PERFORMANCE OF AN ALGORITHM-BASED APPROACH TO THE DIAGNOSIS AND MANAGEMENT OF FUNCTIONAL GASTROINTESTINAL DISORDERS: A PILOT TRIAL

RUNNING HEAD: PERFORMANCE OF ADAM-FGID

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ABSTRACT

Background

Recent advances in the development of diagnostic criteria and effective management options for functional gastrointestinal disorders (FGID) have not yet been integrated into clinical practice. There is a clear need for the development and validation of a simple clinical pathway for the diagnosis and management of FGIDs which can be used in primary care.

Methods

In this controlled pilot study, we designed and evaluated a non-specialist-dependent, algorithm-based approach for the diagnosis and management of FGIDs (ADAM-FGID). Patients referred to one tertiary referral centre with clinically suspected functional gastrointestinal disorders were allocated to waitlist control or algorithm group. The algorithm group was screened for organic disease, and those without clinical alarms received a written FGID diagnosis and management options. All participants were followed up for 1 year.

Key Results

The ADAM-FGID was found to be feasible and acceptable to both patients and primary healthcare providers. The diagnostic component identified that 39% of referrals required more urgent gastroenterological review than original triage category, with organic disease subsequently diagnosed in 31% of these. The majority of patients (82%) diagnosed with a FGID did not receive a relevant alternative diagnosis during follow-up. Patient buy-in to the model was good, with all reading the diagnostic/management letter, 80% entering management, 61% reporting symptom improvement at 6 weeks. Moreover, 68% of patients, and all referring doctors found the approach to be at least moderately acceptable. Patients reported being reassured by the approach, and found the management options useful. Primary health care providers acknowledged the potential of this approach to reduce waiting times for endoscopic procedures and to provide reassurance to both patients and themselves.

Conclusions & Inferences

This pilot study provides preliminary evidence to support a clinical pathway for the diagnosis and management of FGIDs which does not depend upon specialist review. Further rigorous testing within primary care is needed to conclusively establish safety and efficacy. However, this approach is safer than current management and has potential to build capacity by reducing specialist burden and expediting effective care.

Keywords diagnosis, IBS, FGID, Functional gastrointestinal disorders, management, primary care

Key Points

- The referral burden for functional gastrointestinal disorders exceeds resource capacity within many public health institutions, resulting in poor patient outcomes.

The transfer of recent advances in the development of diagnostic criteria and effective management options for functional gastrointestinal disorders into a simple clinical pathway which can be used in primary care, may lead to improved patient care and healthcare resource prioritisation and reduce patient/provider costs.

We designed and trialled an algorithm-based approach for the diagnosis and management of FGIDs. The algorithm-based approach was feasible and acceptable to the majority of patients and referring primary healthcare providers. The screening component enabled the earlier detection and management of organic disease.Functional gastrointestinal disorders (FGIDs) such as irritable bowel syndrome (IBS) and functional dyspepsia (FD) represent a growing burden to healthcare systems around the world [1, 2]. In the past, therapeutic nihilism and frustration expressed by both patients with FGIDs and doctors were prevalent [3, 4]. The recent advent of reliable, accepted diagnostic criteria [5, 6] and effective evidence-based management options have potential to transform the FGID landscape [7-9]. However, clinical practice has not widely adopted these advances: consensus-based diagnostic criteria are not widely used [5, 6, 10] and many primary care providers lack confidence in diagnosing and managing FGIDs, and refer to specialty care [11-13]. The use of unclear diagnostic language and over-investigation in both primary and specialist care are common, as is continued healthcare utilisation in pursuit of a more “acceptable” diagnosis [14-16]. Although newer, effective management options such as the low FODMAP diet, gut-directed hypnotherapy and cognitive behavioural therapy are available, they are not generally used [7-9].

Few models of care for FGID have been evaluated and the need for the development and validation of a simple clinical pathway for the diagnosis and management of FGIDs is evident [17]. Consensus among gastroenterologists is that, in the absence of alarm features and with negative faecal and blood tests, other tests are rarely warranted to diagnose FGIDs [18, 19], and an early, clear diagnosis may mitigate much of the frustration, healthcare utilisation and over-investigation [14]. Thus, to be most effective, a clinical pathway for FGID should incorporate a diagnostic algorithm to successfully move patients from a diagnostic search to an effective management strategy.

In order to integrate new knowledge into practice and to facilitate the provision of effective healthcare to this large patient group, we designed and piloted a non-specialist-dependent, algorithm-based approach for the diagnosis and management of FGIDs (ADAM-FGID) [20]. Our objectives were to evaluate the safety, feasibility, and acceptability of the ADAM-FGID.

METHODS

Recruitment and randomisation

All patients (18-75 y) referred to one gastroenterology outpatient department over a 2-year period (June 2013-July 2015) in a tertiary referral centre (metropolitan city of 1.3 million people), triaged as ‘likely FGID’ were invited. Patients with chronic or recurrent epigastric/abdominal pain with or without altered bowel habit, bloating, nausea and vomiting, and without red flags were included. Referrals indicating predominant reflux symptoms, evidence of current *H. pylori* infection, positive faecal occult blood test or recent symptom onset (<6 months) were excluded. Other exclusions were poor English communication, serious mental health issues and pregnancy. Prior to invitation, patients were randomised to the algorithm or control group in a ratio of 2:1 sequentially in date order of referral. Participants were blinded to the existence of the other group, as knowledge of the algorithm group by controls was deemed likely to introduce bias. Investigators were not blinded to the allocation. (ACTRN12614000602628).

