ANSWERING REVIEWERS

Day 10 March 2015.

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 16313-review.doc).

Title: Esophageal Cancer: Risk Factors, Screening and Endoscopic Treatment in Western and Eastern Countries.

Author: María José Domper, Ángel Ferrández and Ángel Lanas

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 16313

1. Format has been updated. The authors have added an "abstract" to the number of words required by the publisher adjusted and have written a "core tip" as part of the requirements.

2. Revision has been made according to the suggestions of the reviewers.

Reviewer number 3016912:
The reviewer number 3016912 suggested a minor revision of our manuscript:

Reviewer Comment: *"It's an overly exhaustive article about some aspects of esophageal cancer: epidemiology, risk factors and screening, and sometimes difficult to read. - The title is inadequate to the text".*
Authors' Reply: We have tried to capture, from the title, the intention of our editorial. This is a manuscript focuses its strength in the differences between countries mainly at the level of endoscopic screening in order to detect pre-neoplastic lesions or early esophageal cancer, both of them, whit a potentially management by endoscopic treatment. However, many reviewers have suggested to change the title so we have changed the tittle of the article.

Reviewer Comment: "*The abstract should not be numbered; so the numeration should start with the subtitle "Epidemiology of Esophageal Cancer".*
Authors' Reply: We have started numeration of the subheadings with Epidemiology of Esophageal Cancer.

Reviewer: Comment: *"You use the term US and USA".*
Authors' Reply: We have changed all US terms to USA term across the manuscript to refer to the United States of America.

Reviewer Comment: *"Pg. 8, line 8: missing a parenthesis"*
Authors' Reply: A Parenthesis has been included

Reviewer: Comment: *The reviewer suggests using a consistent and appropriate term to refer to the area of Asia with high incidence of carcinoma of the esophagus known as "Asian belt" of esophageal cancer.*
Authors' Reply: We now use the term "Asian Esophageal Cancer Belt" steadily to refer to areas of high incidence of Asia in relation to squamous cell carcinoma.

Reviewer Comment: *"Page 9 you refer: "Barrett's esophagus is the preneoplastic lesion preceding adenocarcinoma in most of the cases."; Pg. 10, line 3: "However, 80-90% of cases of esophageal adenocarcinoma are diagnosed without known Barrett's esophagus." Explain these phrases."*
Authors' Reply: We wanted to capture in the text that the only recognizable predecessor entity of esophageal adenocarcinoma in Barrett's esophagus, however the majority of adenocarcinomas diagnosed are often in advanced stages and out of a screening program, so, in many of them, you can not prove a prior precursor lesion that is generated. We agree that both sentences could be somehow confusing and have explained this better in the text.

Reviewer Comment: *"Pg. 11, line 1 correct the age"*
Authors' Reply: Age has been corrected

Reviewer Comment: *Insist on knowing the reason that the authors have focused editorial in early esophageal cancer.*
Authors´ Reply: We have tried to capture, from the title, the intention of our editorial. This is a manuscript focuses its strength in the differences between countries mainly at the level of endoscopic screening in order to detect pre-neoplasic lesions or early esophageal cancer, both of them, whit a potentially management by endoscopic treatment.

Reviewer Comment: *Pg.17 line 32 you used the term DSE, when you previously always use the term ESD.*
Authors´ Reply: We have used the term "ESD" (endoscopic submucosal dissection) as suggested and steadily unchanged for the entire manuscript.

Reviewer number 1170769:

The reviewer number 1170769 suggested a major revision of our publishing, with the following changes, which have done: (with particular emphasis on spelling errors):

Reviewer Comment*: Since this is a review article, the authors are expected to collect as many as possible original (but not other review articles) clinical/experimental researches in a comprehensive way to support or to overturn a concept or findings, unfortunately, which is not adequately achieved in this manuscript.*

Authors´ Reply: We agree with the reviewer that most of the references should be made to original papers when a review is written. We have included 10 reviews out of a total of 37 references that are mostly published in first and second quartile journals. Moreover, when epidemiology and risk factors are taken in account reviews can be a powerful tool since they sometimes include old references that could have been otherwise not included. We also agree that there might be other excellent reviews to include although we believed that for our purpose the ones we chose fitted better with the aim of the paper.

