Developing a Low Intensity CBT Intervention for GAD in IAPT: A Pilot Feasibility and Acceptability Study

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Thesis declaration form

I confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this had been indicated in the thesis.

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Overview

Volume 1 of this thesis evaluates the development of a low intensity Cognitive Behavioural Therapy (CBT) intervention for Generalised Anxiety Disorder (GAD), its feasibility and acceptability. This volume consists of three parts.

Part 1, the literature review, examines using meta-analysis and network meta-analysis the effectiveness of psychological treatments for pathological worry in Generalised Anxiety Disorder (GAD) using the Penn State Worry Questionnaire (PSWQ) as a primary outcome measure. The review also considers the relative effectiveness of currently available psychological treatments. The quality of the current evidence base and methodological issues are discussed and further research suggested.

Part 2, the empirical paper, is a pilot study, which examines the feasibility and acceptability of the delivery of a brief guided self-help intervention for excessive worry and GAD, which drew on Behavioural Change Theory (Michie, Van Stralen & West, 2011) following a review of current interventions for GAD. The results showed that there was a clinical need for a specific worry and GAD intervention, that Understanding Worry (UW) was as acceptable to patients as Treatment as Usual (TAU) as there was no significant difference in drop out, attendance, cancellations or DNAs. There was no significant difference in post-treatment scores between UW and TAU in observed clinical contact and at session four as predicted by the Mixed Methods Linear Model (MMLM). Implications for treatment and further research are discussed.

Part 3, the critical review, explores critically the empirical study, the background to the research, conceptual issues in the intervention design and the challenges of conducting research in NHS clinical settings. The review particularly focuses on recruitment and the involvement of clinicians the research process and future directions for research.

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Part 1 – Literature Review

The effectiveness of psychological treatments for pathological worry in Generalised Anxiety Disorder (GAD).

Abstract

Aims: The current review sought to update and expand previous reviews of psychological treatments for GAD focusing on pathological worry as a treatment outcome. The review considered the relatively effectiveness of available psychological treatments for GAD. **Method:** Studies had to satisfy inclusion criteria relating to i) disorder ii) research design and iii) outcome measures. Twenty-eight studies were identified from four electronic databases (PsychInfo, OvidMedline, Embase and the Cochrane Central Register of Controlled Trials register) and references in previous systematic reviews. Available data was synthesised using standard two-way meta-analysis and network meta-analysis. **Results:** The review supported the findings of previous reviews suggesting that psychological therapy led to reliable improvement in worry post-treatment. There was evidence that suggested CBT was superior to waitlist but was not superior to applied relaxation. Evidence pointed towards longer CBT treatments reporting greater differences compared to short duration treatments. There was limited evidence for psychodynamic therapy and behavioural activation. Despite reliable changes in worry, post-treatment reductions did not reach a non-clinical level of worry. Network meta-analysis indicated that meta-cognitive therapy was probably the best treatment. **Conclusion:** The current review supported the findings of previous reviews, suggesting that psychological treatments led to reliable reductions in worry. CBT and AR were found to be equally effective and there was limited evidence for psychodynamic and behavioural activation. The network meta-analysis suggested that MCT is probably the best treatment of GAD.

1. Introduction

1.1 History of GAD

Generalised Anxiety Disorder's (GAD) diagnostic history is not without controversy and is a relatively recent addition to the diagnostic taxonomy (Tyrer & Baldwin, 2006). The validity of GAD as a distinct disorder has been widely debated. It has been argued that GAD and Major Mood Disorder (MDD) are indistinguishable due to the high degree of association and substantial overlap and therefore GAD should be classified as agitated depression (Mennin, Heimberg, Fresco & Ritter, 2008; Watson et al., 1995). However, a large longitudinal study questioned whether GAD and MDD were strongly related and concluded that GAD was associated more with anxiety disorders than depression and was a distinct disorder (Beesdo, Pine, Lieb & Wittchen, 2010). The key differentiating symptom of GAD is uncontrollable and pathological worry, which distinguishes GAD from other anxiety disorders and mood disorders (Abel & Borkovec, 1995; Brown, Antony, & Barlow, 1992; Ladoucer, Blasi, Freeston & Dugas, 1998). Previously GAD was subsumed under 'anxiety neurosis' and was a residual category, used when an anxiety disorder could not be classified under any other diagnosis. GAD's recognition as a distinct psychiatric disorder is relatively recent. It was not until the DSM-III revision in 1987 (APA, 1987) that GAD was classified as an independent anxiety disorder. With the introduction of DSM-IV (APA, 1994) the diagnostic criterion was refined further, introducing excessive, uncontrolled pathological worry as a diagnostic marker. This has been maintained in the current diagnostic manual DSM-5 (APA, 2013), which has retained the diagnostic criterion of DSM-IV.

1.2 Symptoms, Course, Co-morbidity and Prevalence of GAD

GAD is characterised by excessive worry that is difficult to control, and can result in reduced social and occupational functioning (Tyrer & Baldwin, 2006). These worries are typically widespread, involve everyday issues and focus on unlikely or remote events in the future (Dugas et al., 1998). To meet DSM-5 criteria

for GAD, excessive worry and anxiety about a number of events must be present for most days for at least six months, causing distress and impaired functioning. The worry experienced is difficult to control and is accompanied by at least three out of six symptoms: restlessness, fatigue, difficulty concentrating, irritability, muscle tension and disturbed sleep. GAD is frequently comorbid with other mental disorders. The rates of comorbidity between epidemiological studies estimate that between 68% to 93% of individuals who meet a diagnostic criteria for GAD will also meet criteria for another Axis 1 mental health disorder (Carter, Wittchen, Pfister & Kessler, 2001; Hunt, Issakidis & Andrews, 2002). The most common comorbid conditions are depressive disorders and other anxiety disorders (Carter et al., 2001; Dugas & Robichaud, 2007; Hunt et al., 2002; Kessler, Chiu, Demler & Walters, 2005).

GAD is a chronic condition with symptoms that wax and wane in response to life stressors (Kessler, Keller & Wittchen, 2001). Clinical studies suggest that there is little remission in symptoms of GAD in the short and medium-term (Yonkers, Warshaw, Massion & Keller, 1996; Greenberg et al., 1999; Kessler, Keller & Wittchen, 2001). Long-term remission from GAD symptoms is reported to be limited, with only 40% of those diagnosed with GAD reporting recovery after 12 years (Tyrer, Sievewright & Johnson, 2004). GAD is associated with a substantial burden of disability that is equivalent to that of depression and other chronic conditions (Wittchen, 2002). Individuals with GAD experience diminished quality of life, reduced work productivity, impaired social relationships and increased reliance on state support. Individuals with GAD are also more likely to make frequent medical appointments, undergo diagnostic testing and represent the most costly patient group in respect to other anxiety disorders (NICE, 2011).

In the United Kingdom it is estimated that 4.4% of the population will meet a diagnosis of GAD (McManus et al., 1999). Wittchen and colleagues (2011) in a European review of mental health disorders estimated that GAD affects

approximately 8.9 million individuals per year. In primary care it is estimated that 8% of individuals seeking treatment meet the diagnostic criteria for GAD (Wittchen, 2002). Individuals with GAD may account for up to account for 25% of primary attendances for psychological problems, and as such it is the most frequent anxiety disorder presenting in primary care settings (Barret, Oxman & Geber, 1988). However, despite its high prevalence in primary care settings GAD is significantly under-detected and undertreated (Wittchen & Jacobi, 2005). Stein and colleagues (2004) suggest that due to the limited recognition of GAD in primary care that general practitioners (GPs) frequently do not provide psychological evidence-based treatment as often as may be indicated. This finding has been supported by the most recent Psychiatric Morbidity survey (McMannus et al., 2009), which reported that only 34% of those with GAD were receiving any treatment. Of those, over half were receiving medication and less than a quarter were receiving psychological treatment.

1.3 Development of Treatment for GAD

Treatments for GAD have reflected changes in the theoretical understanding of GAD. Treatments initially developed for GAD drew on non-specific interventions such as relaxation training and supportive psychotherapy (NICE, 2011). Initial Cognitive Behavioural Therapy (CBT) treatments for GAD developed in the early 1990s (Barlow, Rapee & Brown, 1992; Borkovec & Costello, 1993) focused on the reduction of physical arousal and the modification of dysfunctional cognitive appraisals. First wave CBT approaches focused primarily on addressing the consequence of worry, rather than worry as an underlying process maintaining anxiety. Early cognitive and behavioural interventions applied techniques such as applied relaxation, stimulus control and cognitive restructuring (Wilkins, Mears & Freeston, 2011). More recent second wave CBT treatment packages have emphasised the specific role of worry and the processes of thought and behaviour that maintain anxiety and somatic symptoms (Dugas, Gagon, Ladoucer & Freeston,

1998; Wells, 1999). Second wave CBT approaches focus on reducing behavioural and emotional avoidance, beliefs about worry and problem solving skills. Third wave approaches, which consist of acceptance-based or mindfulness approaches, have also been adapted to address GAD (Behar, DiMarco, Helke, Mohlman & Staples, 2009). The third wave approach focuses on changing the relationship with experience of worry rather than the modification of underlying thinking styles and appraisals.

1.4 Previous Reviews

Several meta-analyses and systematic reviews focusing on therapeutic interventions for GAD have been conducted since 2000. The majority of reviews have had a narrow focus on cognitive therapy (CT) or CBT outcome studies for GAD. Borkovec and Ruscio (2001) reported that CT was effective in reducing anxiety in comparison with placebo, and treatment gains were maintained over time and supported the long-term efficacy of CT as clinical treatment for GAD. Western and Morrison (2001) reported CBT was effective in reducing anxiety at the end of treatment, but treatment gains were not maintained at long-term follow up. However, early reviews, and Western and Morrison's (2001) review in particular, have been criticised in their analysis of anxiety outcomes, which did not address changes in pathological worry which is a key symptom in GAD (Atkins, Hazlett-Stevens, & Craske, 2001). Colvin and colleagues (2008) subsequently conducted a review that focused on evaluation of the effectiveness of CBT interventions for GAD and used the Penn State Worry Questionnaire (PSWQ) (Meyer, Miller, Metzger & Borkovec, 1990) to evaluate changes in pathological worry. Colvin et al. (2008) reported that CBT interventions led to a significant reduction in self-reported worry in comparison to non-treatment controls. They also reported that the largest treatment gains were found in younger adults and that individual treatment was superior to group treatment. More recently Hanrahan and colleagues (2012) conducted a meta-analysis, which focused on evaluation the efficacy of CBT for

GAD and pathological worry. The authors reported that CBT was superior in reducing worry in comparison with non-therapy controls, and 57% of individuals were classed as recovered at 12 months. They concluded CBT treatment approaches were effective in the treatment of GAD.

Two recent systematic reviews conducted focused on the evaluation of all psychological therapies for GAD (Hunot et al., 2007; NICE, 2011). Hunot and colleagues' Cochrane Review for psychological therapies for GAD reported that psychological therapy based on CBT principles was effective in reducing anxiety in comparison with waitlist controls. However, the authors cautioned that the evidence for the effectiveness of CBT in comparison with other psychological therapies was small, heterogeneous, and did not allow any firm conclusions about which psychological therapy was more effective in the treatment of GAD to be made. The more recent National Institute of Clinical Excellence guideline (NICE, 2011) for the treatment of GAD reviewed both Low Intensity (LI) and High Intensity (HI) psychological treatments for GAD. The review reported that there were large treatment effects in the reduction of anxiety for CBT based guided self-help and computer CBT (cCBT) interventions, and that there was a smaller treatment effect for psycho-educational groups. However, the majority of the studies included in the review contained a mixture of diagnoses and the studies were deemed to be of low quality. In regards to the HI interventions the review reported a large effect in the reduction of anxiety for CBT in comparison with waitlist controls and that CBT was equally as effective as applied relaxation (AR), although the evidence for AR's effectiveness was less robust. The review also reported that CBT was superior to psychodynamic therapy, usual care or an active comparator. However, both reviews did not focus specifically on changes in pathological worry as a treatment outcome and analysed anxiety measures, which arguably focus on somatic symptoms of anxiety.

1.5 The Current Review

The current review seeks to update and expand previous reviews of psychological treatments for GAD and focuses on levels of pathological worry as a treatment outcome. The review will also consider the relative effectiveness of available psychological treatments for GAD. The most recent systematic review of psychological therapy for GAD conducted as part of the NICE guideline (2011) identified a relatively small and heterogeneous number of studies, which included mixed anxiety disorders rather than limiting the search to GAD. The literature search for the NICE review was concluded in early 2010; four years have now passed and over this time there has been renewed interest in psychological treatments for GAD and the publication of several new randomised studies in this area. The current review aims to incorporate these new trials into a broader review of psychological therapy rather than focusing on determining the effectiveness of CBT for GAD in reducing pathological worry. It will also seek to delineate CBT approaches into first wave CBT, second wave CBT and third wave approaches. The review defines first wave approaches as traditional Beckian approaches, which focus on worry as a consequence of anxiety. Second wave approaches focus on worry as a maintaining process in anxiety and treatment focuses on addressing intolerance of uncertainty and beliefs about worry. Third wave approaches include acceptance and mindfulness approaches that do not attempt to restructure cognition.

The review uses a network meta-analysis (NWA) to evaluate the comparative effectiveness of different psychological treatments for pathological worry in GAD. NWA is a methodological approach that allows the relative effectiveness of treatment to be assessed when they have not been directly compared in head-to-head in a randomised trial but have been compared to other treatments (Cipriani, Barbui, Rizzo & Salanti, 2012; Lumley, 2002). NWA is a generalisation of standard pairwise meta-analysis. One of the basic assumptions of

NWA is direct and indirect evidence estimate the same parameter, that is, the relative effect between A and B measured directly from an A versus B trial, is the same with the relative effect between A and B estimated indirectly from A versus C and B versus C trials. NWA techniques strengthen inferences in regards to the relative effect of a treatment by including both indirect and direct comparisons between treatments, and at the same time, allowing simultaneous inference on all treatments examined in the pairwise trial while respecting randomisation (Caldewell, Ades & Higgins, 2005). The simultaneous estimation of the relative effect of a number of treatments is possible and is part of a single 'network of evidence', that is, every treatment is linked to at least one other treatment under assessment by a direct or indirect comparison. The NWA method allows treatments that have never been directly compared in a trial head-to-head to be compared against each other and a hierarchical order of relative effectiveness to be considered (Barth et al., 2013). An additional strength of NWA is that it allows the opportunity to understand how much evidence is available for each treatment and a comparison of why and where more research is needed. This method of analysis has yet to be employed in the evaluation of the relative effectiveness of interventions for GAD.

2. Method

2.1 Identification and Selection of Studies

Studies for the current review were identified in a number of ways. Firstly the databases PsychInfo, OvidMedline, Embase and the Cochrane Central Register of Controlled Trials (Central) Trial register were searched for English language studies using an adapted search terms and filters reported in the NICE (2011) GAD guideline. The search included the use of three search filters that specified GAD, randomised study design, High intensity (HI) psychological therapy, which includes CBT, applied relaxation, psychodynamic therapy, non-directive therapies and are delivered by a qualified clinician and Low intensity therapy (LI), which include brief

guided self-help, psychoeducational groups, computer based CBT (cCBT) and are facilitated by healthcare professionals and graduate level workers. The search filters consisted of a combination of medical subject headings (MESH), explosions (exp), subheadings (sh), and text words (ti,ab/tw). A full summary of the terms and filters used can be found in Appendix 1. The filters used in the NICE GAD guideline (2011) were selected to identify studies as they had previously been shown to provide a comprehensive coverage in the identification of psychological therapy studies for GAD and mitigated dissimilarities in bibliographic databases in thesaurus terms, indexing practices and imprecise reporting of study populations by authors. Studies identified in the search were initially included or excluded based on relevance of title and abstract; following this the remaining studies were included or excluded after a review of the complete paper. Secondly, the reference list of previous meta-analyses and systematic reviews were searched to identify any additional studies suitable for inclusion that had not been identified from electronic database searches. This identified a further two studies.

2.2 Inclusion Criteria

Following the searches, studies were included on the basis of the following: population, intervention, comparison and outcomes (PICO) criteria (Pettigrew & Roberts, 2006); Adults (18 years old and above), with a DSM III or DSM IV diagnosis of GAD or those with a baseline score of above 44 on the PSWQ; interventions received were psychological therapies for GAD including both HI and LI interventions; studies included a comparator arm which was either a waitlist control or comparative psychological treatment; reported the PSWQ as a primary or secondary outcome measure. Studies were only included if they were a randomised trial design and had been published in an English language peer reviewed journal.

2.3 Exclusion Criteria

Studies were excluded on the basis of the following criteria: if patients had a co-morbid diagnosis of psychosis, bipolar-affective disorder, panic disorder, seasonal

affective disorder, organic brain disorder, study design was not randomised (e.g. case series designs or single arm trials); studies did not report the PSWQ as either a primary or secondary outcome measure; studies did not report GAD only outcomes for all arms of studies; studies which included participants under the age of 18 years old and studies that were not in the English language.

2.4 Search Strategy

All databases were searched from the database inception to the third of January 2014. Studies were initially screened by title for relevance, remaining studies were screened by abstract against PICO criteria and final full text articles identified were screened. Of the studies reviewed by full text, approximately 18% were excluded for not reported GAD specific outcome data and not providing appropriate data after written request to the author. A further 19% of studies were excluded for not reporting the PSWQ or using a composite measure of anxiety rather than separate anxiety measures, 12% of the studies were excluded as the papers reported a trial protocol without subsequent published data. A single study was excluded as the paper reported a physical exercise as a treatment, which did not constitute a psychological intervention for GAD. A summary of studies excluded after assessment by full text can be found in Appendix 2. Figure 1 outlines the exclusion process by numbers included and excluded at each end point.

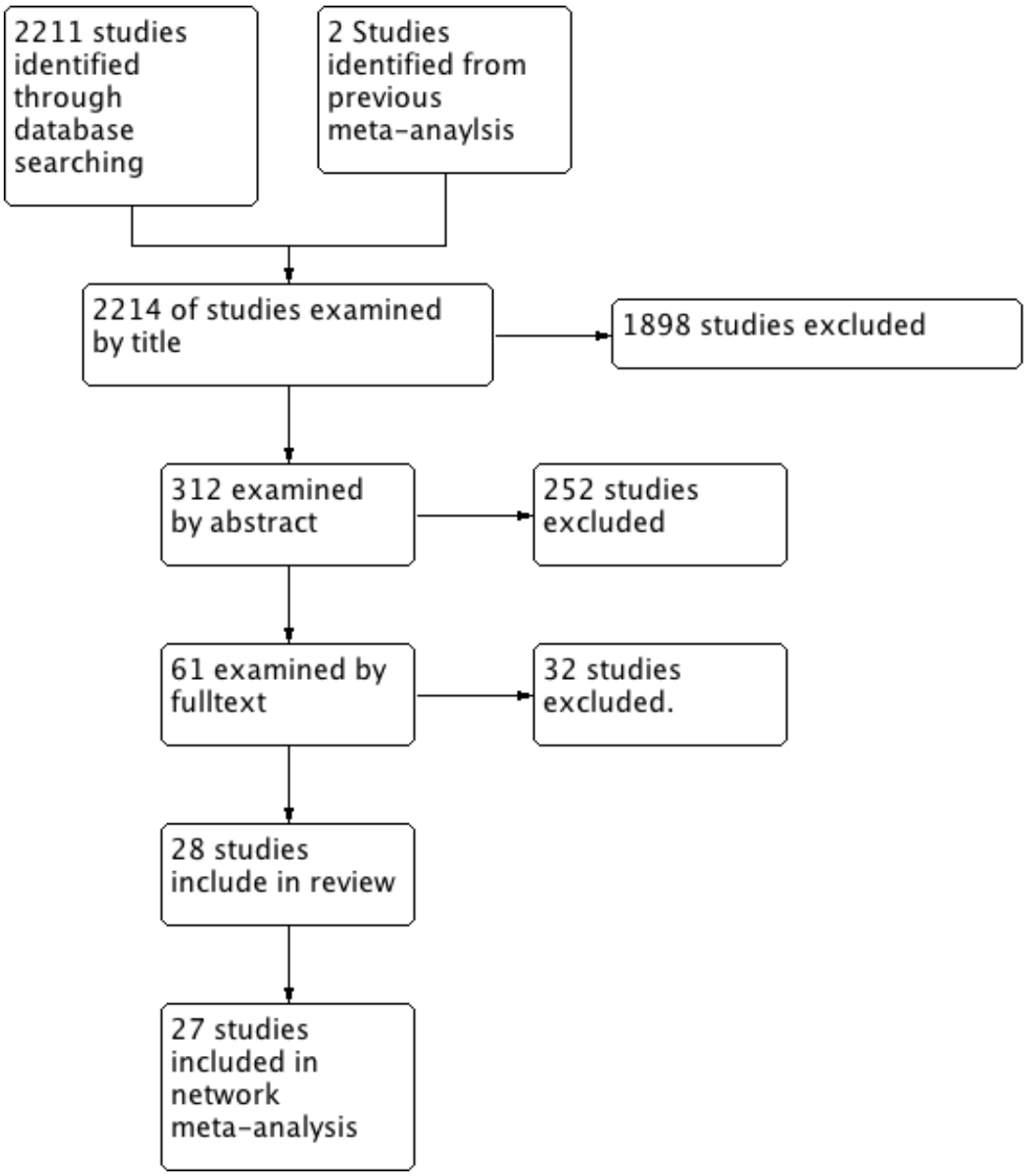

Figure 1: *Flowchart of study selection*

2.5 Risk of Bias

Risk of bias was conducted using Review Manager (Revman) Version 5.2 (http://ims.cochrane.org/revman) using the Cochrane Collaboration risk of bias tool. Studies were rated for selection bias, performance bias, outcome bias, detection, attrition bias, reporting bias and other sources of bias. Ratings of bias were high risk, unclear risk or low risk. A rating of high risk of bias was made when plausible bias that would seriously weaken the confidence of the study results was present, for example a failure to employ random allocation. A rating of unclear risk of bias

was made when plausible bias that could raise doubts was identified by the information provided by the study authors and did not allow a clear decision to be made. A rating of a low risk of bias was made when the plausible risk of bias was unlikely to seriously alter the confidence of the study results (Higgins & Green, 2011).

2.6 Meta-Analysis and Network Meta-Analysis

Studies included in pairwise comparisons were grouped by common intervention. Studies that reported two or more arms were split into separate two-way comparisons and the waitlist control group was split. Meta-analyses were conducted for class of interventions using Review Manager (RevMan) Version 5.2 for all time points where sufficient data was available. In order to assume a more conservative assessment of treatment effect intent-to-treat (ITT) data was used when reported. The comparisons conducted used baseline and end of treatment. The PSWQ was used as the outcome measure of interest, all analysis used reported mean end-point scores on the PSWQ and 95% confidence intervals were calculated.

All available within-study comparisons were then synthesised into a network meta-analysis. The NWA analysis of the available data was conducted using the mean change and standard deviation of change (SD of change) from baseline to post-treatment when reported. If the mean change and SD of change was not reported or could not be calculated using methods described in the Cochrane handbook (Higgins & Green, 2011) then the study reported post-treatment outcome and post-treatment standard deviation (SD) was used (Dias, Welton, Sutton, & Ades, 2011; Senn, Gavini, Magrez and Scheen, 2012). Study interventions included in the network meta-analysis were coded according type of intervention. This resulted in study interventions being classified into 11 different types: first wave, CBT, second wave CBT – Intolerance of Uncertainty (IoU), second wave CBT – Metacognitive Therapy (MCT), third wave CBT, iCBT, Enhanced CBT, Behavioural

Activation (BA), Applied Relaxation (AR), Psychodynamic, Non-Directive Supportive Intervention and Waitlist Control. A description of each intervention type is presented in Table 1. Studies, which used variations of the same treatment, such as two iCBT conditions, were separated into paired comparisons with the common comparator. R version 3.2 (http://www.r-project.org/) and WinBUGS Version 1.4 (Lunn, Thomas, Best & Spiegelhalter, 2000) were used for analysis.

Table 1: *Description of intervention classification*

Intervention Type	Description
1st Wave CBT	Traditional Beckian Cognitive Behavioural Therapy. Interventions include cognitive restructuring, overcoming avoidance and relaxation. The focus of the interventions is on worry as a consequence of anxiety rather than a process that maintains it. Delivered either via group or individual treatment.
2nd Wave CBT - IoU	Second wave CBT that focuses on the worry as a process, focus on problem solving, positive and negative beliefs about worry, intolerance of uncertainty and emotional avoidance. Intervention applies the Dugas et al. (1997) model in either individual or group treatment.
2nd Wave CBT – MCT	Second wave CBT treatment that focuses on worry as a process and the high order meaning and beliefs associated with worry. Interventions employ the Wells (2009) MCT model in either individual or group treatment.
3rd Wave CBT	Interventions that focus on Mindfulness, Acceptance and do not attempt to restructure cognitions. Interventions adopt a more accepting relationship with cognitions and experience. This may also include a spiritual element within the intervention framework, but retains a clear focus on acceptance/ mindfulness. (Romer and Orsillo, 2007) Delivered either via group or individual treatment.
iCBT	CBT models that are primarily delivered using an Internet based computer program with or without clinician support.
Enhanced CBT	First wave CBT with additional elements added to increase effectiveness. This may include interpersonal elements, motivation enhancement, behavioral enhancement or emotional focus. Delivered either via group or individual treatment.
BA	Behavioural Activation approaches where the main focus of the intervention is increasing activity and employing manualised treatment such as Addis and Martell's (2004) BA protocol. Delivered either via group or individual treatment.
AR	The primary focus of Applied Relaxation is the physical de-arousal of the individual and teaching techniques to induce relaxation in response to stimulus. Interventions focus on using protocols such as Öst (1987). Delivered either via group or individual treatment.
Psychodynamic	Interventions that apply psychodynamic theory to the treatment of GAD. The primary objective is to enhance the individual's understanding, awareness, and insight about repetitive conflicts (intrapsychic and interpersonal). Delivered either via group or individual treatment.

Table 1: *Continued*

Intervention Type	Description
Non-Directive Supportive intervention	Interventions that apply non-directive intervention such as the group or individual discussion. Therapists assume a supportive, facilitative role encouraging individuals to share experiences and to provide support for each other, discuss coping skills and think about anxiety symptoms and experience. Therapists teach no specific skills or provide differential reinforcement for any particular mode of coping.
Waitlist Control	No intervention or delayed treatment condition with no intervention. This includes no intervention control. This includes Minimal Contact conditions with no therapeutic intervention.

3. Results

3.1 Description of Studies

Twenty-eight studies met the inclusion criteria. Participants were drawn from populations within the USA (9), Australia (5), Sweden (5), Canada (5), Germany (4), the UK (1), the Netherlands (1) and Iran (1). Gender distribution between studies was highly variable, ranging from 100% women to 48% women. Ninety-six percent of the studies included in the review reported a gender distribution of 50% or greater. The mean age of participants also varied across studies, ranging from 20.1 to 68.3 years old. Twenty-four studies reported the use of a general adult sample with inclusion criteria of 18 years and above. Five studies reported using an older adult sample. The older adult studies varied in the definition of an older adult. Two studies defined older adults as 60 years and over, two studies defined older adults as 65 years and above and a single study used a definition of an older adult as 55 years and above. The mean age of participants in older adult studies varied, ranging from 66.20 to 70.6 years old. The rate of medication use between studies also varied substantially and ranged from 0% to 68.18%. Treating clinicians included clinical psychologists; licensed therapists, doctoral clinical psychology students, counsellors and masters level therapists. Table 2 outlines the demographic features of each study.

All studies employed a randomised control design or randomised assignment design. All studies reported a DSM-III or DSM-IV primary diagnosis of GAD as a study inclusion requirement. A variety of diagnostic methods were used in establishing a diagnosis of GAD. These ranged from using self-reported questionnaires to use of standardised diagnostic clinical interviews for anxiety disorders. Table 3 outlines the design features of each study.

All of the included studies reported the delivery of at least one psychological intervention. Twenty-one studies employed a two-arm trial design; seven studies employed a three-arm trial design. Studies varied in comparison conditions, ranging from waitlist control, minimal contact control, usual care to an active psychological treatment. Sixteen of the included studies employed a waitlist or minimal contact control and 11 studies employed an active treatment comparator. All studies included at least one validated self-report measure, which included the PSWQ. Twenty-seven studies reported the PSWQ as a primary outcome measure; a single study (Leichsenring et al., 2009) reported the PSWQ as a secondary outcome measure. Table 4 summarises the reported outcomes of each study's primary outcome measure at post-treatment and follow up, attrition in studies and the number of individuals judged to be no longer meeting clinical criteria at each time point and risk of bias of each.

