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Cognitive behaviour therapy for distress in people with Inflammatory Bowel Disease: A bench marking study.

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Abstract

Objective: Anxiety and depression are common in inflammatory bowel disease (IBD) and have been linked to clinical recurrence. Previous randomised controlled trials have found no evidence that psychological interventions enhance outcomes for people with IBD but have recruited patients without distress. This study investigates the clinical benefits of a non-randomised uncontrolled study of clinic based cognitive behaviour therapy (CBT) for people with IBD who had moderate to severe levels of anxiety or low mood and compares the results to a previous randomised controlled trial of CBT in this population.

Method: Assessments were completed at baseline and end of treatment and included measures of low mood, generalised anxiety, quality of life and symptomatic disease activity. The patient health questionnaire and generalised anxiety disorder 7 measures were the primary outcomes. Results in the form of a standardized effect size of treatment were compared with a previous randomised controlled trial to consider if CBT had greater benefits for those with distress.

Results: Thirty patients were deemed appropriate for CBT and twenty eight accepted treatment. The results from this clinic based CBT intervention suggest statistically significant reductions in symptoms of anxiety (<0.001), low mood (<0.001) and disease activity ($p<0.01$) and increases in quality of life ($p<0.001$).The uncontrolled effect sizes were large and superior to those found in published RCTs.

Conclusion: This nonrandomised uncontrolled trial of a clinic based CBT intervention suggests CBT may have benefits for those with moderate to severe disturbances to mood and that effect sizes can be improved by targeting those with distress. RCTs are required to establish efficacy.

Keyword: Cognitive behaviour therapy, inflammatory bowel disease, Anxiety, Low mood.

Introduction

The two most common types of inflammatory bowel disease (IBD) are Crohn's disease (CD) and ulcerative colitis (UC). Both conditions are associated with a similar range of unpleasant and incapacitating symptoms which include diarrhoea, fatigue and pain in the abdomen. In UC, this is the consequence of inflammation which is usually restricted to the colon where as in CD any part of the intestines can become affected. Extra intestinal symptoms can also occur, the most common being anaemia (Stein et al, 2010). The course of IBD is changeable and episodic in nature. Its precise aetiology remains elusive and there is currently no conclusive cure. Current IBD treatments target the inflammatory response during flare episodes with regular medication to maintain remission (Kiebles, et al, 2010).

People with IBD are at increased risk of developing anxiety and depression. The empirical evidence demonstrates the life time prevalence rates of these emotional disorders to be as high as 35.8% (Walker et al, 2008). Anxiety and depression are independently associated with clinical recurrence (Mikocka-Walus et al, 2016) and have been linked to increased inflammation (Maunder et al, 2008). Further, psychological distress in IBD can be influenced by disease related factors such as relapses, as well as general psychological factors. A recent systematic review found that emotion focused coping strategies, extreme perceptions of the illness and of being stressed were significantly associated with worse mental health outcomes, and this was maintained when controlling for the influence of disease related variables (Jordan et al, 2016). Psychological factors are potentially modifiable through psychological interventions and consequently interest in the possible efficacy of psychological interventions to improve outcomes in IBD has increased (Knowles et al, 2013).

Several reviews have been published which have examined the impact of psychotherapy on biopsychosocial outcomes for people with IBD (Gracie et al , 2017, Knowles et al, 2013, McCombie, et al, 2013, Timmer et al, 2011). A Cochrane meta-analysis of randomised controlled trials (RCTs)

concluded that there was no evidence that psychological interventions enhanced emotional states, quality of life (QOL) or reduced disease activity in the short term or at 12 months in unselected adults with IBD. It did though suggest that psychotherapy may benefit subgroups of patients with emotional needs and recommended future research should evaluate this (Timmer et al, 2011).

A major problem associated with the RCTs included in the Cochrane meta-analysis is that 19 out of 20 studies included adult patients without distress at the start. Mean scores for mood measures indicated that participants had symptoms in the sub clinical range. This is likely to have significantly reduced any potential treatment effects as participants generally had good mental health (Timmer et al, 2011).

Two trials published subsequently comparing group and computerised cognitive behaviour psychotherapy (CBT) with treatment as usual have continued this trend (Mikocka-Walus et al, 2015, McCombie et al, 2016). Their findings confirm that the impact of CBT is limited for those without disturbance to mood. However, post hoc sub group analysis conducted by Mikocka-Walus et al, (2015), found CBT had a greater impact for participants who had higher scores for anxiety and low mood at baseline. It seems intuitively sensible to target the group with most clinical need (Timmer et al, 2011), as improvements in mood may ultimately alleviate the aspect of disease activity which is linked to or driven by psychological distress.

