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A systematic review of digital self-management therapeutics for Irritable Bowel Syndrome; and exploring the feasibility of an Acceptance and Commitment Therapy smartphone app intervention for Irritable Bowel Syndrome.

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DClinPsychol Declaration of Own Work

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Table of Contents

LIST OF TABLES AND FIGURES

Thesis Abstract

Background and aims: Irritable Bowel Syndrome (IBS) is the most common gastrointestinal (GI) disorder; frequently associated with painful physical symptoms, psychological distress and impaired quality of life. While there is no existing 'gold standard' treatment for IBS; evidence highlighting the link between the gut and the brain has informed new treatment pathways: with a particular emphasis on psychological approaches in managing IBS. However, long waiting times and pressures on healthcare services often result in patients' needs not being adequately met. Digital self-management therapeutics are increasingly applied in the management of health conditions, including IBS. The first chapter of this thesis systematically reviews Randomised Controlled Trials (RCTs) exploring the efficacy of digital self-management therapeutics for IBS. Specifically, this is examined in relation to physical symptomology and quality of life outcomes. In the second chapter, smartphone-delivered Acceptance and Commitment Therapy (ACT) is considered as a therapeutic approach for the management of IBS. While preliminary studies have demonstrated efficacy of ACT for IBS, digital delivery of ACT for IBS has not previously been explored. This study explores the feasibility, acceptability, and efficacy of trialling an ACT smartphone application for IBS patients.

Methods: In Chapter One, the evidence base for digital self-management therapeutics for IBS is systematically reviewed. Relevant databases were searched using inclusion and exclusion criteria to identify studies for review. In Chapter Two, recruitment methods, psychometric measures, app building and contents of the intervention are discussed. 83 eligible participants were identified by four GI Consultants across NHS Lothian, NHS Grampian and Imperial College Healthcare NHS Trust. 44 participants downloaded the app, with 29 participants providing data at two-month follow-up.

Results: In Chapter One, the systematic search identified 12 relevant RCTs for review. Their methodological quality was appraised by two reviewers, using the Cochrane Risk of Bias (RoB 2) tool. These studies demonstrated moderate-large effects in improving physical symptomology and moderate-large effects in improving quality of life, and generally these improvements were maintained at longer-term follow-up. Evidence comparing treatments to active controls, and longer-term comparison to control groups, were lacking. In Chapter

Two, both feasibility and efficacy of the trial were explored. The trial was deemed feasible in terms of recruitment and retention. Paired-sample t-tests demonstrated that use of the ACT self-management application showed significant improvements in IBS acceptance, quality of life, and GI-related anxiety. Similar to a previous ACT self-help trial, improvements in IBS-related avoidance behaviours were not found. Improvements in GI physical symptomology were noted; however contrary to hypothesis, these improvements were not significant.

Discussion: Results from Chapter One indicate the efficacy of digital self-management interventions for IBS; in terms of both physical symptoms and quality of life, with maintained improvements at longer-term follow-up. Large heterogeneity in level of guidance, samples, varying definitions of adherence with interventions, high levels of attrition and methodological quality limit confidence in the results' generalisability. Suggestions are offered for both future systematic reviews and empirical work in the field based on these findings. Results in Chapter Two provide preliminary evidence of the feasibility and efficacy of a digital ACT smartphone intervention for management of IBS. Attrition and adherence with the intervention are discussed in the context of these results, alongside clinical implications for use of such an intervention as part of a stepped-care approach to IBS. This may be informed by screening GI symptomology at baseline to assess suitability of this low-intensity intervention going forward. A future larger-scale trial is warranted to further explore these preliminary findings.

Lay Summary

Irritable Bowel Syndrome (IBS) is a long-term condition that affects the gut and can lead to physical discomfort, distress, and a reduced quality of life. There is a connection between the brain and the gut, and stress can worsen physical symptoms. Psychological treatments have been shown to be helpful in improving symptoms and the overall wellbeing of people with IBS. Due to increased pressure on the health services and large IBS population, there can be delays in getting the necessary care. Digital tools that help people manage symptoms themselves, like smartphone apps, offer a cost-saving solution by providing immediate access to tools to help people better manage living with IBS.

In Chapter One, we have reviewed evidence which shows digital therapies are effective in reducing physical symptoms and improving quality of life for IBS patients. An approach called Acceptance and Commitment Therapy (ACT) helps people to live well alongside their health conditions, though digitally delivered ACT has not yet been explored for IBS. In Chapter Two, this study explored an ACT smartphone app for IBS. This was seen to be feasible and acceptable approach for patients. It led to improvements in wellbeing, quality of life, and IBS-related anxiety. However, the reduction in physical symptoms was not as significant as expected, possibly because the participants had more severe symptoms than the general IBS population. The self-management app may be better suited to people with less severe physical symptoms. Therapeutic guidance alongside the app may also improve outcomes in future trials. A larger study is recommended to explore this intervention further and provide greater confidence in these results.

Chapter 1: Systematic Review

Systematic review of digitally delivered self-management therapeutics for Irritable Bowel Syndrome: exploring the impact on physical symptomology and quality of life (QoL).

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Written according to submission guidelines for Clinical Psychology Review (Appendix 1)

Please note: this paper was written only by the first author. The second author's role was as second quality assessor of the included studies in the systematic review, and the third author's role was as academic supervisor for this paper.

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Abstract

Digitally delivered self-management therapeutic intervention is an emerging field, increasingly applied to supporting physical and psychological outcomes for chronic health conditions, including Irritable Bowel Syndrome (IBS). This is the first paper to systematically review the existing evidence base of digital self-management interventions for IBS, specifically in relation to physical symptomology and quality of life (QoL) outcomes. Medline, EMBASE, PsycINFO, ProQuest Dissertations, MedRXiv, PsycARix and the British Gastroenterology Society (BSG) were systematically searched for randomised-controlled trial (RCT) of digitally delivered self-management intervention studies for IBS, with no limitation on year of publication. 12 studies were included, and their methodological quality was assessed independently by two reviewers. Most studies reported moderate-large effect sizes indicating significant improvements in both physical IBS symptoms and QoL outcomes. Over time, effects were more variable (ranging from small-large) but generally improvements were maintained at longer-term follow-up. High rates of attrition, large heterogeneity in studies and varying measures of adherence with interventions limit conclusions that can be drawn from the methodological quality of the evidence base. Suggestions are offered for the expansion of future research, including greater consistency in the method for evaluating efficacy and adherence with interventions. Digital based self-help interventions for IBS could be used in routine practice as part of a stepped-care approach.

Keywords

Irritable Bowel Syndrome; Digital Health Interventions; Self-Management; Physical Symptoms; Quality of Life; Systematic Review

Introduction

Irritable Bowel Syndrome (IBS) is the most prevalent of all gastrointestinal (GI) disorders; characterised by abdominal pain, bloating, and altered bowel habit (Canavan et al., 2014; Saha, 2014; Tanaka et al., 2011). Worldwide, approximately 15% of the population are affected by IBS: up to 10% in Eastern society and up to 20% in Western society (Lovell & Ford., 2012; Sperber et al., 2021; Zhang et al., 2022). The prevalence of IBS is approximately 1.5- to 3- fold higher in women than men (Canavan et al., 2014). IBS is recognised as a functional disorder, meaning there has been no identification of organic pathophysiology (El-Salhy et al., 2014). It is a chronic condition that can cause significant impairment: with associated workplace absenteeism and subsequent financial burden, repeat medical appointments, costly procedures, burden on healthcare services and increased patient frustration in the often lengthy process of diagnosis and treatment (Canavan et al., 2014; Halpert, 2018). Healthcare utilisation and associated cost for IBS is 50% more than that of the general population (Goodoory et al., 2022; Soares, 2014). Moreover, IBS accounts for approximately 50% of GI referrals and 25% of a gastroenterologist's time in the outpatient clinic (Corsetti & Whorwell, 2017; Shivaji & Ford, 2014; Soares, 2014). Therefore, IBS is burdening in terms of both direct (healthcare use) and indirect (e.g. productivity loss and work absenteeism) costs (Bosman et al., 2023). In turn, IBS is frequently associated with significant psychological distress and reduced quality of life (Canavan et al., 2014; Fadgyas-Stanculete et al., 2014).

Brain-Gut Axis: Biopsychosocial Understanding of IBS

Despite extensive development of clinical guidelines for IBS over the past number of years, there still is no existing 'gold standard' treatment for IBS (Lacy et al., 2015; Soares, 2014). While the exact etiology of IBS remains unknown, it is now understood to be of multifactorial origin: influenced by a combination of biological, psychological and social factors (Riehl, 2022; Tanaka et al., 2011). IBS is coined as a 'disorder of gut-brain interaction': referring to the bidirectional communication between the brain and the gut; connected by the vagus nerve (Kinsinger, 2017). A biopsychosocial framework of IBS provides insight into

the interaction between psychosocial and physiological factors involved in the brain-gut axis (Drossman, 2016). Access to GI-tailored psychological interventions alongside traditional medical interventions is now recommended in the treatment of IBS (Riehl et al., 2022). Keefer et al. (2018) outline best practice guidance to have integrated psychological care available in GI clinics.

Self-Management Therapeutics for IBS

Self-management therapeutic interventions involve an individual accessing materials on their own (unguided) or with minimal guidance from a therapist. A comprehensive review of 'best management' approaches for IBS highlights the importance of self-management for this population, particularly given that treatments aiming to relieve symptomology may not eradicate them completely (Black & Ford, 2021). National Institute for Health and Care Excellence (NICE, 2017) clinical guidelines recommend self-management of IBS symptoms where possible and outline a host of treatment options, including a combination of psychological, dietary and pharmacological interventions. Encouragement of self-management for IBS can play a vital role in revising the current treatment approaches; increasing self-efficacy in managing physical symptoms and improving QoL (Cong et al., 2018; Morton et al., 2017). Self-management strategies also aim to reduce anxiety about an individual's ability to manage symptom fluctuations associated with IBS and subsequently decrease the need for repeated medical appointments to manage such flare-up periods, thus minimising burden on healthcare services.

Digital Self-Management Therapeutics

While recognition of self-management therapeutics in the understanding and treatment of IBS has increased, a difficulty remains with lack of access to therapies, particularly given the large numbers of patients presenting with IBS (Bosman et al., 2023). There are significant barriers to providing psycho-gastroenterology services, and digital therapeutics are recommended to improve access to treatment and outcomes for patients (Riehl, 2022). Such interventions may be delivered on smartphones, computers or tablets; including mobile Health (mHealth), electronic health (eHealth), telemedicine, computerised or web-based

formats. Digitally delivered self-management interventions hold benefit in providing a low-cost treatment that can be accessed immediately, with no or minimal therapist guidance (Riehl, 2022). Furthermore, such interventions are not limited by geographical or personal circumstances (Liegl et al., 2015).

While the majority of existing RCTs exploring digital self-management therapeutics for IBS are CBT-based, preliminary data from recent studies have demonstrated the efficacy of digitally delivered gut-directed hypnotherapy (GDH) for IBS; for both physical and psychological outcomes (Greywoode & Szigethy, 2022; Peters et al., 2023; Zhao et al., 2022). Peters et al. (2023) outlined the preliminary therapeutic potential of a smartphone-delivered GDH self-management approach for IBS (Hasan et al., 2023). Saleh et al. (2023) conducted a recent review of digital therapeutics to highlight CBT and GDH as representing an effort to disrupt the current care model for patients with IBS, demonstrating promising preliminary results for both digitally-delivered CBT (Everitt et al., 2019b; Hunt et al., 2021) and GDH (Peters et al., 2023; Saleh et al., 2023).

Over the last decade, digital health interventions (DHIs) have played a significant role in revolutionizing healthcare delivery, for management of both common mental health conditions (Andersson et al., 2014; Gan et al., 2021; Mohr et al., 2021) as well as associated physical symptomology and QoL for chronic health conditions including tinnitus, headaches, diabetes, cancer and fibromyalgia (Morton et al., 2017; Sasseville et al., 2021; White et al., 2022). The COVID-19 pandemic further highlighted the need for sufficient digital forms of therapy (Chudasama et al., 2020). Among the broad array of applicability, the most prominent focus for research and development of DHIs has been in chronic health conditions. This is attributed to costly management and treatment of chronic health conditions, accounting for as much of 80% of healthcare expenses in several countries (Bashi et al., 2020). However, digital self-help interventions also suffer from high attrition rates (Linardon & Fuller-Tyszkiewicz, 2020). A systematic review and meta-analysis of attrition in mHealth app-based studies for chronic health conditions found a pooled estimate of 43% drop-out (Meyerowitz-Katz et al., 2020). High levels of attrition and low adherence to smartphone-delivered interventions may impact the validity of RCT findings in this field

(Linardon & Fuller-Tyszkiewicz, 2020). Barriers to engagement and prediction of treatment completers remain unknown.

Existing research & gap in the literature

Existing systematic reviews in this field include a review of the efficacy of guided self-help interventions for IBS (Liegl et al., 2015) and self-management interventions for IBS (Cong et al., 2018); with both reviews including studies delivered from a range of angles: in person, via telephone and online. Kim et al. (2022) more recently conducted a systematic review highlighting the efficacy of internet-based Cognitive Behavioural Therapy (CBT) approaches for IBS. However, important differences in the current review are established, alongside critique regarding the reporting of results and inclusion of meta-analysis in the review by Kim et al. (2022). Two research teams conducted the majority of included trials (78%; seven of the nine included papers) which may introduce inherent biases in the meta-analysis. Furthermore, of the seven studies included in meta-analysis conducted by Kim et al. (2022), two papers reported results from the same study (Everitt et al., 2019a, 2019b), with one referring to longer-term follow-up. Inclusion of both studies in this meta-analysis is subject to bias, providing an over-estimation of the effects of the same iCBT intervention. Moreover, the review conducted by Kim et al. (2022) was not limited to 'self-management' interventions; and included only CBT-based interventions; differing from the broader interventional focus in the current review. The review by Kim et al. (2022) also used an older version of the Cochrane Risk of Bias tool to assess study quality. The Cochrane RoB tool has since been updated to provide more stringent assessment of bias; therefore, the updated tool is used in this review and provides different quality assessment outcomes than that of the review conducted by Kim et al. (2022)**.**

The Current Review

The current systematic review aims to evaluate the efficacy of digitally delivered self-management interventions for IBS, both without guidance and/or *minimal* therapist guidance; and not limited to a particular therapeutic approach. To the author's awareness, this is the first systematic review to evaluate digitally delivered self-management

therapeutic interventions for IBS, assessing physiological symptomology and quality of life outcomes.

Methods

Search Procedure

The protocol for this systematic review was registered on PROSPERO on 28/02/23 with registration ID CRD42022373161. This review was conducted in accordance with guidelines recommended by the PRIself-managementA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) statement to guide study design (Moher et al., 2009). A computerised search was conducted using three electronic databases on 24th February 2023 (MEDLINE, PsycINFO and EMBASE) for studies available up to February 2023. A combination of the following search terms was used: mobile health* or mHealth or "m health" or "mobile phone*" or "mobile app*" or smartphone* or eHealth or "e Health" or telemedicine or "tele medicine" or digital or cellphone or "cell phone" or "web" or computer assisted therap* or "online" or "internet" or "electronic health" AND emotion* or mood* or anxiet* or stress or cope* or coping or distress or wellbeing or "well being" or affect or psychol* or "mental health" or "mental ill*" or "quality of life" or depress* or relax* or meditat* or "cognitive behav*" or "psychotherap*" or " psychological therap*" or "psychology" or "acceptance and commitment*" or "CBT" or "ACT" or mindful* AND "Irritable Bowel Syndrome" or "IBS" or "irritable bowel" or "irritable colon" or "mucous colitis". Furthermore, previous systematic reviews of internet-based and guided self-help/minimal self-help interventions for IBS were scanned for potential inclusion of any further relevant studies (Cong et al., 2018; Kim et al., 2022; Liegl et al., 2015). The search was repeated on 27th June 2023 to capture any further studies since the original search. The first author screened the titles and abstracts of the 1,233 records for potentially eligible studies using previously defined inclusion and exclusion criteria. The parameters set for the search were RCTs, journal articles, English language, and adults. The year of publication was not limited to obtain a comprehensive overview of digitally delivered self-management interventions.

Grey Literature

Following identification of two pre-print papers (Kobayashi et al., 2023; Tayama et al., 2022), it was decided to also search grey literature: including ProQuest dissertations, preprints on

MedRXiv and PsyARXiv, and the British Society of Gastroenterology website (BSG) for potential papers. Authors of the pre-print papers were contacted to enquire about the status of these papers: one in the process of submitting to a peer-reviewed journal (Tayama et al., 2022) and no response (Kobayashi et al., 2023). For results that identified abstracts and posters without access to full-text papers, authors were also contacted to enquire about whether full-text was available. The final study selection was performed by the first author (AR) and then the process was reviewed by a colleague (DM, Trainee Clinical Psychologist). Ambiguities and queries on inclusion and exclusion criteria were resolved by consensus.

Eligibility Criteria

The inclusion criteria were based on the PICO framework (Participant, Intervention, Comparator, Outcome): participants were adults diagnosed with IBS, a self-help intervention delivered digitally with either minimal or no therapist guidance, a comparator group of either waitlist control, treatment as usual or active control (e.g., guided intervention or discussion forum), and the primary outcomes were IBS symptom severity and IBS-quality of life.

The following criteria had to be fulfilled for the reviewed study to be included:

(1) The target population for the intervention was adults (aged 16 years or over) with IBS.
(2) The diagnosis of IBS was made either by a medical professional and/or on the basis of ROME I, II, III or IV criteria.
(3) IBS symptom severity was an outcome measure.
(4) Study design was an RCT (randomised controlled trial) that compared a digitally delivered self-help intervention to either a waiting-list control, treatment as usual (TAU), or an active control condition (e.g. guided intervention or discussion forums).
(5) Aspects of psychological self-help interventions were available as part of intervention (e.g. psycho-education, relaxation, etc.). Psychological intervention was defined by the availability of materials for an individual to work through focusing on the mind-

body link in IBS and availability of strategies to manage with emotions, physical symptoms and/or behavioural patterns.

The exclusion criteria were as follows:

(1) Non-RCT or secondary data analysis.
(2) Children or adolescents under the age of 16.
(3) Digitally delivered approaches led by therapist, e.g., weekly support provided fully by therapist rather than a self-management intervention.
(4) No psychological component present in intervention (e.g., purely digitally delivered dietary intervention).
(5) Full-text not available.
(6) Full text not published in English.

A digitally delivered self-management intervention was defined as an online intervention providing educational information and some psychological approach to management of stress-related symptoms, such as relaxation, hypnosis, problem solving. Studies that did not define a pure psychological approach (e.g., CBT) were not excluded. Therefore, some studies included information on IBS, psychological approaches, and dietary advice (e.g., Lindfors et al., 2021; Chen et al., 2022). While self-management was a distinctive part of the intervention, this could include studies where the intervention stood alone (unguided) or those with minimal therapist input. Minimal therapist input was considered as for example contact via email, SMS/online messaging system or telephone, and excluded e.g., face-to-face guidance: in line with the aim to assess the efficacy of such approaches without reliance on geographical location for availability (Liegl et al., 2015).

Data Extraction

The first author (AR) created a tailored data extraction form in an excel spreadsheet to collate the data from the final selected papers. The form was used to collate data on study characteristics, methodology and intervention including: author, year of publication,

country, study design, population characteristics (sample size, percentage female, mean age, symptom duration), diagnostic criteria, randomisation method, intervention (method of delivery, therapeutic approach duration, guidance level, presence/length of follow-up, control group subtype (waitlist, TAU, active control). Furthermore, data on the outcomes of the included studies was also extracted, including: outcome measures (IBS symptom severity and QoL/overall functioning) risk of bias, dropout rate, treatment adherence, and outcomes: within-participant, comparison to control and maintenance at follow-up. Where sufficient data was not available in the full text of studies, supplementary materials were consulted (where available, e.g., Chen et al., 2022, Lindfors et al., 2021).

The primary outcome measure evaluated the impact of a digitally delivered self-help intervention on IBS symptom severity, which was assessed using a number of tools: the IBS Symptom Severity Scale (IBS-SSS) (Francis et al., 1997), the Bowel Symptom Severity Scale (BSSS) (Boyce et al., 2000), the Gastrointestinal Symptom Rating Scale (Wiklund et al., 2003), and two papers used a measure of Abdominal Pain as opposed a globalised measure of IBS symptoms (Oerlemans et al., 2011) and Brief Pain Inventory (Chen et al., 2022).
For the secondary outcome measure of QoL, the majority of studies utilising the IBS-QoL (Drossman et al., 2000; Patrick et al., 1998) as a measurement of IBS-related QoL, and one using the Work and Social Adjustment Scale (WSAS) (Mundt et al., 2002) as valid and reliable psychometric measure of overall functioning (Everitt et al., 2019a; 2019b). The included studies are heterogenous in terms of the nature of intervention, sample, control group and level of guidance. Due to the extent of this heterogeneity, it was decided a meta-analytic approach to the current review would not be appropriate.

Quality Appraisal

Methodological risk of bias in the selected papers was assessed using the revised Cochrane risk-of-bias tool for randomised trials (RoB 2) (Higgins et al., 2011; Sterne et al., 2019).
Bias was assessed across five domains:

(1) Bias arising from the randomisation process
(2) Bias due to deviations from intended interventions
(3) Bias due to missing outcome data
(4) Bias in the measurement of the outcome
(5) Bias in selection of the reported result

The first author completed the RoB 2 template for each of the studies. In line with the guidelines, the relevant version of the tool was used dependent on whether the trial was an individually randomised parallel-group trial, a cluster randomised trial or a crossover trial (Sterne et al., 2019). Risk was determined as per the guidelines for using the RoB 2 tool: risk was deemed 'low' when all domains were rated 'low', studies were deemed to have 'some concerns' when at least one domain was rated as showing 'some concerns', and studies were deemed 'high risk' when they had at least one domain rated as 'high risk' or the study was deemed to have 'some concerns' in several domains in a way that substantially lowers confidence in the reported findings (Sterne et al., 2019). If the risk of bias remained unclear for any of the quality criteria, the criterion was deemed 'not met'. All studies were assessed separately by another researcher, independent from the current review (DM). Inter-rater reliability prior to discussion was deemed to be excellent (k =0.9) (McHugh, 2012). Both reviewers discussed their ratings and minor discrepancies were resolved through discussion.

Results

The titles and abstracts of 1,233 publications were screened after 399 duplicates were excluded from the 1,632 publications identified from the search of three databases and grey literature. The second search on June 27th 2023 had returned 68 further studies, all of which titles were screened and did not identify any further eligible papers for inclusion (see Figure 1 for PRISMA diagram of process). The full text of 66 studies were screened for eligibility. 14 papers were eligible for inclusion; however, two of these papers were longer-term follow-up papers relating to the same study (Everitt et al., 2019a; b; Ljotsson et al., 2010a; b). Therefore, these papers were grouped together for the purposes of this review. In total, 12 studies were selected for the analysis (see Figure 1 – PRISMA flow diagram).

The primary outcome measure evaluated the impact of a digitally delivered self-help intervention on IBS symptom severity, which was assessed using a number of tools: the IBS Symptom Severity Scale (IBS-SSS) (Francis et al., 1997), the Bowel Symptom Severity Scale (BSSS) (Boyce et al., 2000), the Gastrointestinal Symptom Rating Scale (Wiklund et al., 2003), and two papers used a measure of Abdominal Pain as opposed a globalised measure of IBS symptoms (Oerlemans et al., 2011) and Brief Pain Inventory (Chen et al., 2022).
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Figure 1: PRISMA diagram of the systematic search and paper selection process.

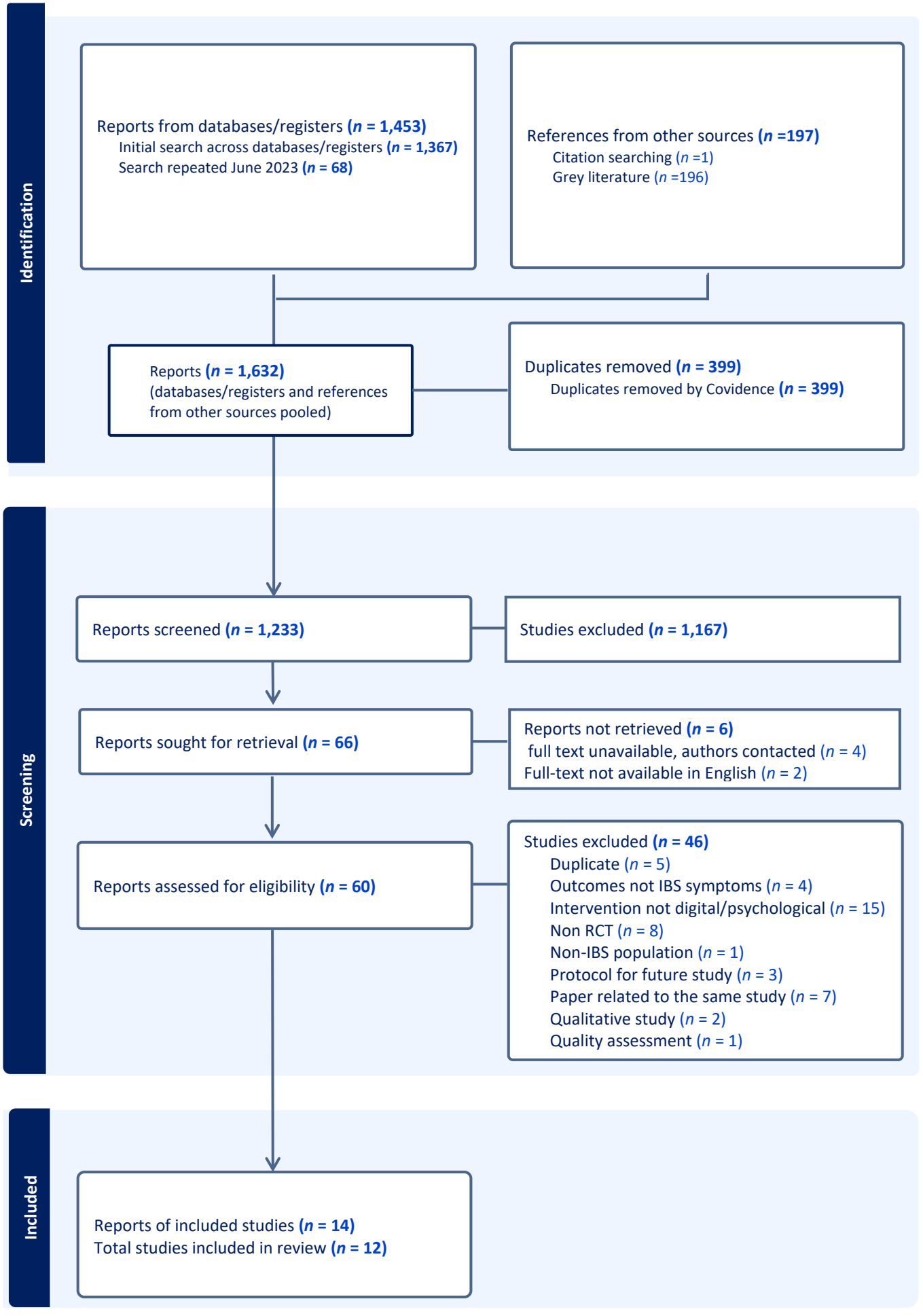

Table 1: A Summary of Study Characteristics, Methodology and Interventions of All the Included Studies in the Current Review

Studies *Country*	Ages	Design	Diagnostic Criteria	IBS duration: mean (SD)	Sample size (% female)	Inter-vention length	Level of Guidance	Randomisation	Long-Term Follow Up *months*	Digital delivery	Therapeutic approach	Digital self-help intervention format
Chen et al., 2022 *US*	Mean age 21 (18-29 limit)	Parallel 3-arm RCT	Diagnosed by a healthcare provider or ROME III criteria	Years since Dx: 2.72 (2.86)	80 (76%)	2 weeks	Unguided	Stratified and blocked randomisation scheme	3	Web-based platform	Self-management intervention including mindfulness, relaxation and guided imagery.	Video content: psychoeducation, Progressive Muscle Relaxation, guided imagery, mindfulness, belly breathing, pain problem solving
Lindsfors et al., 2021 *Sweden*	18-75, mean 38	Parallel 2-arm RCT	Diagnosed by referring physician and verified by a GI physician if necessary	NI	141 (80%)	3 weeks	Unguided	Random number service (random.org) and by a blinder research team member	3 and 6	Web-based platform	Psychoeducati-on, stress management, relaxation exercises, dietary and educational information.	E-reading: Internet-delivered education via pdf book

Studies *Country*	Ages	Design	Diagnostic Criteria	IBS duration: mean (SD)	Sample size (% female)	Inter-vention length	Level of Guidance	Randomisation	Long-Term Follow Up *months*	Digital delivery	Therapeutic approach	Digital self-help intervention format
Hunt et al., 2021 *US*	Range 18-63, mean: 32	Crossov-er, 2-arm RCT	Self-reported previous diagnosis by a physician, or meeting ROME IV criteria	NI	121 (75%)	8 weeks	Unguided	Coin toss feature on random.org	3	Mobile app	CBT	'Zemedy' app: 8 modules focusing on psychoeducation, relaxation training, exercise, stress management, CBT for IBS, exposure, behavioural experiments and dietary information
Owusu et al., 2021 *US*	Mean 39 years (range: 19–61 years)	Parallel 2-arm RCT	Self-reported dx of IBS and clinically significant score >75 on IBS-SSS (mild)	Years with IBS (total sample): 9.6 +/- SD 9.8 (missing =8)	36 (78%)	12 weeks	Unguided	A block randomisation strategy was implemented and stratified by IBS type	3	Website	CBT	Parallel Program (updated version of Regul8 website): 8 modules

Studies *Country*	Ages	Design	Diagnostic Criteria	IB duration: mean (SD)	Sample size (% female)	Inter-vention length	Level of Guidance	Randomisation	Long-Term Follow Up *months*	Digital delivery	Therapeutic approach	Digital self-help intervention format
Tayama et al., 2021 Japan	Range 18-36, mean age 21	Parallel, open label simple RCT	ROME-IV criteria	NI	36 (100%)	4 weeks	Unguided	Randomised to equal groups using a random number table created with Microsoft excel by trial statistician	NA	eHealth program available via computer or mobile phone	Includes elements of CBT hypnotherapy, relaxation	eHealth program accessible on computer or mobile device: digitized an existing self-help book for IBS including 6 chapters: psycho-education, relaxation and stress management, dietary information, CBT, psychotherapy, hypnotherapy
Everitt et al., 2019 (A and B) UK	Range 34-52, mean age 43	Parallel 3-arm RCT	Meet criteria for refractory IBS at screening: ROME III criteria, IBS-SSS score >75, previously offered first line therapies, symptoms >12 months	7.4 years median	557 (76%)	8 weeks	Minimal guidance	Block randomisation with randomly varying block sizes, stratified by recruitment centre	3, 6, 12(a) and 24(b)	Website	CBT	'Regul8' CBT website, 8 online sessions

Studies *Country*	Ages	Design	Diagnostic Criteria	IBS duration: mean (SD)	Sample size (% female)	Inter-vention length	Level of Guidance	Randomisation	Long-Term Follow Up *months*	Digital delivery	Therapeutic approach	Digital self-help intervention format
Everitt et al., 2013 UK	range 16-60, mean age 44	Parallel 3-arm RCT	ROME III criteria recruited in GP practices	10.79 (8.6) years	135 (77%)	6 weeks	Minimal guidance	List computer-generated independent of team. Participants block randomised and stratified by type of IBS	3	Website	CBT	'Regul8' CBT website: digitized from paper manual. Intervention: 8 sessions
Ljotsson et al., 2011 Sweden	mean age 35	Parallel 2-arm RCT	Diagnosed by a GI physician at GI clinic according with ROME III criteria	Years since diagnosis = 11.5 (11.8)	61 (74%)	10 weeks	Minimal guidance	A true random number service (random.org) was used to allocate the participants to groups	12	Web-based platform	Third wave	iCBT protocol including third wave approaches acceptance, mindfulness

Studies	Ages	Design	Diagnostic Criteria	IBS duration: mean (SD)	Sample size (% female)	Inter-vention length	Level of Guidance	Randomisation	Long-Term Follow Up *months*	Digital delivery	Therapeutic approach	Digital self-help intervention format
Ljotsson et al., 2010/11 (A and B) Sweden	mean age 36	Crosso-ver, 2-arm RCT	Self-reported previous dx by a physician, or meeting ROME III criteria	6.3 (7.3) years	85 (85%)	10 weeks	Minimal guidance (text-based response)	Blinded individual received list of anon patient identifier numbers to randomize with a true random number service (random.org)	3 and 15-18 (mean 16.8)	Web-based platform	Third wave	Digital text-based exposure- mindfulness- and acceptance-based treatment for IBS delivered in a self-help format
Oerlem-ans et al., 2011 Netherl-ands	mean age 38	Parallel, 3-arm RCT	Diagnosed by GPs, meeting ROME III criteria	NI	76 (84%)	4 weeks	No live therapist guidance, personali-sed AI feedback	Block randomisation. Excel generated a Randomisation list allocating pts to intervention or control group in order of informed consent date	3	PDA	CBT	Electronic diary on a PDA; gave automated personalised feedback in a CBT format on basis of entries; to intervene on e.g. cognitions, emotions and activities from a mainly CBT perspective

Studies	Ages	Design	Diagnostic Criteria	IBS duration: mean (SD)	Sample size (% female)	Inter-vention length	Level of Guidance	Randomisation	Long-Term Follow Up *months*	Digital delivery	Therapeutic approach	Digital self-help intervention format
Hunt et al., 2009 US	22-59, mean age 38	Crosso-ver, 2-arm RCT	Self-reported previous dx by a medical profession-nal	NI	54 (82%)	5 weeks	Unguided	Randomly assigned to condition based on order of enrolment.	3	Website	CBT	5 modules CBT via website with homework
Lee et al., 2019 China	Mean age 18.5 (18-22 years limit)	Cluster, 3-arm RCT	Diagnosed by a GP using ROME III criteria by a GP	NI	160 (100%)	6 weeks	Guidance to set up online portal a week before starting course unguided	A cluster RCT design was employed. The practicum students in the same practicum unit were randomly assigned to one of the three groups.	3	Web-based platform	CBT	iCBT course based on 'Mind over Mood' online 13 CBT modules: behavioural, emotional, cognitive and stress management.

CBT=Cognitive Behavioural Therapy, iCBT=internet-based Cognitive Behavioural Therapy, IBS= Irritable Bowel Syndrome, GI= Gastrointestinal, NI = no information, Dx=Diagnosis, RCT=Randomised Controlled Trial, PDA=Personalised Digital Assistant, GP= General Practitioner, AI=Artificial Intelligence, IBS-SSS=Irritable Bowel Syndrome Symptom Severity Scale, eHealth = electronic Health.