Procedure

Patients were invited by a group-specific letter, and provided demographics and baseline measures at intake. The algorithm group underwent a structured screening process for organic disease with a medical history/red flag questionnaire and blood/stool tests (Supplementary Table 1). Abnormal results were reviewed by a gastroenterologist and, if appropriate, prompt specialist review offered. Participants without alarms were classified using Rome III criteria, and a letter outlining their FGID diagnosis and evidence-based management strategies and resources, was sent to patients and primary healthcare providers (PHCPs). A low FODMAP food list (21) and self-help psychological resource adapted from a previously evaluated booklet (22) were included. Participants were surveyed and outcomes measured 6 weeks, 6 months and 1 year after intake/diagnosis. The referring PHCPs of the algorithm participants were surveyed at intake and completion to assess the acceptability of the approach to them and the rate of alternative diagnoses in the FGID-diagnosed group at follow-up. Patients who received gastroenterologist review also provided feedback, and non-respondents were contacted to ascertain reasons.

Measures

Patient satisfaction with symptoms was the primary outcome, measured on a 10-point scale: 1, not at all satisfied - to 10, completely satisfied. Secondary outcomes included *symptom severity* (Gastrointestinal Symptom Rating Scale) (23), *mental health* (Visceral Sensitivity Index) (24), Hospital Anxiety and Depression Scale (25), and Depression, Anxiety and Stress Scale (26), GI Cognitions (27), *quality of life* (World Health Organisation Quality of Life questionnaire) (28), and *impact on productivity* (Workplace Absenteeism and Presenteeism Index) (29). Acceptability of the approach was measured on a 4-point Likert scale ranging from 'not at all acceptable', to 'acceptable', and symptom improvement on a 5-point Likert scale from 'no improvement' to 'good improvement in most symptoms'. Open response questions included:

1) How useful was the diagnostic letter, and why?

2) Did you discuss the letter with your referring doctor? If not, why not?

3) What management options were tried, and what were the main reasons for this decision?

Participants also identified resources used to access management options.

Ethical considerations

This study was approved by the Royal Adelaide Hospital Research Ethics Committee. Participants received both verbal and written information about the project and provided informed consent. Both groups were advised that non-participation would not affect their position on the waitlist or subsequent care, and the algorithm group were advised they may be offered an earlier appointment if their test results were abnormal.

Data analysis

Data were analysed using SPSS 24 and R version 3.3.3. Descriptive statistics of baseline demographics, Rome III diagnoses and acceptability to patients and PHCPs are provided as means (standard deviations), medians (inter-quartile range), frequencies and percentages, as appropriate. Groups were compared using the chi-square test and student t-test. Qualitative analysis of patient and PHCP feedback is also provided descriptively. Reasons for missing data were obtained. The effect of the intervention was assessed using mixed-effects logistic regressions. Two models were constructed per outcome assessing the mean difference post-baseline, and the difference in change-over- time between intervention and control groups. Age, gender, wait-list duration and symptom duration were adjusted for as fixed effects, and random intercepts were included per individual. In the mean-difference models baseline response was included as a fixed effect, while in the change-over-time baseline response was included as an outcome. No attempt was made to account for biases due to differences in consent and attrition. Due to the large number of secondary outcomes significance was set at 0.01.

RESULTS

Sample Description

Of the 583 non-urgent referrals, 445 were deemed 'likely FGID', and 307 of these fulfilled inclusion criteria (66% female). Of 211 patients allocated to the algorithm group, 123 consented, 100 completed baseline questionnaires, and 89 completed screening (aged 42 years [SD 15], 62% female) (Figure 1). Of 104 control group patients, 31 consented and 20 completed intake. Non-responders and responders were comparable in age (p=.533), gender (p=.105) and time on waitlist (p=.346). The algorithm and control groups were comparable in age, gender and social demographics. However, the average time on the waitlist was greater for controls (196 days [SD 126] vs 141 days, [SD 106], p=.043), and 55% of the control group had seen a gastroenterologist previously (vs 30% algorithm, p=.036) (Table 1).

Safety of the algorithm-based screening

Of the 89 algorithm patients screened, 35 (39%) had alarms elicited by structured screening and had prompt gastroenterologist (GE) review, in the other 54 (61%), there were no alarms and most (n=45) were diagnosed with a FGID (Figure 1). The number of FGIDs per patient ranged from 1-8 with a median of 3 [IQR 1, 4]; (upper FGID, 7; lower FGID, 11; both upper and lower FGID, 27). Nine patients were excluded with no alarms, non-specific gastrointestinal symptoms but insufficient Rome III criteria to make a FGID diagnosis, leaving a final study sample of n=80 (45 FGID, 35 GE reviewed).

