The Cognitive Behavioural Treatment of Irritable Bowel Syndrome: Feasibility of a Nurse Delivered Model of Guided Self-Help

Andrew David Dainty

MA, BSc Hons, AdvDipN, RN

Thesis submitted to the University of Nottingham
for the degree of Doctor of Philosophy

June 2016

PhD Thesis June 2016 Student ID 4191605

Abstract

Background: Irritable bowel syndrome is a medically unexplained phenomena relating to the lower gastrointestinal tract with symptoms such as altered bowel habit and abdominal pain. Patients experience poor quality of life and consume significant healthcare resources. Mechanisms for the delivery of evidence based psychological interventions for irritable bowel syndrome within the National Health Service are lacking and the feasibility of these interventions is poorly understood.

Methods: A novel, low-intensity, nurse-led psychological intervention has been developed and trialled within a mixed methods feasibility study. Twenty participants were randomly allocated across four treatment conditions consisting of; a treatment as usual control (n = 5), self-help (n = 5), low-intensity (n = 5) and high-intensity (n = 5) cognitive behavioural therapy interventions. A total of ten participants took part in post-intervention interviews analysed using a group thematic analysis.

Results: Recruitment to this feasibility study was a significant challenge with 22 participants recruited of which, 20 were randomised to the feasibility interventions. Of the 104 patients approached within secondary care gastrointestinal clinics, 27.7% of patients volunteered to enrol into the study. Reasons provided relate to difficulties with committing to taking part and personal circumstances. Themes derived from post-intervention interviews suggest participant's valued face-to-face therapist interaction and described their perceived treatment utility along with a variety of barriers and facilitators to engagement in CBT interventions.

Conclusion: Low-intensity and self-help cognitive behavioural therapy may be feasible mechanisms for the delivery of evidence based psychological interventions for patients with IBS, although significant concerns regarding recruitment of participants to future trials will need to be addressed. Further development of these lower-intensity interventions in collaboration with service users is required in order to improve the acceptability and relevance of the interventions.

Acknowledgments

I would first like to acknowledge the support of my PhD supervisors, Professor Patrick Callaghan, Professor Mark Fox, and Associate Professor Nina Ruth Lewis, who have provided extensive knowledge and support throughout my studentship. I would also like to acknowledge the support of the collaborators which I have worked with over the duration of my fellowship; Dr Stephen Timmons, Elizabeth Holtham, Philip Kinsella and Andy Wragg. I have enjoyed working with Dr Melissa Hunt from the University of Pennsylvania, USA, who has devoted her time and energy to the development of the nursing intervention. I would also like to thank our team of gastrointestinal, hepatobiliary and surgical colleagues who have helped with the challenging task of recruiting participants for the feasibility study.

The primary research reported here would not have been possible without the dedication and voluntary involvement of patients who have not only participated within the study, but have also helped to develop the research methods and materials. I am also grateful to the European Academy of Nursing Science (EANS), Professor David Richards (EANS president) and their team of experts, who have provided me with an extensive course of additional education through their complex interventions summer schools for doctoral students.

I am grateful to the many academics within the University of Nottingham who have helped to develop my analytical skills, research knowledge and professional profile. Attending an extensive three year programme of research and education has required a vast amount of energy and dedication, which would not have been possible without the support of my partner, Gary Peter Dawson and my family. The same applies to my PhD colleague Louise Bramley, with whom I have developed a fruitful and enjoyable working relationship throughout our three years of study together. I am very grateful to Dr Joanne Cooper for her inspiration and guidance throughout my early research career.

Abbreviations

5-HT	5-hydroxytryptamine or serotonin
$5HT_4$	5-Hydroxytryptamine receptor 4
ACT	Acceptance and commitment therapy
ANS	Autonomic nervous system
ASI	Anxiety severity index
BABCP	British association for behavioural and cognitive psychotherapies
BDA	British dietetic association
BRU	Biomedical Research Unit
BSSS	Bowel symptoms severity scale
CBT	Cognitive behavioural therapy
CI	Confidence interval
CNS	Central nervous system
CONSORT	Consolidated standards of reporting trials
CPSQ	Consequences of physical sensations questionnaire
CPSR	Composite primary symptom reduction score
CRF	Case report form
CSFBD	Cognitive scale of functional bowel disorders
CT	Cognitive therapy
DBT	Dialectical behaviour therapy
DOH	Department of Health
DSM-IV	Diagnostic and statistical manual of mental disorders, 4th Edition
EANS	European Academy of Nursing Science
EMA	Anti-endomysial antibodies
ENS	Enteric nervous system
FD	Functional diseases
FGID	Functional gastro-intestinal disease
FODMAP	Fermentable oligosaccharides, disaccharides, monosaccharides, and polyols
GAD	Generalised anxiety disorder
GI	Gastrointestinal
GSRS-IBS	Gastrointestinal symptom rating scale for irritable bowel syndrome
HADS	Hospital anxiety and depression score
HI-CBT	High intensity cognitive behavioural therapy
HR-QOL	Health related - quality of life
IAPT	Improving access to psychological therapies
IBD	Inflammatory bowel disease

IBS	Irritable bowel syndrome
IBS-A	Irritable bowel syndrome alternating subtype
IBS-C	Irritable bowel syndrome constipation subtype
IBS-D	Irritable bowel syndrome diarrhoea subtype
IBS-M	Irritable bowel syndrome mixed subtype
IBS-U	Irritable bowel syndrome ungraded subtype
IBS-QOL	Irritable bowel syndrome quality of life
IBS-SSS	Irritable bowel syndrome symptom severity scale
ICC	Inter-class correlation coefficients
ICER	Incremental cost effectiveness ratio
IgA	Anti-gliadin antibodies
ITT	Intention to treat
LI	Lactose intolerance
LI-CBT	Low intensity cognitive behavioural therapy
LM	Lactose malabsorption
LOCF	Last observation carried forward
MANOVA	Multivariate analysis of variance
MMR	Mixed methods research
MRC	Medical Research Council
MUS	Medically unexplained symptoms
NHS	National health service
NICE	National institute for health and clinical excellence
NIHR	National Institute for Health Research
NNT	Number needed to treat
OR	Odds ratio
P	P value
PAG	Patient advisory group
PDA	Personal digital assistant
PEDro	Physiotherapy evidence database tool
PHGG	Partially hydrolysed guar gum
PICO	Patient intervention comparator and outcomes
PI-IBS	Post infectious - irritable bowel syndrome
PNS	Parasympathetic nervous system
PPI	Patient and public involvement
PST	Problem solving therapy
PTSD	Post-traumatic stress disorder
PWP	Psychological wellbeing practitioner
QOL	Quality of life

RBET	Rational behavioural emotive therapy
RCT	Randomised controlled trial
REC	Research ethics committee
SCL-90-R	The symptom checklist-90-R
SD	Somatisation disorder
S.D.	Standard deviation
SF36	Medical outcome short form 36
SH	Self-help
SIT	Stress inoculation training
SMF	Site master file
SNS	Sympathetic nervous system
SSRI	Selective serotonin reuptake inhibitor
TAU	Treatment as usual
TCA	Tricyclic antidepressant
TIC-P	Trimbo's institute of medical technology cost questionnaire for psychiatry
tTGA	Tissue transglutaminase antibodies
UK	United Kingdom
USA	United states of America
VSI	Visceral sensitivity index
WGO	World Gastroenterology Organisation
WLC	Waiting list control
WMA	World medical association

Contents

List of tables and figures

Tables

Figures

Chapter 1 ▪ Introduction

Within this thesis, I present an extensive piece of work undertaken during a three year PhD studentship carried out between October 2012 and December 2015. The subject of this thesis relates to the study of a gastrointestinal phenomenon commonly referred to as the Irritable bowel syndrome or IBS. IBS is one of a number of medically unexplained conditions frequently observed within gastrointestinal medical and nursing practice, both within primary and secondary care settings. IBS is a form of functional gastro-intestinal disease (FGID), characterised by abnormal bowel function with a range of symptoms such as altered bowel habit, bloating and abdominal pain. IBS frequently develops into a chronic and persistent complaint resulting in intermittent episodes throughout the course of the condition.

Within chapter 2, a background of the condition is presented and critically discussed along with the data regarding the prevalence and characteristics of IBS. A case is built for the significant impact IBS has on patients, healthcare systems and society by presenting the reader with a discussion of the latest epidemiological data relating to IBS. The complex picture of IBS is described and critically discussed, which aims to inform the reader of what is known to date about the manifestation and maintenance of the condition. A particular feature of IBS is the co-morbid psychological profiles of people affected by the problem as observed within a variety of study samples. These issues are potentially fundamental to the course of the condition and also have a significant influence on both the onset and management of IBS. The impact that these issues have upon the course of the condition and its treatment are also presented and critically discussed.

Later in chapter 2, a discussion regarding the biopsychosocial models of IBS is presented, particularly the work of leading authors such as Levy et al. (2006), Chey (2013) and Drossman (2006). The concept of psychosomatic illness and how these theories apply to general practice

and our understanding of unexplained medical phenomena such as IBS are also discussed. The origin of cognitive behavioural interventions from the early development of theories described by Beck et al. (1979), through to the modern day application of these methods to a variety of medical and psychological phenomena within modern healthcare are presented. The theory of cognitive behavioural therapy (CBT) and the application of multifaceted evidence based interventions for the treatment of IBS are then presented and discussed. By the end of chapter 2, the reader will have been provided with a complete understanding of IBS, the clinical significance of the condition and its complex characteristics.

Within chapter 3, the evaluation of CBT which offers promise for the treatment and management of IBS is extensively reviewed with a systematic review of the literature, which aims to critically review the current evidence base regarding the use and application of CBT for the treatment of people affected by IBS. There is a focus on the methods used for the delivery of interventions as evaluated with experimental research and an exploration of factors which may have influenced the lack of adoption of these interventions within everyday gastrointestinal nursing practice. There is an extensive discussion of the features of the current evidence base, the development and evaluation of various methods of CBT intervention delivery and the implications these have for implementation within nursing practice.

As a result of the literature review, chapter 3 concludes with a variety of recommendations for future research. There is a great deal of uncertainty regarding the interventions which may be best suited to implementation with NHS settings and how future studies should be designed to evaluate such complex interventions utilising the most robust methods. The study which arises from the systematic review is therefore clearly defined as feasibility work rather than a full scale trial, resulting in the design of the complex feasibility randomised controlled trial (RCT) described within

chapter 4. The feasibility study methods are described in depth, along with extensive justifications for the methods used which have been designed in accordance with the medical research council's (MRC) framework for the evaluation of complex interventions (MRC, 2008).

The feasibility study was designed to evaluate the feasibility of both the methods of evaluation and the application of a new and innovative low-intensity method of CBT treatment, delivered by a registered nurse practicing within gastroenterology at a University teaching hospital. Throughout the methods described, there is an emphasis of the application of interventions within the UK context based within the outpatient gastroenterology speciality. The feasibility study consists of a mixed methods research (MMR) design, with the implementation of concurrent qualitative data collection underpinned by a pragmatic research philosophy. This study described is primarily concerned with the development of methods for evaluating the effectiveness of a novel, nurse delivered CBT intervention within a follow-on program of research.

Within chapter 5, the range of feasibility data collected during the conduct of the feasibility work is presented. A particular feature of the feasibility study relates to the challenges faced during the recruitment phase, which is presented and critically discussed in depth with emphasis on the implications these issues have for further research work. The concurrent qualitative research offers unique and novel insight regarding barriers and facilitators to the use and application of CBT interventions for patients with IBS as implemented within the feasibility study.

Finally, within chapter 6, the findings of previous research studies are contrasted and the relationship discussed between earlier studies and the data observed as a result of the feasibility work. In particular, the concurrent interviews held with study intervention participants offer a novel insight into the perceptions and experiences of service users. These data gathered during feasibility have significant implications for the

design of a follow on study, for which a range of recommendations arising from the research which will need to be taken into account are summarised. Finally, chapter 7 is an extensive bibliography of the literature consulted throughout and chapter 8, a list of appended items which the reader may find useful to consult as indicated within the text.

Chapter 2 · Irritable Bowel Syndrome

2.1 Clinical features and characteristics

IBS is a form of functional gastro-intestinal disease (FGID), characterised by abnormal bowel function with a range of symptoms such as diarrhoea, constipation, bloating and abdominal pain (Schmulson and Chang, 1999). IBS can become a chronic condition with the majority of patients experiencing intermittent episodes throughout the course of the condition (Hahn et al., 1998). Patients with IBS can be divided into certain subsets based on the symptoms experienced and the types of stools associated with their condition. IBS is therefore often referred to by clinicians as either IBS-D (diarrhoea predominant), IBS-C (constipation predominant) or IBS-A (where alternation is present between the two stool patterns).

There is some difficulty in clinicians easily defining IBS due the overlap IBS symptoms may have with a vast range of other conditions. It was in the late 1970's that some of the first attempts to define IBS clearly were made by Manning et al. (1978). Manning and colleagues (1978) originally compared symptomatic patients who were investigated for gastrointestinal complaints and found to have or not to have physiological gastrointestinal disease in order to generate a set of characteristics consistent with a clinical diagnosis of IBS (defined by the absence of biological disease).

The criteria developed by Manning and colleagues (1978), which were recommended to be present for a diagnosis of IBS consisted of the following six characteristics;

1. Onset of pain linked to more frequent bowel movements
2. Looser stools associated with onset of pain
3. Pain relieved by passage of stool
4. Noticeable abdominal bloating
5. Sensation of incomplete evacuation more than 25% of the time
6. Diarrhoea with mucus more than 25% of the time

More recently, the Rome Criteria, having first been reported within the literature in 1990 (Drossman et al., 1990) is now frequently used as diagnostic criteria during the assessment of IBS within clinical practice or during investigational trials. Later editions of the Rome Criteria were reported with the introduction of the Rome II (Thompson et al., 1999) and the current Rome III Criteria (Longstreth et al., 2006).

According to Rome III Criteria (The Rome Foundation, 2016), IBS is defined as;

*Diagnostic criterion**

Recurrent abdominal pain or discomfort** at least 3 days/month in the last 3 months associated with *two or more* of the following:

- Improvement with defecation
- Onset associated with a change in frequency of stool
- Onset associated with a change in form (appearance) of stool

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

** "Discomfort" means an uncomfortable sensation not described as pain.

Assigning diagnostic criteria to patients with IBS is sometimes controversial, and some clinicians feel that IBS is best considered a diagnosis of exclusion based upon a patient's history, physical examination, and the absence of alarming or more serious clinical features (Mearin and Lacy, 2012). It is perhaps the symptom overlap between IBS and other more serious biological conditions and the potential for misdiagnosis which contribute to criticisms of these diagnostic criteria. Nonetheless, many physicians still consider IBS a diagnosis of exclusion, and will combine the use of diagnostic criteria with due clinical judgement, the necessary clinical investigations and appropriate follow up care. A recent study clearly identifies that patients are likely to switch between the phenotypes of IBS-C and IBS-D over time, demonstrating the instability of the current classification system (Marshall et al., 2010).

An accurate diagnosis of IBS can be considered important for a number of reasons, some of which are advocated by Mearin and Lacy (2012) and are summarised below.

i. Patients without a definitive diagnosis may have symptoms which are amenable to treatment following an appropriate diagnosis

ii. Untreated symptoms may directly reduce productivity as a result of presenteeism and absenteeism. Treatment may therefore improve the economic burden in this regard

iii. Patients without a diagnosis may have inappropriate fears and concerns which may contribute to unnecessary testing

iv. A lack of diagnosis may lead to unnecessary procedures and even some types of surgery

For these reasons, the quest for accurate and effective diagnostic criteria continues and the Rome Foundation continues to update their criteria in light of the latest evidence (The Rome Foundation, 2016). Current medical practice is to avoid unnecessary extensive testing in this group of patients, and a confident diagnosis can often be made in the majority of cases with a physical examination and limited laboratory or structural studies such as procto-sigmoidoscopy and a complete blood count (Longstreth, 1997).

Symptoms experienced by patients vary in frequency and intensity. Patients report pain or discomfort to be the most frequent symptom occurring, on average 33% of the time (Hahn et al., 1998). Pain is a particular problem for patients with IBS, and Hungin and colleagues (2005) found that 18% considered the pharmacological treatment of pain to be 'not at all effective' (Hungin et al., 2005). Interestingly, IBS patients appear to demonstrate significant changes and tolerances to the perception of sensations within the gut. These sensations, otherwise referred to as 'visceral hypersensitivity' are often the sensations

described by patients as pain (Guthrie et al., 2004). It is these changes, which experts refer to as visceral hypersensitivity which is also evident within many patients presenting with IBS.

The phenomena are thought to result from the function of neurone chains resulting in changes in visceral perception (Camilleri et al., 2001). Theories which underpin the development of chronic visceral hypersensitivity often seen in some patients with IBS are derived from animal models whereby hypersensitivity appears to follow transient inflammation of the colon (Zhou and Nicholas Verne, 2011). Zhou and Nicholas Verne suggest that the presence of somatic hypersensitivity and an alteration in the neuroendocrine system result from multi-systemic factors such as; nociceptive input from the colon leading to hypersensitivity; increased intestinal permeability which may induce visceral nociceptive drive and alterations in the expression of microRNAs within the gastrointestinal tissue.

Hahn and colleagues (1998) found that patients also reported bloating 28%, altered stool form 25%, altered stool passage 18%, and mucus 7% of the time. On average, IBS patients experience symptoms for around 7 days per calendar month (Hungin et al., 2003). Patients with IBS do not have changes within the gastrointestinal tract which can be successfully visualised with diagnostic techniques such as endoscopy or colonoscopy. Patients with IBS also do not have changes in biochemistry, as would be evident in organic gastrointestinal disease. However, changes in gastrointestinal motility have been observed, and in particular, IBS patients have been associated with irregular contractions within the luminal tract (Simrén et al., 2000). Other observed transit abnormalities include increased frequency of high amplitude propagating contractions within the transverse, descending and sigmoid portions of the colon (Chey et al., 2001). It is for these reasons that IBS is often considered a 'functional' disorder, as although biological features of disease are absent, the gastrointestinal tract is considered not to be functioning as it *normally* would.

Chey and colleagues (2001) suggest that it was the observations in abnormal gastrointestinal motility which perhaps explain a potential causative mechanism for pain experienced by patients with diarrhoea predominant IBS. Prolonged transit time has also been observed within patients with constipation predominant IBS, which was associated with the symptoms of bloating and abdominal distention (Agrawal et al., 2009). Researchers have also found that increasing these delayed transit times with pharmacological interventions has an immediate effect in reducing gas retention and associated levels of pain experienced by some sufferers (Caldarella et al., 2002).

IBS is often considered a heterogeneous condition with an array of treatments which vary in effectiveness (Spiller et al., 2007). The lack of effective treatments for the symptoms experienced by those with IBS is clearly evident within the literature. On average, 41% of patients with constipation and 34% of patients with bloating symptoms report medical treatment to be ineffective (Hungin et al., 2005). Furthermore, around 73% of IBS patients will report that their symptoms have never changed, with as little as 22% finding some improvement in their IBS symptoms following screening and diagnosis (Hungin et al., 2005). Many patients find little relief for their symptoms, and 46% report that they would try 'anything' to alleviate their symptoms (Hungin et al., 2005). IBS patients with a much longer duration of symptoms and associated psychological distress are more likely to have a much poorer prognosis and suffer from treatment refractory symptoms (Lembo et al., 1996). Around 33% of IBS patients have familial history of IBS (Kanazawa et al., 2004).

2.1.1 Prevalence

IBS is one of the most frequent gastrointestinal conditions diagnosed and may be responsible for around 40% of gastrointestinal related consultations (Wells et al., 1997). Approximately 10% to 20% of the general adult population report symptoms compatible with IBS when surveyed (Saito et al., 2002). International studies report a prevalence of IBS between 6% and 22% (Jane Lu et al., 2009). Within the United

Kingdom (UK), a prevalence of 14% among women and 6.6% amongst men is evident (Wilson et al., 2004). The pooled global prevalence of IBS was 11.2% in a recent meta-analysis of 80 international studies (Lovell and Ford, 2012). Some of the pooled results collated by Lovell and Ford are presented in the table below (see table 1).

Pooled prevalence of IBS according to Age, Gender and Socioeconomic Status

	No. of subjects	Pooled prevalence of IBS (95% CI)	Odds Ratio for IBS (95% CI)
Age band (years)			
<30	6909	11.0 (6.0-18.0)	1.00
30-39	7247	11.0 (7.0-16.0)	1.04 (0.85-1.27)
40-49	7543	9.6 (6.0-14.0)	0.86 (0.59-1.24)
50-59	5434	7.8 (5.0-11.1)	0.68 (0.40-1.17)
>60	5540	7.3 (4.3-11.0)	0.63 (0.38-1.04)
Gender			
Male	78’913	8.9 (7.3-10.5)	1.00
Female	83’330	14.0 (11.0-16.0)	1.67 (1.53-1.82)
Socioeconomic status			
High	866	14.0 (9.0-19.0)	1.00
Medium	1732	14.0 (8.0-22.0)	1.02 (0.72-1.44)
Low	2663	13.0 (7.0-22.0)	0.99 (0.71-1.36)

Table.1 Source: Lovell and Ford (2012)

Lovell and Ford (2012) reinforce the results of previous studies within their meta-analysis with a pooled prevalence of IBS much greater in females than males (14% vs. 8.9%). Variation in the prevalence of IBS exist between studies, some of this variation (1.1% to 45%) may be partially explained by inconsistency with various criteria used to define the presence of IBS (Lovell and Ford, 2012). Furthermore, Canavan et al.

(2014) suggest that communities in which there is higher perceived stress or lower perceived quality of life, greater potential gain from receiving a diagnosis, and fewer barriers to accessing health care will report a higher prevalence of IBS. The prevalence of IBS in Europe is 11.5%, with around 9.6% experiencing current symptoms (Hungin et al., 2003). The data presented above also support a tendency for many reported cases to occur in people less than 50 years of age. Symptom onset in IBS is associated with the second and third decades of life (Spiller et al., 2007) and 50% of patients develop IBS before the age of 35 (Maxwell et al., 1997). Around 40% of patients are aged between 35 and 50 years of age (Maxwell et al., 1997).

Some data derived from a household survey of 5430 individuals in the USA suggest an association between lower socioeconomic status and IBS prevalence (Drossman et al., 1993). Other research demonstrates IBS is more prevalent among those with a childhood in a higher socioeconomic group (Mendall and Kumar, 1998). The data which support this notion have been further supported with a recent study carried out by Howell et al. (2004). Areas in which there are a lower number of people employed in manual labour also report a higher prevalence of IBS (Canavan et al., 2014).

Plausible explanations for these observations may include better access to healthcare or a tendency for those with higher socioeconomic status seeking healthcare advice (Cremonini and Talley, 2005). In relation to childhood development, these observations could also be explained by early socialisation experiences, exposure to different infective organisms (which may be dependent upon social class), differences in diet and exposure to certain stressors (Howell et al., 2004). A UK based study has demonstrated no relationship between social class and IBS in adults, which may be explained by universal access to healthcare within the UK (Kennedy and Jones, 2000). On considering the data regarding socioeconomic status, it is likely that no significant association can be

found in relation to socioeconomic status, as found within a recent meta-analyses conducted by Lovell and Ford (2012).

Many studies report that IBS is much more common amongst women, with a female to male predominance ranging from 1:1 to 2:1 (Saito et al., 2002). Reasons for these differences remain unclear, although differences between male and female healthcare seeking behaviour or sociocultural differences have been implicated (Saito et al., 2002). Cultural differences among women are certainly supported in a recent study of the experiences and practices of Asian women (Jane Lu et al., 2009). Within this study, women were shown to have culturally influenced views of the body and gender norms which effect factors such as a willingness to engage with western medication regimens (Jane Lu et al., 2009).

There are some notable differences in the symptoms experienced by gender. For example, women tend to report more IBS-C, whereas men report more IBS-D than women (Lee et al., 2001). Lee and colleagues (2001) suggest that women seem to experience similar symptom severity to men, but tend to report higher levels of a variety of intestinal and non-intestinal sensory symptoms. Women also tend to be affected more by other functional disorders than men such as dysphagia, chronic functional abdominal pain, Sphincter of Oddi dysfunction, faecal incontinence, functional anorectal pain and pelvic floor dysfunction (Chang et al., 2006).

Although the menopause has been suggested to play a role in the observed differences in gender, no differences are evident between pre and post-menopausal women which make this an unlikely explanatory mechanism (Lee et al., 2001). Lee and colleagues (2001) propose that some of the observed gender differences may be a result of altered sensory processes, autonomic responses and cognitive hypervigilance. Differences have also been observed in the regulation of the autonomic nervous system (ANS) between men and women which may partially

explain some of the gender differences (Heitkemper and Jarrett, 2008). There is sufficient evidence to support socialisation as important factors when considering gender differences. For example, feelings of shame and conscientiousness associated with physical appearance may be more on an issue for women than men, particularly in relation to bodily functions (Chang et al., 2006 , Toner and Akmana, 2000). Much more research is needed to explore the complex differences in IBS prevalence, symptom profiles and healthcare seeking behaviours, all of which may be influenced to some degree by gender.

2.1.2 Healthcare seeking characteristics

Around 50% of individuals meeting diagnostic criteria for IBS within the general population will seek consultation for their symptoms (Cremonini and Talley, 2005 , Heaton et al., 1992). IBS is a heterogeneous condition with an array of clinical manifestations and an individual's decision to consult may be influenced by certain clinical features or predisposing factors.

There is evidence to support the fact that psychosocial factors may well be predictors of healthcare seeking behaviour among patients with IBS (Kettell et al., 1992). Hu et al. (2002) concluded that anxiety in particular was an independent factor which significantly predicted healthcare seeking behaviour among subjects with IBS within Chinese community settings. However, other studies have suggested that psychological co-morbidity in the form of anxiety, depression and somatisation have been found not to be significant predictors of healthcare seeking behaviour among primary care patients (Koloski et al., 2003). These results were supported by a later Australian study which suggests neuroticism, psychological morbidity and abuse history are not significant predictors of healthcare seeking behaviour for individuals with IBS (Talley et al., 1997). There is however, further evidence to suggest that anxiety is implicated in the need to seek consultation within secondary care settings (Ringström et al., 2007). Distress has been implicated as a significant predictor of healthcare

seeking behaviour within qualitative research studies (Bourgault et al., 2008).

IBS symptom profiles appear to play a significant role in healthcare seeking behaviour. Pain is one of the predictors most strongly associated with consultation in UK primary care populations, and the likelihood of consulting a physician is directly proportional to the number of overall symptoms experienced by the patient (Heaton et al., 1992). Talley et al. (1997) also support the notion that pain is an important factor in consultation behaviour, particularly when the pain experienced by the individual is of increasing severity and prolonged in duration. Pain and discomfort do not appear to feature independently within the Rome III definition of IBS, whereby patients are said to experience pain or discomfort (The Rome Foundation, 2016). As described within chapter 1, these features are considered to be associated with IBS if 1) they are relieved with defecation, 2) onset is associated with a change in frequency of stool or 3) onset is associated with a change in form (appearance) of stool.

Authors would suggest that pain and discomfort are often used interchangeably in IBS as they are temporally related to change in frequency or stool form (Thompson et al., 1999). Thompson and colleagues also suggest that the pain and discomfort terminology used in IBS definitions were amended within formal diagnostic criteria to 'broaden' symptom descriptions. Authors researching the measurement of pain and discomfort in clinical trials may also use the terms pain and discomfort interchangeably although Skevington (1998) suggests that these experiences are best measured with the consideration of six additional facets; the availability of social care, mobility, activities of daily living, positive mood and to a lesser extent, sleep and dependence on medication.

Despite the tendency for authors to use these terms interchangeably within diagnostic criteria and trial outcome measures, Handa et al.,

(2004) suggest that when considered as two distinct experiences, the discomfort reported by IBS patients was longer in duration than that of pain and the rate of anxiety disorders in pain patients tends to be higher than that of discomfort. These data therefore suggest that pain and discomfort may be considered as different experiences by patients. Patients who choose to consult may have more severe symptom profiles than those who choose not to consult (Kettell et al., 1992). Hillilä et al. (2007) found that symptoms (abdominal pain in particular), were responsible for consultation seeking behaviour rather than psychological co-morbidity in IBS subjects.

It is not just symptoms such as pain that seem to predict consultation behaviour, but rather the perceived severity of symptoms and the potential serious concerns patients may have regarding the possibility of other diseases such as malignancy and other serious disorders (Kettell et al., 1992). Although one might assume that consultation with a physician may abate some of these fears, there is evidence to suggest that these fears remain in all but 26% of UK primary care patients following consultation, which authors suggest may be indicative of unconfident diagnosis or inadequate explanation (Thompson et al., 2000). It does seem that a greater level of patient satisfaction within the patient-physician relationship contributes to increased rates of consultation in patients with IBS and functional dyspepsia (Koloski et al., 2003).

Around 20% of patients managed within general practice surgeries in the UK are referred to a gastroenterologist and around 9% to a surgeon (Thompson et al., 2000). Patients who consult within secondary care are thought to have a higher degree of anxiety, reduced physical functioning and may also experiences problems with food (Ringström et al., 2007). Consultation for IBS related symptoms does not appear to be influenced by socioeconomic status within the UK (Kennedy and Jones, 2000).

Medically unexplained symptoms (MUS) such as IBS are associated with stigma, and patients may find themselves referred to as ‘frequent flyers’

or ‘somatisers’ (Hatcher and Arroll, 2008). Furthermore, doctors who are consulted regarding IBS symptoms are often challenged by their lack of explanation, whilst the patients themselves often feel accused of fabrication (Hatcher and Arroll, 2008). Clinicians observe that patients who consult with IBS often have other MUS related to other organ systems (North et al., 2007). Despite the stigma which may be associated with frequent consultation and high service use, many patients develop autonomy by employing numerous self-management strategies such as altered nutritional behaviour, introspection and acquiring new knowledge (Bourgault et al., 2008). Thompson et al. (2000) also suggest that there is a need for specialists to develop mechanisms which better explain IBS to patients.

IBS patients may also seek consultation with family members or others with similar symptoms which may offer some degree of alternative support, and there is evidence to suggest that having a close relative with similar symptoms reduces healthcare seeking behaviour in patients with IBS (Ringström et al., 2007). In a recent review of the complex literature relating to the various healthcare seeking behaviours in patients with IBS, Al-Huthail (2013) suggest that some of the most important strategies to reduce healthcare seeking behaviour among this group of patients are likely to be interventions which; increase patient education, address patient concerns and educate patients regarding their condition which should include what one should expect from treatment.

2.1.3 Impact, resource use and burden

The lack of pathophysiological origin is perhaps one of the most bothersome predicaments for patients with IBS (Jane Lu et al., 2009). Furthermore, many physicians are challenged when consulted by patients with MUS (Hatcher and Arroll, 2008). It is often the unpredictability of symptoms which many patients find troublesome, which in turn have a significant impact upon daily activities (Whitehead et al., 1996). Furthermore, IBS and its symptoms not only have a significant impact on the activity of those afflicted, but also on body image and serves as a source of worry to patients affected by the condition (North et al., 2007).

IBS patients frequently report impairments in health-related quality of life (HR-QOL (Halder et al., 2004) which is also known to be a significant cause of absenteeism (Hungin et al., 2003).

Many patients with IBS develop chronic symptoms, and research suggests that around 40% of patients will continue to meet diagnostic criteria at 10 years after initial diagnosis, of which 59% will experience current symptoms (Hungin et al., 2003). The chronicity of the condition is demonstrated when patients themselves are asked about their condition. A staggering 60% of IBS patients feel that their condition would last for the duration of their lives (Hungin et al., 2003).

IBS is not thought to be associated with the development of more serious gastrointestinal disease or excess mortality (Spiller et al., 2007). However, worry is often a feature of IBS and in particular, the potential serious nature of symptoms are often troublesome and may provoke fear regarding more serious ailments such as a genuine fear of cancer (Kettell et al., 1992). Some clinicians may understandably feel that ruling out such serious conditions with a negative result on a diagnostic test such as a colonoscopy or barium study may offer some reassurance and result in positive effects (Maxwell et al., 1997). However, a recent study indicates that a negative colonoscopy has no impact whatsoever on levels of reassurance or quality of life (QOL) amongst patients with IBS (Spiegel et al., 2005).

Consultation within primary care appears to have little impact upon alleviating the fears regarding malignancy among IBS patients, which may partially explain repeated consultation regarding symptoms (Thompson et al., 2000). Unfortunately, despite the fact that IBS itself is not thought to lead to malignancy, there is evidence to suggest an increased risk of bowel cancer detection among patients recently diagnosed with IBS. The rate of detecting a colorectal tumour is 26.2 per 10’000 person years in IBS patients compared to 6.2 per 10’000 person years in the general population (García Rodríguez et al., 2000). Around

80% of the colorectal tumours detected within persons with IBS are made within the first year following diagnosis. It is possible that an explanation for these phenomena may be that colorectal adenoma or cancer are detected fortuitously due to the fact IBS patients are more likely to receive investigations (García Rodríguez et al., 2000). The detection rate falls off to near that of the normal population following the first year of diagnosis. These factors may also contribute to repeated presentation of patients with IBS.

There is some data to suggest that only 26% of patients within primary care will be satisfied and feel better about their symptoms following consultation with a physician (Thompson et al., 2000). The data suggests that 29% of the patients in primary care settings will be referred to a secondary care physician or surgeon for specialist opinion (Thompson et al., 2000). Around 50% of IBS patients report that they would feel more in control of their lives if they were free of their IBS symptoms (Hungin et al., 2005).

Work productivity, an ability to concentrate, and time management are adversely effected in individuals with IBS compared those without the condition (Hungin et al., 2005). In the UK, IBS patients on average may take between 1.5 and 1.7 days per calendar month off work (Akehurst et al., 2002). Patients with IBS may also consume vast healthcare resources and require frequent consultation.

Longstreth et al. (2003) have identified the following factors associated with excess healthcare utilisation in subjects with IBS;

- More outpatient visits
- More surgery
- More frequent hospitalisation
- Greater number of outpatient prescriptions
- More laboratory and radiology tests
- 51% greater overall costs than matched controls

IBS has also been associated with a greater risk of surgery for procedures such as appendectomy (Hungin et al., 2003). Longstreth and Yao (2004) also suggest that IBS patients are at a much greater risk of surgical procedures such as cholecystectomy (3-fold increase), appendectomy and hysterectomy (2-fold increase), and back surgery (50% increased overall risk). It is thought that symptom overlap with many co-morbid conditions are often misdiagnosed which may contribute to the increased risk of surgery in some of these patients. It is however, unclear to what degree patients receive surgical procedures such as cholecystectomy as a result of their IBS symptoms or develop them as a consequence of the surgical procedure (Kennedy and Jones, 2000).

IBS is a significant burden on health care resources, and IBS patients may consume over 50% more resources than matched controls (Longstreth et al., 2003). In the US, IBS accounts for around 12% of all primary care visits and around 41% of overall gastroenterology practice (Drossman et al., 1997). After 10 years, 50%–70% of IBS patients continue to report persistent symptoms (Canavan et al., 2014).There is limited recent data available which describes the economic and service use burden of IBS within the UK. A study carried out by Wells et al. (1997), suggests that admissions relating to IBS may account for around 18’000 bed days.

The total cost for primary care prescriptions issued for IBS was estimated to be around £12.5 million based on 1995 prescription charges and IBS patients accounted for 846’349 consultations with primary care physicians per year (Wells et al., 1997). A systematic review found the annual expenditure for IBS in the UK to be somewhere in the region of £45.6 million (Inadomi et al., 2003). Most of the additional treatment costs in the UK are accounted for by direct healthcare costs including hospital stay, higher prescription utilisation and increased use of outpatient services (Akehurst et al., 2002).

2.1.4 Post infectious IBS

Gastrointestinal infection has a relationship to IBS significant enough to warrant critical discussion and consideration when discussing the background of IBS. Around a third of patients recovering from gastrointestinal infection will continue to experience ongoing gastrointestinal symptoms, some of which will meet diagnostic criteria for post infectious IBS (PI-IBS) (DuPont, 2008). PI-IBS was evident within the literature in the 1960's when Chaudhary and Truelove (1962) identified that 34 out of a sample of 130 IBS patients attributed symptom onset to a period of infective dysentery.

Prospective studies have shown that between 3% and 36% of enteric infections may lead to the development of IBS, depending on the type of infective organism responsible (Spiller and Garsed, 2009). Other authors report similar findings of 4% to 32% (DuPont, 2008). It is thought that the wide range of reported prevalence of PI-IBS may be attributable to research conducted using various trial designs, different types of diagnostic criteria and various definitions of enteric infection (DuPont, 2008). Overall, a recent systematic review suggests the odds of developing IBS following an acute infective episode are increased six fold (Thabane et al., 2007).

According to Spiller and Garsed (2009), PI-IBS can be defined as:

"An acute onset of new IBS symptoms in an individual, who has not previously met the Rome criteria for IBS, immediately following an acute illness characterized by 2 or more of the following: fever, vomiting, diarrhoea, or a positive bacterial stool culture"
(Spiller and Garsed, 2009)

A variety of enteric pathogens have been associated with the development of PI-IBS, including *Campylobacter species, Salmonella species, Escherichia Coli and Shigella species* (DuPont, 2008). Viral gastrointestinal infection seems to have only short-term effects, whilst bacterial enteritis, protozoan and helminth infections may be followed by

pro-longed PI-IBS (Spiller and Garsed, 2009). It appears that the duration of the initial infection and factors such as co-existing psychological illness may be predisposing factors for the development of PI-IBS (DuPont, 2008). In particular, a follow up study of 192 individuals following a diagnosis of PI-IBS demonstrated that only one in eight patients with a past history of anxiety and depression recovered compared with 9 of 19 without such a history (Neal et al., 1997).

Various causative mechanisms have been identified which may explain pathophysiological origins for PI-IBS. Enterochromaffin cells which are responsible for the release of serotonin (5-hydroxytryptamine or 5-HT) have been shown to affect gastrointestinal motility, visceral sensation and enterocyte secretion (Coates et al., 2004). Research conducted by Spiller et al. (2000) demonstrates that the number of enteroendocrine cells appear to increase in individuals following infection with *campylobacter* along with other cellular changes (macrophages and T lymphocytes) which may last for more than a year in some individuals. Spiller and colleagues suggest that these increases in 5-HT containing enteroendocrine cells may be an underpinning physiological mechanism for the cause of PI-IBS.

The prognosis for most patients with PI-IBS is promising, as a gradual or spontaneous resolution can be observed in most cases (Thabane and Marshall, 2009). However, data from a sample of 210 individuals meeting IBS criteria following acute gastroenteritis demonstrate that 50% will continue to meet diagnostic criteria at 4 years post infection (Marshall et al., 2010). Around 1 in 7 of these patients will continue to experience symptoms persisting for more than 8 years (Marshall et al., 2010). Risk factors for these long term effects were identified as female gender, anxiety/depression and fever/weight loss experienced during the infective episode. Neal et al. (2002) also found that of 27 PI-IBS patients, only 1/8 patients with a history of anxiety or depression recovered at a six year follow up compared with 9/19 without such concomitant diagnoses. Co-existing psychological problems would

therefore seem to play an important role in the onset and maintenance of symptoms in patients with PI-IBS.

2.1.5 Dietary factors

The role of diet in relation to FGID's such as IBS is poorly understood, which has led to diet playing an adjunctive rather than a primary role in the management of such patients (Chey, 2013). However, diet without doubt plays a crucial role in the symptoms experienced by many patients with IBS which is demonstrated by the abundance of literature available on the subject. Important dietary factors may include (but are not limited to); lactose digestion, gluten exposure, levels of dietary fibre, FODMAPS (Fermentable, Oligo-, Di-, Mono-saccharides And Polyols) and the use of bulking agents, all of which are critically discussed in the following paragraphs. So important are some of these factors, they often warrant careful consideration and assessment sometimes under the care of a professional familiar with the complexity of clinical nutrition such as a qualified dietician. This is particularly important when food diaries or patient report identifies patterns of avoidance toward certain food types (Zigich and Heuberger, 2013). These factors will become relevant during the development of the intervention detailed later within the methods section which include a dietary component in view of the importance of these factors discussed above.

Lactose

Lactose may have a role to play in the symptoms experienced by many patients with IBS. Lactose is s disaccharide sugar, primarily a component of milk and related dietary products. Lactose is broken down during digestion by the enzyme lactase, which enables the absorption of lactose in the form of glucose and galactose. Some patients may fail to produce adequate levels of lactase in order to effectively digest the lactose contained in some foods (otherwise known as hypolactasia). Lactose related digestive problems may be described as either lactose malabsorption (LM – lactose is not absorbed sufficiently during digestion), or lactose intolerance (LI - Lactose is not absorbed and produces a level of intolerance/symptoms) (Yang et al., 2014).

Symptoms in patients with LI are thought to arise from the fermentation of unabsorbed lactose, during which hydrogen, methane and carbon dioxide are produced resulting in bloating, increased transit times and subsequent symptomology (He et al., 2006). It is due to these increased transit times and excess levels of gas that LI produces symptoms which closely mimic those of IBS (particularly diarrhoea predominant IBS). Some patients with LM might also experience constipation and a variety of other nonspecific symptoms relating to other body systems (Matthews et al., 2005). Interestingly, decreased transit times appear to increase the exposure of lactose to the digestive processes, which in some patients may have the effect of reducing these associated symptoms (Vesa et al., 1997).

LM has been shown to co-exist in 24.3% of IBS patients vs. 5.7% of healthy controls (Böhmer and Tuynman, 1996). A UK study identified a prevalence of LM at 27% among a sample of 122 patients with IBS (Parker et al., 2001). However, other research studies have found no difference in the prevalence of LI between patients with IBS and healthy control subjects (Farup et al., 2004 , Gupta et al., 2007).

Grand and Montgomery (2008) describe how the failure to absorb lactose may arise from either primary or secondary causes. Primary causes include; genetic/racial lactase non-persistence (lactase production does not continue after weaning), congenital lactase deficiency or developmental lactase deficiency. Secondary causes include conditions which may injure the small intestinal mucosa such as; viral gastroenteritis, coeliac disease, allergic (eosinophilic) gastroenteritis, and radiation enteritis. LM is diagnosed with the ingestion of a 50 gram dose of lactose and the subsequent measurement of hydrogen breath parameters, ideally for around six hours following lactose ingestion (Matthews et al., 2005).

Although the symptom profiles of patients with IBS and those with IBS and LM may not differ, some authors suggest that LM should always be ruled out when a diagnosis of IBS is made, as a lactose reduction diet may reduce symptoms in patients with both LM and IBS (Böhmer and Tuynman, 1996 , Casellas et al., 2010). However, other authors challenge this notion on the grounds that differentiating IBS patients from patients with LM-IBS offers little benefit, as few LM-IBS patients improve on exclusion diets (39%) and both groups of patients may continue to experience symptoms relating specifically to milk ingestion regardless of absorption status (Parker et al., 2001).

Some authors have gone so far as to argue that on consideration of the evidence (which suggests that most LI patients will tolerate small amounts of dietary lactose), patients who insist on attributing IBS symptoms to small amounts of dietary lactose exposure are more likely to have problems which are 'psychologic' in origin rather than 'physiologic' (Suarez and Levitt, 1996). Although many patients believe they have a problem with foods containing lactose, self-report has been shown to be unreliable as a diagnostic indicator, as many patients who attribute their symptoms to lactose yield negative results when formally evaluated (Casellas et al., 2010). One such study of 63 IBS patients demonstrates that although 60% of such patients felt their symptoms were related to lactose, subsequent formal evaluation revealed a diagnostic rate of just 24% (Vesa et al., 1998).

Dietary exclusion of lactose may only improve symptoms significantly in 52% of lactose intolerant IBS patients (Alpers, 2006). However, some authors would suggest that for individuals with a positive diagnosis of LM, long term dietary restrictions are not thought to be necessary and may contribute to reduced bone mineral densities through a lack of adequate nutrition (Grand and Montgomery, 2008). More recent research carried out by Yang et al. (2014), has shown that lactose intolerance among patients with IBS might also be associated with increased levels of anxiety and mucosal immune system activation.

Gluten

Gluten is often a factor considered during the assessment of patients presenting to a physician with IBS like symptoms. Gluten is a type of protein found in wheat, barley and rye (Verdu et al., 2009). Coeliac disease is primarily an immune response to gluten affecting the small intestine in individuals with a particular genetic susceptibility (Feighery, 1999). This genetic susceptibility is defined with the presence of the human leukocyte antigen (HLA) genotypes (DQ2 and DQ8) associated with the development of the condition (Verdu et al., 2009). Coeliac disease can result in the chronic inflammation of the proximal small intestine, subsequently causing villous atrophy and malabsorption (Verdu et al., 2009).

Coeliac disease may be present in around 1 in 200 persons within the general population (Feighery, 1999). The symptoms of clinically overt coeliac disease include; ulceration, dyspepsia, abdominal bloating and diarrhoea (Feighery, 1999). Coeliac disease is also associated with a variety of symptoms relating to other body systems including peripheral neuropathy, painful paraesthesia of the limbs, depression, anxiety, ataxia, migraines and epilepsy (Mahadev and Green, 2011). Patients are increasingly being diagnosed with coeliac disease during investigation for non-classical symptoms such as anaemia (Van Heel and West, 2006).

Patients with IBS have a four-fold increased risk of coeliac disease (Ford et al., 2008). A potential area of concern is that the symptoms of coeliac disease may closely mimic those of IBS and vice versa (Leeds and Sanders, 2007). A recent study of 364 IBS patients demonstrates a prevalence of coeliac disease at 10.5% among patients with IBS-D (Bakhshipoura et al., 2012). The presence of coeliac disease or other inflammatory bowel diseases (IBD's) does not necessarily suggest that functional gastrointestinal conditions such as IBS do not exist or play some part in the symptom profiles of patients with these problems. For example, many patients with IBD often continue to have symptoms of pain and diarrhoea despite minimal or a complete lack of intestinal

inflammation which authors suggest represents overlap between the symptoms of inflammatory bowel conditions and IBS (Long and Drossman, 2010) . Some authors suggest that such phenomena relate to gut inflammation modulating morphology and function of enteric nerves during periods of remission (Geboes and Collins, 1998). Regardless of the causation, the presence of IBS meeting Rome criteria is found in up to 60 % of people with Crohn's disease (Minderhoud et al., 2004).

The biopsychosocial models which are discussed later within this chapter (see 2.2.3) can also be applied to people with inflammatory conditions in order to understand how aspects of the disease relate to an individual's environment, symptom profiles and experiences (Knowles and Mikocka-Walus, 2014). For example, there are possible mechanisms by which stress could relate to IBD symptoms in similar ways to those seen in IBS which include changes in motor, sensory and secretory gastrointestinal function, increases intestinal permeability and changes in the immune system (Sajadinejad et al., 2012). Psychological distress also stimulates mast-cell degranulation and histamine release, and alters the responsiveness of immune cells (Maunder, 2000).

Another possible mechanism by which IBD patients might experience functional gut symptoms may be through disordered gut microbiota although the mechanisms underpinning these potential causes are not yet clear (Li et al., 2015). Further research is required to determine how low grade inflammation present in IBD may underpin some of the functional gut problems experienced by IBD sufferers (Knowles and Mikocka-Walus, 2014). Guidelines and diagnostic tests to distinguish inflammatory bowel disease from functional gut disorders are lacking (De Schepper et al., 2008).

Coeliac disease is initially identified with a simple blood test. Physicians test for elevated antibodies to gliadin (anti-gliadin antibodies or IgA), antiendomysial antibodies (EMA) or tissue transglutaminase antibodies (tTGA) (Mcloughlin et al., 2003 , NICE, 2009). All of these antibodies tend to return to normal upon the elimination of gluten from the diet.

Small bowel mucosal biopsies demonstrating villous atrophy and crypt hyperplasia are the gold standard for diagnosing coeliac disease, whereas, serological screening are valuable for identification of patients requiring these invasive diagnostic procedures (Wang et al., 2014). A positive blood test therefore necessitates a tissue biopsy for the confirmation of disease and histological assessment of the damaged mucosa (Mcloughlin et al., 2003).

Researchers suggest that tTGA is the preferred serological test for screening asymptomatic individuals for Coeliac Disease (Lewis and Scott, 2006 , Lewis and Scott, 2010). Current NICE guidance (NICE, 2009) suggests that patients experiencing any of the following should be screened serologically for coeliac disease:

- Chronic or intermittent diarrhoea
- Failure to thrive or faltering growth (in children)
- Persistent or unexplained gastrointestinal symptoms including nausea and vomiting
- Prolonged fatigue
- Recurrent abdominal pain, cramping or distension
- Sudden or unexpected weight loss
- Unexplained iron-deficiency anaemia, or other unspecified anaemia.

On average, patients may experience the symptoms of coeliac disease for 4.9 years prior to diagnosis, of which just over a half are diagnosed by a gastrointestinal physician (Sanders et al., 2002). It is also possible for some patients with coeliac disease to remain completely asymptomatic prior to diagnosis (atypical of 'classic' coeliac disease). IBS patients who do not demonstrate tTG serological abnormalities sometimes respond to gluten elimination diets (Biesiekierski et al., 2011), and subsequently may be considered as 'IBS gluten sensitive' and as such, patients do not have diagnoses consistent with true coeliac disease (Verdu et al., 2009).

The identification of patients with coeliac disease is important for a number of reasons. Firstly, patients who are diagnosed with the disease and prescribed a gluten free diet are likely to benefit from significant symptom improvement (Rodrigo et al., 2013) and improved histological findings (Shahbazkhani et al., 2003). Regardless of symptom presentation, treatment following the diagnosis of coeliac disease will improve the QOL of most patients (Lewis et al., 2011). Secondly, coeliac disease is thought to be largely under-diagnosed, which may result in complications such as osteoporosis and infertility (Sanders et al., 2001). Thirdly, patients with coeliac disease also have an increased risk of some forms of malignancy, particularly in the first year of following initial diagnosis (West et al., 2004). Despite this risk, there is also some evidence to suggest these patients are at a decreased risk of developing lung or breast cancers (West et al., 2004).

Fibre

Supplementation of the diet with fibre is perhaps one of the most frequent recommendations given to patients with IBS (Bosaeus, 2004). Whether or not such advice is conducive to symptom improvement in IBS patients is an ongoing debate. Much of the confusion regarding diet and fibre relate to two broad classifications of dietary fibre, namely soluble and insoluble types. These differentiations are particularly important, because soluble fibre (such as Psyllium, Ispaghula, and Calcium Polycarbophil) and insoluble fibre (corn or wheat bran) may have different effects on IBS symptoms (Bijkerk et al., 2004). There is some evidence to suggest that overall; patients with IBS may consume half the dietary fibre of matched control subjects (Malhotra et al., 2004).

Few studies have investigated the role of dietary fibre, particularly changes in symptoms bought about by the consumption of soluble vs. insoluble fibres. A study carried out by Bijkerk et al. (2009) found that dietary intake of soluble fibre (psyllium) in patients with IBS was associated with significant improvements in gastrointestinal symptoms (NNT = 4). The authors found that dietary supplementation with bran did

not improve symptoms in patients with IBS. There is some evidence however to suggest that such positive effects are not sustained as Bijkerk and colleagues (2009) found that the effectiveness of soluble fibre supplementation was no longer significant at three month follow up.

Another study compared an intake of dietary bran vs. partially hydrolysed guar gum (PHGG) (a water-soluble polysaccharide in a beverage form). Researchers found that whilst both bran and PHGG improved symptom scores, PHGG was better tolerated and less likely to be abandoned by participants (Parisi et al., 2002). A recent Cochrane systematic review and meta-analysis concluded that bulking agents (for example psyllium husk) were of no additional benefit over placebo for patients with IBS based upon the outcome measures of abdominal pain, symptom scores or global assessment (Ruepert et al., 2011). The authors also conducted a subgroup analysis of insoluble fibre types which did not change these findings.

It is possible that some improvement may be achieved by increasing the consumption of soluble fibre by 10 to 20 g/day with supplements such as isphaghula or psyllium, although such benefits are unlikely to be evident in IBS patients without constipation predominant forms of IBS (Heizer et al., 2009). Indeed, in some cases, increased supplementation of insoluble fibre may actually worsen symptoms (Bijkerk et al., 2004). A recent systematic review and meta-analysis also found fibre supplementation completely ineffective for the relief of pain (Bijkerk et al., 2004). Although fibre supplementation is frequently used during the treatment of IBS, the cause and effect of these interventions remain unclear (Bosaeus, 2004). The most recent systematic review found insoluble fibres may exacerbate symptoms and provide little relief, whereas soluble fibres are likely to be useful in the management of IBS (Ford et al., 2014).

FODMAPS

FODMAP is an acronym for fermentable oligosaccharides, disaccharides, monosaccharides, and polyols. Discussion regarding FODMPAP's and their role in the management of IBS have been present within the IBS literature since the early noughties when Drs Gibson and Shepherd discussed the benefits of reducing FADMAP's in individuals with FGID's (Gibson and Shepherd, 2010). According to Thomas et al. (2012), oligosaccharides are carbohydrates are made up of molecules composed of a relatively small number of monosaccharide units. According to Magge and Lembo (2012), poor absorption of these short chain carbohydrates may occur for several reasons, in particular when; a) luminal enzymes capable of hydrolysing the glycosidic bonds contained in carbohydrates are absent, b) when there is absence or reduced activity of the brush border enzymes (i.e. lactase), or c) the absence of low-capacity epithelial transporters (fructose, glucose transporter 2 (GLUT-2), and glucose transporter 5 (GLUT-5).

It is thought that symptoms result from the poor absorption of these short chain carbohydrates in the small intestine, which are passed on to be fermented by bacteria in the large bowel potentially causing troublesome symptoms such as flatulence and bloating (Staudacher et al., 2011). It is the production of methane and hydrogen which are thought to contribute to the symptoms experienced by patients with IBS, as healthy control subjects tend to report only the addition of flatulence with a diet rich in fermentable carbohydrates (Ong et al., 2010). It has been suggested that the manifestation and exacerbation of symptoms in patients with IBS relate to the visceral hypersensitivity which is characteristic in many IBS patients (Magge and Lembo, 2012).

The symptoms produced with the excess ingestion of FODMAPS may also relate to the balance of gut micro-flora. This is demonstrated within a recent study whereby the concentration and proportion of luminal bifidobacteria appeared to be reduced in patients randomised to four weeks of the low FODMAP diet (Staudacher et al., 2012). Humans are

colonised with microorganisms that inhabit the skin, oral cavity, vagina and gastrointestinal tract from birth (Ley et al., 2006). Early environmental exposure is of primary importance in shaping the microbiota (Turnbaugh and Gordon, 2009) and in adulthood, between 500 and 1,000 different species of microflora coexist within the gastrointestinal tract (Foxx-Orenstein and Chey, 2012).

Gut microflora are thought to be involved in a two-way interaction between bacteria and gut motor function (Foxx-Orenstein and Chey, 2012). Research suggests that intestinal microbial community have the potential to affect structure and metabolic output (Rajilić-Stojanović et al., 2015) and therefore have a direct effect on gastrointestinal motility (Quigley, 2011). These microorganisms also influence digestive enzyme activity, muscle wall thickness, various immunologic processes (O'Hara and Shanahan, 2006), vitamin synthesis, enterohepatic cycling of bile acids, and cholesterol metabolism (Steer et al., 2000). The composition of the microbiota in the adult is largely influenced by diet, geographic location and the use of oral antibiotics (Hill et al., 2010). FODMAPS include dietary components that may lead to luminal distension due to poor absorption in the proximal small intestine which are then rapidly fermented by bacteria, increasing large bowel bacterial load and methane production leading to distension and subsequent symptoms (Gibson and Shepherd, 2010).

The FODMAP diet necessitates the reduction of FODMAP containing foods, which for most patients with FGID's may prove beneficial for the reduction of functional symptoms (Thomas et al., 2012). Indeed, the assessment and dietary reduction of fermenting carbohydrates are a second line treatment option for patients with IBS in the British dietetic association's (BDA) best practice guidelines (McKenzie et al., 2012). In particular, the FODMAP diet may be an effective dietary intervention for the treatment of bloating, abdominal pain and flatulence (Staudacher et al., 2011 , Halmosemail et al., 2014). Symptom response to a low FODMAP diet may take anything between two to eight weeks to take

effect (Staudacher et al., 2011). Patients may find that more time is required to be invested in the purchase of foods and following the low FODMAP diet requires substantial investment in time and energy (Gearry et al., 2009). Furthermore, the diet can be difficult and complex to follow. Many foods also do not list FODMAP content which makes evaluation of the dietary amounts of FODMAPS challenging (Magge and Lembo, 2012).

2.1.6 Medicines and alternative therapies

Medicines are the most researched aspect of IBS. IBS is considered a heterogeneous condition with a variety of treatments which in general, benefit only a small number of patients (Spiller et al., 2007). Nearly all patients (99%) consulting a physician with IBS will have tried at least one medication for the management of their IBS symptoms, and on average patients will have tried 3.9 different medications (Lembo, 2004). Around 75% of consultations for IBS will result in the issue of a medicine prescription (Everhart and Renault, 1991).

Pharmacological therapy for IBS can be considered in two categories; end organ treatment aimed at relieving abdominal pain or disrupted bowel habit and central treatment such as antidepressants targeted at patients with associated affective disorders (Gunn et al., 2003). First line agents such as anti-muscarinic agents result in relaxation of the intestinal smooth muscle and include agents such as alverine citrate, mebeverine hydrochloride, and peppermint oil (Gunn et al., 2003). Within their recent review of agents used in the management of IBS, the World Gastroenterology Organisation (Quigley et al., 2015) recommends the following broad treatment strategies:

- Antispasmodics for pain
- Laxatives, fibre, and bulking agents for constipation
- Fibre, bulking agents, and anti-diarrhoeal agents for diarrhoea

A variety of agents are therefore used to directly influence gastrointestinal motility, stool form or bowel-function in order to manage or improve the symptoms of IBS. Examples of these agents include

loperamide (an opioid analogue), which has been shown to slow small and large intestinal transit and decreases stool frequency and urgency in patients with IBS (Camilleri, 2001). It has a poor blood-brain barrier penetration and is therefore preferable to opioids owing to the reduced risk of dependence which is a potential complication of with the use of opioids (Camilleri, 2001). Tegaserod is (a specific 5-HT4 partial agonist) may also facilitate enteric cholinergic transmission resulting in acceleration of gastrointestinal transit in individuals with constipation predominant IBS (Prather et al., 2000). Prucalopride (also a 5-HT4 receptor agonist) may also be useful in patients with constipation predominant IBS (Bouras et al., 2001) and increases stool frequency and improves consistency in affected individuals (Coremans, 2008).

Antidepressants are also frequently used for the management of IBS such as tricyclic agents (TCA's) and selective serotonin reuptake inhibitors (SSRI's) (Spiller et al., 2007). Doses of tricyclic TCA's are typically lower than those used in the treatment of depressive disorders. Despite this, constipation, dry mouth, drowsiness, and fatigue may occur in over one third of patients treated with these medicines (Spiller et al., 2007). Eligible candidates for antidepressant treatments are therefore likely to have symptom profiles that are severe enough to justify the potential adverse effects seen and once a benefit is achieved, months of maintenance treatment may be indicated (Clouse, 2003).

Daily administration of TCA's below the psychiatric range for antidepressant effect are usually effective in IBS, producing at least a moderate response in more than 85% of patients in trials of open label use (Clouse et al., 1994). SSRI medications are typically used at full psychiatric dosages with a slow and progressive response which is likely to be associated with improved anxiety or depressive symptoms which have an indirect effect on IBS symptom reporting (Clouse and Lustman, 2002). Despite the widespread use of these agents in IBS, authors suggest that the quality of the evidence base for the use of antidepressants in IBS remains poor, and further studies are required to

support the off-label use of antidepressants in the management of IBS (Rance et al., 2014).

Within their updated guidance, NICE suggest that TCA's should be considered a second line treatment for people with IBS if laxatives, loperamide or antispasmodics have not been effective and SSRI's should be used only if TCA's are ineffective (NICE, 2015). Nice also suggest that the clinician should take into account the possible side effects when offering TCA's or SSRI's to people with IBS and follow up patients taking either of these drugs initially at 4 weeks and then every 6–12 months (NICE, 2015).

New drugs are being developed for the treatment of IBS. However, research is urgently needed which not only evaluates effectiveness of new agents, but identifies which patients are likely to benefit from particular types of treatment (Spiller et al., 2007). Although as many as 84% of patients with IBS may find tablet forms of therapy acceptable (Harris and Roberts, 2008), only 22% of IBS patients are likely to experience a symptom reduction of more than a half when managed routinely in medical practice (Whitehead et al., 2004).

Although advances have been made with the application of $5HT_3$ antagonists and 5-Hydroxytryptamine receptor 4 ($5HT_4$) agonists for IBS, such treatments still carry the risk of serious side effects which include ischaemic colitis and cardiovascular events (Brandt et al., 2009). Drugs originally developed for other applications are increasingly being used 'off license' for the medical management of patients with IBS. One such example is Ondansetron, a drug originally developed as an anti-emetic medication has been trialled with levels of success in patients with diarrhoea predominant IBS which increased stool consistency and reduced frequency (Garsed et al., 2013).

In general, medical therapy aims to provide relief for multiple symptoms or is focused on relieving single symptoms alone, and although some of

these medications may be useful, patients are dissatisfied with their overall efficacy and tolerability (Hulisz, 2004). Research suggests that around 70% of IBS patients discontinue medical therapy due to the side effects experienced, and around 25% of patients will discontinue therapy due to a lack of effectiveness (Lembo, 2004). The majority of traditional medicinal therapies including laxatives and stool softeners are associated with side effects which may further contribute to absenteeism and further consultation with physicians (Lembo, 2004). Currently, no medicines used in the management of IBS appear to be curative. It is perhaps the lack of effective and tolerable treatments which results in patients pursuing a range of alternative therapies for IBS (Shen and Nahas, 2009).

Complementary and alternative medicines consist of interventions which are not typically considered to be a part of traditional medicine (Magge and Wolf, 2013). According to Hussain and Quigley (2006), alternative therapies for IBS generally fall within five domains.

1) Manipulative and body-based methods for example; massage, chiropractice and osteopathic manipulation

2) Mind–body treatments such as meditation, hypnosis, cognitive therapy, patient support groups and prayer

3) Biologically based therapies for example; herbal products, dietary, constituents or additives that are found in nature

4) Energy healing therapies, mainly bio-field therapies which are thought to affect the energy field that surrounds and penetrates the body (examples of which include Qi gong and reiki) and the use of bio-electromagnetic fields and includes such as in pulsed field therapy and magnetic field therapy

5) And finally, alternative medical systems like homeopathy, or traditional Chinese medicine

These alternative therapies are often used by IBS patients either in conjunction or in lieu of conventional therapies despite the fact that many of these interventions have not been subjected to controlled clinical trials (Hussain and Quigley, 2006). Mind–body therapies such as CBT and hypnotherapy used in IBS have well documented efficacy, but have not been well accepted by patients or practitioners (Magge and Wolf, 2013). For example, around 67% of IBS patients have a positive attitude towards complementary and alternate therapy the most frequent of which are homeopathy, herbal medicine and nutrition-based interventions (Lahner et al., 2013). Generally, few physicians well acquainted with these therapies (Spanier et al., 2003). Lahner and colleagues (2013) found that only 26% of gastroenterologists would consider recommending these treatments and suggested that more studies of effectiveness are needed regarding the use of these therapeutic tools in IBS (Lahner et al., 2013). The prevalence of alternative therapy use is thought to be somewhere between 9% to 38% in IBS and is usually employed when conventional medicine has failed or there is a lack of satisfaction with conventional medical care (Usher et al., 2013).

Acupuncture has been used to treat a variety of gastrointestinal symptoms in functional and also in organic diseases, and has been shown to influence visceral activity, gastric emptying, and the secretion of gastric acid (Enck et al., 2007). However, systematic reviews of acupuncture for IBS have found insufficient evidence to support acupuncture having any additional benefit to controls (Lim et al., 2006 , Schneider et al., 2007) with investigational studies often limited by poor study design (Tillisch, 2006). There is, however, evidence to support efficacy for hypnotherapy, some forms of herbal therapy and some types of probiotics in irritable bowel syndrome according to a recent systematic

review of alternative therapies used in IBS management (Hussain and Quigley, 2006).

Hypnotherapy has been used in the form of a gut-directed intervention since the 1980's with a response rate of 100% exhibited by individuals under 50 years of age (Whorwell et al., 1987), although a much lower response rate (less than 25%) was seen in those older than 50 years. Although considered an alternate intervention to conventional medicine, the use of CBT and its application to the treatment of IBS is discussed in great detail later within chapter 3.

Although safety is a concern to some patients using herbal medicines, a recent systematic review of 22 RCTs of herbal medicines for IBS found adverse events occurred only in just 2.97% of cases (Shi et al., 2008). Bishop et al. (2006) found stronger perceived consequences of illness and negative perception of conventional medical care influenced alternative therapy use as did a willingness to treat symptoms with a more natural approach (Bishop et al., 2006). These alternative interventions may be beneficial in addressing negative symptom or treatment perceptions and emotional distress that may accompany IBS symptoms (van Dulmen et al., 1996). Authors conclude that these complimentary therapies may be considered individually as a supplement or alternative to treat IBS which are potentially equal in effect to placebo (Chang and Lu, 2009), although due to the poor quality of research underpinning these interventions, advising clinicians should weigh the potential benefits and uncertainties of these approached when advising patients about their use (Shi et al., 2008).

2.2 Co-morbidities and the biopsychosocial model

2.2.1 Physiological co-morbidities

Many IBS patients have at least one co-existing somatic complaint and many meet diagnostic criteria for other gastrointestinal and extra intestinal functional disorders (Sperber and Dekel, 2010). Other comorbidities which occur in patients with IBS far more often than one would expect to observe by chance are conditions such as gastro-oesophageal reflux disease, genito-urinary symptoms, fibromyalgia syndrome and headaches (Drossman et al., 2000). It is therefore not surprising that IBS patients are often under the care of various hospital specialities for a number of other ailments, particularly those which are medically unexplained.

The literature consistently reports that the conditions advocated by Drossman and colleagues (2000) frequently occur in patients with IBS, with some of the most frequently reported problems being both psychological and physiological in origin. For example; generalised anxiety disorder, depression, agoraphobia, tension headaches and insomnia commonly occur in patients with IBS (Lackner et al., 2013). More on the psychological comorbidities found in IBS is discussed in the following section. Not surprisingly, Lackner and colleagues (2013) have found comorbid conditions to be associated with much more severe symptoms, greater levels of distress and increased levels of pain. Migraine may be present in up to 37% of patients with IBS (Boyd et al., 2012). Whitehead and colleagues (2002) also found 51% of IBS patients to have chronic fatigue syndrome, 64% have temporomandibular joint disorder and 50% report pelvic pain. Decreased sexual drive and sexual dysfunction is also common in IBS (Fass et al., 1998).

One of the functional conditions greatly associated with IBS is fibromyalgia syndrome, which is present in up to 49% of individuals with IBS (Whitehead et al., 2002). Fibromyalgia syndrome is defined as a soft

tissue disorder characterised by diffuse musculoskeletal pain and specific tender points on examination (Wolfe et al., 1990). In terms of how the prevalence of fibromyalgia present in people with IBS compares to that of the general population, Sperber and Dekel (2010) report 31.6% of IBS patients report the syndrome compared to 4.2% of control subjects. Similarly, chronic fatigue syndrome is also reported by 14% of IBS patients (Sperber and Dekel, 2010) compared to 0.4% in the general population (Jason et al., 1999).

In terms of other intestinal complaints, Hungin et al. (2003) have demonstrated that IBS patients report more reflux disease and peptic ulcer diseases than healthy control subjects (Hungin et al., 2003). Indeed, the data suggests that as many as 80% of patients meeting diagnostic criteria for IBS may also experience dyspepsia (Mendall and Kumar, 1998). Patients with constipation-predominant IBS are thought to have higher rates of overlap with dyspepsia than patients with diarrhoea-predominant IBS although the mechanisms underpinning these observations are unclear (Talley et al., 2003). The tendency of medicine to separate functional gastrointestinal disorders into various subtypes (i.e. functional dyspepsia and IBS) has been challenged by researchers. Researchers have suggested that the significance of over 80% of IBS patients also meeting diagnostic criteria for functional dyspepsia suggests that these problems are likely to represent the same disease process (a dysfunctional gastrointestinal tract) in many IBS subjects (Agréus et al., 1995).

There is some evidence to suggest that the risk of IBD is approximately nine times greater in the period following a diagnosis of IBS, which some authors suggest may represent clinical presentations on a pathophysiologic spectrum of disease (Porter et al., 2012). Porter and colleagues also suggest that the misdiagnosis of inflammatory bowel disease (such as microscopic colitis) might also provide an explanation for the observation of these phenomena. This suggests that some

patients with IBS may be at the milder extent of inflammatory processes which are not detected during diagnostic workup. For example, despite the reassurance offered to many patients diagnosed with IBS that their condition is not likely to lead to more serious disease, the relative risk of later receiving an inflammatory bowel disease diagnosis is thought to be around 16.3 (95% confidence interval (CI), 6.6-40.7) (García Rodríguez et al., 2000). Where identified, the time until another gastrointestinal diagnosis is made is on average 1.7 years (SD, 1.8) for inflammatory bowel disease, 2.5 years (SD, 2.8) for colitis, 2.4 years (SD, 2.6) for Crohn's disease, and 2.8 years (SD, 3) for coeliac disease (Boyd et al., 2012). Ascertainment bias may explain some of these observed phenomena, as patients with IBS are more likely to undergo diagnostic testing leading to the fortuitous discovery of this pathology.

IBS is also associated with the reporting of non-intestinal symptoms such as pelvic pain, sexual dysfunction and decreased libido (Lee et al., 2001). Genito-urinary symptoms in general are not uncommon amongst patients with IBS, with bladder dysfunction evident in 50% of IBS patients vs. 13% in carefully matched healthy control subjects (Whorwell et al., 1986). The features of these urinary problems include; increased frequency, urgency, nocturia, hesitancy and incomplete emptying of the bladder. In addition to these genito-urinary symptoms, patients with IBS are also likely to report more gynaecological problems which are thought to be associated with IBS (Longstreth and Yao, 2004). It is likely that symptom overlap may explain these observations as both gynaecological and bowel symptoms may often appear similar (for example; lower abdominal pain or discomfort).

Authors suggest that gynaecological symptoms in this group of patients are particularly important and should be recognised as early as possible as they may potentially lead to misdiagnosis and the implementation of unnecessary treatment (Longstreth, 1997). It is also not unusual for women with IBS to report painful intercourse, chronic pelvic pain, pain

with urination, and increased frequency of urination (Longstreth and Yao, 2004). Not surprisingly, around 9% of IBS patients within primary care are referred to surgeons regarding their gut symptoms (Thompson et al., 2000).

Trying to make sense of why these co-morbid complaints are so strongly associated with IBS is complex. Biopsychosocial models might explain the comorbidity of irritable bowel with other disorders, which may arise as a result of manifestation of varying combinations of interacting physiological and psychological factors (Whitehead et al., 2002). Some authors have suggested that IBS patients are likely to have 'a sensitive mind in a sensitive body' with bodily symptoms associated with psychological distress (Vandvik et al., 2004). However, the association between medically unexplained physical symptoms, anxiety, and depression has been studied and authors conclude that while IBS and other functional disorders such as fibromyalgia syndrome are associated with anxiety and depression, they are not dependent on these psychological traits and cannot be said to represent a spectrum of 'common mental disorders' (Henningsen et al., 2003).

Other potential factors may relate to the perception of symptoms and include symptom hypersensitivity or amplification or more biological explanations such as hypothalamic-pituitary-adrenal axis perturbation, and genetic vulnerability (Tynes and Spiegel, 2013). Whitehead et al (2007) also suggest that comorbidity in IBS is due to a general amplification of symptom reporting and physician consultation suggesting symptom perception rather than shared pathophysiology are putative factors which are influenced by, but not explained by comorbid psychological illness (Whitehead et al., 2007). The current tendency of medicine to characterise these comorbid presentations as distinct entities has been challenged and authors suggest that such distinctions arise as an artefact of the medical specialty making the diagnosis (Wessely et al., 1999).

2.2.2 Psychological co-morbidities

Some of the most prevalent comorbidities associated with IBS are those which are psychological in origin, and a recent published literature review suggests that co-morbid psychological problems identified within samples of research study participants tend to fall in the region of between 50% and 90% for common mental health problems such as anxiety and depression (Dainty, 2012). Earlier research also supports similar levels of co-existing anxiety and depression in patients with IBS (Lydiard and Falsetti, 1999). IBS has a long standing association with psychological illness and was historically thought to be a physiological manifestation of emotional stress (Ryle, 1928).

In 1971, within a study of 67 IBS patients, researchers observed levels of depression of over 73% compared to 17% among control subjects (Hislop, 1971). Hislop (1971) also identified significant levels of anorexia, suicidal ideation, weeping and insomnia. The significance of these findings has been replicated in numerous IBS studies which frequently identify significant psychological co-morbidities associated with IBS. The following table (Table.2) shows the levels of co-existing psychological disorders captured during demographic data collection during some recent randomised controlled trials (RCTs).

Generalised anxiety disorder, depression, agoraphobia, tension headaches and insomnia also commonly occur in patients with IBS (Lackner et al., 2013). IBS is also considered by some physicians to be strongly related to hypochondriasis (Maxwell et al., 1997). These findings are further supported in a recent study, as subjects with IBS and/or functional diseases (FD) score significantly worse on five of the seven abnormal illness behaviour questionnaire scales including those indicating general hypochondriasis, disease conviction, affective disturbance, denial, and irritability (Koloski et al., 2005). There appears to be no difference between the psychological co-morbidities experienced by men and women (Lee et al., 2001) or indeed when compared to other FD's (Chang et al., 2006).

Historically, accounts have been evident within the medical literature whereby symptom onset and resolution has been associated with traumatic life events or stressful life situations. Chaudhary and Truelove (1962) discussed two such case studies conforming to functional bowel disease, one of which was diarrheal symptom onset associated with marriage breakup and another where treatment refractory symptoms resolved once a patient had left her quarrelling parents residence.

Levels of psychological co-morbidity associated with IBS

Study	*N*	Setting	% of psychological co-morbidity
Blanchard et al (2007)	**210**	Tertiary clinics, New York	**66.6%** DSM-IV Axis type 1 disorder
Kennedy et al (2005)	**149**	Primary care, London, United Kingdom (UK)	**43%** Any psychological problem in the past year
Payne and Blanchard (1995)	**34**	Centre for Stress and Anxiety Disorders, State University of New York	**85%** DSM-IV Axis type 1 disorder
Tkachuk et al (2003)	**28**	Community and university medical clinics, Canada	**68%** DSM-IV Axis type 1 disorder

Table.2 Source: Dainty (2012)

The Axis Type 1 disorders reported within table.2 relate to the Diagnostic and Statistical Manual of Mental Disorders or DSM-IV (American Psychiatric Association, 1987) which distinguishes between Axis I and Axis II psychological disorders. Axis II includes personality (and developmental) disorders, whilst others form part of Axis I (Widiger and Shea, 1991). For example, in the study reported by Tkachuk et al (2003), the Axis 1 disorders consist of 39% generalised anxiety disorder

(GAD), 11% major depression, 11% social anxiety disorder, 4% post-traumatic stress disorder (PTSD) and 4% somatoform disorder.

The most important aspect of these psychological co-morbidities is the impact they may have on the onset, progression and maintenance of IBS. Social stressors appear to directly influence the severity of FGID's, particularly IBS (Bennett et al., 1998). Not surprisingly, Lackner and colleagues (2013) have also found the comorbid psychological conditions to be associated with much more severe symptoms, greater levels of distress and increased levels of pain. Such factors also appear to have an influence on healthcare seeking behaviour and the patient's denial of stress playing a role in their IBS symptoms appears to be a significant predictor of referral to secondary care for specialist opinion and treatment (Thompson et al., 2000).

Some studies have demonstrated that the absence of association with stress, worries, or nervousness may in fact be a predictor of symptom resolution in some individuals with IBS (Agréus et al., 1995). Patients with a strong family history of IBS are more likely to suffer from increased levels of distress (Kanazawa et al., 2004). There are data to suggest that patients who develop IBS following a period of dysentery have higher scores for anxiety, depression, somatisation and neurotic trait than patients who returned to normal following an initial gastrointestinal infection, with scores on these instruments remaining unchanged at three months follow up (Gwee et al., 1996). This may suggest that in some patients, psychological co-morbidity may be a significant risk factor for the development of PI-IBS. These findings have been challenged within some subsequent studies (Kanazawa et al., 2004).

Studies have investigated the link between co-existing psychological issues, stress and the manifestation of subjective symptoms (Levy et al., 2006). Despite these on-going efforts and theoretical developments, the causal mechanisms which underpin IBS remain unclear. Guthrie and

colleagues (2004) experimental study involving 107 participants demonstrate significant alterations to the tolerance of bowel sensations when stimulated by balloon distention which appear to be related directly to psychological distress (Guthrie et al., 2004). Researchers have also associated stress with neuroendocrine changes which appear to have significant effects on gastrointestinal motility (Taché et al., 2001). Furthermore, there is a strong correlation between stressful life events, the severity of symptoms and symptom onset (Creed et al., 1988).

Researchers have also identified high levels of sexual and emotional abuse among patients who present with IBS. During a multicentre study, Delvaux et al. (1997) reported levels of sexual abuse around 31% in IBS patients, compared to a rate of 14% in organic gastrointestinal disease and 7.5% in healthy volunteer subjects. Similarly Drossman et al. (1990) observed levels of abuse to be around 44% in IBS. Somatisation disorder (SD) has also been associated with IBS, which is defined as the presence of multiple bodily symptoms in the absence of a physiological cause (Mai, 2004). SD has a prevalence of around 25% in patients with IBS and is associated with more severe symptoms and an increased need to consult (North et al., 2004).

More recent theories suggest that the elevated levels of psychological distress among patients with IBS and the relationship this has to the physiological manifestation of IBS is complex. This results in the presentation of a disease process which does not fit within the same perspectives as organic gastrointestinal diseases with clear pathological origins. Some authors suggest the increased levels of psychological illness within functional disease are a representation of complex interactions between social, physiological and psychological factors (Levy et al., 2006). Levy and colleagues (2006) suggest the role of early life experiences, the perception of symptoms and health seeking behaviours are all potentially fundamental issues for patients with FGID's.

