

## **Author's response to reviews**

**Title:** Increased proton pump inhibitor and NSAID exposure in irritable bowel syndrome: results from a case-control study

### **Authors:**

Daniel Keszthelyi ([daniel.keszthelyi@maastrichtuniversity.nl](mailto:daniel.keszthelyi@maastrichtuniversity.nl))  
Gwen H Dackus ([g.dackus@student.maastrichtuniversity.nl](mailto:g.dackus@student.maastrichtuniversity.nl))  
Gwen M Masclee ([g.masclee@erasmusmc.nl](mailto:g.masclee@erasmusmc.nl))  
Joanna W Kruimel ([j.kruimel@mumc.nl](mailto:j.kruimel@mumc.nl))  
Ad A Masclee ([a.masclee@mumc.nl](mailto:a.masclee@mumc.nl))

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Maastricht, 5<sup>th</sup> July 2012

Bo Shen MD  
Section Head  
Cleveland Clinic  
9500 Euclid Avenue  
Cleveland, OH 44195

Dear Dr Shen,

We hereby submit the revised version of our manuscript entitled "*Increased proton pump inhibitor and NSAID exposure in irritable bowel syndrome: results from a case-control study*" for publication in the *BMC Gastroenterology*. We have altered the paper according to the suggestions and responded to the points raised by the Reviewers. Please find the respective responses and alterations detailed below, we hope that they will be found satisfactory.

Thank you for your kind assistance.

On behalf of the co-authors,

Yours sincerely,

D. Keszthelyi, MD  
Department of Internal Medicine, Division of Gastroenterology  
Maastricht University Medical Center, Maastricht  
PO Box 5800 6202 AZ Maastricht, the Netherlands  
Tel.: +31-43 3881982  
Fax.: +31-43 3875006  
e-mail: daniel.keszthelyi@intmed.unimaas.nl

## **Points raised by Reviewer 1**

We thank the reviewer for evaluating the paper and giving helpful suggestions.

1. According to the reviewer's suggestion, data have been re-analyzed using a multivariate analyses corrected for comorbidities. The new ORs are indicated in table 3. The crude ORs are also indicated in the same table.
  
2. The Cochrane review mentioned by the reviewer concludes that anti-depressants as a group significantly improve abdominal pain and global symptoms in IBS. However, as for abdominal pain, subgroup analyses showed no benefit for SSRIs (RR 2.29; 95% CI 0.79 to 6.68; 197 patients) (Kuiken 2003; Tabas 2004; Tack 2006; Vahedi 2005). Also, no significant improvement was seen in terms of IBS symptom severity. Ladabaum et al. (CGH 2010) found no benefit of citalopram in non-depressed IBS patients. We therefore believe that the apparent symptom global improvement following SSRI therapy in IBS is mainly related to improvement of psychiatric symptoms and not necessarily gastrointestinal symptoms. As far as our study is concerned, the positive association observed between IBS and SSRIs is therefore most probably related to the therapeutic use of SSRIs for a preexistent psychiatric condition.
  
3. Potential controls were selected by a random computerized selection from the municipality residents' register. See also clarification in the manuscript.
  
4. Description of the statistical analyses has been clarified.
  
5. Please see comment under point 1.
  
6. Corrections have been made accordingly.
  
7. Unfortunately, no data are available on the relationship between drug use and IBS symptom severity. A comment has been added in the discussion section.

**Points raised by Reviewer 2:**

We are grateful for the evaluation of our paper and the helpful comments.

1. Patients who have been exposed to the medications in question *after* the initial diagnosis were not included in the analyses. This has been clarified in the manuscript.
2. Statement has been added to the abstract, according to the reviewer's suggestion.
3. Yes, the statement refers to patients having symptoms for less than 6 months. A clarifying note has been added to the manuscript.
4. The initial control group consisted of 408 individuals. From this group, 287 controls were selected by matching to cases by age and gender.