As yet the impact of a clinic based CBT intervention on biopsychosocial outcomes for people with IBD and anxiety and low mood has not been evaluated or considered in relation to the findings of RCTs. This study will therefore evaluate whether a clinic based CBT intervention for people with IBD and moderate-severe anxiety or low mood shows promise. We think it is likely that by targeting those patients with moderate to severe low mood or anxiety that significant changes will be observed in the primary outcome measures. We will then compare the results of this open study to

previous RCT results. The treatment location for this study was a newly developed CBT service which was established as an adjunct to usual IBD treatment and care. It was one of the first of its kind to be located within an inflammatory bowel disease service in the UK. As CBT has proven efficacy for improving mood in other long term conditions, randomly withholding this intervention from patients with significant emotional distress in order to evaluate its efficacy under gold standard RCT conditions raised ethical issues (Harris et al, 2006). We therefore employed a pragmatic approach to investigating the benefits of a clinic based CBT intervention and utilised a non-randomised uncontrolled trial design.

Benchmarking is a useful way of measuring the effectiveness of a clinic based intervention against clinical trials and can provide a direct statistical comparison of pre-post treatment scores (Minami et al, 2008).Often treatment effects are more modest outside of RCT conditions due to for example, lower criteria for inclusion. However given that trials to date have included those without clinical levels of distress and a clinic based intervention focuses on patients with poor mental health, this may not be the case for IBD.

It is important when carrying out a benchmarking study that the treatment location that is being compared to an RCT condition represents a real practice setting .Shadish, et al (1997) and Shadish, Matt, Navarro, and Philips (2000) have developed a set of criteria that can be used to assess the extent to which a setting is clinically representative. These criteria include; representativeness of problems, the setting, how referrals are sourced, representativeness of therapists, structure of service, monitoring of treatment, problem heterogeneity and also pre therapy training, ability to have therapy freedom and use of multiple techniques and flexibility of number of sessions. The CBT clinic which provides the setting for this study fulfilled the majority of the Shadish criteria.

Within the mental health literature, benchmark studies have been produced for CBT for anxiety and depression (Westbrook & Kirk, 2005), chronic fatigue syndrome (CFS) (Quarmby et al, 2007), social phobia (Gaston, et al, 2006), panic (Stuart et al, 1998), post -traumatic stress disorders (Gillespie et al, 2002) and multiple sclerosis (MS) (Askey Jones et al, 2013).These studies revealed comparable effect sizes between RCTs and outpatient clinics. To date there have been no studies comparing results from RCTs of CBT for people with IBD with outcomes achieved with a clinic based CBT intervention focused on those with clinically significant distress. Given the results of previous trials it is important to evaluate whether a psychological intervention could help those in need. We therefore report on the clinical impact of a clinic based CBT intervention for people with IBD who had moderate to severe levels of anxiety or low mood and 2) compare the results to a previous randomised controlled trial (RCT) of CBT in this population. We hypothesise that levels of anxiety and depression will reduce after the clinic based CBT. In addition we hypothesise that the effect sizes after clinic based CBT will be superior to the effect sizes in the comparison RCT.

Methods

Study design

We used a nonrandomised uncontrolled trial to evaluate the impact of a clinic based CBT intervention for people with IBD who have moderate to severe levels of anxiety and/or low mood. We then compared outcomes with the results from an RCT of CBT. The aim of the CBT in the RCT was to prolong remission and improve quality of life and psychological distress in adults with IBD (Mikocka- Walus et al, 2015). Table 1 provides details of the methods employed by the comparison study. We utilised the transparent reporting of evaluations with nonrandomised designs checklist (TREND) to structure the reporting of this study and to ensure clarity (Des Jarlais et al, 2004).

Materials and Procedure

CBT clinic & Participants

The CBT clinic was located within a gastroenterology outpatient department in the UK. Patients were taken from consecutive referrals from the clinical team of gastroenterologists and IBD nurse specialists. Team members were encouraged to use the patient health questionnaire 9 (PHQ9) (Spritzer et al, 1999) and generalised anxiety disorder 7 measure (GAD7) (Spitzer et al, 2006) to screen for symptoms of low mood and anxiety to assist their clinical judgements. People scoring 10 or over on either or both measures (moderate to severe levels of anxiety and/ or low mood) were referred. Most reported difficulty in dealing with or adjusting to an aspect of their diagnosis of IBD or perceived their emotional stress to play a significant role in their experience of disease activity.

Table 1: Basic CBT demographics.

