Author's response to reviews

Title: Symptom attributions in patients with colorectal cancer: a population based study

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Author's response to reviews: see over
Dear Editor,


Thank you for the opportunity to revise this manuscript and thank you for some valuable comments made by each of the reviewer. We have now revised the manuscript and this cover letter provides a detailed description of our responses to each of the points made by the reviewers.

We hope that this will sufficiently answer the raised issues and the article will be suitable for publication. Do not hesitate to contact us if there are any further issues to be handled.

On behalf of the authors,

Yours sincerely,

Line Flytkjær Jensen
PhD Fellow
RE. Reviewer 1:

1) The study is cross-sectional and data on symptom attribution has been collected retrospectively from patients after they received a CRC diagnosis. The authors correctly highlight this important limitation in the discussion section. However, a more thorough discussion in the introduction and in the discussion section would be needed to illustrate how, despite this crucial limitation, the study can still provide a useful contribution to the already available literature on the topic.

Thank you for this comment which we absolutely agree is an essential point. There are indeed limitations in making cancer patients think back to the time before diagnosis and as a consequence recall bias may be present. However, it may also be the most ethical and sound method available to study this important subject. Although the retrospective design may introduce recall bias, other designs are problematic as well. Often it is not feasible to follow a large population and study their symptom experiences over time in detail because only very few will develop cancer and thus be eligible for these kinds of studies. As this discussion is related to the methodology applied in the paper, this discussion is included in the “Discussion of method” section but not the introduction.

Further, in the discussion of methods, we have also elaborated on why we still find the results reliable despite these limitations. These arguments are included at the end of the discussion of methods and reads: “Firstly, we validated the psychometric properties of symptom attribution as a construct in this patient group, which indicated that patients were, in fact, thinking of their disease instead of their symptom when answering the questionnaire [1]. Secondly, we found that experiencing the alarm symptom blood in stool as the most important symptom were associated with both attributing this to cancer and to a benign somatic cause. This could indicate that the patient not in general answered in one direction because they in retrospect knew that the symptoms were due to cancer”.

2) How long after patients received the CRC diagnoses did they complete the study questionnaire?

Data from the DPDB consisted of patients who had been registered with colon and/or rectal cancer between the 1 January to 1 May 2010. The first questionnaire was sent out the 12 July 2010. Hence, the shortest time between diagnosis and the first questionnaire was approximately 3 months and the longest was 7 months as the last questionnaire was sent out the 26 August 2010. Due to ethical considerations we did not send out the questionnaires immediately after the patients had received their diagnosis. We have now mentioned this time interval in the manuscript.

3) How were the questions on ‘symptom attribution’ and on ‘the most important symptom patients had experienced’ formulated? Was the latter question pre-coded or open-ended? According to the methods section (line 110 -‘Included variables’ section) it seems as if the question on symptom attribution was specifically referring to how the patients interpreted ‘their symptom’. However, as patients who had NOT experienced a specific symptom were also asked the relevant question on symptom attribution, it is not clear how the question was formulated. Maybe the question was formulated in more general terms, rather than specifically referring to their own experience with the symptom? This issue can influence the interpretation of the study findings.

The question on ‘the most important symptom patients had experienced’ was formulated as an open-ended question in the following manner: “Which of the symptoms you experienced, did you perceive as the
most important?” The following sentence said: “Please think of this symptom when answering the remaining questionnaire”. This information has now been added in the ‘included variables’ section. Thus, even though the patient experienced more symptoms, the patient should choose which symptom they regarded as the most important.

The questions on ‘symptom attribution’ were formulated in accordance with the part of the Illness Perception Questionnaire concerning perceived causality, where 19 possible causes are listed and the patients are asked to rate on a Likert scale (strongly disagree; disagree; neither agree nor disagree; agree; strongly agree) whether they considered each cause to be the cause of their symptom. This has been elaborated in the manuscript.

