



# Prediction pathways for innate immune pathology, IBS, anxiety and depression in a general population (The POPCOL Study)

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## Introduction

Irritable bowel syndrome (IBS) is a common diagnosis in gastroenterological practice known to be associated with anxiety/ and depression. Although classically considered a functional bowel disorder with no overt pathology, recent studies suggest a role for low-grade mucosal inflammation in producing symptoms. Interaction between innate inflammatory mediators, mast cells, T lymphocytes and eosinophils may disturb neural pathways in IBS causing dysmotility and pain which could lead to anxiety and depression.

## Aim

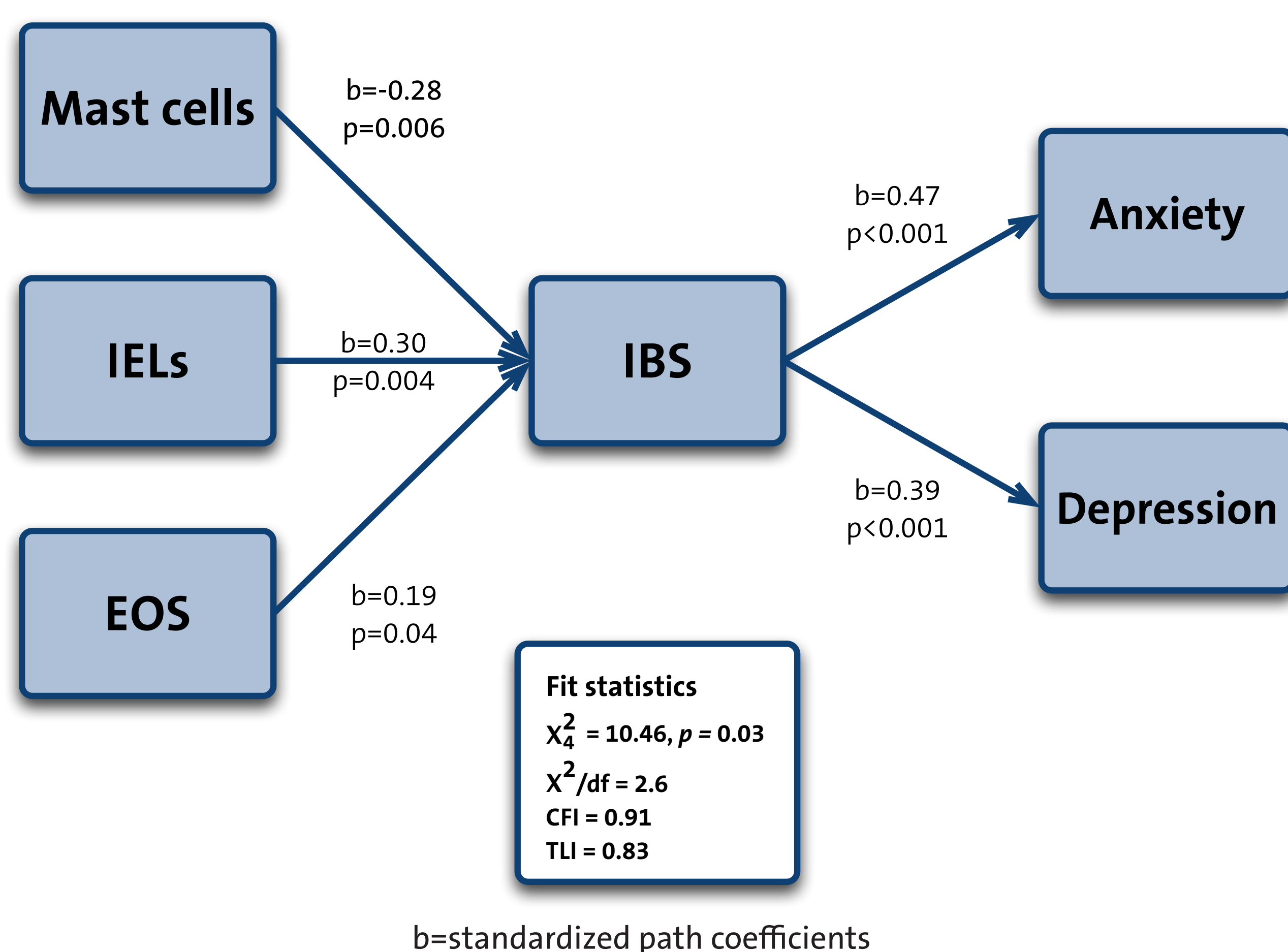
The aim of this study was to ascertain whether low grade innate inflammation contributes to a pathway of depression and anxiety via IBS.

## Methods

- Subjects from the PopCol study including 745 randomly selected subjects from the general population who had a colonoscopy (mean age 51 years;57% women).
- Immune cell counts were evaluated in colonic mucosa in IBS cases (Rome III) and controls
- Intraepithelial lymphocytes (IELs) per 100 enterocytes and eosinophils (eos) per five non-overlapping high power fields (HPF) (90 controls and 100 cases)
- Mast cells (Immunohistochemistry) per 5HPF in (80 controls and 81 cases).
- IELs, mast cells and eos were individually summed over 5 sites (terminal ileum, caecum, transverse colon, sigmoid colon and rectum) to give a total cell load.
- Anxiety and depression scores were calculated from HADS.

A causal model path model which hypothesizes immune cells being associated with IBS which, in turn, is associated with elevated anxiety and depression was tested using path analysis implemented in the MPlus software. The model's fit to the observed variance-covariance structure was assessed in several ways, viz the residual Chi-Square test which is ideally non-significant ( $p > 0.05$ ), the ratio of Chi-Square to degrees of freedom (ideally  $< 5.0$ ) the comparative fit index (CFI, ideally  $> 0.95$ ) and the Tucker-Lewis index (TLI, ideally  $> 0.95$ ).

## Casual path model



## Results

All hypothesized paths reached statistical significance supporting the individual hypothesized pathways, see table. The overall model fit was not ideal in all respects but also was not indicative of a poorly-fitting model.

## Conclusion

In this model there is a significant contribution of innate immune inflammatory load leading to anxiety and depression via IBS. Whether therapy directed to decreasing this inflammatory load also lifts depression and anxiety is an interesting concept which should be further explored.