Author's response to reviews

Title: Factors influencing general practitioners in the referral of elderly cancer patients

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Author's response to reviews: see over
We thank the associate editor and the referees for their valuable comments and suggestions. We have made substantial changes to the article according to your advice to make it clearer and more exhaustive. The modifications are described hereafter and we give a point-by-point response to the concerns.

Reviewer: Jean-Emmanuel Kurtz

1) Overall the English of the manuscript is very weak and should be carefully edited by a native speaker used to medical English
The paper has been reread and corrected by Institut Bergonié’s in-house, native English-speaking medical writer.

2) Table I describes the boundary for old age in the view of the responders, that varies in a 20-years range. One can hardly interpret the study results from a panel of GP, of whom almost 20% consider 80 or more years old as the limit for being old. Was age (as incorporated in the logistic regression model) that fuzzy?

Only 7% consider patients under 70 years as being old, so for the majority of the responders, the boundary for old age varies in a 10-years range.
To clarify variables incorporated in the logistic regression model, we added in the methods section a paragraph.

“For each model, the variable to be explained was the decision to refer a patient (or not) and the explicative variables were GP characteristics (age, gender, practice setting, numbers of year of medical practice, work situation, weekly work time, training in oncology, training in geriatrics) and factors influencing them in the referral or not of their patients (factors from section B liable to influence GP decisions such as patient age, anatomical localisation or presence of good clinical practice guidelines.”

3) The discussion section should be reinforced by thoroughly discussing the present data in the light of similar studies (Townsley et al, Kurtz et al). Eventual discrepancies should be analyzed with regard to healthcare or medical training differences. Conversely, convergent data would reinforce the authors’ conclusions

As per the reviewer’s suggestions, we have incorporated these references and improved the discussion section.

“In studies reported in the literature and conducted in other regions in France and in Canada [10,12], higher referral rates of elderly patients presenting with cancer have been reported according to patient’s age [12] and to stages of the disease [10]. Our referral rates are slightly lower in the general situation, but we have similar high referral rates for both clinical vignettes. Overall, slightly more GPs declared that they always refer for early stages than for advanced disease which is similar to results previously reported [10].”

“In terms of the factors influencing GPs’ referral decisions, we found the same factors to be cited in majority (patient’s wishes and tumor-related factors) as observed previously [10,12].”

“Another decisional factor found, irrespective of disease extension, was the difficulty involved in organising care. This factor is also found in another French two study studies conducted on a sample of GPs where logistic organisational difficulties were found to influence decisions [10,12].”

“For this group, age itself was a determining factor of the referral decision. This association has not been documented in the literature up until now. This difference may not have been observed in the Canadian study as it was performed some time ago and in a different health system [10]. In the French study, the stage was not taken into account when studying referral decisions [12]. Oncology training was found to increase referral rates in our study, but we did not observe an association with geriatric training that has previously been reported in the literature as decreasing referral rates [10,12].”
Minor criticisms
1) “No study has been found in Europe...” (Abstract section). Ref 12 actually reports data from a French study.

We thank the reviewer for this pertinent remark and we have modified this sentence in Abstract section.

“All one European study has been found in Europe that analyses analysed the decision processes leading general practitioners (GP) to refer elderly patients with cancer to oncologists.”

2) Does the pattern of responders match the average profile of GPs in the area? (age, urban/rural practice). Was there any discrepancy in responders according to these factors?

We have added a paragraph in the discussion section on the profile of GPs in the area and the discrepancy in responders.

“In our group of respondents, there were slightly more males and GPs with a rural practice than in the regional GP database. An explanation could be that these GPs see more elderly patients so they were more interested in participating in the study.”

3) The authors mention that 15% of practitioners had a prior training in oncology. So far, and as opposed to geriatrics for which general practitioners residents can graduate, there is no way to be professionally qualified in oncology for a GP. Whether these 15% only reflect a resident training in an oncology unit does matter and should be explained, especially since this data is part of the regression model.

To take this relevant comment into account, we have added a sentence in the methods section.

