Effects of Psychology and Extra-Gastrointestinal Symptoms on Healthcare Use by Subjects With and Without Irritable Bowel Syndrome

David T. McNaughton[1], Anna Andreasson[1,2,3], Brjánn Ljótsson[4], Alissa P. Beath[1], Julia M. Hush[5], Nicholas J. Talley[6], Gunnar Ljunggren[7,8], Peter T. Schmidt[3], Lars Agréus[7], Michael P. Jones[1]

[1]Department of Psychology, Macquarie University

[2]Stress Research Institute, Stockholm University

[3]Department of Medicine Solna, Karolinska Institutet

[4]Department of Clinical Neuroscience, Karolinska Institutet

[5]Department of Health Professions, Macquarie University

[6]Faculty of Health and Medicine, University of Newcastle, Callaghan, NSW, Australia

[7]Division of Family Medicine and Primary Care, Department of Neurobiology, Care Sciences and Society, Karolinska Institutet, Huddinge, Sweden

[8]Public Healthcare Services Committee Administration, Stockholm County Council, Stockholm, Sweden

Short Title

Healthcare utilization in Irritable Bowel Syndrome

Conflict of Interest

All authors have no financial or personal conflicts of interest to disclose.

Abbreviations

FGID = Functional Gastrointestinal Disorder, GI = Gastrointestinal, HADS = Hospital Anxiety and Depression Scale, IRR = Incidence Rate Ratio, IBS = Irritable Bowel Syndrome, PopCol = Population Colonoscopy, Regr = Regression

Correspondence

Prof Michael P. Jones, PhD

Department of Psychology, Macquarie University, 2109, Sydney, Australia

Email: mike.jones@mq.edu.au

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Author Contributions

David McNaughton: Study concept and design; analysis and interpretation of data; drafting manuscript

Anna Andreasson: Study concept and design; acquisition of data and analysis; interpretation of data

Brjánn Ljótsson: Study concept and design

Alissa Beath: Study concept and design; study supervision

Julia Hush: Study concept and design; study supervision

Nicholas Talley: Study concept and design; critical revision of the manuscript for important intellectual content

Lars Agréus: Principal investigator in the original PopCol study; study concept and design; critical revision of the manuscript for important intellectual content

Gunnar Ljunggren: Acquisition of data and analysis

Peter Schmidt: Acquisition of data and analysis: critical revision of the manuscript for important intellectual content

Michael P. Jones: Study concept and design; Statistical analysis; analysis and interpretation of data; study supervision

Abstract:

Background & Aims: There is controversy about whether psychological factors (anxiety and depression) increase seeking of healthcare by patients with irritable bowel syndrome (IBS). We investigated whether psychological factors increase healthcare seeking by patients with IBS and the effects of extra-GI symptoms. **Methods:** We performed a population-based prospective study of healthcare use over a 12-year period in Sweden. From 2002 through 2006, 1244 subjects were randomly selected for an examination by a gastroenterologist and to complete questionnaires, including the Rome II modular questionnaire. Psychological factors were measured with the valid Hospital Anxiety and Depression scale and extra-GI symptoms measured with a symptom checklist. Responses from 1159 subjects (57% female; mean age, 48.65 years) were matched with health records in 2016 (164 were classified as having IBS based on Rome II criteria). **Results:** The overall association between depression or anxiety and healthcare use, in subjects with and without IBS at baseline, varied. The presence of extra-GI symptoms strengthened the relationship between anxiety and depression and prospective psychiatric visits for subjects with IBS and without IBS (incidence rate ratios, 1.14–1.26). Extra-GI symptoms did not alter the association of anxiety or depression with use of GI or extra-GI healthcare. **Conclusions:** In a population-based study in Sweden, we found that individuals with high baseline anxiety or depression were more likely to seek psychiatric healthcare, but not GI or extra-GI healthcare, in the presence of extra-GI symptoms at baseline. Patients with IBS might benefit from more thorough assessments, which examine extra-GI and psychological symptoms, to reduce healthcare utilization.

Introduction

Irritable bowel syndrome (IBS) is a common functional gastrointestinal disorder, impacting 10-15% of the population globally[1]. Diagnosed using either clinical judgement or consensus criteria, IBS is characterized by fluctuating abdominal pain/discomfort and altered bowel habits in the absence of any identifiable organic disease[2]. IBS is associated with a reduced quality of life[3] and increased levels of anxiety and depression[4], compared to those without IBS.