3.2 Quality Assessment and Risk of Bias

The standard reporting of each study design was mixed. To quantify this the quality of study methodology and reporting were assessed for risk of bias using the Cochrane collaboration risk of bias tool using RevMan version 5. Twelve studies were at low risk for sequence generation and 10 of these were at a low risk of bias for allocation of concealment. Two studies (Newman et al., 2011; Westra et al., 2009) were at high risk of bias for allocation of concealment as they both reported that a study researcher used a numbers table to allocate participants. Fifteen studies were at an unclear risk of sequence generation and in 14 of these studies

there was an unclear risk of bias for allocation of concealment, as authors reported randomisation, but reported no specific details of the randomisation process. A single study (Dugas et al., 2003) was at low risk of allocation of concealment as the authors reported that an independent researcher conducted randomisation and allocation occurred at assessment with an independent assessor prior to entry into the study. Two studies were at high risk of bias for sequence generation and allocation of concealment. One study (Borkovec et al., 1993) reported randomisation of participants in waves based on therapist availability. One study (Westra et al., 2009) reported the use of a numbers table in allocation by a member of the research team.

All studies were assessed as having high risk of bias for the blinding of participants and personnel, as it was not possible to blind either the participant or therapist to the intervention received. All studies reported self-rated outcomes as primary measures of assessment and were considered a high risk of bias as blinding of researchers to treatment allocation until after data analysis was not reported. A number of studies reported the use of clinician assessment and this was considered separately. Ten studies were at low risk of bias for assessors, reporting the use of independent assessors blinded to the treatment condition. Nine studies were at an unclear risk of bias for assessors, as they did not report sufficed detail to determine if assessors were blind to participant allocation. For incomplete outcome data 21 studies were at low risk of bias and three were at high risk of bias. Eighteen studies were at a low risk of bias for selective reporting (for example, reporting intent-to-treat data in analysis). Eight studies were a high risk of bias for selective reporting as they reported completer data only. Nineteen studies were at low risk of other sources of bias as they reported the use of adherence measures and treatment manuals in studies, eight studies were at high risk of bias as it was not reported if adherence and integrity checks for the study interventions had been made or reported checks where made as part of clinical supervision by therapist

supervisors. Six studies reported a CONSORT compliant RCT design. Figure 2 provides a summary of the assessed risk of bias of all included studies.

The risk of bias for individual studies is summarised in table 4. Studies were rated as high risk of bias if they reported high risk of bias in areas additional to blinding of participants and personnel and self-repot outcome assessment. Studies were rated as unclear risk if they reported unclear risk in one or more areas. Studies were classified as low risk if the study rated all domains as low risk outside blinding of participants and personnel and self-report outcome assessment.

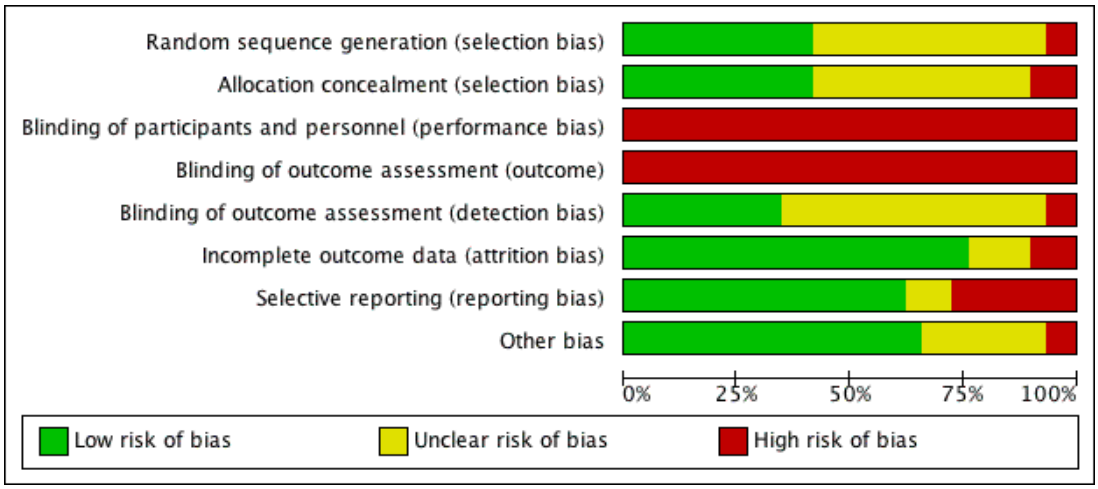

Figure 2: *Risk of bias summary*

3.4 Pairwise Meta-Analysis

The 28 included studies explored the effect of different types of treatments (CBT, AR, Psychodynamic, BA) with 21 studies providing data for two-way comparisons. Where insufficient data was available for comparisons findings are reported narratively. Analysis of CBT was also further delineated into first wave, second wave and third wave CBT treatments, iCBT treatments and CBT treatment for older adults. All comparisons used study post-treatment end point data to assess mean difference between comparators and determine the reduction of self-reported pathological worry as captured by the PSWQ (summarised in Table 5).

Table 2: *Summary of studies' demographic features*

Study	Population	Mean age at recruitment	Size and gender ratio at start of trial	Psychoactive medication use	Treating clinicians
Andersson et al., 2012	Swedish, adult community	41.3	81, 76.5% female	32.1%	Therapists in final year of clinical doctorate, licensed psychologists, CBT therapists.
Borkovec et al., 1993	US, adult community	37.5	63, 65.5% female	19.0%	Therapists with mean experience of 9 years, advanced clinical graduate students.
Chen et al., 2013	Australian, adult community	39.3	49, 77.6% female	6.1%	Psychologist with 2 years experience. Psychology interns with 4 years experience.
Dugas et al., 2003	Canadian, adult community	41.2	52, 71.0% female	26.9%	Licensed clinical psychologists with mean experience 6 years (range 2 to 12 years).
Dugas et al., 2010	Canadian, adult community	38.5	66, 66.2% female	55.4%	Licensed clinical psychologist with 5 years clinical experience.
Hayes Skelton et al., 2013	US, adult community	32.9	81, 65.5% female	28.4%	Post doctoral fellows and advanced doctoral students.
Hoyer et al., 2009	German, adult clinical	45.4	98, 78.0% female	9.6%	Clinical psychologists in postgraduate psychotherapy training.
Kozycki et al., 2009	Canadian, adult community	43.5	20, 60.0% female	68.2%	CBT therapist and counsellor.
Landoucer et al., 2000	Canadian, adult community	39.7	26, 76.9% female	34.1%	Licensed psychologists, post-doctoral researcher, and doctoral students. Mean experience of 4.7 years (range 2 to 10 years.

Table 2: *continued*

Study	Population	Mean at recruitment	Size and gender ratio at start of trial	Psychoactive medication use	Treating clinicians
Leichsenring et al., 2009	German, adult clinical	42.5	57, 80.7% female	0.0%	Licensed CBT therapists with mean experience of 16.3 years (range: 12 to 30 years), licensed psychodynamic therapists with mean experience of 18.7 (range: 4 to 26 years).
Newman et al., 2011	USA, adult community	37.1	83, 75.0% female	33.7%	Doctoral level psychologists with 2 years experience.
Newman et al., 2013	USA, adult community	42.1	34, 58.8% female	38.2%	Post doctoral fellow, graduate students with CBT training with a year experience of GAD treatment protocol.
Öst et al., 2000	Swedish, adult community	40.1	33, 77.2 female	45.0%	Therapists with 8 and 16 years clinical experience.
Paxling et al., 2011	Swedish, adult community	46.9	89, 79.8% female	37.1%	Final year psychology trainee.
Rezvan et al., 2008	Iranian, adult university clinical	20.1	36, 100.0% female	Not reported	University counseling service therapists.
Robinson et al., 2010	Australian, adult community	46.9	150, 68.3% female	32.4%	Clinician, background not described.
Roemer et al., 2008	USA, adult clinical	33.6	31, 71.0% female	25.8%	Doctoral students under supervision of study authors.
Stanley et al., 1996	USA, older adult community	68.3	46, 70.8% female	0.0%	Advance level graduate students trained in both treatment interventions.
Stanley et al., 2003	USA, older adult community	66.2	80, 75.0% female	0.0%	Post doctoral psychological fellows and advanced graduate students trained in CBT.

Table 2: *continued*

Study	Population	Mean at recruitment	Size and gender ratio at start of trial	Psychoactive medication use	Treating clinicians
Stanley et al., 2009	USA, older adult clinical	66.9	134, 78.4 female	41.8%	Masters level CBT therapists, pre-doctoral intern, post-bachelors level therapist with mean experience 2.8 years.
Titov et al., 2009	Australian, adult community	44.0	47, 76.0% female	29.0%	Clinical psychologist.
Titov et al., 2010	Australian, adult community	40.0	34, 68.0% female	47.4%	Clinical psychologist.
Van Der Heiden et al., 2012	Netherlands, adult clinical	35.0	126, 73.0% female	28.0%	Staff psychologists and CBT therapists with a mean experience of 5.6 years.
Wells et al., 2010	UK, adult clinical	49.1	20, 48.0% female	55.0%	Therapist's background not reported.
Westra et al., 2009	Canadian, adult community	41.5	100, 67.0% female	22.4%	Clinical psychologist, doctoral clinical psychology students.
Wetherell et al., 2003	USA, older adult clinical	67.1	75, 80.0% female	40.0%	Clinical psychologist and advanced doctoral clinical psychology students.
Wetherell et al., 2011	USA, older adult clinical	70.8	22, 47.5 female	19.0%	Post doctoral and master level therapists with 2 years clinical experience.
Zinbarg et al., 2007	USA, adult community	41.9	20, not reported	38.8%	Doctoral level therapists, clinical post-doctoral fellow.

Table 3: *Summary of studies' design features*

Study	Design	Comparison Group	Intervention	Individual/ Group delivery	Duration	Manual/ Integrity Checks	Outcomes measures	Assessment points.
Andersson et al., 2012	RCT	Waitlist	Internet-based Psychodynamic therapy (PT): Focus on breaking unconscious patterns contributing to emotional difficulties Internet Based CBT (iCBT): Focus on applied relaxation, problem solving, cognitive restructuring	Individual	8 sessions, PT = 113 minutes CBT = 92 minutes.	PT-.Based on Make the Leap self-help book. iCBT- Based on Paxling et al. 2011 treatment Integrity: Checks not reported	PSWQ, GAD-Q-IV, MADRS-S, QOLI, STAI, BDI-II, BAI	Pre- and post-treatment, 3 and 18 months
Borkovec et al., 1993	Random assignment	Non-directive control: exploration of life experience	Applied Relaxation (AR): Focus on physical relaxation CBT: Focus on exposure, cognitive restructuring challenging dysfunctional assumptions	Individual	12 sessions, 4 X 90 minutes, 9 X 60 minutes	AR: Berstien & Borkovec (1973) manual CBT: Beck & Emery (1985) Integrity: Assessed from audiotapes from 20% of sessions. Checked by clinical graduate students	PSWQ, STAI, ZSRA, RRAQ, BDI	Pre- and post-treatment, 6 and 12 months
Chen et al., 2013	RCT	Waitlist	Behavioural Activation for Worry (BAW): Focus on creating awareness of avoidance relating to worry and developing alternative goals	Group	8 sessions, length not reported	Adaption of Addis & Martell (2004) Overcoming depression one step at a time Integrity checks not reported	PSWQ, GAD-Q-IV, DASS-21, W&SAS, IUS, CBAS	Pre- and post-treatment, 3 months

Table 3: *continued*

Study	Design	Comparison Group	Intervention	Individual/ Group delivery	Duration	Manual/ Integrity Checks	Outcomes measures	Assessment points.
Dugas et al., 2003	RCT	Waitlist	AR: Focus on physical relaxation CBT: Focus on recognition of uncertainty, cognitive exposure, re-evaluation of usefulness of worry	Individual	12 sessions, 60 minutes	AR: Based on Berstein & Borkovec (1973) & Öst (1987) CBT: Based on Dugas et al. (1998) Integrity: Assessed by audio recording. Checked by research assistant	PSWQ, WAQ, STAT-T, BDI-II, CGII- SL	Pre- and post-treatment 6,12 and 24 months
Dugas et al., 2010	RCT	Waitlist	CBT: Focus on recognition of uncertainty, cognitive exposure, re-evaluation of usefulness of worry	Group	14 sessions, 120 minutes	Based on Dugas & Roichaud (2007) Integrity: Assessed by audio recording Checked by advanced graduate student	PSWQ, WAQ, IUS, BAI, BDI, SAS	Pre- and post-treatment 6, 12 and 24 months.
Hayes Skelton et al., 2013	Random assignment	AR: focus on physical relaxation	Acceptance Based Behavioural Therapy (ABBT): Focus on modifying problematic relationship with internal experience	Individual	16 sessions, 4 X 90 minutes, 12 X 60 minutes	AR: Based on Bernstein, Borkevec, Hazlett-Stevens (2000) & Öst (2007) ABBT: Based on Orsillio & Roemer (2011) Integrity: 198 sessions rated for adherence by clinical psychology doctoral students	PSWQ, DASS-21,STAI, BDI-II, QOLI	Pre- and post-treatment, 6 months

Table 3: *continued*

Study	Design	Comparison Group	Intervention	Individual/ Group delivery	Duration	Manual/ Integrity Checks	Outcomes measures	Assessment points.
Hoyer et al., 2009	RCT	Waitlist	AR: Focus on physical relaxation Worry Exposure (CBT): Focus on psycho-education, overcoming avoidance and habituation	Individual	15 sessions, duration not reported	AR: Based on Öst (1987) CBT: Based on Becker and Margraf (2002) Integrity: 25% of sessions reviewed rated by independent clinicians	HAMA, STAI-T, PSWQ, MCQ, WBSI GSI, HAMD, BDI	Pre- and post-treatment, 6 months, 12 months
Kozycki et al., 2009	Random assignment	CBT: relaxation, cognitive restructuring and worry exposure	Spiritually Based Intervention (SBI): Focus on spiritual wellbeing, meditation, acceptance and problematic internal experience	Individual	12 sessions, 50 minutes	CBT: Based on Zinbarg, Craske & Barlow (2006) SBI: Based on Walsh (1999) Essential Spirituality Integrity checks not reported	PSWQ, HAMA, CGI, BAI, IUS, BDI, SAS-SR	Pre-and post-treatment, 3 months, 6 months
Ladoucer et al., 2000	RCT	Waitlist	CBT: Focus on recognition of uncertainty, cognitive exposure, re-evaluation of usefulness of worry	Individual	16 sessions, 60 minutes	CBT: Based on Dugas (1998) Integrity: Audio recording of 3 sessions for each participant. Rated by graduate student	PSWQ, WAQ, BAI, BDI, SORS	Pre- and post-treatment, 6 months, 12 months

Table 3: *continued*

Study	Design	Comparison Group	Intervention	Individual/ Group delivery	Duration	Manual/ Integrity Checks	Outcomes measures	Assessment points.
Lieschernig et al., 2009	RCT	Waitlist	Short Term Dynamic Psychotherapy (STTP): Focus on core conflictual relationship themes associated with symptoms CBT: Focus on relaxation training, worry exposure, cognitive restructuring	Individual	30 sessions, 50 minutes	STTP: Based on Crits-Christoph et al. (1995) CBT: Based on Borkovec & Ruscio (2001) Integrity: All session audiotaped. 57 sessions were rated by between 3-9 independent raters	HARS, PSWQ, STAI-T, BAI, HADS, BDI, IIP	Pre- and post-treatment, 6 months
Newman et al., 2011	Random assignment	CBT+ Supportive Listening (SL)	CBT + Interpersonal Emotional Processing (IEP): Focus on relaxation, cognitive restructuring, addressing interpersonal problems and emotional processing	Individual	14 sessions, 50 minutes CBT, 50 minutes SL or IEP	CBT: Based on Borkovec & Ruscio (2001) IEP: Based on Safran and Segal (1990) Integrity: Audiotapes checked by graduate coders using treatment manuals	PSWQ, HARS, STAI, RRAQ, HADS, IPP	Pre- and post-treatment 6,12 and 24 months
Newman et al., 2013	Random assignment	Group CBT (gCBT)	6-session gCBT: (CBGT): Focus on relaxation training, worry exposure, cognitive restructuring challenging dysfunctional assumptions 6-session computer assisted gCBT (CAGCBT): As above with computer prompted homework tasks	Group	CBGT and CAGCT: 6 sessions, 120 minutes gCBT: 12 sessions, 120 minutes	CBT: Based on Beck & Emery (1985), Bernstien et al., 2000) Integrity checks not reported	HARS, PSWQ, STAI-T	Pre- and post-treatment 6 and 12 months

Table 3: *continued*

Study	Design	Comparison Group	Intervention	Individual/ Group delivery	Duration	Manual/ Integrity Checks	Outcomes measures	Assessment points.
Öst et al., 2000	Random assignment	AR: focus on physical relaxation	CBT: Focus on exposure and cognitive restructuring, and challenging dysfunctional assumptions	Individual	12 sessions, 60 minutes	AR: Based on Öst (1987) CBT: Based on Beck, Emery & Greenberg (1985) Integrity: Checks not reported	HAMA, BAI, PSWQ, CSAQ, BDI	Pre- and post-treatment, 12 months
Paxling et al., 2011	RCT	Waitlist	iCBT: Focus on relaxation, cognitive restricting, worry exposure and problem solving	Individual	8 modules, mean clinician time: 91 minutes Integrity: checks not reported	iCBT: Guided self-help based on Borkovec & Costello (1993) and Öst (1987)	STAI-T, BDI, BAI, PSWQ, GAD-Q-V, QOLI, MADRS-S	Pre- and post-treatment, 12 and 36 months
Rezvan et al., 2008	RCT	Control	CBT: Focus on relaxation, cognitive distancing, worry awareness CBT+IPT: Focus on relaxation, cognitive distancing, worry awareness. Clarification interpersonal difficulty, communication analysis and reappraisal of interpersonal problems	Individual	8 Sessions, duration not reported	No reported manual treatment is based on. Integrity: No check reported	PSWQ, OHI, GAD-Q-V	Pre- and post-treatment, 12 months

Table 3: *continued*

Study	Design	Comparison Group	Intervention	Individual/ Group delivery	Duration	Manual/ Integrity Checks	Outcomes measures	Assessment points.
Robinson et al., 2010	RCT	Waitlist	iCBT: Challenging core beliefs and meta beliefs, graded exposure iCBT Clinician Assisted (CA): Challenging core beliefs and meta beliefs, graded exposure	Individual	6 sessions, iCBT CA-weekly email or telephone contact no longer than 10 minutes	iCBT: Based on Worry program (Titov et al., 2009) Integrity: Checks not reported	PSWQ, GAD-7, PHQ-9, K-10, SDS	Pre- and post-treatment, 3 months
Roemer et al., 2008	RCT	Waitlist	ABBT: Focus on increasing awareness of habitual responding, experimental avoidance, engaging in value directions	Individual	16 sessions, 4 X 90 minutes, 12 X 60 minutes	ABBT: Based on Roemer & Orsillo (2007) Integrity: Two sessions from each participant randomly selected and reviewed by graduate students	PSWQ, DASS, BDI, QOLI, AAQ, MAAS	Pre-and post-treatment, 3 and 9 months
Stanley et al., 1996	Random assignment	Supportive Psychotherapy: focus on non-directive discussion of anxiety symptoms.	CBT: Focus on relaxation, cognitive restructuring, exposure and challenging dysfunctional assumptions	Group	14 sessions, 90 minutes	CBT: Based on Borkovec & Costello (1993) and Craske, Barlow & O'Leary (1992) Integrity: Monitored using checklist for each treatment condition. Videotape monitored by clinical psychologist	WS, PSWQ, STAI-T, HAMA, BDI, HAMD, FQ	Pre- and post-treatment, 1 and 6 months

Table 3: *continued*

Study	Design	Comparison Group	Intervention	Individual/ Group delivery	Duration	Manual/ Integrity Checks	Outcomes measures	Assessment points.
Stanley et al., 2003	Random assignment	Minimal contact: weekly telephone check	CBT: Focus on relaxation, cognitive restructuring, exposure and challenging dysfunctional assumptions	Individual	15 sessions, duration not reported	CBT: Based on Borkovec & Costello (1993) and Craske, Barlow & O'leary (1992) Integrity: 20% of video taped session rated for competence and adherence by independent expert rater	PSWQ, WS, STAI, HAMA, BDI, HAMD, FQ, QOLI,	Pre- and post-treatment, 3, 6 and 12 months
Stanley et al., 2009	Random assignment	Enhanced usual care: Bi weekly telephone symptom check	CBT: Focus on relaxation, cognitive restructuring, exposure, sleep management, problem solving, motivational interviewing	Individual	10 sessions, duration not reported	CBT: Based on Hopko and Diefenbach (2004) Integrity: 20% of session audiotapes rated by treatment manual authors (Hopko & Diefenbach.)	PSWQ, GADSS, HARS, BDI-II, SF-12	Pre- and post-treatment 6,9,12 and 15 months
Titov et al., 2009	RCT	Waitlist	iCBT: Challenging core beliefs and meta beliefs, graded exposure. Clinician assisted contact via email	Individual	6 sessions, over 9 weeks. Mean time per patient 130 minutes	CBT: Worry Program (Titov et al., 2009) Integrity: Checks not reported	GAD-7, PSWQ, PHQ-9, K-10, SDS	Pre- and post-treatment.
Titov et al., 2010	RCT	Waitlist	iCBT: Generic CBT, disorder specific material GAD, social phobia and panic disorder	Individual	6 sessions, over 8 weeks, duration not reported	iCBT: Based on Andrews et al., (2003), Titov et al., (2009), Titov et al., (2008), Wims et al.,(2010)	GAD-7, PHQ-9, PSWQ, PDSS-SR, K-10, DASS-21, NEO-FFi-N	Pre- and post-treatment, 3 months

Table 3: *continued*

Study	Design	Comparison Group	Intervention	Individual/ Group delivery	Duration	Manual/ Integrity Checks	Outcomes measures	Assessment points.
Van Der Heiden et al., 2012	RCT	Waitlist	CBT Intolerance of Uncertainty (IUT): Focus on worry awareness, problem orientation, exposure, re-evaluation of belief about worry CBT – Metacognitive Therapy (MCT): Focus on identifying metacognition, negative and positive metacognition, modifying cognitive bias and attention training	Individual	14 sessions, duration not reported	IUT: Based on Dugas & Robichuad (2007) MCT: Based on Wells (1997) Integrity: Review of 71 randomly selected session recording by trained clinical psychology students	PSWQ, STAI-T, SCL-90, BDI-II, MCQ, IUS	Pre- and post-treatment, 6 months
Wells et al., 2010	Random assignment	AR: focus on physical relaxation	MCT: Focus on identifying metacognition, negative and positive meta cognition, modifying cognitive bias	Individual	8 to 12 sessions, 45 to 60 minutes	AR: Based on Öst (1987). MCT: Based on Wells (1997) Integrity: Therapy notes and active case reviewed in fortnightly supervisor for adherence	STAI-T, PSWQ, BAI, BDI, MCQ	Pre- and post-treatment, 6 and 12 months
Westra et al., 2009	Random assignment	CBT: focus on relaxation, cognitive restructuring, exposure challenging dysfunctional assumptions	CBT+ Motivational Interviewing (CBT+MI): Focus on relaxation, cognitive restructuring, exposure challenging dysfunctional assumptions. Understanding ambivalence, developing self efficacy	Individual	8 sessions, 6 X 120 minutes, 2 X 60 minutes	CBT: Borkovec & Costello (1993) MI: Based on Miller & Rollnick (2002) Integrity: Assessed using CTRS (Young & Beck, 1980) 20% rated by clinical graduate students	PSWQ, DASS-21, SDS, MCQ, GCI, CMOTS	Pre- and post-treatment, 6 and 12 months

Table 3: *continued*

Study	Design	Comparison Group	Intervention	Individual/ Group delivery	Duration	Manual/ Integrity Checks	Outcomes measures	Assessment points.
Wetherell et al., 2003	RCT	Waitlist	CBT: focus on relaxation, cognitive restructuring and worry exposure and challenging dysfunctional assumptions Discussion group (DG): Discussion of worry provoking topics	Group	12 sessions, duration not reported	CBT: Based on Craske, Barlow & O'Leary (1992) DG: Based on Hyman (1980) Integrity: All session audiotaped and review by CBT expert in anxiety disorders.	HARS, PSWQ, BAI, HAMD, BDI, SF-36	Pre- and post-treatment, 6 months
Wetherell et al., 2011	Random allocation	CBT: Focus on symptom monitoring, attention training, thought stopping, relaxation	ACT: Focus on willingness and non-judgmental observation of worry, core values, mindfulness and acting in value directions	Individual	12 sessions, 60 minutes	CBT: Based on Wetherell et al (2009) ACT: Based on Hayes, Strosahl &Wilson (1999) Integrity: Sessions videotaped and reviewed in weekly supervision, external rater evaluated adherence	HAMA, PSWQ, BDI-II, SF-36	Pre- and post-treatment, 6 months
Zinbarg et al., 2007	RCT	Waitlist	CBT: Focus on relaxation training, cognitive restructuring, exposure and challenging dysfunctional assumptions	Individual	12 Sessions, 60-75 minutes.	CBT: based on Master Your Worry (Craske & Barlow, 1994) Integrity: Audio or video tapes were randomly selected for 16 patients, Rated against protocol by two graduate students	PSWQ, BAI, DASS-21,	Not reported

Table 4: *Summary of studies' outcomes and risk of bias*

Study	Outcome at end of treatment	Outcome at follow up	Total study attrition (%)	Percentage rated as recovered*	Study risk of bias
Andersson et al., 2012	Both CBT and Psychodynamic treatment showed moderate within group effects. Waitlist control showed a small within group effect. Post-treatment between group effect sizes were small for both CBT and PD. There was no statistical difference between CBT and PD.	3 months: continued mean reduction on PSWQ for CBT and PD condition. Increase in reported worry in waitlist condition. Moderate between group effect size between intervention and waitlist. Small between group effects favoring CBT over PD, this was not statistically significant. 18 months: further mean reduction in PSWQ score in CBT and PD conditions. Large within group effect sizes reported for both treatments pre-treatment to follow up.	7 (8.64)	End of treatment: 26.1% in CBT condition, 15.4% in the psychodynamic and waitlist conditions were rated as recovered. 3 months: 52.2% in CBT condition, 50% in psychodynamic condition and 10% in waitlist condition were rated as recovered. 18 months: 54.5% in CBT condition and 62% in psychodynamic condition were rated as recovered.	Low Risk
Borkovec et al., 1993	Mean reductions on both the HARS and PSWQ for treatment conditions. CBT and AR were superior to ND. There was no difference between CBT and AR. All treatments showed large within group effect on HARS ND showed a medium within group effect in the reduction on the PSWQ. CBT and AR showed large within group effects in reductions on the PSWQ.	CBT and AR conditions were superior to ND. All treatments continued to show reductions in mean HARS and PSWQ score. There was no statistical difference between CBT and AR.	11 (17.01)	12 months 57.9% of CBT clients reached high-end state functioning status as opposed to 26.7% in ND condition and 37.5% in AR condition.	High Risk

Table 4: *continued*

Study	Outcome at end of treatment	Outcome at follow up	Total study attrition (%)	Percentage rated as recovered*	Study risk of bias
Chen et al., 2013	Greater reduction in worry symptoms in BAW condition in comparison to waitlist with large between group effect sizes. Reduction in depression symptoms with a large effect size. Improvements in cognitive avoidance and intolerance of uncertainty.	Reductions in self-reported worry maintained at follow up. Continued to improvement in self-reported functioning.	0 (0)	At end of treatment 56% of BAW group achieved significant reduction in worry compared to 33% in waitlist condition.	High Risk
Dugas et al., 2003	Reduction on the ADIS-IV, PSWQ, WAQ, IUS, BAI, BDI and SIS. Large pre-post treatment effect sizes for all measures.	Treatment gains were maintained on all measures at all follow up points. Self-reported worry significantly decreased over follow up period in the CBT condition	5 (10.10)	60% of participants no longer met GAD criteria post-treatment, 88% at 6 months follow up and 83% at 12-month follow up and 95% at 24 month follow up.	Low Risk
Dugas et al., 2010	Both AR and CBT conditions were superior to waitlist. Significant reductions in CBT condition compared to waitlist on PSWQ, CSR, WAQ and CGI. Significant reduction on CSR in AR condition in comparison to waitlist.	Treatment gains in GAD severity, pathological worry and clinical improvement were maintained, only CBT condition continued to improve. No significant between group difference between CBT and AR conditions.	7 (10.77)	In CBT condition 70% remission post-treatment, 76% at 6-month follow up, 84% at 24 months. In AR condition 55% were in remission post-treatment, 68% at 6 months, 65% at 12 months and 61% at 24 month follow up.	Unclear Risk