“(in France, GPs can graduate in geriatrics opposed to oncology where they can not graduate in this discipline but can train in an oncology unit during an internship)”

4) There is no description of the « clinical vignettes » that were part of the questionnaire. Responses may considerably vary according to the nature of clinical cases, which should at least appear as appendixes and be discussed. Regardless of age, referring an elderly prostate cancer patient to an urologist does make sense, provided the patient is amenable to surgery or hormonal therapy. Moreover, this depends upon the cancer care organization in the area, that should be described.

As suggested, we have added the questionnaire and the clinical vignettes in the appendix section and we discuss this point in the discussion section:

“The GPs did not refer their patients to the same specialists in the two clinical case vignettes. For prostate cancer patients, GPs referred their patients to a urological specialist. For patients with colon cancer, GPs referred their patients to a gastro-enterologist or to an oncologist. Specialists’ attitudes towards oncogeriatrics and established collaboration relationships can have an important impact on the initial management of patients [17].”

5) Similarly, the questionnaire should appear in the appendix section. It is mandatory to have access to this material to interpret any bias in the questions that may influence answers. The authors should detail the basis for assessing data such as “psychological status” or “degree of mental and physical autonomy”.

We have added the questionnaire in the appendix section. To select elements likely to influence GPs in their decision making such as “psychological status” or “degree of mental and physical autonomy”, we used information from the literature review and the Delphi consensus method. Although we agree that there is a possibility for different interpretations, these factors were chosen by focus group to ensure maximum consensus. This focus group was formed by 10 practitioners: GPs, geriatricians, oncologists, a surgeon, a sociologist and epidemiologists.
6) Did some patients benefit from a geriatric assessment?

As there were no patients directly involved in our study, we are unable to respond to this question. We didn’t ask GPs if they performed a geriatric assessment of their elderly cancer patients in general.

7) Whether a 30% response rate is “acceptable” should be discussed in the light of higher rates that were observed in a previous French study (ref 12)

We have added a sentence in this regard in the discussion section.

“Kurtz et al[12] showed a higher GP response rate but this difference can be explained by the different types of questionnaire (they did not present clinical case vignettes) and they employed a more direct regional communication method to obtain GP responses.”

8) Throughout the manuscript, some locutions regarding age do not make sense, such as ‘chronological age’ or ‘real age’. These are definitely confusing and should be replaced or explained.

We thank the reviewer for pointing out the one occurrence where ‘real age’ was left (in error). This has been corrected with ‘chronological age’ and a definition for chronological age is given in the questionnaire added in the appendix. We believe that chronological age, the period that has elapsed beginning with an individual’s birth and extending to any given point in time, is a relatively commonly-accepted term in research that may have been confused in the initial manuscript by the error of including one occurrence of ‘real age’.

Reviewer: Paul Brocklehurst

It would help the reader if there was more clarity in the methodology about the source of the variables entered into the logistic regression model (see later comment). It would also be helpful to include a copy of the questionnaire so that the reader could more easily relate to the data being collected.

The questionnaire has been added in the appendix section which more clearly identifies the variables that were entered in the logistic regression model.

In the results, it would be appropriate to include more detail on the values of the test statistics and their level of significance.

As suggested we have included more detail on the values of the test statistics and their level of significance.

“In general situation, independents factors associated with the decision to “always” refer an elderly patient with early versus advanced cancer were studied separately. For early cancer, GPs reporting the influence of organisational difficulties relating to care provision (OR=0.35 95%CI[0.24-0.56], p<0.0001) and of the anatomical localisation of the disease (OR=0.58 95%CI[0.37-0.92], p=0.02) were less likely to refer their patients to a specialist team. No GP characteristic was associated with this decision. For advanced cancer, the GPs that had attended training courses in oncology more frequently referred their patients (OR=1.85 95%CI[1.01-3.38], p=0.04), whereas no other individual GP characteristic was associated with this decision. Three subgroups of GPs were identified as being less likely to refer their patients. These were However, the GPs reporting being influenced by patient age (OR=0.55 95%CI[0.35-0.86], p=0.009), organisational difficulties in instituting providing care (OR=0.60 95%CI[0.39-0.92], p=0.02) and the stage of the disease (OR=0.43 95%CI[0.25-0.71], p=0.001) were less likely to refer their patients (table 3)”

The discussion is "light" compared to the introduction and would benefit from comparing the results to further studies, for example, those alluded to in the introduction for comparison. I would also extend this section a little further.