A causative mechanism which clearly describes the link between psychological issues, stress and the manifestation of IBS symptoms is yet to be supported by good quality research. Some theories suggest that these issues may relate directly to the (ANS) with increased activity in the function of the sympathetic nervous system (SNS) and decreased parasympathetic nervous system (PNS) activity (Heitkemper and Jarrett, 2008). Stress related hormones (for example epinephrine) associated with arousal and increased levels of anxiety may also have a central role in the manifestation of IBS symptoms (Maxwell et al., 1997). Maxwell and colleagues suggest that the release of certain cytokines (interleukins 1 and 6) could exacerbate reactions to normally harmless stimuli. Such mechanisms could be associated with the activation of mast cell receptors, which in theory could be activated by peripheral and central nervous systems (Maxwell et al., 1997). Theories also relate to the dysregulation of the hypothalamic-pituitary-adrenal axis, which may result in changes in reactions to acute and chronic stressors (Heitkemper and Jarrett, 2008).

There is not a great deal of data on which to establish the temporal relationship between these common psychological problems, traumatic life events and IBS. Some authors suggest that depending on the type of stressor, stressful life events may precede IBS, with the lag time between the event and the emergence of functional symptoms ranging from decades to weeks (Mayer, 2000). It could be hypothesised that psychological states may increase vulnerability to the development of IBS, although little data exists on which to establish the temporal order of occurrence. Multivariate statistical analyses performed by Whitehead et al (2002) suggest that these are distinct disorders rather than representations of SD's which may play a role in expression, which are likely to be driven by psychological factors. These theories are supported with research which suggests psychological factors are important moderators of symptom severity, symptom persistence, and decisions made my patients to seek treatment, and their response to the treatment sought (Fond et al., 2014).

Some authors suggest that psychological, social and genetic factors appear to be important in the development of IBS symptomatology which might be explained with the dysregulation of HPA axis modulation, enhanced perception of visceral stimuli or psychological vulnerability (Fadgyas-Stanculete et al., 2014). More research is required to establish temporal order in the co-existence of these conditions which currently remains unclear. For potential mechanisms by which common mental health problems relate to IBS see 2.2.3 and 2.2.4.

2.2.3 Biopsychosocial models of IBS

IBS is clearly a condition which is complex in nature and is influenced by a variety of factors such as an individual's environment, psychological profile and exposure to certain stressors. It is unclear how such factors might interrelate, and for these issues to make sense researchers often describe IBS using conceptual models. Levy et al. (2006) suggests that FGID's such as IBS are the result of complex interactions between the biological, psychological and social aspects of the disease process and can only be treated effectively when all of these influential factors are correctly addressed. Levy and colleagues (2006) describe the relationship between these factors in FGID's using a conceptual model presented as the 'biopsychosocial model' (see Figure.1).

Levy and colleagues (2006) suggest that their model describes how early life experiences, the social environment and other social experiences may influence an individual's physiological and psychological responses. These factors are described as related by way of two way interactions between the gut and social factors which Levy and colleagues (2006), referred to as operating within the 'brain gut axis'.

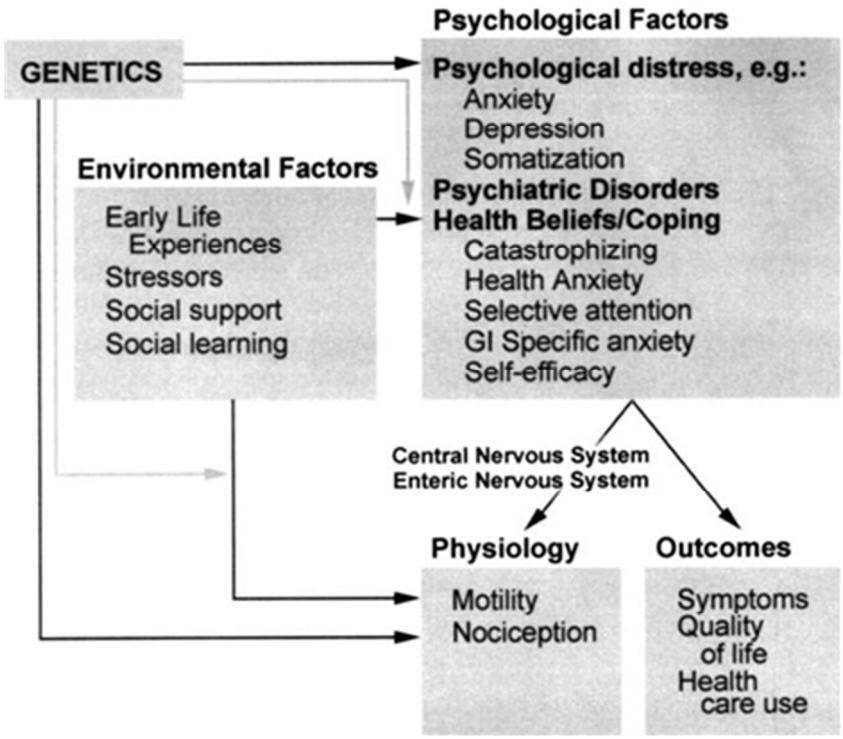


Figure.1

Conceptual model illustrating the relationships among psychological and environmental factors, physiologic variables, and outcome of FGIDs. Source: Levy et al. (2006)

The theory of the biopsychosocial model is underpinned by the assumption that these factors are interrelated as a result of interactions within the central nervous system (CNS) and the enteric nervous system (ENS). Communications between the CNS and ENS (often called the brain-gut axis) involve two branches of the autonomic nervous system which are integrated anatomically and functionally with visceral sensory pathways, and are responsible for the homeostatic regulation of gut function (Tougas., 2007). Camilleri and Di Lorenzo (2013) describe how corticolimbic pontine networks mediate the effect of cognitions and emotions on the perception of homeostatic feelings, and also include visceral experience of pain and discomfort. The system can be thought of as a 'triad' of neural, hormonal and immunological lines of communication which combine to allow the brain to influence the motor,

sensory, autonomic and secretory functions of the luminal tract (Kennedy et al., 2014).

It is thought that for patients with FGID's to receive effective treatment regimens, this model should be implemented into clinical practice and the holistic care of FGID patients routinely (Levy et al., 2006). Other authors such as Tanaka et al. (2011) support the theory of nervous system interactions, particularly those which link distress to the manifestation of physiological symptoms. Tanaka and colleagues (2011) suggest that psychological distress itself is generated by integrative brain structures such as the sub-regions of the hypothalamus, amygdala, the medial thalamus and anterior cingulate cortex. The authors describe how increased hypothalamic-pituitary-adrenal responsiveness to stress produces glucocorticoids, which in turn, increase the expression of inflammation, which may result in the production of cytokines.

Certainly, this theory is in keeping with the immune system activation which would appear to play a fundamental role in PI-IBS discussed within earlier chapters. The brain-gut axis is best described as a bidirectional and integrated system (Tanaka et al., 2011). It is within this system that thoughts, feelings, memories and environmental factors may lead to neurotransmitter release which is likely to affect sensory, motor, endocrine, autonomic, immune and inflammatory functioning (Tougas, 2000). Chey (2013) present a similar conceptual model in their study regarding the role of food in the management of FGID's (See figure 2).

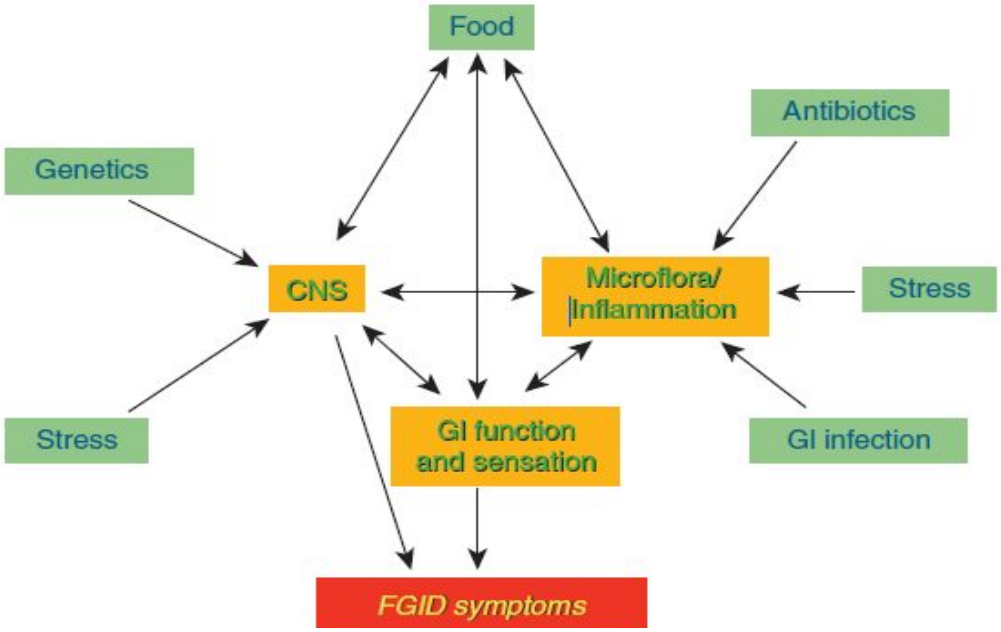


Figure.2

Evolving conceptual model of FGIDs. CNS, central nervous system; FGID, functional gastrointestinal disorder; GI, gastrointestinal. Source: (Chey, 2013)

Similar to the biopsychosocial model presented by Levy and colleagues (2006), Chey et al (2013) describe the relationship between various psychological (stress) and physiological (gut function, microbiota) aspects of FGID's, all of which play fundamental roles in the manifestation of FGID symptoms. Earlier within chapter 2, I described how short chain carbohydrates are fermented by bacteria in the large bowel, potentially causing troublesome symptoms such as flatulence and bloating in some patients with IBS (Staudacher et al., 2011).

In relation to the microbiota concepts put forward by Chey et al (2013), current evidence does not support pronounced IBS-related deviations of entire phylogenetic or functional microbial groups, but suggests IBS patients have alterations in the proportions of commensal organisms with interrelated changes in the metabolic output and overall microbial environment (Salonen et al., 2010). Research reports support that a lower diversity and a higher instability of microbiota may exist in IBS patients when compared to control subjects (Carroll et al., 2012). These

changes in microbiota may relate to mechanisms by which diet components may trigger IBS symptoms through alteration of the gut fermentation processes (Rajilić-Stojanović et al., 2015).

Gut microbiota may have a significant impact on people with IBS, with the potential to alter processes such as intestinal barrier function and immune system regulation (Bennet et al., 2015), as acknowledged within Chey and colleagues (2013) model. However, authors suggests that subtle changes may exist rather than significant alterations in the intestinal microbiota of IBS patients (Salonen et al., 2010). More research is required in order to establish causal links between IBS symptomology and gut microbiota, particularly if therapeutic interventions are to be developed. A particular challenge for researchers working in the field of gut microbiota is the variation which exists, both between individuals and within individuals over time which makes researching the phenomena particularly difficult (Costello et al., 2009)

For Chey and colleagues, their model most importantly demonstrates how food may be fundamental for patients who may have alterations in physiology which may render them hypersensitive to a variety of external cues and stimuli (Chey, 2013). Perhaps one of the most frequently cited conceptual models of FGID's is the work presented by Douglas Drossman and colleagues within a (2006) paper discussing FGID's and the application of the Rome III process (Drossman, 2006). The model is presented on the next page (see figure 3).

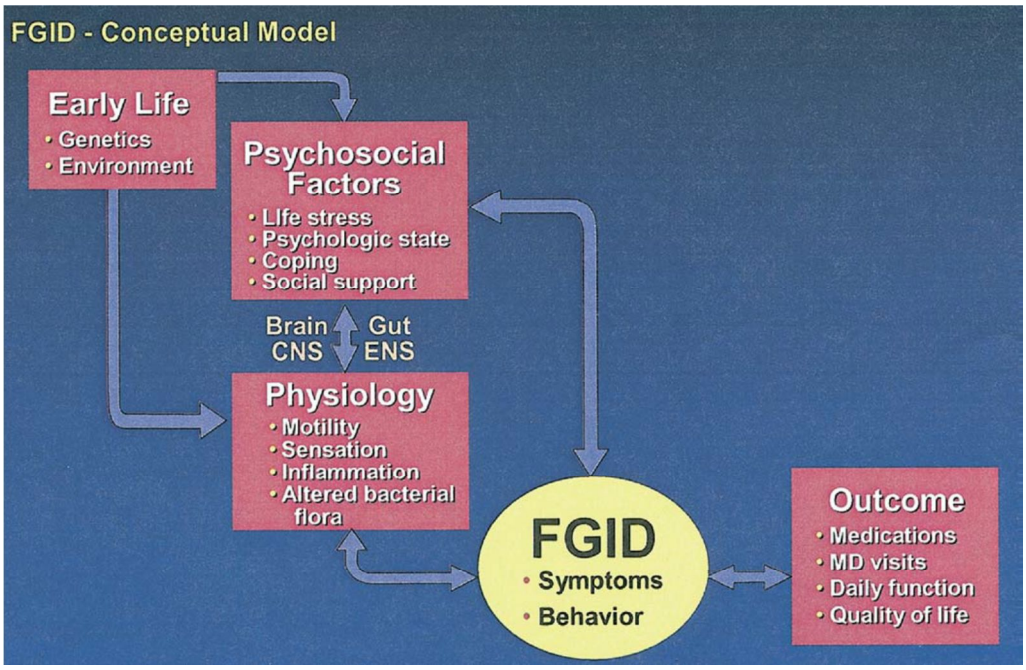


Figure 3

Biopsychosocial conceptualisation of the pathogenesis and clinical expression of the functional GI disorders shows the relationships between psychosocial and physiological factors, functional GI symptoms, and clinical outcome. Source: (Drossman, 2006)

The models presented above help researchers and clinicians better understand how so many confounding variables may become involved in the manifestation of FGID's such as IBS. Although these models recognise the influence such factors have on the maintenance and manifestation of disease, they do not try to establish causal pathways by suggesting that psychosocial issues cause symptom manifestation for example. Instead the models present a complex picture which should be considered during the assessment of diagnosis of FGID's in order for treatment plans and regimens to be maximised and to take account of these important aspects which invariably are likely to affect treatment outcomes.

Tanaka et al. (2011) suggest that a clinician may implement the biopsychosocial model routinely by integrating the following attributes into an assessment of the patient's needs.

i. Make an effort to understand and offer empathy when patients report the experience of the illness
ii. Obtain the history and acknowledge the role of the patient's psychological factors
iii. Clarify any misunderstandings
iv. Provide education how to manage the illness, including psychosocial function
v. Make a plan of treatment in collaboration with the patient

Considering the biopsychosocial model of IBS is perhaps a potential mechanism for resolving some of the broader aspects of the condition in order to improve patient outcomes, reduce chronicity and improve satisfaction with care. Implementation of these methods during routine clinical assessment may also assist the clinician in identifying significant psychosocial stressors which may need to be taken into account in order for medical therapy to become more effective.

These frameworks provide a useful explanation of how the presentation of IBS is often complex and may explain why IBS responds so poorly to medical assessment and therapy which may focus only on limited symptom control. Most importantly, these models of IBS demonstrate a variety of opportunities to intervene, with innovations which address the psychosocial aspects of disease which are discussed within the coming sections. Although these models are useful for addressing many of the psychosocial aspects of IBS, such models are likely to be limited in application without the acceptance and motivation of patients willing to engage in holistic treatment regimens (Tanaka et al., 2011).

Similarities exist between the models described although Drossman's 2006 model makes explicit that coping, psychological state and life stressors are interrelated and play a role in the brain gut axis. This model is therefore of particular relevance during the development of interventions which arise following the review of the literature reported in chapter 3 (see 4.3).

2.2.4 The concept of psychosomatic illness

Psychosomatic illness is of particular relevance to broader context of the work presented here, and as such requires some discussion and consideration within this thesis. Psychosomatic illness is not a term which is easily described or defined in modern medicine. Engel (1967) attempted to define and critically discuss the concept of these complex phenomena;

> *I contend that we have elected as the subject of study the most complex field in all of medicine. There is no other field which must include under its aegis every aspect of life and living, from the social-cultural and physical environments to the finest component of the internal milieu... The psychosomatic approach is concerned with the ways in which psychological and somatic factors interact in the whole sequence of events that constitute a particular disease experience (Engel, 1967 p.4).*

Similar to the concepts put forward in the biopsychosocial models within the chapter 2, Patterson-Kimball (1982) describes how psychosomatic illness is made up of aspects of an individual's psychological, biological and socially conceptualised variables which are present concurrently in the life of the individual. The term psychosomatic is also related to a particular set of disorders which are coined the *'somatoform disorders'* or now more recently defined as the *'somatic symptom disorders'*. Such disorders are those considered to be complaints which appear physical in presentation, but cannot be fully explained or understood in terms of underlying organic pathology (Bass et al., 2001).

According to the American Psychiatric Association (2000), somatoform disorders are those consistent with the following diagnoses: somatisation disorder, undifferentiated somatoform disorder, somatoform disorder (not otherwise specified), conversion disorder, pain disorder, body dysmorphic disorder, and finally; hypochondriasis. These disorders all involve clinically significant distress or impairment in the individuals daily functioning.

Somatoform disorders can also be differentiated from one of the particular diagnoses: SD. SD is used to describe the presence of multiple bodily symptoms in the absence of a physiological cause (Mai, 2004). Like IBS, such patients are troubled with chronic physiological symptoms which are poorly understood, not well treated and are a significant burden to healthcare establishments (Bass et al., 2001). According the American Psychiatric Association (2000), SD is a pattern of many physical complaints (usually presenting prior to 30 years of age) which results in unnecessary medical treatment and/or causes significant impairment in functioning. The somatic symptoms are neither intentionally produced and appear to be unconscious to the patient. The following criteria are required to be met for a formal diagnosis to be established.

i. Four different pain sites (i.e., head, abdomen, back, joints, extremities, chest, rectum) or painful functions (e.g., menstruation, sexual intercourse, urination)
ii. Two gastrointestinal symptoms other than pain (i.e., nausea, bloating, vomiting, or intolerance of several different foods)
iii. One sexual or reproductive symptom other than pain (i.e., erectile or ejaculatory dysfunction, irregular menses, excessive menstrual bleeding)
iv. One pseudo neurological symptom (i.e., impaired balance, paralysis, aphonia, urinary retention)

Engel did not have the range of data available to him researchers have today, which provide plausible evidence based explanations for causal pathways for the complex relations between emotional states and physiological change which may underpin some of these complaints. For example, such changes are those studied by Kiecolt-Glaser et al. (2002), who conclude that there is now sufficient data to support the stimulation of pro-inflammatory cytokines by way of negative emotions and adverse life experiences (presented as distress-related immune dysregulation). Not only may these causal pathways relate to IBS as described earlier within chapter 2, but most importantly they have particular ramifications for the course and presentation of the condition.

As many as a quarter of patients with IBS may also have SD which may exacerbate some aspects of IBS. Most notably, North et al. (2004) were able to identify how patients with IBS and SD were significantly associated with greater numbers of gastrointestinal symptoms and other psychiatric disorders, consulted more physicians including physician telephone calls, they also had more urgent care visits, medication changes, more missed work days and a greater level of treatment dissatisfaction. Examples of those somatoform disorders most frequently associated with IBS are described by North and include; non-ulcer dyspepsia, premenstrual syndrome, chronic pelvic pain, non-cardiac chest pain, hyperventilation syndrome, chronic fatigue syndrome, tension headache, temporomandibular joint dysfunction, globus syndrome, multiple chemical sensitivity, and fibromyalgia (North et al., 2004).

In these somatic conditions, there is continued presentation of physical symptoms coupled with persistent requests for medical investigations, despite negative findings and offers of reassurance by physicians that the symptoms experienced have no physical basis (Tyrer, 2006). As such, these issues require in the least acknowledgement within this work as they relate very closely to the biopsychosocial models of gastrointestinal complaints presented within the previous section and share many characteristics and indeed overlap with IBS. Most importantly psychosomatic conditions which are associated and compounded by psychosocial factors are amenable to psychological intervention, which is described in the context of IBS within the following sections and chapters.

2.2.5 Complexities in the definition of IBS and related theory

Concluding this chapter relating to the underpinning theories and definition of IBS would not be complete without discussing the controversies which surround definition and causation. As mentioned within the previous sections, clear definition and diagnoses of IBS can be considered important for a number of reasons, most importantly to ensure that patients receive timely and accurate diagnosis, effective

therapy and appropriate follow up care (Mearin and Lacy, 2012). Furthermore, it seems logical that best practice should avoid unnecessary extensive testing and some authors would suggest a confident diagnosis of IBS can be made in the majority of cases with a physical examination and limited laboratory or structural tests (Longstreth, 1997).

Issues relating to the accurate detection and definition of IBS are significant enough to be considered responsible for the variation in prevalence presented within the epidemiological data discussed in chapter 2 (Lovell and Ford, 2012). Two of the most sited definitions applied to IBS, particularly within research samples were the earlier criteria developed initially by Manning et al. (1978), and the later Rome criteria first appearing in 1990 (Drossman et al., 1990) and developed by The Rome Foundation (2012). It is prudent to make clear that such criteria are developed by expert consensus rather than research data. The definition of IBS and researchers understanding of IBS continue to evolve, which is demonstrated with the continuous updating of the Rome criteria with the most recent Rome III Criteria being first developed in 2006 (Longstreth et al., 2006). Authors suggest that when such criteria are fulfilled and alarm features are absent, the number of diagnostic tests should be minimal (Soares, 2014)

Assigning diagnostic criteria to patients with IBS is considered by some authors to be controversial, and some clinicians and researchers feel that IBS is best considered a diagnosis of exclusion which should be based upon a patient's history, presentation and absence of alarming or more serious clinical features which might otherwise indicate the presence of serious underlying pathology (Mearin and Lacy, 2012). The criteria for defining IBS have also been criticised in terms of relevance, as the data suggests that patients often switch between the phenotypes used to classify IBS-C and IBS-D over time, which potentially demonstrates the instability of the definitions and current classification systems (Marshall et al., 2010). There is also some data to suggest that the classification of IBS as a lower gastrointestinal disease in isolation may not be all that

useful as 8/10 IBS patients also meet diagnostic criteria for functional dyspepsia which suggests that these problems may represent the same spectrum of disease process in many IBS subjects (Agréus et al., 1995).

Guidelines emphasise that IBS is not a diagnosis of exclusion and encourage clinicians to make a positive diagnostic using the Rome Criteria (Soares, 2014). For example, NICE guidelines offer a pragmatic definition of IBS which suggest symptoms which are of a post-prandial nature support a diagnosis of IBS (NICE., 2008). Although making a positive diagnosis of IBS with minimal testing and investigation seems reasonable, such approaches are largely based on expert opinions and not high quality data derived from clinical research (Talley, 2008).

Many experts and physicians diagnose IBS by exclusion, only after extensively testing patients with typical symptoms and no alarm features (Longstreth, 2005). For those with such a view, the diagnosis of IBS relies on the identification of characteristic symptoms and the exclusion of other organic diseases (Chey et al., 2015). Although the Manning and Rome III criteria have been developed by expert consensus, there has been little validation of the symptom criteria, especially with primary care patients (Longstreth, 2005). Interestingly, a recent survey based research study suggests that experts were less likely than non-experts to endorse IBS as a diagnosis of exclusion. They were also more likely to make a positive diagnosis and spend less money on testing (Spiegel et al., 2010). Furthermore, Spiegel et al. (2010) suggest that care providers who believe IBS to be a diagnosis of exclusion order 1.6 more tests and consume $364 more in resources than those who made diagnoses on the presence of symptoms alone.

In contrast to these views, there is data to suggest that the exclusion of relevant or other causes may contribute to a mutual improved trust and makes the success of indicated treatment approaches more likely (Tkachuk et al., 2008). Reports and guidelines continue to emphasise that IBS is not a diagnosis of exclusion and encourage clinicians to make

a positive diagnostic using Rome Criteria alone (Hammer and Talley, 2008). A particular criticism of the Rome criteria is one which relates to sensitivity, whereby clinicians whom would regard a patients to have typical IBS, but does not meet the specified criteria. This is evident when patients whose symptoms are typical but do not completely fit the 25% Rome III criteria rule on symptom frequency, or experience pain which is intermittent and hence dismissed with the application of strict Rome Criteria (Triantafyllou, 2002).

The cause of IBS is not fully known, although as presented extensively within the previous sections, it is likely to be multifactorial in origin with stress, gastrointestinal infection, abdominal surgery, eating disorders, pelvic disorders, food intolerances, antibiotic therapy and child abuse serving as possible interrelated factors (Silk, 2000). Some authors suggest that views exist whereby patients are often told that IBS does not exist or may be 'all in the head' (Toner et al., 2000). Although psychological factors could play a role in the exacerbation of the condition, the idea that IBS is purely a psychosomatic condition is untenable and unlikely (Silk, 2000). Furthermore, there is evidence beginning to emerge which supports biological (or visible) abnormality as changes in gastrointestinal motility have been observed such as irregular contractions within the luminal tract (Simrén et al., 2000) and increased frequency of high amplitude colonic contractions (Chey et al., 2001).

Hu et al. (2002) conclude that common mental health problems such as anxiety in particular are independent factors which significantly predict factors such as healthcare seeking behaviour among patients with IBS. These views are supported by other authors (Ringström et al., 2007) and are consistent with the multifaceted diseases process explained within various models of IBS causation (Levy et al., 2006 , Drossman, 2006 , Chey, 2013). These biopsychosocial models presented earlier are the most currently accepted basis for IBS (Soares, 2014).

These controversies are likely to continue and represent a spectrum of understanding relating to the causation and definition of IBS. A 2009 position statement issued by the American College of Gastroenterology states that no symptom-based criteria have ideal accuracy for diagnosing IBS (Brandt et al., 2009). The management of patients with IBS is likely to be optimised by an individualised, holistic approach that embraces dietary, lifestyle, medical and behavioural interventions (Chey et al., 2015).

2.2.6 Cognitive Behavioural Therapy and IBS theory

Patients with IBS and psychological co-morbidities currently receive a predominantly medical model of care aimed at bowel symptom control and the regulation of gastrointestinal motility. Physicians do use some forms of medical psychological treatments such as anti-depressants for patients with IBS. However, a therapeutic symptom response (when the aim is to reduce gastrointestinal symptoms) can be observed at much lower doses than used conventionally for psychological illness (Lea and Whorwell, 2003). For example, TCA antidepressants seem to be particularly useful in diarrhoea predominant IBS owing to their ability to alleviate chronic pain coupled with a (desirable) constipation side effect. However, not surprisingly, over a third of patients prescribed these medications will suffer side effects such as dry mouth, constipation, fatigue and drowsiness (Spiller et al., 2007).

Psychological interventions for the treatment of IBS are not new innovations and in fact have been researched as to their application in the treatment of IBS and MUS over the last couple of decades. This is reflected in current best practice guidelines, as the National Institute for Health and Clinical Excellence (NICE) discuss the use and application of treatment approaches such as CBT, Hypnotherapy and Psychotherapy as psychotherapeutic treatment options for patients with IBS (NICE., 2008). However, although NICE support the fact that there may be some desirable effects with some of these interventions; they also recognise that many of the trials which support these notions have methodological

shortcomings and inadequate power. Furthermore, the provision of psychological interventions for treating patients with IBS and psychological co-morbidities within the NHS are rare (Lackner, 2010). Reasons for why this may be the case are discussed within the literature review sections of this thesis.

This thesis is limited to the critical discussion and advancement of CBT techniques for the treatment of IBS, and it is perhaps here that the case should be made for why it concentrates primarily on the use and application of CBT interventions, and not on hypnotherapy or other psychological treatment mechanisms. First of all, CBT certainly has a particular weighting within the literature and would appear to be the most researched form of psychological intervention used for the treatment of IBS. This is perhaps due to the fact that CBT can be very useful for targeting some aspects of IBS which are presented within the biopsychosocial conceptual models within the previous sections. For example, CBT can be used to modify dysfunctional beliefs and help patients understand associations between their thought processes and the manifestation of physical symptoms (Beck et al., 1979 , Beck and Fernandez, 1998). CBT is also particularly useful for addressing negative thought patterns and catastrophizing cognitions and avoidant behaviours (Dainty et al., 2014).

Not only is CBT useful for these particularly troublesome aspects of IBS, many studies have also identified positive effects when using CBT experimentally to treat patients with IBS (Craske et al., 2011 , Drossman et al., 2003 , Gaylord et al., 2011 , Heymann-Mönnikes et al., 2000 , Kennedy et al., 2005 , Lackner et al., 2008 , Ljótsson et al., 2011 , Mahvi-Shirazi et al., 2008 , Tkachuk et al., 2003 , Van Dulmen et al., 1996). It is these promising results from seemingly good quality research studies that have led to the selection of CBT over other forms of psychological treatment approaches as the area on which this work should focus. This is not to say that treatments such as psychotherapy

and hypnotherapy are not effective or less desirable forms of treatment. It is simply a limitation of this work that not all of these treatment approaches could be considered during a period of PhD study.

Furthermore, although there is evidence to suggest CBT may be a particularly useful intervention for patients with IBS, systematic reviews have found the quality of some of the reported studies to be suboptimal (Zijdenbos et al., 2009). More recent reviews report problems with increased risk of bias and limited sample sizes (Altayar et al., 2015) as well as the presence of publication bias (Ford et al., 2014). Nonetheless, the reviews conducted by Ford et al. (2014) and Altayar et al. (2015) recommend CBT as a useful adjunct with clinically significant benefits when used in the management of IBS. It should also be considered that for one reason or another, these seemingly effective treatment approaches do not appear to have been adopted into NHS practice settings to form part of routine care, despite the burden IBS has on NHS resources and the impact IBS has upon patient's lives. These issues clearly require careful and thorough investigation. As a PhD student placed in a school with extensive knowledge and research expertise in the use and application of CBT treatment approaches, I feel well placed to thoroughly investigate and attempt to resolve this dilemma. Therefore, it is a limitation that this work will only focus on the use and application of CBT for the treatment of IBS.

CBT represents a combination of behavioural and cognitive theories relating to various aspects of human behaviour and psychopathology, including emotional, familial and peer influences (Benjamin et al., 2011). It is thought that CBT results largely from the cognitive therapy (CT) developed by Beck (1979) and the work of Ellis (1994) who pioneered rational behavioural emotive therapy (RBET). It is within the modelling of these treatment approaches that the foundations are thought to have emerged which are responsible for the development of the philosophical, theoretical and practical foundations of CBT.

CBT is versatile, complex and represents a broad spectrum of interventional approaches, examples of which include; stress inoculation training (SIT) (Meichenbaum, 1985), problem solving therapy (PST) (D'Zurilla and Nezu, 2007), acceptance and commitment therapy (ACT) (Hayes et al., 2006) and dialectical behaviour therapy (DBT) (Dimeff and Koerner, 2007). These various approaches clearly reflect how CBT can be used to target multiple aspects of psychopathology such as cognitions and behaviours, with the application of a variety of developmentally-guided treatment strategies (Benjamin et al., 2011).

CBT has evolved to accept that cognitive attitudes, beliefs, expectancies, and attributions are essential for understanding and modifying the behaviour of individuals affected by certain psychopathology (Kendall and Hollon, 1979). The basic principles of CBT assume that individuals learn throughout their lives. For example, Jokić-Begić (2010) suggests that;

> *"Both functional and dysfunctional behaviour is learned. Every behaviour that is learned, may be unlearned and replaced by other behaviour that is more functional. CBT helps patients to learn and adopt new knowledge and skills, which will enable them to observe and change their own thoughts, behaviour, and emotional states. After a successful therapy, patients may be expected to be more functional and have better subjective quality of life"* (Jokić-Begić, 2010 p.237)

Jokić-Begić (2010) suggest that CBT is based upon both behavioural and cognitive paradigms; the former underpinning the theories whereby adaptive and maladaptive behaviour is learned, the latter focusing on mental disorders arising from altered cognitive processes. CBT is also based upon the underlying principle that cognitions also play a role in the development and maintenance of emotional and behavioural responses to everyday life situations (González-Prendes and Resko, 2012). CBT elicits new and repeated experiences to stimulate new processes of learning, which result in changes to patterns of behaviour (Fuchs, 2004).

For example, during therapy a patient may learn to self-regulate their unpleasant emotions (Beauregard, 2007).

According to González-Prendes and Resko (2012), there are three main assumptions which underpin CBT models of treatment;

1. Cognitive processes are accessible and can be known, although they may not be known consciously, with proper training awareness of these cognitions may be elicited
2. Cognition mediates responses to environmental cues or stimuli i.e. the way people think about reality is pivotal on how people react to their perceived reality
3. Cognitions can be changed, targeted or modified in ways which are more rational and objective in order to increase adaptability and functionality through self-help (SH) or engagement with a facilitator

During its application during the treatment of IBS, CBT can be particularly useful for dealing with difficult issues such as catastrophizing and negative underlying thought patterns (North et al., 2007). Catastrophizing (a cognitive distortion relating to irrational or exaggerated thoughts) is considered to be a particular issue for many patients with IBS and its presence may be a significant predictor of poor patient outcomes which may be improved with the use of CBT (Hunt et al., 2009). Authors have advocated that CBT is perhaps the most effective approach for dealing with complex and severe co-morbidities such as SD (Mai, 2004). Psychological interventions may also be useful for eliciting and addressing difficult issues such as sexual and emotional abuse (Delvaux et al., 1997).

Stress clearly has a role to play in IBS, and the symptoms which patients experience are thought to be determined to some extent, by the presence and levels of psychological co-morbidity (Stam et al., 1997). Toner (1994) proposed that anxiety may intensify symptoms and in

particular cause a hypersensitivity to the perception and experience of pain. This in turn reinforces the sufferer's belief in an organic cause for their illness leading to further anxiety, states of arousal and more noxious symptoms (Toner, 1994). Many patients with IBS also have distorted views regarding their symptoms (Toner et al., 1998). The underlying theory of CBT lies in correcting these maladaptive thought patterns which results in positive changes in behaviour and affects (Hassett and Gevirtz, 2009).

Researchers such as Blanchard et al. (2007) have used CBT approaches specifically for treating IBS. Their trial conducted in 2007 used CBT which firstly explained and educated participants as to the role of stress in relation to their IBS symptoms. Blanchard et al. (2007) then used methods originally developed by Beck (1976), whereby the therapist worked to address cognitive fallacies. Therapy then focused on the changing of maladaptive beliefs, whilst placing emphasis on a problem solving approach. Participants were then encouraged to keep diaries, to become observers of their cognition and keep records of stressful situations and their efforts to change their own cognitions.

Other authors have used variations of CBT techniques such as mindfulness training (Gaylord et al., 2011) and the combination of CBT approaches with interoceptive exposure to visceral sensations (Craske et al., 2011).

Researchers have developed programs of CBT specifically for treating IBS. Toner et al. (2000) suggest that CBT should have the three following objectives;

- To help clients reconceptualise their views of IBS from feelings of hopelessness to a resourcefulness and hopefulness
- To help clients identify relationships among thoughts, feelings, behaviours, the environment and their IBS symptoms

- To empower clients to develop and implement increasingly more effective ways of coping with IBS in order to improve the quality of their lives

Options for treating IBS patients include group (Tkachuk et al., 2003 , Gaylord et al., 2011) and individual programs of CBT (Payne and Blanchard, 1995). However, some authors would suggest that individual contact is better suited to tailoring therapy to the needs of the client (Toner et al., 2000). A study by Vollmer and Blanchard (1998) showed no significant differences between group and individually delivered programs of CBT (Vollmer and Blanchard, 1998). There are other variations to treatment such as a study of an internet delivered program of exposure therapy (Ljótsson et al., 2011). The various delivery mechanisms of CBT interventions are discussed critically within the appraisal of the literature within the following chapter.

2.3 Summary

IBS is a complex disorder. Although IBS may present to clinicians as a physiological disorder, our understanding of the condition and its aetiology remains poorly understood. IBS is compounded by a multitude of physical, psychological and social factors which may be partially explained by biopsychosocial models suggestive of interactions and interplay between these various factors. Patients with IBS often experience chronic symptoms which appear to reduce quality of life and are a significant concern to healthcare establishments, clinicians and researchers. Many treatments currently used for the medical management of IBS have a limited impact on symptoms or produce undesirable effects. There is currently no medicinal cure for IBS although some patients may experience spontaneous remission or symptom free periods. Coping with this unpleasant and poorly understood condition may be facilitated with the application of various psychological treatment techniques such as CBT. Such treatments are not offered routinely, which necessitates the thorough investigation presented within the chapters which follow.

Chapter 3 ▪ A systematic review of interventions utilised within experimental evaluations of CBT for IBS

3.1 Introduction

As identified within the extensive critical discussion regarding the characteristics of IBS in chapter 2, CBT treatment techniques which may be useful and effective in the management of IBS are not routinely adopted into NHS practice. Reasons for a lack of provision for these alternative treatments are currently unclear and require careful assessment and investigation.

As a research student based within a school with particular expertise in the management of long term conditions and the application of CBT treatment approaches, I feel well placed to thoroughly investigate the literature which underpins the potential use of CBT interventions utilised within studies for the management of IBS. In order for this to be possible, an extensive and review of the literature underpinned by the aims and objectives which are detailed below has been conducted. Most importantly, the literature review aims to review the current evidence base regarding the use and application of CBT for treating patients with IBS, in particular the methods used to deliver interventions to participants.

As RCT's are currently considered the gold standard for assessing the effectiveness of healthcare interventions (Feneck, 2009 , Rothwell, 2005 , Nystrom et al., 1993), and are the mainstay within a systematic review which underpins current practice (Zijdenbos et al., 2009), they are the main focus of the review. It is hoped that by reviewing the various interventions evaluated within the literature, reasons may be sought for why interventions have not been adapted successfully into routine clinical practice.

3.1.1 Aim

To carry out a systematic review of the interventions used within experimental evaluations of CBT treatment approaches evaluated for the management of patients with IBS.

3.1.2 Objectives

1. To critically appraise the delivery methods and underpinning theory used during the CBT treatment of IBS within investigational studies (see 3.2.1)
2. To identify the range of outcomes used within experimental evaluations (see 3.2.2)
3. To identify potential barriers and facilitators to the implementation of CBT interventions evident within experimental evaluations (see 3.2.3)
4. To briefly discuss the quality of studies included within the review (see 3.2.4)
5. To identify opportunities for further research and evaluation of CBT treatment approaches for the management of IBS (see 3.2.6)

3.1.3 Literature search strategy

In order to identify as much relevant material as possible, various databases were extensively searched for relevant literature. CINAHL, Medline (Proquest) and PsycINFO were searched using the subject headings Irritable Bowel Syndrome (IBS) and Cognitive Behavioural Therapy (CBT). As a preliminary search of the literature demonstrated a limited volume of material, no date restrictions were applied to restrict a search of the databases. A search for grey literature (unpublished or not contained within the above mentioned databases) was also conducted during the review. (Please see Appendix 8.1 for the protocol developed for the literature review).

3.1.4 Summary of inclusion criteria

- RCT's evaluating CBT interventions, specifically for the management of adult patients with IBS

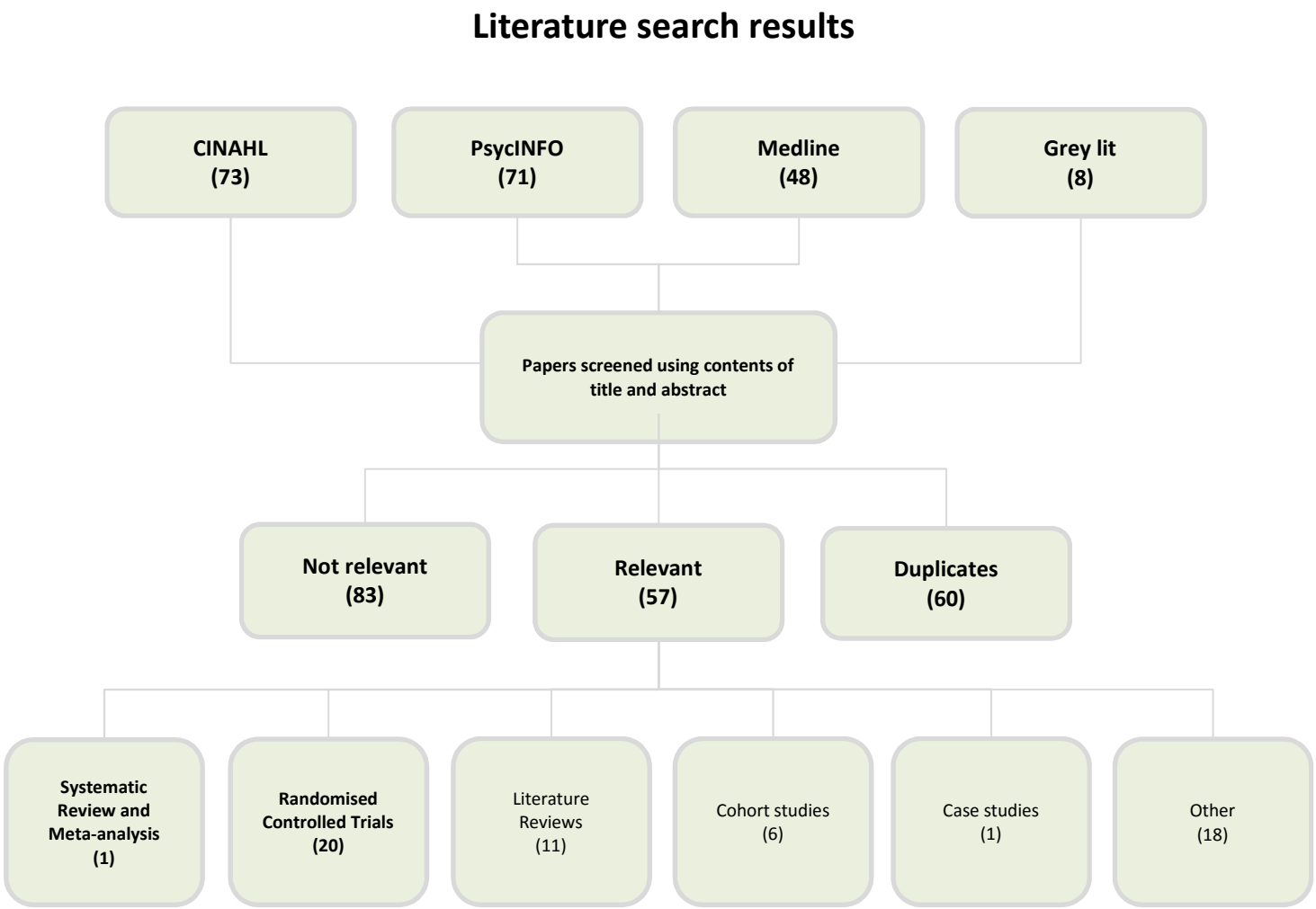
3.1.5 Summary of exclusion criteria

- Papers not written or available in English
- Papers not clearly reporting the evaluation of a CBT intervention
- Evaluations of psychotherapeutic interventions not considered to be CBT
- Evaluations of CBT for the treatment of related FGID's such as gastro oesophageal reflux disease

3.1.6 Summary of search results

The following diagram (figure 4) provides an illustration of the number of papers identified during the search for relevant literature.

Figure 4


Literature search results
CINAHL (73)
PsycINFO (71)
Medline (48)
Grey lit (8)
Papers screened using contents of title and abstract
Not relevant (83)
Relevant (57)
Duplicates (60)
Systematic Review and Meta-analysis (1)
Randomised Controlled Trials (20)
Literature Reviews (11)
Cohort studies (6)
Case studies (1)
Other (18)

A total of 20 RCT's and 1 systematic review were identified during the literature search. No studies were excluded on the basis of unavailability in English. The studies are presented using the patient, intervention, comparator and outcomes (PICO) framework (Huang et al., 2006) within a comprehensive matrix which is presented on the following pages. A PEDro score was calculated and is also included within the matrix which summarises each of the studies. The PEDro framework was originally developed in 2003 (Maher et al., 2003), and was shown to have an interclass correlation coefficient (ICC) of .68 for consensus ratings of quality (95% CI = .57–.76). The scale was developed as a result of Delphi consensus among methodological experts (Verhagen et al., 1998). The reliability ratings of scale items identified as 'fair' to 'substantial', and the reliability of total scores was thought to be 'fair' to 'good' (Maher et al., 2003).

The PEDro scale has since been evaluated for validity and De Morton (2009) found the original PEDro ordinal scores to be a valid measure for assessing the methodological quality of clinical trials. Scores between 1 (minimal quality) and 10 (excellent quality) are included within the matrix of included studies as a summary indicator of quality, which is provided to assist the reader with the interpretation of the studies (see table 4). A copy of the PEDro scale template can be found in Appendix 8.2.

Table. 3 Matrix of experimental evaluations of CBT for the treatment of IBS

Study	Design	*N*	Patients	Intervention	Comparators	Outcomes *(primary in bold)*	Results/findings	Threats to validity & PEDro
Andersson et al. (2011)	**Crossover RCT**	85	Rome III criteria Self-referred (unclear) Suicidal ideation, severe depression, alcohol and substance abuse, mania, anorexia or psychosis were excluded Mean age:34.6 Female:84.7 Co-exist Psych: not reported Stockholm, Sweden	Internet delivered CBT based on exposure and mindfulness exercises for 10 weeks with therapist email support (n=42)	Internet discussion forum with therapist email support (n=43)	**Gastrointestinal symptom rating scale for irritable bowel syndrome (GSRS-IBS)** (Wiklund et al., 2003) Trimbo's institute of medical technology assessment cost questionnaire for psychiatry (TIC-P). Pre, post, 3 months, 15-18 months.	Significant societal cost reductions within intervention group driven by reduced loss of work/productivity Incremental cost-effectiveness ratio (ICER) represents a $16,806 saving per treated case mainly due to reduced loss of work and productivity	Study used 50% reduction in symptoms used as significant improvement Estimated participants salary costs based on levels of education (actual cost data not collected) Randomisation: unclear Blinding: unclear PPI: not evident Economics: cost effectiveness **PEDro score: 6**
Blanchard et al. (2007)	**Crossover RCT**	210	Rome II criteria and severe IBS (moderate to severe) Recruitment: media respondents/outpatients Mean age: 48.8 Female: 84.5 Co-ex Psych: 61.8 New York, USA	Group based CBT delivered by a psychologist for 10 weekly, 90 minute sessions (n=120)	Psycho-educational support (n=46) Intensive symptom and daily stress monitoring (n=44)	**Composite Primary Symptom Reduction (CPSR)** GI Symptom diary McGill pain questionnaire Pre, 2 weeks post, 3 months	ANCOVA's (pre-treatment covariate and pairwise comparisons). Reductions in pain and tenderness for cog ther versus monitoring (p = 0.034)	Older patients (mean age 49 years) 10% drop out rate from treatment, these patients were also notably less chronic cases and more likely to have axis type 1 disorders Unclear interventions Randomisation: double coin flip Blinding: assessor at follow up PPI: not evident Economics: no **PEDro score: 5**

Bogalo and Moss-Morris (2006)	**RCT**	64	Rome I & II diagnosed post infective IBS Recruitment: patients post infection clinics Mean age: 39 Female: 74% Co-ex Psych: not reported Auckland, New Zealand	Self-Help CBT homework manual for 7 weeks, with initial face to face meeting with a Cognitive Behavioural therapist and 2 x 1 hour support sessions at 5 and 7 weeks (n=31)	Study did not report details of control group (n=unclear)	**Subjects global assessment of relief** Retrospective baseline, 8 weeks post, 3 months	Quality of SH homework was not associated with improvement in IBS symptoms post treatment. At 3 months, quality and quantity of homework was associated with symptom improvement (Pearson's correlation coefficient .86 ($p<.001$)	Small sample No control group reported Randomisation: opaque envelope Blinding: not clear PPI: not evident Economics: no **PEDro score: 5**
Boyce et al. (2003)	**RCT**	105	Rome I criteria Recruitment: media respondents Mean age: 42.3 Female: 81% Co-ex Psych: 64.7 New South Wales, Australia	CBT weekly 1 hour sessions delivered by a psychotherapist for 8 weeks (n=35)	Relaxation therapy, 30 minutes per week for 8 weeks (n=36) Routine clinical care (n=34)	**Bowel symptom severity scale (BSSS)** Medical outcome short form (SF36) Hospital anxiety and depression score (HADS) Pre, 4 weeks in, post, 8, 26, 52 weeks	Reductions in bowel frequency scores persisted to 52 week follow up ($F = 39.57$ $p<.001$). However, CBT and relaxation not significantly superior to standard care alone.	Failure to monitor interventions or maximise intervention effectiveness Small sample Randomisation: opaque envelope Blinding: assessors blind PPI: not evident Economics: no **PEDro score: 6**

Craske et al. (2011)	**RCT**	110	Rome II criteria Recruitment: media campaign/OPD Mean age: 39.4 Female: 74.3% Co-ex Psych: 8.1% panic disorder Los Angeles, USA	Ten, 50 minute sessions of CBT with interoceptive exposure to visceral sensations (n=47). Unclear administration of intervention.	Ten, 50 minute sessions of Stress management (n=41) Attention control (n=22)	**Bowel symptom composite score** **Visceral sensitivity index (VSI)** Other secondary outcome measures were also obtained Pre, post and 3 months	Intervention group had greater decline in bowel symptom severity than symptom monitoring [*t* (165) = -2.03, p<.05].	Small sample size High rate of attrition > 25% within control Unclear assignment over groups Randomisation: opaque envelopes Blinding: assessor PPI: not evident Economics : no **PEDro score: 6**
Drossman et al. (2003)	**RCT**	431	Physician opinion Recruitment: media respondents and GI clinics Mean age: 38.6 Female: 100% Co-ex Psych: 23% Michigan, USA	Twelve weeks of individual CBT delivered by a psychologist as detailed in Toner et al. (2000), 1 hour in duration (n=144)	Twelve weeks of modified educational attention control delivered by same therapist (n=71) Education and Desipramine (an antidepressant medication) (n=144) Placebo control (n=72)	**Composite of;** Treatment efficacy questionnaire Global well-being McGill pain questionnaire Irritable bowel syndrome quality of life (IBS-QOL) Pre, 3-6-9-12 months post	Intention to treat analysis (ITT), CBT more effective than education (p = <.001 , response 70% CBT vs. 37% education; number needed to treat (NNT), 3.1	**No primary outcome set** Intervention was delivered over slightly longer period than control Study included women only Small sample Unclear methods for outcome measurement Not all patients (86%) met IBS criteria Randomisation: computer Blinding: assessors blind PPI: not evident Economics: some service use **PEDro score: 7**

Gaylord et al. (2011)	**RCT**	75	Rome II criteria Recruitment: existing participants registry/media campaign Mean age: 42.7 Female: 100% Co-ex Psych: 57% USA	Eight weeks of mindfulness group training for half a day, as detailed in Gaylord et al. (2009) (n=39)	Support group led by masters level social workers (n=36)	**IBS symptom severity scale (IBS-SSS)** IBS-QOL Pre, end of 8 week intervention, 3 months post	Repeated measures ANOVA, ITT analysis, significant intervention x time interaction. Intervention had greater improvements in IBS severity post treatment ($F(1.72) = 7.88$, $P =<.006$) and at 3 months ($F(1,71) = 11.29$, $P<.001$).	Female patients only Randomisation: computer Blinding: assessor blind PPI: not evident Economics: no **PEDro score: 6**
Heymann-Mönnikes et al. (2000)	**RCT**	26	Rome criteria with severe IBS Recruitment: Outpatient clinics Mean age: 37.8 Female: 93% Co-ex Psych: unclear Germany	Ten sessions (60 minutes) of standardised multi-component behavioural therapy in addition to standard medical management (n=12) Intervention delivered by a clinical psychologist	Standard medical treatment (n=12)	**IBS symptom diary specific to study** Various secondary outcome measures were also obtained Pre, 3, 6 months post	ANOVA group x time interaction was significantly in favour of intervention (symptom severity) at post treatment ($F[df = 1:22] =14.95$; $p<.001$) remaining significant at 3 and 6 months.	Very small sample Primary outcome measure without strong evidence base Randomisation: random numbers Blinding: none PPI: not evident Economics: no **PEDro score: 4**

Hunt et al. (2009)	**RCT**	54	Recruitment: Via internet advertisements and self-referral Mean age: unclear Female: 81% Co-ex Psych: unclear USA	Internet based CBT consisting of 5 modules and homework via email to the principal investigator (n=28) Modules included education and relaxation training, stress management, catastrophic thinking, exposure therapy and behavioural experiments	Waiting list control (WLC) (n=26)	**GSRS-IBS** Anxiety severity index (ASI) Visceral anxiety sensitivity IBS-QOL Consequences of physical sensations questionnaire (CPSQ) Pre, Post and 3 months post intervention	ANCOVAs analysis performed, significant effects of intervention at post-treatment ($F(2,28) = 11.31$ ($P<.001$). Maintained at 3 months follow up. Attributed to reductions in catastrophizing behaviour	Significant attrition associated with greater impairments in HR-QOL High rates of attrition within the intervention and WLT group (more than half failed to complete treatment) Atypical sample (more impaired than typical physician referred patients) Lack of diagnostic confirmation Randomisation: unclear Blinding: assessors blind PPI: not evident Economic data: no **PEDro score: 6**
Kennedy et al. (2005)	**RCT**	149	Rome 1 criteria with severe IBS unresponsive to Mebeverine treatment Recruitment: General Practices Mean age: 33.8 Female: 82% Co-ex Psych: 43% Kings College, London	Six, 50 minute sessions of CBT delivered by primary care nurses plus Mebeverine (n=72) Desensitisation procedure as detailed in Lang et al. (1970) Nurses trained 1 day weekly for twelve weeks	Mebeverine alone (n=77)	**IBS-SSS** HADS Pre, 3-6-12 months post	Summary odds ratio (OR) for having severe symptoms after CBT over 12 months was 0.43 (95% CI 0.30 to 0.62). NNT from severe to normal symptoms (3 months) was 5.9 (3.3 to 27.8) Treatment was cost effective in the short term but did not reduce treatment costs overall	Small sample Control and monitoring of intervention unclear Randomisation: unclear Blinding: no PPI: not evident Economics: evident within HTA publication **PEDro score: 5**

Lackner et al. (2008)	**RCT**	75	Rome II criteria Recruitment: community physicians Mean age: 46.6 Female: 86% Co-ex Psych: unclear New York, USA.	Therapist administered skills based CBT, 10 weekly, 1 hour sessions as detailed in Blanchard (2001) (n=25) Both interventions delivered by clinical psychologists	Self-administered (minimal contact) CBT using similar principles to intervention but with only 4 x 60 minute sessions over ten weeks (n=23) WLC (n=27)	**Adequate relief measures** Clinical global impressions scale Pre, two weeks post	At 12 week follow up, both CBT interventions were significantly superior to WLC with percentage reporting relief for therapist CBT at 72%, self-administered CBT 60.9% and WLC 7.4%.	Unclear primary outcome measure Small exploratory sample Randomisation: not stated Blinding: not stated PPI: not evident Economic data: no **PEDro score: 5**
Ljotsson et al. (2010)	**RCT**	85	Rome III criteria (analysis suggests moderate to severe IBS) Recruitment: Self-referred as a result of media advertisements Mean age: unclear Female: unclear Co-ex Psych: unclear Sweden	Ten week CBT internet delivered treatment protocol (Ljotsson et al., 2010), with weekly email contact to psychology student (n=42) Participants also had access to a discussion forum	WLC with online discussion form (which differed from that of the treatment forum (n=43) Participants were also given none CBT email support	**CPSR** GSRS-IBS Various secondary outcomes also obtained which include IBS-QOL Pre, Post and 3 months Follow up conducted with online completion of instruments	Mean CPSR was 0.42 (SD = 0.48) and 0.12 (SD = 0.43) for the treatment and control groups respectively, which was significant (t75 =5.3 p<.001) with large between group effect Cohen's d = 1.19 Follow up period for these observations is unclear.	Three month follow up omitted GI symptom diary Discussion form included within the intervention No therapist controls for adherence Authors felt recruitments from tertiary clinics would have improved generalizability Demographics? Randomisation: random number service carried out by independent persons Blinding: unclear PPI: not evident Economic data: no **PEDro score: 4**

Ljótsson et al. (2011)	**RCT**	195	Rome III criteria Recruitment: media respondents/gastro OPD Mean age: 38.9 Female: 79% Co-ex Psych: unclear Sweden	Internet delivered exposure-based treatment lasting 10 weeks (n=98) Delivered with online psychotherapist support via email	Stress Management (n=97)	**GSRS-IBS** Secondary QOL measures were also obtained Pre, post (10 weeks) and 6 months post	Statistically significant difference in favour of intervention. Differences in GSRS-IBS scores were 4.8 (95% C I 1.2 to 8.4) and 5.9 (95% CI 1.9 to 9.9) at post-treatment and 6 months respectively. (Effect sizes 0.38 and 0.44.)	Limited to internet recruitment and patients who have internet access Internet recruitment may have selected atypical sample Randomisation: simultaneously by independent persons Blinding: assessments online blinding unclear PPI: not evident Economic data: no **PEDro score: 6**
Mahvi-Shirazi et al. (2008)	**RCT**	50	Rome II criteria recruited from a previous study database Recruitment: OPD clinics Mean age: unclear Female: unclear Co-ex Psych: not reported Tehran, Iran	CBT in addition to standard medical treatment (unclear intervention details) (n=unclear assignment over groups)	Standard medical treatment	**Measures of mental health SCL-90-R questionnaire** Unclear follow up procedure	CBT used in conjunction with medical care is superior to Standard medical treatment at follow up. Unclear treatment follow up periods.	Unclear assignment over groups Small sample Unclear methods Randomisation: not stated Blinding: not stated PPI: not evident Economic data: no **PEDro score: 2**

Moss-Morris et al. (2010)	**RCT**	64	Rome II criteria Recruitment: Mean age:39.5 Female: 73% Co-ex Psych: mean HAD 7.9 anxiety (SD 4.2) Auckland, New Zealand	CBT Self-management plus treatment as usual or TAU (n=31) A patient treatment manual administered over 7 to 8 weeks in conjunction with a 1 hour face to face session (psychologist) and 2 x 1 hour telephone sessions	Treatment as usual control (n=33)	**Subjects global assessment of relief** **IBS-SSS** Various secondary outcomes also obtained Pre, post, 3 and 6 months	At 6 months follow up the mean change for the intervention group was 109 vs. 29.5 for the control. 25 of the intervention improved 50 points or more at 6 months vs. 16 in the control (OR 5.3, 95% CI 1.64-17.26).	Small sample Participants less disabled than other in trials of IBS Randomisation: opaque envelopes Blinding: assessor PPI: not evident Economic data: no **PEDro score: 6**
Oerlemans et al. (2011)	**RCT**	76	Rome III criteria Recruitment: from primary care practices and web advertisements Mean age: 40.6 intervention 35.9 control Female: 84% Co-ex Psych: not recorded Netherlands	CBT delivered using Personal Digital Assistant (PDA) as detailed within Oerlemans et al. (2011) <u>in response to individual symptom diaries</u> (n=39) Situational feedback from a psychologist for three weeks	Standard care control (n=37)	Cognitive scale of functional bowel disorders (CSFBD) IBS-QOL The pain catastrophizing scale, abdominal pain and electronic diary Pre, post, 3 months	No significant differences in dysfunctional cognitions found, QOL and pain was improved post intervention but not significant at 3 months. Catastrophizing thoughts were improved post intervention (X^2 =9.33, p<.001, df=1) and at 3 months (X^2 =7.06, p<.001, df=1.	Participants within control condition did not appear to keep symptom diaries as in control Randomisation: unclear Blinding: unclear PPI: not evident Economic data: no **PEDro score: 5**

Payne and Blanchard (1995)	**RCT**	34	Rome criteria Recruitment: unclear Mean age: 39.8 Female: 82% Co-ex Psych: 85% New York, USA	Individualised cognitive therapy based on Greene and Blanchard (1994) Delivered by a therapist 2 x 60 minute sessions per week for 2 weeks then 60 minutes per week for a further 6 weeks (n=12)	Support Group for 1 hour 15 minutes per week for 8 weeks with focus on issues such as stress and diet (n=12) WLC (n=10)	**CPSR** Pre, post, 3 months post	Multilevel analysis of variance (MANOVA) showed significant effect for time ($F(2, 31) = 5.12$, $p<.02$, effect size 0.19 and group x time interaction ($F(2, 31) = 6.84$, $p=<.001$, effect size 0.15 (all pre and post scores of psychological distress – dysphoric psychological state).	Small sample Predominantly male sample Unclear interventions Randomisation: unclear Blinding: none PPI: not evident Economic data: no **PEDro score: 3**
Sanders et al. (2007)	**Crossover RCT**	28	Rome criteria? Recruitment: media campaign and referrals from clinics Mean age: 56.9 treatment 41.8 control Female: 66% Co-ex Psych: New York and Chicago, USA	CBT treatment book as published by Bradley-Bolen (2000) administered in 5 modules for 10 weeks (including 2 weeks of symptom monitoring (n=17) No supportive contact	WLC (n=11)	Albany gastrointestinal history Wide range achievement test reading section CPSR Brief symptom inventory IBS- QOL Structured clinical interview DSM-IV Axis 1 Pre, Post, 3 months	Significantly higher CPSR scores in the intervention condition at post treatment [$t(14) = 2.91$, $p.01$, eta $^2 = 0.38$]. Noted 25% improvement within intervention and 32% decline within WLC.	Small sample High attrition (more likely to have axis I disorder) 43% attrition within control **No primary outcome set** Randomisation: coin flip? Blinding: not evident PPI: not evident Economic data: no **PEDro score: 4**

Tkachuk et al. (2003)	**RCT**	28	Rome criteria Recruitment: university & community practices Mean age: 36 Female: 96% Co-ex Psych: 68% (39% GAD, 11% major depressive disorder, 11% social anxiety disorder, 4% PTSD, 4% somatoform disorder) Canada	Group CBT delivered by 2 therapists with advanced training. Groups of 3 to 8 participants, 10 x 90 minute sessions held over 8 weeks Therapy consisted of education and goal setting, relaxation training, cognitive therapy, assertion training and relapse prevention training (n=14)	No treatment control with weekly symptom monitoring telephone contact (n=14)	Symptom diary Beck depression inventory State-trait anxiety inventory CSFBD Assertiveness questionnaire SF-36 Diaries 2 weeks pre intervention, 9 weeks during, 2 weeks post, 3 months post	Pain and CPSR not significantly affected by intervention. Measures of psychological functioning and QOL were improved within the intervention arm and were significant (Hotelling's T^2 = 1.296, F (6, 21) = 4.536, p= 0.04, effect size = .56	Unclear concealment Very complex intervention consisting of a variety of approaches Long term follow up not possible Randomisation: not stated Blinding: no PPI: not evident Economic data: no **PEDro score: 4**
Vollmer and Blanchard (1998)	**RCT**	32	IBS patients Recruitment: media campaign/physician referral Mean age: 43.6 Female: 72% Co-ex Psych: 84% (41% GAD, 18% major depressive disorder, 15% agoraphobia with panic disorder) New York, USA	CBT Group therapy for 3 to 5 participants, 60-90 minutes in duration for 10 weeks delivered by a therapist (n=11)	CBT individual based on Greene and Blanchard (1994), 60 minutes in duration for 10 weeks (n=11) WLC and symptom monitoring (n=10)	**CPSR** Pre, post, 3 months post	Significant improvement in 64% of the group therapy group, 55% individual and 10% WLC. Maintained at 3 months. MANOVA (of all GI symptoms) demonstrated group F(1, 31) = 1.19, p<.05 and time F(1, 31) = 2.03, p.07.	Small sample Randomisation: not stated Blinding: no PPI: not evident Economic data: no **PEDro score: 5**

3.2 The experimental literature

3.2.1 Treatment intensity and method of delivery

A wide variety of intervention delivery methods were evident within the included RCT's, summary details of which are reported in the matrix of included studies (see table 3). The majority of the CBT interventions were delivered by clinical psychologists (Blanchard et al., 2007 , Boyce et al., 2003 , Drossman et al., 2003 , Heymann-Mönnikes et al., 2000 , Lackner et al., 2008 , Moss-Morris et al., 2010) or cognitive behavioural therapists (Andersson et al., 2011 , Bogalo and Moss-Morris, 2006 , Payne and Blanchard, 1995 , Tkachuk et al., 2003 , Vollmer and Blanchard, 1998).

Some studies offered variations to conventional therapist treatment, delivering their interventions via the internet (Andersson et al., 2011 , Hunt et al., 2009 , Ljotsson et al., 2010 , Ljótsson et al., 2011) or through the use of Personal Digital Assistants (PDA's) (Oerlemans et al., 2011). Bogalo and Moss-Morris (2006), Moss-Morris et al. (2010) and Sanders et al. (2007) used self-administered treatment manuals. The only study within the UK chose to deliver their intervention via primary care nurses trained in the use of CBT (Kennedy et al., 2005).

Issues pertaining to the intensity of treatment and method of delivery should be developed with due care and attention as authors have acknowledged the need for researchers to evaluate a 'second generation' of intervention delivery, which should address concerns relating to potentially prohibitive issues such as cost and treatment accessibility issues (Lackner et al., 2008). Whilst internet interventions may be a potential solution, treatment may not always be adequate on a 'stand-alone' basis without the input of a therapist or facilitator. This is demonstrated when internet or online interventions have been found to require additional therapist support via email (Ljotsson et al., 2010 , Ljótsson et al., 2011). Researchers evaluating internet delivered interventions to treat depression also suggest that stand-alone

interventions appear to yield fewer benefits than those with therapist support and guidance (Titov, 2011). In addition to these concerns, there are also critics who have reservations about the delivery of online interventions with concerns relating to confidentiality, a loss of visual and auditory clues during therapy, a lack of suitability for managing crisis situations and unclear legal and ethical issues (Childress, 1998). A recent survey of 658 patients also suggests that internet delivered CBT would be unacceptable to over 40% of those surveyed (Mohr et al., 2010).

Some interventions were delivered as group based treatments rather than one to one therapy sessions (Blanchard et al., 2007 , Gaylord et al., 2011 , Tkachuk et al., 2003 , Vollmer and Blanchard, 1998). Although this may be another potential solution for increasing access to psychological therapies and reducing the cost of treatment delivery, some authors would suggest that individual contact is better suited to tailoring therapy to the needs of the client (Toner et al., 2000). Interestingly, a study reported by Vollmer and Blanchard (1998) showed no significant differences in affect between group and individually delivered programs of CBT for the treatment of patients with IBS (Vollmer and Blanchard, 1998).

However, Blanchard's findings should be treated with caution as a recent meta-analysis suggests there is insufficient evidence to support the notion that group CBT may be more cost effective for treating conditions such as phobias, anxiety and substance misuse (Tucker and Oei, 2007). Furthermore, whilst assessing treatment acceptability among panic disorder patients, a recent study found that 95% of participants chose individual CBT over group therapy (Sharp et al., 2004) which may suggest that group CBT is less acceptable to patients. The following matrix (table 4) is a summary of the components used and mechanism of delivery of the various interventions within the reviewed studies. A further table (table 5) summarises the types of control and comparator conditions used within the reviewed studies.

Components of CBT interventions and method of delivery utilised within experimental evaluations of CBT treatment approaches for IBS

Study	Intervention components	Sample details
Andersson et al. (2011)	An internet CBT based on exposure and mindfulness exercises for ten weeks in conjunction with therapist email support (n=42). Participants had online contact with a **graduate psychology student**, trained in CBT. • Rationale for the interventions • Mindfulness instructions and coaching • Awareness of IBS symptoms, thoughts, feelings and behaviour • Psychological model of IBS • Promoting an awareness of the detrimental effects of avoidance behaviours • Exposure exercises • Promotion of acceptance of aversive symptoms, thoughts and feelings • Psycho-educational text relating to relapse prevention	Rome III criteria Self-referred (unclear) Mean age:34.6 Female:84.7 Stockholm, Sweden
Blanchard et al. (2007)	A Group based CBT intervention delivered by a **psychologist** for 10 weekly, 90 minute sessions (n=120). • Explanations of the possible role of stress in relation to IBS symptoms • Participants were taught to observe their own cognitions • Attention was focused on addressing cognitive fallacies • Targeting of maladaptive core beliefs • Problem solving • Diaries of stressful situations and efforts to change or counter cognitions	Rome II criteria Recruitment: media respondents/outpatients departments (OPD) Mean age: 48.8 Female: 84.5 New York, USA
Bogalo and Moss-Morris (2006)	A SH CBT homework manual for seven weeks, with initial face to face meeting with a **cognitive behavioural therapist** and two, one hour support sessions at five and seven weeks (n=31). • Rationale for treatment • Education relating to the symptoms of IBS • Irritable Bowel Syndrome explained • Assessing symptoms, self-monitoring and managing IBS symptoms • Cognitive restructuring and relaxation • Stress management and maintenance	Rome I & II diagnosed post infective IBS Recruitment: patients post infection clinics Mean age: 39 Female: 74% Auckland, New Zealand

Boyce et al. (2003)	Weekly one hour CBT sessions delivered by a **psychotherapist** for eight weeks (n=35). • Realistic symptom appraisal • Enhanced coping strategies • Relaxation skills • Cognitive restructuring	Rome I criteria Recruitment: media respondents Mean age: 42.3 Female: 81% New South Wales, Australia
Craske et al. (2011)	CBT with exposure to visceral sensations totalling ten, fifty minute sessions of (n=47). **Unclear administration of intervention**. • Education • Self-monitoring of IBS symptoms • Attentional control skills • Cognitive therapy • Exposure to visceral sensations (e.g., tightening stomach to produce gut sensations, delaying bathroom visits, eating avoided foods) • Exposure to feared or avoided situations	Rome II criteria Recruitment: media campaign/OPD Mean age: 39.4 Female: 74.3% Los Angeles, USA
Drossman et al. (2003)	Twelve weeks of individual CBT delivered by a **psychologist**, one hour in duration (n=144) • Modifying the influence of attention • Personal appraisal • Addressing sex- related cognition and illness attribution • Development of more effective coping strategies	Physician opinion Recruitment: media respondents and GI clinics Mean age: 38.6 Female: 100% Michigan, USA
Gaylord et al. (2011)	Eight weeks of a mindfulness-based stress and pain management program (mindfulness group training) for half a day (n=39). The intervention was delivered by '**mindfulness instructors**'. • Instruction and homework assignments • Sitting and walking meditation, and mindful yoga • Coping with IBS-related symptoms and perceptions • Addressing catastrophizing • Mindfulness practice	Rome II criteria Recruitment: existing participants registry/media campaign Mean age: 42.7 Female: 100% USA

Heymann-Mönnikes et al. (2000)	Ten sessions, sixty minutes in duration, of standardised multi-component behavioural therapy delivered by a **clinical psychologist** (n=12) • Education regarding normal GI functioning and stress • Individual analysis of illness symptoms • Cognitive coping strategies • Problem solving techniques and assertion and social skills training	Rome criteria with severe IBS Recruitment: OPD Mean age: 37.8 Female: 93% Germany
Hunt et al. (2009)	An internet based CBT intervention consisting of five modules and homework via email to the principle investigator (**clinical psychologist**) (n=28) • Education regarding symptoms and stress • Relaxation training • Cognitive approach to stress • Exposure therapy • Behavioural experiments • Weekly symptom checklists	Recruitment: Via internet advertisements and self-referral Mean age: unclear Female: 81% Co-ex Psych: unclear USA
Kennedy et al. (2005)	Six, fifty minute sessions of CBT delivered by **primary care nurses** plus Mebeverine (n=72) • Desensitisation procedure • Education • Cognitive techniques • 270 mg of Mebeverine three times daily	Rome 1 criteria with severe IBS unresponsive to Mebeverine treatment Recruitment: General Practices Mean age: 33.8 Female: 82% Kings College, London
Lackner et al. (2008)	Therapist administered skills based CBT, ten weekly, one hour sessions or minimal contact for four, sixty minute sessions (n=25), interventions delivered by **clinical psychologists**. • Education regarding stress and IBS • Self-monitoring • Muscle relaxation • Cognitive restructuring • Coping strategies & Problem solving	Rome II criteria Recruitment: community physicians Mean age: 46.6 Female: 86% New York, USA.
Ljotsson et al. (2010)	Ten week CBT internet delivered treatment with weekly email contact to **psychology student** (n=42) As described in Anderson et al 2011	Rome III criteria Recruitment: Self-referred as a result of media advertisements Mean age: unclear Female: unclear Sweden

Ljótsson et al. (2011)	Internet delivered exposure-based treatment for ten weeks (n=98), delivered with online **psychotherapist** support via email. • Mindfulness exercises • Exposure to symptoms by engaging in activities that provoke symptoms • Reduction or removal of behaviours • Exposure to situations where symptoms are unwanted	Rome III criteria Recruitment: media respondents/gastro OPD Mean age: 38.9 Female: 79% Sweden
Mahvi-Shirazi et al. (2008)	CBT (**unclear intervention details**)	Rome II criteria recruited from a previous study database Recruitment: OPD Mean age: unclear Female: unclear Tehran, Iran
Moss-Morris et al. (2010)	CBT Self-management (n=31) in the form of a treatment manual administered over seven to eight weeks in conjunction with a one hour face to face session with a **psychologist** and two, one hour telephone sessions. • IBS explained and treatment rationale • Self-monitoring and behavioural management • Personal expectations and activity patterns • Daily thought records • Relaxation and stress management. • Sleep hygiene, managing flare-ups and goal setting	Rome II criteria Recruitment: Previous study Mean age:39.5 Female: 73% Auckland, New Zealand
Oerlemans et al. (2011)	CBT delivered using Personal Digital Assistant (PDA) (n=39) with feedback from a **psychologist**. • Situational feedback • Self-management • Reassurance and comfort • General information about coping with IBS	Rome III criteria Recruitment: from primary care practices and web advertisements Mean age: 40.6 intervention 35.9 control Female: 84% Netherlands

Payne and Blanchard (1995)	Individualised cognitive therapy delivered by a **therapist** in the form of two, sixty minute sessions per week for two weeks then sixty minutes per week for a further six weeks (n=12). • Increasing awareness of stressors, thoughts, and IBS symptoms • Modification of cognitive appraisals and responses • Alteration of underlying depressive or threatening schema • Self-monitoring of thoughts feelings and behaviours	Rome criteria Recruitment: unclear Mean age: 39.8 Female: 82% New York, USA
Sanders et al. (2007)	A CBT treatment book administered in five modules for ten weeks (n=17), with **no support**. • Information • Cognitive restructuring • Relaxation • Exposure	Rome criteria? Recruitment: media campaign and referrals from clinics Mean age: 56.9 treatment 41.8 control Female: 66% New York and Chicago, USA
Tkachuk et al. (2003)	Groups of three to eight participants treated with CBT delivered by **therapists with advanced training**. A total of ten, ninety minute sessions over an eight week period. • Education and Goal Setting • Relaxation Training • Cognitive restructuring and assertion Training	Rome criteria Recruitment: university & community practices Mean age: 36 Female: 96% Canada
Vollmer and Blanchard (1998)	CBT Group therapy for three to five participants, sixty to ninety minutes in duration for 10 weeks delivered by a **therapist** (n=11), as delivered by Payne and Blanchard 1995.	IBS patients Recruitment: media campaign/physician referral Mean age: 43.6 Female: 72% New York, USA

Table 4

Control and comparator conditions used within the reviewed studies

Waiting list control	Hunt et al. (2009), Lackner et al. (2008), Ljotsson et al. (2010), Payne and Blanchard (1995), Sanders et al. (2007), Vollmer and Blanchard (1998)
Treatment as usual control	Boyce et al. (2003), Heymann-Mönnikes et al. (2000), Mahvi-Shirazi et al. (2008), Moss-Morris et al. (2010), Oerlemans et al. (2011), Tkachuk et al. (2003)
Individual CBT	Vollmer and Blanchard (1998)
Support group	Gaylord et al. (2011), Payne and Blanchard (1995)
Educational Support	Drossman et al. (2003)
Self-administered CBT	Lackner et al. (2008)
Education and Dispiramine	Drossman et al. (2003)
Placebo	Drossman et al. (2003)
Stress management	Craske et al. (2011), Ljótsson et al. (2011)
Relaxation therapy	Boyce et al. (2003)
Psycho educational support	Blanchard et al. (2007)
Internet discussion forum	Andersson et al. (2011)
Mebeverine hydrochloride	Kennedy et al. (2005)

Table.5

The studies reviewed employ a variety of treatment protocols based on various CBT theoretical approaches, some of which include; mindfulness training (Andersson et al., 2011 , Gaylord et al., 2011), desensitisation procedures (Kennedy et al., 2005), exposure based treatment (Craske et al., 2011 , Ljótsson et al., 2011) and multi-component therapy (Heymann-Mönnikes et al., 2000). Hunt et al. (2009) used a five module treatment protocol consisting of education and relaxation training, stress management, catastrophic thinking, exposure therapy and behavioural experiments.

Some authors have developed treatment approaches specifically for patients with IBS such as the method developed by Toner et al. (2000) used within the trial carried out by Drossman et al. (2003). Toner's

approach aims to help clients reconceptualise their views of IBS from feelings of hopelessness to a resourcefulness and hopefulness and helps the patient identify relationships among thoughts, feelings, their behaviours, the environment and their IBS symptoms (Toner et al., 2000). Therapy using this approach primarily works to empower clients to develop and implement more effective ways of coping with their IBS.

Other theoretical approaches are methods such as those advocated by Blanchard et al. (2007). The intervention first explained and educated participants as to the role of stress in relation to their IBS symptoms. Blanchard et al. (2007) then used methods originally developed by Beck (1976), whereby the therapist worked to address cognitive fallacies. Therapy then focused on changing maladaptive beliefs, whilst placing an emphasis on a problem solving approaches. Participants were then encouraged to keep diaries, to become observers of their cognitions and keep records of stressful situations and their efforts to change.

The trial carried out by Bogalo and Moss-Morris (2006) developed a treatment protocol using a combination of the approaches advocated by Toner (2000) and Blanchard (2001). This therapy was in the form of a six week brief intervention consisting of the following topics; IBS explained, assessing symptoms and self-monitoring, managing IBS symptoms, cognitive restructuring, personal expectations and activity patterns, relaxation, stress management and maintenance.

