Issues in the Diagnosis and Management of Functional Gastrointestinal Disorders: The Development of a Novel Clinical Pathway

By

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TABLE OF CONTENTS

LIST OF FIGURES AND TABLES

ABSTRACT

Introduction

Functional gastrointestinal disorders (FGIDs) affect one in four people during their lifetime and are a growing public health concern. These disorders are characterised by distressing, chronic recurring symptoms that reduce quality of life, and negatively impact patients physically, psychologically, socially and economically. Although largely managed in primary care, referrals for specialist care represent up to 50% of ambulatory gastroenterology care. New developments in diagnostic criteria and effective management options are available but under-utilised.

Aims

The aims of this study were to 1) determine current issues in the diagnosis and management of FGIDs in primary and tertiary care; 2) explore tested models of care for FGID; and 3) design and evaluate an algorithm-based approach to the diagnosis and management of FGIDs (ADAM-FGID).

Methods

A cross sectional, mixed-methods study was undertaken based on referrals (July 2013-15) to one gastroenterology outpatient department triaged as 'likely FGID'. Patient characteristics, concerns and satisfaction with care, and reasons for referral were explored. The clinical approach to FGID diagnosis and management in tertiary care was assessed via audits of specialist correspondence and endoscopic procedures. A systematic review of FGID models of care was performed and a novel algorithm-based approach to the diagnosis and management of FGIDs was developed and trialled.

Results

There was a clear paucity of research into models of care for FGID, with only 6 low-quality studies. Primary healthcare providers (PHCPs) referring to tertiary care lacked confidence in the diagnosis and management of FGIDs, and patients expressed dissatisfaction with the lack of provision of a diagnosis or effective management options. Within tertiary care, unclear diagnostic language was more prevalent in FGIDs than organic disorders (63% vs. 13%; $p<.001$), as were endoscopic investigations (79% vs. 63%; $p<.05$). Almost 80% of all patients diagnosed with FGID were found to have undergone upper gastrointestinal endoscopy (UGIE) or colonoscopy. Existing endoscopic appropriateness criteria were inadequate in their consideration of functional symptoms, and preliminary evidence

showed locally developed alarm-based appropriateness criteria to have better negative predictive value.

The ADAM-FGID was found to be both safe and effective. 39% of referrals required more urgent gastroenterological review than original triage category, with organic disease subsequently diagnosed in 31% of these. 82% of FGID diagnoses were stable during follow-up. Patient buy-in to the model was good, with 80% entering management and 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.

Conclusion

FGIDs are poorly handled in the public health system and little research into effective models of care has been conducted. This study identifies multiple issues and opportunities to improve patient care and strategies to achieve these improvements are presented. The clinical pathway for the diagnosis and management of FGIDs, which is not dependent upon specialist review, is safe, feasible and acceptable and has potential to capacity build by reducing specialist burden and expediting effective care.

DECLARATION

I certify that this work contains no material which has been accepted for the award of any other degree or diploma in my name, 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. In addition, I certify that no part of this work will, in the future, be used in a submission in my name, for any other degree or diploma in any university or other tertiary institution without the prior approval of the University of Adelaide and where applicable, any partner institution responsible for the joint-award of this degree. I give consent to this copy of my thesis when deposited in the University Library, being made available for loan and photocopying, subject to the provisions of the Copyright Act 1968. I acknowledge that copyright of published works contained within this thesis resides with the copyright holder(s) of those works. I also give permission for the digital version of my thesis to be made available on the web, via the University's digital research repository, the Library Search and also through web search engines, unless permission has been granted by the University to restrict access for a period of time.

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CONFERENCE PRESENTATIONS

The following are published abstracts from national and international conferences that have arisen thus far from the work leading to this thesis: (conference talk presenter underlined).

Linedale, E.C., Shahzad, M.A., Mikocka-Walus, A.M., Gibson, P.R., Andrews, J.M. Referrals to a tertiary hospital: A clinical snapshot of patients with functional gastrointestinal disorders and effectiveness of primary care management. Poster presentation: United European Gastroenterology Journal, vol. 4, 5_suppl: pp. A484 (P0955), October 16, 2016.

Linedale, E.C., M.A., Mikocka-Walus, A.M., Gibson, P.R., Andrews, J.M. Performance of a novel care pathway for functional gastrointestinal disorders: A pilot study-interim results. Poster presentation: United European Gastroenterology Journal, vol. 4, 5_suppl: pp. A293 (P0395), First Published October 16, 2016.

Linedale, E.C., Mikocka-Walus, A.M., Gibson, P.R., Andrews, J.M. Could a structured screening approach be the answer to the avalanche of functional gastrointestinal disorder referrals? (An interim report). Conference talk presented: AGW 2015, Volume: 30 Suppl. 3 Journal of Gastroenterology and Hepatology p.20

Linedale, E.C., Chur-Hansen, A., Mikocka-Walus, A.M., Gibson, P.R., Andrews, J.M. Diagnostic uncertainty signalled by specialists and ongoing investigations may contribute to patient insecurity in functional gastrointestinal disorders. Conference talk presented: AGW 2015, Volume: 30 Suppl. 3 Journal of Gastroenterology and Hepatology p.19

Shahzad, M.A., **Linedale, E.C.,** Mikocka-Walus, A.M., Gibson, P.R., Andrews, J.M. Gastrointestinal outpatient referral quality: safe to use? Poster presentation: WGO International Congress, Gastroenterological Society of Australia Australian Gastroenterology Week 2015. Journal of Gastroenterology and Hepatology 30(Suppl. 3):21-22 . October 2015.

Rizvi,Q. **Linedale, E.C.,** Mikocka-Walus, A.M., Gibson, P.R., Andrews, J.M. Can we better target colonoscopies using standard "appropriateness" guides? Poster presentation: AGW 2015, Volume: 30 Suppl. 3 Journal of Gastroenterology and Hepatology p.58

Rizvi,Q. **Linedale, E.C**., Mikocka-Walus, A.M., Gibson, P.R., Andrews, J.M. Do Criteria to Judge " Appropriateness " of Endoscopic Procedures Improve Diagnostic Yields or Allow Safe Avoidance of Upper Gastrointestinal Endoscopy? A Retrospective review. Poster presentation: AGW 2015, Volume: 30 Suppl. 3 Journal of Gastroenterology and Hepatology p.58-59

Linedale, E.C., Shahzad, M.A., Mikocka-Walus, A.M., Gibson, P.R., Andrews, J.M. How can we better manage functional gastrointestinal disease? Internal Medicine Journal 46:23, January 2016. Conference talk presented: RACP Congress May 2016, Adelaide, South Australia.

ADDITIONAL PUBLICATIONS ARISING FROM THE PHD RESEARCH

Narrative Review: The Diagnosis and Management of Irritable Bowel Syndrome (IBS) in 2017 – a guide for the generalist. Linedale, E.C. & Andrews, J.M. (Invited Review: Medical Journal of Australia, Under Review, 14th May 2017) Appendix H

Linedale, E.C., A. Mikocka-Walus, and J.M. Andrews, Future challenges and directions in FGIDs – Integrated and biopsychosocial care approaches., in Functional Gastrointestinal Disorders: A biopsychosocial approach. S.R. Knowles, J. Stern, and G. Hebbard, Editors. 2017, Routledge Taylor and Francis Group. Appendix I

Chapter 1 : Overview

Functional gastrointestinal disorders (FGID) are a growing health concern worldwide, having a lifetime prevalence of ~40% [1, 2]. These common, chronic disorders impair daily functioning, mental health and workplace productivity [3, 4], and carry significant costs to the patient and community (US$1.7-$10 billion/year in direct costs, and up to $20 billion indirect costs in the USA alone) [5]. Given the high prevalence, cost, and associated reduction in quality of life, these disorders require an effective strategy for overall care.

In the past, there has been therapeutic nihilism and frustration expressed by patients and doctors alike [6]. However, the advent of reliable, accepted diagnostic criteria [7-9] and effective evidence-based management options have potential to transform the FGID landscape [10-12]. Despite this, current practice does not appear to have taken on these advances with diagnostic criteria and newer, effective management options such as the low FODMAP diet, gut-directed hypnotherapy and cognitive behavioural therapy not yet widely used. Therefore, a validated, simple clinical pathway incorporating diagnosis and management was proposed as an effective way to integrate new knowledge into practice by facilitating the provision of effective healthcare to this large patient segment.

This PhD thesis takes a 360 degree look at the current diagnosis and management of FGIDs within a local health care setting. By following patients referred to one tertiary referral centre, a comprehensive exploration of current issues in care was conducted, and issues which may be targeted for improvement, and incorporated into the trial of an FGID clinical care pathway (Figure 1-1). This thesis is to be submitted 'by publication' and several inter-related studies pertaining to FGID management are presented.

Firstly, patients referred with suspected FGID were characterised, and their feedback regarding management to date, and main concerns were explored. Reasons primary healthcare providers referred these patients to tertiary care were also investigated, and the quality of referrals and safety of referral triaging was assessed. These findings are presented in 'Referrals to a Tertiary Hospital - A Window into Clinical Management Issues in Functional Gastrointestinal Disorders', submitted to the Journal of Gastroenterology and Hepatology (Chapter 3).

The clinical approach to FGID diagnosis and management in tertiary care was also examined, through the analysis of specialist correspondence to referring practitioners and a clinical audit of endoscopic procedures. The results are presented in 'Uncertain Diagnostic Language Affects Further Studies, Endoscopies and Repeat Consultations for

Patients with Functional Gastrointestinal Disorders' published in Clinical Gastroenterology and Hepatology 2016;14:1735–1741 (Chapter 4), and 'Comparison of Endoscopic Appropriateness Criteria and Their Utility in Restricting Endoscopic Procedures in Functional Gastrointestinal Disease: A Retrospective Audit', submitted to BMC Gastroenterology (Chapter 5).

To inform the development of an integrated clinical pathway for the diagnosis and management of FGIDs, a systematic review of trialled models of FGID care was conducted. These data are presented in 'The potential of integrated nurse-led models to improve care for people with functional gastrointestinal disorders: Systematic Review' submitted to the Gastroenterology Nursing Journal (Chapter 6). The major focus of this PhD research was the design and evaluation of a novel clinical pathway for FGIDs which does not depend upon specialist consultation. The feasibility, safety, acceptability and performance of this approach are presented in 'Performance of a Non-Specialist Dependent, Algorithm-based Approach to the Diagnosis and Management of Functional Gastrointestinal Disorders: A pilot trial' submitted to Neurogastroenterology and Motility (Chapter 7).

Finally, a discussion summarising the main opportunities to implement changes in the way people with FGIDs are diagnosed and managed is presented. Furthermore, multiple strategies by which improved patient care can be achieved are outlined (Chapter 8)

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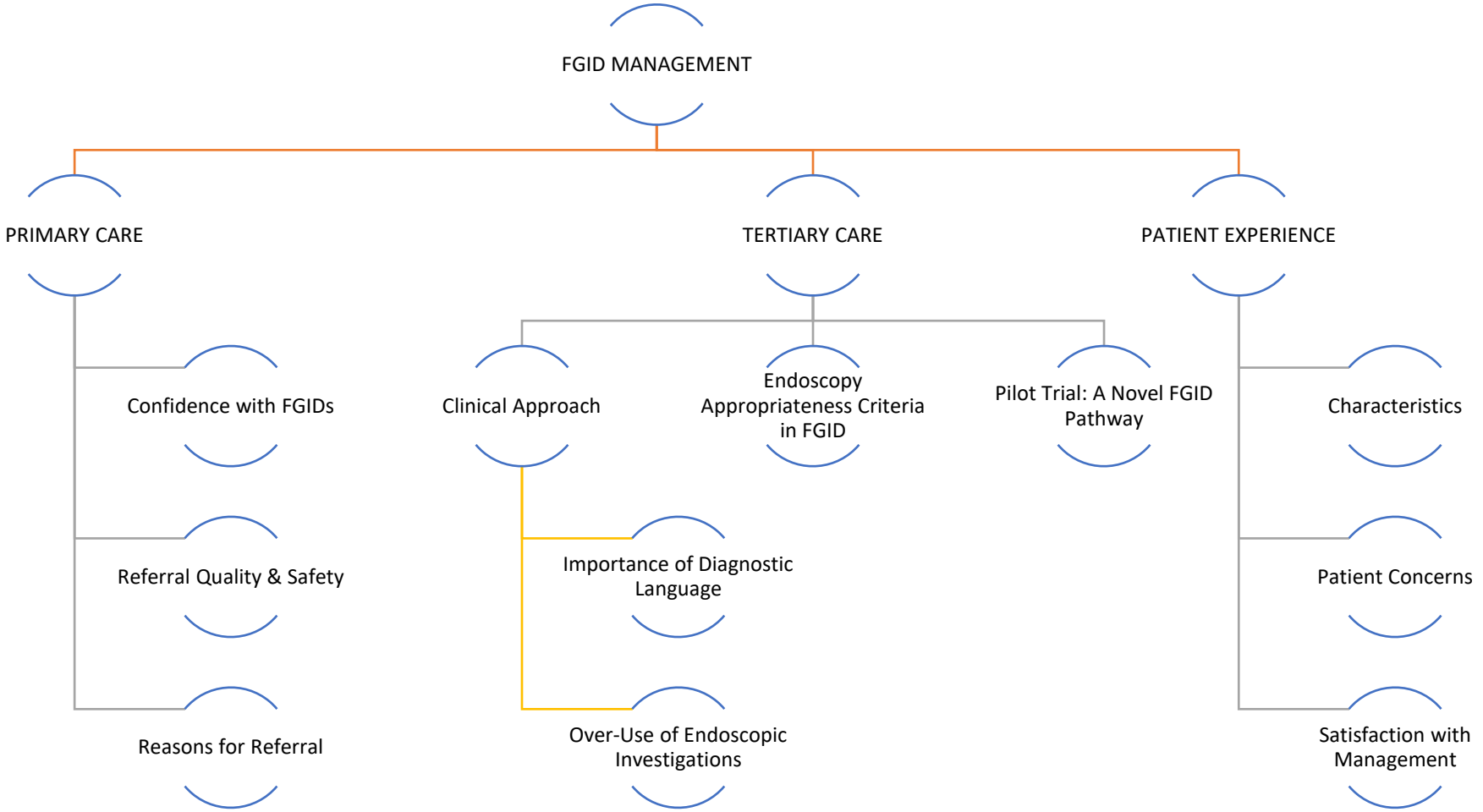

Figure 1-1 Summary of the areas explored in the thesis

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Chapter 2 : Introduction

BURDEN OF FUNCTIONAL GASTROINTESTINAL DISORDERS

Functional gastrointestinal disorders (FGIDs) are chronic disorders with a prevalence of 10-15% [1], and affect at least 40% of the population throughout their lifetime [2]. They are characterised by disturbing, recurrent symptoms such as abdominal or epigastric pain, bloating, diarrhoea, constipation, nausea, and vomiting. The most common FGIDs are irritable bowel syndrome (IBS), which affects approximately 10% of the population [3, 4] and functional dyspepsia (FD), with a prevalence of 15% [4, 5]. There is also a large degree of overlap in FGID symptoms, and patients often suffer from multiple FGIDs [6]. The type of presenting FGID can also change over time [2], and a high incidence of concomitant physical and psychological disorders is apparent [7, 8]. FGIDs severely reduce quality of life (QOL), negatively impacting patients physically, psychologically, socially and economically [9, 10].

FGIDs are mostly managed in primary care, yet there is considerable variability in the approach to diagnosis and management, as reflected in the range of individual referral rates (1-80%) [11]. In Australia, 11% of IBS cases alone are referred to specialist care[12]. Referrals for FGIDs represent a large portion of the workload in gastroenterology, and account for 25-75% of all gastroenterology referrals [3, 13, 14]. In some health systems, such as Australia, referrals for suspected FGIDs are triaged as non-urgent and deferred to very long waiting lists, with many patients never being seen. One Canadian study found that less than 10% of patients referred with un-investigated dyspepsia were seen by a specialist within 6 months [15].

The economic burden of FGIDs is significant, and includes both direct and indirect costs. Direct costs include medical consultations, testing, medication and tertiary care (inpatient/outpatient), whilst indirect costs relate to loss of productivity (presenteeism) and/or absence from (absenteeism) the workplace. In Canada, 75% of the costs were indirect costs [16]. In 2000, an estimated 41 billion dollars (US) was spent on IBS alone in the UK, Japan, Australia, Sweden, Germany, France, and Canada [17]. Since then, costs have continued to grow, with a recent systematic review revealing that the United States alone spends US$1.7-$10 billion (US$1562-$7547/patient) on direct costs, and up to $20 billion in indirect costs for IBS [18]. In Finland, direct IBS costs account for 5% of the national medical expenditure [19]. The total cost of all FGIDs is much greater, as IBS is only one of over 20 FGIDs, and 75% of people with symptoms do not seek medical advice but are

impacted [20, 21]. Furthermore, people with IBS spend at least 50% more on total healthcare than those without IBS [22].

PATHOGENESIS

The mechanism for the pathogenesis of FGIDs is poorly understood and significantly more research is needed to direct diagnostic and treatment strategies. The most commonly accepted explanatory model for FGIDs is a biopsychosocial one with psychological state, increased motor reactivity, visceral hypersensitivity, and altered enteric nervous system regulation implicated (Figure 2-1) [23]. However, not all clinicians accept this model, with some viewing FGIDs as a mixture of organic disorders which are as yet undiscovered, or as normal symptoms which do not require medical attention [24]. Indeed, the role of immune activation [25, 26] and altered microbiome in FGIDs [27] are rapidly evolving areas of research, which will further define the pathogenesis of these disorders. Despite the lack of a well-defined mechanism for the pathogenesis of FGIDs, people with disturbing gastrointestinal symptoms still need a clear accurate diagnoses and effective management options.

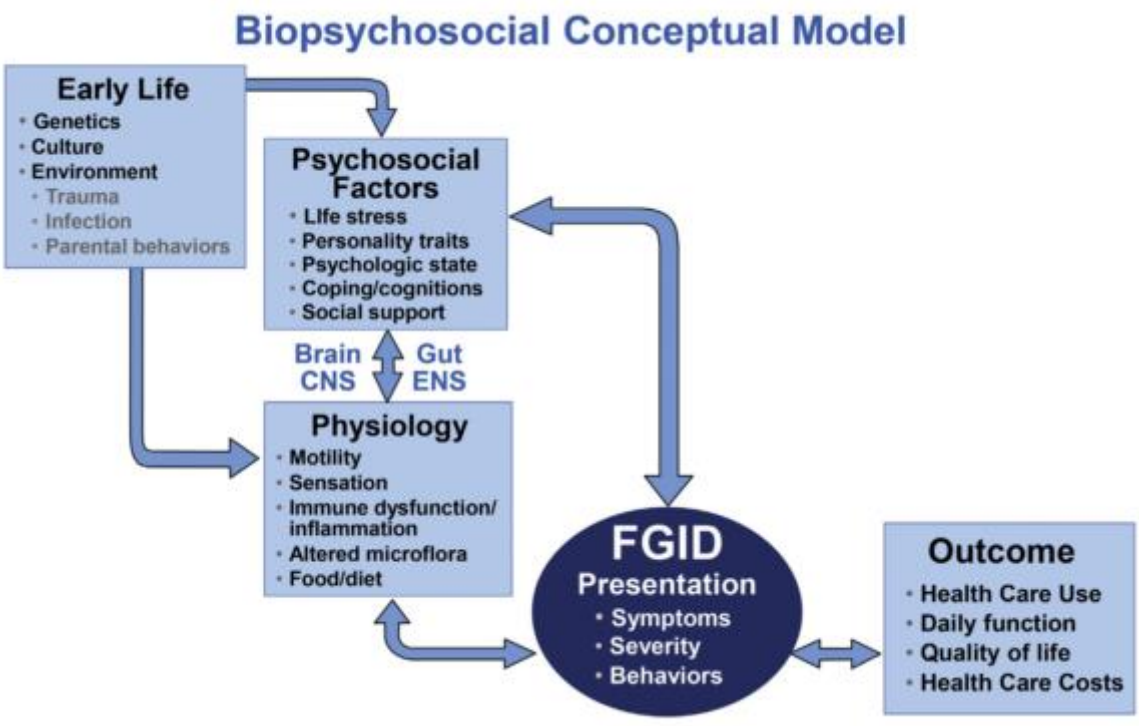

Figure 2-1The biopsychosocial model of functional gastrointestinal disorders.
(Reproduced with permission from Drossman, D.A., Functional Gastrointestinal Disorders: History, Pathophysiology, Clinical Features, and Rome IV. Gastroenterology, 2016. 150(6)

DIAGNOSIS

Importance of Diagnosis

Many clinicians consider a functional diagnosis, but are reluctant to communicate this to the patient [24] or to document it [28]. Many patients are also reluctant to accept a functional diagnosis [29]. Thus, the provision of a timely, clear FGID is critically important. Patients with persistent medically unexplained symptoms (i.e. undiagnosed) use significant amounts of healthcare in a continued search for a diagnosis [30]. A clear diagnosis provides reassurance and alleviates patients concerns and helps move the patient from a diagnostic search to an effective management strategy [24, 31]. Effective management by definition, should in turn reduce the physical and mental distress of patients, the economic burden due impaired workplace productivity, unnecessary investigations and endoscopic procedures. From a strictly economic perspective, a timely diagnosis is necessary for the effective allocation of limited healthcare resources, such as outpatient appointments and endoscopic procedures.

Diagnostic Criteria

Historically, making a confident diagnosis of FGID was hampered by the lack of biological markers and the difficulty in assessing highly variable symptoms. Overlap and co-occurrence of FGID symptoms with other gastrointestinal disorders such as gastroesophageal reflux disease, peptic ulcer, inflammatory bowel disease, colorectal cancer and coeliac disease adds to the complexity. Until recently, an exclusionary approach to diagnosis was widely used, which inevitably led to the over-use of investigations, and high costs [32]. However, symptom-based criteria have been developed which now allow the positive diagnosis with limited testing [33-35].

The first diagnostic criterion for IBS was developed by Manning [34] in 1978, which was followed by the Rome criteria and its revisions (Rome II, III and IV) from 1992-2016 [23, 35, 36]. The Manning criteria are a set of 6 symptoms common to IBS, which were identified in that study comparing patients with organic and functional gastrointestinal disease. These symptoms are abdominal distension, pain relief with bowel movements, more frequent and looser stools with the onset of pain, faecal mucous and feeling of incomplete rectal evacuation. The Rome criteria were established by consensus within a group of IBS experts formed to develop a set of standardised criterion for IBS, primarily for research purposes [37]. Revisions in the Rome criteria over the years, have caused some confusion regarding diagnosis, and poor uptake of the criteria in the clinical setting [38]. The recently released Rome IV criteria, however have a strong emphasis on clinical

diagnosis and care of patients with FGID, particularly the importance of the therapeutic relationship and a severity based approach to symptom management [35].

The Manning criteria have been subjected to greater validation than the Rome criteria. Rome I and II have been validated, but the Rome III and IV have not [39]. Validation of the Rome criteria is a contentious issue in the literature. Some assert that the lack of effort to validate the Rome criteria translates to poor validity [38, 40], yet others regard lack of research interest in validation as a sign of overwhelming clinician agreement with the criteria [24]. A recent systematic review by Dang *et al.,* [38] found the Manning criteria to have a sensitivity of 63-94%, and specificity of 55-93%. Four studies assessing Rome I found sensitivity ranging from 62-85%, and specificity 70-100%; and 3 assessing Rome II found sensitivity 64-89%, and specificity 60-73%. The highest sensitivity (100%) was achieved when the Rome I criteria were used in conjunction with the absence of clinical alarms/red flags [41].

Although the Rome criteria are generally accepted and used by gastroenterologists in research, their use as diagnostic tool has varied. A systematic review of 9 studies in Europe and the United States showed that few primary care providers were aware of (2-36%, median 20.5%) or used (19-35%) diagnostic criteria [39]. An exception was seen in a Romanian study that reported 99% use of Rome II criteria to diagnose IBS, but the majority of these also used colonoscopy, highlighting the lack of confidence in making a positive diagnosis [42]. Current recommendations are that in the absence of alarm features, and with negative faecal and blood tests, other tests are rarely warranted [3, 23, 43]. Alarm features include new onset of symptoms in patients older than age 50, dysphagia, unexplained weight loss, gastrointestinal bleeding, unexplained fever, nocturnal symptoms, and a family history of colon cancer, inflammatory bowel disease or coeliac disease [44]. Although the predictive value of alarm features for organic disease is poor, the specificity of absence of alarm features for FGID is high [45].

However, there appears to be a mismatch between accepted recommendations and current practice with a 'diagnosis of exclusion' approach with investigation over-use still widely used [44, 46, 47]. A recent systematic review found that although two-thirds of IBS patients underwent diagnostic testing in primary care, there was extreme variation in the tests used (29 studies; 6 European countries, United States, Holland) [39]. Common diagnostic tests included faecal occult blood, erythrocyte sedimentation, colonoscopy, coeliac disease screening, complete blood count, electrolyte, liver and thyroid function tests, C-reactive protein, sigmoidoscopy, barium enema, abdominal ultrasound and stool tests for ova and parasites. The age of patients affected the type of investigations ordered,

with several studies showing that patients over 45-50 years were more likely to receive a barium enema, colonoscopy, and laboratory testing than younger patients, who were more likely to be tested for C-reactive protein and coeliac disease [39]. An exclusionary approach to diagnosis is not peculiar to primary care, as the overuse of investigations is widely acknowledged to occur within specialty care.

Testing despite contrary clinical guidelines has been attributed to patient expectations and anxiety [48, 49], patient and clinician's fear of missed pathology [3], clinicians fear of litigation [32] and clinician's belief that diagnostic tests reassure their patients [49]. Yet, contrary to clinicians impressions, patients often prefer a solid explanation and emotional support rather than further testing [50]. Furthermore, investigations have not been shown to reassure anxious patients [48, 49, 51, 52], and reassurance is not a sufficient reason for unnecessary testing. A systematic review of 14 randomised controlled trials (n=3828; in patients with a low pre-test probability of disease) found that investigations had no effect on illness worry, anxiety, or symptom persistence but did slightly reduce subsequent use of health care resources [51]. It should be noted that the cost of testing outweighed any benefit of reduction in follow up consultations [51]. Interestingly, FGIDs accounted for 12 of the 14 studies reviewed, further highlighting the extent of the problem. Missed pathology is always a risk in medicine, even after extensive investigation [24], and fear of litigation is a poor reason to perform unnecessary investigations, especially when a good therapeutic relationship exists [32].

Diagnostic Tests

Mearin and Lacy [24] state the purpose of testing in patients with suspected FGID is to establish a clear diagnosis in a cost-effective way which minimises clinician's concerns and patient risk. The most common differential diagnoses of concern are colorectal cancer, inflammatory bowel disease, peptic ulcer and thyroid disease. However, these are no more prevalent in patients with FGID than the general population, and the judicial use of investigations is recommended [53]. Although several evidence-based guidelines exist, they have been developed by consensus, are yet to be validated, and are debated among clinicians.

The Rome criteria recommend the positive diagnosis of FGIDs based on characteristic symptoms [35]. Similarly, The American College of Gastroenterology Task Force on IBS does not recommend routine testing with complete blood count, serum biochemistry, thyroid function tests, and stool tests for ova an parasites (in developed countries), for suspected functional bowel disorders [45]. Colonoscopies are also not recommended in people under

50 years of age with no alarms, whilst screening for coeliac disease in patients with diarrhoea, and lactose breath testing if symptoms persist after dietary modification are recommended [24, 45]. However, many recommend improving the specificity of symptom-based criteria through the use of blood and stool screening tests [31, 54, 55]. The National Institute for Health and Clinical Excellence (NICE) recommends a full blood count, erythrocyte sedimentation rate or plasma viscosity, C-reactive protein and antibody testing for coeliac disease in patients fulfilling positive FGID symptoms with no alarms [53, 56]. A diagnostic algorithm developed by Fass *et al.,* [57] in 2001, also recommended complete blood count, erythrocyte sedimentation rate, electrolytes, thyroid function tests and flexible sigmoidoscopies in a primary care presentation, and a considerably larger investigative work-up in tertiary care. A recent study conducted by Moore J.S. [58] showed a more accurate diagnosis (of IBS) could be obtained using Rome III together with a panel of routine tests: namely abdominal and rectal physical exam, complete blood count, iron studies, C-reactive protein, thyroid function tests, liver function tests, coeliac antibodies, and kidney function tests together with stool samples for faecal microscopy and culture and faecal calprotectin.

Endoscopic Appropriateness Criteria

Endoscopic investigations such as upper gastrointestinal endoscopy (UGIE) and colonoscopy are often over-used in patients with suspected FGIDs [3]. Although sensitive and specific, endoscopic investigation is expensive and carries a low but significant complication rate [59]. In most countries colonoscopy requests are increasing with the implementation of colorectal cancer screening programs and a general increase in routine referrals. Careful selection of patients in whom invasive investigations are appropriate is necessary. Endoscopic appropriateness guidelines have been developed by the American Society for Gastrointestinal Endoscopy (ASGE) [60-63] and the European Panel on the Appropriateness of Gastrointestinal Endoscopy (EPAGE I and EPAGEII) [64] to better target endoscopic procedures, increase diagnostic yield and improve the quality of patient care.

The ASGE criteria categorises endoscopies as appropriate or inappropriate, and is accepted as an important monitoring tool, particularly in open-access facilities [65]. EPAGE is a decision-making tool which allows the categorisation of indications as necessary, appropriate, uncertain or inappropriate [64]. The full criteria can be accessed via www.epage.ch. Neither is recommended to replace clinical judgement in the context of the individual patient [66, 67]. The validity of these guidelines has not been evaluated in randomised controlled trials, but observational studies have shown a high proportion of inappropriate endoscopies, with higher diagnostic yield in appropriate procedures [66, 68-70].

Rates of inappropriate endoscopies vary widely (10-40%) according to procedure type, patient age, healthcare setting (in- vs. out-patients), the criteria used and the healthcare system of the country [71-78]. Direct comparison of inappropriateness rates is therefore difficult.

The ASGE and EPAGE guidelines for colonoscopy have been found to have good agreement in 80% of indications, with disagreement occurring in a few frequently encountered indications such as uncomplicated abdominal pain and constipation. Such symptoms occur frequently in people with FGID and are, in general, low-yield indications for colonoscopy. Consistent with this, a simple predictive rule based on age, alarm features and family history has been shown to be as effective as ASGE guidelines in identifying appropriate indications for UGIE (n=8252)[71]. The usage of these criteria in clinically suspected FGIDs has not been assessed globally, and there are no studies assessing the rate of unindicated endoscopic procedures in Australia, and how many of these relate to FGID.

TREATMENT

FGID treatment is complicated by the unknown pathophysiology, wide variations in symptoms, lack of a clear therapeutic target and the overlapping role of genetics, biological and psychosocial factors [79, 80]. Current treatment of FGIDs is unsatisfactory, with few people getting adequate symptomatic relief, or experiencing adverse effects, despite using multiple pharmacological treatments as well as complementary and alternative medicines [80]. Although there are several effective pharmacological treatments, there is not a single treatment with proven efficacy in all FGID patients.

Treatment of Functional Bowel Disorders

The most common functional bowel disorder is IBS. Current IBS treatment approaches target symptom management and QOL, and vary according to the predominant symptoms [81]. Treatment options available include pharmacotherapeutic and psycho-pharmacotherapeutic agents, as well as psychotherapy, dietary interventions and complementary and alternative medicines (CAMs). A number of systematic reviews have been conducted, which highlight the variation in efficacy of available treatments, and are summarised in Table 2-1[82-86].

Of interest, peppermint oil is the most effective treatment, but is limited to targeting pain [87]. Similarly, anti-spasmodics although moderately effective, treat only one symptom [87]. Antidepressants are not effective in all patients, with tricyclic antidepressants being

recommended only for patients with diarrhoea (due to significant constipation side effects), and serotonin reuptake inhibitors for those with comorbid major depression [87]. Drugs specifically targeting motility vary in efficacy, but are not recommended due to significant possible adverse effects. Probiotic efficacy is dependent on the bacterial strains used, and this is a growing field of research. Fibre can increase abdominal symptoms in some people, however soluble fibre may be of some benefit [85]. Of interest, is the emerging field of psychological [87-89] and dietary therapies [86], which offer global improvement in symptoms, rather than isolated symptom improvement.

Treatment for Functional Gastroduodenal Disorders

There are fewer effective treatment options available for FD than for IBS, and those with some effect are generally cost prohibitive [90]. Current available treatment approaches include *H. pylori* detection and eradication, anti-secretory (proton pump inhibitors and H2 receptor antagonists) or pro-kinetic drugs as well as lifestyle and dietary modifications [43]. Treatments vary significantly in efficacy showing small-moderate effect sizes in only a small proportion of FD patients and some have significant adverse effects. Research into the efficacy of FD treatments has also been hampered by the inadvertant inclusion of patients with gastroesophageal reflux disease in FD patient samples due to the use of broader diagnostic criteria in some studies.

There is evidence that proton-pump inhibitors are effective in a small proportion of participants with FD, but the results vary significantly [91], and were effective only for epigastric pain. The role of *H. pylori* infection in FD is unclear. A Cochrane review of 12 randomised controlled trials of *H. pylori* eradication found positive effect in 3 trials and no effect in 9 (Table 2-1) [92]. Overall *H. pylori* eradication therapy was found to have a small but significant effect, is cost effective, and justified by the serious potential health effects of an undiagnosed ulcer.

Very few studies have assessed the efficacy of psychological therapies [88, 93], and or dietary therapies [94] in FD. Given the considerable overlap of FD and IBS symptoms, and the proven efficacy of these treatments to reduce global symptoms in IBS, they pose potential furture therapies for FD [86, 87, 94]. In fact, many clinicians believe FGIDs lie on a spectrum rather than being discrete disorders [94, 95]. Giving further weight to the possibility of the effectiveness of these treatments if FD is the similarity of pathogeneis of symptoms: gut motility, gastric emptying, visceral hypersensitivity, immune activation, the microbiome, and psychological factors have been implicated in both IBS and FD [94, 96, 97].

Psychological Interventions for FGIDs

The use of psychological interventions has been investigated largely due to the adverse effects and lack of efficacy of other treatments as well as the effect psychosocial factors appear to have on the maintenance of FGIDs [98]. It is well established that acute stress and anxiety alter gut motility and sensation directly via the brain-gut axis, possibly providing a mechanism whereby they increase the risk of onset of FGID in susceptible individuals [99] and exacerbate symptoms in those with pre-existing FGID [100]. Anxiety disorders are over-represented in FGID patients [7] with anxiety, stress and depression correlating with the severity of symptomology and the extent of somatisation [101, 102]. Psychological factors also mediate the adoption of healthcare seeking behaviour in patients with FGID [99] the screening of all FGID patients for concomitant psychological disorders recommend because of their therapeutic impact [7].

Although the psychological studies to date have been criticised for their lack of rigour [98, 103] there is considerable evidence available to support the use of psychological treatments in both IBS and FD. On the whole, psychological interventions have been shown to be effective in reducing IBS symptoms and psychological distress, as well as increasing QOL [87, 104, 105]. The exact mechanisms by which these reduce FGID symptoms is unknown, but it appears that this may occur independently of psychological distress reduction [104]. However, further research addressing which psychological therapies are more effective in which groups of patients is required [39].

A Cochrane systematic review (25 random controlled studies. 1950-2008) found that psychological interventions improve IBS symptoms post-treatment when compared with waiting list or treatment as usual, but not when compared with placebo [106]. However, placebos are problematic in psychological interventions as the client-therapist interaction is itself therapeutic. This is in agreement with a similar meta-analysis conducted by Ford et al., [105] (20 studies, n=1278) that showed psychotherapy to be equally effective as anti-depressants (13 studies, n=789, NNT=4, RR=0.67), with symptoms persisting in 50.9% of treatment patients as compared with 72.5% control group.

There are many different forms of psychological therapy available which may be beneficial in the treatment of FGIDs with CBT being the most extensively studied. Ford et al's [105] meta-analysis (7 studies, n= 491) showed that CBT is effective in the treatment of IBS symptoms (RR of 0.60, NNT of 3) with symptoms persisting in 42.3% of patients as compared 61.3% of control patients. However, this treatment effect was nullified when three small studies conducted in one centre were removed. There is considerable difficulty in gaining consensus among multiple systematic reviews due to the high degree

of variability in study design and quality. Further rigorous trials of CBT which continue to follow patients up in the long term are required.

A Cochrane systematic review of 4 trials comparing group therapy relaxation techniques (n=103), cognitive therapy (n=100), psychodynamic interpersonal therapy (n=73) and hypnotherapy (n=126) on FD found that all interventions improved dyspepsia symptoms after treatment and at 12 month follow up [107]. However, the trials were of insufficient quality to enable meta-analysis. One trial assessed QOL and found that hypnotherapy significantly improved QOL at one year follow up as compared with medical therapy [90]. Hypnotherapy shows considerable promise as a FGID treatment. Individual studies have shown that hypnotherapy directly affects visceral sensitivity and gastrointestinal motility [108, 109] and improves IBS and FD symptoms and QOL over the long term [90, 110-112]. Although a Cochrane review concluded that there was insufficient quality evidence to recommend the use of hypnotherapy in IBS in 2007 [113], an updated review in 2014 found hypnotherapy to be beneficial [83]. Hypnotherapy as a treatment for FGIDs is at this stage restricted by the cost, time-intensive therapy and the lack of qualified therapists. However, the effect of hypnotherapy on FGIDs reported so far lends further weight to the argument for the use of psychotherapies in general for the treatment of FGIDs.

Despite the well-recognised fact that IBS and FGIDs have a significant psychological aspect, primary care providers do not regularly use psychological treatments [39]. Reasons for this were shown to be lack of knowledge and certainty about these treatments and their efficacy, as well as perceived patient resistance to psychological intervention, and the belief that they could be treated within the primary care setting [39]. In addition the use of psychological treatment has often been impeded by the length and cost of treatment, however recent studies have shown self-administered and minimal-contact psychotherapies to be useful in the symptomatic relief of IBS [114].

Dietary Treatment of FGIDs

Recent studies have shown that fermentable dietary constituents known as FODMAPS (Fermentable Oligo-, Di- and Mono-saccharides and Polyols) contribute to the disturbing symptoms experienced by FGID patients - particularly those with IBS or functional bloating [79]. FODMAPS are poorly absorbed, highly osmotic and rapidly fermentable substances which act to increase the water and gas volume in the intestine resulting in luminal distension. This distension when combined with the visceral hypersensitivity seen in FGIDs can cause abdominal pain, bloating, and/or altered intestinal motility [79, 115, 116]. Two FODMAPS - fructose and lactose - are malabsorbed in 33-75% and 38% of IBS patients

respectively, although population prevalence does vary [117, 118]. Low FODMAP diets have been shown to reduce symptoms in 75% of IBS patients [79], however this dietary approach has not yet been widely adopted in practice. A recent systematic review of 6 randomised controlled trials, and 16 non-randomised trials, showed the low FODMAP diet to be effective in reducing IBS symptoms and improve QOL [86]. In addition a low FODMAP diet has been shown to reduce gastrointestinal symptoms other than those usually characterised by IBS [117].

A prospective study of IBS patients (n=192) who participated in a low FODMAP diet after lactose and fructose malabsorption testing showed a significant correlation between this diet and improvement in bloating, abdominal pain, flatulence, diarrhoea, constipation and energy levels. Patients with fructose malabsorption reported the most significant symptom reduction and 72.1% of participants were satisfied with their symptoms at follow up [117]. Interestingly, a quarter of these patients remained unsatisfied with their symptoms despite the low FODMAP diet, which suggests the need for a combination therapy in order to adequately reduce symptoms in a larger portion of the population affected with FGIDs.

Another randomised control crossover trial conducted by Halmos *et al.,* (119) (n=38), showed that a strictly controlled 21-day low FODMAP diet significantly reduced gastrointestinal symptoms in 70% of participants across all subtypes of IBS, as compared with IBS patients on normal Australian diet. In contrast to the study by de Roest *et al.,* (117) these symptom benefits occurred independent of the presence of fructose malabsorption. However, the strictly controlled study diet is unlikely to reflect the real-life compliance with and utilisation of a low FODMAP diet. In clinical care settings, this diet is generally taught by a dietitian, but could also be learnt from written or electronic resources, although these modalities are yet to have a formal evaluation.

It is therefore feasible to suggest that a low FODMAP diet may reduce symptoms in FGID patients who experience both upper and lower GI symptoms. It may also be possible that reducing the lower abdominal symptoms in patients who experience a large number of symptoms may in fact reduce the overall symptom burden to a level below a symptom perception or symptom complaint threshold and thus increase satisfaction and QOL. It remains to be seen whether the low FODMAP diet is acceptable, utilised and effective in the real-world setting. In addition, low FODMAP diets have only been assessed as dietitian instructed treatments.

Global Treatment

Given the fore-mentioned problems and research, the challenge is how to provide an evidence-based treatment protocol that brings symptomatic relief and increases QOL in the majority of people with FGIDs. There are a number of symptoms and pathophysiological features that are common to both FD and IBS and it has been suggested that these may lie on a spectrum of FGIDs rather than being two distinct disorders [95]. If this is the case, it lends weight to the idea that a common approach to treatment may be effective in a large proportion of FGID patients

THE RESEARCH QUESTION

Rationale

As FGIDs are complex disorders with biopsychosocial triggers, and multi-disciplinary treatment options, holistic, integrated care approaches are needed. An integrated approach (or clinical pathway) that begins with the first medical consultation is required to address the biopsychosocial experience, comorbidities, somatisation and suboptimal acceptance of functional disorders as a valid diagnosis. To be most effective at moving patients from a search for an acceptable diagnosis to an effective management strategy, both a diagnostic algorithm, and widely effective treatments must be included. At present, no such global approach has been trialled in FGID. This thesis explores current issues in the diagnosis and management of FGIDs through the lens of one tertiary referral centre. Additionally, results of a pilot trial into an algorithm-based approach to the diagnosis and management of FGIDS are presented.

Aim

The overall aim of this research is to explore and describe current issues in the diagnosis and management of FGIDs and to perform a pilot trial of a novel algorithm-based clinical pathway. A multi-phase mixed methods design using sequential and convergent studies will be used to investigate this global question.

Research Objectives

The objectives of this research are to:

1) Explore and describe any differences in clinician approach to functional and organic gastrointestinal disorders in tertiary care.
2) Determine the rate of inappropriate endoscopies performed in patients with suspected FGID, and evaluate the utility of alarm-based criteria to reduce inappropriate procedures.

3) Investigate the quality of and reasons for referrals of patients with likely FGID and explore patients' experience of management in primary care.
4) Explore and describe existing trials of models of care for the diagnosis and management of FGIDs.
5) Assess the safety, feasibility, and acceptability of an algorithm-based approach to the diagnosis and management of FGIDs.
6) Explore and describe patient views and experience of this algorithm-based approach to the diagnosis and management of FGIDs.

The Research Process

A multi-phase mixed methods design using sequential and convergent studies was used to investigate this global question, and objectives. A combination of research methods and data collection sources were used in order to fully evaluate the current issues involved in the diagnosis and management of FGIDs. This research is comprised of 4 inter-related phases.

Phase 1: Document analysis

The first phase involved an analysis of current issues in the clinical management of FGIDs in both primary and tertiary care. Source documents included referrals to one metropolitan tertiary care centre, specialist diagnostic letters to referring doctors, booking forms for endoscopic procedures. A systematic review of studies which trialled models of care for the diagnosis and management of FGIDs was also conducted, to identify issues and gaps in available models.

Phase 2: Surveying of Referring Doctors and Referred Patients

In the second phase of the research, patient and referring clinicians were surveyed in order to provide insight into the factors which drive referrals to gastroenterologists for patients with clinically suspected FGID, and to explore patients experience of clinical management preceding referral. These qualitative data were subjected to content analysis and descriptively reported.

Phase 3: Development of a Clinical Pathway for FGID

A clinical pathway which included both the diagnosis and management of FGIDs was developed. As this pathway was to be implemented without specialist consultation, a proforma document of a letter to be sent to referring doctors and their patients following screening for organic disease was developed (Appendix A). This document also contained

basic education about FGIDs, evidenced-based psychological and dietary management options and resources for utilising these options. A self-help booklet and website ("Gut and Mind Matters") were developed as an included resource (Appendix B). These were adapted from a cognitive behavioural therapy booklet for anxiety in functional gastrointestinal disorders, previously designed within this unit [120]. The high/low FODMAP food list from Monash University was also provided [121].

Phase 4: Pilot Study – An Algorithm–Based Approach to the Diagnosis and Management of FGIDS

The last phase of the study involved a pilot trial to assess the performance of the developed FGID clinical pathway – an algorithm-based approach to the diagnosis and management of FGIDs (ADAM-FGID). Specifically, the effectiveness of the ADAM-FGID to safely diagnose FGIDs and improve patient outcomes, and the acceptability of the approach was determined in a non-blinded, parallel group study compared the ADAM-FGID to routine waitlist care.

