Therapeutic Alliance and Outcome in a Treatment Trial of Depressed Adolescents

A Thesis Submitted to the University of Manchester for the Degree of Doctor of Medicine (MD) in the Faculty of Medical and Human Sciences

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ABSTRACT OF THESIS submitted by Dr Rachel Elvins
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Therapeutic alliance is an umbrella term referring to core aspects of the interaction and relationship between patient and practitioner during treatment. It has long been considered an important component of success in psychological and medical treatments. A survey of practitioners in child mental health (Kazdin, 1997) found that 95% thought that the relationship with the patient was the most important predictor of treatment outcome; there is research evidence suggesting the significant impact of alliance quality on outcome in adults and children, for both psychological (Martin et al., 2000, Shirk and Karver, 2003; Shirk, Karver and Brown, 2011) and general medical (Burkitt-Wright et al., 2004) treatments. Alliance, however, has been relatively little researched in childhood and until recently the emphasis (in both research and training) has been much more on the protocol details of treatment methods as opposed to detailed understanding of treatment process and the practitioner-patient relationship. Studies reporting associations between therapeutic alliance and treatment outcome have often been weakened by methodological difficulties in measurement and have failed to settle the direction of causality between symptom change and alliance (Kazdin and Nock, 2003). In treatment trials, alliance is often only measured in the experimental arm; this makes analysis of its effect difficult (Dunn and Bentall, 2007, and Emsley et al., 2010).

This study represents an exceptional opportunity to address these limitations. It makes use of data collected during one of the most rigorous recent studies done in child mental health in the UK (Goodyer et al., 2007). This enables detailed study of the therapeutic relationship during treatment and allows testing of the effects of this relationship on the success of treatment. Sessional audiotapes were available within both arms of this trial. Purposeful selection of tapes from both arms of the trial during treatment were transcribed and rated for treatment alliance. Other data already collected in the trial was included in an analysis to address questions of direction of causality of alliance in relation to symptom change during treatment and the way that alliance may explain treatment effect heterogeneity.

The results indicate a complex effect of alliance upon outcome. There is a relationship between early alliance score and clinical improvement, but the relationship is not straightforward and the predictive effect of alliance appears to depend on differences in patient groups and therapist effects. Analysis of treatment effect heterogeneity suggests that therapeutic alliance is associated with the individual treatment effect and implies that with poor alliance, more treatment may be detrimental. The complexities of the results are discussed with reference to implications for further research in this area as well as clinical practice.

DECLARATION

No portion of the work referred to in the thesis has been submitted in support of an application for another degree or qualification of this or any other university or other institute of learning.

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CHAPTER ONE - INTRODUCTION

1.1 The Concept of Therapeutic Alliance

Therapeutic alliance is an umbrella term referring to core aspects of the interaction and relationship between patient and practitioner during treatment. The term has been widely used in psychotherapeutic and medical literature for many years. Alliance has been broadly studied as a non-specific factor explaining therapeutic outcome and acting independently of the treatment technique. It may be seen to have an effect in, for example, pharmacological treatments of mental and physical illness as well as more psychotherapeutic approaches (Green, 2006a). The theory of alliance, criticisms of the concept, methodological issues in the measurement of alliance and the rationale for the present study are discussed below.

A recent review has explored the origins of the concept of alliance and what is described as its "genealogy" i.e. the evolution of its definition in practice (Elvins & Green, 2008). The paper summarises the development of the theory, from the first description of transference and counter transference as the core mechanism of change in psychoanalytic psychotherapy by Freud (1912), to a more operationalised concept in which the personal alliance or bond between patient and therapist is separated from a joint focus on the purpose of the therapy, for example the works of Hougaard (1994).

Zetzel (1956) was arguably the first to introduce the term "therapeutic alliance", to distinguish between classical analysts and object relations theorists' formulations of the transference. The latter appeared to view alliance as a product of transference

interpretations. Later authors went further in distinguishing alliance from transference. Rogers (1965) defined what he considered to be the active components in the therapeutic relationship: empathy, congruence, and unconditional positive regard, with the concept of the "therapeutic bond" (which describes both empathy and rapport) being established by Anderson (Anderson & Anderson, 1962). Greenson (1967) emphasised rational elements of the relationship (the "working alliance"), postulating that this may draw on either transference or real or "non-transference" elements of the relationship. Anna Freud's (1946) view of the therapeutic relationship was prominent in the early history of child therapy. She observed that an "affectionate attachment" between child and therapist is a "prerequisite for all later work". She described a differentiation of alliance components and distinguished the difference between the emotional relationship and the collaborative relationship (Estrada & Russell, 1999). The collaboration is framed as a functional one; the emotional bond is a catalyst for promoting therapeutic work. Following this, Orlinsky and Howard (1975) went further in describing three dimensions of alliance, proposed from a combination of ideas from empirical data and previous theory. These were *empathic resonance*, *mutual affirmation* (which appears to be similar to the Rogerian concept of the therapist holding the patient in "unconditional positive regard") and *working alliance* (investment of both patient and therapist in the practical purposes of therapy). Bordin (1979) claimed alliance could best be described as a three part division - *goal, task and bond*. This overarching theory takes account of both cognitive behavioural framings of the alliance and psychoanalytic framings; for example Beck's "collaborative empiricism" (1976) and Goldfried and Davisons' "therapeutic contract" (1976). Summers and Barber (2003) state that Bordin was probably the first to suggest that therapeutic alliance is a generic phenomenon, independent of treatment modality. At a similar time, Luborsky (1984) conceptualized a

related division of *'Type 1'* signs (how the therapist is viewed as an expert who can provide the relevant help) and *'Type 2'* signs (the collaborative approach between patient and therapist to work together towards goals). Frank (Frank & Frank, 1991) explicitly separated alliance from therapy techniques, stating that it was independent of modality of treatment. He termed these underlying principles "common active factors" - *accurate empathy, task understanding* and the *badges of office*. Clarkson (1990) identified five components as making up the therapeutic relationship present in all psychotherapies (working alliance, transference/counter transference, reparative, I-You and transpersonal). She stressed the similarities between different conceptualisations in order to make a case for an integrative model of common factors across modalities. Hougaard (1994) further developed a structure based on two factors. This formulation distinguishes the "*personal alliance*" (covering interpersonal aspects between the patient and therapist) and the "*task related alliance*" (addressing the core practical aspects of treatment such as goal related outcomes) (Green, 2006a). Social theory perspectives, however, indicate that the therapist is the agent of change in alliance terms e.g. the work of Strong (1968) was based on the hypothesis that the patient must be convinced of the therapist's competence and ability in order for change to occur.

Orlinsky and Howard (1975) subjected their theory of therapeutic relationships to testing in treatment trials. Treatment engagement as well as the perception of the therapist as an "expert" was found to predict outcome in therapy. Hougaard (1994) emphasized that empirical data showed intercorrelation between different dimensions of the alliance. As Elvins and Green (2008) state, this idea is intuitive but such a "one factor" theory could result in an overestimation of the influence of alliance, through halo effects introduced by common raters. It is suggested that uncertainty surrounding

the concept of alliance itself indicates a need for a more rigorous operationalisation which can be tested empirically.

1.2 Criticisms of the Alliance Concept

Despite some researchers' efforts to systematise the concept of alliance, it remains controversial in some settings. Catty (2004), recently reviewed conceptualisations of the alliance across psychotherapeutic disciplines and concluded that, even within psychoanalytic theory, there are a range of different conceptions and definitions of alliance still current. Some still view therapeutic alliance as essentially an artefact of the treatment situation, founded in positive transference (Nuttall, 2000). Safran, Muran and Eubanks-Carter (2011) argued that there is a danger of making false distinctions between the alliance and the transference, eventually leading to faulty assumptions about the quality of the therapeutic relationship. What may superficially look like a positive alliance may actually be a form of "subtle rupture" of the relationship, in which the patient deals with concerns by withdrawing, deferring to the therapist or being overly compliant. The concept of the alliance may overemphasise rational collaboration between patient and therapist and underestimate unconscious factors. It can be countered, however, that the quality of the alliance is the extent of collaboration, whether consciously or unconsciously mediated.

Catty also considered how the model of alliance has broadened across psychiatric and medical research. Priebe and McCabe (2006) argue that in psychiatry (as opposed to other psychotherapeutic disciplines) there is no clearly defined concept of alliance. They analysed six theoretical models: psychoanalysis, role theory, social constructionism,

systems theory, social psychology and cognitive behaviourism and found that none has been comprehensively investigated in psychiatric settings. However, this analysis addresses itself to the therapeutic relationship in a broad sense and provides little evidence of therapeutic alliance concepts. These theoretical models may offer alternative ways of examining therapeutic relationships, rather than being a reframing of the alliance concept itself.

1.3 Alliance in Treatment

1.3.1. Relationship of Alliance to Outcome

There has recently been a new emphasis on research designs that include the measurement of processes in treatment such as alliance, particularly in children's research, where good quality trials are sparser (Green, 2006b; Green & Dunn, 2008). When clinician's views (Kazdin, 1997) are surveyed, they describe the therapeutic relationship as a crucial factor in determining the outcome of treatment. The importance of therapeutic relationship variables has particularly been emphasised by those who treat adolescents (Karver et al., 2008). Studies of psychotherapeutic interventions over many years suggest that alliance constitutes a major variable in explaining success or failure of treatment (Elvins & Green, 2008). Meta-analyses in both adult (Martin, Garske & Davis, 2000) and child (Shirk & Karver, 2003; Shirk, Karver & Brown, 2011) populations consistently show an association between measures of therapeutic alliance and treatment outcome, even though this effect remains relatively moderate (effect size of 0.26 in child populations and correlation of 0.22 in trials with adults, respectively). Conclusions from most reviews however, particularly those involving trials with a developmental population, have been constrained by the limited number of studies that

actually include an alliance measure based on the conceptualizations discussed above, rather than a general relationship measure, and by the inclusion of studies that assess alliance and outcome concurrently rather than prospectively. The effect of alliance on outcome has been reported to be similar across different treatment modalities (Krupnick et al., 1996). Some meta-analyses, however, have combined results from diverse forms of therapy, for example, group and family therapies, without an adequate sample size to evaluate each form separately. Most individual randomised controlled trials (RCTs) such as Krupnick et al., (1996), examine the effect of alliance by means of conventional multiple regression analyses associating alliance ratings and outcome. Such conventional analysis, however, ignores significant methodological difficulties recently highlighted in both the measurement of alliance and subsequent causal analysis (Dunn & Bentall, 2007).

There appear to be significant deficiencies in the measurement of alliance of previous reported trials from both a theoretical (Green, 2006a; Kazdin & Nock, 2003) and meta-analytic standpoint (Martin et al, 2000; Shirk & Karver, 2003; Shirk, Karver & Brown, 2011). The evidence of the overall impact of alliance on treatment outcomes appears to be fairly robust, but how alliance actually acts in complex treatment trials and how it should best be measured are controversies not as yet resolved (Elvins & Green, 2008).

1.3.2 Explaining Treatment Effect Heterogeneity – How does Alliance Act in Treatment?

Many trials looking at the effect of alliance on treatment have not addressed the methodological difficulties in conducting such trials. The issue of deciding what kind of variable alliance might constitute, and how to take account of it in RCTs, has proved

difficult (Kraemer et al., 2001). Alliance may act in one of several different ways to influence the relationship between treatment and outcome and may not lie directly in the causal pathway. Commentators outline that alliance may take the form of a *moderator* of treatment effect i.e. a variable that affects the direction and/or strength of the relationship between treatment and outcome, or a *mediator* of treatment effect, that to some extent accounts for the relation between treatment and outcome, or as a non specific *predictor* of outcome (see Box 1 below). In essence, a moderator identifies for whom and in what circumstances treatments have different effects and mediators identify why and how treatments have effects (Kraemer et al., 2002). A non specific predictor is a baseline or post treatment measure that is uncorrelated with treatment and has a main effect on outcome, but no interactive effect. An example could be that treatment at a particular site may enhance outcomes whatever the modality of treatment. A moderator of treatment effect precedes treatment i.e. is a baseline or pre randomisation characteristic, for example a characteristic of the individual or treatment site. If alliance is a mediating variable, it would have to measure a change occurring during treatment, correspond with treatment choice (possibly being a result of treatment) and have either a main or interactive effect on outcome. Treatment mediators identify possible mechanisms through which a treatment might achieve its effects. It is plausible that the therapist – patient interaction (therapeutic alliance), which develops during treatment, is an example of a treatment effect mediator thus described, or acts to explain treatment effect heterogeneity.