IBS cohorts utilize a disproportionate use of healthcare resources[5,6]. In the United States it is estimated the total annual cost per patient is up to $US7547, with a projected annual cost to the nation of $US1353 million[6]. A comparison between four European countries estimated that the total annual costs of IBS ranged between €700 to €1600 per patient [7]. Healthcare seeking rates of IBS sufferers reported in the literature do, however, vary substantially, ranging from 10 - 70% of IBS samples, and this number is highly dependent on sampling method and countries or regions' unique healthcare landscape, such as affordability of healthcare[8]. As healthcare demands among IBS sufferers impose a heavy economic burden, identifying predictors of healthcare users has the potential for improving quality and efficacy of care[9].

High symptom intensity and duration of gastrointestinal (GI) symptoms predict only a small proportion of the healthcare seeking behavior seen in IBS individuals[8]. The remaining variance is thought to be associated with a variety of lifestyle and psychological factors such as elevated stress, co-morbidity, history of abuse and lower education level[10]. There is, however, mixed evidence regarding how strongly psychological factors predict healthcare utilization in IBS sufferers. For example, Talley et al. identified no relationship between neuroticism and psychiatric morbidity with healthcare seeking[11], while Ringstrom et al. identified that factors such as anxiety, depression and coping style did predict healthcare

use[12]. Much of this research addressing the relationship between psychological factors and healthcare seeking uses cross-sectional or retrospective methodologies, where prospective, longitudinal designs are lacking.

An understanding of how symptom and non-symptom factors influence healthcare seeking behavior can be conceptualized via the Anderson Model, which is a widely accepted framework for understanding why people access healthcare[13]. The model describes three domains: a predisposition to use services, the ability to use services, and an individual need for those services. Our study is focused on the final stage of the Andersen model where the individual's needs are matched with their local healthcare system. One possible explanation for the current inconsistency in the literature is that studies have not taken into account the burden of extra-gastrointestinal disorders which also influence healthcare seeking. IBS can be considered a complex condition involving the integration of multiple bodily systems and perceptual processes[14]. The presence of comorbid extra-GI symptoms in IBS sufferers has been associated with higher healthcare utilization[15] and increased GI symptom burden[16]. What remains unknown, though, is whether the presence of these extra-GI symptoms can moderate or alter the strength of the relationship between psychological distress and healthcare utilization.

Therefore, the aims of the present paper were to 1) determine the association between psychological factors (anxiety and depression) and prospective healthcare utilization in an IBS and non-IBS cohort, and 2) determine whether this effect is modified by the presence of extra-GI symptoms in an IBS and non-IBS cohort. We specifically hypothesized that the association between psychological factors and healthcare seeking is up-regulated with increasing burden of extra-GI symptoms. It is reasonable to infer that distressed individuals with multiple health complaints will a) be more likely to seek help compared to not seeking help and b) once help is sought, consume more healthcare resources.

Methods

Subjects

This is an analysis of the Swedish population-based study known as PopCol[17]. Between 2002 and 2006, subjects were randomly selected from Stockholm, Sweden, to determine the prevalence of IBS[17]. A random sample of 1244 subjects attended a hospital visit including an interview with a gastroenterologist and completed questionnaires including the Rome II modular questionnaire. July 2016, study data were linked with healthcare utilization data described below using the personal identity number assigned to all Swedish citizens. The baseline investigation was approved by the local ethics committee at Karolinska Institutet, Dnr 394/01. The linkage was approved by the regional ethics board in Stockholm, Dnr 2016/228-31/2.

Measures

IBS Classification

Classification of IBS was based on the Rome II Modular Questionnaire[18], which evaluates symptoms experienced during the last 3 months, some of which must be present at least one day in each week. The Rome criteria are arguably the most well-established and widely used method of Functional Gastrointestinal Disorders (FGID) classification in epidemiological studies[2,18,19]. Subjects classified as non-IBS were those who did not meet the Rome II criteria.

Anxiety and Depression

Self-reported anxiety and depression were measured through the validated Hospital Anxiety and Depression Scale (HADS), which is commonly used to assess the severity of symptoms of mood disorders in clinical and community samples[20]. HADS is comprised of 14 items, seven of which relate to anxiety and depressive symptoms respectively. Each item is rated on a Likert-type scale from 0 to 3. The scores for anxiety and depression can therefore vary from 0 to 21, with higher scores reflecting increased symptom severity. The depression and anxiety

subscales exhibited good internal consistency in the current study with Cronbach's alphas

0.79 and 0.87, respectively.