Table 2-1 Efficacy of treatments for FGIDs: Summary of recent systematic reviews of the evidence

Treatments	FGID	No. of Trials (n)	Odds ratio	Relative risk [CI]	Gain	NNT [CI]	Comments
Pharmacotherapies							
Anti-spasmodics [87]	IBS	22 (n=1718)	1.97		18%	5-6 [1.59-2.45]	*Pain/ Low cost
Motility agents [87]	IBS	31 (n>18000)			5-16%	6-15	Significant adverse effects
Proton pump inhibitors [91]	FD	10 (not stated)		RRR 13% [4-20%]	9%	10 [7-33]	
H. pylori eradication [92]	FD	12 (n=2093)		RRR 10 [6-14%]%		14 [10-25]	Small effect at 12 months
Histamine-H2 antagonists [91]	FD	12 (n=2183)		RRR 23% [8=35%]	14%	7 [5-21]	*Pain and postprandial fullness
Prokinetcs [91]	FD	19 (n=3178)		RRR 13% [13-25%]	10%	6 [5-12]	Poor quality trials Cost/adverse effects
Antacids [91]	FD	1 (n=109)		1.02 [.76-1.36]	No benefit		
Antidepressants [89]	IBS						
TCAs		11 (n=744)		0.66 [.56-.79]	20%	4 [3-6]	IBS-D only
SSRIs		7 (n=356)		0.68 [.51-.91]	22%	4 [2.5-20]	Comorbid depression only

Treatments	FGID	No. of Trials (n)	Odds ratio	Relative risk [CI]	Gain	NNT [CI]	Comments
CAMS							
Peppermint oil [87]	IBS	4 (n=392)	4.11 [2.65-6.36]		39%	2-3	1 symptom (pain); Reflux and other side effects
Iberogast [82, 84, 122]	IBS FD	1 (n=208) 3 (n=425)		1.9 [1.15-3.14] .22 [.11-.47]	15-25% 19%		Global improvement
Psychological Therapies							
Psychotherapy [87]	IBS	22 (n=131)	2.60 [2.01-3.37]		23%	4-5	Global effect; similar effect between all psychotherapies; CBT most evidence
Psychotherapy [88]	FD	4 (n=171)					Insufficient evidence
CBT [83]	IBS	9 (n=610)		.60 [.44-.83]	22%	3 [2-6]	
Relaxation/Stress Management [83]	IBS	6 (n=255)		.77 [.57-1.04]	16%	No benefit	Significant variation
Hypnotherapy [83]	IBS	5 (n=278)		.74 [.63-.87]	23%	4 [3-8]	Global symptom improvement, long term benefits

Treatments	FGID	No. of Trials (n)	Odds ratio	Relative risk [CI]	Gain	NNT [CI]	Comments
Dietary Therapies							
Probiotics [87]	IBS	15 (n=1838)	2.24		13.5%	7-8	Variation with strain; Long term effect not assessed
Fibre [85] Soluble Fibre Bran	IBS	14 (n=906) 7 (n=499) 6 (n=441)		.86 [.80-.94] .83 [.73-.94] .90 [.79-1.03]		10 [6-33] 7 [4-25] No benefit	Can increase abdominal pain; Evidence soluble fibre improves IBS-C
Low FODMAP Diet [86]	IBS	6 RCT 16 non-randomised	1.81 [1.11-2.95] .80 [.72-.86]				Improved global symptom severity & quality of life.

Gain= gain of response over control

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Chapter 3 : Issues with Real World FGID Management

BACKGROUND

Current guidelines recommend that FGIDs are diagnosed and managed within primary care, and referred if patients do not respond to treatment after 12 months. Yet, ambulatory gastroenterology referrals have been estimated to account for anywhere up to 50% of all referrals, and in most public institutions, this is unsustainable. The mismatch between resources and demand results in extremely long waiting lists with many patients never being seen. This problem appears to be amplified by a lack of quality management of FGIDs in the primary care sector – leaving most patients frustrated in their attempts to manage symptoms which are often persistent and disturbing.

The development of an effective clinical pathway for FGID diagnosis and management critically depends on a solid understanding of the way these are currently managed across all healthcare sectors. Exploring the reasons which drive this large group of non-urgent referrals, and barriers that exist to management is extremely important. For example, if limited time, or inability to deal with patients perceived to be difficult are the main reasons for referrals, it is unlikely that a clinical pathway will alleviate the bottleneck of referrals. If, however, the reasons centre more around a lack of knowledge or confidence in dealing with these disorders, a clinical pathway which facilitates upskilling of these areas is likely to be beneficial.

This cross sectional, mixed-methods study explores the current issues in the management of FGIDs from the perspective of the patient and primary healthcare provider. Nested within the pilot trial of 'an algorithm-based approach to the diagnosis and management of FGIDs' (Chapter 7) this study utilises referrals, and surveys of the patients and their referring doctors to gain insight into pertinent issues in diagnosis and management. The patient and primary healthcare provider surveys are provided in Appendices C and E.

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i. the candidate's stated contribution to the publication is accurate (as detailed above);

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|MANUSCRIPT 1| REFERRALS TO A TERTIARY HOSPITAL – A WINDOW INTO CLINICAL MANAGEMENT ISSUES IN FUNCTIONAL GASTROINTESTINAL DISORDERS

Running Head: ISSUES WITH FGID MANAGEMENT

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ABSTRACT

Background

To investigate the quality of and reasons for referrals of patients with likely functional gastrointestinal disorders (FGID) and explore patients' experience of clinical management.

Methods

A cross sectional, mixed-methods study was undertaken. Referrals (July 2013-5) to one gastroenterology outpatient department triaged as 'likely FGID', the referred patients and their referring primary healthcare providers were examined.

Results

69% of patients reported not yet receiving an initial diagnosis, 52% reported persistent/distressing symptoms or reduced quality of life, 24% feared missed or worsening pathology, and 35% were seeking repeat specialist consultation. Most patients were dissatisfied (40%) or only partially satisfied (36%) with current management. Dissatisfaction was significantly related to the lack of provision of a diagnosis and effective treatment options ($p<.001$). Referral quality was poor and with the reason for referral clearly communicated in only 25%. Common referral reasons included repeat presentations (n=32), diagnostic uncertainty (n=19), to ensure nothing is missed (n=19), patient request (n=17), no response to treatment (n=16) and to allay patient fears (n=14). 28/60 primary healthcare providers were confident that their patient had a FGID, yet sought confirmation (n=16), second opinion (n=8) or advice (n=4).

Conclusion

Current management of FGID in usual care is suboptimal, as evidenced by the tertiary referral load, patient dissatisfaction and the lack of provision of diagnoses and effective treatment options. Some clinicians lack confidence in effectively identifying and managing these conditions. Resources and supports to equip and assist clinicians to identify and manage FGID successfully may enhance patient care.

Trial registration: ANZCTR, ACTRN12614000602628

Keywords: Functional gastrointestinal disorders, irritable bowel syndrome, primary care, management, tertiary care

BACKGROUND

Globally, functional gastrointestinal disorders (FGIDs) pose a significant and growing public health problem [1]. It is estimated that 40% of the population will be affected by one or more FGIDs within their lifetime (2), with irritable bowel syndrome (IBS) and functional dyspepsia the most common (prevalence 10-15% each) [1, 2]. These chronic, recurrent conditions impair quality of life and present a significant economic cost due to ongoing patient distress, unnecessary investigations, repeated healthcare visits as well as absenteeism/presenteeism in the workplace [3, 4]. In 2000, an estimated 41 billion dollars (US) was spent on IBS alone in the UK, Japan, Australia, Sweden, Germany, France, and Canada [5].

Historically, FGIDs were regarded as diagnoses of exclusion, leading to unnecessary investigations [6], but can now be positively diagnosed based on symptoms, use of 'red flags' and simple, relevant exclusionary tests [7-11]. Current guidelines from the UK's National Institute of Clinical Excellence (NICE) recommend patients with FGID be diagnosed and managed within primary care and referred to gastroenterology after 1 year if disturbing symptoms persist [12].

Despite this, most clinicians (72%) still regard IBS as a diagnosis of exclusion [13]. A recent systematic review (29 studies, Europe, US, Middle East and South East Asia) showed that few primary healthcare providers (PHCPs) were aware of (2-36%) or used (0-21%) FGID diagnostic criteria [14]. Despite most expressing confidence in diagnosing FGIDs, 4-40% of cases were referred to specialist care [14], with an 11% referral rate in Australia for IBS alone [15]. The considerable variability in the approach to IBS diagnosis and management within primary care is reflected in the range of individual PHCP referral rates (1-80%) [16]. Although most FGID patients are managed within primary care [16], those referred represent a large portion of the workload in gastroenterology, with estimates as large as 30% in the UK [17] and 50% in US [18]. In some health systems, such as Australia, non-urgent disorders such as FGID are deferred to very long waiting lists with many patients never being seen. A Canadian study found that less than 10% of patients referred with uninvestigated dyspepsia were seen by a specialist within 6 months [19].

Referrals without a time limit, large specialist referral loads and limited health resources have resulted in a public health problem that is frustrating for patients, PCHPs and gastroenterologists alike, with many patients facing extraordinarily long wait times. An understanding of the factors that influence the referrals of patients to tertiary referral centres, is needed to address this growing public health problem. Thus, the current study

aimed to describe the quality and drivers of referrals for patients with likely FGID, and explore patient experience of clinical management in the context of Australian health care.

METHODS

This cross sectional, mixed-methods study is nested within an ongoing randomised controlled trial that is examining an algorithm-based approach to the diagnosis and management of FGID (ACTRN12614000602628) [20]. All patients referred to one gastroenterology outpatient department (June 2013-July 2015) in a tertiary referral centre (metropolitan city of 1.3 million people), triaged as 'likely FGID' with chronic or recurrent epigastric/abdominal pain with or without altered bowel habit (diarrhoea, constipation or both), bloating, nausea and vomiting, and the absence of red flags, were invited to participate (n=382) (Figure 3-1 Flowchart of patient progression through the study. . Patients were excluded where the referral indicated predominant reflux symptoms, evidence of current *H. pylori* infection, positive faecal occult blood test or recent symptom onset (<6 months). Additionally, those younger than 18 or older than 75 years of age, pregnant, intellectually or mentally handicapped, or judged to have poor English communication skills were excluded. All participants completed a demographic survey (n=110) and those randomised to the algorithm group (2:1 ratio, sequentially) completed an additional structured medical history questionnaire (n=90). Referring PCHPs of participants in the algorithm group were also invited to complete a patient-specific questionnaire comprising open-ended and multiple-selection questions regarding reasons for referral and confidence in diagnosing FGID. Patient symptom severity was measured by the Gastrointestinal Symptom Rating Scale (GSRS)[21] across 5 dimensions on a 7-point Likert scale with 7 being the most negative. All PCHP responses were anonymous.

Data analysis

Referral quality of the algorithm group was assessed using content analysis, following the steps outlined by Neuendorf (22). Coding categories were prospectively defined by a Senior Gastroenterologist (JMA) and included criteria routinely used to triage referrals. Ten referrals were analysed by two independent coders (EL, MS). Coding was compared and the final categories and rules jointly decided by consensus between all investigators. In total, 90 referrals were coded and frequencies recorded. Referral codes were verified back to the raw data on the first 70 referrals (EL) to ensure coding consistency. Referral data were compared to patient questionnaire responses. Any discrepancies noted between referrals and patient questionnaires were cross-checked for accuracy (MS, EL).

Open-form responses from both patient and PCHP questionnaires were also subject to content analysis (EL, JMA). Where appropriate, codes were combined to explore over-arching themes in the responses. Data were analysed using SPSS 24. Mean and standard deviation (SD) or median and interquartile range (IQR) were reported for ordinal data. Pearson's Chi-square test of association was conducted where appropriate, with significance ≤.05.

Ethics approval

This protocol received Human Research Ethics Approval. All participants received an information sheet and given the opportunity to ask further questions by telephone prior to intake. Receipt of signed consent form or completion of the intake survey signified informed consent.

RESULTS

Patient Description

Demographics

Patients who completed the intake survey (n=110, Figure 3-1) were 64% female, 54% married/de facto, with mean age 42 y (SD 15). The median time on waitlist was 113 days (IQR 69-217). Most were in paid employment (24% part-time, 37% full-time) and had completed high school or further education (80%) (Table 3-1). Non-responders were comparable to responders in age and gender (63% female, M=41.3 years, SD 16.0), and were referred within the same period.

Symptom duration was greater than 2 years in 69% (24% >10 years) of patients. A gastroenterologist had been previously consulted in 35% of patients (53% of these, more than once) and 25% of patients had presented to hospital (79% of these, more than once) for their gastrointestinal symptoms. A third of the repeat-consulters (14/38) had seen the gastroenterologist within the past 2 years. Medical and psychological comorbidities were common (56% and 40% respectively). First-time and repeat specialist consulters were comparable in age, gender, relationship and employment status, and presence of medical and psychological comorbidities. However, repeat consulters had a significantly longer symptom duration (M=20.7 years, SD 29.6) than first-time consulters (M=5.6 years, SD 12.8, $t(105)=3.699$, $p<.001$). Five patients in the algorithm group were diagnosed with organic disease following the algorithm-based screening tests (2 inflammatory bowel disease, 1 neoplasm, 1 pancreatic insufficiency, 1 reflux oesophagitis).

Health characteristics

The majority (78%) of patients were using at least one current FGID treatment (any type) with little or no symptomatic improvement reported in 69% of these. A large portion of patients (60%) had consulted their PCHP in the previous 4 weeks, 61% of these due to the gastrointestinal symptoms indicated in the referral, and three had presented to the Emergency Department for gastrointestinal symptoms in the previous 4 weeks. 67% of patients had spent money on symptom relief in the previous 4 weeks with amount ranging from $5 to $1000 (median $45, IQR $23-$100). One patient spent over $1000 flying interstate to seek medical help from a gastroenterologist perceived to have greater expertise and two patients commented on a lack of funds for treatment (*"I don't have much money to spend"* Patient 73, *$12 for scripts. No other because of lack of funds"* Patient 104). Allied health professionals were consulted by 14% of patients within the previous 4 weeks, with an average associated cost of $90 (IQR $63- $263). Three patients indicated that they had not spent money on allied health because they had *'given up'* (Patients 55, 87) or seen *"little or no effect"* (Patient 83), and a few indicated that they *'cannot afford'* allied health (Patients 75,90).

Overall, patient satisfaction with their current symptoms was low (median=3, IQR 1-5) varying along a 10-point Likert scale (lower values indicating lesser satisfaction). Persistent and/or distressing symptoms were reported by 38% of patients, with an additional 8% who experienced reduced quality of life due to their symptoms (Figure 3-2). At intake, 19 (17%) reported few or no symptoms and attributed this to variability in their symptom presentation. Symptom severity (GSRS) cohort results were: diarrhoea syndrome median=2 (IQR 1-4), indigestion syndrome median=3 (IQR 2-4) constipation syndrome median=2 (IQR 2-4), abdominal pain syndrome median=3 (IQR 2-4), reflux syndrome median=2 (IQR 1-3). First-time and repeat gastroenterologist consulters were comparable in symptom severity, symptom satisfaction, symptom response to current treatment, as well as healthcare utilisation and cost of treatment over the past 4 weeks.

Patient Reported Description of Management

Most patients reported not having been given a diagnosis by their PCHP (76/110, 69%), whilst 18% reported provisional diagnoses of IBS (20/110; 8 being uncertain) and 4% (5/110) reflux-related disorders. Similarly, almost half of the patients who had previously consulted a gastroenterologist reported not receiving a diagnosis from their specialist (18/38) (Table 3-2). The most common specialist diagnoses acknowledged included IBS (n=9; 2 being uncertain) and reflux/gastritis (n=4) with three patients unable to recall the

diagnosis. Patients expressed concern about the presence of painful and/or distressing symptoms (37%) and fear of either missed serious pathology or that the symptoms would progress to something more serious (24%) (Table 3-3).

Satisfaction with management

Patient satisfaction with their clinical management at study intake was poor: 40% dissatisfied and 36% only partially satisfied, with no difference between first-time and repeat consulters (Figure 3-2). Only 12 patients reported being well satisfied with their management. Several themes emerged in patients' responses regarding management, including the lack of provision of a diagnosis and, therefore, lack of effective treatment options, frustration with the 'system', and the belief that further investigations were needed (Table 3-4). Furthermore, dissatisfaction with management was significantly related to the 'lack of provision of a diagnosis/treatment options' ($\chi^2(33) = 76.985$, $p < .001$), with 33% of partial/fully dissatisfied patients reporting lack of diagnosis. In addition, 16% of dissatisfied patients were satisfied with their PHCP but awaited a specialist appointment, 12% reported ineffective management options and 12% dissatisfaction with PHCP.

Description of Referrals

Profile of Referring PCHPs

Referral quality was assessed for patients allocated to the algorithm group who completed the intake survey (n=100, Figure 3-1); 89 were unique referrals from 78 PHCPs in 60 practices, 11 were referrals from other units within the hospital. Of the 90 PHCP requests (to 78 PCHPs) to complete a patient specific survey (patients who completed screening in the algorithm group, (Figure 3-1), 61 (68%) responded (36 males); 42/61 were at least 40 years of age and 50/61 has 6 or more years' experience as a primary healthcare physician (n=39>10 years, 23>20years).

Referral Quality

Overall the quality of referrals was poor; 6% were poorly legible, and many lacked basic important information such as patient age (49%), gender (27%), symptom duration (50%), smoking status (96%), alcohol history (94%), and medical (33%) and psychological (84%) comorbidities. Issues related to mental health and alcohol appeared to be automatically generated and were not integrated into the narrative for referral.

The presence or absence of clinical alarms was not stated in 71% of referrals. Alarms were consistently under-reported when compared to patient responses from the structured health questionnaire (Figure 3-3). Provisional diagnoses and clear reasoning for the referral were not provided in 68% and 75% of referrals respectively. Endoscopic investigation was requested in 33% of referrals and 40% of these failed to provide a reason for the request.

Reasons for Referral

Despite comment from one PCHP that *"there is usually a very good reason to refer to a consultant; unavailability of an investigation, uncertainty of diagnosis, patient anxiety etc."*, reasons were communicated clearly in only 25% of referrals (Figure 3-4). The most common reason stated in the referral was to request investigations or patient request. When directly asked for the reason for the referral, a third of PCHPs did not provide a rationale for the referral; 16 simply relisted the symptoms and 4 declined to answer. Where reasons were stated, common reasons included: persistent symptoms, request for endoscopic procedure, inability to reach a diagnosis and confirmation of diagnosis. Other reasons selected from a structured list included to ensure nothing is missed, non-response to treatment, allay patient fears and inability to meet patients demands.

Approximately half the PCHPs (28/60) were confident that their patient had a FGID in response to the forced multiple-choice question *"Based on your current investigations, are you confident that this patient has a functional gastrointestinal disorder?"*. Of these, 16 sought confirmation of the diagnosis, 4 treatment advice and 8 a second opinion at patient request. A third (27/60) indicated that they were "*unsure"* (n=20) or *"not confident"* (n=7) and would like advice. One PCHP commented *"I am very happy to manage functional GIT disorders and would not refer these to a GI unit unless I felt a SOL* [space-occupying lesion] *needed exclusion".* Five PCHPs were confident of an alternative organic diagnosis (although 3 could not suggest what this was).

DISCUSSION

The referrals together with PCHP and patient survey responses provide a novel, multi-faceted window into the real-world management of FGIDs in Australia. Moreover, the use of both qualitative and quantitative analyses yields rich information on patient and practitioner perspectives to help better explain how and why the model of care for this highly prevalent group of disorders needs changing to deliver better quality care. This is of personal, community and financial importance given the high prevalence and cost of

these disorders. This study identifies four important issues which represent opportunities to improve the management of FGIDs: 1) patient dissatisfaction with management despite recent PCHP consultation for their GI symptoms, and/or previousgastroenterologistconsultation; 2) the lack of provision (and/or acceptance (22)) of a clear diagnosis to patients (in both primary and tertiary care); 3) low real-world confidence of some clinicians in diagnosing and then communicating a FGID diagnosis; and 4) poor referral quality with many omitting routine information and specific alarms which are required for safe, active triage.

Patients and clinicians are known to differ in their perception of symptom frequency and pain levels [23]. Whilst patient-reported symptoms might be considered subjective and exaggerated, (particularly in FGID with high rates of anxiety and/or depression), patient satisfaction with care is a valid and important indicator of effective management. We found that the outcome of both primary and tertiary care management of patients referred with suspected FGID was poor, with a significant proportion of patients dissatisfied despite recent PCHP and/or previous gastroenterologist consultation. Dissatisfaction was related to the lack of diagnosis and treatment options and is a potential driver of repeat consultation. The provision of a clear, timely, accurate diagnosis is recommended to move patients onto a management pathway rather than a prolonged search for an alternative diagnosis. The reported lack of diagnosis may reflect poor patient recall, patient non-acceptance of a functional diagnosis [23], or poor communication of diagnosis by the clinician [24]. Although this study did not differentiate between lack of recall and lack of actual diagnosis, poor recall is less likely, as 1) patients were willing to report 'unsure' or 'possible' IBS diagnoses, 2) patient reports were supported by the lack of diagnoses (provisional or otherwise) within the actual referral and 3) patients with medically unexplained symptoms often report many more diagnoses than can be confirmed [25].

Recent studies have shown that most GEs and PHCPs continue to regard IBS as a diagnosis of exclusion [13, 26]. Only 52% of GEs and 34% of PHCPs were confident diagnosing IBS based on symptoms, history and physical exam, with less than half of these confident to inform the patient without further investigations [13]. This is also supported by the reluctance of PCHPs to add IBS read-codes to patient records until more serious pathology was excluded [27]. Our results, together with the existence of referrals for suspected FGIDs suggest that the real-world confidence of some clinicians in diagnosing FGIDs and communicating this diagnosis is low.

A significant proportion of PCHPs referred to specialist care for confirmation of a FGID diagnosis (not stated in referral), at the request of the patients or for further investigations. The PHCP sample was slightly younger and less experienced than the national average: 31% were under 40 years compared with 24% under 44 years nationally; 43% had been in practice for more 20 years compared to 64% [28]. As PHCP surveys were unidentified, we were unable to explore whether lack of diagnostic confidence was related to age or experience. However, the paucity of provisional diagnoses of IBS flagged in the referrals, suggests this is a problem that crosses experience and age categories. PCHPs' perception of the necessity for further investigations in the absence of alarm features was also reflected in the patients' belief that they could receive no diagnosis or treatment options until endoscopic procedures were performed. The lack of confidence PCHPs have in diagnosing and/or managing FGIDs was found to be the main driver of these referrals.

Paradoxically, chronic symptoms appear to also be driving diagnostic uncertainty and desire for specialist input to exclude other diagnoses and reassure patients, whereas, long term non-progressive symptoms are highly likely to be functional. Although specialist input per-se in these conditions, is not unreasonable, current public health resources cannot fund the demand. Consistent with this reality, current guidelines recommend an initial diagnosis based on symptomatology, followed up with simple investigations, prior to receiving a clinical diagnosis of FGID [12, 29], and NICE guidelines recommend this occurs within the primary care setting (12). Well-defined pathways for diagnosis and management, which can be implemented in primary care, may help reduce referral burden by selecting only those patients failing current evidence-based management options, and assist early, effective diagnosis and management.

These tertiary referrals represent a portion of FGID patients seen in primary care and tertiary care [16, 17] and may reflect a subset of clinicians who struggle to manage FGID or a particularly difficult patient group. FGID management can be challenging; persistent symptoms that fluctuate in severity or even change (for example, dsypeptic to intestinal symtpoms) are not uncommon, with patients rarely becoming totally or durably symptom-free [30, 31]. There is, however, consensus on both the diagnostic and management approach that should be taken. Further studies within primary care are needed to ascertain PCHP awareness of how FGID should be diagnosed and managed according to current best practice. Efforts to develop locally relevant consensus and shared belief between primary and tertiary care on best practice, and clinical pathways which promote quality patient care are needed. An assessment of the quality and availability of PCHP resources (e.g. online pathways, educational sessions), opportunities to partner with

specialists to develop and deliver best practice approaches (which include referrals), and of other barriers such as funding structures and access to FGID specialised allied health professionals will also inform where gains can be made. With this and the data from the current study, the development of FGID clinical pathways may streamline and optimise patient care across primary and tertiary sectors.

The current study may be limited in generalisability, as it was conducted in one tertiary hospital. However, this appears unlikely as a recent systematic review of 29 studies (Europe, North America, Middle East; South East Asia) found 4-40% of patients suspected of having FGID were referred for specialist consultation [32], indicating that our referral load and thus primary care management problems are not unique. A strength of our study is the use of a mixed methods approach to triangulate data from actual referrals, referring PCHPs and the patients themselves, to gain a more comprehensive understanding of FGID management.

CONCLUSION

Current management of FGID is suboptimal, as evidenced by the tertiary referral load, patient dissatisfaction, the lack of provision of diagnoses and effective treatment options long and long waiting lists for specialist review. Some clinicians lack confidence in effectively identifying and managing these conditions. This may stem from a lack of awareness of current best practice and how to access evidence-based management options. Further research into FGID management is needed. Resources such as clinical guidelines, pathways and structured online referrals, may improve patient care by optimising the satisfaction of FGID management in primary care, and facilitating the onward referral of only the subset of people with FGID who struggle to manage after implementing simple evidence-based management options.

List of Abbreviations

FGID, functional gastrointestinal disorder
IBS, irritable bowel syndrome
PHCP, primary healthcare providers
GSRS, gastrointestinal symptom rating scale
SD, standard deviation
IQR, interquartile range
M, mean

Declarations

Ethics approval and consent to participate

Ethics approval was received from the Royal Adelaide Hospital, Human Research Ethics Committee; RAH Protocol No. 140143. Informed consent was obtained prior to patient inclusion in trial.

Consent for publication

Identifiable patient information has not been published. Informed consent included permission to publish unidentifiable patient information.

Availability of data and material

The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests

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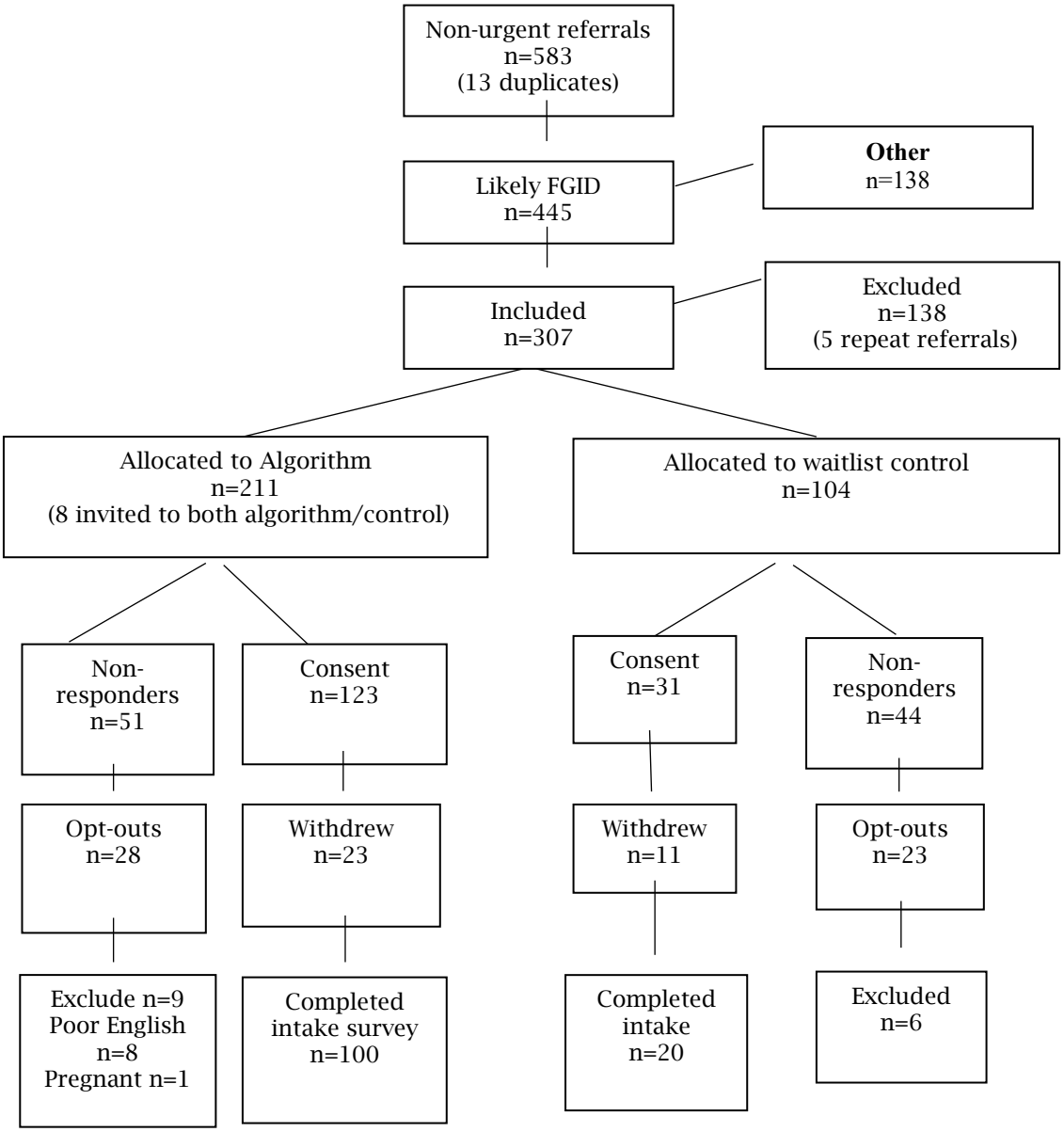

Figure 3-1 Flowchart of patient progression through the study.

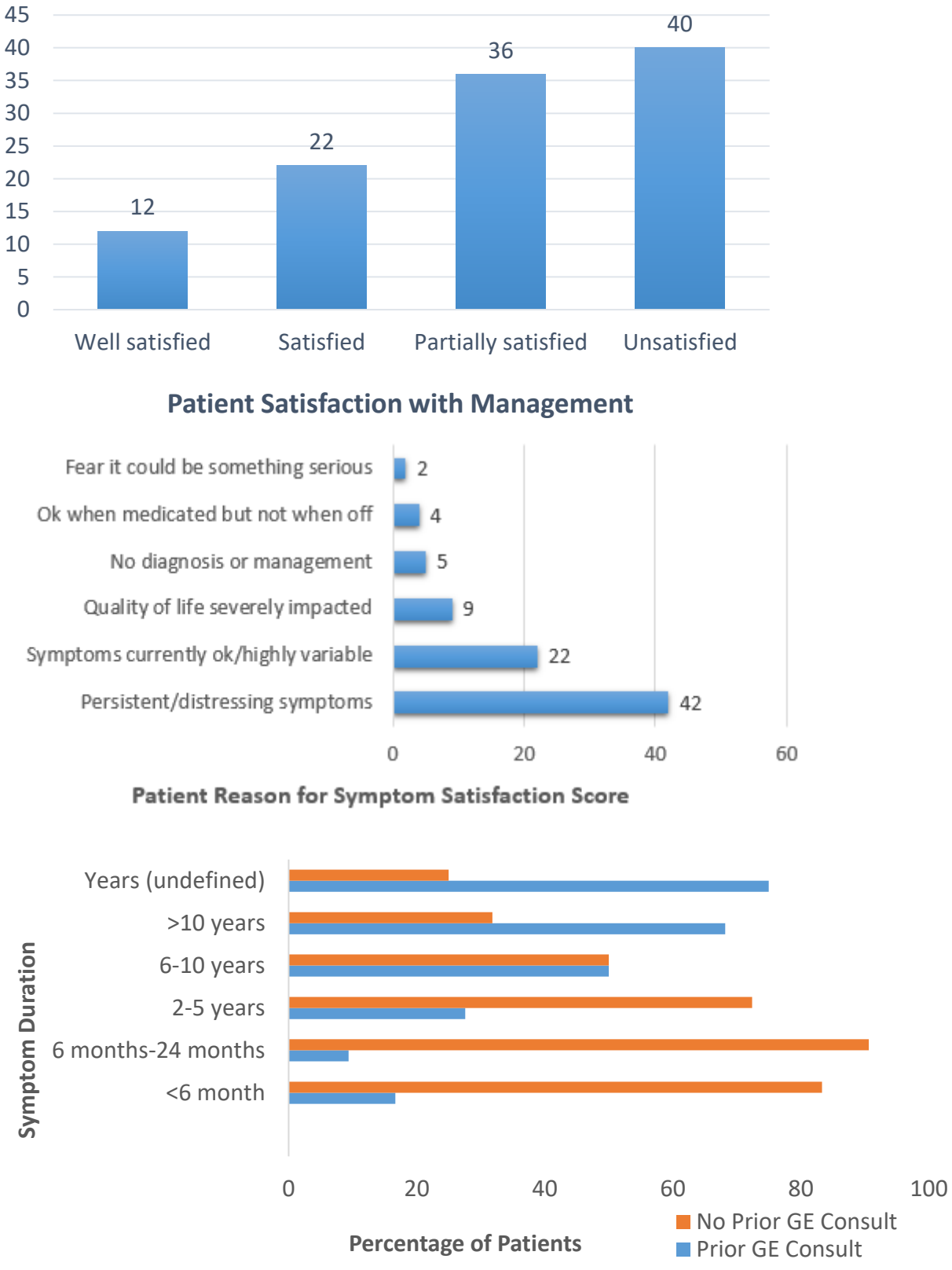

Figure 3-2 Clinical demographics of patients referred with suspected FGID

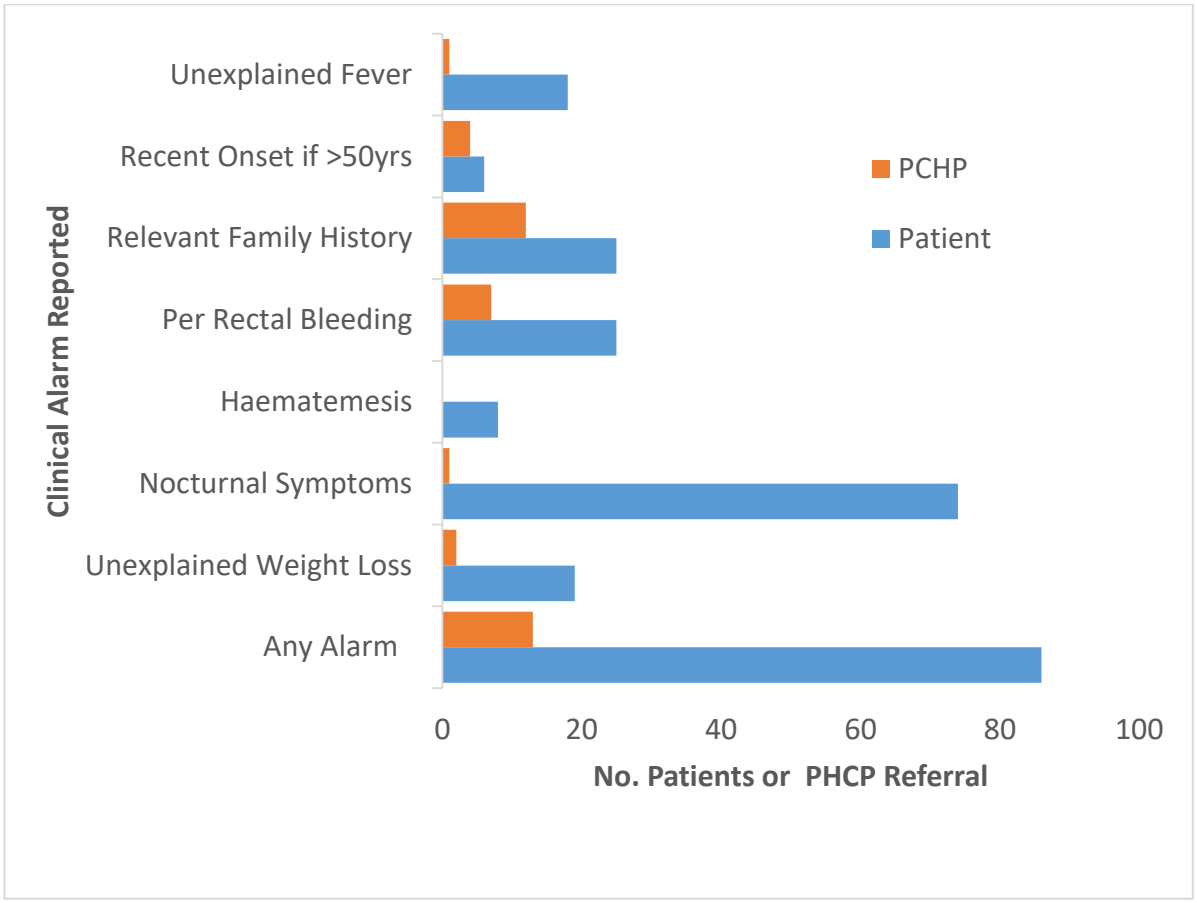

Figure 3-3 Comparison of the frequency of patient reported clinical alarms versus PHCP referrals

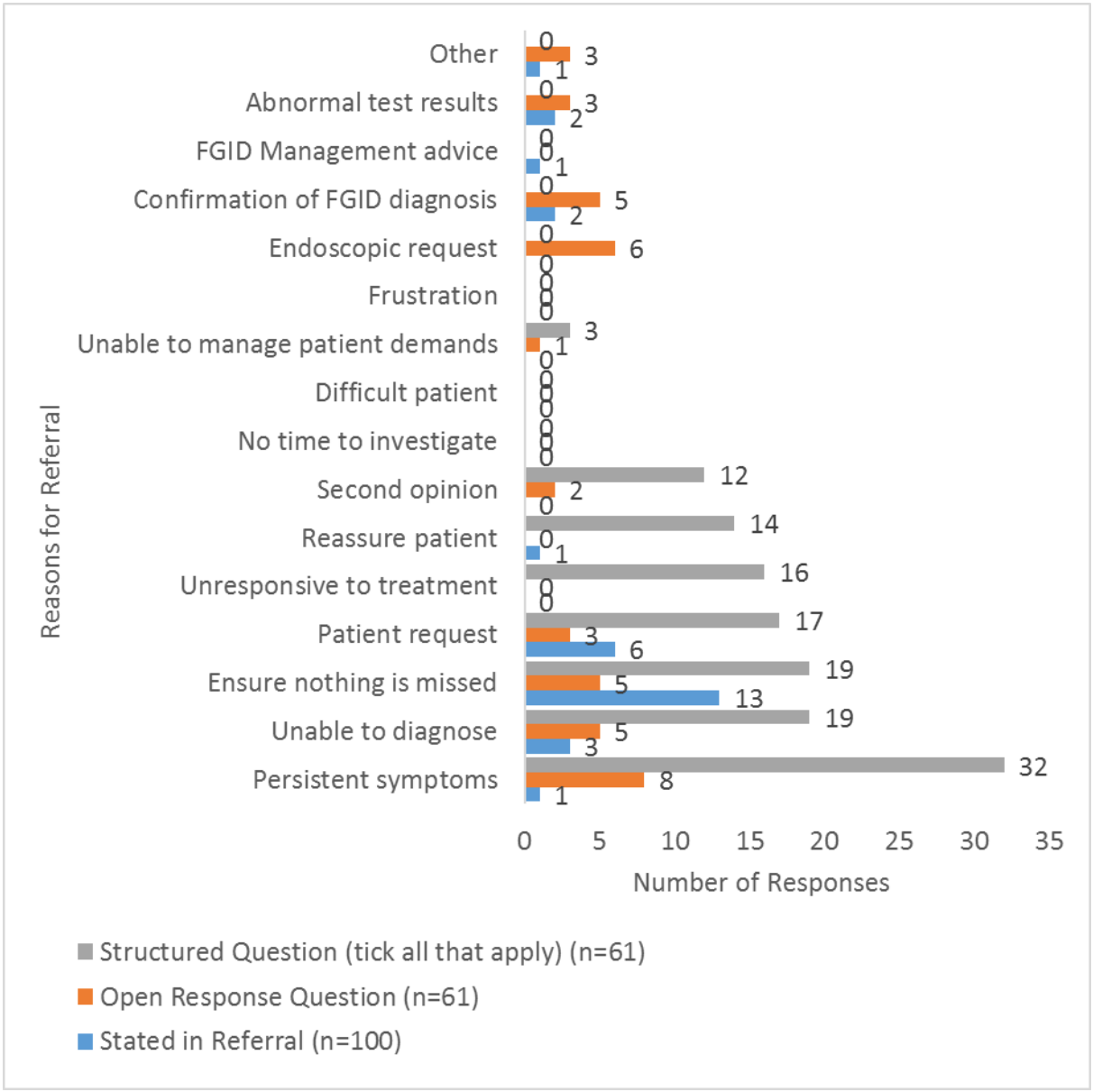

Figure 3-4 Reasons for referrals as stated in referral and primary healthcare provider survey responses.

Table 3-1 Personal and clinical demographics of patients referred with suspected FGID (n=110)

		All patients (n=110)	Prior Gastroenterologist Consultation	
			No (n=72)	Yes (n=38)
Personal Demographics		**n (%)**	**n (%)**	**n (%)**
Gender	Female	71 (64)	46 (64)	24 (63)
Language	English	98 (89)	63 (88)	35 (92)
Relationship	Married/De facto	60 (54)	40 (56)	20 (73)
Employment	Full-time (>35 hrs/week)	41 (37)	28 (39)	13 (34)
	Part-time (<35 hrs/week)	27 (24)	16 (22)	11 (29)
Education	Year 11 or below	23 (21)	15 (21)	8 (21)
	Year 12	22 (20)	15 (21)	6 (16)
	Higher Education	66 (60)	42 (58)	24 (63)
Clinical Demographics				
Medical comorbidities		61 (56)	41 (57)	20 (53)
Psychological comorbidities		44 (40)	29 (40)	15 (40)
Diagnosed by referring PHCP		34 (31)	18 (25)	16 (42)
Satisfaction with management	Well satisfied	12 (11)	6 (8)	6 (16)
	Satisfied	22 (20)	18 (25)	4 (11)
	Partially satisfied	36 (33)	23 (32)	13 (34)
	Unsatisfied	40 (36)	25 (35)	15 (40)
Symptom satisfaction score reason	Persistent/distressing symptoms	42 (38)	28 (39)	14 (37)
	Symptoms currently OK	22 (21)	17 (24)	5 (13)
	Quality of life severely impacted	9 (8)	6 (8)	3 (8)
	No diagnosis or management	5 (5)	4 (6)	1 (3)
	OK when medicated only	4 (4)	2 (3)	2 (5)
	Fear it could be something serious	2 (2)	1 (1)	1 (3)
	No reason given	26 (24)	14 (19.4)	12 (11)

Table 3-2 Patient reported existing or provisional diagnoses

Reported diagnosis	Total	Prior consult with gastroenterologist	
	n=110	No (n=72)	Yes (n=38)
	n (%)	n (%)	n (%)
No diagnosis given	69 (63)	54 (75)	18 (47)
IBS	11 (10)	6 (8)	7 (18)
Possible IBS	8 (7)	5 (7)	2 (5)
IBS plus other	3 (3)		
Reflux/heartburn/dyspepsia/gastritis	3 (3)	1(1)	4 (11)
Possible peptic/gastric ulcer	2 (2)	2(3)	
Gastric ulcer	1(1)	1 (1)	
Diagnosis not reported by patient	2 (2)		2 (5)
Gallstones	1 (1)	1 (1)	
Possible gallstones	1 (1)		
Fatty liver	1 (1)		1 (3)
“Collapsed colon” and fatty liver	1 (1)	1 (1)	
Diverticulosis	1 (1)		
HP Infection	2 (2)		1 (3)
‘A floppy valve-oesophagus’	1 (1)		1 (3)
‘Haemorrhoids, narrow colon near anus’	1 (1)		1 (3)
Hiatus hernia	1 (1)		1 (3)
Lactose intolerance/? underlying issue	1 (1)	1 (1)	

Table 3-3 Frequency table of the main concerns patients have regarding their gastrointestinal symptoms

PATIENT CONCERNS	n (%)
Painful/distressing symptoms	**41 (37)**
"Sometimes very painful. Stomach cramps, diarrhoea. Concerned will throw up in public. Abdominal pain and discomfort."	
Fear of missed pathology	**26 (24)**
"(I'm) scared of the possibility of bowel cancer"	
"(I) hope it isn't anything worse"	
"I do not want it to lead to stomach cancer"	
"By now I could even be at an advanced stage of bowel cancer, which is causing massive fear and anxiety!!!"	
Not knowing the cause	**18 (17)**
"I don't know what is causing it"	
"I want to know what it is and how to manage the illness"	
"I would like a diagnosis to confirm that there is no other reason for them"	
"Would like to know what I have"	
Impaired daily life	13 (12)
"This seriously affects my daily routine"	
"Can't go anywhere. Can't eat foods that I like. Not able to control it. No quality of life"	
"Difficulty in adhering to current work schedule"	
"I am unable to seek or gain employment…. a lot of the time I am unable to cope well with my everyday responsibilities of being a parent caring for two children while experiencing these symptoms"	
Unable to control	5 (5)
"I cannot control the symptoms"	
"I don't know what to do to eliminate the pain"	
Not satisfied with FGID diagnosis	1 (1)
"I am sick and tired of feeling sick and tired, and the classic 'diagnosis of exclusion' IBS. Not to mention Low – FODMAP and countless other fad diets to try to placate patients"	

Table 3-4 Themes regarding patient satisfaction with management

Theme 1: No diagnosis and/or management
• *"… has offered no assistance, has told me I need to learn to live with it"* • *"Have no diagnosis, nor any idea how to treat it"* • *"I…was only given pain relief which seems to put a Band-Aid on the problem but hasn't solved why, or what is causing the problem"* • *"I've seen different PCHP's and at this stage, all they have been able to offer me are various tests. This has been going on for a few years"*
Theme 2: Frustration
• "*My PCHP is trying his best but now I can't afford private health insurance I am on long public waitlists when I'm extremely ill"* • *"Long waiting lists, difficulty getting started / getting healthcare going"* • *"No results, constant hand balling. Ultimately no relief and now on a 12-month waiting list for the next step"* • *"She tries her best; it is not her fault that the system is completely broken"* • *"The public system sucks"*
Theme 3: Belief that further investigations are needed
• *'My current doctor has done all he can but because I haven't had an endoscopy or colonoscopy he can't really do much"* • *"I am still not fully diagnosed, therefore I am concerned to know what my health problem is and how to manage it"* • *"PCHP has investigated with no success then referred to specialist, have not seen a specialist yet"* • *"I doubt my PCHP knew it would be this long and still no colonoscopy. I hope once I have this we can plan treatment"* • *"To cover all bases, she sent me to have an ultrasound, which came back clear. Next step was obviously to have the colonoscopy but the way it looks I won't be seen for a long time. I wish she had another idea of what it could be and how to investigate it but it seems not...pity"*

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Chapter 4 : The Importance of Diagnostic Language In FGIDS

BACKGROUND

The introductory chapter of this thesis highlighted the gap which exists between current guidelines and actual clinical practice. Despite recommendations to diagnose FGIDs on the basis of symptoms and absence of clinical alarms, using minimal tests, many clinicians maintain a clinical approach which focusses on the exclusion of organic disease. Furthermore, although clinicians may consider a differential diagnosis of FGID, they are reluctant to communicate this to the patient or document a FGID as the final diagnosis. It is acknowledged that there may be many reasons for this, not least being fear of missing a serious diagnosis, such as bowel cancer, and/or fear of litigation. In order to develop an effective clinical pathway for the diagnosis and management of FGIDs, to be trialled within the Royal Adelaide Hospital, it was necessary to explore the clinical approach within this local context.

