

**ESPS Peer-review Report****Name of Journal:** World Journal of Gastroenterology**ESPS Manuscript NO:** 6214**Title:** Methylenetetrahydrofolate reductase C677T and A1298C polymorphisms in association with gastric cancer susceptibility: a meta-analysis**Reviewer code:** 02459760**Science editor:** Gou, Su-Xin**Date sent for review:** 2013-10-10 08:43**Date reviewed:** 2014-01-05 22:24

| CLASSIFICATION  | LANGUAGE EVALUATION  | RECOMMENDATION                      | CONCLUSION  |
|---|--|-------------------------------------|---|
| <input type="checkbox"/> Grade A (Excellent)            | <input checked="" type="checkbox"/> Grade A: Priority Publishing | Google Search:                      | <input type="checkbox"/> Accept                                   |
| <input checked="" type="checkbox"/> Grade B (Very good) | <input type="checkbox"/> Grade B: minor language polishing       | <input type="checkbox"/> Existed    | <input checked="" type="checkbox"/> High priority for publication |
| <input type="checkbox"/> Grade C (Good)                 | <input type="checkbox"/> Grade C: a great deal of                | <input type="checkbox"/> No records | <input type="checkbox"/> Rejection                                |
| <input type="checkbox"/> Grade D (Fair)                 | language polishing   | BPG Search:                         | <input type="checkbox"/> Minor revision                           |
| <input type="checkbox"/> Grade E (Poor)                 | <input type="checkbox"/> Grade D: rejected                       | <input type="checkbox"/> Existed    | <input type="checkbox"/> Major revision                           |
|   |  | <input type="checkbox"/> No records |   |

**COMMENTS TO AUTHORS**

no comments.

# ESPS Peer-review Report

**Name of Journal:** World Journal of Gastroenterology

**ESPS Manuscript NO:** 6214

**Title:** Methylenetetrahydrofolate reductase C677T and A1298C polymorphisms in association with gastric cancer susceptibility: a meta-analysis

**Reviewer code:** 00073423

**Science editor:** Gou, Su-Xin

**Date sent for review:** 2013-10-10 08:43

**Date reviewed:** 2014-01-27 20:33

| CLASSIFICATION                                     | LANGUAGE EVALUATION   | RECOMMENDATION                      | CONCLUSION   |
|--|---|-------------------------------------|--|
| <input type="checkbox"/> Grade A (Excellent)       | <input type="checkbox"/> Grade A: Priority Publishing                           | Google Search:                      | <input type="checkbox"/> Accept                        |
| <input type="checkbox"/> Grade B (Very good)       | <input type="checkbox"/> Grade B: minor language polishing                      | <input type="checkbox"/> Existed    | <input type="checkbox"/> High priority for publication |
| <input checked="" type="checkbox"/> Grade C (Good) | <input checked="" type="checkbox"/> Grade C: a great deal of language polishing | <input type="checkbox"/> No records | <input type="checkbox"/> Rejection                     |
| <input type="checkbox"/> Grade D (Fair)            | <input type="checkbox"/> Grade D: rejected                                      | <input type="checkbox"/> Existed    | <input type="checkbox"/> Minor revision                |
| <input type="checkbox"/> Grade E (Poor)            |   | <input type="checkbox"/> No records | <input checked="" type="checkbox"/> Major revision     |

## COMMENTS TO AUTHORS

The meta-analysis on association between common MTHFR polymorphisms and the risk of gastric cancer is presented. There are at least six meta-analyses addressing this association in PUBMED, however, this paper is the first which included stratification according to gastric cancer location and histological subtype. General comments: 1) There are multiple formatting errors and typos within the manuscript that need to be checked. 2) The text needs to be revised by a person proficient in English. There are multiple sentences which feel clumsy, e.g. page 2, line 15: "No matter compared with controls or diffuse-type GC, a positive association was found that C677T polymorphism increased the risk intestinal-type GC in whole population, and in western"; page 6, line 23 "As shown in Table 4, 11 studies including a total of 2007 cases and 3679 controls were performed to analysis the relationship between MTHFR A1298C polymorphism and GC", page 8, line 8" Moreover, no matter compared with controls or diffuse-type GC, a positive association was found that 677TT polymorphism increased the risk intestinal-type GC in whole population, and in western.", etc. Major comments: 1) The authors should present the results of this meta-analysis using the Forrest plots, which are standard in this type of meta-analysis papers. Forrest plots make the article far more comprehensible and illustrative compared to the cumulative tables. 2) Discussion part of the manuscript should be restructured to outline the major findings of this study. The authors should clearly state the advantages of their meta-analyses in relation to previously published 6 meta-analyses. The text is confusing and the English language is poor. The authors often misuse the term "gene function". 3) Conclusions part of the paper should be revised. First of all, it should clearly state the major findings