As suggested, we have the discussion section by adding the following sections:
“Regardless of the stage of the cancer, organisation difficulties were an independent factor influencing the GP’s decision whether or not to refer elderly patients.”

“In studies reported in the literature and conducted in other regions in France and in Canada [10,12], higher referral rates of elderly patients presenting with cancer have been reported according to patient’s age[12] and to stages of the disease [10]. Our referral rates are slightly lower in the general situation, but we have similar high referral rates for both clinical vignettes. Overall, slightly more GPs declared that they always refer for early stages than for advanced disease which is similar to results previously reported [10].”

“In terms of the factors influencing GPs’ referral decisions, we found the same factors to be cited in majority (patient’s wishes and tumor-related factors) as observed previously [10,12].”

“Another decisional factor found, irrespective of disease extension, was the difficulty involved in organising care. This factor is also found in another French two study studies conducted on a sample of GPs where logistic organisational difficulties were found to influence decisions [10,12].”

“For this group, age itself was a determining factor of the referral decision. This association has not been documented in the literature up until now. This difference may not have been observed in the Canadian study as it was performed some time ago and in a different health system [10]. In the French study, the stage was not taken into account when studying referral decisions [12]. Oncology training was found to increase referral rates in our study, but we did not observe an association with geriatric training that has previously been reported in the literature as decreasing referral rates [10,12].”

“The GPs did not refer their patients to the same specialists in the two clinical case vignettes. For prostate cancer patients, GPs referred their patients to a urological specialist. For patients with colon cancer, GPs referred their patients to a gastro-enterologist or to an oncologist. Specialists’ attitudes towards oncogeriatrics and established collaboration relationships can have an important impact on the initial management of patients [17].”

The conclusion does not include the most startling finding that there was no significant difference between the decision to refer early and late cancer (overlapping confidence limits of 48.4-58.0 and 42.1-51.7 p7). This would also need to be added with more prominence to the discussion and the abstract.

We performed a comparison between the decision to refer early or late cancer patients using the Chi^2 test. There was a significant statistical difference (p<0.0001) despite overlapping confidence intervals but the “clinical difference” was not very large ((53% to 46%). We have added this finding in the results and the discussion sections but not in the conclusion section or abstract.

Results section: “Approximately half of the GPs reported “always” referring elderly cancer patients to a cancer team for early cancer cases (230): 53.2% (CI 95%[48.4-58.0]) and for advanced cancer cases (202): 46% (CI 95%[42.1-51.7]) p<0.0001.”

Discussion section: “approximately half of the GPs declared that they always refer elderly cancer patients to a cancer team (this was slightly more frequent for early stages than for advanced disease).”

“Overall, slightly more GPs declared that they always refer for early stages than for advanced disease which is similar to results previously reported [10].”

Specific comments

Introduction

1. I would replace “catered for” by “cared for” - penultimate sentence p3

We have modified this term throughout the text.

2. I would move “using a cross-sectional study” to the end of the sentence describing the aims of the study.

We have moved this to the end of the sentence.

3. I would replace “Secondary aims” as “The detailed objectives of the study were to”

We have replaced this sentence as per the reviewer’s suggestions.
Methodology

4. I would prefer this section to have the subtitles:
Participants
Materials and Methods
Analysis

As suggested, we have inserted these subtitles.

In the participants section:
5. There needs to be more clarity about what the (n=1500) and (n=4006) refer to, otherwise the reader is left confused about what the numbers represent.

We have clarified this point in the participants section:

“One thousand five hundred The GPs in private practice (note that GPs in France have self-employed status) were drawn from exhaustive listings (regional healthcare professional database) including of all GPs in the region (n=4006)”

6. Another sentence is required to detail how the random sampling was undertaken.

We employed a standard statistical method of systematic sampling involving the selection of elements from an ordered sampling frame. The elements chosen in any one sample occupy related positions in the sampling frame, the first element being selected at random [Armitage P, Berry G, Matthews J.N.S. Statistical Methods in Medical Research. Fourth edition. Blackweel. P.651]

7. Was there any ethical requirements that needed to be fulfilled? If so, these would need to be included.

This study was registered with the French national commission on individual privacy: CNIL (Commission Nationale des Libertés Informatiques). We have added this in the methods section.