Table 4: *continued*

Study	Outcome at end of treatment	Outcome at follow up	Total study attrition (%)	Percentage rated as recovered*	Study risk of bias
Hayes Skelton et al., 2013	Improvements on PSWQ, DASS, STAI with large within group effect sizes. No differences between the ABBT and AR conditions.	Treatment gains were maintained at follow up with small effect size post-treatment to follow up. No difference reported between ABBT and AR conditions.	19 (23.45)	Post treatment 90% in ABBT condition and 69.7 % in AR of participants reported meeting diagnostic change criteria post treatment. At follow up 72% in ABBT and 70% in AR conditions no longer met diagnostic criteria.	Low Risk
Hoyer et al., 2009	Reduction on all primary treatment measures pre-post treatment in CBT and AR condition in comparison to waitlist. No difference between CBT and AR conditions.	Treatment gains maintained at follow up. Significant improvement on PSWQ in CBT condition. No significant difference between CBT and AR at either follow up points.	19 (23.45)	Post treatment 56% in CBT condition and 48% in AR condition reached full end-state functioning on HARS.	Unclear Risk
Kozycki et al., 2009	Reduction in HAM-A, BAI and PSWQ post-treatment in both CBT and SBI conditions with large within group effect sizes. There was no difference in treatment outcome between interventions.	Treatment gains maintained at follow up for both CBT and SBI conditions with large pre-treatment to follow up effect sizes. No differences between treatment conditions at either follow up time point.	4 (19.18)	Remission rate for CBT at post-treatment and 3 month follow up were 72.7% and 63.6% at 6 months. For SBI remission was 63.6% post-treatment and 45.4% at 3 and 6 months.	Unclear Risk
Ladoucer et al., 2000	Reduction on ADIS-IV, PSWQ, WAQ, BAI, BDI and SORS. Reductions in CBT condition on all measures with large effect sizes.	Treatment gains maintained and further reduction on all measures at 6 and 12 month follow up. No significant difference in post-test and follow up scores on all measures.	0 (0)	In CBT condition 77% did not reach diagnostic criteria for GAD post-treatment and 12 month follow up.	Unclear Risk

Table 4: *continued*

Study	Outcome at end of treatment	Outcome at follow up	Total study attrition (%)	Percentage rated as recovered*	Study risk of bias
Lieschernig et al., 2009	Improvement on HARS, PSWQ, STAI, BAI, HAD, BDI and IIP for both CBT and STTP with large within group effect sizes. CBT was superior to STTP on reduction in PSWQ and STAI.	Treatment gains were maintained at 6-month follow up with large within group effect sizes. CBT superiority in reductions on PSWQ and STAI was maintained.	5 (8.77)	Not reported.	Unclear Risk
Newman et al., 2011	Reduction on all primary measures pre-post treatment with large within group effect sizes. CBT + IEP was not superior to CBT on any measure.	Treatment gains were maintained across 2 year follow up, with large effect size pre-treatment to follow up on HARS. No statistical difference between CBT + IEP condition and CBT.	13 (15.66)	Post-treatment 73.5% in CBT - IEP condition and 55.6% in CBT condition did not meet criteria for GAD. At 2 year follow up 75% in CBT + IEP condition and 63.6% in CBT condition no longer met the criteria for GAD.	High Risk
Newman et al., 2013	Reduction on all anxiety measures in all treatment conditions with large within group effect sizes. Six-session computer assisted gCBT was superior to six session gCBT on a composite measure of anxiety (PSWQ, HARS, STAI-T). Neither brief group condition was superior to 12 sessions CBT on the anxiety composite.	Computer assisted gCBT was no longer superior to 6 session gCBT. Treatments did not differ at 6 and 12 months.	0 (0)	Not reported.	High Risk

Table 4: *continued*

Study	Outcome at end of treatment	Outcome at follow up	Total study attrition (%)	Percentage rated as recovered*	Study risk of bias
Öst et al., 2000	Reduction on BAI, STAI, CSAQ, BDI, PSWQ scores in both CBT and AR conditions. No difference between treatment conditions.	Reductions in BAI and CSAQ were maintained at follow up for both CBT and AR conditions. Improvements on BDI, STAT-T was maintained at follow up in CBT condition but not in AR condition. The AR group showed significant change on PSWQ post-treatment to follow up, CBT showed no change on PSWQ post-treatment to follow up.	3 (8.33)	Not reported.	Unclear risk
Paxling et al., 2011	Reductions on PSWQ, GAD-Q-IV, STAI, BAI, BDI, MADRSS-R and QOLI scores with large within and between treatment effect sizes for iCBT condition. ICBT was superior to waitlist.	Treatment gains maintained at follow 1 year and 3 year follow up with large effect sizes at 1 year follow up.	7 (7.97)	Post-treatment 42% receiving CBT and 2.3% of the waitlist reached recovery. At 1 and 3 years follow up 48.2% and 57.1% of the CBT group were classified as recovered.	Unclear Risk
Rezvan et al., 2008	Reduction in PSWQ and increase in OCI scores in CBT and CBT + IPT conditions. Both treatment conditions superior to control, there was no difference between treatment conditions.	Treatment gains were maintained at follow up there was no significant difference between treatment conditions.	0 (0.00)	Not reported.	Unclear risk
Robinson et al., 2010	Reduction in mean score on all measures with large within group effect in treatment condition. No difference between treatment groups.	Treatment gains maintained at follow up with large pre-treatment to follow effect size for treatment conditions, no difference between treatment groups.	22 (14.57)	Post-treatment 34% of treatment group and 10% of the control group were classified as recovered on GAD-7. At follow up 64% were classified as recovered.	Low risk

Table 4: *continued*

Study	Outcome at end of treatment	Outcome at follow up	Total study attrition (%)	Percentage rated as recovered*	Study risk of bias
Roemer et al., 2008	Reduction in means score on GAD-CSR, PSWQ, DASS, BDI and increase in QOLI with large within group effect sizes. ABBT treatment superior to waitlist.	Treatment gains were maintained for all outcomes with large effect sizes.	6 (19.35)	Post-treatment 78% of the treatment group no longer met GAD criteria. At 3 months 84% and at 9 months 76% were rated as no longer meeting GAD criteria.	Low risk
Stanley et al., 1996	Reductions on PSWQ, WS, HAMA, STAI, BDI and HAMD, there was no significant differences between CBT and SP conditions, both conditions reported large treatment effects.	Treatment gains were maintained for all outcome measures and no difference between CBT and SP conditions.	15 (32.6)	Recovery not reported. 11% (CBT) and 12% (SP) post-treatment and 22% (CBT) and 31% (SP) at follow up reached high end state functioning.	Unclear risk
Stanley et al., 2003	Improvement in worry, anxiety, depression and quality of life. CBT was superior to MCC conditions post-treatment.	Treatment gains were maintained at follow up for worry, anxiety, depression and quality of life.	10 (11.76)	Not reported.	Unclear risk
Stanley et al., 2009	Improvement on PSWQ in CBT conditions compared to EUC group. Improvement on GADSS in both CBT and EUC conditions. No difference between conditions.	Treatment gain maintained at 3 to 15 month follow up for both group.	18 (13.43)	Not reported.	Low risk
Titov et al., 2009	Improvement in post-treatment GAD-7, PSWQ, PHQ-9, K-10 and SDS favoring iCBT. With large pre-post treatment between group effect. .	N/A	9 (19.14)	63% of treatment group and 10% of controls met definition of recovery.	Low risk

Table 4: *continued*

Study	Outcome at end of treatment	Outcome at follow up	Total study attrition (%)	Percentage rated as recovered*	Study risk of bias
Titov et al., 2010	Improvement post-treatment on GAD-7, PSWQ, PHQ-9, K-10, DASS-21, NEO—FFI-N with medium within group treatment effects for GAD subgroup.	Continued improvement on all measures with larger treatment effect.	3 (8.82)	40% of treatment group and 8% of control group met remission criteria. **	Low risk
Van Der Heiden et al., 2012	Improvement post-treatment on PSWQ, STAI-T with large between group effect sizes, Improvement on SCL-90 and BDI-II. CBT intervention was superior to waitlist. MCT was superior to IUT on all outcome measures.	Maintenance of treatment gains MCT superior to IUT on PSWQ, STAI-T and SCL-90 measures.	32 (25.39)	91% IN MCT condition, 80% in IUT condition and 5% in waitlist group no longer met diagnostic criteria post-treatment. 93% in MCT condition and 90% in IUT condition no longer met diagnostic criteria at follow up.	Unclear risk
Wells et al., 2010	Reductions on PSWQ, STAI-T, BAI, BDI and MCI for both AR and MCT conditions. MCT superior to AR.	Treatment gains maintained at 6 and 12 months on PSWQ, STAI-T and MCQ. MCT superior to AR. MCT improved on all measures, AR improved on 3 measures.	0 (0.00)	Post-treatment: 80% recovery in MCT condition and 10% in AR condition on PSWQ. Follow up: recovery in MCT condition 70% (6 months) and 60% (12 months). AR condition 20% (6 and 12 months).	High risk
Westra et al., 2009	CBT-MI group outperformed CBT group over treatment with a moderate between group effect size on PSWQ. Both CBT-MI and CBT showed improvement on BDI, DASS, SDS, MC-30 and SDS.	Treatment gains maintained at follow up. There was no difference between MI-CBT and CBT at 6 and 12 month follow up.	14 (15.55)	At 12 months 74% of the CBT-MI and 61% of CBT condition no longer met GAD criteria.	High risk

Table 4: *continued*

Study	Outcome at end of treatment	Outcome at follow up	Total study attrition (%)	Percentage rated as recovered*	Study risk of bias
Wetherell et al., 2003	Improvement on PSWQ and BDI with large within group treatment effects. DG group showed medium treatment effect on PSWQ and BDI. CBT superior to DG and waitlist.	Treatment gains were maintained for active treatment conditions, no difference between conditions at follow up.	18 (24.00)	At 3 months 78% of the CBT, 61% of DG and 14% of waitlist conditions no longer met GAD criteria.	High risk
Wetherell et al., 2011	All participants in ACT condition showed an improvement in worry and depression. 5 out of 9 in the CBT condition improvement in anxiety and depressive symptoms, some reduction in worry but not significant.	Post-treatment gains maintained at follow up for both conditions.	6 (28.57)	Not reported.	Unclear risk
Zinbarg et al., 2007	Improvement on PSWQ, DASS with a large effect size. Moderate effect of treatment on BAI. CBT condition superior to Waitlist condition.	Not reported.	1 (5.26)	Not reported.	Unclear risk

Note: *Studies vary in reporting recovery and remission, **Remission reported whole sample, which includes individuals with Social Phobia, Panic Disorder and GAD.

3.4.1 CBT versus Waitlist Control

Fifteen studies compared CBT with waitlist. These included individual CBT (Dugas et al., 2003; Hoyer et al., 2009; Ladoucer et al., 2000; Rezvan et al., 2008; Stanley et al., 2003; Stanley et al., 2009; Van der Heiden et al. 2012; Wetherall et al., 2011, Zinbarg et al., 2007); group CBT (Dugas et al., 2010; Wetherall et al., 2003) and internet based CBT (iCBT) (Andersson et al., 2012; Paxling et al., 2011; Robinson et al., 2010; Titov et al., 2009; Titov et al., 2010). Individual and group treatments lasted between 8 to 15 sessions and iCBT treatments ranged between 6 to 8 sessions. Overall the post-treatment difference between treatment and waitlist groups was statistically significant, favouring CBT (MD= -10.33, 95% CI: -12.57 to -8.10). However there was considerable heterogeneity (I^2= 64%, Chi^2= 46.73, $p<0.01$) and difference between studies. Twelve studies (Andersson et al., 2012; Dugas et al., 2003; Dugas et al., 2010: Ladoucer et al., 2000; Paxling et al., 2011; Rezvan et al., 2008; Robinson et al., 2010: Stanley et al., 2003; Stanley et al., 2009; Titov et al., 2009; Van der Heiden et al. 2012; Zinbarg et al., 2007) reported reliable improvement using the Reliable Change Index of a change score on the PSWQ of seven or more points (Fisher, 2006) and three studies (Hoyer et al., 2009; Wetherall, et al. 2003; Titov et al., 2010) did not report reliable change. In relation to clinical recovery, which is defined as a patient reporting a score under the clinical cut-off of 45 (Behar, Alcaine, Zuelling & Borkovec, 2003), which differentiates dysfunctional from functional populations and also reports a statistically reliable change (Jacobson, Revernstorf & Follette, 1984; Fisher, 2006). Only one study (Rezvan et al., 2008) reported mean post-treatment scores under the clinical cut-off score of 45 on the PSWQ. The remaining studies all reported mean post-treatment scores above the PSWQ clinical cut-off indicating that at mean post-treatment worry remained at a clinically significant level.

Moderator analysis using meta-regression did not find effects for the percentage of medication; mean severity of self-reported worry at baseline and year

of publication. However, there was a trend for more recent studies to report smaller post-treatment differences.

3.4.2 CBT versus Applied Relaxation (AR)

Six studies compared directly CBT with AR (Figure 3). Five studies (Borkovec et al., 1993, Dugas et al., 2010; Hayes Skelton et al., 2013; Hoyer et al., 2009; Öst et al., 2000) reported that CBT was neither superior nor inferior to AR. A single study (Wells et al., 2010) reported a large between group effect size favoring CBT (d= 2.64, 95% CI: 1.35 to 3.71). Combining the studies the post-treatment difference between CBT and AR was not statistically significant (MD= -4.59, 95% CI= -11.54 to 2.36). Heterogeneity was high (I^2= 87%, Chi^2= 35.05, p<0.00001) and there was difference between studies. Exploratory analysis revealed one outlier (Wells et al., 2010) with a large effect size; this might be explained by the small sample size (N= 20). Other explanations include the quality of treatment received and possible researcher or clinician allegiance to the CBT treatment. Without this study the heterogeneity within the comparison was reduced and there was no difference between studies (I^2= 24%, Chi^2= 5.27, p= 0.20) and the overall mean difference between CBT and AR was reduced but did not alter the conclusions about CBT and AR's relative effectiveness (MD= -0.27, 95% CI= -3.29 to 2.75).

Overall five studies reported reliable improvements on the PSWQ post-treatment for the CBT treatment arms and three studies reported reliable improvements post-treatment for AR treatment arms. A single study did not find a reliable improvement for either the CBT or AR treatment arms and two studies reported post-treatment improvements that did not meet the reliable change criteria. A single study (Wells et al., 2010) reported post-treatment improvements for CBT treatment of 25.5 points on the PSWQ and a mean post-treatment score of 39, which reached the criteria for clinical recovery.

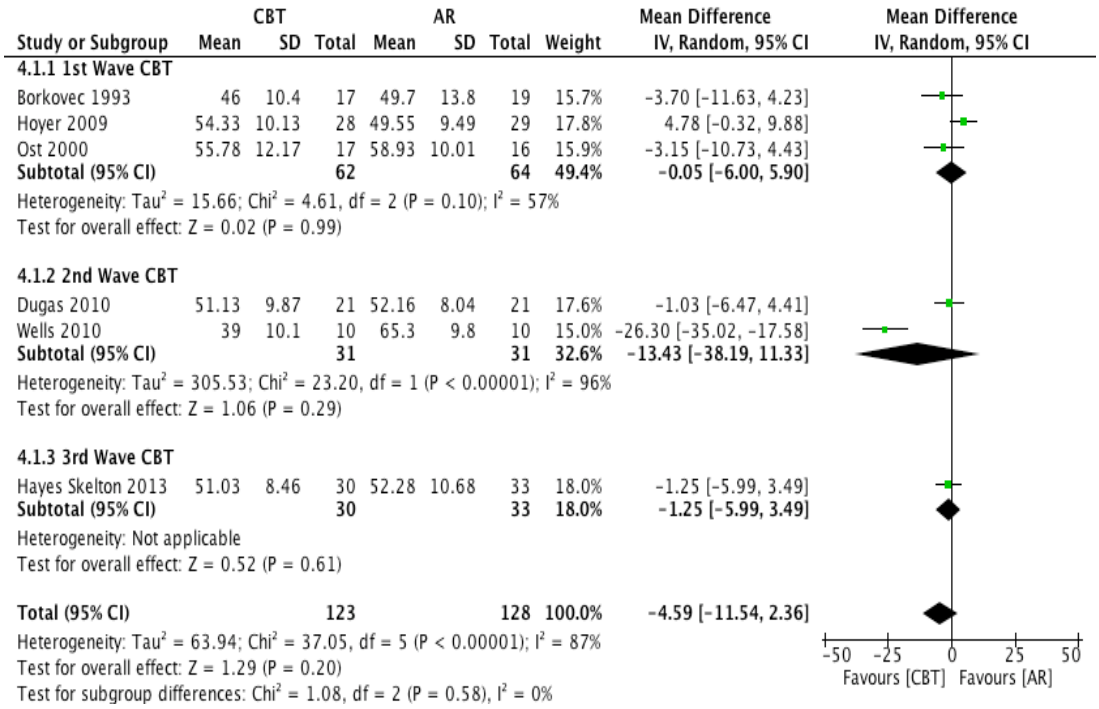

Figure 3: *Post-treatment mean difference CBT compared to applied relaxation*

3.4.4 CBT versus Psychodynamic Psychotherapy

Two studies directly compared CBT with psychodynamic psychotherapy (Andersson et al., 2012; Leichsering et al., 2009). Both studies compared a Short-Term Dynamic Psychotherapy (STDP) with a first wave CBT treatment. Both studies suggested that CBT was neither superior nor inferior to psychodynamic therapy reporting small between group effects for CBT (d= 0.08, 95 % CI: -0.65 to 0.81; d= 0.32, 95% CI: -0.21 to 0.84, respectively). Andersson et al. (2012) reported a reliable improvement on the PSWQ for both CBT (MD= 7.11) and Psychodynamic (MD= 7.53) treatment arms post-treatment. However, neither treatment reported reductions that would meet the criteria for clinical recovery of a score of 44 or below on the PSWQ. Leichsering et al. (2009) reported reliable improvements in self-reported worry for the CBT treatment post-treatment (MD= 13.62), the psychodynamic treatment reported an improvement (MD= 6.10), however this did not meet reliable change criteria. Neither treatment condition met the criteria for recovery post-treatment.

Table 5: *Study information of studies included in comparison*

	CBT versus Waitlist	**CBT versus applied relaxation**	**CBT versus psychodynamic Psychotherapy****	**CBT versus other treatment comparator****	**CBT versus CBT with other additional element****	**Psychodynamic psychotherapy versus waitlist****	**Behavioural activation versus waitlist****
Number of Studies	16	6	2	3	3	1	1
Study	1. Dugas et al., 2003 2. Hoyer et al., 2009 3. Ladoucer et al. 2009 4. Rezvan et al., 2008 5. Stanley et al., 2003 6. Stanley et al., 2009 7. Van Der Heider et al., 2012 8. Wetherall et al., 2003 9. Dugas et al. 2010 10. Zinbarg et al., 2009 11. Andersson et al., 2012 12. Paxling et al., 2010 13. Robinson et al., 2010	1. Borkovec et al., 1993 2. Dugas et al., 2010 3. Hayes Skelton et al., 2013 4. Hoyer et al., 2009 5. Öst et al., 2000 6. Wells et al., 2010	1. Andersson et al., 2012 2. Leichsering et al., 2009	1. Borkovec et al., 1993 2. Neman et al., 2013 3. Stanley et al., 1996 4. Kozycki et al. 2010	5. Rezvan et al., 2008 6. Neman et al., 2011 7. Westra et al., 2009	8. Andersson et al., 2012	9. Chen et al., 2012

Table 5: *Continued*

	CBT versus Waitlist	**CBT versus applied relaxation**	**CBT versus psychodynamic Psychotherapy****	**CBT versus other treatment comparator****	**CBT versus CBT with other additional element****	**Psychodynamic psychotherapy versus waitlist****	**Behavioural activation versus waitlist****
Study	14. Titov et al., 2009 15. Titov et al., 2010 16. Romer et al., 2008						
Pooled pre-treatment severity (PSWQ)	1. 51.63 2. 58.52 3. 62.81 4. 57.83 5. 61.85 6. 55.17 7. 67.46* 8. 64.34 9. 62.38 10. 70.35 11. 68.75 12. 69.05 13. 64.30 14. 66.22 15. 65.71 16. 69.98	1. 67.57 2. 62.38 3. 69.00 4. 58.52 5. 59.58 6. 67.70	1. 68.75 2. 61.21	1. 67.57 2. 68.83 3. 60.57 4. 70.41	1. 57.83 2. 67.55 3. 67.00	1. 68.75	1. 65.40
Severity of Worry (End of Treatment)							
Overall MD (95% confidence interval)	-10.33 (-12.57 to -8.10)	-4.59 (11.54 to 2.36)	-2.05 (5.47 to 1.37)	-4.04 (9.69 to 1.60)	1.11 (-3.64 to 5.85)	-1.00	-9.08

Table 5: *Continued*

	CBT versus Waitlist	**CBT versus applied relaxation**	**CBT versus psychodynamic Psychotherapy****	**CBT versus other treatment comparator****	**CBT versus CBT with other additional element****	**Psychodynamic psychotherapy versus waitlist****	**Behavioural activation versus waitlist****
Overall SMD (95% confidence interval)	-1.12 (-12.57 to-8.10)	-0.30 (-0.84 to 0.22)	-0.23 (-0.61 to -0.16)	-0.34 (-0.76 to 0.08)	0.11 (-0.36 to 0.59)	-0.11	-0.93
Heterogeneity (I^2)	64%	87%	-	-	-	-	-
N	931	251	106	70	79	52	49

Note. *pooled pre-post difference. ** Reported narratively, not suitable for pairwise meta-analysis, MD: Mean Difference, SMD: Standardised Mean Difference.

3.4.5 CBT versus other Treatment Comparator

Four studies compared CBT with a treatment comparator that could not classified under any of the above categories. Due to the variation in comparators the studies could not be entered in a meta-analysis. Borkovec et al. (1993) compared CBT to non-directive therapy in a working adult sample and reported a large improvement in worry on the PSWQ relative to non-directive therapy. The CBT condition reported a reliable improvement in self-reported worry (MD= 19.50); neither treatment condition post-treatment reached the PSWQ criteria for recovery. Stanley et al. (1996) compared CBT to a discussion group in an older adults sample reporting improvements in self-reported worry in both treatment conditions and that the discussion group condition was not statistically different to the CBT condition in its effectiveness in reducing worry. Both treatment conditions reported a reliable improvement post-treatment but did not meet the criteria for recovery. Newman et al. (2013) compared two brief group 6-session group CBT (gCBT) treatments to a standard 12-session gCBT treatment, reporting that at post-treatment brief gCBT treatment with computer assistance was superior to brief gCBT and neither were superior to the standard 12-session gCBT intervention. Reliable improvement was reported for gCBT treatment with computer assistance (MD= 17.37) and standard 12-session gCBT (MD= 12.09) no treatment met the criteria for recovery on the PSWQ. At 6 and 12 month follow up there was no significant statistical difference between any interventions in reported symptoms of worry. Kosyzcki et al. (2010) compared CBT with a spirituality-based intervention (SBI), which focused on acceptance and mindfulness, reporting improvements in worry for both treatment groups, CBT was superior to SBI, but this was not statistically significant, as both interventions reported reliable improvements in worry post-treatment. Treatment gains were maintained at follow up and reported large within group effect sizes (CBT: d= 1.22, 95% CI: 0.27 to 2.08; SBI: 1.08, 95% CI: 0.15 to 1.93) for reduction

in worry. Despite the reported treatment effect neither treatment condition met the PSWQ criteria for recovery.

3.4.6 CBT versus CBT with Additional Elements

Three studies (Rezvan et al., 2008; Newman et al., 2011 and Westra et al., 2009) compared CBT directly to CBT with an additional therapeutic element. Due to the variation in comparators the studies could not be entered in meta-analysis. Revan et al. (2008) compared CBT to CBT with interpersonal therapy, both therapies led to a reliable improvement in worry and reached the criteria for recovery post-treatment, there were no statistically significant differences between the two treatment groups at post-treatment or follow up. Newman et al. (2011) compared CBT to CBT with an interpersonal/ emotional-processing element. Both treatments lead to reliable reductions on the PSWQ but did not reach the criteria for clinical recovery, there was no statistical difference between either treatment conditions post-treatment or at follow up. Westra et al. (2009) compared CBT with CBT following a motivational interviewing (MI) pre-treatment. Both treatments led to reliable improvements in self-reported worry and met the criteria of clinical recovery. The CBT plus MI group outperformed the CBT group post-treatment, this was not maintained at 6 and 12 month follow up.

3.4.7 CBT Subgroup Analysis

A subgroup analysis of CBT was conducted which assessed first wave CBT, second wave CBT, third wave CBT and iCBT (Figure 4). A separate analysis was conducted for an older adult CBT (Figure 5). All subgroup analyses are summarised in Table 6.

3.4.7.1 First Wave CBT versus Waitlist

Five studies directly compared first wave Beckian CBT with waitlist control conditions. Post-treatment there was a statistically significantly difference between conditions, favouring CBT (MD= -11.69, 95% CI: -15.22 to -8.15). There was substantial heterogeneity (I^2= 56%, Chi^2= 9.07, p= 0.06).

3.4.7.2 Second Wave CBT versus Waitlist

Four studies directly compared second wave CBT (Dugas et al.. 1998; Ladoucer et al., 2000; Van Der Heiden et al., 2012; Wells et al., 1999). Post-treatment there was a statistically significant difference between treatment and waitlist favoring CBT (MD= -12.23, 95% CI: -16.48 to -7.97). There was moderate heterogeneity (I^2= 48%, Chi^2= 7.7, p=0.10).

3.4.7.3 Third Wave CBT versus Waitlist

A single trial (Romer et al., 2008) compared third wave CBT with waitlist directly. Romer et al. (2008) reported a mean difference of -14.75 points on the PSWQ post-treatment favouring third wave CBT. The difference between conditions demonstrated a large effect of treatment (d= 1.94, 95% CI: 1.04 to 2.74), however the sample size of the study was small (N=31) and has not been replicated.

3.4.7.4 Internet CBT (iCBT) versus Waitlist

Five studies directly compared iCBT to waitlist. Four studies compared a specific CBT intervention for GAD (Andersson et al., 2012; Paxling et al., 2011 Robinson et al., 2010; Titov et al., 2009) and a single trial compared a trans-diagnostic CBT treatment for anxiety (Titov et al., 2010). The study reported outcomes by diagnostic group and was included in the analysis. Post-treatment there was a statistically significant difference favoring iCBT (MD= -8.42, 95% CI= -12.33 to -4.51). Further analysis focusing on specific iCBT treatments for GAD, excluding Titov et al. (2010) did not alter the findings that iCBT was superior to waitlist (MD= -9.55, 95% CI= -13.36 to -5.74). There was however evidence of substantial heterogeneity (I^2= 60%, Chi^2= 9.91, p= 0.04). There was evidence of a large size effect in three trials (Paxling et al., 2011; Robinson et al, 2010; Titov et al., 2009) favouring CBT post-treatment (MD= -11.43, 95% CI = -14.88 to -8.47) with no heterogeneity (I^2= 0%, Chi^2= 0.73, p= 0.87)

3.4.7.5 Older Adult CBT versus Waitlist

Three studies compared CBT for older adults. Two studies (Stanley et al., 2003, 2009) reported large between group effect sizes post-treatment favouring CBT (d= 1.03, 95% CI: 0.50 to 1.55; d= 0.91, 95% CI: 0.52 to 1.29.respectively) and one study (Wetherall et al., 2009) reported a moderate between group effect size favoring CBT (d= 0.64, 95% CI: -0.02 to 1.27). Combining all studies, post-treatment there was a statistically significant difference between treatment and waitlist control favoring CBT (MD= -9.08, 95% CI =11.82 to 6.34) with no heterogeneity (I^2= 0%, Chi^2= 0.36, p= 0.83).

