

December 26, 2013

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 6107-edited.doc).

Title: Diabetes mellitus increases risk for colorectal adenomas in younger patients

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Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 6107

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) One of the references suggested by reviewer 00054951 (Kanadiya et al) has been incorporated into the manuscript. We thank the reviewer for bringing this to our attention. The other two references (Acevedo et al and Dash et al) were reviewed but not felt to be applicable to our study and discussion. Both were secondary analyses of studies performed for other applications. Acevedo et al was an analysis of pooled data from three prior studies evaluating chemopreventive agents. These studies include patients that were treated with medications designed to prevent development of colorectal neoplasia. Hence, the effect of DM on adenomas cannot be ascertained, as there is confounding bias with use of these treatments. Furthermore, this study evaluated the recurrence of adenomas after all prior polyps had been removed. Dash et al. was a secondary analysis of the Black Women's Health Study based on self-reported questionnaires. The medical records of patients that reported polyps were reviewed, but not the records of those that did not report polyps. In addition, there was no information regarding whether these polyps were found on colonoscopy vs. flexible sigmoidoscopy or the quality of these studies. If these polyps were not found on high quality colonoscopy complete to the cecum, then adenomas were likely missed and under-reported.

(2) Our study showed a slightly stronger association in men (adjusted OR 4.7 in patients ages 40-49 with DM, adjusted OR 4.0 in those ages 50-59 without DM) than in women (adjusted OR 2.5 in patients ages 40-49 with DM, adjusted OR 3.3 in those ages 50-59 without DM). This has been added to the Results section. While interesting, the discussion of the effect of DM on different genders is perhaps beyond the scope of our manuscript. There are at least 10 studies other than the one suggested by reviewer 00054951 (Kramer et al) with conflicting evidence regarding increased risk in either gender. Some conclude that men are at higher risk and others report that women are, such as in Kramer et al. Furthermore, the pathophysiologic mechanism of gender differences is not well understood.

(3) Additional sensitivity analyses suggested by reviewer 00054951 were performed. Despite differences in terms of prevalence of hypertension and hyperlipidemia between the two younger cohorts, sensitivity analyses after further allowances for the two co-morbidities showed a similar significant association (OR 3.2 [95% CI 1.5-7.1] for patients ages 40-49 with DM and OR 3.0 [95% CI 1.5-5.9] for those ages 50-59 without DM). This was added to the Results section.

(4) The statistical analysis section of the Materials and Methods has been expanded.

(5) The odds ratios from the logistic regression analyses have been added to the Results section. This was previously only reported in the tables.

(6) Tables 2 and 3 have been combined

(7) Limitations were expanded to include relatively low sample size.

(8) The abstract has been edited per recommendations. The univariate OR have been removed. The last sentence of the conclusions of has been deleted.

3 References and typesetting were corrected

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

Sincerely,

A handwritten signature in black ink, appearing to read 'Hongha T. Vu', is shown on a light-colored background.

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