Extra-GI Symptoms

The assessment included the symptom questionnaire of the Gothenburg Quality of Life

Assessment, a symptom questionnaire of common somatic and mental symptoms, such as

dizziness, backache, chest pain, and general fatigue[21,22]. The instrument has been shown to

have acceptable reliability, with Cronbach's alpha ranging from $0.72 - 0.85$[22], and correlate

well with several important health constructs, such as depressive symptoms ($r = 0.43$) and

reduced social functioning ($r = -0.39$)[23]. Further, the 30 symptoms included in this instrument

include all 15 of those in another commonly-used somatic symptom checklist, the Patient

Health Questionnaire-15[24]. In the present study, four questions were added to the list of 30

questions from the assessment. Participants were asked: "Have you been troubled by any of

the following symptoms during the last three months?" Respondents answered yes or no,

resulting in a symptom count ranging from 0 to 34, with higher scores reflecting a greater

number of symptoms. To avoid the risk of inducing circularity or gender bias, eight items

containing gastrointestinal, psychological and gender specific symptoms were excluded from

the total score. Thus, the final scores range from 0 to 26 and is subsequently referred to as

extra-GI score.

Healthcare Utilization

The Swedish healthcare system is public-system oriented with a small ($< 5\%$) parallel private

healthcare system where individuals may take out private health insurance or pay out of

pocket. The system is similar in nature to the health systems in Scandinavia, Europe and

other western countries such as Canada and Australia. This system is ideal for this study as it

reduces potentially confounding factors such as financial barriers to accessing healthcare.

Future healthcare utilization was determined using registry data from the Stockholm County

Council over the 12 years (2006-2015). The registry includes almost all physician visits whether as outpatient or as in-patient visits, reimbursed by the Stockholm County Council. International Classification of Disease-10 (ICD-10) codes for the consultations were used to group healthcare utilization in three domains: Gastrointestinal, Psychiatric and Extra-Gastrointestinal. Healthcare utilization is reported as number of consultations within each of these categories, yielding six separate counts of healthcare utilization. A more detailed explanation of this variable is described in the supplemental material.

Statistical analysis

The primary aim of the statistical analysis was to evaluate moderation, or effect modification, of the association between psychological state and level of healthcare seeking by the level of extra-gastrointestinal symptoms. The term moderation here means that the strength of the association between psychological state (the independent variable) and healthcare seeking (the dependent variable) changes (is influenced, or moderated) depending on the level of extra-gastrointestinal symptoms; to put differently, whether level of extra-gastrointestinal symptoms modified the effect of psychological state on healthcare utilisation (see Figure 1). This is formally tested via a statistical interaction in the statistical models described below.

[Insert Figure 1 near here]

Figure 1. Visual representation of the moderation analyses.

Negative binomial or zero-inflated negative binomial models were fit in order to evaluate the moderating effect of extra-gastrointestinal symptoms on the relationship between psychological state (Anxiety or Depression) and prospective healthcare utilization. A more detailed explanation of these statistical techniques are presented in the supplemental material. Results are presented as regression and binary Incidence Rate Ratios (IRR), standard errors and p-values. The IRR were determined via a Z statistic and the criteria for statistical significance level for these analyses was set at 0.05 (two-tailed). A positive regression IRR

value indicates that, conditional upon there being some consultations, increased counts of

healthcare utilization were related with increasing anxiety or depression. Regarding a positive

binary IRR, this measures the increase in odds of consultations occurring or not, with

increasing anxiety or depression. For ease of interpretations of IRRs, the extra-GI score was

divided by five.

Results

Of the 3,556 individuals in the original study population, 2,293 responded to the initial mail out and a total of 1,244 (35%) attended a hospital visit at which the majority of the measures were completed. Data on IBS status were incomplete for 85 subjects, who were subsequently excluded, thus a total of 1,159 (33%) subjects were used in the analyses. A detailed comparison of the demographic factors between the included participants and the Swedish general population can be found in the supplementary material.

Table 1 describes the sample demographics and other characteristics. Of the 1,159 subjects (mean age 49 years, 57% female), 164 were Rome II classified as IBS. IBS subjects were younger, had higher scores of depression and anxiety than non-IBS subjects. Further, IBS subjects experienced higher mean healthcare visits in all domains, except for inpatient extra-GI visits.