4) An important methodological issue regards the fact that symptom attribution is evaluated comparing CRC patients who had experienced a specific symptom and considered it as ‘the most relevant’ with CRC patients who had not considered that symptom as ‘the most important’. Does the comparison group include patients who did not experience the specific symptom, as well as patients who experienced the symptom but did not consider it as ‘the most important’? If this is the case, how should the results be interpreted? In the abstract (line 34) and in the table the findings are presented with the comparison group being described as patients ‘not having’ a specific symptom, e.g. ‘not having blood in the stool’. This does however not correspond to what is described in the methods section (Included variables: line 101-103).

Thank you for bringing our attention to this. It is a valid point that even though the patient did not state the symptom as the most important, this does not necessarily mean that the patient has not experienced the symptom. This essentially means that the reference group of “no blood in stool” may comprise patients that have experienced this symptom. Sub analyses have indicated that among those who did not assess blood in stool to be the most important symptom (i.e. the reference group), 21% (n=61) did in fact state that they had experienced this symptom. So this is naturally important to keep in mind when assessing the results and it is now also mentioned in the discussion section.

Moreover, doing these sub analyses we have come across another important aspect. Thus, actually 52 patients have experienced several symptoms, but have not replied to the question on which symptom they found most important. Earlier these were part of the reference group, but in the updated analyses these patients have now been excluded in the analyses. This information has now been included in the section on ‘design and data collection’.

5) In the results section the tables present the unadjusted and the adjusted PR. However, it would be essential to also show the numbers and % for the examined symptom attributions by the explanatory variables (e.g. experienced symptoms, socio-demographic characteristics and cancer site).

We have now included a table (Table 1) presenting the numbers and proportions that agreed to each of the five causal groups in relation to the experienced symptoms, socio-demographic characteristics and cancer site. It is up to the editor whether this should be included or not.
6) It would be important to report the number of patients with colon and rectal cancer. Cancer site might be an important factor influencing the type of experienced symptoms, symptom attributions and the patient interval. This issue should also be considered when analysing the associations between these variables and it should be addressed in the discussion.

This important information has now been incorporated in the result section and reads: “Among the respondent, 313 were diagnosed with colon cancer, 149 with rectal cancer and 26 with cancer in both the colon and rectum (data not shown)”. We have also added a section in the discussion, where we address this association between the cancer and the experienced symptoms. The precise inserted paragraph is also outlined in response number 6 to reviewer 2.

7) Abstract-Methods section: It should be specified that it is a cross-sectional study and that data on symptom attribution has been collected retrospectively after CRC diagnosis.

This has now been incorporated into the revised manuscript.

8) Abstract-Results section, line 39: As shown by the 95%CI 0.96 to 2.03, the association between symptom attribution and longer patient interval is not statistically significant. This result should be presented accordingly and it should not be over-emphasized both in the abstract and in the results section of the main text (line175-177).

Thank you for this point. We have deleted statements which suggested that this should be interpreted as a statistical significant result and have now only mentioned that a tendency was observed. We still believe that this statement is valid due to a PR of 1.40. The lack of significance may be due to type II error.

9) Main text-Results section: In line 167, the association between older age and attributing symptoms to a benign somatic cause is not statistically significant based on the 95%CI and it should not be presented as such.

Thank you for this as well. We have now deleted this as a significant result from the result section.

10) Main text-Discussion of methods: In line 229, please provide details and references for the theoretical framework the authors are referring to.

We have now specifically stated what theoretical framework we are referring to and have provided a reference as well.
RE. Reviewer 2:

Reviewers report:

Minor essential revisions

1) Lines 59-62 seemed to be a repeated sentence.

Thank you for making us aware about this. We have now deleted the following paragraph: “Secondly, studies have found that people of low socio-economic position experience more difficulties in interpreting health messages than people with a higher socio-economic position”.

2) Lines 223-225 are not very clear and may require better explanation.

We agree that this sentence could be clearer and we have now changed this accordingly. The sentence now reads: “Thus, this study indicates that among patients who later got CRC, the GP can meet patients who are normalising their symptom and attributing it to a benign explanation when presenting their symptom to their GP”.

3) I think something has been lost in translation in relation to the causal attribution ‘scratch or chink’.

I think perhaps this might read better as ‘scratch or cut’ perhaps.

We have now changed ‘chink’ into ‘cut’.

