Article:
Hamilton, J., Saxon, D., Best, E. et al. (3 more authors) (2021) A randomised, controlled pilot study of cognitive analytic therapy (CAT) for stressed pregnant women with underlying anxiety and depression in a routine health service setting. Clinical Psychology & Psychotherapy, 28 (2). pp. 394-408. ISSN 1063-3995

https://doi.org/10.1002/cpp.2520

A randomised, controlled pilot study of cognitive analytic therapy (CAT) for stressed pregnant women with underlying anxiety and depression in a routine health service setting.

Abstract

A pilot study of cognitive analytic therapy (CAT) plus treatment as usual (TAU), versus TAU in stressed pregnant women with anxiety and depression was undertaken as an essential preliminary to any definitive, randomised controlled trial (RCT). The trial was pragmatic, multicentre, parallel, randomised, controlled, and unblinded. Participants were pregnant woman screened using the Hospital Anxiety and Depression Scale (HADS). Treatment was standard 16 session CAT. Main outcome measures: Spielberger State/Trait Anxiety Inventory (STAI) (primary outcome measure) at 24 weeks post-randomisation, therefore one-month post-therapy for the CAT group; HADS; CORE-OM, EPDS; SF36, and a brief 'experience of therapy' questionnaire, completed at baseline, and on average at 12, 24, 40 and 82 weeks post-randomisation. 39 patients (CAT + TAU n=20: TAU =19) were randomised with mean baseline STAI-STATE scores of 50.8 (SD 11.4) and 51.1 (13.3) respectively. 16 patients had missing primary outcome data leaving 23 (n=11, n=12) patients for analysis. The mean STAI-STATE score was 38.5 (SD 13.8) and 45.7 (16.8) in the CAT and TAU groups respectively at 24 weeks post-randomisation; an adjusted difference in means of 7.2 (95% CI: -7.9 to 20.6). No safety issues were reported. Patient retention for the CAT group was high (18/20; 90% of patients completed therapy). 10/11 (90.9%) respondents 'agreed' or 'strongly agreed' that having CAT had been 'very helpful'. The study demonstrated the feasibility of safely undertaking CAT in this setting. Outcomes showed positive trends compatible with a clinically important effect although statistically-definitive conclusions cannot be drawn in such a study.

Key words: Stress, pregnancy, cognitive analytic therapy (CAT), preventive intervention, anxiety, depression.

Practitioner points:

(1) Treatment with CAT during pregnancy is feasible, highly acceptable to patients, and outcome measures demonstrate positive statistical trends consistent with clinical efficacy.

(2) Treatment with CAT may represent an effective 'indicated' preventive intervention to mitigate the damaging effects of stress in pregnancy.

(3) Results of this pilot study support the view that psychological treatment should be available to stressed pregnant women with symptoms of anxiety and depression.

A randomised, controlled pilot study of cognitive analytic therapy (CAT) for stressed pregnant women with underlying anxiety and depression in a routine health service setting.

Introduction

It is increasingly recognised that mental health problems in pregnancy are both very common and distressing and disabling (NICE 2007; 2014). They are frequently a precursor to post-natal disorder. There is a considerable naturalistic and experimental literature in both animals and humans demonstrating that stress in pregnancy damages the developing foetus and causes long-term problems with subsequent emotional, cognitive and physical development (Allen, 1998; Barker, 1995; Barker, 1995; Clarke et al., 1994; Gitau et al., 2001; Glover et al. 2002; Glover, 2019; Henry, 1994; Heron et al., 2004; Lou et al., 1994; O'Connor et al., 2002a and 2002b; O'Connor and Glover, 2009; Schneider et al., 1998; 2001; Thompson, 1957). More broadly-based social stressors such as inequality appear also to contribute to such pathways (Aizer and Currie, 2014) as well as those possibly more cross-culturally specific (Glover et al. 2018).

Whilst early animal studies evaluating the effects of stress used behavioural interventions such as rough handling, overcrowding or unpredictable noise (Thompson, 1957, Schneider et al., 2001), it is clear that in humans stress and psychological trauma is also mediated through relational context and by the meaning of events. The pathways mediating the internalisation and effects of these factors both neurobiologically and psychologically (for example subsequent impairments of mother-baby interactions) remain to be fully elucidated, as do their recognised damaging consequences including transgenerationally (McEwen, 2012). However the importance of antenatal factors, including stress, for subsequent maternal and infant well-being life-long is well-established and of considerable importance (Stein et al., 2014) as is, by implication, the urgency of 'indicated' 'early' or 'preventive' interventions (Mrazek and Haggerty 1994; Albee, 1998; and see discussion by Chanen et al., 2017). These are by now well recognised as important in the field of public mental health. Although stress is a complex and challenging concept theoretically and clinically, in past human studies in the field of perinatal pathophysiology measures of anxiety have been conventionally employed as an indicator or proxy for levels of stress (see Glover, 2002). The confounding problem of 'comorbidity' with regard to symptoms such as anxiety and depression has long been recognised as the rule rather than the exception (see Goldberg and Huxley, 1992; Marshall,

2020; see also discussion in Bjellund et al., 2002) and as effectively vitiating current, symptom-based, psychiatric classifications of so-called, discrete 'disorders'. It would be anticipated that most pregnant women who have symptoms of anxiety will also suffer from depressive symptoms, and vice versa. This has important implications for meaningful research. Many authorities now assert that research needs to be more specifically directed to underlying causative mechanisms and pathways (Insel and Wang, 2010; Marshall 2020), whether more neurophysiological (including e.g. stress), psychological or sociological – or ideally an integration of all of these.

Therapeutic focus in perinatal psychiatry was historically mostly directed toward overt post-natal mental health problems (see reviews in NICE 2007; 2014). In the past pregnancy was frequently an exclusion criterion for psychotherapists and psychological treatment services in the UK although there was little scientific justification for this. Very few studies historically recognised the importance of early detection, intervention or prevention by targeting stressed pregnant women despite increasing recognition of the importance of such measures in the field of public (mental) health in general (Albee 1998, Mrazek and Haggerty, 1994). Previous studies using mixed psycho-educational and/or supportive approaches in pregnancy have shown slight or mixed results (Elliot et al., 1989, Barnett and Parker, 1985) but there have been encouraging studies of treatment for ante-natal depression using interpersonal therapy (IPT) (Spinelli et al., 1997, Spinelli and Endicott, 2003) and, from the same group, light therapy (Oren et al., 2002). Further interventions have included a group-based interpersonal therapy programme (Zlotnick et al. 2001), a psychoeducational intervention aiming to prevent post-partum depression (Lara, Navarro and Navarrete, 2010) and an antenatal group programme aimed at anxiety and depression (Thomas, Komiti and Judd, 2014). We previously collected anecdotal evidence of the effectiveness and feasibility of standard (16 session) CAT for mixed (non-psychotic) mental health problems in pregnancy using mixed outcome measures (Hamilton, unpublished). As far as we are aware no formal therapeutic intervention studies so far reported have explicitly targeted stress in pregnancy. It would also be anticipated that successful early therapeutic intervention in pregnancy would improve the subsequent quality of mother-baby interactions, and also later in childhood when a mother may be still struggling with mental health problems (Glover, 2019).

Cognitive Analytic Therapy

CAT is an increasingly-widely used integrative therapy developed in the UK by Anthony Ryle who aimed to integrate the valid and effective elements of cognitive psychology and psychoanalytic object relations theory as he saw them (Ryle and Kerr, 2002; 2020; Roth and Fonagy, 2005; Parry et al., 2005; Kerr, Hepple, Blunden, 2016). The CAT model was subsequently influenced by insights from developmental psychology stressing the actively intersubjective nature of the infant (see Trevarthen and Aitken 2001; Trevarthen, 2017), by Vygotskyian 'activity theory', and Bakhtinian concepts of the dialogic self, to stress a more radically social model of self**.** Initially developed as a brief therapy in the context of NHS outpatient services for more 'neurotic' types of presentation, it has subsequently become a well-established model with a gradually-emerging evidence base for a broader range of disorders (Kerr, Hepple, Blunden, 2016; Ryle and Kellett, 2018, Ryle and Kerr, 2020).

There is some evidence that CAT may be particularly effective in engaging and retaining patients (Calvert and Kellett, 2014; Ryle and Kerr, 2020), including those who may be more challenging or 'difficult'. CAT also embodies recognised 'common factors' contributing to the effectiveness of psychological treatments, including notably ability to create a strong therapeutic alliance, recognised as critical in treatment outcome of whatever modality (see Gabbard, Beck and Holmes, 2005; Roth and Fonagy, 2005; Castonguay and Beutler, 2006; Lambert, 2013; Calvert and Kellett, 2014; Wampold and Imel, 2015; Hallam et al., 2020).