Table 2: A Summary of Outcomes of All the Included Studies in the Current Review

Studies	Control condition used for analyses	Outcomes Measures: Symptom Severity & QoL	Risk of Bias (Cochrane RoB 2 Tool)	Attrition	Adherence	Within-participant improvement post-intervention	Improvement compared to control	Maintained at follow-up (Time)
Chen et al., 2022	NA no IBS control group: healthy control / nurse-led online intervention	BPI, IBS-QoL	Some concerns	30% drop-out	Engagement/drop-out stage was not reported. Participants considered lost to follow-up after three consecutive reminders to complete video not responded to. Participation recorded by clicking on video link, no record of whether video watched or not (10 videos, 15 mins long each).	BPI 6 weeks *d*=0.17 (small improvement), IBS-QoL 6 weeks *d*= 0.12 (small improvement)	NA (no IBS control group)	<u>Within-group:</u> BPI, *d*= 0.45 (12 weeks) (moderate improvement), QoL: *d*= 0.21 (12 weeks) (small improvement)
Lindsfors et al., 2021	NA: no control group - comparison to face-to-face intervention	IBS-SSS, IBS-QoL	Some concerns	35% drop-out	Adherence measured as completion of midpoint questionnaire or 2 of 3 sessions completed	IBS-SSS *d*= 0.55 (moderate improvement). IBS-QoL *d*= 0.31 (small-moderate improvement)	NA (no IBS control group)	<u>Within-group:</u> IBS-SSS *d*= 0.69 (6 months) (moderate improvement), IBS-QoL *d*= 0.63 (6 months) (moderate improvement)

Studies	Control condition used for analyses	Outcomes Measures: Symptom Severity & QoL	Risk of Bias (Cochrane RoB 2 Tool)	Attrition	Adherence	Within-participant improvement post-intervention	Improvement compared to control	Maintained at follow-up (Time)
Hunt et al., 2021	Waitlist control	GSRS-IBS, IBS-QoL	Some concerns	42% drop-out post-treatment (8 weeks) 61% drop-out at 3-month follow-up.	Adherence not defined: "Of those who completed 8-week follow-up measures, most had not made it through a substantial portion of the app's content." Only one participant completed all modules.	GSRS: *d*=1.01 (large improvement) IBS-QoL: *d* =1.25 (large improvement)	Significant improvement for the treatment group compared with waitlist control group for both primary outcomes: GSRS: (*d*=1.02) (large improvement) IBS-QoL: (*d*=1.25) (large improvement)	Pre to 3-month follow-up: for all participants (both treatment group and waitlist cross-over group) GSRS: *d*=0.8 (large improvement) IBS-QoL: *d*=0.84 (large improvement)
Owusu et al., 2021	TAU	IBS-SSS -	Some concerns	12% dropout intervention group.	Adherence was defined as engaging in half of the modules (4 of 8). More than half of the web-CBT group (*n* = 13) completed at least 50% of the web-CBT program (52% of all participants, 65% of program starters), i.e., ≥4 sessions were completed. Engagement: 80% (*n*=20) started program, 76% complete session 1, 28% completed session 8.	IBS severity: *d*=0.88 (2 months) (large improvement)	IBS-SSS between-group effect sizes (comparing control to web-CBT): There was a small and medium improvement between the two groups at 2 months (*d*=0.43) and 3 months (*d*=0.54), respectively.	<u>Within-group:</u> IBS severity: *d*=1.14 (3 months) (large improvement)

Studies	Control condition used for analyses	Outcomes Measures: Symptom Severity & QoL	Risk of Bias (Cochrane RoB 2 Tool)	Attrition	Adherence	Within-participant improvement post-intervention	Improvement compared to control	Maintained at follow-up (Time)
Tayama et al., 2021	TAU	IBS-SSS, IBS-QoL	Some concerns	0%	Adherence to the study protocol was verified by the access logs of the eHealth system: all participants accessed all content at least once.	eHealth pre post IBS-SSS *d*=0.94 (large improvement); IBS-QoL *d*=0.9 (large improvement)	Between: groups: IBS-SSS *d*=1.09 (large improvement), IBS-QoL *d*=0.85 (large improvement)	NA
Everitt et al., 2019 (A and B)	TAU	IBS-SSS, WSAS	Some concerns	Drop-out not reported, adherence for WCBT group was 69.2% (31.8% completed less than half the web intervention)	Adherence was defined as the number of phone or web sessions undertaken: WCBT completing ≥4 website sessions (half): 69.2% completed four web sessions.	**<u>IBS-SSSS</u>** 3-months: *d*=0.84 (large improvement) 6 months: *d*=0.92 (large improvement) **<u>WSAS</u>** 3 months: *d*=0.41 (moderate improvement) 6 months: *d*=0.64 (moderate improvement)	**<u>IBS-SSS:</u>** 3 months: *d*=0.56 (moderate improvement) 6 months *d*=0.37 (small-medium improvement), 12 months *d*=0.37 (small-medium improvement) **<u>WSAS:</u>** 3 months: *d*=0.35 (small improvement) 6 months: *d*=0.3 (small improvement) 12 months: *d*=0.35 (small improvement)	**<u>IBS-SSS wCBT vs control:</u>** *d*=0.37 (12 months) (A) *small improvement* *d*=0.14 (24 months) (B) *small improvement* **<u>WSAS wCBT vs control:</u>** *d*=0.34 (12 months) (A) small improvement *d*=0.22 (24 months) (B) **<u>Within wCBT IBS-SSS:</u>** *d*=0.98 (12 months) (A) *large improvement* *d*=0.98 (24 months) (B) *large improvement* **<u>Within wCBT WSAS:</u>** *d*=0.66 (12 months) (A) *d*=0.66 (24 months) (B) *moderate improvements*

Studies	Control condition used for analyses	Outcomes Measures: Symptom Severity & QoL	Risk of Bias (Cochrane RoB 2 Tool)	Attrition	Adherence	Within-participant improvement post-intervention	Improvement compared to control	Maintained at follow-up (Time)
Everitt et al., 2013	No website intervention/ TAU (until offered website at end of trial)	IBS-SSS, IBS-QoL	Some concerns	Drop-out not reported, however adherence was defined as engaging with 4 or more sessions in the study: 56% adhered to the self-managed web program and 61% in telephone-supported website group.	91 participants were allocated to either website alone or website with support. The number of sessions undertaken by participants ranged from 0 to 8 (all sessions), with 7 participants completing no sessions and 21 completing 8 sessions, the median was 4 sessions. Adherence was defined as engaging with 4 or more sessions. Overall, 51/ 91 (56%) adhered to the self-management programme.	IBS-SSS *d*=0.66 (6 weeks) (moderate), IBS-QoL *d*=0.34 (small)	*(Authors contacted for further information to calculate effect size, but no response).* There was a statistically significant difference for IBS-SSS scores between control (no website) (162.8) and website (208.9) groups at 6 weeks, but not at 12 weeks: (IBS SS no website (218.2), website (208.9). There were no statistically significant differences between groups for the IBS-QoL at 6 weeks IBS-QoL no website 69.4 (CI 65.7-73.1), website 71.6 (CI 67.9-75.2), or 12 weeks IBS QoL no website 64.3 (59.8-68.9), website 71.6 (67.2-76.1). *	No statistically significant difference in IBS-SSS at 12 weeks: no website (218.2), website (208.9). No statistically significant difference in IBS-QoL at 12 weeks: no website 64.3 (59.8-68.9), website 71.6 (67.2-76.1). *

Studies	Control condition used for analyses	Outcomes Measures: Symptom Severity & QoL	Risk of Bias (Cochrane RoB 2 Tool)	Attrition	Adherence	Within-participant improvement post-intervention	Improvement compared to control	Maintained at follow-up (Time)
Ljotsson et al., 2011	Waitlist control	GSRS-IBS, IBS-QoL	Some concerns	Post treatment: drop-out 18%; Follow-up: 33.3%	Adherence not defined/reported, however the acceptability of ICBT, was measured by the proportions of patients in the ICBT group that stayed in the study (77%) and completed treatment (43%).	Within GSRS pre post: *d*=1.27 (large), IBS-QoL *d*=0.84 (large)	Between group effect size GSRS-IBS *d*=0.77 (large improvement), IBS-QoL *d*=0.79 (large improvement)	**<u>Within (treatment condition only assessed at follow-up):</u>** GSSRS *d*=1.26 (large improvement) (12 months) IBS-QoL *d*=1.13 (large improvement) (12 months)
Ljotsson et al., 2010/11 (A and B)	Waitlist control group with access to group online forum with some IBS suggestive guidance	GSRS-IBS, IBS-QoL	Some concerns	Post-treatment drop-out: 5.9% Follow-up 3 months: 11.9% 15-18 month follow-up: 16.66% .	Adherence reported as reaching final step of treatment: twenty-nine (74%) of the 42 participants in the treatment condition reached the fifth (final) step of the treatment and engaged in exposure exercises (manual divided into 5 steps). Of the remaining 13 participants, 4 never finished the first step, and 1 the first, 6 the second and 2 the third. Participants finishing the fourth step reached the fifth step.	GSRS *d*=1.27 (large improvement), IBS-QoL: *d*=0.89 (large improvement)	Between GSRS *d*=1.21 (large improvement), IBS-QoL *d*=0.93 (large improvement)	**<u>Within (treatment condition only assessed at follow-up):</u>** GSRS *d*=1.31 (large improvement) (12 months) QoL *d*=1.1 (large improvement) (12 months) GSRS *d*=1.11 (large improvement) (15-18 months) IBS-QoL: *d*=0.91 (large improvement) (15-18 months)

Studies	Control condition used for analyses	Outcomes Measures: Symptom Severity & QoL	Risk of Bias (Cochrane RoB 2 Tool)	Attrition	Adherence	Within-participant improvement post-intervention	Improvement compared to control	Maintained at follow-up (Time)
Oerlemans et al., 2011	TAU	Abdominal pain, IBS-QoL	Some concerns	Post treatment: 4% drop-out, Follow-up: 18.7%	Adherence reported as completing follow-up questionnaires: 94.7% completing the post-intervention measurement and 80.3% completing the 3-month follow-up.	Significant within treatment group pre-post effects: abdominal pain T0-T1=0.52 (p<.05), IBS-QoL T0-T1 = -3.84 (p<.05) *	Treatment Vs. Control, Pre-Post abdominal pain: *d*=0.55 (moderate improvement) and for IBS-QoL: *d*=0.48 (moderate improvement)	Follow-up (3 months): no significant differences maintained for treatment group for abdominal pain (*p*=0.23) and/or QoL (*p*=-.370). **Within group:** improvements not maintained for abdominal pain, but improvements maintained for QoL. *
Hunt et al., 2009	Waitlist control	GSRS-IBS, IBS-QoL	Some concerns	Post treatment dropout: 43% Follow-up: 64%	Adherence was defined as completion of treatment & follow-up questionnaire. Treatment group (N=28): 7 (25%) did not complete Module 1, 13 (62%) completed active treatment and 6 weeks follow-up. Of those who completed treatment; 23% were lost to follow-up and 10 participants (77% of completers) provided 3-month follow-up.	GSRS *d*=1.19 (large improvement), IBS-QoL *d*=1.43 (large improvement)	Between groups: GSRS *d*=1.21 (large improvement), IBS-QoL *d*=1.08 (large improvement)	**Within group pre to follow-up (treatment condition only assessed at follow-up):** GSRS *d*=1.38 IBS-QoL *d*=1.47

Studies	Control condition used for analyses	Outcomes Measures: Symptom Severity & QoL	Risk of Bias (Cochrane RoB 2 Tool)	Attrition	Adherence	Within-participant improvement post-intervention	Improvement compared to control	Maintained at follow-up (Time)
Lee et al., 2019	Waitlist control	BSSS, -	Some concerns	0%	Engagement with iCBT program not reported. 100% response rate to questionnaires reported.	Within BSSS improvement *d*=0.17	Lack of significant improvement, not statistically significant on 2nd week (*p*=0.373) or 6th week *(p*=0.09) *	Between iCBT and control: some improvement at 12 weeks, not statistically significant (*p*=0.136) Within BSSS at follow-up (18 weeks): *d*=0.42 *

All effect sizes were calculated where possible to provide Cohen's *d* calculation for consistency across studies (Dunst et al 2004). E.g., calculation used to calculate effect size from Chi Square: $d = (4\chi^2)/(N-\chi^2)$ (Dunst et al., 2004).

*= insufficient data reported/available to calculate Cohen's *d* effect size / *authors contacted for further information in order to calculate effect size, but no response.*

GSRS = Gastrointestinal Symptom Rating Scale, IBS-SSS= Irritable Bowel Syndrome Symptom Severity Scale, IBS-QoL = IBS-related quality of life, BSSS = Bowel Symptom Severity Scale, BPI = Brief Pain Inventory, WSAS = Work and Social Adjustment Scale, NA= not applicable, iCBT = internet-delivered Cognitive Behavioural Therapy, QoL = quality of life, wCBT = web-based Cognitive Behavioural Therapy, TAU= treatment as usual.

Narrative Synthesis

Study Characteristics

Narrative synthesis was conducted following the PRISMA statement (Page et al., 2021) and the Synthesis Without Meta-Analysis guidelines (SWiM) (Campbell et al., 2020). The included RCT studies were published between 2009-2022. The total number of participants in the included studies was 1,415. All participants were aged between 16-75, with a mean age of 32 years. Four studies were conducted in the US, three in Sweden, two in the UK, one in The Netherlands, one in China and one in Japan. The majority (eight) studies were parallel RCT, three were crossover trials (Hunt et al., 2021; Ljotsson et al., 2010a; b; Hunt et al., 2009) and one was a cluster-RCT (Lee et al., 2019). All studies were majority female cohorts, in line with literature highlighting the higher prevalence of IBS in women (Canavan et al., 2014). Two studies were conducted among women only, enrolled in university, therefore limited by educational status (Lee et al., 2019; Tayama et al., 2022), while the remainder of the studies included between 74% and 84.7% female cohorts. All studies excluded participants with comorbid organic GI conditions such as coeliac disease or Irritable Bowel Disease (IBD), psychiatric disorders such as bipolar disorder, schizophrenia or severe depression, infectious diseases or substance misuse.

Half (six) studies included participants based on self-report diagnosis of IBS or previous diagnosis, and/or meeting either ROME (III or IV) criteria or minimum 'mild' IBS-SSS severity, four studies included participants recruited through medical professionals or through referrals detailing an IBS diagnosis (Chen et al., 2022; Lee et al., 2019; Lindfors et al., 2021; Oerlemans et al., 2011) and two studies on basis of meeting ROME criteria (Everitt et al., 2013; Tayama et al., 2022). Length of diagnosis ranged from 2.4 years (Chen et al., 2022) to 11.5 years (Ljotsson et al., 2011). All the studies used a comparator condition: five included a within-subjects waitlist control, five included a control group of treatment-as-usual, two included active treatments of the same intervention delivered with nurse-led guidance (Chen et al., 2022) and as a face-to-face comparator group (Lindfors, 2021).

Duration of interventions ranged from 3 weeks (Lindfors et al., 2021) to 12 weeks (Owusu et al., 2021). Average pre- to post- treatment dropout was 20.34%, with dropout rates ranging

between 0% (Lee et al., 2019; Tayama et al., 2022) to 43% (Hunt et al., 2009) with larger dropout at longer term follow-up: 64% at 3-month follow up (Hunt et al., 2009). All studies included a follow-up, with the follow-up period ranging from 3 months to 24 months (mean: 7.25 months; mode: 3 months).

A summary of the data extraction results is presented in Tables 1 and 2.

Intervention Characteristics

All studies explored the delivery of a digital self-management intervention for IBS and its impact on physical and quality of life related outcomes. Six studies explored the efficacy of a web-based platform intervention (Chen et al., 2022; Hunt et al., 2009; Lee et al., 2019; Lindfors et al., 2021; Ljótsson, Andersson, et al., 2011; Ljótsson et al., 2010), three a website (Everitt et al., 2013; Everitt et al., 2019a; Everitt et al., 2019b; Owusu et al., 2021), one a mobile app (Hunt et al., 2021), one a Personal Digital Assistant (PDA) (Oerlemans et al., 2011) and one an eHealth platform that could be accessed via either computer or mobile (Tayama et al., 2022). Seven studies used a CBT intervention (Hunt et al. 2009; Hunt et al., 2021; Everitt et al., 2013; Everitt et al., 2019; Lee et al., 2019; Oerlemans et al., 2011; Owusu et al., 2021), two were framed from a third-wave perspective (Ljótsson et al., 2010; 2011), and three were non-specified; including a range of mindfulness, relaxation, hypnotherapy and stress management techniques (Chen et al., 2022; Lindfors et al., 2021; Tayama et al., 2022). Seven studies were completely unguided (Chen et al., 2022; Hunt et al., 2021; Hunt et al., 2009; Owusu et al., 2021; Tayama et al., 2022); two of which provided technical support on request (Everitt et al., 2013; Lindfors et al., 2021). Five provided minimal guidance: ranging from asynchronous messaging platforms where participants were encouraged to send weekly messages (Ljótsson, Andersson, et al., 2011; Ljótsson et al., 2010) to weekly automated email reminders, three 30 minute telephone support calls during treatment and two 30 minute booster sessions at 4 and 8 months follow-up (Everitt et al., 2019b). One study provided no live therapist input but provided AI digital personalised feedback (Oerlemans et al., 2011) and one provided an initial meeting to navigate the individual to the online modules; after which there was no further input (Lee et al., 2019). An average of 78% of those who received a digitally delivered self-management intervention completed

treatment (range 56-96%) with two studies reporting a 100% completion rate (Lee et al., 2019; Tayama et al., 2022). The included studies are heterogenous in terms of the nature of intervention, sample, control group and level of guidance. Due to the extent of this heterogeneity, it was decided a meta-analytic approach to the current review would not be appropriate.

Outcomes: Effectiveness of Digital self-management Interventions

IBS Symptom Severity

For evaluating the impact of a digital self-management intervention on IBS symptom severity, most studies used IBS-SSS or GSRS-IBS as outcome measures (*n*=9). One study (Lee et a., 2019) utilised the Bowel Symptom Severity Scale (BSSS). Two studies (Chen et al., 2022; Oerlemans et al., 2011) did not use a global GI symptom severity score; so the abdominal pain score and Brief Pain Inventory scores were utilised for the purposes of this systematic review to calculate effect sizes, as has been conducted in previous guided self-help for IBS systematic review by Liegl et al. (2015). Consistent effect sizes in the form of Cohen's *d* were calculated where possible to make comparison across studies included (Dunst et al., 2004).

Most studies (*n*=10) reported significant within-treatment group improvements in IBS symptom severity, most reporting medium-large effect sizes (range *d*=0.55-1.73). One study reported a significantly smaller within-group treatment effect with the Brief Pain Inventory (Chen et al., 2022) (*d*=0.17), which showed moderate effect at 12-week follow-up (*d*=0.45). For studies that included a comparable control group (e.g. waitlist control/TAU) pre- to post-effect sizes ranged from moderate to large (*d*=0.45-1.21).

Regarding longer-term follow-up, results were more varied. Oerlemans et al. (2011) utilised an Abdominal Pain score, which showed significant improvement post-treatment, but gains were not maintained at 3-month follow-up. Similarly, Everitt et al. (2013) found significant differences at 6 weeks but not at 12-week follow-up for IBS symptom severity scores. Lee et al. (2019) did not find statistically significant effects either post-intervention or at 12-week follow-up. One study (Tayama et al., 2022) did not include follow-up. Most studies

demonstrated maintained moderate-large effects for IBS symptom severity post treatment, e.g., within-participant improvements from pre intervention to follow-up (*d*= 0.45–1.38) for physical symptomology. Only two studies reported follow-up between groups: Lee et al. (2019) reported 3-month follow-up and Everitt et al. (2019b) reported follow-up at 24 months. A small improvement reported in Everitt 2019b (*d*=0.14) highlighted that the effect had decreased over time. The effect size was not possible to calculate for Lee et al. (2019), however, results at 12-week follow-up between groups were not statistically significant. There was significant variability in the follow-up time in included studies, ranging from 3 to 24 months. Furthermore, effect size at follow-up was reported comparing pre- to follow-up measures, rather than post to follow-up. Therefore, the longer-term benefits of digital self-management therapeutic interventions and duration of benefits remains inconclusive.

IBS Quality of Life

For evaluating quality of life, the majority of studies utilised the IBS-QoL (Andrae et al., 2013; Drossman et al., 2000; Patrick et al., 1998) as a measurement of IBS-related QoL, and one using the Work and Social Adjustment Scale (WSAS) (Mundt et al., 2002) as valid and reliable psychometric measure overall functioning (Everitt et al., 2019a; 2019b).
Within treatment group effect sizes ranged mostly between moderate to large for QoL (*d*=0.63-1.25), except for a smaller effect size in Chen et al. (2022) (*d*=0.31).
When compared to waitlist condition, these improvements were larger in comparison; most studies comparing control group to treatment identified a large effect size in QoL, ranging from *d*=0.43-1.25. For most studies, intervention group outcomes were favoured compared with control groups outcomes. One study did not identify statistically significant difference for IBS-QoL between groups at either 6- or 12- weeks (Everitt et al., 2013). However, these outcomes were based on the unguided website group compared with the control group. Everitt et al. (2013) also included a telephone supported website group, with more favourable outcomes reported. Everitt et al. (2013) concluded that therapeutic support alongside the self-management website may be an important feature in future implementation of this intervention.

Regarding longer-term follow-up, maintenance of gains within treatment groups was more variable between small-large effect (range *d*=0.21-1.13). Overall, evidence regarding IBS-related QoL outcomes from digitally delivered self-management interventions is inconclusive and variable. Interventions generally compared favourably to control conditions, though effect sizes ranged from small to large. Regarding between groups follow-up: only one study (Everitt et al. 2019) reported on the WSAS, which showed maintained moderate effect size at 12- and 24- month follow-up. No studies reported on long term follow-up for QoL outcome between groups.

Methodological Risk of Bias

Overall, all twelve studies were rated as raising 'some concerns' using the Cochrane RoB 2 tool by two independent reviewers (see Table 3 and Table 4). After quality assessing one non peer-reviewed paper (Kobayashi et al., 2023) it was agreed by both reviewers to exclude this paper, on the basis of low methodological and quality assessment: due to particularly low recruitment rate (*N*=11) and lacking information reported to provide sufficient data to appropriately assess the study quality. A consensus was reached that the quality of this paper could skew the overall analyses of this review, and therefore was excluded.

For domain one (bias arising from the randomisation process) one study raised some concerns, due to lack of rigorous randomisation and allocation sequence concealment (i.e., allocation based on enrolment order to study) (Hunt et al., 2009).
Domain two related to the risk from deviations from intended interventions and consists of two subcategories: effect of (a) assignment to intervention and (b) adhering to intervention. In domain 2a, all studies (*N*=12) were rated as low risk of bias, all studies rated as using appropriate analysis regarding assignment to intervention and no deviations from the intended intervention noted due to the trial context. For domain 2b, most included studies (*n*=11) delivered interventions to protocol and were therefore considered low risk of bias. One study (Hunt 2009) raised some concerns due to inclusion of both completer and intention-to-treat analyses for all those enrolled in the study (i.e., completing baseline questionnaire), regardless of whether they had started the first module or not.

Domain 3 related to missing outcome data, though all studies (*N*=12) were rated as low risk of bias in this area as missing data was deemed to be dealt with appropriately: with appropriate analyses of data from completers compared with non-completers undertaken. Domain 4 referred to bias in outcome measurement, all studies highlighted some concerns with the risk of bias due to the nature of receiving psychological intervention not possible to be blinded, i.e. participants who were reporting on their outcomes were aware they had received an intervention and therefore may have been influenced by the Hawthorne effect (Adair, 1984; McCambridge et al., 2014).

In domain 5, relating to the selection of reported results, the majority of studies were deemed to be low risk (*n*=11), though some concerns were flagged with one paper (Hunt et al., 2009) due to a lack of availability of a pre-existing protocol outlining the data analysis plan. For all papers, where a protocol was not referred to in the text, the author conducted a search to find one if available and compare against the published papers (eg. Hunt et al., 2009).

Table 3: Methodological Quality Ratings of Rater 1 for Cochrane Risk of Bias Tool (RoB 2)

Study	Domain 1: randomisation process	Domain 2a: deviations from intended interventions (effect of assignment to intervention)	Domain 2b: deviations from intended interventions (effect of adhering to intervention)	Domain 3: Missing outcome data	Domain 4: measurement outcome	Domain 5: selection of reported results	Overall Risk of Bias
Chen et al., 2022	Low	Low	Low	Low	Some concern	Low	**Some concern**
Lindsfors et al., 2021	Low	Low	Low	Low	Some concern	Low	**Some concern**
Hunt et al., 2021	Low	Low	Low	Low	Some concern	Low	**Some concern**
Owusu et al., 2021	Low	Low	Low	Low	Some concern	Low	**Some concern**
Tayama et al., 2021	Low	Low	Low	Low	Some concern	Low	**Some concern**
Everitt et al., 2019 (A and B)	Low	Low	Low	Low	Some concern	Low	**Some concern**
Everitt et al., 2013	Low	Low	Low	Low	Some concern	Low	**Some concern**
Ljotsson et al., 2011	Low	Low	Low	Low	Some concern	Low	**Some concern**
Ljotsson et al., 2010; 2011 (A and B)	Low	Low	Low	Low	Some concern	Low	**Some concern**
Oerlemans et al., 2011	Low	Low	Low	Low	Some concern	Low	**Some concern**
Hunt et al., 2009	Some concern	Low	Low	Low	Some concern	Some concern	**Some concern**
Lee et al., 2019	Low	Low	Low	Low	Some concern	Low	**Some concern**

Table 4: Methodological Quality Ratings of Rater 2 for Cochrane Risk of Bias Tool (RoB 2)

Study	Domain 1: randomisation process	Domain 2a: deviations from intended interventions (effect of assignment to intervention)	Domain 2b: deviations from intended interventions (effect of adhering to intervention)	Domain 3: Missing outcome data	Domain 4: measurement outcome	Domain 5: selection of reported results	Overall Risk of Bias
Chen et al., 2022	Low	Low	Low	Low	Some concern	Low	**Some concern**
Lindsfors et al., 2021	Low	Low	Low	Low	Some concern	Low	**Some concern**
Hunt et al., 2021	Low	Low	Low	Low	Some concern	Low	**Some concern**
Owusu et al., 2021	Low	Low	Low	Low	Some concern	Low	**Some concern**
Tayama et al., 2021	Low	Low	Low	Low	Some concern	Low	**Some concern**
Everitt et al., 2019 (A and B)	Low	Low	Low	Low	Some concern	Low	**Some concern**
Everitt et al., 2013	Low	Low	Low	Low	Some concern	Low	**Some concern**
Ljotsson et al., 2011	Low	Low	Low	Low	Some concern	Low	**Some concern**
Ljotsson et al., 2010; 2011 (A and B)	Low	Low	Low	Low	Some concern	Low	**Some concern**
Oerlemans et al., 2011	Low	Low	Low	Low	Some concern	Low	**Some concern**
Hunt et al., 2009	Low	Low	Low	Low	Some concern	Low	**Some concern**
Lee et al., 2019	Low	Low	Low	Low	Some concern	Low	**Some concern**

Discussion

Principal Results

Since digital delivery of self-management approaches is a relatively novel field, systematic reviews in this area are limited to date. To the author's knowledge, this is the first systematic review to explore the efficacy of digitally delivery self-management interventions for IBS for both physical symptomology and quality of life. This review found that digital self-management interventions for IBS appear to show significant improvements in physical symptomology and quality of life outcomes. Kim et al. (2022) examined efficacy of iCBT-specific interventions for IBS, five of which reviewed studies have been included in the current review (Everitt et al., 2019b; Everitt et al., 2013; Hunt et al., 2009; Lee et al., 2019; Ljótsson et al., 2010). However, as discussed in introduction section of this review, Kim et al. (2022) conducted a meta-analysis including two papers of nine papers relating to the same study (Everitt et al., 2019a; 2019b): thus, increasing the possibility of over-estimated efficacy. Furthermore, an additional seven different papers were also included in the current review.

From the current review, evidence suggests that digitally delivered self-management interventions demonstrate efficacy in improving physical symptomology post-intervention, with moderate-large effect sizes. These effect sizes tended to be maintained at longer-term follow-up. Due to the variable length of time for long-term follow-up in the included studies (range from 3 to 24 months), further research into the sustained benefits, and maintenance of benefit, is needed. Regarding QoL, moderate-large improvements were observed across most studies within treatment groups from pre-to-post treatment. These effect sizes were considerably larger when comparing treatment and control groups. At longer-term follow-up, there was large variability: from small- to large- effect sizes reported for QoL. Inconclusive evidence at longer-term follow-up and variability in length of follow-up warrants further research into the maintenance of these effects. Furthermore, most studies reported maintenance of within-treatment participant effects, with only one study (Everitt et al., 2019) reporting between-group effect sizes at long-term follow-up (24 months): which

highlighted these effects decreasing over time. These findings are consistent with Kim et al. (2022), who reported IBS symptom severity showing medium-large effects post- iCBT with maintenance at follow-up, and moderate effect sizes for QoL. These findings must also be considered in the context of generally small sample sizes. This is significant because it minimizes the chance of detecting a true treatment effect (Type 2 error) as well as potential for unreliable estimates of the effect (Type 1 error). Where very large effect sizes are reported this may over-estimate the efficacy of an intervention.

Attrition/Adherence

Attrition is continually noted as a significant issue for digitally delivered and unguided interventions (Linardon & Fuller-Tyszkiewicz, 2020; Meyerowitz-Katz et al., 2020). Meyerowitz-Katz et al. (2020) highlighted a pooled estimate of 43% drop-out across mHealth interventions for long-term health conditions. In the current review, attrition rates were largely variable (range 0-43% for post-treatment drop-out), with greater attrition at longer-term follow-up (e.g., 64%, Hunt et al., 2009). Furthermore, there were no drop-out rates reported in some included studies (e.g., no data on attrition reported in Everitt et al., 2013; 2019a; b). The considerable variability of reported attrition rates in the current review raises questions as to what may have contributed to such variation in adherence to digital treatment: factors such as baseline presentation differences, intervention length, mode of delivery, content of the intervention, level of guidance provided would be important areas to explore for future reviews and empirical work in the field.

While guidance level varied in the reviewed studies, comparing the outcomes based on guidance level was not a focal point in this review. The benefit of unguided intervention would include a larger scale roll-out of digital interventions and less burden on healthcare staff, however, literature suggests completely unguided self-help interventions may be more appropriate for those who are presenting in the milder symptom range (Gonzalez Salas Duhne et al., 2022). Some included studies may have been biased towards targeting such populations, e.g., Lee et al. (2019) recruited college students between 18-22: limited by age, education status and ability to be in school (i.e., not absent due to severe IBS symptomology). Therefore, there could be considerable variability in the included

populations, and generalisability of these results should be taken with caution. Regarding severity of IBS, it has been suggested that 40% present with 'mild' symptoms, 35% moderate and 25% severe (Drossman et al., 2011). In line with the literature (Gonzalez Salas Duhne et al., 2022) this suggests the majority of those presenting to GI clinics would be suitable for unguided self-help interventions. It may be important to screen the level of severity and therefore appropriateness of offering a digital self-management intervention to patients at baseline as part of a stepped-care approach (Mohr et al., 2019).

Furthermore, included papers in this review measured attrition and adherence in different ways. A challenge exists in evaluating adherence to online therapies, due to the variability in how engagement is defined by numerous trials (Donkin et al., 2011). Completion of the psychometric questionnaires in these studies did not imply that the participants had engaged with the DHI. Some studies measured 'adherence' with the digital intervention as having completed e.g., half of the modules (Everitt et al., 2019; Owusu et al., 2021), others two thirds (e.g., Lindsfors, 2021) and others measured adherence as having completed all modules (e.g., Ljotsson 2010; 2011). Furthermore, Hunt et al. (2021) reported the attrition rate as 36%, though also highlighted that the majority of those who completed a follow-up measure "had not made it through a substantial portion of the app" (Hunt et al., 2021). It is possible that there are over-estimations in our assessment of DHIs: for example, Everitt et al. (2013) and Owusu et al. (2021) showed great variation in completion of the digital intervention: with only 23% and 28% of participants completing all 8 modules while both studies considered those who completed half the modules as 'adherent'. Furthermore, Hunt et al. (2021) did not assess engagement and considered all those who completed the second questionnaire as adherent; however, only one participant in this study completed all modules. Due to the considerable variation in the measurement of engagement with a digital intervention (Donkin et al., 2011; Meyerowitz-Katz et al., 2020) a more conclusive definition of this would be useful going forward, particularly when comparing differing digital intervention deliveries and therapeutic modalities, and to protect against over-estimation of effects from DHI studies. A consistent definition across studies should include a defined engagement metric (e.g., meeting a threshold for module completion), usage frequency, and time spent on the intervention. Using a consistent definition of engagement

in DHI studies going forward will also allow for greater comparison and meta-analyses in the field, with the aim of informing methods to enhance user engagement.

Methodological Quality Assessment

Inclusion criteria for this review limited studies to RCT only. In line with the 'gold standard' approach to assessing bias, the Cochrane RoB tool was utilised to account for a rigorous approach to reviewing current evidence in this field (Sterne et al., 2019; Higgins et al., 2011). Two assessors completed quality assessment, with one assessor completely independent of the study (DM) to reduce the risk of author bias, with discrepancies resolved via discussion. It is also notable that all studies in the review raised 'some concerns' when assessed by Cochrane RoB 2 tool. This is primarily due to participants not being blinded to partaking in a trial, often the case due to the nature of partaking in psychological interventions (Juul et al., 2021). Some previous reviews (e.g., Liegl et al., 2015) have excluded this section of the RoB tool on the basis that this is the nature of psychological interventions. This highlights potential issues in the utilisation of this tool, and a consistent recommendation should be made on inclusion or exclusion of this item in the assessment of psychological interventions.

Given RCTs are generally considered to be the cornerstone of clinical research to rigorously measure efficacy of interventions, and due to the nature of the current review, it was decided to limit the current review to only include RCTs (Hariton & Locascio, 2018). Furthermore, combining estimates of treatment efficacy for both observational and RCT studies is subject to criticism; on account of differences in study design and participant retention (Meyerowitz-Katz et al., 2020). However, given this is an emerging field, particularly for psychological interventions not limited to CBT, some GDH studies using other study design (e.g., pilot, feasibility, pre-post) were not included as a result of the current review's criteria (e.g., Peters et al., 2023; Zhao et al., 2022). On reflection, while limiting the current review to RCTs provided important between group comparisons and randomisation to reduce bias for measuring intervention efficacy, the exclusion criteria has captured majority CBT interventions, as CBT is the most widely researched approach and holds the most published RCTs (David et al., 2018). However, the majority of RCTs have used waitlist control rather than active comparator groups (David et al., 2018). Furthermore, Li et al.

(2014) conducted a systematic review of CBT for IBS and found that while CBT showed efficacy for physical symptomology post-treatment and at short-term follow-up, it did not show superior outcomes compared with other psychological treatments, such as mindfulness and relaxation training (Li et al., 2014). Given these results, it would seem appropriate to evaluate this in digital delivery also. It would be of interest to include other study designs in a future review of online self-management interventions for IBS, particularly with emergence of evidence for other therapies in IBS e.g., GDH and third wave approaches (Greywoode & Szigethy, 2022; Saleh et al., 2023). Due to the emergence of research currently looking into the digital delivery of self-management strategies for IBS in other areas (e.g., GDH), it would be of interest for a future paper to

(a) conduct a review of papers not limited to RCT and
(b) collate a review comparing efficacy with other digitally delivered psychological approaches once they are published in full text.

Grey Literature

With regard to the inclusion of grey literature in this review, the pragmatics and scientific contribution had to be considered in the scope of grey literature that could be accounted for by the one author conducting scoping searches. A decision was made to search for doctoral theses, preprint servers and a gastroenterology-based charity for potential inclusion to minimise publication bias and provide a comprehensive review of the available evidence (Paez, 2017). However, it is acknowledged there are many other preprint servers that could have been utilised for a more rigorous search, and this was limited by the tools available to conduct this in the current review (one author). For future reviews, a more rigorous approach to searching more possible grey literature for inclusion is advised.
Furthermore, while inclusion of grey literature is largely recommended as a way to decrease publication bias in systematic reviews, it may also introduce lower quality studies that have not met peer-review publication standards (Adams et al., 2016). One included preprint study in the current review (Tayama et al., 2022) is considered as grey literature, with the second identified paper (Kobayashi et al., 2023) was excluded on basis of quality assessment. Quality assessment was used to provide further rigour in paper selection for the current

review. The decision to exclude this paper at quality assessment stage was made by both reviewers independently (AR and DM), minimising author bias.

Limitations of the Current Review

The studies included in the current review are largely heterogenous: regarding interventions, delivery method, level of guidance, control groups, sample, and long-term follow-up: which may have influenced the reported findings. While most interventions from included papers take a CBT perspective, others included aspects of various psychological approaches (e.g., third-wave informed approaches, meditation, GDH). The heterogeneity in the included studies confirmed that conduction of a meta-analysis would not be appropriate. Regarding the included papers in this review which assess the longer-term follow up of digitally delivered self-management strategies for IBS, it is important to note that different RCT designs (crossover, cluster, parallel) could have a significant influence on these results, and therefore cannot be adequately compared. This is important to note in our interpretation of longer-term outcomes and provides further rationale for why conducting a meta-analysis would not be appropriate (as was conducted by Kim et al. 2022). Furthermore, there was large variability in the method of recruiting patients with IBS in the reviewed studies: only four studies involved healthcare professionals confirming IBS diagnosis, while most studies relied on self-report symptomology meeting a minimum cut-off point or self-report of a previous diagnosis. This leaves scope for patients to have been included that may not meet criteria for an IBS diagnosis by a healthcare professional or could have co-existing organic pathologies which have not been explored. It would be worthwhile for future studies to include more stringent criteria in recruiting IBS patients, i.e., through GI consultants or healthcare professionals where other diagnoses have been ruled out, as IBS symptomology commonly overlaps with other GI disorders e.g., IBD, coeliac disease (Rani et al, 2016). It is also important to note that a number of studies were not included in the current review due to lack of availability of full-text copies. Where full-text papers were not available, all authors were contacted to enquire about access to the paper: and either advised their paper was undergoing review for publication (Berry et al., 2023) or no response was received (Pedersen, 2015). Furthermore, all comparator control groups were either waitlist control or treatment as usual. It would be important for future studies to include active control groups

for greater generalisability and confidence in findings. Therefore, results of the current review should be interpreted with caution.

Strengths

This is the first paper to systematically review RCT of digital self-management interventions for IBS. Findings from the current review highlight the efficacy of such interventions both post-treatment and at longer-term follow up. This is important for informing future treatment approaches to IBS. Digital delivery of such self-management approaches is a novel and cost saving way to provide immediate access to treatment, in turn positively impacting upon patient care as well as decreasing burden on services: GI, psychology, and dietary services alike (Riehl, 2022). Important clinical implications are highlighted as well as future research directions: such as screening symptom severity at baseline to inform a stepped-care approach, and consistency is recommended for the reporting of engagement and attrition in online interventions going forward. Furthermore, future research evaluating the extent of guidance that may improve the effectiveness of these therapies as part of a stepped-care framework is also recommended. The results of the current review warrant a larger-scale review of online intervention for IBS to provide greater confidence in these results. However, these results add to a body of literature demonstrating the potential to disrupt the current healthcare model by providing immediate access to support, while minimising costs and burden on services.

Theoretical Implications

From a biopsychosocial framework, self-management digital interventions can provide psychologically informed strategies for managing the condition, as well as psychoeducation around the mind-gut link: which is important in the understanding and treatment of IBS. While IBS can be a debilitating physical condition, online therapeutics that can help to alleviate distress can in turn impact upon reported physical symptomology and health-related quality of life, as demonstrated by the reviewed papers. This is in line with what we know about the brain-gut axis: that psychologically informed interventions can have a positive impact on behaviours, cognitions, emotions, and physical symptoms alike (Riehl,

2022; Kinsinger, 2017). Theoretically, the findings suggest that there is use for digital self-management therapeutic interventions for IBS.

Clinical Implications

Clinically, inclusion of a self-management digitally delivered intervention for IBS could be a cost-saving approach to a stepped-care framework to IBS: improving patient outcomes, providing immediate access to care, reducing burden on GI and Psychology services alike (Bosman et al., 2023). It is a direct and easily accessible way to pave towards an integrated pathway between GI and psychology services (Keefer et al., 2018). Furthermore, given evidence suggesting such interventions are more suited to those with less severe IBS, offering this intervention at an earlier stage in the pathway may be an important future development: for example, in primary care. There is also potential for delivery of such interventions by less psychologically qualified staff, such as assistant psychologists, nurses, dieticians, Occupational Therapists, or third sector workers: thus, increasing access and integration of services and holistic care. Digital self-management interventions could also be utilised to organise homework tasks and monitor progress between sessions.

While a plethora of literature focuses on the many benefits that come with increasing access to digital self-management interventions for IBS patients, it is important to take into consideration the digital health inequalities that accompany such approaches. Groups highlighted as more susceptible to digital exclusion are those on lower incomes, disabilities, older people, and rural communities (Toscos et al., 2019). It is notable that the topic of digital inclusion was not considered in any of the included studies in this review and recommended for future consideration in how we work towards accounting for this while digital therapeutics continue to grow and expand over the next number of years: by enhancing digital inclusion strategies such as expansion of public digital access through health and welfare services, working with government and technology providers to promote market innovations that reduce cost of digital access and enhance protection for the marginalised groups. Furthermore, there was a lack of examination into potential reasons for attrition in the reviewed studies, similarly noted in a systematic review of attrition in mHealth self-management apps (Meyerowitz-Katz et al., 2020). This is important to highlight

for empirical work going forward; for example, including qualitative follow-up including user experience of those who dropout, to aid enhancement of future interventions and increase prospective retention rates.

Future Recommendations

It is important for future studies to assess whether there are significant differences in baseline IBS severity for whether people respond to digital self-management interventions as well as how long they have been diagnosed/struggling with IBS symptoms. This could inform future implementation of digital self-management interventions as part of a stepped-care framework: to offer these low-intensity interventions most appropriately to those presenting with mild-moderate symptomology at baseline. There was insufficient information reported in the included papers to assess baseline symptomology presentation in the current review, however exploring baseline scores for those who engage and those who drop-out of digital self-management interventions may provide important insights into such differences to advise future application of such interventions more appropriately. Longitudinal studies are needed to explore the potential impact of DHIs in the longer-term in terms of symptom management and QoL. Suggestions for improving future reviews of digital self-management interventions in IBS include: comparing different digitally delivered treatment modalities (e.g. CBT, GDH, third wave approaches), conducting a systematic review not limited to RCT studies particularly given that this an emerging field for other digital therapeutics, evaluating the impact of guidance level on adherence to interventions and outcomes, and accounting for digital health inequalities and improving access to DHI for the general population, as current findings may be biased to particular population groups who have the means to engage in such interventions (Toscos et al., 2019). From a clinical perspective, it may be important to consider the presentation and severity in the patient in offering a digitally delivered self-management intervention, as part of a stepped-care framework (Donkin et al., 2011).

Conclusion

This review highlights that digitally delivered self-management approaches for IBS show superior outcomes to standard medical care or being on a waiting list for improving IBS symptom severity and quality of life. Furthermore, benefits to treatment groups persisted at long-term follow-up. Digital self-management intervention for IBS is a new and rapidly growing field, with preliminary data providing promising evidence for the efficacy of these interventions (Greywoode & Szigethy, 2022; Saleh et al., 2023). Accounting for the large population of IBS patients and figures demonstrating increased demand for GI-based psychological interventions, digital therapeutics can provide a cost-saving, immediately accessible service to patients to supplement their treatment (Greywoode & Szigethy, 2022). However, there is much more rigorous research to be conducted in this field to demonstrate efficacy at RCT level in diverse patient populations (Saleh et al., 2023) and consideration of mitigating digital health inequalities (Toscos et al., 2019). Results of the current review warrant a larger-scale investigation and review of online intervention for IBS to provide greater confidence in these results. It will also be important for more future research to compare digitized treatment to other evidence-based treatments. Nevertheless, this review provides a comprehensive insight into the efficacy of digital therapeutics for IBS patients, for both physical symptoms and quality of life. Furthermore, these digitized approaches provide immediate access to care, all the while reducing costs and minimising burden on healthcare services.