“The study was approved by the consultative committee on the processing of information in medical research of CNIL (French national commission on individual privacy”

In the materials and methods section:
8. I would replace “tested” with "piloted" - penultimate sentence p4.

We have replaced this word.

9. The description of the questionnaires components requires a little more clarity (this would be helped by the inclusion of the questionnaire in a Table).

We have added the questionnaire.

10. More detail is required about how the clinical cases were developed. For example, why prostrate and colon cancer, was it representative of early or late disease, how much information was included (history, examination, special tests etc), was it validated by a gold standard to determine whether it was appropriate to refer/not refer the case.

We have added the questionnaire and the clinical cases.

In the statistical analysis section:
11. I would add "using a Z-test approximation for proportions" to the sentence describing the statistical test for proportions.

To analyze inter-group comparisons, we performed the Chi² test or the Fisher’s exact test. This has been specified in the text.
12. More clarity is required in the sentence starting "For each of the clinical case vignettes". What does it mean that the attitudes of the GP were described ... and then the elements were set against? Again this would probably be clearer for the reader if the questionnaire was included.

We have added the questionnaire and the sentence has been modified

“For the two clinical case vignettes (questionnaire section E), the attitudes of the GPs were described, and then the elements selected as influencing their decisions were compared against the more general results given in Section B of the questionnaire.”

13. Variables aren’t qualitative or quantitative so I’d phrase this as “the variables from the qualitative section”.

14. Not clear what "depending on conditions of application" means – first sentence p6. Better replaced with "as appropriate"?

15. The section on the variables from the quantitative section requires more clarity, does this include the case vignettes?

16. I would replace "with an alpha risk of error of 5% with "with alpha set at 5%".

We have reworded this paragraph in the light of these remarks:

“To describe the participating physicians and their general attitudes, we used means, standard deviations, medians, range, percentages and frequencies. Inter-group comparisons were performed using the Chi² test, the Fisher’s exact test, the Student’s t-test or Wilcoxon’s test according to the distribution. All tests were performed with alpha set a 5%.”

17. The section on the logistic regression needs more clarity as I was a little unsure about what variables were being used. As highlighted above, did these stem from the first four sections of the questionnaire or the clinical vignettes? I was also ensure what the 20% threshold was referring to in the univariate analysis. I am presuming that all the assumptions of the statistic tests used were satisfied?

We have clarified this paragraph to indicate that associations that were significant in the univariate analyses at p<0.20 were entered into the multivariate model. Concerning the basic assumptions of the statistic test, as long as the sample size is reasonably large (as it is in our case), there are no assumptions for the variable distributions introduced in the logistic regression model [Armitage P, Berry G, Matthews J.N.S. Statistical Methods in Medical Reserch. Fourth edition. Blackweel. P.489].

“Two logistic regression analyses were performed according to the stage of the disease in relation to theon the general decision of whether or not to refer an elderly patient according to the stage of the disease (questionnaire section B). For each analysismodel, the variable to be explained was the decision to refer a patient (or not) and the explicative variables were; being GP characteristics (age, gender, practice setting, numbers of year of medical practice, work situation, weekly work time, training in oncology, training in geriatrics) and factors influencing them in the referral or not of their patients (factors from section B liable to influence GP decisions such as patient age, anatomical localisation or presence of good clinical practice guidelines). The variables that were significant in the univariate regression analyses at p<0.20 for which an association was found at a 20% threshold in the univariate analysis, and also those reported in the literature, were introduced into the multivariate logistic regression models. For each model, explicative variables were removed using a stepwise descending selection procedure, as set out by Hosmer and Lemeshow[11]. This produced a model for each cancer stage (early and advanced), and model fit was ascertained using the Hosmer and Lemeshow goodness-of-fit test [11].”

In the results section:

18. State the response rate

We describe the response rate in the first sentence in the results section.
“Of the 1500 GPs approached in Aquitaine, 30% (436) had responded to the questionnaire after a maximum of two reminders.”