In the 35 participants with alarms, organic disease was subsequently diagnosed in 11 and FGID in 18, with 4 having a FGID and an additional clinically significant finding. In this group, there was a clear discrepancy between the number and type of alarm symptoms mentioned by PHCPs and patients: alarms not mentioned (n=26) or declared absent (n=3) by PHCPs, but reported by 32/35 patients (Table 2).

At study completion (mean 2.7 [SD 0.5] yrs. post-referral), none of the 45 patients diagnosed with FGID had received a gastroenterology consult based on the original referral and most (37/45, 82%) had received no alternative diagnosis (four no longer contactable). Two had additional diagnoses (FGID plus diverticulitis/prostatitis) and two had incidental, clinically significant findings (FGID plus benign adenomatous/sessile GI polyps).

Of those participants not providing formal 12-month follow up, 2 did not accept the FGID diagnosis and 3 consulted a specialist privately. Other reasons for non-response include symptom resolution (n=1), significant other illness (n=1), loss of interest (n=2), loss of contact (n=6). Patient drop-out in the FGID-algorithm group appeared to be unrelated to the level of symptomatic improvement [$\chi^2(3, n=35) = 5.140, p=.162$] or to their confidence in or acceptance of the diagnosis [$\chi^2(1, n=36) = 2.043, p=.219$] 6 weeks after diagnosis.

Feasibility of the Approach

Six-week qualitative feedback was obtained from 36/45 patients diagnosed with FGID by the algorithm (34 completed full questionnaire, 2 completed short phone survey). Responders and non-responders were comparable in age, gender, employment/relationship status and primary language (all p>.05). Tertiary educated participants responded more commonly than those without this level of education (86% vs 64%, p=.032). Non-response reasons included disagreement with the diagnosis/desire to see a specialist (n=2), lack of time (n=1), psychiatric inpatient (n=1), symptom resolution (n=1) and lost contact (n=4).

All but one had read the letter and the majority of respondents (25/36) found it useful (17 useful, 8 partially useful; Supplementary Table 2). Common reasons for usefulness included; receiving management options (n=12), being reassured by the diagnosis (n=7), receiving a diagnosis (n=5). Reasons for non-usefulness included; lack of confidence in diagnosis (n=1), individual case had not been thoroughly considered (n=2), and non-acceptance of diagnosis (n=1). Only 9 patients (25%) discussed the letter with their PHCP by 6 weeks and 13 (36%) by 12 months.

Almost 80% (26/36) of respondents actively engaged in management of their symptoms by 6 weeks (Figure 2). Dietary management options were used almost twice as often as psychological therapies (p=.001) and most tried a combined approach. Participants reported greater acceptance of the link between diet and symptoms, and reported it to be a realistic, manageable and affordable option (Supplementary Table 3). Time, cost and lack of perceived relevance or acceptance of psychological therapies were the main reasons cited for lack of its uptake. Do-it-yourself options were preferred (Figure 2). Even when using psychological management options, some respondents (n=5) did not identify them as such.

Whilst the pilot was not powered for efficacy, symptomatic improvement was reported in 61% (22/36) of 6-week respondents and 86% (18/21) 12-month respondents (Figure 2). A significant beneficial intervention effect over time compared with controls was found for constipation (p=.001) and reflux (p=.01) symptoms, but not for overall patient satisfaction with symptoms or total abdominal symptoms (Supplementary Table 4). A significant intervention effect was not seen for psychological factors of anxiety, depression, stress, gastrointestinal cognitions or quality of life. However, gastrointestinal-related anxiety was increased in the intervention group (p=.04). Improvements in symptom satisfaction (0.04, 95% CI [0.014, 0.066], p=0.003), and indigestion (-0.015, 95% CI [-0.024, -0.006], p=0.001) were seen within the algorithm group compared to their baseline, but ratings were not statistically different to controls.

Acceptability of the Approach

The approach was at least moderately acceptable to 68% (54/80) of patients (Figure 7-2). Of those providing free text responses (n=31) the screening process was rated as relevant/efficient (n=7) and better than a long waiting list (n=5). It reassured the FGID diagnosis group (n=4), provided helpful options for managing their symptoms (n=5), and expedited gastroenterologist review for those with alarms (n=10). Three in the screen-fail group felt cared for with their concerns addressed (n=3) and two liked the ease of the whole approach. Those who found the approach unacceptable or only slightly acceptable expressed dissatisfaction with the healthcare system (n=4) or the FGID diagnosis (n=3), irrelevance of screening questionnaire (n=1) and lack of improvement in symptoms (n=1) (Supplementary Table 5). Only two participants in the screen-fail group found it 'not at all acceptable'; one of these had relocated, missed their endoscopy and was discharged from the system, and another discovered the symptoms were related to taking the wrong medication.

Overall, 60/89 referring PHCPs responded to the intake survey (36 males; 42 aged>40 y, 50 aged ≥ 60 y; clinical experience, 39 >10 y, 23 >20 y). Most (47/60) found the ADAM-FGID to be at least moderately acceptable and did not report any concerns (Figure 2). Those raising concerns cited fear of missed pathology (n=4; leading to litigation n=2) and patient expectation/satisfaction (n=3). At completion, all responding PHCPs found the approach at least moderately acceptable (11-acceptable, 12-moderately acceptable; 23/80 respondents, 18 males, 19 aged>40 years, 17 in practice >10 years; 14 FGID group, 9 screen-fail group), with acceptability unrelated to whether their patient saw a specialist or received a diagnostic letter (p=.507). PHCPs opined that this approach was likely to reduce waiting lists and colonoscopies, and provided reassurance for PHCPs and patients (Supplementary Table 5). Fear of missed pathology or litigation was not raised in the follow-up surveys, although duplication of tests already performed and patient insistence on further investigation were mentioned.