Many of studies reviewed here deliver their interventions to participants over a 10 week treatment period (Andersson et al., 2011 , Craske et al., 2011 , Heymann-Mönnikes et al., 2000 , Lackner et al., 2008 , Ljotsson et al., 2010 , Ljótsson et al., 2011 , Sanders et al., 2007 , Vollmer and Blanchard, 1998 , Blanchard et al., 2007). Within these 10 week treatment periods, therapy sessions ranged from 50 minutes (Craske et al., 2011), to 60-90 minutes weekly (Vollmer and Blanchard, 1998). The longest duration of treatment was 12 weeks of 1 hour therapy sessions within the study carried out by Drossman et al. (2003). There were some

notable exceptions to these treatment periods such as a brief 5 week internet delivered intervention (Hunt et al., 2009) and a 4 week intervention delivered using PDA's (Oerlemans et al., 2011). One of the studies delivered psychotherapy via primary care nurses trained in the use of CBT during 6, 50 minute treatment sessions (Kennedy et al., 2005). Further details regarding treatment durations obtained from the reviewed studies can be seen in summary form within table 4.

3.2.2 Treatment outcomes

Below, within table 6 are the primary outcome measures utilised within the reviewed RCT's. Drossman et al. (2003), Oerlemans et al. (2011), Sanders et al. (2007), Tkachuk et al. (2003), did not set or make clear a primary outcome measure when reporting their studies. The majority of studies reviewed here measure symptom severity or symptom relief as their primary outcome measures (Andersson et al., 2011 , Blanchard et al., 2007 , Bogalo and Moss-Morris, 2006 , Boyce et al., 2003 , Craske et al., 2011 , Gaylord et al., 2011 , Heymann-Mönnikes et al., 2000 , Hunt et al., 2009 , Kennedy et al., 2005 , Lackner et al., 2008 , Ljotsson et al., 2010 , Ljótsson et al., 2011 , Moss-Morris et al., 2010 , Payne and Blanchard, 1995 , Vollmer and Blanchard, 1998). The exception to this trend was Mahvi-Shirazi et al. (2008) who chose to use measures of mental health as their primary outcome measure (referred to as SCL-90-R validated by Derogatis and Melisaratos (1983). The predominant use of symptom scores as primary outcome measures is perhaps due to the fact that authors advocate that it is somatic symptoms which often cause patients to consult (Blanchard et al., 2007).

The CPSR, originally developed by Blanchard and Schwarz (1988) is the most frequently used method of outcome assessment. The measure uses data collected from scores on subjective symptom diaries (tenderness, bloating, diarrhoea and constipation) to calculate a symptom severity score. Only the studies carried out by Boyce et al. (2003), Drossman et al. (2003), Gaylord et al. (2011) and Hunt et al. (2009), report the blinding of assessors during the collection of post intervention outcome observations. Blinding assessors during the collection of follow up data

may be particularly useful for increasing rigour within a study by reducing the potential for investigator bias. Duration of data collection varied among the included studies and was short-term, although the study carried out by Andersson et al. (2011), collected observations in excess of 12 months. Researchers have identified the negative impact that IBS symptoms have upon HR-QOL (Gralnek et al., 2000 , El-Serag et al., 2002 , Hahn et al., 1997). HR-QOL is also though to represent patient centred data, thus ensuring that research better understands the impact of IBS upon the life experience of individuals (Gralnek et al., 2000). Notwithstanding these concerns, few studies have employed QOL outcome measures during intervention evaluation. Researchers also suggest that symptoms, particularly a lack of energy/fatigue and problems with pain (Gralnek et al., 2000), are responsible for patients initially seeking consultation (Blanchard et al., 2007). The impact of IBS symptoms also has significant impact upon everyday activities, mood relationships (Par'e et al., 2006) and upon QOL (El-Serag, 2003). It is therefore not surprising that symptom severity is chosen by many of the researchers as a primary outcome measure.

Primary outcome measures within included studies

Andersson et al. (2011)	GSRS-IBS
Blanchard et al. (2007)	CPSR
Bogalo and Moss-Morris (2006)	Subjects Global Assessment of Relief
Boyce et al. (2003)	Bowel Symptom Severity Scale
Craske et al. (2011)	VSI
Drossman et al. (2003)	Primary outcome unclear
Gaylord et al. (2011)	IBS-SSS
Heymann-Mönnikes et al. (2000)	IBS symptom diary specific to study
Hunt et al. (2009)	GSRS-IBS
Kennedy et al. (2005)	IBS-SSS
Lackner et al. (2008)	Adequate relief measures
Ljotsson et al. (2010)	CPSR
Ljótsson et al. (2011)	GSRS-IBS
Mahvi-Shirazi et al. (2008)	Measures of mental health SCL-90-R questionnaire
Moss-Morris et al. (2010)	Subjects Global Assessment of relief, IBS-SSS
Oerlemans et al. (2011)	Primary outcome unclear
Payne and Blanchard (1995)	CPSR
Sanders et al. (2007)	Primary outcome unclear
Tkachuk et al. (2003)	Primary outcome unclear
Vollmer and Blanchard (1998)	CPSR

Table.6

3.2.3 Barriers and facilitators

Very few of the reviewed studies discuss the acceptability and suitability of the interventions, particularly from the perspectives of the participants. The medical research council (MRC) suggest that these issues are particularly important during the development of complex healthcare interventions (MRC, 2008). Drossman et al. (2003) have produced a study flow diagram which does provide some data regarding acceptability and suitability of the treatment conditions used in their study.

For example, participants who did not complete their allocated trial condition provided information regarding their satisfaction with the treatment or other reasons for not completing the intervention. The flow diagram suggests that 3 of the patients receiving CBT were not satisfied or comfortable with the treatment versus 2 for the education intervention, 8 within the antidepressant condition and 3 within the placebo condition. Such data might suggest that antidepressants are less acceptable or tolerated by patients than CBT. These data also help explain levels of attrition during the conduct of the study. The most obvious shortfall of these studies is that not one of the studies report the collection of qualitative data from their participants, which may have helped explore issues regarding the acceptability and suitability of treatment. Such issues therefore require further investigation within future studies.

3.2.4 Quality of evidence and critical discussion

The studies included within the review consist mainly of simple RCT designs, with the exception of three studies reporting crossover RCT methods (Blanchard et al., 2007 , Andersson et al., 2011 , Sanders et al., 2007). The included RCTs differ in number of comparator conditions and several of the studies reported the use of more than one intervention or treatment condition resulting in complex studies (Blanchard et al., 2007 , Boyce et al., 2003 , Craske et al., 2011 , Drossman et al., 2003 ,

Lackner et al., 2008 , Payne and Blanchard, 1995 , Vollmer and Blanchard, 1998).

A potential threat to the validity of some of the experiments included within this review is that participants who are allocated to the control conditions of the experiments may not receive the intervention at any time during their participation in the research. Indeed, there is some evidence to suggest that this may result in dissatisfaction for participants within the control condition of a trial, a phenomena referred to by methodologists as form of 'resentful demoralisation' (Campbell et al., 2002a). Participants who demonstrate these characteristics may resentfully reflect their discontent during the completion of follow up questionnaires by ensuring responses reflect a poor outcome. This has the potential to elevate the observed treatment effect within some studies.

In this regard, the crossover trial design conducted by Blanchard et al. (2007) may have distinct advantages over the research conducted by other authors as both groups receive the intervention during the research. For example, I note that some of the studies prefer to utilise WLC conditions which may alleviate these problems (Sanders et al., 2007 , Payne and Blanchard, 1995 , Lackner et al., 2008). In this instance, all participants enrolled into a trial receive the intervention following randomisation, or it is delayed until the end of their participation in the research.

The National Institute for Health and Clinical Excellence (NICE) have recognised that many trials which report the evaluation of CBT for the treatment of IBS fail to measure if any desirable effect is maintained upon the withdrawal of treatment (NICE., 2008). Following a review of the RCT's, it would be prudent to suggest that many of the trials appear relatively short in duration producing less than twelve months of follow up data, with exception of the study carried out by (Andersson et al., 2011). Andersson and colleagues (2011) follow up their participants for a period of 18 months.

One of the most striking aspects of the studies reviews is that only two of the trials report economic evaluations (Andersson et al., 2011 , Kennedy et al., 2005). Just one of the trials reviewed reports on the analysis of service utilisation data (Drossman et al., 2003). These factors appear to limit the ability of the current evidence base to demonstrate the economic impact that the various interventions evaluated during the conduct of these trials have upon healthcare and societal expenditure.

Furthermore, the aforementioned study carried out by Kennedy et al. (2005), was unable to support the long term cost-effectiveness of CBT for treating patients with IBS when delivered by primary care nurses trained in the use of CBT techniques combined with Mebeverine (an anti-spasmodic medication frequently prescribed for the treatment of IBS symptoms). With this being only one of two economic evaluations, it is likely that such findings may deter healthcare establishments from investing in these treatments. The way in which therapy was delivered in this trial may have had an impact upon the costs evaluated during the trial, particularly the length of the treatment sessions (six 50 minute sessions). More about this will be discussed within the intervention delivery sections to follow.

The mean PEDro score for trials was 5 (ranging between 2 and 7) with Mahvi-Shirazi et al. (2008) achieving only 2 points out of a possible 10 for the appraisal of quality. Authors suggest that studies scoring between 9 and 10 on PEDro should be considered methodologically *excellent* quality, whilst scores ranging from 6 to 8 and 4 or 5 are considered *good* and *fair* respectively (Foley et al., 2003). Those studies scoring below 4 should be considered *poor* quality. Based upon these observations, the quality of the included studies would appear to range from good to poor, with no studies achieving excellent quality PEDro ratings.

It is not uncommon for authors to fail to report key methodological information (Glasziou et al., 2008). This makes, to some extent the critical review and appraisal of poorly reported trials difficult. The Consolidated Standards of Reporting Trials (CONSORT) was developed to

address many of these issues by providing a framework for the accurate reporting of clinical trials (CONSORT, 2012). The majority of the studies reviewed here fail to clearly report adequate randomisation methods with the exception of three, in which details were evident relating to randomisation procedures including methods of concealment (Boyce et al., 2003 , Gaylord et al., 2011 , Drossman et al., 2003). Bogalo and Moss-Morris (2006) initially appear to report on data gathered during an RCT, but fail to report details relating to a control condition within their study.

Various reporting guidelines such as the CONSORT checklist (see Appendix 8.3) recommend that trials should clearly report the flow of participants during a clinical trial and propose the use of a flow diagram detailing numbers of participants and trial processes. Authors who do not adopt such strategies when reporting research often produce evidence which is difficult to interpret, particularly considering the complexity of some of the experimental evaluations reviewed.

For example, Mahvi-Shirazi et al. (2008) fail to report information which makes clear the assignments of participants over the groups within their study. This makes interpretation of levels of attrition, and the identification of factors which may cause bias during the conduct of their study and participant flow difficult to understand. An example of clear reporting, consistent with the reporting guidelines can be found with the reports published by Ljótsson et al. (2011) and Boyce et al. (2003).

An ideal example of reporting quality can be seen in the flow chart within the original report of the work carried out by Drossman et al. (2003) who provide a detailed flow chart of participant flow through their study including details relating to participant attrition. In relation to basic methodological information, many of the studies presented in table.3 do not clearly report details such as randomisation methods, methods of concealment or blinding. Many of the studies also fail to report sufficient details regarding the interventions used.

Among the 20 RCT's reviewed, the majority report positive effects when CBT is used for the treatment of IBS on a variety outcomes (Andersson et al., 2011 , Blanchard et al., 2007 , Bogalo and Moss-Morris, 2006 , Craske et al., 2011 , Drossman et al., 2003 , Gaylord et al., 2011 , Heymann-Mönnikes et al., 2000 , Hunt et al., 2009 , Kennedy et al., 2005 , Lackner et al., 2008 , Ljotsson et al., 2010 , Ljótsson et al., 2011 , Mahvi-Shirazi et al., 2008 , Moss-Morris et al., 2010 , Oerlemans et al., 2011 , Payne and Blanchard, 1995 , Sanders et al., 2007 , Vollmer and Blanchard, 1998). There were in fact two of the reviewed studies which did not yield positive results on the primary outcomes of interest (Tkachuk et al., 2003 , Boyce et al., 2003).

Settings in which interventions take place during clinical trials are important for a number of reasons. For example, authors have suggested that during a clinical trial, interventions may become enhanced or atypical of their intended use (Stiller, 1992), which may partially relate to the environmental context or setting. As deomonstrated within the previous chapter, CBT is a versatile and adaptable intervention which can be applied to a variety of clinical pathology across a range of settings (Meichenbaum, 1985; D'Zurilla and Nezu, 2007; Hayes et al., 2006; Dimeff and Koerner, 2007).

Within this review, studies have taken place within a variety of locations and only one of the reviewed studies were carried out in the UK (Kennedy at al. 2005). The rainder were carried out in the USA (9), Sweden (3), The Netherlands (1), Iran (1), New Zealand (2), Australia (1), Germany (1) and Canada (1). Kennedy's study took place within primary care settings in the UK and recruited participants from primary care practices. The majority of studies obtained samples from media campaigns such as the methods emplyed by Craske et al. (2013).

3.2.5 Conclusion

The reviewed literature yields some promising results which support the use of CBT as an effective treatment for patients with IBS. In particular, CBT appears to be useful for improving coping, reducing levels of pain and improving quality of life. Within the reviewed studies, there is an emphasis on using CBT as a method for helping patients to cope with the symptoms of IBS and the interaction and impact IBS may have upon quality of life. The methodological quality of many of the studies to be suboptimal and the evidence base should be interpreted with caution (Zijdenbos et al., 2009). Although such interventions are thought to be effective, the availability of skilled therapists experienced in the management of IBS greatly limits the applicability of CBT interventions (Ford et al., 2014). Many of the trials do not represent UK populations with only one of the studies being conducted in the UK. Many other studies have small sample sizes, low statistical power and are inconsistent in the methods used to report their findings.

Although CBT may help patients manage their symptoms and cope with the impact of a persistent and debilitating condition, the administration of CBT is costly and it is widely acknowledged by other researchers that therapists offering IBS speciality clinics are rare (Lackner, 2010). It is perhaps for these reasons that many healthcare establishments choose not to fund psychological interventions for IBS patients. This is particularly important in relation to the review of these experimental evaluations as the majority of studies have used psychologists or therapists with advanced training to deliver their interventions. Within the UK, such health professionals are difficult to access and are not routinely found within clinical settings, particularly within gastroenterology.

There is encouraging activity within the wider UK healthcare system to suggest that the government and policymakers are beginning to recognise the impact that psychological therapies such as CBT have on improving health and reducing loss of productivity (Clark, 2011). In

2006, the NHS launched the improving access to psychological therapies (IAPT) programme (IAPT, 2013). From 2011, the programme broadened its objectives in response to the departments of health's (DOH) paper entitled *'talking therapies: a four year plan of action'* (DOH, 2011a). The paper was developed alongside the governments *'no health without mental health'* paper which set out the government's commitment to improving mental health for people of all ages (DOH, 2011b). Within these papers, the government makes a commitment to improving models of care and levels of access for people with long-term physical conditions and MUS.

Only one study evaluated the delivery of a nurse delivered intervention (Kennedy et al., 2005). The study by Kennedy and colleagues is also the only study carried out with a sample within the UK. There is also a lack of studies which invest in meaningful PPI and which include qualitative or MMR approaches. The incorporation of these methods may create a richer understanding of the use of CBT for treating patients with IBS and improve our understanding of the patient experience, particularly regarding important issues such as treatment acceptability and suitability as advocated by the MRC (2008).

IBS is a complex disease process which is significantly affected by stress and underlying psychological co-morbidity. The disease process is further complicated with high levels of sexual and emotional abuse, the patient's interaction and interpretation of their symptoms and the impact that symptoms have on quality of life. Within this review, encouraging evidence has been appraised which suggests that CBT may be useful for improving the outcomes of patients with IBS. However, there are issues regarding not only the methodological quality of current studies, but most importantly a lack of studies which evaluate practical and implementable psychological interventions within the UK healthcare system. As a result of this review, it is therefore recommended that future research evaluating the use of CBT for treating IBS should address the following concerns summarised in 3.2.6.

3.2.6 Opportunities for further research

Following a review of the literature, future research should;

- Evaluate a new generation of interventions which should aim to address concerns regarding access to treatment, particularly within the UK healthcare system

- Evaluate interventions which are more likely to be implemented within the UK healthcare system

- Incorporate meaningful PPI in order to improve the methodological quality of studies, reduce participant attrition and maximise the suitability and acceptability of CBT interventions

- Consider the incorporation of mixed methods or qualitative research approaches in order to gain a richer understanding regarding the treatment of IBS with CBT which should particularly focus on issues regarding treatment acceptability, suitability and the experience of service users as advocated by the MRC

- Consider the economic impact of CBT interventions used in the treatment of IBS

- Utilise rigorous methods which should be reported in accordance with current reporting standards and guidelines

Chapter 4 ▪ Methods

4.1 Feasibility study design

Within the following sections, details of the methods used for the conduct of a feasibility study designed to address the aims and objectives described within 4.1.1 are reported. Much can be learned from the literature review reported in chapter 3, which largely underpins the direction and design of the investigation designed and reported within the following two chapters.

As demonstrated in chapter 3, few studies have evaluated methods which address concerns regarding access to evidence based CBT interventions within the UK healthcare context. The current evidence base also lacks a richer understanding of phenomena in terms of treatment acceptability, suitability and the experience of service users. In response to these concerns, the feasibility study described here was concerned with both the feasibility of the interventions themselves when implemented within a local context and also the development of the methods used to evaluate the interventions in clinical practice. The study was therefore formulated in accordance with the MRC guidelines for the evaluation of complex interventions (MRC, 2008).

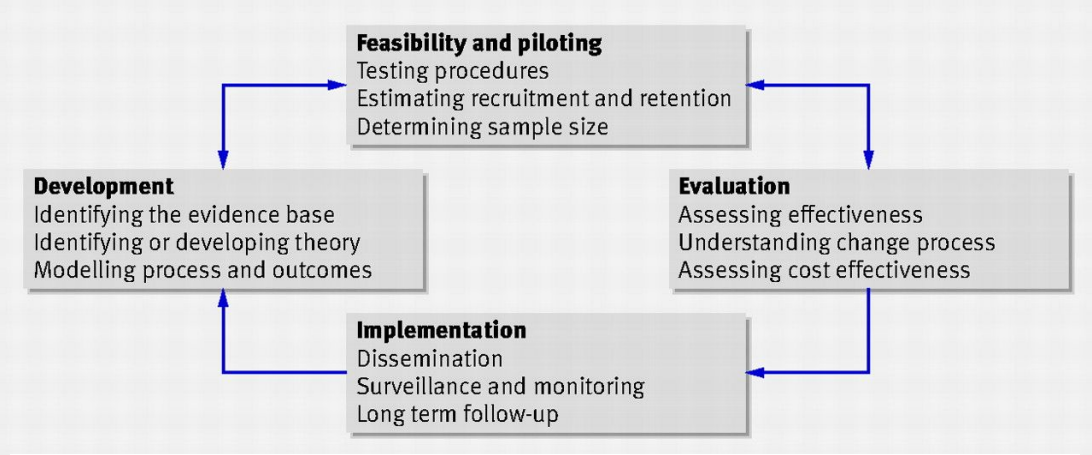


Figure 5

MRC Guidelines for the evaluation of complex interventions (2008)

The guidelines published by the MRC (2008) suggest the four domains of intervention development demonstrated in figure 5 above. This study was concerned with '*feasibility and piloting'*. Modelling and intervention theory is based upon work already carried out within the CBT treatment of IBS, details of which are critically discussed later within 4.3.3.

As identified within the extensive review of the literature in chapter 3, there is a need to adapt and evaluate intervention studies, make judgments about the feasibility of interventions and determine whether comprehensive and multilevel evaluations are justified (Bowen et al., 2009). According to Bowen and colleagues (2009), feasibility studies are concerned with issues such as acceptability; enquiries regarding the demand for the intervention, phenomena surrounding implementation, practicality, adaptability, integration, expansion and in some cases limited efficacy testing. In order to ensure that robust methods were utilised which could be further evaluated and developed for use within a full scale trial, one will observe that the methods are set out within the following sections accompanied by a detailed rationale regarding the methods used.

The principle objective of this study was concerned with the feasibility of the study intervention in terms of acceptability and suitability and the research methods proposed, particularly in relation to the recruitment methods considering difficulties encountered during earlier studies (Dainty at al 2014). The published literature offers little in the way of guidance for the design and evaluation of feasibility studies. Indeed, Hoddinott (2015) refer to such studies as the "*black box*" or "*Cinderella*" of complex intervention trials, as although decision making, process and early intervention development were once seldom reported, editors now express an active interest in publishing such studies (Hoddinott, 2015).

Bowen et al. (2009) suggest that performing a feasibility study is necessary when few studies exist relating to a specific intervention or

technique, or when previous interventions have utilised similar methods but improved versions may be beneficial. Certain aspects of feasibility work such as issues pertaining to '*acceptability*' may be approached with the use of qualitative methods (Bowen et al. 2009), which are also valuable for helping researchers understand institutional and community cultures (NIH, 2001) and when considering the personal perspective to the use of the proposed interventions (Tickle-Degnen, 2013). It's for these reasons that the study reported here was based upon a MMR design which is presented within the following sections (see philosophical and methodological issues for MMR discussion 4.1.2). For more information relating to the integration of qualitative methods and qualitative rigour in particular, please see 4.6.2.

Feasibility relates to assessing the potential for successful implementation of an interventional study and to reduce threats to validity at an early stage (Tickle-Degnen, 2013). As advocated by Tickle-Degnen (2013), the study detailed here will therefore focus upon describing information and generating evidence relating to implementation which will be represented with descriptive statistics and the relevant qualitative data collection and analysis. Such data derived from feasibility trials can also be used to inform sample size power calculations, and estimate recruitment and retention rates when designing future trials (MRC, 2015). Enhancement of validity and intervention development was therefore of particular interest during this study, whereas hypothesis testing and cause and effect will remain the concern of a future RCT (Shanyinde et al., 2011). Feasibility studies of this kind also have the potential to ensure that public funding not wasted on an expensive future trials, which may result from problems with recruitment, the retention of participants or difficulties in the delivery of the intervention (Ioannidis et al. 2014).

The RCT is one of the most powerful tools used in research to establish new knowledge claims (Jadad, 1998 , Anderson et al., 1993 , Muir-Gray, 1997 , Haynes et al., 1997 , Walwyn and Wessely, 2005). Within a fully powered trial, an RCT would enable to study of the cause and effect relationship between CBT and patient outcomes. Campbell et al. (2002b) use a system of notation to clearly describe trial designs. An RCT was proposed, as described in the diagram below, with (R) representing randomisation, (O) observations, (X_A) nurse delivered, low-intensity CBT (LI-CBT), (X_B) psychotherapist delivered CBT, (X_C) SH work books and (X_D), a TAU control condition.

O	**R**	**X_A**	**O**	**O**
O	**R**	**X_B**	**O**	**O**
O	**R**	**X_C**	**O**	**O**
O	**R**	**X_D**	**O**	**O**

Baseline data was collected from all participants for comparison to post intervention observations (Bolig et al., 2002). Post intervention observations were collected on completion of the intervention periods at three and six months. The literature suggests a much longer period of follow up was necessary (Zijdenbos et al., 2009), however longer follow up periods were not within the scope of the PhD project and such timescales did not allow time for the delivery of an intervention to the control group on completion of the study. A much longer follow up period would therefore need to be carefully considered during a full scale follow-on trial and is a significant limitation of this work.

4.1.1 Aims and objectives

Aim

To carry out a feasibility study to explore the use of low-intensity CBT treatment methods for patients with IBS within a single centre, secondary care NHS gastrointestinal clinic

Objectives

- To develop a brief, nurse-delivered CBT intervention for patients with IBS underpinned by established theory and models of IBS
- To examine the number of patients approached and screened in relation to the numbers successfully randomised into the study
- To gather reasons for patients not wishing to take part in CBT treatment approaches for their IBS
- To explore the experience of participants undergoing the study's treatment conditions
- To identify barriers and facilitators to the implementation of the trial interventions
- To measure the follow-up and response rates to study questionnaires
- To describe the range of data with relevant descriptive statistics and obtain measures of mean and variance which may be used for the power requirements of a future trial
- To identify unforeseen factors which may impact upon the conduct and quality of a follow-on study

The research objectives are further defined, with justifications for how decisions were made, using the PICO framework (Huang et al., 2006) within the following sections.

4.1.2 Philosophical and methodological issues

The majority of knowledge which has shaped how IBS is treated has been derived from RCT's based upon quantitative data, statistical analyses and the quest to identify causal effects (positivist paradigms). There are certain characteristics of IBS which may be poorly understood with the use of a positivist philosophy, particularly where aspects of the phenomena are socially constructed. A social constructionist would suggest phenomena are made up of factors independent of conscious beings, so not physiological, but influenced by context and personal experience, which as a result determines the social structure of reality (Burr, 1995). Alfred Shutz (1899-1959) suggests that scientific laws and statistical formulations are simply a shorthand method for the interpretation of society, paying little attention to the presuppositions of the individual or the 'social actor' (Barber, 2011).

Atkinson (2005) suggests that it is important to avoid reductionist views which treat one type of data or a single approach to data analysis as being the only possible source of new social and cultural knowledge. It is for reasons such as these that this research is underpinned by a pragmatic philosophy which is not concerned with epistemologies and their incommensurability (Greene, 2007). Pragmatism is concerned with solving problems that exist in the real world (Feilzer, 2009). Using the pragmatic approach, researchers are not forced to ''*be the prisoner of a particular method or technique*'' (Robson, 1993, p.291). Most importantly, pragmatism focuses on outcomes which gives the researcher methodological freedom of choice (Creswell, 2007). This enables the researcher, most importantly to focus on the relevant questions and subsequent application of the most appropriate methods to enhance knowledge.

Through approaches such as these, research is able to move away from ideologies which separate mind and body, by acknowledging the mind and body as a complete system (Drossman, 2006). Pragmatism also encompasses socially produced knowledge and embraces pluralist methodology (Scott and Briggs, 2009). These so called 'mixed methods' approaches that are better suited to understanding complex phenomena, by providing a solution to reductionist approaches which rely only on single sources by which to derive data (Atkinson, 2005).

Indeed, positivist methods are not without limitations and some critics would suggest that RCT methods struggle to capture the true value of interventions as applied within real clinical settings (Black, 1996). Concerns have also highlighted the limited ability of an RCT to assess a limited number of variables during any one experiment (Amstutz et al., 1994 , Shean, 2014) and the methods applicability to answer innovative research questions (Sanson-Fisher et al., 2007).

Interventions may also become enhanced and atypical of their intended use in clinical environments (Stiller, 1992) and may have little resemblance to real life settings (Hunt, 2012). These issues are particularly relevant to behavioural change interventions such as those described here, due to the RCTs inability to consider the context of interventions (Tarquinio et al., 2015). Authors have suggested that parallel qualitative research might be the ideal solution to understanding the use of interventions in the real world (Bhaskar, 1989). It was hypothesised that the collection of qualitative data during the trial would also help identify barriers to the implementation of CBT interventions within clinical practice (Lancaster et al., 2010 , Bradley et al., 1999).

A MMR approach, underpinned by a pragmatic philosophy, was therefore used to draw from the strengths of both qualitative and quantitative approaches (Johnson and Onwuegbuzie, 2004). MMR is defined as "*collecting, analysing and mixing both quantitative and qualitative data in a single study or series of studies"* (Creswell and Plano-Clark, 2007a,

p.6). The study was designed to robustly address the concerns of combining research methods, as critics of the MMR approach often present the notion of an 'incompatibility thesis', suggesting that MMR violates the epistemological and ontological foundations of research paradigms (Johnson and Onwuegbuzie, 2004).

The growing popularity of MMR approaches would suggest that many researchers recognise the value of the pragmatic approach (Scott and Briggs, 2009). MMR provides robust and rigorous approaches to research (Anaf and Sheppard, 2007) and creates a richer understanding of phenomena (Creswell and Plano-Clark, 2007b). The incorporation of qualitative methods within the RCT ensured that the research was able to consider social experiences and meaning (Denzin and Lincoln, 2000). This ensured the post-intervention interviews would capture the experience of individuals undergoing CBT treatment within their personal circumstances and social contexts. These methods also helped to contextualise the findings of the research (Pluye et al., 2009), and enabled trial participants to provide information regarding their responses to quantitative variables (Wagner et al., 2012).

These methods also underpinned an evaluation of the experiences of participants who received the psychological interventions in order to explore whether they were relevant and tailored to the needs of service users. The qualitative methods were therefore concerned with exploring issues regarding treatment acceptability, suitability and the experience of participants who received the trial interventions as suggested by the MRC (2008). Please see 4.6.2 for more details regarding how these qualitative methods were integrated into the study design.

A particular issue for this project was the differences in sample sizes between qualitative and quantitative research (Bazeley, 2004). Some authors have suggested that the explicit use of an overarching method is a solution to many of the MMR issues which also helps to clarify the position adopted by the researcher (Anaf and Sheppard, 2007). The

primary objective of a full scale study would be concerned with evaluating the efficacy of a nurse delivered model of CBT as a treatment option for patients with IBS. The RCT was therefore the overarching method of enquiry which was used to determine the sample size for this study, and was enhanced and supported by qualitative methods of enquiry. The overall design for this study was therefore a feasibility four armed RCT with concurrent qualitative interviews with intervention participants.

4.1.3 Participant recruitment, sampling and sample size

The ideal participant selection method for this study would have been to select participants at random from the population of IBS patients nationally. However, the entire population of IBS patients remains unknown as many people who potentially have IBS may choose not to consult with a physician (Bourgault et al., 2008). Moreover, confidentiality and the protection of health service data restrict the access researchers have to potential participants who choose to consult with a physician, particularly where patients are cared for in centres outside the researcher's area of clinical practice. This results in many health service research projects employing convenience sampling approaches (Kam et al., 2007). This study was concerned with the treatment of patients with IBS attending secondary care gastrointestinal clinics within a large NHS University Hospital Trust.

It is possible that patients might also have been recruited from primary care to take part in the study. However, as this study received no funding, all interventions used during the conduct of the study were required not to generate excess treatment costs (i.e. not result in cost incurred to the hospital Trust as a result of research taking place in the organisation). Thus, patients would not routinely be referred to the department of psychological medicine from primary care and for patients to be eligible for high intensity CBT (HI-CBT) treatment via this mechanism; patients were required to be registered within the hospital system. It was therefore not possible to recruit IBS patients from primary care for this study. Furthermore, primary care patients were not targeted

during this study in view that such patients are not resulting in secondary care repeat attendance, resource use and associated costs.

Eligible clinic patients were identified by a member of their care team and given participant information sheets in the form of a 'recruitment pack'. This method overcame barriers which prohibit research staff having access to confidential patient information, as reviewing bodies may insist that patients are first approached by a member of their own care team (Dicker and Kent, 1990). The recruitment packs contained an invitation to take part in the research, an information sheet and the contact details of the research team along with a prepaid postage envelope and reply slip (please see appendix 8.4). Ethical approval (see appendix 8.5) was also sought to enable the gastrointestinal outpatient team to write to potentially eligible patients with details regarding the study. Posters were also deployed on clinic notice boards and via hospital media (internet).

Sampling and sample size

This study was concerned only with generating descriptive statistics in the form of measures of mean and variance. Such measures may facilitate the accurate power calculation for a full scale (inferential) trial (Lancaster et al., 2002). Authors suggest that 12 participants per group should be sufficient for calculating the mean and variance which can be used to determine full scale trial sample sizes (Julious, 2005). There is however no consensus on the sample size which should be recruited to feasibility studies.

Within chapter 3, it was evident that previous trials utilising similar interventions in primary care settings suffered significant rates of attrition of over 30% (Kennedy et al., 2005). The sample size of the study was further influenced by the limitations of the study being conducted by a sole researcher during a full time period of PhD study and the limitations of a psychotherapist who agreed to deliver the intervention on a voluntary basis. The psychotherapist had the capacity to treat 15 participants during the study data collection period.

Furthermore, the study was concerned primarily with an evaluation of the study interventions and their feasibility, the use of the study methods and processes and aspects pertaining to the acceptability and suitability of the proposed interventions. A pragmatic decision was therefore made to aim to randomise 60 participants to the treatment conditions (or around 15 participants to each arm of the trial).

4.1.4 Study flow chart

The following diagram (figure 6), summarises the design of the feasibility study including the implementation of qualitative interviews which were collected concurrently during the conduct of the study.

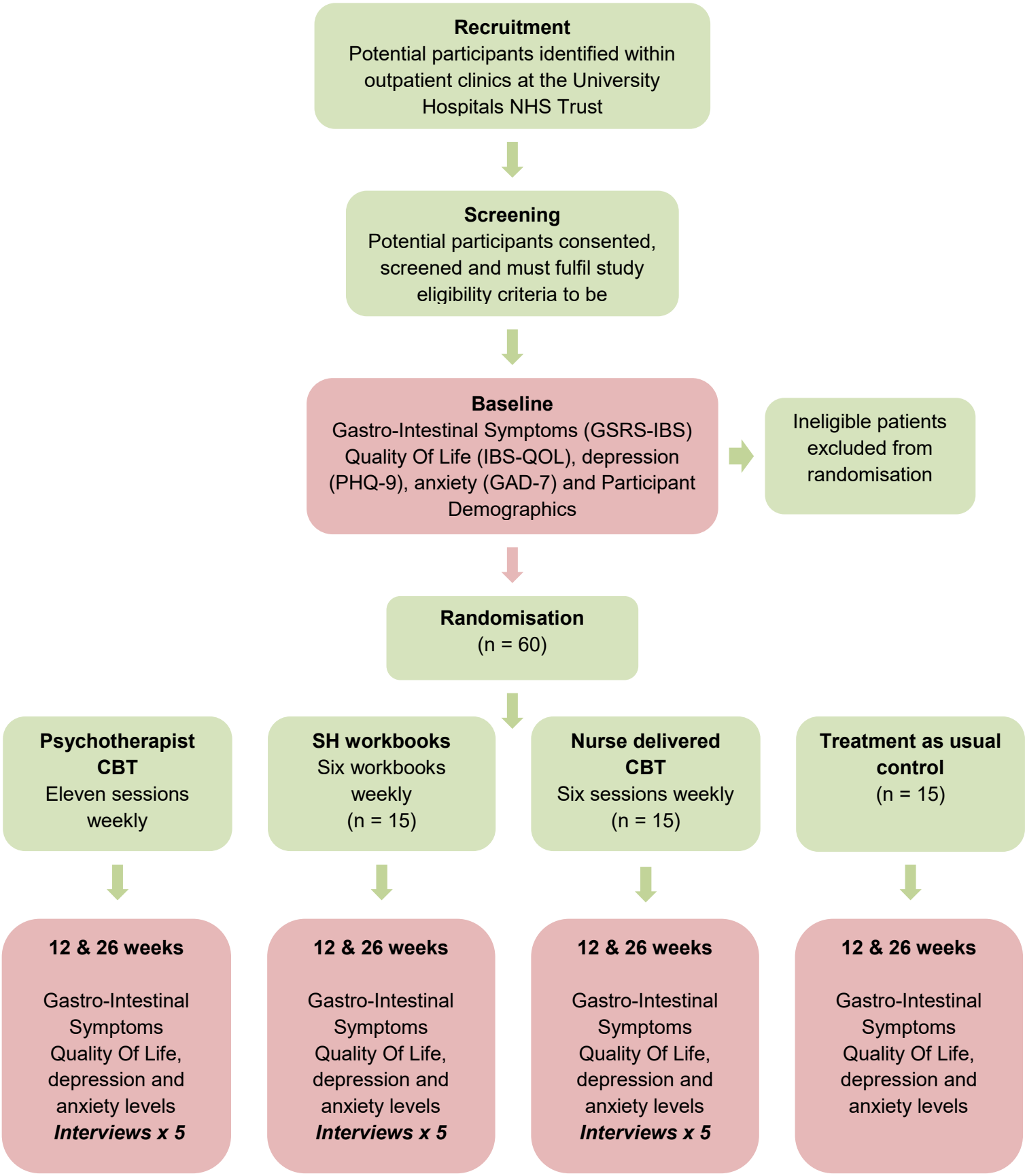


Figure 6: Study Flow Diagram

4.2 Participants

IBS is one of the most frequent gastrointestinal conditions diagnosed and is thought to be responsible for around 40% of gastrointestinal related consultations (Wells et al., 1997). Around 60% of patients referred to gastrointestinal clinics with lower gastrointestinal symptoms are likely to be diagnosed with IBS (Spiller et al., 2007). It is thought that 20% of IBS patients managed within general practice surgeries in the UK are referred to a gastroenterologist and around 9% to a surgeon (Thompson et al., 2000). The local University Hospital secondary care clinics received approximately 6363 gastrointestinal referrals according to a 2011 audit which should have provided a rich source of potential participants for the study. Participants were therefore recruited from gastrointestinal clinics via the following mechanisms.

1. Direct referral to the study team following a secondary care diagnoses of IBS should the patient have wished to find out more about the research study

2. Self-referral from patients attending the clinics via direct advertisement within the clinical areas

3. Advertisement of the study via webpages or hospital media

Adults were chosen as the main group of patients for inclusion as IBS is associated with the third and fourth decades of life (Kumano et al., 2004). Participants were therefore required to be over the age of 18 years upon enrolment into the study.

In order to ensure that participants had symptoms consistent with an evidence based definition of IBS, participants were also screened and must have met Rome III criteria (Drossman, 2006). This tool has been developed by the Rome Foundation with a long-standing history of

development and a strong evidence base (The Rome Foundation, 2016). It has been used successfully as a confirmation tool using symptomatic criteria for IBS in a number of RCT's (Ljótsson et al., 2011 , Craske et al., 2011 , Blanchard et al., 2007 , Gaylord et al., 2011), and is being constantly updated and reviewed in light of changes in the recent literature (Drossman, 2006). Participants with symptoms inconsistent with IBS on Rome III criteria were excluded from the study.

Patients with signs or symptoms of organic disease (rectal bleeding, changes in inflammatory biomarkers), coeliac disease, gastric ulceration, current gastrointestinal infection or alcohol abuse were also excluded, as these conditions had the potential to be confounding factors (see inclusion and exclusion criteria below).

4.2.1 Inclusion criteria

- Adult male and female patients aged 18 years or older at the time of enrolment.
- Documented medical diagnosis of IBS
- Patients with IBS which meets Rome III criteria
- Able to read, write and speak English
- Able to provide written informed consent
- Patients with and without concomitant antidepressant use
- Able to commit to weekly treatment sessions within the intervention arms of the study

4.2.2 Exclusion criteria

- Already receiving psychological therapy or hypnotherapy
- Existing diagnosis of bowel disease based on endoscopic or histological criteria (i.e., Crohn's disease, ulcerative colitis, coeliac disease)
- Presence or history of structural or surgical diseases of the GI tract (not including appendix or gall bladder surgery)
- Evidence of alcohol or substance misuse
- An established cause for bowel symptoms other than IBS (i.e., medication use)

- The presence of current suicidal ideation or self-harm
- Significant psychiatric comorbidity (schizophrenia, bipolar disorder, obsessive compulsive disorder)
- Currently taking part in other research studies

4.3 Intervention

4.3.1 Rationale

The literature review reported in chapter 3 identified the need for research to evaluate a new generation of psychological therapies which address concerns relating to accessibility and relevance to the UK healthcare system. This study was based within a large acute university hospital within a busy gastrointestinal directorate. The gastrointestinal services received over 6000 new referrals in 2011, so it seemed more than feasible to develop the trial intervention based within secondary care. Indeed, CBT has been effective when delivered by nurses within primary care settings (Kennedy et al., 2005). It was therefore possible that similar effects might be achieved if therapy were to be delivered by gastrointestinal nurse within secondary care. Most importantly, the secondary care population is thought to have a higher burden of psychiatric co-morbidity than in the community. In particular, IBS patients within secondary care are thought to have a higher degree of anxiety, reduced physical functioning and may also experience problems with food (Ringström et al., 2007).

Furthermore, the majority of IBS treatment costs in the UK are accounted for by direct healthcare costs which include hospital stay, higher prescription utilisation and increased use of outpatient services (Akehurst et al., 2002). The recruitment methods were therefore aimed at recruiting individuals within secondary care which may have a greater impact on IBS and associated healthcare utilisation and cost. Additionally a lower intensity treatment approach than those employed by other researchers may have been comparable in terms of effectiveness, but more cost effective than higher intensity treatment approaches.

4.3.2 Intervention initial development and outline

It would not have been possible to develop an effective CBT intervention without consulting researchers who already had extensive expertise within this area of research, and thus an alliance was formed with a researcher who has an international reputation and vast experience of developing the CBT treatment of IBS.

A protocol for this study was developed in collaboration with Dr Melissa Hunt, a clinical psychologist based at the University of Pennsylvania, Philadelphia, USA. Dr Hunt had previously developed 'brief' CBT interventions for patients with IBS. In particular, Hunt et al. (2009) developed a brief internet CBT treatment protocol which was successfully trialled and found to be effective in the USA. It was hoped that by collaborating with Dr Hunt, an effective intervention could be further developed and tailored to the needs of patients within the NHS secondary care settings and established expertise could be utilised to ensure the quality of the intervention was achieved.

Various delivery mechanisms were considered during the development of the intervention and the literature regarding the delivery mechanisms of CBT were consulted. Most importantly, during the critical review of the literature reported in chapter 3, it was noted that the majority of the CBT interventions evaluated within previous studies had been delivered by, or required the direct involvement of a psychologist, examples of which include the work of Blanchard et al. (2007), Boyce et al. (2003), Drossman et al. (2003) and Lackner et al. (2008). Some of the studies interventions were also delivered by cognitive behavioural therapists (Andersson et al., 2011 , Bogalo and Moss-Morris, 2006 , Payne and Blanchard, 1995 , Tkachuk et al., 2003 , Vollmer and Blanchard, 1998) or via the internet (Andersson et al., 2011 , Hunt et al., 2009 , Ljotsson et al., 2010 , Ljótsson et al., 2011). At least three studies utilised self-directed methods of treatment administration, namely the treatment manuals reported by Bogalo and Moss-Morris (2006), Moss-Morris et al. (2010) and Sanders et al. (2007). Only one study chose to deliver their

intervention via nurses trained in the use of CBT (Kennedy et al., 2005), although the study was based within primary care.

The group based treatments identified during the review are indeed a viable alternative to individual therapy sessions (Blanchard et al., 2007 , Gaylord et al., 2011 , Tkachuk et al., 2003 , Vollmer and Blanchard, 1998). It is thought however, that one of the advantages of individual contact is that therapy can be tailored to the needs of individual (Toner et al., 2000). Interestingly, the study reported by Vollmer and Blanchard (1998) showed no significant differences in outcomes between group and individually delivered programs of CBT (Vollmer and Blanchard, 1998). Conversely, a recent study found that 95% of patients would choose individual CBT over group therapy when accessing CBT for the treatment of panic disorder (Sharp et al., 2004).

Whilst some of these novel interventions provide alternative methods of intervention delivery such as internet therapy, they are not without disadvantages. For example, internet interventions often do not function on a stand-alone basis, often requiring the input of a therapist or psychologist in order to facilitate therapy and guide the participant through a course of therapy (Ljotsson et al., 2010 , Ljótsson et al., 2011). This is evident within the work of Moss Morris et al. (2010), whereby feedback and support was provided during a brief face to face support session. Furthermore, when these issues are controlled for, researchers using internet delivered interventions to treat depression suggest that stand-alone interventions appeared to yield fewer benefits than those with therapist support (Titov, 2011). Significant concerns have also been raised regarding potential issues with online patient confidentiality, a loss of visual and auditory clues during a face-to-face interaction, difficulty managing crisis situations and unclear legal and ethical issues (Childress, 1998). Internet delivered CBT has also been shown to be unacceptable to over 40% of surveyed patients (Mohr et al., 2010).

Nurses working within secondary care gastroenterology departments fulfil a variety of important roles caring for patients with a wide range of gastrointestinal related disorders. Gastroenterology nursing practice represents a multi-disciplinary specialism whereby nurses provide essential support for patients with distressing symptoms, chronic conditions or support those requiring invasive procedures (Smith and Watson, 2005).

Nursing roles within gastroenterology are expanding and nurses are now fulfilling activities and roles which were once thought to fall within the domain of medical care. For example, nurses work autonomously within a variety of gastrointestinal specialities such as oesophageal cancer, stoma care, endoscopy nursing, inflammatory bowel disease nursing and roles relating to IBS (Norton and Kamm, 2002). Norton and Kamm (2002) suggest that many of the patients seen within gastroenterology and other specialists have functional conditions which may be associated with psychosocial factors such as stress and depression. The authors suggest that the inability of doctors to satisfy these patients is demonstrated by the popularity of alternative therapies. Norton and Kamm (2002) conclude that nurse specialists placed somewhere between the two models of care, may be well suited to meet the complex needs of such patient's.

The intervention detailed here was therefore intended to represent a potential method of expansion to existing nursing roles within gastroenterology, either as part of an existing role or in the development of new future specialist roles. This expansion to the gastrointestinal nursing role may form the basis for a viable mechanism by which to improve access to evidence based CBT interventions and tackle the burden of complex FGID's such as IBS.

4.3.3 Patient involvement in intervention and study design

Service users, when given such opportunity are able to make a valuable contribution to the research process. Despite the suggestions that patient and public involvement (PPI) is often considered a tokenistic activity (Buckley, 2004; Ocloo and Mathews, 2016). It was hoped that the explicit involvement of patients and the public in both the design of the intervention and subsequent feasibility study would enhance quality and rigour. By integrating PPI during the conduct of this research, equilibrium has been achieved in order to address power imbalances between health professionals, researchers and patients (Oliver, 1995). PPI has also been shown to increase the likelihood of research being acknowledged and implemented into routine clinical practice (RCN, 2007). A Patient Advisory Group (PAG) consisting of five gastrointestinal patient volunteers was established, facilitated by a PPI manager within the gastrointestinal research unit within a large university teaching hospital in the East Midlands.

The PAG was established with the following objectives and benefits in mind in relation to intervention development.

- To ensure the intervention incorporated the views and perspectives of service users

- To improve the acceptability and suitability of the intervention through patient involvement in design and development

- To improve the overall quality of the materials used within the intervention and within the study

- To identify barriers to the implementation of the interventions or methods used during the feasibility study

The study co-ordinator and principle investigator for the study initially provided the PAG with an overview of the research project along with a rationale for the trial of the nursing intervention. The PAG reviewed study related documentation, preliminary design, intervention format and made a variety of recommendations. The following (table 7), is a summary of the main recommendations of the PAG along with the responses detailing the changes which were or could be implemented (where possible) to accommodate the views of the PAG.

Recommendations of the patient advisory group and researcher responses

PAG Recommendation	Action
Patients should be treated as a 'special case' which may maximise recruitment	Those involved in recruitment will ensure that patients are approached as an individual case of interest rather than a recipient of a recruitment campaign. As the study PI will be responsible for screening and randomising participants, the PI will ensure that all participants are treated as individuals with their own unique qualities which may be beneficial to the research.
How long will patients have been diagnosed with IBS? What sort of treatments would they have received until that point?	Rome III criteria will be used to ensure all patients meet diagnostic criteria for IBS which requires patients to have had IBS symptoms for more than three months with symptom onset at least six months prior to recruitment. Medications and treatments taken to date will be recorded during baseline data collection. A concomitant medicines form has therefore been devised.
Time commitment – how will the 12 hour treatment regime be prescribed by others?	Trial interventions will be protocolised in order to ensure that treatment is delivered consistently to participants. A sample of sessions will be monitored for compliance
Are they (the patients) ready to open up about their condition? Do they have pre-determined	It is hoped these phenomena will be captured during interviews with trial participants. These issues reinforce the need for the qualitative element of our study. We will ensure these important issues

views of success? **Does it appear like it is all in the mind?**	have been covered within the post intervention interview schedule
Some patients may be unable to see a link between their IBS and psycho-babble?	It is seen as vital that the researcher fully understands these issues and it is hoped these phenomena will be captured during interviews. All of the intervention arms of the study will begin by explaining the potential links between IBS and issues such as stressful life events
Maybe only patients who see a link (between IBS and psychology) will take part in the study and any success may result from a commitment to therapy?	There is already some evidence to suggest that some IBS patients may reject a psychological element to their illness. The researcher will ask patients who refuse to take part for their reasons for not taking part in the study although there are obvious ethical concerns regarding such approaches
What might patient's pre-conceived notions be about what they expect from therapy? Might they expect too much?	Patient expectations have been accommodated during the development of the interview schedule and are considered vital to help the researcher understand more about what the meaningful outcomes might be for patients with IBS undergoing psychological treatment. Participant information will therefore contain information regarding the importance of realistic expectations if participants are randomised to therapy (i.e. promote improved coping mechanisms and not a cure). It is hoped that pre-conceptions about treatment will be covered during the post-intervention interviews.

Might this study raise expectations about what the NHS can achieve within cost parameters?	The study will be conducted in a state of equipoise. By this, the research team mean that we are really not sure if our intervention will be effective. It is likely that the HI therapy will have some positive effects as seen within previous trials. However, it is unlikely that HI CBT will be adopted within gastrointestinal units due to cost and therapist shortages. It is hoped by conducting this research, a feasible alternative could be trialled in a much larger study. The larger study will hopefully provide researchers with information regarding costs
Could this study raise awareness and increase demand on CBT practitioners?	Unfortunately, there are currently no CBT treatments available for patients with IBS in the proposed format. It is possible that the study may increase demand for these kinds of therapies within the NHS, but the research is necessary to help researchers try to identify a practical and deliverable therapy format
Will patients from the four groups mix? May this lead to some people thinking that others are getting better treatment?	It is hoped that contact between participants will not occur. This would be considered a serious threat to the validity of our research as such issues can result in contamination of one group with parts of an intervention from another. It is assumed that contact between participants within this study will be minimal. However, the PI will ensure for example, that participants are not booked in at the same time for therapy which may result in these patients waiting together for treatment.
There seems to be a lot of form filling. Might this put some people off?	The researcher is very conscious of this problem and although data is essential for us to understand the use of these treatment approaches, we realise there is a balance to be sought between data and burden to participants. This will be carefully considered during all stages of study development and the burden data collection will be made as easy as possible with participant convenience in mind

There is a need for more background information, likely benefit and areas CBT might help	More information has been incorporated into the participant information sheet
Is15 per group enough to show any trends?	The study is not powered to detect significant differences between groups but may help to secure funding for a much larger multi-site study which will have groups large enough to detect significant trends
If IBS symptoms improve, will quality of life?	The study will collect data for both symptoms and quality of life to evaluate this during the study
Will the study detect changes in anxiety/depression?	The study will collect data which will help us understand levels of anxiety or depression
There is no mention of age range? Are these patients all adults?	This information has been incorporated into the participant information sheet

Younger age groups may be more reluctant to tell friends and family about their involvement in the psychological aspect of treatment	A limitation of this study is that we are unable to evaluate the use of CBT in children or people younger than 18 years old.
Hopefully the cost of CBT will outweigh the cost of medication and clinic visits	Indeed. It is hoped that a much larger study will factor in the measurement of costs

Table 7

The PAG met for a second time following the review and appraisal of the initial SH materials for IBS in order to evaluate whether the changes made were acceptable and to identify any further issues with the feasibility study methods or interventions. In order for the members of the PAG to become familiar with all aspects pertaining to the intervention, the PAG members were advised to work through the SH materials and provide any feedback which might be useful considering their intended use within secondary care NHS clinics. The following are the factors in addition to those previously raised by the PAG.

- The SH materials and documents were repetitive in places. This sometimes made the text appear patronising
- American idioms were present throughout the intervention SH text which was not felt to be acceptable within the British and local context
- There was too much text in the majority of the workbooks and it was recommended that text be further broken down into subheadings in order to be easier for the reader to digest

The use of American spelling and language was the aspect of the materials which faced heavy criticism from the PAG. The group felt that the materials in their current state were not fit for use with the intended audience. The workbooks therefore underwent further transformations, with these criticisms in mind through extensive work with the author. The author approved all further changes to the materials, which were then prepared for review by the research ethics committee (REC).

It is possible that the PAG could have provided further feedback during the SH material development. However, by the time the workbooks had been further refined in light of the groups review, the study was already well behind schedule and only a limited timeframe existed during the PhD studentship in order for the research to be conducted. It is intended that PPI will continue to feature within follow on studies, with a suitable timeframe allocated to PPI. It was hoped that interviewing patients upon completion of the SH and LI-CBT interventions would provide further information regarding the format and acceptability of the materials. I am grateful to the author, for her patience and extensive support

provided during the review and adaptation of the SH materials in collaboration with the PAG.

4.3.4 Theory underpinning intervention design and modelling

Within chapter 2, three of the biopsychosocial models which underpin a researcher's theoretical understanding of IBS were presented and in particular, the factors which contribute to the presentation and manifestation of the condition (see Drossman (2006), Levy et al. (2006) and Chey (2013). Amongst these models, authors suggest that FGID's such as IBS are the result of complex interactions between the biological, psychological and social aspects, hence the term 'biopsychosocial model'. The three models are revisited and summarised as follows.

Levy et al (2006)

Levy and colleagues describe a multifaceted disease process which is underpinned by early life experiences, social support and learning. These issues in turn shape illness beliefs and coping strategies which are also influenced to some degree by anxiety, depression and somatisation. Health beliefs, coping and psychological aspects elicit the symptoms of IBS through interactions with the central and enteric nervous systems. These interactions affect motility and result in the manifestation of symptoms, excess healthcare utilisation and a poorer quality of life. Genetic predisposition is thought by Levy and colleagues to play a role in some individuals.

Chey et al (2013)

Chey and colleagues describe the relationship between three main mechanisms of causation and interrelated factors (central nervous system functioning, microflora and gastrointestinal function). These factors are influenced by genetics, food, antibiotic use, gastrointestinal infection and the presence of stress. Resultant changes in gastrointestinal function and central nervous system involvement results in the manifestation of physiological symptoms.

Drossman (2006)

As with the model described by Levy and colleagues, Drossman (2006) describe a relationship between the enteric and central nervous system. Psychosocial factors which underpin these interactions are made up of one's early life

experiences, stress, psychological state, coping and social support. There is emphasis on an explicit *two-way* relationship between these factors and altered motility and sensation. The two-way relationship results in the complex process of FGID and resultant behaviour (physician visits, medication use, functioning and poor quality of life). The relationship between these variables suggests that IBS symptoms play a role in levels of stress and life experience (by feeding back into the model). Such phenomena are highly relevant to the forthcoming development of the CBT intervention which is primarily based upon Drossman and colleagues (2006) model.

These frameworks provide a useful underpinning theory by which to design interventions as recommended within the MRC complex interventions guidance (MRC, 2008). There is evidence which supports the theory of the nervous system interactions advocated by Drossman (2006), particularly in relation to the link of stress to the manifestation of physiological symptoms bought about by communication between the central and enteric nervous systems (Tanaka et al., 2011).

Tanaka and colleagues suggest that psychological distress itself is generated by integrative brain structures such as the sub-regions of the hypothalamus, amygdala, the medial thalamus and anterior cingulate cortex. The authors describe how increased hypothalamic-pituitary-adrenal responsiveness to stress produces glucocorticoids, which in turn increase the expression of inflammation, which may result in the production of immunomodulatory cytokines. Unique to Drossman et al's (2006) theory of causation, the brain-gut axis (relationship between central and enteric systems) is described as a bidirectional and integrated system. Although complex, thoughts, feelings, memories and environmental factors are thought to lead to neurotransmitter release which is likely to affect sensory, motor, endocrine, autonomic, immune and inflammatory functioning in susceptible individuals (Tougas, 2000).

As with the theoretical model advocated by Drossman (2006), CBT is based upon cognitive theories relating to various aspects of human behaviour and psychology including emotional, familial, social and peer influences (Benjamin et al., 2011). As suggested earlier within chapter 2, CBT results largely from the

cognitive theory originally developed by Beck and colleagues in the 1970's. It is within the modelling of these treatment approaches that the foundations are thought to have emerged which are responsible for the development of the philosophical, theoretical and practical foundations of CBT, particularly when employed in the management of IBS (Toner et al., 2000).

CBT is versatile, adaptable and can be applied to a variety of clinical pathology across a range of settings (Meichenbaum, 1985; D'Zurilla and Nezu, 2007; Hayes et al., 2006; Dimeff and Koerner, 2007). The flexibility of CBT reflects its usefulness for targeting the multiple aspects of cognitive and behavioural change theorised by Drossman (2006), with the application of a variety of developmentally-guided treatment methods (Benjamin et al., 2011). It is thought that cognitive attitudes, beliefs and attributions are essential for understanding and modifying human behaviour and affects (Kendall and Hollon, 1979). Such cognitions also play a fundamental role in the development and maintenance of emotional and behavioural responses (González-Prendes and Resko, 2012). Within the intervention developed here, CBT has been adapted to help individuals to learn and adopt new knowledge and skills in order to cope and live with the effects of IBS. It is through these mechanisms that people with IBS will become more aware of their thoughts and resultant behaviour, leading to self-directed change, improved function and an improved quality of life (Jokić-Begić, 2010 p.237).

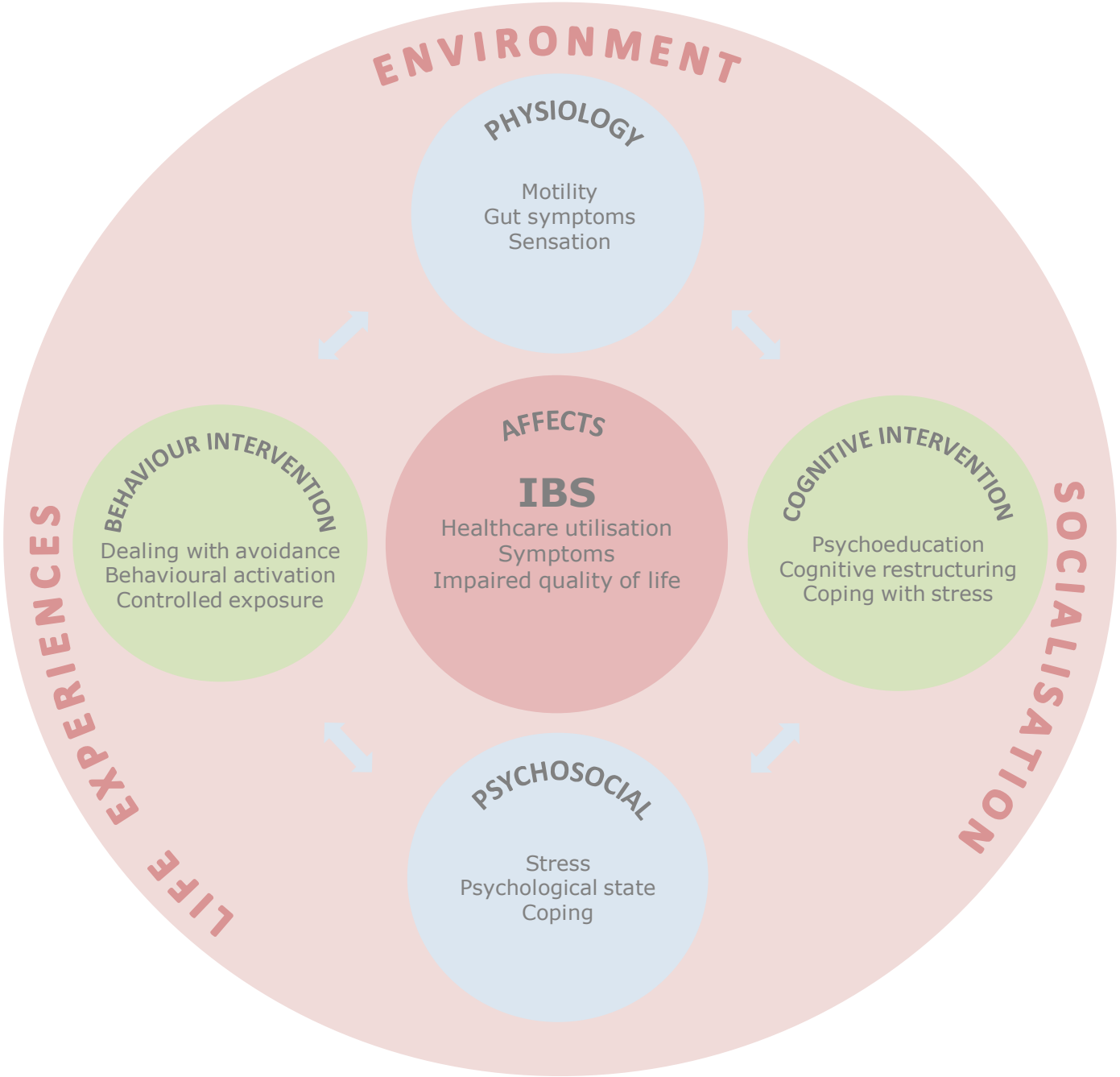
The intervention used within this study has been modelled upon CBT theory, which suggests that repeated experiences should be employed to stimulate new processes of learning, resulting in positive changes in behaviour and affect (Fuchs, 2004). Cognition mediates responses to environmental stimuli, but more importantly can be changed, targeted or modified to processes which are more rational and objective (González-Prendes and Resko, 2012). For example, during therapy, a patient may learn to self-regulate their unpleasant emotions through cognitive appraisal (Beauregard, 2007). CBT is also thought to be useful for addressing issues such as catastrophizing and negative underlying thought patterns in people with IBS (North et al., 2007). Such issues are often predictors

of poor patient outcomes which may be improved following the implementation of CBT (Hunt et al., 2009).

The presence of anxiety is thought to cause hypersensitivity to the perception and experience of pain which has the potential to reinforce an individual's beliefs in an organic cause for their illness leading to further anxiety, states of arousal and more noxious symptoms (Toner, 1994). As with previous studies utilizing CBT for the treatment of IBS, participants undergoing therapy will be educated in relation to the role of stress and in relation to their IBS symptomology (Blanchard et al., 2007).

In addition to managing stress, some individuals with IBS may also have distorted cognitions regarding symptoms (Toner et al., 1998), and as such CBT will focus upon correcting these cognitions in order to elicit positive changes in behaviour and affect (Hassett and Gevirtz, 2009). As advocated by Toner et al. (2000), the intervention must also help participants to reconceptualise their views of IBS and identify relationships between thoughts, feelings, behaviours, their environment and their IBS symptoms in order to develop effective ways of coping with IBS. The following conceptual model (figure 7) illustrates how the feasibility intervention is situated in relation to the theories of cognitive and behavioural change and the relevant elements of the biopsychosocial model developed by Drossman (2006).

Figure 7


ENVIRONMENT
PHYSIOLOGY
Motility
Gut symptoms
Sensation
BEHAVIOUR INTERVENTION
Dealing with avoidance
Behavioural activation
Controlled exposure
AFFECTS
IBS
Healthcare utilisation
Symptoms
Impaired quality of life
COGNITIVE INTERVENTION
Psychoeducation
Cognitive restructuring
Coping with stress
PSYCHOSOCIAL
Stress
Psychological state
Coping
LIFE EXPERIENCES
SOCIALISATION

4.3.5 The low-intensity CBT method and intervention design

Low-intensity CBT (LI-CBT) methods differ considerably from high-intensity CBT (HI-CBT) methods of intervention delivery. LI-CBT is a fairly recent revolution forming part of a stepped model of psychological healthcare, and refers to the low usage of specially trained therapist's time (Bower and Gilbody, 2005). LI-CBT interventions within the UK healthcare system are delivered by Psychological Wellbeing Practitioners (PWP's), specially trained in the used of LI-CBT interventions within the community improving access to psychological therapy (IAPT) services. The LI-CBT method also relates to a variety of CBT delivery mechanisms in the form of workbooks, internet and group type therapies (Bennett-Levy et al., 2010).

Within the literature review reported earlier, it was demonstrated that the majority of experimental evaluations of CBT used for the treatment of IBS utilise HI-CBT methods. LI-CBT treatments are attractive because they are administered using less face to face contact with a therapist than can be seen in some of the experimental evaluations of CBT for IBS. For example, the majority of HI therapy sessions ranged from 50 minutes (Craske et al., 2011), to 60-90 minutes weekly (Vollmer and Blanchard, 1998) lasting for around 10 weeks in duration.

LI-CBT methods have been described by Bennett-Levy et al. (2010) as a revolution in the provision of mental health services. The method represents a significant shift in the wider delivery of psychological services, which according to Bennet-Levy et al (2010) have vastly improved;

- Access and/or speed of access to treatment
- The total number of people who can access evidence-based treatments
- Service flexibility, responsiveness, and capacity
- Patient choice
- Cost-effectiveness of services

Moreover, it is interesting to note that there is evidence to support comparable levels of effectiveness between HI-CBT and LI-CBT methods when used in the treatment of common mental health problems such as mild to moderate anxiety and depression (Cuijpers et al., 2010). The implementation of LI-CBT treatment approaches when used in the management of common mental health issues have also been demonstrated successfully within the IAPT services within the community. These services were initially successfully trialled in two demonstration sites in both Doncaster and Newham (Clark, 2011).

There is no real consensus regarding what may constitute LI-CBT methods. However, Williams and Chellingsworth (2010) describe the use and application of a LI-CBT assessment model defined as the 'five areas approach'. This particular model consists of the following five domains;

- People and events
- Altered thinking
- Altered behaviours
- Altered physical symptoms
- Altered feelings

According to Chellingsworth and Williams (2010), the benefits of using this model allows to practitioner to holistically assess a patients individual needs within a limited timeframe. The five areas approach forms the basis of the assessment process used within the community IAPT services, which according to Richards and Whyte (2011) should also contain the following essential characteristics;

- A clear introduction
- Establishment of relevant expertise
- Positive, non-judgemental attitude
- Non-verbal competences
- Verbal competences

The LI-CBT method focuses on here and now and must be implemented collaboratively (Farrand and Williams, 2010). Risk is also an essential part of an LI-CBT assessment (Myles and Rushforth, 2007) and should at

least include an assessment of suicidal intent, plans or actions, preventative factors and risk to self or others. If risk is identified, the patients should be referred to an appropriately qualified professional. It is these evidence based features of the LI-CBT method which underpinned the development of the nursing intervention and differentiated the methods used here from those employed with the majority of experimental evaluations discussed earlier within the review of the literature (see chapter 3).

4.3.6 Adaptation of self-help intervention materials for IBS

The treatment protocol developed for this study (see appendix 8.6) was based upon the modules originally used within the study carried out by Hunt and colleagues (2009). Collaboration was negotiated during the study and the intervention was designed along with Dr Melissa Hunt and the University of Pennsylvania, Philadelphia, USA. This enabled the development and formulation of the preliminary treatment protocol which was configured (based upon the interventions previous use) to consist of the following evidence based components;

1. An introduction to IBS
2. Relaxation training
3. The cognitive model of stress
4. The cognitive model of IBS
5. Avoidance and exposure
6. Diet and IBS

These modules differ little from those detailed within HI-CBT intervention protocols which have been critically discussed within previous sections (see method of intervention delivery with the literature review section). Indeed, these multicomponent interventions are therefore fully supported by an array of empirical literature and need not be considered new techniques. The intervention protocol is covered by intellectual copyrights which are accredited to the University of Pennsylvania, USA. Adaptation therefore included negotiations with the legal department at the

University of Pennsylvania, in order to ensure that due acknowledgment was given for the intervention protocol outlined within this study. This resulted in an end user agreement between the study sponsor and the author's university. In addition to these legal negotiations, the materials used within the intervention were developed in light of the input of the PAG which were negotiated with the author throughout the process as changes took place. The intervention and self-help materials were also improved to encompass evidence relating to the application of LI-CBT intervention materials as described within 4.3.5. The following descriptions provide further details relating to the components of each of the intervention modules.

An introduction to IBS

The first module of the intervention described IBS to the participant in detail. The module contained information relating to possible causes, rationale for methods of investigation, typical features and evidence based definitions of IBS. The aim of the material was to educate participants regarding their IBS and empower patients to play a role in establishing a diagnosis. The role of stress in relation to IBS was introduced as fundamental in the maintenance of symptoms and symptom exacerbation. The brain-gut axis was described to participants as a vicious cycle consisting of altered behaviours and cognitions. Details of how interventions targeted aspects of the brain-gut axis were provided as part of the intervention rationale.

Relaxation training

The relaxation module provided patients with information regarding three types of relaxation therapy; deep breathing (diaphragmatic breathing), relaxing imagery and progressive muscle relaxation. The materials within the module described how behavioural relaxation exercises help reduce stress and break the stress related IBS cycle. Participants were encouraged to practice relaxation exercises frequently.

The cognitive model of stress

The cognitive model of stress was introduced to patients. The module described how negative automatic thoughts play a role in stress maintenance and exacerbation. The participants were taught how to identify negative automatic thoughts and begin to complete thought diaries in order to identify evidence for and against their thoughts.

The cognitive model of IBS

The cognitive module introduced within the previous module was linked directly to the experience of IBS. Participants were educated around the need to identify automatic thoughts associated with their IBS experience and begin to tackle these using thought records. The module also contained an introduction to behavioural experiments as a method of identifying evidence for and against negative automatic thoughts.

Avoidance and exposure

This module introduced the notion of avoidant behaviours which may be associated with IBS (for example; avoiding social events without toilet provision or avoiding contact with individuals who are thought to be unsympathetic to the experience of IBS). Participants were then taught how to use graded exposure as a method of combating avoidance.

Diet and IBS

The final module contained information relating to IBS and the diet. Participants were educated about dietary factors which may exacerbate IBS symptoms. The module also contained a summary of the activities used throughout the intervention.

Part of an LI-CBT intervention is the use and incorporation of SH materials which facilitate the fundamental aspects of the SH process or related activities. SH materials have been used within previous studies as part of CBT interventions used for the treatment of IBS (Moss-Morris et al., 2010). Indeed, SH materials are a versatile resource and have been empirically validated for a variety of common mental health problems

such as anxiety (Bower et al., 2001), depression (Gregory et al., 2004), eating disorders (Perkins et al., 2006) and panic disorder (Hirai and Clum, 2006).

There was information available to help inform the development of SH materials in relation to the necessary attributes and qualities required for effectiveness. For example, Richards and Farrand (2010) suggest that SH materials should provide patients with a rationale for why a particular approach or intervention may work, along with information about the approach itself and the provision of recording sheets and diaries. Most importantly, CBT SH materials should be based upon CBT methods. Richards and Farrand refer to the individual components of CBT as 'specific factors' which should be used in conjunction with 'common factors' in order to be effective (Richards and Farrand, 2010).

Common factors are the attributes bought about during therapy as a result of the therapeutic alliance between patient and the therapist. They include features such as warmth, empathy, flexibility and genuineness (Richardson et al., 2010). These factors are essential for the maintenance of patient engagement with LI-CBT therapeutic interventions and for supporting patients in their efforts to implement change when using SH materials. In addition to these qualities, authors also suggest that engagement can be further enhanced with the inclusion of real life examples or narratives to enable the patient to relate to the material and to provide examples of how challenges might be overcome (Macdonald et al., 2007). The provision of information alone is seldom sufficient to promote changes (Gellatly et al., 2007). According to the IAPT guide to guided SH materials (IAPT, 2010), the therapist should consider the following important aspects when choosing SH materials for use in LI-CBT interventions;

- Are they technically accurate?
- Do they engage with people?
- Do they develop and maintain that engagement?
- Do they use the language of common factors to do so?

- Do they use personal metaphors for emotional distress?
- Do they use narratives to connect readers to real life experiences?
- Do they help the person make connections between what they are reading and their own life?
- Do they provide a structure that encourages trying out what is learned and helping the person to review the outcomes?
- Are they readable

Williams and Chellingsworth (2010) also suggest that SH materials are much more effective when the material consists of;

- Plain fonts such as Arial
- A minimum font size of 10 (preferably 12)
- White space to break down blocks of text
- Case examples or real life stories
- Use questions to enable the reader to relate their own situation to the material
- Take into account different groups of people when using case examples

A particular challenge during the development of the nursing intervention was the further refinement and adaptation of the SH materials used within this study. This process took several months to complete and necessitated extensive negotiations between establishments, patients, the author and the author's legal representatives as described in 4.3.5. Most importantly, the adaptation of these SH materials took into account the qualities advocated the above authors.

The original SH materials were in the form of a large workbook, 90 pages in length drafted in Times New Roman font script. The majority of the material was black and white and consisted of a variety of information sections, activities and narratives. An example of the workbook format has not been provided as the material is the copyright protected property of the author. The workbook was made up of the following 9 chapters;

1. Do You Have IBS? Differential diagnosis
2. What Causes IBS? The biopsychosocial model
3. Relaxation Training
4. The Cognitive Model of Stress Management
5. Applying the Cognitive Model to IBS Symptoms
6. Behavioural Experiments
7. Eliminating Avoidance
8. Diet and IBS
9. Summary and Review

In light of the qualities of SH materials which are thought to contribute to effectiveness, acceptability and engagement, the following changes were initially made to the SH materials (prior to patient involvement described within the following sections).

- The workbooks were broken down into the modules (individual workbooks) previously described within the nursing intervention (an introduction to IBS, relaxation training, the cognitive model of stress, the cognitive model of IBS, avoidance and exposure, diet and IBS)
- The font style was changed to plain aerial format
- White spacing was introduced to break up large blocks of text
- Colour diagrams were generated to improve sections relating to rationale for 'specific factors'
- Extraneous text was removed
- Text was rearranged to suit the order of the interventions assigned within the study protocol
- American spelling was changed to American English
- A picture of the author was inserted

The workbooks were finally paginated into a consistent glossy blue theme and prepared for review by the author who approved the provisional changes made to the materials. The workbooks were then made available to the study patient advisory group, details of which are described earlier within section 4.3.3.

4.3.7 Training and preparation of the nurse therapist

Authors suggest that SH materials are most effective when coupled with interpersonal support whilst patients put exercises and interventions into practice (Richards and Farrand, 2010). Indeed, the definition of guided SH interventions are treatments which employ structured methods to enable patients to help themselves, which according to authors is usually carried out with support from another person (Lucock et al., 2007). However, the emphasis here was on developing the patient's skills with the ultimate goal of helping patients to help them-selves. Once taught, the concepts which underpin LI-CBT interventions could be applied throughout their lives. Treatment sessions are limited when compared to intensive therapy and patients are often seen in fewer therapy face to face sessions when receiving LI-CBT. There is no consensus on the number of treatment sessions or on the length of treatment required.

As the nurse therapist delivering the intervention within this study, I had previous experience of nursing care within a variety of clinical settings, but in recent years had delivered care to patients within gastroenterology. It was considered essential that the training of the nurse therapist during this study should be replicable and a curriculum for the training undertaken should be clearly defined to facilitate transparent reporting along with the findings of the research.

In General, registered nurses working within gastroenterology are well placed to deliver psychotherapeutic interventions to IBS patients, as they are familiar with the complexity of chronic gastrointestinal symptoms and the impact they have upon patients and their activities of daily living. The preparatory training utilised within this study offers a replicable mechanism for expansion of the professional scope of nursing practice for

nurses working within gastroenterology, while increasing access to evidence-based interventions for patients.

In order to prepare for the therapist role, the first two modules of the National Curriculum for the education of PWP's were completed (IAPT, 2011). The training consisted of 25 days of university-based teaching sessions and simulated clinical skills training. All modules were completed to the nationally accredited and standards, but the eighty supervised practice hours within a mental health services placement were omitted, as this was not felt to be necessary or economically viable for the preparation of the nurse therapist's role. Accessing these practice hours would permit accreditation and registration with the British Association for Behavioural and Cognitive Psychotherapies (BABCP) which is necessary to practice as a PWP within the IAPT services treating common mental health problems such as anxiety and depression.

Another important aspect factored into intervention development was clinical supervision. The main goal of CBT supervised practice is to help the therapist adopt the philosophy of CBT as the basic approach for changing the client's cognitions, emotions and behaviours (Pretorius, 2006). Supervision should also be used with a view to increase the value of the therapeutic process in the client's best interests (Prasko et al., 2012). According to Perris (1993), CBT supervision usually follows a didactic model, with the focus leaning towards the theoretical and technical aspects or the practical conduct of CBT (Perris, 1993).

Liese and Beck (1997) suggest that CBT supervision should cover the following aspects of therapy: diagnosis and identification of problems; associated cognitive models; cognitive case conceptualisation; basic counselling skills; therapy structure; cognitive techniques and behavioural techniques (Liese and Beck, 1997). The practice of the nurse therapist during the conduct of the trial was therefore supervised throughout by a professor of mental health nursing/clinical psychologist. These supervision sessions consisted of structured clinical supervision whereby difficult issues and problems arising during therapy could be

discussed and potential solutions proposed. Finally, the intervention was incorporated into a treatment manual to enable to intervention to be delivered consistently to participants (see more on this subject within the treatment monitoring section).

4.4 Comparator conditions

The aim was for the study to generate a variety of feasibility data essential for helping researchers better understand the use and application of various CBT treatment mechanisms within NHS secondary care gastrointestinal clinics. Moreover, at the feasibility stage of this work, there was uncertainty regarding the interventions which may be feasible to carry forward into a future trial. The intervention was therefore be compared to: a) the services of a fully trained and experienced cognitive behavioural therapist using a HI treatment approach b) a SH CBT workbook as a stand-alone treatment (which forms part of the nursing intervention described above) and c) a treatment as usual (TAU) control condition. Details of each of these comparators along with the relevant rationale are described below. Overall, the aim of providing these comparators within the study was to provide feasibility data on a spectrum of CBT interventions which vary in intensity from stand-alone interventions to intensive treatment regimens, as evaluated in many of the existing experimental evaluations of CBT.

4.4.1 HI-CBT

Comparing the study's nursing intervention with HI-CBT delivered by an experienced cognitive behavioural therapist helped to establish whether the study's nursing intervention might be as effective and acceptable as current evidence based treatment approaches within a full scale trial. Essentially, during feasibility, it was possible to compare the acceptability and suitability of the HI-CBT intervention with LI and SH approaches. The psychotherapist delivered treatment to participants using a protocol developed from the work of Toner et al. (2000) as in previous trials of CBT (Drossman et al., 2003). Full details can be found within the example of the CBT protocol provided within appendix 8.7.

The HI-CBT protocol did not follow the same format as the LI-CBT therapy session and therefore the self-help materials were not used within the HI-CBT intervention.