The alliance literature unfortunately does not deal systematically with these distinctions. Some writers have suggested that alliance may be both a moderator and a mediator (Whisman, 1993), which is confusing. Kraemer et al., (2002) suggest that by their

definition, alliance cannot be a moderator, as it occurs during treatment. If, however, there was a clear baseline patient characteristic that predicted alliance (see below) – then this characteristic could itself be a moderator of treatment effect. This could happen either independently or acting through the alliance. This could be described as "mediated moderation" (Howe et al., 2002).

Box 1

Mediation and Moderation of Treatment Outcomes

(Green, 2006b, adapted from Kraemer et al., 2002)

When is a variable a Mediator, a Moderator or neither?

When measured	**Correlation with treatment**	**Statistical Relationship to Outcome**	**Definition (in relation to treatment outcome)**
Pre-treatment	No	Interaction with the treatment effect and/or main effect	***Moderator***
During/after treatment	Yes	Interaction with treatment effect or main effect	***Mediator***
Pre/during/after treatment	No	Main effect	***Non specific predictor***
During/after treatment	No	Neither main effect or interaction	***Independent outcome of treatment***
During/after treatment	No	Interaction with or without main effect	***Variable moderated by the treatment***

1.3.3 Challenges to Conventional Analysis of Alliance in Treatment

A key, but little discussed, fact about alliance in the context of treatment trial analysis is that it by definition represents a post randomization effect. As it emerges post randomisation, Dunn and Bentall (2007) have argued that there is the possibility of unmeasured confounds in the causal chain between mediator and outcome, which randomisation cannot remove. This could be a hidden or unmeasured confounder i.e. a factor associated with both alliance and outcome which produces a false association or obscures a true association ("mediated confounding"; Howe et al., 2002). Such confounds vary systematically with alliance and have an independent effect on outcome. They will also be in triangular relationship with other variables, rather than being on the causal pathway. Green and Dunn (2008) argue that the probable existence of this unaccounted for variable is a great challenge to making valid inferences from trials regarding the effect of alliance upon outcome. Most trial analyses make the assumption there is no such confounding variable. Traditional approaches to the investigation of mediation, such as Krupnick et al., 1996, and the estimation of direct and indirect effects of treatment (for example using multiple regressions) depend on precisely this assumption. The magnitude of the influence of process variables on the prediction of outcome may therefore be over or under estimated when temporal confounds are not addressed in research designs and data analyses. As noted by Feeley et al. (1999), temporal confounds have often been ignored in studies of alliance–outcome relations. When temporal confounds have been controlled, alliance–outcome findings have been less consistent across studies (Barber, 2009). In a recent study in adults using antidepressant medication combined with cognitive therapy, for example, when prior symptom change and medication were co-varied only behavioural methods remained a significant predictor of outcome, not alliance (Strunk et al., 2012).

Potential effect modifiers measured prior to randomisation may also have an effect on the assumed influence of alliance on outcome. Pre treatment characteristics, for example, may predict both alliance and outcome. Baseline social functioning of parents explained some of the measured parent – therapist alliance in parent management training in a study by Kazdin and Whitley (2006). Prediction of alliance by other patient pre-treatment variables has also been shown, for example patient interpersonal styles (Kivilighan, Patton and Foote, 1998). Howard et al., (2006) suggests that the alliance acts as a mediator between prior patient characteristics and outcome in depression. The Study of Cognitive Realignment Therapy in Early Schizophrenia (SoCRATES trial - Tarrier et al., 2004) suggested that the strength of alliance is associated with an important indicator of prognosis – lower baseline symptom scores. Those with lower scores, even in the control conditions, were those who were better able to form a good therapeutic alliance. This may explain some of the apparent association of alliance with outcome. However, there was also a suggestion that attendance at a higher number of treatment sessions was associated with a poorer outcome, so interpretations from this study are difficult.

There has been much less research examining therapist behaviours and characteristics that predict the therapeutic alliance (Karver et al., 2008) but factors such as warmth and flexibility have been suggested as crucial determinants (Castonguay et al., 2006). Some of these variables have also demonstrated a direct relationship to therapy outcome (Crits-Christoph et al., 2006). Del Re et al., (2012) report a meta-analysis which suggests that therapist variability in the alliance appears to be more important than patient variability for improved patient outcomes. They report that the relationship remains significant even when several potential covariates of this relationship are

controlled for, such as diagnosis and rater of outcome and alliance. Patient participation in the tasks of therapy has also been shown to be a predictor of treatment gains (Chu & Kendall, 2004).

"Ruptures" in alliance i.e. negative fluctuations in alliance score (both across treatment and within session) and subsequent "repair" of the alliance and improvement of score, have been identified as being related to treatment outcome in a recent small meta analysis (Safran, Muran and Eubanks-Carter, 2011). However, the authors recognize that very few treatment trials measure alliance score at different time points in sessions and over treatment in this way and a number of the studies examined were not RCTs.

1.3.4 Early Symptom Change

Early alliance should not be a good predictor of outcome if it is just simply an artefact of unrecognised early symptom improvement, as gains in therapy are said to stabilize and then accumulate over time (Horvath & Luborsky, 1993). Barber, Connolly, Crits-Christoph, Gladis and Siqueland (2000), tried to address the question of whether alliance is explained by early symptom change in a study using repeated measures through treatment. They found that when prior change in symptoms was controlled for, alliance at all time points still significantly predicted outcome i.e. that alliance acts independently of, and is not simply a proxy measure for, early symptom change. Furthermore, one recent study demonstrated that alliance predicted outcome independent of early mood change for two different therapies in depression and baseline symptomatology did not affect change in alliance in early therapy (Weeraskeera et al., 2001). This was however, a small study without a functionally impaired group so the results may not be applicable to clinical populations. Other trials have found largely

contradictory effects. Feeley et al. (1999) found that alliance is no longer associated with treatment outcome when previous symptom reduction is controlled for. Tang et al., (2007) report that "sudden gains" (large improvements in measures of depressive symptoms in between therapy sessions) in cognitive therapy were correlated with a lower risk of relapse and, from an earlier study, reported improved alliance observed in therapy immediately after these sudden gains (Tang and DeRubeis, 1999). There are two posited explanations for this, either that sudden gains and low relapse rates are both caused by common variables such as alliance or that sudden gains trigger a "virtuous circle" of cognitive change, improved alliance, and subsequent symptom relief (Elvins & Green, 2008). Sudden gains have also been found in other psychotherapies, although they appear to predict long-term outcome to a smaller degree (Hardy et al., 2005).

One study in adults has evaluated the alliance – outcome association controlling for both a wide range of patient variables and early or latent symptom improvement (Klein et al., 2003). Early alliance predicted subsequent improvement in depressive symptoms after controlling for these variables. Change in symptoms did not predict subsequent alliance. However, the measure of alliance in this study was patient report alone (see below for discussion of rater effects).

In child and adolescent therapy there are very few rigorous studies attempting to delineate the relationship between alliance and outcome whilst controlling for patient characteristics or early symptom improvement. Pre – treatment diagnosis has been one of the few factors analysed (Shirk, Karver & Brown, 2011) with externalising disorders (e.g. substance misuse) producing small effects.

Methodological developments in medical statistics indicate the possibility of a paradigm shift in analysing the mechanism of action of alliance in complex treatment trials. One of the purposes of this study is to attempt to investigate whether alliance explains treatment effect heterogeneity, and to use more novel statistical analyses to account for hidden variables, such as those proposed by Dunn and Bentall (2007).

1.4 The Therapeutic Alliance Concept in Psychiatric Practice

Additional features may affect the alliance between patient and therapist in psychiatric practice and settings: for example, the statutory nature of psychiatric services and the fact that many psychiatric patients do not attend of their own volition (as opposed to psychotherapy patients). For this reason the concept of the alliance may be conflated with “engagement” (Catty, 2004) or adherence to treatment. There is evidence, however, that increased contact with services (one measure of engagement), may be significantly associated with poorer alliance (Burns et al., 2000). The direction of effect is not clear, which illustrates the difficulty of measuring alliance data in this context. A recent meta- analysis in adults looking at the contribution of therapist competence and adherence to treatment to outcome (Webb, De Rubeis & Barber, 2010) showed that variability in neither adherence nor competence was found to be related to patient outcome and indeed that the aggregate estimates of their effects were very close to zero. Adherence and competence may be relatively inert therapeutic ingredients that play at most a small role in determining the extent of symptom change. They also posit that “therapist responsiveness” helps account for the failure to find significant, positive relations between outcome and these seemingly important therapist variables. Responsiveness refers to the fact that therapists generally do not deliver predetermined

levels of particular interventions but rather adapt their behaviour to the emerging context, in particular, patient behaviours (Stiles, Honos-Webb & Surko, 1998). For example, a therapist might adhere more to the methods of a particular intervention with patients who are not improving and who appear to be at high risk for a relatively poor outcome. The presence of enough such cases in a study would be reflected in small or even negative correlations between method and outcome. Barber et al., (2006) suggest that for patients with low alliance, strict adherence to the model of treatment is necessary for treatment gains whereas for those with high alliance this is not necessary for a good outcome. This applies in this instance to patients with externalizing disorders (drug misuse).

The validity of the concept of alliance in the treatment of severely mentally ill patients and those who are compelled to receive treatment has not been widely investigated (Priebe & McCabe, 2006). Some studies with schizophrenic patients in psychotherapy have been conducted (Frank & Gunderson, 1990). There has been a more recent interest in the effect of alliance on adherence to treatment (usually medication) in severe and enduring mental illness (Montreuil et al., 2012) and its effect in psychological therapies for first episode psychosis (Lecomte et al., 2012). Martin et al., (2000) stated that where a variety of diagnoses are suggested, studies have tended not to analyse their effect, making this impossible to address through meta analysis.

1.5 Developmental Aspects of Alliance

Child and adult alliances are distinguished by a number of developmental features across the described dimensions of personal and task alliance. Theories from

developmental disciplines can be usefully applied in delineating the thinking around alliance processes with children and adolescents (Shirk & Russell, 1996). Attachment theory (Bowlby, 1988) represents a model for use in a personal alliance context (Green, 2006a). A theoretical model of therapy based on attachment ideas has been devised (Eagle, 2006), which contains relevance to alliance constructs in its description of the 'secure base' created for the patient by the therapist and this conceptually unifies attachment and alliance theories across the life span. Several researchers have conducted trials on the effects of attachment patterns on therapeutic alliance, with the overall conclusion that secure attachment in adult clients is related to more positive therapeutic alliances than insecure attachment (Daniel, 2006).

Using an attachment hypothesis, Elvins and Green (2008) suggest that a challenge for researchers will be to formulate experimental designs that test hypotheses regarding the attachment dynamic in alliance and in relation to outcome. Such an approach would enable a test of the relevance of attachment related components of alliance as the treatment progresses. Cox (1989), developed a coding model called "levels of disclosure" where aspects of patient and therapist discourse in therapeutic sessions conceptually reflecting the attachment dynamic (significant affect laden disclosures from the patient, and the therapist's response to these) were operationalised.

1.6 Testing Alliance in Child and Adolescent Populations

Despite the theoretical importance of alliance in the child and adolescent psychotherapeutic literature, a only small selection of studies have evaluated alliance and related process factors in individual treatment (Karver et al., 2008). There are far

fewer methodologically sound studies involving children and adolescents in the alliance literature than there are in the adult population (Faw, Hogue, Johnson, Diamond & Liddle, 2005), for example, Norcross (2002) produced a well regarded review of the evidence base for different process variables within treatment, but omitted research with children. Karver et al., (2005) suggest that relationship variables may be critical with young people as they are typically referred by others (and may be in conflict with the referrer or their care-giver). They may enter into treatment with little insight into their problems or without having given explicit consent to be treated (Elvins & Green, 2008). Adolescents have typically been considered to be difficult to engage in therapy and a complex challenge to treat. Church (1994) reported a pervasive belief amongst clinicians that adolescents are the most difficult group of patients with whom to work. It follows that a strong therapeutic relationship with a young person may be particularly important. Shirk, Karver & Brown (2011) have noticed a more recent emphasis in the literature on an emotional connection (bond) between child and therapist. This view has been recognized in recent approaches to assessing the alliance in child and adolescent therapy (Shirk & Russell, 1996; Shirk, Gudmundsen, Kaplinski, & McMakin, 2008). The “bond” aspect of alliance in childhood may reflect an experience of the therapist as a friend or ally. In adult alliance, however, the therapeutic bond is based on experiencing the therapist as someone who is an expert and who can be accessed to help with emotional problems. The bond may be closely related to task alliance in adult therapy, but this may not be the case with children. This perspective has been criticized for not acknowledging social contractual features of the therapeutic alliance (Di Giuseppe, Linscott, and Jilton, 1996). A component of the working or task alliance, especially with adolescents, consists of agreements regarding treatment goals and the process or methods they might be accomplished. As children and adolescents are

typically referred by others, this makes the establishment of such agreements both difficult and essential for treatment collaboration. In younger children the ability to make agreements may exceed the child's cognitive capacities. Task collaboration with children may therefore be best assessed through observation rather than self-report (Karver et al., 2008; Shirk & Karver, 2006).