[Insert Table 1 near here]

Overall association

The association between psychological factors (anxiety and depression) and prospective healthcare utilization is described in Table 2. Of the IBS cohort, the association between depression symptoms and inpatient GI visits was significant and large, indicating that higher depression is associated with increased number of an inpatient GI visits within an IBS cohort. Regarding anxiety symptoms, a small and negative association was identified with outpatient psychiatric consultations. This indicates higher anxiety relates to a lower probability of seeking (compared with not seeking) psychiatric consultations. Further, a small and positive association was identified with respect to binary inpatient GI visits. This indicates that higher anxiety relates to higher probability of seeking a GI consultation as an inpatient, however it is not associated with an increased number of GI inpatient visits.

Of the non-IBS cohort, the associations between depression symptoms and both outpatient and inpatient extra-GI visits were significant and large. This indicates higher depression is associated with an increased number of consultations which are not of GI or psychiatric origin. Regarding depression symptoms, there was a small and negative association with outpatient psychiatric consultations. This indicates higher depression is related to a smaller probability of seeking (compared with not seeking) an outpatient psychiatric consult. This is similarly identified in the relationship between anxiety symptoms and both outpatient and inpatient psychiatric visits, indicting higher anxiety relates to a lower probability of seeking a psychiatric consult at both an inpatient and outpatient setting.

[Insert Table 2 near here]

Extra-GI symptom moderation

A moderation analysis was undertaken to address the role of extra-GI severity in the relationship between psychological factors (anxiety and depression) and healthcare utilization. Table 3 displays the results of the regression and binary moderation differentiated by the whole sample, IBS-subject and non-IBS subjects.

Significant moderation occurred in the IBS cohort for both anxiety and depression predicting outpatient and inpatient visits. Significant moderation occurred in the non-IBS cohort for anxiety predicting psychiatric inpatient visits. This highlights that among the IBS cohort, increased extra-GI symptoms strengthened the relationship between worse psychological symptoms and both outpatient and inpatient psychiatric visits, while among the non-IBS cohort, increased extra-GI symptoms strengthened the relationship between worsening anxiety and higher inpatient psychiatric visits. Overall, inspection of the moderation findings suggests a more consistent pattern of moderated association between psychological state and healthcare seeking among IBS subjects than in the non-IBS cohort (Table 3). No further moderation was identified with respect to GI or extra-GI visits.

[Insert Table 3 near here]

Discussion

This study sought to investigate the moderating impact of comorbid extra-gastrointestinal (GI) symptoms on the relationship between psychological factors and prospective healthcare utilization in people with IBS. The moderation analysis was used to clarify inconsistencies identified in the literature[11,12] about whether psychological factors predict greater healthcare seeking in subjects with IBS. Our data identified that extra-GI symptoms may moderate the effect of anxiety and depression on future healthcare consumption in IBS subjects, over a 12-year period. This related more to psychiatric consultations, than healthcare visits for gastrointestinal or extra-gastrointestinal symptoms. A similar, albeit weaker, pattern was seen in non-IBS subjects.

Our findings are generally consistent with previous GI-literature, in that IBS subjects experience elevated healthcare utilization compared to non-IBS subjects[25,26]. This was seen in on all measures except for extra-GI consultations. Our results provide new information about the positive associations between psychological factors and GI specific consultations in subjects with IBS, which has been reported in other non-IBS populations[12]. We did also identify negative associations in that higher scores on psychological factors predicted less psychiatric healthcare seeking in both IBS and non-IBS cohorts. This may reflect pre-existing psychological symptoms and/or diagnoses prior to the study period, resulting in individuals not needing to seek psychiatric healthcare during this time. Alternatively, this may reflect healthcare avoidant behavior, where increasing psychological distress has been also identified as a predictor of not seeking help, due to fear of serious illness or death[27].

For people with IBS, the role of psychological factors, such as anxiety and depression, in increased healthcare utilization has been unclear, with some studies finding an association[8,12,28] while others do not[11,29,30]. We hypothesized that a potential explanation for the observed inconsistency in the literature is the presence of a high extra-GI symptom count

as a key moderator of the relationship. Within a biopsychosocial framework, the presence of psychological distress in isolation may not be enough to drive individuals to seek help for their symptoms. However, once extra-GI symptoms occur, this may result in an apparent confirmation of disease or illness to the individual, and thus increase the drive to seek healthcare. Extra-GI symptoms did moderate the association between psychological factors and healthcare seeking, however this was identified for psychiatric consultations only. Furthermore, this pattern was observed more consistently in IBS subjects. This may reflect a somatisation processes, in which the interaction of somatic and mental complaints further exacerbate symptom burden, and thus increase the drive to seek help. Trait somatisation has been consistently identified in IBS[16] and other Functional Somatic Syndromes[31]. This reinforces IBS as a multi-system disorder which requires a comprehensive assessment of GI, extra-GI and psychological symptoms. Early detection of extra-GI complaints and subsequent referral for multi-disciplinary care may be key to reducing the increasing consumption of healthcare resources, which is identified in IBS subjects. Just as decreasing anxiety symptoms may reduce the feedback loop in brain-gut interactions in IBS, early intervention for extra-GI symptoms may have an analogous effect on healthcare resource utilization.