4.4.2 SH

Participants within the SH group of the study were given the same SH treatment workbook as used within the LI-CBT nursing intervention. However, in order for it to be possible to identify any additional benefit that the nurse therapist had within the study's nursing intervention; the treatment workbook was used as a stand-alone treatment. Participants were given the workbooks by the nurse therapist and advised that they should work through the included modules. Participants were informed that they should aim to complete one module per week and were encouraged to complete all of the workbooks activities. No further support was given following issue of the workbooks.

4.4.3 TAU

A systematic review suggested that CBT should be evaluated against TAU conditions (Zijdenbos et al., 2009), which would enable the study of the intervention in comparison to current treatment approaches. Authors have also suggested that a TAU control group is particularly useful during trials where the intervention lies well outside of usual practice (Thompson and Schoenfeld, 2007). Although there may be some concerns regarding levels of discontent among participants of the control condition, this project had insufficient funds and resources to deliver the intervention to control condition participants using a waiting list control condition which might have been possible within a funded full scale trial. It was hoped that the feasibility study would provide further information regarding the acceptability and suitability of a TAU control condition within a future trial.

4.5 Feasibility study outcome measures

Within this section, two types of outcomes are referred to, 1) those which are of concern during the conduct of feasibility i.e. 'feasibility study outcomes' and 2), the outcomes which would be of clinical interest during a full scale trial – the 'clinical outcomes'. In addition to the guidelines offered by the MRC (2008), authors suggest that feasibility studies should address a variety of outcomes. These outcomes include; obtaining the standard deviation for the outcome measure, which is may be needed in some cases to estimate future sample size, establishing the willingness of participants to be randomised and willingness of clinicians to recruit participants, evaluating phenomena relating to the identification of the number of eligible patients, establishing the characteristics of the proposed outcome measures, obtaining the follow-up and response rates to questionnaires and establishing the availability or usefulness of study data (NIHR, 2016; Mubashir et al. 2010). The success of the feasibility study was therefore based upon the following two main feasibility outcomes.

4.5.1 Feasibility study outcome measures

Recruitment and retention of participants

It was expected that some difficulties may arise during the conduct of the feasibility study. However, significant difficulties in recruiting participants may have a significant impact upon the success of a follow on study, particularly where power requirements fall short of a researcher's expectations. A pragmatic decision is therefore based upon the ability of the study to recruit 60 participants as envisaged within section 4.2.

Barriers and facilitators identified during the conduct of feasibility

The second primary objective of this feasibility work is to identify potential barriers and facilitators to the implementation of the trialled interventions. As suggested by the National Institute for Health Research (NIHR, 2016), such factors may relate to the methods used during the feasibility study, the methods used to recruit participants or the willingness of participants to complete the range of clinical outcome measures. The identification of barriers and facilitators, as advocated by the MRC (2008) was therefore pivotal in making decisions in relation to the likelihood of success of the future study.

In addition to these feasibility criteria the following outcomes have been selected as the clinical outcomes which are likely to be of interest within a follow on study. The outcomes are provided along with a justification for their selection and application as follows.

4.5.2 Clinical outcome measures

Primary clinical outcome measure: Symptom severity

Numerous studies have identified the negative impact that IBS symptoms have upon HR-QOL (Gralnek et al., 2000 , El-Serag et al., 2002 , Hahn et al., 1997). Experts also suggest that it is somatic symptoms which may be responsible for patients initially seeking consultation (Blanchard et al., 2007). IBS patients also report a significant impact on energy/fatigue and role limitations caused by physical health and levels of bodily pain (Gralnek et al., 2000). These factors would explain some of the increased consultation amongst patients with IBS and are in keeping with the biopsychosocial model proposed by Drossman et al (2006). For example, researchers have suggested that it is the impact of IBS symptoms on everyday activities, mood and personal relationships that contribute significantly to the impact IBS has on HR-QOL (Par'e et al., 2006).

Moreover, a therapeutic response in IBS symptoms has been associated with marked improvements in HR-QOL (El-Serag, 2003).

It is for these reasons that IBS symptom severity was chosen as the primary clinical outcome of concern for this study. This data was collected at baseline, post intervention and at follow up using the well validated GSRS-IBS (Wiklund et al., 2003). Two-hundred-and-thirty-four patients were involved in Wiklund et al's (2003) psychometric evaluation of GSRS-IBS. The final questionnaire included 13 subdomains; satiety, abdominal pain, diarrhoea, constipation and bloating. Wiklund and colleagues (2003) found the internal consistency reliability to be high, ranging from 0.74 (pain) to 0.85 (satiety). The associations between similar constructs in the GSRS-IBS and the various HRQL scores supported the qualities of the GSRS-IBS construct validity.

Secondary clinical outcome measure: Quality of Life

IBS has been shown to have a significant impact upon HR-QOL, with a level of impact similar to that of chronic conditions such as Gastro-Oesophageal Reflux Disease (GORD) and diabetes mellitus (El-Serag et al., 2002 , Gralnek et al., 2000). Researchers have suggested that the use of HR-QOL within therapeutic trials for IBS is clearly warranted, as the collection of patient centred data will ensure that future research better understands the impact of IBS which will help improve the quality of care for these patients (Gralnek et al., 2000).

Furthermore, HR-QOL is particularly useful for helping policy makers plan resources for the management of chronic diseases such as IBS (Gralnek et al., 2004). HR-QOL will therefore be included as a secondary outcome measure during this study. Various generic instruments such as the Short Form Health Survey (SF-36) have been shown to be useful in measuring HR-QOL in patients with IBS (Simrén et al., 2004).

Other instruments have also been developed to be specifically sensitive to disease specific characteristics not addressed by generic HR-QOL measures such as IBS-36 (Groll et al., 2002), IBS-QOL (Patrick et al., 1998) and the functional digestive disorders quality of life questionnaire (FDDLQ (Chassany et al., 1999). The FDDLQ was not specifically developed for IBS, as the developers felt that there was significant overlap between IBS and FGID symptoms (Chassany et al., 1999).

The IBS-36 and IBS-QOL are both well validated tools which use patient self-rated likert scales. The IBS-36 refers to the experience of respondents in the two month period prior to completion, whereas the IBS-QOL asks patients for responses based on the last months experiences. The latter was therefore better suited to this study design which had a limited follow up period. Furthermore, IBS-QOL has undergone two rigorous evaluations, the first of which demonstrating high reproducibility and internal consistency (Patrick et al., 1998) and the second longitudinal construct validity (Drossman et al., 2000). IBS-QOL was therefore included as a secondary outcome measure during the conduct of the study.

Additional clinical outcome measures: levels of anxiety and depression

Much of the impact that IBS has on quality of life is explained by psychological factors (Halder et al., 2004) which when treated, may reduce IBS related symptoms (Lydiard and Falsetti, 1999). These factors are also recognised as part of the biopsychosocial model of IBS proposed by Drossman et al (2006) as being fundamental in the maintenance of IBS and resultant symptomology. For example, increased levels of psychological distress have also been associated with symptom severity (Roy-Byrne et al., 2008), which is acknowledged in Drossman et al's (2006) model. Around 50-90% of IBS patients suffer with psychological co-morbidities such as anxiety or depression (Lydiard and Falsetti, 1999). Levels of anxiety and depression among the sample were therefore measured during data collection.

The PHQ-9 is a well validated tool for measuring levels of depression. The tools developers suggest that a significant PHQ-9 score above 10, has a sensitivity of 88% and a specificity of 88% for major depression (Kroenke et al., 2001). PHQ-9 scores of 5, 10, 15, and 20 represent mild, moderate, moderately severe, and severe depression, respectively (Kroenke et al., 2001). More recently, a study of 2,642 demonstrates the sensitivity and specificity of the PHQ-9 for the diagnosis of major depression to be around 86% and 78%, respectively (Arroll et al., 2010).

PHQ-9 has also been validated for the screening of depression in community (Nease and Maloin, 2003), secondary outpatient (van Steenbergen-Weijenburg et al., 2010) and prenatal care settings (Sidebottom et al., 2012). With receiver operating curves of n = 127; 0.930, the PHQ-9 is a valid tool for establishing levels of depression among adults from a variety of medical populations (Rathore et al., 2014).

GAD-7 is validated for measuring levels of general anxiety disorder among general populations (Löwe et al., 2008). With a threshold score of 10, GAD-7 has a sensitivity of 89% and specificity of 82% for generalised anxiety disorder (Williams, 2014). Like PHQ-9, GAD-7 has been validated in recent studies when utilised for screening within primary care (Mohd Sidik et al., 2012), perinatal care (Zhong et al., 2015) and when applied to complex medical problems such as MS (Terrill et al., 2015) and addiction (Delgadilloa et al., 2012). The GAD-7 produces a score between 0-21. Scores of 5, 10 and 15 represent mild, moderate and severe anxiety respectively (Spitzer et al., 2006).

Necessary permissions have been sought for all tools to be used during the conduct of this research where necessary. Unfortunately, a limitation of this study was that a pragmatic decision was made not to collect economic data during the conduct of the study. This decision was made to ensure outcome measure data collection was not burdensome to

participants. The properties of the various clinical outcome measures are summarised within table 8 below.

Outcome measure characteristics

Measure	Admin	Components	Data produced	Indications
IBS-GSRS	**Self-report**	13 item likert scale (range 1-7) Subscale; *Pain: 1, 2* *Bloating: 3, 4, 13* *Constipation: 5, 8* *Diarrhoea: 6, 7, 9, 10* *Satiety: 11, 12*	Min. 13 Max. 91	Symptom severity (Symptoms increase with score)
IBS-QOL	**Self-report**	34 item likert scale (range 1-5) Subscale; *Dysphoria: 1, 6, 7, 9, 10, 13, 16, 30* *Interference with activity: 3, 18, 19, 22, 27, 29,31* *Body image: 5, 21, 25, 26* *Health worry: 4, 15, 32* *Food avoidance : 11, 23, 28* *Social reaction: 2, 14, 17, 34* *Sexual: 12, 20 & Relationship: 8, 24, 33*	Min. 34 Max. 170 Score calculation (/100); The sum of the items - lowest possible score/ Possible raw score range x 100	Quality of Life (Quality of life improves with score)

PHQ-9	**Self-report**	9 item likert scale (range 0-3)	Min. 0 Max. 27	Depression/Mood
GAD-7	**Self-report**	7 item likert scale (range 0-3)	Min. 0 Max. 21	Anxiety

Table 8

4.5.3 Intervention monitoring and integrity

Monitoring of interventions within complex interventions research is essential for maximising the validity of the study results and as such, it was felt necessary to evaluate these methods during feasibility. Authors suggest that researchers should ensure that interventions are monitored and optimised in order to increase the likelihood that changes in the dependant variable are bought about by effective treatments rather than unknown confounds which could be unintentionally omitted or added during intervention delivery (Cook and Campbell, 1979).

So important are these factors, that conclusions about proposed treatment effects within an efficacy trial are doomed to failure without careful attention to intervention fidelity. Intervention fidelity can be defined as; "the ongoing assessment, monitoring and enhancement of the reliability and internal validity of a study" (Borrelli et al., 2005). A high level of treatment fidelity improves retention to interventions and reduces rates of attrition (Noel, 2006). Treatment fidelity has the potential to impact upon both the internal and external validity of the study. Internal validity is concerned with ensuring treatment is delivered as intended, whereas external validity represents how interventions might be replicated and applied in real settings (Borrelli, 2011).

These issues were considered during the design of the study to ensure that factors effecting internal and external validity issues had been carefully considered. For example, authors suggest that operationalising interventions should be carried out to ensure they encompass their theoretical and pragmatic roots and therefore contain the 'active ingredients' needed to bring about the desired change in the dependant variable (Moncher and Prinz, 1991). Where interventions demonstrate adherence to theoretical principles, they are also likely to bring about stronger effects (Resnick et al., 2005).

Borrelli et al. (2005) suggests that other measures should also include taping or recording interventions (in order to assess length and

compliance to intervention content), and the standardising of the training of those delivering the interventions. Fidelity to the treatment protocols within the both the psychotherapist and nurse administered treatment arms of the study were therefore monitored. The following measures were implemented during the conduct of the study.

- The study interventions were standardised to ensure that treatment was delivered consistently and in accordance with the theoretical concepts underpinning the interventions (see intervention section 4.3 for more details)
- The number of sessions administered were recorded on a case report form (CRF)
- A CRF required that the therapist declare the sessions were delivered as per protocol and were required to report any deviation from study protocol
- The training of the nurse therapist met nationally recognised and easily replicable standards
- All treatment sessions were audio recorded and a random selection of 10% of the audio recordings were reviewed by a clinician not connected to the delivery of the trialled interventions in order to assess fidelity to the intervention protocols

4.5.4 Randomisation and blinding

Randomisation is used within clinical trials to achieve balance in relation to known and unknown risk factors in the allocation of participants to the treatment conditions within a study (Hewitt and Torgerson, 2009 p. 27). A random permuted block method of randomisation was used to allocate participants across the four treatment conditions of the study. This technique ensured that participants were roughly balanced across all four treatment conditions which may not occur by chance when true randomisation methods are used (Matts and Lachin, 1988). This may result in a decrease in the power of a future study to detect statistically

significant differences between the treatment conditions (Efird, 2011). Blocked randomisation techniques also increase the power of treatment comparisons by dividing experimental units into homogenous strata and then pooling the differences over groups into blocks (Matts and Lachin, 1988). Most importantly during the conduct of this small scale feasibility work, the selection of small block sizes when the list was generated ensured participants were equally assigned over groups should the study fail to recruit 60 participants.

Randomisation was carried out using an online randomisation system (see http://www.sealedenvelope.com). The owners of the randomisation system generously granted the use of their online system without charge for this study. A randomisation list was generated using the services online system, and was carried out by an independent researcher unconnected to the conduct of the research. The researcher selected the block sizes required to generate the list, and uploaded the list once completed to the online system.

The study's investigators had no access at any time during the conduct of the study to the list. A copy of the list was securely stored in the School of Health Sciences should the online system have failed or became unusable. This copy will remain stored securely with the PhD course administrator until such a time as all analysis is complete. In circumstances such as system failure, the study could have reverted to the use of a telephone method of randomisation manned by persons not connected to the conduct of the study.

Blinding

As the allocation of treatment was made clear to participants upon commencing treatment, blinding of participants to their treatment allocation was not possible. Similarly, the investigator was also aware of the allocation of participants as my role within the study encompassed all aspects pertaining to the conduct of the trial. The post intervention data collected during this study was therefore collected by a research

assistant blind to the allocation of study participants. See data collection section for more information.

4.6 Data collection and analysis

4.6.1 Quantitative data collection

Outcome measures were collected at baseline, post intervention and six months as detailed in the outcomes section. As the intervention was being delivered by the investigator, study procedures needed to guard against investigator bias (Schulz, 2000). All follow up observations were therefore collected by a research assistant who was not involved in the delivery of trial interventions and who was blind to the allocation of trial participants. The study's investigator and trial co-ordinator sent out follow up questionnaires to participants at the required intervals to be returned using a prepaid postage envelope. The envelopes were addressed to the research assistant and were identifiable only via the participants study number.

Data collection procedures were detailed in the study protocol and met Good Clinical Practice (GCP) guidance (ICH-GCP, 2012). A summary of outcome measure results were sent to the investigator for entry into a database of results. A full audit trail was maintained and all investigators did not have access to raw data. This study also attempted to collect data regarding the number of patients approached to take part in the study which was used to assess the feasibility of the recruitment methods to be employed within a full-scale trial. A record of study processes, including number of participants approached, screened and randomised was therefore maintained during the trial.

4.6.2 Qualitative data collection and rigour

The 'concurrent triangulation strategy' (Creswell, 2003) facilitated the parallel collection of both qualitative and quantitative data during the conduct of the feasibility study (Creswell, 2009). The qualitative element of this study aimed to capture knowledge located in the minds and

personal experiences of others (Nespor and Barylske, 1991). Interview methods permitted the exploration of these experiences and the subsequent textual portrayal of the phenomena (Patterson and Williams, 2002). Participants within the intervention arms of the study were invited to take part in the qualitative interviews using a convenience sampling approach (participants were invited to take part in the study interviews as they completed the study interventions). Furthermore, this study also sought ethical permission in order to ask patients who refused to take part in the study for reasons for why they might have refused to take part. It was made clear that patients were under no obligation to provide this information to the researcher. This information would be useful for understanding barriers to the successful implementation of the feasibility study's interventions from the perspectives of participants as advocated by the MRC complex interventions framework (2008).

There is some contention among researchers regarding the degree of pre-structure that should be present during participant interviews. It was also anticipated that the reviewing ethics committee would insist on the submission of an interview schedule (Balls, 2009). Some authors would advocate unstructured interview techniques (Huberman and Miles, 1988), whilst others would argue that a semi-structured approach would ensure that information relating to the phenomena of interest is obtained (McNamara, 2009). A semi structured approach would keep the content of the interviews focused and ensure data collected is relevant to the research question. Furthermore, such structure enabled the involvement of the patient advisory group which ensured that patients had been involved in the development of the interview schedule.

The structure of the interviews was carefully considered as authors have recognised how the absence of prescribed sets of rules within qualitative research leave the research process open to the researchers own experiences and intuitions (Kvale, 1996). The structure and content of the interviews was developed as a result of prior knowledge of gastrointestinal research and the subject area as a result of the literature

review. Interview questions were used by the interviewer to seek clarification, illustration and further exploration regarding important issues (Parahoo, 2006). The interview questions were structured around the need to identify barriers to the use of psychotherapy amongst patients with IBS and to explore experiences that participants might have when receiving the trial interventions. It is acknowledged, that although the semi structured interviews may maintain focus, the pre-structure might be a barrier to the elucidation of certain narratives. The interview schedule therefore consisted of open ended questions which allowed participants to freely express their feelings and experiences (see Appendix 8.8 for the study interview schedule).

Knowledge claims which arise from the conduct of qualitative research should be powerful and convincing (Kvale, 1996). The qualitative methods were therefore justifiable and sufficient to demonstrate substantial rigour and quality (Ballinger, 2006). The incorporation of qualitative methods within the feasibility study would ensure that the research was able to consider social experiences and meaning (Denzin and Lincoln, 2000). The qualitative data collection methods would also help to contextualise the findings of the feasibility study (Pluye et al., 2009). Moreover, the qualitative element of the research would also enable trial participants to provide information regarding responses to quantitative variables (Wagner et al., 2012).

The qualitative methods within this proposal must therefore be justifiable and be able to demonstrate sufficient rigour and quality (Ballinger, 2006). Lincoln and Guba (2007) suggest that this can be achieved by ensuring that qualitative research is underpinned by methods which are credible, transferable, dependable and confirmable. Each of these issues are noted in table 9 at the end of this section, along with a definition offered by Baxter and Eyles (1997), and an explanation of how the qualitative methods employed within the feasibility study address each of these important criteria.

There are a variety of other important issues to consider when conducting qualitative research, particularly in relation to critical reflexivity and the involvement of the researcher during the collection and interpretation of qualitative data. For example, there are descriptive approaches used within phenomenological research, underpinned by the early work of phenomenologists such as Husserl (Maggs-Rapport, 2001). Researchers employing such methods would argue that one is able to bracket oneself out from any influence he or she may have during the data collection and analysis process (Lopez and Willis, 2004). When using such approaches, the researcher attempts to separate any bias from the phenomena under study (Koch and Harrington, 1998).

Alternative approaches aim to interpret rather than describe phenomena. The theory of interpretation is largely a result of the work carried out by Heidegger (1962). Such methods reject the philosophy that researchers are able to separate and presuppositions and any influence he or she may have during the interpretation and analysis of qualitative data (Koch, 1995). From the interpretivist's perspective, it is explicitly acknowledged the researchers own experiences have the potential to significantly influence interpretation (Balls, 2009). Authors would suggest that for a researcher to understand the meaning of something held by another, the researcher should remain open to the meaning held by the other (Dowling, 2004). In this sense, it should be acknowledged that the presuppositions held by the researcher should be acknowledged as they are integral to data interpretation and analysis (Pascoe, 1996).

The researcher should have an awareness of his or her personal biases in order to portray the uniqueness of data against his/her own meanings, which has been described by authors as the 'fusing of horizons' (Gadamer, 1989). Within phenomenology for example, the personal involvement of the researcher is thought to take place within a reciprocal process of interpretation (Spence, 2001). Not all of the knowledge and presuppositions held by a researcher should be considered as negative aspects within the research process, as Locke et al. (1993) support the

positive impact that the researcher's knowledge can have on the improving quality and the shaping of their research. Such an arrangement can be achieved through a process of critical subjectivity, whereby the researcher explicitly acknowledges their own experiences as an integral part of the research process (Reason, 1988). Miles and Huberman (1994) support what they refer to as a process of 'reflexivity', which can be employed to enable the researcher to examine their assumptions, expectations and theories, and the impact these issues may have upon the conduct of research.

During the conduct of the research, it is therefore important that I acknowledge my personal presuppositions and any bias they may introduce to the research process as advocated by Huberman (1994). As a researcher with extensive experience of carrying out trials within the gastrointestinal speciality, I have a variety of assumptions based upon my personal experiences and practice. For example, I am aware of the intrusive nature of chronic gastrointestinal conditions and the impact such conditions have upon an individual's quality of life and social experiences. Within professional practice, I spend a great deal of time helping people live with such conditions with a variety of advice and targeted interventions drawn from clinical experience and best practice guidance. What is difficult for me to understand, are the individuals own circumstances, views on the course and progress of their condition and their own mechanisms of adjusting to treatment or new routines.

Such understanding is only reached through a process of interpretation, negotiation and gathering information regarding the circumstances and nature of the individual. This process requires interpretation and clarification which is not without the possibility of misinterpretation, errors in recording circumstances and a whole array of issues regarding the intrusiveness of questioning and gender roles. As such, I acknowledge the influence that I have upon the gathering and interpretation of information regarding phenomena, both in a clinical and research capacity. I therefore formed an alliance with another clinician

and a group of patients in the hope of introducing different perspectives into the research design, data collection and analysis process as advocated by Baxter and Eyles (2007). Further details of how quality and rigour were ensured during the design and conduct of the qualitative research are presented at the end of this section in table 9 in accordance with Baxter's recommendations.

A further example of how introducing others perspectives to the research process have influenced the course of the design and conduct of the research follows the meeting with PAG, who felt it was felt the study interviews should be carried out by an interviewer not involved with the delivery of the trial interventions. This was felt to be of particular importance as the investigator would personally be delivering one of the study interventions which may therefore be a potential barrier to participants providing certain narratives.

Finally, the consolidated criteria for reporting qualitative research (CORE-Q), is a 32-item checklist for ensuring quality and rigour when reporting and conducting empirical research using interviews and focus groups (Tong et al., 2007). The authors of this tool advocate that the implementation of the tool by researchers will improve conduct, and promote a greater recognition of qualitative research which are often viewed as 'second class' research methods (Tong et al., 2007). The proposed qualitative methods were therefore consistent with the standards listed within the CORE-Q checklist (please see Appendix 8.9 for the CORE-Q checklist completed for this study).

All of the post-intervention interviews were conducted as per ethical approval by a co-investigator who was not connected to the delivery of the interventions. The co-investigator was a female trial co-ordinator at the time the interviews took place and held the credentials of a psychology graduate. The interview schedule was developed in collaboration with the interviewer by the study investigator, who was a male PhD student at the time of conducting the research with an MA

Research Methods. Interviews took place within facilities located within a digestive diseases research centre. The interviewer had a background in the delivery of LI psychological interventions and also participated in the formulation of the semi-structured interview schedule. The interviewer was not known to study participants and introductions were carried out in accordance with the interview topic guide (see 8.8) within the BRU at the research centre. No other researchers or healthcare professionals were present at the time of interview.

All interview recordings were transcribed verbatim, and verified by the interviewer and investigator prior to the destruction of interview recordings as required the reviewing REC. The process of interpreting and analysing the interview data was carried out in accordance with the thematic framework analysis described by Ritchie and Spencer (1994) as detailed within 4.6.4.

Table.9

Criteria for ensuring quality and rigour of the qualitative methods

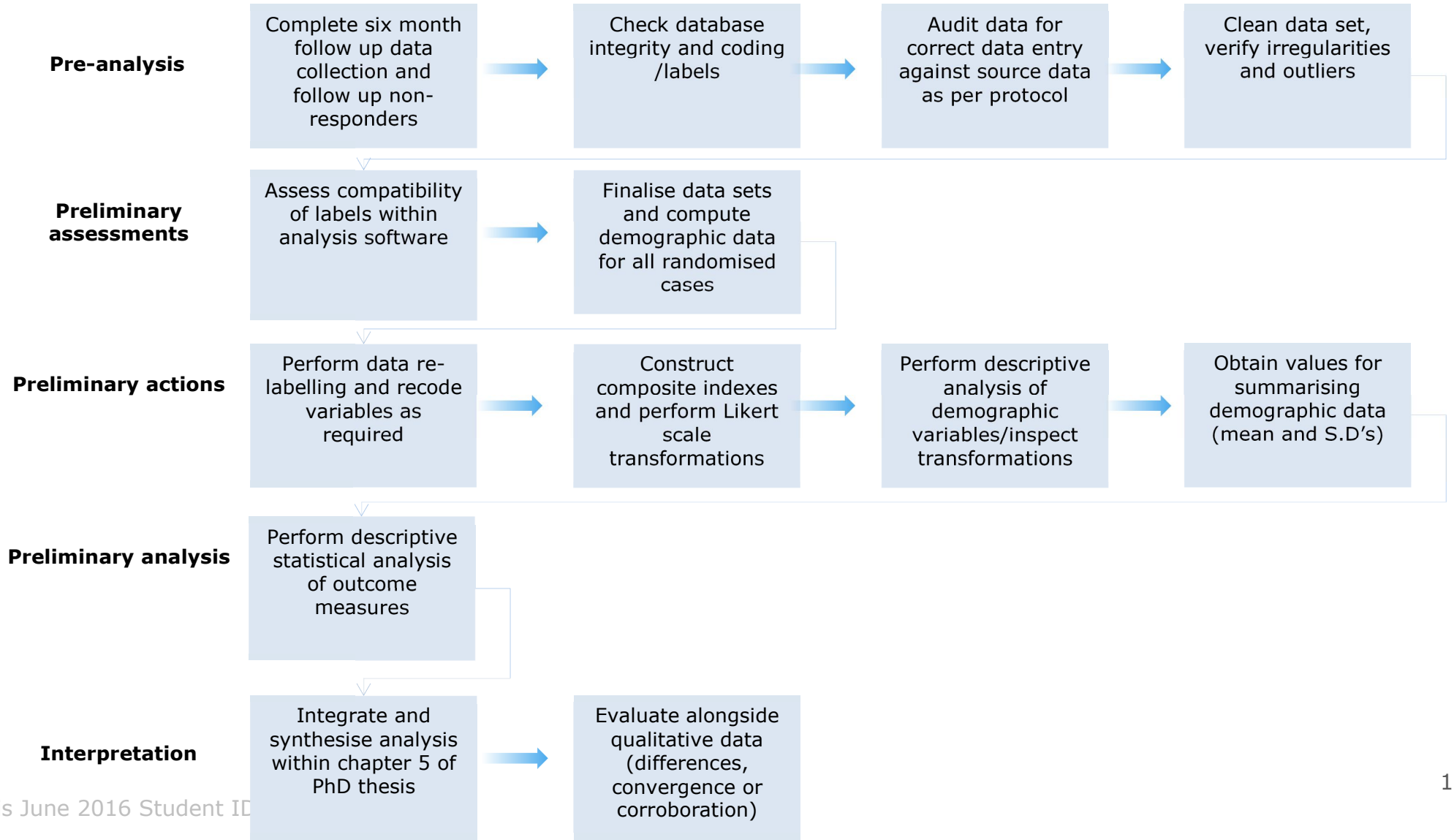
Criteria	Definition	Strategies employed to satisfy criteria
Credibility	Authentic representation of experience	➢ Purposeful sampling of participants receiving trialled interventions
Transferability	Will fit with contexts outside of the study situation	➢ Rich descriptions of experience employed ➢ Detailed description of settings and context upon reporting of findings
Dependability	Minimisation of idiosyncrasies in interpretation Validity tracked to identifiable sources	➢ A group analysis of the interview data carried out in order to incorporate different perspectives and guard against investigator bias ➢ Data recorded and transcribed ➢ Audit trail maintained for peer review and scrutiny
Conformability	Extent to which biases, motivations, interests or perspectives influence interpretations	➢ Audit trail maintained as part of the indexing phase of framework analysis ➢ Audit process explicitly described upon reporting ➢ Presence of self-critical reflection and awareness

Source of definitions: Baxter and Eyles (1997)

4.6.3 Quantitative data analysis

Quantitative data was analysed descriptively as the study was not powered to detect clinically significant effects. The analysis was treated as descriptive in nature and no attempts were made to generalise the results of the study (inferential analysis). Measures of mean and variance including the mean and standard deviations have been used to describe the full range of data at baseline and at follow up. All data were analysed using SPSS version 22 software. Missing data was imputed using the last observation carried forward (LOCF). The overall process for quantitative data preparation and analysis is described within the following diagram of the data analysis plan (Figure 8).

Figure 8 Quantitative Data Analysis Plan: CBT-IBS Feasibility Study



4.6.4 Qualitative data analysis

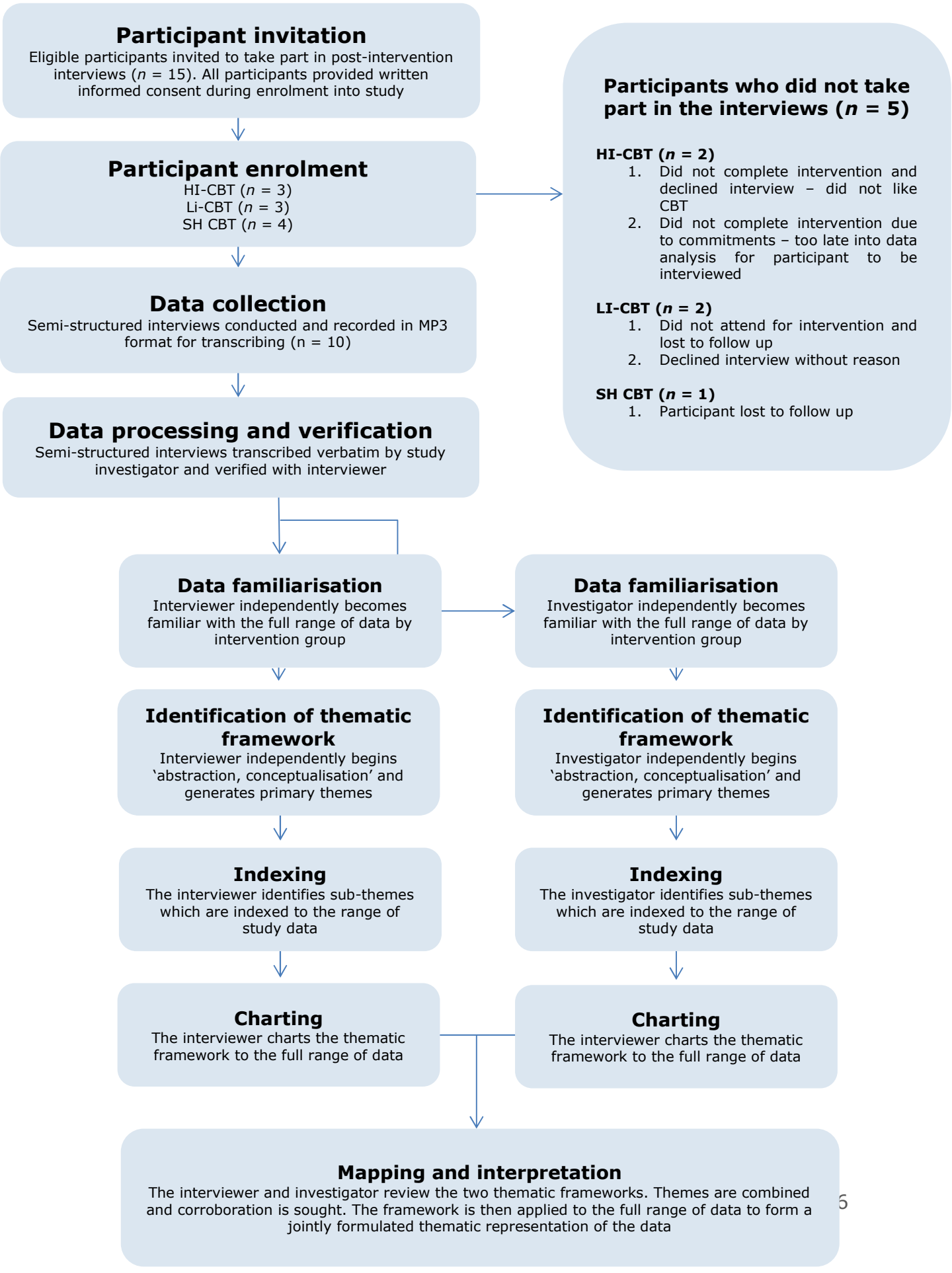
In order to improve the validity of the research project, corroboration was sought between qualitative and quantitative elements of the study during analysis (Doyle et al., 2009). Qualitative data was generated in the form of interview transcripts for analysis. The qualitative data was intended to supplement the quantitative outcome data by identifying convergence and differences between the two databases (Creswell, 2009). Interview data were analysed as collected throughout the study which enabled emerging findings to inform the research process (Wagner et al., 2012). Interview recordings were transcribed verbatim prior to conducting the framework analysis advocated by Ritchie and Spencer (1994) consisting of the following stages.

- **Familiarisation**. The analyst becomes familiar and immersed in the data collected. A process of abstraction and conceptualisation begins with an overview of the richness, depth and diversity of the data.
- **Identification of a thematic framework**. The analyst begins to assemble key issues, concepts and themes by which the data can be referenced.
- **Indexing.** The thematic framework is applied to the transcripts in textual form. The analyst seeks to index transcripts to the framework whilst interpreting meaning.
- **Charting.** In order to build a picture of the data as a whole, parts of the data are lifted away from their original context and rearranged.
- **Mapping and interpretation.** The analyst compares and contrasts the perceptions, accounts, and experiences and searches for patterns or connections. The analyst also searches for explanations weighs up the salience and dynamics of issues, by searching for structure.

In order to improve the rigour during the analysis and guard against investigator bias, a group analysis approach was used to analyse the interview data (Gunaratnam, 2009). Both the investigator and the interviewer analysed the interview transcripts under the supervision of an experienced qualitative researcher. The diagram on the following page describes the process used to conduct the joint analysis of the post-intervention interview data (Figure 9), which is further described within chapter 5.

Figure 9

Process used for the joint thematic analysis and interpretation of interview data



4.7 Ethical issues, data protection and confidentiality

4.7.1 Research ethics

The origins of modern research ethics can usually be traced back to human catastrophe such the development of the Nuremberg Code, which was largely a response to unethical medical experiments carried out on humans during the Nazi regime of WWII (Weindling, 2001). The main focus of the code was the protection of research participants from harm and ensuring that participants in research had provided valid consent (Nuremberg Code, 1949). Later consolidations of ethical principles took the form of the Declaration of Helsinki, developed by the World Medical Association (WMA) which was adopted during the early 1960's and later revised in 2000 (Declaration of Helsinki, 2000).

Consent principles are fundamental during the conduct of clinical research. Consent principles require that the person understands the relevant information provided, believes the information and is able to evaluate the information and make an informed choice (Dalla-vorgia et al., 2001). The ethical literature does not relate to human experimentation alone and participants within qualitative research may be at risk of adverse effects such as anxiety and distress, exploitation, misrepresentation and breaches of anonymity in published papers (Richards and Schwartza, 2002).

Authors suggest that a fundamental approach in the ethical delivery of clinical research is the practice of equipoise. When equipoise is present, there is real uncertainty in relation to the outcomes associated with the treatment under investigation (Freedman, 1987), and a clinician involved in research has no preference about the overall benefit or harm offered by the trialled intervention (Alderson, 1996). Equipoise has also been proposed as a strategy to reduce bias during the design of experimental evaluations (Cook and Sheets, 2011). Equipoise was therefore practiced during the delivery of trial information to participants by the study

investigator with no intervention or treatment conditions portrayed has having favourable benefits over another.

Ethical issues within clinical research are complex and relate to a variety of factors such as; moral standards (Harris, 2005), law (Plomer, 2005), professional codes of conduct (BPS, 2010 , NMC, 2015) and a variety of international directives (European Commission, 2015). Although research ethics represent remarkably complicated phenomena, the following quotation reflects the researcher's responsibilities in a succinct and concise manner.

> *The core ethical principles of respect for autonomy, prevention of harm, promotion of benefit, and justice (which form the basis of professional codes of research conduct) must be applied flexibly to take account of contextual, methodological, personal and practical considerations*
> (Slowther et al., 2006 p.1)

Slowther and colleagues (2006) suggest that researchers have a duty to prevent harm and promote benefit when considering the methodological, personal and practical considerations of research. Such issues are considered throughout the following sections which relate to the ethical considerations identified during the design of the feasibility study. This study has been designed with due attention to ethical detail from the initial conception of the research question, right through to data analysis. Indeed, the improper analysis of research data itself is an ethical issue, as it has the potential to result in the publication of false or misleading conclusions (Wasserman, 2013).

The literature would suggest that investigators need to consider if any aspects of the research design generate unnecessary risks and identify measures required to ensure the protection of participants (WHO, 2009). During the design and implementation of the feasibility study, measures were implemented to ensure, as far as practicably possible, that the safety of participants throughout the conduct of the research was

maintained. These issues require a great deal of attention and due diligence, particularly considering issues such as sexual and emotional abuse, traumatic life events and the prevalence of psychological co-morbidity presented within chapter 2. The following sections summarise the ethical considerations made during the design of the feasibility study.

4.7.2 Psychological issues and IBS

The review of the literature reported within this thesis and the background epidemiological information, highlighted a high rate of psychological co-morbidity evident among IBS patients. Although not all participants recruited for this study had a psychological co-morbidity, some participants may not accept, or may have even rejected, a psychological element to their illness (Toner, 1994). Very little is known about these issues and it was hoped that by conducting interviews with trial participants, these issues would be further explored and better understood.

4.7.3 Experimental design issues

Participants assigned to the treatment as usual condition of the study were intended to not receive any intervention during their participation in the research. A decision to include a treatment as usual control within the RCT was based on a) the need for future research to include treatment as usual controls within a recent systematic review b) a lack of trial resources available to offer an alternative approach such as a waiting list control condition. It is also essential that the full scale study is able to measure the additional benefit that participants receive when subject to the intervention in addition to standard treatment approaches (participants' not currently receiving psychotherapy).

It is acknowledged that some participants may be disappointed when assigned to the treatment as usual condition. In order to minimise these undesirable affects, it was proposed that participants were educated by way of information sheets and discussion with study staff prior to enrolment and at follow up intervals. Participants in the treatment as usual condition were continually advised that they are making an

essential contribution and that their participation within the study may significantly benefit the future healthcare of others.

4.7.4 Participation in a trial of psychological interventions

Some participants might have been concerned regarding the implications of receiving psychotherapy during the trial. The emphasis within this study was to focus on helping participants to live with the impact of their IBS symptoms rather than specifically targeting those only with psychological co-morbidity (such as underlying anxiety or depression). It was therefore considered important that it should be made clear when writing to the participants GP, that participation in the study does not necessarily suggest or confirm that participants are psychologically unwell. This may have been particularly important where a diagnosis of psychological illness may have had negative implications for the participant i.e. insurance implications and those with rigorous occupational requirements.

However, levels of psychological illness were recorded during the participant's journey through the study as these were important and potentially confounding factors. It was predicted that participants within the intervention arms of the study may benefit from CBT if they had underlying anxiety or depression. For participants in the control condition of the study, participants were advised to seek a consultation with their general practitioner for care as usual if they were identified as having anxiety or depression during data collection. Participants were made fully aware of these issues during recruitment and selection and these details were included within the study information sheets as suggested by the PAG.

4.7.5 Emotional distress during participation in the study

It was acknowledged that some participants may have become distressed by talking about their illness during interviews or indeed by undergoing a course of psychotherapy. Participants who displayed significant distress within the intervention arms of the trial would be given the support of their therapist.

4.7.6 Ethical approval

The above issues were reviewed by an NHS REC. This study was granted ethical approval by the Nottingham 2 REC (see appendix 8.5). Host organisation approval was issued by the Research and Innovation department of the hosting organisation prior to the implementation of any research related activity (see appendix 8.10).

4.7.7 Confidentiality and data protection

All data was stored in accordance with ICH-GCP guidance (ICH-GCP, 2012), and stored separately to information which could link participants to data. A Site Master File (SMF) stored all data and correspondence pertaining to the conduct of the trial. A second 'data' folder holds all study collected data and Clinical Report Forms (CRF's) which is identifiable only by unique study identifiers and is stored in a separate and secure location to the SMF.

Quantitative data was entered and stored on an MS Access database for analysis with STATA software. Interview recordings were transcribed verbatim and electronically stored using unique identifiers to protect the confidentiality of trial participants. All electronic data was stored on a University password protected and encrypted server which is automatically backed up. Only study personnel (with explicit permissions on the study's delegation log) were permitted to access the stored data. All data has been stored in accordance with ICH-GCP guidance (ICH-GCP, 2012), and stored separately to information which could link participants to data.

A procedure for auditing the processed data was detailed within the study protocol. All data was subject to monitoring and inspection by the hosting organisation and the regulatory authorities for which consent was obtained at the time of written and informed consent from trial participants upon enrolment into the study. Please see appendix11 for the study Gantt chart.

4.7.8 Resources and funding

The following table (table 10) presents the resources which will be required to carry out the project along with further details which explain how the needs have been met.

Resources	
Full time PhD researcher	A full time PhD studentship has been fully funded by a university studentship. The investigator was personally responsible for the all aspects pertaining the conduct and co-ordination of the trial and assumed the position of principle investigator for regulatory and contractual purposes
Academic and clinical supervision	The research was supervised by the principal and secondary PhD supervisors.
Patient and Public Involvement	A PPI manager is currently facilitating the trial specific PAG. Funds were made available from the gastrointestinal biomedical research unit (BRU) in order to support the initiative which includes reimbursements for participant travel and attendance
Nurse therapist for LI CBT	The investigator was a gastrointestinal nurse researcher with a particular interest in IBS and was trained in the delivery of LI CBT during the study. The training was funded by the gastrointestinal BRU and the school of nursing. There were no additional excess treatment costs for the delivery of the intervention.
Cognitive Behavioural Therapist	A fully trained and qualified therapist from the department of psychological medicine delivered the comparator intervention. The cost of these interventions have been met by the department of psychological medicine and have not been identified as excess treatment costs
Follow up data collection and interviewing	In order to uphold rigour and protect against investigator bias, the investigator was unable to collect post intervention follow up data. Support has been provided for these activities from the gastrointestinal research unit who supported the collection of study data. Interview data was collected by a colleague with an interest in the research on a voluntary basis
Information Technology	IT facilities were provided as part of the PhD studentship which included access to email and data analysis software. NHS IT facilities were accessible.
Interviewing and Consultation Facilities	Participants receiving the intervention of the psychotherapist were seen within outpatient clinics. Participants receiving all other study interventions were seen in the gastrointestinal BRU. The research team had access to outpatient departments within for the recruitment and selection of participants.
Stationery and Printing	Stationery which was necessary for the conduct of the trial was provided by the University who are hosting the studentship.
Total funding required	0.00 GBP

Table 10

4.7.9 Dissemination of the study protocol

This study has been presented throughout the gastrointestinal directorate within the Hospital Trust in order to promote the objectives of the research study and enhance the study recruitment strategy. The study protocol was also presented in poster form at the European Academy of Nursing Science conference in Barcelona, Spain 2015. Furthermore, the study was successfully peer reviewed and published during 2014 within the British Medical Journal Online (see Dainty et al. (2014). The publication has been made available in appendix 12.

This study was also registered on a publically accessible database (ISRCTN) and can be viewed here: http://www.controlled-trials.com/ISRCTN83683687/

Chapter 5 ▪ Findings

5.1 Qualitative and quantitative data findings

Within the following sections a synthesis of both the quantitative and qualitative data findings gathered during the conduct of the feasibility study are presented. In order to assist the reader with linking the findings of the study with the objectives stated within chapter 4, the findings are presented under the heading of the study's feasibility outcomes along with the relevant data.

5.1.1 Recruitment of participants

This chapter begins with the presentation of the findings relating to one of the greatest challenges found during the conduct of this feasibility study - recruitment.

> *"Diligently run feasibility studies are a vital factor for success, but, even with these essential data in place, recruitment still underperforms about 50% of the time…… A poor feasibility study will often lead to poor patient recruitment later"*
> (Wyse, 2006, p.9)

One of the main outcomes of this study was to assess the feasibility of the strategies used to recruit participants and to identify potential barriers and facilitators to the success of future research. Despite the anecdote offered by Wyse (2006) above, one of the most important lessons that can be learned from conducting this feasibility work is that challenges relating to the recruitment processes were grossly underestimated.

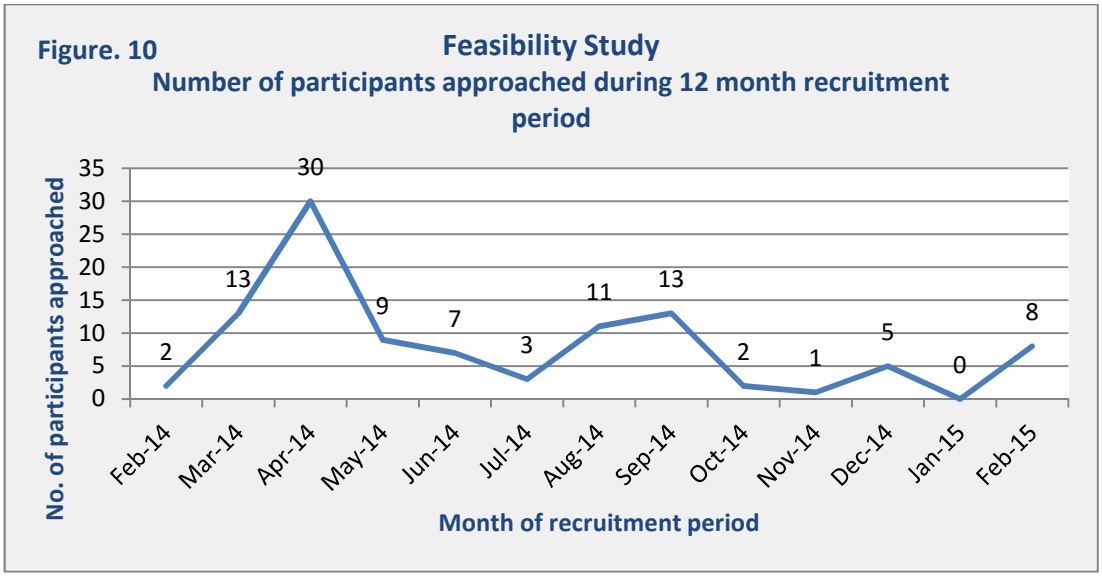
Within the following pages, an overview of the findings relating to the study recruitment period which ran between February 2014 and February 2015 is presented and discussed. As Wyse (2006) suggests, recruitment issues are best identified during a well-designed feasibility study, rather than later during a full scale trial. Furthermore, such issues should not be

underestimated, as they have the potential to affect not only the relevance of a study, but also future funding applications and the researcher's credibility and reputation. During the recruitment period to this study, it was hoped that 60 participants would be recruited and randomised across the four treatment conditions of the RCT. The study only managed to achieve one third of this number, details of which are presented as follows.

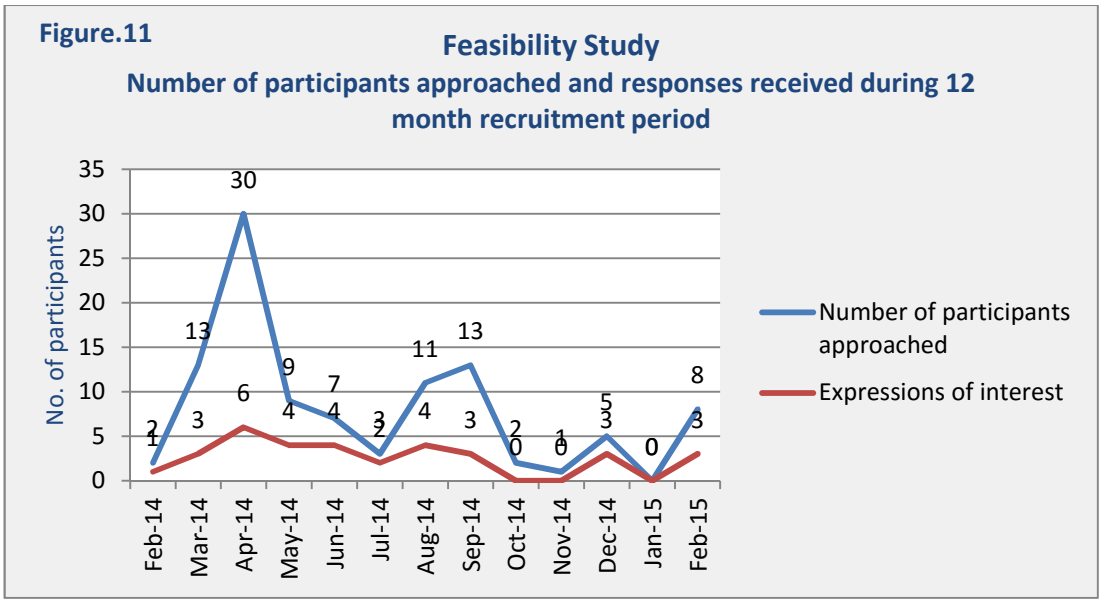
5.1.2 Number of patients approached and randomised

A number of patients (***n*** = 104) were approached with details regarding the study, primarily by way of trial information packs sent to patients via their usual care team or following contact with myself during the conduct of the study (after responding to study posters, the trial website or other trial advertisements). However, one should note that it is not possible for the figures presented here to be entirely representative of the numbers of patients approached, and it is likely that such values underestimate the numbers of patients with whom contact was made. This is due to the fact that some patients may have been given information about the trial during clinic visits or during consultations with their physicians that were not known to the investigator. Indeed many patients may have read information on websites and via study posters, and based upon that information alone may have decided not to take part.

Furthermore, one must appreciate the complexity and importance of patient confidentiality, and when interpreting the figures quoted below, it should be noted that the data presented relate to those who were known to have been approached during the conduct of the study. Where patients were approached directly by their clinician, the investigator was informed of the date and number of patients approached by a member of the care team. The following chart (Figure 10) represents the quantity of information packs (study invitations) distributed to NHS patients during the recruitment period.



The above chart (Figure 10) demonstrates the peak of participants approached to be April 2014. The following chart (figure 11) demonstrates the number of expressions of interest received from patients in relation to the distribution of the study information packs.



Overall, 33 expressions of interest were received which gives a response rate of around 34.4% to the study invite and information packs. The rate of response appears almost proportionate to the number of patients approached (see figure 9). The most successful recruitment period represents the screening of the BRU research database for participants in

March/April 2014. This represents a period when of 30 patients approached, 6 chose to return study invitation information and express an interest in taking part in the study. Very low recruitment rates were seen in October, November and January during the recruitment period. During these times, every effort was made by the study investigator to continue to promote the study and encourage physicians to identify further potential participants. January represents the absence of the investigator due to ill health. No explanations were obtained for poor recruitment rates in October and November. Furthermore, no data was collected from the recruiting physicians regarding the recruitment of participants from the study clinics which is a significant limitation of this work. Further feasibility information in this regard would have been useful for a future study at this centre. Some of the crucial factors relating to these recruitment data are presented on the following pages, which are underpinned by the following questions.

5.1.3 Reasons for patients not wishing to take part

During the design of the study, it was anticipated that some patients may not volunteer to take part in the study or that response rates may even be poor. This was based upon the assumption that some participants may reject a psychosocial element to their IBS (Toner, 1994), and hence not respond to an invite to take part in such a trial. With this in mind, the approval of the REC was sought to ask patients who chose not to take part in the study for reasons why they may not wish to do so, in view that this may explain potential barriers to the success of the interventions or recruitment to a follow-on trial.

This of course would not be possible if the investigator had not made contact personally with the participant. For example, by way of the participant contacting the investigator, or if it were that the participant had been approached by the investigator directly after giving consent to their care team for contact to be made by the research team (making direct contact with a patient purely for the purposes of research whom the investigator would otherwise not have contact with clinically, could be

considered a breach of good clinical research practice and patient confidentiality principles). The following table (table 11) lists the responses of some of the patients approached with information about the study who chose not to express an interest in the research when contacted and asked if there was anything in particular that affected their decision not to express any further interest. These enquiries were carried out by the investigator via telephone.

Reasons for patients not wishing to express further interest in research upon invitation to the study

Patient	Reasons for not expressing interest	Patient source
1	Level of commitment too great	BRU database
2	Generally of no interest	BRU database
3	Does not have the time/symptoms resolved	BRU database
4	Personal circumstances (wife is ill)	BRU database
5	Too busy to take part	BRU database
6	Doesn't want to make stress levels worse	Physician clinic
7	Well controlled on new medicines	Poster advert
8	Too busy to take part	Physician clinic
9	Receiving therapy via community services	Physician clinic
10	Too busy to take part	BRU database

Table 11

How many of the 33 patients who chose to express an interest in the study actually became participants?

Of the 33 patients who responded to the invitations, a total of 22 patients attended screening for enrolment to the study.

Why did some of the 33 patients choose to respond initially, but then not take part?

As presented in table 12 below, issues regarding time and commitment are apparent which provides at least some insight as to why patients may have decided not to take part. Patient number 11 was excluded as she was unable to provide written inform consent to screening procedures.

Reasons for patients who expressed further interest in research not taking part in the study

Patient	Reasons for not taking part	Patient source
1	Does not want to take part due to holidays	BRU database
2	Moved abroad	BRU database
3	Proximity issues and difficulty travelling to trial centre	BRU database
4	Too busy to take part	Physician clinic
5	Unable to make contact with respondent	BRU database
6	Unable to make contact with respondent	Physician clinic
7	Too busy to take part	Physician clinic
8	Too busy to take part due to university work	Physician clinic
9	Did not attend screening due to personal problems	Physician clinic
10	Unable to make contact with respondent	Physician clinic
11	Unable to read or write in English (excluded)	Physician clinic

Table 12

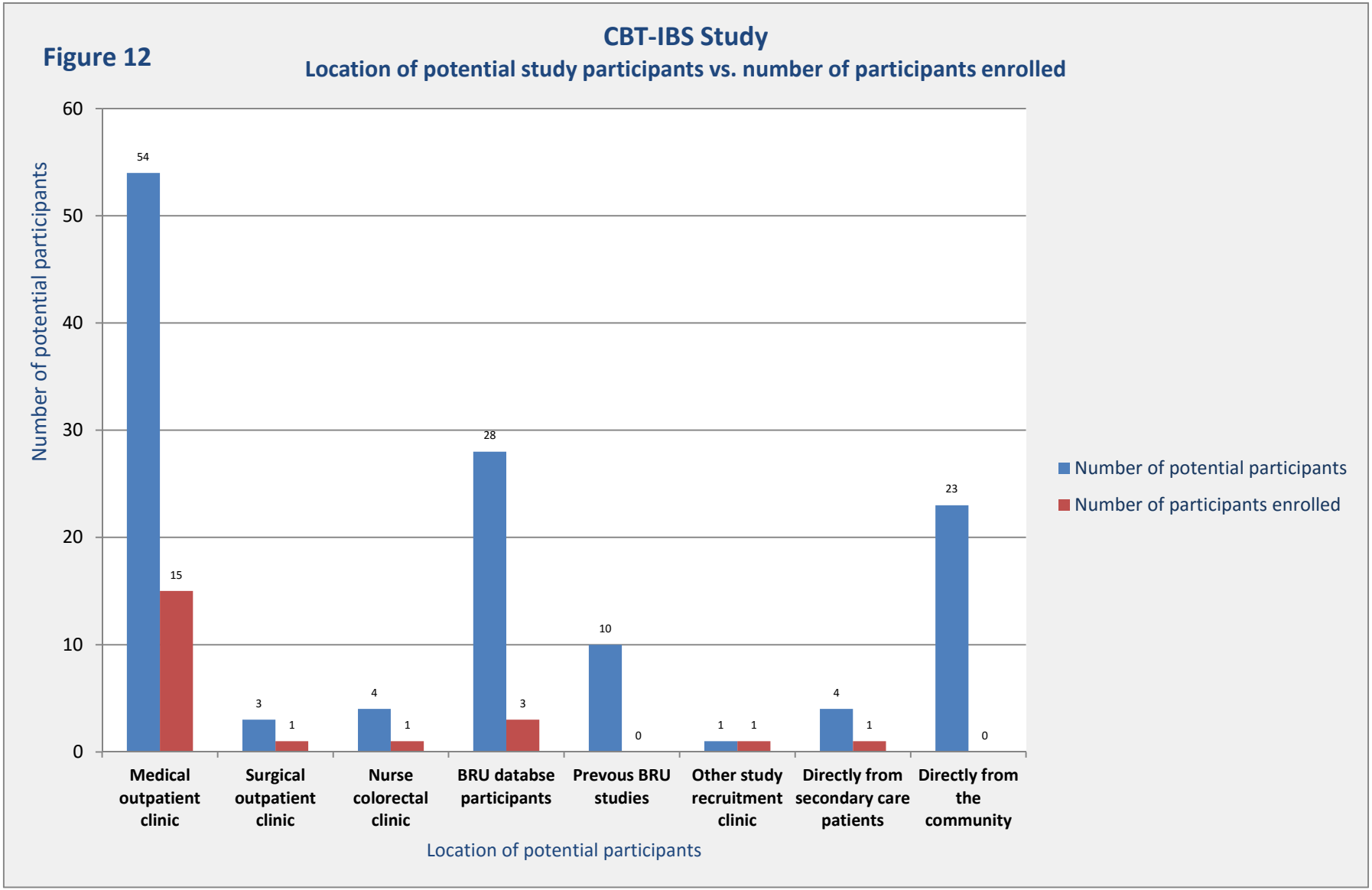
Potential participants for the study were identified from a variety of backgrounds, mostly within secondary care clinics. The following chart (figure 12) demonstrates where potential participants were located in relation to those recruited to the study and provides some further information regarding recruitment to the study. The chart demonstrates that the outpatient medical clinics were the source of the majority of potential participants, and that the conversion rate of those approached to those enrolled into the study was in the region of 27.7%. The

conversion rates for the surgical, nurse colorectal clinic and direct contacts from secondary care patients was similar with conversion rates of 33.3%, 25% and 25% respectively.

Participants approached via the BRU database yield a lower conversion rate of around 10.7%. It may be possible to explain this variation as many details within the BRU database were not current when attempts were made to follow up those contacted with study information. A simple explanation for this observation may therefore relate to the fact that some BRU database participants did not receive the information as intended.

The most valuable information contained within Figure 12 relates to a source of potential participants which was both unexpected and informative. The final column of the chart labelled 'directly from the community' represents a group of people with IBS who contacted the investigator during the conduct of the research in order to enquire about the nature of the study and their ability to participate. When asked, these people had located information about the trial on the publicly accessible trial register (ISRCTN) or via NHS websites (automatically populated and linked to the trials register). Not only is it remarkable that patients are searching the trials register for new and innovative treatments, but this also demonstrates the admirable resilience present among people with IBS who seek out such strategies to manage their condition or who have the desire to help others in similar situations to themselves (through making a contribution to science).

Figure 12


CBT-IBS Study
Location of potential study participants vs. number of participants enrolled
Number of potential participants
60
50
40
30
20
10
0
54
15
3
1
4
1
28
3
10
0
1
1
4
1
23
0
Medical outpatient clinic
Surgical outpatient clinic
Nurse colorectal clinic
BRU databse participants
Prevous BRU studies
Other study recruitment clinic
Directly from secondary care patients
Directly from the community
Location of potential participants
Number of potential participants
Number of participants enrolled

5.1.4 The experience of intervention participants

Qualitative data was collected from participants experiencing the trial interventions with the objective of understanding the experience of participants receiving the study's interventions. A total of ten participants chose to take part in the post-intervention interviews for the study. The distribution of these patients across the three intervention conditions were *n*=3 patients from the HI treatment regimen, *n*=3 from LI and *n*=4 from the pure SH (workbook only) intervention. Participants from all intervention conditions were invited to take part. The average duration of the in-depth interviews was 40 minutes (rounded up to the nearest minute). The average interview times for each of the interview groups was 47 minutes for the HI treatment participants, 41 minutes for LI participants and 30 minutes for those from the SH intervention.

The analysis of the qualitative data was carried out by the study investigator and the study interviewer, supervised by an experienced qualitative researcher according to the strategy described earlier within 4.6.4. The thematic framework was reached by consensus between the two data analysts and was focussed around the aims and objectives of the qualitative research which primarily aimed to identify barriers and facilitators to the use of the trialled interventions. The thematic framework therefore consisted of themes relating to; initial perceptions of treatment, experience of therapeutic task execution, practical considerations for engagement and perceived treatment utility. In addition to these issues, several other main themes were identified within the interview transcripts namely; impact on QOL, wider application of interventions, and reference to traumatic life events. An example of the indexing and the framework used during the analysis of the interview data is provided within Appendix 13.

Although not directly related to the identification of barriers and facilitators to the interventions described within the following section, four themes were evident throughout the qualitative data in relation to

either the experience of participants during the study or their experience with IBS more generally. Participants spoke about their past experiences of care and the impact of IBS on QOL. They also made references to traumatic life events and the application of non-CBT coping mechanisms. All participants have been allocated a pseudonym in order to protect the identity of the participant. Where direct quotes are presented, a reference to the transcript and line number is provided.

Impact of IBS on QOL

Participants described difficulties encountered as a result of suffering with IBS. In particular, the impact that IBS symptoms had on daily life events was evident throughout the range of data. Participants also described significant problems with pain, difficulty working and strain on relationships with other people.

> *"You know, I just want some help, I just want to, you know I know this isn't gonna go away but I just don't want this dull tummy ache and have to have it most days of my life, because I can't go out to work, I can't focus, you know. Going to the toilet in the morning, I go up to, probably three to six times in the morning before I even leave the house, you know it's draining" (Anne, 104-107)*

> *"Obviously when I go out anywhere, the issue of like where's the toilet and stuff my stomach bloats all the time and the pain's quite unbearable, so a lot of the time I'd rather just stay at home, cos I know if I need it I can just go to the toilet, so a lot of my friends get frustrated with it cos they don't really understand and when I say like oh I don't really feel very well, they're just thinking 'oh, she just don't wanna go anywhere'. But it's not that I don't want to go anywhere cos I would like to, it's just that issue like and if I did need it and I was somewhere I can't, I can't hold it in to say, like I know some people are just like hold till when I get home, but I can't do*

that cos if I try to hold it then it just come like, I just mess myself anyway" (Kirsty, 260-268)

Past experience of care

Participants described their frustration with a lack of effective medical treatments and a lack of understanding from healthcare professionals. These issues were captured during interview but were not asked about directly by the interviewer. Some participants also described some degree of stigma experienced either during care or from others around them.

"A lot of the times you talk to people, IBS, it's all in ya head [long pause]. You know when you're in absolute agony, and you think to yourself, cos you feel as though you're in that much pain you think you're gonna die… it's like ya just can't express how painful it is and then someone says it's all in your head. How do you feel when you are in the much pain? And you think 'Jesus Christ, I can't cope', and then someone turns round to you and says it's all in your head" (Janet, 600-604)

The stigma face by participants during previous episodes of care reduced the confidence participants had in clinicians and in some cases left them feeling like a 'nuisance' or 'neurotic'. Participants also felt dissatisfied with the lack of answers they had received regarding the cause of the symptoms they were experiencing which in some cases led to a rejection of their IBS diagnoses.

Coping Mechanisms (non-CBT)

The use of anti-motility agents, dietary manipulation, use of heat packs and laxative use was evident within the interview transcripts.

Reference to traumatic life events

Reference to traumatic life events represents a group of sub-themes which arouse spontaneously during the conduct of the interviews which are significant enough to warrant concern. Throughout the intervention

conditions, participants made reference to traumatic life events such as suicidal ideation, the loss of family members or friends, substance misuse, domestic abuse and violence. Suicidal ideation is discussed in the adverse event sections of this feasibility work as identified during the completion of study questionnaires. However, participants also mentioned these issues spontaneously during the conduct of the in depth interviews.

"I took drugs I had a great time, I thought if I die, I die. That was my attitude. I would never think right I'm gonna do that, but I did feel, like I didn't have anybody, there's nobody to talk to, nobody loved me, you know and this way I'd do this. I'd feel great and I wouldn't give a shit. That was what it was, and if I die, I die". (Anne, 129-132)

"They realised that my behaviour changed when my now ex-husband came to visit me, and they realised that it wasn't post-natal depression that I was suffering from, that It was erm, a mental, it was a mental, it wasn't physical abuse, it was mental-verbal and I'd had it for seven years" (Mandy, 72-74)

"I moved from after a domestic violence relationship and basically I went into safe houses, BnB's, hostels, because this person that I made a silly mistake with, was probably schizophrenic, he was like a loose cannon, he was dangerous" (Anne, 156-158)

"I think by nature I am a worrier anyway and I mean I don't know whether that's relevant for this but I think it was made worse because my mother died of cancer last Christmas" (Isabel, 171-173)

5.1.5 Barriers and facilitators to interventions

There were four main themes evident within the interview data which relate directly to the objectives of the study interviews regarding the

identification of barriers and facilitators to the implementation of the trialled interventions. The four themes consist of; the participant's initial perceptions of treatment, the experience of executing therapeutic tasks, practical considerations for engagement and the perceived utility of treatment. Participants within each of the intervention conditions were also asked if they would recommend the treatment they received to a friend or family member suffering with IBS (otherwise described as the *'friends and family test'*).

SH intervention themes

Initial perceptions of treatment

Understanding the initial perceptions that participants experienced about the interventions or enrolment into the study should be considered essential for a number of reasons. Understanding these factors is likely to give researchers a better understanding of what exactly it is that motivates patients to take part in CBT interventions for the treatment of IBS. These issues are also likely to have implications on how interventions are communicated to patients in routine care and might also affect the nature of information patients are given prior to treatment.

Participants within the SH intervention had negative views about the intervention and in particular, two of the participants stated they would have preferred therapist delivered interventions. This appeared to affect the initial perceptions participants had about treatment and there was some element of doubt regarding the likely benefits of implementing SH.

> *"My initial thought was just to try it and just see what's gonna help but I didn't think it would be that helpful… I didn't think that by reading a book it's gonna make anything better for me"*
> *(Kirsty, 19-22)*

As suggested by Kirsty, she was initially sceptical of the likely benefits of the treatment condition to which she had been randomised. Consistent

with Kirsty's view, three of the SH participants felt that the intervention would not be useful. There was also some evidence that conflicting advice had been received from medical professionals which may have had some bearing on the participant's initial perceptions of treatment as described within the following quotation.

> *"Well the trouble is of course I've been on, well I thought all along that it least it probably had a stress related component but I've been, well not exactly talked out of it but whenever I've mentioned it the person I've been seeing has always directed it back to diet" (Darren, 105-107)*

Darren suggests that although he had been able to self-identify a relationship between stress and IBS, his clinician had insisted upon dietary causation. This created some confusion regarding the perception the participant had with both routine dietary and trialled psychological interventions. The participant felt that for him to have confidence in an intervention for his longstanding IBS, ambiguity between professionals surrounding causation should be resolved.

Experience of therapeutic task execution

The theme relating to therapeutic task execution encompasses the complex phenomena surrounding putting the components of the evidence based interventions into practice in daily life. Participants receiving SH treatments lacked confidence in their ability to understand and execute tasks as described within the workbooks. This was particularly evident with the relaxation exercises which participants struggled to interpret and implement from the descriptions provided. Participants experienced difficulties implementing some components of the intervention or felt that further support was required at some point during the treatment.

> *"The breathing thing, ya know I did have to read it about ten times, if not more and after I understood it, doing it was even more difficult and it got frustrating. It was like, there was no one there to say are you're doing this right or, ya know I just*

couldn't conquer it and I just kind of had to come away an move onto the next book" (Anne, 244-247)

Participants also suggested that it would have been useful to have therapist feedback regarding the practice of relaxation techniques. As suggested by Anne above, not receiving feedback was problematic and the subsequent result was that the intervention was not implemented as intended. Darren describes his difficulties with written relaxation activities as follows.

"The deep breathing I couldn't really follow it too straight forwardly erm… because I found the whole thing a bit counter-intuitive in that when it said I should breathe in I was wanting to breathe out and so on" (Darren, 151-153)

Practical considerations for engagement

The lack of therapist input continued to be problematic for some participants throughout their experience of the intervention. For Darren, these issues not only related to the use of relaxation techniques, but also with regard to the personal applicability of the material.

"It's almost as if this has been too superficial really, and I think that's why probably I realised why, in the first place that I would have preferred to have had the, you know, the interventionist type of approach from either [investigator's name removed] or from the psychiatrist" (Darren, 174-176)

Upon closer investigation, these issues also had a tendency to relate to the amount of social contact or support participants had in general. Darren further described how the lack of social relations impacted upon his ability to carry out relaxation (imagery) as intended due to personal social circumstances.

"I thought if, and I'm not with someone if, I'm not in a relationship where something like this means you know I would enjoy it" (Darren, 162-166)

In contrast to these problems, other SH participants had access to social support in terms of carrying out treatment related activities, but chose to remain autonomous and carry out their activities alone. Interestingly, these participants also felt that reviewing their activities with a therapist would have been helpful. These issues did not relate to confidentiality or concerns relating to sensitive issues although some concern regarding stigma was evident.

"Sort of, yeh, but, in a honest way I thought it makes me feel like I'm a bit mental and need like psychiatric help to overcome it rather than, actually I know that there is actually something wrong" (Anne, 42-44)

Where relaxation techniques were implemented successfully, participants found them useful for reducing stress and for dealing with pain. In relation to the format of the materials, participants suggested the workbooks were useful to refer back to in the future and valued the lack of jargon or complex terminology within the text. One of the participants struggled interpreting the workbook text due to dyslexia.

Perceived utility of treatment

Participants felt that their knowledge relating to IBS was improved. Although one might see increasing knowledge as a factor during the application of SH interventions, participants themselves suggested that increased knowledge had little or no impact upon their IBS.

Participants found the components of the interventions useful for not only IBS, but were also applicable to other aspects of life. This was facilitated by the presence of scenarios and narratives located within the text which were valuable for helping participants identify with themselves within the material. This helped participants to understand that others suffer with similar problems which helped to normalise the experience of IBS.

It also helped participants to think differently about the way that they may be judged by others or accept alternative thoughts about the thoughts, behaviours and attitudes of other people. These narratives and scenarios proved to be very powerful facilitators for changing the cognitions of participants who implemented new ways of thinking about social situations which had practical application to real life situations.

"If I was getting symptoms cramps or gas or whatever, and I'd be a bit worried about what other people would think, but I don't really care now. I've come to the conclusion that I don't think they care and they probably wouldn't even notice anyway" (Yvette, 79-82)

Participants also developed confidence in the notion that IBS may be related to stress or heightened states of arousal as described here by Darren.

"I think you are probably right, it's psychologically based, the problems, the IBS is psychologically based rather than erm food based" (Darren, 187-191)

When participants were able to recognise the relationship between stress and IBS, this facilitated the successful implementation of therapeutic techniques such as relaxing imagery.

"when I feel like I'm in a stressful situation or anything like that, just think of that and it sort of, not necessarily like stops any of the symptoms cos they happen anyway, but if somethings gonna make it worse like in a stressful situation, then that helps just to try an control it to a normal level" (Kirsty, 65-70).

Friends and family test

Participants within all three treatment conditions were asked if they would recommend the intervention to friends or a relative in a similar situation to themselves. Three out of four of the SH participants said that they would recommend the treatment as a useful intervention. The participant that did not recommend the intervention felt that a therapist led intervention would have been much more suitable for applying the intervention components to personal circumstances.

LI-CBT intervention themes

Initial perceptions of treatment

Three participants randomised to the LI-CBT intervention agreed to participate in the post-intervention interviews. Two of the participants described how their motivation to take part in the intervention was driven by the notion that they would have *tried anything* to get some relief from the burden of IBS. There was evidence to suggest that to some extent, the confidence participants had regarding their diagnosis of IBS could influence their initial perceptions of treatment as described by Janet.

> *"Well my initial thought was, I actually don't have IBS?.... But, it would be an absolute waste of my time, and your time. Cos at the end of the day, I didn't feel as though I had IBS" (Janet, 20-22)*

One of the participants described that she would have been disappointed with the workbook only intervention and was positive about receiving LI-CBT.

Experience of therapeutic task execution

Relaxation exercises were a particular feature of the subthemes surrounding the execution of the components of the intervention. Relaxation exercises were described as helpful when carried out alongside the therapist, but could become difficult to implement when

out of session and alone. The participant's quotation below suggests that physically carrying out breathing techniques outside of the session was where such difficulties arose.

"I think it's trying to breathe, like not from my chest and to do the deep breathing properly, that's something I need to practice on" (Hannah, 74-75)

One of the participants described problems interpreting the text due to problems with dyslexia, which was not screened for during study enrolment. These issues were overcome with the support of a partner. The participants valued having the ability to discuss problems with aspects of the intervention with the therapist. There was some evidence to suggest that one of the participants struggled to execute the therapeutic tasks as the treatment protocol used in the study was not flexible enough to accommodate personal circumstances and was bias toward the management of anxiety.

Practical considerations for engagement

Therapist support within the LI-CBT interventions directly influenced the participant's ability to engage with the course of treatment. The data suggests that this was due to the fact that participants valued talking about the experience of IBS or valued face to face contact with the therapist. Treatment experiences were not always shared with others outside of the intervention delivery as participants felt this may be burdensome to friends or family. There was also some evidence to suggest that participants found it both beneficial and challenging to talk about 'toilet habits' or their experiences of IBS with the therapist.

The following quotation highlights these phenomena.

"It's quite personal things that you are actually talking about is extremely personal, and if you have my kind of opinion and judgement on things, there are some things you just don't talk about…And this is definitely that one thing kind of things you

do not talk about and ya know to start off with and that, sitting there and talking to [investigator/therapists name removed], I found it very hard" (Janet, 690-694)

There were other barriers to engagement which closely relate to the quotation provided above. Participants described difficulty implementing intervention components which clashed with personal views regarding acceptable standards of behaviour. For example, breaking wind or frequent toilet visits in social situations was seen as unacceptable regardless of participation in exposure or cognitive restructuring interventions.

Although the LI-CBT format of treatment seemed acceptable to participants, there was some concern regarding the limited length of sessions or too few sessions during the intervention period. For some participants, therapy may have uncovered phenomena which required further intervention which was not covered by the rigid application of the study treatment protocol or within the treatment timeframes permitted. One of the participants also described how she felt obliged not to engage in additional interventions outside of the study during the follow up period.

"The exposure was quite good for me cos I realise that there's a lot of things that like I've supressed, like over the years and stuff that have caused anxiety in certain situations but I never really thought about it. You know, you just feel anxious at the time and you not really think why. So at the moment now, I've got a big list of things that I know I need to address" (Hannah, 170-173)

Perceived utility of treatment

Sub-themes regarding a lack of individualised material (workbooks) and the interventions being too focussed upon the treatment of anxiety continued to feature when participants reflected upon the perceived utility of treatment. However, the treatment protocol enabled participants

to accept and recognise the role of anxiety or stress relating to IBS symptomology and accept a diagnosis of IBS. Relaxation was felt by all participants to be a useful intervention component. Where participants had simultaneously been referred to both the trial team (for potential CBT treatment) and the intervention of a dietician during routine care, the coexistence of these two parallel treatments evaluated particularly well. These phenomena do however highlight the presence of confounds during the feasibility study.

> *"To me, it was like, reading these workbooks and actually going through this and actually getting an understanding I actually do have IBS. Starting the erm, dietician thing an actually, this is actually working for me. But then all this started triggering up things of like, I do have IBS because this workbook and this is what's been happening" (Janet, 41-44)*

There were mixed feelings among the participants regarding whether the intervention had any impact upon IBS, which was described as having no impact whatsoever, to a positive and direct impact on IBS or was beneficial to wider application (for example, other areas of life).

> *"That obviously did have an effect because, it was some things about, like what perceptions people had about me at work, cos obviously going to work made me feel anxious in certain situations, erm so that would affect my IBS but now I'm not anxious about going to work anymore then obviously, that doesn't affect my IBS" (Hannah, 87-90)*

Friends and family test

All three participants interviewed would recommend their treatment to a friend or relative in a similar situation to themselves regardless of whether or not they themselves found the intervention useful.

HI-CBT intervention themes

Initial perceptions of treatment

Participants within the HI-CBT condition of the study described how they had strong belief's regarding a relationship between mind and body and wanted to take control of IBS. There were data to suggest that participants would have been disappointed if randomised to the control or workbook condition of the study and valued to interaction with a therapist. Interestingly, two of the participants also felt that their motivation for taking part in the intervention was derived from the perception that all other treatments had failed or that there was 'nothing else left to try'. In this sense, CBT treatment was seen as a last resort.

Experience of therapeutic task execution

The execution of HI-CBT therapeutic tasks was a challenge for participants. Some examples of these issues involve dealing with 'deep rooted' problems and a lack of awareness regarding the extent to which therapy was perceived to be intrusive as described by Mandy.

"Well, initially I was going to walk out and not come back. So I will tell you, that's how much of a surprise it was"
(Mandy, 25-26)

As portrayed in the quotation provided, these issues had the potential for participants to end participation in the course of treatment during early stages. In this regard, participants suggested that a thorough introduction should inform patients about the nature of CBT interventions so that patients were better prepared for dealing with difficult issues during therapy. Such issues may therefore have led to early discontinuation.

Practical considerations for engagement

There were several strong sub themes evident within the textual data pertaining to issues of engagement with therapy. For participants receiving the HI-CBT treatment regimen, participants felt that the good

personality of the therapist delivering the intervention was crucial to engagement. There was also a strong emphasis on the need for appointment times to be flexible in order for therapy to fit around working patterns and other activities. These issues were influential to the extent that they would have prohibited engagement if flexibility did not exist in relation to session appointment times and flexibility.

"Oh if I'd been working I don't know whether I would have been able to do this… No, I don't think my employer would have given me the time off" (Isabel, 409-411)

A particular feature of the HI-CBT treatment that evaluated particularly well was therapist facilitated relaxation. Participants felt that the therapist carefully demonstrated relaxation techniques alongside the participant which promoted engagement and improved their ability to practice relaxation. In addition to these attributes, participants also valued the face to face contact they had with the therapist which facilitated engagement with the therapeutic task and increased confidence during the execution of treatment related activities.