This paper, explores and describes differences in clinician approaches to functional and organic gastrointestinal disorders in tertiary care. A retrospective audit of letters written to referring doctors following an outpatients' consultation, which communicated a diagnosis of either a FGID or organic disorder, were used as proxy to the specialist consult itself. This was preferred over an observational study of the consultation, as clinicians had no prior knowledge of the study nor opportunity to alter their clinical approach, thus allowing real world insight into the clinical approaches used by specialists dealing with patients with FGID.

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Statement of Authorship

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Principal Author

Name of Principal Author (Candidate)	E.C. Linedale		
Contribution to the Paper	Principal researcher: planning/conducting the study, collecting, analysing, interpreting the data and writing the manuscript.		
Overall percentage (%)	70%		
Certification:	This paper reports on original research I conducted during the period of my Higher Degree by Research candidature and is not subject to any obligations or contractual agreements with a third party that would constrain its inclusion in this thesis. I am the primary author of this paper.		
Signature		Date	20/06/2017

Co-Author Contributions

By signing the Statement of Authorship, each author certifies that:

i. the candidate's stated contribution to the publication is accurate (as detailed above);

ii. permission is granted for the candidate in include the publication in the thesis; and

iii. the sum of all co-author contributions is equal to 100% less the candidate's stated contribution.

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|MANUSCRIPT 2| UNCERTAIN DIAGNOSTIC LANGUAGE IN FUNCTIONAL GASTROINTESTINAL DISORDERS: A POTENTIAL DRIVER OF ENDOSCOPIC INVESTIGATIONS, REPEAT CONSULTATIONS AND DISCARDED DIAGNOSES.

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ABSTRACT

Background and Aims

Despite recommendations that functional gastrointestinal disorders (FGID) can be clinically diagnosed with minimal investigations, they are known to account for high costs from both consultations and investigations. We sought to understand whether this might be driven by specialist clinicians' behaviour. The aim was to examine whether there are definable differences in clinician approach to organic gastrointestinal disease (OGID) as compared to FGID.

Methods

Diagnostic letters and case notes relating to patients with both organic and functional GI disorders were examined. Letters were subjected to content analysis and case files reviewed to determine which investigations had been undertaken and the results of these.

Results

Analyses were conducted on 207 letters, 119 FGID and 108 OGID. Two distinct language types emerged, either clear or 'qualified': consistent with a level of certainty (or lack thereof) on the part of the author. A typical example was "the patient is diagnosed with…." vs. "it is possible that this patient might have….". Qualified diagnostic language was used significantly more often in letters regarding patients with FGID as compared to OGID (63% vs. 13%; $p<.001$). In addition, patients with FGID were found to be endoscopically investigated more often than those with OGID (79% vs. 63%; $p<.05$).

Conclusion

There is a considerable amount of diagnostic uncertainty conveyed by the language specialists' use in correspondence regarding patients with FGID. This may contribute to the suboptimal patient engagement with a diagnosis of a FGID and the use of further "unwarranted" endoscopic investigations.

Keywords functional gastrointestinal disorders; diagnosis; management; endoscopy

INTRODUCTION

Functional gastrointestinal disorders (FGID) are highly prevalent, affecting 40% of the population in their lifetime [1], accounting for 25-50% of gastroenterology referrals [2]. They are associated with reduced quality of life and significant costs to the patient and community [3]. Despite the high prevalence of FGID and the clear impact of these disorders on patients and the community, they are poorly handled in the healthcare system [4].

Historically, FGIDs had been regarded as diagnoses of exclusion, leading to a high investigative burden. However, since the advent of the Manning criteria [5], it is now well documented that a safe, positive diagnosis can be made based on symptoms along with exclusion of relevant differential diagnoses with minimal investigations [6, 7]. Yet, anecdotally, general practitioners appear to persist with a 'diagnosis-of-exclusion' approach to these disorders as judged by the large and increasing number of referrals of patients with suspected FGID for invasive procedures. Even within specialty care, an overuse of investigations is widely acknowledged to occur, with repeat consultation being a major driving factor [8].

Understanding the drivers of repeat consultation is important to the successful management of FGID. Suggested driving factors include patients' fear of a missed organic diagnosis [9], concurrent psychopathology [10], patients' beliefs about symptoms (illness perceptions), faulty cognitions such as catastrophizing and excessive monitoring [11], persistence of symptoms [4], and patients' uncertainty and/or lack of acceptance of diagnosis [4, 12].

Despite the potential impact of a lack of patient acceptance of diagnosis on successful management of FGID, there have only been two small studies conducted to date, in South Korea and Australia [12, 13]. These indicate that the concept of a positive FGID diagnosis is unacceptable to the majority of the population [13], with only one out of 13 patients accepting of the diagnosis [12]. Collins [12] concluded that lack of acceptance was not due to communication failure as the diagnosis was clearly documented in the medical records, nor to a deficit of health literacy. However, given the disagreement in patient and doctor perceptions of communication skills displayed in consultations [14], the possibility remains that the diagnosis noted in the medical records are not being clearly conveyed to patients, thus influencing patient acceptance of the diagnosis. The concept of a "discarded diagnosis" was coined by Collins [12] to describe the occurrence of a patient not acknowledging and/or accepting a FGID diagnosis.

Anecdotally, these issues of discarded diagnoses, repeat consultations and the overuse of investigations do not appear to occur in organic gastrointestinal disease (OGID). We then considered that this difference between how patients with functional and organic gastrointestinal disorders perceive their diagnosis might stem from differences in the language used by the specialist during diagnosis. Without resorting to recorded consultations (which might bias actual behaviour), we sought to examine specialist communication by using the proxy of reviewing their letters dictated after patient consultations. The aim of this study was, therefore, to explore and describe any differences in clinician approach to OGID versus FGID by reviewing their medical communication and use of investigations in these two patient cohorts and to determine whether this related to future healthcare-seeking behaviour. We hypothesised that differences between the care that patients with "functional" gastrointestinal disorders receive compared to recommendations may be related to the language used in specialist communication, and that invasive investigations such as colonoscopy and gastroscopy would be performed in a large proportion of patients diagnosed with FGID. We also hypothesised that the type of language used relates to further healthcare-seeking behaviour.

METHODS

Study Design

A retrospective review of outpatient department (OPD) letters written in a tertiary hospital's luminal Gastroenterology Unit was undertaken. Letters written following a patient consultation between 2008 and 2011 were included if written by a gastroenterologist consultant, trainee (minimum 5 years post medical school), senior trainee (7 or more years' post grad) who had worked in the OPD for at least 12 months at the time of writing. Trainees and senior trainees were supervised by way of post clinic debrief and there was no formal review of letters. Consecutive letters were reviewed by a senior gastroenterologist (JMA) and sorted into diagnostic categories of FGID or OGID according to the primary diagnosis written in the letter by the consultant. No instances of missed or alternative diagnosis were identified by investigators when reviewing letters and patient records.

Selection of letters continued until approximately 100 were obtained in each group (n=213). Incomplete letters, referral letters and non-patient contact letters were subsequently excluded (n=6), leaving 207 letters for content analysis. Letters pertaining to FGID were subsequently analysed to explore factors related to the language used within this subset of disorders. Specific clinical investigations documented in FGID letters were

also noted. Medical records obtained for patients who had undergone a gastroscopy or colonoscopy (as noted in the letter) were assessed for appropriateness using alarms-based criteria. Investigations were considered appropriate where clinical alarms (Table 4-1) or relevant abnormal test results were noted [15].

Content Analysis

Letters were subjected to content analysis following the steps outlined by Neuendorf [16]. Five letters from each group were analysed and categorised according to repetitive content by two independent coders (EL and ACH). The final categories (n=11) and rules were jointly decided by the coders and a senior gastroenterologist (JMA) by means of consensus. The remaining letters were coded by the principal researcher (EL) and frequencies counted. After the first 40 letters were analysed (EL), the codes were verified back to the raw data on a random sample of 10 by a second researcher (ACH) and the codebook was reviewed and adjusted accordingly. Coding was completed on the remaining sample by EL and a 20% random sample by ACH in order to determine inter-rater agreement to ensure consistency. Inter-rater agreement as assessed on a random sample of 20% of the letters coded was 100%.

Outcomes

Primary outcomes were the coding categories identified in the content analysis, which included the type of diagnostic language used and various aspects of the clinical approach taken (Table 4-1). Secondary outcomes were the healthcare-seeking behaviour of the patients as determined by the number of presentations within the public healthcare system 12 months' post consultation.

Data Analysis

The letters were examined to explore whether language type was related to the type of disorder. Other variables that may have influenced the use of clear or qualified diagnostic language were also explored, such as patient age and gender, clinician age, gender, seniority, and clinical load as well as whether the diagnosis was new or pre-existing.

Data were analysed using SPSS 22 with statistical significance reported at the 0.05 level. Categorical coding variables were presented as percentages. The Pearson's chi-square test for independence and Fisher's exact test were used to assess for significant associations between the variables, and Odd's Ratio calculated. Student's t-test for independent samples was used to assess the difference in healthcare seeking behaviour between the two language types in the patients with a functional diagnosis.

Ethics & Bias

Ethics approval was obtained from the Royal Adelaide Hospital Human Research and Ethics Committee prior to review of the letters. Gastroenterologists and patients were not specifically informed of the review of the correspondence as it did not affect care and all letters were de-identified removing patient and clinician details prior to analysis.

Researchers were not blind to the diagnostic category of the letter, but were blind to the clinician author. Three coders were used to minimise potential bias.

RESULTS

Sample description: Letters and clinicians

The 207 letters examined contained 227 diagnoses, 119 being functional and 108 organic. The diagnoses were functional alone in 99 letters (48%), organic alone in 88 (42%) and both in 20 (10%). Diagnoses of FGID comprised irritable bowel syndrome (IBS) (104/119, 87%), functional dyspepsia (FD) (11/119, 9%) and other functional bowel disorders. Diagnoses of OGID comprised inflammatory bowel disease (88/108, 82%), gastro-esophageal reflux disease (10/108, 9%), and other disorders.

The letters were authored by 20 clinicians, 16 of whom were men (145 letters) and four women (62 letters). One specialist (Specialist 3) wrote a large majority of letters in the female group (50/62), and findings are reported with and without this specialist. The specialists varied in level of qualification, and included registrars (specialists in training) (32%, 66/207), fellows (28%, 57/207), consultants (25%, 52/207) and senior consultants (15%, 32/207).

The majority of letters were written by specialists with a clinical load of at least 10 patients in this sample (148/207, 71%). Most of letters (165/207, 80%) were written after a follow-up appointment, with no difference in this proportion between people with functional (83/119, 70%) or organic diagnoses (94/108, 87%). New diagnoses were proposed in 62% (129/207) of all letters, 85% (101/119) of FGID letters and 40% (24/108) of OGID letters, with the remaining pertaining to, or confirming an existing diagnosis.

Sample description: Patients

Patients about whom the letters were written were aged 17-84 (mean 44, SD 17) years, with 61% (127/207) being women. Patients diagnosed with FGID and OGID were comparable in age (mean 45, SD 15 vs mean 44.47, SD 19). Consistent with the usual

Western demographics of FGID, there was a greater proportion of female patients in the FGID letter cohort (77%, 92/119) compared to the OGID cohort (46%, 50/108; p<.01).

Language used in the letters

Two different types of language conveying differing levels of diagnostic certainty were apparent. Examples of 'clear' and 'qualified' language are shown in Table 4-2. The relationships between patient clinical variables and the type of language used are shown in Table 4-3. The category of disorder (i.e. FGID/OGID), whether the diagnosis was new or pre-existing, and the patient gender were all significantly associated with the type of diagnostic language used in all letters. Clinicians were much more likely to use qualified diagnostic language for functional disorders than organic disorders (OR 9.76 [95% CI 5.0-19.05]). Nearly two-thirds of FGID diagnostic letters contained qualified language, compared to the minority (13%) of OGID diagnoses. To determine whether Specialist 3 skewed the data (as she wrote 24% (50/207 of the letters) the analysis was re-run excluding this specialist's data, and an even greater tendency to use qualified diagnoses with functional disorders was seen - increasing from 63% to 70% (p<.001).

Further clinical follow up did not lead to improved diagnostic clarity in FGID letters. Over half of the FGID letters that discussed a pre-established FGID diagnosis continued to use qualified diagnostic language. Overall, qualified diagnostic language was used in more than twice as many letters pertaining to female than male patients, but in equal proportions for both genders in those with FGID. Male clinicians were more likely to use qualified diagnostic language in patients with FGID than female clinicians in our full sample, but when Specialist 3 was excluded no difference was seen.

Investigative Strategy and Clinical Approach to Functional and Organic Disorders

Other differences in the clinical approach used in patients with functional versus organic disorders were also explored. For new diagnoses, the likelihood of endoscopic investigation was high for both FGID and OGID (81% vs 86%). Overall, 79% of patients with FGID underwent gastroscopy/colonoscopy compared with 63% for OGID (p<.05). Gastroscopies were noted in 55% of functional and 20% of organic disorders (p<.001) and colonoscopies in 74% of functional and 58% of organic disorders (p<.05). The average age of patients with FGID endoscopically investigated was under the age of 50 years (gastroscopy: female 43 years, SD 15; male 44 years, SD 12; colonoscopy: female 47 years, SD 15; male, 47 years SD 13).

Medical records of FGID patients were obtained for 44/54 gastroscopies and 50/63 colonoscopies, the remaining procedures were performed elsewhere or more than 2 years prior to the letter. Only 13 gastroscopies were judged definitely appropriate due to the presence of clinical alarms or abnormal test results [15], 11 were clearly unindicated, and 20 uncertain with 'chronic diarrhoea' stated as the indication. Thirty-two colonoscopies were deemed appropriate according to alarm-based criteria. Of the remaining 18 colonoscopies, 3 were conducted in the absence of any clinical alarms features, 10 appeared to be conducted for convenience along with an appropriate gastroscopy, and 5 might be considered appropriate purely for aged-based CRC screening if the patient had never previously undergone colonoscopy.

The use of breath, radiological or stool tests was not found to be associated with the type of disorder. However, blood tests were used more often in organic disorders than functional disorders (50% vs 29%, $p<.001$). Patients with FGID were investigated with radiology to the same extent as those with OGID (26% vs 18%, $p>.05$). Of note is the greater use of tests with a high radiation dose (CT, small bowel series, multiple tests) performed in patients with functional diagnoses as compared with low/no dose options ($t(27)=6.087$ $p<.001$) (Table 4-4).

No differences in the clinical approach to FGID and OGID were detected in terms of the provision of an investigative rationale (documented justification), management plan or prognostic outlook as noted in the letter. An investigative rationale was noted in 25% of all letters regarding FGID and in 40% of FGID letters pertaining to new diagnoses. Only a third of FGID letters explicitly stated that an explanation of the disorder had been given to the patient (36% overall, 38% new diagnoses). Although the provision of a diagnosis did not differ significantly between the FGID and OGID groups for new diagnoses, overall there was a greater chance of a diagnostic explanation being given to patients with FGID (36% vs 19%, $p<.005$). A management plan and patient discussion of this plan was included in the majority of letters regarding both FGID and OGID, but FGID letters were less likely to state that there had been a management discussion with patient (85% vs. 94% $p<0.05$). A prognostic outlook was provided in less than 10% of both FGID and OGID letters ($p>0.05$). The type of follow up arranged was found to be related to the type of disorder with 28% of patients with FGID being discharged to general practitioner care as opposed to only 5.6% of patients with organic disorders ($p<0.05$). Psychological co-morbidities were identified in more FGID than OGID letters (12.6% vs 2.8%, $p<.005$), and the specialists noted the patient's mental health to be relevant to the diagnosis (26% vs 6%, $P<.001$). The number of letters that recorded medical co-morbidities did not vary significantly between disorder types. There was no significant difference in the number of medical encounters

to the hospital in the 12 months following diagnosis between the FGID groups containing clear or qualified diagnostic language (Table 4-5).

DISCUSSION

Despite the high prevalence and costs of FGID there has been a paucity of research regarding the quality and clarity of the communication regarding FGID diagnoses. This study provides new insight into the complex and frustrating problem of the diagnosis and management of FGID, namely that clinicians struggle to provide a clear diagnosis of a FGID to patients and to their referring general practitioners alike. Language conveying diagnostic uncertainty is much more prevalent in FGID than OGID and does not become any more certain with further follow-up appointments. This is surprising given the fact that symptom duration greater than 6 months coupled with absence of alarm features lends itself to a diagnosis of a FGID according to current guidelines [7]. The accuracy of the diagnoses cannot be reliably documented. Diagnosis was however, according to usual specialist practice at that time (using objective markers such as blood in stools, CRP, Hb, Alb, endoscopy to exclude IBD flares; faecal calprotectin was not available). Unexplained symptoms also did not emerge as a coding category as they were not flagged by the specialists.

The communication of diagnostic uncertainty may itself create a significant barrier to a patient accepting that they have a FGID, leading to the so-called discarded diagnosis. This uncertainty may also contribute to ongoing healthcare-seeking behaviour of patients with FGID as has been well documented previously [8, 17, 18]. Although we do not have healthcare seeking data for this particular group, recent data in another of our studies suggests that 66% are consulting the specialist for the first time, and 34% for the 2nd, 3rd or 4th time [19].

This study was not sufficiently powered to detect any difference in the healthcare-seeking behaviour of FGID patients in the clear versus qualified language groups, and this warrants further investigation. Illness perception by a patient can influence important health outcomes such as functioning, treatment adherence and healthcare utilisation and this is informed in part by medical information obtained from the treating clinician [20]. Providing a clear diagnosis at the outset is likely to be beneficial in establishing an understanding of the disorder that acknowledges the functional nature and prognostic outlook: namely the chronic and recurrent nature with management options focussed on the reduction of bothersome symptoms and prevention of dietary and psychological triggers.

Blood tests were found to be used more often in organic disorders than functional, which is consistent with routine use of blood tests regular follow up of IBD and monitoring medication safety. The specific panel of blood tests used was not explored, nor was the 'appropriateness' of these. This was outside the scope of this study, but would be an interesting follow-up. Although data exists exploring the level of appropriateness clinicians assign to different blood tests in FGID in theory [21], current practise has not been evaluated.

The similar rate of endoscopic investigations found in FGID and OGID patients is cause for concern and suggests a diagnosis-of-exclusion approach continues to be applied in mainstream clinical practice. Almost 80% of patients diagnosed with FGID had endoscopic investigations, which is an alarming proportion. It is not possible to evaluate the frequency of repeated diagnostic procedures in this group as some patients have been investigated elsewhere prior to this consult. However, as current guidelines recommend that a positive diagnosis be made without endoscopic investigation, these procedures are therefore inappropriate in the absence of alarms.

One common reason for unindicated procedures was chronic diarrhoea for gastroscopy. Whilst some clinicians may propose that it is reasonable to combine gastroscopy with colonoscopy in these cases the benefit of such an approach is not yet established. Although it is plausible to suggest that, in this tertiary setting, alarm features may have been highly prevalent to account for the high level of endoscopy, this was not supported by our results. Our results showed that about one half of gastroscopies and one third of colonoscopies were conducted in the absence of any clinical alarm features. This is in line with current literature that reports 10-40% of upper gastrointestinal endoscopies and colonoscopies to be unindicated according to current guidelines [22-25]. Additionally, in contradiction to current recommendations, the average age of women investigated by endoscopy or colonoscopy was under 50 years [7, 26].

We did not design this study to look at the drivers for investigations, and so can only speculate. Known drivers of investigation include fear of missed pathology, belief in a diagnosis of exclusion, patient's expectations, litigation [21, 27, 28]. Another possible reason for the high rate of endoscopic procedures is to reassure patients about the absence of organic disease. However, this is not recommended practice as, on the contrary, a recent systematic review including 14 randomized controlled trials (n=3828) found that normal diagnostic tests do little to reassure a patient who is unlikely to have serious disease (such as FGID) and can instead lead to further healthcare-seeking behaviour in the search of an organic cause for their symptoms [29]. Although one randomized controlled trial (n=96) in

patients with chest pain referred for a diagnostic exercise stress test reported that an explanation of the meaning of possible test results prior to testing may provide reassurance and reduce future symptoms [30], this specific approach has not been investigated in FGID. The significant cost and associated risks do not warrant the use of endoscopy as a reassurance tool. The confidence by which the clinician makes the diagnosis from the results of interrogation and tests (if needed) should be sufficient to provide patient reassurance.

Patient characteristics of age and gender were not found to be associated with the tendency to use qualified language. However, it would be interesting to investigate more subjective measures such as perceived patient difficulty, medical understanding, desire for endoscopic procedures and fixation on a single causal cure. In terms of clinician characteristics, experience with patients with FGID as indicated by clinical load, was not related to the type of language used. Although our findings suggest a possible male gender bias towards the use of less certain diagnostic language by specialists when communicating about FGID, further evaluation is warranted due to the small sample of female specialists. Similarly, the significant association between clinician qualifications and the use of qualified language was negated when Specialist 3 was excluded from the analysis, and a larger scale study is needed to adequately power the analysis.

Although there were more new diagnoses in FGID than OGID letters, this is in keeping with the current practice of regular follow up of patients with organic disease and the primary care management of patients with functional disorders. Psychological co-morbidities and relevance of the patient's mental health to the presenting complaint had a higher prevalence in FGID than OGID letters. However, it would appear that, given the high incidence of psychological co-morbidities in patients with FGID [31], the prevalence reflected in the letters is much lower than expected in this population. This may reflect poor psychological screening in the medical consultation.

We are unaware of any factors specific to the Australian healthcare system that would explain the results. Although differences in health care systems exist, most adopt a tiered approach with referral up the specialisation grades which takes time, and adds to costs. System differences will not change the relevance of unclear communication to patients "owning" a diagnosis and moving on to a management pathway instead of remaining within a diagnostic framework. However, there could be a number of reasons for the use of vague diagnostic language in FGID, including fear of litigation, the fact that an exclusionary diagnosis will never be 100% certain, or lack of confidence in the current state of knowledge surrounding these disorders.

Fear of litigation is a very well-known driver of over-investigation in clinical practice in general [32] and in FGIDs [27]. Given the fact that there are as yet no reliable diagnostic tests for FGIDs and diagnosis relies largely upon symptom based criteria such as the Rome III, which do not have 100% certainty [27], and the majority of clinicians still regard it as a diagnosis of exclusion [21] it is possible that this fear also translates into a reluctance to apply a solid diagnostic label to these disorders. Interestingly, even among clinicians who endorse and use a positive diagnosis, there is a reluctance to communicate this to the patient without further testing [21] or to document the diagnosis [33].

Spiegel *et al.,* (21) have suggested that despite the existence and recommendations of well-reasoned evidence-based guidelines, the knowledge regarding FGIDs is still emerging, suggesting the possibility of as yet unknown underlying organic conditions that may contribute to the symptoms of functional disorders. It is possible that the uncertain language used to convey FGID diagnoses may reflect either a lack of confidence in diagnosis, or a lack of confidence in the labelling of the condition itself.

The current study had potential limitations. First, the retrospective methodology provided no opportunity to observe the language used in actual patient discussions, and further analysis of the clinical encounter in real time would be beneficial. However, the analysis of letters permitted real-world insight into the clinical approaches used by specialists dealing with patients with FGID, as clinicians had no prior knowledge of the study nor opportunity to alter their clinical approach. Secondly, although the gastroenterology service in which the study was performed has an active research interest in management of FGID, this was unlikely to bias the content of the letters analysed as they predated such research. Thirdly, the generalizability of the letters is uncertain in terms of currency and applicability to other institutions. Finally, the data retrieved was vulnerable to subjective interpretation and inconsistency inherent in content analysis, particularly as blinding to the diagnostic group to which the letter belonged was not possible. However, this was minimized by using three coders of differing backgrounds and enabled the development of a uniform approach to coding as reflected in the high inter-rater reliability.

CONCLUSION

There is considerable diagnostic uncertainty conveyed by the language specialists use in correspondence to referring doctors of patients with FGID. Contrary to expectations, this uncertainty does not appear to fall over time. Diagnostic uncertainty in specialists may have a flow-on affect to general practitioners and contribute to suboptimal patient acceptance of a functional diagnosis. We postulate that the discarding of a FGID diagnosis

may also be a driving factor in the use of further unwarranted endoscopic investigations. The disparity between the clinical over-use of invasive endoscopic investigations in FGID and the accepted recommendations in making a positive diagnosis indicates that there is room for improvement in the clinical approach taken with patients with suspected FGID. Specifically, the provision of a clear explanation of FGID and their chronic recurrent nature, as well as a rationale for investigations considered or ruled out may be beneficial to patient acceptance of diagnosis, and ongoing management.

Table 4-1 Content analysis coding categories and clinical alarms used to assess the appropriateness of endoscopic investigations

Coding Category
Medical co-morbidities noted
Psychological co-morbidities noted
Diagnosis explained to the patient
Investigative strategy used
Rationale given for the investigations conducted
Management clearly stated
Management discussed with the patients
Prognosis given
Follow up plan noted
Mental health deemed relevant to the diagnosis by clinician
Type of diagnostic language used
Clinical Alarm
New onset of symptoms *(within 6 months and over age 50 years)*
Unexplained weight loss *(> 3 kg or 5% body weight)*
Overt gastrointestinal bleeding *(positive faecal occult blood test, melaena, haematemesis)*
Unexplained fever
Abdominal pain awaking patient from sleep
Nocturnal diarrhoea
Family history of colon cancer *(one first-degree relative <60 years of age; > one first-degree relative any age)*
Family history of inflammatory bowel disease *(one or more first-degree relative)*
Family history of coeliac disease *(one or more first-degree relative)*

Table 4-2 Examples of the types of language used in gastroenterologist letters to referring general practitioners

Language Examples	
Clear	**Qualified**
“he has”	“may be having”
“is suffering from”	“it is possible that”
“has been diagnosed with”	“quite fits the picture of”
“his diagnosis is that of”	“is probably a reasonable label”
“definitely has”	“working impression”
“I have diagnosed with”	“managed as a case of”

Table 4-3 Associations between types of language used and clinical factors in all letters and FGID letters alone.

Factors		Diagnostic Language					
		All Letters[b]			FGID Letters[c]		
		Clear	Qualified	*p*-value[a]	Clear	Qualified	*p*-value[a]
Disorder	Functional	37 (37%)	62 (63%)	<.001			
	Organic	77 (87%)	11 (13%)				
Diagnosis	New	51 (44%)	65 (56%)	<.001	39 (38%)	63 (62%)	0.252
	Pre-established	63.(89%)	8 (11%)		9 (53%)	8 (47%)	
Patient Gender	Male	57 (76%)	18 (24%)	.001	13 (48%)	14 (52%)	.378
	Female	57 (51%)	55 (49%)		35 (38%)	57 (62%)	
Patient Age	<25	22 (76%)	7 (24%)	.206	2 (18%)	9 (82%)	0.349
	25-39	29 (54%)	25 (46%)		14 (37%)	24 (63%)	
	40-49	19 (54%)	16 (46%)		13 (46%)	15 (54%)	
	>50	43 (63%)	25 (37%)		19 (45%)	23 (55%)	
Clinician Load	< 10 Consults	29 (55%)	24 (45%)	.271	12 (32%)	25 (68%)	0.313
	≥ 10 Consults	85 (63%)	49 (37%)		36 (44%)	46 (56%)	
Clinician Gender	Male	79 (59%)	56 (42%)	.384	24 (32%)	50 (68%)	.034
	Female	35 (67%)	17 (33%)		24 (53%)	21 (47%)	
Clinician Gender (Exc-3)	Male				24 (32%)	50 (68%)	.873
	Female				2 (29%)	5 (71%)	
Clinician Qualification	Trainee	38 (61%)	24 (39%)	.977	10 (29%)	25 (71%)	0.041
	Senior Trainee	29 (63%)	17 (27%)		25 (57%)	19 (43%)	
	Consultant	29 (60%)	19 (40%)		7 (29%)	17 (71%)	
	Senior Consultant	18 (58%)	13 (42%)		6 (38%)	10 (63%)	
Clinician Qualification (Exc-3)	Trainee				10 (29%)	25 (71%)	
	Senior Trainee				2 (40%)	3 (60%)	
	Consultant				7 (29%)	17 (71%)	0.889
	Senior Consultant				6 (38%)	10 (63%)	

[a] Pearson's Chi-Squared with significant association p<.05. Data presented excluding specialist 3 (Exc-3) also shown. [b] All letters containing functional diagnoses were included in this analysis (n-119). [c] Letters containing only a functional diagnosis were analysed (n=99).

Table 4-4 Distribution of imaging tests and radiology exposure noted in letters regarding patients with FGID.

Imaging Tests	Radiology Dose	Frequency	Percent
No tests	-	89	74.8
Ultrasound	None	6	5.0
Abdominal X-ray	Low	1	0.8
CT scan	High	13	10.9
Small bowel barium series X ray	High	4	3.4
Multiple radiology tests	High	6	5.0
Total		119	100.0

Table 4-5 Comparison of future healthcare consultations between clear and qualified FGID diagnoses.

Medical Encounters	Clear Diagnosis (n=56)		Qualified Diagnosis (n=33)		Statistic	Significance
	Mean	SEM	Mean	SEM	t	2-tailed
Total Encounters	26.45	6.289	23.52	3.988	-.414	.680
GI Encounters	4.85	1.920	3.16	.679	-.984	.328
Hospital Admissions	2.303	1.2684	1.196	.3432	-1.036	.303
GI Hospital Admissions	.848	.1365	.286	.1365	-.930	.355
Radiology Encounters	9.242	.7564	7.232	2.0003	-.423	.673

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Chapter 5 : Performance of Endoscopic Appropriateness Criteria

BACKGROUND

The previous study found that FGIDs and organic gastrointestinal disease were investigated with endoscopy and/or colonoscopy at similar rates. In fact, almost 80% of patients diagnosed with FGID had undergone endoscopic investigation. Even though alarm features are more likely to be present in patients referred to tertiary care, the results showed a significant proportion of procedures were performed in the absence of clinical alarms (20% gastroscopy, 10% colonoscopy). This is somewhat surprising given the shift in gastroenterology towards a positive diagnosis of FGIDs with minimal investigations and the 'Choosing Wisely' health campaign aimed at reducing unnecessary investigations. The need to reduce inappropriate endoscopic investigations is two-fold: firstly, to reduce unnecessary risk to the patient from invasive procedures, and secondly, to effectively allocate limited healthcare resources.

The prior study however, may not reflect current practice within the Royal Adelaide Hospital. Previous endoscopic investigations were not solely performed within the Royal Adelaide Hospital, or indeed within the past two-years. Furthermore, the specialist letters reviewed were dated between 2008-2011 which pre-dated any active FGID research interest within the department, and as such may not be generaliseable to current practice. In order to determine the current rate of inappropriate endoscopic procedure within this unit, a retrospective audit of all diagnostic endoscopies performed within the prior 3-month period was conducted. Procedures were classified as appropriate or inappropriate according to our local custom alarm-based criteria, and diagnostic yield determined. The performance of the alarm-based criteria was compared to existing criteria established by the American Society for Gastrointestinal Endoscopy (ASGE) and the European Panel on the appropriateness of Gastrointestinal Endoscopy (EPAGEI and EPAGEII). Results are presented for all endoscopies, and the subset of clinically suspected FGID. This manuscript was submitted to BMC Gastroenterology, 9th Feb 2017.

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|MANUSCRIPT 3| PERFORMANCE OF ALARM-BASED CRITERIA AND THEIR UTILITY IN RESTRICTING ENDOSCOPIC PROCEDURES IN FUNCTIONAL GASTROINTESTINAL DISEASE: A RETROSPECTIVE AUDIT

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Running Head: APPROPRIATENESS CRITERIA IN FGID

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ABSTRACT

Background and Aims

With a heavy referral burden on endoscopic services worldwide, careful selection of patients is needed to optimise limited healthcare resources [(1)], particularly in the case of patients with suspected functional gastrointestinal disorders (FGID) [(2)]. This study aimed to determine the inappropriateness rate of endoscopies, and the performance of alarm-based criteria against ASGE and EPAGE criteria in patients with likely FGID.

Methods

A retrospective audit of consecutive medical records of patients with completed endoscopy at one Australian public hospital were reviewed (December 2014-October 2014). Indications were categorised by appropriateness using ASGE, EPAGE and alarm based criteria, and clinical yield determined.

Results

A total of 147 endoscopies (63% male, 67% outpatients) and 196 colonoscopies (50% male, 88% outpatients) were reviewed. 4% of UGIEs and 2% of colonoscopies were inappropriate per ASGE, and 7% (UGIEs) and 10% (colonoscopies) inappropriate per EPAGE. Custom alarms-based criteria in patients suspected of FGID exhibited greater specificity than ASGE or EPAGE ($Z= 3.53$, $p<.001$ for each), and were as sensitive as both ASGE and EPAGE ($p<.001$ each) for UGIEs. Similarly, alarm-based criteria had greater specificity than ASGE (53% vs 11%, $Z= 2.37$, $p=.018$), and comparable specificity to EPAGE (55% vs 20%, $p=.052$) for colonoscopy.

Conclusions

A low rate of inappropriate endoscopies was observed. Although ASGE and EPAGE performed similarly, they had different limitations. In patients with suspected functional symptoms neither ASGE or EPAGE-I appear to perform adequately. The use of an alarm-based criteria in patients with clinically suspected FGIDs may further reduce the rate of unnecessary investigations, and warrants larger scale evaluation.

Keywords Functional gastrointestinal disorders, endoscopy, appropriateness criteria, ASGE, EPAGE

INTRODUCTION

There is a heavy referral burden in endoscopic services worldwide, as referrals continue to increase, at least in part due to colorectal cancer screening programs. It is well recognised that the yield of relevant findings is high for some indications, such as positive faecal occult blood test [3, 4], whilst in other scenarios such as likely functional gastrointestinal disorders (FGIDs), there is a low relevant endoscopic yield [1]. FGIDs are very common, affecting approximately 40% of the population during their lifetime [5] and cause neither tissue damage nor mortality [6]. Yet, because they significantly impair quality of life, they frequently lead to medical consultations, and as current diagnostic practices are suboptimal [7], FGIDs have the potential to add to the endoscopic demand.

Although current recommendations are for minimal use of invasive tests for establishing a diagnosis of a FGID, current practice is at odds with the recommendations [2], with most clinicians adopting an exclusionary approach and continuing to refer for invasive procedures [2, 8-11]. While fear of missed pathology is a recognised driving factor for the over-use of endoscopy [12], this approach cannot be endorsed as a sustainable model of service delivery. It is not efficient, necessary or affordable, and carries avoidable risk to otherwise healthy people. Careful selection of patients for endoscopic procedures is needed to optimise limited healthcare resources [1].

Endoscopic "appropriateness" guidelines have been developed by the American Society for Gastrointestinal Endoscopy (ASGE) [13] and the European Panel on the appropriateness of Gastrointestinal Endoscopy (EPAGEI and EPAGEII) [14], to better target endoscopic procedures, increase diagnostic yield and improve the quality of patient care . However, both sets of criteria are recommended as monitoring/decision-making rather than screening tools [15-17]. The validity of these guidelines has not been evaluated in randomised controlled trials, but a consistent substantial rate of inappropriate upper gastrointestinal endoscopies (UGIEs) and colonoscopies has been documented in observational studies worldwide [18-20].

Rates of inappropriate endoscopic procedures vary significantly (10-40%) according to procedure type, patient age, healthcare setting (in- vs. out-patients), the criteria used and the health system of the country [19, 21-23]. Direct comparison of "inappropriate" endoscopic rates is, therefore, difficult. By way of example, a prospective observational study of 21 centres in 11 European countries (2000-2002, n=5213) found 27% of colonoscopy indications to be inappropriate according to EPAGE, with values ranging from 12-43% across centres [24]. Two recent Italian studies in an open access facility, found

approximately 10% of gastroenterologist referred colonoscopies (n= 2454) and 14% of UGIEs to be inappropriate (n=1777) according to ASGE [25, 26].

There have been only three studies which directly compare ASGE and EPAGE criteria; one in UGIE [27] and two in colonoscopy [28, 29], with only one published in full [27]. Bersani *et al.,* [27] found that the diagnostic yield for clinically relevant endoscopic findings was slightly better using ASGE than EPAGE criteria for UGIE. However, these findings have been debated due to significant methodological issues [30]. Using the same methods, Bersani *et al.,* [29] found that the criteria performed similarly to each other for colonoscopy [29]. Adler *et al.,* [28] report a 5-10% higher yield of relevant colonoscopy findings in ASGE and EPAGE appropriate categories, but full comparative data are not presented in the abstract and cannot be further evaluated [28].

Although the ASGE and EPAGE criteria agree on colonoscopy appropriateness in 80% of indications, disagreement occurs in a few frequently encountered indications such as uncomplicated abdominal pain and constipation [30]. Such symptoms occur frequently in people with FGID and are, in general, low-yield indications for colonoscopy. Consistent with this, a simple predictive rule based on age, alarm features and family history has been shown to be as effective as ASGE guidelines in identifying appropriate indications for UGIE (n=8252) [21].

The rate of 'inappropriate' UGIEs and colonoscopies in Australia has yet to be assessed. The aims of this study are therefore to: 1) explore the rate of unindicated endoscopic procedures being performed, 2) determine what proportion of these "inappropriate" endoscopic procedures are performed in patients clinically suspected of having a FGID and 3) compare the performance of locally developed custom alarm-based criteria against ASGE and EPAGE criteria in the patients with clinically suspected FGID.

METHODS

Consecutive medical records of patients with completed diagnostic and therapeutic colonoscopies and endoscopies (Oct-Dec 2014) in one metropolitan Australian public hospital were retrospectively reviewed. Liver-related procedures were excluded. The indications for each procedure as documented on the booking form were judged appropriate/inappropriate according to ASGE [13], and necessary/appropriate or uncertain/inappropriate using EPAGE criteria (www.epage.ch). EPAGE categories were combined and reported as appropriate (including necessary and appropriate procedures) or inappropriate (uncertain or inappropriate procedures). Where a booking form was not

found, medical notes, outside referral, or procedure reports were used in lieu, in that order of priority. The clinical relevance of endoscopic findings was assessed by a gastroenterology registrar and senior gastroenterologist, and endoscopic findings classified as normal, non-contributory abnormality or relevant abnormality. Patient demographics, symptoms, symptom duration main indications, previous tests, and endoscopic/histological findings were also recorded. Referral demographics included initial source of referral (gastroenterologist, intern, surgeon, primary healthcare provider) and admission status (inpatient/outpatient). A sample size of 139 colonoscopies and 186 UGIEs was powered to detect a prevalence of inappropriate indications of 10% and 14% for colonoscopies and UGIEs respectively, with 5% precision.

A subset of procedures performed in patients judged clinically likely to have FGID were selected for further analysis. Likely FGID was defined as the presence of longstanding (≥6 months), non-specific gastrointestinal symptoms (abdominal/epigastric pain/discomfort, with or without accompanied bloating, flatulence, altered bowel habit, nausea or vomiting). Procedures performed in this subset of patients were additionally categorised as appropriate/inappropriate according to locally developed custom alarms-based criteria (Table 5-1). Procedures were judged as appropriate where one or more clinical alarms were present, and inappropriate in the absence of any alarms, and the subsequent yield of relevant abnormalities was determined.

Data Analysis

Data were analysed using SPSS 24, and expressed as frequencies and counts. Confidence limits for the sample proportion of inappropriate indications were calculated using the Wilson method [31]. Z-scores were calculated to test for significant differences between these proportions, with significance set at $p<.05$ (two-sided). Pearson's Chi square test and Fischer's exact test were used to test for associations between appropriateness categories and clinical relevance of findings, with significance set at $p<.05$ (two-sided). Sensitivity (the ability of the criteria to identify those with clinically relevant findings) and specificity (the ability of the criteria to correctly identify those without clinically relevant findings) of the criteria were calculated for the performance of the criteria using the online calculator (http://vassarstats.net). All authors had access to the study data, and reviewed and approved the final manuscript.

Ethics

As this was a clinical audit conducted retrospectively with the purpose of quality assurance/evaluation, ethical review was not necessary.

RESULTS

Sample Description

The records of 288 patients who underwent either colonoscopy (n=141, M 61y, SD 16), UGIE (n=92, M 61y, SD 18) or both (n=55, M 60y, SD 18) were reviewed. Full demographics are detailed in Table 5-2. Patients were mostly outpatients referred by gastroenterologists. Most UGIE and colonoscopy booking forms/medical records (60%, 61%) did not state whether prior endoscopic procedures had been performed. The procedure was specifically noted to be the initial procedure in only 8% and 7% of UGIEs and colonoscopies respectively. At least one prior endoscopic investigation was noted in 32% of UGIEs and colonoscopies. The status of the remaining procedures was unable to be determined from the medical records.

Appropriateness and yield of UGIEs & colonoscopies by EPAGE and ASGE

The majority of UGIEs were judged to be appropriate by both ASGE (89%) and EPAGE (80%) criteria with only 4% [95% CI (2%, 9%)] and 7% [95% CI (4%, 13%)] inappropriate, respectively (Table 5-3). Although we were unable to categorise a numerically larger number of UGIEs using EPAGE (19 vs 10), the proportions were not statistically different (Z=1.76, p=.078). UGIE indications unable to be coded by ASGE or EPAGE are provided in Supplementary Table 5-1. On clinician review, 1 ASGE-inappropriate, 5 ASGE-uncodeable, and 2 EPAGE-uncodeable UGIE indications were judged appropriate. There were no instances where EPAGE-inappropriate indications were subsequently judged appropriate. Summaries of the categorisation of clinical indications for UGIE and colonoscopy according to ASGE and EPAGE criteria are presented in Supplementary Table 5-2, Supplementary Table 5-3, Supplementary Table 5-4, Supplementary Table 5-5.

Similarly, the majority of colonoscopies were appropriate using ASGE (88%) and EPAGE (72%) with 2% [95% CI (1%, 5%)] and 10% [95% CI (7%, 15%)] inappropriate, respectively (Table 5-3). Again, a larger number of colonoscopies (36/196, 18%) were unable to be categorised with EPAGE as compared to ASGE, and here the difference was significant (19/196, Z=2.64, p=.008). On clinical review 5/19 ASGE-uncodeable indications were deemed appropriate as were 6/19 ASGE-inappropriate; 11/36 EPAGE-uncodeable indications. There were no instances of EPAGE-inappropriate indications being subsequently judged appropriate.

A finding of clinical relevance was not significantly related to the appropriateness category in either ASGE-UGIE [χ^2 (4, n=147) =2.566, p=.633], ASGE-Colonoscopy [χ^2 (2, n=177) =.097, p=.755], or EPAGE-UGIE [χ^2 (2, n=147)=2.477, p=.649]. However,

the appropriateness of EPAGE-Colonoscopy was related to clinical relevance; a higher negative yield was found in the inappropriate colonoscopies (79% vs 69%) and higher positive yield in appropriate colonoscopy indications (44% vs 21 %) [χ^2 (4, n=196) =10.261, p=.036]}. These results should be interpreted with caution, however, due to the small number of inappropriate procedures in this sample.

Performance of custom-alarm based criteria, EPAGE and ASGE in clinically suspected FGID

Likely functional GI symptoms were identified on the referral in 12% (18/147) of UGIEs and 11% of colonoscopy (22/196). All of these procedures were able to be categorised as appropriate or inappropriate using the locally developed alarm-based criteria. However, ASGE was unable to classify 3 UGIEs (17%) and 10 (45%) colonoscopies, and EPAGE was unable to classify 2 UGIEs (11%) and 4 (18%) colonoscopies (Table 5-4). In this subset of procedures, 14/18 UGIEs and almost half of the colonoscopies (10/22) were judged inappropriate using the locally developed alarm-based criteria (Table 5-4).

Clinically relevant findings in patients suspected of FGIDs were seen in only 1 UGIE and 3 colonoscopies, occurring in the "appropriate" category of all 3 sets of criteria including the local custom-alarm based ones (Table 5-4). The alarm-based local criteria applied to UGIEs in patients suspected of FGIDs exhibited greater specificity than ASGE or EPAGE (Z= 3.53, p<.001 for each), and were as sensitive as both ASGE and EPAGE (p<.001 each). When applied to colonoscopies in patients with clinically suspected FGIDs, alarm-based criteria had greater specificity than ASGE (53% vs 11%, Z= 2.37, p=.018), and comparable specificity to EPAGE (55% vs 20%, p=.052). Commonly encountered symptoms that are characteristic of FGIDs and yet deemed appropriate for endoscopic tests by ASGE or EPAGE (but not by local alarm-based criteria) were chronic diarrhoea (sampling of tissue or fluid, or suspected malabsorption) and persistent upper abdominal symptoms (following treatment trial, or uncomplicated dyspepsia) (Supplementary Table 5-5 and Supplementary Table 5-6).

When the custom alarm-based criteria were applied to all diagnostic UGIEs (n=147; not only those performed in people suspected to have a FGID), they were less sensitive than ASGE (89% vs 100, Z =2.298, p<=.021) but as sensitive as EPAGE (89% vs 96% Z=1.12, P=.263) (Table 5-5). Custom alarm based criteria more specific than ASGE (26% vs 4%, Z=3.57, p<.001) and EPAGE (26% vs 6%, Z=3.16, p=.002). Only ASGE captured all relevant findings however. When applied to all diagnostic colonoscopies, local alarm based criteria were as sensitive as both ASGE (94% vs 98%, Z=1.20, p>.05) and EPAGE (94% vs 98%, Z=.942,

p>.05), more specific than ASGE (14% vs 1%, Z= 3.06, p=.002) and as specific as EPAGE (14% vs 16%, Z=.432, p=.667).

DISCUSSION

Local performance

Here we demonstrated a low rate of inappropriate endoscopic procedures according to both ASGE and EPAGE criteria. Our results are on the low end of the spectrum of the published 10-40% rate of inappropriate procedures [19, 21-24, 32, 33], and better than published rates for gastroenterologist referred colonoscopies (2% vs 10%) and UGIEs (4% vs 14%) using ASGE [25, 26]. This study is the first to assess and report the appropriateness of endoscopic procedures in Australia. The low rates of inappropriate procedures may reflect the service pressure to choose wisely [34], and the lack of financial incentives to over-investigate within a publicly funded system. This study was performed in one metropolitan hospital, and further evaluation in the larger Australian context is warranted to establish generalisability.