DISCUSSION

This paper provides the first data on a non-specialist-dependent pathway for the global diagnosis, screening and management of people with FGID. The ADAM-FGID facilitated the provision of a timely, accurate diagnosis and evidence-based management options without gastroenterologist consultation. This pathway has been shown to be feasible to implement, and acceptable to both patients and their referring doctors.

In the local context of this tertiary referral system, in a country with a well-developed healthcare system, this algorithm-based screening approach proved safer than current practice. It facilitated the earlier detection and management of organic disease. Currently referrals with no declared alarms, for clinically suspected FGIDs are triaged as non-urgent and patients are placed on long waiting lists (>2 yrs., with many not being seen). This pilot study identified that one third of those triaged as non-urgent warranted more urgent gastroenterology review, and would have received such if this screening had occurred in primary care and was declared on referral..These pilot data are encouraging, and justify a further larger scale evaluation, with potentially even greater gains within less developed healthcare systems.

Strengths of the Approach

a) Good patient and PHCP buy-in

The results demonstrate the feasibility of a non-specialist-dependent approach conducted via mail/online surveys. Patient buy-in was high, with only one participant finding it too difficult to complete screening. The approach was also well received by PHCPs. Reasons for positive feedback included acknowledgment of the likely outcomes of reduction in both wait list time and unnecessary investigations, along with the value of the written material as an educational resource and a basis for further discussions, which is likely to lead to further capability building via PHCP education and confidence building. No major concerns with the approach were identified by referring clinicians, other than the potential for duplication of tests already performed within primary care, which could be avoided if the approach were embedded in primary care prior to a referral being made.

b) Facilitation of diagnosis

The starting point for this diagnostic pathway was the PCHP referral letter, which was in general poor, as previously reported (11). Information was insufficient to allow safe triage according to urgency as evidenced by the fact that structured screening found that 2 out of 5 patients warranted more urgent gastroenterologist review with a subsequent diagnosis of organic disease in nearly a third of these. These findings are consistent with those of Moore J.S. (30), where 19% of patients previously diagnosed with IBS attending a nurse-specialist IBS clinic were subsequently found to have organic disease. The use of the screening element of the ADAM-FGID alone would enhance the safety of triage by identifying possible organic disease cases, and greater gains made if this occurred in primary care prior to referral. Using this structured screening approach in tertiary care as a triage mechanism, mandates a considerable time commitment by the gastroenterologist, which could be minimised by using a nurse specialist (31, 32).

c) Acceptance of this diagnostic pathway

Most participants found the pathway acceptable, particularly those in whom clinical alarms were identified and a gastroenterologist consult expedited. Almost every patient with clinical red flags also had abnormal test (blood/stool) results, and thus the opportunity to 'game the system', was minimised. Even amongst those diagnosed with a FGID and not offered specialist review, 62% found the approach acceptable, acknowledging its convenience and efficiency, and went on to engage with the management options. Patients were reassured by the screening process.

Opportunities for Refinement

a) Screening questions

Most patients reported nocturnal symptoms, yet on clarification often indicated symptoms during the night rather than pain waking them from their sleep, or nocturnal diarrhoea. A few participants felt the survey did not fully consider their situation. Examples included patients with recent overseas travel, and those on a (non-coeliac) gluten free diet. One important factor easily noted in person, but overlooked in the survey (often asked in clarification phone calls) was patient height and weight to gauge BMI. Future versions of the structured screening survey should include height, weight, restrictive diets, recent travel, and a modified nocturnal alarm question.

b) Shared care

We had anticipated that the letter would provide a shared resource PHCPs and patients could use to tailor an individualised management approach. However, less than a third of participants discussed their diagnostic/management letter with their referring doctor. The importance of continued PHCP management should not be underestimated. PHCPs play an vital role in empowering patients to manage their own symptoms, particularly in chronic disease management [33] and medically unexplained symptoms such as FGIDs [4]. Furthermore PHCPs play a growing role in interpreting knowledge patients gather from various informal sources, such as peers, social media, and websites [4]. Better patient outcomes may have been seen if the letter explicitly stated the importance of arranging an appointment with their GP as the next step in management.

c) Self-management

The patients clearly showed considerable interest in self-management, particularly via dietary manipulation. It has been previously shown that diet is the primary behavioural factor manipulated by women with IBS [34]. The low FODMAP diet is the only dietary approach with a strong evidence-base, with 50-75% [35-37] of patients obtaining considerable symptomatic relief. However, no trials on self-administered low FODMAP diet have been reported, and self-implementation is not currently recommended [38-40]. Furthermore, a profusion of written and electronic low FODMAP resources have been developed and are publicly available, but the accuracy of such resources has been seriously questioned [41]. Given the strong interest in self-management, further efforts to develop a safe and effective dietary self-management approach are warranted.

d) Acceptance of psychological interventions

There is considerable evidence for the efficacy of some psychological interventions (such as cognitive behavioural therapy and gut-directed hypnotherapy) to effectively reduce IBS symptoms and improve quality of life, within a tertiary referral cohort [9, 42, 43, 44]. Participants in this study generally accepted the link between diet and symptoms but not between psychological health and symptoms. Very few consulted a psychologist, and only two participants opted for gut-directed hypnotherapy. Declared barriers to uptake included time, cost, lack of perceived relevance to symptoms and/or nonacceptance of psychological therapy. A clearer explanation of the ability of psychological therapies to utilise the brain-gut axis to influence gut function may improve uptake of these valuable resources.