"I think if you see somebody face to face erm…you…if you read something out of a book, you can take it the wrong way, or you could go off on the wrong track. But when you talk to someone, you're actually getting a response aren't you?" (Jacky, 102-104)

In addition to the contact participants had with the therapist, participants also valued social contact outside of treatment sessions which was helpful for discussing sensitive subjects or for executing tasks such as receiving feedback regarding behaviour. In contrast to these views, there was also evidence of some reluctance to involve others in the treatment process.

"With people other than my partner really, but I don't go into any great detail there either. I have to be careful because he's

younger than me. I don't want to come across as ya know, an old lady" (Isabel, 145-147)

The documentation within the HI-CBT intervention could have been improved as some participants reported problems with the quality and limited quantity of supporting materials. In relation to session length and number of sessions, there were mixed feelings. There was some evidence to suggest that flexibility in the number and time between sessions would have been beneficial. This was particularly evident when participants had come to a natural end to treatment, but continued with sessions as per study protocol. These factors may therefore have contributed to discontinuation of the intervention by two of the intervention participants.

Perceived utility of treatment

Treatment was perceived to be useful for improving the control participants had over the management of their condition and improved understanding of how mood might relate to IBS. Participants described changes in thought processes, felt more relaxed and accepted the role of anxiety, stress or other psychological aspects of IBS.

"I think I am more aware. I was sort of aware of the impact of stress levels on IBS, but I'm even more aware now. If I do feel stressed for some reasons, I think even before anything's happened I think 'oh, if I don't control this my stomach's going to kick off'. So I'm more aware of that now" (Isabel, 519-521)

Relaxation techniques also evaluated well, and were implemented successfully by participants. Scenarios were useful for participants to identify situations where interventions could be implemented and participants also described how aspects of the treatment could be applied to other non-IBS related issues. Two participants described symptom improvements.

Friends and family test

All three HI-CBT participants would recommend the intervention to a friend or family member in a similar situation to themselves. One participant felt that she could only do so if participants were better prepared in relation to the potential intrusiveness of therapy.

Interrelated intervention themes

Initial perceptions of treatment

Themes within the differing treatment modalities have been presented and discussed within the previous sections. There were some similarities and differences between the treatment conditions which may have particular relevance to the feasibility of the interventions. SH participants were mostly disappointed with the treatment to which they had been allocated, some of whom clearly stated that they would have preferred a therapist led course of treatment. These views were also reinforced by participants receiving HI-CBT who also felt that they would have been disappointed with the TAU or SH treatment conditions. Specifically, the prospect of therapist interaction improved initial perceptions of treatment and engagement. There was also doubt regarding the likely benefits of SH treatment prior to intervention delivery.

Throughout the intervention conditions, participants interestingly described how their motivation to participate in CBT treatments was driven by the failure of conventional therapy or that treatment was in fact a 'last resort'. There was also some evidence that contradictory advice received from medical professionals had some bearing on the initial perceptions of treatment. This was particularly evident when participants had detected ambiguity among professionals regarding the cause of IBS.

Experience of therapeutic task execution

Relaxation was a particular feature of the themes derived from each of the treatment conditions and participants described relaxation techniques as useful in the day-to-day management of their IBS. Some participants

struggled with their ability to implement relaxation techniques which also appeared to relate to the mode of treatment. Participants receiving SH found the interventions much more difficult to implement than those with delivered therapies. Therapist facilitated relaxation (the therapist physically doing the relaxation activities alongside participants) was found to be very helpful, particularly for participants within the HI-CBT condition. Feedback from therapists increased confidence in participant's ability to correctly execute relaxation techniques correctly.

The intensity of HI-CBT treatments and in particular, the depth and breadth of treatment could be problematic and preparation for therapy was recommended. These issues were not a feature of the SH or LI-CBT approaches, although some lower intensity treatment approaches were considered to be 'too superficial' or not of sufficient intensity for addressing complex problems. Participants valued the prospect of face to face therapy which could impact directly on the initial perceptions of treatment and their ability to correctly execute tasks. Executing therapeutic tasks was difficult for participants experiencing dyslexia, although such issues may be overcome with therapist or family support.

Practical considerations for engagement

The lack of therapist input was particularly problematic for SH participants and was considered essential by participants within the LI-CBT and HI-CBT forms of treatment. Participants specifically suggested that face to face contact with therapists was highly valued. Social support or interaction was useful for some participants when implementing treatment related activities, whilst others chose to remain autonomous and carry out their activities alone. Interestingly, these participants also felt that reviewing their activities with a therapist would have been helpful. Some participants described how they were reluctant to burden friends or family with IBS related issues. Participants experienced difficulty implementing intervention components which clashed with personal views regarding acceptable standards of societal conduct or behaviour.

Where participants received therapy from a therapist, the personality of the therapist influenced the execution of therapeutic tasks, and a good personality was seen as a facilitator to building a good therapeutic relationship. Interestingly, an additional benefit for participants receiving lower-intensity treatment was that participants suggested the workbooks were a valuable resource. There was some concern that the materials could be difficult to tailor to individual circumstances, although the presence of narratives or real life scenarios helped improve the applicability of the material.

There was also a strong emphasis on the need for therapist delivered therapy to be flexible in order for therapy to fit around working patterns and other activities. These issues were particularly important to participants in work. Documentation within the HI-CBT intervention could have been improved. There were mixed views regarding the length of number of treatment sessions for therapist interventions. Participants suggest that the number of sessions and session duration should be tailored to meet individual needs and remain flexible rather than rigidly applied according to treatment protocols.

Perceived utility of treatment

Participants felt that their knowledge relating to IBS was improved. Narratives within the text helped participants to understand that others suffer with similar problems to themselves which helped to normalise the experience of IBS. Participants developed confidence in the notion that IBS may be related to stress or heightened states of arousal. Where successful, the interventions enabled participants to accept and recognise the role of stress relating to IBS symptoms and reduce doubt they had about IBS diagnoses.

Relaxation was considered a useful intervention component when difficulties implementing relaxation techniques were addressed. There were mixed feelings among participants regarding whether the intervention had any impact upon IBS. Some participants described

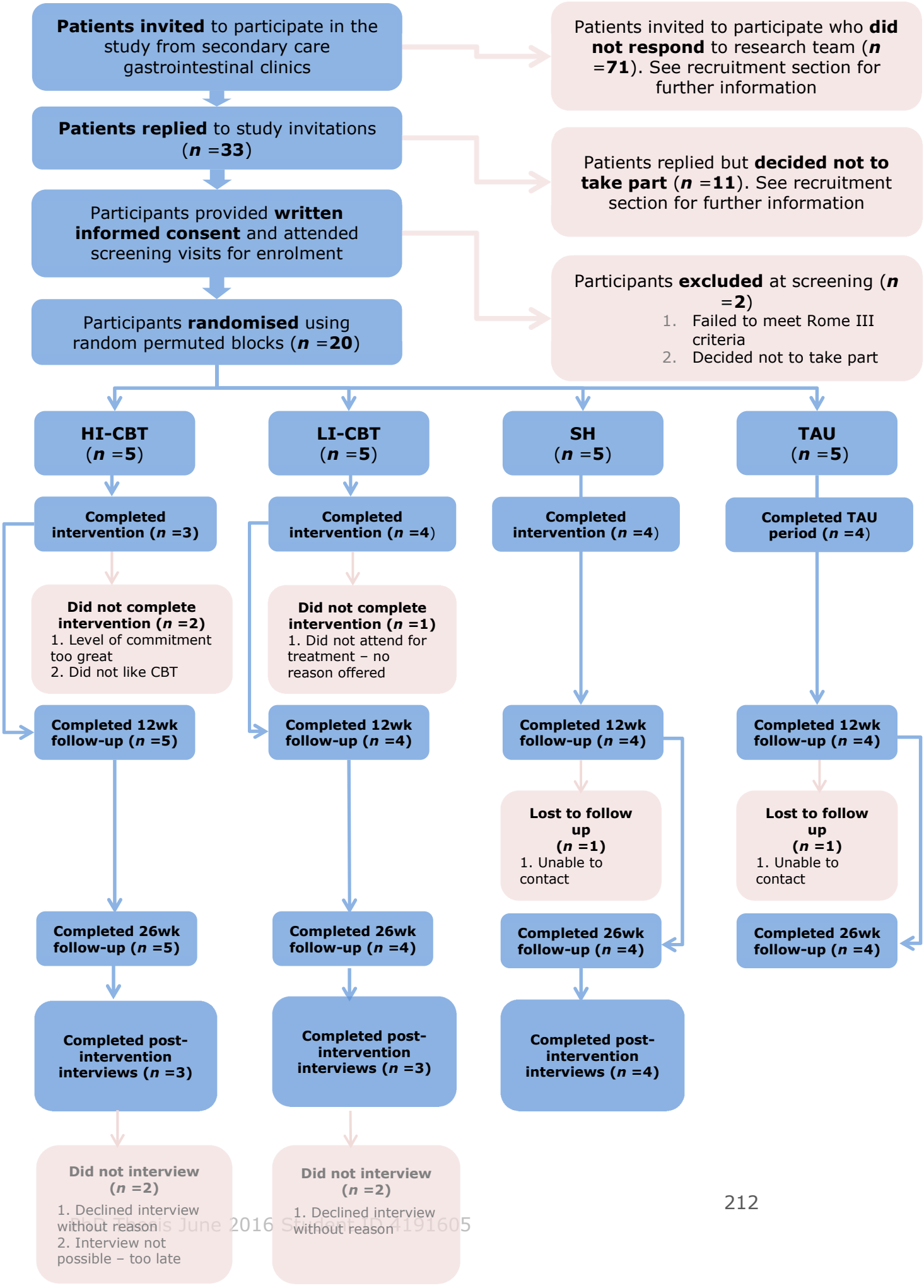
symptom improvement but improved coping mechanisms and the wider application of interventions to other aspects of life was more evident.

5.1.6 Follow-up and response rates

Figure 13 is a representation of the flow of participants throughout the feasibility study as recommended by the CONSORT guidelines (CONSORT, 2012). Participants who chose to drop out of the study or decline participation in post intervention interviews are detailed in the red shaded boxes. Just two of the participants consented to the study failed the screening process. One of these did not meet Rome III criteria for IBS. The second participant decided not to take part in the study once further information was provided, no further explanation was provided in this regard.

Two participants did not complete the HI-CBT intervention because of commitments or did not like CBT. Although these participants chose to withdraw from treatment, they agreed and continued to complete follow up questionnaires. One participant did not arrive for treatment when allocated to the LI-CBT intervention and was lost to follow up or further contact. A total of three participants or 15% were lost to follow up from twelve week follow up period onward. No participants were lost to follow up from the HI-CBT treatment condition. Unfortunately, none of the participants who were lost to follow up were contactable during the study period and did not provide reasons for dropping out.

Figure.13 Feasibility Study Flow Chart



5.1.7 Descriptive analysis of clinical outcome data

The descriptive quantitative data was collected from participants at baseline, 12 weeks and 26 week follow up periods. The data, along with demographic observations were entered onto electronic Microsoft Access CRF forms which were designed to populate the Microsoft Access study database. Strict auditing and checking of imputed data was followed, and prior to analysis, all quantitative variables were checked against the source data for correct entry into the study database as would be the case within a full scale RCT. Data were then transferred from the database into Microsoft Access, which made possible the transfer of data to SPSS V22 software for analysis. The last observation carried forward (LOCF) technique was used to impute data for the three participants which were lost to follow up at 12 and 26 week follow up periods along with other missing data (which included only three missing observations from the 34 item IBS-QOL measure).

The following table (table 13) demonstrates the demographic data collected from participants who were eligible to take part in the study, and were randomised to one of the four treatment conditions.

Table 13 Participant demographic data

		Treatment condition				
		HI-CBT (*n* = 5)	**LI-CBT** (*n* = 5)	**SH** (*n* = 5)	**TAU** (*n* = 5)	**Total** (*n* = 20)
Female, *n* (%)		**5** *(100)*	**4** *(80)*	**4** *(80)*	**4** *(80)*	**17** *(85)*
Age (years), Mean (S.D.)		**56.6** *(14.4)*	**40.0** *(18.9)*	**37.2** *(18.5)*	**44.0** *(15.7)*	**44.5** *(17.4)*
Age diagnosed with IBS (years), Mean (S.D.)		**47.8** *(10.9)*	**37.4** *(18.6)*	**31.4** *(12.1)*	**32.8** *(13.6)*	**37.4** *(14.5)*
Rome criteria, *n* (%)	IBS-C	**0** *(0)*	**1** *(20)*	**1** *(20)*	**0** *(0)*	**2** *(10)*
	IBS-D	**3** *(60)*	**2** *(40)*	**2** *(40)*	**2** *(40)*	**9** *(45)*
	IBS-M	**2** *(40)*	**2** *(40)*	**2** *(40)*	**3** *(60)*	**9** *(45)*
IBS onset associated with infective episode, *n* (%)		**0** *(0)*	**3** *(60)*	**0** *(0)*	**0** *(0)*	**3** *(15)*
Previous received psychotherapy, *n* (%)		**1** *(20)*	**0** *(0)*	**1** *(20)*	**0** *(0)*	**2** *(10)*
Antidepressant use, *n* (%)		**2** *(40)*	**0** *(0)*	**2** *(40)*	**2** *(40)*	**6** *(30)*
Ethnic origin, *n* (%)	White British	**4** *(80)*	**5** *(100)*	**5** *(100)*	**5** *(100)*	**19** *(95)*
	White other	**1** *(20)*	**0** *(0)*	**0** *(0)*	**0** *(0)*	**1** *(5)*
Household income, *n* (%)	< £15000	**0** *(0)*	**1** *(20)*	**1** *(20)*	**0** *(0)*	**2** *(10)*
	£15000-£19999	**0** *(0)*	**2** *(40)*	**0** *(0)*	**0** *(0)*	**2** *(10)*
	£20000-£29999	**2** *(40)*	**1** *(20)*	**1** *(20)*	**2** *(40)*	**6** *(30)*
	£30000-£39999	**2** *(40)*	**0** *(0)*	**1** *(20)*	**0** *(0)*	**3** *(15)*
	£40000-£49999	**0** *(0)*	**0** *(0)*	**1** *(20)*	**1** *(20)*	**2** *(10)*
	£60000-£69999	**0** *(0)*	**1** *(20)*	**1** *(20)*	**2** *(40)*	**4** *(20)*
	£70000-£99999	**1** *(20)*	**0** *(0)*	**0** *(0)*	**0** *(0)*	**1** *(5)*
Marital status, *n* (%)	Divorced or separated	**1** *(20)*	**0** *(0)*	**0** *(0)*	**1** *(20)*	**2** *(10)*
	Living as married	**1** *(20)*	**0** *(0)*	**0** *(0)*	**0** *(0)*	**1** *(5)*
	Married	**3** *(60)*	**1** *(20)*	**1** *(20)*	**3** *(60)*	**8** *(40)*
	Single	**0** *(0)*	**3** *(60)*	**4** *(80)*	**1** *(20)*	**8** *(40)*
	Widowed	**0** *(0)*	**1** *(20)*	**0** *(0)*	**0** *(0)*	**1** *(5)*
Social status, *n* (%)	Living alone	**0** *(0)*	**1** *(20)*	**1** *(20)*	**0** *(0)*	**2** *(10)*
	Shared accommodation	**0** *(0)*	**2** *(40)*	**0** *(0)*	**0** *(0)*	**2** *(10)*
	With relative or friend	**1** *(20)*	**0** *(0)*	**1** *(20)*	**1** *(20)*	**3** *(15)*
	With spouse or partner	**4** *(80)*	**2** *(40)*	**3** *(60)*	**4** *(80)*	**13** *(65)*
Education, *n* (%)	Grammar sch/college	**1** *(20)*	**2** *(40)*	**3** *(60)*	**2** *(40)*	**8** *(40)*
	Primary school	**0** *(0)*	**0** *(0)*	**1** *(20)*	**0** *(0)*	**1** *(5)*
	Secondary school	**2** *(40)*	**0** *(0)*	**0** *(0)*	**2** *(40)*	**4** *(20)*
	Technical/professional	**1** *(20)*	**1** *(20)*	**0** *(0)*	**0** *(0)*	**2** *(10)*
	University degree	**1** *(20)*	**2** *(40)*	**1** *(20)*	**1** *(20)*	**5** *(25)*
Smoking status, *n* (%)	Currently smoking	**0** *(0)*	**0** *(0)*	**2** *(40)*	**1** *(20)*	**3** *(15)*
	Reported never smoked	**5** *(100)*	**4** *(80)*	**3** *(60)*	**2** *(40)*	**14** *(70)*
	Reported previously smoked	**0** *(0)*	**1** *(20)*	**0** *(0)*	**2** *(40)*	**3** *(15)*
Alcohol consumption U/week, mean (S.D.)		**2.0** *(2.9)*	**9.3** *(13.6)*	**.0** *(.0)*	**5.7** *(6.1)*	**4.3** *(7.9)*

The data within table 13 is presented along with the percentage of participants (%) and the Standard Deviation (S.D.) of the mean statistic where applicable. One will observe from the size of the S.D.'s reported within the table, that there was significant variability within this small sample (the distribution of the observations represented by large S.D.'s from the reported mean) in terms of age in years and age diagnosed with IBS. For example, in the LI-CBT condition, the mean age was 40 years with an associated S.D. of 18.9 years representing a broad age range of participants. However, this was similar for the whole study sample (mean age 44.5 years, S.D. 17.4). The mean age diagnosed with IBS within the HI-CBT condition was slightly higher than the sample mean at 47.8 years (S.D. 10.9) vs. 37.4 years (S.D. 14.5) respectively. The study was not sufficiently powered to statistically compare such differences although they should be considered during the interpretation of data.

Eighty five percent of the participants randomised to the study were female and there were no males in the HI-CBT treatment condition. The mean age of participants was 44.5 years (S.D. = 17.4) which was similar within the LI-CBT, SH and TAU conditions. Participants in the HI-CBT intervention were slightly older with a mean age in years of 56.6 (S.D. = 14.4). The sample represents an equal mix of participants with IBS-D and IBS mixed (IBS-M), and just 10% were found to have IBS-C according to Rome III criteria. No participants were found to have IBS ungraded (IBS-U) according to Rome III criteria.

Thirty percent of the sample was using anti-depressant medications at the time of baseline data collection and 15% had previously been exposed to some form of psychological interventions. A variety of changes to these baseline data were noted during the study period which highlight potential confounding factors. One participant within the HI-CBT treatment condition was prescribed an SSRI during the treatment period. Referral to a dietician was not prohibited during the conduct of the study as this formed part of routine gastrointestinal care at the study centre.

Three participants were seen by a dietician between baseline and 26 week follow up, all three of which were in the LI-CBT condition of the study. It is therefore possible that these factors may be responsible for the noted changes described within the following section and should be carefully considered as exclusion criteria within a follow on study if confounds are to be avoided. One participant from the LI-CBT treatment condition was exposed to further psychotherapy upon completion of the intervention following self-referral to a community mental health service. In this case, the participant felt that further psychotherapy would be useful for the treatment of anxiety and depression identified during the conduct of the study. Further details regarding this exposure were not collected and will need to feature within a follow on study if potential confounds are to be fully understood and factored into a statistical analysis.

Sixty percent of participants within the LI-CBT treatment condition associated the onset of IBS with an episode of dysentery. The mean level of alcohol consumption was 4.3 units per week (S.D. = 7.9). The SH sample did not report weekly alcohol consumption. The sample consists mainly of white-British participants (95%) with only 1 participant from a white-other ethnic origin. The sample had a range of household income, ranging from £<15’000 to £99’999, and 30% of the sample had a household income of £20’000 - £29’999. Eighty percent of the sample was living with a relative, friend, spouse or partner with just 10% living alone or within shared accommodation (10%). Eighty five percent of the sample reported not smoking on enrolment.

Symptom severity

The following table (table 14) represents the findings of the study in relation to the observed changes within the treatment conditions on the 5 subdomains of GSRS-IBS. The subdomains were calculated by working out a mean score of each of the following items within each subdomain (sum of the domain scores / number of variables in the domain).

1. **Pain syndrome**; Q1 Abdominal pain, Q2 Pain relieved by a bowel action.
2. **Bloating syndrome;** Q3 Bloating, Q4 Passing gas, Q13 Visible distension.
3. **Constipation syndrome**; Q5 Constipation, Q8 Hard stools.
4. **Diarrhoea syndrome**; Q6 Diarrhoea, Q7 Loose stools, Q9 Urgent need for bowel movement, Q10 Incomplete bowel emptying.
5. **Satiety**; Q11 Fullness shortly after meal, Q12 Fullness long after eating.

Participant GSRS-IBS subdomain mean scores

Table 14

		Treatment condition			
		HI-CBT	**LI-CBT**	**SH**	**TAU**
		(*n* = 5)	(*n* = 5)	(*n* = 5)	(*n* = 5)
Pain					
Baseline	Mean S.D.	**4.3** 1.3	**5.3** 1.1	**4.6** 1.4	**3.4** 0.7
12 weeks		**2.6** 1.3	**3.8** 1.5	**3.9** 1.4	**3.2** 0.7
26 weeks		**2.4** 1.1	**4.1** 1.3	**3.3** 1.1	**3.9** 1.3
Bloating					
Baseline	Mean S.D.	**4.3** 1.4	**4.7** 1.0	**4.3** 1.2	**3.2** 1.2
12 weeks		**2.9** 1.3	**3.7** 1.6	**3.9** 1.4	**3.9** 1.6
26 weeks		**2.6** 1.4	**3.5** 1.5	**4.3** 1.7	**3.7** 1.8
Constipation					
Baseline	Mean S.D.	**2.4** 1.6	**2.9** 2.7	**2.4** 2.4	**2.6** 2.3
12 weeks		**1.9** 1.5	**2.8** 2.3	**2.5** 2.6	**3.0** 1.4
26 weeks		**1.8** 1.1	**2.2** 2.2	**2.2** 2.7	**3.1** 2.1
Diarrhoea					
Baseline	Mean S.D.	**4.5** 2.0	**3.7** 1.8	**4.8** 1.5	**3.2** 0.8
12 weeks		**2.9** 0.9	**2.6** 1.0	**3.9** 1.8	**4.0** 1.4
26 weeks		**3.0** 0.8	**2.6** 1.0	**3.4** 1.3	**4.2** 2.1
Early Satiety					
Baseline	Mean S.D.	**3.0** 2.0	**2.9** 2.2	**1.6** 0.9	**2.2** 1.4
12 weeks		**2.4** 1.7	**2.1** 0.8	**2.5** 1.8	**2.8** 1.5
26 weeks		**2.5** 2.1	**2.2** 1.0	**2.3** 1.2	**2.9** 2.1

The data in table 14 demonstrates that participants receiving HI-CBT reported a reduction in mean pain symptom scores from 4.3 (S.D. = 1.3) to 2.4 (S.D. = 1.1). Differences are apparent between the groups at baseline. The TAU condition did not yield reductions in satiety, constipation, diarrhoea or pain scores between baseline and 26 week follow up. Participants within the HI-CBT and LI-CBT interventions experienced baseline symptom score reductions within all five subdomains. Participants within the SH treatment condition experienced symptom reductions for pain, diarrhoea and constipation, but not for early satiety or bloating.

The greatest symptom score reductions can be observed for pain (-1.9 S.D. = 1.7) and bloating (-1.7 S.D. = 1.2) in the HI-CBT treatment condition. The formula *100/baseline observation * change score* generates a percentage of change statistic. For example, the aforementioned values represent a 44.1% reduction in symptoms of pain, and a 39.5% reduction in bloating for participants within the HI-CBT group. Similar changes were observed in the LI-CBT treatment condition with a reduction of -1.2 (S.D. = 1.8) and -1.2 (S.D. = 1.1) for pain and bloating respectively. Accordingly, a 22.6% reduction in pain and a 25% reduction in bloating were evident within LI-CBT.

Participants within the SH condition had less of a reduction in pain and bloating at -1.3 (S.D. = 1.4) and -.1 (S.D. = .7) respectively. Participants within the TAU condition experienced an increase in pain and bloating by .5 (S.D. = 1.1) and .5 (S.D. = .8) respectively. The percentage change for these values within SH would be a 28.2% reduction in pain and a 2.32% reduction in bloating. For participants within the TAU condition, pain and bloating were increased by 14.7% and 15.6% respectively. The following table (table 15) helps to quantify the observed changes in participants overall GSRS-IBS scores, rather than subdomains.

Participant GSRS-IBS overall scores
and change from baseline to 26 week follow up

Table 15

		Treatment condition			
		HI-CBT	**LI-CBT**	**SH**	**TAU**
		(*n* = 5)	(*n* = 5)	(*n* = 5)	(*n* = 5)
Baseline	Mean	50.4	51.2	49.2	38.6
	S.D.	14.7	11.8	11.2	10.8
12 weeks	Mean	34.2	39.0	45.2	45.4
	S.D.	12.2	11.47	19.2	14.0
26 weeks	Mean	33.2	37.8	42.0	47.4
	S.D.	11.4	9.6	15.1	19.5
Change (baseline to 26 weeks)	Mean	**-17.2**	**-13.4**	**-7.2**	**8.8**
	S.D.	9.2	11.5	10.5	10.6

Table 15 provides data which demonstrates the overall changes that the various treatment conditions may have had upon participant symptom profiles overall. The scores represent a sum of the symptom scores which is calculated by multiplying the maximum of 13 items by 7, which produces a maximum score of 91 points. Participants within the HI-CBT and LI-CBT treatment conditions experienced a mean overall reduction in total symptom scores by -17.2 (S.D. = 9.2) and -14.4 (S.D. = 11.5) respectively between baseline and 26 weeks. The SH treatment condition experienced a mean reduction of symptom scores by -7.2 (S.D. = 10.5). Participants with the TAU condition experienced a mean increase in symptom scores of 8.8 (S.D. = 10.6). The change percentage for these observations (*100/baseline observation * change score*) would be a decrease in symptom profiles by 34.1% for HI-CBT, 26.2% for LI-CBT and 14.6% for SH. Participants within TAU deteriorated with a 22.8% increase in symptom scores.

Table 16 **Degree of change in overall IBS-QOL mean scores**

Treatment condition	HI-CBT (*n* = 5)		LI-CBT (*n* = 5)		SH (*n* = 5)		TAU (*n* = 5)	
	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.
Baseline	50.3	20.1	47.9	18.2	40.4	22.0	56.0	20.0
26 weeks	73.4	23.1	72.1	12.5	50.3	31.5	52.2	23.7
Change	**23.1**	17.2	**24.1**	23.5	**9.9**	19.1	**-3.8**	9.1

Quality of life

Table 16 summarises the overall IBS-QOL scores for participants according to their allocated treatment condition at baseline and 26 week follow up. The IBS-QOL score is the reverse of GSRS-IBS in the fact that an increase in score equals a better QOL. The baseline and 26 week follow up mean scores are displayed within the table along with the mean change which has been computed in SPSS. The conclusions that can be drawn from this table is that IBS-QOL scores increased by a mean of 23.1 (S.D. = 17.2) points for HI-CBT, 24.1 (S.D. = 23.5) for LI-CBT and by 9.9 (S.D. = 19.1) for the SH condition. As observed with GSRS-IBS scores within the previous section, participants within the TAU condition experienced a deterioration in quality of life with a mean score reduction of -3.8 (S.D. = 9.1). These data suggest that HI-CBT and LI-CBT had similar improvements in IBS-QOL whilst SH participants experienced less than half the improvements in IBS-QOL. TAU participants deteriorated during the study.

Depression and anxiety levels

The following table (table 17) shows the mean PHQ-9 and GAD-7 scores for participants according to treatment condition at baseline, 12 and 26 week follow up. As with GSRS-IBS, an increase in score indicates greater levels of anxiety and depression.

Participant PHQ-9 and GAD-7 mean scores

			Treatment condition			
			HI-CBT (*n* = 5)	**LI-CBT** (*n* = 5)	**SH** (*n* = 5)	**TAU** (*n* = 5)
GAD-7 scores						
	Baseline	Mean	**7.8**	**6.8**	**9.8**	**9.2**
		S.D.	3.1	5.3	5.6	4.8
	12 weeks		**5.8**	**5.2**	**10.6**	**8.0**
			5.4	4.6	7.7	6.3
	26 weeks		**4.8**	**5.0**	**7.4**	**7.8**
			5.9	4.9	6.9	5.5
PHQ-9 scores						
	Baseline	Mean	**10.2**	**8.4**	**11.2**	**13.0**
		S.D.	5.5	6.6	6.3	6.6
	12 weeks		**6.8**	**7.8**	**11.0**	**13.8**
			5.8	7.6	8.1	7.5
	26 weeks		**6.8**	**6.8**	**9.2**	**11.6**
Table 17			7.4	7.5	6.9	5.8

Participants within the HI-CBT condition experienced improvements in anxiety from a mean score of 7.8 (S.D. = 3.1) to 4.8 (S.D. = 4.8) and depression from a mean score of 10.2 (S.D. = 5.5) to 6.8 (S.D. = 7.4) at 26 weeks. Participants within the LI-CBT condition also experienced a reduction in anxiety from a mean of 6.8 (S.D. = 5.3) to 5.0 (S.D. = 4.9) and depression scores from a mean of 8.4 (S.D. = 6.6) to 6.8 (S.D. 7.5) from baseline to 26 weeks. Similar changes were seen in the SH and TAU conditions. In order to compare the extent of the changes observed within all four treatment conditions, change scores for GAD-7 and PHQ-9 data are provided within the following tables (tables 18 and 19).

Within table 18, participants experienced on average a -3 (S.D. = 3.4) point reduction in GAD-7 scores within the HI-CBT treatment condition. The mean reduction scores were -1.8 (S.D. = 3.5), -2.4 (S.D. = 3.9) and -1.4 (S.D. = 1.9) for the LI-CBT, SH and TAU treatment conditions respectively. Table 19 summarises the observed changes in levels of depression. Participants within the HI-CBT condition experienced a mean change of -3.4 points (S.D. = 2.1) compared to -1.6 (S.D. = 4.0) within LI-CBT, -2.0 (S.D. = 3.4) within SH and -1.4 (S.D. = 3.4) within TAU.

The data demonstrate that all participants experienced some reduction in GAD-7 and PHQ-9 scores, with the greatest reductions noted within the HI-CBT treatment condition. Participants receiving SH experienced greater mean score reductions than those within LI-CBT and TAU conditions.

Degree of change in GAD-7 mean scores

Table 18

	Treatment condition			
	HI-CBT	**LI-CBT**	**SH**	**TAU**
	(*n* = 5)	(*n* = 5)	(*n* = 5)	(*n* = 5)
Baseline	7.8	6.8	9.8	9.2
S.D.	3.1	5.3	5.6	4.8
26 weeks	4.8	5.0	7.4	7.8
S.D.	5.9	4.9	6.9	5.5
Change	**-3.0**	**-1.8**	**-2.4**	**-1.4**
S.D.	3.4	3.5	3.9	1.9

Degree of change in PHQ-9 mean scores

Table 19

	Treatment condition			
	HI-CBT	**LI-CBT**	**SH**	**TAU**
	(*n* = 5)	(*n* = 5)	(*n* = 5)	(*n* = 5)
Baseline	10.2	8.4	11.2	13.0
S.D.	5.5	6.6	6.3	6.6
26 weeks	6.8	6.8	9.2	11.6
S.D.	7.4	7.5	6.9	5.8
Change	**-3.4**	**-1.6**	**-2.0**	**-1.4**
S.D.	2.1	4.0	3.4	3.4

The study condition in which participants experienced the greatest change in clinical outcomes was the HI-CBT group. Participants within this condition experienced a -17.2 (S.D. = 9.2) mean improvement in symptoms, a -3.4 (S.D. = 2.1) mean reduction in levels of depression and -3.0 (S.D. = 3.4) mean reduction in levels of anxiety. Participants within LI-CBT had marginally better IBS-QOL mean change scores than those within HI-CBT 24.1 (S.D. 23.5) vs. 23.1 (S.D. = 17.2). LI-CBT resulted in a mean overall GSRS-IBS symptom reduction of -13.4 (S.D. = 11.5) and the greatest mean improvement in IBS-QOL scores of 24.1 (S.D. = 23.5). The SH condition participants experienced marginally greater improvements than LI-CBT in mean PHQ-9 scores of -2.0 (S.D. = 3.4) vs. -1.6 (S.D. 4.0) and GAD-7 mean scores of -2.4 (S.D. = 3.9) vs. -1.8 (S.D. = 3.5). These descriptive observations should be taken as an observation of the changes during feasibility and are not intended to infer causation. The final table (table 20) below is a summary of the noted changes during the study.

Summary of overall mean scores and changes

Table 20

		Treatment condition				
		HI-CBT (*n* = 5)	**LI-CBT** (*n* = 5)	**SH** (*n* = 5)	**TAU** (*n* = 5)	**Total** (*n* = 20)
Symptom severity (GSRS-IBS)						
Baseline	Mean	50.4	51.2	49.2	38.6	47.4
	S.D.	14.7	11.8	11.2	10.9	12.4
12 weeks		34.2	39.0	45.2	45.4	40.9
		12.2	11.5	19.2	13.9	14.1
26 weeks		33.2	37.8	42.0	47.4	40.1
		11.4	9.6	15.1	19.6	14.3
Change score		**-17.2**	**-13.4**	**-7.2**	**8.8**	**-7.3**
		9.2	11.5	10.5	10.6	14.0
Quality of Life (IBS-QOL)						
Baseline	Mean	50.3	47.9	40.4	56.0	48.7
	S.D.	20.1	18.2	22.0	20.0	19.3
12 weeks		65.1	64.4	51.6	49.9	57.8
		25.3	19.3	27.5	27.3	24.1
26 weeks		73.4	72.1	50.3	52.2	62.0
		23.1	12.5	31.5	23.7	24.4
Change score		**23.1**	**24.1**	**9.9**	**-3.8**	**13.3**
		17.2	23.5	19.1	9.1	20.2
Levels of anxiety (GAD-7)						
Baseline	Mean	7.8	6.8	9.8	9.2	8.4
	S.D.	3.1	5.3	5.6	4.8	4.6
12 weeks		5.8	5.2	10.6	8.0	7.4
		5.4	4.6	7.7	6.3	6.0
26 weeks		4.8	5.0	7.4	7.8	6.3
		5.9	4.9	6.9	5.5	5.6
Change score		**-3.0**	**-1.8**	**-2.4**	**-1.4**	**-2.2**
		3.4	3.5	3.9	1.9	3.1
Levels of depression (PHQ-9)						
Baseline	Mean	10.2	8.4	11.2	13.0	10.7
	S.D.	5.5	6.6	6.3	6.6	6.0
12 weeks		6.8	7.8	11.0	13.8	9.9
		5.8	7.6	8.1	7.5	7.2
26 weeks		6.8	6.8	9.2	11.6	8.6
		7.4	7.5	6.9	5.8	6.7
Change score		**-3.4**	**-1.6**	**-2.0**	**-1.4**	**-2.1**
		2.1	4.0	3.4	3.4	3.1

5.1.8 Identification of unforeseen factors

Unforeseen events which occurred during the conduct of the trial can be described with the adverse events reported during the study. Such events may highlight shortcomings in the design of the study or treatment procedures implemented during the trial period. They may also identify factors regarding the ethical conduct of the study or safety of participants. Adverse events reported here meet the definition stipulated by the sponsor and the reviewing REC as follows. An Adverse Event (AE) was considered to be any unfavourable and unintended sign, symptom, syndrome or illness that developed or worsened during the period of observation in the study.

An AE included:

1. An exacerbation of a pre-existing illness
2. An increase in frequency or intensity of a pre-existing episodic event or condition
3. A condition detected or diagnosed after the administration of a trial intervention even though it may have been present prior to the start of the study
4. Continuous persistent disease or symptoms present at baseline that worsen following the start of the study

An AE did not include:

1. A medical or surgical procedure (e.g., surgery, endoscopy, tooth extraction, transfusion); but the condition that leads to the procedure may be classified as an AE.
2. A pre-existing disease or conditions present or detected at the start of the study that did not worsen
3. Situations where an untoward medical occurrence has not occurred (e.g., hospitalisations for cosmetic elective surgery, social and / or convenience admissions)

4. Expected variations in the disease or disorder being studied or sign or symptom associated with the disease or disorder (unless more severe than normally expected for the participant's condition)
5. Overdose of concurrent medication without intention to inflict self-harm (i.e. accidental overdose)

There are several important issues which were identified during the conduct of the feasibility work which were not anticipated. No serious adverse events (hospitalisation, surgery or actual harm) were identified during the study period. Three participants responded to item 9 on the PHQ-9 questionnaire at various points during the study. The PHQ-9 question 9, asked participants if they have experienced '*Thoughts that you would be better off dead or of hurting their selves' in some way* during the prior two week period. Participants who scored on this item were assessed in relation to risk. None of the study participants had plans or intentions to commit acts of self-harm or suicide. Accordingly, the participant's general practitioners were notified as required by the study protocol approved by the REC. A participant who was informed her insurance premiums may increase as a result of being identified as having psychological problems did not experience further problems in this regard. Nonetheless, the incident highlights stigma faced by patients with common mental health problems and is an interesting, but disappointing finding.

5.1.9 Delivery of interventions and monitoring

Monitoring of the delivered CBT interventions was carried out in accordance with the research protocol and methods approved by the REC. Participants referred to within this section are identifiable only in terms on study number in order to protect the identity of the individuals concerned.

No breaches of study protocol were reported according to the CRF's returned by therapists during the conduct of the study which would suggest treatment was delivered according to treatment protocol.

However, issues with treatment fidelity were identified within the report carried out by the intervention monitor not connected to the delivery of trial interventions. The report presented below within figure 14 details the results of the report made to the principle investigator upon the completion of the trial.

The first three sessions monitored, detail the fidelity of LI-CBT treatment to the study protocol, with the three other sessions relating to HI-CBT treatment (please see figure 14). The monitoring data for the LI-CBT sessions confirms that treatment was delivered as intended. Within the HI-CBT treatment, several deviations to treatment protocol were noted. The majority of deviations detailed within the report highlight a failure of the therapist to follow up homework activities or review homework within the CBT session. As described within 5.1.6 two participants chose not to complete the full course of HI-CBT and one participant did not attend for LI-CBT interventions. These issues are further explored within the recruitment of participants described earlier within section 5.1.2.

Figure 14 Fidelity to treatment protocol: report to principal investigator

LI-CBT Session Monitoring

Participant: 017
Session: 2 **Duration: 29 minutes**

	Included (Y/N)	Comments
Agenda	Y	
Session Length	Y	
Review questions & concerns about IBS	Y	How have you been since I last saw you?
Review questions & concerns about biopsychosocial model	Y	CBT model
Recap on the content of workbook 1	Y (activities)	Have you looked through the workbook?
Introduce the concept of relaxation training	Y	
Rationale should be clearly stated for the use of relaxation exercises linked to the activation of the parasympathetic nervous system	Y	
Relaxation Training Practice	Y	Deep breathing only
Homework: Read workbook 2	Y	
Homework: Practice relaxation exercises on a daily basis	Y	Practicing daily not advised

Participant: 004 Session: 4 Duration: 33 mins	Included (Y/N)	Comments
Agenda	Y	Not explicit about items to be covered from WB4
Session Length	Y	
Review thought records homework	Y	
Link cognitive model to IBS	Y	
Introduce concept of behavioural experiments (link to negative automatic thoughts)	Y	
Rationale for behavioural experiments and NATS	Y	
Homework: Read workbook 4	Y	
Homework: Complete IBS thought records	Y	
Homework: Identify 2 behavioural experiments	Y	Didn't advise to think of 2 experiments

Participant: 006 Session: 6 Duration: 19 mins	Included (Y/N)	Comments
Agenda	Y	
Session Length	Y	
Review exposure therapy	Y	Therapy not useful - strong emphasis is anxiety which they don't feel they have (participant comment)
Encourage further practice	Y	
Enforce rationale	Y	
Discuss dietary advice	Y	Wheat and honey exclusion has led to no attacks (participant comment)
Introduce the contents of the final workbook	Y	Tailored to individual - participant was seeing a dietician so that is prioritised above dietary advice in workbook
Summarise the treatment program	Y	
Recommend continuing to use the strategies	Y	
Homework: Read workbook 6	Y	
Homework: Continue with experiments, exposure and thought records	Y	

HI-CBT Session Monitoring

Participant: 019
Session: 1 Duration: 1hr, 36 mins

	Included (Y/N)	Comments
Conduct a standard CBT interview looking at predisposing, precipitating and maintenance factors	Y	
Focus will be on the issues of control, bowel performance anxiety, shame, and self-efficacy	Y	
Identify any co-morbid psychiatric diagnoses from assessment and mental state examination	Y	
Consider involvement of co-therapist	N	?
Agree suitability	Y	
Homework: Complete symptom diary	N	

Participant: 002 Session: 9 - 20 mins	Included (Y/N)	Comments
Set agenda	Y	didn't include relapse prevention in agenda
Review of homework: progressive muscle relaxation	?	Just talked about relaxation in general - no specific focus on type
Review of homework: pain management	?	If IBS related pain management - this was not covered. Other pain was discussed.
Review of homework: NAT	Y	
Review of homework: behavioural experiments	N	
Review of homework: exposures	N	
Theme of the day: Relapse Prevention	N	
Homework: complete relapse prevention form	N	

Participant: 013 Session: 9 Duration: 35 mins	Included (Y/N)	Comments
Set agenda	Y	
Review of homework: progressive muscle relaxation	Y	
Review of homework: pain management	?	Asked how her IBS has been
Review of homework: NAT	Y	
Review of homework: behavioural experiments	Y	unrelated to IBS
Review of homework: exposures	N	
Theme of the day: Relapse Prevention	N	
Homework: complete relapse prevention form	Y	very brief explanation of form and asked to complete for next time

We know from intervention monitoring research that unknown confounds can be unintentionally omitted or added during intervention delivery (Cook and Campbell, 1979). Thus, non-adherence to treatment fidelity has the potential to impact upon both the internal and external validity of an investigation (Borrelli, 2011). Monitoring the adherence of the delivered interventions would also establish whether the active ingredients needed to bring about the desired change were present within the independent variable (Moncher and Prinz, 1991). In a correctly powered study, adherence to treatment regimen is likely to result in stronger effects (Resnick et al., 2005).

Research clearly shows that when delivered as intended, fidelity to treatment is linked directly to treatment outcomes (Perepletchikova and Kazdin, 2005). Yates et al. (2005) advocate three indicators of treatment integrity and quality i) manualised treatment, ii) treatment manual adherence, and iii), therapist training. To some degree the former two have been addressed within this study with a manualised treatment protocol and recorded sessions to monitor adherence.

However, the monitoring methods used in this study did not offer therapist's feedback in relation to monitoring on a session by session basis rather than upon completion of the course of treatment (Lu et al., 2012), nor did this study use a validated CBT specific treatment fidelity rating scale to assess the level of CBT content present within the intervention (Lu et al., 2012). Nonetheless, fidelity to an evidence based treatment manual was measured during the delivery of interventions which was found to be largely absent within the trials reviewed within chapter 3. Competence was also not a feature of the intervention monitoring detailed here. Authors suggest that monitoring of interventions should not only consist of intervention content and adherence to protocols, but also assess the levels of therapist competence (McGlinchey and Dobson, 2003). Therapist competence appears to be positively associated with better patient outcomes in recent studies (Simons et al., 2010), and is considered crucial during the

delivery of CBT interventions used in the treatment and management of patients with chronic pain (Ehde et al., 2014)

The data gathered during the conduct of this feasibility study therefore suggests that closer monitoring of the fidelity to treatment is required, and declaration of self-report of conformity to treatment protocol is likely to be insufficient within future studies. Mechanisms by which to correct non-adherence to treatment protocol (such as monitoring in vivo), may also be useful for feeding back the results of intervention monitoring to the therapist during this study. Clearly, intervention monitoring and quality measures need to be reconsidered during a future study.

5.1.10 Randomisation and blinding

Random permuted blocks were used to randomise participants during the trial to one of four treatment conditions which was carried out using an online randomisation system. During the conduct of the study, there were no events associated with the failure of the randomisation system and all participants were notified successfully of their allocation at the time of successful randomisation screening. Two participants were not eligible for randomisation. The first of these participants did not meet Rome III criteria for IBS, whilst the other was unable to read and write in English which was a contraindication to the study protocol and consent process. At no time during the conduct of the study did any of the study investigators become aware of the sequence allocation for randomising participants. A full audit trail of randomisation results were recorded and maintained in the study master file.

Follow up data for the study was collected by a research assistant blind to the allocation of participants. The study investigators had no access to original follow up data and the data collector remained blind as to the allocation of participants throughout the conduct of the study. A full audit trail of data collection returns and CRF's were maintained by the research assistant as approved by the REC.

Chapter 6 ▪ Discussion

6.1 Introduction

Within this chapter, the reader is provided with a critical discussion based on the findings from the qualitative and quantitative aspects of the study. The characteristics of the sample recruited to the feasibility study are discussed and how they relate to samples within other studies evaluating the use of CBT treatments for participants with IBS. Attempts are made to contrast and corroborate the quantitative data with the findings of the in depth interviews and similarities and differences between the two sets of data are discussed. The critical discussion will demonstrate how the two sets of data add a richer and unique understanding of the feasibility of the trialled interventions within this study. Although there is limited information regarding the acceptability and suitability of CBT interventions for IBS as described within chapter 3, in order to situate the observations within the wider body of literature, reference to the work of other authors is made where applicable. Finally, based upon this discussion, the implications the data have for the design of CBT interventions and for future studies are presented.

6.1.1 Participant characteristics

The 22 participants within this study were successfully recruited directly from secondary care gastrointestinal outpatient clinics within a large university teaching hospital. The conversion rate to response was approximately 34% when methods were used to invite patients to take part via postal return. A total of 104 patients were required to be approached to achieve 22 screening visits and 20 randomisations. The conversion rate from patients approached to randomisation was therefore 20.8%. Future recruitment programs utilising the same methods should therefore consider that around 100 patients will need to be approached to achieve n = 20 within the clinical setting where the feasibility study took place.

Retention of study participants was good compared to other studies of minimal contact interventions using similar protocols (Hunt, et al. 2009), losing only *n* = 3 or a 15% rate of attrition. The retention of study participants has recently featured within the methodological literature. Brueton et al. (2014) carried out a systematic review of 38 studies evaluating predictors of retention of participants during trials, during which they identified a variety of strategies for improving the retention of study participants such as;

- Giving a monetary incentives, particularly upon questionnaire completion
- Shorter length questionnaires
- The use of questionnaires which are relevant to the disease/condition
- The use of recorded delivery of questionnaires
- Implementation of a package of postal communication strategies
- Use of an open trial design

Brueton and colleagues (2014) found that non-monetary incentives, prize drawers, behavioural motivation strategies and additional reminders to not be effective strategies for the retention of participants. This study did not consider factors such as those employed within this feasibility study such as meaningful patient and public involvement and good communication with the trial co-ordinator.

There is empirical data to support the notion that quality health care and care team characteristics are critically important as well as attention to privacy and the opportunity to be altruistic when considering participation in research. In contrast to the data presented by Brueton and colleagues (2014), monetary incentives such as compensation for participation did not appear to be a significant factor for recruitment and retention of participants (Stanford et al., 2003). A very recent systematic review supports the implementation of PPI strategies which clearly demonstrate improvements in the rate at which studies retain participants (Jones et al., 2015). Jones and colleagues also found that

PPI improves the identification of relevant research topics, improves the quality of study design and enhances recruitment procedures.

As identified within the literature review reported within chapter 3, the reporting of how PPI is integrated into studies is often lacking (Jones et al., 2015). Although the results of this study demonstrate good retention rates, it is possible that attrition could have been further improved upon with the use of methods advocated by Brueton and colleagues (2014), particularly the use of incentives for returning questionnaires.

The age range of participants when first diagnosed with IBS was consistent with previous work which suggests IBS diagnoses are made within the fourth and fifth decades of life (Spiller et al., 2007) with around half of all new diagnoses developing IBS before the age of 35 years (Maxwell et al., 1997). On average, 40% of patients are thought to be aged between the 35 and 50 years (Maxwell et al., 1997), as observed within this sample of IBS patients with a mean age 44.5 years (S.D. = 17.5).

IBS researchers consistently report IBS as more frequent amongst women, with a female to male ratio as much as 2:1 (Saito et al., 2002). The sample within this study was 85% female, which suggests women may be slightly overrepresented within the small sample. These factors may have consequences for the findings presented within this work, particularly considering differences in IBS symptom profiles relating to gender. Research suggests IBS-C subtypes occur more frequently in women (Lee et al., 2001) which are not in keeping with the observations made within this study, as only 10% of participants met Rome III criteria for IBS-C. Although few differences have been found between the severity of symptoms experienced by men and women, literature suggests that women experience more varied symptom profiles than their male counterparts (Lee et al., 2001) and suffer from a wider variety of additional functional disorders (Chang et al., 2006).

Data regarding other functional complaints were not collected during the study, and did not become evident within the themes of the post-intervention interviews. Assessing these values within future studies may be beneficial.

Participants reporting the onset of their IBS being associated with a period of dysentery represent 15% of the sample, which is not surprising considering the six fold risk of developing PI-IBS following prolonged enteric infection (Thabane et al., 2007). However, these levels may be underestimated as recall of symptom onset was difficult for participants during baseline data collection due to the number of professionals consulted about IBS and related symptoms. Within pilot studies of CBT for the treatment of IBS, researchers have previously identified that gastroenterologists may have a tendency to refer potential participants that they anticipate would benefit from treatment (Ljotsson et al., 2010). These issues were not evaluated during this research, although the description offered by participants as the trial being a 'last resort' to treatment during the post intervention interviews suggests that this may not have been the case.

6.1.2 Recruitment

One of the feasibility outcomes of this study was to assess the feasibility of the strategies used to recruit participants and to identify potential barriers and facilitators to the success of future research. Earlier within the chapter 5, it was demonstrated that the peak of recruitment was around April 2014. This represents a period during the initial recruitment phase where the trial team was able to identify potential participants directly from the BRU patient database and deploy information packs directly to patients.

As with the other patients approached for this study, patients were given the opportunity to express further interest in the study by either contacting the study investigator, their physician or by replying with a prepaid postage envelope and reply slip. During January 2015, no patients were approached with information regarding the study which is

explained by the absence of the investigator early in 2015 due to ill health. Recruitment begins to increase again in February, when unfortunately the trial was required to close as time had run out for participants to be recruited during the allocated period of PhD study and as permitted by the regulatory approvals.

There is some data within chapter 5 which gives some insight as to why patients did not volunteer to participate in the study. It is not clear whether it was the clinical research element (i.e. completion of questionnaires) or the potential commitment to therapy (12 hours if randomised to HI-CBT) which may have deterred potential participants, nor indeed some other unforeseen phenomena relating to commitment.

Although some data was collected regarding a lack of patient interest in the research, the data is relatively limited as it only represents a small number of the patients approached. In reality, calling patients to identify such issues was much more difficult than anticipated. For example, it was not possible to contact patients with whom the investigator had no direct contact, and it is likely that some intent to please bias may have influenced the examples presented within chapter 5 which were reported by participants to the investigator. More than twice the number of patients were approached regarding their reasons for not taking part, but many were not contactable (i.e. telephone numbers were not up to date on the BRU research database).

The majority of reasons gathered related to commitment or not having the time to take part in the study. More details would have been useful, but the REC approvals did not cover the potential to interview these patients and indeed, it could be considered unethical to pursue further enquiries when patients had already indicated a lack of interest via omission (a reluctance to take part). Nonetheless, the data do provide some limited information relating to reasons why patients may not have volunteered to take part in the study.

As described within chapter 5, the 23 patients who made contact via the community could have made a welcome contribution to the study's rate of recruitment. However, there were trial design issues which made it very difficult to recruit patients from within the community. The first of these difficulties related to the fact that the trial was designed to recruit patients only within secondary care. Such patients may be different in terms of symptom profiles and psychological state than those located within the community. There is evidence to support the latter (Canavan et al., 2014), although issues such as these could be controlled for within a statistical analysis in a future study.

The second of the barriers to recruiting these patients relates to the provision of the interventions within one of the four treatment conditions. The HI-CBT treatment was being provided by a therapist contracted to a psychological medicine department which was not commissioned to see patients based within primary care. In order for patients to have been referred to the therapist, they had to be registered within secondary care. This issue was one relating to service provision and was not of a consequence of the study design or methods. Therefore, patients without registration in secondary care were not eligible for treatment should they have been randomised to HI-CBT.

Thirdly, even if these two barriers were overcome, a substantial study amendment would be required to enable community patients to be seen at the research site without routine referrals. The only potential route to recruiting these patients was the possibility that their primary care physician could refer the patient to a gastroenterologist where they would then become eligible for taking part in the study. Of those patients who approached the investigator during the study period, one was referred into the gastrointestinal outpatient clinic and although this patient became eligible to take part, she later withdrew her interest in the research due to time commitments which related to starting a new period of study.

It is difficult to estimate whether the rate of recruitment would have continued to improve if the study were permitted to continue although the increase in recruitment rate towards the end of the study suggests this may have been possible. Several patients were also turned away soon after the study closed in March 2015 (these patients are not included within the data presented within chapter 5). Despite the recruitment difficulties, 22 patients were screened and 20 were randomised to the four intervention conditions and a range of feasibility data was gathered albeit the limited nature of the study.

It is possible that a greater numbers of participants would have changed the data observed during feasibility. Nonetheless, although the study aimed to recruit 60 participants, there is little in the way of guidance for researchers conducting feasibility studies regarding sample size and such a decision was made only on pragmatic grounds and 'rule of thumb' literature. The study was unsuccessful according to the feasibility criteria set in 4.5.1.

6.1.3 The quantitative and qualitative data

This study was limited to a descriptive analysis of the data collected owing to the small feasibility sample size. However, measures of mean and variance (S.D.) within the descriptive analysis were obtained and are useful for discussing the observations made here with the work of other authors reporting S.D's alongside their observations. The baseline GSRS-IBS overall mean score within this sample (*n* = 20) was moderate in severity, at a mean of 47.4 (S.D. = 12.4) points out of a possible score of 91. Ljótsson et al. (2011) report a baseline mean GSRS-IBS score of 47.5 (S.D. = 10.5) among their internet exposure intervention sample (*n* = 98). Following participants up within the same timeframe (26 weeks), Ljótsson et al. (2011) found their internet intervention reduced the mean score to 33.4 (S.D. = 13.4), an overall symptom reduction of 14 points. Within this feasibility study, scores were observed to be reduced on average by -17.2 (S.D. = 9.2) for HI-CBT, -13.4 (S.D. = 11.5) for LI-CBT and -7.2 (S.D. = 10.5) for the SH condition.

In terms of QOL, the mean baseline IBS-QOL score for the total sample (*n* = 20) was around 48.7 (S.D. = 19.3). Drossman et al. (2003) found their participants to have a better QOL in their 2003 study with a baseline mean IBS-QOL score of 65.5 (S.D. = 20.3). Their sample also included a much more diverse range of participants including those self-referred from community settings. Similar QOL levels were evident within the report of the mindfulness work carried out by Gaylord et al. (2011) among their mindfulness group of participants drawn from a variety of settings. It is possible that such data could relate to the recruitment of participants based within secondary care, although greater QOL burden within secondary care IBS populations is not currently supported by empirical data (Canavan et al, 2014).

Ljótsson et al. (2011) report that their baseline IBS-QOL scores among exposure therapy participants were improved from a mean of 57.1 (S.D. = 19.1) to 74.9 (S.D. = 20.8) at 6 months post treatment. This would equate to an IBS-QOL positive change score somewhere in the region of around 17.8 points. Within this feasibility work, a mean 23.1 (S.D. = 17.2) point increase was noted among participants within HI-CBT, 24.1 (S.D. = 23.5) for LI-CBT and by 9.9 (S.D. = 19.1) for the SH condition with TAU participants experiencing a mean reduction of -3.8 points (S.D. = 9.1).

The mean PHQ-9 and GAD-7 scores among this sample were 10.7 (S.D. = 6.0) and 8.4 (S.D. = 4.6) respectively. These scores indicate moderately severe levels of depression and moderate levels of anxiety (Kroenke et al., 2001 , Spitzer et al., 2006). Ljótsson et al. (2011) found mean HAD scores of 8.8 (S.D. = 4.2) for anxiety and 5.4 (S.D. = 3.5) for depression. The baseline HAD scores relate to borderline levels of anxiety and normal levels of depression (Snaith and Zigmond, 1983). These scores were reduced to 7.2 (S.D. = 4.2) and 4.4 (S.D. = 4.1) respectively following exposure therapy within the study reported by Ljótsson et al. (2011) at 6 months. Within this study, the HI-CBT condition experienced improvements in anxiety from a mean GAD-7

score of 7.8 (S.D. = 3.1) to 4.8 (S.D. = 4.8) and depression from a mean PHQ-9 score of 10.2 (S.D. = 5.5) to 6.8 (S.D. = 7.4) from baseline to 26 weeks. Participants within the LI-CBT condition also experienced a reduction in anxiety from a mean GAD-7 score of 6.8 (S.D. = 5.3) to 5.0 (S.D. = 4.9) and depression scores from a mean PHQ-9 score of 8.4 (S.D. = 6.6) to 6.8 (S.D. 7.5) points from baseline to 26 weeks.

The moderate levels of anxiety and depression identified within this sample are consistent with the findings of research relating to the presence of common psychological problems among people with IBS. Research continues to suggest that psychological stresses appear to impact directly upon intestinal sensitivity, motility, secretion and permeability (Qin et al., 2014). Our understanding of the underlying mechanisms which underpin these observations is also improving as researchers have established correlations between stress, mucosal immune activation, changes to the central nervous system, peripheral neurons and gastrointestinal microbiota (Qin et al., 2014).

Authors also suggest that these associations are probably driven by mutual and reciprocal interactions between the brain and the gut via the effects of hormones such as corticotropin releasing hormone (CRH), (involved in the mediation of the stress response in the brain gut axis) which has been shown to increase intestinal permeability and lead to functional disease processes and IBS (Gaber, 2016). For these reasons, understanding the molecular mechanisms of IBS with or without the presence of psychiatric comorbidities is likely to be essential for fully understanding pathophysiology of IBS and for the identification of new therapeutic interventions (Fadgyas-Stanculete et al., 2014). A recent study also suggests a relationship between low-range birth rates which may be contributing factors to the development of anxiety, depression and IBS which is thought to be explained by genetic factors (Bengtson et al., 2015).

It might be possible that participants experiencing common mental health problems may respond differently to those with IBS who do not have comorbid mental health problems. For instance, People with depression may face particular difficulty in complying with treatment due to low mood or motivation (DiMatteo et al., 2000). However, researchers suggest that CBT interventions are effective for patients with and without psychological co-morbidity and positive outcomes cannot completely be accounted for by changes in mood alone (Creed et al., 2005). Research consistently identifies correlations between medically unexplained phenomena and levels of anxiety and depression which are likely to relate to the experience of psychosomatic distress. Some authors might suggest that physical MUS can be described as a single dimension of common distress symptoms associated with depression and anxiety (Henningsen et al., 2003).

It has been especially insightful to consider the qualitative data gathered during this feasibility work alongside the results of the quantitative data analysis. Within the SH intervention, participants were disappointed regarding the lack of therapist interaction and felt that the material contained within the SH materials was difficult to put into practice when they talked about therapeutic task execution. They also had preconceptions about treatment relating to doubt that the SH intervention would help their IBS. It is therefore not surprising to observe that both HI-CBT and LI-CBT interventions may have had a greater impact on QOL and symptom severity than SH. However, participants within the SH condition reported marginally better PHQ-9 and GAD-7 scores than those receiving therapist delivered LI-CBT which seems counterintuitive considering the SH participants' disappointment regarding the lack of face-to-face interaction.

An explanation for these observations within the qualitative data might relate to the presence of interventions conflicting with personal assumptions regarding socially acceptable standards of behaviour or a lack of relevance reported during interviews within LI-CBT. Indeed, these

factors are considered during CBT treatment and may have changed to some degree prior to commencing the trial treatment protocols although this is difficult to speculate without having interviewed participants prior to intervention exposure.

There is little evidence to suggest that patient's attributions for neither their illness, nor their expectations or preferences for interventions influence treatment effectiveness, although some patients may struggle to understand the cognitive behavioural model as applying to them and may therefore be unlikely to engage in CBT (Lackner et al., 2007). Furthermore, ensuring individual applicability and adaptation of a treatment protocol whilst maintaining some degree of standardisation during trials represent a significant challenge which requires further exploration. It is also possible that some of these beliefs may have also represented 'core beliefs' which may not have been addressed or identified sufficiently during therapy. These observations may also have occurred purely by chance within this small sample and may be of limited value.

It is possible that the observations relate to the acceptability of the SH intervention, particularly as researchers have found that medication to be more acceptable than hypnotherapy or other alternative treatments during a survey study which asked 256 IBS patients regarding the acceptability of certain treatments (Harris and Roberts, 2008). This is certainly in keeping with other data which suggests alternative treatment modalities may be considered by patients to be last resorts for the treatment of their IBS (Harris and Roberts, 2008). This theory is consistent with the themes identified during the post intervention interviews reported here. The post intervention interviews provide some data relating to the acceptability of the self-management approach, although other authors plan to use more formal questions in order to establish how patients rate the overall effectiveness of treatment when compared to past treatments and whether or not participants have enjoyed treatment (Everitt et al., 2015). These questions were not asked

directly within this feasibility study and could be employed within a future study.

The findings which suggest participant's valued face-to-face contact with a therapist are of interest, since these issues are currently debated within the literature. For example, the results of a recent study suggest that therapists rate face-to-face therapy as a stronger experience than other types of treatment such as internet based therapy where face-to-face contact is absent (Bengtsson et al., 2015). Authors also suggest that distant psychotherapy such as interventions delivered on the telephone present a variety of challenges, including a lack of control over environments, potential breaches of confidentiality and difficulty developing therapeutic alliance without face-to-face contact (Brenes et al., 2011).

Researchers have also found that therapists reached working alliances faster and more readily during face-to-face therapy (Bengtsson et al., 2015). Nonetheless, interventions underpinned by technology such as internet and telephone increase access to evidence based interventions (Mohr et al., 2012). Telephone CBT may also increase adherence to therapy, although treatment may be less effective than when delivered in person (Mohr et al., 2012). Studies of internet CBT claim equivocal efficacy despite poorer therapy compliance (van Ballegooijen et al., 2014). Despite these observations, internet therapy has been described by some patients as impersonal, non-genuine and inhibitory (Bendelin et al., 2011).

The post-intervention interviews did not fully explore what participants described as a 'good therapist personality'. A participant within HI-CBT provided further clarification suggesting the therapist possessed qualities which were described as *very calm*, *relaxed* and suggested meetings were conducive to *opening up*. Participants in both LI-CBT and HI-CBT described these phenomena. Authors suggest therapists may utilise a variety of sophisticated interpersonal skills, including; verbal fluency,

interpersonal perception, affective modulation and expressiveness, warmth and acceptance, empathy and focus on the other (Wampold, 2016).

Therapist techniques such as exploration, reflection, accurate interpretation of information, facilitating the expression of affect, and attending to the patient's experience have also been associated with an improved therapist-client alliance (Ackermana and Hilsenrothb, 2003). These qualities of course may represent a good therapeutic alliance as part of the CBT intervention or could in fact have been derived from a therapeutic encounter with another. The extent of CBT delivery in terms of content was not evaluated with a formal instrument during therapy delivery other than compliance with treatment protocol which may have provided more information in relation to these phenomena as the extent of general CBT principles or the presence of certain skills used to develop a therapeutic alliance may have become apparent (Strupp and Anderson, 1997).

The value participants placed upon face-to-face contact was not only evident in the post intervention transcripts for participants which had therapy delivered by a LI or HI therapist, but was also discussed by participants receiving SH treatment via the workbooks alone. The quantitative data gathered during the study suggests that the degree of change observed within the treatment conditions, particularly in relation to GSRS-IBS, was potentially proportionate to the dose of treatment. It is however possible that confounding factors may explain some of the observed effects. For example, research has shown that patients who experience a positive therapeutic relationship or a positive interaction with a clinician require less follow-up treatment visits than patients who do not experience such interactions (Owens et al., 1995). This is in keeping with the value participants expressed regarding the ‘good personality’ of the therapist within the delivered treatment conditions.

Indeed, these findings do not reflect the identification of new therapeutic phenomena and have been considered important during the delivery of evidence based CBT interventions by a number of authors. For example, Addington and Gleeson (2005) discuss the importance of the therapist and client developing consensus about treatment goals, which in turn facilitate an atmosphere of trust. Addington and Gleeson (2005) suggest that these factors are part of the engagement phase of therapy, whereby the therapist works to develop a therapeutic alliance. These issues are sometimes considered difficult to build into interventions within the rigid protocols used within experimental evaluations, despite mainstream literature promoting the flexible management and personal aspects of therapeutic engagement (Loewenthal and House, 2010).

CBT therapists propose that this therapeutic relationship is further enhanced when the therapist is able to resolve 'ruptures' by using the relationship as a method to modify cognitive and emotional problems (Leahy, 2008). Common factors which should be present during CBT which may also promote the interpersonal relationship between the therapist and client include the use of empathy, genuineness and warmth (Skinner and Wrycraft, 2014). Such factors perhaps require further evaluation as components of CBT interventions in their own right, which Ehde et al. (2014) suggests may help guide the development of more efficacious treatments.

It could be hypothesised that the interaction between therapist and participant might also be a feature of group CBT interventions in the fact that good therapist traits would be present within the intervention. Group therapy might therefore be a potential option for overcoming these issues, although authors have identified that 95% of participants approached would choose individually delivered CBT over group forms of treatment (Sharp et al., 2004). Nonetheless, the importance of human support needs to be taken into account when designing interventions and such issues have recently featured within the literature. For example, Vigerland et al (2014) suggest that interventions such as computerised

CBT should not be available without professional support which has the ability to provide motivation, feedback and the ability to address queries and problems during therapy. The authors also suggest that it is also possible that limited clinical information is obtained during non-contact interventions on which to base a clinical judgment which might be evident during a traditional face-to-face encounter (Vigerland et al., 2014).

The involvement of a nurse in the delivery of CBT interventions is a concept which has been applied to other settings, for example; in the form of a depression-focused, nurse delivered CBT intervention post cardiac surgery (Doering et al., 2014) or for improving patients access to CBT interventions for the management of patients with chronic pain (Ehde et al., 2014). Working as a nurse therapist could be said to be a much different role to being a nurse, requiring adjustments to a new identity, behaviours, and ways of interacting with patients (Ehde et al., 2014). Difficulty dealing with illness beliefs and resistance to psychotherapy has been identified as a major barrier to the implementation of CBT interventions when used with medically unexplained symptoms (Lyles et al., 2003). Although no difficulties were experienced by the nurse therapist delivering the trialled interventions to the small group of participants within this study, interviewing therapists during the study may have provided additional useful data in this regard.

The assessment of therapist competence was not a feature of the quality of the interventions used here, which following experience of this study, should ideally be considered during a future study. Few studies have reported a transparent and objective training program as with this study, although Turkington et al (2002) report to have provided ten days of intensive training in CBT which was assessed through demonstration, role play, and written examination within their trial evaluating nurse delivered CBT used in Schizophrenia. This study therefore provides a unique contribution to the literature with the application of rigorous training

methods to nationally recognised standards in order to prepare the nurse therapist for delivery of the LI-CBT intervention (IAPT, 2011).

The therapeutic relationship and interactions between technical and interpersonal factors between client and therapist has been shown to influence treatment results in therapy process and outcome research as a result of direct improvements in the therapeutic alliance (Wright and Denise Davis, 1994). It may therefore be, that the observed quantitative data which suggest changes may be proportionate to the treatment dose may actually represent the time spent in direct contact with a therapist, although this would be difficult to support with the findings from such a small sample. Further qualitative evaluation within a future trial is therefore likely to be beneficial.

Participants also described the benefit of relaxation techniques which, when implemented successfully helped participants to manage symptoms during daily life events and activities. Relaxation evaluated particularly well when facilitated by the therapist alongside participants within HI-CBT. The aim of including relaxation techniques within the multi-component interventions trialled within this study was to reduce sympathetic nervous system arousal which may be responsible for the exacerbation of IBS symptoms and maintenance of underlying psychopathology such as anxiety and higher states of arousal. In this context, relaxation utilised in conjunction with other psychological therapy components would reduce levels of psychological distress by promoting a physiological state in opposition to how the body reacts under stressful situations (Brent et al., 2009). These observations are also in keeping with the biopsychosocial models of IBS.

Research has demonstrated these characteristics of relaxation techniques during evaluation of mindfulness interventions, whereby relaxation interventions bring about the physiological effects of decreasing heart and respiratory rates, lowering blood pressure and reducing muscle tension (Ditto et al., 2006). The post intervention interviews conducted

with SH participants suggest that participants had difficulty implementing relaxation techniques without the assistance of a therapist and therefore, SH participants may not have experienced such benefits potentially explaining some of the loss of benefit when compared to HI and LI-CBT.

The ambiguity identified between the delivered interventions and clinician attitude towards CBT may also play a role here, particularly as acceptability of these alternative treatment procedures may improve when recommended by a clinician (Harris and Roberts, 2008). The most relevant findings in relation to the qualitative data were those themes which translate to potential barriers and facilitators to the implementation of the trialled interventions. The main findings in relation to barriers and facilitators within the three interventions themes are summarised as follows.

HI-CBT

Barriers

- × Quality of supporting printed materials
- × Lack of preparation or introduction to therapy
- × Strong client values or beliefs
- × Too many sessions
- × Dietary advice lacking
- × Uncomfortable therapy environment

Facilitators

- ✓ Therapist facilitated relaxation techniques
- ✓ Use of scenarios
- ✓ Good personality of therapist
- ✓ Appointment flexibility
- ✓ Face to face contact – motivation
- ✓ Positive preconceptions

LI-CBT

Barriers

- × Lack of confidence in IBS diagnosis
- × Relaxation difficult out of session
- × Dyslexia
- × Too few sessions
- × Strong personal values or beliefs
- × Sensitive subject discussion (bowels)

Facilitators

- ✓ Flexibility of appointments and therapy
- ✓ Good personality of therapist
- ✓ Therapist input with relaxation
- ✓ Social support
- ✓ Combination of CBT and dietician input

SH

Barriers

- × Preconceptions or doubt about treatment
- × Ambiguity regarding causation amongst professionals
- × Lack of therapist support with relaxation
- × Lack of social support
- × Dyslexia
- × Concerned about stigma
- × Negative experience with previous psychotherapy

Facilitators

- ✓ Narratives and scenarios within workbook text
- ✓ Lack of jargon
- ✓ Positive previous experience with psychotherapy

These issues should be carefully considered during the design of future interventions and research studies. Recommendations regarding these issues are presented within the recommendations for future research and practice sections (see 6.1.6).

The identification of reference to traumatic life events within the qualitative data is a finding which was not actively sought by the interviewer, but emerged spontaneously during interviews. Although these features located within the interview transcripts appear alarming, they are consistent with the high rate of abuse present among persons with IBS and common mental health problems (Delvaux et al., 1997 , Drossman et al., 1990 , Alpers et al., 2001 , Blanchard et al., 2004). Researchers have suggested that these findings reflect reactivity to life stressors which account for two fold increases in levels of distress, as opposed to mere exposure to stressful factors alone (Bolger and Schilling, 1991). It is psychosocial factors such as these that make the presentation of FGID's such as IBS so complex.

Physiological explanations might also explain why these characteristics are so frequently reported by people with IBS, as research suggests that the activation of the stress response has neurological, endocrinological, immunological and cardiovascular consequences (Brosschot et al., 2005). In relation to the traumatic life events reported by participants during interview, as many as 50 percent of people with IBS report exposure to events such as childhood abuse (Nauert, 2011). More recent studies continue to identify the presence of a variety of traumatic experiences among samples of patients with IBS.

For example, when compared to control subjects, Bradford et al. (2012) have recently identified exposure to life events such as; general trauma (78.5% vs 62.3%), physical punishment (60.6% vs 49.2%), emotional abuse (54.9% vs 27.0%) and sexual life events (31.2% vs 17.9%). Furthermore, Bradford and Colleagues (2012) suggest that their data supports that the presence of these adverse life events are associated with the future development of IBS. A second recent study has confirmed similar findings to Bradford et al. (2012), with findings to suggest the presence of general trauma compared at a rate of 74% vs. 59% among control subjects which the authors also conclude to be associated with the future development of IBS (Halland et al., 2014).

Therapists should therefore be in a position to screen out and deal with inappropriate candidates referred for intervention as found in other trials of CBT for IBS (Blanchard and Scharff, 2002). Where issues are identified, previous research suggests that complex cases where specialist mental health interventions are required should be subject to an appropriate stepped referral pathway (Katon et al., 2001). Such factors need to be carefully considered during the design of interventions and research studies should have contingency planning to appropriately handle such complex issues as they arise during research. Such factors a likely to vary significantly between individuals and may relate to the personality of the participant which may be shaped by early life experiences and exposure to trauma or abuse. The findings of research into the effects of life events upon levels of neuroticism suggest that the effects of life events alone are not independent of personality traits (Magnus et al., 1993).

Some participants described concern regarding stigma previously received from healthcare professionals within the transcripts. It is possible that the anonymity afforded by alternative therapies such as internet-based therapy could be attractive to participants who might anticipate stigma during face to face interactions (Beattie et al., 2009). More research regarding these issues would be useful for helping researchers understand how such phenomena may be overcome during the implementation of delivered therapies.

A cross-cutting theme evident within the interview data was an improved level of understanding regarding IBS. Some participants also described how the improved level of understanding did not necessarily result in improvements in symptoms or living with IBS which suggests that the provision of information alone could be insufficient for addressing complex issues relating to IBS. The CBT model relies upon the hypothesis that the manifestation of illness arises from a vicious cycle of psychological and social factors which may become self-perpetuating through an interaction with symptoms causing significant distress and

notable disability (Allen et al., 2002). It was therefore hoped that by providing education during the delivery of the interventions that participants might experience benefit in terms of symptom reduction or improvements in QOL, although not all participants felt that improvements in their knowledge were responsible for these changes where they occurred.

Some of the participants, particularly those receiving SH, described a disappointment with the blanket approach to therapy and lack of individually tailored treatment. Previous qualitative research has identified the importance of CBT implementation utilising person-centred engagement (Kilbridea et al., 2013). Although participants did not necessarily attribute improvements to increased knowledge, authors suggest that CBT should consist of an active process of structured learning, helping the client to improve their personal understanding (Kilbridea et al., 2013). It has also been shown that a lack of understanding of how the cognitive behavioural model applies to an individual results in difficulties engaging in CBT (Lackner et al., 2007).

The quality of written information provided as part of the HI-CBT interventions was found by participants to be suboptimal and will need to be improved during future intervention delivery. A possible mechanism for these issues if that information provided within HI-CBT was not subject to peer review of the PAG as within the LI-CBT intervention where the SH materials were thought to be a more integral part of the intervention.

The provision of information should therefore be considered a necessary part of the interventions despite these qualitative findings. Indeed, some participants felt they were ill prepared for the intrusiveness and depth of the therapeutic encounter. However, more needs to be done to ensure that information is tailored and relevant to the needs of the individual which may improve the impact information giving has upon the experience of IBS. This was particularly evident when participants were

able to identify with themselves during therapy. Previous qualitative studies evaluating the use of computerised CBT have identified how the factors of self-identification along with experienced improvements and the experience of participating in a scientific study were all potential motivators for completing such interventions (Gerhards et al., 2011).

Similar problems have been identified with the use of internet CBT as participants of these interventions have reported therapy to be 'impersonal' (Mohr et al., 2010). Mohr et al (2010) found that individuals with these views may find face to face forms of therapy more acceptable. In addition to the lack of personally tailored treatment described by some participants, a barrier to the implementation of the trialled interventions identified during post-intervention interviews was also the impact that strong, personally held beliefs had upon the participant's ability to engage.

These issues have arisen during similar programs of research which have identified difficulties addressing illness beliefs and resistance to psychotherapy when therapy has been delivered by non-specialist nurses to patients with MUS (Lyles et al., 2003). However, when therapists are able to successfully align treatment and illness beliefs, intervention recipients are more likely to engage in, and complete therapy interventions (Chew-Graham et al., 2010). Issues such as contextual factors and subjective beliefs have also previously been identified as potential factors which may hinder engagement with interventions (Choi et al., 2012).

Participants within HI-CBT did not describe these traits which were apparent in the LI-CBT and SH interventions. Such factors may relate to the provision of HI-CBT overcoming such barriers which might not have been possible with a less experienced nurse therapist. Working as a therapist could be considered a qualitatively different role to being a regular nurse, in the fact that one may require adjustments to one's identity and development of the methods used for interacting with

patients. However, challenges faced by nurses addressing long-term conditions with such interventions are not unusual. For example Marshall and Smith (1995) found that nurses' expertise was often questioned by patients who may have extensive knowledge due to their long-term experience with their condition. These issues may therefore be a feature of long-term conditions management rather than being unique to the delivery of CBT to persons with IBS. Such issues may be overcome with the use of appropriate clinical supervision and guidance.

6.1.4 Implications for a future study

A complex and detailed feasibility study relating to the use of a novel LI-CBT nursing intervention in comparison with HI and SH interventions and a TAU condition when implemented for the treatment of participants with IBS meeting Rome III criteria has been conducted and reported. Although the sample size of the study did not reach the desired sample size, much has been learned from running the feasibility study which has implications for future research and the design of a future trial.

The value participants place upon the face-to-face interaction with a therapist, the disadvantages that arise due to a lack of therapist involvement and how these issues might compare to group and internet delivery mechanisms have been critically discussed. The advantages gained with the addition of therapist interaction may outweigh economic advantages gained when stand-alone interventions are implicated, particularly considering a) the prevalence of concomitant psychological issues b) the presence of domestic, physical and sexual abuse and c) the potential for suicidal ideation and self-harm. It is for these reasons that a future trial should instigate a support mechanism for participants of SH interventions. These support mechanisms may be brief in nature, and need not necessarily be delivered by a highly trained therapist, but should practically ensure that participants are safe from the risk of harm and have the ability to deal with crisis situations. Supporters should also be in a position to identify when a SH intervention is not suitable for the individual.

