Re: Revision of " Helicobacter pylori infection with intestinal metaplasia: An independent risk factor for colorectal adenomas"(**ESPS manuscript NO: 30745**).

Dear Editors,

We thank you and the reviewers for giving us the opportunity to revise our manuscript. We have carefully studied the comments raised by the reviewers and Editors, and revised the manuscript accordingly. The following are the point-by-point responses to the reviewers' comments. All the modifications have been highlighted in yellow in the revised manuscript.

Sincerely,
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Reviewer's code:00503535

Comments to authors

In this manuscript, the authors aimed to explore the association between H. pylori infection status, intestinal metaplasia, and colorectal adenoma, and concluded that H. pylori-related intestinal metaplasia was associated with a high risk of colorectal adenomas in Chinese individuals. The study was well designed and the results were very interesting. Therefore, the reviewer considers it can be accepted after some English correction.

Response:

Thanks for your positive comments and kind reminder.

Reviewer's code: 02922607

Comments to authors

Important topic which should be published.

Response:

We appreciate your positive comment.

Reviewer's code: 02888278

Comments to authors

1) Intestinal metaplasia is assessed on biopsy material which the author has correctly described as the gold standard. However, only 21% had biopsies from multiple sites (number of biopsies not mentioned)and the remaining 79% had biopsy from a single site. Several studies have shown that the yield of intestinal metaplasia correlates directly with the number of endoscopic biopsies obtained. Therefore reliability of presence/absence of IM due to sampling error is questionable. This limitation should be included in the discussion part.

Response:

All the individuals were asymptomatic and healthy. Biopsy specimens were taken from suspicious or abnormal-appearing areas, which helps to explain the low multiple biopsy rate. Biopsies were taken from multiple (i.e., three or more) sites in 21% of individuals, and the remaining 79% had biopsies from one or two sites. We realized this limitation and have already supplemented the Discussion. (page 9 line 15-17)

2) Evaluation of H Pylori colonisation in biopsy tissue with special stains like Giemsa is more reliable than urea breath test and should be added.

response:

We appreciate your suggestion. And we have already added in the discussion part. (page 9 line 17-20)

3)Addiion of more pathological data like presence/absence of gastritis and atrophy is desirable and will add a different dimension to the proposed hypothesis.

Response:

Indeed, the analysis of atrophy could play a role in validating the hypothesis. However, we did not emphasize this aspect in the manuscript. Our research mainly focused on the study of the relationship between *H. pylori*-related intestinal metaplasia and colorectal neoplasms. Moreover, we plan to do further research on the correlation between *H. pylori*-associated gastric diseases and colorectal neoplasia in the near future.

If you are interested in the role of atrophy, please refer to the information below. We hope that this will address your questions. Thank you for taking the time and effort to help us improve the manuscript.

Table. correlation between atrophic and colorectal neoplasam

Parameter	Atrophic(+) 164	Atrophic(-) 1477	OR 95%CI	P
Age	53.8	50.39	1.046(1.028-1.065)	P<0.001
Sex				
Female	60	494	1	
Male	104	983	0.871(0.623-1.218)	P=0.420
Non-polyp	98	960	1	
Adenomas	40	257	1.525(1.030-2.258)	P=0.035
Non-adenomous polyps	26	260	0.980(0.622-1.542)	P=0.929

Correlation between Atrophic(+) and Atrophic(-) by logistic regression analysis.

(The frequency of atrophic was more prevalent in the adenomas group than in the non-polyp group, with a crude OR of 1.525 (95% CI: 1.030-2.258, P=0.035).)