Strengths of the present study include the use of a large population-based study, as well as the prospective design in identifying IBS subjects prior to seeking healthcare which increases the accuracy of the presented associations. Previous studies have recruited IBS subjects once they are already accessed healthcare which may inflate associations[12,32]. Regarding the limitations of the study, there were a small number of subjects (n=85) excluded due to missing data on IBS status. Secondly, our outcome variable of healthcare utilization only took into account the number of visits each subject accrued. Other measures of healthcare utilization, such as number of diagnostic tests ordered, medication use, and/or invasive procedures, may also be related to psychological distress and extra-GI comorbidity,

and future research should aim to investigate these other types of healthcare utilization to see if they offer different perspectives on the matter than what the present results have. Thirdly, as in any non-experimental study, there is the potential for unseen sources of confounding and other forms of bias, which could have influenced our results. To the extent possible, we have investigated potential sources, such as response bias and considered controlling for common confounding variables, such as age and sex. However, we conducted some exploratory analyses and found no evidence to support these concerns. Finally, whilst our aims specifically investigated psychological factors in relation to healthcare seeking, we appreciate there are a number of non-symptom factors such as education level, diet and IBS control beliefs[32], that may also influence the desire to seek help.

An individual's drive to seek medical help remains a complex behavioral process, incorporating psychological, social and symptom specific factors[13]. Our data highlight that anxiety and depressive symptoms at baseline inconsistently predict medical consultations over a 12-year period, with some increasing healthcare utilization, while others lead to reduced tendency to seek help. Further, individuals with high baseline anxiety or depression are more likely to receive a psychiatric diagnosis in the presence of extra-GI symptoms, but not GI or extra-GI diagnoses. This reinforces the importance of a comprehensive assessment of psychological and extra-GI symptoms in subjects with IBS.

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Table 1. Demographic and clinical characteristics of the whole sample, IBS subjects and non-IBS subjects

	Whole Sample (n=1,159)	IBS Subjects (n=164)	Non-IBS subjects (n=995)
Gender (n/%)			
- Female	658 / 57%	106 / 65%	552 / 56%
- Male	501 / 43%	58 / 35%	443 / 44%
Age (m/SD)	48.65 (13.33)	43.5 (13.20)	49.50 (13.17)
College / university (n/%)	678 (58%)	98 (60%)	580 (58%)
People in household (m/SD)	2.17 (1.12)	2.24 (1.09)	2.15 (1.08)
Depression (m/SD)	3.00 (3.00)	4.42 (3.52)	2.77 (2.76)
Anxiety (m/SD)	4.86 (3.97)	7.19 (4.48)	4.48 (3.75)
Extra-GI symptoms (m/SD)	6.5 (4.71)	9.64 (5.18)	5.98 (4.42)
Outpatient visits (m/SD)			
- Psych	1.54 (5.59)	2.44 (6.69)	1.39 (5.38)
- GI	1.19 (3.45)	2.21 (4.66)	1.02 (3.18)
- Extra-GI	22.46 (26.74)	25.15 (25.52)	22.01 (26.92)
Inpatient visits (m/ SD)			
- Psych	0.11 (0.14)	0.14 (1.00)	0.10 (1.50)
- GI	2.00 (0.70)	0.30 (1.02)	0.18 (0.63)
- Extra-GI	2.01 (2.78)	1.96 (2.20)	2.01 (2.85)

Extra-GI symptoms: 0 – 26, Hospital Anxiety and Depression Scale - Depression: 0 - 21, Anxiety: 0- 21

Outpatient visits = general practitioner or specialist consultations in primary care, Inpatient visits = specialist visits in inpatient (hospital) care.

Prospective Healthcare counts relating to: Psych = psychiatric visit, GI = Gastrointestinal visit, Extra-GI = Consults related to complaints other than psychiatric or gastrointestinal origin.

Prospective healthcare use determined over a 12-year period.