3.4.8 Psychodynamic versus Waitlist

A single study (Anderson et al., 2012) compared Internet based psychodynamic psychotherapy with waitlist. Psychodynamic therapy reported a large within group effect on the PSWQ and a reliable post-treatment change on the PSWQ (MD= -7.86, d= 1.16, 95% CI= 0.56 to 1.73) for Internet based psychodynamic psychotherapy. At three-month follow up there was small effect for psychotherapy with it being reported as only marginally better than waitlist.

3.4.8 Behavioural Activation for Worry (BAW) versus Waitlist

A single study (Chen et al., 2013) directly compared BAW to a waitlist. The study delivered group BAW and was adapted from Addis and Martell's (2004) manual. Post-treatment difference favored BAW condition with a mean reduction of 9.08 on the PSWQ in comparison to waitlist, this equated to large post-treatment effect (d= 0.85, 95% CI= 0.43 to 1.61). The change in reported worry in the BA condition indicated a reliable improvement in worry but did not reach clinical recovery. However, this study is based on a small sample size (N= 49) and the authors reported that an administrative error resulted in 10 participants in the waitlist condition (n= 24) not completing the post-treatment PSWQ. The authors conducted multiple imputation (Rubin, 1996) to account for missing data; this may have introduced additional bias and it is likely that additional studies will alter the current conclusions in regards to the effect of BAW as a treatment of GAD.

Table 6: *Study information CBT subgroup comparisons*

	1st Wave CBT versus Waitlist	2nd Wave CBT versus Waitlist	iCBT versus Waitlist	Older Adult CBT versus Waitlist
No of Studies	6	3	5	3
Study	(1) Hoyer et al., 2009 (2) Rezvan et al., 2008 (3) Stanley et al., 2003 (4) Stanley et al., 2009 (5) Wetherell et al., 2003 (6) Zinbarg et al., 2007	(1) Dugas et al., 2003 (2) Dugas et al., 2010 (3) Ladoucer et al., 200 (4) Van Der Heiden et al., 2012*	(1) Andersson et al., 2012 (2) Paxling et al., 2011 (3) Robinson et al., 2010* (4) Titov et al., 2009 (5) Titov et al., 2010	(1) Stanley et al., 2003 (2) Stanley et al., 2009 (3) Wetherell et al., 2003
Pooled pre-treatment severity (PSWQ)	(1) 58.52 (2) 57.83 (3) 61.85 (4) 55.17 (5) 64.34 (6) 70.35	(1) 51.63 (2) 62.38 (3) 62.55 (4) 67.46	(1) 68.75 (2) 69.05 (3) 64.30 (4) 66.22 (5) 65.71	(1) 61.85 (2) 55.17 (3) 64.34
Pre-Post treatment difference (PSWQ)	(1) 2.70 (2) 15.75 (3) 10.20 (4) 8.80 (5) 7.60 (6) 16.10	(1) 10.96 (2) 7.67 (3) 18.94 (4) 12.77*	(1) 2.10 (2) 11.57 (3) 12.37 (4) 9.39 (5) 1.54	(4) 10.20 (5) 8.80 (6) 7.60
Severity of Worry (PSWQ End of Treatment)				
Overall MD	-10.13 (-14.27 to -5.99)	-12.23 (16.48 to -7.97)	-8.42 (-12.33 to -4.51)	-9.08 (-11.82 to -6.34)
Overall SMD	-1.08 (-1.61 to -0.54)	-1.03 (-1.37 to -0.69)	-0.78 (-1.13 to -0.44)	-0.89 (-1.17 to -0.60)
Heterogeneity (I^2)	74%	48%	65%	0%
N	309	246	355	218

Note. *pooled pre-post difference, MD – Mean Difference, SMD – Standardised Mean Difference

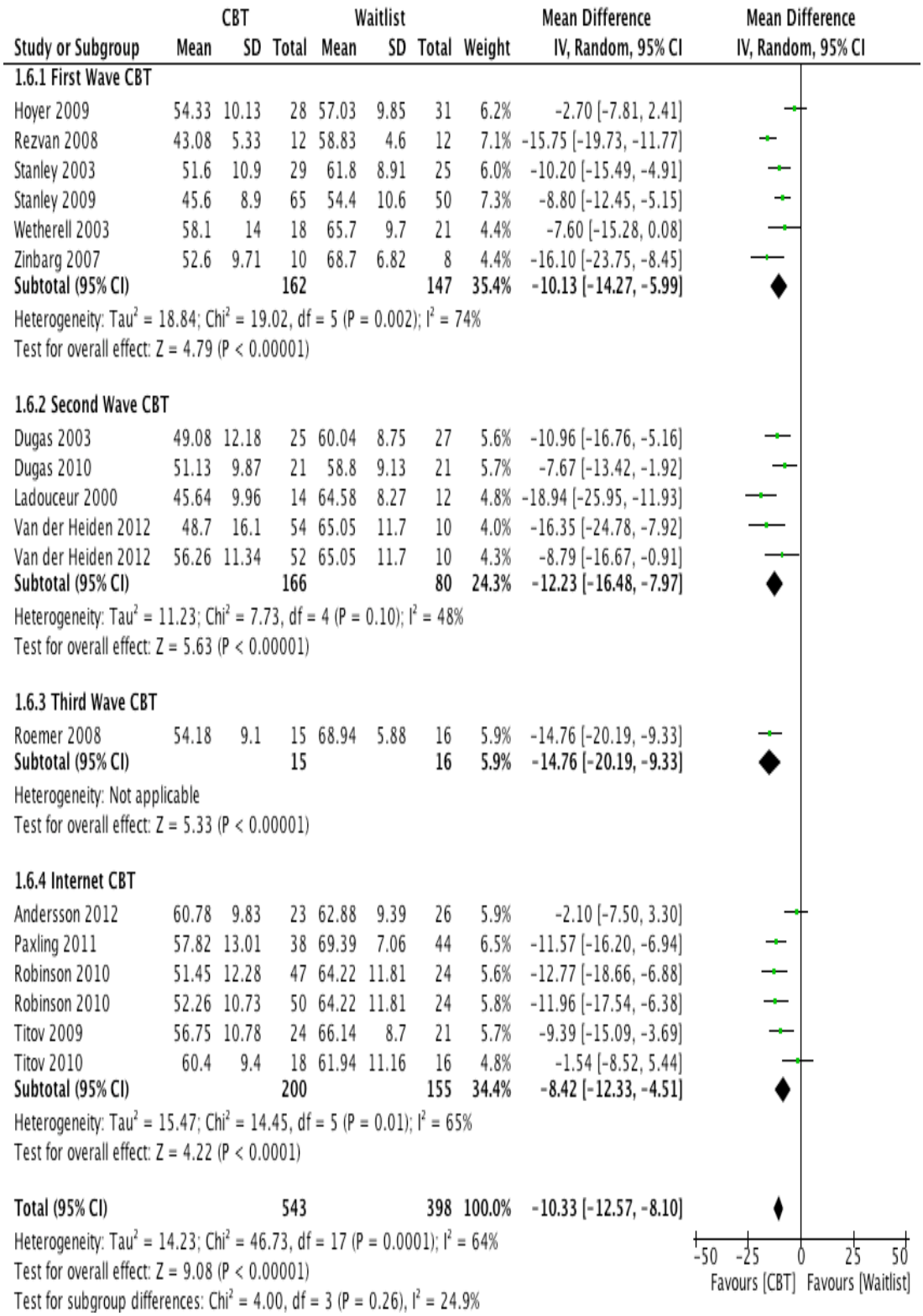

Figure 4: *Post-treatment mean difference CBT compared to waitlist*

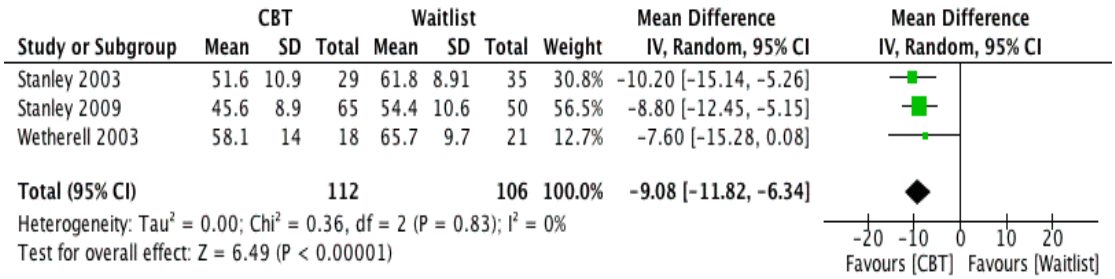

Figure 5*: Post-treatment mean difference older adult CBT*

3.5 Network Meta-Analysis

Of the 28 studies included in the review 27 studies were synthesised with network meta-analysis (NWA). A single study (Robinson et al., 2013) was excluded, as the study did not link to at least one other comparator in the network. The network of evidence included data from 1,545 participants and consisted of 43 between conditions comparisons. Most of the evidence in the network was for the waitlist versus first wave CBT, waitlist versus iCBT and second wave CBT – IoU. The network highlighted that there was a limited amount of evidence for 13 comparisons due to a single comparison between conditions being possible within the network. As such conclusions are tentative and future evidence is likely to lead to changes in the conclusions drawn. Figure 6 summarises the network of evidence, reflecting all available within and between study comparisons and the number of patients investigated for each treatment condition. The thickness of the line represents the number of comparisons (the thicker the line the greater the number of comparisons) and the circle represents the number of participants in each condition (the larger the circle the greater the number of participants).

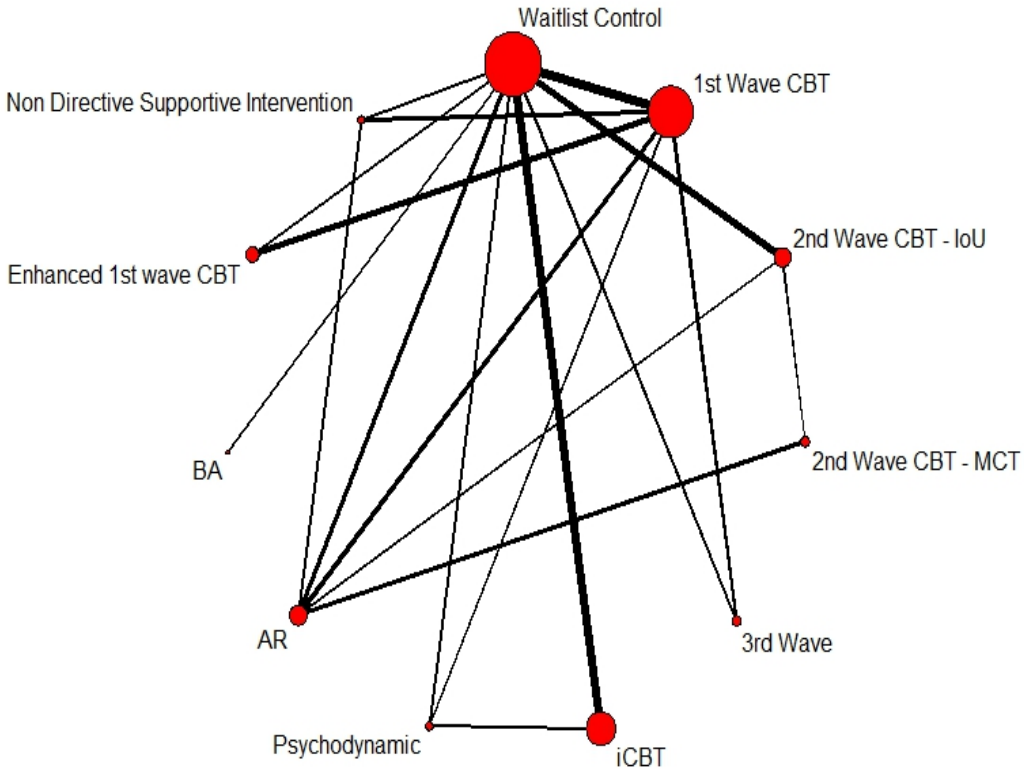

Figure 6: *Network of evidence of all studies*

The post-treatment difference in mean change in worry as measured by the PSWQ is summarised in Table 7. Negative values in the table indicate change favouring treatments in the columns, whereas positive values indicate change favouring treatments in the rows. The difference in self-reported worry between treatments ranged from 0.76 to 23.8 points on the PSWQ. All active treatments out-performed the waitlist condition with a difference ranging from 2.96 to 23.80 points on the PSWQ. CBT based on MCT reported the largest post-treatment difference followed by CBT based on IoU and enhanced first wave CBT. Psychodynamic psychotherapy reported the least change in comparison to the waitlist. Overall CBT based on MCT consistently out-performed all other active treatments with post-treatment differences on the PSWQ ranging from 11.59 to 23.80, however this effect was based on two studies and should be interpreted with caution. Psychodynamic psychotherapy out-performed waitlist reporting a small post-

treatment difference on the PSWQ (2.96) and was inferior to all other active treatments

The performance of individual treatments within the network is summarised in Table 8. The overall ranking of treatment indicated that CBT based on MCT was the best treatment with 98% certainty, however as previously stated this is based on two studies only and must be interpreted with caution. CBT based on IoU, enhanced first wave CBT, third wave CBT, first wave CBT and were all ranked above waitlist and there was considerable overlap of confidence intervals between interventions but none overlapped with waitlist. BA, iCBT, non-directive supportive intervention and psychodynamic therapy had large confidence intervals, which overlapped with waitlist and indicated heterogeneity in the sample. The NWA supported the standard pairwise comparisons.

Table 7: *Table of mean change on PSWQ (and 95% credibility intervals) of psychotherapeutic interventions in NWA*

Therapeutic Intervention/ Control Condition	Wait list	1st Wave CBT	AR	Enhanced 1st Wave CBT	Non Directive supportive intervention	2nd Wave CBT -IoU	2nd Wave CBT -MCT	iCBT	Psycho-dynamic	3rd Wave CBT	BA
Waitlist		-9.844 (-13.28 to -6.42)	-8.08 (-12.58 to -3.45)	-12.22 (-18.21 to -6.27)	-5.53 (-12.19 to 1.14)	-12.33 (-17.16 to -7.34)	-23.8 (-31.45 to -16.34)	-7.29 (-11.30 to -3.20)	-2.96 (-9.32 to 3.37)	-10.50 (-16.68 to -4.23)	-8.52 (-18.25 to 1.30)
1st Wave CBT			1.79 (-2.75 to 6.42)	-2.37 (-7.77 to 3.01)	4.31 (-1.90 to 10.58)	-2.39 (-8.17 to 3.35)	-13.95 (-22.01 to -6.08)	4.92 (-2.15 to 12.15)	6.88 (0.48 to 13.30)	1.72 (-6.34 to 9.90)	3.70 (-7.70 to 15.23)
AR				-4.56 (-11.15 to 2.71)	2.53 (-4.63 to 9.68)	-4.17 (-10.21 to 1.72)	-15.74 (-23.58 to -8.12)	0.76 (-5.29 to 6.81)	5.10 (-2.39 to 12.50)	-2.44 (-8.80 to 3.92)	-0.47 (-0.46 to -11.24)
Enhanced 1st Wave CBT					6.68 (-1.42 to 14.85)	-11.59 (-21.09 to -2.20)	-11.59 (-21.09 to -2.20)	4.92 (-2.15 to 12.15)	9.35 (1.08 to 17.43)	1.72 (-6.34 to 9.90)	3.70 (-7.70 to 15.23
Non Directive supportive intervention						-18.27 (-28.13 to -8.58)	-18.27 (-28.13 to -8.58)	-1.80 (-9.47 to 6.00)	2.57 (-6.19 to 11.27)	-4.97 (-13.49 to 3.58)	-2.98 (-14.80 to 8.84)
2nd Wave CBT - IoU							-11.57 (-19.37 to -3.90)	4.94 (-1.39 to 11.37)	9.27 (1.39 to 17.23)	1.73 (-5.83 to 9.46)	3.71 (-7.44 to 14.66)
2nd Wave CBT - MCT								16.51 (8.06 to 25.23)	20.84 (11.22 to 30.66)	13.30 (4.08 to 22.82)	15.28 (3.06 to 27.72)

Table 7*: Continued*

Therapeutic Intervention/ Control Condition	Wait list	1st Wave CBT	AR	Enhanced 1st Wave CBT	Non Directive supportive intervention	2nd Wave CBT -IoU	2nd Wave CBT -MCT	iCBT	Psycho-dynamic	3rd Wave CBT	BA
iCBT									4.33 (-2.57 to 11.14)	-3.208 (-10.59 to 4.17)	-1.23 (-11.79 to 9.35)
Psycho-dynamic										-7.54 (-16.09 to 1.08)	-5.55 (-17.17 to 6.10)
3rd Wave CBT											1.98 (-9.61 to 13.55)

Table 8: *Ranking of treatments and probability of best treatment*

Treatment	Mean Ranking (SD)	95% Credibility Interval	Mean Probability of Best Treatment (SD)
2nd Wave CBT – MCT	1.0 (0.19)	1 to 1	0.981 (0.14)
Enhanced 1st Wave CBT	3.5 (1.67)	2 to 8	0.007 (0.09)
2nd Wave CBT – IoU	3.5 (1.53)	2 to 7	0.002 (0.03)
3rd Wave CBT	4.7 (2.04)	2 to 9	0.002 (0.05)
1st Wave CBT	5.1 (1.31)	3 to 8	0.001 (0.08)
BA	6.1 (2.80)	2 to 11	0.008 (0.09)
AR	6.6 (1.61)	3 to 9	0.00 (0.04)
iCBT	7.1 (1.63)	3 to 10	0.00 (0.07)
Non Directive Supportive Intervention	8.2 (1.82)	4 to 11	0.00 (0.09)
Psychodynamic	9.5 (1.32)	6 to 11	0.00 (0.05)
Waitlist	10.7 (0.50)	10 to 11	0.00 (0.0)

4. Discussion

4.1 Summary of Aims of Review

This review examined the effectiveness of psychological therapies for GAD in addressing pathological worry as measured by the PSWQ. All studies in the review reported that psychological treatment led to reductions in self-reported worry post-treatment, with large within-group effect sizes. Treatment gains were maintained at follow up, suggesting that psychological treatments were sustained. However due to the substantial variation between studies' follow up time points, which ranged from three months to two years, this data was not able to be incorporated into a formal meta-analysis.

4.2 Summary of Risk of Bias

The risk of bias of studies showed a large variation in the quality of reporting for methodological domains of study design and outcomes. Overall 50% of the studies in the review did not report adequate information for a clear assessment of bias to be made in regards to sequence generation or allocation of concealment. The majority of studies (57%) did not report clear information to determine if raters of outcome assessments were blinded to treatment conditions. Only 36% of the studies in the reviews adequately reported information of blinding for outcome assessors. However, the majority of studies in the review were assessed as being at low risk of bias for selective reporting of data and incomplete data (78% and 64% respectively) as the majority of studies reported intent-to-treat (ITT) data and a single study (Wetherell et al., 2011) additionally reported individual patient data for all study outcomes. Other sources of bias were reported as low in 64% of the studies as they reported use of a treatment manual protocols and independent ratings of adherence. A single study (Andersson et al., 2012) also controlled for therapist allegiance. The risk of bias assessment supported conclusions of previous reviews that the available evidence is mixed and of variable quality with a large proportion of studies being of a moderate to low quality (Hunot et al., 2007; NICE, 2011); there were also indications of the presence of substantial heterogeneity between studies.

4.3 Summary Findings of Pairwise Meta-Analysis

4.3.1 CBT

The findings from the analysis gave limited support to previously reported reviews (Covin et al., 2008; Harahan et at al., 2012; NICE, 2011) that CBT treatment was more effective when compared with waitlist and resulted in reliable change on the PSWQ (Fisher, 2006). The data suggested that those who received a CBT treatment scored a mean of 10.83 points lower on the PSWQ in comparison to waitlist. Subgroup analysis showed that iCBT interventions, which were shorter

than standard CBT interventions and required less clinician input, had smaller reductions on the PSWQ when compared to waitlist. In comparison to waitlist, first generation CBT, second wave CBT and third wave CBT reported larger post-treatment differences. This tentatively suggested that face-to-face CBT was slightly more effective than iCBT. There was also a trend towards more recent CBT approaches (second wave CBT, third wave CBT) reporting increased mean differences between CBT and waitlist post-treatment. Older CBT treatments were also analysed separately as in previous reviews (Colvin et al., 2008), the findings supported previous analysis with older adults reporting a lower post-treatment difference on the PSWQ when compared to a waitlist condition. Moderator analysis using meta-regression did not find statistically significant effects for the percentage of medication use, mean severity of self-reported worry at baseline and year of publication. However, the moderator analysis for medication was limited to the percentage of participants using medication during the trial. Trials did not report in adequate detail the type of medication used or the dosage of medication. Therefore the moderator analysis was unable to control these factors and is limited in its sensitivity as a result.

In comparisons of CBT against other treatments the findings from this review provide some support for the findings of previously reviews (Colvin et al., 2008; Harahan et al., 2012; Hunot et al., 2007; NICE, 2011). CBT did not demonstrate either superiority or inferiority to AR. The differences reported between studies ranged from 1 to 5 points on the PSWQ favouring CBT. A study (Wells et al., 2010) reported a 26 point difference on the PSWQ favouring CBT post-treatment. The overall conclusions of comparison were not altered when this study was excluded, although heterogeneity was reduced. A possible explanation for the lack of difference seen between CBT and AR treatments could be that the majority of CBT treatment incorporates elements of applied relaxation in addition to cognitive therapy. In effect both treatments allow individuals reduce and manage levels of

physical arousal, which lead to a physical state that triggers worry (Borkovec, 1994; Borkovec, Alcaine & Behar, 2004) resulting in less worry being reported. CBT approaches may add alternative strategies for managing previously threatening strategies and facilitate habituation through behavioural approaches.

The limited evidence available also suggests that CBT was neither superior nor inferior to psychodynamic therapy with two studies reporting large within-group effect sizes and small between-group effect sizes post-treatment. However, it is of note that in the Leichsering et al. (2009) study that CBT sessions were matched to the psychodynamic condition of 30 sessions and therefore may not reflect clinical treatment in the UK as NICE (2011) recommends CBT treatment of 12-15 sessions.

CBT was neither superior nor inferior when compared to other active treatments or CBT with an additional element. Studies reported reliable improvements on the PSWQ post-treatment and large within-group effect sizes for both CBT and the comparator treatment, improvements were maintained at follow up. One study (Westra et al., 2009) reported that CBT with motivational interviewing was superior to standard CBT, however this difference was not maintained at follow up.

4.3.2 Psychodynamic Psychotherapy

The effectiveness of psychotherapy as a treatment in comparison to waitlist was limited as a single small study (Andersson et al., 2012) compared Internet based psychodynamic therapy to waitlist. The study's findings suggested that psychodynamic therapy had a large effect in reducing self-reported worry post-treatment. This was not maintained; as psychodynamic therapy was only marginally better than waitlist at follow up.

4.3.3 Behavioural Activation for Worry

The effectiveness of behavioural activation in the treatment of GAD and pathological worry is limited, as only a single study (Chen et al., 2013) to date has compared BAW to waitlist control. The study reported large reductions in worry

post-treatment and a large treatment effect. However, methodological limitations and lack of replication limited the ability to draw any firm conclusions of effectiveness.

4.4 Network Meta-Analysis (NWA)

The NWA allowed the comparison of all available direct and indirect post-treatment data. The network of evidence indicated that most evidence available was for first wave CBT treatments versus waitlist, first wave CBT versus enhanced first wave CBT and first wave CBT versus AR. The network showed that there was limited evidence from psychodynamic psychotherapy, second wave and third wave CBT. Three therapies (non-directive supportive interventions, BA, and psychodynamic therapy) did not differentiate themselves from waitlist, 95% credibility intervals suggested that the treatment effects were no different to waitlist. Of the therapies that did differentiate themselves from waitlist meta-cognitive based CBT therapy demonstrated a consistent superiority over all comparator treatments reporting a post-treatment difference on the PSWQ in excess of 10 points. Meta-cognitive based CBT was estimated by the network meta-analysis to probably be the best treatment for worry out of the available evidence given the available direct and indirect evidence, as the treatment effect did not overlap with the 95% credibility intervals of any other treatment or waitlist.

4.5 Recovery and Remission

Within the studies in the review there was a consistent discrepancy between clinician rated measures of GAD and self-report symptoms of worry. Clinician rated measures reported post-treatment recovery ranging from 26% to 72%, whereas only three studies reported a clinically reliable change in self-reported symptoms of worry and was of a non-clinical level (Meyer et al., 1990). It is striking that the majority of individuals receiving psychological treatment for GAD still appear to

report pathological levels of worry post-treatment despite clinician assessment reporting that individuals no longer met GAD criteria. Given that persistent, excessive and out of control worry is a central symptom of GAD (Behar, Di Marco, Hekler, Mohlman & Staples, 2009) this suggests that current psychological treatments for GAD do not reliably relieve pathological worry for the majority of participants as measured by the PSWQ. It may be that treatments are effective in addressing somatic symptoms of GAD, reducing arousal levels that trigger uncontrollable worry, as a threat state is not reached. It is also possible that the habitual and over-learnt responses that characterise the use of worry as an emotional avoidance strategy (Borkovec et al., 2004) require a longer period of time to become established. Follow up data provided some limited support for this hypothesis. Three studies reported non-pathological levels of worry post-treatment and the number of studies reporting non-pathological levels of worry increased at six months (5 studies) and again 12 months (6 studies), however the majority of studies included in the review still reported the presence of pathological worry at follow up. Alternatively there may be a disproportionate focus in clinician assessment on the reduction in somatic anxiety symptoms. This may lead to an under detection of GAD symptoms as worry is not assessed to the same degree as physical symptoms which has been previously highlighted as an issue in primary care settings (NICE, 2011; Tyrer & Baldwin, 2006). It highlights the possibility that clinicians are still considering worry as a consequence of anxiety rather than an underlying process that maintains worry. Therefore reduction in somatic anxiety

symptoms is equated to a reduction in worry. This may account in part for the waxing and waning profile of GAD as current psychological treatment appears to leave individuals with residual symptoms of pathological levels of worry as current treatments may not address well enough the underlying worry mechanisms in GAD and lead potentially to a higher likelihood of relapse. The network provided support for this hypothesis, as meta-cognitive therapy, a second wave CBT approach, was rated by the network as probably the best treatment. This may be due to the approach addressing underlying processes such as attentional bias and meta-cognitive beliefs about worry.

4.6 Methodological issues and Limitations

This review has several limitations; the decision to include only randomised designed trials of which the majority were RCT may not fully represent actual clinical practice and limit the overall generalisability of findings. Additionally the study sample sizes were small, with only four studies (Robinson et al., 2010; Stanley et al., 2009; Van der Heiden et al., 2012 and Westra et al., 2009) having a sample size over a hundred participants at commencement of the study. As a consequence several studies were underpowered and were described as pilot studies. This highlights the need for large-scale studies in this area. The quality of reporting varied for the included studies with only six studies reporting a CONSORT compliant trial design with a pre-registered trial protocol. A further three studies reported a participant flow CONSORT diagram. The level of reporting of key methodological aspects such as randomisation and concealment varied. Half the studies did not report sufficient detail to allow a judgment of the potential level of bias, which was unclear in the majority of studies.

Studies varied in the reported follow up periods, with the majority of studies reporting time points ranging from three to 12 months. During this time many studies reported further substantial attrition of participants and did not control for other confounders such as further treatment and medication usage, which weakens the conclusions that can be made about treatments long-term effectiveness.

The majority of studies employed a delayed treatment design, which meant that waitlist control data was only available to the end of treatment. This prevented the comparison of treatment follow up data with a non-treatment group, as a consequence natural recovery as a potential confounder could not be definitively excluded, limiting the conclusion about long-term effectiveness. However, it must be considered that withholding treatment for the prolonged periods in long-term follow up is unethical and is a limitation faced by all treatment trials.

Nine of the studies included in the review recruited participants from clinical samples with the remaining employing a community sample. The majority of community studies employed a convenience sampling approach, which may limit the validity of findings when compared to real world clinical population. The majority of studies also excluded other co-morbid disorders and this may further limit the generalisability of findings into real world clinical practice, as GAD is often co-morbid with another Axis I disorder and pure GAD is relatively rare clinical occurrence (NICE, 2011).