CAT is predicated on a concept of 'Self' that is seen as seen as fundamentally constituted by internalised, socially-meaningful, interpersonal experience and is described in terms of a repertoire of formative *reciprocal roles (RRs)* and their procedural coping enactments (*reciprocal role procedures - RRPs*). A '*reciprocal role'* is a complex of implicit relational (possibly traumatic) memory, affect and perception (including beliefs and values) and is often associated with a dialogic voice. A *'reciprocal role procedure'* (RRP) is a stable 'coping' pattern of interaction originating in early internalised relationships that determines current patterns of relations with others and of self-management. The existence and enactment of these underlying psychological structures and processes would be understood in CAT to be essentially unconscious, and a key aspect of therapy would be bringing these into awareness ('recognition') to enable a helpful process of change to them ('revision'), facilitated by a collaborative therapeutic relationship. This relationship itself would also be seen as a place

where these, possibly disruptive or self-sabotaging, enactments will occur and would also be a focus of therapy (see case vignette below).

As a modality of therapy CAT is characterised by a clinical and theoretical focus on time limitation (typical initial treatment length of 16-24 sessions) and a pro-active, structured, genuinely-collaborative *('doing with'),* and empathic style. Therapy aims through an extended assessment phase over the first few sessions at joint description of key problem reciprocal roles (RRs - internalised formative relationships) and reciprocal role procedures (RRPs or 'coping patterns') by means of written (narrative) and diagrammatic reformulations. Subsequent work focuses on the enactments of these (both Self-other and Self-Self), both outside and during sessions, and work on 'transference' and 'counter-transference' understood as enactments of repertoires of reciprocal roles and procedures (Ryle, 1997).

In this trial additional therapeutic focus (and see case vignette below) was directed towards the enactment of internalised *'self-stressful'* RRs and RRPs, enacted as both real-world interactions and also as internal 'self-self' RRs and RRPs, and as previously conceptualised in CAT work with psychotic disorders (Kerr et al., 2003). A brief illustration of some of the specific psychotherapeutic considerations arising in this work, and of the course of a real but fictionalised therapy, is offered below.

Aims of the study

Consistent with more recent formal guidelines and discussion on the role of pilot studies (Thabane et al., 2010; Shanyinde et al., 2011; Eldridge et al., 2016) this study was seen as an essential preliminary to any subsequent, definitive randomised controlled trial (RCT). The purpose of such a pilot is to ensure the design and methods of any future trial are sound, practicable, statistically well-informed, and feasible. The *primary* aims of this pilot were therefore as follows. To test the feasibility, practicality, safety and acceptability of the study design and protocol. These were operationalised as the ability of clinicians and midwives involved in obstetric care for pregnant women to identify and refer women possibly suffering from stress, and the ability of pregnant women to engage with and attend regularly for 16 session CAT, including during mid and later stages of pregnancy. Safety was evaluated in

terms of identification of any possible untoward outcomes, such as worsening of condition or dropping out of routine obstetric care apparently due to involvement in the trial as monitored by clinicians, assessors, and therapists involved in the study. Acceptability was evaluated as the extent to which participating patients had , for example, found therapy 'helpful', 'a strain', 'felt more confident about the future', and 'would recommend it to others', as formulated in a feedback questionnaire (see Table 5). *Secondary* aims of this pilot were to evaluate and resolve any practical issues in relation to the conduct of any future RCT such as the reproducibility of the outcome measures. To investigate the feasibility and acceptability of such a care pathway to colleagues and services, operationalised as their ability to participate through identification and referral of patients to perinatal mental health services, and to refine such a care pathway if need be prior to any full RCT. To obtain some indication of positive or negative statistical trends in relation to outcome measures to help inform future power calculations, and an indication of recruitment and attrition rates.

Method

Background

The study was conceptualised as being aimed at treating stress in pregnant women, given its recognised importance, rather than simply treating specific conventional clinical diagnostic groups, given both the nosological problems associated with these and given the 'transdiagnostic' CAT approach (see discussion above).

The study was a pragmatic, multicentre, parallel, randomised, controlled, unblinded trial. The trial was conducted over two sites in Sheffield and London. Involvement of a further site proved ultimately not possible for service rather than research-related issues. It had been planned that this might have generated an overall sample size (n=68) sufficient for some preliminary analysis of clinical efficacy. The pilot was undertaken and planned on an 'in-service' basis by clinicians involved, volunteer therapists and academic statisticians, and had local NHS management approval and support. It was undertaken however with no external funding.

Ethical approval

The protocol for this study was externally approved by a UK national research ethics committee (accessible via the NREC reference appended at the end of this paper) and was as such pre-registered.

Entry criteria

Patients aged over 18 were recruited from routine out-patient perinatal psychiatry clinics following referral by adult health services (e.g. by midwives, obstetricians, GPs or other mental health professionals). They were offered participation in the trial on the basis of suggestive clinical presentations and psychiatric diagnoses during routine presentations to perinatal clinics or to midwives. Following referral they were screened (score of >10) using the Hospital Depression and Anxiety Scale (Zigmond and Snaith, 1993; Bjelland, et al., 2002)). This was employed as a proxy for stress for the reasons discussed above whilst it was also assumed that it would identify those women with symptoms of anxiety and depression.

Exclusion criteria

Patients who at referral were actively psychotic, or were actively and continuously engaged in substance abuse, or represented a current risk of violence were not recruited since they would be unable to engage in therapy, or it would have been unsafe to offer this. Participation required a good command of English in this context and so those with serious English language problems were not recruited although such patients would ideally be the subject of a further study (e.g. for those from ethnic minorities within the UK, or refugees). Women under 18 were not recruited as the effectiveness of CAT had at the time only been reported in adults, although this could also represent the focus of a further group for study.

Medication

Approximately half of the patients entering such a trial would be expected to be receiving psychotropic medication (mostly anti-depressants). To preclude uneven randomisation of patients receiving medication a stratified randomisation procedure was carried out (see below Results).

Blinding

In such a trial of an active psychological treatment (as opposed e.g. to medication vs placebo) delivered weekly, versus treatment as usual, it is recognised that blinding of participants and of clinicians is evidently not feasible, although blinding of research staff in larger trials is possible. In some studies of briefer treatments time-comparable input has been offered as a 'blind' control through, for example, discussion sessions (see e.g. Hamilton et al., 2000), or through befriending type interventions (see discussion by Harris et al., 1999), but such options were not feasible in this pilot study. Colleagues involved in data management and statistical evaluation in this study were fully blinded to the status of participants. However awareness of patient treatment status by clinicians and patients constitutes a potential source of bias in this study.

Treatment as usual (TAU).

This comprised routine attendance and monitoring at outpatient obstetric clinics, meetings with midwives, and with GPs as per routine NHS practice.

Treatment as usual plus CAT

For the TAU group plus CAT group a standard 16 session CAT was offered on a weekly basis by qualified CAT therapists (i.e. by those who had undergone at least one year ('Level 1' or equivalent) specialist training). They were all given regular weekly supervision by established qualified CAT supervisors. Standard CAT as per the most recent 'manual' available (Ryle and Kerr, 2002) was offered. It was anticipated that patient experience of research assessment meetings with a sympathetic assessor would contribute in both groups to a form of support and possibly some slight treatment effect. This effect is well-recognised to represent a significant modification of treatment as usual (TAU) in most randomised clinical trials.

Assessments

All patients were assessed at initial recruitment (typically at about 12 weeks gestation), 12 weeks later at c. 24 weeks gestation (approximately mid therapy for the CAT treatment group given a typical 4 weeks delay from initial assessment in starting therapy) 12 weeks later at c. 36 weeks gestation (i.e. about one month post-therapy for the treatment group), and at 8 weeks post-partum (i.e. some three months following termination of therapy for that group and at a point when it was presumed that immediate post-natal stresses had subsided). Long

term follow-up was conducted at 11 months post-partum or approximately one year post-therapy for that group.

Following initial screening with the HADS, full demographic and background details were collected. Patients were also asked to complete the self-report questionnaires detailed below. These were repeated at all follow-up assessment points.

Outcome measures

The principal outcome measure was the Spielberger State/Trait Anxiety Measure STAI (Spielberger et al 1970) which has been used in previous studies in this patient group, of pregnant women, as indicator of stress (Glover, 2002). The STAI consists of 20 items for measuring trait anxiety and 20 items for measuring state anxiety. Each item is rated on a four-point scale. The scores for both scales range from 20 to 80 with higher scores reflecting greater levels of anxiety.