As these clinical perspectives suggest, there are important parallels between adult and child models of alliance. Consistent with Bordin's (1979) pan theoretical model, three facets of alliance - emotional bond, task collaboration (work), and agreements (goal consensus) - are prominent in the child and adolescent literature. At least two studies, however, have failed to fully support the three factor model with children. These studies produced a single factor solution, thus suggesting that features of the alliance may be poorly differentiated at younger ages (Di Giuseppe et al., 1996; Faw, Hogue, Johnson, Diamond, & Liddle, 2005). Others have shown that bond and task collaboration represent two distinct but correlated alliance dimensions (Estrada and Russell, 1999; Shirk and Saiz, 1992). Varied measures of alliance appear to be used in children's studies, indicating ongoing uncertainty around the conceptualisation of alliance in developmental populations (Creed & Kendall, 2005).

Meta analytic studies of alliance in child and adolescent mental health (Shirk and Karver, 2003; Karver et al., 2005; Shirk, Karver & Brown, 2011) have found a moderate but robust association with outcome similar to those found in studies with adults. Alliance was found to predict outcome with an equal effect size to factors such as length of illness and number of co morbid diagnoses. The only characteristic which appears to moderate association between alliance and outcome (and has been robustly

considered in treatment trials) is the child's presenting problem. Eltz, Shirk, and Sarlin (1995) found that adolescents with relationship problems and more negative interpersonal styles had more difficulty with alliance formation than a comparable sample of young people without such problems. In contrast to this, Kendall (1994) found minimal associations between alliance and outcome in a sample of young people with anxiety disorders. Nonetheless, these results strengthen the claim that the alliance is an important predictor of treatment outcome in child and adolescent therapy. Shirk, Karver and Brown (2011) point out that future studies need to account for the potential impact of treatment gains prior to alliance measurement, and for other process variables that could share predictive variance with the alliance, as with research in the adult literature.

Behaviours indicative of positive involvement in session tasks were associated with enhanced outcome in one small study where contributions to the task and goal alliance by therapist and child were analysed. This suggests that observing in session behaviours of both parties may be helpful in child and adolescent populations (Braswell et al., 1985). Therapists who attend to adolescents emotional experiences and present themselves as allies are more likely to form meaningful positive alliances with patients (Diamond et al., 2003). Specific therapist behaviours predictive of alliance were identified by Creed and Kendall (2005). These were "collaboration", "pushing the child to talk" and "emphasising common ground". However, directionality could not be determined from the findings. Karver et al., (2006) identified a construct called "therapist direct influence skills". These appear to be measures of directive therapist behaviours such as active structuring of the session and giving specific instructions to the child. In their Meta analysis of therapeutic variables in youth therapy, such

behaviours were moderately correlated with outcome (r = 0.4), but not with alliance measures. However, only five studies were included in this sample. This is in contrast to the adult literature where such behaviours are poorly correlated with outcome (Beutler et al., 2004).

In child and adolescent samples, parallel child and parent alliances with therapists may act together in treatment (Shirk & Karver, 2003). Therapists are faced with establishing and maintaining an alliance with the child and its caregivers, in contrast to work with adults, where the alliance has to be maintained with only the adult patient (Elvins & Green, 2008). Green et al., (2001) showed that individual child and parent alliances with a therapy team do not always correlate. In some therapy contexts it is the child's perception of the alliance that is more predictive of outcome than the parent's (Green, 2006a). Research on the predictive value of parent and child perceptions of difficulties in family work, for instance in eating disorders, is consistent with these findings (North, Gowers and Byram, 1997). Most research on alliance–outcome relations with children and adolescents has focused on the child-therapist relationship in individual work, even though the parent may participate to some extent in the therapy. This has important implications for the measurement of alliance and separation of child and parent alliances with the therapist. An exception is in the area of parent management training where parents are the primary focus of the treatment. Hawley and Weisz (2005) found that parent, but not adolescent, alliance predicted better therapy participation. Alliance with adolescents, but not parent alliance, predicted symptom change. It is possible that alliances with parents and children relate to different sets of outcomes.

Recent meta-analyses looking at the contribution of alliance on outcome in childhood therapy indicate the direction of effect remains unclear even with prospective designs (Shirk, Karver & Brown, 2011). The vast majority of studies have examined direct relations between alliance and outcome (even though one of the most prominent theoretical models posits an indirect link between alliance and outcome) and neither indirect or mediation models have been tested. As with adults, the contribution of the alliance to outcome tends to be evaluated in isolation and the unique contribution of alliance relative to other process predictors remains unknown.

1.7 Measurement of Therapeutic Alliance

The measurement of therapeutic alliance has been approached in several ways. External observation of interactions between therapist and patient and their corresponding behaviours (e.g. rating video or audio tapes of treatment sessions) have been used as have rating scales filled in by patient and therapist at various time points during treatment. It has been argued that the majority of alliance studies have been compromised by common rater and common method problems (Kazdin & Nock, 2003). Significant bias is introduced by the use of patient or therapist measurement of alliance coupled with patient or therapist derived measures of outcome (Klein et al., 2003; Shirk & Karver, 2003). Therapist rated outcome analysed against patient alliance rating is prone to the same error as therapist and patient alliance ratings are usually intercorrelated. Observed measurement of alliance may offer a more robust approach. This cannot, however, directly capture motivational aspects of therapeutic alliance which are by definition, subjective (Elvins & Green, 2008).

Alliance may be particularly predictive of outcome when measured early in treatment. One study in particular showed that poor early alliance predicted client drop out (Constantino et al., 2002). The National Institute of Mental Health (NIMH) collaborative treatment of depression study (Krupnick et al., 1996) found that both early alliance and mean alliance through treatment were predictive and that the quality of the alliance did not differ between treatments (including pharmacotherapy). Clients' and observers' reports of the alliance appear to be more predictive of outcome than therapists. They suggest that overall the evidence indicates that the quality of alliance assessed by independent raters is established quite early in treatment and thereafter does not alter by a significant amount.

1.7.1 Alliance measures

Researchers have attempted to devise scales to measure the alliance over many years. Some have been developed from a particular theoretical standpoint and some to test empirical notions about the alliance in research projects. Ultimately, hypothesis testing and modelling of the effect of alliance on outcome depends on the robustness of the original concept being measured. The plethora of measures in current use, particularly in child and adolescent populations, reflect an uncertainty about this conceptualization (Karver et al, 2008).

1.7.2 Conceptual development of alliance measures

A recent empirical review of the myriad scales used to measure alliance (Elvins and Green, 2008) showed that key measures were developed alongside specific reworking of the alliance concept by different groups and often developed to synthesize (and in some cases test) new theoretical constructs. No single measure has representative items from

all parts of the alliance construct over time. The numbers of items contained in scales vary widely and they purport to measure different alliance dimensions. Furthermore the conceptual subscales proposed by developers of measures do not necessarily reflect item factors. For instance, a conceptual review of the Working Alliance Inventory (WAI, Horvath & Greenberg, 1989), California Scales (CALPAS, Marmar et al., 1989) and Pennsylvania Scales (PENN, Haq; Luborsky et al., 1983) undertaken by Hatcher and Barends (1996) found six factors common to these scales (*confident collaboration, goals and tasks, bond, idealised relationship, dedicated patient* and *help received*) but these bore little relation to the underlying concepts proposed by the developers of the measures. Overall, current alliance scales take a descriptive and sometimes empirical approach to measuring underlying alliance constructs. There has been a lack of systematic experimental approaches designed to investigate the theoretical components of alliance, or to test which parts of the relationship are the crucial "active ingredients" that predict outcome (Shirk, Karver & Brown, 2011).

The WAI, VTAS (Vanderbilt Therapeutic Alliance Scale, Hartley & Strupp, 1983) and CALPAS have received more empirical scrutiny and support in the adult literature than other scales. They have all been used in robust outcome trials and tested against a number of confounding variables (Elvins & Green, 2008). A recent meta-analysis in children reported 10 different instruments in use in the literature (Shirk, Karver & Brown, 2011). The two most frequently used patient and therapist report instruments in the youth literature are the WAI and the Therapeutic Alliance Scale for Children (TASC; Shirk & Saiz, 1992). The WAI has been used primarily with adolescents and the TASC with children and young adolescents. The modified VTAS, WAI and Penn scales have been most often used (Elvins & Green, 2008) in young people when

observer reports are also considered. The VTAS and Penn scales receive some support both for psychometric properties and relation to outcome. The stringent testing suggested by recent commentators (Dunn & Bentall, 2007; Emsley et al., 2010) has not been used in treatment trials with these measures, however.

Alliance continues to be viewed as an important component of psychotherapeutic treatments. Theories of how alliance may act in treatment are varied, but many researchers appear to align with a view of alliance as a mediator or moderator of treatment outcome. The mechanism by which it interacts with prior patient characteristics and early symptom change however, continues to provoke controversy. Common objections to the way that therapeutic alliance has been assessed in outcome trials are as follows: within randomized trials, alliance is commonly only studied in the experimental treatment group. However, factors measured at the time of randomisation such as severity of symptoms are likely to be predictors of both alliance and outcome. Solely looking at associations between alliance and outcome in the treated group will reflect a mix of selection and treatment effects. Treatment effect heterogeneity is not often accounted for in traditional investigations into the effect of alliance on outcome i.e. the effect of alliance on efficacy of treatment in the presence of hidden confounders (hidden common causes of alliance and clinical outcome). Secondly, the apparent direction of causality may be an artefact, due to subtle symptom change early in treatment influencing alliance formation. Thirdly, there are often common method errors in trials, due to non independent information sources. As has been seen, the conceptualisation of alliance itself is still subject to debate within different therapeutic disciplines and this uncertainty is reflected in the plethora of different scales available for its measurement.

CHAPTER TWO – HYPOTHESES AND RESEARCH QUESTIONS

2.1 Addressing Limitations of Published Trials Investigating Therapeutic Alliance

In this study, novel statistical methods are used to investigate treatment effect heterogeneity and the potential effect of hidden confounders, alongside more conventional analysis. This addresses the problem of the mixture of selection and treatment effects in more usual analyses of alliance and outcome. An alliance measure is used very early in treatment in this study. This attempts to address the question of the direction of causality between formation of alliance and early symptom change. An observer rating scale is used in this study. This will prevent results being confounded by common rater errors. The scale used has good psychometric properties for the population under study and has been widely used in previous trials.

2.2. Aims

This study of the effect of therapeutic alliance within a major RCT of treatment for childhood depression (the "ADAPT" trial, Goodyer et al., 2007) strives to address these limitations overall.

This project aims to investigate the relationship between therapeutic alliance and measured outcome (symptom change and change in functioning) during treatment for depression in adolescence, taking into account the recent methods, concepts and objections to previous trials as outlined above.

2.3. Hypotheses and Research Questions

The following experimental hypotheses are investigated:

1. Alliance measured very early in this trial has no relationship to baseline variables of the sample, treatment arm or characteristics of treatment (e.g. site of treatment).

2. Alliance has a predictive effect on outcome in this trial

These hypotheses give rise to the following research questions:

Question 1

a) Does therapeutic alliance measured early in this trial vary with baseline characteristics of the sample and allocated treatments given in the trial?

b) Does therapeutic alliance vary with characteristics of treatment (e.g. treatment site, therapist variables)?

c) Is alliance in the trial stable over time?

Question 2

a) Does early therapeutic alliance predict outcome in this trial?

    I. Does the quality of alliance influence treatment effect?

II. Does variance in baseline characteristics of the sample or other unmeasured variables which are common to both alliance and outcome account for variation in therapeutic alliance and / or its relationship to the effect of treatment?

CHAPTER THREE - METHODS

3.1 Setting for the Study - the "ADAPT" Trial

The Adolescent Depression Antidepressant and Psychotherapy Trial ("ADAPT") was a Health Treatment Agency (HTA) funded randomised trial of medication alone against medication plus cognitive behaviour therapy ("combined treatment") for the treatment of childhood depression (total n = 208). The objective of the trial was to "determine whether a combination of a selective serotonin reuptake inhibitor (SSRI) and cognitive behaviour therapy (CBT) together with routine clinical care is more effective in the short term than an SSRI and clinical care alone in adolescents with moderate to severe major depression" (Goodyer et al., 2007).