Strengths and limitations of the study

There are several potential limitations to the interpretation and generalisability of the results of this study. The study was designed to maximise the potential of having a control comparator group, by randomising to groups prior to invitation. This approach is considered clinically relevant and acceptable, particularly in a pilot study, as people with FGIDs are difficult to recruit due to the chance of being allocated to the control arm [45]. However, the low control group response rate means that we cannot claim successful randomisation. Given the large proportion of non-completers the study was analysed as if it was non-randomized (observational), with no attempt being made to account for biases due to drop-out. Although we did attempt to minimise the effect of attrition by accounting for reasons for drop-out. The small sample size of the control and algorithm groups, is also a potential limitation to generalisability, particularly given the final follow-up sample size. There was also a greater percentage of patients who had previously seen a gastroenterologist for their symptoms, and who had psychological symptoms in the control group, and thus the control group may represent a cohort that is more difficult to treat. A larger size, randomised control trial, with an intent to treat analysis, and imputation of missing data is needed to investigate this model of care further.

Furthermore, this pilot study was conducted within the setting of one local healthcare networkand may not represent other healthcare facilities or systems. However, the controlled, mixed-method design utilising triangulation of data from patient and referring doctor questionnaires, together with quantitative time-series measures enabled a comprehensive assessment of the safety, feasibility, effectiveness and acceptability of this novel model of care within this local healthcare setting. Future trials which assess this model within the primary care setting would be beneficial.

CONCLUSION

We have demonstrated that this novel, comprehensive clinical pathway for the diagnosis and management of FGIDs, which is not dependent upon specialist review is feasible,acceptable and may provide greater safety than the current approach by facilitatingthe earlier detection and management of organic disease. This is important given the size of this patient group and the resultant public health implications. Implementation of this model within primary care would enhance efficiency of care for this large patient group, build capacity, reduce specialist burden (time and cost) and fast-track effective care.

AUTHORSHIP, FUNDING, AND DISCLOSURES

Author Contribution

ECL principal researcher, planning and conducting the study, collecting, analysing, interpreting the data, and writing the manuscript.

AMW assisted in study concept and design, revision of psychological booklet and website, analysis and drafting of manuscript.
PRG assisted in study concept and design, and provided critical revision of the manuscript for important intellectual content
ADV conducted statistical analysis and assisted in interpretation of results and editing of statistical information in the manuscript.
JMA provided conceptual design, review of medical records as required, interpretation of data and critical revision of manuscript.

Conflicts of Interest and Source of Funding

ECL was supported by The University of Adelaide, PhD Scholarship.
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JMA has served as a speaker, a consultant and/or an advisory board member for Abbott, Abbvie, Allergan, Celgene, Ferring, Takeda, MSD, Shire, Janssen, Hospira and Pfizer, and has received research funding from Abbott, Abbvie, Ferring, MSD, Shire,and Janssen.

PRG has served as consultant or advisory board member for AbbVie, Ferring, Janssen, Merck, Nestle Health Science, Danone, Allergan, Pfizer and Takeda. His institution has received speaking honoraria from AbbVie, Janssen, Ferring, Takeda, Fresenius Kabi, Mylan and Pfizer. He has received research grants for investigator-driven studies from AbbVie, Janssen, Falk Pharma, Danone and A2 Milk Company. His Department financially benefits from the sales of a digital application and booklets on the low FODMAP diet. He has published an educational/recipe book on diet.

AMW, ECL and ADV have nothing to declare.

ABBREVIATIONS

FGID	functional gastrointestinal disorder
ADAM-FGID	algorithm-based approach for the diagnosis and management of FGIDs
PHCP	primary healthcare provider

Table 1. Demographic comparison of patients allocated to the algorithm or waitlist control group, and screened patients diagnosed with FGID or requiring GE consult

