# Oct 28, 2012

Title: Consumption of red and processed meat and esophageal cancer risk: a meta-analysis

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Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 580

Dear Dr. Lian-Sheng Ma

Thank you for your kind letter of decision on our manuscript entitled “Consumption of red and processed meat and esophageal cancer risk: a meta-analysis” We also appreciate the referee’s insightful comments and suggestions.

We have carefully revised the original manuscript based on the suggestions and comments by editor and reviewers. We enclosed the point by point responses to the reviewers’ comments and have highlighted (red-color) all the changes.

We believe that the revised manuscript has been improved and hope that this is suitable for publication in the World Journal of Gastroenterology.

Thank you very much for your time and considerations.

Sincerely,

Jung Eun Lee, Sc.D.

**Point-by-point response to comments to the original submission (ESPS Manuscript NO: 580)**

*the authors present a comprehensive review of recent literature and make correct conclusions following to their study data. In regard of our modern era with many different food alternatives and the clear rising of incidence of distal esophageal cancers I would appreciate this study to be published in your journal.*

*I applaud the authors for this comprehensive review of a complex data set for an intriguing issue. They conclude that a high consumption a red meat (but up to now not processed meat) significantly increases the risk for esophageal cancer independently of the histologic subtype. This conslusion is notably based upon recent studies and nicely shows the development of scientific data on time.*

*I have two questions/requests to the authors:*

*1. Is their relevant study data showing an increase in the risk of eosphageal cancer depending on the duration of consumption (not only the relative amount of) of red meat in order to be able to set a sort of a "time cut off".*

🡪 Unfortunately, we could not evaluate the duration of red/processed meat consumption in relation to the risk of esophageal cancer because of a lack of data in each study. But we believe that reviewer’s point could be the interesting questions in further large prospective studies to explore whether daily quantity of red/processed meat consumed as well as duration of consumption are important contributing factors for development of esophageal cancer.

*2. As different mechanisms are responsible for cancer development and red meat may have an influence on other cancer types, it would be of great interest for the reader if you could give more precise explanations for the underlying mechanisms in development of esophageal cancer related to red meat intake.*

🡪 We appreciate reviewer’s comments. We have discussed further the possible mechanisms in the discussion section.

(Page 11, lines 238-244)

“The esophagus is frequently exposed to these dietary mutagenic and/or carcinogenic compounds as stomach and colon, permitting food to pass from the esophagus into the stomach. While the specific mechanism by which meat causes esophageal cancer has not been fully elucidated, one likely reason may involve the potential for increase the susceptibility to carcinogenesis by repeated exposure of esophagus to the mutagenic and/or carcinogenic compounds, given their effects on carcinogenesis in animal models[1,2,3].”

**Reference**

1. **Cross, AJ**, Sinha, R. Meat-related mutagens/carcinogens in the etiology of colorectal cancer. Environ Mol Mutagen 2004; **44**: 44-55
2. **Sugimura, T**, Wakabayashi, K, Nakagama, H, Nagao, M. Heterocyclic amines: Mutagens/carcinogens produced during cooking of meat and fish. Cancer Sci 2004; **95**: 290-299
3. **Mirvish, SS**. Role of N-nitroso compounds (NOC) and N-nitrosation in etiology of gastric, esophageal, nasopharyngeal and bladder cancer and contribution to cancer of known exposures to NOC. Cancer Lett 1995; **93**: 17-48