Discretionary revisions

1) In the Introduction it would be worth mentioning that this research is relevant to the development and evaluation of cancer symptom awareness campaigns as well as how people present to their GP about symptoms associated with cancer. This might also be worth covering in the Discussion.

In the introduction, we have now stated public health campaigns may benefit from incorporating information on patients’ symptom attributions and on the factors associated with these attributions. Also we have elaborated on this in the discussion of results. Thus, we now more thorough discuss the implications for public health campaigns and in relation to awareness, we highlight the challenges of such campaigns in increasing awareness of symptoms related to colorectal cancer without increasing fear of cancer in the population and without overburdening general practice.

In the introduction and discussion, we believe that we already state this research is valuable for the patient-GP encounter.

2) It would be useful to clarify if the questionnaire about the nature of the respondents’ symptoms based on an existing instrument or developed de novo for this study.

In the section on ‘included variables’ we have now made it more clear that the questions regarding the causes attributed by the patients to their most important symptom are based on the causal subscale from the Illness Perception Questionnaire-Revised (IPQ-R). However, some changes have been made as patients in this study were asked to identify the perceived causes of their symptom, whereas the original IPQ-R asks patients to identify causes of their illness. We have chosen not to describe the changes in details as this is already described in our article ‘Measurement properties of the Danish version of the Illness Perception
Questionnaire-Revised for patients with colorectal cancer symptoms’ published in Journal of Health Psychology. Instead we refer to this publication for further information.

3) The authors should present data on the median time since diagnosis to the date they completed the questionnaire. All such studies are subject to potentially important recall bias and so this information is helpful in judging the potential for such bias.

We agree with the reviewer that this information was missing and have already responded to this above (cf. response number 2 to reviewer 1). Thus, the following sentence has been included in the manuscript: “Questionnaire data were collected between 12 July and 26 August 2010 thus the questionnaires were sent out between 3-7 months after diagnosis”.

4) The category ‘Other symptoms’ is relatively large and covers fatigue, nausea, fever and decreased appetite. I understand why they have combined these into a single category for the analyses but it would be useful to present descriptive data on the frequency of each of these symptoms.

This information has now been incorporated in the method section where we added the number of persons who experienced each of these symptoms when we explain the symptoms included in this category.

5) I think the authors have overstated the importance of the non-significant association between the causal attributions and time to diagnosis. I realise that they hoped to find these associations but just because the association does not quite reach a p value of 0.05 does not justify some of their statements.

We have now deleted the statements (cf. in response number 8 to reviewer 1) which overstated the importance of the non-significant association and now merely state that there is a tendency that attribution to benign causes leads to longer patient intervals.

6) In the Discussion it would be useful to discuss the association between rectal cancer and benign explanations from a clinical perspective. I presume that rectal tumours, because of the nature of their bleeding, are more likely to be ascribed to haemorrhoids, compared with rectal bleeding due to a colon cancer. This might be worth discussing briefly.

We have added a section in the manuscript reading: Among our study population, 313 of the patients were diagnosed with colon cancer and 149 with rectal cancer. This distribution reflects the overall incidence in Denmark, where about two thirds of all colorectal tumours develop in the colon [42]. Patients with colon cancer often present with more vague symptoms such as weight loss and fatigue whereas cancer located in the rectum often cause symptoms like abnormal defecation with blood or mucus [43]. Thus, as these cancer types to some degree experience different symptoms this may have affected our results since symptom attributions are associated with the most important symptom experienced.
7) Their main conclusion is that these causal attributions may affect the way symptoms are discussed with a GP and the responses made by the GP. This is an interesting hypothesis. Are the authors aware of any previous research to which they can refer, not just in relation to cancer, which shows that patients' causal attributions affect GPs' diagnostic decision making?

We agree with the reviewer that this is a very interesting hypothesis. However, since we have not been able to find any research on the consequences of patients 'self-labelling’ for the GP’s decision making, the time spent in primary care and ultimately the consequences for the diagnosis of CRC, it remain merely a hypothesis. However, as a last paragraph in the conclusion, we have stated that more research is needed on the consequences of self-labelling.