There are also several limitations of the review that are common to meta-analysis such as the assumption that studies are drawn from the same population. The review found that there were indications of the substantial heterogeneity in the overall class of intervention for CBT; this was retained to a degree in the individual classifications of subtypes.

Network meta-analysis makes an additional assumption to allow conclusions to be drawn from the direct and indirect evidence. It assumes that particular treatments are similar in procedure and rationale, which allows them to be grouped

together. The grouping together of treatments that contain important differences may lead to an underestimation of efficacy and the intervention's effectiveness. The review also did not control for researcher allegiance bias, which may also have introduced a source of bias. Also due to the difference in reporting of data from trials, imputation was employed as only a small number of trials reported change data, and with the majority reporting post-treatment effect any assessment of difference between change and post-treatment effect is not reliable and may be a possible source of bias within the network. Given these limitations the conclusions from the network are tentative.

4.7 Future Directions

The findings of the review suggest several areas of further research in the psychological treatment of GAD. Given the relatively small size of trials it is clear that more large well-conducted trials that adhere to CONSORT standards are required to allow a more definitive assessment of psychological treatment for GAD and worry. There is also a need for further trials of alternative treatments to CBT to establish the effectiveness of other psychological treatments, as there is a paucity of well-conducted trials. The network meta-analysis also confirmed a paucity of trials in the network of evidence and showed that the majority of trials are compared to a waitlist only rather a head-to-head comparison with another active treatment and a control. In order to address heterogeneity further differentiation of treatments active elements and delivery may allow for a reduction in heterogeneity as this would further high quality control trials with high levels of methodological reporting.

Also of interest would be further investigation in post-treatment level of worry as a relapse predictor of GAD given that the majority of treatments in the review do not lead to a sub-clinical level of self-reported worry post-treatment (Behar, Alcaine, Zuelig and Borkovec, 2003).

4.8 Conclusions

Although the findings from this review are tentative as they are based on a small number of studies with a number of methodological issues and limitations in quality, the current review broadly supports the findings of previous reviews, that psychological treatment of GAD leads to a reduction in levels of pathological worry. CBT was superior to waitlist, CBT and AR were equally effective and there was limited evidence for the effectiveness of psychodynamic and behavioral activation approaches. The review also tentatively suggested that newer second wave CBT approaches to GAD treatment lead to increased reductions post-treatment in worry. The network meta-analysis suggested that MCT was probably the best treatment of GAD, although this is based on data from only 64 individuals.

However, despite the evidence that psychological therapy leads to a reliable change in worry post-treatment, few studies reached a level that would indicate clinical recovery post-treatment.

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Part 2: Empirical Paper

Developing a Low Intensity CBT Intervention for GAD in IAPT: A Pilot Feasibility and Acceptability Study

Abstract

Aims: The pilot study investigated the feasibility and acceptability of a Low Intensity (LI) guided self-help intervention for excessive worry and generalised anxiety disorder (GAD). The Understanding Worry (UW) intervention was adapted from current CBT theory and presented in a framework adapted from the COM-B model of intervention design (Michie, Van Stralen & West, 2011). The study also sought to evaluate clinical effectiveness of the new intervention in relation to the current generic LI intervention. **Method:** A randomised trial comparing two groups: Treatment as Usual (TAU) and Understanding Worry (UW). The study planned to recruit 40 patients from primary care NHS clinical settings. However, due to delays in recruitment only 24 were recruited and randomised to treatment conditions. The indicators of acceptability and feasibility were a patient consort diagram, attendance and attrition rates and patient ratings of satisfaction (CSQ-8) at the completion of treatment. The main clinical outcomes were the PSWQ, PHQ-9, GAD-7 and WSAS. Mixed Methods Linear Modeling was used in analysis to utilise all available data and was selected due to the small data set. **Results:** Patient flow indicated that there was a clinical need for a specific worry intervention. Attendance, cancellations and DNAs were not significantly different between the two treatment groups, $X^2=(2,N=102)= 1.665$, $p= 0.44$ suggesting the UW treatment was equally acceptable as TAU. Clinical outcomes showed a reduction in worry and anxiety in both conditions but with TAU reporting larger gains. There was no significant difference in post-treatment scores between UW and TAU. **Conclusions:** The findings of the current evidence suggests that there is a clinical need for an LI intervention that focuses on addressing worry and GAD symptoms within primary care services. Findings also indicate that an intervention adapted from the current HI theory can be delivered by PWPs in routine practice but requires further development and refinement.

1. Introduction

Generalised anxiety disorder (GAD) is one of the most frequently occurring psychological disorders, affecting an estimated 8.9 million people in Europe per year (Lieb, Becker, & Altamura, 2005, Wittchen, 2002). GAD is characterised by excessive and uncontrollable worry about everyday events. Individuals may also experience somatic symptoms such as: increased muscle tension, fatigue, disrupted sleep, impaired concentration and increased irritability (DSM-IV, 1994). Epidemiological studies suggest that symptoms adopt a waxing and waning profile, with the severity of GAD symptoms increasing in response to life stressors, and episodes of the disorder commonly persisting for over 10 years (Kessler, Keller and Wittchen, 2001). GAD is therefore considered to be a pervasive anxiety disorder, with symptoms that are chronic and unremitting in nature (Tyrer & Baldwin, 2006; Yonkers et al., 2000). Those who suffer with GAD are reported to experience a significantly diminished quality of life, reduced work productivity, and impaired social functioning (NICE, 2011). They also constitute a patient group that is highly costly to health services as they are more likely to make frequent medical appointments and undergo diagnostic testing (Massion, Warshaw, & Keller, 1993). The cost and level of disability associated with GAD is reported to be comparable with that of depression (Kessler, 2000).

Despite being the most common anxiety disorder that presents in primary care, accounting for 5% of primary care consultations GAD is under-recognised by General Practitioners (GPs) and undertreated (NICE, 2011). It is estimated that recognition rates by GPs and primary care practitioners are 34.4% for pure GAD and 43% for GAD when it is comorbid with depression (Wittchen & Jacobi, 2005). The current poor recognition rates of GAD in primary care settings are likely to occur for several reasons. A major contributor to the poor recognition of GAD is the diagnostic uncertainty of GAD. There has been substantial debate concerning whether GAD is an independent anxiety disorder or a component of major mood

disorder (MDD) (Mennin, Heimber, Fresco & Ritter, 2008). Both GAD and MDD share common symptoms of fatigue, restlessness, impaired concentration and disturbed sleep (Zbonzienk et al., 2012). However, what differentiates GAD from MDD is the presence of excessive and uncontrolled worry (Ladoucer, Blasi, Freeston & Dugas, 1998). Given the often diffuse picture of somatic symptoms reported by GAD sufferers in the consulting room, GPs may more readily attribute the pattern of symptoms to a general malaise and subsequently neglect to explore the role of uncontrolled worry or anxiety (Arroll & Kendrick, 2009). Therefore, it is possible that GPs more readily diagnose depressive disorders while the anxiety component remains undetected. The challenge in the accurate recognition of GAD has significant implications for individuals' access to evidence-based treatment. It is estimated that only one in four individuals in Europe with mental health disorders receive professional support and only 10% of those are offered any form of treatment (Wittchen, Jacobi & Rhem, 2011). Individuals who receive treatment are more likely to be offered medication, rather than psychological interventions such as cognitive behavioural therapy (CBT) (Stein et al., 2004). It can be argued that due to the high rate of under detection this figure is likely to be inflated in the case of GAD and this represents a group within society with a large unmet treatment need and high health costs.

In an attempt to address the significant unmet treatment needs associated with common anxiety and depression disorders, the UK government has provided unprecedented investment in NHS primary care mental health services with the Improving Access to Psychological Therapies (IAPT) program. The IAPT initiative sought to provide nationwide access to evidence-based psychological therapies that are recommended by National Institute of Clinical Excellence (NICE) (Department of Health, 2011). The IAPT service model adheres to a stepped care approach where the level of intervention is determined by the severity of reported symptoms, with the least restrictive and lowest burden treatment being initially offered to the patient

(Sobell & Sobell, 2000). In order to effectively provide treatment for large numbers of individuals the IAPT model provides both Low Intensity (LI) and High Intensity (HI) psychological treatments. Approximately three quarters of individuals accessing IAPT services receive treatment at the LI treatment level.

HI psychological treatments within IAPT focus on the provision of CBT and are delivered by CBT therapists or other appropriately trained staff. HI CBT interventions are derived from cognitive behavioural models of anxiety disorders and are discrete, time-limited, highly structured interventions, which often follow a clear treatment protocol. The collaborative intervention identifies the links between thoughts, feelings and behaviours and their link to symptoms or problem areas for the individual. The interventions focus on learning coping skills to target problem behaviours, beliefs or thoughts. HI therapies are usually delivered face-to-face and consist of 12 to 15 weekly sessions, which are one hour in duration (NICE, 2011).

In contrast LI psychological therapies are shorter in duration, less resource intensive and consist of a smaller number of sessions, typically four to six, and are 20 to 30 minutes in duration. LI interventions typically involve less face-to-face contact and are delivered by trained practitioners who may not have a formal health professional or HI CBT qualification, such as graduate mental health workers (GMHWs) or Psychological Wellbeing Practitioners (PWPs). The style of LI treatment approaches differs markedly from the traditional HI formal therapy interventions. The focus for the LI practitioner is to provide a coaching role and to support the individual to independently apply CBT techniques using written self-help material, computer delivered CBT (cCBT) or through the facilitation of psycho-educational groups (Bennet-Levy et al., 2010).

HI CBT interventions for GAD have changed substantially over the last 20 years, are well defined and have a clear theoretical framework from which treatments have been developed. GAD CBT treatments can be categorised into first wave interventions, which focus on addressing unhelpful thinking styles including

the view of the self as inadequate and unable to cope, avoidance and address the consequences of worry rather than the process of worry itself (Beck & Emery, 1985). Second wave CBT models seek to address the process of worry (Dugas, Gagon, Ladoucer & Freeston, 1998; Dugas & Robichaud, 2007; Wells, 1999). These CBT approaches conceptualise worry as a coping strategy in response to external events or non-cognitive internal states that are perceived as threatening. These recent models posit that worry is maintained by a combination of positive and negative beliefs about worry itself and this leads to the individual feeling unable to employ problem-solving skills in relation to practical problems. These models of GAD suggest that individuals experience feelings and situations of uncertainty as threatening, intolerable, catastrophic and to be avoided. The second wave CBT approaches seek to address emotional and behavioural avoidance, educate individuals about the affects and physical symptoms of worry, increase confidence in problem solving abilities, modify unhelpful beliefs about worry and increase tolerance to uncertainty. Numerous systematic reviews of HI psychological treatments for GAD have concluded that CBT is an effective treatment (Borkovec & Ruscio, 2001; Hunot et al., 2007; NICE, 2011, Hanrahan, et al., 2012). In the most recent review of psychological therapy for GAD, Cujipers and colleagues (2014) reported a large treatment effect for CBT in comparison to waitlist controls (Hedges' *g*: 0.90, CI; 0.75-1.05) and that the number of needed to treat for a successful outcome using a CBT treatment was two. This suggests that CBT is an effective psychological intervention for GAD.

In contrast the evidence-base for LI interventions for anxiety and depression is mixed. LI interventions for depression have an established evidence-base of effectiveness (Gellatly et al., 2007) and are primarily based on current effective treatments, which include psycho-education, behavioural activation, activity scheduling, cognitive restructuring and problem solving (Bennett-Levy et al., 2010). For example, these interventions show a clear link to the contemporary literature in

the behavioural treatment of depression (Jacobson et al., 1996, 2001). In contrast, LI anxiety interventions have sought to apply a generic approach to anxiety disorders and consist of a combination of psycho-education, cognitive restructuring, graded exposure and de-arousal strategies without a clear tailoring to specific anxiety presentations (White, 1995; White, 2000; Williams, 2003; Williams, 2010). This approach within LI interventions appears to be at significant odds with the well-developed HI intensity disorder specific treatments. Currently the disorder specific approaches to anxiety have so far failed to be successfully integrated into the canon of LI interventions. Current LI anxiety interventions adopt generic first wave CBT approaches in the treatment of GAD. These interventions focus on worry as a consequence of anxiety and do not address worry as a response to uncertainty or as a process that maintains anxiety. Therefore the currently utilised LI treatments for GAD do not reflect current theoretical understandings of the disorder or current treatment approaches for GAD. This gap in the development of anxiety disorder specific LI interventions has led to a position where current LI interventions are less clearly defined, generic and as a consequence the evidence of effectiveness is not as well established (Titov, Andrews & McEvoy, 2010). This perspective is further supported by a systematic review of the literature of LI treatment for GAD that was conducted as part of the recent NICE (2011) guideline for the psychological treatment of GAD. The review concluded that the evidence was small and heterogeneous and it was therefore difficult to make firm conclusions about the effectiveness of LI interventions for GAD.

LI anxiety interventions are in need of development to bring treatments for anxiety disorders in line with HI disorder specific models of treatment. The developing of a disorder specific LI intervention for excessive worry and GAD requires a systematic approach that addresses the core maintaining processes within GAD and leads to behavioural change. Behavioural Change Theory (BCT) (Michie, Van Stralen & West, 2011; Michie & Johnston, 2012) offers a systematic

approach to intervention design that is appropriate to the therapeutic aims of LI interventions. At the heart of BCT is the COM-B model, which describes a behavioural system that can lead to change. The system comprises of three elements: capability, defined as the individual's knowledge and skills that make the behaviour possible; opportunity, which refers to factors outside the individual that prompt behaviour and motivation, which is defined as decision making and regulation of behaviour. Identifying interventions and coherently integrating these elements within an overall treatment plan can increase an individual's capacity to change behaviour and subsequently reduce distress. In utilising the COM-B model approach to psychological interventions by identifying distinct exercises or techniques, which address and increase capacity, motivation and opportunity for alternative behaviours, GAD symptoms can be reduced and unhelpful responses to worry and anxiety can be changed and maintained.

The focus of this study was to seek to (a) develop a coherent intervention for excessive worry and GAD symptoms, which was grounded in current conceptual models, which could be delivered by PWPs at an LI treatment level and was acceptable to patients. The intervention development initially focused on identifying the current conceptual models (Behar et al., 2009) and identifying key processes in worry and GAD. The key areas identified were uncertainty (Dugas et al., 1998), behavioural avoidance and emotional avoidance (Borkovec & Ruscio, 2001), poor problem solving (Dugas et al., 1998), meta-cognitive beliefs and cognitive thought suppression (Wells, 1999). Following the identification of the key processes a review of existing LI and HI treatment material and protocols was undertaken and interventions were dismantled into discrete elements of psycho-education, behavioural, relaxation, cognitive and worry specific strategies. These elements were further divided in to specific tools and exercises, such as goal setting, cognitive restructuring, and exposure (see Appendix 3). After this phase the COM-B model was then applied in the selection of elements with a specific emphasis on

behavioural change that increases the capability, motivation and opportunity in the key areas identified which were suitable for delivery in an LI treatment format. The resulting intervention consisted of six modules that addressed psycho-education of worry, overcoming intolerance of uncertainty, overcoming avoidance, practical approaches to responding to worry, problem solving and relapse prevention. The modules had a clear focus on supporting individuals to change behaviour in response to worry, anxiety and uncertainty and did not address cognitive approaches to GAD, such as challenging meta-cognitions about worry as this was considered to not be suitable for LI treatment.

The current study sought to examine whether this approach to intervention development could be successfully applied to develop a GAD specific LI intervention. The study sought to test whether LI workers could feasibly deliver such an intervention in a routine IAPT setting and to establish whether the intervention was acceptable to patients and led to a reduction in self-reported symptoms. The study also considered how the outcomes of a GAD specific LI intervention compared with the existing generic anxiety based LI interventions currently used in usual treatment. The testing of the intervention sought to answer the following four questions:

1) Is it feasible to develop a GAD specific LI Intervention informed by the current theory and deliver it with PWPs in routine practice?
2) Is the intervention practical and acceptable to individuals who are treated with the GAD specific intervention at LI level?
3) Is the GAD specific intervention comparable to current generic LI interventions for anxiety that are applied to those with a GAD presentation?
4) Is the GAD specific intervention clinically effective in reducing anxiety and worry and is this change reliable and clinically significant?

2. Method

2.1 Participants

The study sought to recruit 40 individuals into the trial, however due to time constraints 24 participants were recruited. Participants were individuals seeking help from two London primary care IAPT services between January 2014 and April 2014. Both services were provided by a large NHS Foundation Trust.

Participants were eligible for this study if they were (a) aged 18 years old or above; (b) presented with excessive worry and anxiety as a primary problem; (c) presented with mild-to-moderate symptoms of anxiety or general anxiety as indicated by a score greater than 4 on the Generalised Anxiety Disorder questionnaire (Lowe et al., 2008); (d) were deemed suitable by IAPT staff for a LI intervention; (e) had consented on the referral to be approached for research and (f) had agreed to randomisation. Participants were excluded from the study if they presented with a primary problem of generalised anxiety or worry which was of a severity that required High Intensity (HI) treatment; a primary presenting problem of depression, obsessive-compulsive disorder (OCD); post-traumatic stress disorder (PTSD); social phobia and panic disorder; current use of anti-psychotic medication; currently receiving psychology treatment; alcohol or drugs dependency, cognitive impairment or declined randomisation. Provisional diagnosis was determined by information provided by an initial screening interview conducted by a PWP, which incorporated the IAPT (2011) screening prompts, and patient's self-reported questionnaires. A qualified clinician prior to the offer of treatment confirmed provisional diagnosis.

2.2 Ethics

Ethical approval was granted by the NHS Heath Research Authority, Brent Research Ethics Committee (Appendix 3), the Research and Development department of the local trust where the study was conducted (Appendix 4) and the

Joint Research Office at University College London who insured the study (Appendix 5).

2.3 Procedure

Participants were recruited from January 2014 and April 2014, from two primary care IAPT Services, both services were provided by a large NHS Foundation Trust. The study adopted a randomised assignment repeated measures pre-post test design using individual participants as randomisation units.

Participants who were suitable for the study were identified by eight Psychological Wellbeing Practitioners (PWPs) during the service's standard initial triage assessment. If individuals met the study's inclusion criteria and had consented to be approached for research they were approached by the PWP to participate in the study. Participants received a participant information sheet (Appendix 6) and completed a consent form (Appendix 7). All PWPs approaching individuals had received training from the intervention's developer in regards to the study and the intervention. If participants consented to participate in the study they completed baseline measures and were randomised to receive either the GAD specific intervention (UW) or the IAPT services standard generic LI treatment as usual (TAU). At each treatment contact participants completed the primary and secondary outcome measures. Data was collected using the IAPT service Patient Care Management Information System (PC-MIS) (http://www.pc-mis.co.uk). Supervision was provided by PWP clinical supervisors, additionally the intervention's developer provided supervision in two three-hour group supervision sessions and via email.

2.4 Randomisation

An independent researcher (CW) not involved with the research project created the study randomisation sequence. The sequence was generated using Stata/IC Version 12.1 for Mac using the ralloc command with random permuted blocks of varying size, stratified by sex and person doing the allocation. An

independent Trainee Clinical psychologist (JB) allocated participants to treatment conditions via email. The author was blind to the randomisation sequence and subsequent allocation of participants until the data analysis of groups had been completed.

2.5 Interventions

2.5.1 Treatment as Usual

The IAPT services routine LI treatments consisted of four to six sessions of guided self-help, sessions were 20 to 30 minutes in duration and treatment followed the service's "stress and worry booklet" and the service's delivery protocol. The stress and worry booklet contained generic CBT approaches for managing stress such as time management, balancing demands and relaxation techniques. The stress and worry booklet's focus on worry was limited to the worry tree, which is a tool to identify if worry is actionable, and worry time, which is a technique to attempt to limit and contain worry to a fixed period during the day.

2.5.2 Understanding Worry (UW) Intervention

The UW intervention consisted of six workbooks, each addressing a different treatment area for GAD. The workbook's content focused on applying tools and management strategies that facilitated behavioural change and developing alternative behavioural responses to worry. The intervention did not address cognitive aspects of GAD such as beliefs about worry as this was considered to be more appropriate for intervention at HI level of treatment. The workbooks followed a clear structure, which included: psycho-education of the main topic of the module, a vignette example and a tool or tools to address the area. Modules also included a review of the learning and an assignment to complete between the support sessions. Participants were provided with workbooks prior to support sessions with a PWP, with the explicit emphasis that they complete the booklets before support sessions. A summary of the content of each module is described in Table 1.

Participants were also offered between four to six structured support sessions with a PWP. Support sessions were between 25 to 45 minutes in duration and followed a clear session outline, which is summarised in Table 2. Support sessions focused on the reviewing of material and learning for a single module, supporting the participant in applying new learning, identifying and collaboratively solving any barriers, identifying how the learning would lead to behavioural change, agreeing the between session task and agreeing the next workbook to be completed. The PWP also provided a standard text prompt between sessions to encourage participants to adhere to between session tasks and to complete the next module's material.

In relation to the workbooks participants were required to compete two core workbooks, Understanding Worry, which focused on psycho-education for worry, goal setting and the identification of which workbooks were most relevant to the participant. The Planning for the Future workbook focused on consolidating the learning over the intervention, identifying high risk situations and relapse prevention planning. The remaining four modules were selected collaboratively between the participant and PWP to allow the treatment to be tailored to the need of the individual and to allow the individual to focus on the areas that were causing most difficulty.

Table 1. *Outline of Understanding Worry intervention workbooks*

Workbook	Description
Understanding Worry	Psycho-education of worry and anxiety, introduction to the adapted IoU model of GAD, identifying motivation to change, goal setting, identification of workbooks to complete in subsequent support sessions.
Understanding Intolerance of Uncertainty	Psycho-education of intolerance to uncertainty, the impact on worries and unhelpful ways of managing uncertainty, building tolerance to uncertainty using behavioural exposure.
Understanding Avoidance	Psycho-education of behavioural and emotional avoidance, the impact on worries and unhelpful ways of managing avoidance, building tolerance to avoidance using behavioural exposure and imaginal exposure.
Practical Ways to Deal with Worry	Psycho-education identifying practical and hypothetical worry, strategies to manage with hypothetical worry, relaxation, attentional training and worry time.
Practical Problem Solving	Psycho-education of how to recognise problems and common unhelpful approaches to problem solving, problem solving in seven stages.
What have I Learnt? Looking Towards the Future	Review of learning from all workbooks. The workbook prompts the individual to identify previous beliefs and behaviours and how these have changed. The workbook also identifies high risk situations of relapse and facilitates the development of a relapse prevention plan.

Table 2: *Support session structure outline*

Session Element	Description
Agenda Setting	Collection of measures, review of assignment; review of new material key areas and between session assignment setting.
Review Between Session Assignment	Discussion of what the individual learnt about their worry, how this differed from expectations, if there were any difficulties and how they will apply the new learning in the future.
Review of New Material	What is the individual's understanding of the psycho-educational material and how does this fit with their experience of worry? What is the individual's understanding of the rationale of the tool that provides an alternative behaviour? Can the individual apply the learning to address their own worry?
Review	What learning will the individual take away from the workbook and session? What will they do differently as a result of their new understanding?
Between Session Assignment	Agree between session assignment using SMART goal settings and address how this will contribute to moving towards identified goals of the individual.

2.6 Outcome Measures

The primary outcome measure was the Penn State Worry Questionnaire (PSWQ) (Meyer, Miller, Metzger & Borkovec, 1990). The PSWQ is a 16 item self-report questionnaire; psychometric data shows that it is a reliable and valid measure of worry in GAD and is able to distinguish those with GAD from other anxiety disorders (Meyer et al., 1990). It is reported to have high consistency and temporal stability (Brown & Barlow, 1992; Fresco et al., 2003).

The secondary measures consisted of the IAPT minimum dataset (IAPT, 2011b):

The nine-item Patient Health Questionnarie (PHQ-9) (Kroenke, Spitzer & Williams, 2001). The PHQ-9 measures symptoms of depression based on the DSM-IV criteria for major depressive disorder. A score of 10 on the PHQ-9 has been identified as threshold for the identification of DSM-IV depression. The PHQ-9 has high internal consistency with a Cronbach's alpha of 0.89 (Kroneke et al., 2001). The PHQ-9 has demonstrated validity for measuring depression (Kroneke, et al., 2001) and has been validated in a UK depressed population (Cameron, Crawford, Lawton & Reid, 2008).

The seven-item Generalized Anxiety Disorder Questionnaire (GAD-7) (Spitzer Kroneke, Williams & Lowe, 2006) is based on the DSM-IV diagnostic criteria for GAD. The GAD-7 questionnaire has been reported to have good internal consistency; Cronbach's alpha is 0.92 (Lowe et al., 2008). However, the GAD-7 does not have good discriminating validity, showing sensitivity to both social phobia and panic disorder and has been increasingly used in research as a generic measure of anxiety and convergence with other measures of anxiety (Clarke et al., 2009).

The five-item Work and Social Adjustment Scale (W&SAS) (Mundt, Marks, Shear & Greist, 2002) measures the perceived impairment of functioning in relation to the problem experienced over five domains (work, home management, social

leisure activities, private leisure activities and family and relationships). Mundt et al. (2002) suggests that a score greater than 18 indicates moderately-severe to severe functional impairment, scores between eight to 18 indicate mild-to-moderate impairment in functioning. A score of seven and below indicates a sub-clinical level of impairment.

The eight-item Client Satisfaction Questionnaire (CSQ-8) (Attikson & Zwick, 2003) enquires about the opinions of respondents and their conclusions of the services they are receiving or have received. Response options are based on a four-point scale ranging from “quiet dissatisfied” to “very satisfied”. Studies of reliability of the CSQ-8 have indicated a coefficient alpha, ranging from 0.83 to 0.93 (Attkisson, & Greenfield, 2004).

2.7 Data Analysis

2.7.1 Indicators of Feasibility and Acceptability

To evaluate feasibility and acceptability a CONSORT diagram was created to provide a graphical summary of patient flow from initial screening to the end of the patient’s participation in the study. Summaries of the number of sessions attended, dropout from each intervention, and withdrawal of consent were included.

Acceptability was evaluated by the reported patient satisfaction from the CSQ-8 measure for each intervention. Satisfaction outcomes were compared between interventions to assess if there was a statistically significant difference between patient satisfaction between the two interventions.

2.7.1.2 Primary and Secondary Behavioural Outcomes

Behavioural outcome measures pre- and post-treatment were compared for each intervention separately and between interventions. The data for each intervention was assessed for clinically significant, reliable change and against the IAPT recovery benchmark (IAPT, 2014). Clinically significant and reliable change was compared between interventions. Effect sizes were calculated for pre-post treatment effects and compared against previously reported outcomes for this

patient group. Potential inflation of type II error was controlled for through the use of appropriate corrections for multiple comparisons.

As a result of delays in the initiation of recruitment and time constraints of the study data collection, the majority of patients were still receiving treatment by the data collection deadline, and data up to session four was available. To address this Mixed Methods Linear Modelling (MMLM) was used to create a model of best fit for the data of the 22 participants eligible for analysis. MMLM is a statistical approach, which can be applied to small, and unequal and incomplete data sets, which use repeated measures, and provides a tool to estimate fixed and random effects using all observation available in the dataset. MMLM uses likelihood algorithms (REML or ML) for estimation and creates a "complete" data set based on a hypothetical scenario, in which there is no missing observation in the dependant variable. A "complete" data set is generated by augmenting observed values on the dependant variable with expected values of the sum of squares and sum of products of the unobserved random effects and residuals (West, Welch & Galecki, 2007). MMLM analysis was conducted using SPSS version 22 and models of best fit were determined by using a likelihood ratio test (LRT) to select the most parsimonious model. The significance of the LRT is determined by use of chi-squared distribution and appropriate degrees of freedom. If the difference is large the more complex model is favoured, if the difference is small the null hypothesis model or nested model is favoured. The model of best fit was then used to generate predicated scores for missing values in a modified Intent-to-treat (ITT) analysis for patients who had not completed four treatment sessions. ITT was considered in regards to predicted change scores.

3. Results

3.1 Patient Flow

Four hundred and twenty four individuals were screened for suitability for the study between 1st January 2014 and 10th April 2014 via the IAPT services initial triage assessment. Of the individuals screened 46 met the study inclusion criteria and were approached to participate in the study and 24 consented to participate and were randomly assigned to either the Understanding Worry (UW) or Treatment as Usual (TAU). Two individuals withdrew consent after randomisation and did not complete pre-treatment measures and were not eligible for analysis. Three individuals did not start treatment but completed pre-treatment measures. Three participants dropped out of treatment and 22 participants were eligible for analysis. Figure 1 summarises the study patient flow.