	Clinic based CBT intervention	**Clinic based CBT intervention**	**RCT**
Method	Nonrandomised trial of clinic based CBT	Nonrandomised trial of clinic based CBT	Online CBT Vs TAU
Trial author & year of publication	Jordan et al, 2018.	Jordan et al, 2018.	MIkocka-Walus et al, 2015.
No in CBT arm of trial	Complete sample n=30	Analysed sample n=27	n=68 baseline n=35 6months
Age, years, M (SD)	38.67 (range 21-68, SD 13.1)	37.4 (range 21-68, SD 12.6)	NR for online CBT group
Gender N (%) **Female** **Male**	 21 (70) 9 (30)	 19 (70.4) 8 (29.6)	NR for online CBT group.
Ethnicity N (%) **White** **Black** **Other**	 27 (90) 3 (10) 0	 25 (92.4) 2 (7.4) 0	NR for online CBT group
Type of IBD N (%) **CD** **UC**	 16 (53.3) 17 (46.7)	 12 (44.4) 15 (55.6)	NR for online CBT group.
Duration of illness **M, (range)**	 5.72 (1-20)	 5.57 (1-20)	NR for online CBT group
Marital status N (%) **Married** **Divorced** **Single**	 13 (43.3) 1 (3.3) 16 (53.3)	 11 (55.6) 1 (3.7) 15 (55.6)	NR for online CBT group

TAU=Treatment as usual, F2F= Face to face, NR=Not reported, CBT=cognitive behaviour therapy

The psychological therapist provided transdiagnostic cognitive behaviour therapy (TD-CBT) for the treatment of anxiety and low mood. This approach targeted the shared cognitive and behavioural processes underlying the development and maintenance of emotional distress (Clarke et al, 2009). It did not require the therapist to determine a primary diagnosis i.e. depression or an anxiety disorder, as is the case with disorder specific CBT. As a consequence it was arguably a more efficient way to work with patients who were presenting with multiple clinical problems (Mansell et al, 2008). A recent meta-analysis which included 24 RCTs found that transdiagnostic CBT treatments outperformed control conditions for reducing anxiety and depression and improving quality of life (Newby et al, 2014).

Routine outcome data was collected in the CBT clinic between November 2014 and September 2016. Unlike previous RCTs, only patients with clinically significant symptoms of anxiety and low mood were referred to the CBT clinic. In addition patients were not excluded if they were experiencing symptomatic disease activity. However patients were excluded if they had cognitive impairment or were unable to speak English to a standard required to engage meaningfully in the therapy. Table 2 provides details of the inclusion and exclusion criteria employed in the CBT clinic and the comparison study. The CBT clinic met the majority of Shadish's et al, (1997) criteria for clinical relevance. Patients were all clinically referred and heterogeneous in age, sex, and focal problem. Although the approach was consistent with a transdiagnostic approach for anxiety and depression there was no written manual, no monitoring of treatment other than routine supervision, the therapist did not participate in any specific training for the purposes of the study and there was flexibility in the number of sessions offered to patients. However, the therapist was a trained and experienced cognitive behavioural therapist.

Table 2: Inclusion and exclusion criteria

	Clinic based CBT intervention	***Mikocka –Walus et al, 2015.***
Inclusion criteria	1) Individuals over aged 18 with a clinically established diagnosis of IBD 2) Moderate to severe symptoms of anxiety and/or low mood indicated by scores of 10 and over on GAD7 and/or PHQ9	1) Individuals over 18 with a clinically established diagnosis of IBD 2) Current clinical remission or mild symptoms only for at least 3 months 2) Sufficient English to understand, answer questionnaires and participate in therapy 3) Competence to consent 4) Willingness to complete CBT sessions.
Exclusion criteria	1) Cognitive impairment or unable to speak English to a standard required to engage meaningfully in the therapy	1) Serious mental illness (e.g. psychosis, schizophrenia) or alcohol/substance dependence as diagnosed by the Clinical psychologist 2) Currently undergoing psychotherapy 3) Significant cognitive impairment
Recruitment strategy	Consecutive referrals from gastroenterologists /IBD nurse specialists	IBD databases at two gastroenterology clinics in Australia were screened by the clinics' IBD nurses. Potentially eligible IBD patients were then contacted by letter

Audit Approval

Advice was sought from the local ethics committee. As the study was part of routine clinical outcome collection ethical approval was not required. However we received audit approval from the gastroenterology directorate to collect clinical outcomes for common mental health problems in IBD. Informed written consent was obtained from all individual participants included in the study. The privacy rights of participants were observed and data was pseudonymised and held in a secure place.