Risk management and the consideration of comorbid mental health problems should feature significantly within a follow-on trial. Stepped care presents a challenge for experimental evaluations of interventions, but the success of such models within primary care should not be overlooked (Clark, 2011). A future trial should therefore ensure that participants are safeguarded from self-harm or neglect and employ mechanisms for stepping up episodes of care where such issues are identified.

The qualitative data demonstrates that participant's value individualised care and interventions which are tailored to meet the needs of the individual. Despite difficulties implementing these qualities with the use of SH interventions, participants found that this was possible where they were able to identify with themselves within written literature or the intervention protocols. The same can be said for allowing sufficient flexibility within treatment protocols to enable therapists to tailor interventions accordingly as would be the case in real-life clinical settings. Such flexibility has the potential to threaten the validity and reproducibility of experiments, and so should be designed with due diligence and attention to scientific rigour.

The recruitment strategies used within this feasibility failed for a number of reasons which were presented earlier within chapter 5. The most notable issue was the presence of the commissioning arrangement which hindered the delivery of interventions to people with IBS from a variety of settings. Conducting a large scale study at a single study site is not likely to be feasible and due attention needs to be given to a multicentre approach following an assessment of feasibility and consideration of commissioning arrangements. This would increase opportunities for people with IBS to be able to take part in the research and address some of the recruitment concerns identified during the feasibility study at a single site.

The qualitative data collected during the conduct of this study has provided valuable information regarding the acceptability and the suitability of the trialled interventions in accordance with the recommendations contained within the MRC complex interventions framework (MRC, 2008). A future trial should continue to draw on the strengths of mixed methods study designs and future qualitative evaluations are warranted. This study did not interview participants within TAU conditions, clinicians recruiting to the feasibility study or the therapist's delivering the interventions which may also be beneficial. A future trial should therefore consider widening the scope of qualitative data collection in order to increase the impact these data have on our understanding of CBT interventions used for the treatment of IBS.

TAU treatment conditions have the potential to disappoint participants upon allocation and although TAU participants were not interviewed during this study, participants within the intervention conditions suggested that they would have been disappointed with being randomised to TAU. Systematic reviews (Zijdenbos et al., 2009) and scientific rigour suggest that such treatment conditions are necessary for demonstrating treatment effects when compared to participants who do not receive the trialled interventions. Other than a single participant in LI-CBT, there was no evidence to suggest that TAU participants within this study sought CBT treatment elsewhere after learning about the interventions within this study at 26 week follow up as reported on the 26 week CRF. A waiting list condition is a potential option for addressing these issues and this approach and the implications it may have upon the scientific quality of a study needs to be carefully considered.

Overall, patients and the public have played a vital role in the design of the nurse led intervention and SH materials used within this study and such involvement should be considered essential within a future trial. The duration of research and funding should consider the necessity of involving patients and the public to become involved in the design and conduct of the research. Timescales of the research should be sufficient

to allow meaningful patient involvement within the development of the trial and its interventions.

With a feasibility study of a small sample of participants experiencing the trialled interventions, it is almost impossible to make any robust claims regarding the effects noted within the four treatment conditions of the study. Nonetheless, there is no evidence to suggest that any of the three trialled interventions should be discontinued although the SH intervention will need to be modified to encompass some form of support. The data gathered and critically discussed here can only improve upon the quality of the interventions which should be developed and potentially utilised within a future study.

6.1.5 Strengths and limitations of the study

Strengths

This study has assessed feasibility of a novel, LI-CBT nursing intervention as applied in the management of participants with treatment refractory IBS. Novel feasibility data relating to the acceptability and suitability of the various interventions has also been gathered which may be used to shape the design of a future study.

The methods used for this feasibility study have been designed with the diligent integration of patient and public involvement throughout. The methods employed during this feasibility work also exceed standards of those forming the current evidence base reviewed within chapter 3. Such methods may be further developed in light of the feasibility data for use within a future trial. Although sample sizes were small, all three treatment conditions have descriptive data relating to positive changes in levels of QOL, subjective symptoms and levels of anxiety and depression. It is possible the noted effects could be improved upon by further developing the interventions with the knowledge obtained during this feasibility work. It is also possible that such observations have occurred by chance alone within a feasibility study of this size.

No research has explored barriers and facilitators to the use of psychotherapeutic treatment regimens as applied to the secondary care population of patients with IBS. Overall this study adds a novel contribution to the body of knowledge regarding the feasibility of lower-intensity CBT treatment modalities as applied to the management of IBS which is particularly relevant to the UK context and expansion to nursing practice. Further details regarding recommendations as a result of this work can be found within the sections which follow.

Limitations

There are several limitations to this research which should be considered carefully when interpreting the results presented throughout this thesis. First of all, one should appreciate that the study experienced significant recruitment problems which result largely from the design of the trial and methods used to recruit potential participants. As a result, the sample size of the study was not achieved during the study timescales. This has resulted in a small sample size in relation to the number of participants assigned to interventions and participants who subsequently agreed to take part in post-intervention interviews.

Nonetheless, this study was not designed to generate inferential data regarding the effectiveness of the trialled interventions, and the observed effects have been described in a descriptive nature without attempts to make generalisations. One should also consider that there is limited guidance available to researchers regarding the optimum sample size for feasibility studies of this kind. It is therefore possible that not recruiting further patients to the study may have impacted upon the quality of the data gathered during feasibility. Participants within the TAU treatment condition were not interviewed, nor the therapists delivering interventions which may have been useful for exploring the experiences of participants randomised to TAU and the experience of therapists delivering the trialled interventions.

A further limitation to the qualitative data collection is that physicians, in particular those with recruitment responsibilities were not interviewed during the conduct of the study. It is possible that by doing so, further information might have been gathered to elicit barriers to the successful recruitment of participants from the gastrointestinal clinics. Considering the poor recruitment rates present in relation to other studies currently taking place within the speciality, a study evaluating the processes of recruitment used within the clinical area is warranted.

PPI played a crucial role in the design of the study materials and development of the intervention from an early stage. Unfortunately, there were limited timeframes for PPI within the scope of the studentship in which this study took place and the amount of time required for extensive user involvement was underestimated. A future study should therefore factor in a sufficient amount of time for the PPI process to provide a maximal contribution to the development of the interventions used within future studies.

It is possible that more themes may have been identified with larger samples of interview participants and it is difficult to suggest if data saturation was achieved during the analysis of interview data. This may be of particular relevance if attempts to generalise the findings of the qualitative component of this study are to be made. The qualitative work should therefore be interpreted with caution, but should reinforce the need for further research to explore phenomena relating to the acceptability and suitability of CBT treatment regimens in order for interventions to reach their full potential. These important phenomena have been largely neglected within previous studies, which makes this work both novel and informative for CBT intervention designers.

The study was conducted as part of a PhD studentship which also relates closely to the decisions made during trial design (regarding the scale of the feasibility work namely; lack of economic evaluations) and the financial implications of conducting an ambitious project without

substantial funding. For these reasons, the study did not consider outcomes such as service utilisation or economic data which may be considered essential for demonstrating the cost-effectiveness, societal benefits and impact of the interventions upon service utilisation. These issues should certainly be considered during follow on work considering the lack of such data highlighted during the systematic review of the literature reported in chapter 3.

The sample included within this study was recruited within a secondary care university teaching hospital within the East Midlands. Recruitment may have been enhanced if participants from community settings were recruited during the study period, although the feasibility of these recruitment methods would need to be established. This was not possible due to the commissioning arrangements as described within the recruitment section presented earlier. If suitable funding is secured for a full scale program of research, further sources of participants should be considered in order for the results of the study to be generalizable to the wider population of patients with IBS. Such methods would need to have their feasibility established prior to the commencement of further trials.

The monitoring methods and methods of measuring intervention quality were found to be suboptimal despite recording treatment sessions and the use of therapist declarations being employed as mechanisms to improve intervention delivery. Furthermore, no data was collected which may have helped identify agents of change during the study such as cognitive or behavioural processes. Further research which uses CBT interventions for the treatment of IBS should therefore employ more robust protocols for ensuring interventions are delivered as intended and the quality of intervention delivery maximised. This study was designed and formulated in accordance with complex interventions development and evaluation guidance, but was not designed using process evaluation research methods which may have been a viable alternative for evaluating the processes and outcomes of interest during the conduct of this feasibility work.

6.1.6 Recommendations for a future trial

I. Clinics for CBT interventions for study participants with IBS should be **flexible** to accommodate varied work patterns and participant availability in order to reduce the burden of interventions on work, social activities and potentially reduce attrition during therapy. Recommendation source: post-intervention interviews.

II. **Patients and members of the public** should continue to be involved in the development of CBT interventions in order to improve the relevance of interventions for participants and improve acceptability. Recommendation source: post-intervention interviews, PPI sections.

III. CBT treatment regimens should be **flexible and delivered according to the needs of individuals**. Recommendation source: post-intervention interviews.

IV. **Adequate information** should be provided to individuals prior to the commencement of CBT treatment. The information should inform patients about the potential breadth and depth of psychological interventions for IBS. The provision of information may promote engagement with interventions, allow preparation for taking part in therapy and potentially reduce attrition. Recommendation source: post-intervention interviews.

V. Materials used within CBT interventions should not include medical jargon, should be written **clearly and accurately** and consider the wider application of interventions to other aspects of life other than IBS. Recommendation source: post-intervention interviews and intervention development process.

VI. Materials used within CBT interventions should use **narratives, case studies and real life examples** which help participants to implement intervention components and to relate their personal circumstances during therapy. Recommendation source: post-intervention interviews.

VII. Therapists should consider **facilitating relaxation techniques** by actively participating in the relaxation experience with participants. SH materials should contain clear instructions of how relaxation techniques should be practiced. Recommendation source: post-intervention interviews.

VIII. The quality of supporting documentation should be improved to ensure that the format and content of the materials are **relevant to participants**. Recommendation source: post-intervention interviews.

IX. Consideration should be given in relation to the number of treatment sessions during a course of therapy and sufficient **time should be given to complete therapeutic tasks** between therapy sessions. Where possible, algorithms should be available for participants who do not require the full course of therapy and extensions to the number of treatment sessions should be possible where additional therapeutic support is required. Source: post-intervention interviews.

X. The **personality of the therapist** is an important factor for promoting and maintaining engagement with CBT interventions although the meaning of these phenomena within this context would benefit from further exploration. These factors should therefore be considered during the designing of new interventions. Source: post intervention interviews.

XI. **Suicidal ideation and self-harm** have the potential to be disclosed during intervention delivery. Clear mechanisms for appropriately dealing with these problems should be formulated prior to intervention delivery. Source: Adverse event reports.

XII. A future study should be **sufficiently funded** in order for the delivery of interventions to be possible for participants from a variety of settings. Source: recruitment processes evaluated during feasibility.

XIII. Protocols for CBT treatments for patients with IBS will need to be **sufficiently flexible** to allow treatment to be delivered in accordance with the needs of individuals. Recommendation source: post-intervention interviews.

XIV. **Healthcare professionals should be educated regarding the implementation and use of psychological interventions**, particularly where the intervention is new to the setting. Education sessions must provide professionals with an understanding of CBT interventions at the time of implementation in order to reduce ambiguity or conflicting advice being delivered to participants. Recommendation source: post-intervention interviews.

XV. Future studies should consider the **impact participation in research has upon participants**. The completion of study questionnaires and timing of data collection processes should enable sufficient flexibility to enable participants to submit responses around work and other commitments. Source: post-intervention interviews.

XVI. Future evaluations of CBT interventions for people with IBS should evaluate the **economic impact of interventions**. Societal benefits, implication on service utilisation and direct healthcare costs should be a feature of such studies. *Source: review of experimental evaluations.*

XVII. Future research should consider utilising mixed methods research approaches in order to explore issues relating to **treatment acceptability, suitability and relevance**. *Source: post intervention interviews and study findings.*

XVIII. Researchers evaluating CBT interventions for patients with IBS should consider the **implementation of interventions** which

should accurately reflect resources present within real clinical settings. *Source: review of experimental evaluations.*

XIX. Future research should evaluate the impact **traumatic life events** have upon patients with IBS. Source: *study findings and post-intervention interviews.*

XX. Experimental evaluations should utilise rigorous methods which should be **reported in accordance with current reporting standards** and guidelines. *Source: review of experimental evaluations.*

XXI. Future research should explore the **relevance of social support** in the context of participants taking part in CBT interventions for the treatment of IBS. Researchers should consider how social support might impact upon outcome. *Source: post-intervention interviews.*

XXII. Future research studies should consider investigating the **prevalence and phenomena of suicidal ideation and risk** which may be present among people with IBS. *Source: post-intervention interviews.*

6.1.7 Conclusion

A systematic literature review has been conducted and highlighted problems with the methods used to deliver CBT interventions to patients with IBS within the UK context. As a result, a new and novel nurse delivered, guided self-help intervention was developed in collaboration with patients and expert clinicians. A complex feasibility study was designed and implemented within a gastroenterology department within a large university hospital Trust within the East Midlands. The LI-CBT intervention was compared to traditional evidence based treatment approaches (HI-CBT), a TAU control and a SH intervention in terms of the descriptive observations and the acceptability and suitability of these methods during post intervention interviews. Both quantitative and qualitative data was collected from participants during the conduct of the feasibility study underpinned by a pragmatic philosophy and a MMR design.

The data generated during this study would suggest that nurse delivered, LI-CBT may be a feasible mechanism for intervention delivery within secondary care outpatient gastroenterology. Regardless of the observations made in relation to the feasibility of the trialled interventions, significant difficulties in recruitment were experienced throughout the duration of this study which may render further investigations unfeasible if problems with recruitment are not addressed.

The themes generated from the qualitative data have highlighted a variety of barriers and facilitators to the implementation of CBT treatment approaches as implemented during the conduct of a clinical trial. Participants struggled with the autonomy required to complete SH interventions, and most participants valued face-to-face interaction with a therapist. Possible mechanisms for overcoming these barriers include introducing a minimal support element to the SH intervention which would require further development in collaboration with patients and experts.

Facilitators to the implementation of the interventions included the successful implementation of relaxation techniques and the explicit use of narratives within SH materials to enable participants to self-identify with the text. Participants also felt that preparation may improve engagement with therapy and improve the acceptability of CBT interventions for IBS. A variety of other themes relevant to feasibility were also identified which have implications for future research.

This study was situated within the feasibility and pilot remit of the MRC's guidelines for the evaluation of complex interventions (2008). Although this study adds knowledge in relation to the potential barriers and facilitators to the successful implementation of the trialled interventions, the significant difficulties in recruiting participants to the feasibility trial suggest that further feasibility and piloting work is required to overcome these barriers if a large scale RCT is to be feasible.

Low-intensity and self-help cognitive behavioural therapy may be feasible mechanisms for the delivery of evidence based psychological interventions for patients with IBS. Further development of these lower-intensity interventions in collaboration with service users is required in order to improve the acceptability and relevance of the interventions within future studies. Problems experienced with the recruitment of participants to this trial warrant further investigation if future trials of this nature are to be feasible.

What is already known?

- IBS is a complex functional gastrointestinal disorder which is influenced by a variety of physical, psychological and sociological factors

- CBT is effective for the treatment of IBS in a variety of settings, but has been poorly utilised within secondary care services

- CBT treatment is a versatile and adaptable intervention which can be provided to patients through a variety of delivery mechanisms such as internet, telephone, group and individual modalities

- Psychological co-morbidities are common amongst people with IBS and have the potential to exacerbate symptoms, prolong the course of the condition and influence healthcare seeking behaviours

- IBS has a significant impact on healthcare systems, society and individuals

- People with IBS can experience chronic and persistent symptoms which may be resistant to pharmacological therapy

- IBS is a heterogeneous condition with no single treatment modality providing relief for the majority of sufferers

What does this study add?

- LI-CBT delivered by a nurse trained in the use of LI-CBT interventions is a potential mechanism for the delivery of evidence based psychological interventions within secondary care gastroenterology subject to further evaluation and feasibility work

- Barriers to the successful implementation of CBT interventions within this study include; a lack of individualised care, a lack of face-to-face interaction, difficulty carrying out relaxation techniques, a lack of preparation for the intrusiveness of therapy, difficulty attending appointments, the presence of dyslexia, strong a-priori personal beliefs and ambiguity in advice provided to patients regarding causation

- Facilitators to the successful implementation of the CBT interventions within this study include; flexibility in the timing and delivery of interventions, therapist-facilitated relaxation techniques, the use of narratives and examples within SH

materials, a perceived utility of treatment, previous positive engagement with CBT and a good therapist personality

- SH interventions are a potential mechanism for the delivery of evidence based psychological interventions within secondary care gastroenterology. Further development is required to improve the acceptability and suitability of the intervention in collaboration with service users

- Formal PWP training to nationally recognised standards of CBT delivery are a potential solution to ensuring the reproducibility of preparation of nurse therapists within future research studies and promote transparency regarding the competencies obtained by clinicians for the delivery of trialled interventions

- Suicidal ideation has been identified as a potential co-morbid presentation within this study which requires further evaluation during future research

- The experience of participants randomly allocated to various methods of CBT delivery has been explored and presented using semi-structured, in-depth qualitative interviews which will help inform researchers regarding the suitability and acceptability of CBT interventions during the conduct of a feasibility RCT

- Recruitment issues need to be rectified in order for future studies of this kind to be feasible at a single secondary care centre

Chapter 7 ▪ References

Ackermana, S. and Hilsenrothb, M. (2003) A review of therapist characteristics and techniques positively impacting the therapeutic alliance. **Clinical Psychology Review** 23(1): pp. 1-33.

Addington, J. and Gleeson, J. (2005) Implementing cognitive–behavioural therapy for first-episode psychosis. **British Journal of Psychiatry** 187(48): pp. 72-77.

Agrawal, A., Houghton, L., Reilly, B., Morris, J. and Whorwell, P. (2009) Bloating and distension in irritable bowel syndrome: the role of gastrointestinal transit. **American Journal of Gastroenterology** 104(8): pp. 1998-2004.

Agréus, L., Svärdsudd, K., Nyrén, O. and Tibblin, G. (1995) Irritable bowel syndrome and dyspepsia in the general population: overlap and lack of stability over time. **Gastroenterology** 109(3): pp. 671-680.

Akehurst, R., Brazier, J., Mathers, N., O'Keefe, C., Kaltenthaler, E., Morgan, A., Platts, M. and Walters, S. (2002) Health-related quality of life and cost impact of irritable bowel syndrome in a UK primary care setting. **Pharmacoeconomics** 20(7): pp. 455-462.

Alderson, P. (1996) Equipoise as a means of managing uncertainty: personal, communal and proxy. **Journal of Medical Ethics** 22(3): pp. 135-139.

Al-Huthail, Y. (2013) Healthcare seeking behavior among subjects with irritable bowel syndrome. **Saudi Medical Journal** 34(3): pp. 225-231.

Allen, L., Escobar, J., Lehrer, M., Gara, M. and Woolfolk, R. (2002) Psychosocial treatments for multiple unexplained physical symptoms: a review of the literature. **Psychosomatic Medicine** 64(6): pp. 939-950.

Alpers, D. (2006) Diet and Irritable Bowel Syndrome. **Current Opinion in Gastroenterology** 22(2): pp. 136-139.

Alpers, D., Clouse, R., Miller, A., North, C. and Wetzel, R. (2001) Irritable bowel syndrome, psychiatric illness, personality, and abuse: is somatization disorder the missing link? **Annals of Clinical Psychiatry** 13(25): pp. 25-30.

Altayar, O., Sharma, V., Prokop, L., Sood, A. and Mohammad, H. (2015) Psychological Therapies in Patients with Irritable Bowel Syndrome: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Available at: http://www.hindawi.com/journals/grp/2015/549308/ [Accessed 6 March 2016].

American Psychiatric Association. (2000) **Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR).** Washington: American Psychiatric Association.

Amstutz, H., Dorey, F. and Grigoris, P. (1994) Making do without randomised trials. **Journal of Joint and Bone Surgery** 76(5): p. 850.

Anaf, S. and Sheppard, L. (2007) Mixing research methods in health professional degrees: Thoughts for undergraduate students and supervisors. **The Qualitative Report** 12(2): pp. 184-192.

Anderson, J., Bjurstam, N., Fagerberg, G., Frisell, J., Larsson, L., Lindgren, A., Lindqvist, M., Nyström, L., Rutqvist, L., Rydén, S., et al. (1993) Breast cancer screening with mammography: overview of Swedish randomised trials. **Lancet** 341(8851): pp. 973-978.

Andersson, E., Ljótsson, B., Smit, F., Paxling, B., Hedman, E., Lindefors, N., Andersson, G. and Rück, C. (2011) Cost-effectiveness of internet-based cognitive behavior therapy for irritable bowel syndrome: results from a randomized controlled trial. **BMC public health** 11(1): pp. 215-215.

Arnstein, S. (1969) A ladder of citizen participation. **Journal of the American Institute of Planners** 35(4): pp. 216-224.

Arroll, B., Goodyear-Smith, F. and Hatcher, S. (2010) Validation of PHQ-2 and PHQ-9 to Screen for Major Depression in the Primary Care Population. **Annals of Family Medicine** 8(4): pp. 348-353.

Atkinson, P. (2005) **Qualitative research: Unity and diversity.** Forum Qualitative Sozialforschung / Forum: Qualitative Social Research [Online]. Available at: http://www.qualitative-research.net/index.php/fqs/article/view/4/9 [Accessed 6 March 2016].

Badia, X., Balboa, A., Baro, E., Caldwell, E., Cucala, M. and Mearin, F. (2002) Burden of illness in irritable bowel syndrome comparing Rome I and Rome II criteria. **Pharmacoeconomics** 20(11): pp. 749-758.

Bakhshipoura, A., Nezama, S., Zakeria, Z., Gharibia, R., Baharib, A. and Kaykhaeia, M. (2012) Coeliac disease in irritable bowel syndrome (Rome III) in Southeast Iran. **Arab Journal of Gastroenterology** 13(1): pp. 24-27.

Ballinger, C. (2006) Demonstrating rigour and quality. In: Finlay, L. and Ballinger, C. (Eds.) **Qualitative research for allied health professionals: challenging choices.** Chichester: John Wiley.

Balls, P. (2009) Phenomenology in nursing research: methodology, interviewing and transcribing. **Nursing Times** 105(32): pp. 30-33.

Barber, M. (2011) **"Alfred Shutz".** Stanford CA: Metaphysics research lab, Stanford Univeristy.

Bass, C., Peveler, R. and House, A. (2001) Somatoform disorders: severe psychiatric illnesses neglected by psychiatrists. **British Journal of Psychiatry** 179(1): pp. 11-14.

Baxter, J. and Eyles, J. (1997) Evaluating qualitative research in social geography: establishing rigor in interview analysis. **Transactions of the Institute of British Geographers** 22(4): pp. 505-525.

Bazeley, P. (2004) Issues in mixing qualitative and quantitative qpproaches to research. In: Buber, R., Gadner, J. and Richards, L. (Eds.) **Applying qualitative methods to marketing management research.** UK: Palgrave Macmillan, pp. 141-156.

Beattie, A., Shaw, A., Kaur, S. and Kessler, D. (2009) Primary-care patients' expectations and experiences of online cognitive behavioural therapy for depression: a qualitative study. **Health Expectations** 12(1): pp. 45-59.

Beauregard, M. (2007) Mind does really matter: Evidence from neuroimaging studies of emotional self-regulation, psychotherapy, and placebo effect. **Progress in Neurobiology** 81(4): pp. 218-236.

Beck, A. (1976) **Cognitive therapy and the emotional disorders.** New York: International Universities Press.

Beck, A. (2008) The evolution of the cognitive model of depression and its neurobiological correlates. **American Journal of Psychiatry** 165(8): pp. 969-977.

Beck, A. (1979) **Cognitive therapy and the emotional disorders.** New York: Meridian.

Beck, A., Rush, A., Shaw, B. and Emery, G. (1979) **Cognitive therapy of depression: a treatment manual.** New York: Guilford.

Beck, R. and Fernandez, E. (1998) Cognitive behavioral therapy in the treatment of anger: a meta-analysis. **Cognitive Therapy and Research** 22(1): pp. 63-74.

Bendelin, N., Hesser, H., Dahl, J., Carlbring, P., Nelson, K. and Andersson, G. (2011) Experiences of guided Internet-based cognitive-behavioural treatment for depression: a qualitative study. **BMC Psychiatry** 11(107): pp. 1-10.

Bengtsson, J., Nordin, S. and Carlbring, P. (2015) Therapists' Experiences of Conducting Cognitive Behavioural Therapy Online vis-à-vis Face-to-Face. **Cognitive Behaviour Therapy** 44(6): pp. 470-479.

Bengtson, M., Aamodt, G., Vatn, M. and Harris, J. (2015) Co-occurrence of IBS and symptoms of anxiety or depression, among Norwegian twins, is influenced by both heredity and intrauterine growth. **BMC Gastroenterology** 15(9): pp. 1-9.

Benjamin, C., Puleo, C., Settipani, C., Brodman, D., Edmunds, J., Cummings, C. and Kendall, P. (2011) History of Cognitive-Behavioral Therapy (CBT) in Youth. **Child and Adolescent Psychiatric Clinics of North America** 20(2): pp. 179-189.

Bennet, S., Öhman, L. and Simrén, M. (2015) Gut Microbiota as Potential Orchestrators of Irritable Bowel Syndrome. **Gut Liver** 9(3): pp. 318-331.

Bennett, E., Piesse, C., Palmer, K., Badcock, C., Tennant, C. and Kellow, J. (1998) Functional gastrointestinal disorders: psychological, social, and somatic features. **Gut** 42(3): pp. 414-420.

Bennett-Levy, J., Richards, D. and Farrand, P. (2010) Low-intensity CBT interventions: a revolution in mental health care. In: Bennett-Levy, J., Richards, D., Farrand, P., Christensen, H., Griffiths, K., Kavanagh, D., Klein, B., Lau, M., Proudfoot, J. and Ritterband, L. (Eds.) **Oxford guide to low-intensity CBT interventions.** New York: Oxford University Press.

Bhaskar, R. (1989) **The possibility of naturalism.** 2nd ed. Brighton UK: Harvester Wheatsheaf.

Biesiekierski, J., Newnham, E., Irving, P., Barrett, J., Haines, M., Doecke, J., Shepherd, S., Muir, J. and Gibson, P. (2011) Gluten Causes Gastrointestinal Symptoms in Subjects Without Celiac Disease: A Double-Blind Randomized Placebo-Controlled Trial. **American Journal of Gastroenterology** 106: (3): pp. 508-514.

Bijkerk, C., de Wit, N., Muris, J., Whorwell, P., Knottnerus, J. and Hoes, A. (2009) **Soluble or insoluble fibre in irritable bowel syndrome in primary care? Randomised placebo controlled trial.** BMJ [Online]. Available at: http://www.bmj.com/content/339/bmj.b3154 [Accessed 6 March 2016].

Bijkerk, C., Muris, J., Knottnerus, J., Hoes, A. and de Wit, N. (2004) Systematic review: the role of different types of fibre in the treatment of irritable bowel syndrome. **Alimentary Pharmacology and Therapeutics** 19(3): pp. 245-251.

Bishop, F., Yardleya, L. and Lewithb, G. (2006) Why do people use different forms of complementary medicine? Multivariate associations between treatment and illness beliefs and complementary medicine use. **Psychology and Health** 21(5): pp. 683-698.

Black, N. (1996) Why we need observational studies to evaluate the effectiveness of health care. **British Medical Journal** 312(7040): pp. 1215-1218.

Blanchard, E. (2001) **Irritable bowel syndrome: Psychosocial assessment and treatment.** Washington, DC: American Psychological Association.

Blanchard, E. and Scharff, L. (2002) Psychosocial aspects of assessment and treatment of irritable bowel syndrome in adults and recurrent abdominal pain in children. **Journal of Consultataion in Clinical Psychology** 70(3): pp. 725-738.

Blanchard, E. and Schwarz, S. (1988) Clinically significant changes in behavioral medicine. **Behavioral Assessment** 10(2): pp. 171-188.

Blanchard, E., Keefer, L., Lackner, J., Galovski, T., Krasner, S. and Sykes, M. (2004) The role of childhood abuse in Axis I and Axis II psychiatric disorders and medical disorders of unknown origin among irritable bowel syndrome patients. **Journal of Psychosomatic Research** 56(4): pp. 431-436.

Blanchard, E., Lackner, J., Sanders, K., Krasner, S., Keefer, L., Payne, A., Gudleski, G., Katz, L., Rowell, D., Sykes, M., et al. (2007) A controlled evaluation of group cognitive therapy in the treatment of irritable bowel syndrome. **Behaviour Research and Therapy** 45(4): pp. 633-648.

Bogalo, L. and Moss-Morris, R. (2006) The effectiveness of homework tasks in an irritable bowel syndrome cognitive behavioural self-management programme. **New Zealand Journal of Psychology** 35(3): pp. 120-125.

Böhmer, C. and Tuynman, H. (1996) The clinical relevance of lactose malabsorption in irritable bowel syndrome. **European Journal of Gastroenterology and Hepatology** 8(10): pp. 1013-1016.

Bolger, E. and Schilling, E. (1991) Personality and problems in everyday life: the role of neuroticism in exposure and reactivity to daily stressors. **Journal of Personality** 59(3): pp. 335-386.

Bolig, E., Maxwell, S. and Venter, A. (2002) Power in randomized group comparisons: the value of adding a single intermediate time point to a traditional pre-test post-test design. **Psychological Methods** 7(2): pp. 194-209.

Borrelli, B. (2011) The assessment, monitoring, and enhancement of treatment fidelity in public health clinical trials. **Journal of Public Health Dentistry** 71(1): pp. 52-63.

Borrelli, B., Sepinwall, D., Ernst, D., Bellg, A., Czajkowski, S., Breger, R., DeFrancesco, C., Levesque, C., Sharp, D., Ogedegbe, G., et al. (2005) A new tool to assess treatment fidelity and evaluation of treatment fidelity across 10 years of health behavior research. **Journal of consultating and clinical psychology** 75(5): pp. 852-860.

Bosaeus, I. (2004) Fibre effects on intestinal functions (diarrhoea, constipation and irritable bowel syndrome). **Clinical Nutrition Supplements** 1(2): pp. 33-38.

Bouras, E., Camilleri, M., Burton, D., Thomforde, G., McKinzie, S. and Zinsmeister, A. (2001) Prucalopride accelerates gastrointestinal and colonic transit in patients with constipation without a rectal evacuation disorder. **Gastroenterology** 120(2): pp. 354-360.

Bourgault, P., Devroede, G., St-Cyr-Tribble, D., Marchand, S. and Barcellos-de-Souza, J. (2008) Help-seeking process in women with irritable bowel syndrome. Part 1: study results. **Gastrointestinal Nursing** 6(9): pp. 24-31.

Bowen, D., Kreuter, M., Spring, B., Cofta-Woerpel, L., Linnan, L., Weiner, D., Bakken, S., Patrick Kaplan, C., Squiers, L., Fabrizio, C., et al. (2009) How We Design Feasibility Studies? **American Journal of Preventative Medicine** 36(5): pp. 452-457.

Bower, P. and Gilbody, S. (2005) Stepped care in psychological therapies: access, effectiveness and efficiency. **British Journal of Psychiatry** 186: pp. 11-17.

Bower, P., Richards, D. and Lovell, K. (2001) The clinical and cost-effectiveness of self-help treatments for anxiety and depressive disorders in primary care: a systematic review. **British Journal of General Practice** 51(471): pp. 838-845.

Boyce, P., Talley, N., Balaam, B., Koloski, N. and Truman, G. (2003) A randomized controlled trial of cognitive behavior therapy, relaxation training, and routine clinical care for the irritable bowel syndrome. **American Journal of Gastroenterology** 98(10): pp. 2209-2218.

Boyd, E., Zhao, W., Mannalithara, A., Sharabidze, A., Singh, G., Chung, E. and Levin, T. (2012) Diagnosis, Comorbidities, and Management of Irritable Bowel Syndrome in Patients in a Large Health Maintenance Organization. **Clinical Gastroenterology and Hepatology** 10(1): pp. 37-45.

BPS. (2010) **The British Psychological Society. Code of Human Research Ethics.** Leicester, UK: British Psychological Society.

Bradley, F., Wiles, R., Kinmonth, A., Mant, D. and Gantley, M. (1999) Development and evaluation of complex interventions in health services research: case study of the Southamptom heart integrated care project (SHIP). **British Medical Journal** 318(7185): pp. 711-715.

Bradford, K., Shih, W., Videlock, E., Presson, A., Naliboff, B., Mayer, E. and Chang, L. (2012) Association between Early Adverse Life Events and Irritable Bowel Syndrome. **Clinical Gastroenterology and Hepatology** 10(4): pp. 385-390.

Bradley-Bolen, B. (2000) **Breaking the bonds of irritable bowel syndrome.** Oakland, CA: New Harbinger Publications Inc.

Brandt, L., Chey, W., Foxx-Orenstein, A., Schiller, L., Schoenfeld, P., Spiegel, B., Talley, N., Quigley, E. and Moayyedi, P. (2009) An Evidence-Based Systematic Review on the Management of Irritable Bowel Syndrome. **American Journal of Gastroenterology** 104(1): pp. 1-35.

Brenes, G., Ingram, C. and Danhauer, S. (2011) Benefits and Challenges of Conducting Psychotherapy by Telephone. **Professional Psychology: Research and Practice** 42(6): pp. 543-549.

Brent, M., Lobato, D. and LeLeiko, N. (2009) Psychological treatments for pediatric functional gastrointestinal disorders. **Journal of Paediatric Gastroenterology Nutrition** 48(1): pp. 13-21.

Brosschot, J., Pieper, S. and Thayer, J. (2005) Expanding stress theory: prolonged activation and perseverative cognition. **Psychoneuroendocrinology** 30(10): pp. 1043-1049.

Brueton, V., Tierney, J., Stenning, S., Meredith, S., Harding, S., Nazareth, I. and Rait, G. (2014) **Strategies to improve retention in randomised trials: a Cochrane systematic review and meta-analysis.** BMJ Open [Online]. Available at: http://bmjopen.bmj.com/content/4/2/e003821.full.pdf+html [Accessed 6 March 2016].

Buckley, J. (2004) **User involvement in care: avoiding tokenism and achieving partnership.** Nursing Times.net [Online]. Available at: http://www.nursingtimes.net/nursing-practice-clinical-research/user-involvement-in-care-avoiding-tokenism-and-achieving-partnership/199293.article [Accessed 7 March 2016].

Burr, V. (1995) **An Introduction to social constructionism.** London: Routledge.

Caldarella, M., Serra, J., Azpiroz, F. and Malagelada, J. (2002) Prokinetic effects in patients with intestinal gas retention. **Gastroenterology** 122(7): pp. 1748-1755.

Camilleri, M. (2001) Management of the irritable bowel syndrome. **Gastroenterology** 120(3): pp. 652-668.

Camilleri, M. and Di Lorenzo, C. (2013) The Brain-Gut Axis: From Basic Understanding to Treatment of Irritable Bowel Syndrome and Related Disorders. **Journal of Paediatric Gastroenterology Nutrition** 54(4): pp. 446-453.

Camilleri, M., Coulie, B. and Tack, J. (2001) Visceral hypersensitivity: facts, speculations, and challenges. **Gut** 48(1): pp. 125-131.

Campbell, D., Cook, T. and Shadish, W. (2002a) Construct validity and external validity. In: Prancan, K. (Ed.) **Experimental and quasi-experimental designs for generalized causal inference.** USA: Wadsworth, pp. 64-102.

Campbell, D., Cook, T. and Shadish, W. (2002b) Randomized experiments: Rationale, designs and conditions conducive to doing them. In: Prancan, K. (Ed.) **Experimental and quasi-experimental designs for generalized causal inference.** USA: Wadsworth, pp. 246-278.

Canavan, C., West, J. and Card, T. (2014) The epidemiology of irritable bowel syndrome. **Clinical Epidemiology** 4(6): pp. 67-80.

Carroll, I., Ringel-Kulka, T., Siddle, J., Klaenhammer, T. and Ringel, Y. (2012) Characterization of the Fecal Microbiota Using High-Throughput Sequencing Reveals a Stable Microbial Community during Storage. **Plos One** 7(10): pp. 1-7.

Casellas, F., Aparici, A., Casaus, M., Roderiguez, P. and Malagelada, J. (2010) Subjective Perception of Lactose Intolerance Does Not Always Indicate Lactose Malabsorption. **Clinical gastroenterology and hepatology** 8: (7): pp. 581-586.

Chang, F. and Lu, C. (2009) Treatment of Irritable Bowel Syndrome Using Complementary and Alternative Medicine. **Journal of the Chinese Medical Association** 72(6): pp. 294-300.

Chang, L., Fukudo, S., Guthrie, E., Locke, R., Norton, N., Sperber, A. and Toner, B. (2006) Gender, Age, Society, Culture, and the Patient's Perspective in the Functional Gastrointestinal Disorders. **Gastroenterology** 130(5): pp. 1435–1446.

Chassany, O., Marquis, P., Scherrer, B., Read, N., Finger, T., Bergmann, J., Fraitag, B., Geneve, J. and Caulin, C. (1999) Validation of a specific quality of life questionnaire for functional digestive disorders. **Gut** 44(4): pp. 527-533.

Chaudhary, N. and Truelove, S. (1962) The irritable colon syndrome. A study of the clinical features, predisposing causes, and prognosis in 130 cases. **Quarterly Journal of Medicine** 31(1): pp. 307-322.

Chew-Graham, C., Brooks, J., Wearden, A., Dowrick, C. and Peters, S. (2010) Factors influencing engagement of patients in a novel intervention for CFS/ME: a qualitative study. **Primary Health Care Research & Development** 12(2): pp. 112-122.

Chey, W. (2013) The role of food in the functional gastrointestinal disorders: introduction to a manuscript series. **American Journal of Gastroenterology** 108(5): pp. 694-697.

Chey, W., Jin, H., Lee, M., Sun, S. and Lee, K. (2001) Colonic motility abnormality in patients with irritable bowel syndrome exhibiting abdominal pain and diarrhea. **American Journal of Gastroenterology** 96(5): pp. 1499-1506.

Chey, W., Kurlander, J. and Eswaran, S. (2015) Irritable Bowel Syndrome: A Clinical Review. **Journal of the American Medical Association** 13(9): pp. 949-958.

Chilcoat, H. and Breslau, N. (1998) Investigations of causal pathways between PTSD and drug use disorders. **Addictive Behaviours** 23(6): pp. 827-840.

Childress, C. (1998) **Potential Risks and Benefits of Online Psychotherapeutic Interventions.** Available at: http://www.ismho.org/potential_risks_and_benefits.asp [Accessed 6 March 2016].

Choi, I., Zou, J., Titov, N., Dear, B., Li, S., Johnston, L., Andrews, G. and Hunt, C. (2012) Culturally attuned Internet treatment for depression amongst Chinese Australians: a randomised controlled trial. **Journal of Affective Disorders** 136(3): pp. 459-468.

Clark, D. (2011) Implementing NICE guidelines for the psychological treatment of depression and anxiety disorders: The IAPT experience. **International Review of Psychiatry** 23(4): pp. 375-384.

Clouse, R. (2003) Antidepressants for irritable bowel syndrome. **Gut** 52(4): pp. 598-599.

Clouse, R. and Lustman, P. (2002) Antidepressants for irritable bowel syndrome. In: Camilleri M, SR. (Ed.) **Irritable Bowel Syndrome: Diagnosis and Treatment.** London: WB Saunders, pp. 161-171.

Clouse, R., Lustman, P., Geisman, R. and Alpers, D. (1994) Antidepressant therapy in 138 patients with irritable bowel syndrome: a five-year clinical experience. **Alimentary Pharmacological Therapy** 8(4): pp. 409-416.

Coates, M., Mahoney, C., Linden, D., Sampson, J., Chen, J., Blaszyk, H., Crowell, M., Sharkey, K., Gershon, M., Mawe, G., et al. (2004) Molecular defects in mucosal serotonin content and decreased serotonin reuptake transporter in ulcerative colitis and irritable bowel syndrome. **Gastroenterology** 126(7): pp. 1657-1664.

CONSORT. (2010a) **CONSORT flow diagram.** Available at: http://www.consort-statement.org/consort-statement/ [Accessed 7 March 2016].

CONSORT. (2010b) **CONSORT checklist for the reporting of clinical trials.** Available at: http://www.consort-statement.org/consort-statement/ [Accessed 7 March 2016].

Cook, C. and Sheets, C. (2011) Clinical equipoise and personal equipoise: two necessary ingredients for reducing bias in manual therapy trials. **Journal of Manual and Manipulative Therapy** 19(1): pp. 55-57.

Cook, T. and Campbell, D. (1979) **Quasi-experimentation: Design and analysis issues for field settings.** Geneva, IL: Houghton Mifflin.

Coremans, G. (2008) Prucalopride: the evidence for its use in the treatment of chronic constipation. **Core Evidence** 3(1): pp. 45-54.

Costello, E., Lauber, C., Hamady, M., Fierer, N., Gordon, J. and Knight, R. (2009) Bacterial community variation in human body habitats across space and time. **Science** 326(5960): pp.1694-1697.

Craske, M., Wolitzky-Taylor, K., Labus, J., Wu, S., Frese, M., Mayer, E. and Naliboff, B. (2011) A cognitive-behavioral treatment for irritable bowel syndrome using interoceptive exposure to visceral sensations. **Behaviour Research and Therapy** 49(6): pp. 413-421.

Creed, F., Craig, T. and Farmer, R. (1988) Functional abdominal pain, psychiatric illness and life events. **Gut** 29(2): pp. 235-242.

Creed, F., Guthrie, E., Ratcliffe, J., Fernandes, L., Rigby, C., Tomenson, B., Read, N. and Thompson, D. G. (2005) Does psychological treatment help only those patients with severe irritable bowel syndrome who also have a concurrent psychiatric disorder? **Australian and New Zealand Journal of Psychiatry** 39(9): pp. 807-815.

Cremonini, F. and Talley, N. (2005) Irritable bowel syndrome: epidemiology, natural history, health care seeking and emerging risk factors. **Gastroenterology Clinics of North America** 34(2): pp. 189-204.

Creswell, J. (2003) **Research design: Qualitative, quantitative, and mixed methods approaches. 2nd ed.** London: Sage.

Creswell, J. (2007) **Qualitative inquiry and research design: Choosing among five approaches. 2nd ed.** London: Sage.

Creswell, J. (2009) Mixed methods procedures. In: Creswell, J. (Ed.) **Research design: Qualitative, quantitative and mixed methods approaches.** London: Sage, pp. 203-236.

Creswell, J. and Plano-Clark, V. (2007a) **Designing and conducting mixed methods research. What is mixed methods research?** Thousand Oaks, CA: Sage, p. 6.

Creswell, J. and Plano-Clark, V. (2007b) Understanding mixed methods research. In: Creswell, J. and Plano-Clark, V. (Eds.) **Designing and conducting mixed methods research.** Thousand Oaks, CA: Sage, pp. 1-19.

Cuijpers, P., Donker, T., Van Straten, A., Li, J. and Andersson, G. (2010) Is guided self-help as effective as face-to-face psychotherapy for depression and anxiety disorders? A systematic review and meta-analysis of comparative outcome studies. **Psychological Medicine** 40(12): pp. 1943-1957.

D'Zurilla, T. J. and Nezu, A. M. (2007) **Problem-solving therapy: A positive approach to clinical intervention.** New York: Springer.

Dainty, A. (2012) Irritable bowel syndrome: psychological comorbidities and cognitive behavioural therapy. A review of the literature. **Gastrointestinal Nursing** 10(10): pp. 44-50.

Dainty, A., Allcock, N. and Cooper, J. (2014) Study of irritable bowel syndrome and co-existing psychological illness. **Nurse Researcher** 21(4): pp. 27-31.

Dainty, A., Fox, M., Lewis, N., Hunt, M., Holtham, E., Timmons, S., Kinsella, P., Wragg, A. and Callaghan, P. (2014) **A mixed methods feasibility study to evaluate the use of a low-intensity, nurse-delivered cognitive behavioural therapy for the treatment of irritable bowel syndrome.** Available at: http://bmjopen.bmj.com/content/4/6/e005262.abstract [Accessed 6 March 2016].

Dalla-vorgia, P., Mason, S., Megone, C., Allmark, P., Bratlid, D., Gill, A., Morrogh, P., Plomer, A. and Reiter-Theil, S. (2001) Overview of European legislation on informed consent for neonatal research. **Archives of Disease in Childhood** 84(1): pp. 70-73.

de Morton, N. (2009) The PEDro scale is a valid measure of the methodological quality of clinical trials: a demographic study. **Australian Journal of Physiotherapy** 55(2): pp. 129-133.

De Schepper, H., De Man, J., Moreels, T., Pelckmans, P. and De Winter, B. (2008) Gastrointestinal sensory and motor disturbances in inflammatory bowel disease - clinical relevance and pathophysiological mechanisms. **Alimentary Pharmacological Therapy** 27(8): pp. 621-637.

Declaration of Helsinki. (2000) **World Medical Association.** Available at: www.wma.net/e/policy/b3.htm [Accessed 6 March 2016].

Delgadilloa, J., Payneb, S., Gilbodyc, S., Godfreyc, C., Gored, S., Jessope, D. and Dalec, V. (2012) Brief case finding tools for anxiety disorders: Validation of GAD-7 and GAD-2 in addictions treatment. **Drug and Alcohol Dependence** 125(1): pp. 37-42.

Delvaux, M., Denis, P. and Allemand, H. (1997) Sexual and physical abuses are more frequently reported by IBS patients than by patients with organic digestive diseases or controls. **European Journal of Gastroenterology and Hepatology** 9(4): pp. 345-342.

Denzin, N. and Lincoln, Y. (2000) The discipline and practice of qualitative research. In: Denzin, N. and Lincoln, Y. (Eds.) **Handbook of qualitative research.** Thousand Oaks, CA: Sage.

Derogatis, L. and Melisaratos, N. (1983) The Brief Symptom Inventory: an introductory report. **Psychological Medicine** 13(3): pp. 595-605.

Dicker, B. and Kent, D. (1990) Physician consent and researchers' access to patients. **Epidemiology** 1(2): pp. 160-163.

DiMatteo, M., Lepper, H. and Croghan, T. (2000) Depression is a risk factor for noncompliance with medical treatment: meta-analysis of the effects of anxiety and depression on patient adherence. **Archives of Internal Medicine** 160(14): pp. 2101-2107.

Dimeff, L. A. and Koerner, K. (2007) **Dialectical behavior therapy in clinical practice: Applications across disorders and settings.** New York: Guilford.

Ditto, B., Eclache, M. and Goldman, N. (2006) Short-term autonomic and cardiovascular effects of mindfulness body scan meditation. **Annals of Behavioral Medicine** 32(3): pp. 227-234.

Doering, L., Chen, B., Eastwood, J., McGuire, A., Cross-Bodán, R. and Irwin, M. (2014) **Beyond Depression: Benefits of Cognitive Behavioral Therapy in Cardiac Surgery Patients.** Available at: http://circ.ahajournals.org/content/130/Suppl_2/A16389.abstract [Accessed 3 March 2016].

DOH. (2011a) **Talking therapies: A four-year plan of action. A supporting document to No health without mental health: A cross-government mental health outcomes strategy for people of all ages.** London: Department of Health.

DOH. (2011b) **No health without mental health.** London: Department of Health.

Dowling, M. (2004) Hermeneutics: an exploration. **Nurse Researcher** 11(4): pp. 30-41.

Doyle, L., Brady, A. and Byrne, G. (2009) An overview of mixed methods research. **Journal of Research in Nursing** 14(2): pp. 175-185.

Drossman, D. (2006) The functional gastrointestinal disorders and the rome III process. **Gastroenterology** 130(5): pp. 1377-1390.

Drossman, D., Corrazziari, E., Talley, N., Thompson, W. and Whitehead, W. (2000) **Rome II: The Functional Gastrointestinal Disorders. Diagnosis, Pathophysiology, and Treatment: A Multinational Consensus.** McLean, VA: Degnon Associates.

Drossman, D., Leserman, J., Nachman, G., Li, Z., Gluck, H., Toomey, T. and Mitchell, C. (1990) Sexual and physical abuse in women with functional or organic gastrointestinal disorders. **Annals of Internal Medicine** 113(11): pp. 828-833.

Drossman, D., Li, Z., Andruzzi, E., Temple, R., Talley, N., Thompson, W., Whitehead, W., Janssens, J., Funch-Jensen, P. and Corazziari, E. (1993) US householder survey of functional gastrointestinal disorders. Prevalence, sociodemography, and health impact. **Digestive Disease Science** 38(9): pp. 1569-1580.

Drossman, D., Patrick, D., Whitehead, W., Toner, B., Diamant, N., Hu, Y., Jia, H. and Bangdiwala, S. (2000) Further validation of the IBS-QOL: A disease-specific quality-of-life questionnaire. **American Journal of Gastroenterology** 95(4): pp. 999-1007.

Drossman, D., Thompson, W., Talley, N., Funch-Jensen, P., Janssens, J. and Whitehead, W. (1990) Identification of subgroups of functional gastrointestinal disorders. **Gastroenterology International** 3(1): pp. 159-172.

Drossman, D., Toner, B., Whitehead, W., Diamant, N., Dalton, C., Duncan, S., Emmott, S., Proffitt, V., Akman, D., Frusciante, K., et al. (2003) Cognitive-behavioral therapy versus education and desipramine versus placebo for moderate to severe functional bowel disorders. **Gastroenterology** 125(1): pp. 19-31.

Drossman, D., Whitehead, W. and Camilleri, M. (1997) Irritable bowel syndrome: A technical review for practice guideline development. **Gastroenterology** 112(6): pp. 2120-2137.

DuPont, A. (2008) Postinfectious Irritable Bowel Syndrome. **Clinical Infectious Diseases** 46(4): pp. 594-599.

Efird, J. (2011) Blocked Randomization with Randomly Selected Block Sizes. **International Journal of Environmental Research and Public Health** 8(1): pp. 15-20.

Ehde, D., Dillworth, T. and Turner, J. (2014) Cognitive-behavioral therapy for individuals with chronic pain efficacy, innovations, and directions for research. **American Psychologist** 69(2): pp. 155-166.

Ellis, A. (1994) **Reason and emotion in psychotherapy: A comprehensive method of treating human disturbances.** Rev. New York: Citadel.

El-Serag, H. (2003) Impact of irritable bowel syndrome: prevalence and effect on health-related quality of life. **Gastroenterology Disorders** 3(2): pp. 3-11.

El-Serag, H., Olden, K. and Bjorkman, D. (2002) Health-related quality of life among persons with irritable bowel syndrome: a systematic review. **Alimentary pharmacology and therapeutics** 16(6): pp. 1171-1185.

Enck, P., Martens, U. and Klosterhalfen, S. (2007) The psyche and the gut. **World Journal of Gastroenterology** 13(25): pp. 3405-3408.
Engel, G. (1967) The concept of psychosomatic disorder. **Journal of Psychosomatic Research** 11(550): pp. 3-9.

European Commission. (2015) **Medicinal products for human use. Clinical trials.** Available at: http://ec.europa.eu/health/human-use/clinical-trials/index_en.htm [Accessed 6 March 2016].

Everhart, J. and Renault, P. (1991) Irritable bowel syndrome in office-based practice in the United States. **Gastroenterology** 100(4): pp. 998-1005.

Everitt, H., Landau, S., Little, P., Bishop, F., McCrone, P., OReilly, G., Coleman, N., Logan, R., Chalder, T. and Moss-Morris, R. (2015) Assessing cognitive behavioural Therapy in Irritable Bowel (ACTIB): protocol for a randomised controlled trial of clinical-effectiveness and cost-effectiveness of therapist delivered cognitive behavioural therapy and web-based self-management in irritable bowel syndrome in adults. **British Medical Journal Open** 5(1): pp. 1-14.

Fadgyas-Stanculete, M., Buga, A., Popa-Wagner, A. and Dumitrascu, D. (2014) The relationship between irritable bowel syndrome and psychiatric disorders: from molecular changes to clinical manifestations. **Journal of Molecular Psychiatry** 42(4): pp. 1-7.

Farrand, P. and Williams, C. (2010) Low-intensity CBT assessment: in person or by phone. In: Bennett-Levy, J., Richards, D., Farrand, P., Christensen, H., Griffiths, K., Kavanagh, D., Klein, B., Lau, M., Proudfoot, J., Ritterband, L., et al. (Eds.) **Oxford guide to low-intensity CBT interventions. .** New York: Oxford University Press.

Farup, P., Monsbakken, K. and Vandvik, P. (2004) Lactose malabsorption in a population with irritable bowel syndrome: prevalence and symptoms. A case-control study. **Scandanavian Journal of Gastroenterology** 39(7): pp. 645-649.

Fass, R., Fullerton, S., Naliboff, B., Hirsh, T. and Mayer, E. (1998) Sexual dysfunction in patients with irritable bowel syndrome and non-ulcer dyspepsia. **Digestion** 59(1): pp. 79-85.

Feighery, C. (1999) Coeliac disease. **British Medical Journal** 319(7204): pp. 236-239.

Feilzer, M. (2009) Doing mixed methods research pragmatically: Implications for the rediscovery of pragmatism as a research paradigm. **Journal of Mixed Methods Research** 4(1): pp. 6-16.

Feneck, O. (2009) Clinical research in anaesthesia: randomized controlled trial or observational studies? **European Journal of Anaesthesiology** 24(1): pp. 1-5.

Foley, N., Teasell, R., Bhogal, S. and Speechley, M. (2003) Stroke Rehabilitation Evidence-Based Review: methodology. **Topics in Stroke Rehabilitation** 10(1): pp. 1-7.

Fond, G., Loundou, A., Hamdani, N., Boukouaci, W., Dargel, A., Oliveira, J., Roger, M., Tamouza, R., Leboyer, M. and Boyer, L. (2014) Anxiety and depression comorbidities in irritable bowel syndrome (IBS): a systematic review and meta-analysis. **European Archives of Psychiatry and Clinical Neuroscience** 264(8): pp. 651-660.

Ford, A., Chey, W., Talley, N., Malhotra, A., Spiegel, B. and Moayyedi, P. (2008) Utility of diagnostic tests for celiac disease in irritable bowel syndrome: systematic review and meta-analysis. **Gut** 57(2): pp. 651-658.

Ford, A., Moayyedi, P., Lacy, B., Lembo, A., Saito, Y., Schiller, L., Soffer, E., Spiegel, B. and Quigley, E. (2014) American College of Gastroenterology monograph on the management of irritable bowel syndrome and chronic idiopathic constipation. **American Journal of Gastroenterology** 109(1): pp. 2-26.

Ford, A., Quigley, E., Lacy, B., Lembo, A., Saito, Y., Schiller, L., Soffer, E., Spiegel, B. and Moayyedi, P. (2014) Effect of antidepressants and psychological therapies, including hypnotherapy, in irritable bowel syndrome: systematic review and meta-analysis. **American Journal of Gastroenterology** 109(9): pp. 1350-1365.

Foxx-Orenstein, A. and Chey, W. (2012) Manipulation of the Gut Microbiota as a Novel Treatment Strategy for Gastrointestinal Disorders. **American Journal of Gastroenterology** 1(1): pp. 41-46.

Freedman, B. (1987) Equipoise and the ethics of clinical research. **New England Journal of Medicine** 317(3): pp. 141-145.

Fuchs, T. (2004) Neurobiology and psychotherapy: An emerging dialogue. **Current Opinion in Psychiatry** 17: (6): pp. 479-485.

Gaber, O. (2016) The Relationship between Irritable Bowel Syndrome Depression, Anxiety, and Stress among a Sample of Irritable Bowel Patients: Predictive Study. **Journal of Sociological Research** 7(44): pp. 44-64.

Gadamer, G. (1989) **Truth and method. (2nd Ed).** London: Sheed & Ward.

García Rodríguez, L., Ruigómez, A., Wallander, M., Johansson, S. and Olbe, L. (2000) Detection of colorectal tumor and inflammatory bowel disease during follow-up of patients with initial diagnosis of irritable bowel syndrome. **Scandanavian Journal of Gastroenterology** 35(3): pp. 306-311.

Garsed, K., Chernova, J., Hastings, M., Lam, C., Marciani, L., Singh, G., Henry, A., Hall, I., Whorwell, P. and Spiller, R. (2013) **A randomised trial of ondansetron for the treatment of irritable bowel syndrome with diarrhoea.** Available at: http://gut.bmj.com/content/early/2013/12/12/gutjnl-2013-305989.full.pdf+html [Accessed 6 March 2016].

Gaylord, S., Palsson, O., Garland, E., Faurot, K., Coble, R., Mann, J., Frey, W., Leniek, K. and Whitehead, W. (2011) Mindfulness training reduces the severity of irritable bowel syndrome in women: results of a randomized controlled trial. **The American Journal of Gastroenterology** 106(9): pp. 1678-1688.

Gaylord, S., Whitehead, W., Coble, R., Faurot, K., Palsson, O., Garland, E., Frey, W. and Mann, J. (2009) Mindfulness for irritable bowel syndrome: protocol development for a controlled clinical trial. **BMC Complement Altern Med** 9(1): pp. 24-24.

Gearry, R., Irving, P., Barrett, J., Nathan, D., Shepherd, S. and Gibson, P. (2009) Reduction of dietary poorly absorbed short-chain carbohydrates (FODMAPs) improves abdominal symptoms in patients with inflammatory bowel disease: a pilot study. **Journal of Crohn's and Colitis** 3(1): pp. 8-14.

Geboes, K. and Collins, S. (1998) Structural abnormalities of the nervous system in Crohn's disease and ulcerative colitis. **Neurogastroenterology Motility** 10(3): pp. 189-202.

Gellatly, J., Bower, P., Hennessy, S., Richards, D., Gilbody, S. and Lovell, K. (2007) What makes self-help interventions effective in the management of depressive symptoms? Meta-analysis and meta-regression. **Psychological Medicine** 37(9).

Gerhards, S., Abma, T., Arntz, A., de Graaf, L., Evers, S., Huibers, M. and Widdershoven, G. (2011) Improving adherence and effectiveness of computerised cognitive behavioural therapy without support for depression: a qualitative study on patient experiences. **Journal of Affective Disorders** 129(1): pp. 117-125.

Gibson, P. and Shepherd, S. (2010) Evidence-based dietary management of functional gastrointestinal symptoms: The FODMAP approach. **Journal of Gastroenterology and Hepatology** 25(2): pp. 252-258.

Glasziou, P., Heneghan, C., Meats, E. and Shepperd, S. (2008) What is missing from descriptions of treatment in trials and reviews. **British Medical Journal** 336(7659): pp. 1472-1474.

González-Prendes, A. and Resko, S. (2012) Capter 2: Cognitive Behavioral Theory. In: Ringel, S. and Brandell, J. (Eds.) **Trauma: Contemporary Directions in Theory, Practice, and Research.** London: SAGE Publications.

Gralnek, I., Hays, R., Kilbourne, A., Chang, L. and Mayer, E. (2004) Racial differences in the impact of irritable bowel syndrome on health-related quality of life. **Journal of Clinical Gastroenterology** 38(9): pp. 782-789.

Gralnek, I., Hays, R., Kilbourne, A., Naliboff, B. and Mayer, E. (2000) The impact of irritable bowel syndrome on health-related quality of life. **Gastroenterology** 119(3): pp. 654-660.

Grand, R. and Montgomery, R. (2008) Lactose malabsoprtion. **Current treatment options in Gastroenterology** 11(1): pp. 19-25.

Greene, B. and Blanchard, E. (1994) Cognitive therapy for irritable bowel syndrome. **Journal of consulting and clinical psychology** 62(3): pp. 576-582.

Greene, J. (2007) **Mixed methods in social enquiry.** Chichester, UK: Wiley.

Gregory, R., Canning, S., Lee, T. and Wise, J. (2004) Cognitive bibliotherapy for depression: a meta-analysis. **Professional Psychology: Research and Practice** 35(3): pp. 275-280.

Groll, D., Vanner, S., Depew, W., DaCosta, L., Simon, J., Groll, A., Roblin, N. and Paterson, W. (2002) The IBS-36: A new quality of life measure for Irritable Bowel Syndrome. **American Journal of Gastroenterology** 97(4): pp. 962-971.

Gros, D., Antony, M., McCabe, R. and Swinson, R. (2009) Frequency and severity of the symptoms of irritable bowel syndrome across the anxiety disorders and depression. **Journal of Anxiety Disorders** 23(2): pp. 290-296.

Gunaratnam, Y. (2009) **Narrative and stories in health care: Illness, dying, and bereavement.** Oxford: Oxford University Press.

Gunn, M., Cavin, A. and Mansfield, J. (2003) Management of irritable bowel syndrome. **Postgraduate Medicine** 79(929): pp. 154-158.

Gupta, D., Ghoshal, U., Misra, A., Misra, A., Choudhuri, G. and Singh, K. (2007) Lactose intolerance in patients with irritable bowel syndrome from northern India: a case-control study. **Journal of Gastroenterology and Hepatology** 22(12): pp. 2261-2265.

Guthrie, E., Barlow, J., Fernandes, L., Ratcliffe, J., Read, N., Thompson, D., Tomenson, B. and Creed, F. (2004) Changes in tolerance to rectal distension correlate with changes in psychological state in patients with severe irritable bowel syndrome. **Psychosomatic Medicine** 66(4): pp. 578-502.

Gwee, K., Graham, J., McKendrick, M., Collins, S., Marshall, J., Walters, S. and Read, N. (1996) Psychometric scores and persistence of irritable bowel after infectious diarrhoea. **Lancet** 347(8995): pp. 150-153.

Hahn, B., Kirchdoerfer, L., Fullerton, S. and Mayer, E. (1997) Patient-perceived severity of irritable bowel syndrome in relation to symptoms, health resource utilization and quality of life. **Alimentary Pharmacology and Therepeutics** 11(3): pp. 553-559.

Hahn, B., Watson, M., Yan, S., Gunput, D. and Heuijerjans, J. (1998) Irritable Bowel Syndrome Symptom Patterns: Frequency, Duration, and Severity. **Digestive Diseases and Sciences** 43(12): pp. 2715-2718.

Halder, S., Fett, S., Locke, G., Melton, L., Talley, N. and Zinsmeister, A. (2004) Impact of functional gastrointestinal disorders on health-related quality of life: a population-based case-control study. **Alimentary Pharmacology Therapeutics** 19(2): pp. 233-242.

Halland, M., Almazar, A., Lee, R., Atkinson, E., Larson, J., Talley, N. and Saito, Y. (2014) A case-control study of childhood trauma in the development of irritable bowel syndrome. **Neurogastroenterology Motility** 26(7): pp. 990-998.

Halmosemail, E., Power, V., Shepherd, S., Gibson, P. and Muir, J. (2014) A Diet Low in FODMAPs Reduces Symptoms of Irritable Bowel Syndrome. **Gastroenterology** 146(1): pp. 67-75.

Hammer, J. and Talley, N. (2008) Value of different diagnostic criteria for the irritable bowel syndrome among men and women. **Journal of Clinical Gastroenterology** 2(42): pp. 160-166.

Handa, M., Nukina, H., Ando, K. and Kubo, C. (2004) What Does Pain or Discomfort in Irritable Bowel Syndrome Mean? **Digestive Disease and Sciences** 49(4): pp. 575-578.

Harris, J. (2005) Scientific research is a moral duty. **Journal of Medical Ethics** 31(1): pp. 242-248.

Harris, L. and Roberts, L. (2008) Treatment for irritable bowel syndrome: patients' attitudes and acceptability. **BMC Complementary and Alternative Medicine** 8(65): pp. 1-11.

Hassett, A. and Gevirtz, R. (2009) Nonpharmacologic treatment for fibromyalgia: Patient education, Cognitive-Behavioral Therapy, relaxation techniques, and complementary and alternative medicine. **Rheumatic Disease Clinics of North America** 35(2): pp. 393-407.

Hatcher, S. and Arroll, B. (2008) Assessment and management of medically unexplained symptoms. **British Medical Journal** 336(7653): pp. 1124-1128.

Hayes, S. C., Luoma, J. B., Bond, F. W., Masuda, A. and Lillis, J. (2006) Acceptance and commitment therapy: Model, processes, and outcomes. **Behaviour Research and Therapy** 44(1): pp. 1-25.

Haynes, R., Richardson, W., Rosenberg, W. and Sackett, D. (1997) **Evidence Based Medicine: How to practice and teach EBM.** New York: Churchill Livingstone.

He, T., Priebe, M., Harmsen, H., Stellaard, F., Sun, X., Welling, G. and Vonk, R. (2006) Colonic fermentation may play a role in lactose intolerance in humans. **Journal of Nutrition** 136(1): pp. 58-63.

Heaton, K., O'Donnell, L., Braddon, F., Mountford, R., Hughes, A. and Cripps, P. (1992) Symptoms of irritable bowel syndrome in a British urban community: consulters and nonconsulters. **Gastroenterology** 102(6): pp. 1962-1967.

Heidegger, M. (1962) **Being and time.** New York: Harper and Row.

Heitkemper, MM. and Jarrett, ME. (2008) Update on irritable bowel syndrome and gender differences. **Nutrition in clinical practice** 23(3): pp. 275-283.

Heizer, W., Southern, S. and McGovern, S. (2009) The role of diet in symptoms of irritable bowel syndrome in adults: a narrative review. **Journal of American Dietetic Association** 109(7): pp. 1204-1214.

Henningsen, P., Zimmermann, T. and Sattel, H. (2003) Medically unexplained physical symptoms, anxiety, and depression: a meta-analytic review. **Psychosomatic Medicine** 65(4): pp. 528-529.

Hewitt, C. and Torgerson, D. (2009) Randomization: What is it and how to do it. In: Domanski, M. and McKinlay, S. (Eds.) **Successful Randomized Trials.** Philadelphia, USA: Wolters Kluwer, p. 27.

Heymann-Mönnikes, I., Arnold, R., Florin, I., Herda, C., Melfsen, S. and Mönnikes, H. (2000) The combination of medical treatment plus multicomponent behavioral therapy is superior to medical treatment alone in the therapy of irritable bowel syndrome. **The American Journal of Gastroenterology** 95(4): pp. 981-994.

Hill, D., Hoffmann, C., Abt, M., Du, Y., Kobuley, D., Kirn, T., Bushman, F. and Artis, D. (2010) Metagenomic analyses reveal antibiotic-induced temporal and spatial changes in intestinal microbiota with associated alterations in immune cell homeostasis. **Mucosal immunology** 3(2): pp. 148-158.

Hillilä, M., Siivola, M. and Färkkilä, M. (2007) Comorbidity and use of health-care services among irritable bowel syndrome sufferers. **Scandanavian Journal of Gastroenterology** 42(7): pp. 799-806.

Hirai, M. and Clum, G. (2006) A meta-analytic study of self-help interventions for anxiety problems. **Behaviour Therapy** 37(2): pp. 99-111.

Hislop, I. (1971) Psychological significance of the irritable colon syndrome. **Gut** 12(6): pp. 452-457.

Hoddinott, P. (2015) A new era for intervention development studies. **Pilot and Feasibility Studies** 38(1): pp. 82-96.
Howell, S., Talley, N., Quine, S. and Poulton, R. (2004) The irritable bowel syndrome has origins in the childhood socioeconomic environment. **American Journal of Gastroenterology** 99(8): pp. 1572-1578.

Hu, W., Wong, W., Lam, C., Lam, K., Hui, W., Lai, K., Xia, H., Lam, S. and Wong, B. (2002) Anxiety but not depression determines health care-seeking behaviour in Chinese patients with dyspepsia and irritable bowel syndrome: a population-based study. **Alimentary Pharmacological Therapy** 16(12): pp. 2081-2088.

Huang, X., Lin, L. and Demner-Fushman, D. (2006) **Evaluation of PICO as a knowledge representation for clinical questions.** Available at: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1839740/?tool=pmcentrez [Accessed 6 March 2016].

Huberman, A. and Miles, M. (1988) Assessing local causality in qualitative research. In: Berg, D. and Smith, K. (Eds.) **The self in social inquiry: Researching methods.** Newbury Park, CA: Sage, pp. 351-381.

Hulisz, D. (2004) The Burden of Illness of Irritable Bowel Syndrome: Current Challenges and Hope for the Future. **Journal of Managed Care Pharmacy** 10(4): pp. 299-309.

Hungin, A., Chang, L., Locke, G., Dennis, E. and Barghout, V. (2005) Irritable bowel syndrome in the United States: prevalence, symptom patterns and impact. **Alimentary Pharmacological Therapy** 21(11): pp. 1365-1375.

Hungin, A., Tack, J. and Whorwell, P. (2003) The prevalence, patterns and impact of irritable bowel syndrome: an international survey of 40,000 subjects. **Alimentary Pharmacology and Therapeutics** 17(12): pp. 643-650.

Hunt, M., Moshier, S. and Milonova, M. (2009) Brief cognitive-behavioral internet therapy for irritable bowel syndrome. **Behaviour Research and Therapy** 47(9): pp. 797-802.

Hunt, N. (2012) **Methodological Limitations of the RCT in Determining the Efficacy of Psychological Therapy for Trauma.** Available at: http://www.scitechnol.com/methodological-limitations-of-the-rct-in-determining-the-efficacy-of-psychological-therapy-for-trauma-J9uG.php?article_id=43 [Accessed 6 March 2016].

Hunt, M., Moshierb, S. and Milonovab, M. (2009) Brief cognitive-behavioral internet therapy for irritable bowel syndrome. **Behaviour Research and Therapy** 47(9): pp. 797-802.

Hussain, Z. and Quigley, E. (2006) Systematic review: Complementary and alternative medicine in the irritable bowel syndrome. **Alimentary Pharmacological Therapy** 23(4): pp. 465-471.

IAPT. (2010) **Good practice guidance on the use of self-help materials within IAPT services.** Available at: http://www.iapt.nhs.uk/silo/files/good-practice-guidance-on-the-use-of-selfhelp-materials-within-iapt-services.pdf [Accessed 6 March 2016].

IAPT. (2011) **National curriculum for the education of Psychological Wellbeing Practitioners (PWPS).** Available at: http://www.iapt.nhs.uk/silo/files/national-curriculum-for-the-education-of-psychological-wellbeing-practitioners-pwps-.pdf [Accessed 6 March 2016].

IAPT. (2013) **About IAPT.** Available at: http://www.iapt.nhs.uk/about-iapt/ [Accessed 6 March 2016].

ICH-GCP. (2012) **International Conference on Harmonisation of technical requirements for registration of pharmaceuticals for human use.** Available at: http://ichgcp.net/ [Accessed 6 March 2016].

Inadomi, J., Fennerty, M. and Bjorkman, D. (2003) Systematic review: the economic impact of irritable bowel syndrome. **Alimentary Pharmacological Therapy** 1(18): pp. 671-682.

Ioannidis, JP., Greenland, S., Hlatky, MA., Khoury, MJ., Macleod, MR. and Moher, D. (2014) Research Waste series: increasing value and reducing waste in research design, conduct, and analysis. **Lancet** 383(9912): pp. 166–75.

Jadad, A. (1998) **Randomised controlled trials: a user's guide.** London: BMJ Books.

Jane Lu, Z., Chen, W., Chen, H. and Ou, M. (2009) Irritable Bowel Syndrome: The Bodily Experiences of Taiwanese Women. **Journal of Nursing Research** 17(1): pp. 42-51.

Jason, L., Richman, J., Rademaker, A., Jordan, K., Plioplys, A., Taylor, R., McCready, W., Huang, C. and Plioplys, S. (1999) A community-based study of chronic fatigue syndrome. **Archives of Internal Medicine** 159(18): pp. 2129-2137.

Johnson, B. and Onwuegbuzie, A. (2004) Mixed methods research: A research paradigm whose time has come. **Educational Researcher** 33(7): pp. 14-26.

Jokić-Begić, N. (2010) Cognitive-Behavioral Therapy and Neuroscience: Towards Closer Integration. **Psychological Topics** 19(2): pp. 235-254.

Jones, E., Williams-Yesson, B., Hackett, R., Staniszewska, S., Evans, D. and Francis, N. (2015) Quality of reporting on patient and public involvement within surgical research. **Annals of Surgery** 261(2): pp. 243-250.

Julious, S. (2005) Sample size of 12 per group rule of thumb for a pilot study. **Pharmaceutical Statistics** 4(4): pp. 287-291.

Kam, C., Wilking, J. and Zechmeister, E. (2007) Beyond the ‘‘Narrow Data Base’’: Another convenience sample for experimental research. **Political Behaviour** 29(4): pp. 415-440.

Kamm, M. (2002) The complexity of drug development for irritable bowel syndrome. **Alimentary Pharmacological Therapy** 16(3): pp. 343-351.

Kanazawa, M., Endo, Y., Whitehead, W., Kano, M., Hongo, M. and Fukudo, S. (2004) Patients and nonconsulters with irritable bowel syndrome reporting a parental history of bowel problems have more impaired psychological distress. **Digestive Diseases Science** 49(6): pp. 1046-1053.

Kaptchuk, T., Kelley, J., Conboy, L., Davis, R., Kerr, C., Jacobson, E., Kirsch, I., Schyner, R., Nam, B. and Nguyen, L. (2008) Components of placebo effect: randomised controlled trial in patients with irritable bowel syndrome. **British Medical Journal** 2(336): pp. 999-1003.

Katon, W., Von Korff, M., Lin, E. and Simon, G. (2001) Rethinking practitioner roles in chronic illness: the specialist primary care physician, and the practice nurse. **General Hospital Psychiatry** 23(3): pp. 138-144.

Kendall, P. and Hollon, S. (1979) Cognitive-behavioral interventions: Overview and current status. In: Kendall, P. and Hollon, S. (Eds.) **Cognitive-behavioral interventions: Theory, research, and procedures.** New York: Academic Press, pp. 1-9.

Kennedy, P., Cryan, J., Dinan, T. and Clarke, G. (2014) Irritable bowel syndrome: A microbiome-gut-brain axis disorder? **World Journal of Gastroenterology** 20(39): pp. 14105-14125.

Kennedy, T. and Jones, R. (2000) Epidemiology of cholecystectomy and irritable bowel syndrome in a UK population. **British Journal of Surgery** 87(12): pp. 1658-1663.

Kennedy, T., Jones, R., Darnley, S., Seed, P., Wessely, S. and Chalder, T. (2005) Cognitive behaviour therapy in addition to antispasmodic treatment for irritable bowel syndrome in primary care: Randomised controlled trial. **British Medical Journal** 331(7514): pp. 435-437.

Kettell, J., Jones, R. and Lydeard, S. (1992) Reasons for consultation in irritable bowel syndrome: symptoms and patient characteristics. **British Journal of General Practice** 42(364): pp. 459-461.

Kiecolt-Glaser, J., McGuire, L., Robles, T. and R., G. (2002) Psychoneuroimmunology and psychosomatic medicine: back to the future. **Psychsomatic Medicine** 64(1): pp. 15-28.

Kilbridea, M., Byrnea, R., Pricea, J., Wooda, L., Barratta, S., Welforda, M. and Morrisona, A. (2013) Exploring service users' perceptions of cognitive behavioural therapy for psychosis: A user led study. **Behavioural and Cognitive Psychotherapy** 41(1): pp. 89-102.

Kim, H. (2013) Statistical notes for clinical researchers: assessing normal distribution using skewness and kurtosis. **Restorative Dentistry and Endodontics** 38(1): pp. 52-54.

Knowles, S. and Mikocka-Walus, A. (2014) **Psychological Aspects of Inflammatory Bowel Disease: A Biopsychosocial Approach.** New York: Routledge, p. 90.

Koch, T. (1995) Interpretive approaches in nursing research: the influence of Husserl and Heidegger. **Journal of Advanced Nursing** 21(5): pp. 827-836.

Koch, T. and Harrington, A. (1998) Reconceptualizing rigour: the case for reflexivity. **Journal of Advanced Nursing** 28(4): pp. 882-890.

Koloski, N., Boyce, P. and Talley, N. (2005) Is health care seeking for irritable bowel syndrome and functional dyspepsia a socially learned response to illness? **Digestive Disease Science** 50(1): pp. 153-162.

Koloski, N., Talley, N., Huskic, S. and Boyce, P. (2003) Predictors of conventional and alternative health care seeking for irritable bowel syndrome and functional dyspepsia. **Alimentary Pharmacological Therapy** 17(6): pp. 841-851.

Kroenke, K., Spitzer, R. and Williams, J. (2001) The PHQ-9: validity of a brief depression severity measure. **Journal of General Internal Medicine** 16(9): pp. 606-613.

Kumano, H., Kaiya, H., Yoshiuchi, K., Yamanaka, G., Sasaki, T. and Kuboki, T. (2004) Comorbidity of irritable bowel syndrome, panic disorder, and agoraphobia in a Japanese representative sample. **American Journal of Gastroenterology** 99(2): pp. 370-376.

Kvale, S. (1996) **Interviews: An introduction to qualitative research interviewing.** London: Sage, p. 84.

Lackner, J. (2010) How can cognitive behavioural therapy help irritable bowel syndrome? **Gastrointestinal Nursing** 8(4): p. 11.

Lackner, J., Jaccard, J., Krasner, S., Katz, L., Gudleski, G. and Blanchard, E. (2007) How does cognitive behavior therapy for irritable bowel syndrome work? A mediational analysis of a randomized clinical trial. **Gastroenterology** 133(2): pp. 433-444.

Lackner, J., Jaccard, J., Krasner, S., Katz, L., Gudleski, G. and Holroyd, K. (2008) Self-administered cognitive behavior therapy for moderate to severe irritable bowel syndrome: Clinical efficacy, tolerability, feasibility. **Clinical Gastroenterology and Hepatology** 6(8): pp. 899-906.

Lackner, J., Ma, C., Keefer, L., Brenner, D., Gudleski, G., Satchidanand, N., Firth, R., Sitrin, M., Katz, L., Krasner, S., et al. (2013) Type, rather than number, of mental and physical comorbidities increases the severity of symptoms in patients with irritable bowel syndrome. **Clinical gastroenterology and hepatology** 11(9): pp. 1147-1157.

Lahner, E., Emerenziani, S., Cicala, M., Arullani, P. and Annibale, B. (2013) Complementary and Alternative Medicine in Irritable Bowel Syndrome: A Survey amongst Italian Gastroenterologists. **Journal of Gastroenterology and Hepatology Research** 2(4): pp. 385-393.

Lancaster, G., Campbell, M., Eldridge, S., Farrin, A., Marchant, M., Muller, S., Perera, R., Peters, P., Prevost, A. and Rait, G. (2010) Trials in primary care: statistical issues in the design, conduct and evaluation of complex interventions. **Statistical Methods in Medical Research** 19(4): pp. 349-337.