Reviewer Comment*: Suggests change the title of the editorial.*

Authors´ Reply: We have changed the title according to the suggestions of the reviewer.

Reviewer Comment*: There are spelling errors and many terms are used inconsistently. The reviewer suggested on using systematically the term "Asian Esophageal Cancer Belt" to refer to the area of Asia with a high incidence of squamous cell esophageal cancer.*

Authors´ Reply: We have made the proper changes to refer such area as the Asian Esophageal Cancer Belt, as proposed by the reviewer.

Reviewer Comment: *We drew attention to the province of China to which we referred in our text was not "Lixian" and we have to find the correct name.*

Authors´ Reply: We have corrected the typo, and changed Lixian by Linxia

Reviewer Comment*: Objective commas as an error in the OR of adenocarcinoma and tobacco, which were to be exchanged for points.*

Authors´ Reply: We have changed commas by points: OR 2.7 (95% CI, 1.64-4.45).

Reviewer Comment*: Table 2 "Modified TNM cancer esophagus". The table is not complete. It includes only "T" but no information on "NM". In addition, "cancer esophagus" should be changed to "esophageal cancer".*
Authors´ Reply: We have added the staging of esophageal carcinoma according to the AJCC. We have also changed the Footnotes to "Modified TNM esophageal cancer from 2010 AJCC" as suggested.

Reviewer number 3088280:
The reviewer number 3088280 suggested accept our revision, but suggested the following recommendations:

Reviewer Comment*: The quality of Figure 1 is low.*
Authors´ Reply: We have made the proper changes to upgrade this figure.

Reviewer Comment: *In sentences of 'the province of Lixian, China', 'Henan, Hebei, Lixian and Shanxi', and 'Chinese region of Linxian',* ***the 'Lixian' and 'Linxian' should be "Linxia".***
Authors´ Reply: We have corrected the typo, and changed Lixian by Linxia.

Reviewer number 3090352:
The reviewer number 3090352 suggested accept our revision without any recommendations.

Reviewer number 580061:
The reviewer number 580061 suggested a minor revision of our publishing, with the following changes, which have done:

Reviewer Comment*: The reviewer suggests changing the title to correspond better form and content of the publisher.*
Authors´ Reply: We have changed the title according to the reviewer suggestions.

Reviewer Comment *: The reviewer says the need to change the following sentence because it was so long and so hard to understand "The trend Towards dominance of adenocarcinoma subtype is not limited only to North America, since in European countries country like the UK, France or Norway the Increased age-adjusted incidence by 39.6% for men and 37.5% for women in the last five years (1) Which are rated higher than Those Observed in Australia, with an annual Increase in the incidence of adenocarcinoma around 4.2%. "*
Authors´ Reply: We have shorten the sentence as suggested. It currently says "The trend towards dominance of adenocarcinoma subtype is not limited only to North America. In European countries like the UK, France or Norway the age-adjusted incidence increased by 39.6% for men and 37.5% for women in the last five years [1] "

Reviewer Comment*: pg 2: Please indicate in the text where you are referring to age-standardized rates.*
Authors' reply: We have indicated it in the text.

Reviewer Comment*: Clarify Figure 1, specifying to which we refer in the right and left side. Men and women ??*
Authors´ Reply: We have changed Figure 1 and included clarifications suggested by the reviewer.

Reviewer Comment*: This reviewer told us we had made an error in transcription of names related to the pathogenesis of esophageal carcinoma genes and that we should review it.*
Authors´ Reply: We have changed "enzyme phospodiesterase C" by "enzyme phospholipase C " as suggested by the reviewer.

3 References and typesetting were corrected

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,

Signature:__  **_____Date:_10/03/2015 _____**

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