The trial was carried out in 6 outpatient clinics in Manchester and Cambridge. The participants were 208 adolescents, aged 11-17, with moderate to severe major or probable major depression who had not responded to a brief initial intervention (BII). Adolescents with depressive psychosis, or a diagnosis of conduct disorder or suicidality were all included.103 adolescents received an SSRI and routine care; 105 received an SSRI, routine care, and CBT. The trial lasted 12 weeks, followed by a 16 week maintenance phase (28 weeks in total). The main outcome measure was change in score on the Health of the Nation Outcome Scales for Children and Adolescents (HoNOSCA - Gowers et al., 1999) from baseline. Primary outcomes were measured at 12 weeks. Outcomes were also measured at 28 weeks at the end of the maintenance phase. Secondary measures were change in scores on the adolescent rated Mood and Feelings Questionnaire (MFQ - Wood et al., 1995)**,** the observer rated revised Children's

Depression Rating Scale (CDRS-R reporting the t score - Poznanski et al., 1984), the Children's Global Assessment Scale (CGAS, Dyrborg et al., 2000), and the Clinical Global Impression Improvement Scale (CGI-I, Guy, 1976). Please see pages 41 - 42 for more about these rating scales.

At 12 weeks the treatment effect for the primary outcome (HoNOSCA) was −0.64 (95% confidence interval −2.54 to1.26, P = 0.50). The authors carried out a longitudinal analysis, no difference being seen in the effectiveness of treatment for the primary (average treatment effect 0.001, −1.52 to 1.52, P = 0.99) or secondary outcome measures. On average there was a decrease in suicidal thoughts and self harm but cognitive behaviour therapy did not confer a protective effect on suicidal ideation or attempts. By 28 weeks, 57% overall were either much or very much improved with 20% not improving. The authors concluded that for adolescents with moderate to severe major depression "there is no evidence that the combination of CBT plus an SSRI in the presence of routine clinical care contributes to an improved outcome by 28 weeks compared with the provision of routine clinical care plus an SSRI alone" (Goodyer et al., 2007 page 1 of 8).

Permission for this alliance and outcome analysis of the trial was obtained from the ADAPT steering group under the original national and local ethics committee approvals (see Appendix A).

3.2 Sampling Strategy

Sessional audiotape transcripts, previously unanalysed, were obtained from both trial arms at multiple time points: a combination that has rarely been undertaken in adult psychiatry and, to my knowledge, the first in child mental health. The project arguably represents the most systematic study of this kind on therapeutic alliance yet undertaken in child mental health and follows the general model of one of the most important studies of alliance in adult depression (Krupnick et al; 1996). This study aimed to replicate the successful aspects of the National Institute of Mental Health (NIMH) trial investigating the predictive effect of therapeutic alliance on outcome, which was undertaken with depressed adults i.e. use of a robust alliance measure; investigating multiple time points during treatment and use of several outcome measures. This project further aimed to improve upon the analysis methodology used in the NIMH trial.

Audiotapes of sessions were already collected within both arms of the ADAPT trial. Patients in the medication only arm were offered nine outpatient sessions over 28 weeks; more could be offered depending on clinical need. CBT was offered weekly for 12 weeks, then fortnightly for 12 weeks with a final session at 28 weeks (total 19 sessions). Assertive efforts were made to ensure participants continued even if they missed appointments. Tapes of the sessions were unanalysed prior to this study. 202 patients were included in the primary end point analysis in the trial - 101 in each arm (6 refused the final research assessment). 140 subjects were recorded on the original database as having at least one session taped at or prior to 12 weeks and 121 patients had at least one session taped at or prior to 6 weeks.

In order to be able to assess the stability of the alliance over time, cases with both early

(baseline – 6 weeks) and late (6 - 12 weeks) treatment tapes were first selected.

A strategy was agreed with Chris Roberts, statistician (Professor in Medical Statistics, University of Manchester) in order to select cases. This strategy was based on the likelihood of tapes being available at these time points (or propensity to have a tape as an inverse probability weight of being included in the sample), using logistic regression adjusted for baseline variables (age, sex, site, co morbidity, HoNOSCA, CGAS, MFQ and CDRS). This was used to estimate the probability of having a tape and then cases were sorted from low probability to high. Cases in the medication only arm were then paired with cases with a similar probability in the medication and CBT arm. This gave a total of 64 cases across both arms with tapes at both time points (128 tapes). A random sample was not used as we would expect those who are less likely to have a tape to differ systematically from those who are highly likely. A propensity score is a way of removing effects of confounding variables i.e. removes the confounding effect of the likelihood of having a tape. A purposeful sample was required to be able to investigate hypotheses surrounding outcome.

Some tapes were unavailable (mislabelled or not found) or of very poor quality. These two difficulties limited the number of tapes available for use. Out of a potential 64 identified cases (128 tapes), 45 patients had tapes that were actually available and of sufficient quality to be transcribed at both time points (90 tapes).

A database of available tapes was created. For each case the sessional tapes nearest 3 and 9 weeks from baseline were transcribed for analysis i.e. 45 nearest week 3 and 45 nearest week 9. To expand the number of tapes available a further propensity analysis

was carried out looking only at tape availability between 0-6 weeks. 71 additional cases had available tapes near to week 3. Tapes were transcribed by professional transcribers.

3.3. Measures

3.3.1. Therapeutic Alliance

A modified version of the Vanderbilt Therapeutic Alliance Scale (VTAS) was used to rate the strength of the therapeutic alliance for both treatment conditions. In its original form (Hartley & Strupp, 1983), the VTAS is a 44-item measure composed of three subscales, Therapist, Patient, and Therapist-Patient Interaction. This instrument was selected because, on the basis of a review of therapeutic alliance measures (Elvins and Green, 2008), it was seen as broadly applicable to the treatments under investigation, and one of the few measures with available psychometric data on its use by clinical raters. In assessing its feasibility for this study, I used a modified version of the VTAS created by Krupnick et al., 1996, in their NIMH trial of psychotherapies and medication for depression in adults (see Appendix B for the scale). They judged that the original VTAS was not fully applicable nor its rating manual sufficiently comprehensive to CBT and pharmacotherapy conditions. Seven items from the original scale that applied to psychodynamic therapies were deleted, and the rating manual was revised, making the scale and manual more applicable to the different treatments. Additional "decision rules" were added to the coding manual to help anchor items, providing examples for each of the treatments and aimed at increasing interrater reliability. The scale and the manual were obtained from the original authors.

3.3.2. Symptom change during the course of treatment

Study data already collected includes independent symptom ratings at baseline and weeks 6, 12 and 28 from child (Mood and Feelings Questionnaire) and therapist (Child Depression Rating Scale Revised). The MFQ (Wood et al., 1995) consists of a series of descriptive phrases regarding how the subject has been feeling or acting recently. Codings reflect whether the phrase was descriptive of the subject most of the time, sometimes, or not at all in the past two weeks. The CDRS (Poznanski et al., 1984) is a brief rating scale based on a semi-structured interview with the child. The interviewer rates 17 symptom areas. In clinical settings it can be used to aid the diagnosis of depression (based on DSM-IV criteria – American Psychiatric Association, 1994) and monitor treatment response.

3.3.3. Global Adjustment

Independent standardised researcher ratings of symptoms and general functioning (Health of the Nation Outcome Scales, HoNOSCA), blind to treatment allocation, have been made at baseline and weeks 6, 12 and 28. The HoNOSCA (Gowers et al., 1999) is an outcome measurement tool that assesses the behaviours, impairments, symptoms, and social functioning of children and adolescents with mental health problems. It provides a global measure of an individual's current mental health status, and a means of evaluating the success of attempts to improve health and social functioning. Other ratings of global functioning have also been obtained at baseline and weeks 6, 12 and 28. The CGAS (Dyrborg et al., 2000) is a numeric scale (1 to 100) used to rate the general functioning of children under the age of 18 independent of a clinical diagnosis. A lower score indicates poorer function. Scores on the Clinical Global Impression

Improvement Scale, CGI-I have been obtained at 6, 12 and 28 weeks. The CGI-I (Guy, 1976) is a 7-point scale that requires the clinician to rate the severity of the patient's illness at the time of assessment.

HoNOSCA was the primary outcome measure from the ADAPT trial. There was no main effect of treatment arm on this primary outcome measure in the original trial.

The research questions identified in this current study aim to investigate whether variations in therapeutic alliance in both arms of the trial will provide an explanation of treatment effect, in terms of these outcomes (as it did in an equivalent study in adult depression, Krupnick et al., 1996).

3.4. Coding Procedures

Audio tapes were transcribed and the transcriptions used to rate the alliance. This is essential for coding accuracy and interrater reliability. Interrater reliability on the therapeutic alliance measure was gained using triple coding of 25 transcripts with a trained MSc candidate and another trained researcher. Regular meetings were held to reach a common understanding of rating methods. Rater training began with an orientation session in which the theoretical rationale and general approach of each treatment were reviewed.

The raters met once a month to score the VTAS, and compare and discuss their ratings and decision criteria.

Audiotapes from the purposeful sample were scored only after the raters achieved acceptable levels of reliability on a subset of training cases. Audiotapes were randomly ordered, and raters were kept unaware of session number, type of therapy, and patient outcome (once rating began, it was not difficult to tell what type of treatment was being conducted, but raters were unable to anticipate what type of therapy they would be rating next.)

3.4.1 Coding of Audio Tapes - Interrater Reliabilities

Interrater reliabilities between the three raters on 25 transcripts were calculated pair wise. The table below shows variance estimates; the coefficient alpha is calculated by var (idno)/var (idno) +var (rater) +var (error) i.e. there is a large variance between individual patients' scores (as one might expect), but a low variance between raters on the same patient and a low variation explained by error.

Table 1

Variance Estimates

Component	Estimate
Var (idno)	272.829
Var (rater)	.000 (a)
Var (error)	11.680

Dependent Variable: sum
Method: Restricted Maximum Likelihood Estimation
a This estimate is set to zero because it is redundant.

The coefficient alpha was 0.95 for total alliance scores, which indicates good interrater reliability. This compares with 0.91 for total alliance scores in the equivalent study in

adults (Krupnick et al., 1996). The table below shows a selection of raw total alliance scores for transcripts by rater.

Table 2

Rater, Identification Number of the Transcript (idno) and Total VTAS Score

RATER	IDNO	TOTAL VTAS SCORE
DK	1	87
GC	1	81
RE	1	100
DK	2	142
GC	2	143
RE	2	141
DK	3	143
GC	3	144
RE	3	144

3.5. Data Handling

All 161 transcripts have been coded using the VTAS. 25 were used as the interrater sample.

An SPSS (Statistical Package for Social Sciences Version 16) database has been produced of the sub scores and total scores for each transcript. Stata 10.1 has also been used for some of the statistical analysis.

CHAPTER FOUR – ANALYSIS PLAN

The analyses carried out consist of both conventional statistical analysis and causal modelling analysis designed to look at treatment effect heterogeneity. Analysis is discussed by research question below:

4.1 Research Question 1

a) Does therapeutic alliance measured early in this trial vary with baseline characteristics of the sample and allocated treatment given across the trial?
b) Does therapeutic alliance vary with characteristics of treatment (e.g. treatment site, therapist variables)?

Descriptive statistics were used to illustrate the characteristics of the sample used and to define and describe the spread and variation of the alliance and baseline measures of functioning. T-tests / analysis of variance and non-parametric tests such as chi-square were used to look at any differences in characteristics of the sample at different treatment sites and arms of the trial.

Data reduction was used to factor analyse the VTAS in this sample. Factor analysis was necessary in order to understand if there were coherent underlying constructs operating within the many original variables of the scale and to reduce the data to a manageable size whilst retaining as much original information as possible. A factor analysis was also carried out in the equivalent trial in adults (Krupnick et al., 1996). The result of the factor analysis was used to investigate the relationship between early alliance factors,

baseline characteristics and outcome measures.

Correlations were used to investigate the relationship between early alliance and baseline measures of impairment, alliance and adherence to treatment (sessional attendance) and relationship of alliance to therapist variables.

c) Is alliance in this trial stable over time?

The stability of the alliance through treatment was investigated using correlations between early and late alliance.

4.2. Research Question 2

a) Does early therapeutic alliance predict outcome in this trial?

Correlations and linear regressions were carried out between alliance factors and outcome measures at 6 and 12 weeks (main outcome point) in both arms of the trial and at both sites to investigate the predictive effect of alliance. Multivariable analysis i.e. analysis of covariance was used to look at the relationship between treatment group allocation, the alliance and outcome (where treatment group is the independent variable and alliance is the co-variate). It aims to show the relationship between alliance and outcome measures and the effect of treatment after accounting for the effect that alliance has on the outcome. The value of the treatment by alliance interaction was also analysed to make sure that the relationship between the outcome and alliance is the same in each treatment group.