Comparison of ASGE/EPAGE

Although ASGE and EPAGE criteria were comparable in the yield of clinically relevant findings in those endoscopic investigations judged appropriate, they differed in utility. ASGE was broader in its inclusions, covering the vast majority of clinical scenarios without consideration of time-frames, whilst EPAGE was more stringent and did not address therapeutic procedures (e.g. stricture dilatation, or intervention for Barrett's oesophagus) [35]. According to ASGE, all UGIEs are appropriate in patients over 45 years of age with upper abdominal symptoms irrespective of the presence or absence of clinical alarms [36] . There were however a number of indications which were unable to be classified by each set of criteria which were clearly appropriate according to current clinical practice, suggesting that these criteria could benefit from updating. The rigid format of EPAGE resulted in more indications being unable to be categorised. Specifically, EPAGE required flexible sigmoidoscopy results to determine appropriateness of colonoscopy for iron deficiency anaemia, however sigmoidoscopy is now rarely performed and thus, this resulted in an inability to categorise this indication. Similarly, UGIE endoscopy for caustic/foreign body ingestion was uncodeable in EPAGE whereas they are clearly appropriate based on current data and clinical experience. [37-40].

UGIE is regarded as an important diagnostic procedure for patients with upper abdominal and reflux symptoms, however, the logic is mainly due to a fear of missing significant pathology. However, symptomology/clinical alarms do not correlate well with the yield

of endoscopic procedures [42]. One study (n=7159) has shown that less than 1% of patients with gastroesophageal reflux symptoms had Barrett's or adenocarcinoma [43]. Similarly, a random population study in Sweden (n= 3000) found that although gastroesophageal reflux symptoms were reported in 40% of the general population, only 16% were found to have erosive oesophagitis upon UGIE whilst 6 of 20 (30%) patients with gastric ulcer and 2 of 21 (10%) with duodenal ulcer did not have any symptoms [44]. In patients with epigastric or upper abdominal symptoms, it is generally accepted that UGIE is not needed in those with clinical diagnosis of functional dyspepsia.

A potential limitation of this study is the small sample size. The final number of UGIEs examined was not powered to detect the estimation of 14% inappropriate indications at 5% precision. However, this had negligible effect on the results or subsequent interpretation, as a precision of 6% was achieved. In addition, the number of clinically relevant findings was small, and it is therefore possible that a Type II error has occurred when examining for associations between appropriateness and clinical yield. A larger, prospective comparison of ASGE/EPAGE would be valuable.

Utility of local alarm-based criteria

When applied to patients referred with clinically suspected functional symptoms, the custom alarm-based criteria performed as well as ASGE and EPAGE in terms of sensitivity. In addition, they were more specific that ASGE or EPAGE. Furthermore, the alarm-based criteria enabled categorisation of all indications unlike ASGE or EPAGE. There were a number of indication categories under which potentially functional symptoms (such as chronic diarrhoea and persistent symptoms) could be coded in both ASGE/EPAGE. These categories could be viewed as "escape clauses" for over-investigating functional symptoms, resulting in more endoscopic procedures than truly necessary according to current guidelines [(2)].

The use of our alarm-based approach to determining the appropriateness of endoscopic investigation in patients with symptoms suggestive of functional disease may be useful to reduce the number of unnecessary investigations, freeing up valuable endoscopic resources and reducing unnecessary risk to patients. However, this subset of endoscopic procedures performed in potential FGID patients was small and further large-scale evaluation of our custom alarms-based criteria in patients with likely functional symptoms seems justified on these preliminary data.

CONCLUSION

The targeting of appropriate endoscopic investigations in this unit is very good, with results at the low end of published rates for inappropriate procedures world-wide. Although the ASGE and EPAGE appropriateness criteria performed similarly, both were limited in patients with possible functional symptoms, and less specific than alarm-based criteria. The use of our alarm-based criteria in patients with suspected functional gastrointestinal disorders may further reduce the rate of unnecessary investigations, and this warrants larger scale evaluation.

Table 5-1 Locally developed algorithm-based alarm criteria for the appropriateness of endoscopies

Upper GI Endoscopy	Colonoscopy
Abnormal physical exam	
Abnormal Imaging	
New onset symptoms if > 50 years of age (within 6 months)	
Unexplained weight loss (> 3 kg or 5% body weight)	
Iron deficiency +/- anaemia	
Haematemesis	Melena, faecal occult blood, overt rectal bleeding
Dysphagia/odynophagia	Abdominal pain awaking patient from sleep
Family History of Coeliac Disease in symptomatic patient (1 FDR)	Nocturnal diarrhoea/faecal incontinence
	Unexplained fever
	Family history of colon cancer (1 FDR* <60, or > 1 FDR any age)
	Family History of IBD in symptomatic patient (1 FDR)

* FDR, first-degree relative

Table 5-2 Demographics of patients undergoing UGIE and colonoscopy

Demographics		UGIE n (%)	Colonoscopy n (%)
Number of procedures		147	196
Gender	Female	69 (47)	97 (50)
	Male	78 (53)	99 (50)
Admission Status	Outpatient	98 (67)	172 (88)
	In-patient	43 (29)	18 (9)
	In-patient/for the procedure	6 (4)	6 (3)
Referral Source	Gastroenterologist	99 (67)	101 (52)
	Primary healthcare provider	4 (3)	3 (1)
	Surgeons	19 (13)	80 (41)
	Other	25 (17)	12 (7)
Prior procedures	Multiple prior	25 (17)	11 (6)
	At least one prior	22 (15)	53 (27)
	No prior	12 (8)	15 (8)
	Not stated	88 (60)	117 (60)

Table 5-3 Comparison of the performance of ASGE, EPAGE for UGIE and colonoscopy

	AGSE n (%)			EPAGE n (%)		
	A	I	X	A/N	I/U	X
UGIE Indications	131 (89%)	6 (4%)	10 (7%)	117 (80%)	11 (7%)	19 (13%)
Clinical Alarms (88)	86	0	2	83	0	5
Persistent Symptoms/No Alarms (21)	17	2	2	14	4	3
Surveillance (20)	14	2	4	8	3	9
Post-operative assessment/complications (3)	3	0	0	2	0	1
Pre-operative Assessment (2)	0	1	1	1	1	0
Metastatic cancer-seeking primary (3)	2	1	0	2	1	0
Persistent symptoms despite treatment (3)	3	0	0	3	0	0
Achalasia (2)	2	0	0	2	0	0
Operative endoscopy (2)	1	0	1	1	1	0
Diarrhoea/Immunocompromised (2)	2	0	0	0	1	1
Food bolus (1)	1	0	0	1	0	0
Clinical Relevance of Findings						
Clinically Relevant	64 (49%)	2 (33%)	3 (30%)	53 (45%)	6 (55%)	10 (53%)
Non-contributory abnormality	28 (21%)	2 (33%)	2 (20%)	27 (23%)	3 (27%)	2 (11%)
Normal	39 (30%)	2 (33%)	5 (50%)	37 (32%)	2 (18%)	7 (37%)

A= appropriate, I= inappropriate, X=un-codeable, A/N= appropriate or necessary, I/U= inappropriate or uncertain.

UGIE: Surveillance (Barrett's oesophagus n=12, varices n=6, stricture n=1, gastric ulcer n=1), Post-operative assessment for complications (fundoplication n=2, gastric bypass n=1), Preoperative assessment (gastric bypass surgery n=2). 3/10 ASGE-uncodeable and 3/11 EPAGE-uncodeable UGIEs, were unable to be coded due to insufficient information in the medical records. Colonoscopy: IBD Follow Up (active disease n=4, cancer n=6, post-operative n=3), Surveillance (benign disease n=2, colorectal cancer n=3, polyps n=14, post colorectal cancer n=8), Preoperative assessment (benign disease n=2, colorectal cancer n=2, fistula n=1). 4/18 ASGE-uncodeable and 11/36 EPAGE-uncodeable colonoscopies, were unable to be coded due to insufficient information in the medical records

	AGSE n (%)			EPAGE n (%)		
	A	I	X	A/N	I/U	X
Colonoscopy Indications	173 (88%)	4 (2%)	19 (10%)	141 (72%)	20 (10%)	35 (18%)
Clinical Alarms (124)	121	0	3	95	10	19
Persistent Symptoms/No Alarms (13)	4	1	8	10	1	2
Surveillance (27)	21	2	4	13	4	10
IBD Follow Up (12)	12	0	0	9	2	1
Pre-operative Assessment (5)	4	0	1	5	0	0
Metastatic cancer-seeking primary (4)	3	0	1	3	1	0
Persistent symptoms despite treatment (2)	2	0	0	1	0	1
Completion colonoscopy (3)	2	0	1	2	0	1
Operative colonoscopy (2)	2	0	0	1	1	0
Diarrhoea/Immunocompromised (2)	2	0	0	1	0	1
Unindicated (2)	1	0	1	1	0	1
Clinical Relevance of Findings						
Clinically Relevant	70 (40)	2 (50%)	2 (11%)	62 (44%)	4 (21%)	8 (22%)
Non-contributory abnormality	46 (24%)	1 (25%)	4 (22%)	35 (25%)	4 (21%)	12 (33%)
Normal	58 (33)	1 (25%)	12 (67%)	44 (31%)	11 (58%)	16 (44%)

Table 5-4 Performance of alarm-based, ASGE, EPAGE criteria for UGIE and colonoscopy in patients with clinically suspected FGID symptoms

UGIE	Custom Alarm-Based Criteria (n)			AGSE (n)			EPAGE (n)		
	A	I	X	A	I	X	A/N	I/U	X
Indications	4	14	0	13	2	3	14	2	2
Clinical Relevance									
Relevant	1	0	0	1	0	0	1	0	0
Non-contributory/Normal	3	14	0	12	2	3	13	2	2
Sensitivity [95% CI]	100% [5-100]			100% [5-100]			100% [5-100]		
Specificity [95% CI]	82% [56-95]			14% [3-44]			13% [2-42]		
Colonoscopy	**Custom Alarm-Based Criteria (n)**			**AGSE (n)**			**EPAGE (n)**		
	A	I	X		A	I	X		A
Indications	12	10	0	11	1	10	15	3	4
Clinical Relevance									
Relevant	3	0	0	3	0	0	3	0	0
Non-contributory/Normal	9	10	0	8	1	10	12	3	4
Sensitivity [95% CI]	100% [31-100]			100% [31-100]			100% [31-100]		
Specificity [95% CI]	53% [29-75]			11% [1-49]			20% [5-49]		

I= inappropriate, A= appropriate, A/N= appropriate or necessary, I/U= inappropriate or uncertain. UGIE relevant finding (hiatus hernia with antral gastritis). Colonoscopy relevant findings (tubular adenoma with low grade dysplasia, benign hyperplastic polyp, active chronic colitis consistent with IBD).

Table 5-5 Comparison of the performance of alarm-based, ASGE, EPAGE criteria in patients undergoing diagnostic UGIE and colonoscopy.

UGIE	Custom Alarm-Based Criteria (n)			AGSE (n)			EPAGE (n)		
	A	I	X	A	I	X	A/N	I/U	X
Diagnostic UGIE Indications (n=119)	95	24	0	112	3	4	104	6	9
Clinical Relevance									
Relevant	42	5	0	47	0	4	43	2	2
Non-contributory/Normal	53	19	0	65	3	0	61	4	7
Sensitivity [95% CI]	89% [76-96]			100% [91-100]			96% [84-99]		
Specificity [95% CI]	26% [17-38]			4% [1-13]			6% [2-16]		
Colonoscopy	**Custom Alarm-Based Criteria (n)**			**AGSE (n)**			**EPAGE (n)**		
	A	I	X	A	I	X	A/N	I/U	X
Colonoscopy Indications (n=149)	132	16	0	133	2	13	111	13	25
Clinical Relevance									
Relevant	51	3	0	53	1	0	49	1	4
Non-contributory/Normal	81	13	0	80	1	13	62	12	20
Sensitivity [95% CI]	94% [84-99]			98% [89-100]			98% [88-100]		
Specificity [95% CI]	14% [8-23]			1% [0-8]			16% [9-27]		

I= inappropriate, A= appropriate, A/N= appropriate or necessary, I/U= inappropriate or uncertain.

Supplementary Table 5-1 Comparison of endoscopic indications unable to be categorised using ASGE/EPAGE

UGIE	ASGE	EPAGE	Allowed
Iron deficiency in the setting of previous gastric cancer - not anaemia	X	X	AC
Follow up/surveillance of gastric polyps	X	U	AC
Follow up/surveillance Barrett's oesophagus	X	I	AC
Follow up/surveillance of varices	X/I	A/N	AC
Pre-operative assessment for gastric bypass	X	X	AC
To assess caustic ingestion	A	X	
Treatment of stricture/dilation of stenotic lesion	A	X	
Assess healing of gastric ulcer	I	X	
Treatment of Barrett's oesophagus	A	X	
Colonoscopy	**ASGE**	**EPAGE**	**Allowed**
Altered bowel habits, previous right hemicolectomy for caecal volvulus query malabsorption	X	A	
Anaemia on the background of oesophageal cancer treated with CRT	X	X	
Hartmann's for perforated diverticulitis, assess rectal stump	X	A	
Change in bowel habits, increased constipation and tenesmus, chronic pain	X	U	
Constipation	X	N	
Ischaemic colitis	X	X	
Renal transplant, increased risk surveillance	X	N	
Change in bowel habit	X	A	
Abdominal pain associated with unintentional weight loss and satiety	X	I	
Iron deficiency, not anaemia	X	N	
Recheck post-polypectomy	X	I	
Iron deficiency anaemia for investigation	A	X	
Caecal polyps for therapy	A	X	

Endoscopic indications encountered in our cohort which were unable to be categorised using ASGE/ EPAGE criteria, as well as those which were "allowed" (deemed appropriate) per current clinical practice. X= uncodeable, I=inappropriate, A=appropriate, U=uncertain, N=necessary, AC=appropriate as per current practice.

Supplementary Table 5-2 Referral indications for UGIE according to ASGE

UGIE Indications (n=147)	Frequency	%
Upper abdominal symptoms, persistent despite therapy	10	6
Upper abdominal symptoms with alarms (or in patients aged>45 y)	5	3
Dysphagia or odynophagia	15	10
Esophageal reflux symptoms, persistent despite therapy	7	4
Suspected neoplastic lesion	2	1
Upper tract stricture or obstruction	1	1
GI Bleeding	1	1
Active or recent bleeding	23	15
Presumed chronic blood loss/iron deficiency anaemia	35	23
When sampling of tissue or fluid is indicated	12	8
Suspected portal hypertension/ document or treat esophageal varices	2	1
Acute injury after caustic ingestion	2	1
Banding or sclerotherapy of varices	2	1
Removal of foreign bodies	1	1
Removal of selected polypoid lesions	1	1
Dilation of stenotic lesions	4	3
Endoscopic therapy for intestinal metaplasia	6	4
Indications not included in ASGE guidelines	19	7
Iron deficiency (previous gastric cancer)- not anaemia	1	
Follow up/surveillance of gastric polyps	1	
Follow up/surveillance Barrett's oesophagus	2	
Follow up/surveillance of varices	2	
Pre-operative assessment for gastric bypass	1	
Persistent symptoms (trial of medication not mentioned)	2	
Positive FOBT, past hx malignant polyp, also upper GI discomfort, >45 yrs	1	

Supplementary Table 5-3 Referral indications for UGIE according to EPAGE

UGIE Indications (n=147)	Frequency	%
Uncomplicated dyspepsia	11	8
GERD or history of reflux-associated mucosal disease of the esophagus, without alarm symptoms and without Barrett's esophagus	5	3
Known Barrett's esophagus, without alarm symptoms	2	1
Alarm symptoms	78	53
Risk factors and pre-malignant conditions of the UGI tract	1	1
Miscellaneous indications	20	14
Indications not included in EPAGE guidelines	**19**	**13**
Barrett's treatment	4	
Barrett's surveillance	3	
Caustic ingestion	3	
Persistent symptoms/no treatment mentioned in notes	2	
Variceal surveillance	1	
Variceal bleed	1	
Post-op assessment for complications	1	
Check ulcer healing	1	
Stricture treatment	1	
Iron deficiency in the setting of previous gastric cancer/not anaemia	1	
? Infective GI source, febrile and diarrhoea in immunosuppressed patent	1	

Supplementary Table 5-4 Referral indications for colonoscopy according to ASGE

Colonoscopy Indications (n=173)	Frequency	%
Abnormality on barium enema or other imaging study	14	7
Evaluation of unexplained GI bleeding	1	0.5
Hematochezia	30	15
Melena after an upper GI source has been excluded	2	1
Presence of faecal occult blood	43	22
Unexplained iron deficiency anaemia	16	8
Screening and surveillance for colon neoplasia	41	22
Dysplasia and cancer surveillance in patients with ulcerative or Crohn's colitis	13	7
Clinically significant diarrhoea of unexplained origin	10	5
Excision or ablation of lesions	2	1
Marking a neoplasm for localisation	1	0.5
Indications not included in ASGE guidelines	**19**	**10**
Persistent symptoms/no alarms	7	
Abdominal pain associated with unintentional weight loss and satiety	1	
Altered bowel habits, previous right hemicolectomy for caecal volvulus query malabsorption	1	
Anaemia on the background of oesophageal cancer treated with CRT	1	
Family History of Crohn's (insufficient information in notes)	1	
Hartmann's procedure for CRC 2014	1	
Hartmann's for perforated diverticulitis, assess rectal stump	1	
Iron deficiency, not anaemia	1	
Ischaemic colitis	1	
Completion colonoscopy (insufficient information in notes)	1	
Recheck post-polypectomy	1	
Post polypectomy bleed/ischaemic colitis	1	
CRC surveillance in renal transplant patient with increased risk	1	

Supplementary Table 5-5 Referral indications for colonoscopy according to EPAGE

Colonoscopy Indications (n=173)	Frequency	%
Iron-deficiency anaemia (malabsorption syndrome excluded)	1	1
Screening for colorectal cancer	49	35
Miscellaneous indications	31	22
Hematochezia (without IBD). Patient hemodynamically stable.	25	18
Lower abdominal symptoms of at least 3 months duration, without known inflammatory bowel disease/anemia/FOBT positive stools, with or without empirical IBS therapy. No risk factors for colorectal cancer.	6	4
Uncomplicated diarrhea (infectious or malabsorption origin excluded and without known IBD).	7	5
Evaluation of known Crohn's disease (CD), excluding surveillance for cancer.	6	4
Surveillance for colorectal cancer in patients with inflammatory bowel diseases.	1	2
Surveillance after colonic polypectomy	7	5
Surveillance after curative intent resection of colorectal cancer	6	4
Indications not included in EPAGE guidelines	**35**	**20**
Completion colonoscopy (insufficient information in notes to code)	1	
Iron deficiency anaemia (no flexible sigmoidoscopy done)	15	
Surveillance polyps (insufficient information in notes to code)	6	
Surveillance ischaemic colitis	1	
Removal of polyps	1	
Surveillance post CRC (insufficient information in notes to code)	2	
Overt bleeding associated with perianal itch, past hx of colonic polyps and iron deficiency anaemia (insufficient information in notes to code)	1	
Persistent symptoms/no alarms	3	
Family history of Crohn's	1	
IBD Surveillance (insufficient information in notes to code)	1	
Anaemia	2	
Persistent diarrhoea in immunosuppressed patient (insufficient information in notes to code)	1	

Supplementary Table 5-6 Frequency table of ASGE/EPAGE appropriateness categories used for UGIE/Colonoscopy in patients with suspected functional symptoms.

UGIE/ ASGE Category Used		**Colonoscopy/ ASGE Category Used**	
Main Indication (n=18)	#	**Main Indication (n=22)**	#
Persistent symptoms-no alarms	11	Persistent symptoms-no alarms	10
Clinical alarms	5	Clinical alarms	9
Persistent symptoms-despite treatment	2	Completion colonoscopy	2
		Surveillance -polyps	1
Uncodeable	5	Uncodeable	11
Upper abdominal symptoms, which persist despite an appropriate trial of therapy	7	Clinically significant diarrhoea of unexplained origin	3
For presumed chronic blood loss/iron deficiency anaemia when the clinical situation suggests an upper GI source or when colonoscopy result is negative	2	Hematochezia	2
Upper abdominal symptoms associated with other symptoms or signs suggesting serious organic disease (eg, anorexia and weight loss) or in patients aged>45 years	1	Presence of faecal occult blood	2
Dysphagia or odynophagia	1	Evaluation of an abnormality on barium enema or other imaging study that is likely to be clinically significant	1
Esophageal reflux symptoms, which are persistent or recurrent despite appropriate therapy	1	Unexplained iron deficiency anaemia	1
When sampling of tissue or fluid is indicated	1	Surveillance of patients with neoplastic polyps	1
		Surveillance of patients with a significant family history of colorectal neoplasia	1

UGIE/EPAGE Category		Colonoscopy/EPAGE Category	
Uncodeable	3	Uncodeable	4
Uncomplicated dyspepsia	10	Lower abdominal symptoms of at least 3 months' duration, without known inflammatory bowel disease, anemia. FOBT positive stools. No risk factors for colorectal cancer.	8
Alarm symptoms	3	Hematochezia (without IBD). Patient hemodynamically stable.	3
Gastroesophageal reflux disease (GERD) symptoms, without alarm symptoms/Barrett's esophagus	1	Miscellaneous indications	3
Miscellaneous indications: assess healing of benign gastric ulcer, follow-up of sclerotherapy/banding, suspected malignant lesion on UGI series, suspected malabsorption syndrome	1	Uncomplicated diarrhea (infectious or malabsorption origin excluded and without known IBD). No anemia. No bleeding. No risk factors for colorectal cancer. No HIV / AIDS. With or without empirical treatment.	3
		Screening for colorectal cancer	1

Abbreviations

FGID Functional gastrointestinal disorders
UGIE Upper gastrointestinal endoscopy
ASGE American Society for Gastrointestinal Endoscopy
EPAGE European Panel on the appropriateness of Gastrointestinal Endoscopy
M Mean
SD Standard deviation
CI Confidence interval

Declarations

Ethics approval and consent to participate: As this was a clinical audit conducted retrospectively with the purpose of quality assurance/evaluation, ethical review was not necessary.

Consent for publication –Not applicable

Availability of data and material: The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests: The authors declare that they have no competing interests

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Authors' contributions: E.C. Linedale: Principal researcher planning/conducting the audit, collecting, analysing, interpreting the data and writing the manuscript. Q Rizvi: Assisted in the medical records audit, including interpretation of medical records, and clinical relevance of procedural findings. Also contributed to analysis of the practical performance of criteria and writing of manuscript. A. Mikocka-Walus: Provided oversight in data analysis and drafting of manuscript. P.R. Gibson: Provided research oversight, data analysis, and editing of manuscript. J.M. Andrews: Provided conceptual design, research oversight, medical interpretation of findings, and drafting of manuscript. All authors have approved the final draft for submission for publication.

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Chapter 6 : Models of Care For FGID

BACKGROUND

Several issues pertaining to the diagnosis and management of patients with FGIDs have been identified in the previous chapters. These issues are not isolated within a particular healthcare sector, but rather represent systemic difficulties faced by all clinicians caring for this large patient segment. Primary health care providers express a lack of confidence in correctly identifying and managing FGIDs. This is also reflected in the large number of referrals to tertiary care. In the public health sector, demand for specialist input exceeds capacity, resulting in extremely long waiting lists, with many patients never been seen. Within public healthcare, patients are triaged into urgency categories according to the information provided in the referrals. However, the quality of these referrals is poor, and many do not mention the presence of absence of relevant clinical alarms. Thus, it is possible that those triaged as non-urgent require warrant more urgent review. Patients who are referred to public health tertiary care report dissatisfaction with management to date, related to the lack of diagnosis or effective management options. Many experience persistent, distressing symptoms, and are anxious about the possibility of missed or worsening pathology. Within tertiary care, clinicians continue to over-use endoscopic procedures in patients with clinically suspected FGID, and struggle to clearly communicate a diagnosis of a FGID.

A timely, accurate diagnosis that relies on minimal investigation and is communicated effectively is a key component in the care of patients with FGIDs, and facilitates patients moving successfully onto a management pathway, rather than a continued search for organic disease. Although there has been much research into management strategies for patients with FGIDs, we propose that strategies divorced from the diagnostic process fail to address one of the critical components of FGID. The aim of this study, was therefore to explore and describe the evidence (or lack thereof) for models of care in FGID which integrate both diagnosis and management.

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|MANUSCRIPT 4| THE POTENTIAL OF INTEGRATED NURSE-LED MODELS TO IMPROVE CARE FOR PEOPLE WITH FUNCTIONAL GASTROINTESTINAL DISORDERS: A SYSTEMATIC REVIEW

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Running Head: FGID MODELS OF CARE

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ABSTRACT

Functional gastrointestinal disorders (FGID) such as irritable bowel syndrome (IBS) and functional dyspepsia (FD) are extremely common, debilitating and costly. Although diagnostic guidelines and effective management options exist, management is sub-optimal, with long waiting lists, delayed diagnosis and poor patient outcomes. The aim of this systematic review was to explore and evaluate evidence for existing models of care for functional gastrointestinal disorders. 38 studies pertaining to the diagnosis or management of FGIDs were found, however only 6 investigated a full model of care. Five studies assessed a nurse-led model and one a structured gastroenterologist consultation. Nurse-led models were cheaper to current treatments, and resulted in symptomatic improvement, high patient satisfaction, reduced healthcare usage, and improved psychosocial functioning and quality of life, whilst standard gastroenterological care did not improve pain or quality of life. There are minimal research trialling integrated models of care for the diagnosis and management of functional gastrointestinal disorders. This represents a lost opportunity for timely, effective, healthcare provision to a large patient group. Although low in quality, preliminary data suggest that integrated nurse-led models of care are economically viable and may facilitate timely diagnosis and management, and improve patient outcomes. Further, studies to robustly evaluate the efficacy, safety and acceptability of such models are needed.

INTRODUCTION

Functional gastrointestinal disorders (FGIDs) are common [1, 2], chronic and complex, with biopsychosocial triggers, shifting symptomatology over time [3] and the frequent presence of other unexplained, somatic complaints [4]. The most common FGIDs are irritable bowel syndrome (IBS) which affects approximately 10% of the population globally [5, 6] and functional dyspepsia (FD) with a prevalence of 15% worldwide [6, 7]. Symptoms of FGID significantly impair daily life, lead to high healthcare use and costs [8-12] overuse of investigations [13] and high levels of absenteeism and presenteeism [14]. Although FGIDs are common and significantly impact both the patient and community, they are poorly handled in the healthcare system creating frustration in patients and doctors alike [15].

Recent developments of reliable, accepted diagnostic criteria [16, 17] and effective evidence-based management options [18, 19] do not appear to have been incorporated into current routine practice. Many primary healthcare providers lack confidence and continue to refer for specialist input [20-22], with capacity restraints resulting in extraordinarily long wait lists. The delay in diagnosis and implementation of effective management options represents a lost opportunity to improve symptoms, quality of life and workplace productivity, and reduce unnecessary societal expenditure on repeat consultation, unnecessary investigations, and ineffective treatments.

Given the chronic nature of FGIDs and the clear interplay of biological, psychological and social factors in triggering symptoms [23], an integrated model of care (IMoC) is needed. Integrated models of care (IMoC) have been successfully established in other chronic illnesses such as diabetes [24] and asthma [25], yet have received little attention in FGID.

A model of care is a multidimensional concept that defines the way in which healthcare services are delivered (Queensland Health, 2004). There are several elements of effective care of FGID patients which could be addressed in an IMoC. The provision of a clear diagnosis and patient acceptance of this diagnosis are critical to the successful management of patients with FGIDs. Research has shown that both patient acceptance of functional diagnoses and diagnostic communication from the physician are poor [26-28] . Thus, a model of care incorporating the first point of patient contact with the medical system is likely to greatly improve patient outcomes and reduce costs. Other important elements of such a model include diagnostic criteria and the coordinated use of newer treatments with proven efficacy for global symptom relief, including cognitive behavioural therapy, gut-directed hypnotherapy and the low FODMAP diet [18, 19].

Although there are many recommendations as to how FGID should be diagnosed and managed [29-31], few designs have been tested to date. We therefore undertook a systematic review to explore and evaluate models of care for FGID.

METHODS

Types of Studies

The protocol for this quantitative systematic review was registered at PROSPERO International prospective register of systematic reviews 15/01/2016 (PROSPERO 2016:CRD42016033146) and the search conducted in January 2016. No new publications were identified in Jan-Dec 2016.

Inclusion criteria

Primary studies concerning the diagnosis and management of FGID, irritable bowel syndrome (IBS) or functional dyspepsia (diagnosed in primary, secondary or tertiary care) were included. Studies of any quantitative research design published 1995-2016 and reporting patient related outcomes (i.e. quality of life, symptom severity) in an adult population were included. Both full text and abstracts were included.

Exclusion criteria

Studies regarding patients with organic disease, or functional abdominal pain were excluded, as were reviews, opinion pieces, dissertations, or secondary analyses. Qualitative studies, and those reporting cost or health-care use alone were excluded, as were studies trialling a treatment.

Search methodology

Sources

Databases searched were PubMed, Medline, Embase, Web of Science, Cochrane, CINAHL, PsychInfo and the ISCRTN registry. Reference lists of all included studies were also searched, experts in the field were contacted to identify additional references, and authors contacted for further information as required.

Search strategy

The search strategy covered three main concepts: functional gastrointestinal disorders, models and care, as indicated in Table 6-1.

Study selection

A systematic review was conducted according to the 5 steps outlined by Khan *et al.,* (32). The framing question was 'what models of care have been evaluated for functional gastrointestinal disorders'. In the first phase, titles and abstracts of the search results were screened by the primary researcher (EL) to assess suitability for inclusion. Studies whose suitability was uncertain were also screened by the second reviewer (AMW) and consensus reached on inclusion. Where uncertainty regarding inclusion or disagreement occurred, a third researcher (JMA) was consulted and a joint decision regarding selection was reached. In the second phase, full papers deemed suitable from the initial search were screened by both reviewers (EL, AMW) and checked against a pre-designed relevance checking proforma based on the inclusion/exclusion criteria.

Data Analysis

Data extraction

Data including author, year of publication, country of origin, design, model of care, sample size and characteristics, disease type (for example, FGID, irritable bowel syndrome, functional dyspepsia), outcomes measured and results, were extracted by the primary researcher (EL), using a customised extraction table. Extracted data was checked against the original articles by the second reviewer (AMW).

Data synthesis

Due to the limited number of available studies, and heterogeneity in study design and outcomes measured, we provided a narrative synthesis of the findings regarding full models of care (including both diagnosis and management). Studies pertaining to components of a model (such as diagnosis, patient education, or management) were summarised in Figure 6-1, but not synthesised.

Assessment of quality and risk of bias

Quality assessment of the 7 included studies was conducted (Supplementary Table 6-1) using the Quality Assessment Tool for Quantitative Studies (Effective Public Health Practice Project) [33] as recommended by the Cochrane group [34]. This scale allows all quantitative study designs to be assessed with one tool. Studies were assessed in 6 domains: selection bias, study design, confounders, blinding, data collection methods, withdrawal and dropouts, intervention integrity and analyses and scored according to the rules [33]. An overall global rating was given based on the number of weak domain ratings (strong=no weak ratings, moderate=1 weak rating, weak=2 or more weak ratings). Studies

were appraised independently by EL and AMW, and an overall rating reached by consensus. All studies regardless of quality rating were included in this review due to the scarcity of research found.

RESULTS

Search results

Out of the 95 full text articles identified, 57 were excluded (Figure 6-1) for reasons that included: non-primary research (n=14), treatment trial (n=10), duplicate abstract, protocol or secondary analysis of full-text article already included (n=15), not pertaining to FGID (n=4), or IMoC (n=6), assessed outcomes not in inclusion criteria (n=7), data unpublished (n=1). Of the 38 unique primary research studies that pertained to diagnosis or management of FGIDs (Figure 6-1), only 6 were deemed suitable for inclusion as a full IMoC, including both a diagnostic and management component. A summary of the studies that considered only one of these components of care (i.e. diagnosis OR management) is presented in Supplementary Table 6-2. An overview of these studies is included, as the examined components may be relevant to inform the development of a full IMoC for FGID (Figure 6-2). A review of individual components is outside the scope of this review.

Nature of studies

Included studies were all low in quality (Supplementary Table 6-1). Two studies were published in abstract form only, and full data were unable to be analysed [35, 36], and one described subjective changes in patient outcomes without reference to baseline or statistical analysis [37]. One study was a randomised controlled trial [38], 3 observational [26, 37, 39] and 2 non-randomised controlled designs [35, 36]. Four studies evaluated IBS IMoCs in Sweden [38], USA [37], Canada [26] and New Zealand [39], and 2 studies, in abstract form only, evaluated IMoCs for functional dyspepsia in Canada [35, 36]. No studies presented an IMoC for FGIDs in general. Due to the small number, studies regarding irritable bowel syndrome and functional dyspepsia are not discussed separately. Five articles assessed some form of a nurse-led care model [35-39], and one evaluated the performance of a structured gastroenterologist consultation [13].

Summary of full models of care

Nurse–led models

Five studies evaluated a nurse-led model [35-39]. These models differed in the setting, role and timing of nurse management. Roles included the provision of active triage and patient education prior to a consult with a gastroenterologist [36, 38], ongoing holistic management

post-diagnosis [37], screening and treatment trials prior to gastroenterologist consultation [35] and independent nurse diagnosis and management [39]. Full description of the models and findings are presented in Table 6-2.

Four of the 5 nurse-led studies measured symptom severity and patient satisfaction. Symptomatic improvement was seen in all [36-39]. One study reported subjective improvement following the intervention (no baseline comparator) [37], 2 compared to baseline at 3 [39] and 6 months [36] follow-up, and 1 compared to control group (mean GOS change -0.6±0.1, $p<0.001$) [38]. Patient satisfaction was high [36, 37] or improved compared to baseline [39], with the exception of the model reported by Bengtsson *et al.,* [38] where the nurse's role was to implement a care plan prior to consultation with a gastroenterologist. Two studies evaluated healthcare utilisation and showed reduced gastroenterologist visits compared with treatment as usual controls [38], and reduced doctor visits following the intervention [37]. Psychosocial health was measured in various forms in 4 studies with overall improvement found in all [35, 37, 39] except that reported by Bengtsson *et al.,* ([38]. Studies that assessed quality of life [35, 39] and psychosocial functioning [37] showed improvement, but Moore *et al.,* [39] found no simultaneous improvement in coping strategies. The cost of a nurse-led model was assessed in two studies and found to be significantly reduced compared to current treatments [35, 37].

Structured gastroenterologist care

Only 1 observational cohort study investigated the value of a structured gastroenterologist consultation [26]. The consultation included establishing a positive diagnosis, investigations as indicated, education and reassurance, and psychological referrals as appropriate. Ambulatory gastroenterology visits returned to and remained at baseline levels for 2 years' post-consultation. However, other ambulatory and psychiatric healthcare utilisation remained unchanged. In addition, quality of life and pain also remained unchanged at 1-year follow up, although a reduction in pain was seen at the 2-year mark.

DISCUSSION

This systematic review demonstrates that, despite FGIDs being highly prevalent, there is a paucity of data examining IMoC for FGIDs. This represents a lost opportunity for effective and efficient provision of care to this large patient group, which can be ill-afforded considering the need for cost constraint and optimal outcomes in healthcare systems worldwide. While a number of studies relate to the management of FGIDs, there is minimal research into IMoC which incorporate both diagnosis and management. This

review considers IBS and FD together, as they often co-occur and thus are best treated as one clinical group. Many patients with IBS will subsequently have FD and visa-versa. In general, our healthcare systems function more efficiently when related conditions affecting one large patient group receive a similar (but not rigidly identical) approach. The current approaches to the diagnosis and management for IBS and FD are very similar; namely exclude alarms, offer reassurance, explanation, and recommend lifestyle changes, psychological and/or dietary therapies and medication when needed.

FGIDs are significant and growing public health problem [14], with up to 40% of the population affected within their lifetime [2], and referrals representing up to 50% of gastroenterology workload [21, 22]. There is a high economic cost of FGIDs, with an estimated annual cost of 41 billion dollars (US) for IBS alone, in the UK, Japan, Australia, Sweden, Germany, France, and Canada in 2000 [40]. These costs are driven by persistent and/or unmanaged symptoms, unnecessary investigations, repeated healthcare visits and workplace impairment [6, 41], and represent a significant opportunity for improved healthcare service delivery.

Dill and Dill [37] describe the first nurse-led IBS model and its effectiveness in a single private practice in the USA in 1995. This study provides preliminary evidence to suggest the economic and clinical benefit of a nurse-led IMoC. Surprisingly, further assessment of this model did not occur for another 25 years. However, recent studies show benefits of integrated nurse-led models on symptoms, psychosocial well-being and quality of life [35-37, 39]. In addition, nurse-led clinics were more cost-effective and may enable a larger volume of patients to be seen in specialist care. The use of a nurse to screen referrals and implement treatment trials in patients with no alarm features was effective, both independently of gastroenterology consultation [39] and in conjunction with specialist review [35-37]. The only ineffective nurse-led model was dependent upon an accurate primary care diagnosis (which was found to be lacking), giving further credence to the importance of including diagnosis in a model of care. Traditional gastroenterological care was assessed in only 1 study and was not effective in reducing symptoms, or improving quality of life. However, this study was not controlled, and the approach to diagnosis and management was not standardised.

Although these studies differed in the clinicians used and the role they played, several common features were apparent. All models included a standardised diagnostic pathway, provided patient education and reassurance, and focussed on enabling the patient to self-manage their condition. The nurse-led models also provided continuing review, support and co-ordination of care.

The overall quality of included studies is low, with most having design, sampling, or reporting limitations. All studies used convenience samples of referred patients, and most study designs were observational or non-randomised control designs. In addition, all studies assessed either functional dyspepsia or irritable bowel syndrome, not a model of care for all FGIDs, and the long-term effect of these models was not assessed. Despite the low quality of evidence, these studies do provide preliminary evidence for the potential effectiveness of nurse-led, integrated models of care in FGID, and further larger scale, high quality trials are warranted.

The lack of research (and interest) in models of care for FGID to date, is most likely influenced by a poor understanding of the mechanism for pathogenesis in FGIDs, lack of diagnostic tests and uniformly effective management options, as well as differences between and changes within healthcare systems worldwide [42, 43]. However, with recent advances in the development of positive diagnostic criteria and effective global symptom management strategies, it is now possible to develop a model of care which can be implemented in virtually any developed country.

This review specifically targeted only those studies pertaining to an integrated approach to the diagnosis and management of FGIDs. The process of diagnosis is a critical component to the model of care. Many clinicians consider a functional diagnosis, but are reluctant to communicate this to the patient [44] or to document it [45], and many patients are reluctant to accept a functional diagnosis [46]. However, a timely, clear, accurate diagnosis is critical in FGIDs, as it provides reassurance, alleviates patients' concerns and helps move the patient from a diagnostic search to an effective management strategy [35, 42].

Recommendations

Despite the shortcomings in our understanding, we do have a useful biopsychosocial model (implicating psychological state, increased motor reactivity, visceral hypersensitivity, changes in mucosal immune/inflammatory function and altered enteric nervous system) [47], diagnostic guidelines [29] and effective dietary/psychological treatment options [18, 48]. Although guidelines recommend a biopsychosocial approach to the management of FGIDs, little direction is given on how [16, 29, 49, 50]. The Rome IV criteria recommend a tiered approach to the management of FGIDs according to symptom severity [16]. Current recommendations from the National Institute for Health and Clinical Excellence (NICE) are that FGIDs are diagnosed in primary care based on characteristic symptoms without alarms, with the judicious use of investigations (Dalrymple & Bullock,

2008). Referral for psychological interventions are recommended if no symptom improvement after 12 months' treatment with lifestyle modification and symptom based pharmacotherapy. The development of a standard IMoC that incorporates both a diagnostic and evidence-based management pathway is the next step forward in improving patient care for FGIDs. Key components of such a model, include the provision of a timely, clear diagnosis, patient education, empowerment, care co-ordination, multi-disciplinary teams, and individual care plans [51].

Future Directions

This review highlights the paucity of research into the development and assessment of integrated models of care for FGIDs. However, the preliminary evidence indicates a role for nurse-led models of care in FGIDs. Future studies should be large, randomised controlled trials, comparing standard gastroenterological care with integrated models, with both patient outcomes and cost evaluated. Detailed descriptions of the content of both the diagnostic and management arms of the model of care are also needed to evaluate whether components of IMoC are evidence-based, and effective. Furthermore, evidence of the standardisation of the IMoC within the trial is also necessary to ensure accuracy of the findings.

In conclusion, there is minimal research to date trialling models of care which incorporate a standardised approach to diagnosis as well as evidence-based management. Furthermore, no studies have assessed FGIDs in general, but restricted to either functional dyspepsia or irritable bowel syndrome. Existing research on full models of care is of low quality, with most pertaining to nurse models of care. However, these preliminary data suggest that models of care that incorporate protocol driven assessment and diagnosis, in conjunction with ongoing holistic care are economically viable, can be delivered by nurses, and may facilitate timely diagnosis and management, and improve patient outcomes.