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Chapter 2: Empirical Study

Investigating the delivery of an acceptance and commitment therapy (ACT) smartphone app intervention on symptomology in adult IBS patients: a feasibility study.

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Please note: this paper is written only by the first author. The second author and last author wrote the 'Better Living with IBS' (2012) workbook; the materials that were adapted for the digital intervention. The last author is academic supervisor for this paper.

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Abstract

Irritable Bowel Syndrome (IBS) is a common chronic gastrointestinal (GI) condition with significant burden on patients and associated healthcare costs. More recently, digitized psychological therapeutics are being trialled to meet the need of the numbers of patients presenting to psychological services for chronic health conditions. Acceptance and Commitment Therapy (ACT) is increasingly applied to chronic health conditions and has been successfully delivered digitally for conditions such as chronic pain and diabetes. This is the first study to trial the feasibility of a smartphone-app self-help ACT therapeutic for IBS. 83 participants diagnosed with IBS were identified by GI Consultants across three UK Health Services: NHS Lothian, NHS Grampian and Imperial College Healthcare NHS Trust. Participants had access to the ACT self-help app for a period of 8-weeks and completed the same questionnaire at two timepoints: pre-intervention and post-intervention. 44 participants downloaded the app and 29 completed the 8-week follow-up questionnaire. Results demonstrated preliminary feasibility and acceptability of delivery of this intervention as a self-help intervention. In terms of preliminary efficacy, results highlighted the smartphone app intervention showed significant changes in IBS acceptance, IBS-related quality of life and GI-related anxiety. Contrary to hypothesis, results did not show significant IBS behavioural change. In terms of physical symptomology in the current study, improvements were observed though did not reach significance. Possible reasons for the results are discussed such as baseline symptom severity, as well as potential implications for screening GI symptomology at baseline to offer the most appropriate level of intervention intensity, as part of a stepped-care framework. Strengths, limitations, future research, and clinical implications from the current study are discussed. This study offers preliminary evidence of feasibility to disrupt the current healthcare model, proving a stepped-care solution to increasing access to psychological therapies while minimising burden on over-stretched healthcare services.

Background

Irritable Bowel Syndrome (IBS) is a gastrointestinal (GI) disorder causing significant burden for patients and healthcare services: affecting approximately 15% of the population worldwide (Lovell & Ford., 2012; Zhang et al., 2022). IBS is characterized by abdominal pain, altered bowel habit and bloating (Canavan et al., 2014; Saha, 2014). It is recognised as a functional disorder, meaning no organic pathophysiology has been identified. Tests for inflammatory markers can rule out other conditions which have similar symptomology to IBS, such as Irritable Bowel Disease (IBD) and coeliac disease. ROME-IV criteria is the validated measure used for diagnosing IBS (Camilleri, 2020).

IBS patients represent the largest subgroup of functional disorders seen in GI clinics, and 12% of those seen in primary care practices (Saha, 2014). IBS is twice as common in females compared with males (Boeckxstaens et al., 2016). Symptomology can vary from mild to severe for patients and can be debilitating; frequently resulting in absenteeism and loss of productivity at work (Weaver et al., 2017; Tack et al., 2019). In fact, IBS is cited as the second most common cause of work absence, after the common cold (Qureshi et al., 2016). IBS is therefore one of the most burdening conditions in terms of both direct costs (e.g. healthcare appointments and procedures) and indirect costs (e.g. absenteeism from work and productivity loss) (Bosman et al., 2023; Canavan et al., 2014; Soares, 2014).

Brain Gut Axis

The brain-gut axis refers to the bidirectional communication between the brain and the gut: connected by the vagus nerve (Kinsinger, 2017). The GI tract is highly sensitive to stress, and psychological pathology has been identified as a significant contributor to dysregulation of the brain-gut axis in IBS (Carabotti et al., 2015). IBS is therefore coined as a ‘disorder of gut-brain interaction’ (Kennedy et al., 2014). This

bidirectional relationship between the brain and the gut is important in informing a biopsychosocial approach to diagnosis, understanding and treatment of IBS.

Providing a biopsychosocial understanding and positive diagnosis of IBS is important in supporting both the patient and healthcare provider in feeling confident in diagnosis and treatment plan (NICE, 2016). However, IBS can often be viewed as a diagnosis of exclusion both by patients and physicians: increasing anxiety, undermining confidence, and often resulting in further unnecessary and costly procedures, appointments and testing to rule out other possible conditions (Spiegel et al., 2010). IBS is associated with increased rates of psychological distress and negative impact on patients' quality of life (QoL) (Kinsinger, 2017). A recent cost analysis of direct healthcare use for IBS highlighted that the majority of costs were associated with mental health services rather than GI services (Bosman et al., 2023).

Psychological approaches for IBS

Increasingly, psychological therapies are recommended as a component of treatment for IBS, from a biopsychosocial understanding of the condition. Psychological approaches for IBS with the strongest evidence base include: Cognitive Behavioural Therapy (CBT), hypnotherapy and mindfulness-based therapies (Ballou & Keefer, 2017). CBT has been the most rigorously tested psychological approach for IBS, comprising the majority of published randomized controlled trials (RCTs) (Laird et al., 2016). However, meta-analyses have found CBT to be effective for IBS when compared with non-active controls, but not when compared with basic support, standard medical care, or other active psychological treatments (Laird et al., 2016; Li et al., 2014). Other studies have compared the efficacy of CBT and mindfulness-based techniques for IBS and found mindfulness to have superior outcomes (Zomorodi et al., 2014). Ljotsson et al. (2010, 2011a; b) have conducted several studies demonstrating the significant impact of psychological interventions for IBS. While these interventional studies are titled 'CBT', these interventions include third-wave elements of acceptance-based approaches and mindfulness. This is significant as the importance of 'acceptance' has been highlighted in recent years in adjusting to

chronic health conditions (Helgeson & Zajdel, 2017), and particularly applied to IBS (Ferreira et al., 2013); as well as shifting focus towards management of symptoms, rather than eradication (Ballou & Keefer, 2017). Furthermore, Lackner et al. (2007) found that cognitive change (a key component of CBT) was not associated with significant changes in IBS outcomes. While CBT and hypnotherapy promote a focus on gaining a sense of control over IBS symptoms, for many patients, this can consequently lead to further avoidance of daily activities in efforts to control symptoms (Ferreira et al., 2011). Therefore, approaches targeting other mechanisms have been suggested for treating IBS: particularly Acceptance and Commitment Therapy (ACT) (Naliboff et al., 2008).

ACT for IBS

Acceptance and Commitment Therapy (ACT) (Hayes et al., 2012) encourages psychological flexibility: contact with the present moment and acceptance of thoughts and emotions, including those that are unwanted, in the service of moving towards valued living (Hayes et al., 2013). Psychological flexibility encourages acceptance and willingness to move in the direction of meaningful and valued living, as opposed to experiential avoidance in an effort to control unwanted inner events (Kashdan & Rottenberg, 2010). Avoidance is highlighted as the primary strategy in coping with IBS, even in the absence of physical symptoms (Ballou & Keefer, 2017; Bowers et al., 2020; Melchior et al., 2022). Situations commonly avoided include food-related events, social or work situations, leisure, personal relationships, and intimate contact (Ballou et al., 2019; Sánchez et al., 2017). Avoidant coping in IBS has been linked to poorer quality of life (QoL) and psychological wellbeing (Rutter & Rutter, 2007) as well as lower psychotherapeutic treatment success (Reme et al., 2010). Avoidance of meaningful activities enhances the IBS patients' suffering: becoming stuck in rigid patterns and reducing QoL. ACT encourages engaging with such activities and allowing space for both positive and negative thoughts and feelings in the service of living well alongside the condition, rather than a focus on symptom control (Hayes et al., 2012). ACT has been successfully applied to several chronic health conditions in increasing psychological flexibility and promoting better

self-management of health conditions; including chronic pain (Du et al., 2021) Irritable Bowel Disease (IBD) (Dober et al., 2021), diabetes (Sakamoto et al., 2022) and cancer (Mathew et al., 2021).

Ferreira et al. (2017) conducted a pilot study where participants took part in a one-day ACT for IBS workshop and used a self-help workbook for 8 weeks: 'Better Living With IBS' (Ferreira & Gillanders, 2012). This pilot study demonstrated a significant increase in participants' acceptance of IBS, and QoL, and significant decrease in symptom severity, avoidance and GI-specific anxiety (Ferreira et al., 2018). This protocol was then extended for trial as a stand-alone 8 week self-help workbook: which found improvements in symptoms severity, GI-specific anxiety and IBS willingness (Gillanders et al., 2017). Contrary to hypothesis, the bibliotherapy self-help intervention did not show significant differences in terms of QoL, avoidance or greater activity. These results suggest the workshop element had been an important aspect in patient outcomes: which could be related to accountability, peer support and/or therapist support. However, neither of these studies formally measured engagement with the self-help workbook, which could have provided useful insight into the extent to which participants engage with the materials. Nevertheless, both studies provide promising preliminary data in the application of ACT for IBS and highlight further research is warranted.

Digital therapeutics for IBS

Despite the evidence base for psychological therapies in IBS, a difficulty remains with lack of access to therapies, particularly given the large numbers of people presenting with IBS (Lovell & Ford., 2012; Zhang et al., 2022). Digital self-help interventions are a solution for this: providing immediately accessible treatment for patients, while minimising burden on healthcare services (Hasan et al., 2023). Over the last decade, digital health interventions (DHIs) have played a significant role in revolutionizing healthcare delivery for chronic health conditions such as tinnitus, headaches, diabetes, cancer, fibromyalgia (Morton et al., 2017; Sasseville et al., 2021; White et al., 2022). DHIs can provide a viable method to support self-management for patients managing chronic health conditions (Baumeister et al., 2022).

Digital self-help interventions can encourage confidence in patients' abilities to manage IBS flare-ups and provide support while minimising the need for repeat medical appointments and costly, unnecessary procedures (Hetterich & Stengel, 2020). Black and Ford (2021) highlight the importance of encouraging self-management approaches for the IBS population, particularly given its fluctuating nature. Self-management strategies also aim to reduce anxiety about an individual's ability to manage symptom fluctuations associated with IBS and subsequently decrease the need for repeated medical appointments to manage such flare-up periods. Saleh et al. (2023) conducted a review of current digital therapeutics highlighting CBT and gut-directed hypnotherapy (GDH) approaches for IBS representing an effort to disrupt the current care model. Digital interventions to date have included both CBT (Zemedy smartphone application) (Hunt et al., 2021); and 'Parallel' web-based platform (formerly 'Regul8') (Everitt et al., 2019; Everitt et al., 2013; Everitt; et al., 2015) and GDH, e.g. smartphone applications 'Regulora' and 'Nerva' (Greywoode & Szigethy, 2022; Peters et al., 2023). There has been preliminary promising feasibility for the digital delivery of psychological therapeutics in these studies; presented as feasible and acceptable modes of delivering psychological self-management interventions to the IBS population, with larger scale RCTs warranted (Saleh et al., 2023).

A gap in the literature exists with no current digitally delivered ACT intervention for IBS. Preliminary evidence highlights the effectiveness of ACT for IBS (Ferreira et al., 2018) and ACT as a self-help standalone intervention for IBS (Gillanders et al., 2017). Furthermore, a systematic review of technology-assisted ACT interventions in several chronic health conditions showed promising results in improving functioning, QoL, and distress across several LTCs: including chronic pain, obesity, cancer, hearing loss, HIV, multiple sclerosis, and tinnitus (Herbert et al., 2022). However, digital delivery of an ACT intervention for IBS has not yet been explored.

Aims

The current study is an extension of Gillanders et al. (2017) and Ferreira et al. (2018) utilising the same protocol of ACT for IBS ('Better Living With IBS'; (Ferreira &

Gillanders, 2012) with materials delivered via mobile phone application to evaluate the efficacy of a digitally delivered ACT intervention on both physical and psychological symptomology in IBS patients.

This feasibility project is designed to answer a number of key questions regarding the principal objective: whether or not a larger scale, definitive controlled trial for a digitally delivered ACT intervention in reducing IBS symptomology is feasible and justified. The main outcomes included feasibility of the recruitment process and measurement tools, acceptability of the intervention for participants and adherence to the programme.

These questions include:

(a) Is a smartphone intervention for IBS a sufficiently accessible and acceptable method of intervention delivery?
(b) Can sufficient numbers of participants be recruited and retained across multiple NHS sites?
(c) Will participants engage in the intervention sufficiently?
(d) What are the likely effect sizes for this kind of intervention with this population across the measures of interest?

Secondary research questions/objectives:

1. Does use of an ACT smartphone application increase acceptance/psychological flexibility in IBS patients?

2. Does use of an ACT smartphone application increase levels of self-reported quality of life in IBS patients?

3. Does engagement with the ACT smartphone intervention improve IBS-related avoidance behaviours in patients?

4. Does use of an ACT smartphone application improve reported symptom severity in IBS patients?

5. Does use of an ACT smartphone application decrease GI-symptom related anxiety in IBS patients?

6. Does greater app use correlate with better IBS outcomes (e.g., greater psychological flexibility/acceptance)?

Methodology

Participants

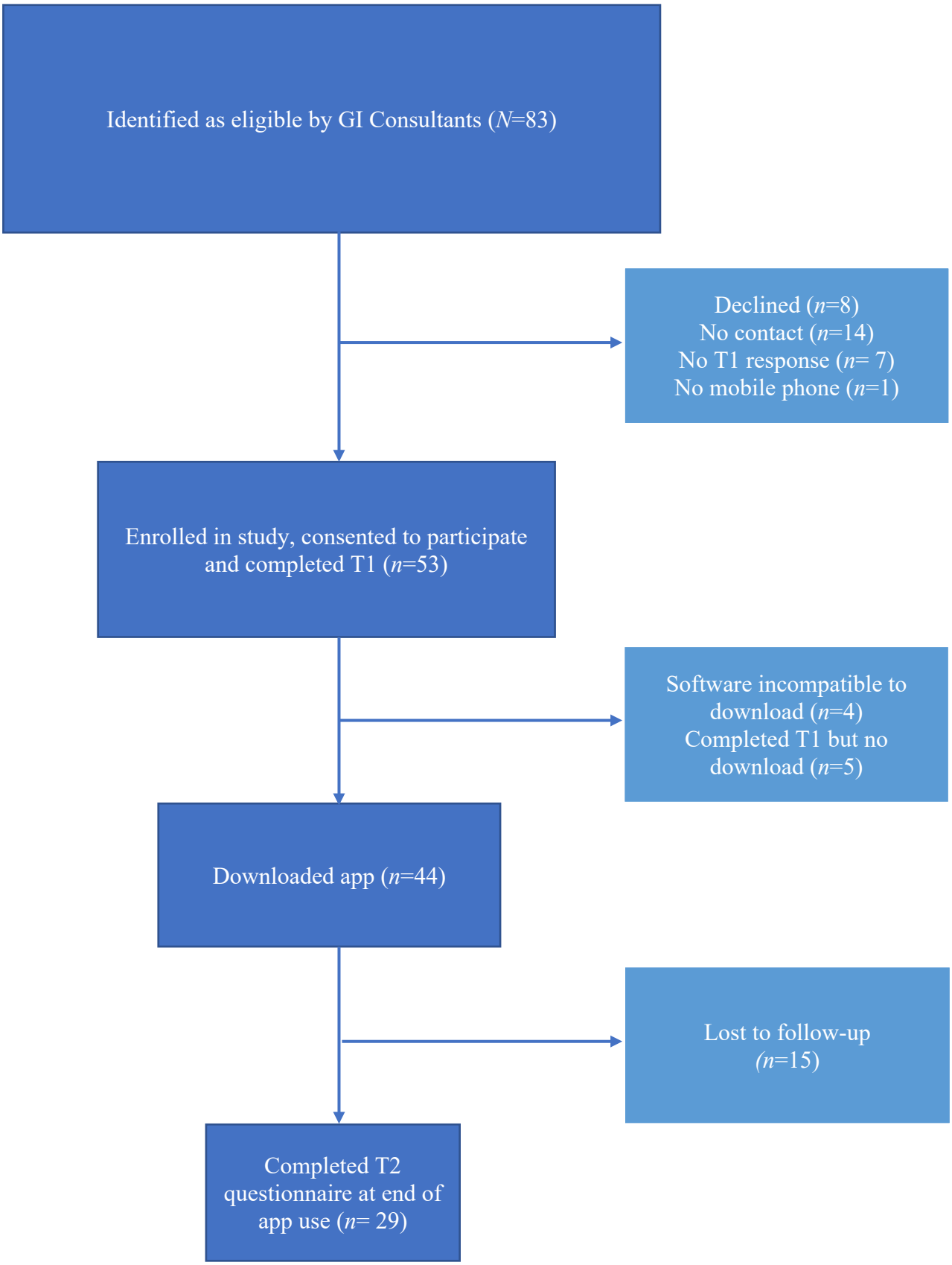
Participants were recruited from GI clinics across three NHS health service areas: NHS Lothian (Western General Hospital), NHS Grampian (Aberdeen Royal Infirmary) and Imperial College Healthcare NHS Trust London (St Marys Hospital and Charing Cross Hospital), between November 2022-May 2023. GI Consultants confirmed IBS diagnosis using both clinical interview and the ROME IV criteria (Longstreth et al., 2006) as recommended by the British Society of Gastroenterology (Spiller et al., 2007). The GI Consultants identified suitable participants to offer participation in this trial. Exclusion criteria included patients under the age of 18, symptoms suggestive of organic disease (e.g., IBD, coeliac disease), severe psychiatric difficulties, terminal illness, substance misuse, cognitive impairment, inability to give informed consent in English and inability to understand written and spoken English.

Figure 2 highlights an overview of the participant flow through the study. A total of 83 patients were identified by the GI Consultants as eligible for participation in the study. Contact details were passed to the first author, who then phoned the identified patients to provide them with further information about the trial before offering the decision to participate or decline. A total of 30 of the eligible patients (36%) were not enrolled into the trial, with reasons outlined in Figure 2. Of the remaining participants, 53 (64% of all eligible) completed the initial questionnaire (T1), 44 (53%) downloaded the app and 29 (35% of all eligible and 66% of all those that began the intervention) completed the second questionnaire at end of app use (8 weeks) (T2).

Of the 53 individuals who consented to participate in the trial and completed T1, participants were predominantly female (*n*=47; 88.7%) consistent with IBS research in tertiary settings (Boeckxstaens et al., 2016). The mean age was 41.8 years (SD=14.06) ranging between 20-70 years, and mean time of managing IBS was 14.63 years (SD=

3.79, range 1-60 years). With regard to educational status, 34% of participants had attended college or further education, 9.4% a postgraduate degree, 30.2% had obtained an undergraduate degree and 26.4% had completed secondary school. 43.3% of participants were single, 32.1% married, 13.2% co-habiting, 7.5% divorced and 3.8% separated.

Figure 2: Flowchart of Participation in Study



Measures

Participants completed self-report psychometric questionnaires using the online platform JISC surveys at two time points: upon enrolment in the study prior to downloading the app (T1) and after 8 weeks (expected time for completion of self-help materials, consistent with previous studies: (Gillanders et al., 2017; Ferreira et al., 2018)) (T2).

Demographic variables of gender, age, education, marital status, and length of illness were collected alongside the psychometric questionnaires. Treatment adherence was analysed using the Firebase Realtime Database to assess the materials the patient had accessed on their app (e.g. number of pages/chapters read, access to workbook exercises and audio exercises played). Firebase is a cloud-hosted database that allows the app owner to store and sync data in real time across participants' devices.

Psychometric questionnaires to assess the self-reported physical and psychological symptomology at T1 and T2 were collected at both time points using the following instruments:

Irritable Bowel Syndrome Acceptance and Action Questionnaire (IBSAAQ)

The IBSAAQ assesses the individual's level of acceptance of IBS: consisting of 20 items on a 7-point scale, from 0 ('never true') to 6 ('always true') (Ferreira et al., 2013). Higher scores indicate higher levels of acceptance of IBS. The IBSAAQ has been identified as a valid and reliable measure of acceptance in IBS, with good reliability (α =0.89) and good validity (Ferreira et al., 2011). Furthermore, this test has been recommended for use in evaluating the effectiveness of ACT-based approaches in IBS (Ferreira et al., 2013). The IBSAAQ consists of two subscales: 'activities engagement' and IBS 'willingness' measures. Cronbach's alpha at baseline for the current sample was calculated: α= 0.88.

Irritable Bowel Syndrome Impact on Quality of Life Scale (IBS-36)

The IBS-36 is a 36-item IBS-specific measure of the impact of IBS on quality of life: including areas such as food, family relations, daily activities, social and emotional impact, symptomology, fatigue, and sexual relations (Groll et al., 2002). This 36-item questionnaire is scored on a 7-point Likert scale ranging between 0 ('Never') and 6 ('Always'), with higher scores indicating greater impact on QoL. It shows high internal consistency (α=0.95) and high test-retest reliability (r=0.92). The IBS-36 is a well validated measure of QoL specific to IBS, which has demonstrated sensitivity to clinical intervention and correlated highly with patient reported symptom scores (Groll et al., 2002). Cronbach's alpha at baseline was calculated for the current sample: α= 0.92.

Irritable Bowel Syndrome Symptom Severity Scale (IBS-SSS)

The IBS-SSS has been identified as a valid and reliable method of introducing a scoring system to IBS symptomology (Francis et al., 1997). The questionnaire incorporates measures of pain, distension, bowel dysfunction and quality of life/global wellbeing; and scores are ranked into categories of 'mild', 'moderate' or 'severe'. The questionnaire is composed of five questions (scored from 0-100) and the maximum available score is 500. Mild, moderate, and severe were indicated by scores in a range of 75-175, 175-300 and >300 respectively. Scores below 75 indicate normal bowel function. This scale has been shown to have satisfactory reliability and to be sensitive to change, with a decreased score change of 50 reliably indicating improvement (Gonsalkorale et al., 2003). Cronbach's alpha at baseline was calculated for the current sample: α= 0.68.

Visceral Sensitivity Index (VSI)

The VSI provides a measurement of GI symptom-specific anxiety (GSA): anxiety specifically related to GI sensations and symptoms as well as the contexts in which these may occur (Labus et al., 2004). Higher scores indicate higher levels of GI-related anxiety. This 15-item scale asks the responder to rate their level of agreement with

each statement: from 1 ('Strongly Agree') to 6 ('Strongly Disagree'). The items are reverse scored and collated to get a possible score between 0 (no GSA) to 75 (severe GSA). The VSI demonstrates good validity and internal consistency (Labus et al., 2007). Cronbach's alpha at baseline was calculated for the current sample: α= 0.93.

IBS Behaviour Response Questionnaire (IBS-BRQ)

The IBS-BRQ scale was developed to assess specific avoidant coping behaviours related to IBS which are often a targeted and expected outcome of change in psychological interventions (Reme et al., 2010). The 28-item scale is scored on a Likert scale from 1 ('Never') to 7 ('Always'), indicating the frequency a behaviour is engaged with. Higher scores are indicative of greater avoidance or control behaviour. The item identifies avoidance of situations such as avoidance of certain foods, social situations, work, exercise, intimacy, medication use and toilet habits. It has been identified as a reliable and valid measure with a high internal consistency for both IBS patients (α =0.86) and controls (α=0.89) (Reme et al., 2010). Cronbach's alpha at baseline was calculated for the current sample: α= 0.89.

Dose/ App Use

Usage was measured according to the number of modules completed. The mobile app sent usage data to the Firebase system each time a participant visited the app. Data include the time and date of each session on the app, pages read, workbook exercises completed, and audio exercises played.

App Development

Collaboration with both Informatics and Design Informatics Departments at the University of Edinburgh was established to build the digital intervention. Firstly, a Masters Degree Design Informatics student (QoL) was recruited for a summer internship and guided to create a protocol design of the app, working with the first author and their supervisor to consider the development of this over the months of June-

September 2021 (see Appendix 19a, 19b and 19c for details of app intervention building process outline). A workflow and protocol for the app was developed using Figma software (see images in Appendix 19b and 19c). From September 2021-April 2022, an undergraduate Informatics student (EW) worked collaboratively with the first author in planning the building of the app. EW built and coded the app using Ionic framework, Xcode and VS Studio. Over the period of April-May 2022, the first author tested the app and a number of issues with playback, design interface, processing speed and flow of the app materials, which were resolved with the Informatics student to create a finalised version of the app (see Figure 3 for sample images). The app experience could be customised by the user: font choice, size, background colour of the app could all be tailored by the individual (see Appendix 23).

App Intervention

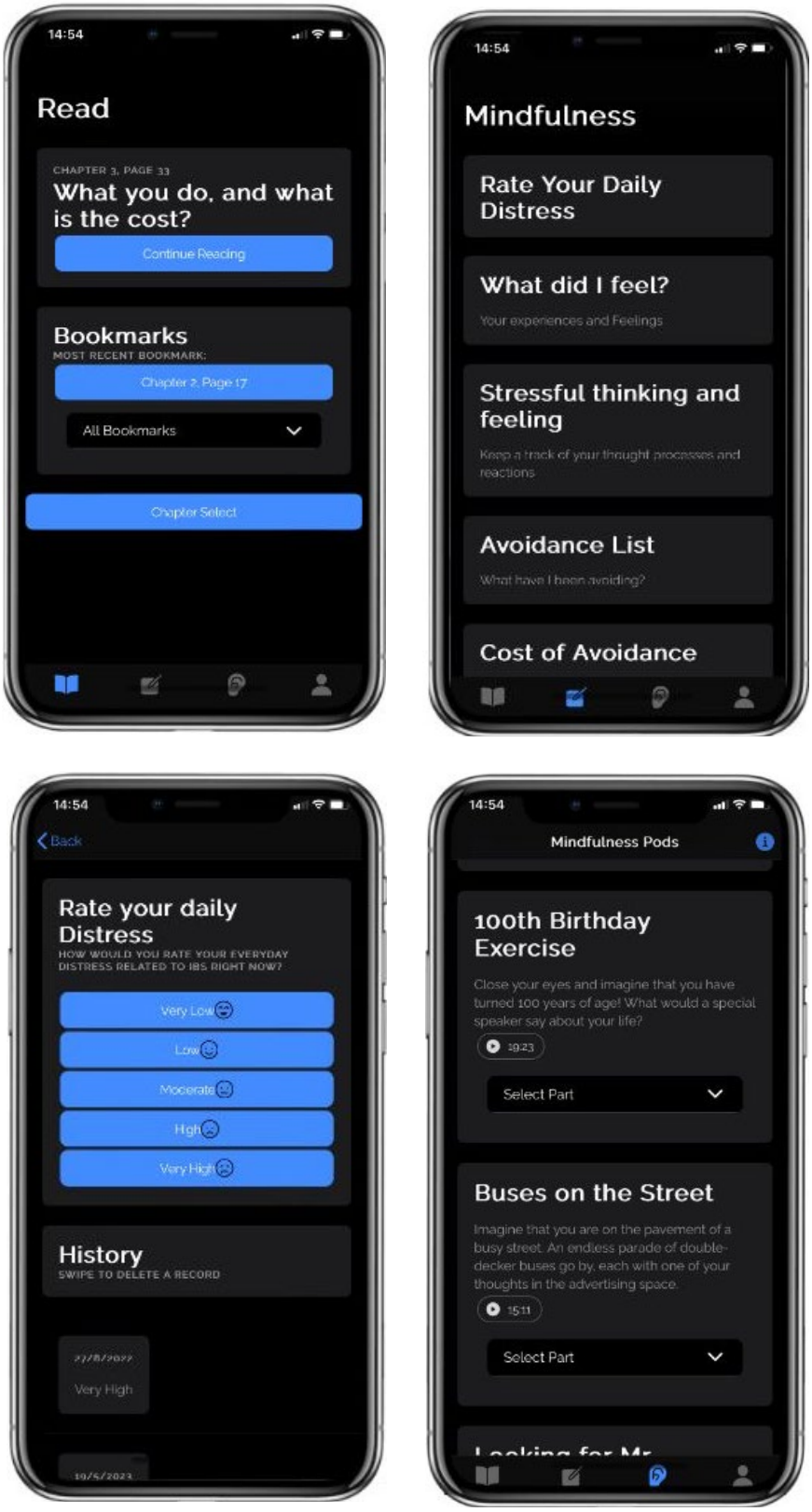
The intervention consisted of access to a smartphone application delivering ACT-based self-help for IBS. The materials were adapted from the self-help book 'Better Living with IBS' for digital delivery (Ferreira & Gillanders, 2012). The mobile app consisted of reading materials, workbook exercises and audio materials: divided into nine chapters. An outline of the materials and chapters can be found in Table 5 and some images of the app materials in Figure 3. The app contained psycho-education about IBS, the brain-gut axis and relation between physical and psychological symptoms, stress, reflective exercises and information about values, cognitive defusion, mindfulness, self-as-context, willingness and committed action. No specific protocol or amount of time to spend on the app was provided: instead, the benefit of regular use of the app and engagement with the materials were encouraged. Participants were provided with access to the app materials for 8 weeks, to work through at their own pace. Participants received a phone call from the first author prior to getting set up on the app, typically lasting between 10-20 minutes. Some participants required assistance with downloading the app and ad-hoc support was available for this from the first author through phone call, email and text during the 8-week trial period. The first author checked in with all participants half-way (4 weeks) through app use to offer any

support needed and covered any difficulties with engagement, clarification of how to use the app or the exercises in the app, and encouragement of using the strategies. The app provided an automated reminder to users if they had not opened the app for 3 days, each time they had accessed the app. If they did not open the app again, they did not receive further reminders. All participants were contacted again at the end-point (T2, 8 weeks) with a request to complete the final questionnaire.

Table 5: Summary of treatment protocol content included in mobile app

Chapter	Content
1: What is IBS?	Psychoeducation about IBS
2: Psychological Stressors & IBS	Brain-gut connection and mutual influence between symptoms and emotional reactions to symptoms.
3: What you do, and what is the cost?	Exploring the short- and long-term effects of strategies directed at controlling/eliminating or avoiding IBS symptoms
4: Mapping Your Direction	Exploring the patient's valued paths through: The compass metaphor and "100th Birthday" exercise
5: When to use your mind, when to lose your mind	Exploring how minds work (fusion and relating): using ACT metaphors through audio and workbook exercises.
6: Mindfulness: A New Perspective	Extended version of the "Buses on the street" Exercise, adapted from the ACT classic 'Leaves on a Stream': used to point out the observer perspective, seeing thoughts as thoughts, and being aware of experiences here and now.
7: Are you willing to have IBS?	Exploring concepts of acceptance and willingness
8: Committing to make your own music	Introduction to committed action, values, making a commitment plan
9: Staying Committed	Exploring potential barriers to commitment and how to manage these, creating an action plan to manage potential barriers, building a support team to staying committed.

Figure 3: sample image from the app: including the e-reader, workbook exercises and audio exercises.



Procedure

As the app was published as a beta testing app and therefore not publicly available on either the Apple or Google Play stores, the first author was able to gatekeep access only to participants who had been recruited through the GI Consultants and consented to participate in the trial. Once participants expressed interest in enrolling in the trial via phone, text or email, they were provided a link to an online consent form and initial questionnaire on the JISC platform: where they indicated whether they had an Apple or Android phone. Following completion of the JISC survey, individual email addresses were added to either the Apple Developer Test Flight account or Google Play Console accounts, and an invitation email with a link was sent to participants so that they could access the app. Once the initial questionnaire was completed, participants were then emailed with the relevant instructions (see Standard Operating Procedures (SOPs) Appendices 21 and 22) to download the app. Participants were aware they could contact the first author for technical guidance to download the app. Halfway through the intervention (at 4 weeks) all participants were contacted by the first author to check-in on app use, offer any guidance needed and reminder about half-way timepoint. Post-intervention (at 8-weeks), all participants were contacted to complete the final questionnaire.

Statistical Analysis

Data were analysed using SPSS Version 27 (IBM Corporation, 2020). Histograms and distribution statistics were used to confirm parametric assumptions. Baseline data between non-completers and completers were compared using independent t-tests and chi-square tests. Feasibility of the intervention was analysed by evaluating recruitment, uptake, engagement with the app, and the accessibility and acceptability of the app as a method of intervention delivery. Preliminary intervention effectiveness and within-participant effect sizes were analysed using paired sample t-tests.

Missing Data

Within assessment phases, there was no overt pattern to missing data. Little's MCAR test indicated a missing completely at random pattern ($\chi 2 = 5.17$, $p = .396$). This means that the likelihood of data being missing is unrelated to the values of the missing data itself, or any other variables in the dataset (Little & Rubin, 2019). Therefore, to handle the missing data, maximum likelihood estimation was employed based on the recommendations of Enders (2011) and Newman (2014). This approach was chosen for its ease of implementation within SPSS, its relatively conservative nature, and its ability to yield comparable estimates to more complex methods like multiple imputation (Enders, 2011; Newman, 2014).

In order to assess the robustness of the outcomes of different missing data handling approaches, a sensitivity analysis was conducted by comparing the results obtained from complete case analysis and maximum likelihood estimation (MLE) in SPSS. Complete case analysis involved excluding cases with missing data, while MLE imputation was used to estimate the missing values based on the observed data patterns. The aim of this sensitivity analysis was to evaluate the potential impact of missing data handling on our study outcome and determine if the conclusion and inferences remained consistent across the two approaches. As results were largely consistent, missing data was dealt with using the MLE approach: providing greater power, decreasing risk of type II error, and providing a more representative sample of app engagement (i.e., including baseline and implementation data of those who dropped out).

Dose-Dependent Response

The amount of engagement with the intervention (i.e., number of chapters read) and change over time was also evaluated using correlation: with more engagement with the app hypothesised to be positively associated with greater improvement in symptomology.

Ethical approval

Ethical approval for this study was sought through the NHS Integrated Research Approval Service and the Berkshire Research Ethics Committee and HRA Wales both provided approval on 15th February 2022 (reference 22/SC/0039; Appendices 4, 5 and 6). The School of Health in Social Science at University of Edinburgh approved the study on 2nd March 2022 (see Appendix 12) and the Research & Development departments in NHS Grampian, NHS Lothian and Imperial College Healthcare NHS Trusts gave approval on 27th June 2022, 29th July 2022 and 3rd October 2022 respectively (Appendices 8, 9, and 10; Reference 22/SC/0039). Participant Information Centre (PIC) Approval between sites was also sought (see Appendix 11).

Power Analysis

Appropriate sample size for this study was approached two ways. As the primary outcome is considered feasibility, the primary focus was the numbers of eligible participants recruited and retained over the course of the study. Taking Gillanders et al. (2017) low-intensity ACT intervention for IBS as a guide: over a period of 8 months, 70 participants met eligibility criteria, of which 45 provided baseline data, 36 at two months and 24 were retained at six-month follow-up. This is an approximate 53% retention rate from initial recruitment, and 34% of all those eligible. For the current study, based on the aforementioned recruitment and retention rates from Gillanders et al. (2017) pilot study and taking guidance on the successful implementation of feasibility trials (Bowen et al., 2010) into account, the trial was considered feasible if it is able to recruit 40% of eligible participants and retain a minimum of 60% of these participants at two months.

The second way to approach sample size estimation for the study is to be sufficiently powered to detect within participant effects similar to those found in Gillanders et al. (2017). This was calculated using the G*Power programme. As IBS acceptance (measured by the IBS-AAQ) is the primary outcome measure of interest in the current study, the effect size of this measure in the previous paper was used for power

calculation. With the parameters of a within-participant effect size based on the previous low intensity IBS paper by Gillanders et al. (2017) (*d*=0.46) using an alpha of .05 and a beta of .8, proposing use of a paired sample t-test with one group and two measurement points, the sample size needed to detect a change would be 31 participants. Accounting for the 47% attrition rate that was observed in the previous study by Gillanders et al. (2017), the current study aimed to recruit at baseline a sample size of 60 participants.

Results

Feasibility

83 participants met eligibility criteria and were invited to the study. 64% of those eligible for the trial were recruited and completed baseline data *(n*=53). Of those who completed baseline data, 83% downloaded the app (*n*=44). Retention of those who downloaded the app (*n*=44) to those who completed T2 measure at 2 months follow-up (*n*=29) is 66%. Therefore, based on the parameters set for the current trial, the trial meets feasibility criteria.

Treatment engagement

Overall time spent on the app was calculated from the Firebase database. Greater time spent using the app and the greater number of chapters accessed was weakly associated with improvements across all outcome measures, however no correlations showed significance (range r = -0.14 - 0.2; p>.05). Table 6 outlines app chapter completion. 93% of participants commenced use of the app. 13.6% completed all nine modules of the app.

Table 6: Outline of app chapter engagement (*n*=44)

Chapter	Participants (*N* %)
1	41 (93%)
2	30 (68%)
3	22 (50%)
4	16 (36%)
5	11 (25%)
6	6 (13.6%)
7	6 (13.6%)
8	6 (13.6%)
9	6 (13.6%)

Table 6: Cumulative demonstration of participant engagement, i.e. same six participants who completed chapter 6, completed chapter 9

Completers and Non-Completers

Parametric assumptions were met, and normality of the data was assessed visually using histograms. There were no significant baseline differences on any demographic or outcome variables found between completers and non-completers using independent sample t-tests and chi squared analyses (all $p>.05$); aside from baseline scores on the Visceral Sensitivity Index (VSI) a measure of GI-related anxiety was significantly lower at baseline in completers ($p<.05$) (see Table 7 for further details).

In terms of app usage, non-completers (n=15) completed a mean of 1.53 chapters (SD=1.19), ranging from 0-4 chapters. Therefore, the greatest number of chapters completed by non-completers was 4. Completers of T2 (n=29) completed a mean of 4.48 chapters (SD=2.67), ranging from 1-9 chapters.

Table 7: Baseline descriptives: completers and non-completers (n=53)

Variable	Completers baseline	Lost to follow up baseline	χ2
	n = 29	*n = 24*	
	Frequency	Frequency	
Gender			
Male	3 (10.3%)	3 (12.5%)	
Female	26 (89.7%)	21 (87.5%)	*.805, ns*
Education			
Secondary school	8 (27.6%)	6 (25.0%)	
College/further education	10 (34.5%)	8 (33.3%)	
Undergraduate degree	8 (27.6%)	8 (33.3%)	
Postgraduate degree	3 (10.3%)	2 (8.3%)	*.971, ns*
Marital Status			
Single	12 (41.4%)	11 (45.8%)	
Married	11 (37.9%)	6 (25%)	
Co-habiting	3 (10.3%)	4 (16.7%)	
Separated	2 (6.9%)	0 (0.0%)	
Divorced	1 (3.4%)	3 (12.5%)	*.377, ns*
	Mean (SD)	**Mean (SD)**	***t (53)***
Age (years)	44.59 (15.62)	39.42 (11.56)	*1.3, ns*
Duraion of IBS (years)	16.46 (16.48)	12.83 (10.42)	*0.9, ns*
IBS AAQ Total	54.00 (18.39)	50.42 (17.08)	*0.7, ns*
IBS AAQ Activity Engagement	25.66 (8.63)	22.63 (10.40)	*1.2, ns*
IBS AAQ Willingness	25.76 (12.08)	24.88 (9.35)	*0.3, ns*
IBS36 Quality of Life	118.26 (36.83)	133.42 (37.17)	*1.5, ns*
Visceral Sensitivity Index	57.65 (17.47)	68.79 (14.74)	*2.5 **
IBS Behavioural Response	96.90 (27.80)	110.54 (24.78)	*1.9, ns*
IBS Symptom Severity	294.17 (85.19)	313.17 (79.59)	*0.8, ns*

*p<.05

Treatment Outcomes

Table 8 shows results of the t-test for pre- (T1) and post- (T2) intervention for all participants who downloaded the app intervention (*n*=44). Participants showed significant improvements in IBS acceptance, quality of life and GI-related anxiety. Contrary to hypothesis, participants did not show significant changes in either physical symptom severity or behavioural responses to IBS. For IBS-AAQ Total and subscales of AAQ activities and AAQ willingness, improvements are shown by higher scores. For IBS-36 QoL, VSI, BRQ and IBS-SSS, a decrease in score demonstrates improvement.