I. Does the quality of treatment alliance influence treatment effect?

II. Does variance in baseline characteristics of the sample or other unmeasured variables which are common to both alliance and outcome account for variation in therapeutic alliance and/or its relationship to the effect of treatment?

To investigate these questions i.e. how alliance may affect or explain treatment effect heterogeneity, Structural Mean Modelling (SMM) was used. Related methodology has recently been employed successfully in the evaluation of heterogeneity in the effects of treatment by the advisor to this project (Dunn et al., 2012) and in other recent complex treatment trials in medicine (Follman, 2006). The analysis employed seeks to determine the effect of alliance on efficacy of treatment in the presence of hidden confounders (unmeasured potential causes which are common to both alliance and clinical outcome). Traditional approaches to the analysis of clinical trials use data from treated groups and then correlate outcome and alliance (as discussed in the introduction above). However, this approach cannot distinguish treatment–free (or different treatment) prognosis from prediction of treatment effects.

In the ADAPT trial, half the participants received treatment as usual plus medication and half received treatment as usual plus medication and CBT (combined treatment). Although the average treatment effect from the original intention to treat (ITT) analysis in ADAPT was not statistically significantly different from zero, this does not imply that the treatment effect for everyone in the trial is zero. Treatment could have been beneficial for some and detrimental for others. The key task is therefore to investigate whether the individual's treatment effect (ITE) is associated with therapeutic alliance.

Structural mean modelling allows us to estimate the treatment effect as if everyone in the trial received all interventions. For each individual there are two potential outcomes – Yt and Yc, where Yt is their outcome if they receive one intervention (combined treatment) and Yc is the outcome if in the other arm of the trial (medication). The effect of intervention on every individual is the difference between the predicted outcome in the additional treatment group and that in the medication group i.e. the individual treatment effect (ITE) is the Yt–Yc. The fundamental problem is that we can never observe both Yt and Yc in a given individual, but we can use baseline predictors of outcome under the two treatment conditions to get an estimate (imputed value) for that individual's individual treatment effect. The remaining question is then "is the individual treatment effect related to alliance under treatment?"

The SMM algorithm is as follows:
Regress total alliance on treatment centre, age, gender and baseline measure (e.g. baseline HoNOSCA) for those in the CBT group only. Predict the alliance for everyone in the trial (both treatment arms). Regress change in outcome measure (e.g. baseline HoNOSCA to HoNOSCA at week 12) on the same variables in the CBT group only. Predict change after CBT for everyone in the trial (A). The same procedure is used for the medication only group (B). The predicted individual treatment effect (ITE) is change in outcome measure after CBT minus change in outcome measure after control i.e. ITE = A-B.

The ITE is then regressed against the predicted CBT total alliance (with and without zero intercept – to look at the effect of assuming the intervention has no impact when

the alliance is zero). The analyses above are then bootstrapped (with 1000 iterations) to get valid standard errors and confidence intervals within the analysis. Bootstrapping constructs a number of re samples of the observed dataset as a method for assigning measures of accuracy to sample estimates (Efron & Tibsharani, 1993). This technique allows estimation of the sampling distribution of almost any statistic using only very simple methods (Varian, 2005).

CHAPTER FIVE – RESULTS

Descriptive statistics were used to illustrate the characteristics of the sub sample of the original ADAPT trial and to define and describe the spread and variation of the alliance and baseline measures of functioning. T-tests / analysis of variance and non-parametric tests such as chi-square were used to look at any differences in characteristics of the sample at different treatment sites and arms of the trial.

Data reduction was used to factor analyse the VTAS in this sample. Factor analysis was necessary in order to understand if there were coherent underlying constructs operating within the many original variables of the scale and to reduce the data to a manageable size whilst retaining as much original information as possible. The result of the factor analysis was used to investigate the relationship between early alliance factors and baseline characteristics and outcome measures.

Correlations were used to investigate the relationship between early alliance and baseline measures of impairment, alliance and adherence to treatment (sessional attendance) and relationship of alliance to therapist variables.

These analyses were carried out to answer the questions: “Does therapeutic alliance measured early in this trial vary with baseline characteristics of the sample and allocated treatment given across the trial?” and “Does therapeutic alliance vary with characteristics of treatment (e.g. treatment site, therapist variables)?”

5.1. Characteristics of the Whole Sample

116 cases were identified using the strategy defined in the methods; producing 161 available tapes (45 tapes from week 9). 64 patients were identified in the Manchester cohort and 52 in the Cambridge cohort.

5.1.1 Distribution and Demographics

Table 3

Distribution of Sample by Treatment Arm and Site of Treatment

	Treatment Allocation: Medication Group (%age)	**Treatment Allocation: Medication and CBT (%age)**
Whole Sample	43 (37.1)	73 (62.9)
Manchester Site	17 (26.6)	47 (73.4)
Cambridge Site	26 (50.0)	26 (50.0)

In the whole sample, 63% were allocated to combined treatment (medication plus CBT). The treatment allocation was equal in Cambridge with a higher percentage of combined treatment in the Manchester sample. In the original trial the treatment allocation was broadly equal (105 combined arm compared to 103 medication arm). This disparity in the Manchester sample probably reflects the difficulty of obtaining tapes of adequate quality (see sampling strategy above).

Table 4

Mean Age, Gender Distribution and Presence or Absence of Behaviour Disorder

Sample	Age at trial entry (mean)	No. Female (%age)	No. Male (%age)	Behaviour Disorder Present (%age)
Whole Sample	14.23	83 (71.6)	33 (28.4)	32 (27.6)
Manchester Site	14.09	45 (70.3)	19 (29.7)	25 (39.1)
Cambridge Site	14.40	38 (73.1)	14 (26.9)	7 (13.5)
Medication arm	14.37	31 (72.1)	12 (27.9)	8 (18.6)
Combined Treatment (Medication and CBT) arm	14.15	52 (71.2)	21 (28.8)	24 (32.9)

The mean age of the whole sample was 14.2 years, with a slightly older age at the Cambridge site compared to Manchester (14.4 compared to 14). The age ranges from 11 to 17 years. Those aged 14 and over account for 75% of the whole sample. This is consistent with the original trial (whole sample 14.0 SD 1.5). The samples were normally distributed for age (see Appendix C for graphs).

71.6% of the whole sample was female with a female preponderance at both sites. There were a slightly higher percentage of females in Cambridge (73.1% compared to 70.3%). This is broadly consistent with the original trial where the percentage female was 74.0%.

27.6% of the whole sample had a co morbid behaviour disorder. The Manchester sample had a much higher percentage of behaviour disorder present than Cambridge (39.1% compared to 13.5%). This is reflective of the original trial. 32.9% of the combined treatment group had a comorbid behaviour disorder compared to 18.6% in the medication group. Chi-square was used to see if there were any statistically significant differences between sites in terms of behaviour disorder.

Pearson's Chi-Square 9.413, df 1, sig 0.002, shows there is a significant difference between sites in terms of numbers of patients with co-morbid behaviour disorder. Manchester had a statistically significantly greater number of patients with co-morbid behavioural disorder than Cambridge.

Chi-square was used to look at difference between treatment arms in terms of behaviour disorder, Chi-square = 2.76, df = 1, sig = 0.097. This indicates there is no significant difference between treatment arms in terms of diagnosis of behaviour disorder.

5.1.2 Socioeconomic Data

92% of this sample was white British and there was no difference between the groups. This is reflective of the original trial where 94% of the sample was white British.

In the whole sample, 73% lived with biological mother and 30% with biological father. A slightly higher percentage of the sample (94.0% compared with 91.8%) lived with a biological parent in Cambridge than in Manchester. More patients lived with their biological father in Cambridge (40% compared to 14%). A variable amount of this data is, however, missing from the original trial database.

A higher percentage of family respondents had a degree or higher in Cambridge than in Manchester (32.7% compared to 17.2%), as had their partners, and a higher percentage were in paid employment, as were their partners (67.3% in Cambridge compared with 50% in Manchester).

Overall the socioeconomic data indicate that participants in Cambridge come from a broadly more economically affluent group, with parents who have been educated to a higher level and who are more likely to be within "intact" biological families.
There were 116 patients in the early alliance sample, 64 in the Manchester cohort and 52 in the Cambridge cohort.

5.1.3 Therapist Cohort

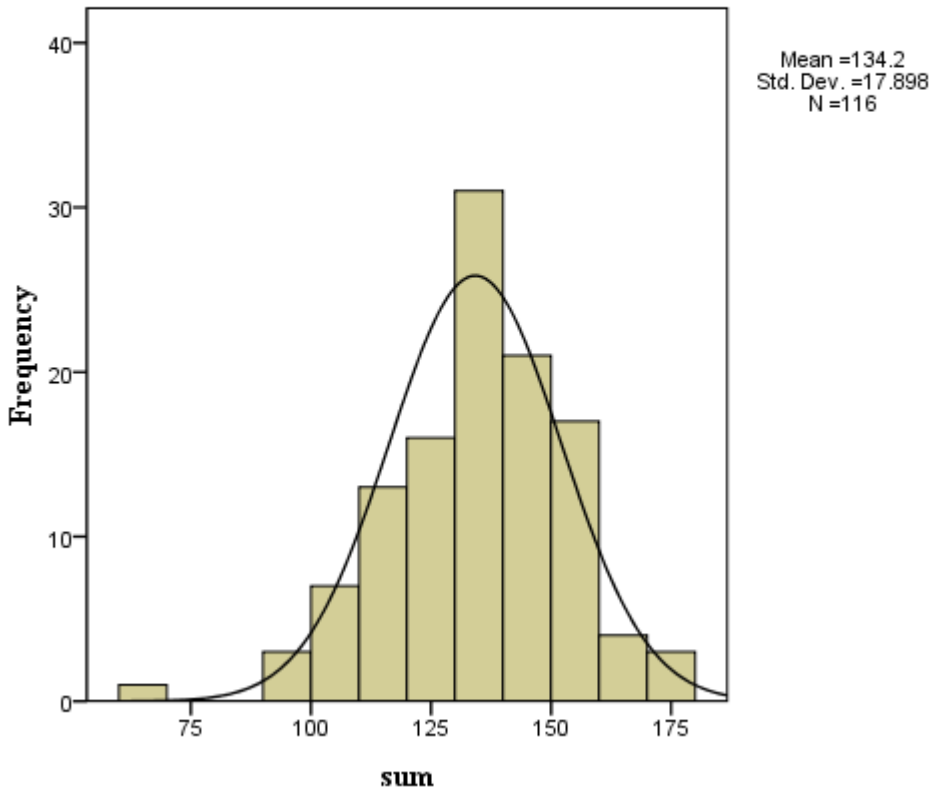
There was one main therapist in Cambridge, (98% of Cambridge cases) who carried out both CBT and medication management (in both arms of the trial) and was a psychiatrist. In Manchester there were 11 therapists, of whom 3 were psychiatrists and the rest were psychologists (CBT sessions only). However, one therapist (psychiatrist) saw 31 (nearly 50%) of these patients. The rest of the therapists saw between 7 and 1 patient each.

5.2 Characteristics of Early Alliance

The mean early total alliance score was 134.2 with a SD of 17.8. The maximum score that could be gained by using the scale is 185. Minimum score in the whole sample was 65 (one patient), maximum was 178. The sample was slightly skewed to the right, with fewer low scores, but the scores fall within a wide range (113).