Table 6-1 Search strategy used

Concepts	Synonyms	Search Terms
Functional gastrointestinal disorders	FGIDs functional gastrointestinal disorders functional bowel disease IBS irritable bowel syndrome irritable colon functional dyspepsia epigastric pain syndrome postprandial distress syndrome non-ulcer dyspepsia pseudo-ulcer syndrome pyloro-duodenal irritability nervous dyspepsia	FGIDs "colonic diseases, functional"[Mesh] OR functional gastrointestinal disorder* [all] OR FGID [all] OR FGIDs [all] OR functional bowel disorder* [all] OR functional bowel disease*[all] OR “irritable bowel syndrome” [all] OR IBS [all] OR irritable Colon [all] OR functional dyspepsia [all] OR epigastric pain syndrome [all] OR postprandial distress syndrome [all] OR non-ulcer dyspepsia [all] OR pseudo-ulcer syndrome [all] OR pyloro-duodenal irritability [all] OR dyspepsia/psychology [mh] OR colonic diseases, functional [mh] functional colonic disease*[all]
Models	integrated multidisciplinary team based models interdisciplinary holistic, wholistic nurse-led student led approach self-management biopsychosocial approach	integrat* [all] OR mutlidisciplin* [all] OR team [all] OR model [all] OR Models [all] OR interdisciplin* [all] OR holistic [all] OR wholistic [all] OR nurse-led [all] OR student-led [all] OR approach* [all] OR manag* [all] OR self manage* [all] OR biopsychosocial approach [all]
Care	health care primary care outpatient services interventions patient care	health care [all] OR Healthcare [all] OR primary care[all] OR outpatient service* [all] OR nurse-led intervention* [all] OR student-led intervention* [all] OR patient care [all] OR usual care [all] OR standard care [all]

Figure 6-1 PRISMA flow diagram

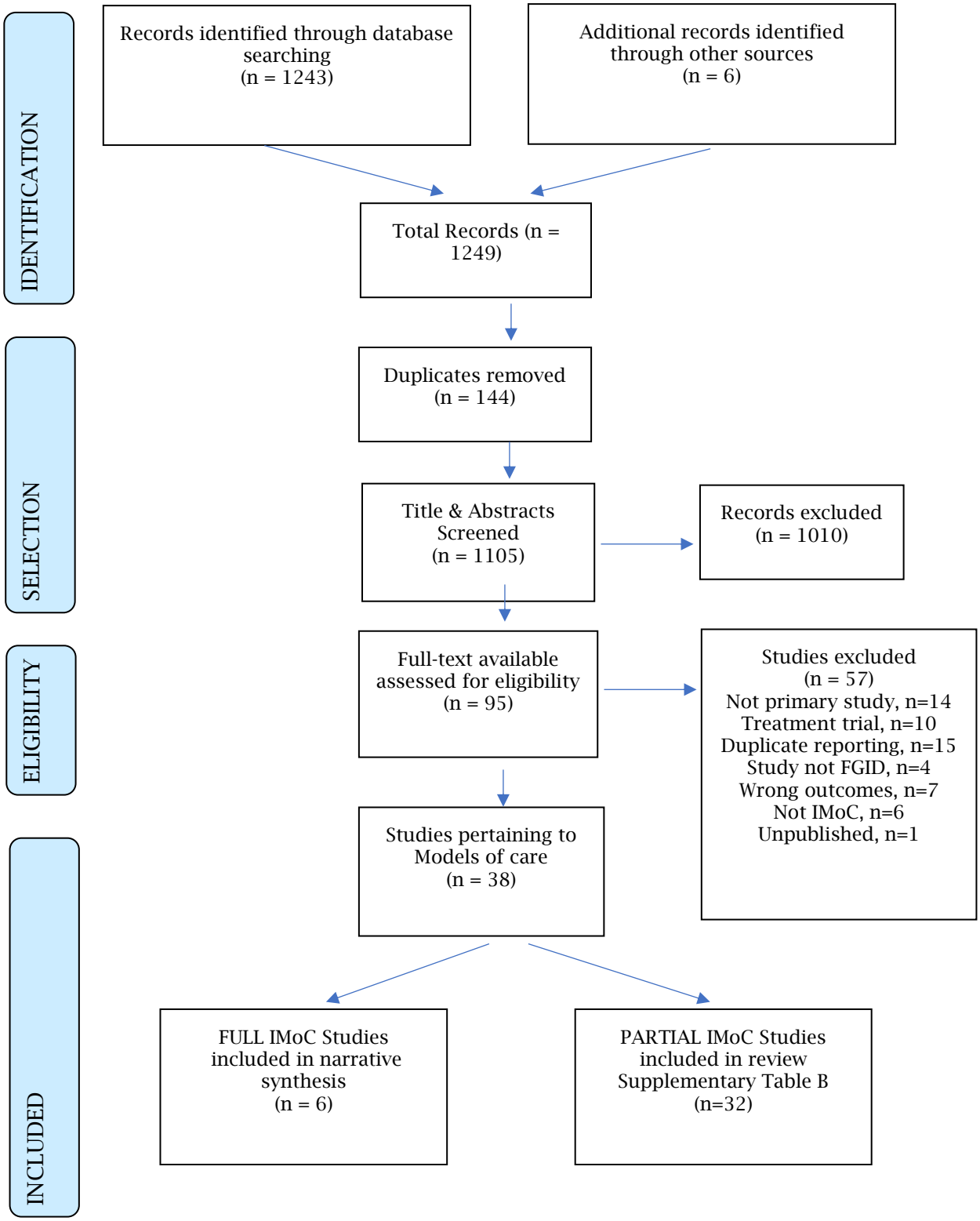

Figure 6-2 Graphical summary of all studies pertaining to models of care

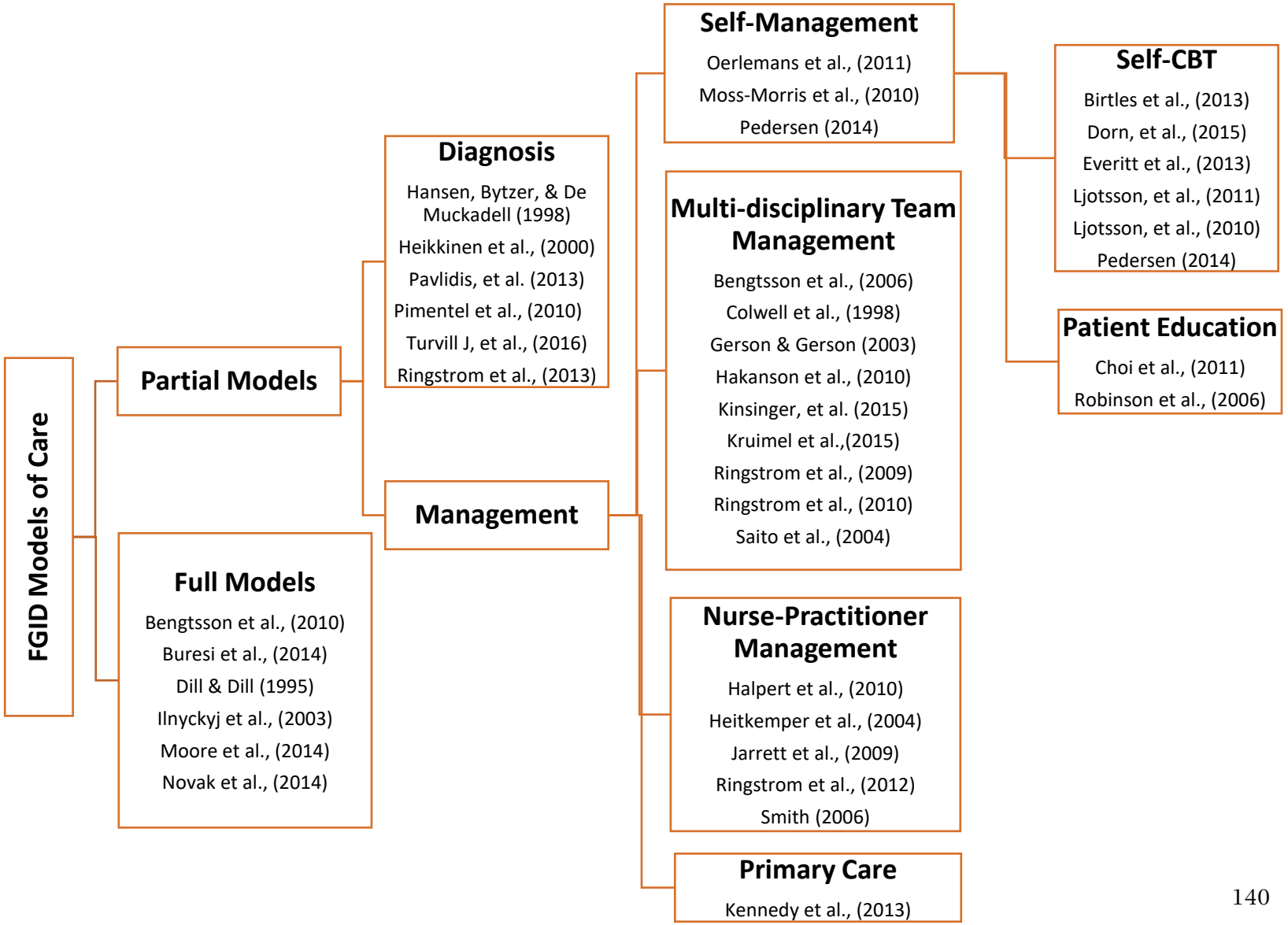

Table 6-2 Summary of studies included in the systematic review

Reference	Study Design/Sample	Details of Service Provided	Comparators/Outcomes	Results/Limitations
Bengtsson et al., (2010) – Sweden	*Design:* RCT (2-arm) *Sample:* Women 18-65 years, referred 2003-2005 with preliminary diagnosis of IBS *Sample Size*: Invited n=50 Responded n=39 Intervention n=19 Control n=20 *Alternative diagnosis:* 19/19 (100%)	*Setting:* Tertiary care *Model:* Nurse-led clinic *Delivery Mode:* Patient consult *Timing:* Prior to GE review *Further details:* Nurse takes patient history, blood tests & formulates care plan of with patients diagnosed with IBS prior to GE review	*Comparators:* Treatment as usual (GE Consult); Patients in both groups received medical consult with GE, investigations, dietitian visit as required *Primary Outcomes:* Gastrointestinal symptoms (GSRS) and psychological well-being and distress (PGWB) *Secondary Outcomes:* Patient acceptance of model, healthcare usage during intervention	*Results:* Symptom severity and well-being unchanged at follow-up. Nurse diagnosis was not acceptable as a standalone. Intervention group used less GE visits than control (p value not assessed). *Limitations:* Preliminary diagnoses were incomplete/inaccurate and nurse model unable to be adequately tested
Buresi et al., (2014) – Canada	*Design:* Cohort analytic *Sample:* Adult patients with uninvestigated dyspepsia without alarm symptoms *Sample Size*: not stated *Alternative diagnosis*: not stated	*Setting:* Tertiary care *Model:* Nurse Navigator clinic *Delivery Mode:* Multi-disciplinary group session (nurse, dietitian, mental health therapist), *Timing:* instead of GE review *Further details:* Nurse performs coeliac screen, urea breath test, trial of proton pump inhibitors, and facilitates multi-disciplinary group session by nurse, dietitian and mental health therapist (and EGD for non-responders)	*Comparators:* 1. Current therapy (Test/Treat or PPI) +gastroenterologist consult and EGD in non-responders, 2. prompt upper endoscopy & gastroenterologist review, 3. prompt thin scope endoscopy & gastroenterologist review *Outcomes:* Cost, quality adjusted life years (QALYs) gained, and incremental costs per QALYs gained	*Results:* Nurse-Navigator is the most effective strategy, thin scope endoscopy is the cheapest, but less effective than NURSE-LED *Limitations:* Abstract only: full data unavailable

Reference	Study Design/Sample	Details of Service Provided	Comparators/Outcomes	Results/Limitations
Dill & Dill (1995) – United States	*Design:* Audit survey (n=42) *Sample:* Convenience sample of adult patients referred to tertiary referral center diagnosed with IBS (1997-1998). *Sample Size*: Invited n=100 Responded n=42 *Alternative diagnosis:* Study reports only on those patients diagnosed with IBS, no data on prevalence of other diagnoses.	*Setting:* One solo, private gastroenterology practice *Model:* Gastroenterologist consult/investigations/diagnosis followed by nurse-led IBS school for ongoing management *Delivery Mode:* Individual consult *Timing:* 1x 3hr class *Further details:* 1st Visit = GE -review with minimal tests, patient told possibility of IBS; 2nd Visit = GE-Flexi sig performed & IBS diagnosis (where indicated), enrolled into nurse GI clinic with concurrent GE review; Nurse Clinic-pathophysiology plus educational material, review of meds, lifestyle, stressors and dietary advice (elimination) + fibre supplements (psyllium);3rd – Nurse Clinic. Evaluation of symptoms, continuing education, food challenge, consideration of psychosocial issues	*Comparators:* n/a *Outcomes:* Subjective patient reported changes in symptoms, symptom control, work productivity, healthcare utilisation, satisfaction with program	*Results:* Patients reported subjective improvement in symptoms, job and social functioning, and had less Dr visits, and were satisfied with the program. Cost reduction 38% *Limitations:* Observational study, not a trial. Results not statistically analysed. Baseline and follow-up data not presented, only subjective patient reported improvement since participation. 42% responders, no information on non-responders
Ilnyckyj et al., (2003) – Canada	*Design:* Observational, 2-year longitudinal follow-up *Sample:* Adult patients, referred to gastroenterologist, meeting Rome I criteria for IBS with symptom duration of 1 year or more (1996-1997) (n=70)	*Setting:* Tertiary care *Model:* Standardised diagnosis and management *Delivery Mode:* Individual consult *Timing:* Initial consult -at least 30min; follow up at 6 wks. -at least 15min *Further details:* 1. Provide positive diagnosis (history, physical exam, testing as needed); 2. Patient education (inc. material) and reassurance; 3. Standard initial and follow up times and duration	*Comparators:* Baseline *Primary Outcomes:* Healthcare utilisation *Secondary Outcomes:* Psychological functioning, pain, and patient morbidity	*Results:* Healthcare usage returned to baseline levels following consultation; No change in psychological distress or general functioning at 1 year *Limitations:* No comparator, measures at 1 year may have overlooked changes in the short-term; GE consults were not standardised in investigative approach or treatment provided; needs repeating according to current clinical approach

Reference	Study Design/Sample	Details of Service Provided	Comparators/Outcomes	Results/Limitations
Moore et al., (2014) –New Zealand	*Design:* Observational, 3-month follow up *Sample:* Adult patients previously diagnosed with IBS fulfilling Rome II criteria, attending IBS clinic *Sample Size*: Invited n=55 Responded n=45 *Alternative diagnosis:* 24/55 (43%)	*Setting:* Secondary care *Model:* Private IBS service conducted by nurse practitioner *Delivery Mode:* Individual consult *Timing:* Initial consult, plus follow-up 2 weeks later *Further details:* Protocol driven assessment; 1. Abdominal and rectal physical exam; 2. Blood tests (CBE, iron studies, C-reactive protein, thyroid function, liver function, coeliac antibodies, kidney function); 3. Stool tests (faecal microscopy and culture, faecal calprotectin). Follow-up consult: review results, discuss management strategy (education, lifestyle management, onward referrals)	*Comparators:* n/a *Primary Outcomes:* Symptom severity, patient satisfaction, quality of life, and coping skills.	*Results:* Improved symptoms, satisfaction with healthcare, and quality of life. No change in coping strategies *Limitations:* No control group
Novak et al., (2014) – Canada	*Design:* Prospective, non-randomly controlled study; 6-month follow-up *Sample:* Adult patients with uninvestigated dyspepsia without alarm symptoms, from one primary care area (n=359) *Sample Size*: Invited n=not stated Intervention n=247 (107/247 endoscopy), Control n=112 *Alternative diagnosis:* 6/107 in endoscopy group. Data not provided on non-endoscopy group.	*Setting:* Tertiary care *Model:* Nurse-led, triage, multidisciplinary group management, followed by physician consult *Delivery Mode:* Group session plus individual consult *Timing:* 1 hr group session, followed by brief physician consult *Further details:* 1. Nurse triage of alarm vs non-alarm patients; 2. Non-alarm patients participated in session (dietitian, nurse, pharmacist); 3. Followed by brief physician consult immediately after group	*Comparators:* Treatment as usual in patients referred from another primary care area (mainly waitlist control) *Outcomes:* Symptom severity, patient satisfaction, satisfaction with group format	*Results:* Symptom severity improved in intervention group at 6 months follow up. 99% of patients reported benefit and support, 84% liked the group format. *Limitations:* Abstract only: Full data unavailable for analysis. Details of intervention brief

Supplementary Table 6-1 Critical appraisal using The Quality Assessment Tool for Quantitative Studies

Reference	Selection Bias	Study Design	Confounders	Blinding	Data Collection Method	Withdrawals and Dropouts	Global Rating
Bengtsson et al., (2010) [1]	Weak	Strong	Moderate	Weak	Strong	Weak	Weak
Buresi et al., (2014) [2]	Weak	Moderate	Weak	Weak	Weak	Weak	Weak
Dill & Dill (1995) [3]	Weak	Weak	n/a	Weak	Weak	Weak	Weak
Ilnyckyj et al., (2003) [4]	Moderate	Moderate	n/a	Weak	Strong	Weak	Weak
Moore et al., (2014) [5]	Weak	Moderate	Moderate	Moderate	Weak	Strong	Weak
Novak et al., (2014) [5]	Moderate	Strong	Strong	Weak	Strong	Weak	Weak

Scoring rules: Strong (no weak ratings), Moderate (one weak rating), Weak (two or more weak ratings)

Supplementary Table 6-2 Summary of the studies excluded from the systematic review

Reference	Model Component (Disorder)	Study Design & Sample	Details of Service Provided	Comparators & Outcomes	Results & Limitations	Practical Implications
Begtrup, et al. (2013) – Denmark (6)	Diagnosis (IBS)	*Design*: RCT (2-arm) *Sample*: Patients aged 18-50 years suspected of having IBS referred from primary care (n=302)	*Setting:* Tertiary care *Service:* Positive diagnosis-provided by gastroenterologist *Delivery Mode:* Patient consult *Timing:* Initial consult, testing and follow-up all completed within 4 weeks	*Comparators:* Diagnosis of exclusion *Outcomes:* Health related quality of life, gastrointestinal symptoms, satisfaction with management, use of resources. Diagnosis at 1 year	*Results:* Positive diagnostic strategy is cheaper. No difference in outcomes between two strategies was observed *Limitations:* Long-term differences in the two groups were not assessed. Patients were young <50 years of age	Positive diagnosis for IBS in patients under 50 years of age is safe and cost-effective, and does not decrease patient satisfaction with management or increase subsequent use of healthcare resources
Bengtsson et al., (2006) – Sweden (7)	Management-Patient Education (IBS)	*Design:* Before-After, 1,6 & 12-month follow-up *Sample:* Women 18-65 years, diagnosed in-house with IBS 1998-2002 (n=29)	*Setting*: Tertiary care *Service :* Multidisciplinary team management (dietitian, physician, nurse & social worker, plus care nurse) *Delivery Mode:* Group workshop *Timing:* One 8-h session	*Comparators:* Diagnosis of exclusion *Outcomes:* Psychological well-being, health care and medicine use, sick leave	*Results:* No change in symptoms/psychological well-being/hospitalisations/medicine use/sick leave; reduced abdominal pain and increased vitality; reduced healthcare utilisation *Limitations:* No control group. Women only sample. Small sample size. Tertiary referral sample rather than primary care.	MDT workshops may be useful in reducing pain and healthcare utilisation. Differences in tertiary vs primary care patients not known. Timing/type of workshop may inadequate to maximise outcomes.

Reference	Model Component (Disorder)	Study Design & Sample	Details of Service Provided	Comparators & Outcomes	Results & Limitations	Practical Implications
Birtles et al., (2013) – Australia [8]	Management-Self CBT (IBS)	*Design:* RCT (2-arm) *Sample:* Specialist and community patients fulfilling Rome III criteria for IBS; no other details provided	*Setting:* Primary and tertiary care *Service:* Self-CBT *Delivery Mode:* Online website *Timing:* Available 8 weeks	*Comparators:* Waitlist *Outcomes:* Patient coping, symptom severity	*Results:* Patients with low-moderate symptoms and positive coping significantly improved in outcomes after intervention, as compared to other groups; Comparison to control NOT reported *Limitations:* Abstract only: full data unavailable, control group data not presented	Patients with low-moderate symptoms may benefit from web based CBT self-management
Choi et al., 2011 – United States [9]	Management-Patient Education (FD)	*Design:* RCT (2-arm), 6-month follow-up *Sample:* Patients fulfilling Rome III criteria recruited from a GI and from an internal medicine clinic; (n=30); no other details provided	*Setting:* Not stated *Service:* Patient education *Delivery Mode:* Written, and reviewed with someone *Timing:* Not stated	*Comparators:* Treatment as usual *Outcomes:* Understanding of FD, symptom severity, health related quality of life	*Results:* Patient understanding was improved, although still low; no difference observed in symptom severity or quality of life *Limitations:* Abstract only: full data unavailable, control group data not presented	Interventions need to be more than just education regarding pathophysiology.
Colwell et al., (1998) – United States [10]	Management-Patient Education	*Design:* Observational study - 1 & 6-month follow-up *Sample:* Adult outpatients with IBS (n=52)	*Setting:* Tertiary care *Service:* Nurse-led multidisciplinary team management (Registered nurse, dietitian, physical therapist, and behavioural psychologist) *Delivery Mode:* Group workshop *Timing:* One 3-h class (1-6 patients	*Comparators:* n/a *Outcomes:* Health-Promoting Lifestyle Profile, frequency and severity of symptoms	*Results:* Reduced pain at 1 & 6 m, variable improvement in exercise and stress management; reduction in lifestyle interference and physician visits at 6m, no change in medications used *Limitations:* No control group.	Nurse led model of management may improve patient health outcomes.

Reference	Model Component (Disorder)	Study Design & Sample	Details of Service Provided	Comparators & Outcomes	Results & Limitations	Practical Implications
Dorn, et al., (2015) – United States [11]	Management-Self	*Design:* Observational, pilot study *Sample:* Adults aged 18–80y with physician-diagnosed, Rome III criteria-positive IBS (n=40)	*Setting:* Not stated *Service:* Self-CBT *Delivery Mode:* Web-based with email support *Timing:* Access to website for 12 weeks	*Comparators:* Web-based without email support *Outcomes:* Program utilization, self-efficacy and quality of life	*Results:* Significantly improved knowledge about IBS. 75% reported at least some relief relative to baseline. No clinically meaningful changes in self-efficacy or health-related quality of life. *Limitations:* No control group. Patients had very mild symptoms at baseline. Differences in outcomes with levels of access of the site not analysed. Rolling recruitment led to low activity in forum. Website was static for duration of access.	Web-based self-management improves knowledge and may reduce symptoms. Unknown which patient group it might be more effective in, and whether forums are useful.
Everitt et al., (2010) – United Kingdom [12]	Management-Self (IBS)	*Design:* RCT, 6 week, 3,6 & 12-month follow-up *Sample:* Patients aged 16-60y presenting to general practice with symptoms of IBS fulfilling Rome III criteria (n=135)	*Setting:* Primary care *Service:* Self-CBT *Delivery Mode: Interactive w*eb-based with expert chatrooms and peer-to-peer networks *Timing:* 8 sessions over 6 weeks	*Comparators:* No website access, With/without Mebeverine or Methylcellulose *Outcomes:* Symptom severity, quality of life, global assessment of relief	*Results:* No observed differences in outcomes between groups. Subjects global assessment of relief was improved at 12-week mark *Limitations:* Factorial design combining drug trial led to very small sample size in pure web based groups (n=15), possible Type II error	Web-based CBT may be useful, but larger scale trials needed

Reference	Model Component (Disorder)	Study Design & Sample	Details of Service Provided	Comparators & Outcomes	Results & Limitations	Practical Implications
Gerson & Gerson (2003) – United States [13]	Management-Collaborative Treatment (IBS)	*Design*: RCT (3-arm) *Sample:* Patients diagnosed IBS 1998-2001, aged 20-60y, fulfilling Rome I criteria (n=41)	*Setting:* Tertiary care *Service:* Combined gastroenterologist & psychologist consultation *Delivery Mode:* Individual patient consult *Timing:* Timing: 3 x 45 min sessions (bi-weekly)	*Comparators:* Gastroenterology care alone (2 visits in 6 weeks) versus psychological care alone (6 x 45 min weekly visits) *Outcomes:* Symptom severity, quality of life, quality of personal relationships, anxiety, depression, global *assessment.*	*Results:* Collaborative group had improved global assessment and symptom severity, whereas the other treatment groups did not improve. Psychological measures were also stable in all 3 groups *Limitations:*	Combining psychological management with gastroenterology management leads to improved patient outcomes.
Hakanson et al., (2011) – Sweden [14]	Management-Patient Education (IBS)	*Design:* Before-After *Sample:* Patients with IBS symptoms > 3 years, fulfilling Rome II criteria, on the waiting list for the education program (n=51)	*Setting:* Tertiary care *Service:* Nurse-led, multidisciplinary team management (IBS Nurse, GE, Psychologist, Biofeedback nurse, Anaesthesiologist, Dietitian, Physiotherapist, Hospital deacon) *Delivery Mode:* Group workshop *Timing:* 1-h individual nurse appointment ; plus groups workshops 5 h/day for 5 consecutive days	*Comparators: Baseline* *Outcomes:* Symptom severity & coping	*Results:* Significant and clinical reduction in symptom severity following group program, which was associated with changes in coping strategies used *Limitations:* No control group, short follow-up time frame	Nurse-led group based management program is effective in the short-term

Reference	Model Component (Disorder)	Study Design & Sample	Details of Service Provided	Comparators & Outcomes	Results & Limitations	Practical Implications
Halpert et al., (2010) – United States [15]	Management-Patient Education (IBS)	*Design:* RCT (2-arm), 1,3 & 6-month follow-up *Sample:* People with IBS - No other details provided (n=100)	*Setting:* Tertiary care *Service:* Tailored education provided by gastroenterology nurse practitioner that builds on learner's past experience and focuses on problem solving not information giving *Delivery Mode:* Individual consult *Timing:* One, 30 min session	*Comparators:* Read IBS brochure for 30min *Outcomes:* IBS specific quality of life, disease related cognition/coping, severity, and health care utilization	*Results:* Improved symptom severity, and health beliefs and attitudes at 1 and 3 months, but no difference to control group. No differences in other outcomes *Limitations:* Abstract only: full data unavailable	1) NURSE-LED educational consultation may improve patient outcomes, 2) IBS brochure may be just as effective, 3) Effect of more than one NURSE-LED session is unknown
Hansen, Bytzer, & De Muckadell (1998) – Denmark [16]	Diagnosis (FD)	*Design:* Clinical study (Not RCT) *Sample:* All adults with dyspeptic symptoms seen in primary care in one city (n=668)	*Setting:* Primary care *Service:* Primary health care provider stated provisional diagnosis and proposed management strategy. Upper endoscopy performed to determine predictive value of provisional diagnosis. *Delivery Mode:* Individual consult *Timing:* At diagnosis	*Comparators:* 1. Non-responders 2. Another group referred for open access endoscopy *Outcomes:* Predictive value of symptom based provisional diagnosis and management	*Results:* 1/3 patients categorised inappropriately, low predictive value of unaided provisional diagnosis *Limitations:* study conducted prior to Rome criteria, standardised form of positive diagnosis was not used	Non-standardised, symptom based diagnosis for dyspepsia may be unreliable

Reference	Model Component (Disorder)	Study Design & Sample	Details of Service Provided	Comparators & Outcomes	Results & Limitations	Practical Implications
Heikkinen et al., (2000) – Finland [17]	Diagnosis (FD)	*Design:* Clinical study (Not RCT) *Sample:* Dyspepsia patients in primary care 1993-1994 (n=400)	*Setting:* Primary care *Service:* Primary care working diagnosis *Delivery Mode:* Individual consult *Timing:* At diagnosis	*Comparators:* GE diagnosis following structured testing and extra investigations if needed *Outcomes:* Sensitivity, specificity and positive/negative predictive values of GP diagnosis, and management outcomes	*Results:* Clinical diagnoses of dyspepsia unreliable *Limitations:* PHCP decision to investigate or not was purely theoretical as all were investigated as part of the study.	Standardised clinical pathways utilising criteria predictive of organic disease in dyspepsia might be useful.
Heitkemper et al., (2004)– United States [18]	Management-Self (IBS)	*Design:* RCT (3-arm), 6 & 12-month follow-up *Sample:* Women with IBS (Rome I) aged 18-48 years, recruited through community advertisement and local health organisation (n=144)	*Setting:* Not stated *Service:* Psychiatric nurse practitioner led, multi-component, non-pharmacologic intervention (Diet, education and reassurance, relaxation, and CBT). *Delivery Mode:* Individual consult *Timing:* 8, 1-h weekly sessions	*Comparators:* Treatment as usual or brief multi-component intervention (one 90 min session plus workbook) *Outcomes:* symptoms, psychological distress, health-related quality of life, and stress-related hormones at after completion	*Results:* Reduced gastrointestinal symptoms, psychological distress, disruption to daily living, and enhanced quality of life out to 12 months. Comprehensive intervention more effective than the Brief intervention *Limitations:* Delivered by advanced practice nurses with Masters and experience in mental health.	Nurse-led group based management program is effective over the long term

Reference	Model Component (Disorder)	Study Design & Sample	Details of Service Provided	Comparators & Outcomes	Results & Limitations	Practical Implications
Jarrett et al., (2009)–United States [19]	Management-Self (IBS)	*Design:* RCT (2-arm), 12-month follow-up *Sample:* Adults with IBS (Rome II) diagnosed in primary care, with current symptoms, recruited through community advertisement (n=188)	*Setting:* Not stated *Service:* Comprehensive self-management facilitated by psychiatric nurse practitioner *Delivery Mode:* Individual consult *Timing:* 9-weekly in-person sessions versus 9-weekly sessions (3 in person, 6 telephone)	*Comparators:* Treatment as usual *Outcomes:* Symptom severity, disease specific quality of life; psychological distress, cognitive beliefs, workplace productivity and activity.	*Results:* Improved patient outcomes in intervention not controls, and persisted to 12-month follow-up *Limitations:* Telephone intervention also had 3 in-person consults, so not strict non-contact intervention.	In person and combined in person/telephone delivered management are viable options. Allows flexibility for patient preferences.
Kennedy et al., (2013)–United Kingdom [20]	Management-Self (IBS)	*Design:* RCT (2-arm) *Sample:* One primary care trust, 2009-2012. Patients with diabetes, chronic obstructive pulmonary disease, or IBS (n=5599)	*Setting:* Primary care *Service:* Primary health care provider practices trained in 1. use of wide range of resources; 2. Tools to assess the support needs of patients; 3. Guidebooks on self-management; 4. Web-based directory of local self-management : 1. Education, 2. Diet (food diary reviewed by dietitian to tailor advice), 3. Relaxation, 4. CBT strategies] *Delivery Mode:* Individual consult *Timing:* n/a	*Comparators:* Treatment as usual *Outcomes:* Shared decision making, self-efficacy, and health related quality of life; General health, psychological well-being, self-care activity, enablement, social or role limitations, and energy and vitality	*Results:* Primary care practices using WISE did not differ from control primary care practices in any patient outcome *Limitations:* No standard approach to WISE. Implementation was variable.	Embedding self-management supports into primary care is difficult.

Reference	Model Component (Disorder)	Study Design & Sample	Details of Service Provided	Comparators & Outcomes	Results & Limitations	Practical Implications
Kinsinger, et al. (2015)– United States [21]	Management-Multidisciplinary (FGID)	*Design:* Retrospective, cross sectional study *Sample:* Patients referred to in-house health psychology unit with chronic gastrointestinal conditions (2101-2011) (n=259)	*Setting:* Tertiary care *Service:* Onsite, integrated GI health psychology service *Delivery Mode:* Individual consult *Timing:* as needed	*Comparators:* n/a *Outcomes:* Uptake of service by referred patients, and health care utilisation	*Results:* Half of referred patients attended psychological service, and a third participated in ongoing treatment; fewer medical procedures in psychological service attenders. *Limitations:* Sample well educated and affluent - may influence generalisability. Measures of patient improvement not taken, only healthcare utilisation. Psychological services were covered by medical insurance - this is not necessarily the case in every healthcare system	Integrating psychological services within a gastroenterology clinic is practically feasible, used by a significant number of patients, and reduces ongoing medical procedures.
Kruimel et al.,(2015)– Netherlands [22]	Management-Multidisciplinary (FGID)	*Design:* Prospective, observational, naturalistic, 12-month longitudinal design *Sample:* All FGID patients (Rome III) with moderate-severe symptoms non-responsive to standard treatment, suspected of having psychiatric co-morbidity referred to FGID clinic	*Setting:* Tertiary care *Service:* Multidisciplinary outpatient joint consultation with gastroenterologist and psychiatrist; Evaluation of diagnosis and management. Focus on somatic and psychosocial factors and how they interact. *Delivery Mode:* Individual consult *Timing:* as needed	*Comparators:* n/a *Outcomes:* Gastrointestinal symptoms, anxiety and depression, health related quality of life	*Results:* Reduction in depression/anxiety and health related quality of life persisting to 12 months; independent of symptomatic improvement (no change except diarrhoea) *Limitations:* No control group; standardised treatment prior to referral not discussed	Use of multi-disciplinary approach to management improves quality of life and psychosocial functioning in patients with persisting symptoms. Joint consultation is a novel approach - possibly restricted by billing criteria.

Reference	Model Component (Disorder)	Study Design & Sample	Details of Service Provided	Comparators & Outcomes	Results & Limitations	Practical Implications
Ljotsson, et al., (2011)–Sweden [23]	Management-Self	*Design:* RCT (2-arm) 12 month longitudinal *Sample:* Clinical setting: All adult patients diagnosed with IBS (Rome III) in a tertiary clinic 2008-2009 (n=61)	*Setting:* Primary and tertiary care *Service:* Self-CBT *Delivery Mode:* Online website with group discussion forum and access to psychologist via chat *Timing:* Available 10 weeks	*Comparators:* Waitlist *Outcomes:* Gastrointestinal symptoms, health economic data, quality of life, cognitive patterns, disability, healthcare use	*Results:* Reduced symptoms, IBS-related anxiety and improved IBS-related quality of life *Limitations:* Only 43% completed the treatment	Although beneficial to a subset of patients, use of internet CBT may not be acceptable to all patients in a clinic.
Ljotsson et al., (2010)–Sweden [24]	Management (IBS)	*Design:* RCT (2-arm), 3 month longitudinal **Sample:** Self-referred, diagnosed IBS patients (May-June 2008) currently filling Rome III criteria (n=85)	*Setting:* Primary and tertiary care *Service:* Self-CBT *Delivery Mode:* Online website with group discussion forum and access to psychologist via chat *Timing:* Available 10 weeks	*Comparators:* Online discussion forum *Outcomes:* Symptom severity, quality of life, cognitive patterns, disability, depression, treatment credibility	*Results:* Reduced symptoms post treatment and at 3 month follow up, improvement in all secondary outcomes *Limitations:* Control group expectation of improvement was low, as they were offered crossover to intervention at completion - limiting comparison of the two groups	In self-selected patients, web-based, CBT grounded self-help with access to groups forum is beneficial in reducing symptoms and improving quality of life

Reference	Model Component (Disorder)	Study Design & Sample	Details of Service Provided	Comparators & Outcomes	Results & Limitations	Practical Implications
Moss-Morris et al., (2010)-New Zealand [25]	Management (IBS)	*Design:* RCT (2-arm), 8 month longitudinal (n=64) *Sample:* Adult patients recruited from previous study database of confirmed IBS patients (Rome I or II)	*Setting:* Primary care *Service:* Self-management for a chronic condition *Delivery Mode:* Manualised program, plus one in-person consult, and two telephone consult *Timing:* 7-week manualised program plus one-hour face to face therapy (beginning), and 2 x 1-h phone therapy sessions (middle and end)	*Comparators:* Treatment as usual *Outcomes:* Global assessment of relief, and symptom severity; work and social adjustment, anxiety and depression	*Results:* Improvement in symptom severity and impact on life, which persisted to 6 months. Intervention group had reduced anxiety at 6 months compared to baseline, but comparable to control. Patient acceptability of program was high *Limitations:* Educated cohort, also with low-moderate symptoms - possible generalisability issues.	Self-management with minimal psychologist input is acceptable and effective for some patients.
Oerlemans et al., (2011)-Netherlands [26]	Management (IBS)	*Design:* Open label RCT (2-arm), 3 month follow up *Sample:* Patients with IBS (Rome III) aged 18-65 y recruited from primary care 2007-2008 (n=76)	*Setting:* Primary care *Service:* Self-management plus e-psychologist feedback *Delivery Mode:* Personal digital assistant (PDA) plus written feedback (sms) *Timing:* Patients completed electronic diary 3x per day, for 3 weeks.	*Comparators:* Standard care *Outcomes:* GI symptom related cognitions, disease specific quality of life, pain catastrophising, abdominal pain	*Results:* Improved quality of life, pain, catastrophising at 4 weeks, with improvement in catastrophising persisting at 3 months *Limitations:* Long term follow-up not conducted. Unknown whether continued monitoring is beneficial or not	Use of monitoring system in conjunction with tailored feedback is beneficial. PDA also acceptable format for some patients

Reference	Model Component (Disorder)	Study Design & Sample	Details of Service Provided	Comparators & Outcomes	Results & Limitations	Practical Implications
Pavlidis, et al. (2013)–United Kingdom (27)	Diagnosis (IBS)	*Design:* Retrospective clinical practice study *Sample:* Patients aged 18-45y, with GI symptoms (with/without alarms) tested for faecal calprotectin in primary care 2010-2011 in a primary trust	*Setting:* Primary care *Service:* Faecal calprotectin pathway *Delivery Mode:* Individual consult *Timing:* at diagnosis	*Comparators:* n/a *Outcomes:* Final diagnosis	*Results:* Faecal calprotectin useful in ruling out organic disease. Cut-off values and re-testing strategies are needed *Limitations:* Individual variation in investigative strategies used may lead to partial verification bias.	Faecal calprotectin is a useful component of a diagnostic pathways
Pedersen (2014)–Denmark (28)	Management (IBS)	*Design*: Case report *Sample:* Patients with IBS (Rome III) aged 18-74 y (2011-2012((n=19)	*Setting:* Tertiary care *Service:* Self-based symptom tracker *Delivery Mode:* Web-based *Timing:* Weekly for 12 weeks	*Comparators:* n/a *Outcomes:* symptoms, quality of life	*Results:* Symptom improvement achieved during control period of symptom tracking as well as when dietary intervention applied. Quality of life improved in dietary intervention, not control period *Limitations:* Small sample size. Impact of adherence to low FODMAP diet not assessed. Short time frame of follow up	The use of a symptom tracker which flags symptoms with a traffic light symptom, may help patients to identify factors which contribute to symptoms and self-manage their condition

Reference	Model Component (Disorder)	Study Design & Sample	Details of Service Provided	Comparators & Outcomes	Results & Limitations	Practical Implications
Pimentel et al., (2010)–United States [29]	Diagnosis (IBS)	*Design:* Observational *Sample:* Patients aged 18+y, diagnosed with IBS-D, IBD, coeliac disease (n=99)	*Setting:* Tertiary care *Service:* Questionnaire regarding stool form and frequency *Delivery Mode:* Questionnaire *Timing:* at diagnosis	*Comparators:* Compare IBS stool form and frequency to IBD/coeliac stool form and frequency *Outcomes:* Utility of a single question regarding stool form and frequency	IBS-D patients had greater number of stool forms per week, this feature was diagnostically significant. Utility in distinguishing other types of IBS is unknown, as is utility in patients with co-existing organic/functional disorders	History regarding stool form and frequency may be a useful tool in distinguishing between IBS-D and IBD/coeliac disease. More research is needed
Ringstrom et al., (2009)–Sweden [30]	Management-Patient Education (IBS)	*Design:* Before-After, 3, 6, 12-month follow-up *Sample:* IBS patients (Rome II) attending tertiary outpatient gastroenterology clinic (n=12)	*Setting:* Tertiary care *Service:* Multidisciplinary team management (nurse, gastroenterologist, dietitian, physiotherapist, psychologist) *Delivery Mode:* "IBS School" Group (5-7 people) *Timing:* 6 weekly, 2-h sessions	*Comparators:* Baseline *Outcomes:* Perceived knowledge about IBS, symptom severity, health related quality of life	*Results:* Symptom and quality of life improvement at 3 and 6 months; improved knowledge and satisfaction with knowledge *Limitations:* Small sample size; Tertiary care patients may have more severe symptoms and be more motivated to attend	Group based education programs might be effective in helping patients manage their FGID.
Ringstrom et al., (2010)–Sweden [31]	Management-Patient Education (IBS)	*Design:* RCT (2-arm), 3 & 6-month follow-up *Sample:* IBS patients (Rome II) aged 18-70y referred from primary, secondary & tertiary care (n=143)	*Setting:* Tertiary care *Service:* Multidisciplinary team management (nurse, gastroenterologist, dietitian, physiotherapist, psychologist) *Delivery Mode:* "IBS School" Group (8-10 people) *Timing:* 6 weekly, 2-h sessions	*Comparators:* Booklet *Outcomes:* Perceived knowledge about IBS, symptom severity, health related quality of life, anxiety, depression	*Results:* IBS School participants had greater reduction in symptom severity, anxiety, increased perceived knowledge; no difference in depression noted *Limitations:* Most patients were recruited from secondary/tertiary care, thus generalisability to primary care patients is unknown	Group based education is superior to written information and might be a valuable management tool for patients

Reference	Model Component (Disorder)	Study Design & Sample	Details of Service Provided	Comparators & Outcomes	Results & Limitations	Practical Implications
Ringstrom et al., (2012)– Sweden [32]	Management-Patient Education (IBS)	*Design:* RCT (2-arm), 3 & 6-month follow-up *Sample:* IBS patients (Rome II) aged 18-70y referred from primary, secondary & tertiary care (n=80)	*Setting:* Tertiary care *Service:* Short nurse-led patient education *Delivery Mode:* "IBS School" Group (8-10 people) *Timing:* 3 weekly, 2-h sessions	*Comparators:* Multi-disciplinary group sessions, 6 weekly, 2 hr sessions *Outcomes:* Perceived knowledge about IBS, symptom severity, health related quality of life, anxiety, depression	*Results:* Participants in both groups had reduced symptom severity, anxiety, and increased perceived knowledge. *Limitations:*	Short nurse led version of IBS School is as effective as longer multi-disciplinary team
Ringstrom et al., (2013)– Sweden [33]	Diagnosis (IBS)	*Design:* Qualitative *Sample:* Patients diagnosed with IBS referred to a FGID clinic 2003-2007 (n=20)	*Setting:* Tertiary care *Service:* 1. Structured diagnostic workup of patients already diagnosed with IBS (small bowel manometry, rectal balloon distension, oro-anal transit time); 2. Follow up inc. explanation of mechanisms underlying symptoms and how to reduce, symptoms. *Delivery Mode:* Individual consults with nurse and physicians *Timing:* 4 visits over 6-month period	*Comparators:* n/a *Outcomes:* Patients lived experiences	*Results:* 1) Suffering caused by symptoms and poor management; 2) Patients were motivated to endure discomfort and pain in the diagnostic workup; 3) Increased capacity for resilience because of learning more about their body and IBS during the workup; 4) validation of their experience *Limitations:* Delay between workup and interview. Unable to determine whether the workup or the clinician approach was more important	Diagnostic workup in conjunction with adequate explanation, reassurance, validation is valued by patients. However, this workup is extensive and not recommended by current guidelines

Reference	Model Component (Disorder)	Study Design & Sample	Details of Service Provided	Comparators & Outcomes	Results & Limitations	Practical Implications
Robinson et al., (2006)– United Kingdom (34)	Management-Patient Education (IBS)	*Design:* RCT (3-arm), 12-month follow-up *Sample:* Patients diagnosed with IBS (by primary healthcare provider or specialist) aged 18+y	*Setting:* Primary care *Service:* Self-management using guidebook *Delivery Mode:* Written material *Timing:* *n/a*	*Comparators:* 1) Guidebook plus 1, 2 hr group session, 2) Treatment as usual *Outcomes:* Number of primary care consultations, global assessment of symptoms, quality of life.	*Results:* Number and cost of healthcare use was reduced in both intervention; symptoms and quality of life were not improved in either intervention; Concluded no additional benefit from group session *Limitations:* Lack of effect of guidebook conflicts with other studies and may reflect content rather than the mode of delivery. Likewise, the group results differ from published studies and may reflect the ineffectiveness of 1 short session rather than group based educational interventions. The content of the group based session and qualification of the facilitator is not described and may be a limiting factor.	Guide books and group based interventions can reduce patient healthcare use. Whether the cost of the group offsets the healthcare savings is not known. Attendance at group session was low, suggesting groups may appeal to subsets of patients. Attention to content of the self-help material is required.
Smith (2006)– United Kingdom (35)	Management (IBS)	*Design:* Before-After *Sample:* Patients aged 18-64, with IBS (Rome II) (n=75)	*Service:* Nurse led treatment program including education, support and gut-directed hypnotherapy *Delivery Mode:* Individual consult *Timing:* 5-7 half hour hypnotherapy sessions over 5 months	*Comparators:* Baseline *Outcomes:* Symptoms, psychosocial aspects, health related quality of life	*Results:* Symptoms, quality of life, and anxiety improved following gut-directed hypnotherapy, whilst depression did not *Limitations:* No control group; information pertaining to support and educational components not described or accounted for in results	Hypnotherapy can be successfully implemented by nursing staff in a clinic setting. However, education and support may also play a role in symptomatic improvement

Reference	Model Component (Disorder)	Study Design & Sample	Details of Service Provided	Comparators & Outcomes	Results & Limitations	Practical Implications
Saito et al., (2004)– United States [36]	Management-Patient Education (IBS)	*Design:* Prospective, observational study, 6-month follow-up *Sample:* All adult patients referred to tertiary referral center diagnosed with IBS (1997-1998) (n=211)	*Setting:* Tertiary care *Service:* Nurse-led, multidisciplinary team; Includes dietitian, psychologist, and physical therapist *Delivery Mode:* Group session *Timing:* 1 x 3-h class	*Comparators:* Non-attendees *Outcomes: S*ymptom severity, quality of life, health related behaviours, psychological distress	*Results:* Pain and quality of life improved in both attendees and non-attendees; class attendees had improved symptoms and overall health behaviours compared to non-attendees; no difference in healthcare use between the two groups *Limitations:* Comparison group is a gastroenterologist consult group within the same centre. It is unknown whether patients would be getting the same advice in their individual consult as the group participants	Group educational session can improve symptoms and promote better health behaviours. Which aspects of the intervention are efficacious is unknown, as is the optimal length/number of sessions
Turvill J, et al., (2016)– United Kingdom [37]	Diagnosis (IBS)	*Design:* Clinical evaluation of primary care pathway *Sample:* Patients aged 18-60 presenting to primary care with new lower GI symptoms where cancer is not suspected (n=262)	*Setting:* Primary care *Service:* Faecal calprotectin primary care pathway to differentiate between IBS and IBD; >100 μg/g repeat test, >250 μg/g prompt colonoscopy, <100 μg/g IBS *Delivery Mode:* Individual consult *Timing: at diagnosis*	*Comparators:* Gastroenterology activity in a neighbouring trust *Outcomes:* Positive and negative predictive value compared with GP diagnosis	*Results:* Faecal calprotectin pathway had 97% negative predictive value, 40% positive predictive value; diagnostic yield of colonoscopies was greater in the pathway group than gastroenterology comparison group *Limitations:*	Use of faecal calprotectin as part of a clinical pathway is effective in ruling out IBD in primary care and identifying indicated colonoscopies

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Chapter 7 : Performance of A Novel FGID Clinical Pathway

BACKGROUND

The research presented thus far, provides evidence for the mismatch between current guidelines and clinical practice. Referrals for tertiary care of patients with clinically suspected FGIDs have been shown to be driven by the lack of confidence in diagnosing and managing these conditions in primary care. Furthermore, within tertiary care specialists struggle to clearly communicate the diagnosis of a FGID and continue to over-use invasive investigations such as upper gastrointestinal endoscopy and colonoscopy. The lack of a timely, clear diagnosis is likely to perpetuate the search for an organic cause for symptoms, and prevent patients transitioning to effective management of their symptoms with evidence-based options currently available.

In order to address this growing public health problem, we developed an algorithm-based approach to the diagnosis and management of FGIDs and trialled it against waitlist control within one tertiary referral centre. The trial was not a treatment trial per se, but rather an exploration of whether timely/appropriate screening, the provision of a clear diagnosis and educational to both the patient PHCP could facilitate the development of a successful, individualised management strategy. This manuscript outlines the performance of this novel pathway in terms of feasibility, safety, acceptability, and symptom relief. Additionally, substantial data pertaining to the experience, perception and feedback of patients and doctors is presented in order to identify opportunities to further improve the pathway. The use of open-ended questions in the feedback surveys alongside quantitative outcomes, provided a rich source of experiential data allowing further insight into the effectiveness of this novel approach.

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Overall percentage (%)	70%
Certification:	This paper reports on original research I conducted during the period of my Higher Degree by Research candidature and is not subject to any obligations or contractual agreements with a third party that would constrain its inclusion in this thesis. I am the primary author of this paper.
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By signing the Statement of Authorship, each author certifies that:

i. the candidate's stated contribution to the publication is accurate (as detailed above);

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|MANUSCRIPT 5| PERFORMANCE OF AN ALGORITHM-BASED APPROACH TO THE DIAGNOSIS AND MANAGEMENT OF FUNCTIONAL GASTROINTESTINAL DISORDERS: A PILOT TRIAL

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ABSTRACT

Current guidelines recommend that functional gastrointestinal disorders are diagnosed and managed within primary care, with referral after one year of unsuccessful treatment. 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. In this pilot study, we designed and piloted a non-specialist-dependent, algorithm-based approach for the diagnosis and management of FGIDs (ADAM-FGID).

The ADAM-FGID was found to be both safe and effective. The diagnostic component identification 39% of referrals requiring more urgent gastroenterological review than original triage category, with organic disease subsequently diagnosed in 31% of these. The ADAM-FGID diagnosis was safe, with 82% receiving no 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. This study shows that a clinical pathway for the diagnosis and management of FGIDs, which is not dependent upon specialist review, is safe, feasible and acceptable and has potential to capacity build by reducing specialist burden and expediting effective care.

INTRODUCTION

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

(Appendix C, Supplementary Table 7-1). 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 (Appendix B) 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 (Appendix D). The referring PHCPs of the algorithm participants were surveyed at intake (Appendix E) and completion (Appendix F) 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 consultation 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 after structured screening.

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, and significance was set at 0.05.

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 7-1). 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 waitlist control had seen a gastroenterologist previously (vs 30% algorithm, p=.036) (Table 7-1).

Safety of the algorithm-based screening

Of the 89 algorithm patients screened, 35 (39%) had alarms elicited by structured screening and had prompt specialist review, in the other 54 (61%), there were no alarms and most (n=45) were diagnosed with a FGID (Figure 7-1). 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 review).

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 7-2).

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. 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 7-2). 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 7-2). 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 7-3). 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 7-2). 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 7-2). 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 7-4). 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 7-5). 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 ≥ 6 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 7-2). 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 7-5). 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 safe, and importantly safer than current triaging of referrals, and was feasible to implement, and acceptable to both patients and their referring doctors. These pilot data are encouraging, and justify a further larger scale evaluation.

