

**Six studies pointing to the need for a biopsychosocial
approach to treating common gastrointestinal and
hepatologic disorders**

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Abstract

Background and aims

This interdisciplinary thesis was designed to deepen understanding of the co-morbidity of anxiety and depression with chronic diseases of the digestive tract, and inflammatory bowel disease (IBD) in particular. The first part of the thesis aimed to explore the prevalence of psychological problems in IBD compared to irritable bowel syndrome (IBS) and chronic hepatitis C (HCV) groups. It also explored the relationship between the number of co-morbid functional gastrointestinal disorders and the severity of psychological problems in IBD and IBS. It also aimed to determine whether there is a relationship between psychological problems and the response to standard medical treatment/physical outcomes in patients with IBD, IBS and HCV. Furthermore, it aimed to explore whether disclosure of the psychological status of depressed and/or anxious IBD patients to their gastroenterologists influences doctors' behaviour and affects patients' responses to treatment/physical outcomes. The second part of the thesis aimed to investigate the potential role of antidepressants in IBD and to determine the feasibility of future randomised controlled trials on the role of antidepressants in IBD.

Methods

Overall, a cohort of 139 outpatients (64 IBD, 41 HCV, and 34 IBS) and 18 gastroenterologists participated in the six studies comprising this thesis. A mixed methods design was applied. Two cross-sectional studies, an observational cohort prospective management study, a randomised controlled trial, a systematic review and an exploratory interview study were conducted. Differences between the groups for continuous variables were assessed with one way analysis of variance (ANOVA) and independent samples t-tests. Differences in categorical variables were assessed with contingency tables with the

Chi-Square test and the Fisher's Exact Test. Propsective analyses were conducted with repeated measures ANOVA, logistic regression and Poisson regression. Qualitative data were analysed using content analysis.

Results

Overall, 42% of participants were anxious and 19% were depressed. Participants with HCV had higher levels of psychological impairment compared with the IBS, the IBD group and the general population ($p<0.05$). Those IBD participants with fewer co-morbid functional disorders had better physical quality of life than participants with a greater number of these disorders ($p=0.025$). Moreover, depression/anxiety at baseline did not explain medical outcomes after 12 months in this cohort of patients with chronic diseases of the digestive tract. Doctors' knowledge of patients' psychological status was found to have no impact on IBD patients' outcomes after 12 months. However, interestingly, the level of anxiety in IBD participants significantly dropped between the baseline and nine months indicating a possible benefit from participating in the study. In the literature review, insufficient evidence was found to conclude that antidepressants are efficacious for treatment of psychological co-morbidities or somatic complaints in IBD. However, the qualitative interview study indicated a potential positive impact of treatment with antidepressants on coping with disease symptoms and general wellbeing in patients with IBD.

Conclusion

The thesis confirms that there is a significant burden of psychological co-morbidity in patients with chronic gastroenterological diseases. Interdisciplinary approaches to the management of these diseases are therefore warranted in Australian gastroenterology clinics. Anxiety targeted interventions and research in this setting are urgently needed,

especially with respect to patients with HCV. Larger studies exploring the gastroenterologists' role in treatment of co-morbid psychological problems in their patients are recommended. Longer prospective studies on homogenous samples of patients are also needed to clarify the nature of the relationship between psychological problems and relapse of somatic symptoms. Finally, randomised controlled trials exploring the efficacy of antidepressants in IBD are warranted.

Statement page

This work contains no material which has been accepted for the award or any other degree or diploma in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text.

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List of studies and hypotheses/research questions

Part 1

Study 1: A cross-sectional study comparing the prevalence of psychological problems and the level of quality of life in patients with IBD, IBS and HCV.

- Hypothesis 1: Patients with IBD are most affected by psychological problems compared to patients with IBS and HCV.

Study 2: A cross-sectional investigation into the prevalence of functional gastrointestinal disorders in IBD and IBS patients and exploring the relationship between the number of these disorders and the severity of psychological problems.