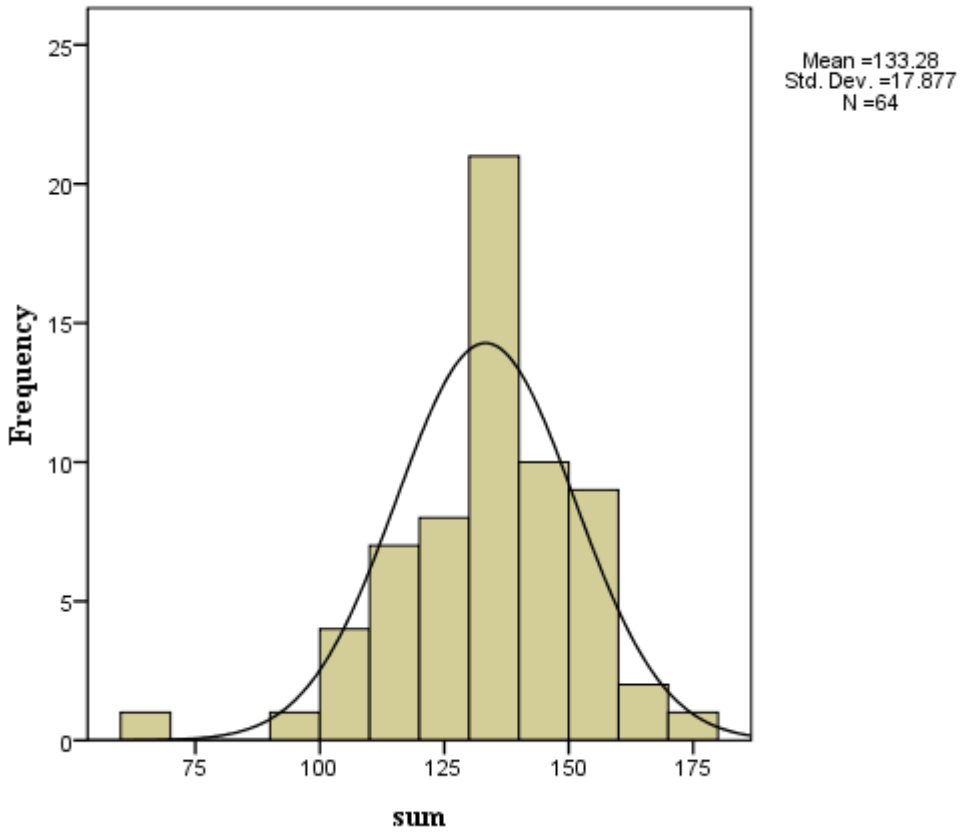
Histogram 1 shows the spread of total alliance scores for the whole sample:

Histogram1: Sum of Early Alliance Scores for Whole Sample

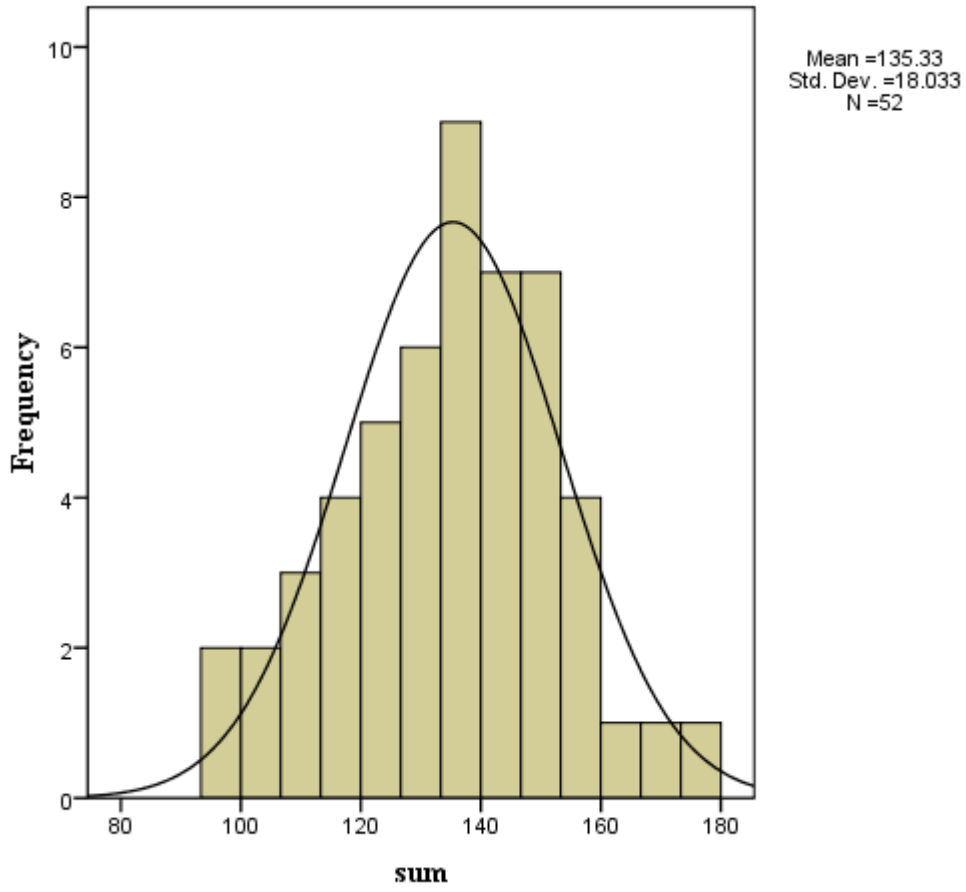


The following two graphs show the spread of early alliance scores in each site:

Histogram 2: Sum of Early Alliance Scores for Manchester Site



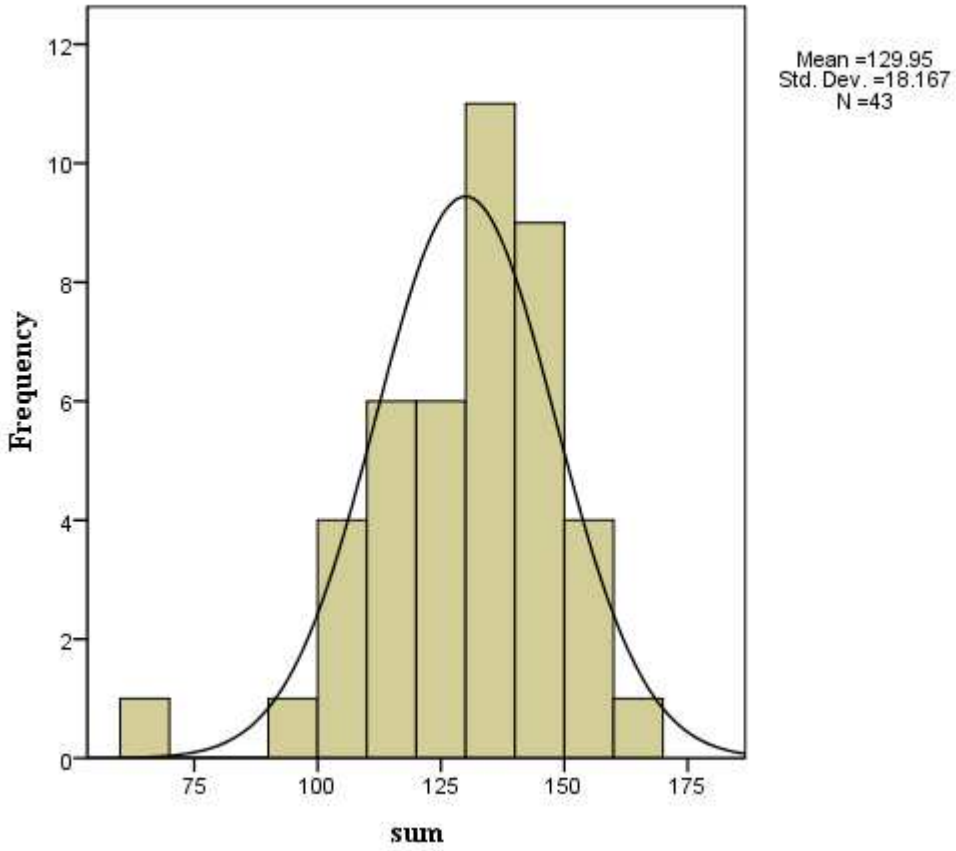
Histogram 3: Sum of Early Alliance Scores for Cambridge Site



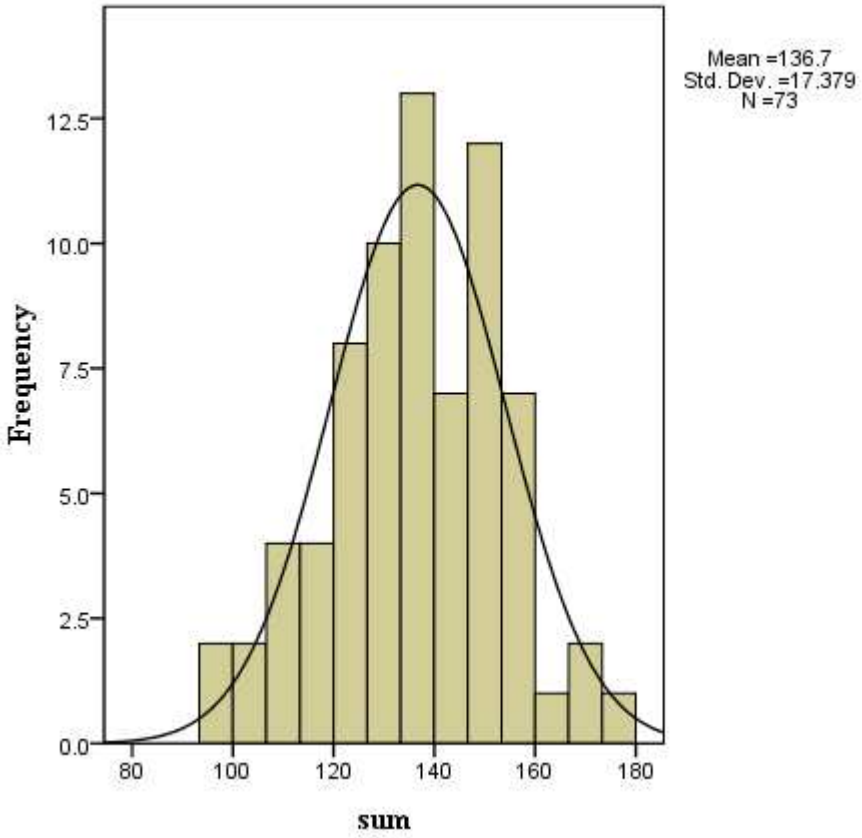
The graphs above show that mean total early alliance scores across both sites are very similar (133 compared to 135) with similar standard deviations. However, the Manchester data accounted for the lowest scores in the whole sample (65).

The following two graphs show spread of early alliance scores by arm of treatment:

Histogram 4: Sum of Early Alliance Scores for Medication Arm



Histogram 5: Sum of Early Alliance Scores for Combined Treatment Arm



The graphs above show that the combined treatment arm overall had a higher mean early alliance score compared to the medication arm (136 compared to 129). The medication arm accounted for the lowest scores.

In summary the above graphs show that the medication arm had a lower mean total alliance score than the combined treatment arm (129 compared to 140). The Cambridge combined treatment arm accounted for the highest scores in the whole sample (180). Overall there was a trend towards the mean score in Cambridge being slightly higher and SD slightly wider. This seems to be accounted for by the combined treatment arm in Cambridge which had a higher mean alliance score than the medication arm (140

compared to 129). Scores across both arms in Manchester were more similar (134 and 130). The medication arm sample overall had a lower total alliance score than the combined treatment arm.

5.3 Data Reduction - Factor Analysis of VTAS Scores

To identify dimensions of the revised VTAS, the instrument was factor analysed. Some items were reverse keyed. A principal components analysis was followed by varimax rotation (N = 116 patients). The Kaiser-Meyer-Olkin measure verified the sampling adequacy for the analysis, KMO = .86 which is well above the generally accepted limit of .5. Bartlett's test of sphericity chi –square (666) = 3020.67, p <.001, indicated that correlations between items were sufficiently large for principle components analysis.

5.3.1 Data Reduction – Correlations

The correlations between the questions (components) in the VTAS are summarized as follows:

Mean 0.327

Minimum value 0.018

Maximum value 0.762

An initial analysis was run to obtain eigenvalues for each component in the data. The scree plot and the following table show eigenvalues and percentage of variance explained by each component.