19. Given overlapping CIs on the two proportions (early vs late) for "always" referring (2nd paragraph p7) - would be worth undertaking a Z-test approximation of the difference in proportions in order to state whether there was a significant difference. Or state given their overlap, there was not a significant difference. This was one of the most interesting results from the study.

We performed a comparison between the decision to refer early and late cancer using the Chi² test. There was a significant statistical difference (p<0.0001) but the "clinical difference" was not very large ((53% to 46%) so we have added this result in the results and the discussion sections.

Results section: “Just over half of the GPs reported that in general, they "always" referring referred elderly cancer patients to a cancer team for early cancer cases (230): 53.2% (CI 95%[48.4-58.0]) and just under half “always” referred for advanced cancer cases (202): 46% (CI 95%[42.1-51.7]) (p<0.0001).”

Discussion section: “approximately half of the GPs declared that they always refer elderly cancer patients to a cancer team (this was slightly more frequent for early stages than for advanced disease)”

20. Were the difficulties reported/detailed? (4th paragraph)

In the final section of the questionnaire we asked GPs for their suggestions to improve the care of elderly patients. They were mainly relating to care provision in the home, multidisciplinary care, integration of the GP into decision-making procedures, psychological care of the patients and their families and the improvement of palliative care. However, the questionnaire didn’t allow GPs to report difficulties in referring a patient to a team of cancer specialists. This is an interesting area for possible future research.

21. I would replace "respectively nearly 10% and just over 5%" with "approximately 10% and 5% respectively".

We have replaced this section.

22. A little more clarity in the second paragraph starting "An exploration..." would be helpful.

We have clarified this paragraph.

“The response patterns were different indicating the patient factors were most commonly selected as influencing general referral decisions, whereas tumor-related factors were most commonly selected for specific cases.”

23. Important to include statistical test values and levels of significance in the text too e.g. the OR (and CIs) for the logistic regression and their p values. How many responses were entered into the regression - was their sufficient power?

We have modified this section in the results section.

In the logistic regression model regarding the decision to refer an elderly patient or not, there are: 417 GPs (96% total population) for early cancer and 397 GPs (91% total population) for advanced stages. We have added this information in table 3.

“In general situation, independent factors associated with the decision to "always" refer an elderly patient with early versus advanced cancer were studied separately. For early cancer, GPs reporting the influence of organisational difficulties relating to care provision (OR=0.35 95%CI[0.24-0.56], p<0.0001) and of the anatomical localisation of the disease (OR=0.58 95%CI[0.37-0.92], p=0.02) were less likely to refer their patients to a specialist team. No GP characteristic was associated with this decision. For advanced cancer, the GPs that had attended training courses in oncology more frequently referred their patients (OR=1.85 95%CI[1.01-3.38], p=0.04), while whereas no other individual GP characteristic was associated with this decision. Three subgroups of GPs were identified as being less likely to refer their patients. These were However, the GPs reporting reported being influenced by patient age (OR=0.55 95%CI[0.35-0.86], p=0.009), organisational difficulties in instating providing care (OR=0.60 95%CI[0.39-0.92], p=0.02) and the stage of the disease (OR=0.43 95%CI[0.25-0.71], p=0.001) were less likely to refer their patients (table 3).”
24. The term "organ specialists" would be better replaced with "secondary care specialist"

We propose to replace “organ specialists” by “specialist” as per the editorial of Terret [Terret C, Droz J-P. Editorial. Crit Rev Oncol/Hematol (2010). In press]

In the discussion section:

25. Final sentence on p8 and first sentence on p9 are a little unclear and need clarification.

We have clarified this sentence.

“In Canada, as in France today, patients encountering a health problem consult as a first-resort the first instance the family practitioner (GP) who decides if referral to a specialist is required. It is possible that in the present study the figure for referral is underestimated on account of the absence in France of a clear definition of a "team of cancer specialists", so that the GPs may not have included organ specialists practising oncology under the term.”

26. The paper would benefit from more contrast with related studies, which are referenced in order to elaborate and strengthen the discussion.