Procedure and treatment

Once referred to the CBT clinic by the IBD nurse specialists or gastroenterologists, all patients were asked to sign a consent form confirming they were agreeable to having their data recorded and used anonymously for any future papers following service evaluation. All participants consented to this. The therapist provided an initial assessment of all referrals and asked patients to complete self-report questionnaires. Following the initial assessment patients were offered TD-CBT if appropriate. This approach is based on traditional CBT principles with a particular emphasis on helping people change the way they respond to their emotions. A range of TD-CBT strategies were utilised in sessions to target the common psychological processes underlying anxiety and depression, rather than targeting the symptoms of the specific disorders. Strategies included psychoeducation to introduce the main components of an emotional experience, namely thoughts, physical sensations and behaviour and the reciprocal relationships between these domains. This three component model was then employed across sessions to recognise and track emotional experiences. This enabled the patient to understand their cognitive, behavioural and emotional responses to triggers and assess the short and long term consequences of their emotion driven behaviour. Where behaviour was identified as unhelpful, patients worked towards acting in alternative ways. For example, a patient may have identified that when traveling on trains they experienced anxiety about

having access to a toilet and their response was to stay close to a toilet during the journey and monitor and time its occupation. On consideration, they may have recognised that this behaviour maintained attention and focus on the feared event and amplified their anxiety. An alternative response might therefore be to sit slightly further away and focus attention on a more neutral activity thus lessening preoccupation and anxiety. Mindfulness and attention training exercises were employed to encourage such present focused awareness and to support the development of alternative adaptive emotional responses. Further, to encourage flexibility in thinking patients were taught to identify and evaluate maladaptive automatic appraisals as well as identify and overcome emotional avoidance. Therapy concluded with relapse prevention whereby patients were encouraged to identify goals to maintain treatment gains and for continued progress (Barlow et al, 2011). The treatment received was not manualised, but was instead based on individual case formulations. Therapy was undertaken on 1:1 basis, weekly for 50 minutes. The amount of sessions offered varied and was determined by the severity of the clinical problem and the individual's response to the intervention. We used the Template for intervention Description and Replication (TDieR) checklist (Hoffman et al. 2014), to promote completeness in reporting and replicability of the intervention, please see appendix 6.

Training and supervision

The therapist was trained in cognitive behavioural psychotherapy at a post graduate level with 15 years' experience of working with anxiety disorders and depression. Supervision was provided by a cognitive behavioural psychotherapist familiar with IBD (TC) on a monthly basis and consisted of face to face case supervision. The therapist had experience of working with people with IBD and anxiety and depression and this was consolidated by spending time with the IBD nurse specialists and gastroenterologists to gain further insight into the biopsychosocial impact of IBD.

Outcome measures

During the initial appointment demographic information (such as age, gender, marital status) as well as type of IBD, length of diagnosis, current medications and previous psychiatric history was elicited from participants. The clinical service collected routine data from all participants seen over a two year period (November 2014 and September 2016).

Primary outcomes

We chose two primary outcomes, anxiety (generalised anxiety disorder 7 (GAD7) and low mood (patient health questionnaire (PHQ9) as both were being targeted in the transdiagnostic treatment. The GAD7 is a self- report questionnaire which measures symptom severity for the four most common anxiety disorders (generalised anxiety disorder, panic disorder, social phobia and post-traumatic stress disorder). Scores in the 10-14 range are indicative of a moderate level of symptoms, whilst 15 and above implies severe (Spitzer et al, 2006). Symptoms of low mood were measured by the patient health questionnaire, a multiple choice self -report inventory (PHQ9). Scores in 10-19 range signpost moderate to moderately severe symptoms of low mood, a score of 20 or more severe (Spritzer et al, 1999). Both of these measures are widely used to screen for clinically significant levels of symptoms within general medical and outpatient settings and to monitor treatment response over time (Spitzer et al, 2006). All patients completed these measures at pre therapy and immediately at the end of therapy.

Secondary outcomes

We selected two secondary outcomes, health related quality of life and symptomatic disease activity. As these outcomes are associated with anxiety and low mood we hypothesised that improvements to mood may lead to improvements in these domains. Health related quality of life was quantified by the short inflammatory bowel disease questionnaire (SIBDQ) which measures this construct across the 3 domains of physical, social and emotional status. Scores range from 10-70,

with higher scores indicating a better quality of life (Irvine et al, 1996). Current levels of symptomatic disease activity were measured by the Harvey Bradshaw Index (HBI) (Harvey et al, 1980), for participants with Crohn's disease and the Simple Clinical Colitis Activity Index for participants with ulcerative Colitis (SCCAI) (Walmsley et al, 1998). The score derived from the HBI is based on 5 items that assess general well-being, abdominal pain, number of liquid stools per day, abdominal mass, and complications or extra intestinal manifestations. The score derived from the SCCAI is based on 6 items that assess daytime and night time bowel movements, urgency, and presence of blood in the stool, general well-being, and extra intestinal manifestations. Scores of <5 on the HBI and <3 on SCCAI are considered to suggest remission (Higgins et al, 2005). All patients completed these measures at pre therapy and immediately at the end of therapy.