		Group Allocation		Significance	Result Post Screening		Significance
		Algorithm (n=89)	**Control (n=20)**	***P* (2-tailed)**	**FGID (n=45)**	**GE Reviewed (n=35)**	***P* (2-tailed)**
Clinical Demographics		[mean (SD)]/ n (%)	[mean (SD)]/ n (%)		[mean (SD)]/ n (%)	[mean (SD)]/ n (%)	
Gender	Female	54 (61%)	15 (75%)	.307	30 (67%)	21 (60%)	.538
Age (y)		42 (14)	42 (16)	.923	45 (14)	39 (15)	.108
Time on waitlist (days)		141 (106)	196 (126)	.043	166 (112)	118 (104)	.055
Symptom duration (y)		6.5 (7.9)	6.6 (11.0)	.941	8.2 (9.2)	5.3 (6.6)	.045
Psychological comorbidities		33 (37%)	10 (50%)	.285	17 (38%)	14 (40%)	.840
Prior GE consult	Seen previously	27 (30%)	11 (55%)	.036	16 (36%)	10 (29%)	.508
		Group Allocation		Significance	Result Post Screening		Significance
		Algorithm (n=89)	**Control (n=20)**	***P* (2-tailed)**	**FGID (n=45)**	**GE Reviewed (n=35)**	***P* (2-tailed)**
Clinical Demographics		[mean (SD)]/ n (%)	[mean (SD)]/ n (%)		[mean (SD)]/ n (%)	[mean (SD)]/ n (%)	
Last specialist visit	< 2 years	9 (10%)	4 (20%)		2 (4%)	6 (17%)	

GE=gastroenterologist

Table 2. Screening results and final diagnosis of FGID and GE consult groups.

Patient Reported Alarm Symptoms (n)			Abnormal Test Results (n)			Final Diagnosis (n)	
	FGID Group (n=45)	GE Reviewed Group (n=35)		FGID Group (n=45)	GE Reviewed Group (n=35)	FGID Group (n=45)	GE Reviewed Group (n=35)
Alarms present (any)	40	32	Abnormal Tests (any)	24	31	Functional (37)	Functional (18)
Nocturnal Symptoms	35	25	Blood Tests				
PR Bleeding	7	13	Iron Deficiency	3	13	Functional and additional (2)	Functional and Incidental (5)
Unexplained fever	4	11	*H. pylori*	10	4	FGID/diverticulitis (1)	FGID/polyps (2)
Weight Loss	6	10	Complete blood exam	5	4	FGID/prostatitis (1)	FGID/dietary iron deficiency (2)
FHx IBD	3	9	Coeliac serology	1	3		FGID plus reflux oesophagitis (1)
FHx CRC	1	4	C-reactive protein	2	3	Functional and Incidental (2)	Organic (6)
New onset	1	3	Thyroid function tests	0	3	FGID/benign adenomatous polyps (1)	Inflammatory bowel disease (2)
Haematemesis	2	1	Biochemistry	11	2	FGID/sessile polyps (1)	Neoplasm (1)
FHx Coeliac	0	1	Stool Tests				Pancreatic insufficiency (1)
			Faecal elastase	0	7	Non-contactable (4)	Reflux oesophagitis (1)
			Faecal calprotectin >100µg/g	0	7		Iron deficiency – no GI cause (1)
			Faecal calprotectin 50-100µg/g	0	7		Patient did not attend (6)

FHx=Family history; IBD=inflammatory bowel disease; CRC= colorectal cancer; FGID=functional gastrointestinal disorder

Supplementary Table 1. Screening for organic disease in patients in the algorithm group.

Screening for alarm symptoms (patient survey)	Screening Tests Performed
New onset symptoms (within 6 months) if age > 50 y	Complete blood exam: (screening for clues to other disease)
Unexplained weight loss (> 3 kg or 5% body weight)	C-reactive protein: exclude infectious or inflammatory disease
Iron deficiency ± anaemia	Iron studies: exclude iron deficiency
Haematemesis	Serum biochemistry: liver and renal function, calcium (screening for clues to other disease)
Melena, faecal occult blood, overt rectal bleeding	Coeliac serology: exclude coeliac disease
Abdominal pain awaking patient from sleep	Thyroid function tests: exclude thyroid dysfunction as reason for motility abnormality
Nocturnal diarrhoea/faecal incontinence	*H. pylori* serology (upper GI symptoms): exclude peptic ulcer
Unexplained fever	Faecal calprotectin (lower GI symptoms): exclude inflammatory bowel disease
Family history of colon cancer (1 FDR* <60, or > 1 FDR any age)	Faecal elastase (upper abdominal pain, diarrhoea): exclude pancreatic exocrine insufficiency.
Family history of IBD in symptomatic patient (1 FDR)	
Family history of coeliac disease in symptomatic patient (1 FDR)	

FDR=first degree relative, IBD=inflammatory bowel disease

Supplementary Table 2. Patients' feedback on the usefulness of the letter outlining the screening results, diagnosis and management options.

Usefulness of the letter	(n)/36	Example of Response
Useful	17	*"It was good to know what was wrong with me and that there were options for managing it".*
		"Stopped me worrying it was something serious".
		"It has help to reduce my stress level… I am able to manage my health problem better and is feeling much better".
		"Now know that the condition is manageable and have options as to the management of the conditions".
Partially useful	8	*"Confirmed possible diagnosis. But would prefer to have a colonoscopy to double check all is ok"*
		"At least I know what is causing the pain, I just need some sort of medication for the pain. I just don't know why it took so long to diagnose"
Uncertain	3	*"Not sure, I do not know whether the diagnosis is correct, there can be something else going on".*
		"I've unfortunately not had the chance to look at it yet, nor do I know where it is".
Not useful	8	*"I did not find the letter and diagnosis useful, I felt that my case had not been thoroughly considered and that that I had many questions left unanswered".*
		"No. All my problems were not included or asked about, fat malabsorption or floaty stool, lactose intolerance…"
		"Not really useful. Confirmed what I already knew re dietary restrictions e.g. FODMAP"
		"I know it was meant to be reassuring that there is nothing sinister, but without definite proof I find it hard to relax"