Lancaster, G., Dodd, S. and Williamson, P. (2002) Design and analysis of pilot studies: recommendations for good practice. **Journal of Evaluation in Clinical Practice** 10(2): pp. 307-312.

Lang, P., Melamed, B. and Hart, J. (1970) A psychophysiological analysis of fear modification using an automated desensitization procedure. **Journal of Abnormal Psychology** 76(2): pp. 220-234.

Lea, R. and Whorwell, P. (2003) New insights into the pschosocial aspects of Irritable Bowel Syndrome. **Current Gastroenterology Reports** 5(4): pp. 343-350.

Leahy, R. (2008) The Therapeutic Relationship in Cognitive-Behavioral Therapy. **Behavioural and Cognitive Psychotherapy** 36(6): pp. 769-777.

Lee, O., Mayer, E., Schmulson, M., Chang, L. and Naliboff, B. (2001) Gender-related differences in IBS symptoms. **American Journal of Gastroenterology** 96(7): pp. 2184-2193.

Leeds, J. and Sanders, D. (2007) Is there an association between coeliac disease and irritable bowel syndrome? **Gut** 56(9): pp. 1326-1327.

Lembo, A. (2004) Irritable bowel syndrome medications side effects survey. **Journal of Clinical Gastroenterology** 38(9): pp. 776-781.

Lembo, T., Fullerton, S., Diehl, D., Raeen, H., Munakata, J., Naliboff, B. and Mayer, E. (1996) Symptom duration in patients with irritable bowel syndrome. **American Journal of Gastroenterology** 91(5): pp. 898-905.

Levy, R., Olden, K., Naliboff, B., Bradley, L., Fransisconi, C., Drossman, D. and Creed, F. (2006) Psychosocial aspects of the functional gastrointestinal disorders. **Gastroenterology** 130(5): pp. 1447-1458.

Lewis, N. and Scott, B. (2006) Systematic review: the use of serology to exclude or diagnose coeliac disease (a comparison of the endomysial and tissue transglutaminase antibody tests). **Alimentary Pharmacological Therapy** 24(1): pp. 47-54.

Lewis, N. and Scott, B. (2010) Meta-analysis: deamidated gliadin peptide antibody and tissue transglutaminase antibody compared as screening tests for coeliac disease. **Alimentary Pharmacological Therapy** 31(1): pp. 73-81.

Lewis, N., Hubbard, R., Sanders, D., Logan, R., Holmes, G. and West, J. (2011) Treating occult coeliac disease with a gluten-free diet is associated with a significant improvement in quality of life. **Gut** 60(1): pp. 1-3.

Ley, R., Peterson, D. and Gordon, J. (2006) Ecological and evolutionary forces shaping microbial diversity in the human intestine. **Cell** 124(4): pp. 837-848.

Li, J., Butcher, J., Mack, D. and Stintzi, A. (2015) Functional impacts of the intestinal microbiome in the pathogenesis of inflammatory bowel disease. **Inflammatory Bowel Disease** 21(1): pp. 139-153.

Liese, B. and Beck, J. (Eds.) (1997) **Cognitive therapy supervision**. New Jersey: John Wiley & Sons.

Lim, B., Manheimer, E., Lao, L., Ziea, E., Wisniewski, J., Liu, J. and Berman, B. (2006) Acupuncture for treatment of irritable bowel syndrome. **Cochrane Database of Systematic Reviews** 18(4): p. CD005111.

Lincoln, Y. and Guba, E. (2007) But is it rigorous? Trustworthiness and authenticity in naturalistic evaluation. **New Direction for Program Evaluation** 1986(30): pp. 73-84.

Ljótsson, B., Andersson, G., Andersson, E., Hedman, E., Lindfors, P., Andréewitch, S., Rück, C. and Lindefors, N. (2011) Acceptability, effectiveness, and cost-effectiveness of internet-based exposure treatment for irritable bowel syndrome in a clinical sample: a randomized controlled trial. **BMC Gastroenterology** 11(110): pp. 1-13.

Ljotsson, B., Andreewitch, S., Hedman, E., Ruck, C., Andersson, G. and Lindefors, N. (2010) Exposure and mindfulness based therapy for irritable bowel syndrome-An open pilot study. **Journal of Behavior Therapy and Experimental Psychiatry** 41(3): pp. 185-190.

Ljotsson, B., Falk, L., Vesterlund, A., Hedman, E., Lindfors, P., Ruck, C., Hursti, T., Andreewitch, S., Jansson, L., Lindefors, N., et al. (2010) Internet-delivered exposure and mindfulness based therapy for irritable bowel syndrome - A randomized controlled trial. **Behaviour Research and Therapy** 48(6): pp. 531-539.

Ljótsson, B., Hedman, E., Andersson, E., Hesser, H., Lindfors, P., Hursti, T., Rydh, S., Rück, C., Lindefors, N. and Andersson, G. (2011) Internet-delivered exposure-based treatment vs. stress management for irritable bowel syndrome: a randomized trial. **The American Journal of Gastroenterology** 106(8): pp. 1481-1491.

Locke, L., Spirduso, W. and Silverman, S. (1993) **Proposals that work: A guide for planning dissertations and grant proposals. 3rd ed.** Newbury Park: Sage, pp. 48-49.

Loewenthal, D. and House, R. (2010) **Critically engaging in CBT.** Berkshire: Open University Press.

Long, M. and Drossman, D. (2010) Inflammatory bowel disease, irritable bowel syndrome, or what?: A challenge to the functional-organic dichotomy. **American Journal of Gastroenterolgy** 105(8): pp. 1796-1798.

Longstreth, G. (1997) Irritable bowel syndrome. Diagnosis in the managed care era. **Digestive Disease Science** 42(6): pp. 1105-1111.

Longstreth, G. (2005) Definition and classification of irritable bowel syndrome: current consensus and controversies. **Gastroenterology Clinics of North America** 34(2): pp. 173-187.

Longstreth, G. and Yao, J. (2004) Irritable bowel syndrome and surgery: a multivariable analysis. **Gastroenterology** 126(7): pp. 1665-1673.

Longstreth, G., Thompson, W., Chey, W., Houghton, L., Mearin, F. and Spiller, R. (2006) Functional bowel disorders. **Gastroenterology Disorders** 130(5): pp. 1480-1491.

Longstreth, G., Wilson, A., Knight, K., Wong, J., Chiou, C., Barghout, V., Frech, F. and Ofman, J. (2003) Irritable bowel syndrome, health care use, and costs: a U.S. managed care perspective. **American Journal of Gastroenterology** 98(3): pp. 600-607.

Lopez, K. and Willis, D. (2004) Descriptive versus interpretive phenomenology: their contributions to nursing knowledge. **Qualitative Health Research** 14(5): pp. 726-735.

Lovell, R. and Ford, A. (2012) Global prevalence of and risk factors for irritable bowel syndrome: a meta-analysis. **Clinical gastroenterology and hepatology** 1(7): pp. 72-721.

Löwe, B., Decker, O., Müller, S., Brähler, E., Schellberg, D., Herzog, W. and Herzberg, P. (2008) Validation and standardization of the Generalized Anxiety Disorder screener (GAD-7) in the general population. **Medical Care** 46(3): pp. 266-274.

Lu, W., Yanos, P., Gottlieb, J., Duva, S., Silverstein, S., Xie, H., Rosenberg, S. and Mueser, K. (2012) Using Fidelity Assessments to Train Frontline Clinicians in the Delivery of Cognitive-Behavioral Therapy for PTSD in Persons with Serious Mental Illness. **Psychiatric Services** 63(8): pp. 785-792.

Lucock, M., Barber, R., Jones, A. and Lovell, J. (2007) Service users' views of self-help strategies and research in the UK. **Journal of Mental Health** 16(6): pp. 795-805.

Lydiard, R. and Falsetti, S. (1999) Experience with anxiety and depression treatment studies: implications for designing irritable bowel syndrome clinical trials. **American Journal of Medicine** 107(5): pp. 65-73.

Lyles, J., Hodges, A., Collins, C., Lein, C., Given, C., Given, B., D'Mello, D., Osborn, G., Goddeeris, J., Gardiner, J., et al. (2003) Using nurse practitioners to implement an intervention in primary care for high-utilizing patients with medically unexplained symptoms. **General Hospital Psychiatry** 25(2): pp. 63-73.

Macdonald, W., Mead, N., Bower, P., Richards, D. and Lovell, K. (2007) A qualitative study of patients' perceptions of a 'minimal' psychological therapy. **International Journal of Social Psychiatry** 53(1): pp. 23-35.

Magge, S. and Lembo, A. (2012) Low-FODMAP Diet for Treatment of Irritable Bowel Syndrome. **Gastroenterology and Hepatology** 8(11): pp. 739-745.

Magge, S. and Wolf, J. (2013) Complementary and alternative medicine and mind–body therapies for treatment of irritable bowel syndrome in women. **Women's Health** 9(6): pp. 557-567.

Maggs-Rapport, F. (2001) 'Best research practice' in pursuit of methodological rigour. **Journal of Advanced Nursing** 35(3): pp. 373-383.

Magnus, K., Diener, E., Fujita, F. and Pavot, W. (1993) Extraversion and neuroticism as predictors of objective life events: a longitudinal analysis. **Journal of Personality and Social Psychology** 65(5): pp. 1046-1053.

Mahadev, S. and Green, P. (2011) Celiac Disease: A Challenge for All Physicians. **Gastroenterology and Hepatology** 7(8): pp. 554-556.

Maher, C., Sherrington, C., Herbert, R., Moseley, A. and Elkins, M. (2003) Reliability of the PEDro Scale for Rating Quality of Randomized Controlled Trials. **Physical Therapy** 83(8): pp. 713-721.

Mahvi-Shirazi, M., Fathi-Ashtiani, A., Rasoolzade-Tabatabaei, S. and Amini, M. (2008) Irritable bowel syndrome treatment: Cognitive behavioral therapy versus medical treatment. **Archives of Medical Science** 8(1): pp. 123-129.

Mai, F. (2004) Somatization Disorder: A practical review. **Canadian Journal of Psychiatry** 49(10): pp. 652-662.

Malhotra, S., Rana, S., Sinha, S. and Khurana, S. (2004) Dietary fiber assessment of patients with irritable bowel syndrome from northern India. **Indian Journal of Gastroenterology** 23: (6): pp. 217-218.

Manning, A., Thompson, W., Heaton, K. and Morris, A. (1978) Towards positive diagnosis of the irritable bowel. **British Medical Journal** 2(6138): pp. 653-654.

Marshall, A. and Smith, R. (1995) Physicians' emotional reactions to patients: recognizing and managing countertransference. **American Journal of Gastroenterology** 90(1): pp. 4-8.

Marshall, J., Thabane, M., Garg, A., Clark, W., Moayyedi, P. and Collins, S. (2010) Eight year prognosis of postinfectious irritable bowel syndrome following waterborne bacterial dysentery. **Gut** 59(1): pp. 605-611.

Martin, G. and Larson, S. (2008) Analysis of Variance. **Circulation.** 117(1): pp. 115-121.

Matthews, S., Waud, J., Roberts, A. and Campbell, A. (2005) Systemic lactose intolerance: a new perspective on an old problem. **Postgraduate Medicine** 81(953): pp. 167-173.

Matts, J. and Lachin, J. (1988) Properties of permuted-block randomization in clinical trials **Controlled Clinical Trials** 9: (4): pp. 327-344.

Maunder, R. (2000) Mediators of stress effects in inflammatory bowel disease: not the usual suspects. **Journal of Psychosomatic Research** 48(6): pp. 569-577.

Maxwell, P., Mendall, M. and Kumar, D. (1997) Irritable Bowel Syndrome. **Lancet** 350(9092): pp. 1691-1695.

Mayer, E. (2000) The neurobiology of stress and gastrointestinal disease. **Gut** 47(6): pp. 861-869.

McGlinchey, J. and Dobson, K. (2003) Treatment integrity concerns in cognitive therapy for depression. **Journal of Cognitive Psychotherapy** 17(4): pp. 299-318.

McKenzie, Y., Alder, A., Anderson, W., Wills, A., Goddard, L., Gulia, P., Jankovich, E., Mutch, P., Reeves, L., Singer, A., et al. (2012) British Dietetic Association evidence-based guidelines for the dietary management of irritable bowel syndrome in adults. **Journal of Human Nutrition and Dietetics** 25(3): pp. 260-274.

Mcloughlin, R., Sebastian, S., Qasim, A., Mcnamara, D., O'conner, H., Buckley, M. and O'morain, C. (2003) Coeliac disease in Europe. **Alimentary Pharmacological Therapy** 18(3): pp. 45-48.

McNamara, C. (2009) **General guidelines for conducting interviews.** Available at: http://managementhelp.org/evaluatn/intrview.htm [Accessed 17 May 2012].

Mearin, F. and Lacy, B. (2012) Diagnostic criteria in IBS: useful or not? **Neurogastroenterology Motility** 24(9): pp. 791-801.

Meichenbaum, D. H. (1985) **Stress inoculation training.** New York: Pergamon.

Mendall, M. and Kumar, D. (1998) Antibiotic use, childhood affluence and irritable bowel syndrome (IBS). **European Journal of Gastroenterology and Hepatology** 10(1): pp. 59-62.

Miles, M. and Huberman, A. (1994) **Qualitative data analysis: An expanded source book. 2nd ed.** Newbury Park, CA: Sage, p. 18.
Minderhoud, I., Oldenburg, B., Wismeijer, J., van Berge Henegouwen, G. and Smout, A. (2004) IBS-like symptoms in patients with infl ammatory bowel disease in remission; relationships with quality of life and coping behavior **Digestive Disease and Sciences** 49(3): pp. 469-474.

Mohd Sidik, S., Arroll, B. and Goodyear-Smith, F. (2012) Validation of the GAD-7 (Malay version) among women attending a primary care clinic in Malaysia. **Journal of Primary Health Care** 4(1): pp. 5-11.

Moher, D., Liberati, A., Tetzlaff, J. and Altman, D. (2009) Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. **Plos Medicine** 6(7): pp. 1-6.

Mohr, D., Ho, J., Duffecy, J., Reifler, D., Sokol, L., Burns, M., Jin, L. and Siddique, J. (2012) Effect of telephone-administered vs face-to-face cognitive behavioral therapy on adherence to therapy and depression outcomes among primary care patients: a randomized trial. **Journal of the American Medical Association** 307(21): pp. 2278-2285.

Mohr, D., Siddique, J., Ho, J., Duffecy, J., Jin, L. and Fokuo, J. (2010) Interest in behavioral and psychological treatments delivered face-to-face, by telephone, and by internet. **Annals of Behavioural Medicine** 40(1): pp. 89-98.

Moncher, F. and Prinz, F. (1991) Treatment fidelity in outcome studies. **Clinical Psychology Review** 11: (3): pp. 247-266.

Moss-Morris, R., McAlpine, L., Didsbury, L. and Spence, M. (2010) A randomized controlled trial of a cognitive behavioural therapy-based self-management intervention for irritable bowel syndrome in primary care. **Psychological Medicine** 40(1): pp. 85-94.

MRC. (2008) **Complex interventions guidance.** Available at: http://www.mrc.ac.uk/Utilities/Documentrecord/index.htm?d=MRC004871 [Accessed 15 February 2012].

MRC. (2015) **Public Health Intervention Development Scheme (PHIND).** Available at: http://www.mrc.ac.uk/funding/browse/public-health-intervention-development-scheme-phind/ [Accessed 3 March 2016].

Mubashir Arain, M., Campbell, MJ., Cooper, CL and Lancaster, GA. (2010) What is a pilot or feasibility study? A review of current practice and editorial policy. **BMC Medical Research and Methodology** 10(67) pp.1-7.

Muir-Gray, J. (1997) **Evidence based healthcare.** New York: Churchill Livingstone.

Myles, P. and Rushforth, D. (2007) **The complete guide to primary care mental health.** London: Constable and Robinson.

Nauert, R. (2011) **Psychological Trauma Tied to Irritable Bowel Syndrome.** Available at: http://psychcentral.com/news/2011/11/01/psychological-trauma-tied-to-irritable-bowel-syndrome/30933.html [Accessed 6 March 2016].

Neal, K., Barker, L. and Spiller, R. (2002) Prognosis in post-infective irritable bowel syndrome: a six year follow up study. **Gut** 51(3): pp. 410-413.

Neal, K., Hebden, J. and Spiller, R. (1997) Prevalence of gastrointestinal symptoms six months after bacterial gastroenteritis and risk factors for development of the irritable bowel syndrome: postal survey of patients. **British Medical Journal** 314(7083): pp. 779-782.

Nease, D. and Maloin, J. (2003) Depression screening: a practical strategy. **Journal of Family Practice** 52(2): pp. 118-124.

Nellesen, D., Yee, K., Chawla, A., Lewis, B. and Carson, R. (2013) A systematic review of the economic and humanistic burden of illness in irritable bowel syndrome and chronic constipation. **Journal of Managed Care Pharmacy** 19(9): pp. 755-764.

Nespor, J. and Barylske, J. (1991) Narrarive discourse and teacher knowledge. **Americal Educational Journal** 28(4): pp. 805-823.

NICE. (2008) **Irritable bowel syndrome in adults: Diagnosis and management of irritable bowel syndrome in primary care.** London: National Institute for Health and Clinical Excellence.

NICE. (2009) **Recognition and assessment of coeliac disease.** London: National Institute for Health and Clinical Excellence.

NICE. (2015) **Irritable bowel syndrome in adults: diagnosis and management** Available at: https://www.nice.org.uk/guidance/CG61/chapter/1-Recommendations [Accessed 3 March 2016].

NIH. (2001) **Qualitative methods in health research: opportunities and considerations in application and review.** Available at: https://obssr-archive.od.nih.gov/pdf/Qualitative.PDF [Accessed 3 March 2016].

NIHR. (2016) **Feasibility Sutides** [Online]. Available at: http://www.nets.nihr.ac.uk/glossary/feasibility-studies (Accessed 3 March 2016)

NMC. (2015) **Professional standards of practice and behaviour for nurses and midwives.** Available at: http://www.nmc.org.uk/standards/code/ [Accessed 29th September 2015].

Noel, P. (2006) The impact of therapeutic case management on participation in adolescent substance abuse treatment. **American Journal of Drug and Alcohol Abuse** 32(3): pp. 311-327.

North, C., Downs, D., Clouse, R., Alrakawi, A., Dokucu, M., Cox, J., Spitznagel, E. and Alpers, D. (2004) The presentation of irritable bowel syndrome in the context of somatization disorder. **Clinical Gastroenterology and Hepatology** 2(9): pp. 787-795.

North, C., Hong, B. and Alpers, D. (2007) Relationship of functional gastrointestinal disorders and psychiatric disorders: implications for treatment. **World Journal of Gastroenterology** 13(14): pp. 2020-2027.

Norton, C. and Kamm, M. (2002) Specialist nurses in gastroenterology. **Journal of the Royal Society of Medicine** 95(7): pp. 331-335.

Nuremberg Code. (1949) **Trials of War Criminals Before the Nuremberg Military Tribunals Under Control Council Law.** Available at: https://www.loc.gov/rr/frd/Military_Law/pdf/NT_war-criminals_Vol-II.pdf [Accessed 6 March 2016].

Nystrom, L., Wall, S., Rutqvist, L., Lindgren, A., Lindqvist, M. and Ryde´n, S. (1993) Breast cancer screening with mammography: overview of Swedish randomised controlled trials. **Lancet** 341(8851): pp. 973-978.

O'Cathain, A., Nicholl, J. and Murphy, E. (2009) Structural issues affecting mixed methods studies in health research: a qualitative study. **BMC Medical Research Methodology** 9(82): pp.1-8.

Ocloo, J. and Matthews, R. (2016) From tokenism to empowerment: progressing patient and public involvement in healthcare improvement**. British Medical Journal of Quality and Safety**. Available at: http://qualitysafety.bmj.com/content/early/2016/03/18/bmjqs-2015-004839.full.pdf [Accessed 6 March 2016].

Oerlemans, S., Van Cranenburgh, O., Herremans, P., Spreeuwenberg, P. and Van Dulmen, S. (2011) Intervening on cognitions and behavior in irritable bowel syndrome: A feasibility trial using PDAs. **Journal of Psychosomatic Research** 70(3): pp. 267-277.

O'Hara, A. and Shanahan, F. (2006) The gut flora as a forgotten organ. **EMBO reports** 7(7): pp. 688-693.

Oliver, S. (1995) How can health service users contribute to the NHS research and development agenda? **British Medical Journal** 310(1318): pp. 1315-1318.

Ong, D., Mitchell, S., Barrett, J., Shepherd, S., Irving, P., Biesiekierski, J., Smith, S., Gibson, P. and Muir, J. (2010) Manipulation of dietary short chain carbohydrates alters the pattern of gas production and genesis of symptoms in irritable bowel syndrome. **Journal of Gastroenterology and Hepatology** 25(8): pp. 1366-1373.

Owens, D., Nelson, D. and Talley, N. (1995) The irritable bowel syndrome: long-term prognosis and the physician-patient interaction. **Annals of Internal Medicine** 122(2): pp. 107-112.

Parahoo, K. (2006) **Nursing research: principles, process and issues.** Hampshire: Palgrave Macmillan.

Par'e, P., Gray, J., Lam, S., Balshaw, R., Khorasheh, S., Barbeau, M., Kelly, S. and McBurney, C. (2006) Health-related quality of life, work productivity, and health Care resource Utilization of Subjects with Irritable Bowel Syndrome: Baseline results from LOGIC (Longitudinal Outcomes Study of Gastrointestinal Symptoms in Canada): a naturalistic study. **Clinical Therepeutics** 28(10): pp. 1726-1735.

Parisi, G., Zilli, M., Miani, M., Carrara, M., Bottona, E., Verdianelli, G., Battaglia, G., Desideri, S., Faedo, A., Marzolino, C., et al. (2002) High-Fiber Diet Supplementation in Patients with Irritable Bowel Syndrome (IBS): A Multicenter, Randomized, Open Trial Comparison Between Wheat Bran Diet and Partially Hydrolyzed Guar Gum (PHGG). **Digestive Diseases and Sciences** 47(8): pp. 1697-1704.

Parker, T., Woolner, J., Prevost, A., Tuffnell, Q., Shorthouse, M. and Hunter, J. (2001) Irritable bowel syndrome: is the search for lactose intolerance justified? **European Journal of Gastroenterology and Hepatology** 13(3): pp. 219-225.

Pascoe, E. (1996) The value to nursing research of Gadamer's hermeneutic philosophy. **Journal of Advanced Nursing** 24(6): pp. 1309-1314.

Patrick, D., Drossman, D., Frederick, I., Dicesare, J. and Puder, K. (1998) Quality of life in persons with Irritable bowel syndrome: development and validation of a new measure. **Digestive Disease Science** 43(2): pp. 400-411.

Patterson, M. and Williams, D. (2002) **Collecting and analysing qualitative data: Hermeneutic principles, methods and case examples.** Champaign, USA: Sagamore.

Patterson-Kimball, C. (1982) Stress and psychosomatic illness. **Journal of Psychosomatic Research** 26(1): pp. 63-71.

Payne, A. and Blanchard, E. (1995) A controlled comparison of cognitive therapy and self-help support groups in the treatment of irritable bowel syndrome. **Journal of Consulting and Clinical Psychology** 63(5): pp. 779-786.

Perepletchikova, F. and Kazdin, A. (2005) Treatment integrity and therapeutic change: Issues and research recommendations. **Clinical Psychology Science and Practice** 12(1): pp. 365-383.

Perkins, S., Murphy, R., Schmidt, U. and Williams, C. (2006) Self-help and guided self-help for eating disorders. **Cochrane Database of Systematic Reviews** 19(3): pp. 1-90.

Perris, C. (1993) Stumbling blocks in the supervision of cognitive psychotherapy. **Clinical Psychology and Psychotherapy** 1(1): pp. 29-43.

Plomer, A. (2005) **The Law and Ethics of Medical Research: International Bioethics and Human Rights.** London: Cavendish Publishing.

Pluye, P., Gagnon, M., Griffiths, F. and Johnson-Lafleur, J. (2009) A scoring system for appraising mixed methods research, and concomitantly appraising qualitative, quantitative and mixed methods primary studies in mixed studies reviews. **International Journal of Nursing Studies** 46(4): pp. 529-546.

Porter, C., Cash, B., Pimentel, M., Akinseye, A. and Riddle, M. (2012) Risk of inflammatory bowel disease following a diagnosis of irritable bowel syndrome. **BMC Gastroenterology** 12(55): pp. 1-10.

Prasko, J., Vyskocilova, J., Slepecky, M. and Novotny, M. (2012) Principles of supervision in cognitive behavioural therapy. **Biomedical papers of the Medical Faculty of the University Palacký, Olomouc, Czechoslovakia** 156(1): pp. 70-79.

Prather, C., Camilleri, M., Zinsmeister, A., McKinzie, S. and Thomforde, G. (2000) Tegaserod accelerates orocecal transit in patients with constipation-predominant irritable bowel syndrome. **Gastroenterology** 118(3): pp. 463-468.

Pretorius, W. (2006) Cognitive Behavioural Therapy Supervision: Recommended Practice. **Behavioural and Cognitive Psychotherapy** 34(4): pp. 413-420.
Quigley, E. (2011) Microflora Modulation of Motility. Journal of **Neurogastroenterology Motility** 17(2): pp. 140-147.

Qin, H., Cheng, C., Tang, X. and Bian, Z. (2014) Impact of psychological stress on irritable bowel syndrome. **World Journal of Gastroenterology** 20(39): pp. 14126-14131.

Quigley, E., Fried, M., Gwee, K., Khalif, I., Hungin, P., Lindberg, G., Abbas, Z., Fernandez, L., Bhatia, S., Schmulson, M., et al. (2015) **World Gastroenterology Organisation Global Guidelines: Irritable Bowel Syndrome: a Global Perspective**. Available at: http://www.worldgastroenterology.org/guidelines/global-guidelines/irritable-bowel-syndrome-ibs/irritable-bowel-syndrome-ibs-english [Accessed 3 March 2016].

Rajilić-Stojanović, M., Jonkers, D., Salonen, A., Hanevik, K., Raes, J., Jalanka, J., de Vos, W., Manichanh, C., Golic, N., Enck, P., et al. (2015) Intestinal Microbiota And Diet in IBS: Causes, Consequences, or Epiphenomena? **American Journal of Gastroenterology** 110(2): pp. 278-287.

Rance, M., Lindner, L. and Ford, A. (2014) A Systematic Review Of Antidepressants In Irritable Bowel Syndrome: A Qualitative Analysis. **Gut** 63(1): p. 203.

Rathore, J., Jehi, L., Fan, Y., Patel, S., Foldvary-Schaefer, N. and Ramirez, M. (2014) Validation of the Patient Health Questionnaire-9 (PHQ-9) for depression screening in adults with epilepsy. **Epilepsy and Behavior** 37pp. 215-220.

RCN. (2007) **User involvement in research by nurses. RCN guidance.** London: RCN.

Reason, P. (1988) **Human inquiry in action: Developments in new paradigm research.** Newbury Park, CA: Sage, pp. 1-17.

Reme, S., Stahl, D., Kennedy, T., Jones, R., Darnley, S. and Chalder, T. (2011) Mediators of change in cognitive behaviour therapy and mebeverine for irritable bowel syndrome. **Psychological Medicine** 41(12): pp. 2669-2679.

Resnick, B., Bellg, A., Borrelli, B., Defrancesco, C., Breger, R., Hecht, J., Sharp, D., Levesque, C., Orwig, D., Ernst, D., et al. (2005) Examples of implementation and evaluation of treatment fidelity in the BCC studies: where we are and where we need to go. **Annals of Behavioral Medicine** 29(1): pp. 46-54.

Richards, D. and Farrand, P. (2010) Choosing self-help books wisely: sorting the wheat from the chaff. In: Bennett-Levy, J., Richards, D., Farrand, P., Christensen, H., Griffiths, K., Kavanagh, D., Klein, B., Lau, M., Proudfoot, J. and Ritterband, L. (Eds.) **Oxford guide to low-intensity CBT interventions.** New York: Oxford University Press.

Richards, D. and Whyte, M. (2011) **Reach out. National Programme Student Materials to Support the Delivery of Training for Psychological Wellbeing Practitioners Delivering Low Intensity Interventions.** London: Rethink.

Richards, H. and Schwartza, L. (2002) Ethics of qualitative research: are there special issues for health services research? **Family Practice** 19(2): pp. 135-139.

Richardson, R., Richards, D. and Barkham, M. (2010) Self-help books for people with depression: the role of the therapeutic relationship. **Behavioural and Cognitive Psychotherapy** 38(1): pp. 67-81.

Ringström, G., Abrahamsson, H., Strid, H. and Simrén, M. (2007) Why do subjects with irritable bowel syndrome seek health care for their symptoms? **Scandanavian Journal of Gastroenterology** 42(10): pp. 1194-1203.

Ritchie, J. and Spencer, L. (1994) Qualitative data analysis for applied policy research. In: Bryman, A. and Burgess, R. (Eds.) **Analysing Qualitative Data.** London: Routledge.

Robson, C. (1993) **Real World Research.** Oxford, UK: Blackwell, p. 291.

Rodrigo, L., Blanco, I., Bobes, J. and J de Serres, F. (2013) Remarkable prevalence of coeliac disease in patients with irritable bowel syndrome plus fibromyalgia in comparison with those with isolated irritable bowel syndrome: a case-finding study. **Arthritis Research and Therapy** 15(6): pp. 1-12.

Rothwell, P. (2005) External validity of randomized controlled trials: 'To whom do the benefits apply? **Lancet** 365(9453): pp. 82-93.

Roy-Byrne, P., Davidson, K., Kessler, R., Asmundson, G., Goodwin, R., Kubzansky, L., Lydiard, R., Massie, M., Katon, W., Laden, S., et al. (2008) Anxiety disorders and comorbid medical illness. **General Hospital Psychiatry** 30(3): pp. 208–225.

Ruepert, L., Quartero, A., de Wit, N., van der Heijden, G., Rubin, G. and Muris, J. (2011) Bulking agents, antispasmodic and antidepressant medication for the treatment of irritable bowel syndrome. **Cochrane Database of Systematic Reviews** 10(8): pp. 1-63.

Ryle, J. (1928) An address on chronic spasmodic affections of the colon and the diseases which they simulate. **Lancet** 212(5492): pp. 1115-1119.

Saito, W., Schoefeld, P. and Locke, R. (2002) The epidemiology of irritable bowel syndrome in North America. **American Journal of Gastroenterology** 97(8): pp. 1910-1915.

Sajadinejad, M., Asgari, K., Molavi, H., Kalantari, M. and Adibi, P. (2012) **Psychological Issues in Inflammatory Bowel Disease: An Overview.** Available at: http://www.hindawi.com/journals/grp/2012/106502/ [Accessed 3 March 2016].

Salonen, A., de Vos, W. and Palva, A. (2010) Gastrointestinal microbiota in irritable bowel syndrome: present state and perspectives. **Microbiology** 156(11): pp. 3205-3215.

Sanders, D., Carter, M., Hurlstone, D., Pearce, A., Ward, A., McAlindon, M. and Lobo, A. (2001) Association of adult coeliac disease with irritable bowel syndrome: a case-control study in patients fulfilling ROME II criteria referred to secondary care. **Lancet** 358(9292): pp. 1504-1508.

Sanders, D., Hurlstone, D., Stokes, R., Rashid, F., Milford-Ward, A., Hadjivassiliou, M. and Lobo, A. (2002) Changing face of adult coeliac disease: experience of a single university hospital in South Yorkshire. **Postgraduate Medical Journal** 78: (915): pp. 31-33.

Sanders, K., Blanchard, E. and Sykes, M. (2007) Preliminary study of a self-administered treatment for irritable bowel syndrome: comparison to a wait list control group. **Applied psychophysiology and biofeedback** 32(2): pp. 111-119.

Sanson-Fisher, R., Bonevski, B., Green, L. and D'Este, C. (2007) Limitations of the Randomized Controlled Trial in Evaluating Population-Based Health Interventions. **American Journal of Preventive Medicine** 33(2): pp. 155-161.

Schmulson, M. and Chang, L. (1999) Diagnostic approach to the patient with irritable bowel syndrome. **The American Journal of Medicine** 107(5): pp. 20-26.

Schneider, A., Streitberger, K. and Joos, S. (2007) Acupuncture treatment in gastrointestinal diseases: a systematic review. **World Journal of Gastroenterology** 13(25): pp. 3417-3424.

Schulz, K. (2000) Assessing allocation concealment and blinding in randomised controlled trials: why bother? **Evidence Based Medicine** 5(1): pp. 36-38.

Scott, P. and Briggs, J. (2009) A pragmatist argument for mixed methodology in medical informatics. **Journal of Mixed Methods Research** 3(3): pp. 223-241.

Shahbazkhani, B., Forootan, M., Merat, S., Akbari, M., Nasserimoghadam, S., Vahedi, H. and Malekzadeh, R. (2003) Coeliac disease presenting with symptoms of irritable bowel syndrome. **Alimentary Pharmacological Therapy** 18(2): pp. 231-235.

Shanyinde, M., Pickering, R. and Weatherall, M. (2011) Questions asked and answered in pilot and feasibility randomized controlled trials. **BMC Medical Research Methodology** 11(117): pp. 1-11.

Sharp, D., Power, K. and Swanson, V. (2004) A comparison of the efficacy and acceptability of group versus individual cognitive behaviour therapy in the treatment of panic disorder and agoraphobia in primary care. **Clinical Psychology and Psychotherapy** 11(2): pp. 78-82.

Shean, G. (2014) **Limitations of Randomized Control Designs in Psychotherapy Research.** Available at: http://www.hindawi.com/journals/apsy/2014/561452/ [Accessed 6 March 2016].

Shen, Y.-H. A. Y. H. and Nahas, R. R. (2009) Complementary and alternative medicine for treatment of irritable bowel syndrome. **Canadian family physician Médecin de famille canadien** 55(2): pp. 143-148.

Shi, J., Tong, Y., Shen, J. and Li, H. (2008) Effectiveness and safety of herbal medicines in the treatment of irritable bowel syndrome: a systematic review. **World Journal of Gastroenterology** 14(3): pp. 454-462.

Sidebottom, A., Harrison, P., Godecker, A. and Kim, H. (2012) Validation of the Patient Health Questionnaire (PHQ)-9 for prenatal depression screening. **Archives of Women's Mental Health** 15(5): pp. 367-374.

Silk, D. (2000) Irritable bowel syndrome and diet - exploring the controversies. **The Pharmaceutical Journal** 264(7096): pp. 731-736.

Simons, A., Padesky, C., Montemarano, J., Lewis, C., Murakami, J., Lamb, K., DeVinney, S., Reid, M., Smith, D. and Beck, A. (2010) Training and dissemination of cognitive behavior therapy for depression in adults: a preliminary examination of therapist competence and client outcomes. **Journal of Consulting and Clinical Psychology** 78(5): pp. 751-756.

Simrén, M., Brazier, J., Coremans, G., Dapoigny, M., Müller-Lissner, S., Pace, F., Smout, A., Stockbrügger, R., Vatn, M. and Whorwell, P. (2004) Quality of life and illness costs in Irritable Bowel Syndrome. **Digestion** 69(4): pp. 254-261.

Simrén, M., Castedal, M., Svedlund, J., Abrahamsson, H. and Björnsson, E. (2000) Abnormal propagation pattern of duodenal pressure waves in the irritable bowel syndrome (IBS). **Digestive Diseases Science** 45(11): pp. 2151-2161.

Skevington, SM. (1998) Investigating the relationship between pain and discomfort and quality of life, using the WHOQOL. **Pain** 76(3): 395-406.

Skinner, V. and Wrycraft, N. (2014) **CBT fundamentals, theory and cases.** Berkshire: Open University Press.

Slowther, A., Boynton, P. and Shaw, S. (2006) Research governance: ethical issues. **Journal of the Royal Society of Medicine** 99(2): pp. 65-72.

Smith, G. and Watson, R. (2005) **Gastrointestinal Nursing.** Oxford: Blackwell Science.

Snaith, R. and Zigmond, A. (1983) The Hospital Anxiety And Depression Scale. **Acta Psychiatrica Scandinavica** 67(6): pp. 351-370.

Soares, R. (2014) Irritable bowel syndrome: A clinical review. **World Journal of Gastroenterology** 20(34): pp. 21244-12160.

Spanier, J., Howden, C. and Jones, M. (2003) A systematic review of alternative therapies in the Irritable Bowel Syndrome. **Archives of Internal Medicine** 163(3): pp. 265-274.

Spence, D. (2001) Hermeneutic notions illuminate cross-cultural nursing experiences. **Journal of Advanced Nursing** 35(4): pp. 624-630.

Sperber, A. and Dekel, R. (2010) Irritable Bowel Syndrome and Co-morbid Gastrointestinal and Extra-gastrointestinal Functional Syndromes. **Journal of Neurogastroenterology Motility** 16(2): pp. 113-119.

Spiegel, B., Farid, M., Esrailian, E., Talley, J. and Chang, L. (2010) Is irritable bowel syndrome a diagnosis of exclusion?: a survey of primary care providers, gastroenterologists, and IBS experts? **American Journal of Gastroenterology** 105(4): pp. 848-858.

Spiegel, B., Gralnek, I., Bolus, R., Chang, L., Dulai, G., Naliboff, B. and Mayer, E. (2005) Is a negative colonoscopy associated with reassurance or improved health-related quality of life in irritable bowel syndrome? **Gastrointestinal Endoscopy** 62(6): pp. 892-899.

Spiller, R. and Garsed, K. (2009) Postinfectious irritable bowel syndrome. **Gastroenterology** 136(6): pp. 1979-1988.

Spiller, R., Aziz, Q., Creed, F., Emmanuel, A., Houghton, L., Hungin, P., Jones, R., Kumar, D., Rubin, G., Trudgill, N., et al. (2007) Guidelines on the irritable bowel syndrome: mechanisms and practical management. **Gut** 56(12): pp. 1770-1798.

Spiller, R., Jenkins, D., Thornley, J., Hebden, J., Wright, T., Skinner, M. and Neal, K. (2000) Increased rectal mucosal enteroendocrine cells, T lymphocytes and increased gut permeability following acute Campylobacter enteritis and in post-dysenteric irritable bowel syndrome. **Gut** 47(6): pp. 804-811.

Spitzer, R., Kroenke, K., Williams, J. and Löwe, B. (2006) A brief measure for assessing generalized anxiety disorder: the GAD-7. **Archives of Internal Medicine** 166(10): pp. 1092-1097.

Stam, R., Akkermans, L. and Wiegant, V. (1997) Trauma and the gut: interactions between stressful experience and intestinal function. **Gut** 40(6): pp. 704-709.

Stanford, P., Monte, D., Briggs, F., Flynn, P., Tanney, M., Ellenberg, J., Clingan, K. and Rogers, A. (2003) Recruitment and retention of adolescent participants in HIV research: findings from the REACH (Reaching for Excellence in Adolescent Care and Health) Project. **Journal of Adolescent Health** 32(3): pp. 192-203.

Staudacher, H., Lomer, M., Anderson, J., Barrett, J., Muir, J., Irving, P. and Whelan, K. (2012) Fermentable Carbohydrate Restriction Reduces Luminal Bifidobacteria and Gastrointestinal Symptoms in Patients with Irritable Bowel Syndrome. **Journal of Nutrition** 142(8): pp. 1510-1518.

Staudacher, H., Whelan, K., Irving, P. and Lomer, M. (2011) Comparison of symptom response following advice for a diet low in fermentable carbohydrates (FODMAPs) versus standard dietary advice in patients with irritable bowel syndrome. **Journal of Human Nutrition and Dietetics** 24(5): pp. 487-495.

Steer, T., Carpenter, H., Tuohy, K. and Gibson, G. (2000) Perspectives on the role of the human gut microbiota and its modulation by pro- and prebiotics. **Nutrition Research Reviews** 13(2): pp. 229-254.

Stiller, C. (1992) Centralised treatment, entry to trials, and survival. **British Journal of Cancer** 70(7): pp. 352-362.

Strupp, H. and Anderson, T. (1997) On the Limitations of Therapy Manuals. **Clinical Psychology: Science and Practice** 4(1): pp. 76-82.

Suarez, F. and Levitt, M. (1996) Abdominal symptoms and lactose: the discrepancy between patients' claims and the results of blinded trials. **American Journal of Clinical Nutrition** 64(2): pp. 251-252.

Taché, Y., Martinez, V., Million, M. and Wang, L. (2001) Stress and the gastrointestinal tract III. Stress-related alterations of gut motor function: role of brain corticotropin-releasing factor receptors. **American Journal of Physiology - Gastrointestinal and Liver Physiology** 280(2): pp. 173-177.

Talley, N. (2008) Controversies in NICE guidance on irritable bowel syndrome. **British Medical Journal** 336(7643): pp. 558-559.

Talley, N., Boyce, P. and Jones, M. (1997) Predictors of health care seeking for irritable bowel syndrome: a population-based study. **Gut** 41(43): pp. 394-398.

Tanaka, Y., Kanazawa, M., Fukudo, S. and Drossman, D. (2011) Biopsychosocial Model of Irritable Bowel Syndrome. **Journal of Neurogastroenterology Motility** 17(2): pp. 131-139.

Tarquinio, C., Kivits, J., Minary, L., Coste, J. and Alla, F. (2015) Evaluating complex interventions: perspectives and issues for health behaviour change interventions. **Psychological Health** 30(1): pp. 35-51.

Terrill, A., Hartoonian, N., Beier, M., Salem, R. and Alschuler, K. (2015) The 7-Item Generalized Anxiety Disorder Scale as a Tool for Measuring Generalized Anxiety in Multiple Sclerosis. **International Journal of MS Care** 17(2): pp. 49-56.

Thabane, M. and Marshall, J. (2009) Post infectious irritable bowel syndrome. **World Journal of Gastroenterology** 15(29): pp. 3591-3596.

Thabane, M., Kottachchi, D. and Marshall, J. (2007) Systematic review and meta-analysis: The incidence and prognosis of post-infectious irritable bowel syndrome. **Alimentary Pharmacology Therapeutics** 26(4): pp. 533-544.

The Rome Foundation. (2012) **To Improve the lives of people with functional GI disorders.** Available at: http://www.romecriteria.org/ [Accessed 6 March 2016].

The Rome Foundation. (2016) **Rome lll Criteria for Irritable Bowel Syndrome.** Available at: http://romecriteria.org/assets/pdf/19_RomeIII_apA_885-898.pdf [Accessed 6 March 2016].

Thomas, J., Nanda, R. and Shu, L. (2012) A FODMAP Diet Update: Craze or Credible? **Practical Gastroenterology** 36(12): pp. 37-46.

Thompson, B. and Schoenfeld, D. (2007) Usual care as the control group in clinical trials of nonpharmacologic interventions. **Proceedings of the American Thoracic Society** 4(7): pp. 577-582.

Thompson, W., Heaton, K., Smyth, G. and Smyth, C. (2000) Irritable bowel syndrome in general practice: prevalence, characteristics, and referral. **Gut** 46(1): pp. 78-82.

Thompson, W., Longstreth, G., Drossman, D., Heaton, K., Irvine, E. and Müller-Lissner, E. (1999) Functional bowel disorders and functional abdominal pain. **Gut** 45(2).

Thompson, W., Longstreth, G., Drossman, D., Heaton, K., Irvine, E. and Müller-Lissner, E. (1999) Functional bowel disorders and functional abdominal pain. **Gut** 45(2): pp.43-47.

Tickle-Degnen, L. (2013) Nuts and Bolts of Conducting Feasibility Studies. **American Journal of Occupational Therapy** 67(2): pp. 171-176.

Tillisch, K. (2006) Complementary and alternative medicine for functional gastrointestinal disorders. **Gut** 55(5): pp. 563-596.

Titov, N. (2011) Internet-delivered psychotherapy for depression in adults. **Current Opinion in Psychiatry** 24(1): pp. 18-23.

Tkachuk, G., Graff, L., Martin, G. and Bernstein, C. (2003) Randomized controlled trial of cognitive-behavioral group therapy for irritable bowel syndrome in a medical setting. **Journal of Clinical Psychology in Medical Settings** 10(1): pp. 57-69.

Toner, B. (1994) Cognitive-behavioral treatment of functional somatic syndromes: Integrating gender issues. **Cognitive and Behavioral Practice** 1(1): pp. 157-178.

Toner, B. (2005) Cognitive-behavioral treatment of irritable bowel syndrome. **CNS Spectrums** 10(11): pp. 883-890.

Toner, B. and Akmana, D. (2000) Gender role and irritable bowel syndrome: literature review and hypothesis. **American Journal of Gastroenterology** 95(1): pp. 11-16.

Toner, B., Segal, Z., Emmott, S. and Myran, D. (2000) **Cognitive-behavioral treatment of irritable bowel syndrome: The brain-gut connection.** New York: Guilford Press.

Toner, B., Stuckless, N., Ali, A., Downie, F., Emmott, S. and Akman, D. (1998) The development of a cognitive scale for functional bowel disorders. **Psychosomatic Medicine** 60(4): pp. 492-497.

Tong, A., Sainsbury, P. and Craig, J. (2007) Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. **International Journal of Qualitative Healthcare** 19(6): pp. 349-357.

Tougas, G. (2000) The autonomic nervous system in functional bowel disorders. **Gut** 47(4): pp. 78-80.

Triantafyllou, K. (2002) Problems and challenges in the design of irritable bowel syndrome clinical trials. Focusing on the future with the experience from the past. **Annals of Gastroenterology** 15(3): pp. 263-270.

Tucker, M. and Oei, T. (2007) Is Group More Cost Effective than Individual Cognitive Behaviour Therapy? **Behavioural and Cognitive Psychotherapy** 35(1): pp. 77-91.

Turnbaugh, P. and Gordon, J. (2009) The core gut microbiome, energy balance and obesity**. Journal of Physiology** 587(17): pp. 4153-4158.

Tyrer, S. (2006) Psychosomatic pain. **British Journal of Psychiatry** 188: (1): pp. 91-93.

Usher, L., Fox, P., Lafarge, C. and Mitchellb, K. (2013) Factors Associated With Complementary and Alternative Medicine Use in Irritable Bowel Syndrome: A Literature Review. **Psychology Community and Health** 2(3): pp. 1-15.

van Ballegooijen, W., Cuijpers, P., van Straten, A., Karyotaki, E., Andersson, G., Smit, J. and Riper, H. (2014) Adherence to Internet-based and face-to-face cognitive behavioural therapy for depression: a meta-analysis. **Plos One** 9(7): pp. 1-10.

Van Dulmen, A., Fennis, J. and Bleijenberg, G. (1996) Cognitive-behavioral group therapy for irritable bowel syndrome: effects and long-term follow-up. **Psychosomatic Medicine** 58(5): pp. 508-514.

van Dulmen, A., Fennis, J., Mokkink, H. and Bleijenberg, G. (1996) The relationship between complaint-related cognitions in referred patients with irritable bowel syndrome and subsequent health care seeking behaviour in primary care. **Family Practice** 13(1): pp. 12-17.

Van Heel, D. and West, J. (2006) Recent advances in coeliac disease. **Gut** 55: (7): pp. 1037-1046.

van Steenbergen-Weijenburg, K., de Vroege, L., Ploeger, R., Brals, J., Vloedbeld, M., Veneman, T., Hakkaart-van Roijen, L., Rutten, F., Beekman, A. and van der Feltz-Cornelis, C. (2010) Validation of the PHQ-9 as a screening instrument for depression in diabetes patients in specialized outpatient clinics. **BMC Health Services Research** 10(1): p. 235.

Verdu, E., Armstrong, D. and Murray, J. (2009) Between Celiac Disease and Irritable Bowel Syndrome: The "No Man's Land" of Gluten Sensitivity. **American Journal of Gastroenterology** 104(6): pp. 1587-1594.

Verhagen, A., de Vet, H., de Bie, R., Kessels, A., Boers, M., Bouter, L. and Knipschild, P. (1998) The Delphi list: a criteria list for quality assessment of randomized clinical trials for conducting systematic reviews developed by Delphi consensus. **Journal of Clinical Epidemiology** 51(12): pp. 1235-1241.

Vesa, T., Marteau, P., Briet, F., Boutron-Ruault, M. and Rambaud, J. (1997) Raising milk energy content retards gastric emptying of lactose in lactose-intolerant humans with little effect on lactose digestion. **Journal of Nutrition** 127(12): pp. 2316-2320.

Vesa, T., Seppo, L., Marteau, P., Sahi, T. and Korpela, R. (1998) Role of irritable bowel syndrome in subjective lactose intolerance. **American Journal of Clinical Nutrition** 67(4): pp. 710-715.

Vigerland, S., Ljótsson, B., Bergdahl Gustasson, F., Hagert, S., Thulin, U. and Andersson, G. (2014) Attitudes towards the use of computerized cognitive behavior therapy (cCBT) with children and adolescents: A survey among Swedish mental health professionals. **Eva SerlachiusaInternet Interventions** 1(3): pp. 111-117.

Vollmer, A. and Blanchard, E. (1998) Controlled comparison of individual versus group cognitive therapy for irritable bowel syndrome. **Behaviour Therapy** 29(1): pp. 19-33.

Wagner, K., Davidson, P., Pollini, R., Strathdee, S., Washburn, R. and Palinkas, L. (2012) Reconciling incongruous qualitative and quantitative findings in mixed methods research: Exemplars from research with drug using populations. **International Journal of Drug Policy** 23(1): pp. 54– 61.

Walwyn, R. and Wessely, S. (2005) RCTs in psychiatry: challenges and the future. **Epidemiologia e Pschiatria Sociale** 14(3): pp. 127-131.

Wampold, E. (2016) **Qualities and actions of effective therapists.** Available at: https://www.apa.org/education/ce/effective-therapists.pdf [Accessed 8 March 2016].

Wang, N., Truedsson, L., Elvin, K., Andersson, B., Rönnelid, J., Mincheva-Nilsson, L., Lindkvist, A., Ludvigsson, J., Hammarström, L. and Dahle, C. (2014) Serological Assessment for Celiac Disease in IgA Deficient Adults. **PLos One** 9(4).

Wasserman, R. (2013) Ethical Issues and Guidelines for Conducting Data Analysis in Psychological Research. **Ethics and Behavior** 23(1): pp. 3-15.

Weindling, P. (2001) The Origins of Informed Consent: The International Scientific Commission on Medical War Crimes, and the Nuremberg Code. **Bulletin of the History of Medicine** 75(1): pp. 37-71.

Wells, N., Hahn, B. and Whorwell, P. (1997) Clinical economics review: irritable bowel syndrome. **Alimentary Pharmacological Therapy** 11(6): pp. 1019-1030.

Wessely, S., Nimnuan, C. and Sharpe, M. (1999) Functional somatic syndromes: one or many? **Lancet** 7(354): pp. 936-939.

West, J., Logan, R., Smith, C., Hubbard, R. and Card, T. (2004) Malignancy and mortality in people with coeliac disease: population based cohort study. **British Medical Journal** 329(716): pp. 1-4.

West, S., Finch, J. and Curran, P. (1995) Structural equation models with nonnormal variables: problems and remedies. In: Hoyle, R. (Ed.) **Structural equation modeling: Concepts, issues and applications.** Newbery Park, CA: Sage, pp. 56-75.

Whitehead, W., Burnett, C., Cook, E. and Taub, E. (1996) Impact of Irritable Bowel Syndrome on Quality of Life. **Digestive Diseases Science** 41(11): pp. 2248-2253.

Whitehead, W., Levy, R., Von Korff, M., Feld, A., Palsson, O., Turner, M. and Drossman, D. (2004) The usual medical care for irritable bowel syndrome. **Alimentary Pharmacological Therapy** 20(11): pp. 1305-1315.

Whitehead, W., Palsson, O. and Jones, K. (2002) Systematic Review of the Comorbidity of Irritable Bowel Syndrome With Other Disorders: What Are the Causes and Implications? **Gastroenterology** 122(4): pp. 1140-1156.

Whitehead, W., Palsson, O., Levy, R., Feld, A., Turner, M. and Von Korff, M. (2007) Comorbidity in Irritable Bowel Syndrome. **American Journal of Gastroenterology** 102(2): pp. 2767-2776.

WHO. (2009) **Casebook on Ethical Issues in International Health Research.** Geneva: World Health Organisation.

Whorwell, P., Lupton, E., Erduran, D. and Wilson, K. (1986) Bladder smooth muscle dysfunction in patients with irritable bowel syndrome. **Gut** 27(9): pp. 1014-1017.

Whorwell, P., Prior, A. and Colgan, S. (1987) Hypnotherapy in severe irritable bowel syndrome: further experience. **Gut** 28(4): pp. 423-425.

Widiger, T. and Shea, T. (1991) Differentiation of Axis I and Axis II disorders. **Journal of Abnormal Psychology** 100(3): pp. 399-406.

Wiklund, I., Fullerton, S., Hawkey, C., Jones, R., Longstreth, G., Mayer, E., Peacock, R., Wilson, I. and Naesdal, J. (2003) An irritable bowel syndrome specific symptom questionnaire: development and validation. **Scandinavian Journal of Gastroenterology** 38(9): pp. 947-954.

Williams, C. and Chellingsworth, M. (2010) **A clinicians guide to using the five areas approach** London: Hodder Arnold.

Williams, N. (2014) The GAD-7 questionnaire. **Occupational Medicine** 64(3): pp. 224-226.

Wilson, S., Roberts, L., Roalfe, A., Bridge, P. and Singh, S. (2004) Prevalence of irritable bowel syndrome: a community survey. **British Journal of General Practice** 54(504): pp. 495-502.

Wolfe, F., Smythe, H., Yunus, M., Bennett, R., Bombardier, C., Goldenberg, D., Tugwell, P., Campbell, S., Abeles, M. and Clark, P. (1990) Criteria for the Classification of Fibromyalgia. Report of the Multicenter Criteria Committee. **Arthritis and Rheumatology** 33(2): pp. 160-172.

Wright, J. and Denise Davis, D. (1994) The therapeutic relationship in cognitive-behavioral therapy: Patient perceptions and therapist responses. **Cognitive and Behavioral Practice** 1(1): pp. 25-45.

Wyse, R. (2006) **Accelerating Patient Recruitment in Clinical Trials.** Oxford, UK: NetworkPharma Ltd.

Yang, J., Fox, M., Cong, Y., Chu, H., Zheng, X., Long, Y., Fried, M. and Dai, N. (2014) Lactose intolerance in irritable bowel syndrome patients with diarrhoea: the roles of anxiety, activation of the innate mucosal immune system and visceral sensitivity. **Alimentary Pharmacology and Therapeutics** 39(3): pp. 302-311.

Yates, S., Morley, S., Eccleston, C. and Williams, A. (2005) A scale for rating the quality of psychological trials for pain. **Pain Practice** 117(3): pp. 314-325.

Zhong, Q., Gelaye, B., Zaslavsky, A., Fann, J., Rondon, M., Sánchez, S. and Williams, M. (2015) Diagnostic validity of the generalized anxiety disorder- 7 (GAD-7) among pregnant women. **PLos ONE** 10(4): pp. 1-28.

Zhou, Q. and Nicholas Verne, G. (2011) New insights into visceral hypersensitivity —clinical implications in IBS. **Nature Reviews Gastroenterology and Hepatology** 8(6): pp. 349-355.

Zigich, S. and Heuberger, R. (2013) The relationship of food intolerance and irritable bowel syndrome in adults. **Gastroenterology Nursing** 36(4): pp. 275-282.

Zijdenbos, I., De Wit, N., Van der Heijden, G., Rubin, G. and Quartero, A. (2009) **Cochrane Review: Psychological treatments for the management of irritable bowel syndrome.** Chichester, UK: John Wiley & Sons.

Chapter 8 ▪ Appendix

8.1 Literature search strategy

The literature review conducted as part of this report was carried out to assess the current evidence base for the use of CBT for treating patients with IBS. As RCT's are currently considered the gold standard method assessing the effectiveness of interventions (Feneck, 2009 , Rothwell, 2005 , Nystrom et al., 1993), they were a particular feature of the review. The results of the appraisal are presented in a PICO formatted matrix which facilitated the interpretation of the current evidence base.

Databases were searched using the subject headings Irritable Bowel Syndrome combined with Cognitive Behavioural Therapy. Databases were also searched using the abbreviations IBS and CBT. The American spelling of behaviour (behavior) was also factored into the search of the included databases where this was not built into the databases search facility. Where required Boolean operators which included 'AND' and 'OR' were used to search the databases for relevant literature and combine search terms. Papers which were available or written in English were included within the review.

All included studies were of adult patients (aged 18 years or older). A preliminary search of the literature demonstrated limited material, therefore no date restrictions were applied during the subsequent search. A search for grey (unpublished or not contained within the above mentioned databases) literature was also conducted during the review. A limitation to this literature review is that no clinical trial registers were searched during the review as only published studies were included.

Medline

An all text search was conducted using the headings described above. An English filter was applied during the search, filters were also used to include studies of adults only (over 18 years old). A total of 71 papers were identified for screening.

CINAHL

An all text search was used with the subject headings detailed above which were then merged using the 'AND' function. Papers returned included 35 using American spelling, 27 with English spelling and 11 with abbreviations. A total of 73 papers were identified for screening.

PsycINFO

A keywords search was used with the subject headings described above, search results were then merged by using the 'AND' function. Papers returned included 32 using American and English spelling and 16 with abbreviations. A total of 48 papers were identified for screening.

Grey literature

A recent systematic review was used to identify any papers which may have been missed searching the above databases. Furthermore, search engines such as Google scholar were used to identify further RCT's. A 'snowballing' technique was also used to identify RCT's referenced within other papers. A total of 8 papers were identified in addition to those retrieved from the above databases for screening.

Screening

Papers were initially screened for inclusion using the paper title and abstract. Papers were only included if they were relevant to evaluating the effectiveness of CBT as a treatment method for patients with IBS. Details of papers included within the review are detailed using a flow diagram within the literature review text.

8.2 The Pedro Scale

PEDro scale

1.	eligibility criteria were specified	no ❑ yes ❑ where:
2.	subjects were randomly allocated to groups (in a crossover study, subjects were randomly allocated an order in which treatments were received)	no ❑ yes ❑ where:
3.	allocation was concealed	no ❑ yes ❑ where:
4.	the groups were similar at baseline regarding the most important prognostic indicators	no ❑ yes ❑ where:
5.	there was blinding of all subjects	no ❑ yes ❑ where:
6.	there was blinding of all therapists who administered the therapy	no ❑ yes ❑ where:
7.	there was blinding of all assessors who measured at least one key outcome	no ❑ yes ❑ where:
8.	measures of at least one key outcome were obtained from more than 85% of the subjects initially allocated to groups	no ❑ yes ❑ where:
9.	all subjects for whom outcome measures were available received the treatment or control condition as allocated or, where this was not the case, data for at least one key outcome was analysed by "intention to treat"	no ❑ yes ❑ where:
10.	the results of between-group statistical comparisons are reported for at least one key outcome	no ❑ yes ❑ where:
11.	the study provides both point measures and measures of variability for at least one key outcome	no ❑ yes ❑ where:

The PEDro scale is based on the Delphi list developed by Verhagen and colleagues at the Department of Epidemiology, University of Maastricht (*Verhagen AP et al (1998). The Delphi list: a criteria list for quality assessment of randomised clinical trials for conducting systematic reviews developed by Delphi consensus. Journal of Clinical Epidemiology, 51(12):1235-41*). The list is based on "expert consensus" not, for the most part, on empirical data. Two additional items not on the Delphi list (PEDro scale items 8 and 10) have been included in the PEDro scale. As more empirical data comes to hand it may become possible to "weight" scale items so that the PEDro score reflects the importance of individual scale items.

The purpose of the PEDro scale is to help the users of the PEDro database rapidly identify which of the known or suspected randomised clinical trials (ie RCTs or CCTs) archived on the PEDro database are likely to be internally valid (criteria 2-9), and could have sufficient statistical information to make their results interpretable (criteria 10-11). An additional criterion (criterion 1) that relates to the external validity (or "generalisability" or "applicability" of the trial) has been retained so that the Delphi list is complete, but this criterion will not be used to calculate the PEDro score reported on the PEDro web site.

The PEDro scale should not be used as a measure of the "validity" of a study's conclusions. In particular, we caution users of the PEDro scale that studies which show significant treatment effects and which score highly on the PEDro scale do not necessarily provide evidence that the treatment is clinically useful. Additional considerations include whether the treatment effect was big enough to be clinically worthwhile, whether the positive effects of the treatment outweigh its negative effects, and the cost-effectiveness of the treatment. The scale should not be used to compare the "quality" of trials performed in different areas of therapy, primarily because it is not possible to satisfy all scale items in some areas of physiotherapy practice.

Last amended June 21st, 1999

8.3 CONSORT checklist

ection/Top	Item No	Checklist item	Reported on page No
itle and abstra			
	1a	Identification as a randomised trial in the title	
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	
ntroducti			
ackground ar	2a	Scientific background and explanation of rationale	
bjectiv	2b	Specific objectives or hypotheses	
etho			
rial desi	3a	Description of trial design (such as parallel, factorial) including allocation ratio	
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	
articipar	4a	Eligibility criteria for participants	
	4b	Settings and locations where the data were collected	
nterventio	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	
utcom	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	
	6b	Any changes to trial outcomes after the trial commenced, with reasons	
ample si	7a	How sample size was determined	
	7b	When applicable, explanation of any interim analyses and stopping guidelines	
andomisatic			
Sequence generation	8a	Method used to generate the random allocation sequence	
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	
lindi	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	
	11b	If relevant, description of the similarity of interventions	
tatistical metho	12a	Statistical methods used to compare groups for primary and secondary outcomes	
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	
esu			
articipant flow	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	
iagram is strong	13b	For each group, losses and exclusions after randomisation, together with reasons	

ecommende			
ecruitme	14a	Dates defining the periods of recruitment and follow-up	
	14b	Why the trial ended or was stopped	
aseline da	15	A table showing baseline demographic and clinical characteristics for each group	
umbers analys	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	
utcomes and estimati	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	
ncillary analys	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	
arr	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	
iscussi			
imitatio	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	
eneralizabil	21	Generalizability (external validity, applicability) of the trial findings	
nterpretati	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	
ther informati			
egistrati	23	Registration number and name of trial registry	
roto	24	Where the full trial protocol can be accessed, if available	
undi	25	Sources of funding and other support (such as supply of drugs), role of funders	

8.4 Participant information sheet

The University of Nottingham
UNITED KINGDOM · CHINA · MALAYSIA

Nottingham University Hospitals NHS
NHS Trust

Cognitive Behavioural Therapy for Irritable Bowel Syndrome (Feasibility Study)
Participant Information Sheet

Final Version 1.0: 28th October 2013

Name of Researcher: Andrew David Dainty

We would like to invite you to take part in our research study. Before you decide if you would like to consider taking part, we would like you to understand why the research is being done and what it would involve for you. One of our team would be happy to discuss the study with you and answer any questions you have. Talk to others about the study if you wish. Ask us if there is anything that is not clear.

What is the purpose of the study?

This study will help researchers better understand the use of a particular kind of 'talking therapy' called Cognitive Behavioural Therapy (CBT), which may help to improve the symptoms of patients with Irritable Bowel Syndrome (IBS). CBT is a type of psychotherapy which has been used to help people with IBS develop new ways of living and coping with certain aspects of their IBS. There is already some evidence to suggest that this may be useful for people with IBS, although there are currently no practical solutions for delivering CBT cost effectively within gastrointestinal NHS clinics. By carrying out this study, researchers at the University of Nottingham hope to learn more about the use of three different kinds of CBT which might be beneficial to patients like you with IBS. We also hope to interview some of the participants during our study which will also help us better understand how patients might experience and feel about the different ways in which CBT could be provided to patients within the NHS.

Why have I been invited?

You have been invited to take part in this study because you have IBS. Your hospital doctor has provided you with this information sheet because he/she feels that you might be eligible to take part in our study. We are inviting sixty patients like you, over the age of eighteen years old, to take part in our study.

Do I have to take part?

It is up to you to decide whether you would like to consider taking part in our study. If you do decide to take part, you will be given this information sheet to keep and will be given the opportunity to ask questions and find out more about our study. If you decide to take part, you will be asked to sign a consent form before taking part in any research activities. If you do decide to take part, you are still free to withdraw at any time and without giving a reason. You are under no obligation to consider taking part in this research and if you choose not to take part, your care and legal rights will not be affected.

What will happen to me if I take part?

If you decide to take part in the study, you will be invited to attend an initial appointment with the nurse researcher. It may be possible to do this in conjunction with your next hospital appointment so that you do not have to make a special journey for the visit. This will provide you with the opportunity to clarify anything you may be unsure about and ask any questions you might have. The nurse may ask for your permission to have access to your hospital notes prior to attending the screening visit in order to become familiar with your medical history. If you decide to take part, the nurse will ask you to sign a consent form. The nurse will then talk to you about your IBS, ask you to complete some forms about your symptoms and will decide if you are eligible to take part in the study. At this point, **some participants will <u>not</u> be able to continue to the next part of our stud**y (randomised to the four treatment options detailed below). It is important that you are aware that this should not be taken personally, as there are strict criteria which have to be met in order for you to take part. The criteria relate to the extent of your IBS and any other health conditions you may have. If you are not eligible to be randomised to the study, the research team would still like to collect some information about you in order to help us better understand certain characteristics about people who have IBS by completing our first set of questionnaires.

If you are eligible to take part in our study, we will ask you to complete the first set of questionnaires which ask about the severity of your symptoms and how these might impact on your quality of life. We will also ask you to complete forms which will help us measure the level of anxiety and depression that participants might have prior to taking part in our study. We will then randomly allocate you to one of four arms of the trial. The nurse researcher has no control over this process, which will be carried out by someone who is not involved with our study. There is an equal chance of you being allocated to any one of the four groups described below.

<u>High Intensity CBT</u>

Participants in this arm of the study will receive CBT delivered by a Cognitive Behavioural Therapist. This is a highly intensive programme of talking therapy which will involve up to 12 hours of face to face therapy spread over 11 weekly treatment appointments at the hospital. The final session (referred to by therapists as a follow up session) will be arranged for 3 months after you have completed weekly session 10. During this treatment, the therapist will work in partnership with you to try and find ways of helping you cope with the symptoms of your IBS using a variety of activities such as relaxation techniques. You will also be asked to complete homework activities in between your appointment sessions. We would like to interview five participants about their experiences of taking part in the high intensity treatment and will try to meet you at your final treatment session if you are selected for this part of the study. Where this is not possible, we will arrange to meet you at another time or to interview you at home should you prefer. It is anticipated that the interview will take no longer than an hour to complete.

<u>Guided self-help CBT</u>

Participants in this arm of the study will receive CBT under the guidance of a nurse therapist over 6 weekly treatment appointments, the first of which is 60 minutes in duration. All other sessions are 30 minutes in duration. The first session consists of a thorough psychotherapy assessment with the therapist. The nurse will then guide you through activities in a series of treatment booklets and offer any support that you may require. There are also homework activities in between the treatment sessions that you would need to complete and supporting material to read and work through. Similar to the first arm of the study, we would like to interview five participants about their experiences of taking part in the guided self-help and will try to meet you at your final treatment session if you are selected for this part of the study. Where this is not possible, we will arrange to meet you at another time or to interview you at home should you prefer. It is anticipated that the interview will take no longer than an hour to complete.

Self-help workbooks

Participants who are in this arm of the study will be given a series of weekly self-help workbooks with homework activities to complete over a 6 week period. The workbooks are completely self-directed and you will not be required to attend any treatment sessions with a nurse or therapist. You will be required to read through the workbooks and complete the activities on a weekly basis. Like the other arms of the study, we would like to interview five participants about their experiences of taking part in the self-help and you may be selected for this part of the study. This can be arranged at a time to suit you at the hospital or where this is not possible we will arrange to meet you at home should you prefer. It is anticipated that the interview will take no longer than an hour to complete.

Usual care

Participants who are in this group of the study will not receive anything which differs to the high quality care they receive from their team of hospital specialists. This is a very important part of our study, because without knowing how our patient's symptoms improve with our current treatment practices alone, we would not understand if any of the trial treatments described above offer any additional benefit.

For all participants

The research team will contact you around 12 weeks after your first appointment with the nurse researcher and after 6 months by mail. The research team will ask you to complete the same forms you completed with the nurse researcher during your first appointment. During the therapy sessions, the therapist may be required to record the contents of the session for the process of supervision and to clarify that treatment has been provided as intended. If your session needs to be recorded, your therapists would talk to you about this first and ask for your permission to do so. You will be asked to consent to these recordings if you agree to take part in the study but we will always ask before making any recordings of the treatment sessions.

When will the study end?

Your participation in the research study will end upon completion of the 6 month follow up postal questionnaires regardless of which group you are in. If you are not eligible to be randomised into the main part of the study, your participation will end once you have completed the questionnaires at your first appointment with the researcher. This means that participants who were eligible for the main part of the study will be enrolled for approximately 6 months from consent to completion. During participation in the study, you should continue to receive the usual care of your hospital doctor and general practitioner.

Expenses and payments

Participants will be able to be reimbursed for their travel expenses for any visits to the hospital which they have incurred as a result of taking part in the study. We are unable to offer any inconvenience allowance or any other payments for taking part in this study.

What are the possible disadvantages and risks of taking part?

Some participants may find talking about their IBS and the impact this has on their daily activities distressing, either during the study treatments or by taking part in the interviews. Participants in any part of the study will have full control over their participation in the research project and may stop a treatment session or an interview at any time. Taking part in the study will result in random allocation to any of the four groups. Participants should consider the amount of time and level of commitment that may be required to take part in the study. We hope to better understand these issues by carrying out the interviews with fifteen of our study participants during the study.

What are the possible benefits of taking part?

There is not yet enough evidence for us to make promises about any benefits there may be to receiving one of the study treatments. However, it is possible that some participants who take part in one of the trial treatments may experience an improvement in their symptoms or feel more able to cope with the symptoms of their IBS.

What happens when the research study stops?

When the research study closes we will analyse all of the data collected during the conduct of the study. Participants will complete their participation in the study upon completion of the 6 month follow up postal questionnaires. The information gathered during the study will hopefully be used to apply for funding for a much larger research project.

What if there is a problem?

If you have a concern about any aspect of this study, you should ask to speak to the researcher who will do their best to answer your questions. The researchers contact details are given at the end of this information sheet. If you remain unhappy and wish to complain formally, you can do this by contacting NHS Patient Advice and Liaison Service (PALS), c/o PALS, Freepost, NEA 14614, Nottingham, NG7 1BR or Tel: 0800 183 0204.

Will my taking part in the study be kept confidential?

We will follow ethical and legal practice and all information about you will be handled in the strictest of confidence and in accordance with the Data Protection Act 1998. During participation in the study, we will collect data from the questionnaires completed at the beginning, middle and end of the study period. We will also collect data during interviews from fifteen participants in the treatment arms of our study. Interview data will be recorded using a digital recording device and will then be transcribed for analysis. During the conduct of the study, we will also collect some information from participant's medical records. If you join the study, some parts of your medical records and the data collected for the study may be examined by authorised persons from the University of Nottingham who are organising the research. They may also be looked at by Nottingham University Hospitals NHS Trust to check that the study is being carried out correctly. All will have a duty of confidentiality to you as a research participant and we will do our best to meet this duty.

All information which is collected about you during the course of the research will be kept **strictly confidential**, stored in a secure and locked office, and on a password protected database. Any information about you which leaves the hospital will have your name and address removed (anonymised), a unique code will be used so that you cannot be recognised. Your personal data (address, telephone number) will be kept for 6 months after the end of the study so that we are able to contact you about the results of the study and possible follow-up studies if you have indicated that you would like to receive this information. After this time, your personal data will be destroyed. All other data (research data) will be kept securely for 7 years. After this time your data will be disposed of securely. During this time all precautions will be taken by all those involved to maintain your confidentiality, only members of the research team will have access to your personal data.

With your permission, we would also like to share anonymised research data collected during this study with other researchers and healthcare professionals. This will enable us to ensure that the data collected during this study will have the greatest impact upon the way we care for patients with IBS. Any information such as interview transcripts which are used in reports or shared with other researchers will be completely anonymised. Although information gathered during participation in this study will be treated with the strictest of confidence, you should be aware that should you disclose anything to us which we feel puts you or anyone else at any risk of harm, then we may have a professional obligation to pass on such information to the relevant authorities. We would always try to discuss this with you first, unless we felt that doing so may further increase the risk to yourself or others. These procedures do not differ to confidentiality practices within the NHS healthcare system.

What will happen if I don't want to carry on with the study?

You may leave the study at any time without giving any reason. If you choose to withdraw, information collected so far cannot be erased and this information may still be used in the project analysis. The care you receive and your legal rights will not be affected in any way if you decide to leave our study. We would value any information you could provide us with that might help us understand why you chose to leave. This information may help us improve the studies we carry out in the future and help us better understand how we can improve the way we use CBT to treat IBS in the future. You are under no obligation to provide the researcher with this information and we would not be disappointed if you should choose not to share your reasons for leaving with us.

Involvement of your General Practitioner and hospital care team

We will write to your family doctor and inform them about your participation in the study. Your family doctor will receive a letter along with a copy of this information sheet, we will also provide your doctor with the details of the research team should they require any further information about the research study are taking part in. We will also place a copy of this information within your hospital notes so that your hospital care team are aware that you are taking part in our study. If the questionnaires you complete during the study tell us that you may have moderate to severe scores potentially indicating anxiety or depression, we would also like to notify your general practitioner and hospital team as would be the case if you were being treated routinely in a gastrointestinal clinic.

What will happen to the results of the research study?

We will share our findings with other researchers and healthcare professionals by way of conference presentations and publications within peer reviewed journals, websites and other media. The results of the study may also be used to apply for funding for a much larger research project. The results of the study will also be published within the researchers PhD thesis at the University of Nottingham. Any research data which is used in a publication or report about our findings will be completely anonymised and you will not be identifiable in any way. The researcher will ask if you would like to be notified about the results of the study during your first study appointment.

Who is organising and funding the research?

This research is being organised by the University of Nottingham, School of Health Sciences and is being carried out by the recipient of a PhD studentship funded by the University of Nottingham and the Nottingham NIHR Biomedical Research Unit.

Who has reviewed the study?

All research in the NHS is looked at by independent group of people, called a Research Ethics Committee, who provide us with an ethical opinion and relevant permission to carry out our research in the NHS. This study has been reviewed and given favourable opinion by the Nottingham Local Research Ethics Committee 2.

Contact details

Principal Investigator

Mr Andrew David Dainty, Nottingham University Hospitals NHS Trust, Nottingham Digestive Diseases Centre & Biomedical Research Unit, University Of Nottingham, E Floor, West Block, Queen's Medical Centre Campus, Nottingham, NG7 2UH, Tel: +44 (0)115 9709966, Fax: +44 (0)115 9709955, Email: ntxad9@nottingham.ac.uk

Chief Investigator

Professor Patrick Callaghan, Professor of Mental Health Nursing/Head of School, University of Nottingham, School of Health Sciences, Queens Medical Centre Campus, Derby Road, Nottingham, NG7 2HA, Tel: 0115 82 30812 Email: Patrick.Callaghan@nottingham.ac.uk

8.5 Ethical approval

NHS
Health Research Authority
NRES Committee East Midlands - Nottingham 2
The Old Chapel
Royal Standard Place
Nottingham
NG1 6FS

Telephone: 0115 8839695

05 December 2013

Professor Patrick Callaghan
Professor of Mental Health Nursing
University of Nottingham, School of Nursing, Midwifery and Physiotherapy
A Floor, School of Nursing, Midwifery and Physiotherapy,
Queens Medical Centre,
Nottingham
MG7 2AH

Dear Professor Callaghan,

Study title:	**A mixed methods feasibility study to evaluate the use of low-intensity, nurse delivered Cognitive Behavioural Therapy in the treatment of Irritable Bowel Syndrome**
REC reference:	**13/EM/0428**
Protocol number:	**13127**
IRAS project ID:	**131205**

The Research Ethics Committee reviewed the above application at the meeting held on 25 November 2013.

We plan to publish your research summary wording for the above study on the NRES website, together with your contact details, unless you expressly withhold permission to do so. Publication will be no earlier than three months from the date of this favourable opinion letter. Should you wish to provide a substitute contact point, require further information, or wish to withhold permission to publish, please contact the REC Manager - Liza Selway on 0115 8839695

Ethical opinion

The chair introduced themselves and thanked the researchers for attending the meeting and thanked the researchers for an interesting study

The committee asked the researcher who will be assessing the database of potential participants. The researchers advised that the Principal Investigator will be accessing the information and that they have a clinical contract with the Biomedical Research Unit

The committee asked the researchers if the Principal Investigator would be recruiting potential participants from their own cohort of patients. The researchers confirmed that this will not be the case and participants will be recruited WHO are known to the hospital gastroenterology clinics

The committee asked the researchers who will be transcribing the interviews with participants. The researchers advised that the Principal Investigator will transcribe and all data will be disposed of once completed. The transcribing will be from a digital recording and consequently be stored on a secure university server

The members of the Committee present gave a favourable ethical opinion of the above research on the basis described in the application form, protocol and supporting documentation, subject to the conditions specified below.

Ethical review of research sites

Non NHS sites

The Committee has not yet been notified of the outcome of any site-specific assessment (SSA) for the non-NHS research site(s) taking part in this study. The favourable opinion does not therefore apply to any non-NHS site at present. I will write to you again as soon as one Research Ethics Committee has notified the outcome of a SSA. In the meantime no study procedures should be initiated at non-NHS sites.

Conditions of the favourable opinion

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

Management permission or approval must be obtained from each host organisation prior to the start of the study at the site concerned.

Management permission ("R&D approval") should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements.

Guidance on applying for NHS permission for research is available in the Integrated Research Application System or at http://www.rdforum.nhs.uk.

Where a NHS organisation's role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre"), guidance should be sought from the R&D office on the information it requires to give permission for this activity.

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 approvals from host organisations

Registration of Clinical Trials

All clinical trials (defined as the first four categories on the IRAS filter page) must be registered on a publically accessible database within 6 weeks of recruitment of the first participant (for medical device studies, within the timeline determined by the current registration and publication trees).

There is no requirement to separately notify the REC but you should do so at the earliest opportunity e.g when submitting an amendment. We will audit the registration details as part of the annual progress reporting process.