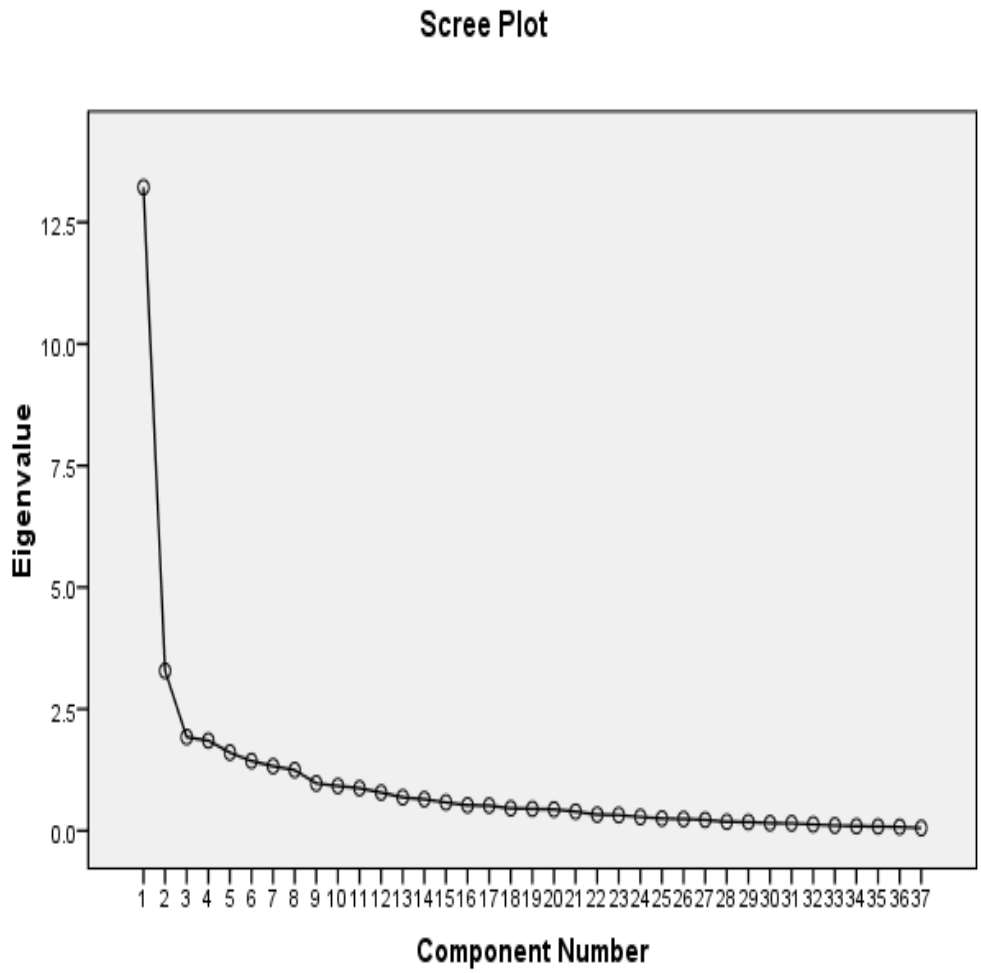


Table 5

Eigenvalues and Percentage of Variance for Early Alliance Scores

	Initial Eigenvalues		
Component	**Total**	**% of Variance**	**Cumulative %**
1	13.221	35.731	35.731
2	3.285	8.879	44.611
3	1.924	5.201	49.811
4	1.853	5.008	54.820
5	1.605	4.339	59.158
6	1.433	3.874	63.033
7	1.326	3.583	66.616
8	1.246	3.367	69.982
9	.972	2.628	72.610
10	.920	2.487	75.098
11	.873	2.359	77.457
12	.784	2.118	79.575
13	.686	1.853	81.428
14	.648	1.752	83.180
15	.583	1.575	84.755
16	.521	1.409	86.164
17	.515	1.393	87.556
18	.459	1.241	88.797
19	.449	1.214	90.011
20	.437	1.182	91.193
21	.394	1.065	92.258
22	.331	.895	93.152
23	.322	.869	94.021
24	.282	.761	94.783
25	.252	.680	95.463
26	.240	.649	96.112
27	.223	.604	96.715
28	.182	.492	97.208
29	.178	.481	97.689
30	.157	.423	98.112
31	.151	.409	98.521
32	.129	.348	98.869
33	.107	.289	99.157
34	.091	.245	99.403

Table 5

Eigenvalues and Percentage of Variance for Early Alliance Scores Continued

	Initial Eigenvalues		
Component	**Total**	**% of Variance**	**Cumulative %**
35	.087	.236	99.639
36	.078	.210	99.849
37	.056	.151	100.000

The scree plot shows inflexions that would justify retaining components 1 and 2. Eight components had eigenvalues over Kaisers' criterion of one, but two components in combination explained 44.6% of the variance. Given the relatively large sample size and the convergence of the scree plot and percentage of variance on two components, this is the number of components that were retained in the final analysis.

The following table shows the factor loadings after rotation. The items that cluster on the same components suggest that component 1 represents a patient factor, component 2 a therapist factor. Printing of loadings / coefficients less than 0.4 has been suppressed.

Table 6

Component Scores of the VTAS after Rotation for the Whole Sample (Key: page 65)

	Component 1	Component 2
t conveying confidence		.715
t expressing hope		.448
t committing himself		.737
t show acceptance respect compassion		.765
t acknowledge validity of p problems		.746
t make sure patient understands therapy		.448
t makes interventions that preserve patient dignity		.796
t intrude own values		.442
t express own reactions appropriately		.737
t fosters undue dependency		
t makes irrelevant uncalled for comments		.476
t builds sense of mutuality		.523
t misses interventions		.523
patient expresses feels better		
p indicates experiences t as understanding	.659	.534
p assumes therapeutic tasks by self	.612	
p expects therapist to change him	.625	
p carries out therapeutic procedures asked of him	.681	
p acknowledges has problems that t can help him with	.719	
p indicates desire to overcome problems	.697	
p talks freely openly honestly with t	.668	.485
p acts hostile or attacking to t		
p acts mistrustful or defensive	.787	

Table 6

Component Scores of the VTAS after Rotation for the Whole Sample Continued

	Component 1	Component 2
p becomes so anxious interferes with therapy		
p misses appointments or comes late		
p and t show enthusiasm	.683	.508
work together in joint effort	.670	.622
share common viewpoint	.643	.454
p and t relate in realistic straightforward way	.642	.590
agree on goals and tasks	.592	.589
focus on therapeutic task		.556
seem engaged in power struggle	.789	
express possibility of premature termination	.713	
allow session to become empty or boring		
accept different roles and responsibilities	.582	.524
refer back to experiences together		.558
awkward silences or pauses		

Key:
Extraction Method: Principal Component Analysis
Rotation Method: Varimax with Kaiser Normalisation
Rotation converged in 3 iterations
t = therapist
p = patient

Table 6 and the scree plot indicate that two factors, a therapist factor and a patient factor, accounted for the vast majority of the variance and will be used for the present analyses along with the total alliance score. This is the same as the equivalent trial in adults (Krupnick et al., 1996), which identified 2 factors, a patient factor and a therapist

factor. These results do not corroborate previous literature suggesting that the alliance in adolescents is more of a “one factor” phenomenon (Di Giuseppe, Linscott and Jilton, 1996).

5.3.2 Internal Consistency

The internal consistency was calculated for both components of the scale. Both had high internal consistency, Cronbach’s alpha = 0.870 and 0.930 respectively. This statistic is calculated from pair wise correlations between scale items within the components. High internal consistency indicates that within the components, items on the scale probably measure the same general construct. The SpSS commands used were Analyze, Scale, Reliability Analysis, selected the scale items as variables and chose alpha as the model to analyse them.

5.4. Baseline Measures of Functioning and Early Treatment Alliance Factors

The following analyses seek to describe and explain the relationship between baseline functioning and early alliance factor scores.

The following table shows the baseline severity of depression, global functioning and early alliance factor scores in this sub sample of the original trial.

Table 7

Spread of Baseline Variables and Early Alliance Factors for Whole Sample

Baseline Variable	Minimum	Maximum	Mean	Std Deviation
HoNOSCA	13.00	37.00	25.38	5.45
CGAS	30.00	60.00	41.21	6.13
CDRS	35.00	84.00	58.37	10.29
MFQ	6.00	61.00	37.10	12.78
Therapist alliance factor	-2.50	2.65	0.00	1.00
Patient alliance factor	-4.11	1.82	0.00	1.00
Total alliance factor	-3.65	2.57	0.00	1.00

(N = 116)

The spread of baseline functioning scores are reflective of the sample in the original trial and show that overall the sample had at least moderate depressive symptoms (CDRS mean of 58) and were quite impaired at baseline (HoNOSCA mean of 25).

Table 8:

Spread of Baseline Variables and Early Alliance Factors in Manchester

Variable (Baseline)	Minimum	Maximum	Mean	Std Deviation
HoNOSCA	13.00	37.00	25.60	4.79
CGAS	30.00	60.00	40.31	6.40
CDRS	35.00	84.00	58.65	9.78
MFQ	6.00	61.00	36.33	13.38
Therapist alliance	-3.65	2.07	-0.06	0.98
Patient alliance	-2.42	1.79	-0.14	0.94
Total alliance	-4.11	1.83	0.06	1.05

(N = 64)

Table 9

Spread of Baseline Variables and Early Alliance Scores in Cambridge

Variable (Baseline)	Minimum	Maximum	Mean	Std Deviation
HoNOSCA	14.00	37.00	25.12	6.21
CGAS	31.00	55.00	42.32	5.64
CDRS	39.00	82.00	58.04	10.98
MFQ	15.00	57.00	39.98	11.80
Therapist alliance	-1.93	2.57	0.08	1.02
Patient alliance	-2.50	2.65	0.18	1.06
Total alliance	-3.73	1.39	-0.07	0.94

(N = 52)

The summary tables above indicate there are no obvious large differences between the samples in terms of baseline functioning and alliance scores. The patients at the Manchester site are slightly more impaired at baseline (HoNOSCA mean of 25.6 compared to 25.1) and their depressive symptoms are slightly worse than at Cambridge on patient reported scores (MFQ).

Analysis of variance (ANOVA) was carried out to see if any of the differences in mean scores on these variables between the sites were significant at the $p<0.05$ level.

Table 10

ANOVA analysis of Baseline Scores and Early Alliance by Site

Variable (Baseline)	df between groups	df within groups	F	Sig. (p)
HoNOSCA	1	114	0.219	0.640
CGAS	1	114	3.170	0.078
MFQ	1	114	2.400	0.127
CDRS	1	113	0.100	0.752
Therapist alliance	1	114	2.990	0.086
Total alliance	1	114	0.525	0.470
Patient alliance	1	114	0.475	0.492

There are no significant differences between the sites in terms of baseline HoNOSCA scores F (1, 114) = .219 (p value = .640), Children's' Global Assessment Scale F (1, 114) = 3.172 (p value = .078), Mood and Feelings Questionnaire, F (1, 114) = 2.40 (p value = .127), Children's Depression Rating Scale F (1, 113) = .100 (p value = .752)

and alliance scores. There are no significant differences between the sites in terms of early therapist, patient or total alliance.

This indicates that there are no statistically significant differences between sites in terms of baseline functioning, researcher assessed and patient reported symptoms of depression, and early alliance scores.

An analysis of variance (ANOVA) showed there were no significant differences in total alliance ($F(1, 62) = .075$, p value = .785), therapist alliance ($F(1, 62) = .014$ p value = .905) or patient alliance ($F(1, 62) = .066$ p value = .799) at the Manchester site between groups of those with behaviour disorder and those without.

The following tables show the spread of baseline scores by treatment allocation Although the groups were of course randomised in the original trial so one would not expect there to be statistically significant differences in baseline functioning between treatment arms, my sample is a subgroup of the original and it is important to check that at baseline functioning and severity of depression remains equal between groups.

Table 11:

Spread of Baseline Scores and Early Alliance in Medication Arm

Variable (Baseline)	Minimum	Maximum	Mean	Std Deviation
HoNOSCA total	14.00	37.00	25.80	5.65
CGAS	30.00	54.00	40.40	5.70
CDRS	39.00	79.00	58.90	10.09
MFQ	7.00	61.00	38.40	13.93
Therapist alliance	-2.50	1.05	-0.22	0.88
Patient alliance	-4.11	1.24	-0.16	0.89
Total alliance	-3.65	1.50	-0.27	0.99

(N = 43)

Table 12

Table to show Spread of Baseline Scores and Early Alliance in Combined Arm

Variable (Baseline)	Minimum	Maximum	Mean	Std Deviation
HoNOSCA	13.00	37.00	25.14	5.35
CGAS	30.00	60.00	41.69	6.35
CDRS	35.00	84.00	58.06	10.47
MFQ	6.00	57.00	37.72	12.13
Therapist alliance	-2.42	2.64	0.13	1.05
Patient alliance	-3.73	1.82	0.10	1.05
Total alliance	-1.99	2.57	0.16	0.98

(N = 73)

There do not appear to be large differences between the scores in each treatment group. Patients in the combined treatment arm appear to be slightly more impaired at baseline on some measures (MFQ of 37.7 compared to 38.4, CGAS of 41.7 compared to 40.4) but not all, and to have slightly better early alliance

Analysis of variance (ANOVA) was carried out to see if any of the differences in mean scores on these variables between treatment arms were significant at p value <0.05.

Table 13

ANOVA Analysis of Baseline Scores and Early Alliance by Treatment Arm

Variable (Baseline)	df between groups	df within groups	F	Sig. (p)
HoNOSCA	1	114	0.387	0.535
CGAS	1	114	1.220	0.272
MFQ	1	114	0.080	0.784
CDRS	1	113	0.180	0.670
Therapist alliance	1	114	3.440	0.066
Total alliance	1	114	5.240	0.054
Patient alliance	1	114	1.820	0.181

The table above shows that there are no significant differences between treatment arms in terms of baseline functioning, patient and researcher assessed symptoms of depression and early alliance scores.

5.5. Relationship between Early Alliance Scores and Baseline Measures of Impairment in the Whole Sample

Correlations were carried out between baseline measures and early alliance factor scores (therapist, patient and total) to investigate the relationship between impairment and severity of depression and early alliance.