Supplementary Table 3. Factors influencing the management option decision of participants

The Low FODMAP Diet		Psychological Therapies	
Reasons FOR trying	**(n)**	**Reasons FOR trying**	**(n)**
Realistic/manageable	8	Perceived benefit/ more chance of success	3
Link between food and symptoms evident	6	Link between stressors and symptoms evident	1
Open to trying it	5	Recommended by clinician	1
Natural/ not harmful	3	Trying everything	2
Currently using dietary restrictions	3		
Cheaper	2		
Recommended by clinician	2		
Shown to be effective	2		
Participating in psychotherapy already	1		
Reasons AGAINST trying	**(n)**	**Reasons AGAINST trying**	**(n)**
Low FODMAP diet too complicated	1	Lack of time	6
Further dietary restrictions not possible	1	Not relevant for me	4
		Lack of money	3
		Dietary treatment is working	3
		Disagree/not comfortable with 'psychology'	2
		Laziness	1
		Previously tried and ineffective	1
		"Over it"	1
		Symptoms aren't bad enough	1

Supplementary Table 4. Statistical analysis of intervention effect compared with controls using mixed model logistic regression

Outcome	Baseline difference [95%CI]	p	Mean Effect [95%CI]	p	Change [95%CI]	p
Primary Outcome						
Satisfaction with symptoms	-0.32 [-1.6, 0.96]	0.62	0.57 [-0.88, 2]	0.44	0.03 [-0.01, 0.07]	0.18
Symptom Measures						
Diarrhoea (GSRS)	0.18 [-0.64, 0.99]	0.66	-0.21 [-0.9, 0.49]	0.56	-0.01 [-0.03, 0.01]	0.48
Indigestion (GSRS)	-0.013 [-0.69, 0.66]	0.97	-0.65 [-1.2, -0.08]	0.03	-0.01 [-0.02, 0.01]	0.27
Constipation (GSRS)	0.33 [-0.42, 1.1]	0.38	-0.64 [-1.3, -0.01]	0.05	-0.03 [-0.05, -0.01]	0.001
Abdominal Pain (GSRS)	-0.56 [-1.2, 0.12]	0.11	-0.42 [-0.9, 0.06]	0.09	-0.01 [-0.02, 0.01]	0.85
Reflux (GSRS)	0.25 [-0.44, 0.95]	0.47	-0.73 [-1.4, -0.06]	0.04	-0.02 [-0.04, -0.00]	0.01
Total Score (GSRS)	-0.24 [-0.88, 0.4]	0.45	-0.56 [-1.1, -0.06]	0.03	-0.01 [-0.02, 0.00]	0.15
Psychological Measures						
Depression (DASS)	-2.5 [-5.2, 0.21]	0.07	-0.38 [-2.1, 1.3]	0.66	0.03 [-0.02, 0.08]	0.19
Anxiety (DASS)	-2 [-3.9, -0.11]	0.04	-1.1 [-2.6, 0.37]	0.14	0.02 [-0.02, 0.05]	0.4
Stress (DASS)	-2.8 [-5.4, -0.29]	0.03	-0.77 [-2.7, 1.2]	0.44	0.05 [0.00, 0.10]	0.03
Depression (HADS)	-1.4 [-3.8, 0.98]	0.24	-0.13 [-1.7, 1.5]	0.87	0.02 [-0.02, 0.05]	0.27
Anxiety (HADS)	0.02 [-0.02, 0.05]	0.27	-1.1 [-3, 0.76]	0.24	0.01 [-0.03, 0.05]	0.68
GI symptom-specific anxiety	9.4 [-0.93, 20]	0.07	11 [2.5, 20]	0.01	0.2 [0.01, 0.4]	0.04
Pain life interference	-0.34 [-0.89, 0.21]	0.22	-0.2 [-0.57, 0.18]	0.3	-0.00 [-0.01, 0.01]	0.58

Outcome	Baseline difference [95%CI]	p	Mean Effect [95%CI]	p	Change [95%CI]	p
Psychological Measures (cont.)						
Social anxiety	-0.18 [-0.75, 0.4]	0.54	-0.27 [-0.67, 0.13]	0.19	-0.01 [-0.29, 0.00]	0.10
Disgust sensitivity	0.08 [-0.57, 0.72]	0.82	-0.27 [-0.74, 0.19]	0.24	-0.00 [-0.02, 0.01]	0.6
Daily Functioning Measures						
Physical health (WHO-QoL)	1.6 [-0.11, 3.4]	0.07	0.05 [-1.1, 1.2]	0.92	0.01 [-0.02, 0.03]	0.64
Psychological health (WHO-QoL)	1.6 [-0.02, 3.2]	0.05	-0.29 [-1.3, 0.69]	0.56	-0.03 [-0.06, -0.01]	0.01
Social relationships (WHO-QoL)	0.99 [-0.81, 2.8]	0.28	-0.68 [-1.9, 0.5]	0.26	-0.00 [-0.04, 0.03]	0.83
Environment (WHO-QoL)	0.24 [-1.1, 1.6]	0.72	1.6 [0.56, 2.7]	0.004	0.06 [0.04, 0.09]	<0.001
Percent worktime missed	-8.5 [-19, 1.9]	0.11	-3.3 [-13, 6.3]	0.50	0.19 [-0.13, 0.51]	0.24
Percent impairment while working	-31 [-46, -15]	0.0003	-0.49 [-24, 23]	0.97	0.65 [0.18, 1.1]	0.01
Percent overall work impairment	-38 [-55, -22]	<0.001	9.5 [-17, 36]	0.48	0.62 [0.18, 1.1]	0.01
Percent activity impairment	-8.6 [-21, 4.1]	0.18	-12 [-26, 1.2]	0.07	-0.12 [-0.53, 0.28]	0.55