Table 2. Overall association between psychological factors with healthcare utilization

	Healthcare	Whole Sample: IRR (SE), p				IBS Subjects: IRR (SE), p				Non-IBS Subjects: IRR (SE), p			
		Anxiety		Depression		Anxiety		Depression		Anxiety		Depression	
		Regr	*Binary*	*Regr*	*Binary*	*Regr*	*Binary*	*Regr*	*Binary*	*Regr*	*Binary*	*Regr*	*Binary*
Outpaitnt Visits	Psych	1.04 (0.03), p = 0.07	**-0.25 (0.06)****	1.06 (0.03), p = 0.06	**-0.23 (0.06)****	1.02 (0.04), p = 0.70	**-0.32 (0.12)***	1.03 (0.05), p = 0.59	-0.49 (0.29), p = 0.10	1.04 (0.03), p = 0.13	**-0.26 (0.08)****	1.05 (0.04), p= 0.15	**-0.20 (0.07)****
	GI	**1.05 (0.02)***	-0.52 (0.68), p = 0.44	**1.05 (0.02)***	-0.03 (134.64), p=1.00	1.05 (0.03), p = 0.16	32.66 (7636.65), p = 1.00	1.05 (0.04), p = 0.22	0.07 (314.72), p = 1.00	1.01 (0.03), p = 0.51	-0.39 (0.40), p = 0.33	1.00 (0.04), p =0.92	-0.39 (1.10), p = 0.73
	Extra-GI	1.00, p = 0.49	_	**1.02 (0.01)***	_	1.00 (0.02), p = 0.75	_	1.01 (0.02), p = 0.65	_	1.00 (0.008), p = 1.0	_	**1.02 (0.01)***	_
Inpatient Visits	Psych	0.94 (0.05), p = 0.25	**-0.16 (0.08)***	1.00 (0.12), p = 0.97	-0.22 (0.15), p = 0.14	0.95 (0.07), p = 0.54	-0.08 (0.10), p = 0.42	0.82 (0.18), p = 0.38	-0.39 (0.40), p= 0.34	0.93 (0.06), p =0.22	**-0.19 (0.09)***	1.13 (0.22), p =0.54	-0.15 (0.16), p = 0.35
	GI	(0.03), p = 0.98	-1.35 (1.03), p=0.19	1.06 (0.04), p = 0.12	-9.63 (757.08), p = 1.00	1.10 (0.06), p = 0.10	**0.17 (0.08)***	**1.29 (0.12)***	0.24 (0.13), p = 0.07	0.96 (0.04), p= 0.31	-1.28 (0.80), p =0.11	1.03 (0.05), p =0.47	-3.7 (14.89), p =0.80
	Extra-GI	1.00 (0.007), p = 0.50	0.003 (522.38), p = 1.00	**1.03 (0.01)****	0.001 (1141.01), p= 1.00	1.00 (0.12), p = 9.96	-0.008 (918.30), p = 1.00	1.01 (0.02), p = 0.49	-0.01 (1950.03), P = 1.0	0.99 (0.008), p = 0.28	0.004 (3933.29), p = 1.00	**1.04 (0.1)****	0.004 (1021.36), p = 1.00

Anxiety and depression measured through hospital anxiety and depression (HADS) subscales

Psych = psychiatric visit, GI = Gastrointestinal visit, Extra-GI = Consults related to complaints other than psychiatric or gastrointestinal origin

Outpatient Other = Negative Binominal Regression, All others Zero-inflated Binominal Regression

IRR = Incidence rate ratio. Standard error and p-value

Binary = probability of consults occurring or not occurring with higher anxiety or depression, Regr = conditional upon there being consultation, does higher anxiety or depression relate to increased healthcare consultation.

Prospective healthcare use determined over a 12-year period.

