Author’s response to reviews

Title: Impact of comorbid conditions on participation in an organised colorectal cancer screening programme: a cross-sectional study

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Author’s response to reviews:

Dr. Matejka Rebolj
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Dear Dr. Matejka Rebolj,

We appreciate the opportunity to revise the manuscript entitled "Impact of comorbid conditions on participation in an organised colorectal cancer screening programme: a cross-sectional study". The manuscript has been modified to reflect the very helpful comments provided by yourself and the Reviewers. Our responses to them are outlined in this point-by-point letter, and highlighted in the revised main manuscript.

Editorial Office

1. The eligibility for the programme was gathered from the Central Registry of Insured from the Primary Healthcare Information System (1). At the beginning of the RCT, the BCCSP technical office provided a list of individuals invited to participate in the programme and their corresponding primary care centre.

The BCCSP was launched in December 2009 and the first round lasted until May 2012. The target population comprised 197,795 individuals invited based on the primary care centre they had been assigned to. More specifically, the specific cohort of individuals enrolled in the cluster-RCT involved those individuals assigned to the last 10 primary care centres that were invited from July 2011 to May 2012. The appropriateness of including the entire population (130 GPs with their 41,042 patients) was considered.

These points have been clarified in the Methods section (page 7 and 9).

2. To our clinical experience the proportion of patients that change GP practices is low. Moreover, the RCT was analysed under an intention-to-treat approach; consequently, although patients had been moved to another centre that did not participate in the RCT, all individuals included in the study were analysed.

3. Upon statistical consultation, we fully agree with the editor regarding the use of OR. Now we have changed OR to incidence rate ratios (IRR). Although there are some changes in table 3 (actually table 2), results lead to similar conclusions. We have made, according with this issue, changes at the Statistical Analysis, Results, Discussion, Conclusions and Table 3 (actually table 2) sections.

In addition:
- Two typographical errors in the email addresses has been amended (page 1), and the postal address of the corresponding author (page 2), due to a recent change in GP practice.

- The words “primary care physician” have been changed to “general practitioner” or “GP” throughout the revised document; accordingly, “GP” has been added to the list of abbreviations (page 18).

- Moreover, CRG has been added to the list of abbreviations and CCSPB has been changed to BCCSP (see page 18).

- The improvements to the English language requested by the Editorial office and the Reviewers have been revised throughout the revised main manuscript.

Reviewer 1 (Patricia Valery):

1. According to the Reviewer’s suggestion, in paragraph 2, page 11, the sentence "Colorectal cancer risk factors, as smoking, high-risk alcohol intake or obesity, were significant negative predictors to participate in the screening programme (Table 2)", has been changed by “There was a higher proportion of current smoking, high-risk alcohol intake or obesity in the non-participation group versus the participation one (Table 2)”.

2. Following the Reviewer’s suggestion, in paragraph 2, page 11, the sentence "On the other hand, a statistically significant lower participation was observed in individuals allocated in the lower comorbid groups (39.4% for healthy and 40.6% for acute disease category).", has been changed by “there was a lower proportion of participants classified as lower comorbid groups (39.4% for healthy and 40.6% for acute disease category) in the participation group compared to those who did not participate in screening”.

3. As the Reviewer suggested, in paragraph 2, page 13, "The total crude participation rate (48%) found in this study,..." has been reworded to “The total crude participation rate in the CCSPB (48%) found in this study,...”