Secondary standard outcome measures included the 10 item Edinburgh Post Natal Depression Questionnaire (EPDS – Cox et al (1987) – a measure specifically validated for use in pregnancy as well as post-partum). The EPDS is scored on a 0 to 30 scale with higher scores indicating more depressive symptoms. The 'CORE' brief routine outcome battery (an increasingly widely used general baseline indicator of subjective well-being, risk of self- harm, symptoms and functioning (Barkham et al., 1998; 2005). The 34-item CORE total is scored on a 0 to 134 with higher scores indicating more severe client distress. CORE scores also correlate with those of the Beck Depression Inventory (BDI) enabling direct comparison and indication of depressive symptoms (Leach et al., 2006). The 36-item SF-36 MCS (mental component summary) and PCS (physical component summary) scores are standardised to have a mean of 50 and a standard deviation of 10 the same as the reference population, with higher scores indicating better physical and mental health.

Outcomes were collected at five time points or stages: baseline (randomisation) and four post-randomisation assessments. These were intended to be at approximately 12 weeks post-randomisation (at c.24 weeks gestation and approximately mid-therapy for the treatment group), 24 week post-randomisation (at c. 36 weeks gestation and at about one month post therapy for the treatment group), at 36 weeks post-randomisation (and 8 weeks months post-

partum i.e. some three months following termination of treatment for that group) and 76 weeks post-randomisation (11 months post-partum). The actual average post-randomisation follow-up data collect points were 11, 21, 41 and 83 weeks respectively.

Monitoring of safety issues and adverse outcomes

Any possible untoward outcomes, such as worsening of condition or dropping out of routine obstetric care apparently due to involvement in the trial was monitored by clinicians, assessors, and therapists involved in the study.

Sample size

The primary outcome was the STAI scale at 24 weeks post-randomisation at 36 weeks gestation at about one-month post therapy for the treatment group. From a study of (n=571) pregnant women at mean 30 weeks gestation the mean STAI score was 34.2 (SD 10.1) (Glover et al., in preparation). We assumed similar levels of variability in our sample and that a mean difference of 7 points in STAI scores between the intervention and controls groups is the smallest difference that was clinically and practically important, then to have an 80% power of detecting this difference or greater between the groups as statistically significant, at the 5% two sided level, this study would require 34 patients per group (68 in total). This seven-point difference in mean STAI scores between the control and treatment groups is equivalent to a standardized effect size of 0.7 standard deviations. This figure is consistent with the reported and anticipated effect for CAT in out-patient settings and with the effects of other comparable therapies for a range of disorders. Although evaluation of clinical efficacy is not understood to be a core part of early pilot studies as articulated in more recent guidelines (Eldridge et al., 2016), it was planned that some helpful preliminary indication might be obtained.

Statistical analysis

As the study was a two-parallel group RCT, the study was reported according to the CONSORT guidelines for randomised controlled trials (Moher et al., 2001) and subsequently for pilot studies (Eldridge et al., 2016). However, this study was commenced before the publication of the latter (pilot study) guidelines which could not therefore be used to inform its initial design.

The statistical analysis of the data was conducted on an as "as randomised" basis with the primary analysis directed to estimating the difference between post treatment (24-weeks post-randomisation or stage 3) follow-up scores on the STAI outcome measures.

For the primary outcome, STAI score at 24-weeks post-randomisation (c.36 weeks gestation and at about one month post therapy for the treatment group) scores at follow up were compared between the two arms (CAT and TAU), with analyses unadjusted and adjusted for covariates. The unadjusted analysis used a two independent samples *t*-test to compare mean post-treatment STAI scores between the CAT and TAU groups. A ninety-five percent confidence interval for the mean difference in post-treatment scores between the two treatment groups was reported. The adjusted analysis used an ANCOVA model with post-treatment STAI score as the outcome and baseline STAI score, treatment centre and treatment group as covariates (Frison and Pocock, 1992). A ninety-five percent confidence interval for the treatment group regression coefficient effect was also reported.

For the four post-randomisation repeated STAI measures, a simple summary measure for each individual patient the average post-randomisation score was calculated. Average post-randomisation STAI scores were compared between the two arms (CAT and TAU), again with analyses unadjusted and adjusted for covariates. The unadjusted analysis used a two independent samples *t*-test to compare average post-randomisation STAI scores between the CAT and TAU groups. A ninety-five percent confidence interval for the mean difference in post-randomisation scores between the two treatment groups was reported. The adjusted analysis used an ANCOVA model with average post-randomisation STAI score as the outcome and baseline STAI score, treatment centre and treatment group as covariates (Frison and Pocock, 1992). A ninety-five percent confidence interval for the treatment group regression coefficient effect was also reported. The secondary outcomes of EPDS, CORE and SF-36 were analysed in a similar way.

Results

The trial randomised 39 participants. 20 and 19 were allocated to the intervention (TAU + CAT) and TAU control groups, respectively (Figure 2). Sixteen participants were lost to follow-up, or had missing primary outcome data at 24 weeks, leaving 23/39 (59%) participants in the primary analysis (11 intervention; 12 control). Baseline characteristics of the participants are displayed in Table 1. The two groups appear to have similar characteristics at baseline.

As shown in the CONSORT flow diagram (Figure 2) some 39 patients were randomised in the study but only 23 (i.e. 59% of the original cohort) had primary outcome data, STAI score at c.36 weeks gestation (at about one month post therapy for the treatment group or stage 3), that could be analysed. In the original cohort of 39 patients Tables 1 and 2 clearly shows that the two groups were well matched.

Table 2 compares the baseline characteristics of those patients who were randomised with those who were actually analysed (had stage 3 data). This table shows that those subjects actually analysed were similar between the intervention and control group at baseline, and the subjects analysed were similar to those randomised.

~~Intention to treat (ITT)~~ The analysis found no difference in the primary outcome, the STAI scale at 24 weeks post-randomisation (36 weeks gestation at about one-month post therapy for the treatment group- stage 3) between the groups (Table 3); an adjusted difference in means of 6.1 points (95% CI: -4.2 to 16.3) in favour of CAT for the STATE domain and 6.2 points (95 CI% -2.8 to 15.2) for TRAIT domain. If the minimum clinically important difference for the STAI STATE and TRAIT dimensions is seven or more points then Table 3 shows the although the 95% CI confidence interval includes zero (which is compatible with no difference in outcomes), the CIs includes a difference of seven points so are potentially compatible with a clinically important effect. The CI for the other secondary outcomes at 24 weeks post-randomisation (CORE, EPDS SF-36 MCS and SF3-6 PCS also include zero which is compatible with no difference in outcomes between the randomised groups.

Figures 3 and 4 show how the STAI State and Trait domain scores vary over time for the women by the randomised group, with the CAT + TAU group having lower (better) STAI scores at all four post-randomisation assessment points than the TAU group.

For the four post-randomisation repeated STAI measures; a simple summary measure for each individual patient the average post-randomisation score was calculated. Average post-randomisation STAI scores were compared between the two arms (CAT and TAU), again with analyses unadjusted and adjusted for covariates. Table 4 shows that all the 95% confidence intervals for the difference in mean follow-up scores between the CAT and TAU groups, include zero which is compatible with no difference in outcomes between the randomised groups.

Summary vignette of a successful therapy (fictionalised but based on actual case material)

Presentation: 'Alison' was a woman in her late thirties with a first pregnancy. She presented to her GP with increasing anxiety about coping with pregnancy (about which she said she had mixed feelings) and about then coping with a baby. She felt she "ought" to be able to cope but was increasingly exhausted by trying to keep working (as an administrator in a Human Resources department) and also cope at home. She said she felt she "can't" burden her (second) husband or her mother, with whom she has a wary relationship. At times she said she felt very hopeless and gloomy about the future.

Background: 'Alison' was the elder of two sisters brought up in an impoverished background. Her father was frequently away from home with work; she remembered him as a distant and intimidating figure. Her mother was probably depressed herself and was apparently emotionally unavailable and highly critical. Alison was expected to look after herself and younger sister. She thought she was probably 'naturally sensitive'. She did reasonably well at school (it felt 'safe and good') but also experienced some teasing due to her late development. She met her first boyfriend (whom she subsequently married) at college. She says she 'tolerated' this relationship for 10 years despite his being very critical and at least verbally abusive towards her. She was evidently very committed to her work in a Human Resources

department where she said she had a reputation for 'going out of the way for others', but set high standards, and it transpired she could be very critical of colleagues herself.

Figure 1 (a) Initial SDR or 'map' for 'Alison' showing formative reciprocal roles

Figure 1(b) full SDR or 'map' for Alison showing also 'self-stressful' role procedures and their consequences.

- *TPP/Key Issue*: Because of your formative experiences of having been put down and criticised and told you ought to cope, tending then to keep things to yourself and to go out of your way for others, and to cope alone, which leaves you however isolated, 'stressed out' and hopeless.
- *Aim*: Try out communicating your feelings and needs to trusted others (e.g. in therapy or with your husband) - and see what happens.

- *TPP/Key Issue*: Accepting the 'criticising' and 'putting down' voice you grew up with, and so tending to put yourself down and to feel that you don't deserve help (including sometimes through therapy).
- *Aim*: Try to identify this 'voice' when it occurs and consider, as we have discussed, whether it is valid and whether you really need to accept it.