P-value: < 0.05 = * and < 0.005 = **

	Healthcare	Whole sample: IRR (SE), p				IBS Subjects: IRR (SE), p				No-IBS Subjects: IRR (SE), p			
		Anxiety		Depression		Anxiety		Depression		Anxiety		Depression	
		Regr	Binary	Regr	Binary	Regr	Binary	Regr	Binary	Regr	Binary	Regr	Binary
Outpatient Visits	Psych	**1.05 (0.02)***	-0.04 (0.05), p=0.36	**1.06 (0.03)***	-0.11 (0.09) p = 0.21	**1.15 (0.06)***	-0.001 (0.09), p =0.98	**1.15 (0.07)***	0.006 (0.12), p = 0.96	1.04 (0.03), p =0.14	-0.06 (0.10), p = 0.54	1.04 (0.04), p = 0.29	-0.13 (0.12), p =0.29
	GI	1.01 (0.02), p = 0.48	-1.38 (1.24), p = 0.27	1.04 (0.03), p = 0.19	-1.15 (1.12), p = 0.31	0.95 (0.03), p = 0.11	-0.06 (0.08), p = 0.48	0.99 (0.04), p = 0.82	-0.03 (0.09), p = 0.77	1.02 (0.03), p = 0.51	-1.51 (1.17), p = 0.20	1.01 (0.04), p =0.71	-0.98 (0.98), p =0.32
	Extra-GI	1.00 (0.007), 0.51	N/A	1.00 (0.01), 0.78	N/A	1.02 (0.02), p = 0 .16	N/A	1.01 (0.02), p = 0.71	N/A	1.00 (0.008), p = 1.00	N/A	1.01 (0.01), p = 0.68	N/A
Inpatient Visits	Psych	**1.14 (0.07)***	0.02 (0.06), p = 0.71	1.06 (0.11), p = 0.43	0.08 (0.08), p = 0.30	**1.14 (0.05)***	-0.02 (0.10), p = 0.85	**1.26 (0.13)***	0.06 (1.15), p = 0.70	**1.24 (0.11)***	-0.002 (0.15), p = 1.00	0.84 (0.15), p = 0.32	-0.04 (0.16), p = 0.79
	GI	1.02 (0.03), p = 0.45	-0.83 (1.18), p = 0.48	0.95 (0.43), p= 0.27	0.73 (0.50), p = 0.14	0.99 (0.05), p = 0.85	-0.05 (0.08), p = 0.56	1.01 (0.13), p = 0.95	0.10 (0.12), p = 0.38	1.00 (0.04), p = 0.91	-0.70 (1.10), p = 0.53	0.98 (0.05), p =0.74	0.45 (0.33), p = 0.17
	Extra-GI	1.01(0.007), p = 0.43	-0.004 (845.57), p = 1.00	1.00 (0.01), p =0.79	-0.009 (1180.77), p=1.00	1.00 (0.01), p = 0.77	-0.01 (22060.47), p =1.0	0.98 (0.27), p =0.46	-0.02 (6463.55), p = 1.0	1.00 (0.008), p = 0.72	-0..005 (587.85), p =1.00	1.01 (0.01), p= 0.30	-0.01 (840.86), p = 1.00

Table 3. Moderation of the relationship between psychological factors and healthcare utilization by extra-GI symptoms

Anxiety and Depression: Hospital anxiety and depression (HADS) subscales, extra-GI symptoms: Gothenburg Quality of Life Assessment

Psych = psychiatric visit, GI = Gastrointestinal visit, extra-GI = Consults related to complaints other than psychiatric or gastrointestinal origin

Outpatient Other = Negative Binominal Regression. All others = Zero-inflated Binominal Regression

IRR = Incidence rate ratio. Standard error and p-value

Binary = change in odds of consultations occurring or not with higher anxiety or depression, Regr = conditional upon there being some consultations, does higher anxiety or depression relate to increased healthcare consultation.

Prospective healthcare use determined over a 12-year period.

P-value: < 0.05 = and < 0.005 = **

Extra-gastrointestinal symptoms

Psychological state
(Anxiety or Depression)

Prospective healthcare utilization
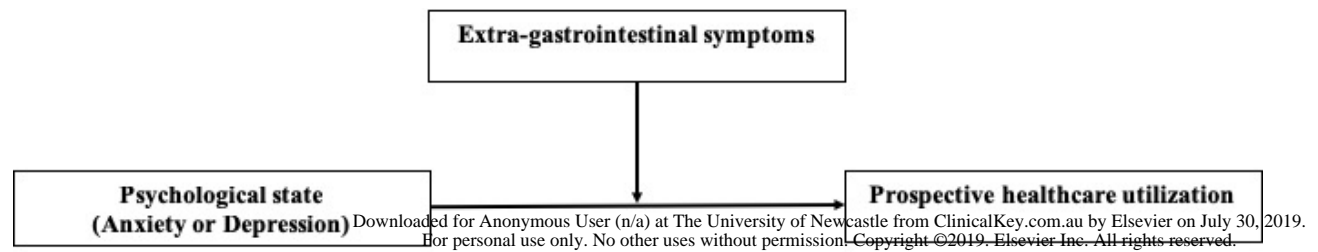
Effects of Psychology and Extra-Gastrointestinal Symptoms on Healthcare Use by Subjects With and Without Irritable Bowel Syndrome

What You Need to Know

Background: We investigated whether psychological factors increase healthcare seeking by patients with IBS and the additional effects of extra-gastrointestinal (GI) symptoms.