To ensure transparency in research, we strongly recommend that all research is registered but for non clinical trials this is not currently mandatory.

If a sponsor wishes to contest the need for registration they should contact Catherine Blewett (catherineblewett@nhs.net), the HRA does not, however, expect exceptions to be made. Guidance on where to register is provided within IRAS.

It is 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).

Approved documents

The documents reviewed and approved at the meeting were:

Document	*Version*	*Date*
Advertisement	CBS-IT Study poster for clinics notice boards V1	28 October 2013
Covering Letter		05 November 2013
Evidence of insurance or indemnity	CBT-IBS Study Clinical Trials Evidence - Insurance letter	30 July 2013
GP/Consultant Information Sheets	CBT-IBS V1	28 October 2013
Interview Schedules/Topic Guides	Study Post Intervention V1	28 October 2013
Investigator CV	Patrick Callaghan	14 October 2013
Letter from Sponsor		01 November 2013
Letter of invitation to participant	CBT-IBS study Irvite V1	28 October 2013
Other: CV Supervisor	Nina Lewis	04 October 2013
Other: CV Student	Andrew Dainty	04 October 2013
Other: CBT-IBS Study GRGS-BS Form (validated questionnaire 2 of 5)	1	28 October 2013
Other: CBT-IBS Study IBS-QOL form (validated questionnaire 3 of 5)	1	28 October 2013
Other: CBT-IBS Study GAD-7 Form (validated questionnaire 4 of 5)	1	28 October 2013
Other: CBT-IBS Study PHQ-9 Form (Validated questionnaire 5 of 5)	1	28 October 2013
Other: CV Phillip Kinsella		04 October 2013
Other: CBT-IBS Study demographics form (completed but the study PI but provided for information	1	28 October 2013

Other: CBT-IBS Study Poster for doctors room only	1	28 October 2013
Other: CBT-IBS Study Missed appointment letter	1	28 October 2013
Other: CBT-IBS Study Reply slip	1	28 October 2013
Other: CBT-IBS Study Follow up letter	1	28 October 2013
Other: CBT-IBS Study Follow up reminder letter	1	28 October 2013
Other: CBT-IBS Study Workbook 1	1	28 October 2013
Other: CBT-IBS Study Workbook 2	1	28 October 2013
Other: CBT-IBS Workbook 3	1	28 October 2013
Other: CBT-IBS Workbook 4	1	28 October 2013
Other: CBT-IBS Study Workbook 5	1	28 October 2013
Other: CBT-IBS Study Workbook 6	1	28 October 2013
Participant Consent Form: CBT-IBS Study Consent Form	1	28 October 2013
Participant Information Sheet: CBT -IBS Study Participant	1	28 October 2013
Protocol	CBT-IBS V1	28 October 2013
Questionnaire: CBT-IBS Study Rome 111 IBS Module Form (validated questionnaire 1 of 5)		28 October 2013
REC application	131205/523643/1/45	01 November 2013

Membership of the Committee

The members of the Ethics Committee who were present at the meeting are listed on the attached sheet.

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.

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

The NRES website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

Feedback

You are invited to give your view of the service that you have received from the National Research Ethics Service and the application procedure. If you wish to make your views known please use the feedback form available on the website.

Further information is available at National Research Ethics Service website > After Review

13/EM/0428	**Please quote this number on all correspondence**

We are pleased to welcome researchers and R & D staff at our NRES committee members' training days – see details at http://www.hra.nhs.uk/hra-training/

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

Yours sincerely

Dr Martin Hewitt
Chair

Email: NRESCommittee.EastMidlands-Nottingham2@nhs.net

Enclosures: *List of names and professions of members who were present at the meeting and those who submitted written comments*
"After ethical review – guidance for researchers" SL-AR2

Copy to: *Paul Cartlege, University of Nottingham*
Charlotte Davies, Nottingham University Hospitals NHS Trust

8.6 Nurse delivered, guided self-help treatment protocol

Participants randomised to this arm of the study will attend a much less intensive program of CBT guided by a nurse therapist. The nurse therapist will be the study's principal investigator who is a registered nurse trained in the use and delivery of low-intensity CBT. The nurses training has consisted of accessing and completing the first two modules of the Improving Access to psychological Therapies national curriculum for the education of psychological wellbeing practitioners, see IAPT (2011). It is for these reasons that the study's principal investigator will not collect post intervention data (in the form of interviews or quantitative data) directly from participants. The nurse therapist will receive clinical supervision from the study's chief investigator.

Participants within this arm of the study will work through six workbooks derived from an intervention developed by Hunt et al. (2009). These workbooks will be provided to the REC, Sponsor and R&D departments as supporting documentation and are not considered a new intervention. However, the workbooks have been modified in light of knew knowledge relating to the quality of guided self-help materials in the hope that their format and layout will be more acceptable to service users. The patient advisory group for this study are also involved in the checking of these workbooks format. The treatment schedule will follow the format as detailed below and will consist of six weekly treatment sessions of face to face contact with the nurse therapist.

Session 1 (60 minutes)
The nurse therapist will begin by explaining his/her role as a gastrointestinal nurse trained in the administration of CBT (in order to establish relevant expertise). The session must begin with an agenda and the therapist will advise the person of the time that is available for the session. This will help ensure the session is delivered in a timely fashion. The format of this and all subsequent sessions will follow the structure of information gathering, information giving and collaborative/shared decision making supported within the material produced by Richards and Whyte (2011).

The therapist will begin by carrying out a full assessment of the person using a five areas approach as advocated by Williams and Chellingsworth (2010). This will help ensure that the therapist is able to use examples during subsequent therapy sessions and relate the interventions within the CBT workbooks to the person's individual circumstances. The therapist will make full use of the specific factors, common factors and collaborative methods of working advocated by Richards and Whyte (2011) in order to maximise the effectiveness of the program interventions and maintain client engagement in therapy. An assessment of risk will also feature within the first therapy session as advocated by Farrand and Williams (2010). The assessment of risk will consist of an assessment of suicidal intent, plans or actions and self-harm intent, plans or actions, protective factors and access to means (all of which are considered routine in a psychotherapy assessment). Where risk is identified, such risk will be dealt with as described within the *Ethical and Regulatory Aspects section*. Where suicidal ideation or self-harm is identified, the participant will be withdrawn from the study as detailed within the *removal of participants from therapy or assessments* section. A problem statement will be formulated in order to summarise information gathered during the session.

Session 1 (60 minutes)
The therapist should introduce the psychoeducation chapter of the first workbook and begin to help the person understand and unpick how they have arrived at the diagnosis of IBS. The person should be encouraged to review their own medical history with their doctor/care team as the first step on the ladder to taking control of their IBS. The therapist should introduce the biopsychosocial model of IBS

contained within workbook one. This should be reinforced with a rationale for why CBT might help people better manage their IBS. It should be reinforced that the program is about the person gaining control of their lives and reducing the impact that IBS has upon it.

Set homework for next session: Read workbook 1 and complete suggested activities

Session 2 (subsequent sessions 30 minutes)
The session will begin with an agenda and the therapist will advise the person of the time that is available for the session. The therapist should start by reviewing questions and concerns about IBS or the biopsychosocial model introduced during the previous session and recap on the content of workbook one. The therapist should then introduce the concept of relaxation training and the person should be given the opportunity to practice these skills under the guidance of the therapist. A rationale should be clearly stated for the use of relaxation exercises which can be linked to the activation of the parasympathetic nervous system discussed within the previous workbook.

Set homework for next session: Read workbook 2 and practice relaxation exercises on a daily basis

Session 3
The session will begin with an agenda and the therapist will advise the person of the time that is available for the session. The therapist should review the persons experience with relaxation exercises briefly, then introduce basic cognitive model of stress management detailed within workbook three. The therapist should work with the patient to identify some situations which the person may recall and complete a thought diary collaboratively with the therapist in session.

Set homework for next session: Read workbook 3 and practice completing thought records

Session 4
The session will begin with an agenda and the therapist will advise the person of the time that is available for the session. The therapist should facilitate a review of the persons thought records completed as homework set during the previous session and give corrective and collaborative feedback. The therapist should then link the cognitive model to IBS. The therapist should then also introduce the concept of behavioural experiments which can be used to generate data in relation to negative automatic thoughts. The session should include a detailed rationale for both of the interventions detailed within the following workbook.

Set homework for next session: Read workbook 4 and complete some IBS thought records and identify two behavioural experiments

Session 5
The session will begin with an agenda and the therapist will advise the person of the time that is available for the session. The therapist should facilitate a review of the persons experience with the cognitive model of IBS and the two behavioural experiments and give corrective and collaborative feedback. The therapist should then introduce the concept of reducing unhelpful avoidance using exposure. The therapist should then work with the person to identify avoidance behaviours that the person would like to work on for homework and ensure the person has a thorough understanding of the rules underpinning exposure therapy.

Set homework for next session: Read workbook 5 and try out exposure exercises

Session 6

The session will begin with an agenda and the therapist will advise the person of the time that is available for the session. The therapist should facilitate a review of the person's experiences with exposure therapy and encourage further practice of these activities and reinforce rationale as required. The therapist should then discuss any dietary advice and introduce the contents of the final workbook. The therapist should also summarise the treatment program and ask the person to continue using the strategies covered during the program.

Set homework for on-going use of self-help interventions: Read workbook six and continue with experiments, exposure and thought records

8.7 High intensity CBT treatment protocol

Participants randomised to this arm of the study will undergo a program of high intensity CBT, provided by a designated cognitive behavioural therapist within the department of psychological medicine at the Queens Medical Centre Campus. Therapy will consist of 11 sessions of face to face contact with the psychotherapist and the completion of homework tasks between sessions based upon the model of CBT for IBS advocated by Toner et al. (2000), brief details of which are provided below. Participants will be referred to the department of psychological medicine by way of referral letter to the high intensity therapist who will liaise with the participant, and arrange a suitable time and date to commence therapy. A visit notification and monitoring form will accompany the referral letter for the purposes of stipulating the visit due dates and to enable the monitoring of deviations from protocol.

Every session
The therapist will set the session agenda; do progressive muscle relaxation with patient; review homework; introduce theme of the day and set new homework tasks.

Session 1 (two hours)
Conduct a standard CBT interview looking at predisposing, precipitating and maintenance factors. Focus will be on the issues of control, bowel performance anxiety, shame, and self-efficacy. The therapist will identify any co-morbid psychiatric diagnoses from assessment and mental state examination. Consider involvement of co-therapist. Agree suitability.
New homework: ask patient to complete symptom diary.

Session 2 (all subsequent sessions one hour)
Set agenda; progressive muscle relaxation; review of homework
Theme of the day: reinforce rationale for CBT, and develop formulation. Review symptom diary-focus on areas of 'stress'. Do 'problem and target statements' and rate these.
New homework: patient to continue symptom diary and review formulation.

Session 3
Set agenda; progressive muscle relaxation; review of homework
Theme of the day: Introduce concept of Negative Automatic Thought (NAT) diary, and of Behavioural Experiments to address negative cognitions, ensuring coverage of bowel performance anxiety.
New homework: related to NAT diary and Behavioural Experiments.

Session 4
Set agenda; progressive muscle relaxation; review of homework
Theme of the day: Review of NAT diary work with focus on behavioural experiments, and exposure work.
New homework: related to NAT diary and Behavioural Experiments/exposure work

Session 5
Set agenda; progressive muscle relaxation; review of homework;
Theme of the day: Continue review of NAT diary work. Focus on behavioural experiments and exposure work.
New homework: related to NAT diary and Behavioural Experiments.

Session 6
Set agenda; progressive muscle relaxation; review of homework; Continue review of NAT diary work. Focus on behavioural experiments and exposure work.
Theme of the day: Introduction to pain management concepts and strategies if pain is a problem.
New homework: related to pain management.

Session 7
Set agenda; progressive muscle relaxation; review of homework; relating to pain management, and also NAT/ behavioural experiments /exposure.
New homework: relating to pain management and on-going NAT/ behavioural experiments /exposure.

Session 8
Set agenda; progressive muscle relaxation; review of homework; Addressing of 'other problematic issues' that have been identified, potentially shame; excessive need for control; perfectionism; excessive need for approval; poor self- efficacy.
New homework: related to 'other problematic issues'.

Session 9
Set agenda; progressive muscle relaxation; review of homework; Review of 'other problematic issues' homework, and review of NAT/pain management as appropriate. Theme of the day: Relapse prevention.
New homework: To complete Relapse prevention form.

Session 10
Set agenda; progressive muscle relaxation; review of homework; Review of relapse prevention and other homework as appropriate.
New homework: Continuing therapy and implementing relapse prevention.

Session 11 - follow up at three months
Set agenda; progressive muscle relaxation; review of homework: relapse prevention and other homework as appropriate. No new themes. Discharge.

8.8 Study interview schedule

Cognitive Behavioural Therapy for Irritable Bowel Syndrome (Feasibility Study)

Post intervention interview schedule

Final version 1.0 28th October 2013

Introduction	***Please start your recording device.*** The interviewer should introduce him/herself and explain the rationale for conducting the interview. Participants should be advised that the interviews will help researchers better understand how patients experience one of the three trial treatments. Participants should also be advised that any feedback they give, whether negative or positive will be welcomed by the research team as this will help us develop treatments for IBS in the future. Participants should therefore be encouraged to be open and honest about the way they feel about their treatment experience.
The experience	*It would be useful for us to understand how you feel about the overall experience of the treatment you received during the study. Please describe your journey, in your own words, from when you first heard about the study right through to completion of your treatment.*
Initial perceptions	*What were your initial thoughts about being offered a form of psychological therapy to help you manage your IBS symptoms?* *Have you ever received psychological help for issues you may have experienced in the past?* *If yes, do you remember the type of therapy you received and whether you found it useful?* *Prior to enrolment into this study did you have any knowledge or experience of Cognitive Behavioural Therapy?* *If yes, what did you know about CBT and what were your perceptions of it as a form of treatment?* *Did you have any initials thoughts about the usefulness of this treatment in relation to managing your IBS symptoms and if so what were they?* *Why did you decide to try this form of treatment?*
Acceptability	
Positive aspects	*Are there any elements of the treatment that you found*

	especially effective in reducing or helping you to manage your IBS symptoms? If so what are they and how have they impacted on your experience of IBS now? *If you received one of the treatments delivered by a therapist, was there anything you found particularly helpful about receiving face-to-face support/therapy?* *If you received treatment via the self-help manual alone, was there anything in particular that helped keep you engaged with the material?* *Can you describe any other benefits you have experienced as a result of the treatment you have received in this study?*
Negative aspects	*Are there any elements of the treatment that you found unhelpful or difficult to understand? If so what are they and do you have any suggestions for improvement?* *If you received one of the treatments delivered by a therapist, do you have any suggestions that could improve the way a therapist interacts with their client/patient during the sessions?* *Were there any elements of the treatment you received that had a negative impact on your IBS symptoms that haven't been discussed already – if so please describe these?*
Practical issues	If the participant has not talked about any of the points below, the interviewer should prompt the participant to share their experiences of these aspects. *What do you think about the level of commitment that was required to complete the treatment?* *Were there any tasks set by the therapist or workbook that you found difficult to complete? If there were, which tasks were difficult to complete and what were the barriers to completing them?* *Did you spend the suggested amount of time on the therapeutic tasks?? If not, which tasks were you unable to spend the suggested amount of time on and what were the barriers?* *If not, did you spend more or less time on the activities?*
Peer support/understanding	*Did you let your family and/or friends know about your participation in this study? If so did you tell them about the type of treatment you were receiving? How did you describe it to them if you did?* *Can you describe anything your family or friends have done to support you with your treatment activities?*

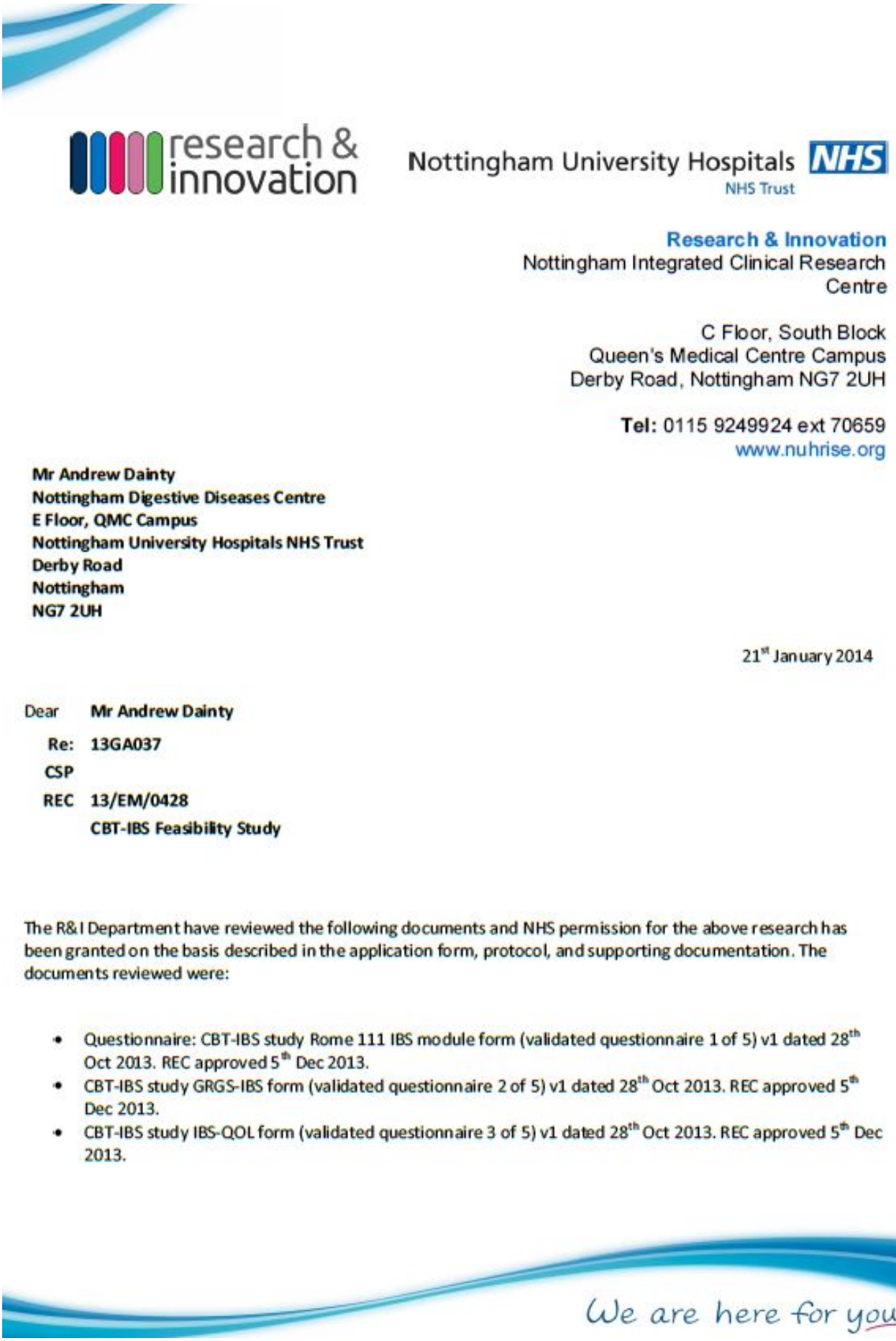
Impact	*Has the treatment you received changed your understanding of your IBS? If so, what is different about your understanding of your IBS since receiving the treatment?* *Do you think that the treatment you have received has had an impact on any other part of your life apart from the management of your IBS symptoms?* *If you are working, how has the treatment affected your work life, if at all?* *What would you say are the most important benefits you gained from your treatment (if anything)?* *Would you recommend this form of treatment to a friend or relative and why?*
Other issues	*Is there anything else that you would like to tell me that you think might help us to develop treatments like this in the future?*
End of interview	***Please stop your recording device*** The participant should be thanked for taking part in the study to date and for taking part in the interview. Participants should be told how important their participation in the research is and that by taking part in the study they have played a vital role in shaping the way that IBS will be treated in the future. Participants should be advised that they will be contacted in around six months and asked to complete the same forms that they have completed previously. It should be stressed that completing and returning the forms is vitally important for us to see if anything has changed. Participants should be asked at this point if they are happy to continue taking part in our study and for us to contact them in around six months by post.

8.9 Study CORE-Q checklist

No. Item	Guide questions/description	Reported in section/information
Domain 1: Research team and reflexivity		
Personal Characteristics		
1. Inter viewer/facilitator	Which author/s conducted the interview or focus group?	4.6.2 p.169-170
2. Credentials	What were the researcher's credentials? E.g. PhD, MD	4.6.2 p.169-170
3. Occupation	What was their occupation at the time of the study?	4.6.2 p.169-170
4. Gender	Was the researcher male or female?	4.6.2p.169-170
5. Experience and training	What experience or training did the researcher have?	4.6.2 p.169-170
Relationship with participants		
6. Relationship established	Was a relationship established prior to study commencement?	Appendix 8.8
7. Participant knowledge of the interviewer	What did the participants know about the researcher? e.g. personal goals, reasons for doing the research	4.6.2 p.170 Appendix 8.8
8. Interviewer characteristics	What characteristics were reported about the inter viewer/facilitator? e.g. Bias, assumptions, reasons and interests in the research topic	4.6.2 p.169, interviews carried out by another
Domain 2: study design		
Theoretical framework		
9. Methodological orientation and Theory	What methodological orientation was stated to underpin the study? e.g. grounded theory, discourse analysis, ethnography, phenomenology, content analysis	MMR pragmatic philosophy 4.1.2
Participant selection		
10. Sampling	How were participants selected? e.g. purposive, convenience, consecutive, snowball	4.1.3 and 4.2
11. Method of approach	How were participants approached? e.g. face-to-face, telephone, mail, email	4.1.3
12. Sample size	How many participants were in the study?	4.1.3
13. Non-participation	How many people refused to participate or dropped out? Reasons?	5.1.4
Setting		
14. Setting of data collection	Where was the data collected? e.g. home, clinic, workplace	4.6.2
15. Presence of non-participants	Was anyone else present besides the participants and researchers?	4.6.2
16. Description of sample	What are the important characteristics of the sample? e.g. demographic data, date	4.1.3 and 6.1.1
Data collection		
17. Interview guide	Were questions, prompts, guides provided by the authors? Was it pilot tested?	Appendix 8 Not piloted but approved by the PAG see 4.3.3.
18. Repeat interviews	Were repeat inter views carried out? If yes,	No

	how many?	
19. Audio/visual recording	Did the research use audio or visual recording to collect the data?	4.6.2
20. Field notes	Were field notes made during and/or after the interview or focus group?	No
21. Duration	What was the duration of the inter views or focus group?	5.1.4
22. Data saturation	Was data saturation discussed?	6.1.5
23. Transcripts returned	Were transcripts returned to participants for comment and/or correction?	No
Domain 3: analysis and findings		
Data analysis		
24. Number of data coders	How many data coders coded the data?	6.1.3
25. Description of the coding tree	Did authors provide a description of the coding tree?	5.1.4, 5.1.5 identification of themes and Appendix 13.
26. Derivation of themes	Were themes identified in advance or derived from the data?	4.6.4
27. Software	What software, if applicable, was used to manage the data?	N/A
28. Participant checking	Did participants provide feedback on the findings?	Not at the time of writing
Reporting		
29. Quotations presented	Were participant quotations presented to illustrate the themes/findings? Was each quotation identified? e.g. participant number	5.1.4, 5.1.5 extensively
30. Data and findings consistent	Was there consistency between the data presented and the findings?	5.1.4, 5.1.5 but limited to very small sample as described in 6.1.6
31. Clarity of major themes	Were major themes clearly presented in the findings?	5.1.4, 5.1.5
32. Clarity of minor themes	Is there a description of diverse cases or discussion of minor themes?	5.1.4

8.10 Research and innovation approval



research & innovation

Nottingham University Hospitals NHS
NHS Trust

Research & Innovation
Nottingham Integrated Clinical Research Centre

C Floor, South Block
Queen's Medical Centre Campus
Derby Road, Nottingham NG7 2UH

Tel: 0115 9249924 ext 70659
www.nuhrise.org

Mr Andrew Dainty
Nottingham Digestive Diseases Centre
E Floor, QMC Campus
Nottingham University Hospitals NHS Trust
Derby Road
Nottingham
NG7 2UH

21st January 2014

Dear **Mr Andrew Dainty**

Re: 13GA037
CSP
REC 13/EM/0428
CBT-IBS Feasibility Study

The R&I Department have reviewed the following documents and NHS permission for the above research has been granted on the basis described in the application form, protocol, and supporting documentation. The documents reviewed were:

- Questionnaire: CBT-IBS study Rome 111 IBS module form (validated questionnaire 1 of 5) v1 dated 28th Oct 2013. REC approved 5th Dec 2013.
- CBT-IBS study GRGS-IBS form (validated questionnaire 2 of 5) v1 dated 28th Oct 2013. REC approved 5th Dec 2013.
- CBT-IBS study IBS-QOL form (validated questionnaire 3 of 5) v1 dated 28th Oct 2013. REC approved 5th Dec 2013.

We are here for you

- CBT-IBS study GAD-7 form (validated questionnaire 4 of 5) v1 dated 28th Oct 2013. REC approved 5th Dec 2013.
- CBT-IBS study PHQ-9form form (validated questionnaire 5 of 5) v1 dated 28th Oct 2013. REC approved 5th Dec 2013.
- CBT-IBS study demographics form v1.1 dated 9th Dec 2013. REC approved 9th Jan 2014.
- CBT-IBS study poster for doctor's room only v1 dated 28th Oct 2013. REC approved 5th Dec 2013.
- CBT-IBS study missed appointment letter v1 dated 28th Oct 2013. REC approved 5th Dec 2013.
- CBT-IBS Study reply slip v1 dated 28th Oct 2013. REC approved 5th Dec 2013.
- CBT-IBS study follow up letter v1 dated 28th Oct 2013. REC approved 5th Dec 2013.
- CBT-IBS study follow up reminder letter v1 dated 28th Oct 2013. REC approved 5th Dec 2013.
- CBT-IBS study self-workbook 1 v1.1 dated 9th Dec 2013. REC approved 9th Jan 2014.
- CBT-IBS study self-workbook 2 v1.1 dated 9th Dec 2013. REC approved 9th Jan 2014.
- CBT-IBS study self-workbook 3 v1.1 dated 9th Dec 2013. REC approved 9th Jan 2014.
- CBT-IBS study self-workbook 4 v1.1 dated 9th Dec 2013. REC approved 9th Jan 2014.
- CBT-IBS study self-workbook 5 v1.1 dated 9th Dec 2013. REC approved 9th Jan 2014.
- CBT-IBS study self-workbook 6 v1.1 dated 9th Dec 2013. REC approved 9th Jan 2014.
- Participant information sheet: CBT-IBS Study participant v1 dated 28th Oct 2013. REC approved 5th Dec 2013.
- Participant consent form: CBT – IBS study consent form v1 dated 28th Oct 2013. REC approved 5th Dec 2013.
- Interview Schedules/ Topic Guidelines Study post Intervention v1.1 dated 9th Dec 2013. REC approved 14th Jan 2014.

Your study now has NHS permission , on the understanding and provision that you will follow the conditions set out below.

Conditions of Approval

The Principal Investigator is responsible for

1. Compliance with all relevant laws, regulations and codes of practice applicable to the trial including but not limited to, the UK Clinical Trials Regulations, Medicines for Human Use (Clinical Trial) Regulations 2004, principles of Good Clinical Practice, the World Medical Association Declaration of Helsinki entitled 'Ethical Principles for Medical Research Involving Human Subjects' (1996 version), the Human Rights Act 1998, the Data Protection Act 1998 the Medicines Act 1968, the NHS Research Governance Framework for Health and Social Care (version 2 April 2005). Should any of these be revised and reissued this will apply. Copies of the up-to-date regulations are available from the R&I Office or via the R&I website http://nuhrise.org

2. Submission of study amendments to the Ethics committee and MHRA in accordance with the IRAS guidelines. Amendments and information with regards to changes in study status must be sent to R&I, (this includes changes to the local study team). Within 35 days from the receipt of a valid amendment submission, NUH will inform you if may not locally implement the amendment. If no objections are raised NHS permission is valid and the amendment may be implemented.

When submitting documents for studies adopted into the NIHR portfolio please send the information to

NUHNT.TRENTCLRN@nhs.net
When submitting documents for all other studies please use the email address rdamend@nuh.nhs.uk

3. Ensuring all study personnel, not employed by the Nottingham University Hospitals NHS Trust hold either honorary contracts/letters of access with this Trust, before they have access to any patients or staff, their data, tissue or organs or any NUH facilities.

4. In accordance with the Department of Health's Plan for Growth, for initialising and delivering research within the NHS the 'first patient, first visit should occur 70 days from receipt of a valid submission in R&I. Therefore for all research where :

    - The sponsor is a commercial partner
    - NUH holds a funding contract with the National Institute for Health Research (NIHR)
    - The research is classed as a "clinical trial "on the IRAS filter page.

The research team is expected to collaborate with the department of R&I in reporting recruitment data to rdmon@nuh.nhs.uk.

1. For GTAC-approved studies, the NHS permission should be forwarded to GTAC via the sponsor. GTAC should then issue a site authorisation letter which must be received by each site prior to recruitment commencing. A copy of this letter must be forwarded to R&I.

2. Comply with requests from NUH R&I to allow monitoring of research to comply with the Research Governance framework.

3. Record *all* types of adverse events (including Suspected Unexpected Serious Adverse Drug Reaction - SUSARS) in the patient medical records and study documentation and report to the sponsor as required by the protocol. Further guidance can be found in R&I SOP 11 - "Adverse Event Monitoring, Recording and Reporting for investigators".

4. Report any Serious Breach of the UK Clinical Trial regulations in connection with the trial or Serious Breach of the protocol, immediately after becoming aware of the breach to the study sponsor.

For NUH sponsored studies only, the Chief Investigator is responsible for:

i. All duties as detailed in the "Clinical Trial Delegation of Sponsorship responsibilities to Chief Investigator" agreement.
ii. Contacting the sponsor for review of all amendment documentation prior to submission to NRES and MHRA. Please note that according to NRES and MHRA regulations, all submissions of amendments need to be signed by the authorised sponsor's representative. All relevant documentation should be emailed to rdappl@nuh.nhs.
iii. Send copies of the completed Annual Safety, Progress reports and End of Study reports required by the

Ethics Committee and the MHRA (if appropriate) to the Quality Assurance manager at NUH R&I.

iv. Notify NUH R&I of all SAEs by completing and sending the *"Serious Adverse Event reporting form"* to R&I **(only via fax, e-mail or by hand)**, within 24hrs of becoming aware of the event. If the event is defined as a SUSAR then a follow up report must also be submitted to R&I, via the above channels-**no longer than 7 days after the original report was submitted**

v. Reporting any Serious Breach of the UK Clinical Trial regulations in connection with the trial or Serious Breach of the protocol, immediately after becoming aware of the breach to NUH R&I as sponsor. Further guidance can be found in R&I SOP 12 "Protocol Violation and Serious Breach Reporting"

This approval letter constitutes a favourable Site Specific Assessment (SSA) for this site.

Please note that the R&I department maintains a database containing study related information, and personal information about individual investigators e.g. name, address, contact details etc. This information will be managed according to the principles established in the Data Protection Act.

Yours sincerely,

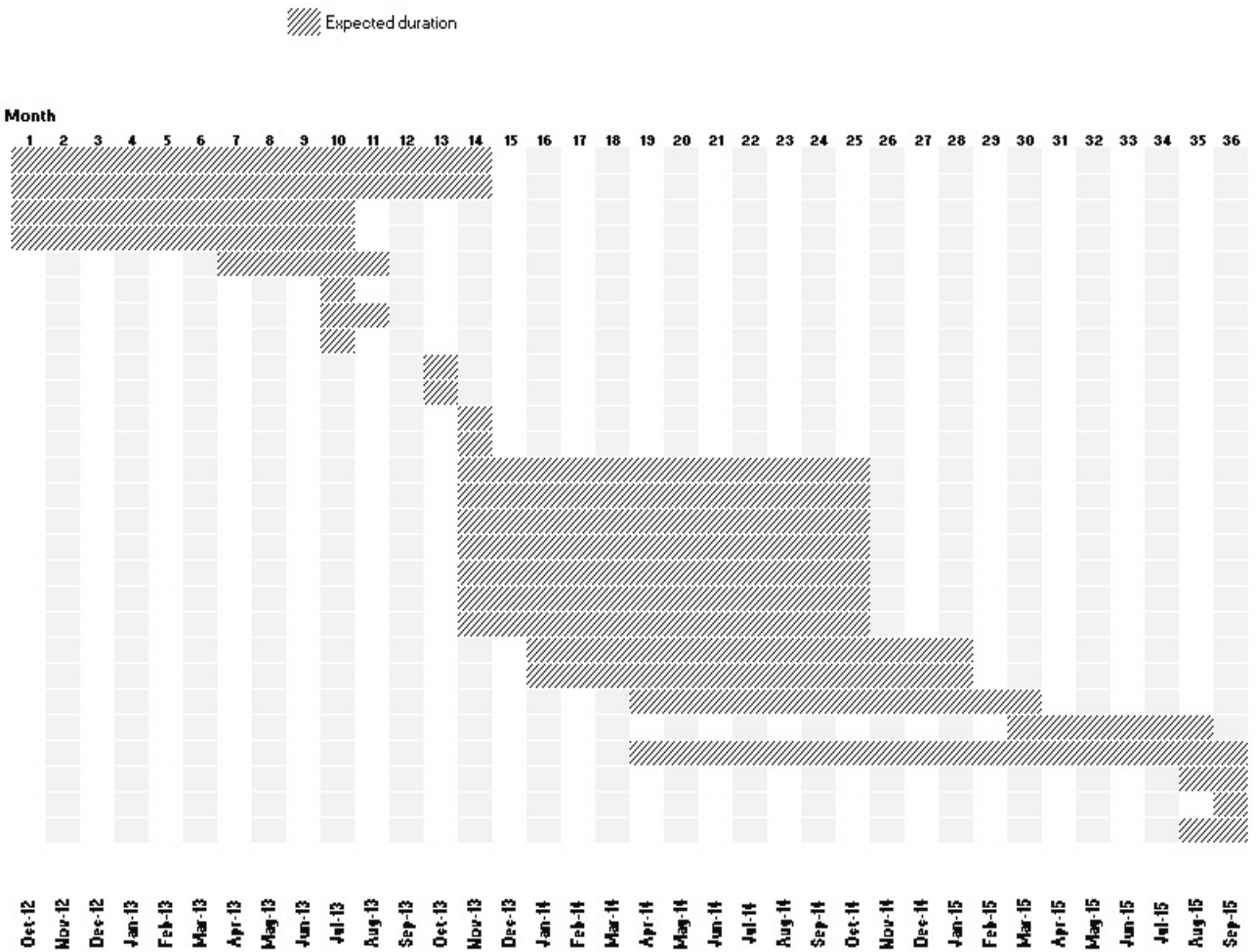
Dr Brian Thomson / Dr Maria Koufali
Director of Research and Innovation / Deputy Director Research and Innovation

cc Nottingham Research Ethics Committee

8.11 Study Gantt chart

Study Timescales

Activity	Month start	Expected duration (months)
PPI planning	1	14
PPI input	1	14
Nurse delivered CBT intervention development	1	10
Proposal development	1	10
Protocol and supporting documents development	7	5
Confirmation review	10	1
Implement confirmation review recommendations	10	2
IRAS data set completion	10	1
Study sponsor approval	13	1
Study ethics approval	13	1
Study NHS R&D approval	14	1
Study launch	14	1
Study recruitment	14	12
Study screening	14	12
Baseline data collection	14	12
Nurse delivered CBT	14	12
Psychotherapist delivered CBT	14	12
Self-help treatment manual	14	12
TAU control	14	12
Post intervention interviews	16	13
Post intervention outcome measures	16	13
6 month follow up data collection	19	12
Data analysis	30	6
PhD thesis write up	19	18
Begin to consider app for substantive trial funds	35	2
Study submission and completion deadline	36	1
Dissemination begins	35	2



8.12 Study protocol publication

A mixed methods feasibility study to evaluate the use of a low-intensity, nurse-delivered cognitive behavioural therapy for the treatment of irritable bowel syndrome

Andrew David Dainty, Mark Fox, Nina Lewis, et al.

BMJ Open 2014 4:
doi: 10.1136/bmjopen-2014-005262

BMJ Open

A mixed methods feasibility study to evaluate the use of a low-intensity, nurse-delivered cognitive behavioural therapy for the treatment of irritable bowel syndrome

Andrew David Dainty,[1] Mark Fox,[2] Nina Lewis,[3] Melissa Hunt,[4] Elizabeth Holtham,[5] Stephen Timmons,[6] Philip Kinsella,[7] Andrew Wragg,[8] Patrick Callaghan[6]

To cite: Dainty AD, Fox M, Lewis N, *et al*. A mixed methods feasibility study to evaluate the use of a low-intensity, nurse-delivered cognitive behavioural therapy for the treatment of irritable bowel syndrome. *BMJ Open* 2014;**4**:e005262. doi:10.1136/bmjopen-2014-005262

► Prepublication history for this paper is available online. To view these files please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2014-005262).

Received 14 March 2014
Revised 15 May 2014
Accepted 2 June 2014

For numbered affiliations see end of article.

Correspondence to
Andrew David Dainty;
ntxad9@nottingham.ac.uk

ABSTRACT

Introduction: Irritable bowel syndrome (IBS) is characterised by symptoms such as abdominal pain, constipation, diarrhoea and bloating. These symptoms impact on health-related quality of life, result in excess service utilisation and are a significant burden to healthcare systems. Certain mechanisms which underpin IBS can be explained by a biopsychosocial model which is amenable to psychological treatment using techniques such as cognitive behavioural therapy (CBT). While current evidence supports CBT interventions for this group of patients, access to these treatments within the UK healthcare system remains problematic.

Methods and analysis: A mixed methods feasibility randomised controlled trial will be used to assess the feasibility of a low-intensity, nurse-delivered guided self-help intervention within secondary care gastrointestinal clinics. A total of 60 participants will be allocated across four treatment conditions consisting of: high-intensity CBT delivered by a fully qualified cognitive behavioural therapist, low-intensity guided self-help delivered by a registered nurse, self-help only without therapist support and a treatment as usual control condition. Participants from each of the intervention arms of the study will be interviewed in order to identify potential barriers and facilitators to the implementation of CBT interventions within clinical practice settings. Quantitative data will be analysed using descriptive statistics only. Qualitative data will be analysed using a group thematic analysis.

Ethics and dissemination: This study will provide essential information regarding the feasibility of nurse-delivered CBT interventions within secondary care gastrointestinal clinics. The data gathered during this study would also provide useful information when planning a substantive trial and will assist funding bodies when considering investment in substantive trial funding. A favourable opinion for this research was granted by the Nottingham 2 Research Ethics Committee.

Trial registration number: ISRCTN: 83683687 (http://www.controlled-trials.com/ISRCTN83683687).

Strengths and limitations of this study

- This study will provide essential feasibility data regarding the use of nurse-delivered, low-intensity cognitive behavioural therapy (CBT) treatment approaches with secondary care gastrointestinal clinics.
- The mixed methods study design will produce qualitative and quantitative data for analysis which will provide a range of feasibility data.
- The study will not collect economic or service use data, although this should ideally be a concern of a follow-on study.
- This study does not consider the application of other CBT treatment mechanisms such as group-based or internet therapy.

BACKGROUND

Irritable bowel syndrome (IBS) is a functional gastrointestinal (GI) disease that is characterised by the presence of altered bowel habit (diarrhoea and constipation) and the presence of symptoms including bloating and abdominal pain.[1] The cause of IBS remains unexplained, although it is known that a proportion of patients will develop IBS following an initial insult such as GI infection.[2 3] Research has also established that food intolerance, the balance of gut microflora and certain changes within the immune system might be underlying mechanisms in IBS.[4 5] However, routine investigations fail to identify abnormal pathology for IBS and patients are left with a range of symptoms which are managed empirically by antispasmodics, low-dose antidepressants and other medications. The daily activities of patients with IBS are often adversely affected and patients may be troubled by concerns related to the cause

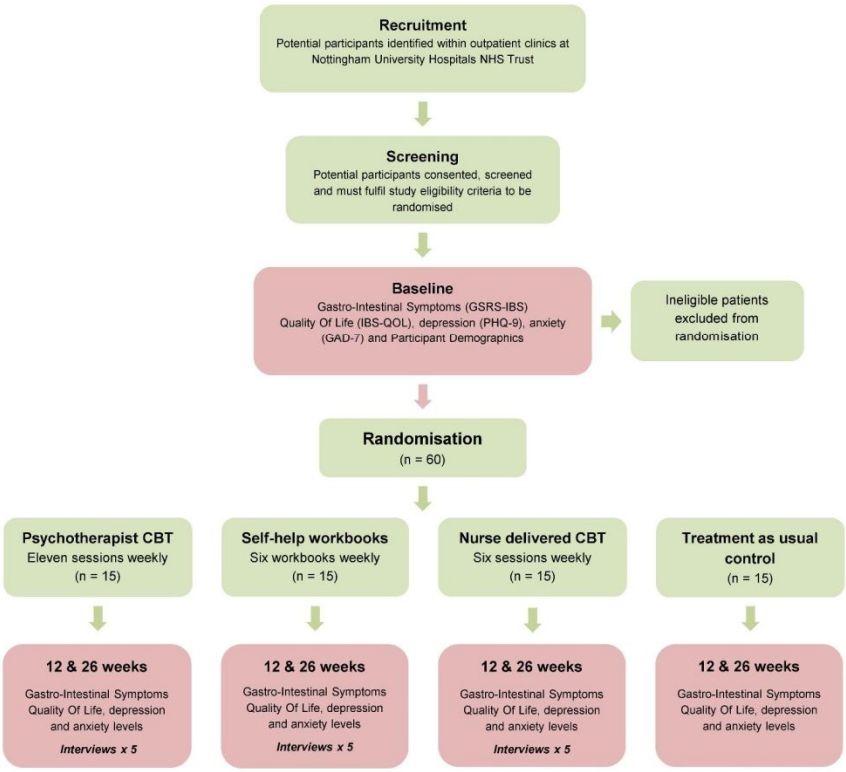


Figure 1 Study flow diagram detailing numbers of participants and participant flow through the study-related procedures and follow-up data collection periods. CBT, cognitive behavioural therapy; GSRS-IBS, Gastrointestinal Symptom Rating Scale for irritable bowel syndrome.

and the effects of their condition.[6] Patients with IBS tend to report a poor quality of life (QOL) and often experience absenteeism.[7] Moreover, IBS places a significant strain on healthcare resources and service utilisation, with patients with IBS consuming over 50% more resources than carefully matched controls.[8 9] Health professionals may also find themselves challenged with the management of such a complex and persistent disorder.[10]

Psychological aspects of IBS

Psychosocial factors and stress are related to the maintenance and manifestation of IBS symptoms in many patients.[11] Indeed, historically, clinicians felt that IBS was purely a physical manifestation of emotional problems.[12] In recent years, the association IBS has with psychological issues has been supported with experimental data. For example, Guthrie *et al*'s[13] study involving 107 participants demonstrates that the perception of bowel sensations may relate directly to psychological distress. The literature reports a prevalence of psychological comorbidity ranging anywhere between 50% and 90% for common mental health problems such as anxiety and depression.[14] Traumatic events or stressful experiences which shape an individual's life experiences may also play a fundamental role in IBS. Indeed, it is not uncommon for patients with IBS to report some history of physical or sexual abuse.[15 16] Stressful life events, in general, are associated with symptom onset and severity.[17] These psychological factors and the complex manifestation of IBS symptoms are widely acknowledged as a disease process which involves an individual's social environment, physiology and psychology.[11] These elements form part of the 'biopsychosocial model' which offers a holistic and rational explanation for the presentation and persistence of IBS symptoms in many individuals.

Because the mechanisms of IBS can be explained by a biopsychosocial model, effective treatment approaches may include psychological interventions such as cognitive behavioural therapy (CBT). Best practice guidelines suggest that CBT, hypnotherapy and psychotherapy are useful interventions for patients with IBS.[18] CBT is particularly useful for addressing negative thought patterns[6] and catastrophising cognitions and avoidant behaviours.[19] CBT can also be used to target maladaptive thought processes[20] and help patients understand the interactions between their thoughts and their symptoms.[21] CBT is well supported empirically as an effective intervention for patients with IBS.[22–24] Although the

results of many of these investigations are promising, a recent systematic review identified issues regarding the methodological quality and power of trials which support these interventions.[25]

Rationale

There is a need for CBT to be further evaluated using robust methods.[14] Furthermore, there is a need for future research to evaluate psychological therapies which address concerns regarding treatment provision and accessibility.[26] Many patients within the National Health Service (NHS) healthcare system have no routine access to psychological interventions for the treatment of their IBS symptoms. Notwithstanding these concerns, there is encouraging activity within the wider UK healthcare system to suggest that the government and policymakers are beginning to recognise the impact that psychological therapies such as CBT have on improving health and reducing loss of productivity.[27] This study will evaluate the feasibility and acceptability of a novel, nurse-delivered, low-intensity CBT, guided self-help intervention for the treatment of IBS. It is hoped that the nursing intervention will provide a feasible mechanism for the delivery of CBT which may be economically viable, more accessible to patients and implementable within the UK healthcare system. Qualitative research performed during the course of this study will provide researchers and funding bodies with essential information on the acceptability and practical application of CBT interventions in patients with IBS.

METHODS AND ANALYSIS

Study aim

To carry out a feasibility study to explore the use of various CBT treatment delivery mechanisms for patients with IBS within secondary care GI clinics.

Study objectives

- To develop a tailored, nurse-delivered CBT treatment for patients with IBS.
- To examine the number of patients needed to screen in relation to the numbers successfully randomised into the study.
- To gather reasons for patients not wishing to take part in CBT treatment approaches for their IBS.
- To explore the experience of participants undergoing the study's treatment conditions.
- To identify barriers and facilitators to the implementation of the trial interventions within real clinical settings.
- To measure the follow-up and response rates to study questionnaires.
- To describe the range of data with relevant descriptive statistics.
- To test the data collection procedures and time required to collect study data.

Study design

The randomised controlled trial (RCT) is considered one of the most powerful tools used in research to establish new knowledge claims.[28 29] The proposed RCT will establish the cause and effect relationship between CBT and patient outcomes. A mixed methods research (MMR) approach, underpinned by a pragmatic philosophy, will draw from the strengths of qualitative and quantitative approaches.[30] MMR is defined as "collecting, analysing and mixing both quantitative and qualitative data in a single study or series of studies."[31] The growing popularity of MMR approaches would suggest that many researchers now recognise the value of this pragmatic approach.[32] MMR provides robust and rigorous approaches to research[33] and creates a richer understanding of phenomena.[34] Many of the RCTs which have investigated the use of CBT for patients with IBS lack a qualitative research component. This limits our understanding of the suitability and acceptability of these interventions for this group of patients. The incorporation of qualitative methods will ensure the research considers problematic moments and meanings in individuals lives.[35] These methods will also contextualise the findings of the research[36] and enable trial participants to provide information regarding their responses to quantitative variables.[37]

Patients

Around 60% of patients referred to GI clinics with lower GI symptoms are diagnosed with IBS.[38] Adults (over 18 years of age) have been chosen as the main group of patients for inclusion as IBS is typically associated with the third and fourth decades of life.[39] In order to ensure that participants have symptoms consistent with IBS, they will be screened and required to fulfil Rome III criteria. This tool has been developed by the Rome Foundation with a long-standing history of development and a strong evidence base.[40] It has been successfully utilised as symptomatic criteria for IBS in a number of RCTs[22 41 42] and is being constantly updated and reviewed in the light of changes in the recent literature.[43] Participants with symptoms inconsistent with IBS according to Rome III criteria will be excluded from randomisation.

Inclusion criteria

- Adult male and female patients aged 18 years or older at the time of enrolment.
- Documented medical diagnosis of IBS.
- Patients with IBS which meets Rome III criteria.
- Able to read, write and speak English.
- Able to provide written informed consent.
- Patients with and without concomitant antidepressant use.
- Able to commit to weekly treatment sessions within the intervention arms of the study.

Exclusion criteria

- Already receiving psychological therapy or hypnotherapy.
- Existing diagnosis of bowel disease based on endoscopic or histological criteria (ie, Crohn's disease, ulcerative colitis, coeliac disease).
- Presence or history of structural or surgical diseases of the GI tract (not including appendix or gall bladder surgery).
- Evidence of alcohol or substance misuse.
- An established cause for bowel symptoms other than IBS (ie, medication use).
- The presence of suicidal ideation or self-harm.
- Significant psychiatric comorbidity (schizophrenia, bipolar disorder, obsessive compulsive disorder).
- Currently taking part in other research studies.

Intervention

Many studies which have investigated the use of CBT for patients with IBS utilise high-intensity treatment protocols. Several RCTs have used 10-week treatment programmes,[22 26 44 45] with most sessions over 50 min in duration. Some researchers have experimented with much lower intensity treatment methods and have altered delivery mechanisms in order to improve the provision of CBT interventions such as internet CBT.[19] However, there is concern regarding the delivery of online interventions relating to confidentiality, a loss of visual and auditory clues during therapy and a lack of suitability for managing crisis situations.[46] A recent survey of 658 patients suggests that internet-delivered CBT would be unacceptable to over 40% of those surveyed.[47] Other delivery mechanisms include group-based treatments,[42] although some authors suggest that individual contact is better suited to tailoring therapy to the needs of the client.[48] CBT has been effective when delivered by trained nurses within primary care settings.[24] It is therefore possible that similar effects might be achievable if therapy were to be delivered by GI nurses within secondary care utilising a lower intensity, guided self-help treatment approach which could be less time consuming to deliver and further increase access to evidence-based interventions for patients.

Registered nurses working within gastroenterology are well placed to deliver psychotherapeutic interventions to these groups of patients as they are familiar with the complexity of chronic GI symptoms and the impact they have on patients and their daily activities. The preparatory training utilised within this study offers a replicable mechanism for expansion of the professional scope of nursing practice for nurses working with the GI specialty, while increasing access to evidence-based intervention patients may not otherwise receive.

We have adapted the protocol and self-help materials originally developed by Hunt *et al*[19] at the University of Pennsylvania USA, while working in collaboration with service users to maximise the quality and suitability of our nursing intervention. The nursing intervention consists of an initial 60 min assessment session, with five further 30 min treatment sessions over a 6-week treatment period. Participants will work through six guided self-help treatment modules with a nurse therapist, consisting of:

- an introduction to IBS,
- relaxation training,
- the cognitive model of stress management,
- the cognitive model of IBS and behavioural experiments,
- managing avoidance using exposure,
- diet and IBS.

The nurse therapist (ADD) undertook the first two modules of the National Curriculum for the education of Psychological Wellbeing Practitioners[49] in order to prepare for the nurse therapist's role. This training consisted of 25 days of university-based teaching sessions and simulated clinical skills training. The therapist completed all assessments for these modules to the nationally accredited assessed standard, but did not access the supervised practice hours within a mental health services placement as this was not felt to be necessary or economically viable for the preparation of the nurse therapist's role for the treatment of IBS.

Comparators

The nursing intervention will be compared to: (A) the services of a fully trained and experienced cognitive behavioural therapist using high-intensity treatment; (B) a six module, CBT-based self-help workbook as a stand-alone intervention; and (C) a treatment as usual (TAU) control condition. Participants in all four treatment conditions will be permitted to continue with the routine medical management of their IBS.

Psychotherapist

Comparing the nursing intervention with the services of a cognitive behavioural therapist during a substantive trial will help establish whether the study's nursing intervention is as effective and acceptable as current evidence-based treatment approaches. The psychotherapist will deliver treatment to participants using a protocol developed from the work of Toner *et al*,[48] not dissimilar to previous trials of CBT.[23] Participants will attend 11 treatment sessions at weekly intervals, the first 2 h in duration and subsequent sessions will last for up to an hour.

Self-help workbooks

Participants will be given the same six module self-help treatment workbooks as used within the nursing intervention. However, in order to identify any additional benefit that the nurse therapist has within the study's nursing intervention, the treatment workbooks will be used as a stand-alone treatment. Participants will be given the workbooks by the nurse therapist and advised that they should work through the modules on a weekly basis. No further therapist support will be provided.

Treatment as usual

A TAU condition will enable the study of the intervention in comparison to current treatment approaches and may also be required for economic evaluations within a definitive study. It is hoped that the feasibility study will provide further information regarding the suitability of a TAU control condition.

Outcomes

The literature would suggest that an extended period of follow-up is necessary in order for researchers to establish whether the positive treatment effects of CBT diminish over time.[25] However, longer follow-up periods are not feasible within the scope of this PhD project and will be the concern of a definitive trial. Similarly, although an important feature of a definitive study may be a cost-effectiveness data collection and analysis, a limitation is that such data will not be collected during this feasibility work. All outcome measures will be assessed at baseline, and at 12 and 26 weeks postrandomisation. The study flow diagram (figure 1) demonstrates the various data collection points throughout the study period.

IBS symptom severity

Numerous studies have identified the negative impact that IBS symptoms have on QOL,[50 51] and suggest that symptoms are largely responsible for patients seeking consultation.[42] IBS symptom severity will be the primary outcome for this study and will be measured with participant responses on the Gastrointestinal Symptom Rating Scale for IBS (GSRS-IBS).[52] GSRS-IBS consists of 13 items with five symptom subdomains including: abdominal pain, bloating, diarrhoea, constipation and satiety. Participants are asked to record the previous 7 days' symptoms indicating responses on a seven-point Likert scale. Mean item scores (between 1 and 7) are calculated for each of the five subdomains. Treatment responders will be defined by a reduction in IBS symptom scores of more than 50%.

Quality of life

IBS has also been shown to impact on QOL to a similar degree as chronic conditions such as diabetes mellitus.[51] Researchers have suggested that the measurement of QOL within therapeutic trials for IBS is clearly warranted.[50] QOL will therefore be included as a secondary outcome measure utilising IBS-QOL.[53] IBS-QOL consists of 34 self-report Likert scales specific to IBS. IBS-QOL also makes possible the analysis of eight subdomains which include: dysphoria, interference with activity, body image, health worry, food avoidance, social reaction and sexual relationships.

Comorbid anxiety and depression

Much of the impact that IBS has on QOL is explained by psychological factors[7] which, when treated, may reduce IBS-related symptoms.[54] Levels of depression will be measured with the Patient Health Questionnaire (PHQ) -9,[55] and levels of anxiety using the Generalised Anxiety Disorder (GAD)-7.[56] Both of these well-validated measures consist of nine-item and seven-item self-report Likert scales, respectively, indicating depression and anxiety severity scores. Necessary permissions have been sought for all measures utilised during the conduct of this research.

Randomisation and blinding

Participants will be allocated to one of four treatment conditions using random permuted blocks. The principal investigator will screen all potential participants and randomise eligible participants using an online randomisation system (see http://www.sealedenvelope.com). All quantitative, postintervention outcome data will be collected by a research assistant blind to the allocation of participants. The study's investigators will be aware of the allocation of study participants.

Sample size

This study is concerned with generating descriptive statistics that will be used to evaluate the feasibility of the proposed methods and not to establish the effectiveness or generalisability of the interventions. A pragmatic decision was made to randomise 60 participants across four treatment conditions. Approximately 15 participants will be assigned to each of the study conditions (see study diagram).

Recruitment and participant selection

Potentially eligible clinic patients will be identified by a member of their care team and given participant information packs or will be sent information relating to the trial via their hospital physician. Participants may express an interest in taking part in the research study by returning a reply slip using a prepaid postage service. Posters will also be deployed on clinic and hospital notice boards. We will also write to potentially eligible participants on our Biomedical Research Unit research database.

Data collection

The quantitative measures will be collected by the principal investigator (ADD) at screening and sent to participants by mail at 12 and 26 weeks postrandomisation. Postintervention outcome data will be returned to a research assistant blind to the allocation of participants. Interview data will be collected by a coinvestigator (EH) not connected to the delivery of the trial interventions.

The qualitative element of the study aims to capture the knowledge which is located in the minds and personal experiences of others.[57] Although some authors advocate unstructured interview techniques,[58] a semi-structured approach will ensure that information relating to the phenomena of interest is obtained.[59] Furthermore, the prestructure has provided a mechanism for the involvement of our patient advisory group, which has helped shape the contents of the interview schedule. The structure and content of the interviews

was initially developed as a result of the researcher's prior knowledge of GI research and the subject area as a result of a literature review. Interview questions will be used by the interviewer to seek clarification, illustration and further exploration regarding important issues.[60] The qualitative element of our study aims to evaluate the experiences of service users undergoing the three trial treatment protocols in order to identify potential barriers and facilitators to the use of the interventions. Five participants from each of the intervention arms of the study will be recruited to qualitative interviews. This study has also received ethical permission to make enquiries into the reasons patients may have for not taking part in the research. It will be made clear that patients are under no obligation to provide this information to the research team. This information will be useful for helping researchers understand barriers to the successful implementation of psychological therapies for IBS within the NHS.

Data analysis

Quantitative data

Quantitative data will be analysed descriptively. Measures of mean and variance including CIs and SD will be used to describe the full range of data at baseline and at follow-up. An intention to treat analysis will be facilitated as missing data will be rectified using the last observation carried forward. Outcome-related data will be analysed using SPSS version 22.

Qualitative data

Corroboration will be sought between qualitative and quantitative elements of the study.[61] Qualitative data will be generated in the form of interview transcripts for analysis. The qualitative data will supplement the quantitative outcome data by identifying convergence and differences between the two databases.[62] Interview recordings will be transcribed verbatim prior to conducting the framework analysis advocated by Ritchie and Spencer.[63] In order to improve the rigour during the analysis and guard against investigator bias, a group analysis approach will be used to analyse the interview transcripts.[64] The study's principal investigator and the interviewer will jointly conduct the thematic analysis of the interview transcripts supervised by an experienced qualitative researcher.

Patient and public involvement

Patient and public involvement (PPI) is defined by the National Institute for Health Research (NIHR) as "research that is done with or by the public and not to, about or for them."[65] Many awarding bodies expect to see evidence of PPI within major grant applications.[66] Our research team has developed an excellent working alliance with a group of six patient/public volunteers who have helped shape and improve the design of the study. The patient advisory group has also helped to review study documents and highlight potential barriers to the recruitment and selection of participants. By involving service users in the conduct of the research, it is hoped that equilibrium has been sought in order to address any power imbalances between health professionals and patients.[67] It is also hoped that PPI has helped maximise the quality of our nursing intervention.

Ethical issues

Psychological issues and IBS

Although not all participants recruited for this study will have a psychological comorbidity, some participants may not accept, or may even reject, a psychological element to their IBS.[68] It is hoped that by conducting interviews with study participants, barriers to the implementation of psychological therapies relating to these phenomena will be further explored.

Implications for participants taking part in a trial of psychological interventions

Some participants may be concerned regarding the implications of receiving psychotherapy during the trial. The emphasis within our study is to focus on helping patients to live with the impact of their IBS symptoms rather than specifically targeting those only with psychological comorbidity (such as underlying anxiety or depression). It will be made clear when writing to the participant's doctor that participation in our study does not necessarily suggest or confirm that participants are psychologically unwell. This may be particularly important where a diagnosis of psychological illness may have negative implications for the participant, that is, those with rigorous occupational requirements. However, levels of psychological illness will be recorded during a participant's journey through the study as we are interested in the effects that treatment may have on these underlying issues. We will ensure that participants are made fully aware of these issues during recruitment and selection and that these details are included within the study information sheets. A participant's hospital care team and general practitioner will be notified where a moderate-to-severe level of anxiety or depression is detected during measurement, as per current practice within our GI clinics.

Host organisation approval was sought from the Nottingham University Hospitals NHS Trust prior to the start of any research-related activity.

Author affiliations
[1]Nottingham Digestive Disease Centre Biomedical Research Unit and School of Health Sciences, University of Nottingham, Nottingham, UK
[2]Functional GI Diagnostics Laboratory, Division of Gastroenterology and Hepatology, Centre for Reflux and Swallowing Disorders, University Hospital, Zürich, Switzerland
[3]Nottingham University Hospitals NHS Trust, Nottingham, UK
[4]University of Pennsylvania, Philadelphia, PA, USA
[5]Faculty of Medicine & Health Sciences, University of Nottingham, Nottingham, UK
[6]School of Health Sciences, University of Nottingham, Nottingham, UK

[7]Institute of Mental Health, University of Nottingham, Nottingham, UK
[8]Nottingham Digestive Disease Centre Biomedical Research Unit, Nottingham University Hospitals, Nottingham, UK

Acknowledgements An adapted version of the irritable bowel syndrome self-help intervention originally developed by Dr Melissa Hunt at the University of Pennsylvania is being used within this study, as permitted under a research license issued by the University of Pennsylvania, Philadelphia, USA.

Contributors ADD developed the initial protocol draft. PC, MF, PK and NL were responsible for the development, refinement and approval of the study protocol. PC and PK provided mental health expertise while physicians MF and NL provided gastrointestinal expertise for the protocol development. ADD is conducting the project as part of his PhD studies. MH and ADD collaborated on the adaptation and development of the nurse-delivered treatment protocol and associated materials. ADD and EH developed the qualitative elements of the protocol which is supervised and edited by ST. AW is the study's patient and public involvement manager responsible for facilitating patient and public involvement in the development of the study. All authors have approved the final version of this manuscript.

Competing interests ADD's PhD studentship was funded by the University of Nottingham and the NIHR Gastrointestinal Biomedical Research Unit at Nottingham University Hospitals NHS Trust.

Ethics approval Nottingham 2 Local Research Ethics Committee.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

1. Schmulson M, Chang L. Diagnostic approach to the patient with irritable bowel syndrome. *Am J Med* 1999;107:20–6.
2. Spiller R, Garsed K. Postinfectious irritable bowel syndrome. *Gastroenterology* 2009;136:1979–88.
3. DuPont A. Postinfectious irritable bowel syndrome. *Clin Infect Dis* 2008;46:594–9.
4. Yang J, Fox M, Cong Y, *et al*. Lactose intolerance in irritable bowel syndrome patients with diarrhoea: the roles of anxiety, activation of the innate mucosal immune system and visceral sensitivity. *Aliment Pharmacol Ther* 2014;39:302–11.
5. O'Mahony L, McCarthy J, Kelly P, *et al*. Lactobacillus and bifidobacterium in irritable bowel syndrome: symptom responses and relationship to cytokine profiles. *Gastroenterology* 2005;128:541–51.
6. North C, Hong B, Alpers D. Relationship of functional gastrointestinal disorders and psychiatric disorders: implications for treatment. *World J Gastroenterol* 2007;13:2020–7.
7. Halder S, Fett S, Locke G, *et al*. Impact of functional gastrointestinal disorders on health-related quality of life: a population-based case-control study. *Aliment Pharmacol Ther* 2004;19:233–42.
8. Canavan C, West J, Card T. The epidemiology of irritable bowel syndrome. *Clin Epidemiol* 2014;4:67–80.
9. Longstreth G, Wilson A, Knight K, *et al*. Irritable bowel syndrome, health care use, and costs: a U.S. managed care perspective. *Am J Gastroenterol* 2003;98:600–7.
10. Hatcher S, Arroll B. Assessment and management of medically unexplained symptoms. *BMJ* 2008;336:1124–8.
11. Levy R, Olden K, Naliboff B, *et al*. Psychosocial aspects of the functional gastrointestinal disorders. *Gastroenterology* 2006;130:1447–58.
12. Ryle J. An address on chronic spasmodic affections of the colon and the diseases which they simulate. *Lancet* 1928;212:1115–19.
13. Guthrie E, Barlow J, Fernandes L, *et al*. Changes in tolerance to rectal distension correlate with changes in psychological state in patients with severe irritable bowel syndrome. *Psychosom Med* 2004;66:578–82.
14. Dainty A. Irritable bowel syndrome: psychological comorbidities and cognitive behavioural therapy. A review of the literature. *Gastrointest Nurs* 2012;10:44–50.
15. Drossman D, Thompson W, Talley N, *et al*. Identification of subgroups of functional gastrointestinal disorders. *Gastroenterol Int* 1990;3:159–72.
16. Delvaux M, Denis P, Allemand H. Sexual and physical abuses are more frequently reported by IBS patients than by patients with organic digestive diseases or controls. *Eur J Gastroenterol Hepatol* 1997;9:345–52.
17. Creed F, Craig T, Farmer R. Functional abdominal pain, psychiatric illness and life events. *Gut* 1988;29:235–42.
18. NICE. *Irritable bowel syndrome in adults: diagnosis and management of irritable bowel syndrome in primary care*. London: National Institute for Health and Clinical Excellence, 2008.
19. Hunt M, Moshier S, Milonova M. Brief cognitive-behavioral internet therapy for irritable bowel syndrome. *Behav Res Ther* 2009;47:797–802.
20. Hassett A, Gevirtz R. Nonpharmacologic treatment for fibromyalgia: patient education, cognitive-behavioral therapy, relaxation techniques, and complementary and alternative medicine. *Rheum Dis Clin N Am* 2009;35:393–407.
21. Beck A, Rush A, Shaw B, *et al*. *Cognitive therapy of depression: a treatment manual*. New York: Guilford, 1979.
22. Craske M, Wolitzky-Taylor K, Labus J, *et al*. A cognitive-behavioral treatment for irritable bowel syndrome using interoceptive exposure to visceral sensations. *Behav Res Ther* 2011;49:413–21.
23. Drossman D, Toner B, Whitehead W, *et al*. Cognitive-behavioral therapy versus education and desipramine versus placebo for moderate to severe functional bowel disorders. *Gastroenterology* 2003;125:19–31.
24. Kennedy T, Jones R, Darnley S, *et al*. Cognitive behaviour therapy in addition to antispasmodic treatment for irritable bowel syndrome in primary care: randomised controlled trial. *BMJ* 2005;331:435–7.
25. Zijdenbos I, De Wit N, Van der Heijden G, *et al*. *Cochrane review: psychological treatments for the management of irritable bowel syndrome*. Chichester, UK: John Wiley & Sons, 2009.
26. Lackner J, Jaccard J, Krasner S, *et al*. Self-administered cognitive behavior therapy for moderate to severe irritable bowel syndrome: clinical efficacy, tolerability, feasibility. *Clin Gastroenterol Hepatol* 2008;6:899–906.
27. Clark D. Implementing NICE guidelines for the psychological treatment of depression and anxiety disorders: the IAPT experience. *Int Rev Psychiatry* 2011;23:375–84.
28. Jadad A. *Randomised controlled trials: a user's guide*. London: BMJ Books, 1998.
29. Muir-Gray J. *Evidence based healthcare*. New York: Churchill Livingstone, 1997.
30. Johnson B, Onwuegbuzie A. Mixed methods research: a research paradigm whose time has come. *Educ Res* 2004;33:14–26.
31. Creswell J, Plano-Clark V. *Designing and conducting mixed methods research. What is mixed methods research?* Thousand Oaks, CA: Sage, 2007.
32. Scott P, Briggs J. A pragmatist argument for mixed methodology in medical informatics. *J Mixed Methods Res* 2009;3:223–41.
33. Anaf S, Sheppard L. Mixing research methods in health professional degrees: thoughts for undergraduate students and supervisors. *Qual Rep* 2007;12:184–92.
34. Creswell J, Plano-Clark V. Understanding mixed methods research. In: Creswell J, Plano-Clark V, eds. *Designing and conducting mixed methods research*. Thousand Oaks, CA: Sage, 2007: 1–19.
35. Denzin N, Lincoln Y. The discipline and practice of qualitative research. In: Denzin N, Lincoln Y, eds. *Handbook of qualitative research*. Thousand Oaks, CA: Sage, 2000.
36. Pluye P, Gagnon M, Griffiths F, *et al*. A scoring system for appraising mixed methods research, and concomitantly appraising qualitative, quantitative and mixed methods primary studies in mixed studies reviews. *Int J Nurs Stud* 2009;46:529–46.
37. Wagner K, Davidson P, Pollini R, *et al*. Reconciling incongruous qualitative and quantitative findings in mixed methods research: exemplars from research with drug using populations. *Int J Drug Policy* 2012;23:54–61.
38. Spiller R, Aziz Q, Creed F, *et al*. Guidelines on the irritable bowel syndrome: mechanisms and practical management. *Gut* 2007;56:1770–98.
39. Kumano H, Kaiya H, Yoshiuchi K, *et al*. Comorbidity of irritable bowel syndrome, panic disorder, and agoraphobia in a Japanese representative sample. *Am J Gastroenterol* 2004;99:370–6.
40. The Rome Foundation. To improve the lives of people with functional GI disorders. 2012. http://www.romecriteria.org/ (accessed 13 Jul 2012).
41. Ljótsson B, Hedman E, Andersson E, *et al*. Internet-delivered exposure-based treatment vs. stress management for irritable bowel

syndrome: a randomized trial. *Am J Gastroenterol* 2011;106:1481–91.
42. Blanchard E, Lackner J, Sanders K, *et al*. A controlled evaluation of group cognitive therapy in the treatment of irritable bowel syndrome. *Behav Res Ther* 2007;45:633–48.
43. Drossman D. The functional gastrointestinal disorders and the Rome III process. *Gastroenterology* 2006;130:1377–90.
44. Andersson E, Ljótsson B, Smit F, *et al*. Cost-effectiveness of internet-based cognitive behavior therapy for irritable bowel syndrome: results from a randomized controlled trial. *BMC Public Health* 2011;11:215.
45. Heymann-Mönnikes I, Arnold R, Florin I, *et al*. The combination of medical treatment plus multicomponent behavioral therapy is superior to medical treatment alone in the therapy of irritable bowel syndrome. *Am J Gastroenterol* 2000;95:981–94.
46. Childress C. Potential risks and benefits of online psychotherapeutic interventions. 1998. http://www.ismho.org/potential_risks_and_benefits.asp (accessed 10 Jan 2013).
47. Mohr D, Siddique J, Ho J, *et al*. Interest in behavioral and psychological treatments delivered face-to-face, by telephone, and by internet. *Ann Behav Med* 2010;40:89–98.
48. Toner B, Segal Z, Emmott S, *et al*. *Cognitive-behavioral treatment of irritable bowel syndrome: the brain-gut connection*. New York: Guilford Press, 2000.
49. IAPT. National curriculum for the education of Psychological Wellbeing Practitioners (PWPS). 2011. http://www.iapt.nhs.uk/silo/files/national-curriculum-for-the-education-of-psychological-wellbeing-practitioners-pwps-.pdf (accessed 28 Feb 2013).
50. Gralnek I, Hays R, Kilbourne A, *et al*. The impact of irritable bowel syndrome on health-related quality of life. *Gastroenterology* 2000;119:654–60.
51. El-Serag H, Olden K, Bjorkman D. Health-related quality of life among persons with irritable bowel syndrome: a systematic review. *Aliment Pharmacol Ther* 2002;16:1171–85.
52. Wiklund I, Fullerton S, Hawkey C, *et al*. An irritable bowel syndrome specific symptom questionnaire: development and validation. *Scand J Gastroenterol* 2003;38:947–54.
53. Patrick D, Drossman D, Frederick I, *et al*. Quality of life in persons with irritable bowel syndrome: development and validation of a new measure. *Dig Dis Sci* 1998;43:400–11.
54. Lydiard R, Falsetti S. Experience with anxiety and depression treatment studies: implications for designing irritable bowel syndrome clinical trials. *Am J Med* 1999;107:65–73.
55. Kroenke K, Spitzer R, Williams J. The PHQ-9: validity of a brief depression severity measure. *J Gen Intern Med* 2001;16:606–13.
56. Löwe B, Decker O, Müller S, *et al*. Validation and standardization of the Generalized Anxiety Disorder screener (GAD-7) in the general population. *Med Care* 2008;46:266–74.
57. Nespor J, Barylske J. Narrarive discourse and teacher knowledge. *Am Educ J* 1991;28:805–23.
58. Huberman A, Miles M. Assessing local causality in qualitative research. In: Berg D, Smith K, eds. *The self in social inquiry: researching methods*. Newbury Park, CA: Sage, 1988:351–81.
59. McNamara C. General guidelines for conducting interviews. 2009. http://managementhelp.org/evaluatn/intrview.htm (accessed 17 May 2012).
60. Parahoo K. *Nursing research: principles, process and issues*. Hampshire: Palgrave Macmillan, 2006.
61. Doyle L, Brady A, Byrne G. An overview of mixed methods research. *J Res Nurs* 2009;14:175–85.
62. Creswell J. Mixed methods procedures. In: Creswell J, ed. *Research design: qualitative, quantitative and mixed methods approaches*. London: Sage, 2009:203–36.
63. Ritchie J, Spencer L. Qualitative data analysis for applied policy research. In: Bryman A, Burgess R, eds. *Analysing qualitative data*. London: Routledge, 1994:173–94.
64. Gunaratnam Y. Narrative and stories in health care. 2009. http://goldsmiths.academia.edu/YasminGunaratnam/Papers/386158/Narrative_Interviews_and_Research (accessed 17 May 2012).
65. NIHR. What is patient and public involvement in research? 2012. http://www.peopleinresearch.org/find-out-about-involvement/what-is-public-involvement-in-research/ (accessed 6 Apr 2012).
66. NIHR. Health Technology Assessment programme. 2012. http://www.hta.ac.uk/PPIguidance/ (accessed 6 Apr 2012).
67. Oliver S. How can health service users contribute to the NHS research and development agenda? *BMJ* 1995;310:1315–18.
68. Toner B. Cognitive-behavioral treatment of functional somatic syndromes: integrating gender issues. *Cogn Behav Pract* 1994;1:157–78.

8.13 Example of thematic framework derived from the joint analysis of interview data

Joint Schema of Post-Intervention Themes

High Intensity Intervention (HI-CBT)

Main theme	Sub-theme	Data source
Initial perceptions of treatment	Would have been disappointed with control	IG002:23-24
	Would have been unmotivated with workbooks	IG002:29-31
	Belief in a connection between mind and body	IG002:42-44
	Positive about CBT treatment	IG002:63-64
	Wanted to take control of IBS	MS013:36
	Nothing else left to try	JC003:22-23; IG002:79
Experience of therapeutic task execution	Thought diary columns overlapped (repetition)	IG002:237-241
	Introduction to therapy would be useful	IG002:701 MS013:166-167
	Thought diaries difficult-complete - needed therapist help	JC003:62-65
	Perception that symptoms were in the mind	MS031:542-543, 545-546, 550, 558, 560
	Feeling very low impacted on engagement in sessions	MS013:688-689
	Difficulty dealing with deep routed non-IBS problems	MS013:28-30, 118-119, 171-172
	Own values and beliefs impacted upon engagement with interventions	MS013:313-315, 317-318
	Motivation face-face appointments provide	IG002:48-51
	Not aware of how intrusive therapy would be	MS013:152-153
	Initially difficult to engage	MS013:25-26
Practical considerations for engagement	The therapist "expert" for support, motivation and guidance	IG002:48-51, 111-113; JC003:102-104, 197-198
	Reluctance to utilise social support	MS013:515-516; IG002:137-143, 145-147; (JC003:319-321)
	Too many sessions	JC003:249-251, 260-264

	Dietary advice lacking	IG002:605-607
	Lack of preparation for sessions caused distress	MS013:25, 32, 164-165
	Longer between sessions may have been beneficial	JC003:200-201
	Disclosure about IBS to others beneficial	MS013:246, 252-253
	Valued social support outside of sessions	IG002:502-504; MS013:249-254; MS013:715-720
	Thinking about what a friend would advise - very helpful	IG002:461-463
	Seeking support would burden others	IG002:110 and 121-123
	Dealing with sensitive subjects (bowels)	JC003:319-323; IG002:383; MS013:263-265; MS013:487-495; IG002:110-111
	Good personality of therapist improved engagement	IG002:122-125; IG002:291; JC003:215-219
	Flexibility of appointments valuable	IG002:346-349; IG002:391; IG002:409; IG002:417-425; JC003:116-122; JC003:336-339; MS013:432-449; JC003:236-238 (leaving work); JC003:113-118
	Flexibility of activities around events	IG002:446-448
	Valued face to face intervention and contact	IG002:48-51; IG002:110-113; JC003:62-66; JC003:102-104*; JC003:192-195; MS013:199-213
	Environment uncomfortable	IG002:285
	Length of sessions sufficient	IG002:333-335
	Format of worksheets/materials could be improved	IG002:237-241; MS013:370 and 384-385
	More printouts would have been useful for further reading/information after sessions finished	IG002:652-653
	Persevered to "break the cycle" of feelings surrounding IBS	MS013:32-33
	Therapist facilitated relaxation useful	IG002:291-292; JC003:222-228; IG002:93-94, 99-101, (207-209) difficult at first
Perceived utility of treatment	Thought diaries useful	IG002:88-89; JC003:56-57
	Benefits of wider (non-IBS) application	IG002:170-171, 553-554, 585-586; JC003:36-37
	Understanding role of stress/low mood in affecting IBS to a greater extent has helped manage symptoms/feel in control	IG002:519-521, 554-555; JC003:337-339
	More relaxed and easy going	IG002:596
	Change in thought processes	MS013:405-407
	Scenarios valuable for relating personal circumstances	IG002:464-469

	Accepted and recognised the role of anxiety, stress and psychological aspects	IG002:519-521 and 523; JC003:36-38; JC003:337-344; MS013:64-68
	Relaxation useful	IG002:160-161; IG002:92-94; JC003:36-38 and 42-44; MS013:181-185
	Symptoms improved	IG002:305-306; MS013:601-602
	More in control	MS013:61; MS013:114-116; MS013:518-520; MS013:522-523; MS013:620-623; IG002:570; MS013:132-133; MS013:580-583, 591
Past experience of care	Medicine not effective	JC003:28-29
	Lack of understanding	IG002:72-24; JC003:414-433; IG002:73, 614-615
	Stigma	JC003:414-417
	No dietary advice (FODMAPS)	IG002:79-81
	Felt like a nuisance - neurotic	IG002:72-74
Impact on QOL	Restrictions imposed by symptoms	MS013:40-41
Wider application of interventions	Dealing with worry	IG002:170-173; IG002:578; MS013:471
Coping mechanisms (non-CBT)	Use of anti-motility drugs	MS013:270-271
Reference to traumatic life events	Suicidal ideation	MS013:74-76
	Domestic abuse	MS013:70-72
	Loss of family or friends	IG002:170-181*; MS013:94-98
Other	Friends and family test	IG002:yes:599; JC003:yes:402 ; MS013:yes:650 (if prepared)