Course of therapy: Alison attended regularly despite some initial ambivalence and gradually began to be more confident in opening up. There were some difficult and tearful moments early on when the therapist attempted to explore her 'countertransference' (RR) feelings of frustration that she was being excluded from Alison's real and possibly painful underlying emotions and that this might possibly be due to Alison enacting a historic reciprocal role procedure (or 'defence') of keeping things to herself others out and feeling she 'ought' to cope (for fear of being put down and criticised). This was explored with the aid of an initial rudimentary SDR where therapist and patient were able to locate themselves and their

enactments. It also enabled a discussion about the costs of this RRP in that this typically left her feeling isolated, 'stressed out' and feeling hopeless (see TPP/Key Issue 1 above and 'map'). She was moved and obviously engaged by the subsequent reformulation letter shared in session 4. She said that it seemed 'strange' to have this "*pulled together*" in a sympathetic and non-critical manner, although in a way she knew most of its contents already. She was encouraged to work eventually on her TPPs/key issues and aims despite a feeling of "not deserving it". She began to try to talk to and confide in her husband; she returned to one session with a broad smile stating that he actually had been sympathetic and encouraging and had responded by talking about how he had felt about things. She gradually became more adept at recognising the '*criticising*', '*putting down*' voice but still found challenging it much harder. As the ending of therapy drew near she again became more anxious and reported feeling stressed again, and reported reverting at times to old coping procedures such as keeping things to herself and feeling she ought to cope alone. However she said she now recognised these (and their costs) much better and agreed with the therapist's observation that their interaction felt by this point very different from how it had been early in therapy. She wrote a brief 'goodbye' letter herself in response to that of the therapist in which she expressed gratitude for the help she had received and acknowledged these changes and the progress she felt she had made, even if they often feel often fragile and she still often felt some anxiety about the future. At three month routine follow-up (two months post-partum) she reported that she was doing well despite her initial anxiety after finishing therapy. She felt she was able to be much more openly engaged and 'in dialogue' with other people (including with her baby) and less 'stressed out' - despite often sleepless nights. There were significant reductions on routine questionnaires (both anxiety and depression) at follow up. She was the referred back to routine follow-up in primary care.

Discussion

A pilot trial such as this represents an essential preliminary to any definitive RCT. The study demonstrated the feasibility of safely undertaking a brief, structured, relational form of therapy (CAT) in pregnancy in a routine health service setting. Trial results were encouraging with regard to the feasibility, practicality, safety, acceptability in pregnancy, and potential efficacy of this intervention. These were evidenced in line with the *primary aims* of the study set out in the introduction above. They included demonstration of the ability of clinicians and

midwives involved in obstetric care for pregnant women to identify and refer women possibly suffering from stress, and the ability of pregnant women to engage with and attend regularly for 16 session CAT, including during mid and later stages of pregnancy. Safety was demonstrated in terms of lack of report or identification of any possible untoward outcomes, such as worsening of condition or dropping out of routine obstetric care apparently due to involvement in the trial as monitored by clinicians, assessors, and therapists involved in the study. Acceptability was demonstrated formally through the overall very positive feedback from patients (see Table 5) and lack of informal negative feedback to clinicians from patients. *Secondary* aims of this pilot were demonstrated through the apparent absence of practical issues in relation to the conduct of any future RCT such as the reproducibility of the outcome measures. The feasibility and acceptability of such a care pathway to colleagues and services, operationalised as their ability to participate through identification and referral of patients to perinatal mental health services was demonstrated. It was observed that difficulties on a second site in relation to recruitment occurred due to lack of dedicated or clinically involved research staff rather than inability identify such patients. Finally, some indication of positive or negative statistical trends in relation to outcome measures was obtained to help inform future power calculations, along with indication of recruitment and attrition rates for patients who were referred into the trial. These positive trends were compatible with a possible clinically important effect although statistically-definitive conclusions cannot be drawn in such a pilot study.

This pilot trial did not recruit to its original target sample size (due to difficulties in recruitment on a second site and for service-related issues on a further planned third site, rather than issues related to study design or feasibility of offering CAT) and the attrition to follow up data of 41% was higher than anticipated. The trial randomised 39 participants and 59% (23/39) provided outcome data at 24 weeks post-randomisation. This is not unusual as many trials fail to reach their planned sample size within the envisaged trial timescale and trial funding envelope. A review of 151 RCTs published in the UK's National Institute for Health Research (NIHR) Health Technology Assessment (HTA) Programme journal found the final recruitment target sample size was achieved in 56% (85/151) of the RCTs and the median retention rate (proportion of participants with valid primary outcome data at follow up) was estimated at 89% (IQR 79–97%) (Walters et al., 2017).

Difficulty in obtaining and processing follow up outcome data could have occurred for various reasons in this setting. These could include, for example, dissatisfaction with trial participation (although there was no evidence of this), other health problems pre- and post-natally, or simply preoccupation with tasks of motherhood and family life. It may also reflect logistic issues in storing and processing data in a small study undertaken by colleagues on a voluntary basis and in the absence of any dedicated full-time support or grant funding. However it is noteworthy that the majority (n=18/20; 90%) of patients receiving treatment with CAT completed therapy as defined *per protocol* by attending >12/16 sessions. Of the 2 patients who failed to complete therapy one woman had been admitted to hospital due to an ante-partum haemorrhage, and one had to move from the area for family reasons (information received from participating therapists).

In future studies the apparently high attrition rate for capture of follow-up outcome measures should be routinely addressed in larger scale RCTs by ensuring dedicated, focussed support (e.g. a full-time research assistant) to collect, store and manage data. This would clearly require adequate grant funding. Nonetheless the very high treatment retention rate (90%) and positive patient feed-back (Table 5) clearly suggest that 'CAT in addition to TAU' for those recruited was feasible and welcome. This is a remarkably high engagement and retention rate for a psychological treatment and is line with observations made previously with regard to the particular effectiveness of CAT in this regard (see reviews by Calvert and Kellett, 2014; Hallam et al., 2020). This is particularly noteworthy for therapy undertaken during pregnancy which can in itself be an arduous and exhausting experience. It is remarkable that there was only one negative voice amongst the patient feedback data given that enactment of psychopathology (e.g. due to borderline or narcissistic traits) by patients in therapy trials would be an anticipated issue, notwithstanding the need to investigate all dissatisfaction with services seriously. No adverse events or safety issues were reported in relation to trial participants and the only drops outs from therapy, as noted above, occurred for external reasons.

The clinical outcomes reported here as measured by routine psychometric analysis are entirely typical of pilot studies of this kind which are by definition insufficiently powered to generate definitive statistically significant conclusions. However in comparison to many pilot studies the sample size is large (n=39) and the trends observed across all psychometric outcome measures are all positive and potentially clinical significant, and justify extension of

this work into larger trials evaluating both overall outcome and their effective elements through 'dismantling' type studies. Our current results should also help to enable sample size calculations to be made for such further studies.

The estimates of the variability of the outcomes suggest that if we assume a primary outcome of the STAI at 21 weeks and a standard deviation of 17 points and a target difference of 7-points, 5% two-sided significance and 90% power then a main trial might need to randomise and follow-up around 250 women. However, such sample size calculations would also be informed by generic evidence for the efficacy of CAT (see Calvert and Kellett, 2014; Hallam et al., 2020; Ryle and Kerr, 2020). The results of this pilot trial certainly suggest that a main of definitive trial is potentially feasible within a reasonable timescale, number of centres, and resource envelope.

Offering effective treatment to his patient group is clearly important given its consequences not only for the well-being of pregnant women (see also NICE 2007; 2014), but also for their children potentially life-long. If stress during pregnancy can be mitigated by whatever means (e.g. therapy, appropriate pharmacotherapy, social support, befriending), even if it is not maintained subsequently, this could have important consequences. The data in Figure 3 suggests a positive trend favouring treatment during pregnancy and although inferences around efficacy cannot be made from this study, these data support the case for further trials of this intervention designed to evaluate clinical efficacy. The data in Figure 3 suggest a potential treatment effect at this stage for therapy in this study. Such treatment would therefore also constitute a form of public health 'indicated' preventive intervention (Mrazek and Haggerty, 1994) and would be a matter of some urgency. In any future, more extended, RCTs focussing on stress in pregnancy it would be ideal to make use of additional psychological and physiological measures of stress along with the proxy markers used here for the reasons discussed above. Although this study focussed on use of CAT as an individual therapy it is possible that future studies may usefully evaluate its effectiveness as a group-based treatment given the increasing use of CAT-based groups (see Kerr, Hepple, Blunden et al., 2016; Ryle and Kerr, 2020) and some of the advantages offered by this treatment format.