4. We agree with the Reviewer that the representability of the study population should be clarified.

* Firstly, of the 11 primary care centres invited to take part in the RCT (n = 148 general practitioners (GP) and 57,020 patients), one refused to participate (n = 18 GP and 5,953 patients). Subsequently, 10,025 patients who did not have a GP assigned to a participating centre at the start of the study were excluded. Therefore, they were not eligible to receive the RCT intervention. Following the above exclusions, we considered the appropriateness of including the entire population - 130 GPs with 41,042 individuals. Following the Reviewer suggestion this paragraph has been briefly added in Methods section (see page 7).
As it was mentioned in comment #1 to the Reviewer 1, the BCCSP was launched in December 2009 and the first round lasted until May 2012. The target population comprised 197,795 individuals invited based on the primary care centre they had been assigned to. More specifically, the specific cohort of individuals enrolled in the cluster-RCT involved those individuals assigned to the last 10 primary care centres that were invited from July 2011 to May 2012. These centres, run by the Catalan Institute of Health, were waiting to start the first round of the BCCSP at the time the intervention was started. The population of the 10 centres included in the RCT is representative of the population invited to the first round of the BCCSP, based on published sociodemographic data (2,3), as well as the population of the second screening round according to data presented at the CAPRI 2017 Congress (4). Nevertheless, it is important to mention that this study had an urban population as the BCCSP was carried out in the city of Barcelona and more studies would be required to extrapolate these data to the entire population at average risk of developing colorectal cancer in Catalonia. This information has been briefly added to the Methods (see page 7) and the Discussion (page 15,16) sections.

* Second: In Figure 1, 3,100 patients were excluded because they presented some of the BCCSP’s exclusion criterion. Of them, 835 patients were excluded because they were up-to-date with colorectal cancer screening; that is, they were patients who had reported to the BCCSP having a colonoscopy performed in the last 5 years or a fecal occult blood test in the last two years. This point has been added in Figure 1 legend (page 27).

* Third: In comparison with the group of patients included in the study, in the group of patients with no information on the variable CRG status (n = 1,734) we observed a greater proportion of men (54% vs. 46%), of individuals in the fifth deprivation quintile (25% vs. 19%), of individuals who did not attend their health centre in the last year (55% vs. 23%) and of smokers (34% vs. 24%). The differences were statistically significant for all the variables mentioned (p<0.001). This information has been added in the Results (see page 11) and in Discussion section (page 16).

In addition, according with the Reviewer comment the term “broadly representative” has been changed for “large”, and “as well as an evaluation of several colorectal cancer risk factors as smoking, alcohol consumption and obesity” has been removed (page 15).

* Finally, according to the Reviewer suggestion Tables 1 and 2 have been combined (page 23, Table 1).

Reviewer 2 (Gwenn Menvielle):

Major comments
1. The Catalan Institute of Health incorporated the CRG tool as a model for grouping morbidities. Its use involves a computerised calculation based on a patient's basic information as collected in their electronic medical record (age, sex, International Classification of Diseases 10) and the assignment and visualisation of the CRG stratification results for each user in the computerised medical record used by primary care physicians. This variable was collected from the electronic medical record and provided by the Primary Care Services Information System of the Catalan Health Institute at the beginning of the study. These issues about CRG have been added to the Methods section (page 8).

2. According with the Reviewer suggestion the impact of the different sources of information used to classify an individual as healthy or with some comorbidity, and to compare results between the different studies, has been considered in the Discussion section (page 13) and in the limits of the study (page 15 and 16).

3. As it was mentioned in comment #1 to the Editorial Office and in comment #4 to the Reviewer 1 possible selection issues to the restriction to the 10 primary care centres of Barcelona included in the study have been clarified in Introduction (see page 7) and in Methods section (see pages 15 and 16).

4. We agree with the reviewer about adjustment variables issues, but we can not exclude almost half of the sample only to perform an adjusted analysis by smoking, alcohol and body mass index. Then, now we show the results (table 3) for the 33,943 subjects with the basic set of adjusting variables (sex, age, socioeconomic deprivation index, number of visits, study group of the colo-alert randomised trial). A comment has been added into the Results section to inform of the unadjusted results with the whole sample (36,208) and with covariates (33,943) (see page 12). Results with additional adjusting by smoking, alcohol and body mass index were similar with those obtained without these covariates, and a text note have been added in the Results section (page 12). Statistical analysis shows now the issue with missing values (see page 10).

5. Following the Reviewer suggestion Discussion section has been restructured to facilitate the reader understand the paper.

6. We agree with the Reviewer that healthier lifestyles are not comorbid conditions and it has been removed in the Discussion section (Page 13, second paragraph).

7. The exclusion criteria for participating in the population-based colorectal cancer screening programmes are defined by the Official Guides and in this regard, according to the reviewer's comment, the related sentences have been removed to facilitate the reader understand the paper (page 15 and 16).
Minor comments

1. In page 5 “de” has been replaced by “the”

2. In page 10 “both in unadjusted and adjusted models” has been removed.