3.2 Demographic Data

Table 3 summarises the available demographic data of patients who participated in the study as an overall sample and by allocated treatment arm. In the overall sample 77.3% were female and were referred to IAPT via their GP. The majority of the sample was in of employment (59.1%) and were white British (59.1%). The most common provisional diagnoses at assessment were GAD (59.1%), moderate depression (18.2%), mixed anxiety and depression (13.6%) and recurrent depression (4.5%). Post-randomisation there was a mean difference of 5.28 years between the UW and TAU groups. The main reason for difference between the two groups was that five of the participants in the UW condition were under 24 years of age and half of the group were over 30 years old with two individuals above the age of 50. There was very little difference between conditions in relation to primary diagnosis, employment and ethnicity.

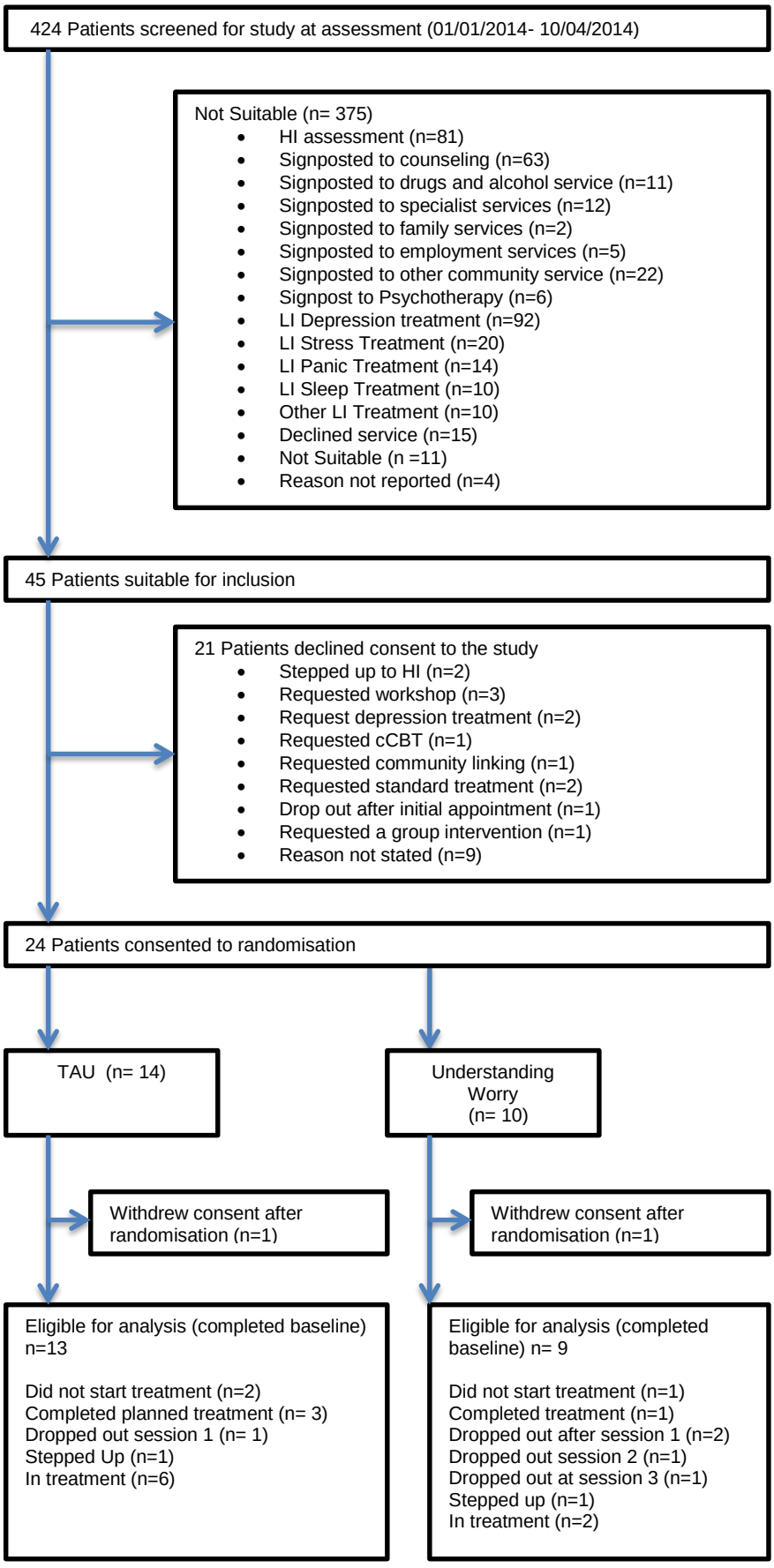

Figure 1: *Consort diagram*

Table 3*:* *Demographic description of participants*

		Overall Sample		**TAU**		**Understanding Worry**	
Variable	Sub-variable	N	%	n	%	n	%
Gender	Male	5	22.7	4	30.8	1	11.1
	Female	17	77.3	9	69.2	8	88.9
Age	Mean Age (SD)	31 (10.01)		28.85 (7.09)		34.11 (13.18)	
	Range	19-59		19-44		22-59	
Referral Source	GP	17	77.3	11	84.6	6	66.7
	Self	5	22.7	2	15.4	3	33.3
Provisional Primary Diagnosis	GAD	13	59.1	8	61.5	5	55.6
	Mixed Anxiety & Depression	3	13.6	1	7.7	2	22.2
	Moderate Depression	4	18.2	2	15.4	2	22.2
	Recurrent Depression	1	4.5	1	7.7	-	-
	Not Reported	1	4.5	1	7.7	-	-
Medication Use	Yes	7	31.8	3	23.1	4	44.6
	No	15	68.2	10	76.9	5	55.6
Employment Status	Employed	13	59.1	8	65.1	5	55.6
	Unemployed	6	27.3	3	23.1	3	33.3
	Receiving Benefits	1	4.5	1	7.7	-	-
	Homemaker or Carer	2	9.1	1	7.7	1	11.1
Ethnicity	White British	14	63.6	7	53.8	7	77.8
	White Other	4	18.1	4	30.8	-	-
	Asian	1	4.5	1	7.7	-	-
	Mixed Other	3	12.6	1	7.7	2	22.2

Note: SD: Standard Deviation

3.3 IAPT Caseness Pre-treatment

Pre-treatment every patient scored eight or above on the GAD-7 meeting the IAPT criteria (IAPT, 2011) for clinical caseness; 14 patients (63.6%) scored 10 or above on the PHQ-9 meeting clinical caseness and 14 patients (63.6%) met the criteria of IAPT caseness on both PHQ-9 and GAD-7 measures. All patients who completed baseline measures scored above 44 on the PSWQ, indicating substantial levels of worry and what would be seen as above caseness of GAD.

3.4.1 Indicators of Feasibility

3.4.1.1 Recognition and Detection

Over a 15-week period PWPs identified 10.8% of referrals as experiencing excessive worry and anxiety as a primary problem. This represented the second largest patient group after low mood, indicating that there is an adequate level of clinical need to justify a specific LI intervention for worry and GAD. However, it is likely that the number of referrals identified over this time period is an underestimation of individuals who experience worry or GAD as a primary problem. Pre-treatment PSWQ scores in the overall sample were high (M= 69.55, SD= 6.10), with all individuals in the trial reporting an initial PSWQ score above 60.

3.5 Behavioural Outcome Measures

Due to the small sample, as a result of data collection time constraints, all available session data for patients who attended a minimum of two clinical contacts were included in the analysis using a Mixed Model Linear Modeling (MMLM). Table 4 summarises the pre-treatment and up to the last recorded clinical contact for all patients with a minimum of two clinical contacts. Table 5 summarises the adjusted means and change score for imputed ITT data up to session four. ITT data will be considered in relation to the predicted change scores of each treatment arm.

3.5.1 PSWQ

MMLM, using all available session data, indicated that there was no significant effect of treatment group on self-reported worry, *F* (1,22)= 0.91, p= 0.35 but a significant effect of time, *F* (4,38)= 3.740, p= 0.01. Within group effect sizes were 0.38 (95% CI: -0.41 to 1.14) and 0.72 (95% CI: -0.09 to 1.49) for UW and TAU respectively; there was also a medium between group effect size (d= 0.56, 95% CI: -0.32 to 1.41). ITT analysis based on the predicted values from the MMLM model predicted reductions in PSWQ score at session four of 12.24 points (95% CI: 8.06 to 16.42) in the TAU condition and 7.68 points (95% CI: 3.39 to 11.97) in the UW condition. The difference between treatment conditions (MD= 4.56) was not significant, t (20)= 1.64, p= 0.12.

Based on the reliable change index (Jacobson & Truax, 1991) previously reported by Fisher (2006), a change of seven points on the PSWQ constitutes reliable change in reported symptoms. Recovery was defined as meeting the reliable change criteria in addition to reporting a score below the measures clinical cut-off of 45. Two patients (22.2%) from the UW condition reported a reliable improvement in worry. Whereas in the TAU condition five patients (38.5%) reported reliable improvements in worry and one patient (7%) reported a reliable increase in worry. One patient in the TAU condition met the criteria for recovery.

3.5.2 PHQ-9

MMLM, using all available session data, indicated that there was no effect of treatment groups for self-reported symptoms of depression, *F* (1,22)= 0.06, p= 0.94 or time, *F* (4,38)= 0.764, p= 0.55. Both within group effect sizes for both the TAU (d= 0.05, 95% CI: -0.81 to 0.72) and UW conditions (d= 0.19, (-0.74 to 1.11), there was also a small between group effect size (d =0.23, 95% CI: -0.63 to 1.07). ITT analysis predicted a change score at session of 2.17 (95% CI: -0.55 to 2.17) in TAU and 2.61 (95% CI: 0.01 to 5.22) in the UW condition. The difference between treatments (MD= -0.44) was not statistically significant, t(20)= -2.50, p= 0.81.

At the last clinical contact one patient reported a reliable improvement in depressive symptoms and one patient reported a reliable deterioration in the UW condition. In the TAU condition, one patient reported a reliable deterioration.

3.5.3 GAD-7

MMLM, using all available session data, indicated that there was no significant effect of treatment group on self-reported symptoms of anxiety, *F*(1,22)= 091, p= 0.35 but a significant effect of time, *F*(4,38) 3.740, p= 0.01. Within group effect sizes were 1.30 (95% CI: 0.23 to 2.24) and 0.88 (95% CI: 0.05 to 1.65) for Understanding Worry and TAU respectively, there was also small between group effect size (d= 0.20, 95% CI: 0.66 to 1.05). ITT analysis predicted a change score of 7.87 (CI: 5.27 to 10.47) for TAU and 6.57 (95% CI: 3.75 to 9.39) in the UW condition, the difference in predicted change scores (MD= 1.31) between to the two treatments was not statistically significant, t (20)= 0.74, p= 0.47.

Four patients (44.4%) in the UW condition achieved reliable reductions in anxiety and five patients (38.4%) in the TAU condition reported a reliable improvement in TAU condition.

3.5.4 WSAS

MMLM using all available session data indicated that there was no significant effect of treatment groups in regards to functioning, *F*(1,22)= 0.034, p=0.86 but a significant effect of time, *F*(4,31)= 2.87, p= 0.04. There was a medium within group effect size (d= 0.30, 95% CI: -0.48 to 1.07) for TAU condition and a medium between group treatment effect size (d= 0.34, 95% CI: -0.53 to 1.19). The ITT model predicted a change score at session of four in the TAU condition of 3.86 (95% CI: 0.57 to 7.15) and 2.34 (95% CI: -1.28 to 5.83) in the UW condition. A comparison of the difference in predicted change scores (MD= 1.51) indicated that there was no statistical difference between treatment conditions, t (20)= 0.66, p= 0.50. No patients in either arm met the criteria for reliable clinical change.

Table 4: *Outcome measures pre-treatment to last clinical contact: Means, standard deviations, confident intervals and effect sizes (Cohen's d) for each group (N=22)*

Outcome Measure	Group	Pre-Treatment Mean (SD)	Last Clinical Contact Mean (SD)	Mean Change (95% CI)	Within Group ES (95% CI)	Between Group ES (95% CI)
PSWQ	TAU	69.00 (5.77)	62.00(12.43)	7.00 (1.12 to 12.88)	0.72 (-0.09 to 1.49)	0.56 (-0.32 to 1.41)
	UW	70.33 (6.76)	67.86 (6.23)	4.43 (0.97 to 7.78)	0.38 (-0.41 to 1.14)	
PHQ-9	TAU	11.23 (5.42)	11.54 (7.56)	-0.31 (-2.46 to 1.85)	-0.05 (-0.81 to 0.72)	0.23 (-0.63 to 1.07)
	UW	11.00 (4.58)	10.00 (5.48)	0.14 (-3.21 to 3.50)	0.19 (-0.74 to 1.11)	
GAD-7	TAU	15.31 (4.27)	10.31 (6.81)	5.00 (1.95 to 8.05)	0.88 (0.05 to 1.65)	0.20 (-0.66 to 1.05)
	UW	13.67 (3.46)	9.14 (3.53)	4.71 (0.49 to 8.94)	1.30 (0.23 to 2.24)	
W&SAS	TAU	16.62 (7.07)	14.31 (8.16)	2.31 (-0.29 to 4.80)	0.30 (-0.48 to 1.07)	0.34 (-0.53 to 1.19)
	UW	17.00 (9.95)	16.96 (7.03)	0.57 (-4.34 to 3.20)	0.01 (-0.92 to 0.93)	

Note. UW – Understanding Worry, TAU – Treatment as Usual, ES –Effect Size

3.7 IAPT Recovery

Recovery data was reviewed for all individuals who attended two clinical contacts. IAPT recovery is defined as a pre-treatment score on the PHQ-9 above nine or a score on the GAD-7 above 7 and a post-treatment scope or below 10 on the PHQ-9 and below eight on the GAD-7 (Richards & Borglin, 2011). Using this criterion, three patients (33.3%) in the Understanding Worry condition and four patients (30.8%) in the TAU treatment met the criteria for recovery.

Table 5*: ITT Pre-treatment to Session 4: Adjusted Means, standard deviations, confident intervals and effect sizes (Cohen's d) for each group (N=22)*

Outcome Measure	Group	Pre-Treatment Adjusted Mean (SD)	Session 4 Adjusted Mean (SD)	Adjusted Mean Change (95% CI)	Within Group Adjusted ES (95% CI)	Between Group Adjusted ES (95% CI)
PSWQ	TAU	69.00 (5.77)	56.76 (8.96)	12.24 (8.06 to 16.42)	1.62 (0.69 to 2.45)	0.81 (0.10 to 1.66)
	UW	70.33 (6.76)	62.65 (3.48)	7.68 (3.39 to 11.97)	1.43 (0.43 to 2.39)	
PHQ-9	TAU	11.23 (5.42)	9.06 (5.79)	2.17 (-0.55 to 4.89)	0.39 (-0.40 to 1.15)	0.08 (-0.77 to 0.93)
	UW	12.11 (5.21)	9.50 (4.29)	2.61 (0.01 to 5.22)	0.55 (-0.42 to 1.46)	
GAD-7	TAU	15.31 (4.28)	7.44 (4.76)	7.87 (5.27 to 10.47)	1.74 (0.79 to 2.58)	0.09 (-0.77 to 0.93)
	UW	13.67 (3.46)	7.10 (2.33)	6.57 (3.75 to 9.39)	2.23 (0.97 to 3.28)	
W&SAS	TAU	16.62 (7.07)	12.75 (6.18)	3.86 (0.57 - 7.15)	0.58 (-0.22 to 1.35)	0.32 (-0.55 to 1.16)
	UW	17.00 (6.94)	14.65 (5.70)	2.34 (-1.28 to 5.83)	0.37 (-0.58 to 1.28)	

Note. UW – Understanding Worry, TAU – Treatment As Usual, ES –Effect Size

3.8 Indicators of Acceptability

3.8.1 Attrition and Attendance

Prior to the start of treatment five individuals dropped out or withdrew from the study. Two individuals, one from each intervention arm, withdrew consent to participate and received the service's standard treatment. Two individuals from the TAU condition did not start treatment. In the Understanding Worry condition one individual did not start treatment. The overall attrition rate from randomisation was

22.7%, as a total of five individuals dropped out of treatment, the attrition rate for UW condition and TAU condition were 7.6% and 33.3% respectively. However, it is of note that an individual in the UW condition dropped out of treatment as they emigrated from the country, taking this into account the attrition rates between the two conditions equated to one patient in the UW condition and two patients in the TAU, indicating that attrition was similar across both treatments.

The pattern of attendance is summarised in Table 6. There was no difference in pattern of attendance, cancellation or did not attend (DNA) between treatment conditions, X^2= (2, N=102)= 1.665, p= 0.44, suggesting that both treatments were equally acceptable.

Table 6: *Summary of attended clinical contacts, cancellations and DNAs (N=22)*

	Overall Sample	**TAU**	**Understanding Worry**
	Mean (SD)	**Mean (SD)**	**Mean (SD)**
Attended Clinical Contacts	3.09 (1.02)	3.45 (0.82)	2.89 (1.05)
Cancellations	1.09 (1.02)	1.27 (1.27)	1.00 (0.71)
DNA	0.36 (0.58)	0.27 (0.65)	0.44 (0.53)

3.8.2 Implementation

The number mean of days individuals had to wait between scheduled clinical appointments for both treatments exceeded 14 days, and was longer in the Understanding Worry condition (Mean= 21.75, SD= 13.49) than in the TAU condition (Mean= 17.02, SD= 6.08). There was no significant difference between treatments in the mean number of days between appointments, *F* (1,20)= 1.26, p= 0.28.

The number of sessions offered to individuals in treatment varied with individuals in the UW condition (Mean= 3.56, SD= 1.74) receiving fewer treatment sessions offered than in the TAU condition (Mean= 5.23, SD= 1.58). There was a significant difference between the two treatment groups in regards to the number of

sessions offered (*F* (1,20)= 5.47, p= 0.03). However, this may be accounted for by more individuals being randomised into the UW condition later in the study, which limited the number of sessions that could have been offered within the duration of the study, and the reported difference should be treated with caution.

The majority of both treatments were delivered via face-to-face sessions, with 76.5% and 77.6% of clinical contacts being face-to-face in the UW condition and TAU condition**,** respectively. There was no difference between treatments in regards to the type of session offered (X^2=1, 101)= 0.17, p=0.90.

3.8.3 CSQ-8

During the duration of the study four individuals completed planned treatment and completed a CSQ-8. In the UW condition one individual completed treatment and reported a satisfaction score of 24 out 32. In the TAU condition patients reported a satisfaction score of 31, 23 and 24 and a mean satisfaction score comparably to the UW condition (Mean= 26, SD= 4.36). This tentatively suggests that individuals who completed treatment were similarly satisfied with the treatment they received. However conclusions are tentative and limited by the small sample size.

3.8.4 Clinician Feedback

PWPs were asked to provide their feedback in their experience of delivering the new UW intervention, and 57% of clinicians completed the brief survey. PWPs reported the materials were easy to follow, that content was more in depth than TAU and the use of examples within the intervention helped individuals relate to the material. PWPs reported that the ability to select modules, the clear objectives, the examples that supported the psycho-education material, and the use of visual scales to measure progress were all strengths of the intervention. PWPs also commented that they had increased in confidence as they delivered the intervention more often and felt more knowledgeable about GAD. However, PWPs also identified that given the limited time in guided support sessions the modules

contained too much material to cover in detail during the session and session preparation required more time than the TAU intervention. They also reported that if the individual had not completed the module material before the session it provided a challenge to cover the material in the allotted time. PWPs also felt that there was limited time to review the learning between sessions and the homework assignment and felt that perhaps more time could be allocated in sessions to this area. PWPs commented that reducing the amount of information in the modules and the provision of additional training would be future improvements, as the concepts underpinning the UW intervention were not currently taught in IAPT PWP training courses.

4. Discussion

The study sought to develop and pilot a LI intervention specifically for excessive worry and GAD symptoms (UW). It was delivered by PWPs in a routine clinical setting. The main aims of the study were to assess the feasibility and acceptability of the UW intervention and to establish an indication of clinical effect and performance in comparison to the current treatment.

The initial question of whether it was feasible to deliver a structured LI intervention adapted from HI theory, which specifically addressed excessive worry and GAD symptoms, was supported. Referrals screened during the study period indicated that those with excessive and uncontrolled worry and GAD as a primary presenting problem represented the second largest patient group after those presenting with low mood. This demonstrated that there was a current level of clinical need to justify a specific LI intervention focusing on excessive worry and GAD symptoms. Additionally, the clinical need identified was likely to be an underestimate as pre-treatment scores on the PSWQ were high and exceeded pre-treatment scores of previous published LI studies (Titov et al., 2010; Robinson et al., 2011) and were equivalent or higher than several published HI GAD treatment

studies (Landoucer et al., 2000; Dugas et al., 2003; Dugas et al., 2010; Wells et al., 2010). This suggests that individuals with less severe or mixed anxiety and depression presentation were not reliably identified by practitioners, and raises broader questions about the assessment of suitability for LI interventions as the pre-treatment anxiety scores on the GAD-7 were at the high end of the moderate range. Several patients in the study may well have met the criteria for HI treatment rather than LI intervention according to the IAPT step cared model (IAPT, 2008), as 50% of the sample reported pre-treatment anxiety scores in the severe symptom range. This suggests PWPs in routine practice appear to be working with patients who are reporting clinical levels of severity that LI interventions were not conceptualised to accommodate, which suggests robust interventions at an LI are required.

The question of whether the specific Understanding Worry (UW) intervention would be acceptable to patients was supported. The hypothesis that UW was practical to delivery at an LI level was partially supported.

There was no difference between the UW and TAU in patterns of attendance, cancellation and DNA of clinical sessions. The attrition rates between the treatments were comparable, indicating that both treatments were equally acceptable to patients. The four patients who completed the treatment as planned and completed post-treatment satisfaction measures reported a high level of satisfaction with the treatment received, which suggested that UW as an LI treatment was as acceptable as TAU. Attrition after the start of treatment was similar to previously reported rates of attrition in clinical interventions (Hunot et al., 2007). However, the study's patient flow showed a considerable number of suitable patients declining entry into the study and withdrawal after initially consenting to participate, demonstrating that those with worry and anxiety may be a challenging group to recruit. It is possible that processes such as intolerance of uncertainty contributed to difficulty in recruitment into the study and may highlight a wider clinical issue in the treatment of anxiety disorders.

In relation to the implementation of the UW treatment, patients were offered fewer sessions than in the TAU condition, with a longer gap between sessions. Possible explanations for this discrepancy may be that PWPs felt less confident in the delivery of new material and implementation of the treatment protocol and prioritised TAU treatment sessions, as this was more familiar, which resulted in greater clinical contact and a higher treatment effect. However, the differential number of offered clinical contacts may be an artifact of the randomisation process given the small numbers in each arm. Reviewing the randomisation matrix after the data was analysed showed that a high number people were randomised to TAU in the early stages of recruitment. The consequence of patients being randomised to the UW condition later in the trial meant that there was less opportunity for sessions to be offered before the end of data collection.

In regards to the delivery of the intervention PWPs reported positive experiences in the delivery of the UW intervention and highlighted the clear and consistent format and focus on uncertainty and avoidance, the behavioural framework, the modular format, clear objectives, clinical examples and the clear session framework as strengths of the intervention. However, PWPs believed that the amount of content in modules was too much to cover in support sessions and should be reduced. Practitioners also commented that there should be more time to focus on the learning from the between session tasks as this was challenging to facilitate given the high level of content to review in support sessions. It is possible that refining the material based on this feedback may facilitate increased effectiveness, as the UW treatment may become more focused, accessible to patients and practitioners.

The question of whether the UW intervention was comparable to TAU was partially supported. The available clinical data and ITT modeled data both suggested that the UW treatment was no more effective than TAU. Both treatments showed reductions in worry and anxiety symptoms at the last observed clinical

contact and the ITT modeled data and indicated that change in worry and anxiety symptoms were greater in the TAU condition, but the difference between UW and TAU was not statistically significant. Treatment effect sizes were within previously reported confidence intervals for IAPT LI treatments (Richards & Borglin, 2011), but were slightly lower in comparison to previously reported controlled trials of LI GAD treatments (Titov et al., 2009; Robinson et al., 2010).

The observed treatment effects could be explained in part by the differences in treatment dosage between treatments. A larger number of TAU patients completed planned treatment, with a shorter duration between treatment sessions, in comparison to UW. It can be argued those in TAU had the opportunity to engage more with treatment and received a higher dose of treatment than those in the UW condition and as a result showed a greater improvement in reported symptoms. Whereas the UW condition in comparison received fewer sessions with longer gaps between them, as a result patients receiving the UW treatment may have experienced a lower treatment dosage and consequently reported limited reductions in symptoms. Alternatively the differences between TAU and UW could be accounted for by the relative effects of experience and confidence in delivery of the interventions, as PWPs first experience of delivering UW treatment was limited to eight hours of training and zero hours clinical delivery prior to the start of the trial. The relatively weaker clinical effect of UW may reflect that PWPs were still in the process of understanding the material and how to effectively deliver it clinically. PWPs may not have held an understanding of the underlying theory as clearly and confidently as their understanding of the first wave CBT theory that underpinned the TAU condition. It is probable that the observed difference in reported symptoms between interventions would diminish as PWPs confidence and understanding improved through the further training in the delivery of the UW intervention and training.

However, there are several alternative explanations as to why the TAU condition reported larger reductions in self-reported symptoms of worry and anxiety in comparison to UW. It may be that a brief LI intervention which draws on second wave CBT approaches for GAD is no more clinically effective than first wave Beckian CBT approaches. This may be due to more complex concepts such as intolerance of uncertainty and emotional avoidance not translating well into an LI time-limited format and may reflect the level of practitioner training. Second wave CBT content for GAD may require a longer treatment duration input and a higher-level practitioner to be delivered effectively. Additionally, UW treatment did not attempt to address meta-cognitive aspects of GAD such as beliefs about worry, which could be have led to a reduction in clinical effectiveness as the complete model was not included in LI treatment. Given the complexity of cognitive work it was considered to be more suitable to HI interventions. However, any firm conclusions in regards to effectiveness are limited by the study's small sample size.

The final question of whether the UW intervention would lead to reliable change in anxiety and worry was partially supported. The ITT model suggested that individuals who received the UW condition would achieve a change score on the PSWQ and GAD-7 that would reach the criteria for reliable clinical change by session four of treatment. In the observed clinical contacts 22.2% showed a reliable improvement on the PSWQ and 44% showed a reliable improvement on the GAD-7 measure. In regards to clinical recovery, 33.3% of those who received the UW treatment met the IAPT recovery criteria at their last clinical contact. The relative low levels of attended sessions in the UW condition (M= 2.89) may explain the relatively low rate of recovery and it is likely this would have improved if patients had completed the UW treatment and received the planned treatment dose.

Limitations

There are several limitations of the current pilot study. Firstly, as a consequence of challenges in recruitment, the sample size is small and therefore

the current study is statistically underpowered. This limits the generalisability of findings and all conclusions should be treated tentatively and with the appropriate level of caution. However, it is of note that despite the early ending of the study the obtained sample size was comparable with that of other published GAD pilot studies (Wetherall et al., 2011; Wells et al., 2010). A substantial limitation was the lack of a delayed treatment or active placebo control group, which means that the rate of natural remission of symptoms could not be established and cannot be discounted as a possible explanation for the observed symptom reduction. The pilot study used practicing clinicians as both assessors and therapists, which may have introduced demand and allegiance effects. Additionally bias may have been introduced as practitioners delivered both interventions, the possibility of leakage between interventions cannot be discounted as no formal measure of adherence was used and was only assessed via clinical supervision, which provided a limited check on intervention fidelity. Practitioner and participant expectations prior to intervention were not assessed formally, which may have introduced additional bias. Other sources of potential bias such as the use of medication and previous psychological treatments were not assessed in this study. The use of pure self-report measures rather than an independent diagnostic interview is also a potential limitation of the current study as provisional diagnosis was reached using the IAPT screening algorithm following assessment which is not a structured diagnostic interview. It is possible that reported provisional diagnoses of GAD were a consequence of the assessor's bias and expectancy effects.