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

Participants generally accepted the link between diet and symptoms but not between psychological health and symptoms. Very few consulted a psychologist. Psychological interventions overall, effectively reduce IBS symptoms and psychological distress, and improve quality of life [9, 42, 43]. Gut-directed hypnotherapy is as effective as the low FODMAP diet in reducing IBS symptoms and has the added benefit of improving psychological health [44]. Despite this strong evidence-base, only two participants opted for gut-directed hypnotherapy. Lack of uptake of gut-directed hypnotherapy was not related to lack of availability of practitioners, but may in fact relate to a perceived (and negative) link to psychological therapy. Clearer explanation and marketing of gut-directed hypnotherapy as a stand-alone treatment that uses the brain-gut axis to influence gut function (rather than influence psychological functioning), may improve uptake of this valuable resource.

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 within the setting of one local healthcare network is also a potential limitation to generalisability. 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. A larger size, randomised control trial, with an intent to treat analysis, and imputation of missing data should be performed to investigate this model of care further.

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 safe, feasible and acceptable. 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.

Figure 7-1 Flowchart of patient progression through the study.

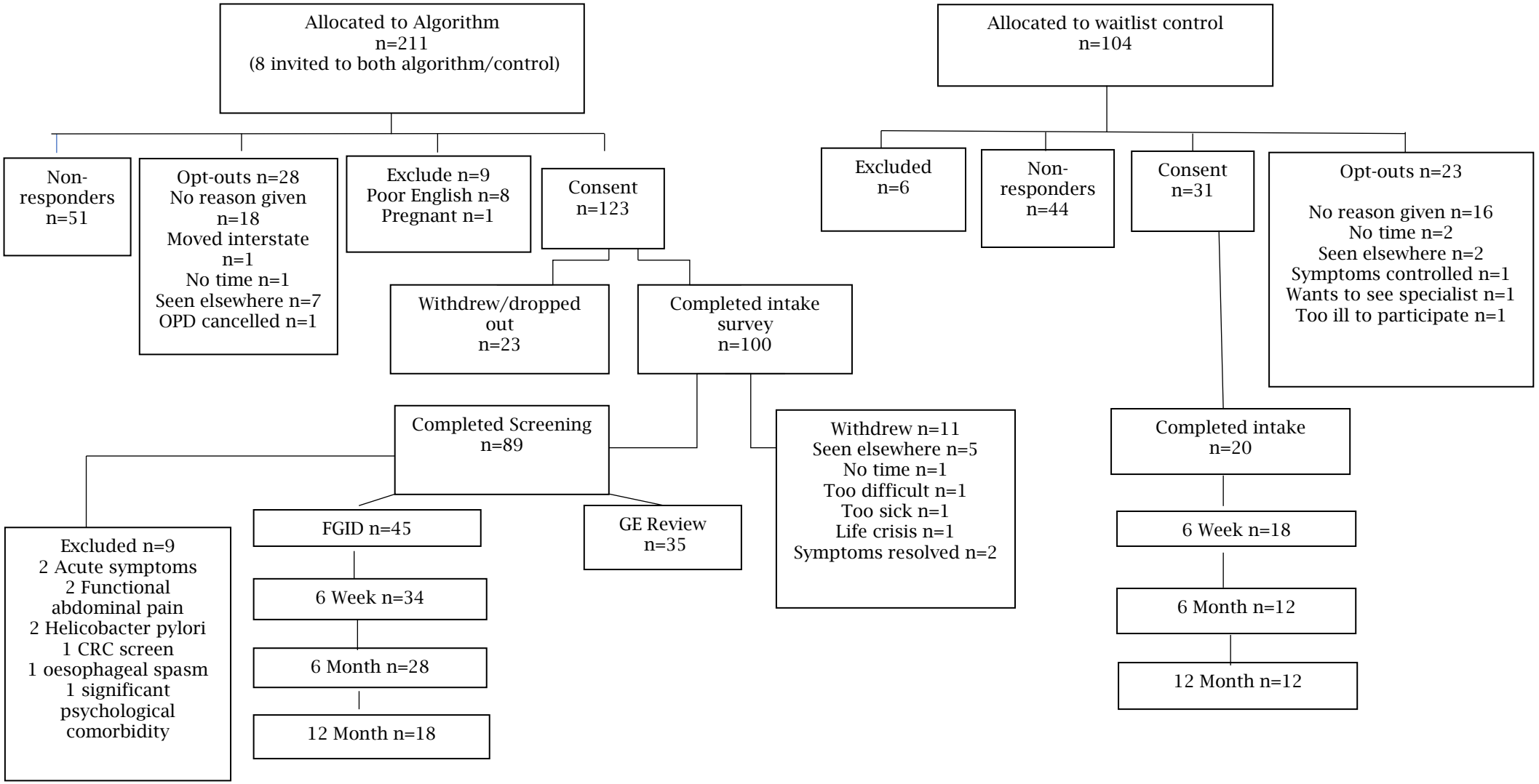


Table 7-1 Demographic comparison of patients allocated to the algorithm or waitlist control group, and screened patients diagnosed with FGID or requiring GE consult

		Group Allocation		Significance	Result Post Screening		Significance
		Algorithm (n=89)	Waitlist (n=20)	*P* (2-tailed)	FGID (n=45)	GE Consult (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
Medical comorbidities		46 (52%)	12 (60%)	.501	22 (49%)	19 (55%)	.632
Psychological comorbidities		33 (37%)	10 (50%)	.285	17 (38%)	14 (40%)	.840
Previous psychologist consult		36 (40%)	10 (50%)	.435	19 (42%)	15 (43%)	.955
Prior GE consult	Seen previously	27 (30%)	11 (55%)	.036	16 (36%)	10 (29%)	.508
	Once	12 (13%)	5 (25%)		7 (16%)	5 (14%)	
	Twice	6 (7%)	1 (5%)		4 (9%)	2 (6%)	
	≥ 3 times	8 (9%)	5 (25%)		5 (11%)	2 (6%)	
	Unsure	1 (1%)	-		0	1 (3%)	

		Group Allocation		Significance	Result Post Screening		Significance
		Algorithm (n=89)	**Waitlist (n=20)**	***P* (2-tailed)**	**FGID (n=45)**	**GE Consult (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%)	
	2-5 years	3 (3%)	3 (15%)		2 (4%)	1 (3%)	
	5-10 years	7 (8%)	4 (20%)		6 (13%)	1 (3%)	
	>10 years	4 (4%)	0		4 (9%)	0	
Social Demographics							
Primary language	English	81 (91%)	16 (80%)	.640	41 (91%)	31 (89%)	.707
Relationship	Married/De facto	49 (55%)	10 (50%)	.935	28 (62%)	15 (43%)	.085
Employment	Full-time>35 hrs/wk)	35 (39%)	5 (25%)	.862	18 (40%)	11 (31%)	.168
	Part-time<35 hrs/wk)	21 (23%)	8 (40%)		12 (27%)	7 (20%)	
	Unemployed	33 (38%)	7 (35%)		15 (33%)	17 (49%)	
Education	Year 11 or below	18 (20%)	5 (25%)	.640	8 (18%)	9 (26%)	.021
	Year 12	17 (19%)	4 (20%)		5 (11%)	10 (29%)	
	Higher Education	54 (61%)	11 (55%)		32 (71%)	16 (45%)	

GE=gastroenterologist

Table 7-2 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 Group (n=35)		FGID Group (n=45)	GE Consult Group (n=35)	FGID Group (n=45)	GE Consult Group (n=35)
Alarms present (any)	40	32	Abnormal Tests (any)	24	31	Functional (37)	Functional (18)
Nocturnal Symptoms	35	25	Blood Tests				FGID (18)
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			Non-contactable (4)	Pancreatic insufficiency (1)
			Faecal elastase	0	7		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

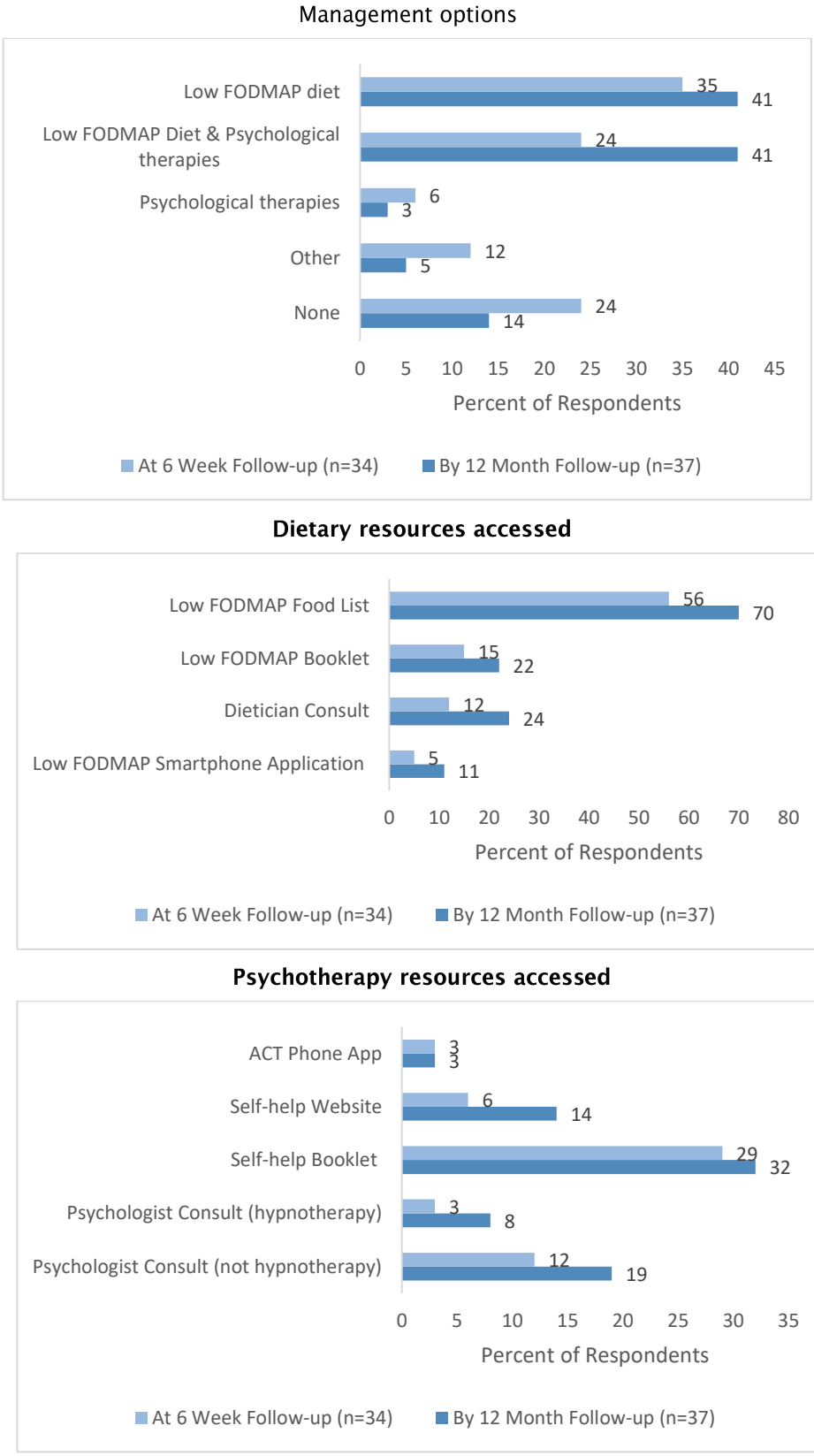
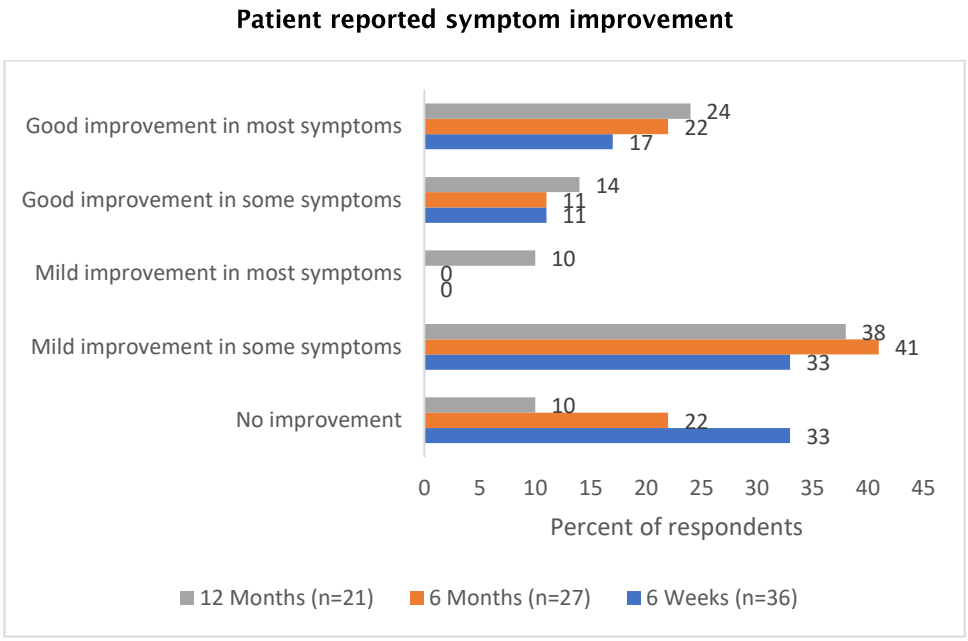


Figure 7-2 Patient reported management choice, symptom response and acceptability of the approach.



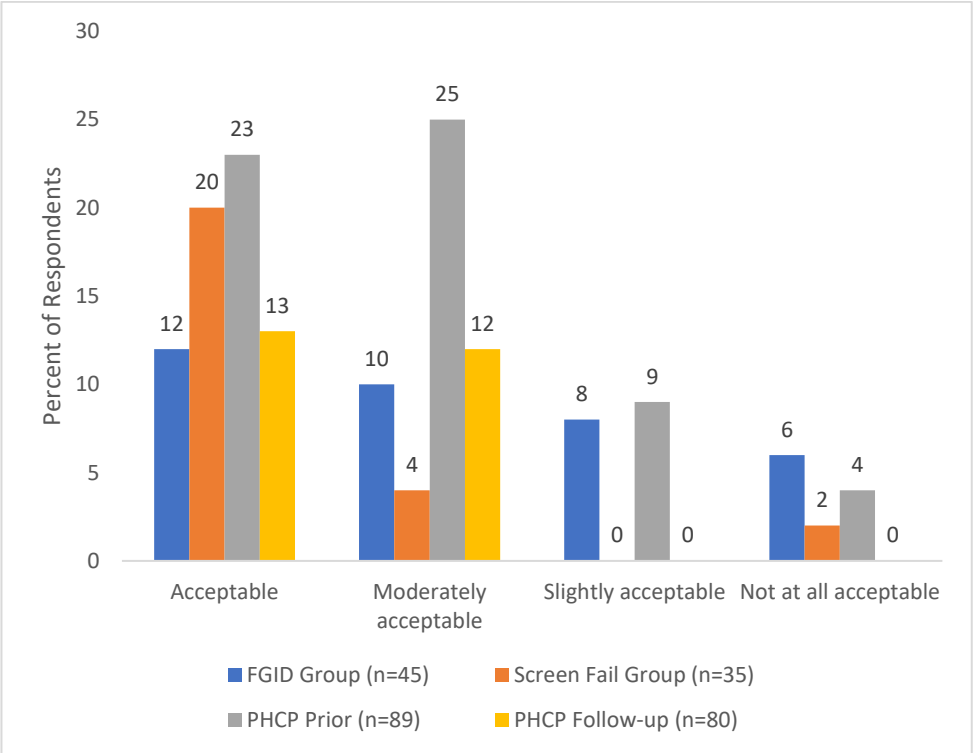


Figure 7-2 (cont). Patient reported management choice, symptom response and acceptability of the approach.

Supplementary Table 7-1 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 7-2 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 7-3 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 7-4 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 7-5 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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Chapter 8 : Discussion

The body of research presented, is the first to comprehensively investigate the management of FGIDs within Australia. Data obtained from patients, referring doctors and gastroenterologists within one local public healthcare network, were used to explore diagnostic and management issues, and identify opportunities to improve the quality of healthcare provided to this large patient group. Several key issues within the existing model of care in primary and tertiary sectors have been identified. These are summarised in Figure 8-1. Additionally, evidence for the safety, feasibility, acceptability and performance of a novel clinical pathway for patients with FGIDs has been presented. In this chapter, the key findings, future research, and clinical implications are discussed.

The small sample size and the setting of one local healthcare network pose potential limitations to the generalisability of the findings presented. However, the benefit of restricting the focus to one institution was to allow a more comprehensive exploration of all issues influencing patient care for those with suspected FGIDs. Multipronged analysis of data from patient and referring doctor questionnaires, referrals, endoscopic records and specialist letters, together with the mixed method design enabled much greater insight into the opportunities to improve patient care.

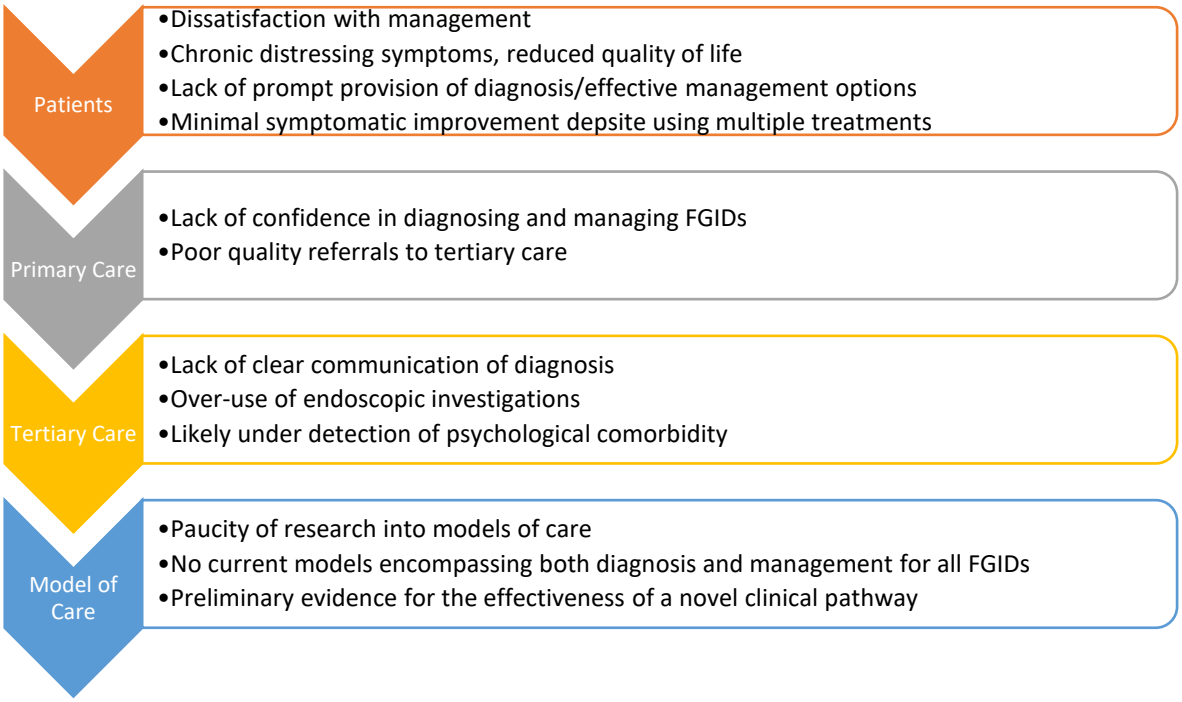


Figure 8-1 Opportunities for improvement in FGID care

KEY OUTCOMES & FUTURE RESEARCH

PATIENT CARE: THE EXISTING SYSTEM IS FAILING THE PATIENT

Most people referred to the outpatient gastroenterology department with clinically suspected FGIDs were presenting for the first time with chronic symptoms, not improving despite the use of multiple treatments. Patients with medically-unexplained symptoms such as FGIDs are often perceived as difficult and overly anxious repeat consulters [1-4]. However, only 35% had previously consulted a specialist (13% within the past 2 years) and had longer symptom duration than those presenting for the first time. Indeed, most patients had symptoms for over 2 years and a quarter for over 10 years. This is in keeping with the finding by Williams *et al.,* [5] that healthcare-seeking behaviour is related to impaired social and physical functioning caused by gastrointestinal symptoms, and the presence of comorbid conditions, rather than mental health status.

The majority of patients were dissatisfied with their management, and had not received a diagnosis and/or effective management options prior to referral. This finding is not unique to the local setting, as other studies have shown that although clinicians may consider a functional diagnosis, most are reluctant to communicate or document this without further investigations [6, 7]. Neither was suboptimal management isolated within primary care. Almost half of those who had previously seen a gastroenterologist also reported not being given a diagnosis. Many had concerns about their persistent distressing symptoms and the possibility these might indicate a serious condition. A timely diagnosis is critically important in reassuring patients, mitigating concerns, preventing continued healthcare seeking in search of a diagnosis, facilitating effective management and reducing economic burden [4, 8, 9].

Data detailing patient characteristics and experiences highlight the existing problem of poor diagnosis and management in some sectors of primary care and tertiary care, with many patients waiting unnecessarily for specialist review. As these disorders can be diagnosed and effectively managed in primary care; strategies to facilitate this are needed.

PRIMARY CARE: OPPORTUNITY TO UPSKILL

Since triaging of referrals according to medical priority is common practice in public health care, the quality of referrals is paramount to effective patient care. Previous studies have consistently shown referral letter quality to be unsatisfactory. Information regarded as important, but often lacking, includes reason for the referral, medical history, test results, relevant social and psychological factors, and information about treatments

already tried [10, 11]. Our analysis of gastroenterology referrals is consistent with this. Many lacked the basic information such as age, gender, length of duration of symptoms and relevant medical, psychosocial and psychological history. A reason for the referral or statement of suspected provisional diagnosis was also rarely provided.
As their name suggests, clinical alarms or red flags indicate that further consideration of organic pathology is needed. However, we found that the presence or absence of alarm features was rarely included in referrals and, when included, not all relevant alarms were considered. Yet, alarms were consistently reported by patients. When the non-specific question related to nocturnal symptoms was excluded, 55% of patients screened in the pilot trial reported red flags, consistent with previously reported prevalence of any alarm symptom of 60% in IBS patients [12, 13]. The discrepancy between patient and PHCP reported alarms is not suspected to be due to patient over-reporting, but rather under-documentation of relevant alarms by primary healthcare providers, as even family history of relevant organic disease was under-reported by PHCPs.

The pilot trial of an algorithm-based approach to the diagnosis and management of FGIDs found the quality of referrals insufficient to allow safe triage. Almost 40% of referrals for clinically-suspected functional symptoms warranted more urgent specialist review due to red flags and/or abnormal blood and stool tests, with organic disease being found in almost one third of these. Structured screening for organic disease in primary care would have fast-tracked gastroenterologist consultation if declared in the referral. Referring doctors lacked confidence in diagnosing and/or managing FGIDs, and this was the main driver for referral. The referrals represent only a portion of FGID patients seen in primary care [14, 15] and may reflect a subset of clinicians who struggle to diagnose/manage FGID or a patient subset with particularly difficult problems. However, the referral load is large and growing, and cannot be managed within the current healthcare setting. Efforts to develop local consensus around patient pathways and a shared understanding of FGID diagnosis/management between primary and tertiary care to promote quality patient care are needed.

TERTIARY CARE: OPPORTUNITY TO IMPROVE CLINICAL APPROACH

Suboptimal management of patients with FGIDs is not unique to primary care and several opportunities to improve patient care in the tertiary sector have also been identified. Almost a third of the patients referred with clinically-suspected functional symptoms had previously seen a gastroenterologist. Repeat presentation may be due to several factors, such as dissatisfaction with diagnosis or management, failure to respond to treatment, or worsening symptoms. Of note, is the fact that half the patients reported not being given

a diagnosis at prior specialist consultation. This is in keeping with previous studies reporting the non-acceptance of functional diagnoses [16, 17]. We therefore explored specialist-related factors that might contribute to this known phenomenon of discarded functional diagnoses.

Using specialist letters sent to referring doctors after consultation as a proxy for specialist communication with the patient, we found that clearly-communicated diagnoses were rare. The language used by specialists conveyed considerable diagnostic uncertainty, which surprisingly did not decrease over time, despite chronicity without overt "disease progression" being highly suggestive of FGID. Diagnostic uncertainty as documented in specialists' language is likely to have exacerbated uncertainty in patients and referring doctors, and further contribute to poor patient acceptance of a functional diagnosis, and may drive additional unwarranted endoscopic investigations. Indeed, an alarming 80% of patients diagnosed with FGID had undergone endoscopic examination. Whilst it might be suggested that this high rate of investigation is appropriate in a tertiary sample where the level of alarms suggestive of organic disease is much higher, this was not found to be the case. A separate clinical audit of endoscopic procedures found half of gastroscopies and one third of colonoscopies performed in patients with suspected FGID were inappropriate according to alarm-based criteria [18]. Although the rate of inappropriate endoscopies was on the low end of published rates around the world, these still represent an opportunity to reduce both system costs and unnecessary patient risks. Perhaps as an additional driver to overuse of endoscopic testing, existing appropriateness criteria were found to be at odds with current recommendations for minimal investigations in the absence of clinical alarms in this patient group [18]. Analysis of specialist letters to referring doctors also revealed a much lower level of identified psychological comorbidity than expected from pervious publications (13% vs 40-60%) [19]. This may partly reflect the lack of routine, purposeful psychological screening during the medical consultation. Due to the established link of psychological comorbidity with symptom severity [20, 21] and the potential impact on healthcare seeking behaviour [22], screening of all FGID patients for concomitant psychological disorders is recommend [23].

The analysis of tertiary care performance was restricted to observation of correspondence and audit of endoscopic bookings as proxy for real-time observation. Retrospective analyses were used to observe behaviour without inducing observer effect. However, a letter clearly cannot convey the full details of the clinical encounter, and thus the data are a limited representation of the clinician's approach. It would be difficult to achieve unbiased observation of a clinical encounter. However, detailed interviews of

gastroenterologists across locations and healthcare settings should be used in future research to explore the clinician approach to the diagnosis and management of FGIDs.

TOWARDS AN EFFECTIVE MODEL OF CARE FOR FGID

Given the fact that FGIDs are chronic conditions with a complex interplay between biological, psychological, and social factors and symptoms, an integrated approach – or model of care - is needed. The provision of a clear diagnosis and patient acceptance of that diagnosis are important initial factors in the successful management of FGIDs. Therefore, models of care that incorporate both diagnosis and management are required. Although there are many recommendations as to how FGID should be diagnosed and managed [24-26], few designs have actually been tested to date. Only six, low quality studies pertaining to models of care for either functional dyspepsia (FD) or irritable bowel syndrome (IBS) have been conducted. However, it is well known that FGIDs often co-occur and shifting between FGIDs is common [27]. Thus, they are best treated as one clinical group. The clinical approach to IBS and FD are very similar, consisting of the exclusion of alarms, provision of a diagnosis, reassurance, explanation, and recommendation of lifestyle changes along with psychological and/or dietary therapies and medication if specific therapy is needed. Preliminary data suggest that integrated models of care are economically viable and may facilitate timely diagnosis and management, and improve patient outcomes.

The lack of an integrated model of care for FGIDs represents a lost opportunity for timely and effective healthcare provision to this large patient group. Therefore, we conducted a pilot trial of a novel model of care which was not dependent upon specialist consultation and could be implemented within either primary or tertiary care. This approach consisted of screening for organic disease using routine blood and stool tests, the provision of a clear diagnosis, explanation of functional disorders and information about effective evidence-based management options and how to access these (Figure 8-3). The process of screening and diagnosis without in-person consultation was not only feasible to conduct, but was also appreciated by some patients. We also found that transparency of likely waiting time resulted in some choosing to access private care instead. Patient buy-in to the model was good, with most completing screening, reading the diagnostic letter and entering active self-management.

Several opportunities to improve upon this model have been identified. Firstly, this trial was implemented by a non-clinical researcher, and, as most patients reported alarm symptoms or returned test results outside of the normal range, gastroenterologist review

of records was required. If this model of care were implemented by a clinician, the necessity for review of records by a specialist would be reduced and care more efficiently fast-tracked. Patients were also often contacted for clarifying information regarding reported alarm symptoms (such as colour, quantity and location of per rectal bleeding), which would be unnecessary if conducted via an in-person clinical consultation. The alarm question "does abdominal pain wake you from your sleep" was found to be non-specific and required follow-up clarification in most cases. Upon clarification, many cases were found not to be true alarms, but rather an indication that the patients noticed their symptoms during the day and the night. Again, this could be clarified quickly and easily via an in-person consultation. There may be opportunity to refine the algorithm so that patient rated frequency and total number of alarm-symptoms provide clinical identification of those requiring a specialist appointment. Although we did not formally assess the total number of alarm symptoms, the number of red flags has been shown to be predictive of organic disease in patients with suspected IBS [13, 28], and those citing alarms occurring 'most of the time' or 'all of the time' went on to receive specialist review.

The ADAM-FGID was safer than current care, as a large proportion of referred patients initially triaged as non-urgent (and unlikely to be seen) were found to warrant gastroenterology review due to the presence of clinical alarms not specified in the referrals. Cases of inflammatory bowel disease, neoplasm, pancreatic insufficiency, reflux oesophagitis, iron deficiency and incidental findings of polyps were identified via this screening. Screening in either primary or tertiary care would improve patient care by ensuring rapid identification of patients likely to have organic disease, and facilitating timely access to gastroenterological care for this group. The diagnosis of FGID was also found to be safe and stable. No patients diagnosed with FGID had received an alternate diagnosis to account for their gastrointestinal symptoms in the 2.7 years (SD 0.5 y) following diagnosis.

This model of care was acceptable to most participants. It facilitated fast-tracking of specialist appointment for those with clinical alarms, and provided reassurance and helpful management options to those diagnosed with a FGID. Reasons for dissatisfaction centred around frustration with a healthcare system that does not facilitate consultation with a specialist when the PHCP is unable to diagnose or manage effectively. A small number of patients did not accept the FGID diagnosis and pursued endoscopy and colonoscopy privately, for personal reassurance. It could be argued that this screening process at least provided patients and their PHCPs with enough information to decide whether to engage in private care (where that was an option). A few patients indicated that they felt that the survey did not allow full consideration of their individual situation.

Examples included patients who had recently travelled overseas, and those on a gluten free diet. One important factor that clinicians can quickly gauge in person, but was overlooked in the survey (yet often asked for in clarification phone calls) was patient height and weight. Future versions of the screening survey could be improved by including questions regarding height, weight, restrictive diets, and recent travel.

Most respondents reported some level of symptomatic improvement, and both constipation and reflux symptoms improved to a statistically significant degree in those in the model of care as compared with waitlist controls. The changes were, however, not as large as previously reported RCT trial results with psychological therapies [29-35] and the low FODMAP diet [36, 37]. Furthermore, the model of care was not found to improve psychological health or quality of life; in fact, gut-specific anxiety increased in the intervention group. Given the acceptability of the model to patients and the reported symptomatic improvement, there are several reasons why greater symptomatic improvement might not have been demonstrated. Firstly, the study was designed to maximise the potential of having a control comparator group, by randomising to group 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. However, a low response rate in the control arm means that we cannot consider randomisation to have been successfully achieved. Additionally, attrition has the potential to significantly bias results. As this was a pilot trial, data was analysed using mixed model logistic regression, with no attempt made to account for biased accrual. A larger size, randomised control trial, with an intent to treat analysis, and imputation of missing data should be performed to investigate this model of care further.

One important, clinically relevant factor that may have contributed to the lower than expected symptomatic benefit is the method of engagement with management options chosen by participants. There was a poor uptake of clinician-led therapies, such as consulting a dietitian or psychologist, with many choosing do-it-yourself approaches to management without discussion with their PHCP. Although self-administered and minimal-contact psychological interventions for FGIDs have proven efficacy [38, 39], little research on the efficacy or long-term safety of a self-taught low FODMAP diet has been performed and dietitian-led management is currently recommended [24, 40, 41]. The resource pack included a list of high/low FODMAP foods, alongside links to the Monash University low FODMAP website and e-application resources. In future trials, perhaps the recommended ways of accessing treatment methods should be made more explicit and consultation with PHCP more directly advised. It is possible that patients did not

understand the principles (particularly regarding the low FODMAP diet) and engaged haphazardly, thus not seeing optimal results. The abundance of, and difficulty assessing the credibility of online information, poses a serious problem for patients choosing to self-manage [40]. However, this pilot study shows a clear and considerable interest in self-management of FGIDs, and thus efforts to develop safe and effective self-management options are likely to be used and are therefore needed. Online self-management programs have been successfully implemented in a range of chronic health disorders such as diabetes and arthritis, [42, 43] and the development of integrated self-management programs for FGIDs are likely to be beneficial.

Empowerment of the patient to manage their own symptoms is a cornerstone of medical practice, particularly in chronic disease management [44] and medically unexplained symptoms such as FGIDs [4]. The relationship between a doctor and patient is most highly valued when patients are facing significant health problems [45]. Although participants in our pilot trial opted to self-manage without PHCP input, the role and importance of the clinical consult should not be underestimated. PHCPs plays a particularly important role in interpreting knowledge gathered by patients from a variety of sources, such as friends and relatives, social media, online forums and blogs [4]. The ADAM_FGID pilot study provided both patients and PHCPs with diagnostic and management information, yet most patients and PHCPs did not co-discuss this further. Better patient outcomes may have been seen if the letter itself provided the basis for ongoing doctor-patient partnership in co-developing an appropriate management strategy and facilitation of patient empowerment to self-manage. Such improvements in outcomes, however, would be dependent on the confidence and ability of PHCPs to manage FGIDs, which has been shown lacking in at least a portion of PHCPs. A key component of a future FGID clinical pathway by necessity must include the education of PHCPs and fostering of clinical environments that promote the sharing of information and provision of needed resources.

PUBLIC HEALTH IMPLICATIONS

FGIDs affect 4 in 10 Australians in their lifetime, cost over a quarter of billion dollars annually to the Australian healthcare system (Appendix F), and thus warrant a more focussed whole clinical systems approach. A major issue with the management of FGIDs in Australia is the delay in receiving a diagnosis and advice on effective management options. This may be due to a lack of confidence in diagnosing, communicating and managing these disorders combined with a desire to extensively investigate, and restricted access to tertiary care in the public health system. Impaired social and physical functioning drives health-care seeking behaviour. Therefore, access to an early, accurate

diagnosis, along with clear communication, reassurance, and education about FGIDs is paramount to reducing the personal and economic burden of healthcare. Ultimately an integrated, multi-disciplinary approach to FGIDs is needed.

OPTIONS FOR INTEGRATED CARE

There are many strategies which could be used to facilitate better care for patients with symptoms suggestive of a FGID. These are detailed below and in **Error! Reference source not found.**.

1) Firstly, PHCPs could be upskilled with the latest recommendations on diagnosis and management of FGIDs. This could be achieved via professional development courses run by a multi-discplinary team (i.e. gastroenterologists, dietitians, psychologists). In addition, to be truly beneficial, opportunity should be provided for PHCPs to contribute to discussions around barriers they face in caring for these patients, to better inform pathway development.

2) The ADAM-FGID could be used as a launchpad for the development of an evidence-based FGID clinical pathway established through Delphi consensus with a team of mutlidisciplinary clinicians. Transformation of healthcare will not occur in isolation, but requires all relevent stakeholders work together to find a joint understanding and create a consensus position, on quality care for this patient group within the local context, based on current evidence. Additionally, successfully practical implementation requires a PDSA (plan-do-study-act) approach to critically evaluate and revise the pathway [46]. An FGID pathway, could facilitate improved referral quality where needed, and guide primary care management where not. Opportunity to convert this tool to an e-health platform would also allow wider dissemination. A clinical pathway would facilitate earlier care of FGID patients and more accurate identification of patients who require gastroenterologist review. Upskilling of PHCPs in FGID diagnosis and management is the ideal long-term goal, as PHCPs are perfectly placed to understand their patient, how their symptoms impact their life, and tailor an individualised, effective management approach. However, immediate change to patient care in this area is needed.

3) Immediate, specialised care could be implemented by nurse-led clinics, based in either primary and/or tertiary care. Drawbacks to this include the current lack of suitably-trained GI nurses and the cost to primary health care clinics. Future research into the health savings afforded by the implementation of a nurse-led clinic would be beneficial to establish true cost savings of reduced healthcare, reduced morbidity, reduced

workplace abseenteeism, and reduced number of unnecessary endosocpic investigations afforded by early, effective diagnosis and management.

4) A mixed-care model could present a commercially viable way to provide quality care to public patients. In this model, a nurse - (or GP-) led clinic could operated within a private healthcare facility. The operating cost of a bulk-billing or low-cost clinic could be offset against the increased time and capacity of the specialists to focus on conditions that may be more medically urgent, perceived as more interesting and/or more financially rewarding. As not all specialists enjoy or are good at manageing patients with FGIDs, this would also facilitate better patient care by providing alternate quality care options for the treating gastroenterologist within the same practice. Many business organisations are now embracing this hybrid business model that incorporates a 'not-for-profit' and the main 'for-profit' business. Known as a "profit for purpose" business model, it channels a portion of the profits towards the busineses given mission, as a way of giving back to the community and to come in line with recent movement towards ethical business practice and social responsibility [47]. In line with this, a private specialist practice could channel a portion of their profits to the establishment of a nurse-led clinic to provide timely, quality care for public patients. Unless incentivised, this solution would rely on entreprenurial clinicians with a social/clinical conscience driven to providing equitable care.

5) An FGID-focussed tertiary clinic is an effective means of ensuring both the immediate provision of quality care in the public health system and the upskilling of the next generation of PHCPs and specialists. This could be housed within public teaching hospitals, and be staffed by medical students and specialist trainees under gastroenterologist supervision. This would solve multiple problems with minimimal capital outlay. As FGIDs are common and represent up to 50% of gastroenterologist care, the need for both PHCPs and gastroenterologists to receive quality training in these disorders is clear. If patients with non-urgent symptoms such as FGIDs are being triaged into a category unlikely to ever be seen, trainee clinicians are not receiving comprehensive training and the lack of confidence and ineffective care will be perpetuated. Student-led clinics have been successfully implemented in a number of Australian healthcare settings [48, 49] and are used to develop clinical skills whilst providing healthcare to underserviced communities or patient groups. Such a clinic could also often a phone hotline as a resource to facilitate quality gastroenterolgoical care within primary care. However, a tertiary FGID clinic as a stand-alone option could serve to perpetuate and possibly exaccerbate the problem of PHCP lack of confidence in diagnosis and management and of FGIDs by providing a parallel route of care. It is envisaged that this option is best used in

conjuction with options one or two (the development and implementation of an evidence-based clinical pathway in primary care).

6) The provision of up-to-date resources for clinicians is also greatly needed. This could include:

- Information about diagnostic tests and evidence-based management options,
- A database of local FGID specialised dietitians and psychologists,
- Pamphlets outlining examples of good communication and FGID metaphors, to ensure consistent explanations across primary, tertiary and allied health,
- Links to online resources regarding diagnosis, management and communication skills such as the Drossman Care You Tube channel [50]
- Templates of FGID chronic disease management plans.

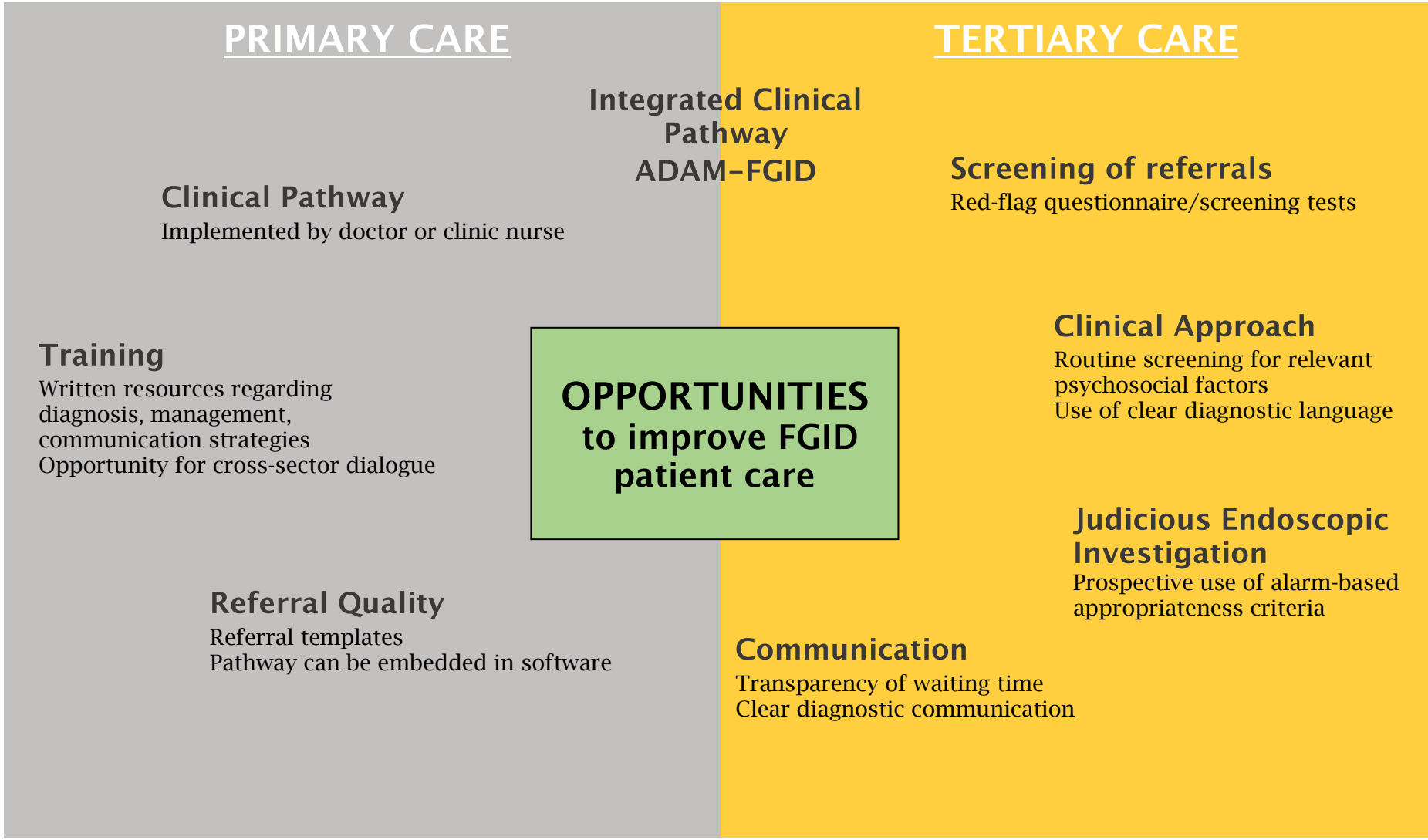
In feedback provided at a local IBS Management Update, PHCPs queried the acceptability of chronic disease management plans for FGIDs, and how to access these [51]. Medicare does not list conditions eligible for chronic disease management plans, but states they are available for medical conditions present (or are likely to be present) for 6 months or longerm and provide rebates for at least 2 specialists involved in the treatment of FGID alongside PHCP care [52]. Medicare states that "these items are designed for patients who require a structured approach to their care and to enable GPs to plan and coordinate the care of patients with complex conditions requiring ongoing care from a multidisciplinary team" [52]. Thus, in FGIDs a chronic disease healthcare plan should provide access to the most effective treatments, namely psychological and dietary therapies.

7) Improved public awareness of FGIDs and health literacy of these disorders is also needed. Organisations such as The IBS Network (UK) [53] and the International Foundation for FGIDs [54] produce quality information for patients and have growing online and social media presence. Further gains in public awareness could be achieved by targetted efforts to raise awareness in the general public, so that people are aware of and understand the nature of these disorders before they develop symptoms. This would greatly aid acceptability of FGIDs as a diagnosis and subsequent openness to effective management strategies.

8) Finally, considerable multidisciplinary effort should be put into developing a self-management program. Healthcare is being transformed by e-health and it is imperative that experts in FGID lead the way in the provision of online self-help information. If online programs for the low FODMAP diet can be proven safe and effective, this information

could be expanded to include basic psychological therapies such as gut-directed hypnotherapy, acceptance and commitment therapy, and basic cognitive behavioural therapy, in conjunction with recommended basic lifestyle changes. These programs could be made commercially viable through the use of subscription, and facilitated online by a team of trained nurses, psychologists, dietitians, gastroenterologists and/or PHCPs. A fully stand-alone self-management website with links to local providers is an alternative option.

Figure 8-2 Strategies to Improve Patient Care and Service Delivery for Functional Gastrointestinal Disorders



BARRIERS TO INTEGRATED CARE

A major barrier to providing quality care in primary practice, are the current perverse financial incentives of the Medicare system. PHCPs are incentivised for higher consult volumes rather than high quality care [55]. Significant amounts of time are required to adequately educate the patient on the nature of FGIDs, address related psychosocial issues, explain and get buy-in to psychological or dietray management options. The absence of suitable financial rewards reflects a lack of value the system places on PHCP time and quality care, and perpetuates poor management, over-reliance of ineffective tests and pharmaceuticals, and excess referrals to tertiary care. This system-based focus on transactional rather than longitudinal care forces PHCPs whom provide quality care for patients with chronic disorders, to carry the cost of such care. If PHCPs are to effectviely engage in the current recommendations that FGIDs be diagnosed and managed in primary care, the issue of disincentivising quality care needs to be addressed.

CONCLUSION

Timely and effective diagnosis and management of functional gastrointestinal disorders is a challenge for public health in Australia. Failing to achieve this creates ongoing avoidable morbidity, and costs our society significant amounts in direct and indirect costs. The implementation of a model of care that is simple, affordable, acceptable and effective is needed.

