

Bilbao, February 21st 2017

Dear Editor in chief:

Thank you for all your suggestions, questions and required amendments. On behalf of my co-authors, I have already taken them into account in order to solve any of the possible mismatches.

General remarks and requirements:

Regarding the question [Q1]: all the changes have been made and corrected in the article and the 5 questions have been answered in a separate sheet with my signature.

Regarding the question [Q2]: As English Non-Native Speakers, you can find enclosed a pdf including the language editing certificate, verifying that the language of the manuscript has reached Grade A.

Regarding the question [Q3]: the Grant number has been already introduced in the text and the PDF file duly signed. Project name: Factors affecting the balance between indicators of benefits and adverse effects in colorectal cancer screening programmes, Carlos III Health Institute, Spanish Government, Grant number: PI12/02547.

Regarding the question [Q4]: all files have been signed and provided in a PDF format.

Regarding the question [Q5]: all the reference numbers have been changed as required.

Regarding the question [Q Wang JL6]: we have added to the text a short comment maintaining the suggested structure and epigraphs.

Regarding the comments TO Authors:

Reviewer 1:

- the abbreviations have been already reviewed where first used such as Colorectal cancer (CCR), American Joint Committee on Cancer (AJCC), Faecal Inmunochemical test (FIT), Interval Cancer FIT (IC-FIT), Interval Cancer Colonoscopy (IC-Colonoscopy)
- As you say, the second sentence in the "Introduction" section required a reference and we have added the following one: **Lopez de Munain A.** Incidencia del cáncer en la comunidad autónoma de Euskadi, 2013. Vitoria-Gasteiz: Departamento de Salud, Servicio de Registros e Información Sanitaria, 2017. [Available: 2017-02-16]

http://www.osakidetza.euskadi.eus/contenidos/informacion/estado_salud/es_5463/adjuntos/INFORME_Bilingue_2013nuevo.pdf

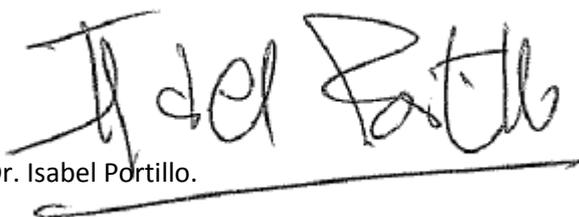
- The explanation if the other risk factors related with ICs are absent in registries, we have included in our own registry all the known factors associated to CRC in the literature, up to now.
- SCs acronym has been standardized through the whole text.
- In last part of discussion. We have properly written "diagnostic group" (HR 0.45, 95% CI 0.29-0.69, P<0.0001) as SCs.

Reviewer 2:

- No comments required to be made.

Should you need further comments or requirements, do not hesitate to contact us.

Yours sincerely

A handwritten signature in black ink, appearing to read 'Isabel Portillo', written in a cursive style. The signature is positioned above a horizontal line that underlines the text 'Dr. Isabel Portillo.' below it.

Dr. Isabel Portillo.