These results overall are consistent with the view that distressed pregnant women with mental health problems may be helped clinically, and that ante-natal stress may be mitigated, by a treatment such as CAT. Successful therapy at this time point could also have important

beneficial consequences for subsequent mother-baby interactions post-natally and later in childhood. As noted above, the pathways mediating the neurobiological and psychological internalisation and effects of stress are still being fully elucidated and will involve many factors including possibly genetic (O'Donnell and Meaney, 2017; Glover et al., 2016). Although elevated expression of cortisol appears to be one such critical mechanism, it is of interest that in a parallel study involving these patients salivary cortisol levels were not significantly reduced following treatment, in this context at least (Glover, unpublished data). Overall our results offer support to the increasingly widely-held view (see Zlotnick et al. 2001; NICE, 2007, 2014; Lara, Navarro and Navarrete, 2010; Thomas, Komiti and Judd, 2014; Glover, 2014) that such treatments should be routinely available in health services for pregnant women where indicated.

References

Aizer, A., Currie, J. (2014). The intergenerational transmission of inequality: maternal disadvantage and health at birth. *Science,* 344, 856–861.

Albee, G.W. (1998). Primary prevention of mental disorder and promotion of mental health. *Journal of Mental Health*, 7, 437-439.

Allen, N.B., Lewinsohn, P.M., and Seeley, J.R. (1998). Prenatal and perinatal influences on risk for psychopathology in childhood and adolescence. *Development and Psychopathology* 10; 513-529.

Barker, D.J.P. (1995). The foetal origins of adult disease. *Proc.R.Soc. London. B. Biol.Sci.* 262, 37-43.

Barkham, M., Evans, C., Margison, F., McGrath, G., Mellor-Clark, J., Milnes, D. & Connell, J. (1998). The rationale for developing and implementing core outcome batteries for routine use in service settings and psychotherapy outcome research. *Journal of Mental Health*, 7, 35-47.

Barkham, M., Gilbert, N, Connell, J, Marshall, C, Twigg, E. (2005). Suitability and utility of CORE-OM and CORE-A for assessing severity of presenting problem in psychological therapy services based on primary and secondary settings. British Journal of Psychiatry, 186, 239-246.

Barnett, B. and Parker, G. (1985). Professional and non-professional intervention for highly anxious primiparous mothers*, British Journal of Psychiatry*, 146, 287-293.

Bjelland, I., Dahl, A., Tangenhaug, T. and Neckelmann,S. (2002). The validity of the Hospital Anxiety and Depression Scale: An updated literature review*. Journal of Psychosomatic Research*, 52, 69-77.

Brazier, J., Roberts, J., Deverill, M. (2002) The estimation of a preference-based single index measure for health from the SF-36. *Journal of Health Economics*, 21, 271-292.

Calvert, R and Kellett, S. (2014). Cognitive analytic therapy: A review of the outcome evidence base for treatment. *Psychology and Psychotherapy Research: Theory, Research and Practice,* 87, 253-277. https://doi.org/10.1111/papt.12020

Castonguay, L.G. and Beutler, L. (2006). *Principles of Therapeutic Change That Work*, Oxford, Oxford University Press.

Chanen, A. M., Sharp, C., Hoffman, P., & Global Alliance for Prevention and Early Intervention for Borderline Personality Disorder. (2017). Prevention and early intervention for borderline personality disorder: A novel public health priority. *World Psychiatry*, *16*, 215‐216. doi:10.1002/wps.20429

Clarke, A.S., Wittwer, D.J., Abbott, D.H. and Schneider, M.L. (1994) Long term effects of prenatal stress on HPA axis activity in juvenile rhesus monkeys. *Dev. Psychobiol.* 27, 257-268.

Cox, J.L., Holden, J.M., Sagovsky, R. (1987). Detection of post natal depression: development of the Edinburgh Post Natal Depression Scale. British Journal of Psychiatry, 140, 111-117.

Diggle P.J., Heagerty P., Liang K-Y., Zeger S.L. (2002). *Analysis of Longitudinal Data. 2nd edition.* Oxford University Press, Oxford.

Eldridge, S.M., Chan, C.L., Campbell, M.J., Bond, C.M., Hopewell, S., Thabane, L., Lancaster, G.A. and on behalf of the PAFS consensus group. (2016). CONSORT 2010 statement: extension to randomised pilot and feasibility trials. *Pilot and Feasibility Studies.* 2:64 DOI 10.1186/s40814-016-0105-8

Elliot, S. (1989). Psychological strategies in the prevention and treatment of postnatal depression. *Clinical Obstetrics and Gynaecology,* 3, 879-903.

Entringer, S., Elissa S. Epel, E.S., Kumsta, E., Lind, J., Hellhammer, D.H., Elizabeth H. Blackburn, E.H., Wüst, S. and Wadhwaa, P.D. (2011). Stress exposure in intrauterine life is associated with shorter telomere length in young adulthood. *Proc. Natl. Acad. Sci.* (USA), 108, E513-518. doi/10.1073/pnas.1107759108.

Frison L. & Pocock S.J. (1992). Repeated Measures in Clinical Trials: Analysis Using Mean Summary Statistics and Its Implications for Design. In, *Statistics in Medicine.* 11, 1685-1704.

Gabbard, G.O., Beck J.S., Holmes, J. (2005). (Eds) *Oxford Textbook of Psychotherapy*. Oxford, Oxford University Press.

Gitau, R., Fisk, N.M. and Glover, V. (2001). Maternal stress in pregnancy and its effect on the human foetus: an overview of research findings. *Stress,* 4, 195-203.

Glover, V. (2014). Maternal depression, anxiety, and stress during pregnancy and child outcome: what needs to be done. *Best Pract. Res. Clin. Obstet. Gynaecol.,* 28, 25–35.

Glover, V. (2019). Is the association between maternal stress during pregnancy and the child's depression partly causal, and what should we do about it? *Acta Psychiatr. Scand*., 139,301-303.

Glover, V. and O'Connor, T.G. (2002). Effects of ante-natal stress and anxiety: implications for development and psychiatry. *British Journal of Psychiatry*, 180, 389-391.

Glover, V., O'Donnell, K.J., O'Connor, T.G. and Fisher, J. (2018). Prenatal maternal stress, fetal programming and mechanisms underlying later psychopathology – a global perspective. *Development and Psychopathology*, *30*, 843-854. Goldberg, D. P., & Huxley, P. (1992). *Common mental disorders: A bio-social model.* Tavistock/Routledge.

Hallam, C., Simmonds-Buckley, M., Kellett, S. Greenhill, B. and Jones, A. (2020) The acceptability, effectiveness, and durability of cognitive analytic therapy: Systematic review and meta-analysis. *Psychology and Psychotherapy Research: Theory, Research and Practice,* https://doi.org/10.1111/papt.12286.

Hamilton, J., Guthrie, e., Creed, F., Thompson, D., Tomenson, B., Bennett, R., Moriarty, K. , Stephens, W. and Liston, R.. (2000). A randomised controlled trial of psychotherapy in patients with chronic functional dyspepsia. *Gastroenterology*, **119**, 661–669. https://doi.org/10.1053/gast.2000.16493.

Harris, T. Brown, G.W. and Robinson, R. (1999). Befriending as an intervention for chronic depression among women in an inner city. 1: Randomised controlled trial, *The British Journal of Psychiatry,* 174: 219-224.

Henry, C. Kabbaj, M., Simon, H., et al (1994). Prenatal stress increases the hypothalamo-pituitary-adrenal axis response in young and adult rats. *Journal of Neuroendocrinology,* 6, 341-345.

Heron, J. O'Connor, T.G., Evans, J. Golding, J, Glover, G. and the ALSPAC Study Team (2004). The course of anxiety and depression through pregnancy and the post-partum in a community sample. *Journal of Affective Disorders*, 80, 65-73.

Insel, T. R., & Wang, P. S. (2010). Rethinking mental illness. *JAMA*, *303*, 1970‑1971.

Kerr, I.B., Burkitt, P. and Chanen, A. (2003). Clinical and service implications of a cognitive analytic therapy (CAT) based model of psychosis. *Australian and New Zealand Journal of Psychiatry*, 37, 515-523.

Kerr, I.B., Hepple, J. and Blunden J. (2016). Cognitive analytic therapy. In: J. Yakeley, J. Johnstone, G. Adshead, and L. Allison (Eds) *Medical Psychotherapy.* Oxford: Oxford University Press.

Lambert, M. (2013). (Ed.) *Bergin and Garfield's Handbook of Psychotherapy and Behaviour Change* (6th Ed.) New York: John Wiley and Sons.

Lara, M,A., Navarro, C., Navarrete, L. (2010). Outcome results of a psycho-educational intervention in pregnancy to prevent PPD: a randomized control trial. *J. Affect. Disord.* 122, 109–117.