Table 8: paired t-test analysis with maximum likelihood imputed missing data (*n*=44)

Variable	Pre-intervention Mean (SD)	Post-intervention Mean (SD)	Effect Size (*d*)	Significance
IBS-AAQ Total	51.39 (18.82)	58.91 (17.64)	*d* = 0.53	*p* = .001 **
AAQ Activities	23.36 (9.68)	26.94 (8.19)	*d* = 0.39	*p* = .013 *
AAQ Willingness	25.45 (11.7)	29.21 (10.72)	*d* = 0.45	*p* = .004 **
IBS-36 (QoL)	121.36 (37.39)	102.3 (31.30)	*d* = 0.49	*p* = .002 **
VSI	61.09 (16.80)	53.18 (16.05)	*d* = 0.46	*p* = .004 **
BRQ	99.41 (27.16)	98.24 (23.49)	*d* = 0.05	*p* = .764
IBS-SSS	300.19 (86.05)	281.66 (73.72)	*d* = 0.22	*p* = .155

* p<.05.
** p<.01.
[d] effect size conventions for *d* are: small > .20, medium > .50, large > .80 (Cohen, 1992).

IBS-AAQ = Irritable Bowel Syndrome Acceptance and Action Questionnaire (and two subscales: 'activity engagement' and 'willingness'; IBS-36 (QoL) = IBS-related quality of life; VSI = Visceral Sensitivity Index, IBS-BRQ = IBS Behaviour Response Questionnaire; IBS-SSS= IBS Symptom Severity Scale

Pre-treatment, one participant (2.3%) scored in the range of 'healthy bowel function', three participants (6.8%) reported 'mild IBS', 18 (40.9%) reported moderate IBS' and 22 (50%) reported 'severe IBS'. At two months, one participant (2.3%) reported 'healthy bowel function', three participants (6.8%) reported 'mild IBS', 28 (63.6%) reported 'moderate IBS, and 12 (27.3%) reported 'severe IBS'. A related samples McNemar test showed that the proportion of people no longer meeting diagnostic criteria following the intervention was not significant (p=.094). A score reduction of ≥50 points indicate clinically meaningful improvements in IBS symptom severity (Francis & Whorwell, 1997). Using these parameters, 41% (n=18) showed clinically significant improvement in physical symptomology from T1 to T2.

Discussion

This study sought primarily to assess the feasibility of delivering an ACT smartphone intervention for IBS. Feasibility was assessed by recruitment and retention of participants in the trial, on the parameters set based on Gillanders et al. (2017) self-help intervention trial and guidance on feasibility trials by Bowen et al. (2010). The trial was to be considered feasible if it is able to recruit 40% of eligible participants and retain a minimum of 60% of these participants at 2 months. Therefore, the delivery of this intervention is considered feasible: recruiting 64% of all those identified as eligible and retaining 66% of those who accessed the intervention at 2-month follow-up.

Engagement & App Use

There is a challenge to find a widely accepted definition of engagement in online therapies, and there is large variation in engagement assessment across digital therapeutic studies (Donkin et al., 2011; Meyerowitz-Katz et al., 2020). Furthermore, engagement in the current study is challenging to define due to variability in materials accessed, for example, variation in use of the e-reader, workbook and/or audio exercises. The greater number of chapters accessed weakly correlated with improved outcomes, though these correlations were not significant ($p>.05$). Furthermore, these correlations were underpowered, and so limits confidence in drawing conclusions from these results.

A systematic review of engagement with digital self-guided interventions for depression and anxiety defined 'moderate engagement' as completion of 40-60% of programs (Fleming et al., 2018). Using these parameters, approximately half of participants (52.3%) showed 'moderate' engagement with the app (i.e., engaged with at least 40% of materials; or 3.6 chapters). However, only 6 (13.6%) participants completed all nine chapters of the intervention. This is greater in comparison to the CBT smartphone application trial by Hunt et al. (2021), where only one participant completed all modules. A systematic review of digital therapeutics highlighted that

between 0.5 - 28.6% of participants complete all modules of unguided self-help apps (Fleming et al., 2018). Attrition is a continually noted issue in web-based self-help interventions, and further research into reasons for attrition would be worthwhile. A systematic review of mHealth interventions for long-term health conditions highlighted a pooled estimate drop-out rate of 43% (Meyerowitz-Katz et al., 2020), slightly higher than that of the current study (34%). Qualitative feedback of app user experience could provide richer data on reasons for dropout or disengagement, and potential to enhance future engagement. Furthermore, qualitative feedback on reasons for drop-out would inform whether this was related to personal circumstances or the intervention itself (Lawler et al., 2021). Based on the current study, given the severe symptom severity of most presenting patients at baseline, it is also wondered whether this may have had an impact on attrition and engagement with the app (Staudacher et al., 2023). Lawler et al. (2021) also highlight that dropout from online self-help interventions can be related to improvements and needs already being met; qualitative feedback would provide further insight into reasons for disengagement aswell as enhance user experience for future use of the app (Meyerowitz-Katz et al., 2020). Furthermore, the current study was unstructured, meaning participants could use the app as frequently as they liked, and no guidance on frequency of use was provided. As a feasibility trial, this provides important implementation data on app usage which could inform future use of the intervention, for example, by providing guidance to participants on how long to spend on each chapter per week based on these outcomes. However, Meyerowitz-Katz et al. (2020) also highlight that low retention can be related to an unguided approach; and it would be of interest to trial whether asynchronous guidance alongside the app may impact retention rates. It is also worth highlighting that the entire self-help e-reader and workbook was included in the app intervention (total 131 reading pages). This is quite long, particularly to be read on a mobile phone device. It would be of interest to trial editing the materials, include video and audiobook option for these materials in future trials to assess potential improved engagement. Furthermore, inclusion of gamification features such as tracking days of unbroken practice, progress bars and personalisation in the app could further enhance user engagement (Bitrián et al., 2021).

Treatment Outcomes

Regarding efficacy of the intervention, the primary outcome measure of 'acceptance' showed moderate significant improvement comparing pre to post intervention; for the total IBSAAQ measure as well as on both the 'activities engagement' and 'IBS willingness' subscales (d = 0.53, d = 0.39, d = 0.45 respectively). IBS-related quality of life demonstrated significant moderate improvements from pre to post intervention (d = 0.49; p<.01). GI-related anxiety also showed moderate significant improvement from T1 to T2 (d = 0.46, p<.01). Similar to results from the self-help workbook delivery in Gillanders et al. (2017), the BRQ measuring IBS behavioural response did not show significant improvements comparing pre- and post-intervention (p>.05). It is possible that further time to practice and consolidate skills from the intervention is needed to influence overt behaviour change, though the current study did not assess participants at longer-term follow-up. However, these results did not change in Gillanders et al. (2017) study at 6-month follow-up. Results from Ferreira et al. (2018) study, which included a one-day workshop, showed superior outcomes for behavioural change compared to both stand-alone self-help interventions. This suggests there may be a vital component to the face-to-face aspect in terms of behaviours including peer support, normalisation, and public commitment in producing overt behavioural changes. This is consistent with studies by Ljotsson et al. (2010; 2011; 2014) highlighting therapist and peer support and explicit exposure strategies as important factors in contributing to changing IBS avoidance. Owusu et al. (2021) similarly found an unguided web-based CBT intervention did not show significant differences in IBS behavioural change. This is in line with the literature highlighting that even in the absence of symptoms, avoidance is the primary coping strategy in managing IBS (Ballou et al., 2019; Melchior et al., 2022). Results of the current study further reinforce the suggestion that public commitment and exposure-based strategies may be key for successful IBS behavioural change, though longer-term follow-up of the current study would provide more conclusive evidence.

Regarding physical IBS symptomology, improvements were observed from pre- to post- intervention. However, contrary to Gillanders et al. (2017) bibliotherapy study,

these results were not significant (p = .155). Comparing baseline symptom severity (IBS-SSS) scores across both self-help studies, the majority of participant baseline symptom severity scores were in the 'severe' category in the current study *(mean 300.19; SD 75.85);* compared with 'moderate' baseline symptom severity in Gillanders et al. (2017) *(mean 207.08; SD 97.6).* This is important to highlight, as literature shows low-intensity interventions are most appropriately offered to patients with mild-moderate GI symptomology (Staudacher et al., 2023). In fact, both the current study and Gillanders et al. (2017) found at baseline, non-completers had higher mean scores of GI symptomology; suggesting the self-help interventions did not meet their needs and may have contributed to drop-out (*mean 313.17; SD 79.59 / mean 275.7; SD 114.2*; respectively). This provides a possible explanation for the lack of significant change for those presenting at baseline with more severe GI symptoms, who may be more suited to a more intensive intervention as suggested by other recent studies (Staudacher et al., 2023). Furthermore, the current study recruited participants from secondary care GI services, presumably capturing a population presenting with more severe levels of GI symptomology than that of the general IBS population. It is also important to highlight that the IBS-SSS measure showed only moderate internal consistency among items in the scale (α=0.68), indicating a lack of confidence in the reliability of this scale for the current sample. This is worth noting particularly given literature suggesting the current sample (majority 'severe' symptomology) is not representative of the general IBS population (majority mild-moderate severity). Consequently, caution should be exercised when interpreting composite scores derived from this questionnaire and may impact the generalisability of these findings for the wider IBS population. Despite this, 41% (n=18) showed clinically significant change in physical symptomology (IBS-SSS score reduction of ≥50 points) from T1 to T2 (Francis & Whorwell, 1997). Due to lack of control group, it was impossible to assess whether these participants may have shown improvements over time irrespective of the intervention. However, given the average length of illness (mean 14.63 years), this is considered unlikely.

Limitations

There are several limitations to acknowledge in the current study.

Results of this study are limited by a small sample size of T2 completers (*n*=29). Missing data was found to be missing completely at random (MCAR) and therefore, in line with recommendations, missing data was dealt with using maximum likelihood imputation analysis (Enders, 2011). This decision was also guided by Newman (2014): who argue that listwise deletion results in partial respondents becoming discarded and converts construct-level missingness into person-level missingness (Newman, 2014). Particularly given the feasibility aspect of this trial, it was deemed important to include all participants who had downloaded and accessed the intervention: to provide a more accurate estimate of engagement and attrition from the intervention. However, the handling of missing data is subject to criticism, particularly given the large number of missing data at T2 (*n*=15); meaning 34% of follow-up data was missing. As a rule of thumb, it is recommended to manage missing data with imputation methods for missing data not exceeding 40% (Jakobsen et al., 2017). As data was MCAR, partial responses are deemed representative of the entire dataset, and therefore maximum likelihood imputation may lead to unbiased results (Sterne et al., 2009). Furthermore, a sensitivity analysis was also employed to confirm this decision: by comparing outcomes of listwise deletion (*n*=29) and maximum likelihood imputation (*n*=44). As outcomes were generally consistent, maximum likelihood imputation analysis was deemed most appropriate method to handle the missing data: to provide greater power, minimise risk of Type II error, and include participants who dropped out and had provided both baseline data (T1) as well as implementation data (app use). While deemed the most appropriate way to handle missing data in the current study, it remains a limitation when interpreting trial results and therefore these outcomes should be interpreted with caution (Jakobsen et al., 2017). Furthermore, the current study did not follow-up with those who dropped out of the study for feedback on reasons contributing to dropout, which would be of interest to inform future empirical work.

The pre-post design without a control group also precludes conclusions about causality of these findings, and it is possible that participants may have improved without any intervention. However, this is deemed unlikely given the average length of time the sample were managing symptomology (mean 14.63 years).

As the current intervention was available as a 'beta testing' app prototype, there were more steps required for participants to gain access to the app as it was not available for public download (described in SOPs Appendices 21; 22). This may have impacted uptake, as opposed simply downloading an existing app from the app store. It also could have had an impact on those eligible to participate in the trial, who may have been more motivated to use the app. Future research should also include 'non-treatment seeking' participants who would typically be encountered in healthcare settings, for a more generalisable sample. As the intervention was developed by an undergraduate IT student who was also working to their own deadline, the 'functionality' of the app was prioritised over the design interface. Improved engagement could be explored with greater enhancement of user design interface, using the current app as a prototype for such developments. As literature highlights, 'enhanced user interface' positively impacts on behavioural engagement with psychological smartphone app interventions (Hentati et al., 2021). It would also be of interest for a future qualitative study to assess participant's experience of using the app to provide further refinement to ways to enhance future user engagement (Meyerowitz-Katz et al., 2020). User testing and feedback was planned for the current project, however due to time constraints and unforeseen delays with building the app intervention, feedback on the app was only provided by the first author (AR) and supervisor (DG) and focused on the 'functional' aspects of the app.

This interventional study was also limited by resources available, for example, the lack of technical support resulted in some eligible participants unable to download the app due to software incompatibilities (*n*=4). For future studies, technical support assistance would be required to mitigate such instances, as well as a prototype developed and informed by the current study to prevent recurrence of technical issues in future app developments. Furthermore, informed by the current results, potential inclusion of a chat space for peer support and asynchronous messaging therapist guidance may enhance future use of this app: with the aim of these public commitment spaces targeting IBS behavioural change outcomes (Melchior et al., 2022).

Strengths

There are also several notable strengths to acknowledge in the current study.
This is the first study to trial the feasibility of an ACT smartphone app for IBS and has provided preliminary evidence of feasibility and acceptability as a method of delivery. Results from the current study warrant a larger scale trial, with enhancements to design interface and greater resources, such as technical support, research assistance to assist with recruitment and potential for asynchronous guided support provided through the app; to assess whether this may improve engagement.
While the current study is limited by a relatively small sample size, it meets the power requirements to detect significant change and found moderate improvements in IBS acceptance, GI-related anxiety, and IBS-related quality of life from pre to post intervention. These preliminary findings warrant further investigation on a larger scale pilot trial.
Recruitment was another notable strength in the current trial. Participants were identified by GI Consultants in GI clinics with a confirmed IBS diagnosis using both clinical interview and the ROME IV criteria, as recommended by the British Society of Gastroenterology (Spiller et al., 2007). Many IBS studies include self-identified patients (e.g. Hunt et al., 2021; 2009; Owusu et al., 2021) and due to large overlap in IBS symptoms with other conditions (e.g. IBD, coeliac disease) (Card et al., 2014; Rani et al., 2016), it was important that those included in the current study were identified as IBS patients by GI Consultants.

Reporting of implementation data in the current study is another notable strength as this is often lacking in digital self-help intervention studies (Fleming et al., 2018; Meyerowitz-Katz et al., 2020). Eysebach (2005) and Meyerowitz-Katz et al. (2020) highlight that a substantial proportion of users drop out of all eHealth trials and consequently these results are often not highlighted in online trials; particularly in online self-help interventions where high dropout rates are well established (Lawler et al., 2021). In line with recommendations, usage metrics and attrition are analysed and discussed in this trial, which could provide important implications for the future development and use of the current intervention. Implementation data such as time

spent on the app, number of times accessed, engagement with e-reader/workbook exercises/audio exercises, provides a gauge that could inform a more structured approach to future studies. For example, providing guidance or in-app prompting on how much time to spend on the app per week, to facilitate completion of modules within the eight-week timeframe. However, Lawler et al. (2021) also highlight a predefined number of modules is not always necessary for clinical benefit from online self-help interventions. Suggestions for future research have also been made on the basis of this preliminary trial including enhanced design interface for hypothesised increased engagement; screening GI symptomology at baseline to assess this intervention as part of a stepped-care framework; and potential for increased asynchronous therapist support and exposure-based strategies to target behavioural avoidance, the key coping strategy in IBS (Ballou et al., 2019; Melchior et al., 2022).

Clinical Implications

Several important clinical implications are drawn from the current study. Firstly, this study provides preliminary evidence of the feasibility and acceptability of an ACT self-help app for IBS. Further research on a larger scale is recommended to provide more conclusive evidence. Comparing results from the current trial to the previous bibliotherapy approach using the same intervention materials (Gillanders et al., 2017) suggests that this intervention may be better suited for those with mild-moderate IBS symptomology at baseline. This is in line with literature suggesting that low-intensity interventions may be most appropriate for mild-moderate GI symptomology (Staudacher et al., 2023). Results of the current study suggest screening baseline GI symptom severity, and therefore appropriateness of a digital self-management intervention, could inform offering this intervention in a stepped-care approach (Mohr et al., 2019). For example, offering the digital self-help intervention to those presenting with mild-moderate symptomology, and more intensive interventions for those with 'severe' GI symptoms, such as guided self-help, as suggested by Owusu et al. (2021). It would be of interest for future studies to explore a stepped-care

framework on a larger scale, to provide more conclusive evidence around efficacy for those presenting with mild-moderate symptomology. Moreover, the current study recruited participants from secondary care, presumably capturing a population presenting with more severe levels of IBS. Going forward, it would be of interest to also trial this intervention at an earlier stage in the pathway: for example, in primary care GP practices.

Due to the high numbers of people suffering with IBS (Zhang et al., 2022), results suggest ACT-based self-help apps could be rolled out as a prescription to supplement medical treatment; providing increased access to psychological self-help materials. Regarding IBS baseline severity, it has been suggested that 40% of patients present with 'mild' symptoms, 35% 'moderate' and 25% 'severe' (Drossman et al., 2011). Therefore, this level of treatment may be adequate for the majority of IBS patients (75%) and further research is needed to explore this (Gonzalez Salas Duhne et al., 2022). There is also scope to explore the app's use and efficacy in conjunction with guidance from a health professional, which could in turn reduce the level of contact needed. Further research offering this treatment for mild-moderate baseline GI severity is an important next step in empirical work in this field. This could in turn have significant economic impact in terms of; improved accessibility to immediate treatment for most 'mild-moderate' IBS patients; decreased wait-time for GI Psychology for 'severe' presentations; and a positive impact on both direct and indirect healthcare costs (e.g., reduced workplace absenteeism, reduced healthcare use and related costs).

Moreover, digital health inequalities are important to highlight in the emergence of more digital interventions (Honeyman, 2020). This study was limited to participants owning a smartphone device which may have excluded particular age groups, abilities, educational and financial levels (Toscos et al., 2019). Consideration of ways to mitigate such inequalities for future work in this field is important, for example, access to the same materials is provided via website for those without a smartphone or tablet device, or printed manual of the self-help material for those without access to internet.

Conclusion

Conclusions from the current trial include preliminary evidence of feasibility and acceptability of an ACT smartphone app for IBS. Results demonstrate significant improvements in IBS acceptance, IBS-related quality of life and GI-related anxiety, but not overt behavioural changes. Improvements were observed in symptom severity; however, these improvements were not significant. Results warrant a larger scale pilot trial and suggestions for future research include exploring efficacy of this intervention for those presenting at baseline with mild-moderate symptom severity, inclusion of a comparator control condition, inclusion of exposure-based strategies, and comparing unguided and guided version of this app intervention. In line with all studies of online self-help interventions for IBS, engagement and attrition were issues in the current trial; and enhanced design interface based on user testing feedback for this app is recommended for future trials. This is the first study to explore the efficacy of an ACT smartphone app intervention for IBS and demonstrates the feasibility for a larger scale roll-out as part of a stepped-care approach. On a wider front, this study contributes to the body of digital therapeutics disrupting the current healthcare model: aiming to increasing immediate access to care in a cost-effective way, while minimising burden on over-stretched healthcare services.

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List of Appendices

Appendix 19(b): Workflow planning adaptation of self-help workbook ino app format: flow, content and design

Appendix 19(c): Prototype of app with Design Informatics

Appendix 20: Standard Operating Procedures (SOPs) for Users and Owners

Appendix 21: Android SOP User Guide

Appendix 22: iOS SOP User Guide

Appendix 23: Welcome tutorial screenshots from app

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Reference style

References should be arranged first alphabetically and then further sorted chronologically if necessary. More than one reference from the same author(s) in the same year must be identified by the letters "a", "b", "c", etc., placed after the year of publication. **References should be formatted with a hanging indent (i.e., the first line of each reference is flush left while the subsequent lines are indented).**

Examples: Reference to a journal publication: Van der Geer, J., Hanraads, J. A. J., & Lupton R. A. (2000). The art of writing a scientific article. *Journal of Scientific Communications,* 163, 51-59.

Reference to a book: Strunk, W., Jr., &White, E. B. (1979). *The elements of style.* (3rd ed.). New York: Macmillan, (Chapter 4).

Reference to a chapter in an edited book: Mettam, G. R., & Adams, L. B. (1994). How to prepare an electronic version of your article. In B.S. Jones, & R. Z. Smith (Eds.), *Introduction to the electronic age* (pp. 281-304). New York: E-Publishing Inc.

[dataset] Oguro, M., Imahiro, S., Saito, S., Nakashizuka, T. (2015). *Mortality data for Japanese oak wilt disease and surrounding forest compositions.* Mendeley Data, v1. http://dx.doi.org/10.17632/xwj98nb39r.1

Appendix 2: Cochrane RoB 2 Tool Risk of Bias: Cribsheet Rating Form

Revised Cochrane risk-of-bias tool for randomized trials (RoB 2)
SHORT VERSION (CRIBSHEET)

Edited by Julian PT Higgins, Jelena Savović, Matthew J Page, Jonathan AC Sterne
on behalf of the RoB 2 Development Group

Version of 22 August 2019

The development of the RoB 2 tool was supported by the MRC Network of Hubs for Trials Methodology Research (MR/L004933/2- N61), with the support of the host MRC ConDuCT-II Hub (Collaboration and innovation for Difficult and Complex randomised controlled Trials In Invasive procedures - MR/K025643/1), by MRC research grant MR/M025209/1, and by a grant from The Cochrane Collaboration.

Preliminary considerations

Study design

- ☐ Individually-randomized parallel-group trial
- ☐ Cluster-randomized parallel-group trial
- ☐ Individually randomized cross-over (or other matched) trial

For the purposes of this assessment, the interventions being compared are defined as

Experimental: _____ Comparator: _____

Specify which outcome is being assessed for risk of bias _____

Specify the numerical result being assessed. In case of multiple alternative analyses being presented, specify the numeric result (e.g. RR = 1.52 (95% CI 0.83 to 2.77) and/or a reference (e.g. to a table, figure or paragraph) that uniquely defines the result being assessed. _____

Is the review team's aim for this result…?

- ☐ to assess the effect of *assignment to intervention* (the 'intention-to-treat' effect)
- ☐ to assess the effect of *adhering to intervention* (the 'per-protocol' effect)

If the aim is to assess the effect of *adhering to intervention*, select the deviations from intended intervention that should be addressed (at least one must be checked):

- ☐ occurrence of non-protocol interventions
- ☐ failures in implementing the intervention that could have affected the outcome
- ☐ non-adherence to their assigned intervention by trial participants

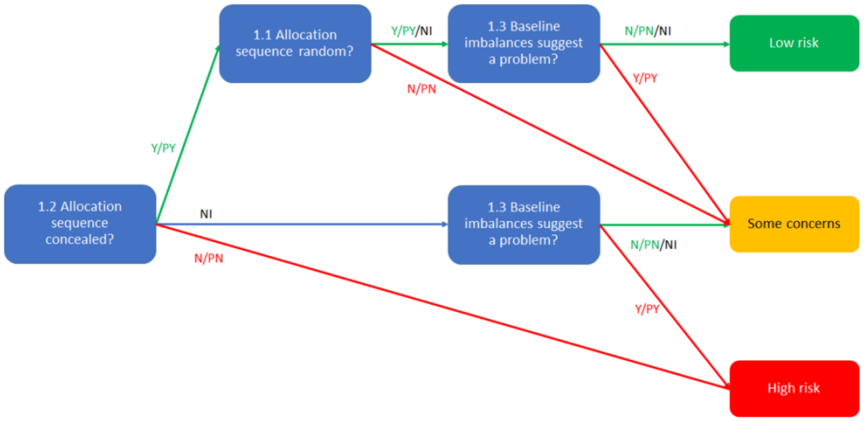
Which of the following sources were <u>obtained</u> to help inform the risk-of-bias assessment? (tick as many as apply)

- ☐ Journal article(s)
- ☐ Trial protocol
- ☐ Statistical analysis plan (SAP)
- ☐ Non-commercial trial registry record (e.g. ClinicalTrials.gov record)
- ☐ Company-owned trial registry record (e.g. GSK Clinical Study Register record)
- ☐ "Grey literature" (e.g. unpublished thesis)
- ☐ Conference abstract(s) about the trial
- ☐ Regulatory document (e.g. Clinical Study Report, Drug Approval Package)
- ☐ Research ethics application
- ☐ Grant database summary (e.g. NIH RePORTER or Research Councils UK Gateway to Research)
- ☐ Personal communication with trialist
- ☐ Personal communication with the sponsor

Domain 1: Risk of bias arising from the randomization process

Signalling questions	Elaboration	Response options
1.1 Was the allocation sequence random?	Answer 'Yes' if a random component was used in the sequence generation process. Examples include computer-generated random numbers; reference to a random number table; coin tossing; shuffling cards or envelopes; throwing dice; or drawing lots. Minimization is generally implemented with a random element (at least when the scores are equal), so an allocation sequence that is generated using minimization should generally be considered to be random. Answer 'No' if no random element was used in generating the allocation sequence or the sequence is predictable. Examples include alternation; methods based on dates (of birth or admission); patient record numbers; allocation decisions made by clinicians or participants; allocation based on the availability of the intervention; or any other systematic or haphazard method. Answer 'No information' if the only information about randomization methods is a statement that the study is randomized. In some situations a judgement may be made to answer 'Probably no' or 'Probably yes'. For example, , in the context of a large trial run by an experienced clinical trials unit, absence of specific information about generation of the randomization sequence, in a paper published in a journal with rigorously enforced word count limits, is likely to result in a response of 'Probably yes' rather than 'No information'. Alternatively, if other (contemporary) trials by the same investigator team have clearly used non-random sequences, it might be reasonable to assume that the current study was done using similar methods.	Y/PY/PN/N/NI
1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?	Answer 'Yes' if the trial used any form of remote or centrally administered method to allocate interventions to participants, where the process of allocation is controlled by an external unit or organization, independent of the enrolment personnel (e.g. independent central pharmacy, telephone or internet-based randomization service providers). Answer 'Yes' if envelopes or drug containers were used appropriately. Envelopes should be opaque, sequentially numbered, sealed with a tamper-proof seal and opened only after the envelope has been irreversibly assigned to the participant. Drug containers should be sequentially numbered and of identical appearance, and dispensed or administered only after they have been irreversibly assigned to the participant. This level of detail is rarely provided in reports, and a judgement may be required to justify an answer of 'Probably yes' or 'Probably no'. Answer 'No' if there is reason to suspect that the enrolling investigator or the participant had knowledge of the forthcoming allocation.	Y/PY/PN/N/NI
1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?	*Note that differences that are compatible with chance do not lead to a risk of bias. A small number of differences identified as 'statistically significant' at the conventional 0.05 threshold should usually be considered to be compatible with chance.* Answer 'No' if no imbalances are apparent or if any observed imbalances are compatible with chance. Answer 'Yes' if there are imbalances that indicate problems with the randomization process, including: (1) substantial differences between intervention group sizes, compared with the intended allocation ratio; or (2) a substantial excess in statistically significant differences in baseline characteristics between intervention groups, beyond that expected by chance; or (3) imbalance in one or more key prognostic factors, or baseline measures of outcome variables, that is very unlikely to be due to chance and for which the between-group difference is big enough to result in bias in the intervention effect estimate. Also answer 'Yes' if there are other reasons to suspect that the randomization process was problematic: (4) excessive similarity in baseline characteristics that is not compatible with chance. Answer 'No information' when there is no *useful* baseline information available (e.g. abstracts, or studies that reported only baseline characteristics of participants in the final analysis). The answer to this question should not influence answers to questions 1.1 or 1.2. For example, if the trial has large baseline imbalances, but authors report adequate randomization methods, questions 1.1 and 1.2 should still be answered on the basis of the reported adequate methods, and any concerns about the imbalance should be raised in the answer to the question 1.3 and reflected in the domain-level risk-of-bias judgement. Trialists may undertake analyses that attempt to deal with flawed randomization by controlling for imbalances in prognostic factors at baseline. To remove the risk of bias caused by problems in the randomization process, it would be necessary to know, and measure, all the prognostic factors that were imbalanced at baseline. It is unlikely that all important prognostic factors are known and measured, so such analyses will at best reduce the risk of bias. If review authors wish to assess the risk of bias in a trial that controlled for baseline imbalances in order to mitigate failures of randomization, the study should be assessed using the ROBINS-I tool.	Y/PY/PN/N/NI
Risk-of-bias judgement	See algorithm.	Low / High / Some concerns

Optional: What is the predicted direction of bias arising from the randomization process?	If the likely direction of bias can be predicted, it is helpful to state this. The direction might be characterized either as being towards (or away from) the null, or as being in favour of one of the interventions.	NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable



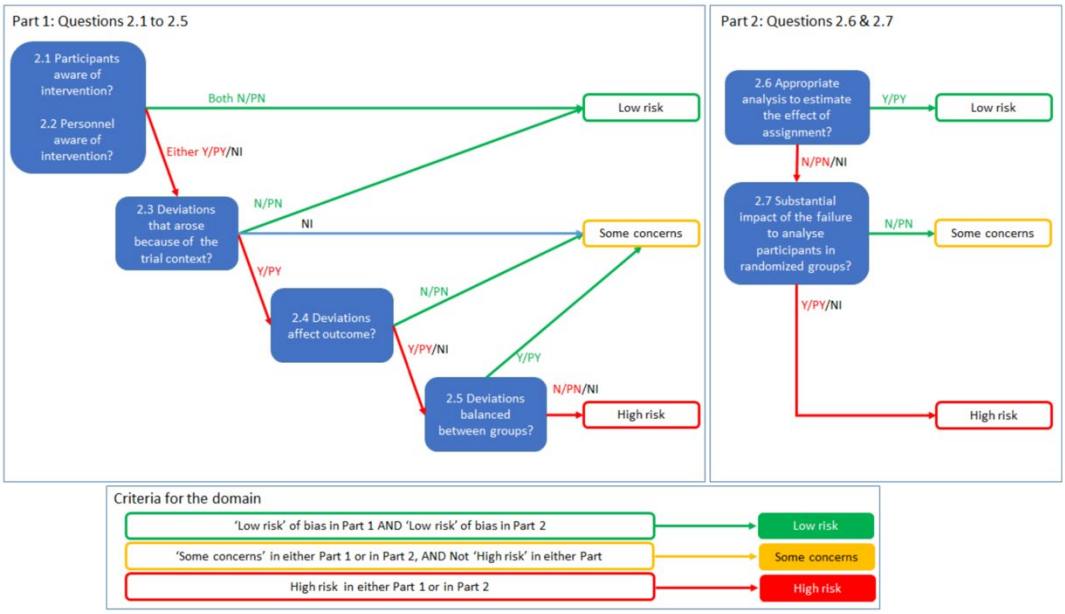
Algorithm for suggested judgement of risk of bias arising from the randomization process

Domain 2: Risk of bias due to deviations from the intended interventions (*effect of assignment to intervention*)

Signalling questions	Elaboration	Response options
2.1. Were participants aware of their assigned intervention during the trial?	If participants are aware of their assigned intervention it is more likely that health-related behaviours will differ between the intervention groups. Blinding participants, most commonly through use of a placebo or sham intervention, may prevent such differences. If participants experienced side effects or toxicities that they knew to be specific to one of the interventions, answer this question 'Yes' or 'Probably yes'.	Y/PY/PN/N/NI
2.2. Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	If carers or people delivering the interventions are aware of the assigned intervention then its implementation, or administration of non-protocol interventions, may differ between the intervention groups. Blinding may prevent such differences. If participants experienced side effects or toxicities that carers or people delivering the interventions knew to be specific to one of the interventions, answer question 'Yes' or 'Probably yes'. If randomized allocation was not concealed, then it is likely that carers and people delivering the interventions were aware of participants' assigned intervention during the trial.	Y/PY/PN/N/NI

2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the trial context?	For the effect of assignment to intervention, this domain assesses problems that arise when changes from assigned intervention that are inconsistent with the trial protocol arose because of the trial context. We use the term **trial context** to refer to effects of recruitment and engagement activities on trial participants and when trial personnel (carers or people delivering the interventions) undermine the implementation of the trial protocol in ways that would not happen outside the trial. For example, the process of securing informed consent may lead participants subsequently assigned to the comparator group to feel unlucky and therefore seek the experimental intervention, or other interventions that improve their prognosis. Answer 'Yes' or 'Probably yes' **only** if there is evidence, or strong reason to believe, that the trial context led to failure to implement the protocol interventions or to implementation of interventions not allowed by the protocol. Answer 'No' or 'Probably no' if there were changes from assigned intervention that are inconsistent with the trial protocol, such as non-adherence to intervention, but these are consistent with what could occur outside the trial context. Answer 'No' or 'Probably no' for changes to intervention that are consistent with the trial protocol, for example cessation of a drug intervention because of acute toxicity or use of additional interventions whose aim is to treat consequences of one of the intended interventions. If blinding is compromised because participants report side effects or toxicities that are specific to one of the interventions, answer 'Yes' or 'Probably yes' only if there were changes from assigned intervention that are inconsistent with the trial protocol and arose because of the trial context. The answer 'No information' may be appropriate, because trialists do not always report whether deviations arose because of the trial context.	NA/Y/PY/PN/N/NI
2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?	Changes from assigned intervention that are inconsistent with the trial protocol and arose because of the trial context will impact on the intervention effect estimate if they affect the outcome, but not otherwise.	NA/Y/PY/PN/N/NI

2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?	Changes from assigned intervention that are inconsistent with the trial protocol and arose because of the trial context are more likely to impact on the intervention effect estimate if they are not balanced between the intervention groups.	NA/Y/PY/PN/N/NI
2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	Both intention-to-treat (ITT) analyses and modified intention-to-treat (mITT) analyses excluding participants with missing outcome data should be considered appropriate. Both naïve 'per-protocol' analyses (excluding trial participants who did not receive their assigned intervention) and 'as treated' analyses (in which trial participants are grouped according to the intervention that they received, rather than according to their assigned intervention) should be considered inappropriate. Analyses excluding eligible trial participants post-randomization should also be considered inappropriate, but post-randomization exclusions of ineligible participants (when eligibility was not confirmed until after randomization, and could not have been influenced by intervention group assignment) can be considered appropriate.	Y/PY/PN/N/NI
2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized?	This question addresses whether the number of participants who were analysed in the wrong intervention group, or excluded from the analysis, was sufficient that there could have been a substantial impact on the result. It is not possible to specify a precise rule: there may be potential for substantial impact even if fewer than 5% of participants were analysed in the wrong group or excluded, if the outcome is rare or if exclusions are strongly related to prognostic factors.	NA/Y/PY/PN/N/NI
Risk-of-bias judgement	See algorithm.	Low / High / Some concerns
Optional: What is the predicted direction of bias due to deviations from intended interventions?	If the likely direction of bias can be predicted, it is helpful to state this. The direction might be characterized either as being towards (or away from) the null, or as being in favour of one of the interventions.	NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

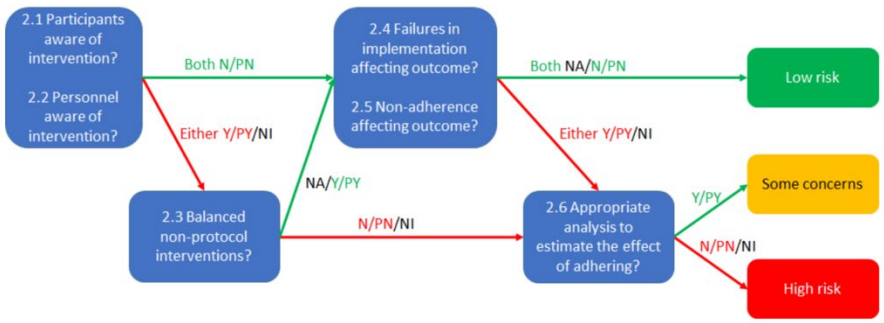


Algorithm for suggested judgement of risk of bias due to deviations from the intended interventions (effect of assignment to intervention)

Domain 2: Risk of bias due to deviations from the intended interventions (*effect of adhering to intervention*)

Signalling questions	Elaboration	Response options
2.1. Were participants aware of their assigned intervention during the trial?	If participants are aware of their assigned intervention it is more likely that health-related behaviours will differ between the intervention groups. Blinding participants, most commonly through use of a placebo or sham intervention, may prevent such differences. If participants experienced side effects or toxicities that they knew to be specific to one of the interventions, answer this question 'Yes' or 'Probably yes'.	Y/PY/PN/N/NI
2.2. Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	If carers or people delivering the interventions are aware of the assigned intervention then its implementation, or administration of non-protocol interventions, may differ between the intervention groups. Blinding may prevent such differences. If participants experienced side effects or toxicities that carers or people delivering the interventions knew to be specific to one of the interventions, answer 'Yes' or 'Probably yes'. If randomized allocation was not concealed, then it is likely that carers and people delivering the interventions were aware of participants' assigned intervention during the trial.	Y/PY/PN/N/NI
2.3. [If applicable:] If Y/PY/NI to 2.1 or 2.2: Were important non-protocol interventions balanced across intervention groups?	This question is asked only if the preliminary considerations specify that the assessment will address imbalance of important non-protocol interventions between intervention groups. Important non-protocol interventions are the additional interventions or exposures that: (1) are inconsistent with the trial protocol; (2) trial participants might receive with or after starting their assigned intervention; and (3) are prognostic for the outcome. Risk of bias will be higher if there is imbalance in such interventions between the intervention groups.	NA/Y/PY/PN/N/NI
2.4. [If applicable:] Were there failures in implementing the intervention that could have affected the outcome?	This question is asked only if the preliminary considerations specify that the assessment will address failures in implementing the intervention that could have affected the outcome. Risk of bias will be higher if the intervention was not implemented as intended by, for example, the health care professionals delivering care. Answer 'No' or 'Probably no' if implementation of the intervention was successful for most participants.	NA/Y/PY/PN/N/NI
2.5. [If applicable:] Was there non-adherence to the assigned intervention regimen that could have affected participants' outcomes?	This question is asked only if the preliminary considerations specify that the assessment will address non-adherence that could have affected participants' outcomes. Non-adherence includes imperfect compliance with a sustained intervention, cessation of intervention, crossovers to the comparator intervention and switches to another active intervention. Consider available information on the proportion of study participants who continued with their assigned intervention throughout follow up, and answer 'Yes' or 'Probably yes' if the proportion who did not adhere is high enough to raise concerns. Answer 'No' for studies of interventions that are administered once, so that imperfect adherence is not possible, and all or most participants received the assigned intervention.	NA/Y/PY/PN/N/NI