Statistical analysis

Statistical analysis was performed using the statistical package for the social sciences (SPSS) version 23. Descriptive statistics were generated to describe the study population The pre and post measures of health related quality of life (SIBDQ) and disease activity (HBI & SCCAI) for all participants were analysed using the paired t-test. The Shapiro-Wilks test for normality indicated that data may be skewed for post measures of anxiety (GAD7 W=.053 df=27 p=0.01) and low mood (PHQ9 W=.758 df=27 p=0.001) so the two sample Wilcoxon rank sum (Mann Whitney) test was used for analysis. The one drop out was not included in the analysis as post therapy measures had not been completed at the time of leaving the service.

Benchmarking & comparison of effects

A systematic review of psychological interventions for adults with IBD (Knowles et al, 2013), identified five studies investigating the effect of CBT focused interventions on clinical disease parameters as well as anxiety, low mood, disease related concerns and quality of life (Mussell et al, 2003, Kaneko, 2009, Schwarz et al, 1990, Diaz Sibaja et al, 2007, longhorst et al, 2007). Subsequently

two further trials have been published (Mikocka-Walus et al, 2015, McCombie et al, 2016). None of these studies included participants with IBD who report clinically significant symptoms of anxiety or low mood either through structured clinical interview or validated measurement tools, although these domains have often been evaluated as secondary outcomes (Fiest et al, 2016). There is also considerable variation across studies regarding the content of the intervention, as CBT was often used in combination with other strategies.

In order to create a benchmark we therefore selected studies that investigated a 1:1 intervention which was informed by a cognitive behavioural paradigm (including Computerised CBT, (CCBT) for people with IBD and that reported pre and post mean scores and standard deviations for measures of either anxiety, low mood or quality of life, as well as disease activity. This led to the exclusion of three studies which failed to report outcomes in the required format (Kaneko, 2009, Schwartz et al, 1990, McCombie et al, 2016) and three which evaluated a group intervention (Mussell et al, 2003, Diaz Sibabja et al, 2007, longhorst et al, 2007). The one remaining study consisted of two interventions (group CBT and online CBT) tested against standard care (Mikocka-Walus et al, 2016) (See table 9.1). For the purpose of this study only the outcome data from online CBT condition was used (Mikocka-Walus et al, 2016) (since the CBT clinic only included an individual CBT treatment group) to compose a benchmark indexing the mean change of CBT under RCT condition.

Details of the recruitment strategies and inclusion/exclusion criteria utilised in the RCT study ((Mikocka-Walus et al, 2016) which composed our benchmark are reported in table 3. Primary outcomes included symptomatic disease activity measured by the Crohn's disease activity index (CDAI) (Best, 1976) and simple clinical colitis activity index (Walmsley et al, 1998). Secondary outcomes considered were anxiety and low mood measured by the Hospital anxiety and depression scale (HADS) (Zigmond et al, 1983).

As it is not possible to directly compare these differing outcome measurements, uncontrolled effect sizes for each of these outcomes were calculated to standardize the treatment effects (Streiner, 1991). Such an uncontrolled effect size is likely to inflate the effects of therapy as compared to a conventional controlled effect size, because it effectively assumes that there would be no change without therapy. It does however provide a crude benchmark for comparison with other studies. Uncontrolled effect sizes were calculated as (*M* Start _ *M* End) / *SD* Start) (Cohen, 1988; Westbrook et al, 2004). As outcomes were reported at multiple time points (e.g., post treatment and follow-up), we calculated the effect size with the outcome closest to the time interval of the clinical service which was 6 months. Conventionally effect sizes are classed as 0.2 (small), 0.5 (medium) and 0.8 (large).

Results

Number of sessions, attrition and drop out.

The mode number of CBT sessions received was six (range 4-10, mean 6.70, SD 1.68). Of the 36 patients screened; 30 were eligible for CBT. Two declined treatment due to being unable to attend the appointments slots offered. Of the remaining 28, 27 completed therapy and 1 dropped out of treatment. The reason given for this was that the participant changed employment and was no longer able to attend the clinic (See fig. 1). On inspection there were no differences in gender ($\chi 2$= 2.19 pr=0.139), ethnicity ($\chi 2$ =3.11 pr=0.375) or marital status ($\chi 2$=0.6710 pr=0.715) between starters and non-starters of therapy.

Baseline severity of anxiety, low mood, quality of life and disease activity.