As suggested we have improved the discussion section:

“Regardless of the stage of the cancer, organisation difficulties were an independent factor influencing the GP’s decision whether or not to refer elderly patients.”

“In studies reported in the literature and conducted in other regions in France and in Canada [10,12], higher referral rates of elderly patients presenting with cancer have been reported according to patient’s age[12] and to stages of the disease[10]. Our referral rates are slightly lower in the general situation, but we have similar high referral rates for both clinical vignettes. Overall, slightly more GPs declared that they always refer for early stages than for advanced disease which is similar to results previously reported [10]”

“In terms of the factors influencing GPs’ referral decisions, we found the same factors to be cited in majority (patient’s wishes and tumor-related factors) as observed previously [10,12].”

“Another decisional factor found, irrespective of disease extension, was the difficulty involved in organising care. This factor is also found in another French two study studies conducted on a sample of GPs where logistic organisational difficulties were found to influence decisions [10,12].”

“For this group, age itself was a determining factor of the referral decision. This association has not been documented in the literature up until now. This difference may not have been observed in the Canadian study as it was performed some time ago and in a different health system [10]. In the French study, the stage was not taken into account when studying referral decisions [12]. Oncology training was found to increase referral rates in our study, but we did not observe an association with geriatric training that has previously been reported in the literature as decreasing referral rates [10,12].”

“The GPs did not refer their patients to the same specialists in the two clinical case vignettes. For prostate cancer patients, GPs referred their patients to a urological specialist. For patients with colon cancer, GPs referred their patients to a gastro-enterologist or to an oncologist. Specialists’ attitudes towards oncogeriatrics and established collaboration relationships can have an important impact on the initial management of patients [17].”

27. I would add "..., however, the results should be interpreted with this in mind" to the penultimate paragraph (first para on limitations)

We have added this sentence in the beginning of this paragraph.

“Finally, there are two main limitations to this study to keep in mind when interpreting results”

In the conclusions section:

28. I would add that there was no difference between early and late stage disease.
As previously mentioned, we performed a comparison between the decision to refer early and late cancer using the Chi² test. There was a significant statistical difference (p<0.0001) but the "clinical difference" was not very large ((53% to 46%). We have thus added this result in the results and discussion sections but not in the conclusion section or abstract.

In Table 2:

29. Worth adding an extra column and dividing the first two columns into "early" and "late" cancers

Table 2 illustrates descriptions of elements influencing GPs that were present in question 5 of the questionnaire and in the two clinical vignettes. In table 3, there are multivariate analyses performed according to the stage of the disease. We added the questionnaire in the appendix section so that this will be clearer.