Leach, C., Lucock, M., Barkham, M., Stiles, W.B., Noble, R. and Iveson, S. (2006). Transforming between Beck Depression Inventory and CORE-OM scores in routine clinical practice. *British Journal of Clinical Psychology*, 45, 153-166. https://doi.org/10.1348/014466505X35335

Lou, H., Hansen, D., Nordentoft, M. et al (1994). Prenatal stressors of human life affect foetal brain development. *Developmental Medicine and Child Neurology,* 36, 826-193.

Marshall, M. (2020). The hidden links between mental disorders. *Nature Research* https://www.nature.com/articles/d41586-020-00922-8.

McEwen, B.S. (2012) Brain on stress: How the social environment gets under the skin. *Proceedings of the National Academy of Sciences,* 109, 17180-17185.

Moher D., Schulz K.F., Altman D.G., for the CONSORT Group. (2001). The CONSORT statement: revised recommendations for improving the quality of reports of parallel-group randomised trials. *Lancet,* 357, 1191-1194.

Murray, L., Fiori-Cowley, A., Hooper, R. and Cooper, P. (1996) The impact of post-natal depression and associated adversity on early mother-infant outcome. *Child Development*, 76, 2512-26.

Mrazek, P.J. & Haggerty, R.J. (Eds) (1994) *Reducing risks for Mental Disorders: Frontiers for Preventive Intervention Research*. Washington, DC: National Academy Press.

NICE (2007). *Antenatal and Postnatal Mental Health.* National Institute for Clinical Excellence, London.

NICE (2014). *Antenatal and Postnatal Mental Health: Clinical Management and Service Guidance.* Clinical guideline [CG192] London, National Institute for Clinical Excellence. (Available at https://www.nice.org.uk).

O'Connor, T.G., Heron., J., Glover, V. et al (2002a) Antenatal anxiety predicts child behavioural/emotional problems independently of postnatal depression. *Journal of the American Academy of Child and Adolescent Psychiatry.* 41, 1470-1477.

O'Connor, T.G., Heron, J., Golding, J. Beveridge, M. and Glover, V. (2002b) Maternal anxiety and children's behavioural/emotional problems at 4 years. *British Journal of Psychiatry*, 180, 502-508.

O' Donnell, K., O' Donnell, T.G., Glover, V. (2009). Prenatal Stress and Neurodevelopment of the Child. *Developmental Neuroscience*, 31, 285-295.

O'Donnell K.J., Glover, V., Barker, E.D., et al. (2014). The persisting effect of maternal mood in pregnancy on childhood psychopathology. *Development and Psychopathology*, 26, 393–403.

O'Donnell, K. J. and Meaney, M.J. (2017). Fetal Origins of Mental Health: The Developmental Origins of Health and Disease Hypothesis. *American Journal of Psychiatry,* 174, 319–328. doi: 10.1176/appi.ajp.2016.16020138.

Oren, D.A., Wisner, K.L., Spinelli, M. et al. (2002). An open trial of morning light therapy for treatment of antepartum depression. *American Journal of Psychiatry,* 159, 666-669.

Parry, G.D., Roth, T., Kerr, I.B. (2005). Brief and Time Limited Psychotherapy, In, *Oxford Book of Psychotherapy*, (Eds Gabbard, G., Holmes, J. and Beck, J.), Oxford University Press.

Pilotandfeasibilitystudies.qmul.ac.uk/introduction (2016).

Roth, T., and Fonagy, P. (2005). (2nd Ed) *What Works for Whom? A Critical Review of Psychotherapy Research.* Guilford, New York.

Ryle, A., & Kellett, S. (2018). Cognitive analytic therapy. In W. J. Livesley & R. Larstone (Eds.). *Handbook of personality disorders: Theory, research and treatment* (2nd ed.). New York, NY and London, UK: Guilford Press.

Ryle, A, and Kerr, I.B. (2002). *Introducing Cognitive Analytic Therapy: Principles and Practice*, Chichester, John Wiley and Sons.

Ryle, A, and Kerr, I.B. (2019 – In press). (2nd Ed.) *Introducing Cognitive Analytic Therapy: Principles and Practice of a Relational Approach to Mental Health*, Chichester, John Wiley and Sons.

Shanyinde M, Pickering RM, Weatherall M. (2011). Questions asked and answered in pilot and feasibility randomized controlled trials. *BMC Medical Research Methodology*. 11, 117.

Schneider, M. L., Clarke S.A., Kraemer G.W. et al. (1998). Prenatal stress alters brain biogenic amine levels in primates. *Development and Psychopathology*, 10, 427-440.

Schneider, M.L., Moore, C.F., Roberts, A.D. et al. (2001). Prenatal stress alters early behaviour, stress reactivity and learning in non-human primates: a brief review. *Stress*, 4, 183-193.

Spielberger, C.D., Gorsuch, R.L., Lushene, R. (1970). *State-Trait Anxiety Inventory manual*. Consulting Psychologists Press, Paolo Alto, CA.

Spinelli, M. (1997). Interpersonal psychotherapy for depressed antepartum women: a pilot study. *American Journal of Psychiatry*, 154, 1028-1030.

Spinelli M., Endicott J. (2003). Controlled Clinical Trial of Interpersonal Psychotherapy Versus Parenting Education Program for Depressed Pregnant Women*. American Journal of Psychiatry*, 160, 555-562.

Stein, A., Pearson, R.M., Goodman, S.H., Rapa, E., Rahman, A., McCallum, M., Howard, L.M., Pariante, C.M. (2014). Effects of perinatal mental disorders on the foetus and child. *Lancet,* 384, 1800–1819.

Thabane L, Ma J, Chu R, Cheng J, Ismaila A, Rios LP, et al. (2010). A tutorial on pilot studies: the what, why and how. *BMC Medical Research Methodology*. 10, 1.

Thomas, N., Komiti, A. and Judd, F. (2014). Pilot early intervention antenatal group program for pregnant women with anxiety and depression. *Archives of Women's Mental Health*, 17, 503-509.

Thompson, W.R. (1957). Influence of prenatal anxiety on emotionality in young rats*. Science*, 125, 698.

Trevarthen, C. (2017). The affectionate intersubjective intelligence of the infant and its innate

motives for relational mental health. *International Journal of CAT and Relational Mental Health*, *1*, 11‑53.

Trevarthen, C, and Aitken K.J. (2001). Infant intersubjectivity: research, theory and clinical applications*. Journal of Child Psychology and Psychiatry.* 42: 3-48.

Walters, S.J,, Bonacho dos Anjos Henriques-Cadby, I., Bortolami, O. et al., (2017). Recruitment and retention of participants in randomised controlled trials: a review of trials funded and published by the United Kingdom Health Technology Assessment Programme. *BMJ Open, 7:e015276.doi:10.1136/bmjopen-2016-015276*

Wampold, B. E. and Imel, Z.E. (2015) *The Great Psychotherapy Debate: Models, Methods and Findings*. (2nd Ed) New York: Routledge.

Zigmond, A.S. and Snaith, R.P. (1983) The Hospital Anxiety and Depression Scale. *Acta Psychiatrica Scandinavica,* 67, 361-370.

Zlotnick, C., Johnson, S,L., Miller, I.W., Pearlstein, T., Howard, M. (2001). Postpartum depression in women receiving public assistance: pilot study of an interpersonal-therapy-oriented group intervention. *American Journal of Psychiatry.* 158, 638–640.