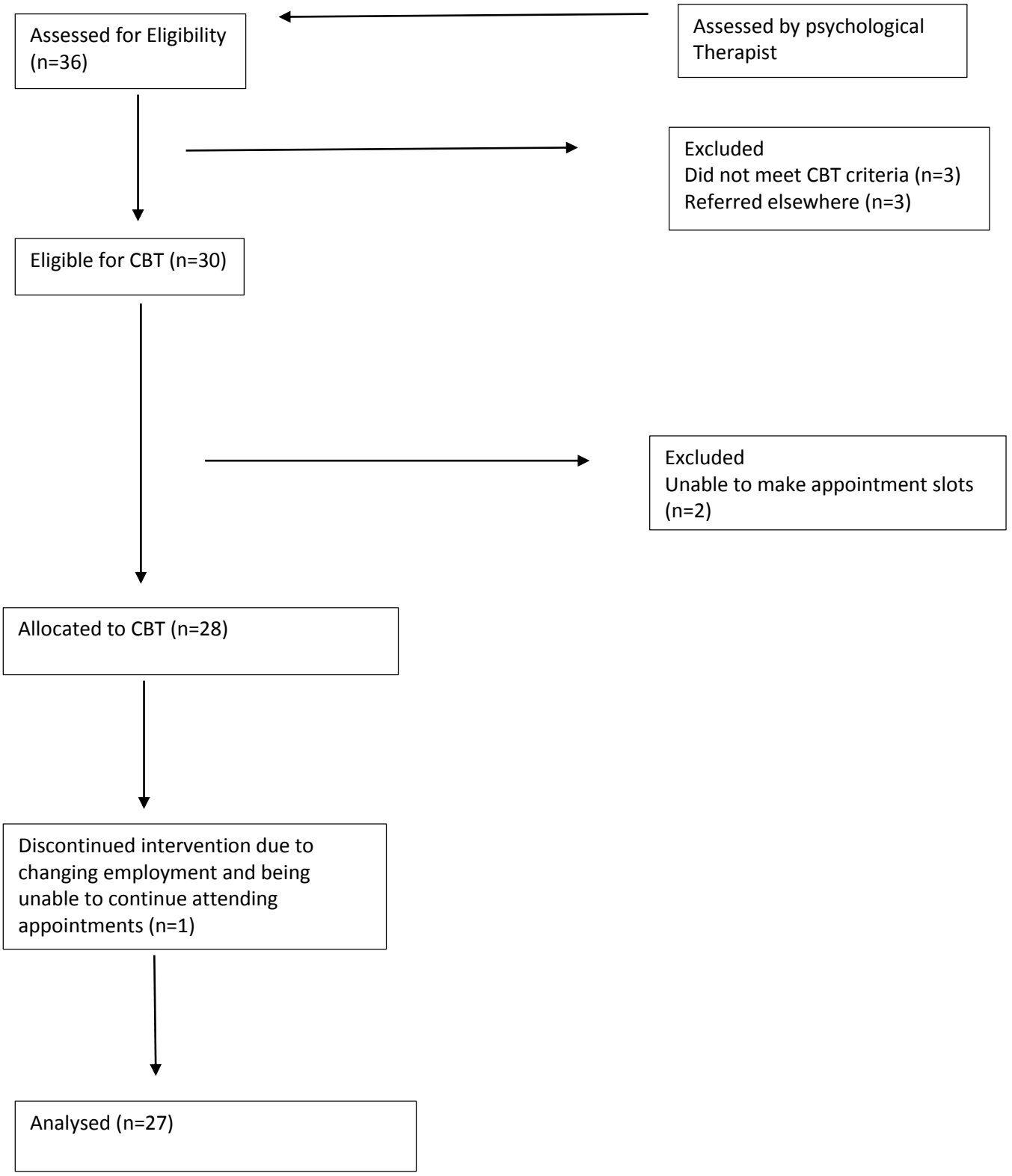
The majority of participants presented with moderate to severe levels of anxiety and low mood (n=20 scored 10 and above on PHQ9 & GAD7). On inspection there were no differences between starters (n=28) and non -starters (n=2) of therapy on baseline scores for the SIBDQ (t (28) =2.81 p=0.08), GAD7 (z=-0.67 p=0.31) or PHQ9 (z=-1.17 p=0.29).

Further analysis Indicated that 65% of the participants with Crohn's disease scored <5 on HBI and 66% of participants with ulcerative Colitis scored <3 on SCCAI which suggests the majority of participants were experiencing a remission in disease activity.

Treatments outcomes

Analyses were conducted on 27 people who had completed pre and post scores on the PHQ9, GAD7, SIBDQ and either the HBI for Crohn's disease or SCCAI for Ulcerative Colitis, at base line and end of therapy. There was a statistically significant decrease in scores for low mood on the PHQ9 from time 1 (M 13.44, 5.31) to time 2 (M 3.44 SD 2.23, Z=.000 p<0.001). Statistically significant decreases in anxiety scores on the GAD7 were also observed from time 1 (M 12.67 SD 4.67) to time 2 (M 3.22 SD 2.55, z=.000, p<0.001). In addition statistically significant decreases in symptomatic disease activity were observed for Crohn's disease on the HBI from time 1 (M 7.00 SD 3.95) to time 2 (M 4.25 SD 3.19, t (25) =4.01 P=0.002) and ulcerative colitis on the SCCAI at time 1(M 4.93 SD 2.46) to time 2 (M 2.27 SD 1.79, t (25) =4.28 P<0.001). Finally statistically significant increases in scores for quality of life on the SIBDQ were detected from time 1 (36.22 SD 9.01) to time 2 (M 55.04 SD 6.39 t (25) =-14.65 p<0.001).