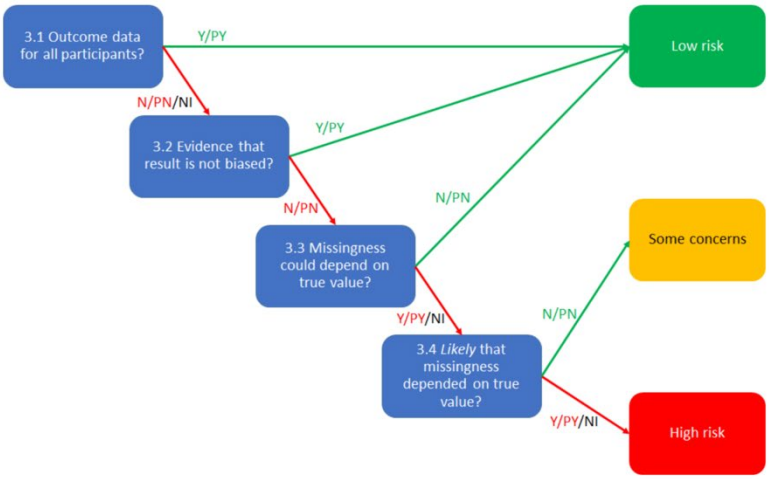
2.6. If N/PN/NI to 2.3, or Y/PY/NI to 2.4 or 2.5: Was an appropriate analysis used to estimate the effect of adhering to the intervention?	Both ' naïve 'per-protocol' analyses (excluding trial participants who did not receive their allocated intervention) and 'as treated' analyses (comparing trial participants according to the intervention they actually received) will usually be inappropriate for estimating the effect of adhering to intervention (the 'per-protocol' effect). However, it is possible to use data from a randomized trial to derive an unbiased estimate of the effect of adhering to intervention. Examples of appropriate methods include: (1) instrumental variable analyses to estimate the effect of receiving the assigned intervention in trials in which a single intervention, administered only at baseline and with all-or-nothing adherence, is compared with standard care; and (2) inverse probability weighting to adjust for censoring of participants who cease adherence to their assigned intervention, in trials of sustained treatment strategies. These methods depend on strong assumptions, which should be appropriate and justified if the answer to this question is 'Yes' or 'Probably yes'. It is possible that a paper reports an analysis based on such methods without reporting information on the deviations from intended intervention, but it would be hard to judge such an analysis to be appropriate in the absence of such information. If an important non-protocol intervention was administered to all participants in one intervention group, adjustments cannot be made to overcome this. Some examples of analysis strategies that would not be appropriate to estimate the effect of adhering to intervention are (i) 'Intention to treat (ITT) analysis', (ii) 'per protocol analysis', (iii) 'as-treated analysis', (iv) 'analysis by treatment received'.	NA/Y/PY/PN/N/NI
Risk-of-bias judgement	See algorithm.	Low / High / Some concerns
Optional: What is the predicted direction of bias due to deviations from intended interventions?	If the likely direction of bias can be predicted, it is helpful to state this. The direction might be characterized either as being towards (or away from) the null, or as being in favour of one of the interventions.	NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable



Algorithm for suggested judgement of risk of bias due to deviations from the intended interventions (effect of adhering to intervention)

Domain 3: Risk of bias due to missing outcome data

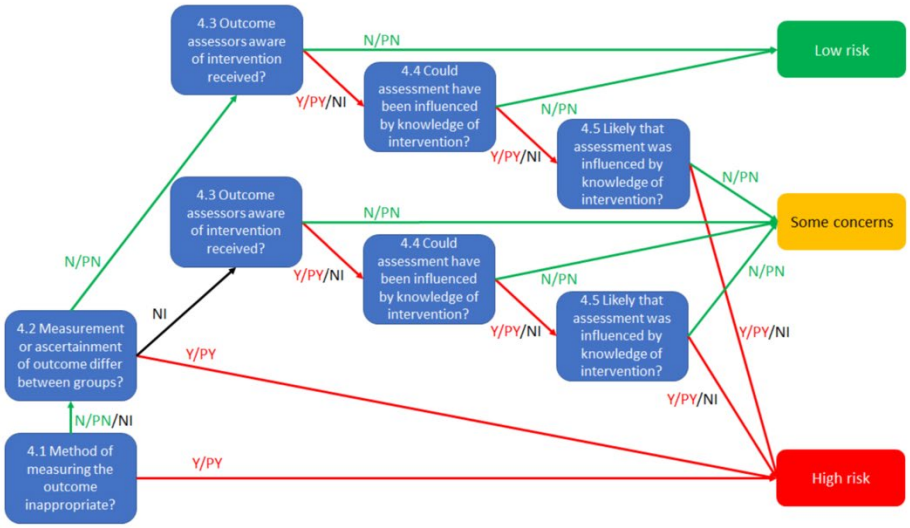
Signalling questions	Elaboration	Response options
3.1 Were data for this outcome available for all, or nearly all, participants randomized?	The appropriate study population for an analysis of the intention to treat effect is all randomized participants. "Nearly all" should be interpreted as that the number of participants with missing outcome data is sufficiently small that their outcomes, whatever they were, could have made no important difference to the estimated effect of intervention. For continuous outcomes, availability of data from 95% of the participants will often be sufficient. For dichotomous outcomes, the proportion required is directly linked to the risk of the event. If the observed number of events is much greater than the number of participants with missing outcome data, the bias would necessarily be small. Only answer 'No information' if the trial report provides no information about the extent of missing outcome data. This situation will usually lead to a judgement that there is a high risk of bias due to missing outcome data. Note that imputed data should be regarded as missing data, and not considered as 'outcome data' in the context of this question.	Y/PY/PN/N/NI
3.2 If N/PN/NI to 3.1: Is there evidence that the result was not biased by missing outcome data?	Evidence that the result was not biased by missing outcome data may come from: (1) analysis methods that correct for bias; or (2) sensitivity analyses showing that results are little changed under a range of plausible assumptions about the relationship between missingness in the outcome and its true value. However, imputing the outcome variable, either through methods such as 'last-observation-carried-forward' or via multiple imputation based only on intervention group, should not be assumed to correct for bias due to missing outcome data.	NA/Y/PY/PN/N
3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	If loss to follow up, or withdrawal from the study, could be related to participants' health status, then it is possible that missingness in the outcome was influenced by its true value. However, if all missing outcome data occurred for documented reasons that are unrelated to the outcome then the risk of bias due to missing outcome data will be low (for example, failure of a measuring device or interruptions to routine data collection). In time-to-event analyses, participants censored during trial follow-up, for example because they withdrew from the study, should be regarded as having missing outcome data, even though some of their follow up is included in the analysis. Note that such participants may be shown as included in analyses in CONSORT flow diagrams.	NA/Y/PY/PN/N/NI
3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	This question distinguishes between situations in which (i) missingness in the outcome could depend on its true value (assessed as 'Some concerns') from those in which (ii) it is likely that missingness in the outcome depended on its true value (assessed as 'High risk of bias'). Five reasons for answering 'Yes' are: 1. Differences between intervention groups in the proportions of missing outcome data. If there is a difference between the effects of the experimental and comparator interventions on the outcome, and the missingness in the outcome is influenced by its true value, then the proportions of missing outcome data are likely to differ between intervention groups. Such a difference suggests a risk of bias due to missing outcome data, because the trial result will be sensitive to missingness in the outcome being related to its true value. For time-to-event-data, the analogue is that rates of censoring (loss to follow-up) differ between the intervention groups. 2. Reported reasons for missing outcome data provide evidence that missingness in the outcome depends on its true value; 3. Reported reasons for missing outcome data differ between the intervention groups; 4. The circumstances of the trial make it likely that missingness in the outcome depends on its true value. For example, in trials of interventions to treat schizophrenia it is widely understood that continuing symptoms make drop out more likely. 5. In time-to-event analyses, participants' follow up is censored when they stop or change their assigned intervention, for example because of drug toxicity or, in cancer trials, when participants switch to second-line chemotherapy. Answer 'No' if the analysis accounted for participant characteristics that are likely to explain the relationship between missingness in the outcome and its true value.	NA/Y/PY/PN/N/NI
Risk-of-bias judgement	See algorithm.	Low / High / Some concerns
Optional: What is the predicted direction of bias due to missing outcome data?	If the likely direction of bias can be predicted, it is helpful to state this. The direction might be characterized either as being towards (or away from) the null, or as being in favour of one of the interventions.	NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable



Algorithm for suggested judgement of risk of bias due to missing outcome data

Domain 4: Risk of bias in measurement of the outcome

Signalling questions	Elaboration	Response options
4.1 Was the method of measuring the outcome inappropriate?	This question aims to identify methods of outcome measurement (data collection) that are unsuitable for the outcome they are intended to evaluate. The question *does not* aim to assess whether the choice of outcome being evaluated was sensible (e.g. because it is a surrogate or proxy for the main outcome of interest). In most circumstances, for pre-specified outcomes, the answer to this question will be 'No' or 'Probably no'. Answer 'Yes' or 'Probably yes' if the method of measuring the outcome is inappropriate, for example because: (1) it is unlikely to be sensitive to plausible intervention effects (e.g. important ranges of outcome values fall outside levels that are detectable using the measurement method); or (2) the measurement instrument has been demonstrated to have poor validity.	Y/PY/PN/N/NI
4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	Comparable methods of outcome measurement (data collection) involve the same measurement methods and thresholds, used at comparable time points. Differences between intervention groups may arise because of 'diagnostic detection bias' in the context of passive collection of outcome data, or if an intervention involves additional visits to a healthcare provider, leading to additional opportunities for outcome events to be identified.	Y/PY/PN/N/NI
4.3 If N/PN/NI to 4.1 and 4.2: Were outcome assessors aware of the intervention received by study participants?	Answer 'No' if outcome assessors were blinded to intervention status. For participant-reported outcomes, the outcome assessor is the study participant.	NA/Y/PY/PN/N/NI
4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	Knowledge of the assigned intervention could influence participant-reported outcomes (such as level of pain), observer-reported outcomes involving some judgement, and intervention provider decision outcomes. They are unlikely to influence observer-reported outcomes that do not involve judgement, for example all-cause mortality.	NA/Y/PY/PN/N/NI
4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	This question distinguishes between situations in which (i) knowledge of intervention status could have influenced outcome assessment but there is no reason to believe that it did (assessed as 'Some concerns') from those in which (ii) knowledge of intervention status was likely to influence outcome assessment (assessed as 'High'). When there are strong levels of belief in either beneficial or harmful effects of the intervention, it is more likely that the outcome was influenced by knowledge of the intervention received. Examples may include patient-reported symptoms in trials of homeopathy, or assessments of recovery of function by a physiotherapist who delivered the intervention.	NA/Y/PY/PN/N/NI
Risk-of-bias judgement	See algorithm.	Low / High / Some concerns
Optional: What is the predicted direction of bias in measurement of the outcome?	If the likely direction of bias can be predicted, it is helpful to state this. The direction might be characterized either as being towards (or away from) the null, or as being in favour of one of the interventions.	NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable



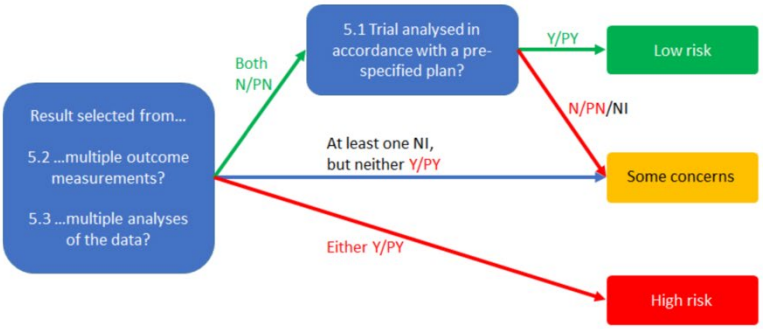
Algorithm for suggested judgement of risk of bias in measurement of the outcome

Domain 5: Risk of bias in selection of the reported result

Signalling questions	Elaboration	Response options
5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?	If the researchers' pre-specified intentions are available in sufficient detail, then planned outcome measurements and analyses can be compared with those presented in the published report(s). To avoid the possibility of selection of the reported result, finalization of the analysis intentions must precede availability of unblinded outcome data to the trial investigators. Changes to analysis plans that were made before unblinded outcome data were available, or that were clearly unrelated to the results (e.g. due to a broken machine making data collection impossible) do not raise concerns about bias in selection of the reported result.	Y/PY/PN/N/NI
Is the numerical result being assessed likely to have been selected, on the basis of the results, from...		
5.2. ... multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	A particular outcome domain (i.e. a true state or endpoint of interest) may be **measured** in multiple ways. For example, the domain pain may be measured using multiple scales (e.g. a visual analogue scale and the McGill Pain Questionnaire), each at multiple time points (e.g. 3, 6 and 12 weeks post-treatment). If multiple measurements were made, but only one or a subset is reported on the basis of the results (e.g. statistical significance), there is a high risk of bias in the fully reported result. Attention should be restricted to outcome measurements that are eligible for consideration by the RoB 2 tool user. For example, if only a result using a specific measurement scale is eligible for inclusion in a meta-analysis (e.g. Hamilton Depression Rating Scale), and this is reported by the trial, then there would not be an issue of selection even if this result was reported (on the basis of the results) in preference to the result from a different measurement scale (e.g. Beck Depression Inventory). Answer 'Yes' or 'Probably yes' if: There is clear evidence (usually through examination of a trial protocol or statistical analysis plan) that a domain was measured in multiple eligible ways, but data for only one or a subset of measures is fully reported (without justification), and the fully reported result is likely to have been selected on the basis of the results. Selection on the basis of the results can arise from a desire for findings to be newsworthy, sufficiently noteworthy to merit publication, or to confirm a prior hypothesis. For example, trialists who have a preconception, or vested interest in showing, that an	Y/PY/PN/N/NI

	experimental intervention is beneficial may be inclined to report outcome measurements selectively that are favourable to the experimental intervention. Answer 'No' or 'Probably no' if: There is clear evidence (usually through examination of a trial protocol or statistical analysis plan) that all eligible reported results for the outcome domain correspond to all intended outcome measurements. or There is only one possible way in which the outcome domain can be measured (hence there is no opportunity to select from multiple measures). or Outcome measurements are inconsistent across different reports on the same trial, but the trialists have provided the reason for the inconsistency and it is not related to the nature of the results. Answer 'No information' if: Analysis intentions are not available, or the analysis intentions are not reported in sufficient detail to enable an assessment, and there is more than one way in which the outcome domain could have been measured.	
5.3 ... multiple eligible analyses of the data?	A particular outcome measurement may be analysed in multiple ways. Examples include: unadjusted and adjusted models; final value vs change from baseline vs analysis of covariance; transformations of variables; different definitions of composite outcomes (e.g. 'major adverse event'); conversion of continuously scaled outcome to categorical data with different cut-points; different sets of covariates for adjustment; and different strategies for dealing with missing data. Application of multiple methods generates multiple effect estimates for a specific outcome measurement. If multiple estimates are generated but only one or a subset is reported on the basis of the results (e.g. statistical significance), there is a high risk of bias in the fully reported result. Attention should be restricted to analyses that are eligible for consideration by the RoB 2 tool user. For example, if only the result from an analysis of post-intervention values is eligible for inclusion in a meta-analysis (e.g. at 12 weeks after randomization), and this is reported by the trial, then there would not be an issue of selection even if this result was reported (on the basis of the results) in preference to the result from an analysis of changes from baseline. Answer 'Yes' or 'Probably yes' if:	Y/PY/PN/N/NI

	There is clear evidence (usually through examination of a trial protocol or statistical analysis plan) that a measurement was analysed in multiple eligible ways, but data for only one or a subset of analyses is fully reported (without justification), and the fully reported result is likely to have been selected on the basis of the results. Selection on the basis of the results arises from a desire for findings to be newsworthy, sufficiently noteworthy to merit publication, or to confirm a prior hypothesis. For example, trialists who have a preconception or vested interest in showing that an experimental intervention is beneficial may be inclined to selectively report analyses that are favourable to the experimental intervention. Answer 'No' or 'Probably no' if: There is clear evidence (usually through examination of a trial protocol or statistical analysis plan) that all eligible reported results for the outcome measurement correspond to all intended analyses. or There is only one possible way in which the outcome measurement can be analysed (hence there is no opportunity to select from multiple analyses). or Analyses are inconsistent across different reports on the same trial, but the trialists have provided the reason for the inconsistency and it is not related to the nature of the results. Answer 'No information' if: Analysis intentions are not available, or the analysis intentions are not reported in sufficient detail to enable an assessment, and there is more than one way in which the outcome measurement could have been analysed.	
Risk-of-bias judgement	See algorithm.	Low / High / Some concerns
Optional: What is the predicted direction of bias due to selection of the reported result?	If the likely direction of bias can be predicted, it is helpful to state this. The direction might be characterized either as being towards (or away from) the null, or as being in favour of one of the interventions.	NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable



Algorithm for suggested judgement of risk of bias in selection of the reported result

Overall risk of bias

Risk-of-bias judgement		Low / High / Some concerns
Optional: What is the overall predicted direction of bias for this outcome?		Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable / NA

Overall risk-of-bias judgement	**Criteria**
Low risk of bias	The study is judged to be at **low risk of bias for all domains** for this result.
Some concerns	The study is judged to raise **some concerns** in at least one domain for this result, but not to be at high risk of bias for any domain.
High risk of bias	The study is judged to be at **high risk of bias** in at least one domain for this result. Or The study is judged to have **some concerns** for **multiple domains** in a way that substantially lowers confidence in the result.

The development of the RoB 2 tool was supported by the MRC Network of Hubs for Trials Methodology Research (MR/L004933/2- N61), with the support of the host MRC ConDuCT-II Hub (Collaboration and innovation for Difficult and Complex randomised controlled Trials In Invasive procedures - MR/K025643/1), by MRC research grant MR/M025209/1, and by a grant from The Cochrane Collaboration.

Appendix 3: Journal of Contextual Behavioural Science Review Author Guidelines

Before You Begin

Authors should prepare their manuscript for double anonymized review, so that only the handling editors have access to author details. Authors must take special care to delete all potentially identifying information from any files that are not the Title Page with author details and the Cover Letter. Note: these two documents are submitted separately to the main manuscript. Any potential author identifying information including, but not limited to, name(s), affiliation(s), geographic location(s), identifying acknowledgments, author notes or funding details, should be removed from all other files. In-text citations to previous work by the authors should be presented in such a way that it is not clear that it was written by the same authors or should be removed for masking with a note (e.g., "citation removed for anonymized review"). For authors resubmitting revisions of manuscripts, please ensure that the "Response to reviewers" is also free from author identifying information. Manuscripts that are not appropriately anonymized will be rejected without a full content review, although in many cases authors will be Study and Analysis Registration to re-submit manuscripts without author identifying information. This process will, however, delay review and manuscript processing times and should be avoided if at all possible.

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A study is considered pre-registered if study details are registered in a repository prior to when the study began. Some examples of repository sites include ClinicalTrials.gov and Open Science Framework, but there are others. For instructions on how to mask your registration details for peer -review, see "Double Anonymized Review" under Preparation.

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Authors should include a statement in the manuscript that informed consent was obtained for experimentation with human subjects. The privacy rights of human subjects must always be observed.

All animal experiments should comply with the ARRIVE guidelines and should be carried out in accordance with the U.K. Animals (Scientific Procedures) Act, 1986 and associated guidelines, EU Directive 2010/63/EU for animal experiments, or the National Research Council's Guide for the Care and Use of Laboratory Animals and the authors should clearly indicate in the manuscript that such guidelines have been followed. The sex of animals must be indicated, and where appropriate, the influence (or association) of sex on the results of the study.

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Reporting guidance

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Definitions

Sex generally refers to a set of biological attributes that are associated with physical and physiological features (e.g., chromosomal genotype, hormonal levels, internal and external anatomy). A binary sex categorization (male/female) is usually designated at birth ("sex assigned at birth"), most often based solely on the visible external anatomy of a newborn. Gender generally refers to socially constructed roles, behaviors, and identities of women, men and gender-diverse people that occur in a historical and cultural context and may vary across societies and over time. Gender influences how people view themselves and each other, how they behave and interact and how power is distributed in society. Sex and gender are often incorrectly portrayed as binary (female/male or woman/man) and unchanging whereas these constructs actually exist along a spectrum and include additional sex categorizations and gender identities such as people who are intersex/have differences of sex development (DSD) or identify as non-binary. Moreover, the terms "sex" and "gender" can be ambiguous—thus it is important for authors to define the manner in which they are used. In addition to this definition guidance and the SAGER guidelines, the resources on this page offer further insight around sex and gender in research studies.

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Divide your article into clearly defined sections. Each subsection is given a brief heading. Each heading should appear on its own separate line. Subsections should be used as much as possible when cross-referencing text: refer to the subsection by heading as opposed to simply 'the text'.

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If there is more than one appendix, they should be identified as A, B, etc. Formulae and equations in appendices should be given separate numbering: Eq. (A.1), Eq. (A.2), etc.; in a subsequent appendix, Eq. (B.1) and so on. Similarly for tables and figures: Table A.1; Fig. A.1, etc.

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Immediately after the abstract, provide a maximum of 6 keywords, using

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Electronic artwork

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You are urged to visit this site; some excerpts from the detailed information are given here.
Formats
If your electronic artwork is created in a Microsoft Office application (Word, PowerPoint, Excel) then please supply 'as is' in the native document format. Regardless of the application used other than Microsoft Office, when your electronic artwork is finalized, please 'Save as' or convert the images to one of the following formats (note the resolution requirements for line drawings, halftones, and line/halftone combinations given below):
EPS (or PDF): Vector drawings, embed all used fonts.
TIFF (or JPEG): Color or grayscale photographs (halftones), keep to a minimum of 300 dpi.
TIFF (or JPEG): Bitmapped (pure black & white pixels) line drawings, keep to a minimum of 1000 dpi.
TIFF (or JPEG): Combinations bitmapped line/half-tone (color or grayscale), keep to a minimum of 500 dpi.
Please do not:
• Supply files that are optimized for screen use (e.g., GIF, BMP, PICT, WPG); these typically have a low number of pixels and limited set of colors;
• Supply files that are too low in resolution;
• Submit graphics that are disproportionately large for the content.

Color artwork
Please make sure that artwork files are in an acceptable format (TIFF (or JPEG), EPS (or PDF) or MS Office files) and with the correct resolution. If, together with your accepted article, you submit usable color figures then Elsevier will ensure, at no additional charge, that these figures will appear in color online (e.g., ScienceDirect and other sites) in addition to color reproduction in print. Further information on the preparation of electronic artwork.

Figure captions
Ensure that each illustration has a caption. Supply captions separately, not attached to the figure. A caption should comprise a brief title (**not** on the figure itself) and a description of the illustration. Keep text in the illustrations themselves to a minimum but explain all symbols and abbreviations used.

Tables

Please submit tables as editable text and not as images. In accordance with APA style, tables should be placed on separate page(s) at the end of the manuscript. Number tables consecutively in accordance with their appearance in the text and place any table notes below the table body. Be sparing in the

use of tables and ensure that the data presented in them do not duplicate results described elsewhere in the article. Please avoid using vertical rules and shading in table cells.

References

Citation in text

Please ensure that every reference cited in the text is also present in the reference list (and vice versa). Any references cited in the abstract must be given in full. Unpublished results and personal communications are not recommended in the reference list. If these references are included in the reference list they should follow the standard reference style of the journal and should include a substitution of the publication date with either 'Unpublished results' or 'Personal communication'. Citation of a reference as 'in press' implies that the item has been accepted for publication.

Appendix 4: Email issuing Ethical Approval by NHS Integrated Research Approval Service with documents attached

From: berkshireb.rec@hra.nhs.uk <noreply@harp.org.uk>
Date: Tuesday, 15 February 2022 at 08:45
To: RYAN Anna < >, GILLANDERS David
< >
Cc: CAHSS Research ethics <Cahss.res.ethics@ed.ac.uk>, RYAN Anna <
>, < >
Subject: IRAS 304810. HRA & HCRW Approval issued

Dear Miss Ryan

RE: IRAS 304810 ACT web-based intervention for IBS patients: a feasibility study. . HRA & HCRW Approval issued

Please find attached your HRA and HCRW letter of Approval.

Please also find attached your REC Favourable Opinion letter. Please note, the standard conditions referenced in your REC favourable opinion letter as being attached ("After ethical review – guidance for researchers") can now be accessed through the HRA website.

You may now commence your study at those participating NHS organisations in England and Wales that have confirmed their capacity and capability to undertake their role in your study (where applicable). Detail on what form this confirmation should take, including when it may be assumed, is provided in the HRA and HCRW Approval letter.

User Feedback

The Health Research Authority is continually striving to provide a high quality service to all applicants and sponsors. You are invited to give your view of the service you have received and the application procedure. If you wish to make your views known please use the feedback form available on the HRA website: https://www.hra.nhs.uk/about-the-hra/governance/quality-assurance/.

If you have any queries please do not hesitate to contact me.

Kind regards

Claudia Bywater
Approvals Manager
T. 0207 104 8253
E. berkshireb.rec@hra.nhs.uk
W. www.hra.nhs.uk

Appendix 5: HRA Approval (England sites)

Ymchwil Iechyd a Gofal Cymru
Health and Care Research Wales

NHS
Health Research Authority

Miss Anna Ryan
284 Rosemount Place
2nd Floor Right
Aberdeen
AB25 2YAN/A

Email: approvals@hra.nhs.uk
HCRW.approvals@wales.nhs.uk

15 February 2022

Dear Miss Ryan

HRA and Health and Care Research Wales (HCRW) Approval Letter

Study title:	**Investigating the delivery of an acceptance and commitment therapy (ACT) web-based intervention on symptomology in adult IBS patients: a feasibility study.**
IRAS project ID:	**304810**
Protocol number:	**CAHSS2109/15**
REC reference:	**22/SC/0039**
Sponsor	**University of Edinburgh**

I am pleased to confirm that **HRA and Health and Care Research Wales (HCRW) Approval** has been given for the above referenced study, on the basis described in the application form, protocol, supporting documentation and any clarifications received. You should not expect to receive anything further relating to this application.

Please now work with participating NHS organisations to confirm capacity and capability, in line with the instructions provided in the "Information to support study set up" section towards the end of this letter.

How should I work with participating NHS/HSC organisations in Northern Ireland and Scotland?
HRA and HCRW Approval does not apply to NHS/HSC organisations within Northern Ireland and Scotland.

If you indicated in your IRAS form that you do have participating organisations in either of these devolved administrations, the final document set and the study wide governance report (including this letter) have been sent to the coordinating centre of each participating nation. The relevant national coordinating function/s will contact you as appropriate.

Please see IRAS Help for information on working with NHS/HSC organisations in Northern Ireland and Scotland.

How should I work with participating non-NHS organisations?
HRA and HCRW Approval does not apply to non-NHS organisations. You should work with your non-NHS organisations to obtain local agreement in accordance with their procedures.

What are my notification responsibilities during the study?

The standard conditions document "*After Ethical Review – guidance for sponsors and investigators*", issued with your REC favourable opinion, gives detailed guidance on reporting expectations for studies, including:

- Registration of research
- Notifying amendments
- Notifying the end of the study

The HRA website also provides guidance on these topics, and is updated in the light of changes in reporting expectations or procedures.

Who should I contact for further information?
Please do not hesitate to contact me for assistance with this application. My contact details are below.

Your IRAS project ID is **304810**. Please quote this on all correspondence.

Yours sincerely,
Claudia Bywater

Approvals Manager

Email: approvals@hra.nhs.uk

Copy to: *Miss Charlotte Smith*

List of Documents

The final document set assessed and approved by HRA and HCRW Approval is listed below.

Document	*Version*	*Date*
Evidence of Sponsor insurance or indemnity (non NHS Sponsors only)		
IRAS Application Form [IRAS_Form_14012022]		14 January 2022
Letters of invitation to participant [Reminder: web-based ACT for IBS]	1	23 December 2021
Other [Response to Action Points]		
Participant consent form [Consent Form]	2	04 February 2022
Participant information sheet (PIS) [PIS]	2	04 February 2022
Research protocol or project proposal [Protocol]	2	11 February 2022
Summary CV for Chief Investigator (CI) [CV CI]		20 September 2021
Summary CV for supervisor (student research)		01 March 2021

IRAS project ID	304810

Information to support study set up

The below provides all parties with information to support the arranging and confirming of capacity and capability with participating NHS organisations in England and Wales. This is intended to be an accurate reflection of the study at the time of issue of this letter.

Types of participating NHS organisation	Expectations related to confirmation of capacity and capability	Agreement to be used	Funding arrangements	Oversight expectations	HR Good Practice Resource Pack expectations
NHS organisations in this study will act as Participant Identification Centres (PICs).	PIC activities should not commence until a PIC Agreement is in place. HRA and HCRW recommend use of the standard Participating NHS Organisation to PIC agreement available here.	HRA and HCRW recommend use of the standard Participating NHS Organisation to PIC agreement.	No application for external funding has been made.	The chief investigator will be responsible for all PIC related activities.	It is not expected that any HR arrangements will be necessary.

Other information to aid study set-up and delivery

This details any other information that may be helpful to sponsors and participating NHS organisations in England and Wales in study set-up.
The applicant has indicated that they do not intend to apply for inclusion on the NIHR CRN Portfolio.

Appendix 6: HRA Approval (Scotland sites)

NHS
Health Research Authority
South Central - Berkshire B Research Ethics Committee
The Old Chapel
Royal Standard Place
Nottingham
NG1 6FS

Telephone: 0207 104 8253

Please note: This is the favourable opinion of the REC only and does not allow you to start your study at NHS sites in England until you receive HRA Approval

15 February 2022

Miss Anna Ryan
284 Rosemount Place
2nd Floor Right
Aberdeen
AB25 2YA

Dear Miss Ryan

Study title:	**Investigating the delivery of an acceptance and commitment therapy (ACT) web-based intervention on symptomology in adult IBS patients: a feasibility study.**
REC reference:	**22/SC/0039**
Protocol number:	**CAHSS2109/15**
IRAS project ID:	**304810**

Thank you for your letter of 09 February 2022, responding to the Proportionate Review Sub-Committee's request for changes to the documentation for the above study.

The revised documentation has been reviewed and approved on behalf of the PR sub-committee.

Confirmation of ethical opinion

On behalf of the Research Ethics Committee (REC), I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised.

Good practice principles and responsibilities

The UK Policy Framework for Health and Social Care Research sets out principles of good practice in the management and conduct of health and social care research. It also outlines the responsibilities of individuals and organisations, including those related to the four elements of research transparency:

1. registering research studies
2. reporting results
3. informing participants
4. sharing study data and tissue

Conditions of the favourable opinion

The REC favourable opinion is subject to the following conditions being met prior to the start of the study.

Confirmation of Capacity and Capability (in England, Northern Ireland and Wales) or NHS management permission (in Scotland) should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements. Each NHS organisation must confirm through the signing of agreements and/or other documents that it has given permission for the research to proceed (except where explicitly specified otherwise).

Guidance on applying for HRA and HCRW Approval (England and Wales)/ NHS permission for research is available in the Integrated Research Application System.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of management permissions from host organisations.

Registration of Clinical Trials

All research should be registered in a publicly accessible database and we expect all researchers, research sponsors and others to meet this fundamental best practice standard.

It is a condition of the REC favourable opinion that **all clinical trials are registered** on a publicly accessible database within six weeks of recruiting the first research participant. For this purpose, 'clinical trials' are defined as:

- clinical trial of an investigational medicinal product
- clinical investigation or other study of a medical device
- combined trial of an investigational medicinal product and an investigational medical device
- other clinical trial to study a novel intervention or randomised clinical trial to compare interventions in clinical practice.

Failure to register a clinical trial is a breach of these approval conditions, unless a deferral has been agreed by the HRA (for more information on registration and requesting a deferral see: Research registration and research project identifiers).

If you have not already included registration details in your IRAS application form you should notify the REC of the registration details as soon as possible.

Publication of Your Research Summary

We will publish your research summary for the above study on the research summaries section of our website, together with your contact details, no earlier than three months from the date of this favourable opinion letter.

Should you wish to provide a substitute contact point, make a request to defer, or require further information, please visit:
https://www.hra.nhs.uk/planning-and-improving-research/application-summaries/research-summaries/

N.B. If your study is related to COVID-19 we will aim to publish your research summary within 3 days rather than three months.

During this public health emergency, it is vital that everyone can promptly identify all relevant research related to COVID-19 that is taking place globally. If you haven't already done so, please register your study on a public registry as soon as possible and provide the REC with the registration detail, which will be posted alongside other information relating to your project. We are also asking sponsors not to request deferral of publication of research summary for any projects relating to COVID-19. In addition, to facilitate finding and extracting studies related to COVID-19 from public databases, please enter the WHO official acronym for the coronavirus disease (COVID-19) in the full title of your study. Approved COVID-19 studies can be found at:
https://www.hra.nhs.uk/covid-19-research/approved-covid-19-research/

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

After ethical review: Reporting requirements

The attached document "After ethical review – guidance for researchers" gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study, including early termination of the study
- Final report
- Reporting results

The latest guidance on these topics can be found at
https://www.hra.nhs.uk/approvals-amendments/managing-your-approval/.

Ethical review of research sites

The favourable opinion applies to all NHS/HSC sites taking part in the study, subject to

management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" above).

Approved documents

The documents reviewed and approved by the Committee are:

Document	*Version*	*Date*
Evidence of Sponsor insurance or indemnity (non NHS Sponsors only)		
IRAS Application Form [IRAS_Form_14012022]		14 January 2022
Letters of invitation to participant [Reminder: web-based ACT for IBS]	1	23 December 2021
Other [Response to Action Points]		
Participant consent form [Consent Form]	2	04 February 2022
Participant information sheet (PIS) [PIS]	2	04 February 2022
Research protocol or project proposal [Protocol]	2	11 February 2022
Summary CV for Chief Investigator (CI) [CV CI]		20 September 2021
Summary CV for supervisor (student research)		01 March 2021

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

User Feedback

The Health Research Authority is continually striving to provide a high quality service to all applicants and sponsors. You are invited to give your view of the service you have received and the application procedure. If you wish to make your views known please use the feedback form available on the HRA website:
http://www.hra.nhs.uk/about-the-hra/governance/quality-assurance/

HRA Learning

We are pleased to welcome researchers and research staff to our HRA Learning Events and online learning opportunities– see details at:
https://www.hra.nhs.uk/planning-and-improving-research/learning/

IRAS project ID: 304810	**Please quote this number on all correspondence**

With the Committee's best wishes for the success of this project.

Yours sincerely

Pp

Ms Sue Harrison
Chair

Email: berkshireb.rec@hra.nhs.uk

Enclosures: "After ethical review – guidance for researchers"

Copy to: Miss Charlotte Smith

Lead Nation England: approvals@hra.nhs.uk

Appendix 7: Substantial Amendment approval (Imperial)

NHS
Health Research Authority

South Central - Berkshire B Research Ethics Committee
The Old Chapel
Royal Standard Place
Nottingham
NG1 6FS

Tel: +442071048276

Please note: This is the favourable opinion of the REC only and does not allow the amendment to be implemented at NHS sites in England until the outcome of the HRA assessment has been confirmed.

10 August 2022

Miss Anna Ryan
284 Rosemount Place
2nd Floor Right
Aberdeen
AB25 2YA

Dear Miss Ryan

Study title:	**Investigating the delivery of an acceptance and commitment therapy (ACT) web-based intervention on symptomology in adult IBS patients: a feasibility study.**
REC reference:	**22/SC/0039**
Protocol number:	**CAHSS2109/15**
Amendment number:	**Substantial Amendment 1**
Amendment date:	**24 June 2022**
IRAS project ID:	**304810**

The above amendment was reviewed by the Sub-Committee in correspondence.

Ethical opinion

The members of the Committee taking part in the review gave a favourable ethical opinion of the amendment on the basis described in the notice of amendment form and supporting documentation.

Approved documents

The documents reviewed and approved at the meeting were:

Document	*Version*	*Date*
Completed Amendment Tool [Updated AT with correct categorisation]	1.6	20 July 2022

Membership of the Committee

The members of the Committee who took part in the review are listed on the attached sheet.

Working with NHS Care Organisations

Sponsors should ensure that they notify the R&D office for the relevant NHS care organisation of this amendment in line with the terms detailed in the categorisation email issued by the lead nation for the study.

Amendments related to COVID-19

We will update your research summary for the above study on the research summaries section of our website. During this public health emergency, it is vital that everyone can promptly identify all relevant research related to COVID-19 that is taking place globally. If you have not already done so, please register your study on a public registry as soon as possible and provide the HRA with the registration detail, which will be posted alongside other information relating to your project.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

HRA Learning

We are pleased to welcome researchers and research staff to our HRA Learning Events and online learning opportunities– see details at: https://www.hra.nhs.uk/planning-and-improving-research/learning/

IRAS Project ID - 304810:	**Please quote this number on all correspondence**

Yours sincerely

Dr Thomas Woodcock
Meeting Chair

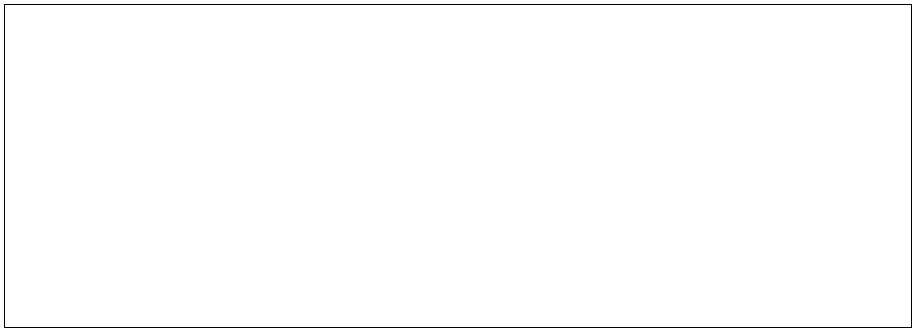
E-mail: berkshireb.rec@hra.nhs.uk

Enclosures: *List of names and professions of members who took part in the review*

Copy to: *Miss Anna Ryan*

Appendix 8: NHS Lothian Research and Development Department Approval

Queen's Medical Research Institute



Substantial amendments to the protocol will require approval from the ethics committee which approved your study and the MHRA where applicable.

Data controllers and processors have a legal obligation to hold a register of all its information assets (e.g. personal information (data) and/or special categories of personal data held in paper or electronic format for the purpose of clinical research). This R&D management approval is given on the understanding that you, as a potential information asset owner, will register any information assets associated with this research project with your employing organisation (where the data is held) in accordance the Data Protection Act 2018.

Please keep this office informed of the following study information, **which is a condition of NHS Lothian R&D Management Approval**:

1. Date you are ready to begin recruitment, date of the recruitment of the first participant and the monthly recruitment figures thereafter.
2. Date the final participant is recruited and the final recruitment figures.
3. Date your study / trial is completed within NHS Lothian.

I wish you every success with your study.