Figure 2: Participant progress through the trial – CONSORT flow chart

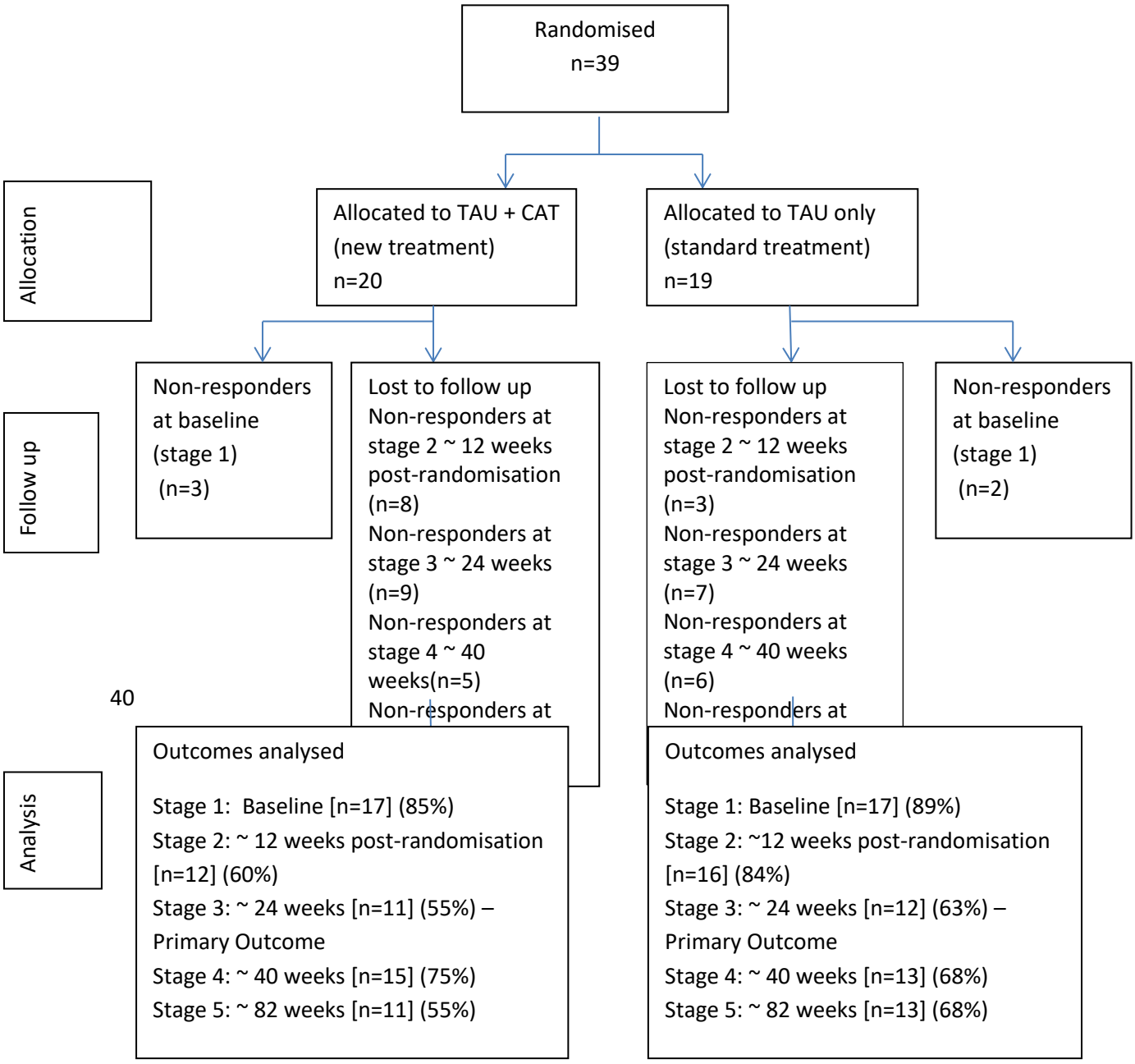

Table 1: Baseline demographic characteristics of women by treatment group

		TAU (n=19)			TAU + CAT (n=20)		
		N	Mean	SD	N	Mean	SD
Age		16	31	2.9	18	30.2	6.4
STATE		17	51.1	13.3	17	50.8	11.4
TRAIT		17	60.9	11.2	17	59.8	10.3
EPND		17	18.1	5.3	18	18.4	5.6
Total CORE		15	17.7	7.5	16	19.2	7.5
MCS		16	22.8	15.4	17	23.4	12.2
PCS		16	50.2	8.9	17	50.4	9.4
		n	%		n	%	
Site	Sheffield	17	89%		17	85%	
	London	2	11%		3	15%	
		19			20		
Marital Status	Married	15	88%		10	56%	
	Partner	1	6%		7	39%	
	Single	1	6%		0	0%	
	Divorced	0	0%		1	6%	
		17			18		
Ethnicity	White/European	17	100%		16	89%	
	Afro-Caribean	0	0%		1	6%	
	British Asian	0	0%		1	6%	
		17			18		
On Medication	No	13	68%		13	65%	
	Yes	6	32%		7	35%	
		19			20		
Anti-depressant Medication	No	8	57%		9	60%	
	Yes	6	43%		6	40%	

*The Spielberger STATE/TRAIT anxiety measure dimensions are scored on a 20 to 80 scale with higher scores reflecting greater levels of anxiety.

The EPDS is scored on a 0 to 30 scale with higher scores indicating more depressive symptoms.

The CORE total is scored on a 0 to 34 with higher scores indicating more severe client distress.

*MCS (mental component summary) and PCS (physical component summary) scores are standardised to have a mean of 50 and a standard deviation of 10 the same as the reference population, with higher scores indicating better physical and mental health.

Table 2: Baseline questionnaire characteristics for patients depending on whether follow-up data was obtained at Stage 3 (~ 24 weeks post-randomisation) or not.

		TAU (n=19)						TAU + CAT (n=20)					
		Follow up at 21 weeks (n=12)			No follow up at 21 weeks (n=7)			Follow up at 21 weeks (n=11)			No follow up at 21 weeks (n=9)		
		N	Mean	Range or SD	N	Mean	Range or SD	N	Mean	Range or SD	N	Mean	Range or SD
Age		11	32	26-36	5	29	27-31	11	31	22-40	7	29	18-35
STATE		12	52.8	13.6	5	47.2	13.1	11	50.3	10.8	6	51.8	13.6
TRAIT		12	62.3	13.1	5	57.8	4	11	59.2	8.9	6	60.8	13.6
EPND		12	18	6	5	18.2	3.9	11	17.6	5.5	7	19.7	5.7
Total CORE		10	16.9	9	5	19.5	3	10	17.3	7	6	22.4	7.9
MCS		12	24.4	17.4	4	17.7	5.6	11	25.9	13.2	6	18.8	9.3
PCS		12	48.9	9.6	4	54.1	5.8	11	51	10.1	6	49.3	8.8
Site		n	%		n	%		n	%		n	%	
	Sheffield	12	100%		5	71%		10	91%		7	78%	
	London	0	0%		2	29%		1	9%		2	22%	
		12			7			11			9		
Marital Status	Married	12	100%		3	60%		5	45%		5	71%	
	Partner	0	0%		1	20%		5	45%		2	29%	
	Single	0	0%		1	20%		0	0%		0	0%	
	Divorced	0	0%		0	0%		1	9%		0	0%	

		12		5		11		7	
Ethnicity	White/European	12	100%	5	100%	10	91%	6	86%
	Afro-Caribean	0	0%	0	0%	1	9%	0	0%
	British Asian	0	0%	0	0%	0	0%	1	14%
		12		5		11		7	
On Medication	No	7	58%	6	86%	6	55%	7	78%
	Yes	5	42%	1	14%	5	45%	2	22%
		12		7		11		9	
Anti-depressant medication	No	5	50%	3	75%	5	56%	4	67%
	Yes	5	50%	1	25%	4	44%	2	33%
		10		4		9		6	

Table 3: Unadjusted and adjusted differences in outcome scores between CAT and Treatment as Usual (TAU) groups post treatment (2nd post-randomisation (stage 3) assessment ~ 21 weeks post-randomisation)

Outcome	Group						Unadjusted*				Adjusted**		
	CAT+TAU			TAU			Mean	95% CI			Mean	95% CI	
	N	Mean	SD	N	Mean	SD	Diff	Lower	Upper	P-value*	Diff	Lower	Upper
STATE	11	38.5	13.8	12	45.7	16.8	-7.2	-20.6	6.2	0.28	-6.3	-20.6	7.9
TRAIT	11	48.3	12.0	12	56.4	16.2	-8.1	-20.6	4.3	0.19	-5.9	-17.2	5.4
CORE	10	11.0	7.5	10	13.8	8.5	-2.7	-10.3	4.8	0.45	-2.3	-9.5	5.0
EPDS	11	9.7	5.7	12	14.3	7.6	-4.6	-10.5	1.2	0.12	-4.2	-10.3	1.8
MCS	11	43.5	12.9	12	34.8	17.3	8.7	-4.6	22.1	0.19	7.1	-6.2	20.4
PCS	11	39.1	11.4	12	40.9	14.9	-1.8	-13.3	9.8	0.75	-2.2	-12.8	8.3

The Spielberger STATE/TRAIT anxiety measure dimensions are scored on a 20 to 80 scale with higher scores reflecting greater levels of anxiety.

The EPDS is scored on a 0 to 30 scale with higher scores indicating more depressive symptoms.

The CORE total is scored on a 0 to 134 with higher scores indicating more severe client distress.

The MCS (mental component summary) and PCS (physical component summary) scores are standardised to have a mean of 50 and a standard deviation of 10 the same as the reference population, with higher scores indicating better physical and mental health.

**P-value from independent samples t-test.*

***Adjusted Mean difference calculated from a linear regression model with stage 3 score as the outcome and baseline, treatment centre and treatment group as covariates.*

For the STATE, TRAIT, CORE & EPDS outcomes a negative mean difference shows that the TAU+CAT group has a smaller score/value and better outcome. Conversely for the SF-36 PCS and PCS outcomes a positive mean difference shows that the TAU+CAT group has a larger score/value and better outcome.

Figure 3: Mean STAI State domain scores over time by randomised group

Bars are standard errors.