Figure 1. Modified Consort flow diagram for recruitment to the CBT clinic.



B*enchmark comparison*

Uncontrolled effect sizes comparing the CBT clinic and the RCT self- report outcome scores are provided in table 3. Overall the mean effect sizes reported from the RCT for low mood, anxiety and symptomatic disease activity were small to medium (0.2-0.5) whilst for the CBT clinic large mean effect sizes were observed for these outcomes (close to or over 0.8).

Discussion

The results indicate that CBT may be of benefit for people with IBD and clinically significant emotional distress. Scores on measures of anxiety, low mood and disease activity significantly decreased over the course of the study whilst scores for quality of life significantly increased.

The treatment effects of CBT on all outcomes for people with IBD compared to the RCT were favourable. This is likely to be due to the inclusion of participants with moderate to severe symptoms of anxiety and low mood. These findings suggest that it is this sub group of patients with significant levels of distress who benefit most from psychological intervention. The results of the majority of previous RCTs suggest that CBT has limited effect on self-reported disease course for people with IBD without disturbance to mood (Gracie et al, 2017). Based on our findings, future RCT' may show improved disease related outcomes if participants with clinically significant symptoms of anxiety and low mood are recruited. As mood improves it may be that inflammation is reduced in combination with a shift in symptom perception. In contrast, as mood worsens reports of disease activity may increase and vice versa. This reciprocal interaction is likely to be mediated by cognitive, behavioural and emotional responses. Our findings suggest that by identifying and addressing unhelpful responses with cognitive behaviour therapy both mood and reports of disease activity may improve (Jordan et al, 2016).

Table 3: Mean scores at pre & post treatment and effect sizes for the CBT clinic and the RCT

Name of trial authors	**CBT clinic.**	**Mikocka –Walus et al, (2015).**
CBT type	Individual	CCBT
Pre-treatment scores (M, SD): Depression	PHQ9: 13.44 (5.308)	HADSD: 4.1 (3.6)
Post treatment scores (M,SD) : Depression	PHQ9: 3.44(2.23)	HADSD 6M: 3.3 (3-1)
Effect size-Depression	**1.9**	**0.22**
Pre-treatment scores (M,SD): Anxiety	GAD7: 12.67 (4.666)	HADSA: 6.7 (4.2)
Post treatment scores (M, SD): Anxiety	GAD7: 3.22 (2.55)	HADSA 6Months : 5.8 (3.8)
Effect size -Anxiety	**2.0**	**0.21**
Pre-treatment scores (M,SD): Quality of life (higher score higher Quality of life)	SIBDQ: 36.22 (9.01)	NR
Post treatment scores(M,SD) : Quality of life	SIBDQ: 55.04 (6.39)	NR
Effect size-quality of life	**-2.09**	**NR**

Pre- treatment scores :(M,SD) Disease Activity		
CD	HBI: 7.0 (3.95)	CDAI : 101.2 (65.5)
UC	SCCAI: 4.93 (2.46)	SCCAI:3.2 (1.5)
Post treatment scores :(M, SD) DA activity:		
CD	HBI: 4.25(3.19)	CDAI 6Months : 97.3 93.7)
UC	SCCAI: 2.27(1.79)	SCCAI 6Months : 3 (1.9)
Effect size-disease activity:		
CD	**0.71**	**0.06**
UC	**1.1**	**0.13**

This study's findings may have been influenced by our choice of measures. We used the GAD7 (Spitzer et al, 2006) to measure symptoms of anxiety and the PHQ9 (Spitzer et al, 1999) for symptoms of low mood and it is possible that these measures are more sensitive to change in the IBD population than the HADS which was used in the comparison trial (Mikocka- Walus et al, 2015). There is some controversy surrounding the HADS with some studies showing it to be equally good at detecting anxiety and low mood as the GAD7 & PHQ9. However recent psychometric systematic reviews have found it to be a measure of general distress rather than distinct mood states (Norton et al, 2013, Costco et al, 2012). As yet it is unclear which questionnaires are best suited to measuring anxiety and low mood in IBD. Further work on the validity of measures for this population would be useful.