Yours sincerely

Fiona McArdle (Jul 29, 2022 16:05 GMT+1)

Ms Fiona McArdle
Deputy R&D Director

CC: Miss Anna Ryan, Chief Investigator, University of Edinburgh
Miss Charlotte Smith, Research Governance Coordinator, University of Edinburgh
Mr Chris Stirling, Hospital Director, WGH, NHS Lothian
Ms Caroline Whitworth, Associate Medical Director for Surgery, RIE, NHS Lothian

Approval - LOT (2022.0036), 29.07.22

Final Audit Report 2022-07-29

Created:	2022-07-29
By:	Lesley Saeed (v1lmore@exseed.ed.ac.uk)
Status:	Signed
Transaction ID:	CBJCHBCAABAA8w0XJpBTfVRXJWTUg5K24QKW14kg7vf0

"Approval - LOT (2022.0036), 29.07.22" History

Document created by Lesley Saeed (v1lmore@exseed.ed.ac.uk)
2022-07-29 - 2:56:22 PM GMT- IP address: 62.253.82.232

Document emailed to Fiona McArdle (fiona.mcardle@nhslothian.scot.nhs.uk) for signature
2022-07-29 - 2:57:09 PM GMT

Email viewed by Fiona McArdle (fiona.mcardle@nhslothian.scot.nhs.uk)
2022-07-29 - 3:04:55 PM GMT- IP address: 104.47.1.254

Document e-signed by Fiona McArdle (fiona.mcardle@nhslothian.scot.nhs.uk)
Signature Date: 2022-07-29 - 3:05:07 PM GMT - Time Source: server- IP address: 62.253.82.231

Agreement completed.
2022-07-29 - 3:05:07 PM GMT

Adobe Acrobat Sign

Appendix 9: Approval from NHS Grampian Research and Development Department

Research and Development

Dr Francesca Moroni
NHS Grampian
Gastroenterology
Aberdeen Royal Infirmary
Foresterhill
Aberdeen

Dear Dr. Moroni,

Management Permission for Non-Commercial Research

STUDY TITLE:	Investigating the delivery of an acceptance and commitment therapy (ACT) web-based intervention on symptomology in adult IBS patients: a feasibility study
PROTOCOL NO:	304810
REC REF:	22/PR/0050
IRAS REF:	V2, 11.2.22

Thank you very much for sending all relevant documentation. I am pleased to confirm that the project is now registered with the NHS Grampian Research & Development Office. The project now has R & D Management Permission to proceed locally. This is based on the documents received from yourself and the relevant Approvals being in place.

All research with an NHS element is subject to the UK Policy Framework for Health and Social Care Research (2017 v3), and as Chief or Principal Investigator you should be fully committed to your responsibilities associated with this.

R&D Permission is granted on condition that:

1) **The R&D Office will be notified and any relevant documents forwarded to us if any of the following occur:**
   - **Any Serious Breaches in Grampian (Please forward to pharmaco@abdn.ac.uk).**
   - **A change of Principal Investigator in Grampian or Chief Investigator.**
   - **Any change to funding or any additional funding**

2) **When the study ends, the R&D Office will be notified of the study end-date.**

3) **The Sponsor will notify all amendments to the relevant National Co-ordinating centre. For single centre studies, amendments should be notified to the R&D office directly.**

We hope the project goes well, and if you need any help or advice relating to your R&D Management Permission, please do not hesitate to contact the office.

Yours sincerely

Susan Ridge
Non-Commercial Manager

cc: CI Ms Anna Ryan
Research Monitor
Dr Nicola Price
Dr Rituka Richardson
Ms Louise Osborne

Sponsor: University of Edinburgh

Appendix 10: Approval from Imperial College Healthcare NHS Trust PIC Site

Dear Dr Casburn-Jones,

Study Title: Investigating the delivery of an acceptance and commitment therapy (ACT) web-based intervention on symptomology in adult IBS patients: a feasibility study.

Documas No.: 22SM7813

REC Reference No.: 22/SC/0039

Initial study capacity and capability confirmation up to amendment SA1

I can confirm that Imperial College Healthcare NHS Trust has the capacity and capability to deliver the above referenced study as a PIC site. This means participants referral to the research site(s) may now start at Imperial College Healthcare NHS Trust sites.

The capacity and capability is confirmed based on the following approvals:

Documents	Date
Initial approvals	
HRA Approval	15/02/22
NRES – Favourable opinion	15/02/22
SA1	
HRA confirmation of amendment assessment	10/08/22
NRES – favourable opinion	10/08/22

Before you commence your research, please note that you must be aware of your obligations to comply with the minimum requirements for compliance with the UK policy framework indicators – Researcher teams (9.6) and Research sites (9.14) (Details of the requirements to be met can be found in the on the UK policy framework for health and social care on https://www.hra.nhs.uk/

Under the UK policy framework regulations, Serious Adverse Event Reports and amendments to the protocol or other supporting documents must be forwarded to the Joint Research Compliance Office.

In accordance with the UK Policy Framework for health and social care, research projects carried out in the Trust will be randomly chosen by the Research Governance Integrity Team for auditing.

Thank you.

Kind Regards,

Tara

Tara Tamang | Senior Research Facilitator - Medicine & Integrated Care | Imperial College Healthcare NHS Trust

✉ | ☎ Working from home | www.imperial.nhs.uk | @ImperialNHS

***KIND** - We are considerate and thoughtful | **EXPERT** - We draw on our diverse skills | **COLLABORATIVE** - We actively seek others' views and ideas | **ASPIRATIONAL** - We are receptive and responsive to new thinking*

In relation to the set-up of your study, the Division would like to receive feedback on your experience with our feasibility service. Please complete the survey here.

Appendix 11: Participant Information Centre (PIC) Agreement between Imperial College Healthcare NHS Trust and NHS Grampian

MODEL NON-COMMERCIAL PARTICIPANT IDENTIFICATION CENTRE AGREEMENT (TRIAL SITE TO PIC)

Grampian Health Board constituted pursuant to the National Health Service (Scotland) Act 1978 (as amended) and having its headquarters at Summerfield House, 2 Eday Road, Aberdeen. AB15 6RE

(referred to as "**the Trial Site**")

AND

Imperial College Healthcare NHS Trust
The Bays
South Wharf Road
St Mary's Hospital
London W2 1NY

(referred to as "**the PIC**")

Which are collectively referred to as the "**Parties**" or individually referred to as a "**Party**"

NOW

WHEREAS the Sponsor is a University of Edinburgh

WHEREAS there is no external funding (student project)

WHEREAS the Trial Site wishes to sub-contract with the PIC to undertake Data Processing for the purpose of identifying potential Participants for the Study;

WHEREAS the Study is multi-centred, having more than one investigator site;

WHEREAS the Study is a Qualitative study

In respect of the clinical research Study entitled INVESTIGATING THE DELIVERY OF AN ACCEPTANCE AND COMMITMENT THERAPY (ACT) WEB-BASED INTERVENTION ON SYMPTOMOLOGY IN ADULT IBS PATIENTS: A FEASIBILITY STUDY **the above Parties HEREBY AGREE AS FOLLOWS:**

1. Definitions

1.1 The following words and phrases have the following meanings:

- **Agent(s)**
  includes, but shall not be limited to, any person undertaking a function in connection with this Agreement (including the Principal Investigator, any nurse or other health professional), any such person's principal employer in the event it is not the Trial Site or PIC and where such person is providing services to a Party under a contract for services or otherwise (including clinical academics), and/or any contracted third party providing services to a Party under a contract for services or otherwise;

- **Agreement**
  this Agreement, together with the schedules annexed hereto;

- **Controller**
  shall have the meaning set out in the Data Protection Legislation;

- **Data Protection Legislation**
  means the GDPR, the Data Protection Act 2018, the Privacy and Electronic Communications (EC Directive) Regulations 2003, as well as any legally enforceable NHS requirements, Codes of Practice or Guidance issued by the Information Commissioner's Office, in each case in force from time to time in England, Northern Ireland, Scotland and/or Wales;

- **Data Subject**
  as defined in the Data Protection Legislation;

- **GDPR**
  means Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, as it forms part of the law of England and Wales, Scotland and Northern Ireland by virtue of section 3 of the European Union (Withdrawal) Act 2018 and as amended by the Data Protection, Privacy and Electronic Communications (Amendments etc) (EU Exit) Regulations 2019;

- **Participant**

  any person who consents (where consent is necessary) and is enrolled to take part in the Study. All references to Participants in this Agreement should be construed to include potential Participants who are identified by and referred by or through the Trial Site;

- **Trial Site**
  the NHS/HSC organisation named on page one of this Agreement, being an NHS/HSC organisation contracted by the Sponsor to Process Personal Data on behalf of the Sponsor to identify potential Participants for the Study;;

- **Personal Data**
  any and all information, data and material of any nature received or obtained by any Party in connection with this Agreement which is personal data as defined in Data Protection Legislation and which relates to any Participant or their treatment or medical history;

- **Participant Identification Centre (PIC)**
  the organisation named on page one of this Agreement, being an organisation sub-contracted by the Trial Site to Process Personal Data on behalf of the Sponsor to identify potential Participants for the Study;

- **Principal Investigator or PI**
  the leader responsible for a team of individuals conducting the Study at the Trial Site;

- **Process**
  as defined in the Data Protection Legislation (and "Process" and "Processed" shall be construed accordingly);

- **Processor**
  shall have the meaning as set out in the Data Protection Legislation;

- **Protocol**
  the full description of the Study with the reference number set out on the front page of this Agreement, together with any amendments thereof, and incorporated into this Agreement by reference. Reference in the Agreement to Protocol should be construed to include reference to the clinical investigation plan for the Study, where the Study is a clinical investigation of a medical device;

- **Sponsor**
  the individual, company, institution or organisation that is (or the institutions or organisations, where there is more than one sponsor under a co-sponsorship or joint-sponsorship arrangement, that are), that takes responsibility for the initiation, management and financing (or arranging the financing) of the Study;

- **Study**
  the clinical research study that is the subject of this Agreement;

- **Sub-Processor**
  the PIC contracted by the Trial Site to Process Personal Data on behalf of the Sponsor (as per GDPR Article 28, 2).

1.2 Any reference to a statutory provision, code or guidance shall be deemed to include reference to any subsequent modification or re-enactment of it.

2. General

2.1 As the mutual exchange of obligations and promises is regarded as consideration, this Agreement forms a legally binding contract.

2.2 The PIC will Process Personal Data to identify potential Study Participants as follows:

2.2.1 The PIC will undertake identification of potential Participants by Gastroenterologists identifying suitable participants attending outpatient appointments meeting the following criteria:

a. INCLUSION CRITERIA

Individuals aged 18 and over diagnosed with IBS according to the ROME-IV criteria by NHS-based Gastroenterology consultants. Individuals with access to a device which can access the online intervention.

EXCLUSION CRITERIA

Individuals continuing testing for other gastroenterology-related issues or experiencing symptomology suggestive of Inflammatory Bowel Disease (or similar). Patients with severe psychiatric difficulties, suicidality, psychosis, terminal illness, intellectual disability, cognitive impairment, brain injury, substance misuse; inability to give informed consent in English and an inability to understand written and spoken English.

2.2.2 The PIC will be provided with the following information to provide to potential participants:

a. Current Patient Information sheet

2.2.3 Potential Participants will be approached by PIC staff at usual clinic visits

2.2.4 The PIC will use its best endeavours to identify as many potential Participants as possible until March 2023 inc.

2.3 By entering into this Agreement, the Parties agree that the conduct of the Study at the PIC is governed by and subject to the national laws and regulations of the PIC. However any other issue, including any issue as to the construction of this Agreement, shall be governed and construed in accordance with the laws governing the country of the United Kingdom in which the Sponsor is established (or by which the mNCA, to which this Agreement is a sub-agreement, is governed

and construed in accordance with Clause 18.2 of that mNCA), namely, the laws of England and Wales or Scotland and shall be subject to the exclusive jurisdiction of the Courts of that country. Save, that where both Parties agree, having taken into consideration that it would be more reasonable and expeditious both as to time and costs, in such instance to do so, for the agreed issue pertaining to this Agreement, to be subject to the jurisdiction of the defendant.

3. Confidentiality and Data Protection

Confidentiality

3.1 The Parties agree to comply with all applicable statutory requirements and mandatory codes of practice in respect of confidentiality (including medical confidentiality) in relation to Participants and persons identified as potential Participants.

3.2 The PIC agrees to treat the Confidential Information in this Agreement (including the Protocol) and the Results, excluding any Clinical Data of the Study, as Confidential Information of the Trial Site and the Trial Site agrees to treat Personal Data and confidential patient information as Confidential Information.

Data Processing Terms

3.3 For the purposes of the Data Protection Legislation, the Sponsor is the Controller, the Trial Site is the Sponsor's Processor and the PIC is the Sub-Processor of the Trial Site in relation to all Processing of Personal Data that is Processed for the purpose of this Study and for any future research use under the Controllership of the Sponsor, that would not have taken place but for this Agreement regardless where that Processing takes place.

3.4 The Parties acknowledge that whereas the Sponsor is the Controller in accordance with Clause 3.3, the PIC is the Controller of the Personal Data Processed for the purpose of providing clinical care to the persons identified as potential Participants. This Personal Data may be the same Personal Data, collected transparently and processed for research and for care purposes under the separate Controllerships of the Sponsor and PIC.

3.5 Where the PIC is the Trial Site's Sub-Processor and thus where the Processing is undertaken by the PIC for the purposes of the Study, Clauses 3.6 to 3.10 below will apply. For the avoidance of doubt, such Clauses do not apply where the PIC is Processing the Participant Personal Data as a Controller.

3.6 The PIC agrees only to Process Personal Data for and on behalf of the Trial Site in accordance with the instructions of the Trial Site or Sponsor and for the purpose of the Study and to ensure the Sponsor's and Trial Site's compliance with the Data Protection Legislation.

3.7 The PIC agrees to comply with the obligations applicable to Processors described by Article 28 GDPR including, but not limited to, the following:

3.7.1 to implement and maintain appropriate technical and organisational security measures sufficient to comply at least with the obligations imposed on the Controller by GDPR Article 28(1);

3.7.2 to not engage another Processor without the prior written authorisation of the Sponsor (GDPR Article 28(2));

3.7.3 to Process the Personal Data only on documented instructions from the Trial Site or Sponsor unless required to do otherwise by legislation, in which case the PIC shall notify the Trial Site before Processing, or as soon as possible after Processing if legislation requires that the Processing occurs immediately, unless legislation prohibits such notification on important grounds of public interest (GDPR Article 28(3)(a));

3.7.4 to ensure that personnel authorised to Process Personal Data are under confidentiality obligations (GDPR Article 28(3)(b));

3.7.5 to take all measures required by GDPR Article 32 in relation to the security of processing (GDPR Article 28(3)(c));

3.7.6 to respect the conditions described in GDPR Article 28(2) and (4) for engaging another Processor (GDPR Article 28(3)(d));

3.7.7 to, taking into account the nature of the Processing, assist the Trial Site and/or the Sponsor, by appropriate technical and organisational measures, insofar as this is possible, to respond to requests for exercising Data Subjects' rights (GDPR Article 28(3)(e));

3.7.8 to assist the Controller, to ensure compliance with the obligations pursuant to GDPR Articles 32 to 36 taking into account the nature of the Processing and the information available to the PIC (GDPR Article 28(3)(f));

3.7.9 to, at the choice of the Sponsor, destroy or return all Personal Data to the Sponsor at the expiry or early termination of the Agreement, unless storage is legally required (GDPR Article 28(3)(g)) or where that Personal Data is held by the PIC as Controller for the purpose of clinical care or other legal purposes; and

3.7.10 to maintain a record of Processing activities as required by GDPR Article 30(2).

3.8 The PIC shall ensure that:

3.8.1 its Agents do not Process Personal Data except in accordance with this Agreement (and in particular the Protocol);

3.8.2 it takes all reasonable steps to ensure the reliability and integrity of any of its Agents who have access to the Personal Data and ensure they:

a. are aware and comply with the PIC's duties under this clause;

b. are subject to mandatory training in their information governance responsibilities and have appropriate contracts including sanctions, including for breach of confidence or misuse of data; and

c. are informed of the confidential nature of the Personal Data and understand the responsibilities for information governance, including their obligation to Process Personal Data securely and to only disseminate or disclose for lawful and appropriate purposes.

3.9 The PIC agrees to:

3.9.1 allow the Trial Site and/or Sponsor(s) or another auditor appointed by the Trial Site and/or Sponsor(s) to audit the PIC's compliance with the obligations described by this Agreement, Data Protection Legislation in general and GDPR Article 28 in particular, on reasonable notice subject to the Trial Site/Sponsor complying with all relevant health and safety and security policies of the PIC and/or to provide the Trial Site or Sponsor with evidence of its compliance with the obligations set out in this Agreement; and

3.9.2 obtain prior agreement of the Sponsor to store or Process Personal Data outside of the UK and the European Economic Area.

3.10 Where the PIC stores or otherwise Processes Personal Data outside of the UK and the European Economic Area as the Sponsor's Processor, it warrants that it does so in compliance with the Data Protection Legislation.

Data Sharing Terms

3.11 Personal Data shall not be disclosed to the Trial Site or Sponsor by the PIC, save where this is required directly or indirectly to satisfy the requirements of the Protocol, or in relation to a claim or proceeding brought by a Participant in connection with the Study.

3.12 The Trial Site agrees to use Personal Data solely in connection with the operation of the Agreement, or otherwise for purposes not incompatible with this original purpose (GDPR Article 5(1)(b)), and not otherwise. In particular:

3.12.1 not to disclose Personal Data to any person except in accordance with applicable legal requirements and codes of practice.

3.13 The Trial Site represents that the Sponsor has agreed to comply with the obligations placed on a Controller by the Data Protection Legislation. This is not limited to, but includes, being responsible for and able to demonstrate compliance with the principles relating to Processing of Personal Data (GDPR Article 5).

3.14 The Trial Site agrees to ensure persons processing Personal Data under this Agreement are equipped to do so respectfully and safely. In particular:

3.14.1 to ensure any persons (excluding employees, honorary employees, students, researchers, consultants and subcontractors of the PIC) Processing Personal Data understand the responsibilities for information governance, including their obligation to Process Personal Data securely and to only disseminate or disclose for lawful and appropriate purposes;

3.14.2 to ensure any persons (excluding employees, honorary employees, students, researchers, consultants and subcontractors of the PIC) have appropriate contracts providing for personal accountability and sanctions for breach of confidence or misuse of data including deliberate or avoidable data breaches.

3.15 The Trial Site agrees to proactively prevent data security breaches and to respond appropriately to incidents or near misses. In particular to:

3.15.1 ensure that Personal Data are only accessible to persons who need it for the purposes of the Study and to remove access as soon as reasonably possible once it is no longer needed;

3.15.2 ensure all access to Personal Data on IT systems processed for Study purposes can be attributed to individuals;

3.15.3 review processes to identify and improve processes which have caused breaches or near misses, or which force persons Processing Personal Data to use workarounds which compromise data security;

3.15.4 adopt measures to identify and resist cyber-attacks against services and to respond to relevant external security advice;

3.15.5 take action immediately following a data breach or near miss.

3.16 The Trial Site agrees to ensure data are Processed using secure and up to date technology. In particular, to:

3.16.1 ensure no unsupported operating systems, software or internet browsers are used to support the processing of Personal Data for the purposes of the Study;

3.16.2 put in place a strategy for protecting relevant IT systems from cyber threats which is based on a proven cyber security framework such as Cyber Essentials;

3.16.3 ensure IT suppliers are held accountable via contracts for protecting Personal Data they Process and for meetings all relevant information governance requirements.

Intellectual Property Rights

3.17 All Background Intellectual Property Rights (including licences) and Background Know How and their improvements used in connection with the Study shall remain

the property of the Party introducing the same and the exercise of such rights for purposes of the Study shall not knowingly infringe any third party's rights.

3.18 All Intellectual Property Rights and Know-How in the Protocol and other documents and information disclosed by the Sponsor, and in the Study Data, excluding clinical procedures developed or used by the PIC independently of the Study, shall belong to the Sponsor. The PIC hereby assigns all such Intellectual Property Rights, and undertakes to disclose all such Know-How, to the Trial Site.

3.19 At any time within the duration of the Study, the PIC shall at the request of the Trial Site or Sponsor and at the expense of the Sponsor execute all such documents and do all acts necessary to fully vest the Intellectual Property Rights in the Sponsor. To give effect to this Clause 3.19, the PIC shall ensure that its Agents involved in the Study assign such Intellectual Property Rights and disclose such Know-How to the Trial Site.

4. Sign Off*

Each Party represents that it has 'redlined' or otherwise called attention to all changes that it made and sent to the other Party in previously sent drafts of this Agreement, including but not limited to drafts of the schedule.

Signed by the duly authorised representatives of the Parties.

SIGNED ON BEHALF OF THE TRIAL SITE

[redacted]	[redacted]	[redacted]	29/9/22
Name	Position	Signature	Date

SIGNED ON BEHALF OF THE PIC

Paul Craven, Head of Research Operations			29 September 2022
Name	Position	Signature	Date

* Duly authorised scanned signatures shall be mutually acceptable and e-mail deemed a valid medium for exchanging signed copies of this Agreement, which may be executed in counterpart.

View Menu

Schedule 1

Study Support Arrangements

A. Financial Arrangements

Where no payments are to be to made to the PIC under this Agreement tick this box ☒ and delete the rest of this Section A.

B. Supplies Arrangements

Where no items are to be provided to, or procured for/by, the PIC under this Agreement tick this box ☒ and delete the rest of this Section B.

Appendix 12: Approval Email from School of Health in Social Science at University of Edinburgh

From: HISS Research Ethics <ethics.hiss@ed.ac.uk>
Date: Wednesday, 2 March 2022 at 10:22
To: RYAN Anna < >, HISS Research Ethics <ethics.hiss@ed.ac.uk>
Subject: Re: CLPS166 - Uni Ethics Application

Dear Anna,

Thank you for your email and for providing us with all the relevant documents. We have now checked that your project adheres to any University governance concerns and your application has been logged. As your project has been reviewed and received a favourable opinion by Caldicott, it does not require further review by the Clinical Psychology Ethics Committee database.

If you need to make any changes to the protocol these would go through the REC, but I would appreciate if you could also copy University ethics into any correspondence.

Wishing you all the best with your project.

Best wishes,

Ingrid

Ingrid Obsuth, PhD Lecturer in Clinical Psychology

Ethics & Integrity Lead—

From: RYAN Anna < >
Sent: 25 February 2022 15:48
To: HISS Research Ethics <ethics.hiss@ed.ac.uk>
Subject: CLPS166 - Uni Ethics Application

To whom it may concern,

Please find attached my Ethics application for my Doctoral thesis, alongside IRAS approval, sponsorship letter, proposed measures and PIS.

I am still awaiting R&D approval from Grampian and Lothian, this has all been applied for and will be forwarded in due course once received.

If I can send anything further in the meantime, please let me know.

Many thanks,
Anna

Appendix 13: Participant Information Sheet

PARTICIPANT INFORMATION SHEET

Investigating the delivery of an acceptance and commitment therapy (ACT) web-based intervention on symptomology in adult IBS patients: a feasibility study.

You are being invited to take part in research on Irritable Bowel Syndrome (IBS).

As a Doctoral thesis, Anna Ryan (Trainee Clinical Psychologist) at the University of Edinburgh is leading this research. This is a feasibility study: meaning this will be an initial trial to explore whether providing web-based self-help materials at IBS clinics is something that may be feasible or helpful to do in the future.

Before you decide whether to take part it is important you understand why the research is being conducted and what it will involve. Please take time to read the following information carefully.

WHAT IS THE PURPOSE OF THE STUDY?

The purpose of the study is to investigate whether using a web-based application may impact on symptoms associated with IBS. The research is investigating how participants respond to the guided self-help web-based materials, and whether this may have an impact on associated symptomology. This will involve logging onto a Psychology web-based app for IBS, to work through the guided materials and answer an approximate 10-minute questionnaire at two timepoints: prior to starting the materials and on completion of the materials (approx. 8 weeks). This will guide the research question of whether it is feasible to trial as a larger scale intervention in the future; and whether this method of intervention may have an impact on symptomology in IBS patients.

WHY HAVE I BEEN INVITED TO TAKE PART?

You are invited to participate in this study because you have been diagnosed with IBS and are over the age of 18. As this is an initial feasibility trial, we are interested to see how many individuals may wish to partake in this research. Approximately 60 participants will be recruited across the UK.

DO I HAVE TO TAKE PART?

No – it is entirely up to you. If you do decide to take part, you are still free to withdraw at any time and without giving a reason. Deciding not to take part or withdrawing from the study will not affect your healthcare in any way.

Please note that as your data will be anonymised it will not be possible to withdraw any data already collected before your withdrawal.

WHAT WILL HAPPEN IF I DECIDE TO TAKE PART?

If you do decide to take part, please keep this Information Sheet. You will be asked to complete an Informed Consent Form online to show that you understand your rights in relation to the research, and that you are happy to participate. A link to access the Consent form is provided at the bottom of this sheet.

You will be asked a number of questions regarding your experience of IBS, psychological symptoms and quality of life. The questionnaires will be available to complete online once you have completed the consent form. The questionnaires should take around 10 minutes to complete. The web-based application can be used as desired, though an 8-week timeframe is recommended as a guide to use the materials within. Your app usage will be assessed over this 8-week timeframe, from signing up to the app. You will then have access to use a web-based application, which will include reading materials, audio and interactive exercises to partake in. You will be asked to complete the same online questionnaires again at completion of the program (Week 8), see how you are finding the application. You will be sent a reminder at these time points with a link to the questionnaires.

If you decide to partake in the research, there will be an Informed Consent Form to complete which will ask whether you would also consent to being contacted further about research related to this study prior to May 2023. You are completely free to decide whether or not you wish to consent to further contact regarding this study, and of course may change your mind about this at any point on the duration of the study. If you decide to consent to being contacted further, this is not a guarantee that further contact will be made. If you choose to consent to further contact and contact is made, this would be to hear a bit more about your own individual experience with the web-based materials: for example, what you may have liked more, liked less or your individual recommendations of what you may have preferred. This would again be to inform potential future research and tailored interventions in this field.

WHAT ARE THE POSSIBLE BENEFITS OF TAKING PART?

There are no direct benefits but by sharing your experiences with us, you will be helping the researcher and the University to better understand how psychological interventions may impact physical healthcare.

ARE THERE ANY RISKS OR DISADVANTAGES ASSOCIATED WITH TAKING PART?

There are no significant risks associated with participation. Taking part will involve the time you wish to spend on the material over a period of 8 weeks.

WILL MY TAKING PART BE KEPT CONFIDENTIAL?

All the information we collect during the course of the research will be anonymised, encrypted and kept confidential and there are strict laws which safeguard your privacy at every stage. The only person who will have access to your data will be the Chief Investigator. Your data will be stored in password-protected files on an NHS computer only. Data will be stored for

HOW WILL WE USE INFORMATION ABOUT YOU?

People who do not need to know who you are will not be able to see your name or contact details. Your data will have a code number instead.

We will need to store information from you for this research project.

You will sign up to use the web-based app using an email address, meaning there will be a link between this and your app usage, though stored on separate databases. All personal identifiable data (email addresses) will be stored in a separate datafile and identified using a Unique Identifier Code and encrypted. People will use this information to do the research or to make sure that the research is being done properly. We will keep all information about you safe and secure. Your data will only be viewed by the research team. All electronic data will be stored on a password-protected computer file. Questionnaires will be completed via JISC Surveys, a secure online base. Data will be stored in an Excel database in a limited access folder. No identifiable data will be kept on any University computers. When the research is completed, all electronic data will be deleted. Usage and fidelity data collected via the web-based intervention will be anonymised using randomized numerical identifiers. Your consent information will be kept separately from your responses in order to minimise risk.

Once we have finished the study, we will keep some of the data so we can check the results. We will write our reports in a way that no-one can work out that you took part in the study. Anonymous data collected from this study will be stored for 3 years. Personal data collected from this study (eg. email addresses) will be deleted after a maximum timeframe of 12-months.

What are your choices about how your information is used?

- You can stop being part of the study at any time, without giving a reason, but we will keep information about you that we already have.
- We need to manage your records in specific ways for the research to be reliable. This means that we won't be able to let you see or change the data we hold about you.

Where can you find out more about how your information is used?

You can find out more about how we use your information at
https://www.ed.ac.uk/records-management/privacy-notice-research

- by asking one of the research team
- by sending an email to Anna Ryan:

The University of Edinburgh is the sponsor for this study based in the United Kingdom. We will be using information from you in order to undertake this study and will act as the data controller for this study. This means that we are responsible for looking after your information and using it properly. The University of Edinburgh will keep your anonymised data for a minimum of 3 years and this may be used in future ethically approved research.

WHAT WILL HAPPEN WITH THE RESULTS OF THIS STUDY?

The results of this study may be summarised in published articles, reports and presentations. You will not be identifiable from any published results. Quotes or key findings will always be made anonymous in any formal outputs unless we have your prior and explicit written permission to attribute them to you by name. With your consent, your anonymised information may also be kept for future research.

WHO IS ORGANISING THE RESEARCH?

This study has been organised by Anna Ryan and sponsored by the University of Edinburgh.

WHO HAS REVIEWED THE STUDY?

All research in the NHS is looked at by an independent group of people called a Research Ethics Committee. A favourable ethical opinion has been obtained. NHS Management Approval has also been obtained.

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WHO CAN I CONTACT?

If you have any further questions about the study, please contact the lead researcher, Anna Ryan ( ).

If you would like to discuss this study with someone independent of the study please contact Paul Morris ( ).

If you wish to make a complaint about the study, please contact: Research Governance Team (cahss.res.ethics@ed.ac.uk)]

HOW DO I TAKE PART IN THIS STUDY?

Please email lwibs.team@gmail.com to partake in this study and access the mobile phone app.

Appendix 14: Consent Form (Online, Page 1 of JISC Survey)

PARTICIPANT CONSENT FORM

Study Title: Investigating the effectiveness of an acceptance and commitment therapy (ACT) web-based intervention on symptomology in adult IBS patients: a feasibility study.

Researcher's name and contact details:

Anna Ryan

Contact Email: lwibs.team@gmail.com

I confirm I have read the Participant Information Sheet provided at my Gastroenterology appointment regarding the current study.
Yes

I understand that my participation is voluntary and that I can ask to withdraw at any time without giving a reason and without my medical care or legal rights being affected.
Yes

I understand that relevant sections of my data collected during the study may be looked at by individuals from the Sponsor (University of Edinburgh), or from the NHS organisation where it is relevant to my taking part in this research. I understand that my email address may be linked to app usage data, however this will be stored on an encrypted file on an NHS computer and accessed only by the researchers. No data in the written research will be identifiable. I give permission for these individuals to have access to my data.
Yes

I understand that my data will be stored for a minimum of 3 years and may be used in future ethically approved research.
Yes

I agree to take part in the above study.
Yes
No

Further contact regarding this research: I understand that I am completely free to decide whether or not I wish to consent to further contact regarding this study, and of course may change my mind about this at any point in the duration of the study. If I decide to consent to being contacted further, this is not a guarantee that further contact will be made. If I choose to consent to further contact and contact is made, this would be to hear a bit more about my own individual experience with the web-based materials: for example, what I may have liked more, liked less or my individual recommendations of what I may have preferred. This would again be to inform potential future research and tailored interventions in this field. I consent to being contacted further about research related to this study between now and May 2023.
Yes

No

I confirm that a completed copy of this document will be retained by the research team.

Yes

Appendix 15: NHS Lothian IG/IT Security Risk Assessment Agreement

- Data can be removed in an irretrievable manner if deletion is requested.
- All software used to process participant data (inc embedded) to be supported for the full lifecycle of the application.
- Security patches on the app to be installed within 14 days, as per Cyber Essentials requirements, where the patch fixes a vulnerability with a severity the product vendor describes as 'critical' or 'high risk'.
- University of Edinburgh must notify NHS Lothian of any Data Loss Event relating to this project of which it becomes aware within twenty-four (24) hours.
- Any changes to the transfer or storage of NHS Lothian PII data, to be approved by NHS Lothian IG/IT Security.
- Information Asset to be registered with Information Governance for any patient data collected and stored within NHS Lothian / University of Edinburgh.

Confirmation of compliance with the above requirements has been received on 21st July 2022.

Yours sincerely

Pavlina Yaneva McGovern
R&D Information Governance Lead

P.Y.McGovern (Jul 21, 2022 15:57 GMT+1)

Research and Development, NHS Lothian

On behalf of: Miss Tracey Gillies, Executive Medical Director and Caldicott Guardian for NHS Lothian

Cc: Ms Anna Ryan, Trainee Clinical Psychologist, University of Edinburgh

Appendix 16: Outgoing Subcontract Request Form

THE UNIVERSITY of EDINBURGH
Edinburgh Research Office

Research Contracts, Governance and Integrity Team

REQUEST FORM

OUTGOING SUBCONTRACT

This form is to be used when you are subcontracting part of a research project to a third party.

The form is designed for you to use:

- as a checklist of the information, documents and approvals you need in order to put in place a subcontract; and
- as a request for support from the Research Contracts, Governance and Integrity (**RCGI**) Team for putting in place a subcontract.

When you have completed the details and answered the questions below, please send the completed form, together with the relevant documents, to the RCGI Team at ERO.contracts@ed.ac.uk.

A member of the RCGI Team will acknowledge receipt, review, and liaise with you as needed.

In order for the RCGI Team to be able to put in place your subcontract effectively and speedily, please ensure you provide all the details below to the RCGI Team.

QUESTION	PROVIDE DETAILS	DOCUMENT(S) TO BE SENT TO RCGI TEAM
Your Details		
Name of Edinburgh researcher/requester	*Anna Ryan*	N/A
Name of Edinburgh Principal Investigator	*David Gillanders*	N/A
Name of Research Institute / Centre / School	*Health in Social Science*	N/A
Related WorkTribe project number	*N/A*	N/A
Date of submission of request form	*14 June 2022*	N/A
Subcontractor Details		

QUESTION	PROVIDE DETAILS	DOCUMENT(S) TO BE SENT TO RCGI TEAM
Who is the subcontractor? (Please give full name and address of the institution or company)	Ed Walpole University of Edinburgh Informatics Undergraduate Student	N/A
Who is your contact at the subcontractor? (Please give full name, job title, email and phone number)	Ed Walpole (as above)	N/A
Have you worked with them before (If yes, please give details)	☐ *Yes* ☒ *No*	N/A

Due Diligence for international parties		
What is the status of due diligence checks on the other party? (If ongoing, please give details of current status and who is carrying out due diligence checks. If Completed and requires contractual provisions as mitigation of risks, please provide details of contractual provisions required e.g. payment in instalments/ payment in arrears/ other specific invoicing and payment or termination requirements.) Find guidance on due diligence checks at https://www.ed.ac.uk/research-office/winning-research-funding/craft-application/working-with-overseas-partners-due-diligence	☒ *N/A* ☐ *Ongoing* *Status:* *DD contact:* ☐ *Completed and no issues* ☐ *Completed and requires the following contractual provisions to be included as mitigation of risks identified:*	N/A
Wider Project		

What is the wider project? (Please provide title and short summary here and, where applicable, send copy of / link to, the full project description)	*Investigating the effectiveness of an acceptance and commitment therapy (ACT) web-based intervention on symptomology in adult IBS patients*	Send copy of, or link to, full project description / final research proposal submitted to funder ☐ Attached
Subcontractor Role		
What role will the subcontractor have in the wider project and what tasks will the subcontractor be carrying out? (If the subcontractor is carry out tasks referred to in the original project application please specify the relevant tasks)	Subcontractor programmed app, delivered the app to us for purposes of Doctoral thesis project with the University of Edinburgh, and the Subcontractor is now no longer in contact/involved in the project – the contact is now Chris Swift, Director of IT at University of Edinburgh, and the app is under thr UoE.	Send copy of, or link to, full subcontractor work description ☐ N/A as no longer involved in project.
Please confirm the start date and end date for the subcontract.	September 2021-June 2022	
Materials		
Are any materials being transferred between the parties as part of the project? (If yes, please give details)	☒ *Yes* ☐ *No* The original workbook (Living with IBS, published workbook written by Dr. Nuno Ferriera and Dr. David Gillanders, UoE) has been transferred into digital format to be delivered in this app. This workbook has been described in thesis project Better Living with IBS: Ferreira, Nuno & Gillanders, David. (2012) https://www.researchgate.net/publication/235917273_Better_Living_with_IBS/citation/download . This workbook has also previously been utilised in the following research project: https://era.ed.ac.uk/handle/1842/6312	N/A

Is the material human tissue? See Human Tissue Authority guide to relevant material for guidance on which materials constitute human tissue	☐ *Yes* ☒ *No*	N/A
Data		
Is data being transferred between the parties as part of the project? (If yes, please give details)	☐ *Yes* ☒ *No*	N/A
Is identifiable personal data being collected / transferred / accessed by parties as part of the project? Find guidance on data protection requirements for research at https://www.ed.ac.uk/records-management/guidance/research/data-protection	☒ *Yes* ☐ *No* Email addresses and free-text responses being collected which participants are made aware of in PIS (attached) – DPIA also completed and attached,	If yes, send copy of the Data Protection Impact Assessment for the project ☒ Attached
Is pseudonymised / de-identified data relating to people being generated / transferred / accessed by the parties as part of the project? (If yes, please give details)	☐ *Yes* ☒ *No*	N/A

Research Ethics Committee (REC) Approvals		
Do you have REC approval for the project? (NB this may be required where the research involves humans or animals, or use of human tissue or identifiable or pseudonymised personal data) Find your College ethics contacts at https://www.ed.ac.uk/research-office/research-integrity/need-help	☒ *Yes* ☐ *Not required*	If yes, send copy of REC approval ☒ Attached
Costs		
Is UoE paying the subcontractor (If not, please give details of the payment arrangements)?	☐ *Yes* ☒ *No* The Subcontractor is no longer involved in the project. They were involved for the capacity that it was their undergraduate research project to develop the app. It has now been handed over to us and is now under the UoE.	Send copy of, or link to, full description of the budget / costs / financials / payment schedule ☐ Attached
Funding Terms		
Who is funding the wider project?	N/A	N/A
Which funder programme applies? (e.g. UKRI GCRF, EU Horizon 2020, EU IMI-JU)	N/A	N/A

What funder terms and conditions apply?	N/A	Send copy of, or link to, funder grant award & terms and conditions ☐ Attached
Are any parts of the funder terms and conditions to be redacted before sending out to the subcontractor? (If yes, please specify which parts are to be redacted)	☐ *Yes* ☒ *No* *N/A*	N/A
Related Agreements		
Are there any other agreements relating to the wider project (e.g collaboration agreement)? (If yes, please send copies and give applicable RCGI Contracts Database or WorkTribe reference number if known)	☐ *Yes* ☒ *No*	Send copy of, or link to, all related agreements ☐ Attached

Results		
Is UoE to own all results and intellectual property rights arising from subcontractor's work? (If no, please give details)	☒ *Yes* ☐ *No*	N/A
Publications		
Is the subcontractor to have any publication rights? (If yes, please give details)	☐ Yes X No No automatic rights, though he could be a part of the the author team of the Doctoral Thesis, though not required.	If specific publications policy, send copy of, or link to, policy ☐ Attached
Timescales and Impact		
Are there any external requirements on timescales for putting in place the subcontract that we should be aware of? (If yes, please give details and specify dates)	No	N/A

About the Research Contracts, Governance and Integrity Team

We work alongside researchers providing expertise and legal advice in negotiating, drafting, reviewing and signing research related contracts on behalf of the University.