30. Worth ordering "variables" according to "P", "T" and "O"?

We have modified this table as suggested

```
"Table 2 - Elements influencing the decision by general practitioners (436) to refer an elderly cancer patient"

<table>
<thead>
<tr>
<th>Elements influencing GPs</th>
<th>Cancer (non specified)</th>
<th>Prostate cancer</th>
<th>Sigmoid colon cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wish or reluctance of patient (P)</td>
<td>364 (83.5)</td>
<td>158 (36.2)</td>
<td>66 (15.2)</td>
</tr>
<tr>
<td>Presence of and/or wish of family (P)</td>
<td>348 (79.8)</td>
<td>21 (4.8)</td>
<td>107 (24.6)</td>
</tr>
<tr>
<td>Presence or absence of serious comorbidity (P)</td>
<td>347 (79.5)</td>
<td>79 (18.1)</td>
<td>115 (26.4)</td>
</tr>
<tr>
<td>Invasive investigations unsuitable (P)</td>
<td>334 (76.6)</td>
<td>52 (11.9)</td>
<td>33 (7.6)</td>
</tr>
<tr>
<td>Degree of mental and physical autonomy (P)</td>
<td>328 (75.2)</td>
<td>126 (28.9)</td>
<td>93 (21.4)</td>
</tr>
<tr>
<td>Short patient life expectancy (P)</td>
<td>300 (68.4)</td>
<td>32 (7.3)</td>
<td>24 (5.5)</td>
</tr>
<tr>
<td>Patient's psychological state (P)</td>
<td>307 (70.0)</td>
<td>108 (24.8)</td>
<td>63 (14.5)</td>
</tr>
<tr>
<td>Awareness of diagnosis by patient (P)</td>
<td>254 (58.1)</td>
<td>36 (8.3)</td>
<td>36 (8.3)</td>
</tr>
<tr>
<td>Chronological Age of patient (P)</td>
<td>243 (56.3)</td>
<td>113 (25.9)</td>
<td>81 (18.6)</td>
</tr>
<tr>
<td>Patient's financial resources (P)</td>
<td>82 (18.4)</td>
<td>1 (0.2)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Side effects and tolerance towards treatment (expected) (T)</td>
<td>348 (79.8)</td>
<td>24 (5.5)</td>
<td>14 (3.2)</td>
</tr>
<tr>
<td>Seriousness of cancer symptoms (T)</td>
<td>345 (79.1)</td>
<td>131 (30.0)</td>
<td>143 (32.8)</td>
</tr>
<tr>
<td>Stage of the disease (T)</td>
<td>314 (71.9)</td>
<td>90 (20.6)</td>
<td>192 (44.1)</td>
</tr>
<tr>
<td>Anatomical localisation of the cancer (T)</td>
<td>294 (67.4)</td>
<td>172 (39.4)</td>
<td>151 (34.7)</td>
</tr>
<tr>
<td>Presence of good clinical practice guidelines(T)</td>
<td>293 (67.2)</td>
<td>34 (7.8)</td>
<td>23 (5.3)</td>
</tr>
<tr>
<td>In the habit of collaborating with specialised cancer teams (O)</td>
<td>337 (77.2)</td>
<td>46 (10.6)</td>
<td>58 (13.3)</td>
</tr>
<tr>
<td>Time lapse before care is instated (O)</td>
<td>314 (71.9)</td>
<td>27 (6.2)</td>
<td>25 (5.7)</td>
</tr>
<tr>
<td>Organisational difficulties in providing care (O)</td>
<td>222 (50.2)</td>
<td>34 (7.8)</td>
<td>31 (7.1)</td>
</tr>
<tr>
<td>Other</td>
<td>55 (12.8)</td>
<td>32 (7.3)</td>
<td>19 (4.4)</td>
</tr>
</tbody>
</table>
```

*: Patient-related factors (P); †: the three elements mainly influencing the GPs in the three different situations ; ‡: Tumor-related factors (T); §: organisational factors (O)"
In Table 3:

31. I would include B and its SE, R squared and chi squared
   We have completed table 3 with B and its SE, R squared and chi squared

   "Table 3 - Determinants of the decision to refer elderly patients at early and advanced stage
   (multivariate analyse)

<table>
<thead>
<tr>
<th>Element influencing GPs</th>
<th>β</th>
<th>SE</th>
<th>OR</th>
<th>[CI 95 %]</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early disease model (417 GPs)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Organisational difficulties (care provision)</td>
<td>-0.99</td>
<td>0.21</td>
<td>0.37</td>
<td>[0.24-0.56]</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Anatomical localisation of the cancer</td>
<td>-0.53</td>
<td>0.23</td>
<td>0.58</td>
<td>[0.37-0.92]</td>
<td>0.02</td>
</tr>
</tbody>
</table>

   R-Squared = 0.08 ; Chi-Squared Hosmer and Lemeshow = 0.02 (p = 0.99)

| Advanced disease model (397 GPs)                |      |      |      |                |         |
| GP characteristics                              |      |      |      |                |         |
| Training in oncology (ref: not influenced)      | 0.61 | 0.31 | 1.85 | [1.01-3.38]    | 0.046   |
| Elements influencing GPs                        |      |      |      |                |         |
| Chronological age of patient (ref: not influenced) | -0.59| 0.23 | 0.55 | [0.35-0.86]    | 0.009   |
| Organisational difficulties (care provision)    | -0.51| 0.22 | 0.60 | [0.39-0.92]    | 0.02    |
| Disease stage (ref: not influenced)             | -0.85| 0.26 | 0.43 | [0.25-0.71]    | 0.001   |

   R-Squared = 0.11 ; Chi-Squared Hosmer and Lemeshow = 4.31 (p = 0.63)