Finally, due to time constraints data collection was stopped early. As a direct consequence of this a number of patients in both arms did not receive the full intervention as planned, therefore the cumulative treatment effect is uncertain. Also it is possible that treatment arms did not receive equivalent dosages of treatments. Dedicated trial therapists were not used which contributed to the reported challenges in the implementation of the intervention, as PWPs were required to

provide the study interventions alongside a full clinical caseload. Also the long-term clinical effect of both the TAU and UW interventions was not assessed in the pilot.

Future Research

Further research that focuses on the replication of this pilot should focus on the further refinement of the treatment material and following that testing the impact of alternative forms of delivery such as group, pure self-help and Internet treatment. The use of dedicated and more comprehensively trained therapists may enable a more robust assessment of effectiveness given the described difficulties in the implementation of the intervention in the context of a high clinical caseload. Research should also seek to assess the long-term effect of treatment through follow up, and in order to be suitably powered to reliably detect large between group treatment effect should aim to recruit a minimum sample of 84 people. However, as the current study compared a novel treatment with an active treatment it is likely that any difference between treatments would be a small to medium effect. Trials that would be appropriately powered to reliably detect a medium or small effect between treatments would require a total sample of 580 and 5200 people respectively**.** Due to the difficulties reported in the recruitment process future studies may need to consider research design carefully and the use of a randomised cluster design may improve recruitment, as the prospect of individual randomisation appeared to be difficult to tolerate for those reporting high levels of worry. Future research may also choose to focus on whether underlying processes such as intolerance of uncertainty using the Intolerance of Uncertainty scale (Freeston, Rhéaume, Letarte, Dugas, & Ladouceur, 1994) predicts treatment response or the early termination of treatment. A greater understanding of the underlying processes of worry and GAD and their impact on engagement may improve treatment retention and clinical outcomes.

Clinical Implications

It is clear that those who experience pathological levels of worry and GAD symptoms are a challenging group to engage in treatment. The study also indicates within routine IAPT practice that the recognition of GAD symptoms may be limited only to those with high levels of worry. Existing literature suggest GAD is often comorbid with other disorders, 29% to 62% of individuals with GAD are estimated to have comorbid depression (Hoge, Ivkovic & Fricchoine, 2012) and there is also significant comorbidity with other anxiety disorders (NICE, 2011). This suggests that PWPs may require more training in the recognition and assessment of GAD. The use of the PSWQ as a screening tool for uncontrollable worry should be considered to aid identification of patients with excessive worry where GAD is suspected. Finally, the approach to intervention design adopted within the current pilot may provide a useful framework and further opportunities for the development of LI interventions for other disorders.

Conclusion

The primary goal was to establish whether a specific GAD intervention based on HI theory could be delivered by PWPs at an LI treatment level. The findings of the current pilot study suggest that there is a clinical need for an LI intervention that focuses on addressing worry and GAD symptoms within primary care IAPT services. Findings tentatively indicate that an intervention adapted from the current HI approaches can be delivered by PWPs but this requires further development, refinement and the provision for further training. The study also highlighted several challenges of implementing intervention research for anxiety disorders in clinical settings.

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Part 3: Critical Appraisal

Introduction

This appraisal will critically evaluate the empirical study, focusing on the background to the research, the conceptual issues in the intervention design and the challenges of conducting research in NHS clinical settings, particularly focusing on recruitment and the involvement of clinicians in the research process. The appraisal will also consider future directions for research, clinical implications and the learning points from the research process.

Background

After my undergraduate and postgraduate studies I worked for two years at a second wave IAPT site as a Psychological Wellbeing Practitioner (PWP) and a senior PWP. During this time I was involved in the evaluation of a Low Intensity (LI) psycho-educational depression group and saw that the routine collection of clinical outcomes could be used to aid the development and evaluation of interventions' clinical effectiveness. I also saw how the IAPT service design lent itself to the testing and development of interventions in routine clinical settings.

During my clinical work it became apparent that there was a gap in the provision of treatments that addressed excessive and distressing worry and GAD at an LI level. My experiences of using the available tools taught on the IAPT training course was that they were generic and advised cognitive restructuring, worry containment and problem solving. Often when my colleagues or I attempted to apply these techniques in guided self-help sessions or psycho-educational anxiety groups it appeared that these tools triggered more worries and led to an increase in anxiety. The treatment outcomes for this patient group also seemed to be worse. This group of patients often showed minimal improvement on IAPT outcome measures, dropped out of treatment more frequently and were often re-referred to the service soon after discharge. It seemed that all the intervention had achieved was to provide the person with additional tools to engage in worry rather than

alleviate any distress or anxiety. As a consequence of this I, as my colleagues did, drew on other sources such as the Centre for Clinical Interventions (CCI, 2014) GAD workbooks and supervision, which led to a hodge-podge of material being selected in an ad-hoc manner with little consistency. Guided self-help sessions would sometimes stray into a diluted version of CBT rather than adhering to the conceptual ethos of LI interventions. The result was that I felt treatment techniques delivered for worry often did not form a coherently treatment package and were varied across the service generally. I wondered if our service and other IAPT sites were providing no more than a 'sticking plaster therapy' for this patient group (Martin & Helmore, 2006). Consequently when the opportunity arose to conduct my own research it was an area I wanted to focus on and hoped to establish if the current LI interventions for GAD could be improved by drawing on High Intensity (HI) theory and adapted into a structured brief intervention that adhered to the principles of LI treatment.

Reflections on Conceptual Issues in Intervention Design

As I had to design the project myself, and it was not part of an existing project, I felt it was important to initially spend time meeting with local IAPT services, PWPs and teaching staff on the PWP training course to gain a sense of their experiences of providing LI interventions for worry and GAD, especially since I had been of out the IAPT services since I started my clinical training. In listening to them I noticed the same concerns were still present and this was still an area in need of development. However, there were a large variety of opinions regarding what was felt to be needed to address this gap and the way in which it should be delivered. It was also clear that there was a concern that any intervention developed adhered to the LI principles and was not CBT-lite. This diversity of opinion is reflected in the emerging LI literature (Bennett-Levy Richards and Farrand et al.,

2010). This presented a challenge in balancing the views of what theoretical material the LI treatment should include and how this was best adapted.

To address this I adopted a pragmatic approach of reviewing the current LI interventions for GAD and worry and deconstructed the interventions into their individual elements; this helped give a sense of how the interventions were structured, what were the most common elements and what was missing. I also reviewed the evidence for the theoretical CBT models of GAD, which allowed me to decide on a coherent theory to base the intervention on. This was the Intolerance of Uncertainty (IoU) model (Dugas et al., 1998), the model with the most established evidence base. Although this took longer than anticipated I hoped that it help to engage the PWPs who would be delivering the intervention, so they could see that this was a new intervention not just a repackaging of existing LI approaches but based on a clear model. I also hoped the modular structure would allow them to exercise their existing clinical skills and provide a treatment which was tailored to the patient but retained a clear structure.

This led to the issue of how to structure the material and how PWPs should deliver it so the intervention kept the CBT in the material and utilised PWPs skills in guidance, support and scaffolding of the patient's reflective learning processes (Bennett-Levy et al., 2010). To achieve this I was aware that the material and support sessions needed to focus on process and the encouragement of positive behavioural change. The Behavioural Change Theory (BCT) framework of intervention (Michie, Van Stralen & West, 2011) appeared to fit well with the ethos of LI intervention and the COM-B approach ensured that each element in the intervention was included for a clear definable reason. It also provided a clear rationale for the structure support sessions, which I hoped would allow PWPs to adopt the intervention as a whole rather than just the patient materials. The explicit focus on behaviour allowed the focus of worry to move away from the content and focus on process and behaviour.

The initial idea for the intervention was a fixed six-session structured intervention, which while providing a consistent intervention would almost certainly have lost individuals, as the material may not have been immediately relevant, and motivation for treatment could be lost. As a solution a modular format was constructed, which included a mandatory psycho-educational and last session review, with sessions in between benefiting from a flexible selection of modules that address different areas of GAD such as uncertainty, problem solving and avoidance. The advantage of this approach was that it provided a consistent format but allowed flexibility to tailor interventions to maximise engagement, as what was most meaningful for the individual could be addressed first. However, on reflection this choice of which areas to address may have inadvertently increased patients' anxiety as it introduced uncertainty in where to begin. It is also possible that by offering a choice individuals may well have avoided the areas of the intervention that would bring the most anxiety. Additionally, the choice element in of the intervention may have been perceived as an additional burden to the PWPs delivering the intervention and resulted in them delivering the modules they preferred. I attempted to address this by consulting with PWPs throughout the design of the materials and modified the material in line with the feedback I received. By doing this I aimed to engage and motivate the PWPs and encourage them to view the project as something other than an academic piece of work.

A weakness in the overall design of the intervention was that it did not include any service user involvement. In hindsight this may have provided valuable information and feedback to ensure the content of the intervention was engaging and connected with the experience of worry and GAD in a way that supported motivation for change. Also I was aware that I wanted to provide a clear explanation of the approaches in the intervention and as such brevity may have been sacrificed to an extent. This may have been off-putting and made working

through the modules feel like a chore; service user involvement could have provided valuable guidance in this regard.

Reflections on Conducting Research in Clinical Settings

There were several challenges that became apparent during the course of the research. The main challenges that will be focused on are the methodological compromises made and the process of study recruitment.

The research was conducted in a busy and strictly commissioned clinical setting, which as a consequence led to pragmatic constraints in study design and the recruitment process, as the process was required to fit within service's existing assessment and treatment targets. Due to the timescale of the research, methodologies such as a cluster randomised trial design, where multiple sites would deliver one intervention, were not realistic given the service assessment system or the time scale of the study. Similarly the concern of waiting list breaches meant that a delayed treatment control or placebo condition could not be used. This meant that a natural rate of reduction in symptoms could not be measured and controlled, as worry and GAD have a characteristic waxing and waning course (NICE, 2011). Given the practical restrictions a randomised design was considered the most suitable for the piloting of the intervention, as this would reduce selection bias and threats to interval validity (Barker, Pistrang & Cooke, 2002) while being implementable within the service's normal practice. Despite these limitations the main advantage was that the study compared the service's existing treatment to the experimental intervention, which I hoped would provide immediate clinically useful information, and allowed the acceptability to be assessed directly against the service's current treatment.

The recruitment into the study was a challenge as there were significant delays in gaining ethical approval due to the concerns of the use of a novel treatment in a clinical setting. This delay resulted in recruitment beginning four

months later than planned. Recruitment into the study was slow and it became apparent that PWPs were not completing the number of assessments that had been used in the preliminary calculation for recruitment. It also appeared that a bystander effect (Lantané & Nida, 1981) was partially present with recruitment rates varying between PWPs and this appeared to be exacerbated by the fact that PWPs were often working at different GP surgeries isolated from each other. This may have led to some PWPs leaving the task of recruitment to the other practitioners involved in the study. It may also have been explained by the service's highly active contribution to research as PWPs were simultaneously recruiting for other studies, and experienced a level of general research fatigue. I tried to encourage and remind the PWPs by arranging meetings with them and sending regular emails to update them. However, on reflection my attempts to be supportive and to recapture the earlier motivation present in the intervention development and training phase and may have been perceived by the PWPs as nagging and inconsiderate of the high volume caseload that they consistently carried. I believe that I underestimated the amount of extra work that was created for the PWPs who I was relying on to recruit and deliver of the study interventions. My intention had been to integrate the research design as much as possible into the normal services practiced, by the addition of the PSWQ to session MDS, and by providing a clear manual and training in how to deliver the experimental intervention. In the feedback I received from the PWPs during scheduled meetings and more casual conversations it appeared that delivering the experimental intervention required more preparation than I had anticipated and that the style of the intervention was different to what they had been used to. In hindsight it may have been helpful to provide more training in the delivery of the intervention and include more experiential practice of reviewing the material. However, given the high workload and clinical commitments of the PWPs and their supervisors it was not possible to arrange this. Perhaps establishing

regular contact with their supervisors could have helped provide more support and guidance as the clinicians got used to the new intervention.

Another major issue was recruiting suitable participants into the study. I had not expected that a primary care patient group would be so challenging to recruit into a research study. On meeting the PWPs to discuss recruitment they reported that often they would assess an individual and identify them as suitable but the patient would decline to participate in the study or would agree and then withdraw when contacted to collect the baseline measures. When I explored this with the PWPs they frequently reported individuals expressing worries that they would not be able to do the treatment to a good standard, would ruin the research by not getting better or would be at a disadvantage to the people who received the other intervention, or would want normal treatment as it had been delivered many times before.

This reaction from participants surprised me, however on reflecting about the patient group that was the subject of the study this reaction to the uncertainty could have been expected. Research shows that those who experience GAD and high levels of worry tend to respond more negatively to uncertain situations, are more likely to interpret them as threatening and demonstrate higher levels of indecisiveness (Koerner & Dugas, 2008; Rassin & Muris, 2005). Given this dispositional characteristic, the consent process may have been highly anxiety provoking and experienced as aversive. The prospect of an additional contact with the PWP to confirm consent and to collect the initial study measures may have proved too much and led to a characteristic response of avoidance by dropping out of treatment or deciding to not enter the study. This difficulty in the recruitment of individuals with GAD or high levels of worry appears to be widely reflected across the published GAD literature (NICE, 2011; Hanrahan et al., 2012) as the majority of studies report small numbers of participants entering trials and substantial recruitment durations (Dugas, et al., 2003; Dugas et al., 2010; Hayes Skelton et al.,

2013). It is possible that higher levels of intolerance of uncertainty may have led to those with a relative higher tolerance to uncertainty participating in research more readily than those with lower tolerance of uncertainty and arguably more severe and disabling GAD symptoms. This may be an avenue for further study in regards to developing an understanding of how underlying constructs of GAD may contribute to response treatment and dropout. This understanding may aid clinicians in retaining patients in treatment once they have made contact with a treatment service. It also may suggest that researchers in the future need to carefully consider study designs and recruitment procedures to ensure they do not introduce large amounts of uncertainty that may reduce the likelihood of a suitable individual participating in the research study.

Reflections on Clinical Implications and Future Directions of Research

The empirical study has tentatively shown that it is possible to adopt HI theory to a structured guided self-help LI intervention for GAD and worry, using the BCT model of intervention design as a framework. It is possible that further research could further develop this approach by exploring its application in respect to other disorders at an LI level in both a group and individual treatment format. However, clinically it appears that a clear and shared understanding of what constitutes an LI intervention across IAPT sites and practitioners is still needed and perhaps the above approach to intervention design can aid to an extent this endeavor. Additionally given the experienced difficulty in recruitment it may be prudent for future research with GAD to adopt designs that minimise exposure to uncertainty such as a randomised cluster design where a single intervention is delivered in a single site by dedicated clinical staff.

Clinically the challenges of recruitment have highlighted the difficulties that services may experience in engaging and retaining individuals with GAD in treatment and research. This may give rise to the perception similar to Anorexia

Nevosa that it is a difficult disorder to treat and research due to problems with dropout and recruitment into studies (Agras et al., 2004). Further research that addresses how underlying dispositional characteristics of intolerance of uncertainty impacts engagement in both treatment and research could allow strategies to be developed that could support engagement and retention in treatment. An improved understanding of these factors may also aid the production of larger appropriately powered studies that are more economically viable due to the reduction in recruitment time. These findings may also apply more generally to other disorders such as OCD where intolerance of uncertainty is a significant factor.

Learning Points

The main learning point taken from this experience of conducting research in clinical settings is the importance of groundwork. This is essential in the early stages of a project in terms of gaining a full understanding of a service and existing demands of the clinicians in order to ensure the successful implementation of a study. Also I have learned the importance of considering how disorder process may actively impact the recruitment of individuals into the study and that this needs to be considered at the early stage of the research process. I will also take away the importance of maintaining contact with service leads and supervisors in addition to the clinicians delivering the intervention to ensure consistent support for the study. I have also learned that intervention design is more complex than I first expected and requires the balance to be struck between what is theoretically ideal and what is pragmatic and can be clinically delivered. Also service user input in the early stages of intervention design is important in ensuring the intervention accurately captures and addresses the experience of the disorder being treated.

Conclusion

Whilst there are many other questions that could be addressed in this area, I hope the findings presented here prove useful to other researchers and IAPT services who want to further develop the provision of LI interventions within IAPT for GAD and other psychological disorders.

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Appendix 1: Literature Review Search Terms and Database Filters

Search filter combination strategy:

1) Generalised anxiety disorder filter + Randomised trial filter + General psychology terms.
2) Generalised anxiety disorder filter + Randomised trial filter + Low intensity terms.
3) Generalised anxiety disorder filter + Randomised trial filter + High intensity terms.

Filter search terms:

Filter	Terms
Generalized anxiety disorder filter	1. Anxiety or anxiety disorders).sh. 2. Generali?ed$ anxiet$ Disorder$ or GAD NOT (Glutmic acid dexcarboxylase or gultmaic decarboxylase or gad sad) ti.ab. 3. (anxiety$ or anxious$ or (chronic$ or excessive$ or intens$ or intens$ or ongoing or persit$ or serious$ or sever$ or pathological or uncontrol$ or un control) adj2 worry. Ab.ti 4. Or 1-3.
Randomized trial filter	1. Randomi?ed Control$ Trial$ (ti.ab.) 2. Exp control group or control system 3. Randomized controlled trial .sh. 4. Or 1-3
General Psychology Terms	1. Psychotherapy 2. psychotherap$ or psycho therap$ or psychotherapeutic or (non pharmacological or psychologic$) adj3 (approach$ or assist$ or coach$ or educat$ or instruct$ or intervene$ or manag$ or module$ or program$ or rehab$ or strategy$ or support$ or technique$ or therap$ or train$ ot treat$ or workshop$ or work shop$) adj2 therap$.ti,ab. 3. 1 or 2 4. psychotherapy, brief.sh 5. (brief or short term or time limited) adj2 (intervention$ or program$ or psycho-analy$ or psychotherapy$ or solution$ or therap$ or treat$) .ti.ab. 6. or 4-5 7. or 1-6
LI Terms	1. bibliotherapy.sh 2. (bibliotherap$ or biblio therap$ or (audio$ or book$ or booklet$ or brochure$ or cd or cd rom or cdrom or computer$ or cyber$ or internet$ or phone$ or sms$ or telephon$ or text or texting or video or virtual or web$ or workbook$ or work book$ or written%) adj5 (approach$ or assist$ or coach$ or educat$ or empower$ or psychoanal& or psychotherapy$ or help$ or instruct$ or intervene$ or manag$ or module$ or program$ or rehab$ or strategy$ or support$ or technique$ or therap$ or train$ ot treat$ or workshop$ or work shop$) or (listen$ or read$ or watch$) adj4 (aido$ or book$ or booklet$ or brochure$ or cd$ or cdrom or computer$ or dvd$ or internet$ or manual$ or material$ or multimedia$ or multi media or pamphlet$ or poster$ or read$ or video$ or virtual$ or workbook$ or writtern or www) ab.ti. 3. Self adj (administer$ or care$ or change or direct$ or help$ or instruct$ or manag$ or regulat$ or reinforce$ or re inforc$ or self help$) .ti.ab. 4. Self adj (administer$ or care$ or chang$ or directed$ or help$ or instruct$ or manag$ or monitor$ or regulate$ or reinforc$ or re inforc$ or self help$ ti.ab 5. Guid$ self help or low intensity or brief intervent$ .ab.ti 6. Or /1-5 7. Exp health education 8. (adult$ or client$ or consumer$ or patient$ or participant$ or service use$) adj4 (educat$ or empower$ or knowledge or information$ or instruct$ or promot$ or teach$ or train$) or (anxiet$ or anxious$ or worry or worring) adj4 (educat$ or empower$ or knowledge or information$ or instruct$ or promot$ or teach$ or train$) or booklet$ or brochure$ or leaflet$ or pamphlet$ or poster$ or workbook$ or psychoeducat$ or psycho educate$ or (oral or printed or written) adj5 (book$ or manual$ or material$ or multimedia or mutli media or video$) Adj5 (intervent$ or program$ or therap$ or treat$) .ti, ab. 9. Or 7-8 10. Hotlines.Sh

	11. (call in or callin$ or call lin$ or help lin$ or helplin$ or hot lin$ or hot lin$ or phone in or phonein or caller$) adj3 (intervene$ or program$ or therap$ or treat$).ab.ti. 12. Or/10-11 13. Exp exercise 14. (active living or a?robic$ or exercise$ or physical$) adj3 (active$ or agil$ or educat$ or fitness$).ab, ti. 15. Or/ 13-14 16. (caccbt or ccbt or cbt). Id,kw. 17. (beating adj2 blues) or fearfighter or ffeducation or ff education or internet or moodgym or (living life adj2 full) or stress control or oc fighter or ocfighter or overcoming depression or pain online or (restoring adj2 balance) or standaloneff or stand alone ff or theraput$ learning program$. ab, ti. 18. (bt step$ or calypso$ or climate or climategp$ or climateschool$ or climatemh$ or climateclinic$ or climatetv$ or crufad$ or gpcare$ or ultrasis or (anxiety or anxious) adj3 package$. ad.,ti. 19. (anxiety$ or stress$ or worry$) adj3 (package$ or program$ or course$).ab.ti. 20. (etherap$ or e therap$ or telehealth or tele health) ab.,ti. 21. (e communication$ or emcommunication$ or e consult$ or econsult$ or e visit$ or e visit$ or e therap$ or etherap$ or tele health or telehealth) ti.,ab. 22. (audio$ or cd$ or cd rom or computer$ or dvd or electronic$ or interactive$ or internt$ or multimedia or multi media or online or sms or telephone or text or texting or video$ or virtual$ or web$ or www) abj5 (advocacy or approach$ or coach$ or discussion$ or educate$ or exchange$ or guide$ or help$ or instruct$ or interact$ or intervene$ or learn$ or manag$ or meeting$ or module$ or network$ or online or participant$ or program$ or psychoanal$ or psychotherap$ or rehab$ or retrain$ or re train$ or self guide$ or self help or self-guide$ or selfhelp or skill$ or strategy$ or support$ or teach$ or technique$ or telephone$ or therap$ or train$ or treat$ or work shop& or workshop$) .ab, ti. 23. (audio$ or cd$ or cd rom or cdrom or computer$ or dvd or electronic$ or interactiv$ or internet$ or multimedia or multi media or online or sms or telephone$ or text or texting or video$ or virtual or web$ or www) abj2 (assist$ or based).ab,ti. 24. (audio$ or cd$ or cd rom or cdrom or computer$ or dvd or electronic$ or interactiv$ or internet$ or multimedia or multi media or online or sms or telephone$ or text or texting or video$ or virtual or web$ or www) adj5 (aid or aided or appointment$ or booking% or communicat$ or consult$ or deliver$ or feedback or forum or guided or imput$ or interactive$ or letter$ or message$ or referral$ or remind$ or send$ or transfer$ or transmit$ or visit).ab,ti. 25. audio$ or cd$ or cd rom or cdrom or computer$ or dvd or electronic$ or interactiv$ or internet$ or multimedia or multi media or online or sms or telephone$ or text or texting or video$ or virtual or web$ or www) adj 5 group$.ab.ti 26. (client$ or patient$) adj5 (audio$ or cd$ or cd rom or cdrom or computer$ or dvd or electronic$ or interactiv$ or internet$ or multimedia or multi media or online or sms or telephone$ or text or texting or video$ or virtual or web$ or www).ti,ab. 27. (client$ or patient$ or service user$ or health or information or web or internet) adj3 portal$.ab,ti. 28. Or 16-27 29. exp psychotherapy 30. (audio$ or cd$ or cd rom or cdrom or computer$ or dvd or electronic$ or interactiv$ or internet$ or multimedia or multi media or online or sms or telephone$ or text or texting or video$ or virtual or web$ or www).ti.ab. 31. interactive voice response.ab,ti. 32. Or/ 30-31 33. 29 and 32 34. Or/ 26 and 33 35. Or/1-12,34
HI Terms	1. exp counseling/ 2. (counsel$ or (client or person) adj2 (centred or centered or focus?ed) or non directive$ or nondirective$ or rogerian) adj5 (approach$ or assist$ or coach$ or educat$ or instruct$ or intervene$ or manag$ or module$ or program$ or rehab$ or strategy$ or support$ or technique$ or therap$ or train$ ot treat$ or workshop$ or work shop$) or pastoral care or (individual or personal or talk$) adj (psycho$ or therap$) .ti,ab. 3. Or 1-2 4. Interpersonal relations and (psychotherapy$ or therap$ or treatment) .hw. 5. (Interpersonal$ or inter personal$ or interrelation$ or relation$) adj5 (approach$ or assist$ or coach$ or educat$ or instruct$ or intervene$ or manag$ or module$ or program$ or rehab$ or strategy$ or support$ or technique$ or therap$ or train$ ot

	treat$ or workshop$ or work shop$) or (interpersonal$ or inter personal$ or interrelation$ or relation$) adj5 (analy$ or approach$ or assit$ or coach$ or communication$ or counsel$ or educat$ or help$ or instruct$ or intervene$ or manage$ or module$ or network$ or program$ or psychoanaly$ or psychotherapy$ or rehab$ or skill$ or straterg$ or support$ or teach$ or technique$ or therap$ or train$ or workshop$ or work shop$) or (intermittent preventative adj (therap& or treatment$) adj social rhythm$).ti,ab. 6. Or/4-5 7. (patient acceptance or health care.sh) and (psychotherap$ or therap$ or treatment.).hw 8. acceptance adj (based or centred or centered) or acceptance adj2 (commitment or mindfulness) or act adj (psychotherapy$ or therap$) or (contextual adj2 approach$ or assist$ or coach$ or educat$ or instruct$ or intervene$ or manag$ or module$ or program$ or rehab$ or strategy$ or support$ or technique$ or therap$ or train$ ot treat$ or workshop$ or work shop$) or comprehensive distancing) ti.,ab. 9. Or/ 7-8 10. Exp behavior therapy or psychotherapy or rational emotive. sh. 11. (cognit$ or behavior?r or metacognit$) adj5 (analy$ or interven$ or modif$ or program$ or psychoanaly$ or psychotherapy$ or restructur$ or psychotherapy$ or restructure$ or retrain$ or technique$ or therap$ or train$ or treat$) or behavio?r$ activat$ or cbt).ti.ab. 12. Or/ 10-11 13. exp biofeedback 14. bifoeed$ or bio feed$ or neuro feed$ or psychophysiology$ or psycho physiology$ or (alpha or brainwave$ or electromyography or emg or physiological) adj2 feed$ .ab,ti. 15. /13 or 14 16. (expos$ adj3 fear) or (exposure or fear) adj3 (intervene$ or psychoanaly$ or psychotherapy$ or therap$ or treat$) or fear$ adj5 (decreas$ or diminish$ or extinct$ or lessen$ or prevent$ reduc$) adj5 (approach$ or assist$ or coach$ or educat$ or instruct$ or intervene$ or manag$ or module$ or program$ or rehab$ or strategy$ or support$ or technique$ or therap$ or train$ ot treat$ or workshop$ or work shop$) .ab, .ti 17. breathing exercise or mediation or relaxation.sh 18. or/ 16 or 17 19. exp psychoanalytic therapy or psychoanalysis.sh 20. free association or psychoanal$ or psycho anal$ or psychodynamic$ or psycho dynamic$ adj3 (approach$ or assist$ or coach$ or educat$ or instruct$ or intervene$ or manag$ or module$ or program$ or rehab$ or strategy$ or support$ or technique$ or therap$ or train$ ot treat$ or workshop$ or work shop$) .ti.ab. 21. exp group processes or exp psychotherapy, group or self help group or (community network or peer group or social support) .sh. 22. (conjoint therap$ or family responsive or family relation$) or (couples or family or group$ or martial or marriage$ or support$) adj (based or cent$ or focu?ed) or (couples or famil$ or martial or marriage$) adj3 (approach$ or assist$ or coach$ or educat$ or instruct$ or intervene$ or manag$ or module$ or program$ or rehab$ or strategy$ or support$ or technique$ or therap$ or train$ ot treat$ or workshop$ or work shop$) .ab.ti 23. or/ 21-22 24. (anxiety$ or fear or stress or worry$) adj3 (control$ or manag$) .ti.ab. 25. (multisystemic or systemic) adj2 (intervene$ or therap$ or treat$). ab, ti. 26. dialectic$ ab, ti. 27. (signpost$ or sign post$) .ti, .ab. 28. problem based learning or problem solving.sh. 29. (identif$ or deal$ or resolve$ or solution$ or solv$) adj3 (difficult$ or problem$) or (skil$ adj3 problem) .ti.ab. 30. or/24-29 31. solution focused therapy.sh. 32. solution$ adj2 (build$ or focus$).ab,ti. 33. Or /31-32 34. Or/ 1-33

Appendix 2: Table of Excluded Studies

Study	Design	Trial Size	Comparison Group	Intervention	Assessment Points	Outcome Measures	Reason for Exclusion
Bell et al., 2012	RCT	83	Waitlist control	Computerised CBT	Baseline, 3 and 6 months.	PGI, WSAS, GADI, PSWQ, PDSS, LSAS, FNE, FQ, BAI, BDI-I.	GAD subgroup not reported. Author did not respond to data request.
Brenes et al., 2012	RCT	60	Non-directive supportive therapy	Telephone delivered CBT	Not reported.	Not reported.	Full RCT data not reported reflective article.
Brenes et al., 2012 (a)	RCT	60	Non-directive supportive therapy	Telephone delivered CBT	Baseline, end of treatment and 12 months.	PSWQ, STAI, HARS, ASI, BDI, SF-36.	GAD data subgroup not reported. Author did not respond to data request.
Bressi et al., 2010	RCT	60	TAU	Short-Term Dynamic Psychotherapy	Baseline, 12 months.	CGI, SCL-90, CSI, IPP.	PSWQ not used in trial.
Craske et al., 2011	RCT	1004	Usual Care	Combination CBT and pharmacotherapy	Baseline, 6 and 12 months.	GADSS, PDS-SR, SPI, PTSD Checklist- CV.	PSWQ not used in trial.
Christensen et al., 2010	RCT	N/A	Attentional Control	Internet based CB.	Baseline, post-treatment, 6 and 12 months.	GAD-7, PSQW, PHQ, K-10.	Protocol no published data for trial.
Dear et al., 2011	Single Group open trial	32	N/A	Internet CBT	Baseline, post-treatment, 3 months.	MINI-v5, DASS-21, PHQ-9, PSWQ,SiAs6, GAD-7,PDSS-R, K-10.	Not randomised trial.
Delgado et al., 2010	Randomised assignment	36	Progressive muscle relaxation	Mindfulness	Baseline, end of treatment.	PSWQ, BDI, STAI, PANAS, SHC, TMMS-24.	Sample did not use diagnostic criteria, PSWQ below cut off.