In the CBT clinic patients were offered transdiagnostic CBT based on individual case formulations meaning that treatment strategies targeted the specific psychological processes underpinning the symptoms and situations the patient described as problematic (Barlow et al, 2011). This contrasts with the CBT provided in the RCT which followed a protocol and was delivered online. As many

people with IBD present with multiple co-morbidities a transdiagnostic approach may be more suitable. A recent preliminary evaluation of the impact of a one day transdiagnostic CBT group intervention on distress in IBD found anxiety scores were significantly reduced at 3 month follow up (Hou et al, 2017). In addition the therapy within the clinic was delivered by a psychological therapist which may be more acceptable and engaging for the majority of patients. Drop outs reported for the CBT service (n=1, 3.5%) were small whilst attrition at 6 months from the CCBT group in the comparison trial was high at 48%. This is also likely to have reduced any treatment effects (Mikocka-Walus et al, 2015).

Previous benchmark studies have suggested that the experience of the therapist as well as waiting times may influence participation and outcomes (Scheeres et al, 2008). In this study the therapist had 15 years of experience and this was a newly established psychological service. To the authors knowledge it is the first to be located geographically within an IBD clinical service in the UK. This may serve to lessen any perceived stigma in regards to seeking or receiving treatment for a mental health problem as it does not involve attending a psychiatric outpatient setting. This new service was received enthusiastically by both clinicians and patients. Further, there was no waiting time to commence treatment. It is likely that all these factors positively affected engagement in therapy.

Limitations and future directions

The pragmatic design of this study and the absence of a control group means that the benefits of a clinic based CBT intervention for mood and quality of life must be interpreted with some caution. As no comparison data can be provided we cannot say with any certainty whether these promising results are truly due to the intervention, or for example repeated testing, spontaneous recovery or changes in treatment conditions. It has been suggested that in recent onset cases of depression spontaneous remittance is common and the benefits of psychological intervention may be modest

(Clark et al 2008). In addition the statistical principle of regression to the mean predicts that elevated scores are likely to decline over time even without intervention. To control for the effects of confounding variables future studies would benefit from randomisation and a control condition. This may prove difficult in a clinical setting but a waiting list control group may be feasible next step. Equally important is the inclusion of participants with clinically significant emotional distress in future RCTs.

Measurements of anxiety, low mood, quality of life and disease activity in our study were all based on self- report measures. We therefore cannot say with any certainty whether improvements in disease activity were due to a reduction in inflammation or changes to the appraisal of symptoms. Ideally prospective studies would include objective measurements such as endoscopy and faecal calprotectin analysis and structured clinical interview (Jordan et al, 2016). Future studies should also consider assessing objectively any changes to medication or treatment regimens as potentially confounding variables.

Further, this pragmatic study of CBT implementation embedded within an outpatient gastroenterology service did not follow a specific treatment manual and no treatment integrity checks were carried out. It is therefore possible that the intervention may have deviated from a CBT paradigm. Patients also received a variable number of sessions in comparison to the RCT and this may have further confounded results. In addition the number of participants undertaking CBT was small (n=27). In order to enhance generalisability further studies should consider a larger sample.

Finally, three of the 27 people entered in CBT were taking antidepressants. However, only one had commenced them in the last month. The two other participants had been receiving pharmacological treatment for more than 8 months prior to commencing CBT. This reduces the likelihood that change could be attributed to the pharmacological intervention.

The CBT clinic fulfilled the majority of the criteria for clinical representative as set out by Shadish et al , (2000) in that it (a) took clients who had clinically representative problems, (b) took place in a clinical setting, (c) saw clients who were referred through normal clinical routes from IBD nurse Specialists and gastroenterologists, (d) used a psychological therapist who had CBT training and held a caseload of IBD patients, (e) followed a typical structure for the clinical practice, (f), treatment was not monitored closely to impact the psychological therapists behaviour, (g) the population had heterogeneous problems and were clinically representative, (h) the psychological therapist did not receive specific training immediately prior to the clinic, (i) the psychological therapist could use a variety of techniques and (j) there was not a limited number of sessions. This is important as it adds further evidence for a clinic based CBT intervention being able to match and in this case better effect sizes of RCTs.

Conclusion

In summary, the results of this study suggest that CBT for people with IBD and symptoms of anxiety and low mood is beneficial when implemented in clinical practice for the majority of participants and that large effect sizes can be observed. Clinically significant levels of anxiety and low mood should be considered as inclusion criteria for the selection of participants in future RCTS and the addition of a control group should be considered for future clinic based intervention studies. Finding an effective psychological intervention for people with IBD is of vital importance given the impact that these mood disorders have been observed to have on disease parameters.

Given the established association between anxiety, low mood and disease activity and the potential impact that CBT may have on improving these outcomes, clinicians working with people with IBD in gastroenterology clinics should be trained to recognise symptoms of mood disorders and to refer to psychologically trained therapists. As there is some debate as to the cost-effectiveness of

widespread screening of mental health in primary care (Thombs et al, 2014) and higher-risk populations (Goldberg, 2014) this may be a more effective means of facilitating referrals to psychological services for further evaluation and treatment where indicated.