

Format for ANSWERING REVIEWERS



October 7, 2013

Dear Editor,

Title: The Accuracy of the early detection of colorectal tumor by stool methylation markers: A Meta-Analysis

Author: Hu Zhang, You-Qing Zhu, Jian Qi, Sha-Sha Cai, Si-Ying Zhu, Qi-Xian Wang, Xiao-Wen Zhu and Xin-Tao Wang

Name of Journal: World Journal of Meta-Analysis

ESPS Manuscript NO: 4604

The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer

(1) I am not sure why colorectal adenoma was included in the study. However, since it has been included, it should be reflected in the title.

Answers:

We think your opinion is reasonable, so we change the title of “colorectal cancer” to “colorectal tumor”. Historically, colorectal adenoma has been recognized as the most important precancerous lesion to CRC. Our previous study found that there were frequently methylation DNA in colorectal adenoma, therefore it is helpful for early screening of CRC by detection of DNA methylation in stool samples.

(2) The authors should describe clearly the “Inclusion and Exclusion Criteria” in the Methods.

Answers:

Eligible studies had to meet all of the following criteria: (a) Data was independent. (b) The CRC was diagnosed using the analysis of DNA methylation in stool sample. (c) The patients were diagnosed as colorectal cancer or colorectal adenomas by pathology. (d) The colonoscopy result of the control individuals was normal.

Exclusion criteria for this meta-analysis were: (a) Studies on secondary CRC or primary CRC with other organs’ metastasis. (b) Studies on CRC patients receiving chemotherapy or curative surgery.

(3) I don’t understand what is meant by “344 articles excluded for duplicates”. Please clarify further.

Answers:

There were 344 articles were excluded because they were repetitions.

(4) Some key outcomes such as diagnostic odds ratio (DOR) and summary receiver operative characteristic (SROC) curve should be defined in the Methods.

Answers:

Yes. We have described them clear in the methods.

Diagnostic odds ratio (DOR) reflects the relationship between the result of the diagnostic test and the disease. The summary receiver operation characteristic (SROC) curve displays the trade-off between sensitivity and specificity and represents a global summary of test performance. We used Q-value, the intersection point of the SROC curve with a diagonal line from the left upper corner to the right lower corner of the receiver operation characteristic (ROC) space, which corresponds to the highest value of

sensitivity and specificity for the test.

(5) There are three curves in Figures 2c as well as 3c. Please describe them clearly.

Answers:

Yes. We have described them clear in the article.

(6) The presentation of QUADAS score should be made appropriately. You may present the exact overall score for each of the studies in Table 1, and label Tabl4 as a supplementary table.

Answers:

We think your opinion is reasonable, label Table4 may be as a supplement table for QUADAS score in Table1. We have deleted the Table4.

Quality Assessment of studies of Diagnostic Accuracy (QUADAS) was used to assess the quality of primary studies of diagnostic accuracy. Quality scoring was appraised by the empirical evidence, the experts' opinions and the formal consensus. Score 1, 0 and -1 was given to the articles in compliance with the standards completely, unclear and out of standards, respectively. The full score was 14.

(7) Discussion may focus on your major findings, and their clinical significance. Also, any limitations of your meta-analysis should be commented.

Answers:

Yes, the discussion has been revised and we have described the limitations in the discussion.

Our meta-analysis had several limitations. (1) None of the included studies were multicentre or large blinded randomized controlled trials; (2) The conference abstracts, non-English and non-Chinese language studies were excluded, which might have led to publication bias; (3) Studies on DNA methylation with statistical significance tend to be published and cited; (4) Due to the absence of case-mix differences analysis, the smaller trials may show larger treatment effects than larger studies (e.g., patients with only localized vs metastatic disease).

(8) Study characteristics: (Spain, et al). Delete et al. The same in Table 1: Vimentin et al.

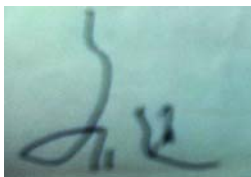
Answers

We think your opinion is reasonable. We have deleted "et al" all, and supplement the missing data.

3 References and typesetting were corrected

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

Sincerely yours,

A handwritten signature in black ink, appearing to be 'Jian Qi', on a light blue background.

Jian Qi, MD, PhD

Zhongnan Hospital of Wuhan University

Wuhan

Hubei Province

China

Fax: +86-27-87336141

E-mail: qiqidelizi @ aliyun.com