of the study, because after reading it is not clear whether MTHFR C677T increases or decreases GC risk. The authors should also briefly state their findings regarding GC location and histological subtype. The last sentence of conclusion section “studies with larger sample size should be performed to assess the function of MTHFR gene in different ethnic groups” is not correct. The function of the gene is the same in all ethnic groups; the authors should be more accurate in using these terms. Minor comments: 1) Page 2, Line 5, Abstract section: the sentence “A total of 35 studies from 26 eligible publications were included in this meta-analysis” is confusing and needs to be checked. The same applies to the result section page 5, line 23. 2) Page 2, Line 15: GCC and NCGC abbreviation explanation missing 3) What is ment by “further clinical trials” in the abstract (Page 2 line 23)? The authors should be more careful about such conclusions. 4) SNP “rs” numbers should be included in the paper for the polymorphisms that have been analyzed. 5) Page 7, line 27: Our data were consistent with four previously published meta-analyses [38-40] – only three meta-analysis are cited here? Besides, there are at least three additional meta-analyses on the topic that the authors did not cite: Zacho et al. 2011; Lv et al. 2013; Yan et al. 2013. 6) Page 8, ln 12: Citation is missing to support the statement “To our knowledge, the distributions of the MTHFR polymorphism were different between various ethnic populations which may lead the different results in eastern and western populations” 7) Page 10, ln 2: The statement “The authors of this study indicate no financial conflict of interest” has nothing to do with the acknowledgement section.

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**ESPS Manuscript NO:** 6214

**Title:** Methylenetetrahydrofolate reductase C677T and A1298C polymorphisms in association with gastric cancer susceptibility: a meta-analysis

**Reviewer code:** 00182188

**Science editor:** Gou, Su-Xin

**Date sent for review:** 2013-10-10 08:43

**Date reviewed:** 2014-02-12 22:30

| CLASSIFICATION                                     | LANGUAGE EVALUATION  | RECOMMENDATION                      | CONCLUSION   |
|--|--|-------------------------------------|--|
| <input type="checkbox"/> Grade A (Excellent)       | <input checked="" type="checkbox"/> Grade A: Priority Publishing     | Google Search:                      | <input checked="" type="checkbox"/> Accept             |
| <input type="checkbox"/> Grade B (Very good)       | <input type="checkbox"/> Grade B: minor language polishing           | <input type="checkbox"/> Existed    | <input type="checkbox"/> High priority for publication |
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| <input type="checkbox"/> Grade D (Fair)            | <input type="checkbox"/> Grade D: rejected                           | <input type="checkbox"/> Existed    | <input type="checkbox"/> Minor revision                |
| <input type="checkbox"/> Grade E (Poor)            |  | <input type="checkbox"/> No records | <input type="checkbox"/> Major revision                |

## COMMENTS TO AUTHORS

Methylenetetrahydrofolate reductase C677T and A1298C polymorphisms in association with gastric cancer susceptibility: a meta-analysis This meta-analysis is a well-written and well-conducted study, which evaluated the association of MTHFR polymorphisms in the susceptibility to gastric cancer. It has a large sample size, which allowed consistent conclusions in relation to the general population. However, in subgroup analysis, when considering histology, tumor's location and populations, the sample size are quite small and the conclusions become less consistent. But, authors commented about these important limitations in the discussion. I recommend the exhibition of the data of the tables 4 and 5 in Forest Plot form. It would be much more comprehensible. In discussion, in third paragraph, authors said that "In regard to the A1298C polymorphism, we found CC genotype conferred susceptibility to GC in western". This affirmative is not correct, because in Table 4, CC genotype has OR 1.11 (95% CI 0.81 - 1.51), which did not reach statistical significance. Moreover, this affirmative was not said in the results, only in the discussion. Thus, I recommend the exclusion of that affirmative. The latter affirmative "and protection in eastern and the relationship was statistically significant in the latter" is correct and should be maintained. In Results, in "Subgroup analysis", second paragraph, it was written (TT vs. CT+CC: OR = 1.36 [1.15 , 1.67], P = 0.0006). According to the table 4, the correct number is OR = 1.38. Table 3 and 5 change intestinal by intestinal