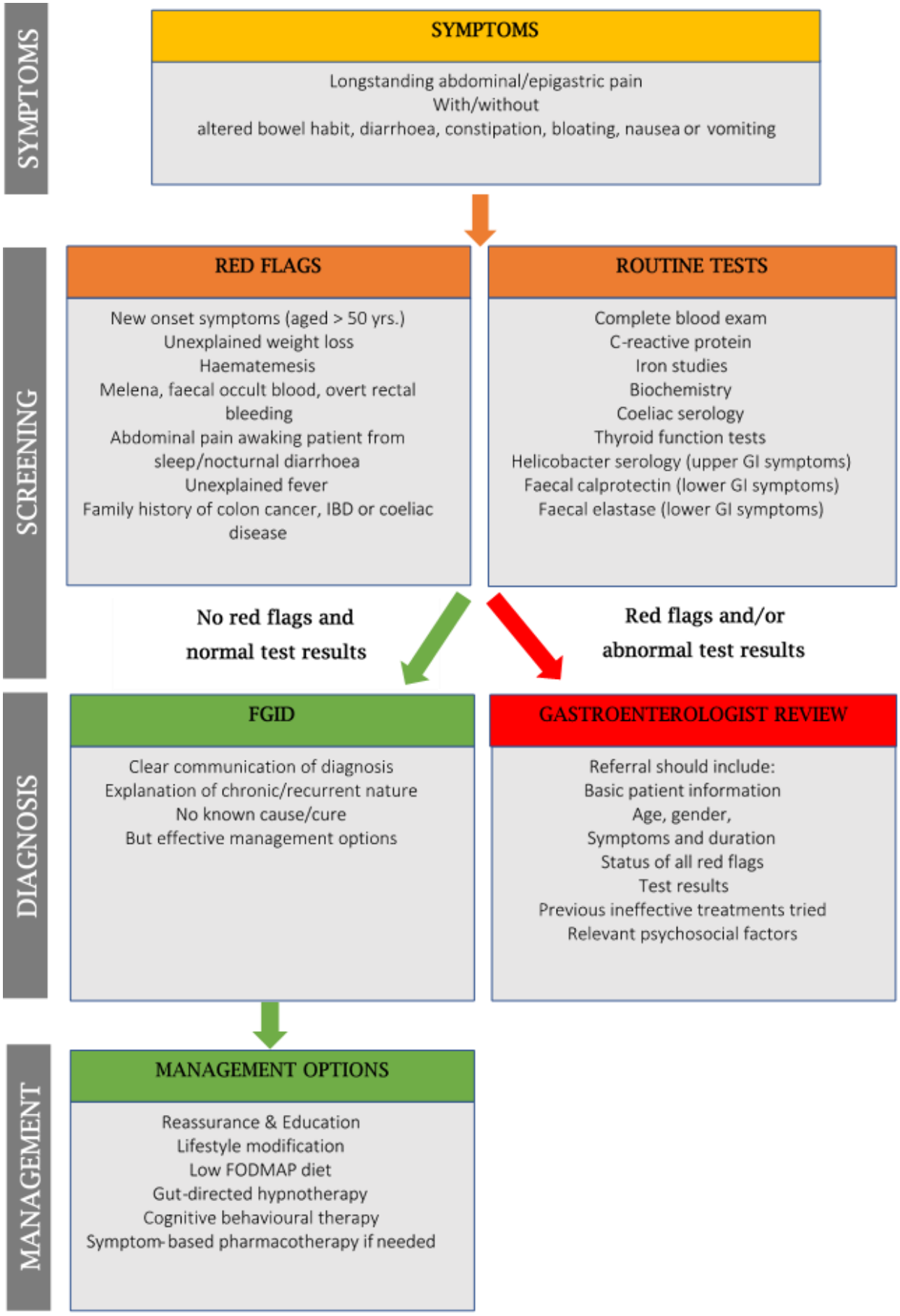
This PhD research has identified significant opportunities for gains to be made in patient care through:

1) raising the standard of referrals for specialty care to ensure safe and timely triage
2) improving confidence in identifying and diagnosing FGIDs, particularly within prmary care
3) facilitating the supports and cross-polination of specialties needed to manage these disorders in both primary and tertiary care
4) providing clearly identified referral criteria for patients failing treatment
5) reducing unnecessary investigations and costs
6) improving the communication of functional diagnoses to patients and
7) providing evidence-based management options

We provide here evidence for the safety, acceptability, feasibility and efficacy of an algorithm-based approach to the diagnosis and management of FGIDs. Refinement of this

approach and development of a consensus-based clinical pathway for larger-scale testing is the next step in transforming healthcare for this large patient group.

Figure 8-3 Clinical pathway for the diagnosis and management of FGIDs



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Appendix A: Proforma of Diagnostic/Management Letter to Patients and Referring Doctors

Government of South Australia
Central Northern Adelaide Health Service

ROYAL ADELAIDE HOSPITAL
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P Kuo
M Le Mire
NQ Nguyen
G Nind
CK Rayner
MN Schoeman
W Tam
E Tse

Dear < Dr > and <Patient>

Re: Patient < name >

<PATIENT NAME> was referred to us with gastrointestinal symptoms for evaluation and has now undergone several blood and faecal screening tests with all results normal. <PATIENT NAME> has also been evaluated with a family and personal history questionnaire and had his/her GI symptoms assessed according to the Rome criteria for functional gastrointestinal disorders. Specifically, the screening tests show no evidence of colitis, Crohn's disease, coeliac disease, blood loss or malabsorption. All the test results have also been sent to the original referring doctor. The symptoms reported show that <PATIENT NAME> has a functional gastrointestinal disorder (FGID).

<PATIENT NAME> has (Specify which irritable bowel syndrome and/or functional dyspepsia).

The good news is that the cause of these symptoms is functional. This means that there is no tissue damage or disease state, and the symptoms are thought to be due to nerve sensitivity or dysfunction.

FGIDs are common conditions affecting up to 40% of the population. All patients with FGID experience different levels of pain or distress from their symptoms and these symptoms may also affect day-to-day tasks, reduce quality of life and cause or worsen stress/anxiety. Whilst FGiDs cannot be cured, there are a number of proven ways in which patients can reduce symptoms and improve their ability to cope with them. Below, we describe a number of management approaches that have a good scientific evidence base for use in FGiD management. Many of them have not been widely used as yet, as much of the evidence for their effectiveness is new.

Dietary Approaches - Low FODMAP diet

The low FODMAP diet has been shown to reduce abdominal symptoms in patients with **Irritable Bowel Syndrome** when administered and overseen by a dietitian. A dietitian can be accessed through a standard Health Care Plan (set up by your GP).

Alternatively, The Monash University provide extensive resources via their website www.med.monash.edu/cecs/gastro/fodmap for those who prefer a self-help approach. A low FODMAP food chart is also included with this letter.
Patients without IBS who experience bloating or fullness may also benefit from the low FODMAP diet.

Additional dietary/lifestyle Modifications for patients with Functional Dyspepsia or upper abdominal pain/discomfort or bloating are also recommended. These include:

1) Reduction in caffeine/alcohol intake
2) Reduction of fizzy drinks, chewing gum and lollies which cause excess gas
3) Eating 6 or more smaller portions throughout the day rather than 3 big meals.
4) Weight loss which reduces pressure/crowding in the abdomen.

Psychological/Stress Management Approaches

These have been used successfully to reduce FGiD symptoms in patients because there is a highly active two-way communication pathway between the brain and the gut (the brain-gut axis) which influences gut symptoms. This treatment approach has been successful in patients who do not have an underlying anxiety disorder as well as in patients who already have significant stress or anxiety. These approaches can reduce stress and anxiety as well as gut symptoms. Commonly used psychological therapies include Cognitive Behavioural Therapy (CBT), mindfulness-based therapies, and hypnosis.

A psychologist of your choice can be accessed through a Mental Health Care Plan (set up by your GP). This can provide up to 10 sessions per year. A psychologist can be recommended by your GP or found through the Australian Psychological Society website http://www.psychology.org.au/findapsychologist. We have also included a list of psychologists (last page) who currently treat FGIDs, which you may like to use.

Self-Help Psychology
For those who prefer a self-help approach, you may wish to consider the booklet provided with this letter and/or the online FGID course http://ecushlalinedale.wix.com/test (under construction, will have own domain name).

Please see the attached sheet for a list of these treatment options and ways in which they can be accessed.

It is up to you how much/little you use of these evidence-based management suggestions. We recommend that this letter is discussed between each patient and their GP in order to clarify the information given and tailor an approach specific to each patient's needs. We will be following you up in 6 weeks to see how you are going and to get you to complete the questionnaires. We will then contact you at 6 and 12 months for follow up surveys.

Kind regards

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Supervisory Panel: Prof. Jane Andrews (RAH), Dr Antonina Mikocka-Walus (York University) and Prof. Peter Gibson (The Alfred Hospital/Monash University).

Management Resources Available

	Psychological Therapies	Dietary Therapies
Specialists	**Psychologist** (your choice OR) Listed local psychologists	**Dietitian** (your choice OR) Listed local dietitians
Self-Help Material	**Booklets** Mind & Gut Matters booklet (attached)	**Booklets** Low FODMAP chart (attached)
	Online Resources Mind & Gut Matters http://www.gutandmindmatters.com	Monash University Low FODMAP Diet FAQs http://www.med.monash.edu/cecs/gastro/fodmap
	Smartphone Applications ACT Companion http://www.actcompanion.com	Smartphone Applications The Monash University Low FODMAP Diet App www.med.monash.edu/cecs/gastro/fodmap/iphone-app.html
	Books Change Your Thinking by Sarah Edelman The Happiness Trap by Russ Harris The Happiness Trap Pocketbook by Russ Harris	**Books** The Monash University Low FODMAP Diet Book. http://ecommerce.med.monash.edu.au/product.asp?pID=317&cID=11&c=18103

Appendix B. Self Help Booklet "Gut and Mind Matters"

Gut & Mind Matters

A self-help booklet for people with functional gastrointestinal disorders




2nd Edition: Created By

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Note from authors

We hope you find this self-directed approach to coping with functional gastrointestinal disorders useful and easy to follow. We hope that the exercises and skills demonstrated here are applicable and useful to you. We must note that the information presented comes from reliable and academic sources. The sources for some of these exercises are provided on page 17 of this booklet for personal use. Please do not distribute the material in this booklet or present it in public forums.

WHO IS THIS BOOKLET FOR? This booklet is for people who are affected by functional gut disorders (FGIDs). These are disorders where no tissue damage or disease state can be detected and symptoms are thought to be due to nerve sensitivity or dysfunction.

FGIDs are common conditions affecting up to 40% of people. Symptoms vary from person to person, and can be painful, distressing, stressful, not to mention embarrassing!

The good news is, that these gut symptoms can be reduced by harnessing the communication highway between the brain and the gut (called the brain-gut axis). The brain can directly stimulate the gut to alter gut symptoms. However, the gut also transmits messages to the brain about pain and discomfort, which increases stress and anxiety. Stress and anxiety in turn increase brain signals to the gut making the symptoms even worse.

Thankfully particular skills can be learnt that change the messages between the brain and gut to reduce these symptoms.

WHAT IS THE AIM OF THIS BOOKLET? The aim of this booklet is to train you in skills that reduce gut symptoms by reducing stress and anxiety. Stress and anxiety can be caused by functional gut disorder, everyday life and anxiety disorders. The tools and techniques covered will help regardless of the cause of the stress.

HOW DO I USE THIS BOOKLET? This booklet is set out to be used over four weeks, reading one section and completing the matching exercise each week. It is important to take the time to do the exercises properly in order to benefit from them fully. If you use the week to practice the exercise and then apply it to an appropriate situation in that week you will become very familiar with the exercise. Once you are familiar with the exercise you will be able to use it whenever needed.

Week 1 Relaxation

This week's skill is known as diffusion. It is easy to get "caught up" in our thoughts. Diffusion is the act of separating or distancing ourselves and our actions from our thoughts.

In the process of diffusion we:

- **Look at** thoughts rather than from thoughts
- **Notice thoughts** rather than getting caught up in them
- **Allow thoughts to come and go** rather than holding on to them

The aim of diffusion is to learn to respond to thoughts in terms of how helpful they are rather than how true they are.

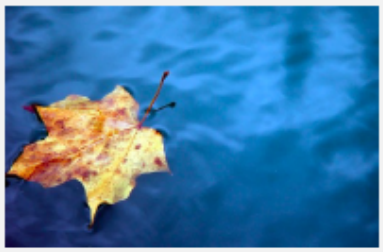
Diffusion is a mindfulness skill. Mindfulness is a process of awareness that focuses on paying attention to the present moment rather than getting caught up in our thoughts. In order for mindfulness to work successfully you will need to adopt an attitude of openness and curiosity.

Mindfulness exercises such as diffusion are helpful techniques to use for relaxation. Learning to anchor yourself in the present moment and allow your thoughts to come and go can give you a great sense of calmness. This exercise will help you to feel centred and in control of your actions.

Exercise 1 Leaves on a stream

Read through all of the instructions before attempting this exercise.

1. Find a comfortable position in a quiet space. Either close your eyes or fix your eyes on a spot, whichever you prefer.



2. Imagine you are sitting by the side of a gentle flowing stream, and there are leaves flowing on the surface of the stream. Allow the scenery to take on any form you wish.

3. Now for approximately ten minutes (you may use a timer if you wish) take every thought that pops into your head, place it on a leaf, and let it float on by. Do this regardless of whether the thought is positive or negative, pleasurable or painful. Even if it is the most wonderful of thoughts, place it on a leaf and let it float on by.

4. If your thoughts stop, just watch the stream. Sooner or later your thoughts will start up again.

5. Allow the stream to flow at its own rate. Do not speed it up. You are not trying to wash the leaves away, you are allowing them to come and go in good time.

Continue exercise on next page

6. If a leaf gets stuck, let it hang around. Do not force it to float away.
7. If a difficult feeling arises such as boredom or impatience, acknowledge this feeling. Say to yourself, "Here is a feeling of boredom" or "Here is a feeling of impatience". Then, place those words on a leaf, and let the leaf float on by.
8. From time to time your thoughts will hook you, and you will lose track of the exercise. This is normal and natural, and it will keep happening. As soon as you realise this has happened, gently acknowledge it, and then continue on with the exercise.

Once you have completed the exercise, it will be useful to reflect on it by asking yourself the following questions.

- What sort of thoughts hooked you?
- What was it like to let your thoughts come and go without holding on to them?
- Was it hard to let go of any thoughts?
- What feelings came up? Did you find acknowledging this feeling useful?

Week 2 Accepting Pain

Most people suffering from functional gut disorders will experience some abdominal pain or discomfort. Pain can be physical and is commonly described as aching, squeezing, cramping or bloating in the abdomen. "Pain" can also be emotional, and may include anxiety and embarrassment.

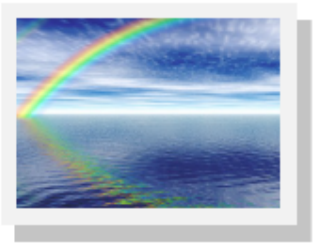
Pain is usually experienced as an unpleasant feeling that we wish would go away. Therefore, we tend to struggle against our pain.

Typical thoughts include:

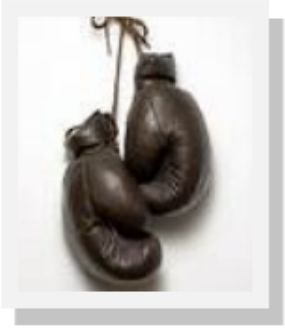
"Oh no! My pain is back. Why does this keep happening to me? What if it never goes away?"

These thoughts cause us to worry about our pain, resulting in anxiety. This anxiety can then make the pain, and our perception of it, worse. This can be thought of as a negative spiral as the anxiety and pain make one another worse. All this anxiety and pain also drains our energy causing us to feel tired.

However, instead of struggling there is another way to approach pain. This approach involves accepting the pain rather than struggling against it.



Accepting pain does not mean liking it or wanting to feel it, the pain is still unpleasant. The difference is that you do not waste your physical or mental energy struggling with it.



Typical thoughts from a person accepting their pain could include:

"Okay here is that cramping feeling in my abdomen again. This pain will pass because it always does. I just need to continue to breathe and focus my mind on something else"

Without struggling, a natural level of physical and emotional pain or discomfort can be experienced. This pain or discomfort will not get worse because you will not create that negative spiral of pain and anxiety.

The exercise for this week will focus on learning the skill to control your "struggle switch". You can teach yourself to turn off your struggle switch at times when you are experiencing physical or emotional pain or discomfort. This exercise is to be used when experiencing physical or emotional pain or discomfort. It is best to use the template on the next page while learning. It is recommended that you read aloud and write your answers in the spaces provided. Once you become familiar with the exercise you can do it in your head whenever you are experiencing pain or discomfort.

Exercise 2 The Struggle Switch

Scan your body and identify where you are feeling the pain or discomfort

_____

_____

On a scale of 1-10 with 1 being no pain and 10 being unbearable, how would you rate your pain?

☐

Imagine your struggle switch. Allow the switch to take on any appearance you wish. Circle whether the struggle switch is currently

ON or OFF

Now imagine your struggle switch is a dial. On a scale of 1-10 with 1 being no struggle and 10 being fully on, how much are you struggling with this feeling of pain?

☐

Now let's see if you can bring the struggle down a few notches. Notice the feeling, where is it and where is it most intense?

_____

_____

Now focus on taking slow, deep breaths. Notice the feeling of pain or discomfort and gently breathe into it. Create space around the feeling. See if you can open it up a little. This feeling is unpleasant and you do not want to feel it. You do not have to like it, just allow it to sit there for a moment, allow it to be there.

Think back to the struggle switch dial. Re-rate your struggle with this feeling on a scale of 1-10

☐

Now rate your feeling of pain or discomfort again on a scale of 1-10

☐

Week 3 Thought Awareness

This week will focus on becoming aware of unhelpful thoughts and learning a skill to change them. Thoughts, feelings and behaviours are all connected and influence each other.

Therefore, understanding our thought patterns will help us understand the reasons for our feelings and behaviour. Furthermore, changing our thought patterns will help us feel and behave more

positively.

Sometimes we are very aware of our thought patterns, while at other times our thoughts become "automatic". Automatic thoughts are thoughts that we are not aware of but still influence our feelings and behaviour. Automatic thoughts are usually connected to deep, underlying beliefs that can be either positive or negative. Examples include:

"I am weak" or "I am strong"

"Nobody cares" or "I have a lot of people looking out for me"

Automatic thoughts can often be the reason behind strong feelings such as anger, sadness, or joy. These thoughts can be

words, images or memories.

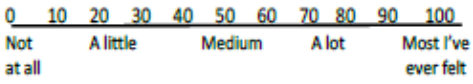
This week's exercise will ask you to identify a situation where you experienced a strong positive or negative feeling. You will need to give a brief description of the situation. For example

In the middle of presenting a talk at a work meeting I have to excuse myself to go to the toilet

You will then need to identify your feeling and rate it's intensity. Feeling intensity can be rated on a scale from 1-100% . For example

Anxious 80%

You should then list all your automatic thoughts related to



this feeling (use the questions in the box as a guide if needed). For example

- *Everyone will think I'm unprofessional*
- *People will laugh at me*
- *I am such a failure*

Once your automatic thoughts have been listed you can attempt to identify and circle the hot thought.

QUESTIONS TO HELP IDENTIFY AUTOMATIC THOUGHTS

What was going through my mind just before I started to feel this way?

What am I afraid might happen?

What does this mean about me, the other people involved, my life, and my future?

A hot thought is the thought that carries the greatest emotional charge.

- *Everyone will think I'm unprofessional*
- *People will laugh at me*
- *I am such a failure*

Now that you have identified your hot thought you will need to ask yourself "Is it really true?" To do this you will need to provide evidence to support and refute your hot thought as though you are trying to persuade a jury. For example

Evidence to support

- *My talk will no longer have the same effect*
- *I will not look professional and prepared*

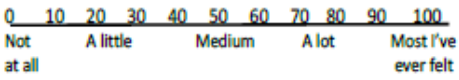
Evidence to refute

- *I was chosen for this talk because I am the best person for it*
- *I was promoted last year*

Now you can change the hot thought to an alternative or balanced thought that summarises the evidence that you provided in the previous step. You may ask yourself, "Is there another way of understanding this situation?" E.g.

Although my talk has been interrupted, interruptions are a part of everyday life. Even successful people get interrupted. Although it may come across disjointed, my talk will still have an impact because I am an expert in this field.

Your last task is to rate your feeling again to see if there is a difference from your first rating.



Anxious 15%

A template is provided on the next page to further assist you with this exercise . This exercise is best completed within 2 hours of experiencing a strong feeling.

EXERCISE 3: IDENTIFY THE HOT THOUGHT

Situation (When, Where, What, Who)	Mood Rating (0-100)	Automatic Thoughts Circle the hot thought	Evidence To Support Hot Thought	Evidence That Goes Against Hot Thought	Alternative/ Balanced Thoughts	Mood Rating (0-100)

13

Week 4 Self-esteem & Assertiveness

Self-esteem is the value and worth that we place on our own identity. This includes our beliefs, values, attitudes and opinions.

People who have low self-esteem often have trouble asking others for what they want, as they feel as though other people's wants are more important than their own.

People with low self-esteem tend to neglect their essential needs such as security, respect, understanding and belonging by viewing them merely as wants rather than necessities.

You are the only person who can judge the strength of your needs and wants. **Chances are if you feel that something you want is important for you, then it is important and you have the right to ask for it.**

Assertiveness is a style of communicating that involves respecting the needs and wants of both yourself and other people. It allows you to feel comfortable asking for what you want and doing it in a way that does not violate the feelings of the other people involved.

The exercise for this week will focus on putting your wants into words. To do this you will need to get the facts and then summarise them in a clear statement.

- From = the person who can give you what you want
- I want = spell out what you want the other person to do
- When = indicate the deadline of getting what you want, the time of day or the frequency

- Where = the places where you want something
- With = specify any other people who are involved with your request

However, it is often not enough to just say what you want. It is more helpful for people to understand your perspective and your feelings. That way they will know why you want what you do. When we tell people what we want using our thoughts, feelings and a clear want statement, we are communicating a *whole message.*

Example:

From = Tom (my husband)

I want = No more jokes that my pain is "all in my head"

When = Usually after dinner when pain occurs

Where = At home

With = Tom alone

Feeling = I feel hurt when you do not believe that I am experiencing pain

Perspective = I struggle with this pain and sometimes feel like I am crazy. Your support and empathy might help me cope.

Exercise 4: Asking for what you want

If asking for things is hard for you, it is helpful to prepare your request in advance. This will help you to make your statement clear and assertive. It will also ensure you are asking using a "whole message". To become familiar with this technique you may first use it for simple wants before trying it to get something you are having difficulty asking for.

From = _____

I want = _____

_____

_____

When = _____

Where = _____

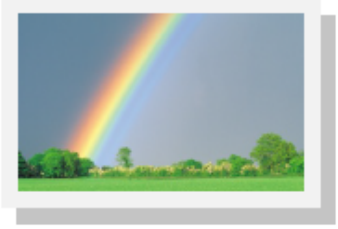
With = _____

My feelings = _____

_____

My perspective = _____

_____



16

Thank you for taking the time to use this booklet. We hope that the exercises and skills demonstrated in this booklet were applicable and useful to you. These exercises have been adapted from general cognitive behavioural and acceptance commitment therapy techniques. The sources for some of these exercises are provided below for your convenience if you are interested in learning more.

Greenberger, D., & Padesky, C.A. (1995). *Mind over mood*, New York, NY: The Guilford Press.

Harris, R. (2009) *ACT made simple.* Oakland, CA: New Harbinger Publications Inc.

McKay, M. & Fanning, P. (2000). *Self-esteem.* 3rd ed. Oakland, CA: New Harbinger Publications Inc.

Note: An extra copy of the templates for the exercises are located in the following pages. These templates may be photocopied for personal use if needed while familiarising yourself with the techniques. However, please do not distribute these templates or present them in public forums.

Appendix C: Patient Intake Survey

PATIENT DETAILS AND CURRENT HEALTH QUESTIONAIRRE

1. What is today's date?

2. What is your full name?

3. What is your current address?

4. What is your email address? (if applicable)

5. Home phone number (if applicable)

6. Work phone number? (if applicable)

7. Mobile phone number? (if applicable)

8. What is your date of birth?

9. Please provide the name, address and telephone number of your GP (regular doctor).

10. What is your gender?

○ Male ○ Female

11. Are you pregnant?

○ Yes ○ No

* 12. What is your age?

- ○ 18-24
- ○ 25-34
- ○ 35-44
- ○ 45-54
- ○ 55-64
- ○ 65-74
- ○ 75+

13. What is your relationship status?

- ○ Single
- ○ In a relationship but not living together
- ○ Married
- ○ Living with partner
- ○ Divorced or separated
- ○ Widowed

14. Which best describes your current employment situation?

- ○ Retired
- ○ Unable to work due to disability
- ○ Student
- ○ Homemaker
- ○ Not currently employed
- ○ Working part-time (less than 35 hours a week)
- ○ Working full-time (35 hours a week or more)
- ○ Other (please specify)

15. What level of education have you completed?

- ○ Year 11 or below
- ○ High School (Yr 12)
- ○ TAFE/ Other training
- ○ University Degree
- ○ Post Graduate Degree

16. What language do you speak at home?

- ○ English
- ○ Other (please specify)

17. How long have you had the current symptoms that led to your referral to the RAH Gastroenterology Outpatients Department?

18. Have you seen a gastroenterologist specialist for your symptoms previously?

- ○ Yes
- ○ No

19. How many times have you seen a specialist for these symptoms previously?

20. Did your specialist give you a diagnosis? If yes, please write the diagnosis down.

- ○ No
- ○ Yes (Please specify)

21. How many years ago, did you see the specialist? (Please list all visits that you can remember)

22. Has your referring GP given you a diagnosis for these symptoms?

- ○ No
- ○ Yes (please specify)

23.How long have you been on the waiting list to be seen by the specialist? If you can recall.

24. What treatments are you currently using for these symptoms? Please include all prescribed and over the counter medicines, as well as herbal supplements, dietary supplements, and any complementary or alternative therapies such as psychological therapy, acupuncture, hypnosis etc.

25. What level of improvement in your symptoms do you get with the treatments you are currently using?

- ○ No improvement
- ○ Mild improvement in some symptoms
- ○ Mild improvement in most symptoms
- ○ Good improvement in some symptoms
- ○ Good improvement in most symptoms

26. Please indicate which treatments you think are effective for you and why?

27. In the last 4 weeks, how much money do you estimate that you have spent on medications and treatments for your gastrointestinal disorder? Include all medicines including over the counter, vitamins, herbal supplements as well as prescription medicine.

28. In the last 4 weeks, how much money do you estimate that you have spent on appointments with alternative health practitioners (such as naturopaths, chiropractors, dietitians etc) for your gastrointestinal disorder?

29. How satisfied are you with your gastrointestinal symptoms at the moment? Please rate your satisfaction on a scale of 0-10 where 0=completely unsatisfied, and 10=completely satisfied

Please give reasons

30. Have you previously tried any treatments for your gastrointestinal symptoms that were not effective? If yes, please give details.

- ○ No
- ○ Yes (please specify)

31. How satisfied are you with your GP/Specialist management of your symptoms?

- ○ Well satisfied
- ○ Satisfied
- ○ Partially satisfied
- ○ Unsatisfied

Please give reasons

32. In the last 4 weeks, how many times have you seen your GP/doctor because of your current symptoms?

33. In the last 4 weeks how many times have you visited your GP/doctor for ANY other problems?

34. In the last 4 weeks have you presented to the hospital for your current symptoms or any other conditions? If yes, please provide details of each visit.

- ○ No
- ○ Yes (please give details)

35. Have you had any hospital admissions for your current symptoms previously?

- ○ Yes
- ○ No
- ○ Unsure

36. How many times have you been to hospital because of the same symptoms that you currently have?

37. What are your main concern(s) about your gastrointestinal symptoms?

38. What other illnesses do you have? (please include physical and/ or and psychological e.g. depression, anxiety etc).

39. Have you previously taken antidepressants?

- ○ Yes
- ○ No

If yes, please name the medication if you can remember

40. Did your previous antidepressant treatment help you?

- ○ Yes
- ○ No
- ○ Unsure

Please give details of how it helped you. i.e. how did your health improve?

41. Have you ever seen a psychologist?

- ○ Yes
- ○ No

If yes, please state the reason

42. Did therapy with a psychologist help you?

- ○ Yes
- ○ No
- ○ Unsure

MEDICAL AND FAMILY HISTORY (Algorithm Group Only)

43. In the last 3 months, how often have you noticed blood in your stools (bowel motions)?

- ○ Never or rarely
- ○ Sometimes
- ○ Often
- ○ Most of the time
- ○ Always
- ○ Other (please specify)

44. In the last 3 months, have you vomited blood?

- ○ Never or rarely
- ○ Sometimes
- ○ Often
- ○ Most of the time
- ○ Always

45. In the last 3 months, have you had a fever (greater than 38 degrees Celsius on a thermometer) with no typical explanation (such as a sore throat, ear infection, flu etc.)?

- ○ Never or rarely
- ○ Sometimes
- ○ Often
- ○ Most of the time
- ○ Always

46. In the last 3 months have you unintentionally lost more than 3kg or more than 5% of your body weight?

- ○ Yes
- ○ No

47. If you are over 50, have these gastrointestinal symptoms begun in the last 6 months?

- ○ Yes
- ○ No
- ○ Does not apply

48. Do you have a first-degree relative who was diagnosed with colon (bowel) cancer when they were less than 60 years of age? (e.g. mother, father, sister or brother)

- ○ Yes (please list all)
- ○ No

49. Do you have any first-degree relatives (e.g. mother, father, sister or brother) diagnosed with Ulcerative colitis or Crohn's disease at any age?

- ○ Yes (please list all)
- ○ No

50. Do you have any first-degree relatives (e.g. mother, father, sister or brother) diagnosed with Coeliac disease?

- ○ Yes (please list all)
- ○ No

51. Do abdominal complaints wake you up from sleep?

- ○ Never or rarely
- ○ Sometimes
- ○ Often
- ○ Most of the time
- ○ Always

If yes, please give more detail

Appendix D: Patient Follow Up Survey (Algorithm group)

We are very interested to hear which aspects of the 'system of care' we are trialling that you found to be helpful (or not helpful) and why. In order to tailor this management approach to meet the current needs of patients we would appreciate as much detail and reasoning as you can give in your answers.
Thank you for your time and honest opinions.

1. Did you find receiving the letter which stated your diagnosis and management options to be useful? Please give reasons (as much detail as you are able)

2. Did you discuss this letter with your GP? Please explain whether discussing the letter with your GP was helpful or not, and why, or provide any reasons you had for choosing not to discuss this letter with your GP.

3. Which management options recommended in the letter did you decide to try?

- ○ Dietary intervention (low FODMAP diet, dietitian)
- ○ Psychological intervention (CBT website, psychologist, or self-help booklet)
- ○ Both
- ○ None
- ○ Other (please specify)

4. What were your reasons for choosing these options? (Please list as many as you can)

5. Please give any reasons you have for not trying the other management recommendations? (This will help direct future research)

6. What method did you use to access these management options?

- ○ None
- ○ Dietitian appointment/s
- ○ Psychologist appointment/s (not including hypnotherapy)
- ○ Psychologist appointment/s (including hypnotherapy)
- ○ The Monash University Low FODMAP diet booklet (purchased)
- ○ The Low/High FODMAP Food List (provided)
- ○ Gut and Mind Matters Self-help booklet (provided)
- ○ Gut and Mind Matters Website
- ○ Low FODMAP Smartphone App
- ○ ACT smartphone APP
- ○ Other (please specify)

7. What level of improvement in your symptoms do you get with the treatments you are currently using?

- ○ No improvement
- ○ Mild improvement in some symptoms
- ○ Mild improvement in most symptoms
- ○ Good improvement in some symptoms
- ○ Good improvement in most symptoms

8. Which management options do you feel have helped reduce your symptoms? Please explain how/why they have helped, where you can?

9. For each option you used, can you indicate to what extent you have used it. (e.g.. regularly, only when symptoms flare up, when I remember, for 4 weeks only, continued regular use etc.)

10. What other treatments are you currently using for these symptoms?
Please include all prescribed and over the counter medicines, as well as herbal supplements, dietary supplements, and any complementary or alternative therapies
11. How satisfied are you with your gastrointestinal symptoms at the moment?
Please rate your satisfaction on a scale of 0-10 where 0=completely unsatisfied, and 10=completely satisfied. (Please give reasons)

12. In the last month, how much money do you estimate that you have spent on medications and treatments for your gastrointestinal disorder? (Include all medicines including over the counter, vitamins, herbal supplements as well as prescription medicine).

13. In the last month, how much money do you estimate that you have spent on appointments with alternative health practitioners (such as naturopaths, chiropractors, dietitians etc.) for your gastrointestinal disorder?

14. In the last 4 weeks, how many times have you seen your GP/doctor because of your current symptoms?

15. In the last 4 weeks how many times have you visited your GP/doctor for ANY other problems?

16. In the last 4 weeks have you presented to the hospital for your current symptoms or any other conditions? If yes, please provide details of each visit.

- ○ No
- ○ Yes

If Yes (please give details)

17. The current practice for patients with your symptoms involves a greater than 12 month waiting list to see a specialist (with many patients never being seen). In view of this fact, do you find the approach used in this study to be acceptable?

- ○ Not at all acceptable
- ○ Slightly acceptable
- ○ Moderately acceptable
- ○ Very acceptable

Please give reasons where you can.

Appendix E: PHCP Intake Survey

Thank you for completing this very brief survey. All responses in this survey are unidentifiable. These questions do however refer to the SPECIFIC patient you have referred as indicated in the letter we sent to you.

1. Are you male or female?

- ○ Male
- ○ Female

2. Which category below includes your age?

- ○ 21-29
- ○ 30-39
- ○ 40-49
- ○ 50-59
- ○ 60 or older

3. How many years have you been practicing as a General Practitioner?

- ○ Less than a year
- ○ 1-5 years
- ○ 6-10 years
- ○ 11-20 years
- ○ 20+ years

4. What is the main reason for your referral for this specific patient to the RAH Gastroenterology OPD?

5. Please tick ANY reasons for the referral of THIS SPECIFIC PATIENT to the RAH Gastroenterology OPD which apply (all responses are unidentifiable)

- ○ Second opinion of diagnosis already made
- ○ Unable to provide diagnosis
- ○ Patient keeps presenting with the same problem
- ○ To allay patient fears
- ○ To ensure I haven't missed something
- ○ I do not have time to investigate further
- ○ Patient unresponsive to treatments tried
- ○ The patient requested a referral
- ○ The patient is difficult
- ○ I am unable to manage this patients' demands
- ○ Frustration

6. On the basis of your current investigations are you confident that this patient has a functional gastrointestinal disorder?

- ○ Yes, but the patient wants a second opinion
- ○ Yes, but I would like confirmation of my diagnosis
- ○ Yes, and I would like treatment recommendations
- ○ Unsure and I would like advice
- ○ No and I need specialised advice
- ○ No and I think they have another diagnosis

7. Currently patients suspected of having Functional Gastrointestinal Disorders face a greater than 12-month waitlist to see a specialist at the RAH Gastroenterology OPD (if they are seen at all). We are interested in trialling a new algorithm based approach to these patients which will incorporate the screening of referrals, testing to exclude other diagnoses and the provision of a FGID diagnosis and management recommendations to both the referring doctor and the patient.

   In comparison to the current system would you find this approach acceptable?

- ○ Not at all acceptable
- ○ Slightly acceptable
- ○ Moderately acceptable
- ○ Very acceptable
- ○ Completely acceptable

8. Do you have any concerns, comments or feedback on this proposed approach?

Appendix F: PHCP Follow Up Survey

Thank you for completing this very brief survey. These questions relate to the SPECIFIC patient you have referred as indicated in the letter we sent to you.

1. Are you male or female?

- ○ Male
- ○ Female

2. Which category below includes your age?

- ○ 21-29
- ○ 30-39
- ○ 40-49
- ○ 50-59
- ○ 60 or older

3. How many years have you been practicing as a General Practitioner?

- ○ Less than a year
- ○ 1-5 years
- ○ 6-10 years
- ○ 11-20 years
- ○ 20+ years

4. Since this trial, has <patient name, dob> received any other diagnosis (other than functional), which accounts for their GI symptoms? (Please name the diagnosis).

- ○ No
- ○ Yes (please specify) _____

5. Did you discuss the diagnostic/management letter with the patient?

- ○ Yes, I recalled the patient to discuss
- ○ Yes, we discussed at a subsequent appointment
- ○ Can't remember
- ○ No (could you tell us why not)? _____

7. Were there any particular aspects of the trial/letter which you found useful?

8. Currently patients suspected of having Functional Gastrointestinal Disorders face a greater than 12 month waitlist to see a specialist at the RAH Gastroenterology OPD (if they are seen at all). This trial assessed a non-specialist dependent approach where patients were screened for alarm features and tested to exclude other diagnoses. A letter stating the FGID diagnosis and management recommendations was provided to both the referring doctor and the patient. (Where alarms or abnormal test results were present, a senior gastroenterologist reviewed the notes and a prompt consultation offered when indicated - as per usual triage classification).

   In comparison to the current system do you find this approach acceptable?

- ○ Not at all acceptable
- ○ Slightly acceptable
- ○ Moderately acceptable
- ○ Very acceptable
- ○ Completely acceptable

9. Do you have any other feedback you would like to give?

Appendix G: Health Economics Analysis for FGIDS in Australia

There is little information regarding the economic burden of FGIDs to the Australian healthcare system. This analysis does not propose to be a comprehensive, health economic analysis but rather an initial estimate of the cost of FGIDs based on publicly accessible Australian data and population studies. Data includes government and industry reports, current AMA and national hospital costings, and small isolated studies assessing healthcare usage and workplace productivity. The estimates produced here are can be used as a foundation to inform future full-scale health economic analyses.

1. Based on "Bettering the evaluation and care of health data", the average rate of GP encounters for IBS between 1998-2005 was 0.3/100 [(1)].

2. In 2014, there were an estimated 2.57 million GP–patient encounters per week (133 640 000/yr) [(2)]. Estimated number of IBS encounters is 400 920 consultations/yr.

3. An Australian population study in 2002, found that 4.4% of Australians had IBS and 8.5% FD according to Rome I criteria. 81% of people with IBS had sought healthcare for their IBS in the last 12 months, compared with 76% of those with FD [(3)].

4. Thus, 6.5% of the Australian population consulted for FD, and 3.6% for IBS

5. Annual number of IBS-GP consultations =400920 (3.6%) [(1)]

6. For this analysis, we will assume that the rate of GP encounters is the same for IBS and FD. Although Koloski *et al.,* (3) found that Australians with FD have a higher level of GP encounters than those with IBS [(3)].

7. Koloski *et al.,* (3) also found that 2.5% of the population had both IBS and FD. Thus, the adjusted consultation rates are as follows:
   i. IBS= 211597 (1.9%)
   ii. IBS & FD=278417 (2.5%)
   iii. FD=501150 (4.5%)
   iv. Total number of GP-encounters=991164

8. Cost of annual GP-consultations, based on AMA GP level B consult $78 [4] = $77,310,792

9. Between 1998-2005 9.1 % of IBS patients were referred for specialist care [1](gastroenterologist, surgeon, colonoscopy). All gastroenterology referrals increased from 0.4/100 encounters to 0.6/100 encounters between 2003-2014, which represents a total increase in referrals of 33% [5]. If we assume comparative increase across all disorders, and apply this 33% increase to IBS and FD referrals (not compounding), this equates to a referral rate increase from 9.1% to 12.1% (25,603 IBS referrals).

10. Previous population studies in the United States [6] and Canada [7] have shown that 13-23% of primary care consults are referred for specialist care, and 50-53% undergo upper GI endoscopy. Taking a conservative approach, an equal referral rate for IBS and FD in Australia (12.1%) will be used for FD for this analysis. Thus, the total number of referrals is 110,251.

11. Using an initial consult cost (MBS 110) of $315, the total cost of initial specialist consults is 34,729,065.

12. Of patients referred with suspected FGID, it has been shown that 79% undergo endoscopic investigation [8] .

    i. IBS= 211,597 x12.1%x79%=20,227 colonoscopy
    ii. IBS & FD=278,417 x12.1% x79%=26,614 colonoscopy & UGIE
    iii. FD=501,150 x12.1%x79%=47,905 UGIE
    iv. Total 46,841 colonoscopies, 74,519 UGIEs

13. The national estimated cost of colonoscopies in 2014 was $1632 ($1246 direct costs, $386 indirect costs), and gastroscopies, $1453 ($1116 direct costs, $338 indirect costs) [9].

14. Total cost colonoscopy = $1632 x 46841 =76,444,512

15. Total cost UGIE=$1453 x 74519= $108,276,107

16. Assuming approximately 30% of these endoscopic procedures will also include biopsy and histopathology (MBS 78213) at a cost of $71.50 per procedure. Total procedural costs including pathology tests are estimated at $187,323,770

17. Patients referred to a gastroenterologist in the public health system generally receive at minimum an initial consult plus follow-up consult, regardless of whether endoscopic investigations are performed. Total follow-up consultation costs are $12,716,308, based on MBS 116 fee of $146.

18. Thus, the total annual cost for GP and specialist consultation for IBS and FD is $312,079,935.

19. Some patients also present to hospital outside of the Outpatients clinic and are admitted. The number of overnight admissions per year for IBS alone was 670 in 2010, and this has been stable for the past decade [10]. The average length of stay was 4 days, with an average separation cost of $3535 [9]. There are no admission data available for FD, and so this is omitted from this analysis. As IBS is just one of over 20 FGIDs, with functional dyspepsia being as prevalent, the likely admission rate is greater.

20. Contrary to expectation, the ongoing costs of total healthcare and gastrointestinal related healthcare are higher than the initial diagnostic workup [11]. In fact, the cost of diagnostic workup in this US study [11], was relatively small when compared to overall healthcare utilisation and costs in established IBS patients. In our recent pilot study of patients with FGID referred to the Royal Adelaide Hospital, we found that the average cost of treatment prior to referral was $50/4 weeks[SD $116], with 1.15 (SD 1.49) GP visits in the prior 4 weeks (GI related, 0.46 [SD 0.862], other 0.70 [SD 0.105]) [12, 13]. This gives an estimated monthly cost (GI related medication plus GP appointments) of $86 per patient, or $123,088,626 annually.

21. There are no Australian data regarding the effect of FGIDs on workplace productivity. However, Another study has shown workplace productivity to be reduced by 20%, or 8 hours/ week in IBS patients [14]. With an Australian average weekly wage of $1163.50 [15] this loss amounts to $233 per patient employer per week ($12,095 per year). With 110,251 patients referred to specialist care each year, this is a cost of 1.33 billion dollars in lost productivity to the Australian workforce.

22. Thus, the estimated annual costs of IBS/FD, (two of the most prevalent FGIDs) in Australia total $1.77 billion ($312 million direct/diagnostic, $1.33 billion indirect/ongoing, gut-related costs).

Figure 1. Annual Diagnostic Costing of IBS/FD in Australia

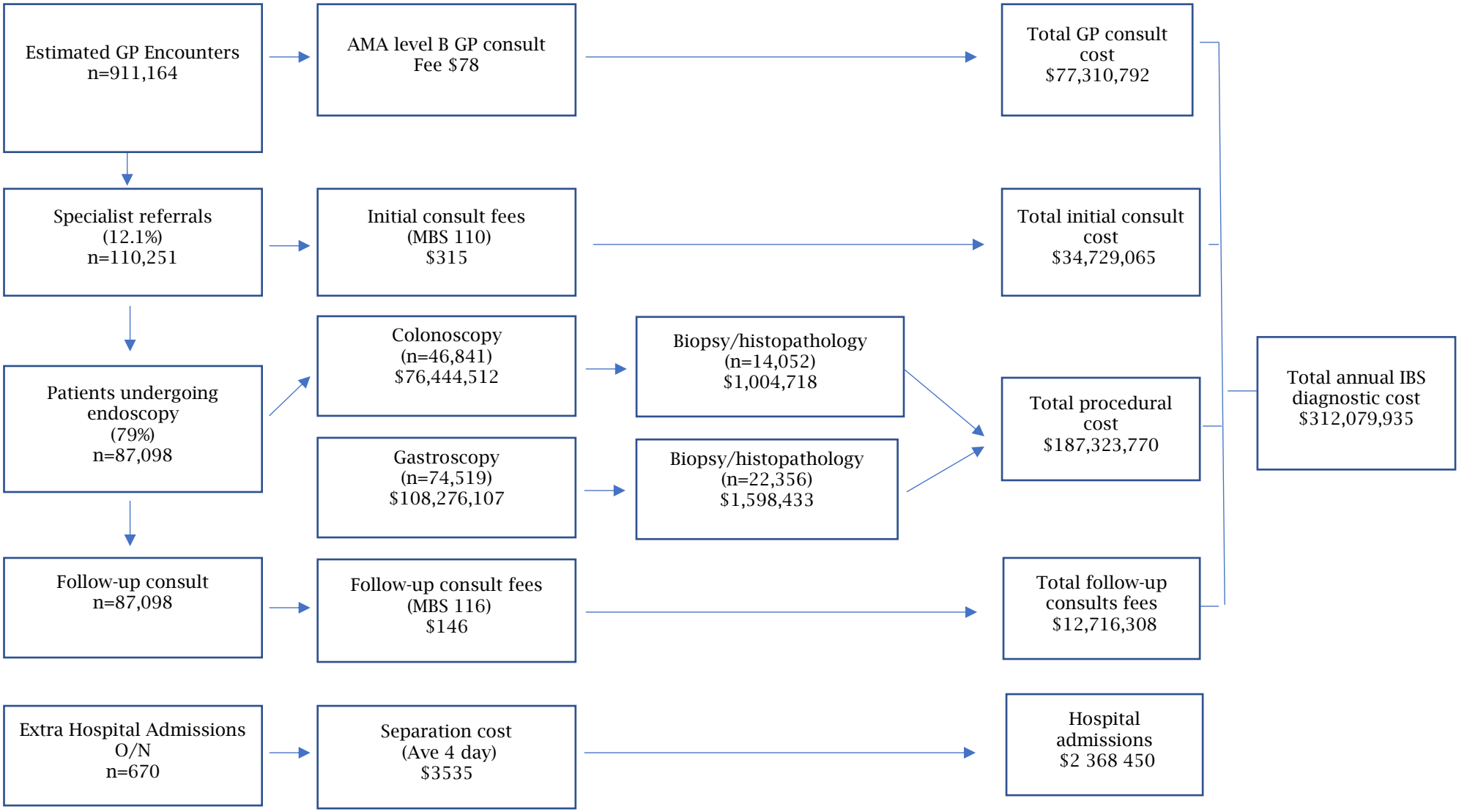
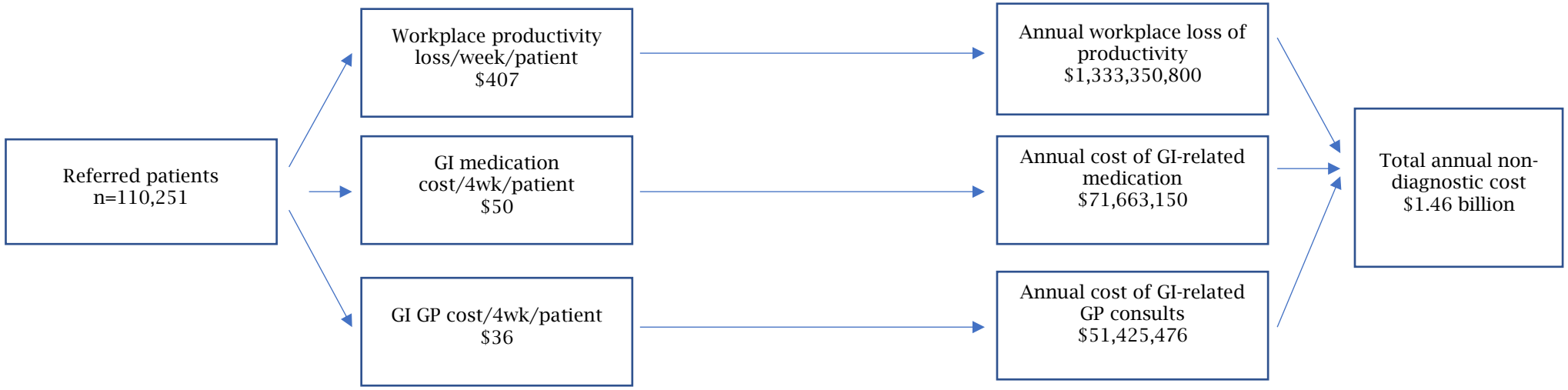


Figure 2. Annual Additional Gut-related Healthcare and Workplace Productivity Loss Costs of IBS in Australia



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Appendix H: Narrative Review

Narrative Review: The Diagnosis and Management of Irritable Bowel Syndrome (IBS) in 2017 – A Guide for the Generalist

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SUMMARY

- Irritable bowel syndrome (IBS) is so prevalent it cannot reasonably have its diagnosis and management based within specialty care. However, currently delayed diagnosis and lengthy wait times for specialist review are common, as are over-investigation and lack of clear diagnostic communication

- Its intrusive symptoms impair patient functioning and reduce quality of life. IBS comes with significant costs to individual patients and our healthcare system, which could be reduced with timely diagnosis and effective management.