Mean effect = is the difference between groups of the average post-intervention scores (6w, 26w and 52w) adjusting for baseline differences.

Change =differences in change over time by group. Clinical significance where change and mean effect significant.

Supplementary Table 5. Acceptability of the algorithm-based approach to the diagnosis and management of FGIDs to patient and PHCPs

EXAMPLES OF PATIENT ACCEPTABILITY RESPONSES
Acceptable
“I found this study to be great, as I haven’t had to go to any appointments” (Female, 47 y FGID group)
“This approach can pick up if anything is seriously wrong before a specialist/hospital and offer some alternative solutions. However, should not replace a specialist visit or treatment; In my circumstances, the heath management plan and the dietitians support have completely kept me symptom free” (Female, 56 y FGID group)
“GP tells you it’s a long (wait) list, and this creates fear and worry because you don't know what's wrong. The letter and tests help you find out quickly if there’s anything seriously wrong” (Female, 27 y FGID group)
“Quicker, useful. Good idea if it helps pick up people who need to be seen quicker or to get help to people rather than just sitting on a waiting list” (Female, 44 y FGID group)
“It was great to be able to skip the line, but also to do the surveys in my own time” (Female, 32 y FGID group)
“It's assisted in dealing with current issues and pains. Has helped a lot considering how much pain I was in compared to now”. (Female, 32 y FGID group)
“I wish I had this information 20 years ago. Better than nothing” (Male, 65 y FGID group)
“It showed that somebody paid attention. I felt well looked after. I like the smoothness the process and professionalism of the people”. (Female, 40 years old, iron deficiency and functional pain, screen-fail group)
“My feeling is that when one is worried about their health and full of questions and concerns, each passing week feels like an eternity. It was reassuring for me to know what was happening with me and what I needed to be doing about my dietary habits. Although I was given the all-clear, if I had had an issue, waiting a year or more could have resulted in me doing further damage to my gastrointestinal system by not having timely intervention”. (Female, 39 years old, IBS, screen-fail group)

EXAMPLES OF PATIENT ACCEPTABILITY RESPONSES
Moderately acceptable
“There is something wrong and I feel we haven't really got to the bottom of it”. (Female, 68 y FGID group)
“All recommendations are good suggestions, I've learn to tried new methods at home to reduced my symptoms while waiting to see the specialist”. (Female, 21 y FGID group)
Slightly acceptable
“Useful to have symptoms confirmed and to motivate regarding diet”. (Female, 70 y FGID group)
“It’s good to know how long the waiting list is, and get tested for serious things while you wait. But I wasn’t reassured and wanted the endoscopy and colonoscopy for peace of mind re bowel cancer”. (Female, 38 y FGID group)
“This is absolutely outrageous!!!!! Makes Australia feel like a 3rd world country, appalling!!” (Female, 51 y FGID group)
Not at all acceptable
“If <politician named> had suffered what I and many other people have no doubt suffered I am sure a solution would be hastily arranged for him to gain treatment. Need I say more”. (Male, 60 y FGID group)
I've simply been template matched. I grew up with familial Mediterranean fever, but there hasn't been a multiple-choice option for that, so it can't be figured into the algorithm, because I'm a human, not a computer program. Template matching doesn't work, there is a far greater history to learn. If only there was some kind of specialist in this field that could help me. (Male, 39 y FGID group)

EXAMPLES OF PRIMARY HEALTHCARE PROVIDER ACCEPTABILITY RESPONSES
Acceptable
“Hopefully it will help reduce waiting lists” “I think it is very useful. Perhaps some funding for nurse to do questionnaire?”
“Likely to lead to a reduction in unnecessary colonoscopies.” “The screening and educational components were useful”
“Able to get second opinion promptly.” “A great idea”
“Patient seemed happy with the service she was provided”
“Shorter wait time for urgent non-functional disease referrals”
Moderately Acceptable
“The general approach is OK-but these are things I do already” “Provided a good summary/talking points”
“Prevents unnecessary investigation”. “Had FODMAP diet – good”
“More timely assessment by specialist clinic rather than being placed on an indefinite waiting list” “In a lot of cases doing all those investigations is doubling up on what has already been done”.
“Some patients insist on being investigated and do not accept a functional diagnosis”.
“Patient and GP reassured that specialist assessment has occurred and further tests are being performed. GP will need to monitor patients’ progress and be able to refer back to specialist clinic if symptoms persist”.
“Reduces unnecessary tests”

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