- Hypothesis 2: Patients with IBD and patients with IBS with the greater number of functional gastrointestinal disorders have higher levels of depression and anxiety and poorer quality of life than those with smaller number of functional disorders.
- Hypothesis 3: Patients with IBD with co-morbid IBS have higher rate of psychological problems and poorer quality of life than patients with IBD without co-morbid IBS.

Study 3: A cohort prospective management study exploring the temporal relationship between psychological co-morbidities and the likelihood of a successful response to standard medical treatment/better physical outcomes in patients with IBD, IBS and HCV.

- Hypothesis 4: Patients with psychological co-morbidities are less likely to have a satisfactory response to standard treatment/good physical outcomes at 12 months.

Study 4: A pilot randomised controlled trial examining whether disclosure of IBD patients' psychological status to their treating doctors influences patients' responses to the clinical treatment/their physical outcomes.

- Hypothesis 5: Physicians' knowledge of patients' psychological status alters physicians' behavior and/or improves patients' clinical outcomes.

Part II

Study 5: A systematic review of the literature designed to quantitatively and qualitatively explore the problem of using antidepressants in IBD.

- Are antidepressants effective in maintaining or inducing remission of inflammatory bowel disease?

Study 6: Standardised semi-structured interviews enabling in-depth exploration of gastroenterologists' experiences, opinions and attitudes about treating IBD patients with antidepressants.

- What are the gastroenterologists' attitudes and experiences of using antidepressants in patients with inflammatory bowel disease?

Abbreviations

| | |
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| BDI: | Beck Depression Inventory |
| BMI: | Body Mass Index |
| CAI: | Colitis Activity Index |
| cAMP: | Cyclic Adenosine Monophosphate |
| CBT: | Cognitive-Behavioural Therapy |
| CD: | Crohn's Disease |
| CDAI: | Crohn's Disease Activity Index |
| CES-D: | Center for Epidemiological Studies Depression Scale |
| CRS: | Clinical Rating Scale |
| DIS: | Diagnostic Interview Schedule |
| DSM-III: | Diagnostic and Statistical Manual of Mental Disorders-III |
| EPI: | Eysenck Personality Inventory |
| FGIDs: | Functional Gastrointestinal Disorders |
| GI: | Gastrointestinal |
| GSI: | Global Severity Index |
| GSRS: | Gastrointestinal Symptom Rating Scale |
| HADS: | Hospital Anxiety and Depression Scale |
| HAM-D: | Hamilton Depression Inventory |
| HCV: | Hepatitis C |
| HCVRNA: | Hepatitis C Ribonucleic Acid |
| IBD: | Inflammatory Bowel Disease |
| IBDQ: | Inflammatory Bowel Disease Questionnaire |
| IBS: | Irritable Bowel Syndrome |
| MAOI: | Monoamine Oxidase Inhibitor |

| | |
|---------|--|
| MCS: | Mental Component Summary |
| PCS: | Physical Component Summary |
| PGWB: | Psychological General Well-Being Index |
| POMS: | Profile of Mood States |
| PSDI: | Positive Symptom Distress Index |
| PSQ: | Perceived Stress Questionnaire |
| PST: | Positive Symptom Total |
| RFIPC: | Rating Form of Inflammatory Bowel Disease Patient Concerns |
| SADS-L: | Schedule for Affective Disorders and Schizophrenia |
| SCCAI: | Simple Clinical Colitis Activity Index |
| sCDAI: | Simplified Crohn's Disease Activity Index |
| SCL-90: | Symptom Check List 90 |
| SF-12: | Short Form 12 Health Survey |
| SF-36: | Short Form 36 Health Survey |
| SIP: | Sickness Impact Profile |
| SNRI: | Serotonin-Norepinephrine Reuptake Inhibitor |
| SSRI: | Selective Serotonin Reuptake Inhibitor |
| STAI: | State and Trait Anxiety Inventory |
| TNF: | Tumour Necrosis Factor |
| UC: | Ulcerative Colitis |
| y.o: | Years Old |
| Yr: | Year |