We work with researchers, research leaders and a range of internal and external stakeholders to ensure that the University upholds its commitments to the highest standards of research integrity.

We work closely with colleagues across the University's other legal and contracts teams, with Edinburgh Innovations and with NHS Lothian (through the ACCORD partnership) in order to deliver high-quality, joined-up support.

Appendix 17: Data Protection Impact Assessment (DPIA)

DATA PROTECTION IMPACT ASSESSMENT
Student Research

PROJECT NAME:	Investigating the delivery of an acceptance and commitment therapy (ACT) web-based intervention on symptomology in adult IBS patients: a feasibility study.

OVERVIEW

1. Project outline – what and why

Explain broadly what the project aims to achieve and what type of processing it involves. You may find it helpful to refer or link to other documents, such as a project proposal.

Irritable bowel syndrome (IBS) is a chronic condition associated with symptoms of abdominal pain, bloating and changes in bowel habits. IBS is considered a 'functional' disorder; meaning there is no evidence of an organic pathology. IBS can have a significant impact on an individuals' quality of life, psychological distress and behaviours.

Acceptance and Commitment Therapy (ACT) interventions have been recommended as a line of treatment for IBS and have been found to be effective in helping people to manage symptoms, reduce distress and live more effectively with their condition. However, there are problems with access to psychological therapy for IBS, because there aren't enough Psychologists to deliver to everyone that needs it. Therefore, self-help materials have been developed to provide support for people with IBS. We propose that a more interactive online intervention will be more accessible and lead to greater retention.

Patients diagnosed with IBS by their Consultant will be offered the option to partake in this study. Participants will be recruited following consultation with their Gastroenterologists: in Grampian, Edinburgh and London. Consenting participants will be granted access to the web-based application, alongside some questionnaires to monitor both physical and psychological symptoms.

The current study proposes exploring the feasibility of delivering a web-based ACT intervention for IBS alongside usual treatment. We want to test whether we can recruit people in a study of online therapy for IBS, to see if this mode of delivery leads to greater retention and increased access to treatment, and judge how effective the intervention is. This will help to inform whether future larger-scaled trials in this area are justified. This study will also examine whether use of a web-based ACT application may impact upon an individual's symptoms and quality of life.

2. Describe the information flow

You should describe the collection, use and deletion of personal data here and it may also be useful to refer to a flow diagram or another way of explaining data flows – where you are getting the data from, where it will be stored and where it could be transferred to. You should also say how many individuals are likely to be affected by the project.
e.g. Data will be collected from research participants via online forms

↓

Data will be stored encrypted on departmental drives

↓

Pseudonymised dataset will be provided to Department X along with report

Data will be collected via participant app frequency usage, eg how often they log onto app, how many pages they read/whether they listen to audio exercises and/or engage in the psychological workbook exercises.

Data will be stored on encrypted departmental devices on a secure encrypted password-protected file which only the researcher can access

Data is pseudoanonymised, ie. participants sign up to app using email address however random number will be generated to identify participants and protect identity.

3. Privacy law compliance

Note: Data Protection legislation is relevant to any DPIA, and a DP compliance check should always be carried out. The Data Protection Officer will be able to advise you on the relevance of other privacy laws.

3.1 General Data Protection Regulation (GDPR) and Data Protection Act 2018 (DPA)

	Question	**Answer**
1.	What personal data is going to be processed? See here for definition	Data is pseudoanonymised, ie. participants sign up to app using email address however random number will be generated to identify participants and protect identity.
	Principle 1 – Fairness, Lawfulness, Transparency	
2.	Are you processing the personal data under Article 6 (1) (e) – task carried out in the public interest? If not, explain what other legal basis you rely on.	Task carried out in public interest to protect anonymity.

3.	If special categories of personal data are going to be processed, are you (in addition to the Article 6(1) legal bases) relying on the legal basis in Article 9 (2)(j) – necessary for research in the public interest? Note – special categories of personal data are personal data consisting of information as to (a) the racial or ethnic origin of the data subject, (b) political opinions, (c) religious beliefs, (d) Trade Union membership, (e) physical or mental health, (f) sexual life, (g) genetic data and (h) biometric information.	Physical or mental health – the app will contain exercises prompting users to reflect on BS symptoms and living alongside IBS. However, questionnaires assessing physical and mental health will not be linked to app – these will be circulated separately via JISC surveys.
4.	How are individuals being made aware of how their personal data will be used? If you supply participants with a PIS, please attach the PIS.	PIS attached
	Principle 2 – Purpose Limitation	
5.	Does the project involve the use of existing personal data for new purposes?	No
	Principle 3 – Adequacy, Relevance, Data Minimisation	
6.	What procedures will be in place for checking that the data collection procedures are adequate, relevant and not excessive in relation to the purpose for which the data will be processed?	Pseudonymised data JISC surveys to collate response to questionnaires separate from app No data stored on phone App has very limited access to phone – simply can enable or disable notifications, no other allowances.
	Principle 4 – Accuracy	
7.	How will the personal data be checked for accuracy?	Will be accepted at face value as part of feasibility trial.
	Principle 5 – Storage Limitation	
8.	Will there be set retention periods in place in relation to the storage of the personal data or are you applying the research exemption that the data are intended for future use? If so, is this included in your PIS?	Duration of doctoral thesis – data to be collected until project completion with expected end date of May 2023, outlined in PIS.
	Principle 6 – Security	
9.	What technical and organisational security measures will be in place to prevent any unauthorised or unlawful processing of the personal data?	Data is securely stored and processed, using standard encryption in both storage and end to end transfer and processing. The data stored will only be accessed by the

		researchers, and it is password protected. App has password constraints (min 8 characters, 1 upper 1 lower case, 1 special character, 1 number).
10.	Has the personal data been evaluated to determine whether its processing could cause damage or distress to data subjects?	This data is just the frequency of app usage and its processing will not cause damage to the data subjects
11.	Will you be transferring personal data to a country outside of the European Economic Area? If so where, and what arrangements will be in place to ensure that there are adequate safeguards over the data? If you have answered 'yes' and provided an explanation of safeguards, a separate approval procedure is required involving the Head of School. Advise your supervisor to consult the Data Protection Officer for further guidance and to initiate the approval procedure.	No, stored on Google Cloud in London.
12.	If the data will be anonymised, is it likely that a 'motivated intruder' will be interested in attempting re-identification by linking the data with other information available to them? Check the guidance for more information on the 'motivated intruder' test.	De-identification of data in line with GDPR. A variety of techniques will be used in order to pseudonymise data: data encryption, shuffling and masking out numbers to work against possibility of 'motivated intruder'. The data itself will have no financial value and would not be of interest.
A Data Protection compliance check has been carried out as part of this DPIA, the details of which are below From this we have concluded: (state whether your project is data protection compliant) …….		
3.4 Common Law duty of confidence		
Note: This only applies when you use, for example medical data or similar types of data that individuals would not expect to see disclosed. Describe how you have obtained consent.		
N/A		
3.3 Human Tissue Act and the Medicines for Human Use (Clinical Trials) Regulations (if relevant)		
Note: This only applies to medical research. Describe how you have obtained consent.		

N/A

4. Screening questions	
Explain what practical steps you will take to ensure that you identify and address privacy risks. Who should be consulted about potential risks (members of your research team, supervisor, research sponsor…)? Then list the risks identified under 5. **Answer the questions by ticking the box if 'yes'.**	
Will the project involve the collection of new identifiable or potentially identifiable information about individuals?	X
Will the project compel individuals to provide information about themselves, i.e. where they will have little awareness or choice?	☐
Will identifiable information about individuals be shared with other organisations or people who have not previously had routine access to the information?	☐
Are you using information about individuals for a purpose it is not currently used for r in a new way, i.e. using data collected to provide care for an evaluation of service development.	☐
Where information about individuals is being used, would this be likely to raise privacy concerns or expectations, i.e. will it include health records, criminal records or other information that people may consider to be sensitive and private and may cause them concern or distress?	☐
Will the project require you to contact individuals in ways which they may find intrusive, i.e. telephoning or emailing them without their prior consent?	☐
Will the project result in you making decisions in ways which can have a significant impact on individuals, i.e. will it affect the care a person receives?	☐
Does the project involve you using new technology which might be perceived as being privacy intrusive, i.e. using biometrics, facial recognition or automated decision making?	☐
Is a service being transferred to a new supplier (re-contracted) and the end of an existing contract?	☐
Is processing of identifiable/potentially identifiable data being moved to a new organisation (but with same staff and processes)	☐

4. identification of risks

Note: You should carry out the risk analysis using exactly the same methodology as you do for other project risks. Enter the key risks that have been identified, and the options for avoiding or mitigating those risks, into the table below. Below are some of the most common risks – choose from these and add any other risk that might be specific to your work. *

Risk description	*Options for avoiding or mitigating this risk	Residual Privacy Risk after implementation of mitigation		
		High	Medium	Low
Potentially identifiable information (email address to sign up to app).	A unique identifier code will be assigned to each participant randomly to link their app use to questionnaires, as such once this is complete the email addresses will be removed and no such potentially identifiable link will be available. Participants are made aware of the collection of email address upon signup to this research project (outlined in PIS).			X

* For each privacy risk, there could be a number of options for avoiding or mitigating that risk. You should list all the options then consider the residual risk for each one

5. Approval by academic supervisor (date and signature)

David Gillanders, Clinical Psychology, School of Health in Social Science

Example risks

i. Inadequate disclosure controls increase the likelihood of information being shared inappropriately.
ii. The context in which information is used or disclosed can change over time, leading to it being used for different purposes without people's knowledge.
iii. New surveillance methods may be an unjustified intrusion on their privacy.
iv. Measures taken against individuals as a result of collecting information about them might be seen as intrusive.
v. Identifiers might be collected and linked which prevent people from using a service anonymously.
vi. Vulnerable people may be particularly concerned about the risks of identification or the disclosure of information.
vii. Collecting information, matching and linking identifiers or whole datasets might mean that you are no longer using information which is safely anonymised.
viii. Information which is collected and stored unnecessarily, or is not properly managed so that duplicate records are created, presents a greater security risk.
ix. If a retention period is not established information might be used for longer than necessary.
x. Public distrust about how information is used can damage an organisation's reputation and lead to loss of business.
xi. Data losses which damage individuals could lead to claims for compensation.
xii. Without proper security, the possibility of external unlawful access to the data such as hacking increases.
xiii. Even with proper security, a hacking attack is a possibility.
xiv. Since the European Court of Justice decision in July 2020, a special risk assessment is required for transfer of personal data in particular to the US but also to other non-EEA countries. Please assess how likely it is that despite the use of the Standard Contractual Clauses the data is likely to be accessed, for example under the Patriot Act in the US. If the answer to this question is 'yes', then draw your supervisor's attention to the fact and ask them to get in touch with the Data Protection Officer.

Appendix 18: Non-CTIMP Study Protocol

<IBS>
<V2_11.01.22>
< CAHSS210915>

Non-CTIMP Study Protocol

Investigating the delivery of an acceptance and commitment therapy (ACT) web-based intervention on symptomology in adult IBS patients: a feasibility study.

	The University of Edinburgh
Protocol authors	**Anna Ryan**
Chief Investigator	**Anna Ryan (Trainee Clinical Psychologist)**
Sponsor number	CAHSS2109/15
REC Number	**Insert REC number before finalisation**
Project registration	**If applicable trials should be registered on a publically accessible database. ACCORD can provide log-in credentials for clinicaltrials.gov. Please email resgov@accord.scot to arrange**
Version Number and Date	Version 2, 11/02/22.

<IBS>
<V2_11.01.22>
< CAHSS210915>

CONTENTS

To update the table of contents, highlight the existing table of contents; right click "update fields" and OK

LIST OF ABBREVIATIONS

Insert abbreviations as required

This is not an exhaustive list.
Any additional abbreviations used within the protocol must also be added here.

	Academic and Clinical Central Office for Research & Development - Joint office for The University of Edinburgh and Lothian Health Board
	Chief Investigator
	Case Report Form
	Good Clinical Practice
	International Conference on Harmonisation
	Principal Investigator
	Quality Assurance
	Research Ethics Committee
	Standard Operating Procedure
IBS	Irritable Bowel Syndrome
CBT	Cognitive Behavioural Therapy
ACT	Acceptance and Commitment Therapy

1 INTRODUCTION

1.1 BACKGROUND

Should include:

Irritable bowel syndrome (IBS) is a functional gastrointestinal (GI) condition characterized by abdominal pain and altered bowel habit in the absence of an organic pathology. The condition affects 10-22% of the UK population, with annual NHS associated costs of more than £200 million (Everitt et al., 2015). IBS is associated with increase rates of psychological distress and negative impact on patients' quality of life (QOL) (Kinsinger, 2017). Additionally, IBS has been coined as a 'disorder of gut-brain interaction' (Kennedy et al., 2014). The brain-gut axis refers to the bidirectional communication between the brain and the gut (Kinsinger, 2017). The GI tract is highly sensitive to stress, and psychological pathology has been identified as a significant contributor to dysregulation of the brain-gut axis in IBS (Carabotti et al., 2015).

Psychological interventions in IBS

Given the evidence for the brain-gut interaction and bidirectional relationship between stress and IBS symptomology, psychological interventions are increasingly applied as treatment for IBS; showing significant improvements in both physical and psychological associated symptoms (Ballou & Keefer, 2017). Cognitive behavioural therapy (CBT) has demonstrated the strongest evidence in treating IBS to date. Meta-analyses have highlighted CBT efficacy for IBS when compared to controls, though not in comparison to standard medical care (Li et al., 2014). Furthermore, CBT self-help interventions have shown benefits in IBS. Hunt, Ertell, Coello & Rodriguez (2015) highlighted benefits in IBS symptoms, QOL and psychological distress following a self-help CBT intervention. However, Sanders et al. (2007) conducted a similar self-help CBT intervention and found a decrease in GI symptom scores but no significant improvements in QOL or distress. Both studies involved a CBT self-help workbook intervention without therapist support and showed high attrition rates. Hunt et al. (2015) showed only 53% of participants in the treatment group completed measures post-treatment; meaning that a large proportion of eligible participants may not have found the treatment acceptable. Furthermore, at 3-month follow-up only 19% of participants completed measures, leading to inconclusive evidence regarding treatment persistence.

A CBT web-based intervention 'Regul8' was developed from the paper-based self-help manual by Moss-Morris, McAlpine, Didsbury and Spence (2010) which had demonstrated improvements in IBS symptom severity and psychological distress (Everitt et al., 2013). While it was hypothesized that the web-based program Reglu8 would similarly show improvements; no significant differences were identified between the intervention and control group, in IBS symptom severity or IBS-related QOL. Possible reasons contributing to such outcomes may include that therapist contact alongside the intervention was significantly lower in the web-based intervention in comparison to the paper-based trial. Furthermore, later trials which included greater therapist input alongside the Regul8 program demonstrated superior outcomes in both IBS symptomology and QOL (Everitt et al., 2019). This is in line with other interventions for for IBS (Hunt et al., 2009; Ljótsson, Falk, et al., 2010) that suggest that therapeutic engagement is important for adherence to a web-based intervention.

While CBT is the most widely examined psychotherapy for IBS management, in more recent years studies have highlighted the impact of Acceptance and Commitment (ACT) based interventions in the management of symptom reporting in IBS patients (Ferreira, Eugenicos, Morris & Gillanders, 2011). CBT focuses on gaining control over IBS symptoms; a mechanism that has since been found to often result in further restriction of functioning. Furthermore, as highlighted above, the efficacy of CBT for IBS has shown inconsistent outcomes, and a review of mind-body approaches to IBS has identified third wave approaches to be

particularly beneficial in this population (Sánchez et al., 2017). ACT focuses on acceptance, mindfulness and defusing from thoughts to facilitate working towards overarching life goals. ACT has been identified as an effective treatment in health conditions by promoting an accepting perception of their condition (Aghalar et al., 2020).

A pilot trial identified the efficacy of ACT in an IBS population when delivered via a self-help workbook and one-day workshop, which showed an increase in participants' IBS acceptance (Ferreira et al., 2018). This increase in IBS acceptance in turn mediated improvements in reported physical symptoms, QOL, avoidance behaviours and distress. A trial was subsequently conducted to examine the effects of bibliotherapy alone. This trial identified significant increases in IBS acceptance, reduced symptoms and lower GI-related anxiety. However, by contrast to the study including a face-to-face workshop, no significant changes were identified in IBS-related behaviour or QOL (Gillanders et al., 2017). This finding suggests that a peer component may be vital in encouraging overt behavioural changes. Furthermore, the study including the workshop showed greater reductions in GI-specific anxiety, reinforcing the idea that normalising and sharing of IBS experiences with peers may be particularly important part of the process: which could be considered a form of exposure. This idea is in line with studies by Ljotsson et al. (2010,2011) which found inclusion of both therapist and peer support alongside exposure contributed to changes in both behavioural avoidance and quality of life. Furthermore, attrition rates in the ACT self-help intervention alone reflected this: with almost half (47%) of participants lost to follow-up, suggesting that the intervention did not feel sufficient for those a large proportion of eligible participants. This is consistent with existing literature which suggests that purely self-help interventions without therapist support are not as effective as those with therapeutic guidance (Gerhards et al., 2010). The differences in outcomes in the ACT-based studies suggests that both therapist and peer support are important factors not only in the retention of participants, but also patient outcomes regarding behavioural change and QOL.

Web-based intervention delivery

Recent research found that the delivery of web-based CBT for IBS patients showed positive feedback from patients regarding the level of engagement and flexibility the online approach offered (Hughes et al., 2020). White et al. (2020) conducted a systematic review and meta-analysis of web-based psychological interventions and identified a need for further research into the efficacy of online psychological interventions for specific chronic health conditions. A systematic review highlighted preliminary evidence that web-based mindfulness-based interventions (MBIs) show promising results for patients with chronic health conditions, particularly those tailored to specific condition symptomology (Toivonen et al., 2017). Ljótsson et al. (2010; 2011) highlighted benefits of incorporating elements of a 'third wave' approach in a web-based mindfulness and exposure intervention, supported by a peer online chat room and asynchronous therapeutic support. Large effect sizes were identified across QOL and reported symptoms and continued at 15-18 month follow-up (Ljótsson et al., 2011). Furthermore, a systematic review and mental analysis identified internet-based ACT (iACT) targeting psychological flexibility as improving and maintaining psychological wellbeing across diverse populations (Thompson et al., 2021). While some preliminary studies have identified ACT web-based interventions as beneficial in chronic pain (Slattery et al., 2019) and

depression (Pots et al., 2016); no study has yet examined the impact of the web-based delivery of an ACT intervention for IBS patients.

1.2 RATIONALE FOR STUDY

Based on the existing literature on psychological interventions in IBS as outlined above, common themes that emerged regarding retention, engagement and patient outcomes include: the importance of therapeutic support alongside a self-help intervention and inclusion of peer-support components in facilitating behavioural change. While self-help ACT interventions have recently demonstrated promising results in IBS, no online intervention has yet been trialled in this population. Therefore, the current study proposes exploring the feasibility of a web-based ACT intervention with asynchronous therapeutic support and peer support in increasing user engagement and adherence for IBS patients. This study hypothesizes that 'prescribing' a web-based ACT intervention alongside TAU will have a positive impact on patients' IBS symptoms, improve psychological flexibility, QOL and psychological wellbeing. This feasibility study will examine whether this method of delivery is achievable in terms of recruitment and acceptability as an intervention, prior to the implementation of a larger-scale controlled trial (Bowen et al., 2009).

Furthermore, this feasibility study will be able to determine an estimated effect size for a larger-scaled trial. If this method of delivery is found to be feasible and acceptable, it could have many clinical implications for further studies to explore this novel treatment pathway. Development of an effective digital pathway in the treatment of IBS would be both time- and cost- effective. Rationale for delivery of the intervention online is for ease of immediate accessibility, and flexibility with 24-hour availability to materials for the patient to engage in the intervention and work at their own pace: particularly important as the majority of IBS patients are of working age (Canavan et al., 2014). Due to the large population of patients presenting with psychological distress as well as a diagnosis of IBS; a web-based ACT intervention could have significant impact in reaching a large population and minimize wait-times for accessing treatment as well as burden on the NHS. The disorder frequently results in absenteeism and loss of productivity at work (Zacker et al., 2004) as well as repeated medical appointments (Tack et al., 2019). The web-based intervention has the potential for large-scale roll-out and a positive impact economically: minimizing recurring appointments and waiting times for the NHS and reducing absenteeism from work (Ballou et al., 2019).

STUDY OBJECTIVES

1.3 OBJECTIVES

1.3.1 Primary Objective

This project is designed to answer a number of key questions regarding the principal objective: whether or not a larger scale, definitive controlled trial for a web-based ACT intervention in reducing IBS symptomology is feasible and justified. The main outcomes will include feasibility of the recruitment process and measurement tools, acceptability of the intervention for participants and adherence to the programme.

These questions include:

(a) Is a web-based intervention for IBS a sufficiently accessible and acceptable method of intervention delivery?
(b) Can sufficient numbers of participants be recruited and retained across multiple NHS sites?
(c) Will participants engage in the intervention sufficiently?
(d) What are the likely effect sizes for this kind of intervention with this population across the measures of interest?

1.3.2 Secondary Objectives

1. Does use of an ACT-based smartphone intervention alongside treatment as usual (TAU) reduce symptom reporting in IBS patients?

2. Does engagement with the ACT web-based intervention improve IBS-related behaviours in patients?

3. Does use of an ACT smartphone application increase psychological flexibility in IBS patients?

4. Does use of an ACT smartphone application increase levels of self-reported quality of life in IBS patients?

5. Does use of an ACT-based smartphone intervention reduce psychological disress in IBS patients?

2 STUDY DESIGN

Detail:

Participants

Participants meeting ROME-IV criteria for a diagnosis of IBS will be recruited from outpatient gastroenterology clinics at NHS Grampian, NHS Lothian and Imperial College Healthcare NHS Trust, London. Gastroenterology consultants from each of the aforementioned health boards have agreed to offer IBS patients information allowing them to consider participation in the study. These participants will be identified by the gastroenterology consultants and offered to partake in this study alongside recommended treatment-as-usual (TAU).

Design

This study aims to employ a single-arm repeated measures feasibility study of a web-based ACT intervention for IBS. The purpose of this study is to evaluate the feasibility of a web-based ACT intervention in order to explore the whether a larger-scaled controlled trial is justified. A feasibility study design will be used as, to date, no study has assessed the feasibility and acceptability of a web-based application employing ACT-principles in the management of IBS. As outlined by the NIHR, a feasibility study is necessary to identify whether something can be done, should be proceeded with; and if so, how. Furthermore, a feasibility study should either lead to subsequent more definitive research providing valuable evidence, help to avoid wasting resources or inform a different way of approaching the research question. The current study aims to trial the implementation of a web-based application alongside treatment as usual for IBS patients, to assess whether this can impact on the way an individual lives with their condition (reported symptomology, acceptance of IBS, quality of life and psychological wellbeing). The current study also aims to identify participant uptake of app use during the study period, how many complete the modules, engagement and attrition rates. This data will be collected via online questionnaires, which the participants will be provided by link upon signing up to the app and/or emailed by the Researcher. The outcomes regarding app use and engagement will be important in informing subsequent trial work in this field.

This study will assess participants at two ime points, and each participant will act as their own baseline.

T1: Pre-intervention
T2: Post-intervention

Intervention

The intervention will be delivered on an online platform, which can be accessed from any smartphone, tablet or computer. The materials used will be adapted from the published IBS workbook 'Better Living With IBS' (Gillanders & Ferreira, 2012). These materials will include psycho-education around ACT and management of IBS with audio files and exercises to engage with. The web-based intervention will be broken down into 8 modules, with a suggested rate of working through the course over 8 weeks. The web-based intervention will have interactivity programmed into it, with a chat function inviting questions, check-in and general support where the researcher will respond asynchronously to queries raised. There will also be a discussion board, where app users can chat amongst themselves to increase engagement. Based on previous literature outlining that a purely self-help intervention was less effective and showed lower retention rates in comparison to the workshop with self-help (Gillanders et al.,2017), this level of interactivity and peer support is an important factor to include in the current web-based intervention.

3 STUDY POPULATION

3.1 NUMBER OF PARTICIPANTS

Appropriate sample size for this study was approached two ways. As the primary outcome is considered feasibility, the primary focus will be investigating the numbers of eligible participants recruited and retained over the course of the study. Taking Gillanders et al. (2017) low-intensity ACT intervention for IBS as a guide: over a period of 8 months, 70 participants met eligibility criteria, of which 45 provided baseline data, 36 at 2 months and 24 were retained at 6 months follow-up. This is an approximate 53% retention rate from initial recruitment, and 34% of all those eligible. For the current study, based on the aforementioned recruitment and retention rates from Gillanders et al. (2017) pilot study and taking guidance on the successful implementation of feasibility trials (Bowen et al., 2010) into account, the trial will be considered feasible if it is able to recruit 40% of eligible participants and retain a minimum of 60% of these participants at 3 months.

The second way to approach sample size estimation for the study is to be sufficiently powered to detect within participant effects similar to those found in Gillanders et al. (2017). This was calculated using the G*Power programme. With the paramaeters of a within participant effect based on the previous low intensity IBS paper by Gillanders et al. (2017) (ηp2=.09, 90% CI=.01−.18) using an alpha of .05 and a beta of .8, proposing use of a repeated measures ANOVA with one group and four measurement points, the sample size needed to detect a change of .09 is 16 participants. Moreover, as a conservative estimate to power the study to be able to detect effects half way between the mean and the lower level of the confidence interval (0.01), taking an effect size of ηp2 = .05, the sample size required to detect it would be 28 participants. Accounting for the 47% attrition rate that was observed in the previous study by Gillanders et al. (2017), the current study aims to recruit at baseline a sample size of 60 participants.

3.2 INCLUSION CRITERIA

Individuals aged 18 and over diagnosed with IBS according to the ROME-IV criteria by NHS-based Gastroenterology consultants. Individuals with access to a device which can access the online intervention.

3.3 EXCLUSION CRITERIA

Individuals continuing testing for other gastroenterology-related issues or experiencing symptomology suggestive of Inflammatory Bowel Disease (or similar). Patients with severe psychiatric difficulties, suicidality, psychosis, terminal illness, intellectual disability, cognitive impairment, brain injury, substance misuse; inability to give informed consent in English and an inability to understand written and spoken English.

4 PARTICIPANT SELECTION AND ENROLMENT

4.1 IDENTIFYING PARTICIPANTS

Participants meeting ROME-IV criteria for a diagnosis of IBS will be recruited from outpatient gastroenterology clinics at NHS Grampian, NHS Lothian and Imperial College Healthcare NHS Trust, London. Gastroenterology consultants from each of the aforementioned health boards have agreed to offer IBS patients information allowing them to consider participation

in the study. These participants will be identified by the gastroenterology consultants and offered to partake in this study alongside recommended treatment-as-usual (TAU).

4.2 CONSENTING PARTICIPANTS

Consenting participants will be provided with a Participant Information Sheet to consider for as long as they wish prior to making a final decision to sign up to the app, and can withdraw at any point, without penalty.

4.2.1 Withdrawal of Study Participants

Participants are free to withdraw from the study at any point or a participant can be withdrawn by the Investigator. If withdrawal occurs, the primary reason for withdrawal will be documented in the participant's case report form, if possible. The participant will have the option of withdrawal from:

(i) all aspects of the trial but continued use of data collected up to that point . To safeguard rights, the minimum personally-identifiable information possible will be collected.

Detail reasons and procedures for a study participant stopping early i.e. "stopping rules" and "discontinuation criteria"

4.3 STORAGE AND ANALYSIS OF DATA

All participant data will be anonymised and encrypted. Questionnaires will be completed via JISC Surveys, a secure online base. Data will be stored in an Excel database in a limited access folder. No identifiable data will be kept on any University computers. When the research is completed, all electronic data will be deleted. Usage and fidelity data collected via the web-based intervention will be anonymised using randomized numerical identifiers.

5 DATA COLLECTION

Demographic data
Relevant demographic data will be collected at the start of the study: including gender, age, ethnicity, employment status and marital status.

All individuals will complete the following questionnaires at two time-points: pre-study (baseline; T1), and post-intervention (T2).

1. IBSAAQ (psychological flexibility/ acceptance)
2. IBS-36 (IBS-related quality of life)
3. IBS-SSS (physical symptom severity)
4. VSI (GI-related anxiety)
5. IBS-BRQ (IBS Behaviours Response Questionnaire)

All questionnaires will be completed online, either via tablet, phone, computer or any web-based device. All data collected will be anonymised and encrypted.

6 DATA MANAGEMENT

6.1.1 Personal Data

No personal data will be collected, all data will be anonymised using a Unique Identifier Number and encrypted.

6.1.2 Transfer of Data

Data collected or generated by the study (including personal data) will not be transferred to any external individuals or organisations outside of the Sponsoring organisation(s).

6.1.3 Data Controller

A data controller is an organisation that determines the purposes for which, and the manner in which, any personal data are processed.

The University of Edinburgh is the data controller along with any other entities involved in delivering the study that may be a data controller in accordance with applicable laws (e.g. the site)

6.1.4 Data Breaches

Any data breaches will be reported to the University of Edinburgh and NHS to the appropriate timelines if required.

7 STATISTICS AND DATA ANALYSIS

7.1 SAMPLE SIZE CALCULATION

Appropriate sample size for this study was approached two ways. As the primary outcome is considered feasibility, the primary focus will be investigating the numbers of eligible participants recruited and retained over the course of the study. Taking Gillanders et al. (2017) low-intensity ACT intervention for IBS as a guide: over a period of 8 months, 70 participants met eligibility criteria, of which 45 provided baseline data, 36 at 2 months and 24 were retained at 6 months follow-up. This is an approximate 53% retention rate from initial recruitment, and 34% of all those eligible. For the current study, based on the aforementioned recruitment and retention rates from Gillanders et al. (2017) pilot study and taking guidance on the successful implementation of feasibility trials (Bowen et al., 2010) into account, the trial will be considered feasible if it is able to recruit 40% of eligible participants and retain a minimum of 60% of these participants at 3 months.

The second way to approach sample size estimation for the study is to be sufficiently powered to detect within participant effects similar to those found in Gillanders et al. (2017). This was calculated using the G*Power programme. With the paramaeters of a within participant effect based on the previous low intensity IBS paper by Gillanders et al. (2017) ($\eta p2$=.09, 90% CI=.01–.18) using an alpha of .05 and a beta of .8, proposing use of a

repeated measures ANOVA with one group and four measurement points, the sample size needed to detect a change of .09 is 16 participants. Moreover, as a conservative estimate to power the study to be able to detect effects half way between the mean and the lower level of the confidence interval (0.01), taking an effect size of ηp2 = .05, the sample size required to detect it would be 28 participants. Accounting for the 47% attrition rate that was observed in the previous study by Gillanders et al. (2017), the current study aims to recruit at baseline a sample size of 60 participants.

7.2 PROPOSED ANALYSES

SPSS will be used to analyse the data. Descriptive analysis will be used to gather an insight into recruitment, retention and the calculation of effect sizes to inform later research. Descriptive analysis will also be used on data gathered surrounding app use, user engagement and outcomes, which will be imorotant in informing potential future research and web-based design for interventions in this field. A paired samples t-test will be used to analyse whether there is a significant difference in scores on the above measures over time. The data will be analysed on an intention-to-treat basis.

8 OVERSIGHT ARRANGEMENTS

8.1 INSPECTION OF RECORDS

Investigators and institutions involved in the study will permit trial related monitoring and audits on behalf of the sponsor, REC review, and regulatory inspection(s). In the event of audit or monitoring, the Investigator agrees to allow the representatives of the sponsor direct access to all study records and source documentation. In the event of regulatory inspection, the Investigator agrees to allow inspectors direct access to all study records and source documentation.

8.2 STUDY MONITORING AND AUDIT

The ACCORD Sponsor Representative will assess the study to determine if an independent risk assessment is required. If required, the independent risk assessment will be carried out by the ACCORD Quality Assurance Group to determine if an audit should be performed before/during/after the study and, if so, at what frequency.

Risk assessment, if required, will determine if audit by the ACCORD QA group is required. Should audit be required, details will be captured in an audit plan. Audit of Investigator sites, study management activities and study collaborative units, facilities and 3rd parties may be performed.

9 GOOD CLINICAL PRACTICE

9.1 ETHICAL CONDUCT

The study will be conducted in accordance with the principles of the International Conference on Harmonisation Tripartite Guideline for Good Clinical Practice (ICH GCP).

Before the study can commence, all required approvals will be obtained and any conditions of approvals will be met.

9.2 INVESTIGATOR RESPONSIBILITIES

The Investigator is responsible for the overall conduct of the study at the site and compliance with the protocol and any protocol amendments. In accordance with the principles of ICH GCP, the following areas listed in this section are also the responsibility of the Investigator. Responsibilities may be delegated to an appropriate member of study site staff.

9.2.1 Informed Consent

The Investigator is responsible for ensuring informed consent is obtained before any protocol specific procedures are carried out. The decision of a participant to participate in clinical research is voluntary and should be based on a clear understanding of what is involved.

Participants must receive adequate oral and written information – appropriate Participant Information and Informed Consent Forms will be provided. The oral explanation to the participant will be performed by the Investigator or qualified delegated person, and must cover all the elements specified in the Participant Information Sheet and Consent Form.

The participant must be given every opportunity to clarify any points they do not understand and, if necessary, ask for more information. The participant must be given sufficient time to consider the information provided. It should be emphasised that the participant may withdraw their consent to participate at any time without loss of benefits to which they otherwise would be entitled.

The participant will be informed and agree to their medical records being inspected by regulatory authorities and representatives of the sponsor(s).

The Investigator or delegated member of the trial team and the participant will sign and date the Informed Consent Form(s) to confirm that consent has been obtained. The participant will receive a copy of this document and a copy filed in the Investigator Site File (ISF) and participant's medical notes (if applicable).

9.2.2 Study Site Staff

The Investigator must be familiar with the protocol and the study requirements. It is the Investigator's responsibility to ensure that all staff assisting with the study are adequately informed about the protocol and their trial related duties.

9.2.3 Data Recording

The Principal Investigator is responsible for the quality of the data recorded in the CRF at each Investigator Site.

9.2.4 Investigator Documentation

- The Principal Investigator will ensure that the required documentation is available in local Investigator Site files ISFs.

9.2.5 GCP Training

For non-CTIMP (i.e. non-drug) studies all researchers are encouraged to undertake GCP training in order to understand the principles of GCP. However, this is not a mandatory requirement unless deemed so by the sponsor. GCP training status for all investigators should be indicated in their respective CVs.

9.2.6 Confidentiality

All evaluation forms, reports, and other records must be identified in a manner designed to maintain participant confidentiality. All records must be kept in a secure storage area with limited access. Clinical information will not be released without the written permission of the participant. The Investigator and study site staff involved with this study may not disclose or use for any purpose other than performance of the study, any data, record, or other unpublished information, which is confidential or identifiable, and has been disclosed to those individuals for the purpose of the study.. Prior written agreement from the sponsor or its designee must be obtained for the disclosure of any said confidential information to other parties.

9.2.7 Data Protection

All Investigators and study site staff involved with this study must comply with the requirements of the appropriate data protection legislation (including the General Data Protection Regulation and Data Protection Act) with regard to the collection, storage, processing and disclosure of personal information.

Computers used to collate the data will have limited access measures via user names and passwords.

Published results will not contain any personal data and be of a form where individuals are not identified and re-identification is not likely to take place

STUDY CONDUCT RESPONSIBILITIES

9.3 PROTOCOL AMENDMENTS

Any changes in research activity, except those necessary to remove an apparent, immediate hazard to the participant in the case of an urgent safety measure, must be reviewed and approved by the Chief Investigator.

Amendments will be submitted to a sponsor representative for review and authorisation before being submitted in writing to the appropriate REC, and local R&D for approval prior to participants being enrolled into an amended protocol.

9.4 MANAGEMENT OF PROTOCOL NON COMPLIANCE

Prospective protocol deviations, i.e. protocol waivers, will not be approved by the sponsors and therefore will not be implemented, except where necessary to eliminate an immediate hazard to study participants. If this necessitates a subsequent protocol amendment, this should be submitted to the REC, and local R&D for review and approval if appropriate.

Protocol deviations will be recorded in a protocol deviation log and logs will be submitted to the sponsors every 3 months. Each protocol violation will be reported to the sponsor within 3 days of becoming aware of the violation. All protocol deviation logs and violation forms should be emailed to QA@accord.scot

Deviations and violations are non-compliance events discovered after the event has occurred. Deviation logs will be maintained for each site in multi-centre studies. An alternative frequency of deviation log submission to the sponsors may be agreed in writing with the sponsors.

9.5 SERIOUS BREACH REQUIREMENTS

A serious breach is a breach which is likely to effect to a significant degree:

(a) the safety or physical or mental integrity of the participants of the trial; or

(b) the scientific value of the trial.

If a potential serious breach is identified by the Chief investigator, Principal Investigator or delegates, the co-sponsors (seriousbreach@accord.scot) must be notified within 24 hours. It is the responsibility of the co-sponsors to assess the impact of the breach on the scientific value of the trial, to determine whether the incident constitutes a serious breach and report to research ethics committees as necessary.

9.6 STUDY RECORD RETENTION

All study documentation will be kept for a minimum of 3 years from the protocol defined end of study point. When the minimum retention period has elapsed, study documentation will not be destroyed without permission from the sponsor.

9.7 END OF STUDY

The end of study is defined as the last participant's last visit.

The Investigators or the sponsor have the right at any time to terminate the study for clinical or administrative reasons.

The end of the study will be reported to the REC, and R+D Office(s) and co-sponsors within 90 days, or 15 days if the study is terminated prematurely. The Investigators will inform participants of the premature study closure and ensure that the appropriate follow up is arranged for all participants involved. End of study notification will be reported to the co-sponsors via email to resgov@accord.scot

A summary report of the study will be provided to the REC within 1 year of the end of the study.

9.8 INSURANCE AND INDEMNITY

The sponsor is responsible for ensuring proper provision has been made for insurance or indemnity to cover their liability and the liability of the Chief Investigator and staff.

The following arrangements are in place to fulfil the co-sponsors' responsibilities:

- The Protocol has been designed by the Chief Investigator and researchers employed by the University and collaborators. The University has insurance in place (which includes no-fault compensation) for negligent harm caused by poor protocol design by the Chief Investigator and researchers employed by the University.
- Sites participating in the study will be liable for clinical negligence and other negligent harm to individuals taking part in the study and covered by the duty of care owed to them by the sites concerned. The co-sponsors require individual sites participating in the study to arrange for their own insurance or indemnity in respect of these liabilities.
- Sites which are part of the United Kingdom's National Health Service will have the benefit of NHS Indemnity.
- Sites out with the United Kingdom will be responsible for arranging their own indemnity or insurance for their participation in the study, as well as for compliance with local law applicable to their participation in the study.

10 REPORTING, PUBLICATIONS AND NOTIFICATION OF RESULTS

10.1 AUTHORSHIP POLICY

Ownership of the data arising from this study resides with the study team.

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Appendix 19 (a): Timeline of building app intervention

This serves as an outline of the work conducted on the building of this app intervention between April 2021 to May 2023: planning, collaborations, prototype developed, first draft of app coded and built, internal testing and feedback, final draft of app built, handover period to first author (AR). An outline of the timeline, summary of events and people involved is provided below.