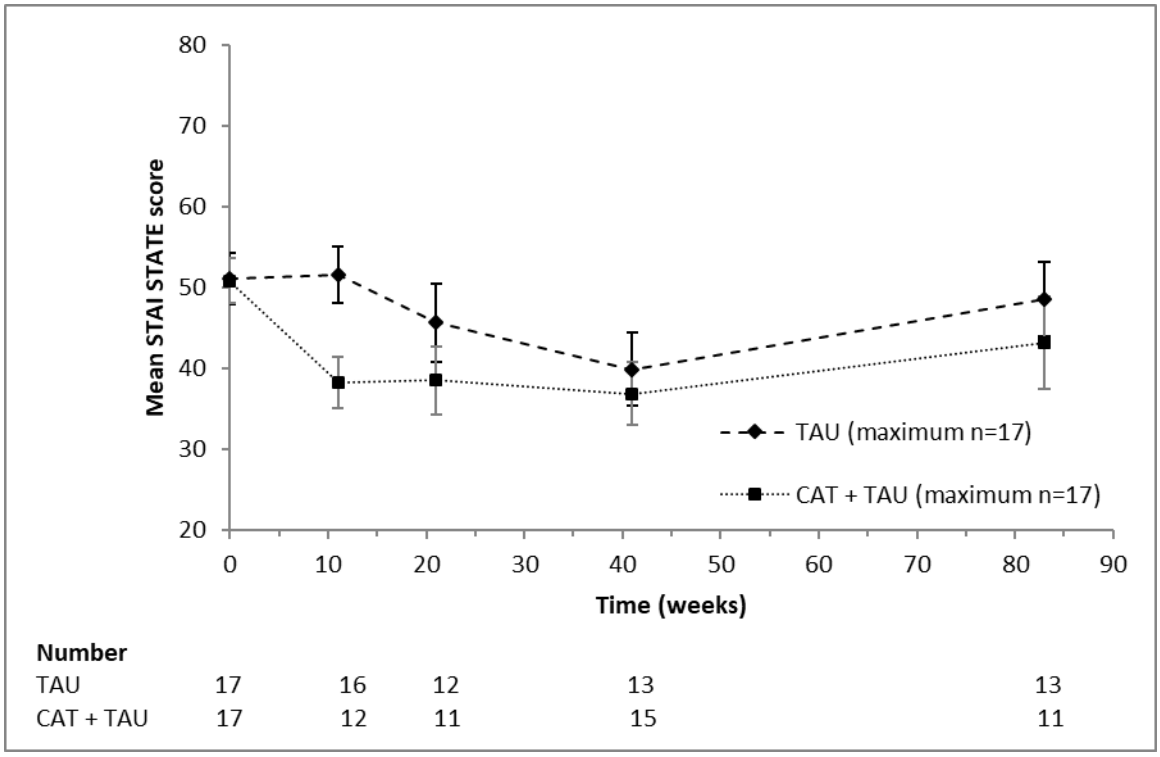

Figure 4: Mean STAI Trait domain scores over time by randomised group. Bars are standard errors.

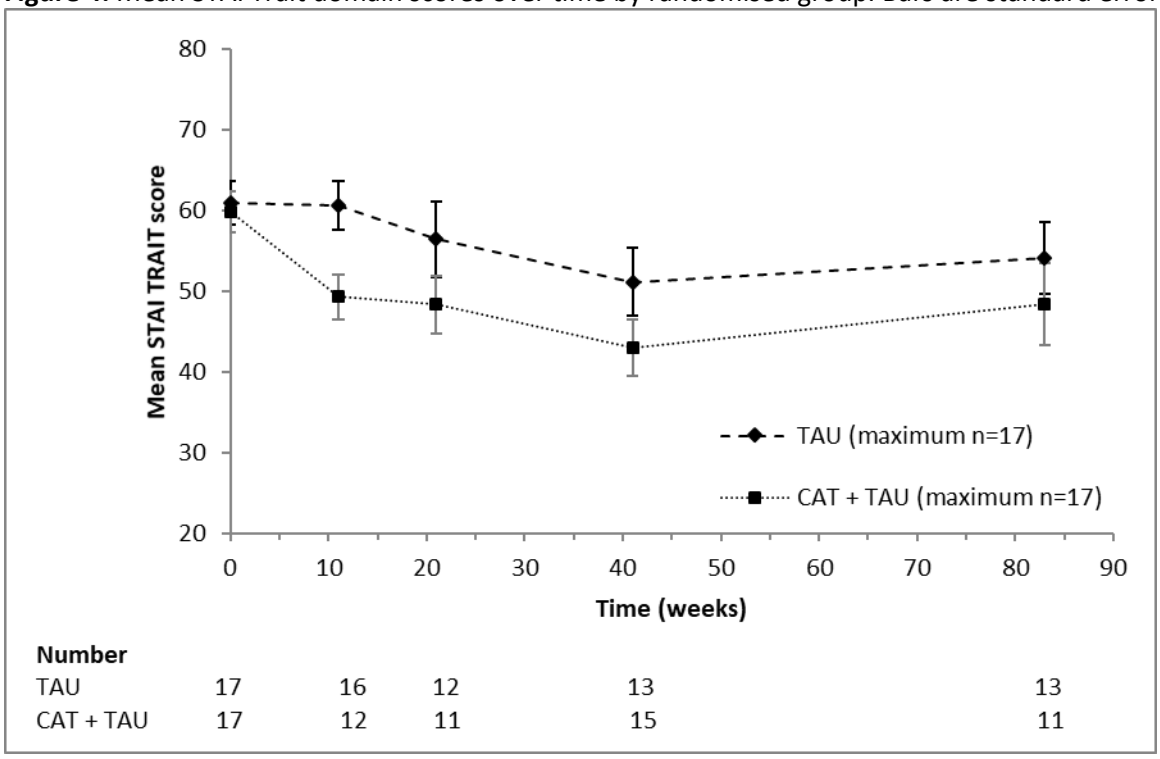

Table 4: Unadjusted and adjusted differences in mean post randomisation follow-up come scores between the CAT and Treatment as Usual groups

	Group						Unadjusted*				Adjusted**		
	CAT+TAU			TAU			Mean	95% CI			Mean	95% CI	
Outcome	N	Mean	SD	N	Mean	SD	Diff	Lower	Upper	P-value	Diff	Lower	Upper
STATE	15	39.8	14.0	16	47.4	13.9	-7.6	-17.8	2.7	0.143	-6.1	-16.3	4.2
TRAIT	15	46.7	12.1	16	55.8	14.3	-9.1	-18.9	0.7	0.067	-6.2	-15.2	2.8
CORE	15	10.5	6.1	16	14.6	7.8	-4.1	-9.3	1.1	0.12	-2.7	-7.5	2.1
EPDS	15	11.0	6.3	16	13.8	6.2	-2.7	-7.3	1.9	0.233	-1.4	-5.2	2.4
MCS	15	40.7	13.8	16	32.8	14.9	8.0	-2.6	18.5	0.133	4.5	-5.0	14.0
PCS	15	48.0	9.0	16	45.2	9.5	2.8	-4.0	9.6	0.407	2.1	-2.7	6.9

The Spielberger STATE/TRAIT anxiety measure dimensions are scored on a 20 to 80 scale with higher scores reflecting greater levels of anxiety.

The EPDS is scored on a 0 to 30 scale with higher scores indicating more depressive symptoms.

The CORE total is scored on a 0 to 134 with higher scores indicating more severe client distress.

The MCS (mental component summary) and PCS (physical component summary) scores are standardised to have a mean of 50 and a standard deviation of 10 the same as the reference population, with higher scores indicating better physical and mental health.

**P-value from independent samples t-test.*

***Adjusted Mean difference calculated from a linear regression model with stage 3 score as the outcome and baseline, treatment centre and treatment group as covariates.*

For the STATE, TRAIT, CORE & EPDS outcomes a negative mean difference shows that the TAU+CAT group has a smaller score/value and better outcome. Conversely for the SF-36 PCS and PCS outcomes a positive mean difference shows that the TAU+CAT group has a larger score/value and better outcome.

Table 5: Results of 'Experience of Therapy' Questionnaire

Q1: The treatment seemed to be very helpful.

agree strongly:	*agree :*	*unsure:*	*disagree :*	*disagree strongly*
7	3	0	1	0

Q2: I would recommend this form of therapy to other stressed pregnant women if it were routinely available.

agree strongly:	*agree :*	*unsure:*	*disagree :*	*disagree strongly*
7	3	0	1	0

Q3: The reformulation letter was particularly helpful.

agree strongly:	*agree :*	*unsure:*	*disagree :*	*disagree strongly*
2	4	4	1	0

Q4: Attending weekly for therapy was a considerable strain.

agree strongly:	*agree :*	*unsure:*	*disagree :*	*disagree strongly*
0	4	1	5	1

Q5: I feel more confident about the future having had this course of therapy.

agree strongly:	*agree :*	*unsure:*	*disagree :*	*disagree strongly*
5	3	2	1	0