

Date: 10-10-2016

manuscript no: 28029

Title: : "Systematic review: The placebo effect of psychological interventions in the treatment of irritable bowel syndrome"

To : Professor Bonino.
Editor

Dear professor Bonino,

Thank you very much for the comments of reviewers and editor, and the opportunity to submit a revised version of our manuscript.

We have used the comments to improve the content. Please find attached a detailed reply and a revised version of the manuscript.

We hope you will consider our work suitable for publication in the World Journal of Gastroenterology

With best wishes,

Carla Flik
Department of General Practice
Julius Centre for Health Sciences and Primary Care
University Medical Centre, Utrecht, the Netherlands

Reviewer 1:

A supportive doctor-patient relationship with empathy and listening with understanding may maximize and influence the placebo response to the pharmacological agent. This would be helpful to comment on.

Response:

In the **Discussion** we added the sentence:

A positive interpersonal encounter with affective communication and adequate information from the health professional can positively influence the patient's expectations and result in an improvement in health status^[31].

2. Given the high placebo response rate in IBS, it would be helpful to note if the placebo response been studied systematically in other disease states, and if differences in the placebo rate noted in psychotherapy control groups.

Response:

In the **Discussion**, we added the following sentence:

It would be interesting to compare the PRR in studies on psychological interventions for irritable bowel syndrome to that in studies on psychological interventions for other diseases. In the systematic review entitled 'Psychological Interventions for treatment of inflammatory bowel disease' located in the Cochrane database and published in 2011^[37], none of the control groups in the included studies met our criteria for control groups. In a study by Keefer et al.^[38] on gut-directed hypnotherapy for ulcerative colitis, published in 2013, a control group that met our criteria was used. The placebo rate was 40%, which was comparable to the placebo rate found in our research. In a systematic review published in 2005, Enck & Klosterhalfen^[39] compared the PRRs for functional bowel disorders with those of non-intestinal diseases and other organic gastrointestinal diseases. Most of the studies focused on drug treatment. The authors stated that the placebo effects in functional bowel disorders were similar to those in non-intestinal diseases (depression, pain and Parkinson's disease) and not too dissimilar to those in other gastrointestinal diseases (duodenal ulcer, inflammatory bowel disease).

Reviewer 2: Very good manuscript overall. Please review abstract for clarity and grammar.

Response:

We adapted the abstract

Introduction could be written with more flow to it; please review.

Response:

We adapted the introduction in order to make it more fluent.

Please, if plot could be made more presentable with clear and consistent listing of publications included for meta-analysis, that would enhance the manuscript.

Response:

We adapted figure 2

Reviewer 3:

Good study and well conducted. I agree with the conclusions drawn.