Findings: In a population-based study in Sweden, we found that individuals with high baseline anxiety or depression were more likely to seek psychiatric healthcare, but not GI or extra-GI healthcare, in the presence of extra-GI symptoms at baseline.

Implications for Patient Care: Patients with IBS might benefit from more thorough assessments for extra-GI and psychological symptoms to reduce healthcare utilization.

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Online supplementary material

Healthcare utilization variable

Future healthcare utilisation was determined using registry data from the Stockholm County Council over the 12 years (2006-2015). The registry includes almost all physician visits (as well as other professionals), whether as outpatient (primary care general practitioner or specialist) or as in-patient visits (hospitalization), reimbursed by the Stockholm County Council. International Classification of Disease-10 (ICD-10) codes for the consultations were used to group healthcare utilisation in three domains: Gastrointestinal (all codes with the prefix K, denoting a gastrointestinal consultation), Psychiatric (F31.5, F32, F32.1, F32.2, F32.8, F32.9, F33.0, F40.0, F40.1, F40.2, F40.2E, F40.2F, F40.2G, F40.2W, F40.8, F40.9, F41.0, F41.1, F41.2, F41.3, F41.8 and F41.9) and Extra-Gastrointestinal (any code which does not have a K or F prefix, denoting consultations not relating to psychiatric or gastrointestinal disorders). Hence, it is the diagnosis group and not the type of practice that determines if the visit is GI, psychiatric or extra-GI. Healthcare utilization variables were grouped as either an outpatient or inpatient visits depending on the type of practice the diagnosis originated at.

Description of statistical models

All healthcare measures were found to have quite skewed distributions with most people reporting relatively few occasions of care but a small proportion reporting greater utilisation. Regarding other inpatient visits, the shape of the distribution was an overdispersed Poisson distribution, and consistent with a negative binomial distribution and hence negative binomial regression was employed for these. For all other utilisation measures, a significant proportion of the sample had used zero occasions of service and this is not consistent with a single skewed distribution. For these measures, zero-inflated negative binomial regression was employed. In two cases (both containing the outpatient GI variable) it was necessary to truncate the extreme upper tail of the utilisation distribution due to difficulties with numerical estimation. This was manually done by constraining consultations to a maximum of 10 visits.

Using the appropriate model (negative binomial or zero-inflated negative binomial), moderation of extra-GI score on the association between a psychological predictor (anxiety or depression) and a healthcare utilisation outcome, based on the statistical interaction between psychological predictor and extra-GI score was evaluated. Moderation findings are presented as interaction incidence rate ratios (IRR), standard error and p-value based on the score test which follows a standard normal distribution. This was conducted separately within the IBS and non-IBS subgroups to qualitatively describe any group differences and to determine how specific any moderation identified was to IBS individuals.

Results are presented as regression and binary Incidence Rate Ratios (IRR), standard errors and p-values. The IRR were determined via a Z statistic and the criteria for statistical significance level for these analyses was set at 0.05 (two-tailed). A positive regression IRR value indicates that, conditional upon there being some consultations, increased counts of healthcare utilisation were related with increasing anxiety or depression. Regarding a positive binary IRR, this measures the increase in odds of consultations occurring or not, with

increasing anxiety or depression. For ease of interpretations of IRRs, the extra-GI score was

divided by five.

Comparison of demographic factors between study participants and the Swedish general population

Compared with the Swedish population, the original study population included slightly more women (49% verses 55%) and a slightly higher percentage of individuals who had college or university education (46% verses 57%)[1]. There were no significant differences between the age or number of people living in the household with the Swedish population. Of the responders to the initial mail out and those who attended the hospital visit, hospital participants were slightly older (mean = 49, range 18-70 years verses mean = 46, range 18-70 years). There were no differences between groups in education level, number of persons living at home or mean healthcare visits. Further, the level of anxiety and depression measured through the HADS is similar to previously reported data from the general Swedish population[2].

References

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2. Lisspers J, Nygren A, Söderman E. Hospital Anxiety and Depression Scale (HAD): some psychometric data for a Swedish sample. *Acta Psychiatrica Scandinavica.* 1997;96(4):281-286.