Timeframe	Summary	People Involved
April-May 2021 *Ideas developed, team built, plan for prototype building, feedback from inner team and testing.*	• Contact established with Perdita Stevens (Informatics, UoE) and Maria Wolters (Design Informatics, UoE) regarding interest in recruiting students as part of Undergraduate Thesis (Informatics) and Summer Internship (MSc Design Informatics). • Two students noted their interest and were recruited for this collaborative project (WW and EW).	Perdita Stevens Maria Wolters David Gillanders Anna Ryan
May-Sept 2021 *Collaborative meetings.* *Plan to handover to Informatics undergraduate student to build and code app, assistance in design from Trainee Clinical Psychologist (AR).*	• AR arranged and chaired meetings with wider team for timeline planning and logistics. • WW to work on User Interface Design element of app over the Summer, at which point EW will be able to take over to build app. This will meet requirements for his Undergraduate thesis, at which point the app will be used for purposes of current research project.	Wayne Wu Edward Walpole Perdita Stevens Maria Wolters Nuno Ferreira David Gillanders Anna Ryan
May-Sept 2021 *Prototype developed*	• AR worked with WW, Design Informatics, who created a prototype of the app using Figma software (see Appendix 19b and 19c).	Wayne Wu Anna Ryan

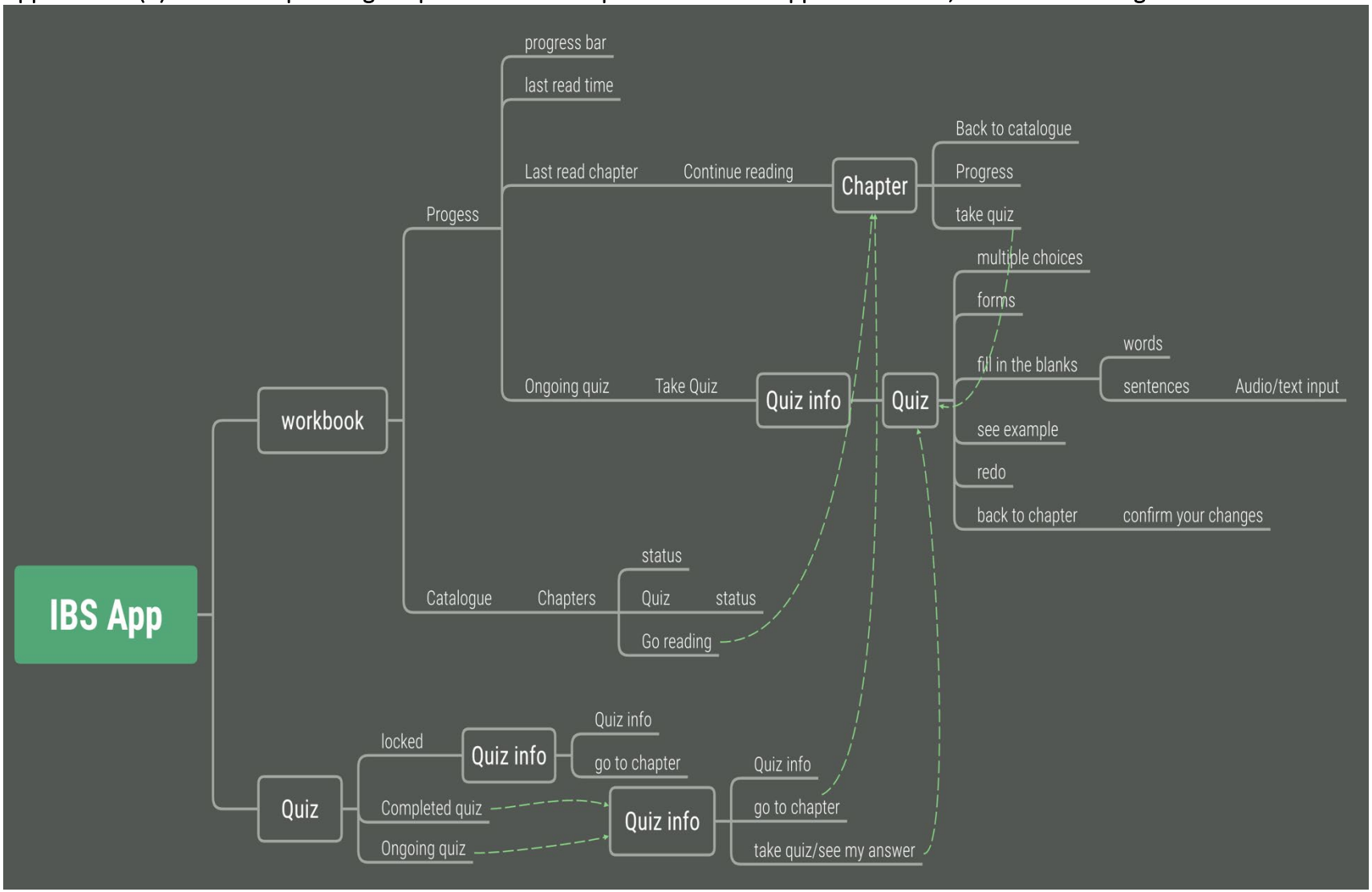
	• Regular meetings between AR and WW to project manage and guide creation of the prototype. • Presentation of prototype to wider team for feedback before handover to EW for basis upon which to build app (Informatic Undergraduate student).	
August 2021 *'Plan B' explored: to use existing IBS app MyGutSolution for purposes of project in case of complications arising in building of app.*	• Meeting with 'MyGutSolution': potential collaboration and use of existing app for purposes of thesis, however it was later decided by MyGutSolution that they were not in the position to collaborate at this time.	Niall Moloney Nuno Ferreira David Gillanders Anna Ryan
September 2021-April 2022 *Building app*	• Weekly meetings between AR and EW to guide project management, address concerns, Gantt chart deadline planning for deadline targets. • Plan was for app to be built by Jan 2022. • The first draft of the app was available for initial testing by the AR in April 2022.	Edward Walpole Anna Ryan
April-May 2022 *Internal testing: app feedback and editing*	• AR tested first draft of the app where a number of issues were identified: including playback and audio difficulties, improving design interface, updates required to password restrictions, adding a tutorial on how to use app upon initial login. This feedback was given to EW who worked upon rectifying the identified areas. • This testing, feedback and re-drafting process lasted 2 months between AR and	Edward Walpole David Gillanders Anna Ryan

	EW to make required edits and think of practical solutions where edits were not possible (e.g., was not possible to upload audio exercises as one recording, therefore they were added as separate files that played sequentially). • DG also contributed to internal testing and feedback. • Due to limitations of the Ionic framework the app was built on, this meant it was necessary to work around its own infrastructure to provide a functioning app primarily before improving design and user interface. Some requests for improving design interface and engagement with the app had to be de-prioritised due to the Informatics student's timescale for the project.	
June-September 2022 *Attempts for gaining technical support for app within remit of DClinPsychol project*	• A number of unexpected issues arose with the building of the app: for iPhone, app needs to be re-published every 90 days, after which time student will no longer be collaborating in this project. • As apps are published in beta testing mode and not publicly available, it is necessary to add testers to the app via email. • AR met with EW to learn how to support technical issues and process of adding participants on both Apple Developer Account for iPhone and Google Play console for Android users and assessing progress of app use on Firebase platform.	Chris Swift Edward Walpole Anna Ryan Charlotte Smith Filip Horvat Anne Robertson *(Head of Services and User Engagement, EDINA)* Ian Stuart *(Software Engineer, EDINA)*

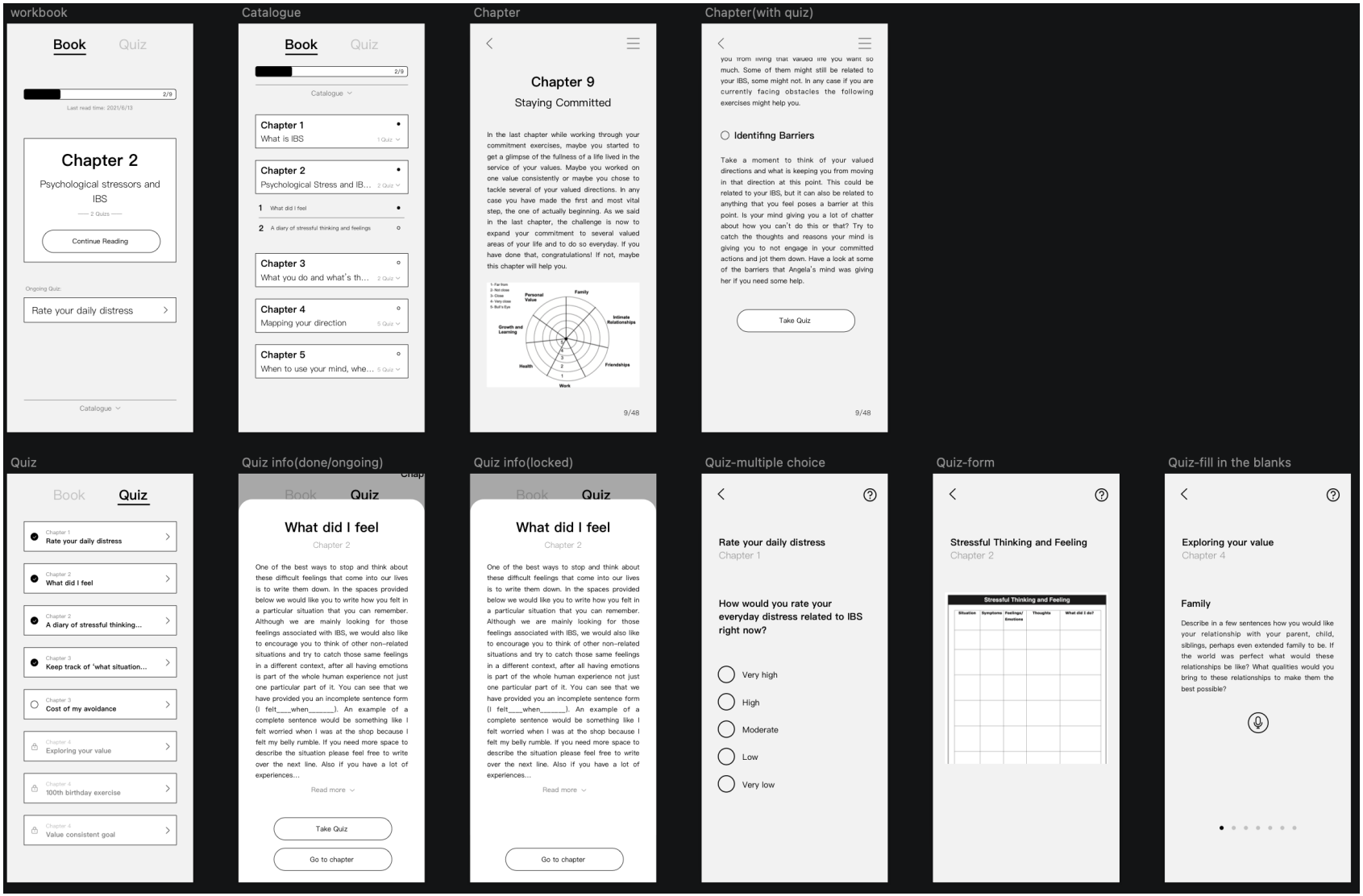
	• Several meetings and contacts were attempted to recruit technical support for this project following the end of the student's deadline: including meetings with EDINA at the UoE (too far out of budget to provide support), contacting the Informatics team at UoE, Digital Innovation Team UoE, IS UoE: none of the aforementioned were able to provide support. C. Swift (Learning and Information Technology Manager at UoE), agreed to provide technical support where possible and supported particularly with the development of the Android re-publication of the app and SOPs. • Process to ensure app meet requirements for IT Lothian approval as well as hand over from student to AR: IT Security meetings between AR, C. Smith and FV. NHSL R&D IT Security Risk Assessment granted on agreed conditions. Risk Assessment Agreement, Outgoing Subcontract and DPIA completed by AR (see Appendices 15, 16 and 17).	
August-September 2022 *Handover*	• A meeting was held between EW, AR, DG and CS to handover the process of re-publishing the app. • This meeting was recorded and referred back to for notes on re-publishing the Apple version of the app every 90 days, by AR and DG. • CS re-published the Android version of the app, which did not require further re-publication during the testing period.	Edward Walpole David Gillanders Chris Swift Anna Ryan

October 2022 *Consult Apple Developer for guidance on appropriate restrictions and testing parameters.*	• AR consulted support from Apple Developer regarding the internal and external testing to ensure we added participants with the appropriate user profile restrictions.	Anna Ryan
October 2022 – May 2023 *Re-publishing App (Apple Version)*	• A total of 4 re-publications (each a 90-day cycle) of the Apple (iOS) version of the app were conducted over the course of the testing period: using XCode, VS Studio software and Apple Developer Account, with the coding commands learned from the re-publication handover.	David GIllanders Anna Ryan
November 2022-May 2023 Technical support	• AR provided ad-hoc technical support where required for participants downloading and using app: supported by telephone call, email and text and Standard Operating Procedures developed by EW, CS and AR (see Appendices 20, 21, 22). • Some devices were unable to support download of the app (*n*=1 Apple Device due to being an older version of the phone and unable to download 'Test Flight' (required to test the iOS app); *n*=3 Android devices unable to download – app not supported on these devices). • Efforts to resolve included the AR consulting the student who built the app (EW), Chris Swift (IT, UoE), and external IT support; however, these issues were unresolvable in the scope of the current project (*n*=4).	Chris Swift Edward Walpole Anna Ryan

Appendix 19 (b): Workflow planning adaptation of self-help workbook into app format: flow, content and design



Appendix 19 (c): First Prototype of app with Design Informatics



Appendix 20: Standard Operating Procedures (SOPs) (Users and Owners)

LWIBS SOPs

Users

iOS

Users will have to download the 'TestFlight' app which allows them to download beta testing apps. They will also have to provide their Apple ID. Given their Apple ID, invites will be sent to participants. Once they have accepted these invites, they will be able to view the LWIBS app on TestFlight. They can then download and install the app on their iPhone.

Android

Users will provide their Gmail accounts, and will then receive an email invitation, which will take them to LWIBS's page in the Google Play Store. From here they can install the application.

Once the app is installed, the usage is the same on both platforms. Users can create an account with an email address and password. Once logged in they will have access to the app's features. These are an e-reader, an audio player, and diary style mindfulness exercises.

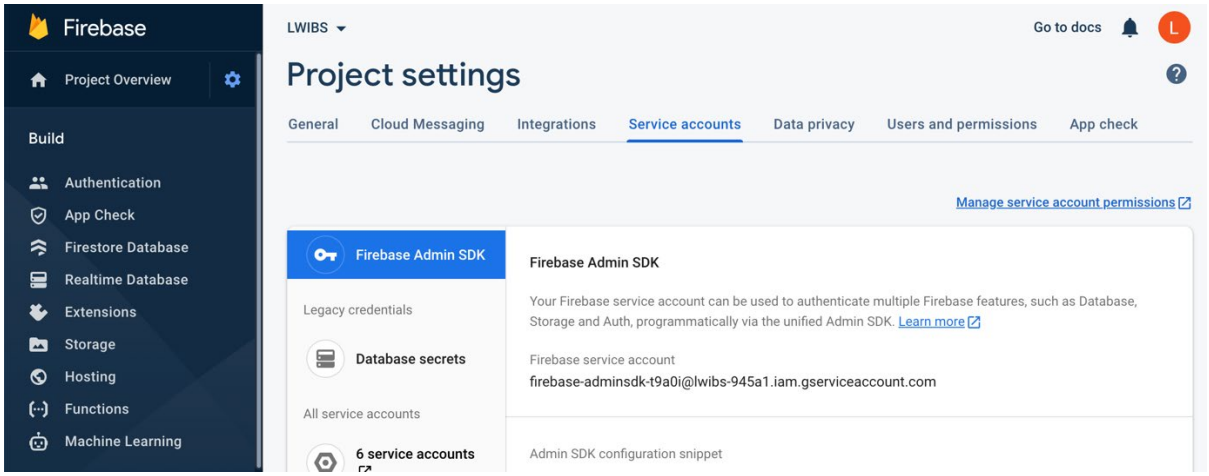
Owners

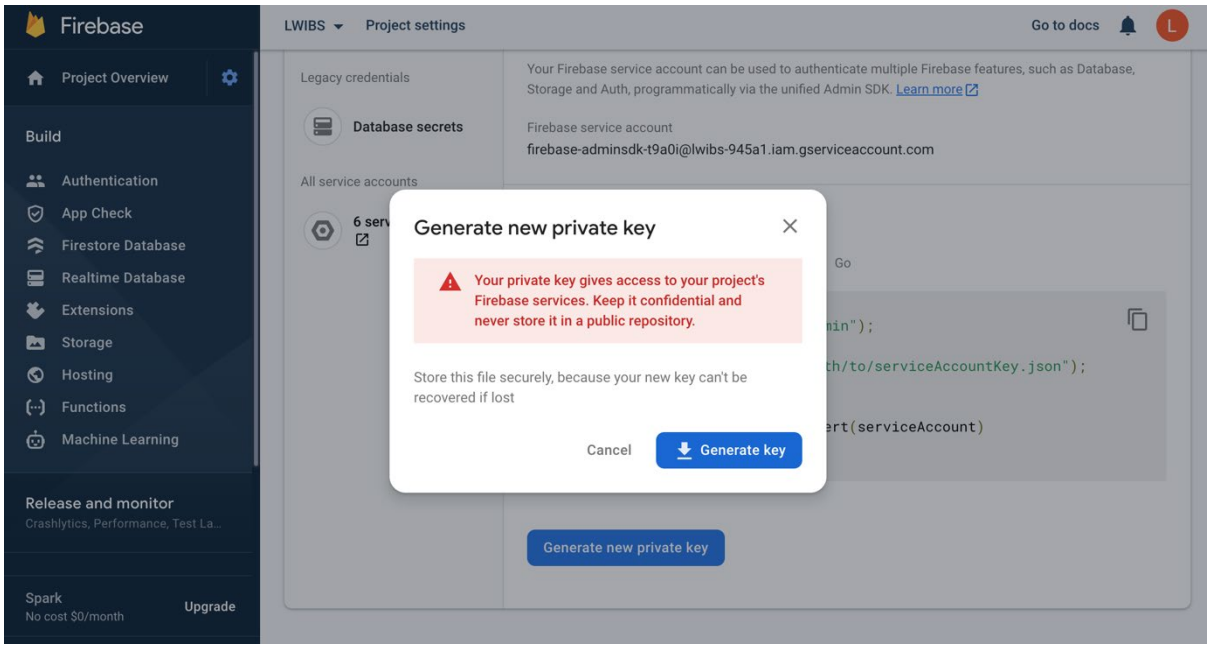
Invites can be sent to users through the various platforms' developer consoles. On Google Play, only one invite has to be sent. However, on Apple's developer console, users will first have to be invited to part of the development team, before they can receive their TestFlight invite.

To download the user data from Google's Firebase, owners will have to install Node Package Manager on their machine. They will have to temporarily revert the Firestore security roles to allow for any read and write access. They can then export all data using the following command from https://gunargessner.com/firestore-backup.

```
npx -p node-firestore-import-export firestore-export -a
credentials.json -b backup.json
```

Where credentials.json can be generated by logging in to Google Firebase, accessing Settings, then Service Accounts, then generating a new private key.





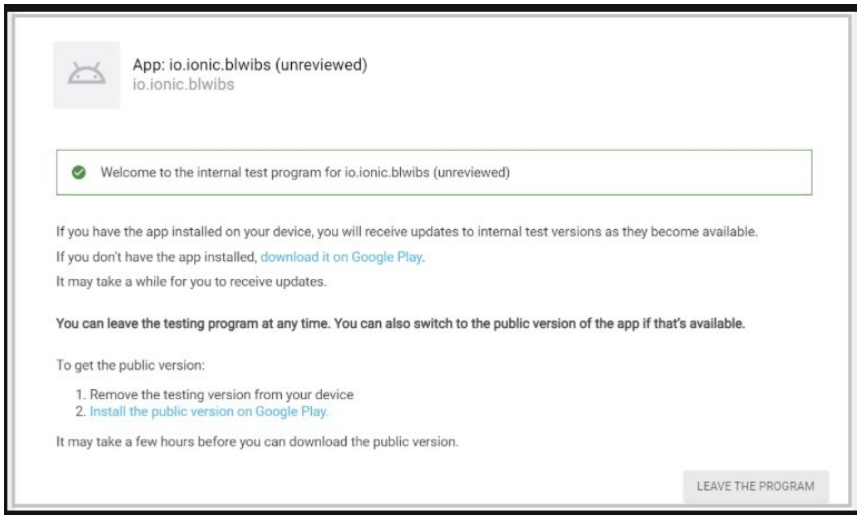
This command will create a new JSON document which will contain all the raw data. Owners should be careful to reinstate the Firebase security rules once this operation is completed.

Appendix 21: Android User SOP Guide

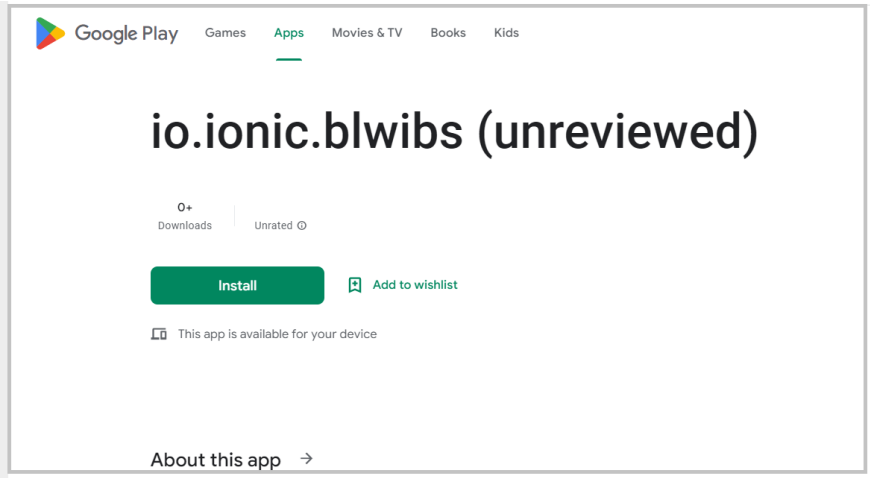
Accessing the 'Living with IBS' app: Android User Guide

1. Once you have contacted our team with your email linked to your Google Android account (ie. the email account you use to download Android apps), you will receive a link in your Google account email. Please click on this link.

2. The link can be opened on Android phone or Windows laptop and brings you to this screen. There's two options to *download it on Google Play* or *Install the public version on Google Play*. Choose to *download on Google Play.*



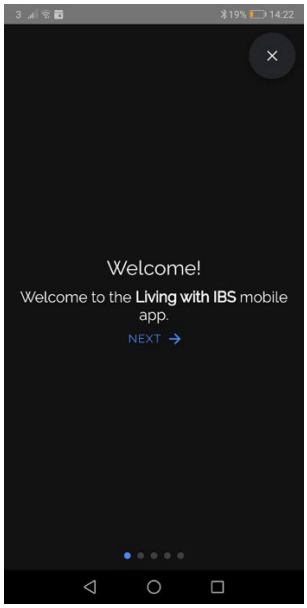
3. It will give you a prompt to install the app on Google Play. You may be asked to confirm your email address and password. After a few minutes the app should install on your device.



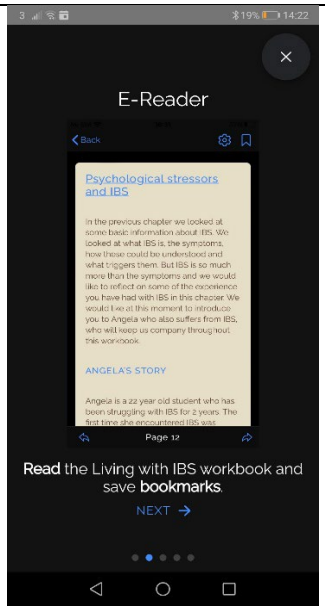
4. You may get a pop up notification saying the app has been installed. Or, the app will appear amongst the other apps on your phone. The app icon looks like this

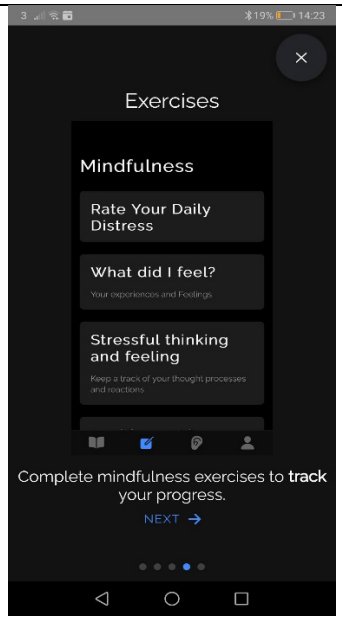
Using the app

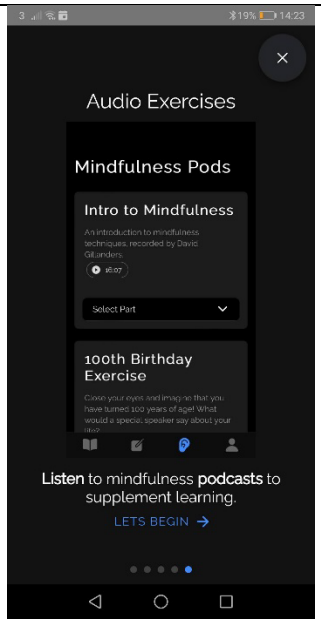
1. Open up the app you'll see a Welcome screen



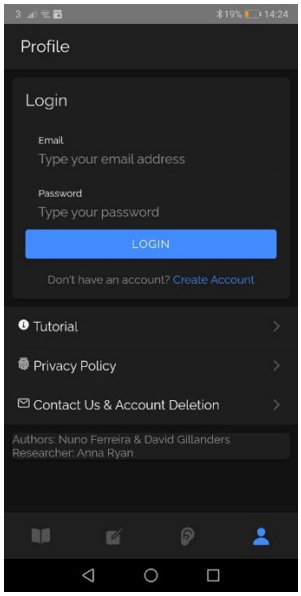
2. At the bottom are a few scrollable pages that give a little bit of information about the app and how you can use it. Click Next to scroll through these



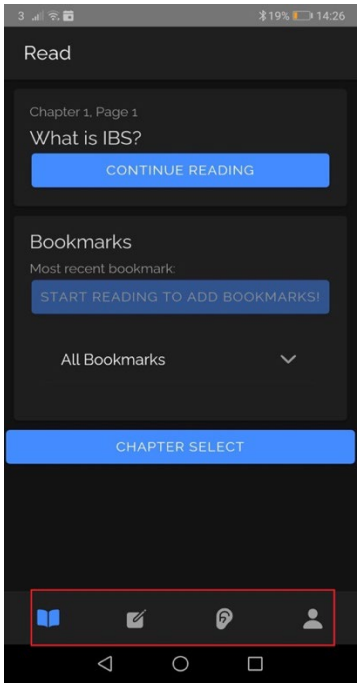




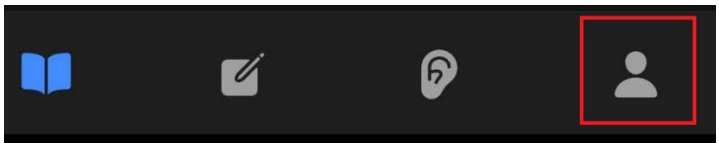
3. Once you've scrolled through these welcome pages you will come to a login screen where you'll be asked to either login or create an account if you are a first time user. When creating an account, the password must be at least 8 characters long and contain one each of an upper case character, lower case character, number, and special character.



4. When your account is created you will see the four sections of the app at the bottom of the screen: Read, Mindfulness, Mindfulness Pods, and Profile. Click on each one to see the resources available.



5. The section on the far right is your Profile

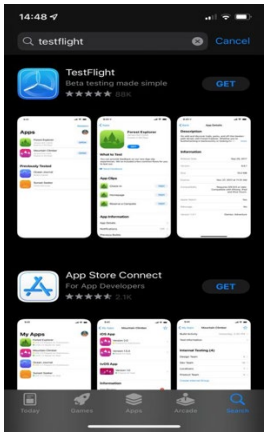


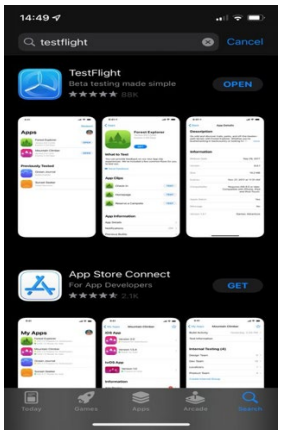
In here you can log out, read our privacy policy, run through a short tutorial, contact us, or request that your account be deleted.

If you encounter any difficulties following this guide, please do not hesitate to contact us for assistance by emailing:
lwibs.team@gmail.com

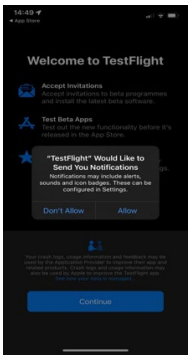
Appendix 22: iOS SOP User Guide

Downloading Living With IBS App for iOs: User Guide (approx. 5 mins setup). (if you have already downloaded TestFlight app, please skip to step 6).

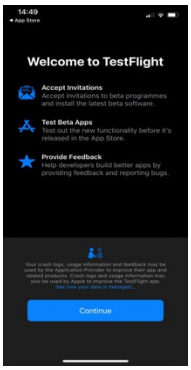
1. Download 'TestFlight' app from the Apple Store (free to download). Once downloaded, Open the TestFlight app.
2. 



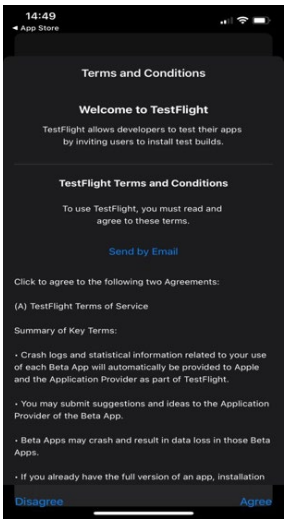
2. Welcome to TestFlight page – click 'allow' to notifications (to allow for any notifications regarding updated versions of the app)



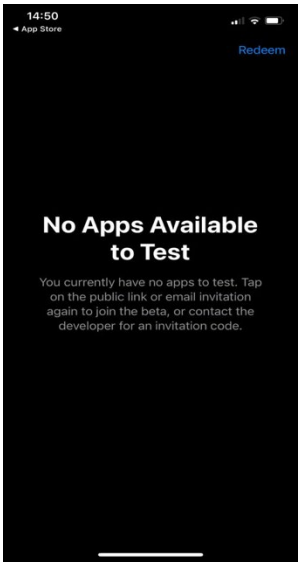
3. Welcome to TestFlight page – press 'Continue'.



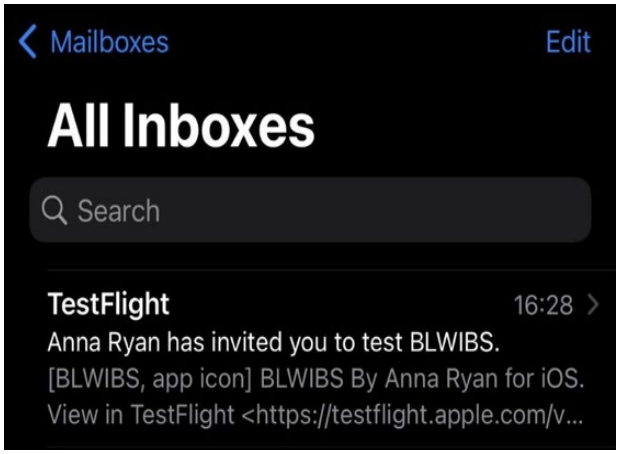
4. TestFlight terms and conditions – press ‘Agree’

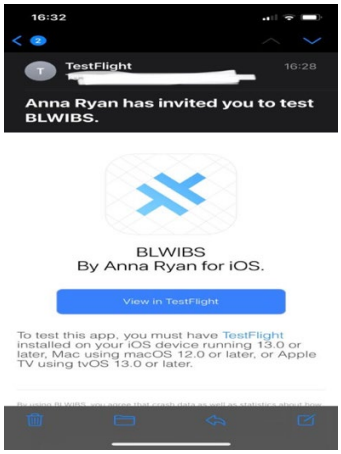


5. The next page will read ‘no apps available to test’. You can now click out of this app and open your email linked to your Apple ID.

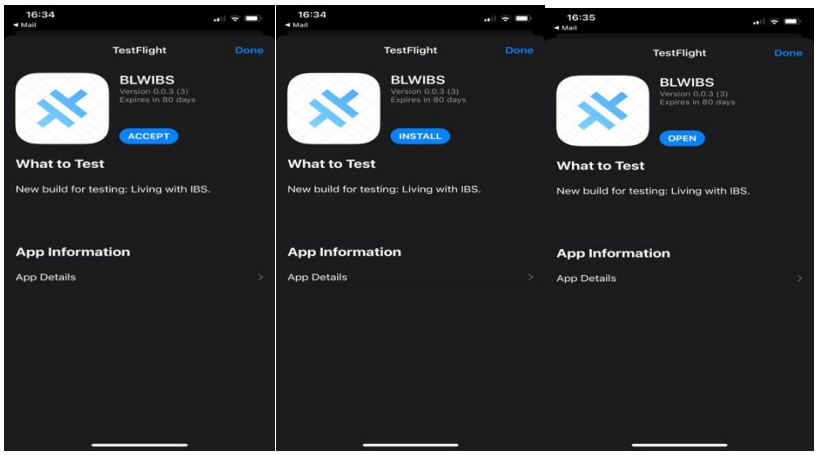


6. At this point, if you have not already, please send an email from your email address linked to your Apple ID (ie. email which you can use to download Apps from the App store/sign into iCloud) to indicate your interest in participating in the study. If you have already emailed us your Apple ID, please check for an email from ‘TestFlight; which will appear in your Inbox like so: (once opened, click ‘view in TestFlight’)

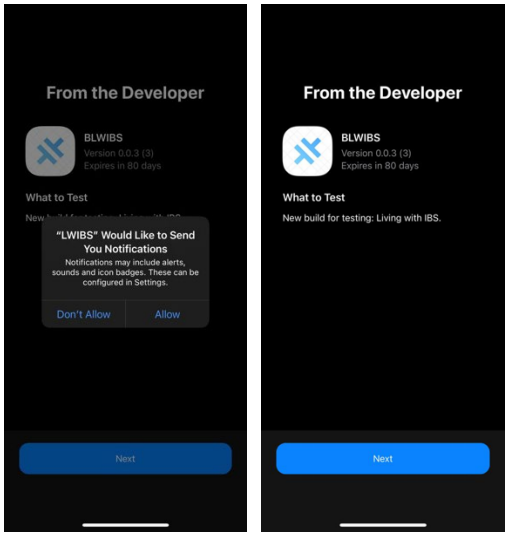




7. Click (a) ‘Accept’, (b) ‘Install’ and (c) ‘Open’

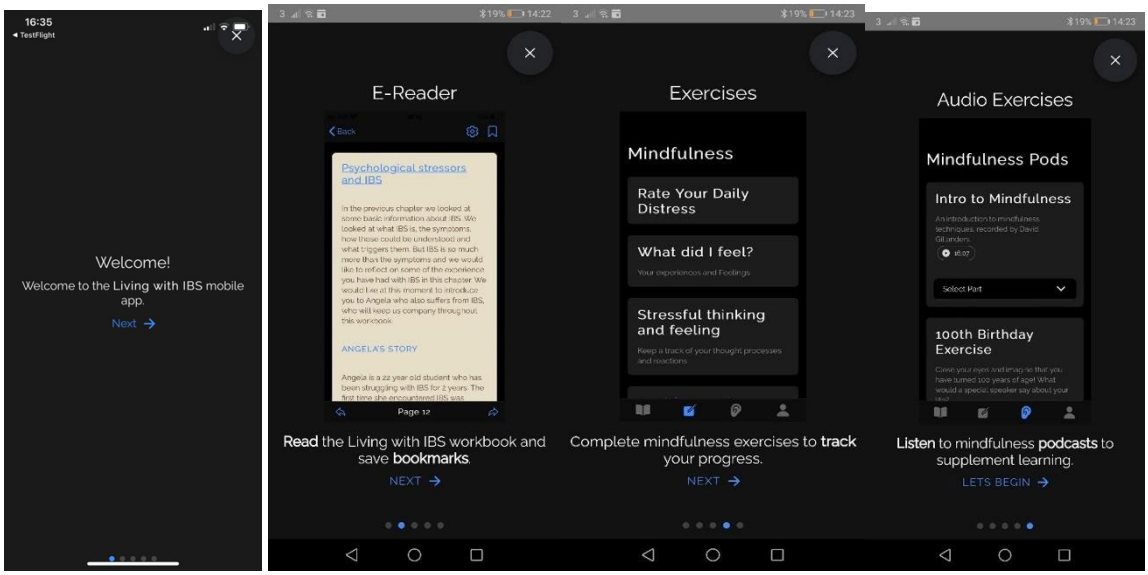


8. Click ‘allow’ to notifications. Then, click ‘Next’.



9. Click ‘Start Testing’

10. You have arrived at the Welcome page of the app. Click through these items as a Tutorial of how to use the app, how you can customise the experience to suit you (ie. font size, shape, background colours) and introduce you to the various aspects of the app: workbook, interactive exercises and audio exercises. Once familiarised, click Next to scroll through these.



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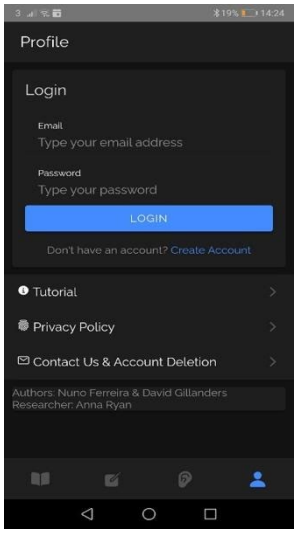
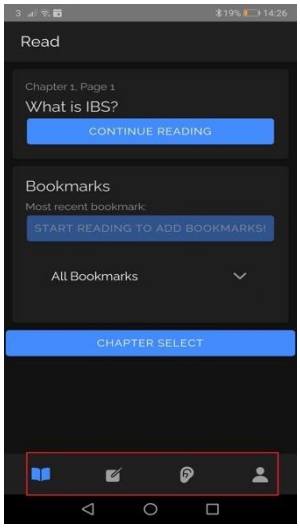
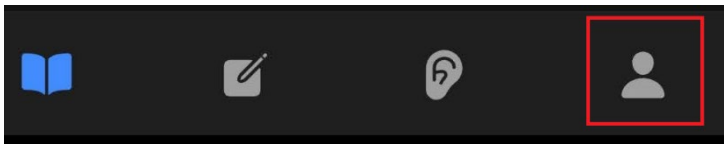


13. When your account is created you will see the four sections of the app at the bottom of the screen: Read, Mindfulness, Mindfulness Pods, and Profile. Click on each one to see the resources available.



14. The section on the far right is your Profile.



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If you encounter any difficulties following this guide, please do not hesitate to contact us for assistance by emailing: lwibs.team@gmail.com

Appendix 23: Welcome Tutorial Screenshots of App