- It is no longer a diagnosis of exclusion and there are now effective dietary and psychological therapies which can be accessed without specialist referral.

- Faecal calprotectin, is widely available, yet not on the medical benefit schedule and a normal result it reliably discriminates between people with IBS and those who warrant specialist referral.

INTRODUCTION

Irritable Bowel Syndrome (IBS) is a highly prevalent condition affecting 10% of the population at any time-point and ~40% over a lifetime [1-3]. It causes disturbed gut function and intrusive symptoms which impair quality of life [2, 4, 5], without there being overt structural or biochemical abnormalities [6]. Due to its prevalence and symptom burden, it results in a large societal cost via both direct and indirect expenditure [7-9]. Yet, despite the high prevalence, it does not appear to be generally well handled within our current healthcare system, and leads to frustration and dissatisfaction in patients and doctors alike [10]. This frustration appears to begin with the diagnostic process and flows through to either insufficient or excess investigations [11-14], repeat consultations and reinvestigation, and low and late uptake of therapies which are proven to be effective, yet are infrequently used outside of specialty care centres with an IBS focus. This represents an opportunity cost to our community, as IBS can be easily and safely diagnosed with few investigations and effective therapeutic options can be implemented and accessed from primary care. Herein, we review the current best-practice approach to making and delivering a safe and effective diagnosis of IBS, and then proceed to outline newer, effective treatment strategies which can be initiated without specialist Gastroenterology input.

MAKING A DIAGNOSIS OF IBS: WHY DOES IT MATTER?

It may seem self-evident, but without a diagnosis which is accepted and owned by the patient, she/he cannot move out of the diagnostic process and into effective management. Thus, the formulation and delivery of a safe, confident and effective diagnosis is an essential starting point in the therapeutic pathway. Logically, there are 3 key components to the diagnostic process:

- Making the diagnosis (provisional diagnosis on positive criteria);
- Ensuring it is a correct diagnosis (targeted investigations to exclude other relevant differential diagnoses) and
- Communicating it effectively to patients to ensure “ownership”.

These three components of the diagnostic process are true for any disease, however, they take on a greater importance for IBS, where there is no definitive diagnostic test and no abnormality can be “shown”, making it more likely that uncertainty around the diagnosis will be perceived by either patient or doctor. Many people – both patients and doctors – are uncomfortable with uncertainty and this is thought to be a driver of more testing and specialist referrals in IBS.

Repeat healthcare utilisation is a common phenomenon in people with IBS [3]. Drivers for repeat consultation include increasing perceived symptom severity and duration [15], with common reasons for specialist referral including persistent symptoms, diagnostic uncertainty (in the clinician) and patient fears [16]. In addition, healthcare utilisation by people with IBS, for unrelated conditions, is significantly higher than the general population and is partly driven by somatisation, whereby psychological distress is perceived in the form of somatic symptoms [17-19].

A crucial step in reducing symptoms and healthcare utilisation, is the early provision of a clinical diagnosis of IBS, along with an explanation of the chronic recurrent nature of the disorder and the biopsychosocial factors which may influence symptoms (anxiety, stress, depression, hypervigilance, catastrophising) [20]. Without this, patients will remain in the diagnostic process and may recurrently seek an organic cause for their symptoms. Where IBS is present, a prolonged search for an alternative explanation/diagnosis is futile, financially inefficient, time consuming and encourages unrealistic expectations along with delaying effective management. Thus, a delayed diagnosis does not help either the patient or society. In recognition of this, the UK National Institute for Health and Care Excellence (NICE) quality standards for IBS [21] specifically recommend giving a positive diagnosis to reduce unnecessary anxiety for patients and to promote effective management. Moreover, they recommend this diagnosis is most often provided in primary care.

MAKING A DIAGNOSIS OF IBS: KEY PRINCIPLES

Ever since the initial publication of the Manning Criteria [22], the diagnosis of IBS ceased to be “a diagnosis of exclusion”. This old approach led to never ending rounds of investigations with diminishing returns, and has encouraged the perception amongst patients that if only another test were done, an alternative diagnosis would be found. In addition, ongoing testing encourages the belief that the doctor is uncertain and this also heightens anxiety – often contributing to worsening symptoms. Formulating an IBS diagnosis consists of the positive component in recognising IBS according to its typical symptomatology and the negative component in excluding other relevant possibilities [23, 24]. Both these aspects can be largely addressed by a careful, structured clinical history and a physical examination. Where symptoms are typical and long standing, there is no family history of concern and no clinical alarms are present, the diagnosis may even be made without any testing.

Current recommendations are to make a positive diagnosis based on characteristic symptoms and confirm with minimal investigations [21, 25]. Which investigations are

reasonable to perform will depend on the patient's age and pre-test probability, and should not represent an exhaustive search. IBS is the most commonly recognised functional bowel disorder, others include functional bloating, functional diarrhoea and functional constipation. Essentially these distinctions are probably more important in research than in clinical medicine, where all functional bowel disorders are appropriately grouped under the umbrella label of IBS [26]. The current criteria (Rome IV) [27] for diagnosing functional bowel disorders, including IBS, are shown in Table 1. It is important to note that not only does one need the relevant symptoms but also to meet the time criteria. This makes an incorrect diagnosis much less likely, as infection is likely to have resolved and inflammatory bowel disease (or other organic pathology) is likely to have progressed within the 6-month time frame. Once one has recognised the positive criteria for a diagnosis, a structured approach to elicit/exclude the relevant clinical alarms (Table 2) can be applied. When this approach is combined with a physical examination, including a digital rectal exam – essential where anorectal symptoms including bleeding, incontinence and pain are described – one can often make a firm diagnosis with no further testing.

Where there are specific concerns, limited tests might be performed, which should be tailored to the symptoms, age and presentation of the patient. These are detailed in the upper right corner of Figure 1. It is important to note, that many commonly performed investigations are actually not recommended, and there are moves internationally to address overuse of diagnostics as part of initiatives such as "Choosing Wisely" [28] and "Evolve"[29]. One test worthy of mention here is faecal calprotectin (FC). It is not as widely used in Australia as it could be, due to a lack of MBS funding, however it is very good at discriminating between functional and organic lower gastrointestinal disease, such that in a young patient, with at least 6 months' symptom duration and no clinical alarms, a negative FC essentially seals the diagnosis [21, 30-32] and allows one to safely move into the management phase. Colonoscopy in young woman without clinical alarms is very low yield [33] and should be discouraged.

MAKING A DIAGNOSIS OF IBS: WHAT EVIDENCE DO WE HAVE THAT THERE IS A PROBLEM?

We, and others, have shown that many patients with an existing diagnosis of IBS do not own it, and often continue to seek further diagnoses, investigations, explanations and treatments [10, 34, 35]. This is difficult to fully explain, but might relate to patient, primary care, or specialty care factors. The exploratory work by Collins *et al.,* (36), found that there is quite a divergence in the understanding of symptom burden, perceived cause and best

treatment options in people with functional gastrointestinal disorders (FGIDs) especially IBS. This might be viewed as a failure in clear medical communication and a lost opportunity for patient education. The issue of specialist communication has been further investigated by examining the language doctors use to convey the diagnosis [37]. It was striking that in letters back to referring doctors, even gastroenterology specialists were using uncertain diagnostic language much more often in patients with functional gastrointestinal disorders (like IBS) than in patients with other organic gastrointestinal conditions such as reflux disease, Crohn's disease, peptic ulcer. Of concern, the uncertain language continued even with follow-up visits, even though further time had elapsed and investigations had returned negative results. This represents an opportunity for doctors to more clearly and confidently deliver an IBS diagnosis and likely prevent ongoing fear of missed pathology in patients and referring doctors alike.

There are also documented problems in primary care with formulating and delivering an IBS diagnosis. A recent study exploring current issues in the management of FGIDs such as IBS, found that whilst most patients from primary care were presenting to tertiary referral for the first time, they had longstanding symptoms with no firm diagnosis and no improvement despite multiple treatments [16]. Referring doctors lacked confidence in diagnosing and managing these disorders, and patients' dissatisfaction was related to remaining undiagnosed with no effective management options. Furthermore, often the demand for specialist review of 'non-urgent' disorders like IBS exceeds capacity, resulting in very long waiting lists with many patients never being seen. Providing a timely, clear diagnosis is critically important. Other studies have also shown that although clinicians may consider a functional diagnosis, most are reluctant to communicate or document this without further investigations [13, 38]. Patients with persistent medically unexplained symptoms (i.e. undiagnosed) use significant amounts of healthcare in a continued search for a diagnosis [39]. A clear diagnosis provides reassurance and alleviates patients concerns and helps move the patient from a diagnostic search to an effective management strategy [23, 24]. This in turn reduces the physical and mental distress of patients and the economic burden due impaired workplace productivity, unnecessary investigations and endoscopic procedures. From a strictly economic perspective, a timely diagnosis is necessary for the effective allocation of limited healthcare resources, such as outpatient appointments and endoscopic procedures

So, there are clearly both primary and specialty care issues we, as doctors, can address. If we fail to manage this well, patients will turn to alternative practitioners and advice via the web, and are likely to be vulnerable to false claims, high cost, and unproven therapies.

MAKING A DIAGNOSIS OF IBS: WHAT EVIDENCE DO WE HAVE THAT IT IS SAFE?

Fortunately, there is a wealth of data to show that a well-made clinical diagnosis of IBS is safe and reliable over time. There is no increase in mortality in those with a diagnosis of IBS [40-44] and no increase in colorectal cancer – except in the first year, in older patients – where perhaps a better structured evaluation might have been applied [45]. Fluctuating symptoms are very common, and when strict Rome categories are applied, people often move between various functional bowel disorder categories, but are rarely durably symptom-free [2, 46].

MANAGEMENT OF IBS: WHERE TO NEXT?

Once there is consensus between doctor and patient that IBS is the diagnosis, we can move into the management phase. Management needs to take the patient's desires, beliefs and main concerns into account, as IBS of itself does not "need" or mandate management. This is important to remember as many people need only to know why they have symptoms and whether they should be concerned.

For those requiring management, there are a number treatment options, of varying efficacy [47-51] (Table 3). Of particular interest, are the non-pharmacological options (psychological and dietary therapies), which offer the benefit of global rather than targeted symptom control. On the whole, psychological interventions have been shown to be effective in reducing IBS symptoms and psychological distress, as well as increasing quality of life [52-54], and are as effective as anti-depressants [54]. Almost 50% treated with psychological treatments experience symptomatic improvement compared to only 25% of controls who received 'usual physician treatment', 'supportive therapy' or 'symptom monitoring' [54]. Although many different forms of psychological therapy have been tested, cognitive behavioural therapy (CBT), hypnotherapy and multicomponent therapies are effective with a number needed to treat of 3-4 which is comparable with anti-depressants (NNT=4) [54], and without side effects. Despite the well-recognised fact that IBS and FGIDs have a significant psychological aspect, primary care providers do not regularly use psychological treatments [55]. Patient resistance to psychological interventions may contribute to this low uptake, however it is also likely to be related to a lack of positive endorsement by the doctor recommending it. Given the convincing efficacy data, practitioners should be more convincing when proposing psychological therapies to people with FGIDs. Moreover, gut-directed hypnotherapy directly affects visceral sensitivity and gastrointestinal motility [56, 57] and improves symptoms and quality of life over the long term [58-61] and thus shows considerable promise as an IBS treatment [62]. In

fact, marketing of gut-directed hypnotherapy as a stand-alone treatment, rather than a psychological treatment may improve patient uptake of this valuable treatment [14, 55].

The low FODMAP diet is effective in reducing IBS symptoms and in the short term, is the treatment with greatest gains, reducing symptoms in 70-75% of IBS patients [63, 64] and improving quality of life [51]. FODMAPS (Fermentable Oligo-, Di- and Mono-saccharides and Polyols) are poorly absorbed, highly osmotic and rapidly fermentable substances that act to increase the water and gas volume in the intestine resulting in luminal distension. High FODMAP foods are not harmful per se, and in people without visceral hypersensitivity cause no problems. However, distension resulting from fermentation of these foods, when combined with visceral hypersensitivity, causes abdominal pain, bloating, and/or altered intestinal motility [63, 65, 66]. Current recommendations (and evidence) are for this diet to be supervised by a qualified dietitian [21, 67, 68], as it is complex, and needs to be tailored to the individual. It is not recommended to be followed lifelong [68], and the re-introduction of some tolerated FODMAP containing foods is important, to ensure a wide variety of food choices and reduce risk of impairing nutritional adequacy [68, 69].

In general, non-pharmacological options are preferred in the first instance, as they can be used long term without ongoing cost, risk or healthcare utilisation. Once the techniques are learnt, patients can "self-treat" and use them as much or as little as desired to control symptoms. Lack of affordability of psychological and dietary therapies is often cited as a barrier to access. However, when one considers the amount spent on non-evidence-based, non-subsided therapies for IBS, this does not stand up as a reasonable explanation. Perhaps those selling alternative therapies do a better job of selling their therapies than medical practitioners do of endorsing evidence based, non-drug approaches? The existing good quality data suggest we need to market our therapies better, for community benefit. It is likely that if these approaches were adopted more widely and earlier in primary care, there would be considerable health, quality of life and financial gains made across the community. Moreover, it is likely that many fewer patients would need referral to specialty care with all the costs entailed.

MANAGEMENT OF IBS: WHEN NON–PHARMACOTHERAPY IS NOT ENOUGH.

In a subset of patients' further management will be needed to control symptoms and improve quality of life. Whilst there are many options marketed to manage IBS symptoms, the quality of evidence and the effect size is sub-optimal for many commonly used approaches. As the focus of this article is to highlight the substantial gains which can be made in formulating and delivering an IBS diagnosis and increase the knowledge and

uptake of effective, accessible non-drug therapies by non-gastroenterologists, a detailed review of IBS pharmacotherapy is beyond the scope of this review.

For people with significant urgency and fear of incontinence, daily loperamide taken first thing in the morning, with the dose titrated to effect, can be useful although it will not reduce other symptoms. In addition, drug therapies may be used in combination with non-pharmacological treatments, perhaps whilst initiating psychological or dietary therapy or when symptoms are in periods of flare.

There are several pharmacological treatments with some efficacy (Table 3), however gains over placebo are generally modest. Peppermint oil is the most effective treatment, but is limited to targeting pain. Similarly, anti-spasmodics although moderately effective, treat a single symptom. Antidepressants are not effective in all patients, with tricyclic antidepressants being recommended for patients with diarrhoea (due to significant constipation side effects), and serotonin reuptake inhibitors for those with comorbid major depression [52]. Drugs specifically targeting motility demonstrate some efficacy, yet have been plagued by safety concerns and no longer widely available. Probiotics' efficacy varies and is dependent on the bacterial strains used with this being a growing field of research. Fibre may increase abdominal symptoms in some people, however soluble fibre may be of some benefit. Newer agents on the horizon for IBS are now being targeted to specific issues, such as constipation (prucalopride, lubiprostone, linaclotide), diarrhoea (eluxadoline) or pain (eluxadoline), however most are not currently TGA registered or PBS funded in Australia, and their use is appropriately limited to within subspecialty units.

CONCLUSION

IBS is a highly prevalent condition where we should no longer be bound by the past focus on a diagnosis of exclusion with resultant therapeutic nihilism. There are substantial individual and community gains to be made if current knowledge around effective diagnosis and management can be rolled out from specialty practice into broader care, especially via general practitioners. A diagnosis can be safely made by following basic principles with few tests and is reliable over time. Failing to make and deliver a confident diagnosis, creates ongoing avoidable morbidity, and costs our society significant amounts in direct and indirect costs. Once a diagnosis is made, and an explanation of symptoms provided, we have access here and now to effective therapies. To achieve these gains, doctors need to be better advocates for these proven therapies or leave patients at the mercy of those with better marketing skills.

Table 1. Diagnostic Criteria for Functional Bowel Disorders Using Rome IV Criteria

<table>
<tr><th colspan="2">Rome IV [a]</th></tr>
<tr><td colspan="2">Irritable Bowel Syndrome
Recurrent abdominal pain
≥1 day per/week in the last 3 months
Associated with 2 or more of the following criteria:
• Related to defecation
• Associated with a change in frequency of stool
• Associated with a change in form (appearance) of stool</td></tr>
<tr><td>Functional Abdominal Bloating/Distension

Must include both of the following:
1. Recurrent bloating and/or distention occurring on average, at least 1 day per week; abdominal bloating and/or distention predominates over other symptoms[a].
2. There are insufficient criteria for a diagnosis of irritable bowel syndrome, functional constipation, functional diarrhoea, or postprandial distress syndrome.
[a] Mild pain related to bloating may be present as well as minor bowel movement abnormalities</td><td>Functional Diarrhoea

Loose or watery stools, without predominant abdominal pain or bothersome bloating, occurring in >25% of stools

Patients meeting criteria for diarrhoea-predominant IBS should be excluded</td></tr>
<tr><td>Functional Constipation
1. Must include two or more of the following:
In more than 25% of defecations:
• Straining
• Lumpy or hard stools
• Sensation of incomplete evacuation
• Sensation of anorectal obstruction/blockage
• Manual manoeuvres to facilitate (e.g., digital evacuation, support of the pelvic floor
• Or fewer than three spontaneous bowel movements per week

2. Loose stools are rarely present without the use of laxatives
3. Insufficient criteria for irritable bowel syndrome</td><td>Opioid Induced Constipation
1. New, or worsening, symptoms of constipation when initiating, changing, or increasing opioid therapy that must include 2 or more of the following:
In more than 25% of defecations:
• Straining
• Lumpy or hard stools
• Sensation of incomplete evacuation
• Sensation of anorectal obstruction/blockage
• Manual manoeuvres to facilitate (e.g., digital evacuation, support of the pelvic floor
• Or fewer than three spontaneous bowel movements per week

2. Loose stools are rarely present without the use of laxatives</td></tr>
</table>

Rome IV [a]	
Unspecified Bowel Disorders Bowel symptoms not attributable to an organic etiology that do not meet criteria for IBS or functional constipation, diarrhoea, or abdominal bloating/distention disorders.	Centrally Mediated Abdominal Pain Syndrome[b] Must *include all* of the following: • Continuous or nearly continuous abdominal pain • No or only occasional relationship of pain with physiological events (e.g., eating, defecation, or menses)[c] • Pain limits some aspect of daily functioning[d] • The pain is not feigned • Pain is not explained by another structural or functional gastrointestinal disorder or other medical condition [b]CAPS is typically associated with psychiatric comorbidity, but there is no specific profile that can be used for diagnosis. [c]Some degree of gastrointestinal dysfunction may be present. [d]Daily function could include impairments in work, intimacy, social/leisure, family life, and caregiving for self or others

[a] Criterion fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis

Lacy, B.E., et al., *Bowel Disorders.* Gastroenterology, 2016. **150**(6): p. 1393-1407.e5. [(1)]

Table 2: Clinical Alarms to elicit/exclude in diagnostic consultation

CLINICAL ALARMS
New onset symptoms if > 50 years of age (within 6 months)
Unexplained weight loss (>3 kg or 5% body weight)
Iron deficiency +/- anaemia
Melena, overt rectal bleeding, positive FHH[a]
Abdominal pain awaking patient from sleep
Diarrhoea disturbing sleep or faecal incontinence
Documented unexplained fever
Family history of colon cancer (1 FDR* <60, or > 1 FDR any age)
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,

FHH=Faecal Human Haemoglobin

[a]FHH testing only appropriate in people at average risk of colorectal cancer, > 50 years of age – not recommended for investigation of symptomatic patient

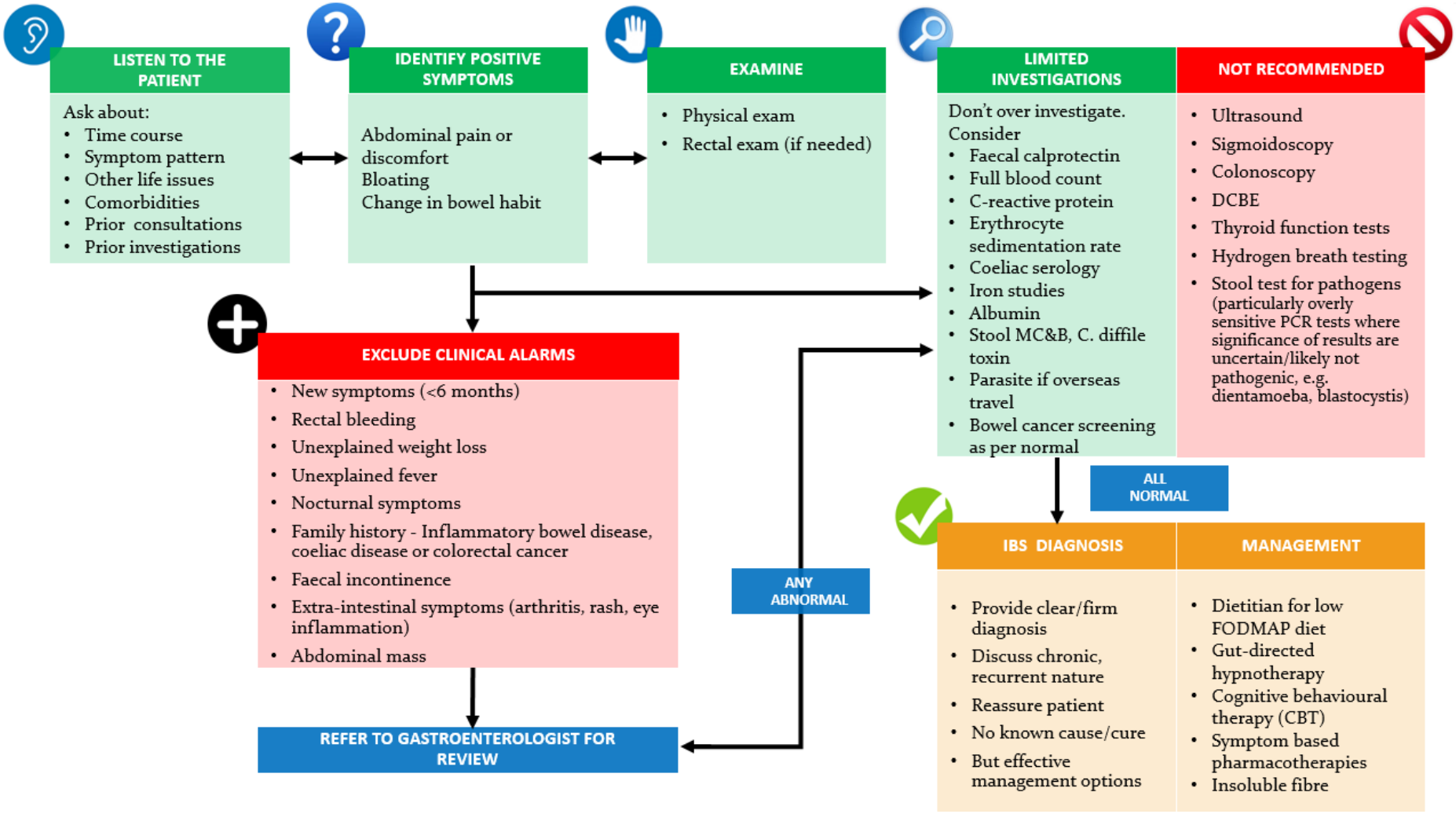
Table 3. Efficacy of Treatments for FGIDs: Summary of recent systematic reviews of the evidence

Treatments	No. of Trials (n)	Odds ratio	Relative risk [CI]	Gain	NNT [CI]	Comments
Psychological Therapies						
Psychotherapy [1]	22 (n=131)	2.60 [2.01-3.37]		23%	4-5	Global effect; similar effect between all psychotherapies; CBT most evidence
CBT [2]	9 (n=610)		.60 [.44-.83]	22%	3 [2-6]	
Relaxation/Stress Management [2]	6 (n=255)		.77 [.57-1.04]	16%	No benefit	Significant variation
Hypnotherapy [2]	5 (n=278)		.74 [.63-.87]	23%	4 [3-8]	Global symptom improvement, long term benefits
Dietary Therapies						
Low FODMAP Diet [3]	6 RCT 16 non-RCT	1.81 [1.11-2.95] .80 [.72-.86]				Improved global symptom severity & quality of life
Probiotics [1]	15 (n=1838)	2.24		13.5%	7-8	Variation with strain; Long term effect not assessed
Fibre [4] Soluble Fibre Bran	14 (n=906) 7 (n=499) 6 (n=441)		.86 [.80-.94] .83 [.73-.94] .90 [.79-1.03]		10 [6-33] 7 [4-25] No benefit	Can increase abdominal pain; Evidence soluble fibre improves IBS-C

Treatments	No. of Trials (n)	Odds ratio	Relative risk [CI]	Gain	NNT [CI]	Comments
Pharmacotherapies						
Anti-spasmodics [1]	22 (n=1718)	1.97		18%	5-6 [1.59-2.45]	*Pain/ Low cost
Motility agents [1]	31 (n>18000)			5-16%	6-15	Significant adverse effects
Antidepressants [5]						
TCAs	11 (n=744)		0.66 [.56-.79]	20%	4 [3-6]	IBS-D only
SSRIs	7 (n=356)		0.68 [.51-.91]	22%	4 [2.5-20]	Comorbid depression only
CAMS						
Peppermint oil [1]	4 (n=392)	4.11 [2.65-6.36]		39%	2-3	1 symptom (pain); Reflux and other side effects
Iberogast [6-8]	1 (n=208) 3 (n=425)		1.9 [1.15-3.14] .22 [.11-.47]	15-25% 19%		Global improvement

CAM= complementary and alternative medicines; CBT=cognitive behavioural therapy; NNT =number needed to treat; CI=confidence interval; RRR= relative risk reduction; Gain= gain of response over control

Figure 1. IBS Clinical Management Tool. Adapted from 1. "Differentiating IBS and IBD "(2013). Clinical Insights Steering Committee [1] 2. "Irritable bowel syndrome in adults": NICE quality standard [QS114] (2016) [2]



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Appendix I: Future challenges and directions in FGIDs – Integrated and biopsychosocial care approaches.

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ABSTRACT

The biopsychosocial nature of FGIDs together with the high prevalence of comorbidities and somatisation calls for the use of holistic, integrated care from each patient's initial presentation. The aim of this chapter is to review the current evidence for holistic care for FGID and suggest avenues for future gains. Specific areas reviewed in this chapter include the need for an integrated healthcare approach, current recommendations for integrated care, benefits of integrated approaches, gaps between recommendations and practice and the evidence for models of integrated care. Despite the limited number of studies evaluating the efficacy of an integrated approach to FGIDs available to date, research does identify significant benefits in terms of patient outcomes, reduced costs, and creation of greater capacity within a clinic.

LEARNING POINTS Integrated care for individuals with FGID should be patient-centered and holistic to facilitate accurate and timely diagnosis, effectively communicate both the cause of the symptoms and evidence-based information about treatment approaches, and co-ordinate relevant multi-disciplinary care-givers, all with the specific purpose of enabling the individual to self-manage.

- Integrated care for FGID has been shown to be effective in nurse-navigated models in secondary and tertiary care and via remote care in the tertiary setting.
- Evaluation of integrated care in primary care settings is lacking.
- Practical and accessible guidelines to support FGID diagnosis and management, and clinical pathways for evidence-based treatment approaches are needed.

INTRODUCTION

It is well established that individuals with FGIDs are likely to experience multiple comorbidities, somatisation and require an ongoing high level of health care [1]. Integrated care approaches are therefore necessary to address the multiple comorbid challenges associated with FGIDs. A holistic, integrated healthcare approach that begins with the first medical consultation is required to address the biopsychosocial experience, comorbidities, somatisation and suboptimal acceptance of functional disorders as a valid diagnosis. This type of integrated care requires a number of professionals including, general practitioners, gastroenterologists and allied health professionals (i.e. psychologists, dietitians) to optimally address these chronic complex conditions.

Defining Integrated Care

Integrated care has been a popular concept in healthcare since the 1960s, recommended by the World Health Organisation as current best practice in the management of people with complex, long term conditions, offering a number of benefits (Figure 1) [2, 3].

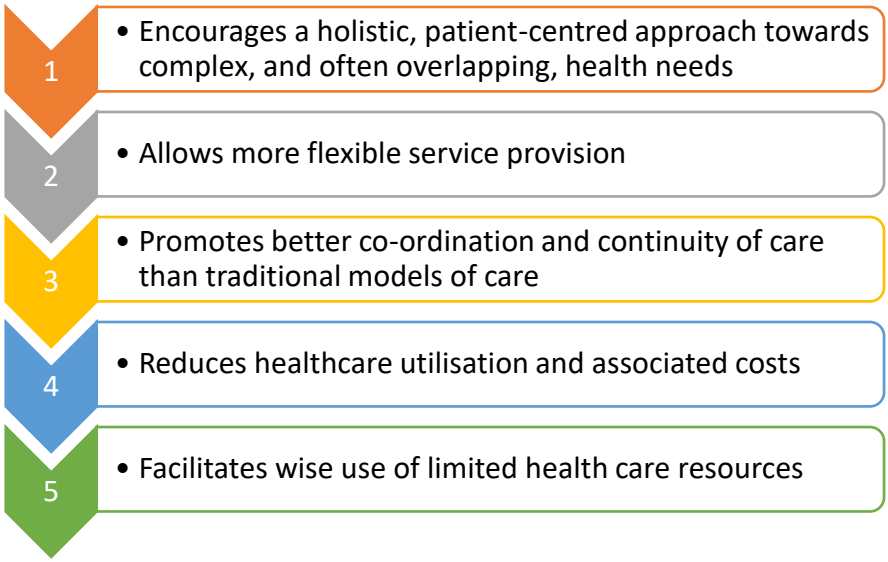

Figure 1. Benefits of an Integrated Approach to Healthcare

Integrated care is an umbrella term which is used to describe multi-component care [4]. Although there is no universally accepted definition of integrated care, it incorporates both the delivery and management of health care services, in order to provide efficient, effective, high quality, person-centered care [5]. Although the meaning of 'integrated care' and the individual elements of an integrated healthcare program vary between countries and healthcare systems, the founding principles include a holistic patient-centred approach (i.e. partnering with patients and carers) and facilitating access to, and communication between health care providers and services [4, 6]. While integrated care systems are not quick or easy to establish, integrated approaches have been shown to be successful in a number of global and financial settings and can be practically applied in any health system [5, 7].

The Need for Integrated FGID Care

FGIDs are indeed both chronic and complex, with biopsychosocial triggers, shifting symptomology over time [8] and often involving multiple unexplained somatic complaints [9]. Many patients have symptoms which impair daily life and need to access a number of health care services to maintain both physical and mental functioning [6]. This results in high levels of healthcare utilisation and costs [10-13], and often an over-use of unnecessary investigations [14]. An integrated approach to the diagnosis and management of FGIDs, beginning at the first point of medical contact, could greatly improve patient outcomes and reduce costs.

McKinsey research has identified 4 elements which are critical to successful integrated care: patient education and empowerment, care co-ordination, multi-disciplinary teams, and individual care plans (Figure 2)[7].

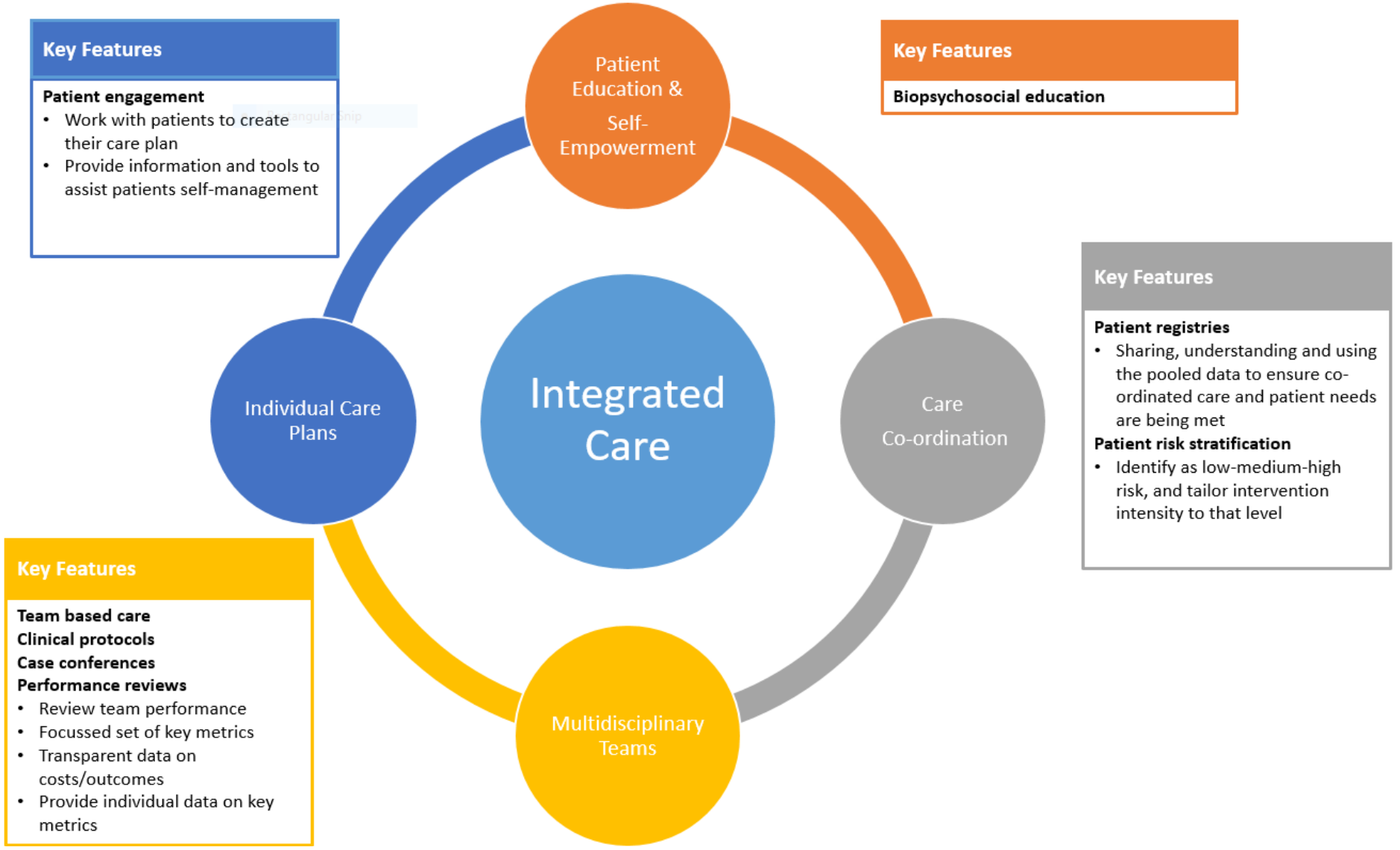

Figure 2. Key components of successful integrated care systems

Current Recommendations for Integrated Care

Although most clinical guidelines highlight the biopsychosocial approach to the management of FGIDs, which may involve the primary healthcare provider (PHCP), gastroenterologists, dietitians and/or psychologists, little direction is given on the manner in which this should occur [1-4]. The recently published Rome IV criteria recommend a tiered approach to the management of FGIDs, according to symptom severity (Figure 3) [3]. In the UK, NICE guidelines recommend that patients with FGID be diagnosed and managed within the primary care setting, and that psychologists, dietitians, or gastroenterologists be consulted when symptoms do not improve after one year of implementing general lifestyle changes [5]. Regardless of the restraints of a country's health system or FGID guidelines, there is current opportunity to provide better patient care by integrating and co-ordinating the biopsychosocial providers/treatments.

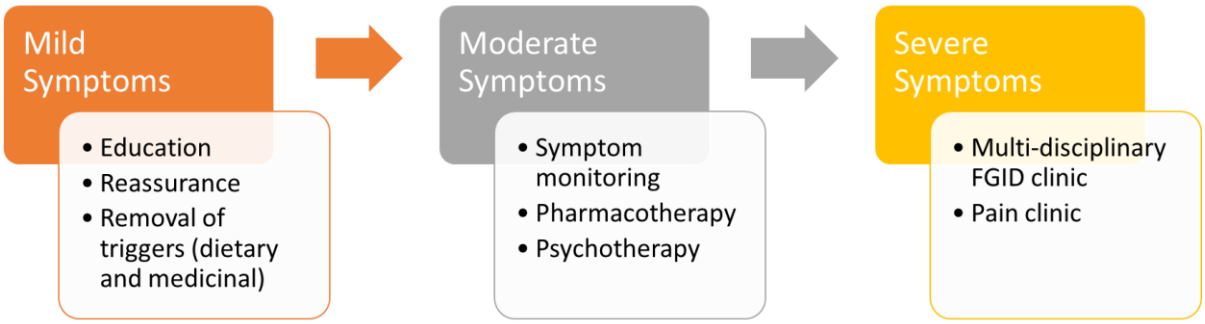

Figure 3. A symptom severity based approach to FGID management

With the potential number of specialty practices involved, the challenge remains to ensure patient care is integrated [6]. Ultimately, primary care may be ideally placed to facilitate integration and continuity of care for patients with FGIDs in health settings where PHCPs co-ordinate secondary and tertiary care (such as Australia)[7]. However, there are significant barriers that need to be overcome. For example, in Australia, changes to funding incentives are required in order to facilitate the longer consultations needed in FGID care to provide reassurance, education, and co-ordinated multi-disciplinary care. Even with this in place, significant resourcing of PHCPs with diagnostic criteria, evidence-based management pathways, and a network of multi-disciplinary FGID specialists is required.

THE EVIDENCE FOR MODELS OF INTEGRATED CARE

Despite the current recommendations for a biopsychosocial approach to the diagnosis and management of FGIDs, to date, only five published studies evaluated an integrated model of care for FGIDs from diagnosis through to management (Table 1). Studies assessed models of care for functional dyspepsia in Canada [8, 9] and the United States [10], for irritable bowel syndrome (IBS) in New Zealand [11] and FGIDs in general in Australia [12]. Four studies assessed variation of nurse-led care models [8-11], and one an algorithm-based approach to integrated care [12]. There is a lack of robust peer-reviewed data, as several of these have been published only in abstract form [8, 9, 12]. Whilst all studies demonstrated the benefit of integrated models of care, much more high-quality research is required to evaluate the best model of care.

Nurse–Navigator Models

The nurse-led or nurse navigator (NN) models differ from each other in the role assigned to the nurse and at what point in the patient journey nurse-led care was initiated (see Table 1 for advantages and disadvantages of each model).

The first NN model of integrated care for IBS consisted of an initial consult and provisional diagnosis by a gastroenterologist, 30-minute nurse-led educational session covering pathophysiology, review of medications ordered and discussion on lifestyle, stressors and triggers/elimination, diet, followed by 30 min follow-up sessions (as needed) [10]. Supportive counselling surrounding stress and psycho-social issues was also provided made as needed.

The second NN model (2014) used a nurse to perform active telephone triage of patients referred to the tertiary centre with gastroesophageal reflux or functional dyspepsia and involved a 1-hour multi-disciplinary small group session with an expert nurse, pharmacist and dietitian, followed by a brief physician visit for medication/endoscopic evaluation as needed.

In another functional dyspepsia NN model, the nurse conducted initial screening (coeliac screen, urea breath test), and arranged a trial of PPI therapy prior to leading the multi-disciplinary group session with a dietitian and mental health therapist [8]. Patients with persisting symptoms were referred on to the specialist for upper endoscopy. Only one small study in New Zealand, trialled an integrated model of care in a secondary care setting in the form of a private nurse-led IBS clinic [11]. The initial nurse consult included a full history, systems review, family history, physical exam (including rectal exam), blood and stool tests (including faecal calprotectin and coeliac antibodies), as well as a food and symptom diary and IBS questionnaire. A follow up nurse consult was conducted to review findings a fortnight later. Abnormal test results or physical exam findings triggered a

referral back to the GP, gastroenterologist or other specialists. Normal test results were used as a basis for reassurance and education, and management strategies were tailored to the individual. Strategies offered included low FODMAP diet, referral to dietitian, nurse reassurance and discussion of psychosocial issues with referral to psychologist where needed and accepted.

Non-Specialist Dependent Algorithm-Based Model

Early results from a small Australian trial, suggest the usefulness of an algorithm-based approach to the diagnosis and management of FGIDs which does not depend on specialist consultation [12] (Table 1). Patient referrals to a tertiary centre triaged as 'likely' FGID were screened for organic disease with a standard online questionnaire for alarms and routine panel of blood/stool tests (CBE, CRP, iron studies, TFTs, biochemistry, coeliac serology, and *H. pylori* serology and/or faecal calprotectin and elastase). Where clinical alarms or abnormal tests resulted, records were reviewed by a gastroenterologist and, if appropriate, prompt appointment offered. Those without screening concerns were classified according to Rome III criteria, and received a letter (copied to their PHCP), explaining their FGID diagnosis and dietary/psychological management options.

Model/Setting	Description	Evidence	Advantages/Disadvantages
Nurse Navigator (Tertiary care) **Prior to GE Consult**	- Initial screening, treatment trials - Multi-disciplinary group session with nurse, dietitian, mental health therapist -Onward referrals for persistent symptoms	Abstracts [8, 9]	**Advantages:** Cheaper for patients, enhanced patient care, experience, and outcomes, and more efficient to the practice Not reliant on GE consult, able to be implemented in primary care.
Nurse Navigator (Tertiary care) **Following GE Consult**	-To provide ongoing holistic management - Including education, counselling & referrals	Level IV [10]	**Advantages:** Patient more likely to accept diagnosis and management recommendations following specialist consultation. **Disadvantages:** Dependent upon specialist consultation
Private Nurse Clinic (Secondary care) **Independent of GE consult**	-To provide diagnosis, reassurance, education, management strategies -including low FODMAP diet and exploration of psychosocial issues -Onward referral as needed	Level IV [11]	**Advantages:** Improves patient satisfaction, QoL and reduces frequency and severity of symptoms One-stop shop for diagnosis and management by a specialised practitioner Could be integrated into primary or tertiary setting **Disadvantages:** Requires a specialist nurse practitioner
Algorithm-based Approach (Primary/Tertiary Care) **Independent of GE consult**	-To screen and diagnose, FGID, and identify patients requiring GE review without face-to-face contact -To provide reassurance, education, management strategies, resources which can be discussed with PHCP -including low FODMAP diet and psychological therapies	Abstract [12]	**Advantages:** Reduces stress, anxiety and maladaptive cognitions and improves symptoms Clinical pathway for use in primary or tertiary care Can be implemented by nurse, physician or GE Allows rapid triage and assessment in health systems with long waiting lists **Disadvantages:** Patient is not assessed in person No guarantee of patient follow-up in primary care

Table 1. Models of care for FGID diagnosis and management.

MOVING FORWARD & CONCLUSIONS

Although there are very few studies to date, research suggests that integrated care for patients with FGID is likely to improve patient outcomes. Key features of all models include a standardised diagnostic pathway, patient education and reassurance, and resourcing the patient to self-manage their condition. Most models reviewed centre around an on-going supportive relationship with a nurse who co-ordinates and reviews care. It is envisaged that integrated care approaches will also facilitate patient education, diagnostic acceptance, access to and uptake of, multi-disciplinary management and improve outcomes such as symptoms, daily functioning, healthcare costs, stress, anxiety and maladaptive cognitions. Its uptake is also likely to decrease the frustration currently experienced by patients and PCHPs alike in dealing with these highly prevalent conditions by providing earlier access and building capacity for effective management.

Practical recommendations:

- Integrated, multidisciplinary care is an emerging field in the management of FGIDs.
- Integrated care should begin at diagnosis.
- An early confident diagnosis with minimal investigation and reassurance of lack of organic causes is required.
- Patient education about the chronic, recurrent nature of the disorders, and effectiveness of the low FODMAP diet and psychological interventions are key tools in integrated care.
- Team-based care coordinated by a central figure is recommended as is the use of standardised clinical pathways and multi-disciplinary case management reviews.

Current limitations/future considerations:

- There is no published research into the long-term effectiveness of integrated models of care in FGIDs.
- Small care providers may struggle to run specialist nurse-led clinics; this limitation may be circumvented through the use of a virtual FGID network.
- Healthcare systems need to review funding models to ensure financial incentives for specialist or doctor-led care do not prevent novel solutions.

e-Health, if well designed/supported, has the potential to assist with structured screening and advice in these common conditions with both GP and patient support tools (once validated).

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