Study	Design	Trial Size	Comparison Group	Intervention	Assessment Points	Outcome Measures	Reason for Exclusion
Donegan et al., 2012.	RCT	57	AR	CBT	Baseline, end of treatment.	ADIS, PSWQ, BDI, WAQ-SOM,.	Secondary analysis of previously reported RCT.
Gorini et al., 2010	Randomised assignment	20	Non Biofeedback	Biofeedback	Baseline, post-treatment.	PSWQ, BAI, STAI, HAM-A.	Biofeedback not psychological intervention. Pre-post scores not reported.
Herring et al., 2012	RCT	30	Waitlist Control	Aerobic exercise training Resistance exercise training	Baseline, 2,4 and 6 weeks.	ADIS-IV, PSWQ, BDI.	Physical exercise intervention, not psychological therapy.
Johnson et al., 2011	RCT	131	Waitlist Control	Internet CBT	Baseline, post-treatment, 3 month.		Trans-diagnostic trial GAD specific data not reported for all arms.
Johnson et al., 2013	RCT	129	Waitlist Control	Internet CBT	Baseline, post treatment, 3 month.		Trans-diagnostic trial GAD specific data not reported for all arms.
Kitchener et al., 2009	RCT	73	Waitlist Control Anxiety Management	Stress control	Baseline, post-treatment, 1 month.	GHQ-28, FQ, BDI, LSAS, GHQ-28.	PSWQ not used in trial.

Study	Design	Trial Size	Comparison Group	Intervention	Assessment Points	Outcome Measures	Reason for Exclusion
Mohlman et al., 2003	RCT	42	Waitlist Enhanced CBT	CBT	Baseline, post-treatment.	BAI, PSWQ, BDI, SCL- Anxiety, SCL-GSI. STAI-T.	Use composite of anxiety and did not report PSWQ scores separately. Author did not respond to information request.
Monnaze et al., 2013	Randomised assignment	45	CBT	MCT	Baseline, post-treatment.	GADS, MCQ.	PSWQ not reported. Not published in English.
Muntingh et al., 2009	Randomised assignment	N/A	Care as Usual	Collaborative stepped care	Baseline, 3, 9 and 12 months.	BAI, SF-36, EQ-5D, PSQ, OASIS, PHQ-9, UCL.	Study protocol not full published study.
Newman et al., 2013	Randomised assignment	49	Self-control desensitization	CBT	Baseline, post-treatment, 6,12 and 24 months.	STAIT, HARS, PSWQ.	Secondary analysis.
Norton et al., 2012	Randomised assignment	87	Relaxation	CBT	Baseline, pre-treatment, post - treatment.	STAI, ADDQ, BAI, PDSS, GAD-IV, SPDQ.	PSWQ not used in trial.
Repetto et al., 2013	RCT	25	Waitlist control Virtual reality and mobile phone	Biofeedback Virtual Reality and mobile phone	Baseline, post-treatment.	PSWQ, BAI, STAI, HAM-A.	Technological intervention not psychological intervention.

Study	Design	Trial Size	Comparison Group	Intervention	Assessment Points	Outcome Measures	Reason for Exclusion
Roy-Bryne et al., 2010	RCT	1004	Usual Care	Combination CBT and pharmacotherapy	Baseline, post-treatment, 6. 12 and 18 months.	BSI-12.	PSWQ not used in trial.
Salzer et al., 2011	Randomised assignment	59	CBT	Short Term Psychodynamic Psychotherapy	Baseline 12 months.	HARS, PSWQ, BAI, HADS, BDI IIP.	Follow up report of Leichsering 2009 study. Secondary analysis.
Schmidt et al., 2012	RCT	96	Waitlist control	False Safety Behaviour Elimination Therapy	Baseline, post-treatment, 6 months.	ASI, BDI, MI, DIS, SPRAS, CGI.	PSWQ not used in trial.
Seekes et al., 2011	Randomised assignment	120	Usual care	Stepped Care	Baseline, 8, 12 and 24 weeks.	IDS, HADS, W&SAS.	Model of care not specific psychological intervention.
Smith, 2010	Single case	1	N/A	Short-term Psychodynamic Psychotherapy	Baseline, post-treatment, 3 months.	GHQ-12.	Single case design not randomised study.
Treanor et al., 2010	Randomised assignment	31	Delayed treatment Waitlist	ABBT	Baseline, post-treatment.	DERS, ACS, ACQ-R, GAD CSR, PSWQ.	Report identical data of Roemer et al. 2008 trial. Secondary Analysis.
Titov et al., 2012	RCT	77	Waitlist	Internet CBT	Baseline, post-treatment, 3 months.	DASS-21, PHQ-9, PSWQ, SP-12, PDSS-SR, NEO-FFI-N.	Trans-diagnostic trial. GAD specific data not reported for all arms.

Study	Design	Trial Size	Comparison Group	Intervention	Assessment Points	Outcome Measures	Reason for Exclusion
Wong et al., 2011	RCT	N/A	Usual care Psycho-education + usual care	MCBT	Baseline, post-treatment, 6 and 9 months.	PSWQ, BAI, CES-D, SF-12.	Trial protocol only, no published data of trial.
Zager et al., 2012	RCT	18	Control group	ABBT	Baseline, post-treatment.	GAD-7, PSWQ, SF-12.	Anxiety composite used. PSWQ not reported separately. Author did not respond to data request.
Zager et al., 2013	Randomised assignment	22	AR	ABBT	Baseline, post-treatment.	VLQ, AQQ, SF-12.	PSWQ not used in trial.

Appendix 3: Intervention Matrix

Component	Reach Out IAPT	C&I Stress & Worry	Chris Williams 5 Areas Approach	Lava Model: Dugas	Overcoming Worry Self Help Freestone	Meta Cognitive Therapy: Wells	StressPack : White	Centre Clinical Interventions (CCI)	This Way Up ICBT Titov
General									
Psycho-Education		X	X	X	X	X	X	X	X
Worry Information		X	X	X	X	X		X	X
Types of Worry		X		X	X	X		X	X
Sleep Hygiene		X	X		X		X		
Formulation	X	X	X	X	X	X	X	X	X
Goals	X	X	X	X	X			X	X
Behavioural									
Behavioural Experiments				X	X	X	X	X	
Avoidance			X	X	X		X		X
Exposure	X		X	X	X		X		X
Behavioural Activation									X
Relaxation				X			X	X	
Progressive Muscle Relaxation							X	X	
Controlled Breathing		X	X					X	X
Exercise			X				X		X
Problem Solving	X	X	X	X	X	X	X	X	X
Cognitive						X		X	X
Detached Mindfulness									X
Distraction		X		X	X				X
Recognising Cognitive Bias	X	X	X	X	X	X	X	X	X
Thought Challenging	X	X	X		X	X	X	X	X
Evidence For/ Against Worry	X	X	X	X	X	X	X	X	X
Beliefs About Worry				X	X	X			
Worry Specific Strategies									
Worry Box									
Worry Tree		X							
Worry Time/		X				X		X	X
Postponement									
Worry Diary		X	X	X	X			X	
Reduce Demands		X							
Time Management		X							
Relapse Prevention		X	X	X	X	X	X	X	
Length of Material			335 pages choice of modules, online modules		446 Pages		Session Handouts 8-10 pages	8 modules – 8-10 pages approx	320 slides PDF Handout 10-20 pages
Clinician Guide	Curriculum manual	Local protocol	Can be bought separately	CBT for GAD Dugas and Robichaud	None	Meta Cognitive therapy for Anxiety Wells	Treatment for Anxiety and Stress White	Can be purchased for $40	N/A – Pure Internet Self Help

Appendix 4: NHS Ethical Approval Letter

NHS
Health Research Authority
NRES Committee London - Brent
80 London Road
Skipton House
London
SE1 6LH

Telephone: 02033117294
Facsimile: n/a

28 August 2013

Prof Stephen Pilling
Director Centre of Outcomes and Effectiveness
University College London
Centre of Outcomes and Effectiveness,Clinical Health Psychology
1-19 Torrington Place, London
WC1E 7HB

Dear Prof Pilling

Study title:	**Developing a low intensity CBT intervention for GAD in IAPT: A Feasibility and Acceptability Study**
REC reference:	**13/LO/1206**
IRAS project ID:	**121623**

The Research Ethics Committee reviewed the above application at the meeting held on 19 August 2013. Thank you for attending to discuss the application.

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 Co-ordinator Danyal Enver, (nrescommittee.london-brent@nhs.net).

Ethical opinion

1. The Committee requested additional background on the novel intervention that would be trialled during the study. You explained that low intensity interventions were widely used. You stated that the study intervention would also use a low intensity deliverance of a different intervention and confirmed that this would be done by 'power professionals'. You stated additionally that those not benefiting from the treatment could be withdrawn from the study and switched to high intensity interventions by the study team. The Committee was satisfied with this background.
2. The Committee raised some concerns that the normal care offered to the participants after the trial may be refused following a bad experience with the study care. It was noted that their being offered by the same clinical team may put participants off normal care and hinder their treatment. You explained that this had not happened in previous trials and that he did not think it would be an issue. The Committee was happy to accept

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

this response as a resolution to this issue.

3. The Committee noted that telephone calls to people, as anxious as the study population were likely to be, may cause problems regarding support. You stated that this was not anticipated to be an issue as well as outlining the ease at which follow up sessions could be organised if the participant had not found them satisfactory. The Committee was happy to accept this response as a resolution to this issue.
4. You confirmed that the study would be registered on a database.
5. The research team agreed to submit proof of insurance.
6. They also agreed to submit a full Scientific Peer Review as only excerpts and summaries had been submitted originally.

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

NHS Sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

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.

1. Proof of insurance cover for the study to be submitted.
2. Scientific Peer Review to be submitted.

You should notify the REC in writing once all conditions have been met (except for site approvals from host organisations) and provide copies of any revised documentation with updated version numbers. The REC will acknowledge receipt and provide a final list of the approved documentation for the study, which can be made available to host organisations to facilitate their permission for the study. Failure to provide the final versions to the REC may cause delay in obtaining permissions.

Management permission or approval must be obtained from each host organisation prior to the start of the study at the site concerned.

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

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*
Covering Letter		19 April 2013
Evidence of insurance or indemnity		19 April 2013
Interview Schedules/Topic Guides	1	10 April 2013
Investigator CV		19 April 2013
Letter from Sponsor		19 April 2013
Other: Summary CV for supervisor		19 April 2013
Other: Summary CV for student		19 April 2013
Other: West London REC letter		22 May 2013
Other: Interview guide	1	10 April 2013
Other: Ethics submission feedback		28 February 2013
Participant Consent Form	2	17 March 2013
Participant Information Sheet	4	03 July 2013
Protocol	2	24 January 2013
Questionnaire: PHQ9		
Questionnaire: GAD7		
Questionnaire: W&SASD		
Questionnaire: PSWQ		
Questionnaire: CSQ8		
REC application	2	19 April 2013
Referees or other scientific critique report		19 April 2013

Summary/Synopsis	1	22 February 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/LO/1206	**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

p.p.

NHS
Health Research Authority

NRES Committee London - Brent
80 London Road
Skipton House
London
SE1 6LH

Telephone: 020 7972 2552

07 October 2013

Professor Stephen Pilling
Director Centre of Outcomes and Effectiveness
University College London
Centre of Outcomes and Effectiveness,Clinical Health Psychology
1-19 Torrington Place, London
WC1E 7HB

Dear Professor Pilling

Study title:	**Developing a low intensity CBT intervention for GAD in IAPT: A Feasibility and Acceptability Study**
REC reference:	**13/LO/1206**
IRAS project ID:	**121623**

Thank you for your email of 2nd October 2013. I can confirm the REC has received the documents listed below and that these comply with the approval conditions detailed in our letter dated 28 August 2013

Documents received

The documents received were as follows:

Document	*Version*	*Date*
Referees or other scientific critique report		02 October 2013

Approved documents

The final list of approved documentation for the study is therefore as follows:

Document	*Version*	*Date*
Covering Letter		19 April 2013
Evidence of Insurance or Indemnity		19 April 2013
Interview Schedules/Topic Guides	1	10 April 2013
Investigator CV		19 April 2013

Letter from Sponsor		19 April 2013
Other: Summary CV for supervisor		19 April 2013
Other: Summary CV for student		19 April 2013
Other: West London REC letter		22 May 2013
Other: Interview guide	1	10 April 2013
Other: Ethics submission feedback		28 February 2013
Other: Letter from UCL Insurance		08 February 2013
Participant Consent Form	2	17 March 2013
Participant Information Sheet	4	03 July 2013
Protocol	2	24 January 2013
Questionnaire: PHQ9		
Questionnaire: GAD7		
Questionnaire: W&SASD		
Questionnaire: PSWQ		
Questionnaire: CSQ8		
REC application	2	19 April 2013
Referees or other scientific critique report		19 April 2013
Referees or other scientific critique report		11 October 2012
Referees or other scientific critique report		02 October 2013
Summary/Synopsis	1	22 February 2013

You should ensure that the sponsor has a copy of the final documentation for the study. It is the sponsor's responsibility to ensure that the documentation is made available to R&D offices at all participating sites.

13/LO/1206 **Please quote this number on all correspondence**

Yours sincerely

[redacted]

Appendix 5: Local R&D Approval

noclor NHS
Research Support Service

Bedford House, 3rd Floor
125-133 Camden High Street
London, NW1 7JR

Tel: 020 3317 3045
Fax: 020 7585 5830/5788
www.noclor.nhs.uk

26 November 2013

Professor Stephen Pilling
Department of Education and Health Psychology
University College London
1-19 Torrington Place
London
WC1 7HB

Dear Professor Stephen Pilling

I am pleased to confirm that the following study has now received R&D approval, and you may now start your research in **the trust identified below**:

Study Title: Low Intensity GAD Intervention: A Feasibility and Acceptability Study
R&D reference: Non CSP 121623
REC reference: 13/LO/1206

This NHS Permission is based on the REC favourable opinion given on **04 September 2013**.

Name of the trust	Name of current LC	Date of permission issue(d)
Camden & Islington NHS Foundation Trust	Dr Judy Leibowitz	26 November 2013

If any information on this document is altered after the date of issue, this document will be deemed INVALID

Specific Conditions of Permission (if applicable)
This letter is for permission for the following services only: Camden IAPT Services, 211 Kings Road, London, WC1X 9DN Islington IAPT Services, iCOPE, The Psychology Department, 5th Floor Hill House, 17 Highgate Hill, London, N19 5NA
If any information on this document is altered after the date of issue, this document will be deemed INVALID

Yours sincerely,

[redacted]

Mabel Sali
Research Management & Governance Manager

Cc: Dr Judy Leibowitz (Local Collaborator),

Dr Clara Kalu, UCL (Sponsor Contact)

noclor NHS
Research Support Service

Bedford House, 3rd Floor
125-133 Camden High Street
London, NW1 7JR

Tel: 020 3317 3045
Fax: 020 7686 5830/5788
www.noclor.nhs.uk

May I take this opportunity to remind you that during the course of your research you will be expected to ensure the following:

- **Patient contact:** only trained or supervised researchers who hold the appropriate Trust/NHS contract (honorary or full) with each Trust are allowed contact with that Trust's patients. If any researcher on the study does not hold a contract please contact the R&D office as soon as possible.
- **Informed consent:** original signed consent forms must be kept on file. A copy of the consent form must also be placed in the patient's notes. Research projects are subject to random audit by a member of the R&D office who will ask to see all original signed consent forms.
- **Data protection:** measures must be taken to ensure that patient data is kept confidential in accordance with the Data Protection Act 1998
- **Health & safety:** all local health & safety regulations where the research is being conducted must be adhered to.
- **Serious Adverse events:** adverse events or suspected misconduct should be reported to the R&D office and the Research Ethics Committee.
- **Project update:** you will be sent a project update form at regular intervals. Please complete the form and return it to the R&D office.
- **Publications:** it is essential that you inform the R&D office about any publications which result from your research.
- **Ethics:** R&D approval is based on the conditions set out in the favourable opinion letter from the Research Ethics Committee. If during the lifetime of your research project, you wish to make a revision or amendment to your original submission, please contact both the Research Ethics Committee and R&D Office as soon as possible.
- **Monthly / Annually Progress report:** you are required to provide us and the Research Ethics Committee with a progress report and end of project report as part of the research governance guidance.
- **Recruitment data:** if your study is a portfolio study, you are required to upload the recruitment data on a monthly basis in the website: http://www.crncc.nihr.ac.uk/about_us/processes/portfolio/p_recruitment/
- **Amendments:** if your study requires an amendment, you will need to contact the Research Ethics Committee. Once they have responded, and confirmed what kind of amendment it will be defined as, please contact the R&D office and we will arrange R&D approval for the amendment.
- **Audits:** each year, noclor select 10% of the studies from each service we have approved to be audited. You will be contacted by the R&D office if your study is selected for audit. A member of the governance team will request you complete an audit monitoring form before arranging a meeting to discuss your study.

Appendix 6: UCL Study Insurance Confirmation

University College London Hospitals NHS
NHS Foundation Trust

UCL

ROYAL FREE
world class care and expertise

Joint Research Office

Office Location:
1st Floor Maple House
149 Tottenham Court Road
London W1T 7DN

Postal Address:
UCL,
Gower Street
London WC1E 6BT

Email: david.wilson@ucl.ac.uk Tel No. 020 3447 5199 Fax No 020 7380 9937
Web-sites: www.uclh.nhs.uk; www.ucl.ac.uk

6th February 2013

Mr Alan Underwood
Department of Clinical, Educational & Health Psychology
UCL
4th Floor, 1-19 Torrington Place
London
WC1E 7BH

Dear Alan,

Chief Investigator: **Professor Stephen Pilling**

Study/Trial Title: **Developing Low Intensity CBT Intervention for GAD in IAPT**

Funder: **Departmental**

UCL Project ID No: **12/0562**

Re: Insurance for studies not involving a Clinical Trial of an Investigational Medicinal Product (non-CTIMP) sponsored by UCL

Thank you for completing UCL Insurance Registration Form of 11th January 2013. I am pleased to inform you that the above study, as described in the registration form, is now insured under UCL's Policy. A copy of the current insurance summary (Certificate of Currency) is attached to this letter.

The policy provides for the legal liabilities (negligence) of UCL and its employees or agents.

This confirmation letter together with the attached summary needs to be submitted to the Research Ethics Committee in support of question A76 for both your NHS REC and, where applicable, NHS R&D applications submitted via the Integrated Research Application System (IRAS).

The UCL insurance policy is renewed annually but studies included in the UCL insurance portfolio will be automatically rolled over into subsequent insurance period(s) until the study terminates. Indemnity and insurance arrangements for any participating sites will be detailed in individual Site Agreements.

Yours sincerely,

[redacted]

DAVID WILSON
Database & Information Officer

cc. Professor Stephen Pilling, UCL Centre for Outcomes Research & Effectiveness
Dr Clara Kalu, Senior Research Co-ordinator

Appendix 7: Participant Information Sheet

Camden and Islington NHS
NHS Foundation Trust

UCL

Low Intensity GAD Intervention: A Feasibility and Acceptability Study

Participant Information Sheet

You are being invited to take part in a research study. Before you decide whether to take part, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and feel free to discuss with others if you wish. If there is anything that is not clear or if you would like more information, please ask us. Your participation in this study is completely voluntary.

What is purpose of the study?
This study also forms part of a University College London Doctorate of Clinical Psychology research thesis by Alan Underwood (Trainee Clinical Psychologist) and is supervised by Professor Stephen Pilling and Dr. Peter Scragg.

Generalized anxiety disorder (GAD) is one of the most common anxiety disorders in primary care and is categorized by excessive worry and has been shown to cause distress. It has been reported to have a disabling effect similar to depression. Because of this it is important to find ways of working with anxious people effectively to reduce distress and prevent problems mild to moderate problems developing in severe problems. We would like to find out whether this can be done by improving the delivery of existing low intensity psychological treatment services for patients with anxiety, within the Improving Access to Psychological Therapies (IAPT) program. We would like to test a brief guided self-help treatment (LI-GAD) delivered by an IAPT Psychological Wellbeing Practitioner (PWP), which addresses specifically generalized anxiety and excessive worry. We hope to find out if this approach to treatment is feasible and acceptable to those who receive it and if the intervention is effective in reducing symptoms of anxiety and worry. We would also like to compare this specific low intensity generalized anxiety intervention with standard IAPT low intensity treatments for anxiety and worry.

We are carrying out this small study work out whether a larger study would be practical. The study will involve IAPT services from Camden and Islington. If this study is successful, it will help us determine if a larger study is possible, as well as providing us with important information about the effective treatment of generalized anxiety at the low intensity treatment level.

Why we would like your help
In order to conduct our pilot study, we will compare a group of people who get a GAD specific low intensity intervention (LI-GAD) with a group of people who get the current standard low intensity intervention (LI-SD).

Why have you been chosen?

Information Sheet 03.07.2013 v4 Rec Ref 13/LO/1206

We are inviting people aged 18+ who have recently entered participating IAPT services seeking treatment for excessive worry or generalized anxiety and are suitable for a low intensity (Step 2) treatment intervention. You have been chosen because you fit our selection criteria.

What does taking part involve?

If you agree to take part, you will be asked to sign a consent form. The researcher will arrange to contact you to arrange a time and date to answer any question you may have and collect a pre-treatment measure before you start the intervention.

Following this you will be randomly assigned either to receive the LI-SD or LI GAD interventions. Both interventions will be delivered as part of the IAPT services routine practice and be between 6 to 8 sessions of face-to-face or telephone contact with a PWP and working in a structured way through session materials. Sessions will last between 45-60 minutes. The reason for randomly assigning participants to either the LI-SD or LI-GAD is to ensure that no participant is favored over another and all participants have a chance of being allocated to either intervention allowing a fair comparison of the two interventions. To ensure this is fair an independent researcher will oversee the allocation.

As part of the low intensity treatment you will be asked to complete questionnaires about you mood (anxiety, depression), levels of functioning and level of worry. This will help us assess how effective the intervention is and its effectiveness in comparison to the other treatment in the study.

We are also interested in finding out what it was like to be part of this study, and we will be giving some of our participants the opportunity to describe their experiences and the ways in which the study could be improved. This will be done through an interview with a member of the research team, which will last about 90 minutes. If you are identified as someone suitable to take part in this kind of interview we will contact you nearer the time with further information.

The study is unable to offer reimbursement for travel expenses.

What will happen to my Information?

All information collected about you during the course of the study will be kept strictly confidential and will be stored in secure premise at UCL. Your name and contact details will be stored separately from the data collected. Both sets of information will be kept securely according to the requirements of the Data Protection Act 1998. Your GP will be informed about your participation in the study with your permission.

The results from this study will form part of the researchers research thesis, which is part of the UCL Doctorate in Clinical Psychology, only group results will be presented and no individual's health will be discussed. Your name will not appear on any publication or report about this research. Your participation is strictly confidential.

Do I have to take part?

No. It is up to you to decide whether or not to take part in this study. In other words, this is voluntary. If you *do not* take part, you will still have access to standard IAPT services. If you *do* decide to take part you are still free to stop your participation at any time and have the right to request that any research data is withdrawn without giving a reason. If you decide to take part, you will be given this information sheet to keep and be asked to sign a consent form.

Are there any risks?

There are minimal risks in taking part in this study. Trained professionals will monitor your progress for the duration of the study. As the intervention will involve discussing emotions and experiences as part of treatment there may be times when you feel upset. If this is the case, your PWP will be able to help.

This study has received ethical approval from Brent Rec (Ref: 13/LO/1206). All information gathered as a result of this study will be kept strictly confidential.

What are the benefits of this research?
By taking part in this study, you will contribute to a better understanding of low intensity treatment of anxiety while also receiving high-quality care from PWPs as part of standard IAPT services.

If we find that LI-GAD reduces symptoms of generalized anxiety and worry it may allow a further larger study and become part of standard IAPT service. The study may also support development of further for other low intensity anxiety treatments.

What happens when the research study stops?
Throughout the study and afterwards, your PWP will continue to treat you as s/he feels is best for you and with your agreement.

If I have concerns
If you wish to complain, or have any concerns about any aspect of the way you have been approached or treated by members of staff due to your participation in the research, NHS or UCL mechanisms are available to you. Please as your PWP if you would like more information on this.

In the unlikely event that you are harmed by taking part in this study, compensation may be available to you. If you suspect that harm is the result of that the harm is the result of negligence on the part of the Sponsor (University College London) or your IAPT service you may be able to claim compensation. After discussing this with your PWP, please make a claim in writing to Professor Stephen Pilling who is the Chief Investigator for the research and is based at University College London. The Chief Investigator will then pass on the claim to the Sponsor's insurers, via the Sponsor's office. You may have to bear the costs of legal action initially, and you should consult a solicitor about this.

Next steps
If you had read through this information sheet and are happy to take part, then the first thing to do is to complete the enclosed consent form and return it to your PWP or send it to the contact details below.

Contact details
If you need any further information to help you decide whether to take part in the study or if there is anything you do not understand, please contact:

Alan Underwood
Department of Clinical, Educational & Health Psychology
University College London, 1-19 Torrington Place, London WC1E 7HB
Email: alan.underwood.11@ucl.ac.uk, phone: 07739350431

Thank you for taking the time to read this information Sheet

Appendix 8: Participant Consent Form

Patient Identification Number for this study:

CONSENT FORM

Title of Project: Developing a low intensity CBT intervention for GAD in IAPT: A Feasibility and Acceptability Study

Name of Researcher: Prof .Stephen Pilling / Alan Underwood

Please initial all boxes

1. I confirm that I have read and understand the information sheet dated [17.03.2013] (version 2) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐

2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected. ☐

3. I understand that relevant sections of my medical notes and data collected during the study, may be looked at by individuals from UCL from regulatory authorities or from the NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records. ☐

4. I understand that the information collected will form part of Alan Underwood's research and may be used by him in publications, reports and presentations – but I will not be identified in these. ☐

5. I agree to my GP being informed of my participation in the study. ☐

6. I agree to take part in the above study. ☐

Name of Participant	Date	Signature
Name of Person taking consent.	Date	Signature

Consent form date of issue: [17.03.2013] REC REF:13/LO/06845
Consent form version number: [VERSION 2]