Table 14

Correlations between Alliance Factors and Baseline Measures of Impairment in Whole Sample

	Therapist Alliance		Patient Alliance		Total Alliance	
	Pearson Correlation	**Sig (two-tailed)**	**Pearson Correlation**	**Sig (two-tailed)**	**Pearson Correlation**	**Sig (two-tailed)**
Therapist Alliance	1.000		0.000	1.000	0.708*	<0.05
Patient Alliance	0.000	1.000	1.000		0.706*	<0.05
Total Alliance	0.708*	<0.05	0.706*	<0.05	1.000	
HoNOSCA	-0.061	0.516	0.147	0.116	0.060	0.519
CGAS	0.002	0.984	-0.110	0.240	-0.076	0.416
MFQ	-0.180	0.053	0.031	0.744	-0.106	0.258
CDRS	-0.072	0.445	0.023	0.804	-0.034	0.715

*(N = 116)*indicates significance at p<0.05*

There is trend towards a negative correlation between mood and feelings score at baseline and therapist early alliance score (r = -0.180 p value = 0.053) i.e. as MFQ score decreases (meaning the patient is reporting fewer symptoms) Therapist early alliance factor increases. However, this trend is not corroborated by a similar relationship between MFQ at baseline and Patient or Total early alliance score - there is no

relationship between MFQ score at baseline and Patient or Total alliance score (r = .031, p value = .744 and r = -0.106, p value = 0.258 respectively). There is a significant correlation between Total alliance and Patient alliance (r = 0.706, p value 2 tailed = <0.05) and Total alliance and Therapist alliance (r = 0.708, p value 2 tailed = <0.05).

There are no statistically significant correlations between baseline measures of impairment and symptoms and early alliance factors in the whole sample e.g. Therapist alliance and HoNOSCA at baseline r = -0.061 p= 0.516.

This implies that baseline impairment does not adequately explain any variation in early alliance scores.

5.6 Relationship between Alliance Factors and Baseline Measures in Each Site

The above correlations were repeated when the sample was looked at by site:

Table 15

Correlations between Alliance Factors and Baseline Measures in Manchester

Alliance Factor		HoNOSCA	CGAS	MFQ	CDRS t score
Therapist Alliance	Pearson Correlation	-0.032	-0.087	-0.197	-0.020
	Sig. (2-tailed)	0.801	0.497	0.120	0.873
Patient Alliance	Pearson Correlation	0.230	-0.227	0.159	0.084
	Sig. (2-tailed)	0.068	0.071	0.210	0.512
Total Alliance	Pearson Correlation	0.152	-0.230	-0.013	0.049
	Sig. (2-tailed)	0.232	0.068	0.921	0.699

(N = 64)

The above table indicates there are no statistically significant correlations between alliance factors and baseline scores in Manchester.

Table 16

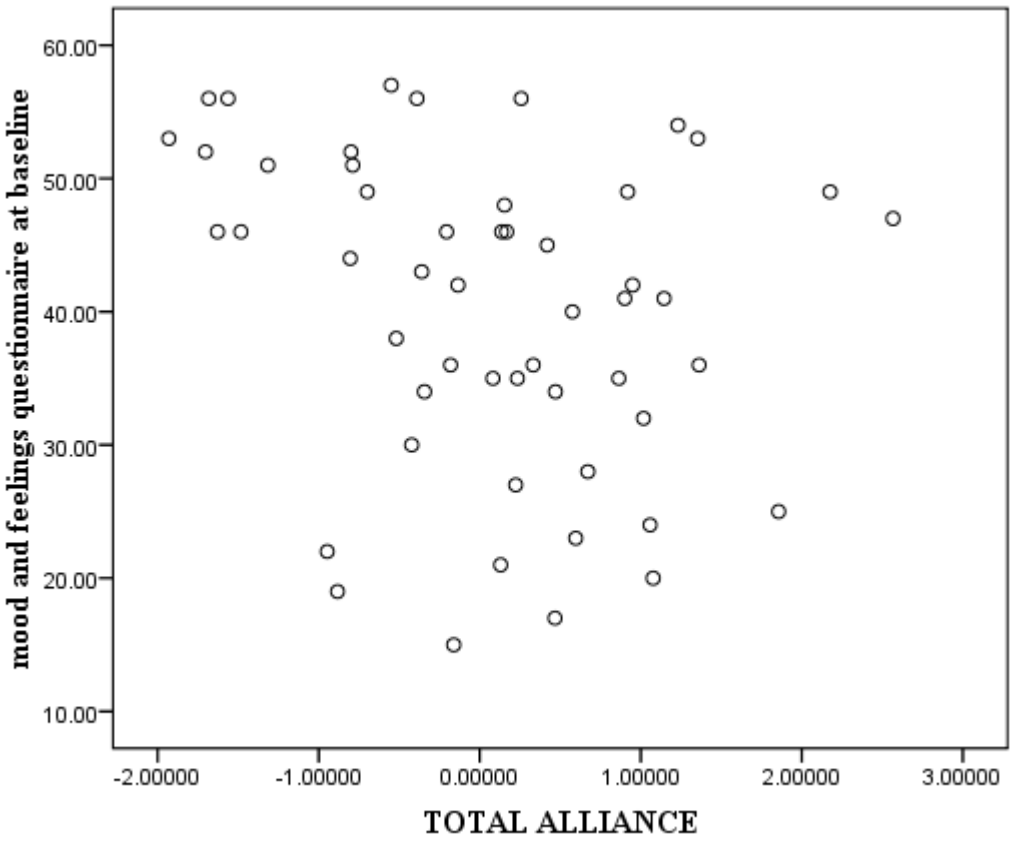
Correlations between Alliance Factors and Baseline Measures in Cambridge

Alliance Factor		HoNOSCA	CGAS	MFQ	CDRS t score
Therapist Alliance	Pearson Correlation	-0.074	0.051	-0.225	-0.120
	Sig. (2-tailed)	0.603	0.721	0.109	0.396
Patient Alliance	Pearson Correlation	0.058	0.098	-0.145	-0.053
	Sig. (2-tailed)	0.683	0.491	0.305	0.708
Total Alliance	Pearson Correlation	-0.016	0.100	-0.258	-0.122
	Sig. (2-tailed)	0.909	0.479	0.065	0.388

(N = 52)

The previous table and following graph show that there is a trend towards a negative correlation between mood and feelings score at baseline and total early alliance score (r = -0.258 p value = 0.065) i.e. as MFQ score improves (decreases) total early alliance score improves (increases). However there are no other correlations between early alliance score and other baseline characteristics.

Scatter Plot 1: Relationship between Early Total Alliance Factor and Baseline Mood and Feelings Questionnaire Score in Cambridge



The above correlations were repeated in Cambridge when the sample was divided into treatment arms but no correlations between alliance factors and baseline measures were found (see Appendix C for tables of correlations).

5.7. Alliance and Sessional Attendance / Adherence

Correlations were conducted to see if there was any relationship between early alliance and sessional attendance (one measure of adherence to treatment) by 12 weeks and 28 weeks. Patients in the medication only arm were offered nine outpatient sessions over 28 weeks; more could be offered depending on clinical need. CBT was offered weekly for 12 weeks, then fortnightly for 12 weeks with a final session at 28 weeks (total 19 sessions).

Table 17

Correlations between Early Alliance Factors and Number of Sessions Attended for Whole Sample

Alliance Factor		**total sessions attended by 12 weeks (N = 116)**	**total sessions attended by week 28 (N = 110)**
Therapist Alliance	**Correlation coefficient**	.096	.024
	Sig. (2-tailed)	.304	.802
Patient Alliance	**Correlation coefficient**	.052	.083
	Sig. (2-tailed)	.578	.374
Total Alliance	**Correlation coefficient**	.105	.076
	Sig. (2-tailed)	.262	.420

The above table shows there is no evidence of correlation between early alliance factor scores and number of sessions attended by 12 weeks and 28 weeks. This implies there is

no relationship between early alliance and how many sessions are attended by patients. The same held true when the sample was divided by site (see Appendix C for correlations).

5.8. Relationship to Therapist Variables

There was one main therapist in Cambridge, (98% of Cambridge cases) who carried out both CBT and medication management (in both arms of the trial) and was a psychiatrist. In Manchester there were 11 therapists, of whom 3 were psychiatrists and the rest were psychologists (CBT sessions only). However, one therapist (psychiatrist) saw 31 (nearly 50%) of these patients. The rest of the therapists saw between 7 and 1 patient each.

The following table shows each therapist identifier and mean total alliance:

Table 18

Mean Total Early Alliance Scores for each Therapist

Therapist	N	Mean	Standard Deviation	Minimum	Maximum
1	6	136.170	9.368	123	152
2	31	133.650	19.678	65	171
3	7	128.710	16.500	102	155
4	1	122.000	n/a.	122	122
5	7	140.570	11.588	129	159
6	2	130.000	35.355	105	155
7	2	137.000	5.657	133	141
8	2	128.000	41.012	99	157
9	2	135.000	25.456	117	153
10	3	130.000	19.672	109	148
11	1	113.000	n/a.	113	113
12	51	135.390	18.207	98	178
13	1	132.000	n/a	132	132

Therapist 2 (main therapist in Manchester) has the widest range of alliance scores but also treated the highest percentage of the sample in Manchester (31/64). The main therapist in Cambridge (12) gained the highest individual alliance score, but a wide range of scores overall (98 – 178).

An analysis of variance (ANOVA) shows no significant differences between therapists $F(12, 103) = .335$ (p value = .981) in terms of mean alliance scores.

In the combined treatment arm, patients who had two therapists (one for medication management, one for CBT) had lower total alliance scores than those who had one therapist (mean of 133.4, s.d. 17.7 compared to mean of 138.0 s.d. 17.3). The difference was not significant $t(71) = 1.04$, $p > 0.05$.

5.9 Summary - Characteristics of Early Alliance and Relationship to Baseline Variables, Characteristics of Treatment and Number of Sessions Attended

To summarise the results reported above, 116 patients were identified in the selected sample for analysis. 64 of these patients were treated in Manchester and 52 in Cambridge. The mean and age and gender mix of the sample reflects the original trial, as does the severity of symptoms and impairment. Some differences between sites in the selected sample were identified. A greater number of patients are identified in the combined treatment group in Manchester (possibly reflecting the difficulty of obtaining tapes of sufficient quality). A difference between sites in terms of both patient factors and therapist factors was also identified. There is a significant difference between Manchester and Cambridge in the number of patients with co-morbid behaviour

disorder, with the greater number in Manchester. There were a far greater number of therapists in Manchester, from different professional disciplines. In Cambridge one therapist treated 98% of the sample. An analysis of variance did not show any significant differences in the alliance scores obtained for sessions with different therapists overall, but there was a trend towards a lower alliance score in patients who had more than one therapist in the combined treatment group.

A wide range of alliance scores were obtained over the whole sample. Scores were slightly skewed to the right, with fewer low scores. Lower scores were obtained in the medication group compared to the combined group. Slightly higher scores were obtained in the Cambridge cohort. However, these differences were not seen to be statistically significant.

There is no consistent relationship between early alliance and baseline measures or between early alliance and sessional attendance.

5.10 Stability of alliance

The following analysis was performed to answer the research question “Is alliance in this trial stable over time?”

A correlation was used to investigate the relationship between early and late alliance. There is a statistically significant correlation between total alliance scores measured at early (3 weeks) and late (9 weeks) $r = 0.371$, p (two-tailed) < 0.05.

This indicates that alliance established early in the relationship between patient and therapist is strongly related to the alliance as measured much later in the process of treatment. Alliance is stable throughout the process of treatment i.e. a positive alliance established early on continues to be positive towards the end of treatment.

5.11 Relationship between Early Alliance and Outcome Measures

In order to answer the question "Does early therapeutic alliance predict outcome in this trial?" the following analyses were carried out.

Correlations were undertaken to see if there was a relationship between early alliance and outcome measures. Correlations were firstly undertaken for the whole sample at 6 and 12 weeks (main outcome point of the trial). Kendall's Tau was used for the CGI-I scale as it is ordinal data, and a small data set with a number of tied ranks. Pearson's r was used for all other correlations.

Table 19

Correlations between Total, Patient and Therapist Alliance Factors and Outcome Measures at 6 and 12 weeks for Whole Sample

		Patient Alliance	Therapist Alliance	Total Alliance
HoNOSCA total at 6 weeks	Pearson Correlation	.042	-.014	.019
	Sig. (2-tailed)	.661	.880	.840
	N	111	111	111
HoNOSCA total at 12 weeks	Pearson Correlation	.129	-.050	.054
	Sig. (2-tailed)	.171	.599	.570
	N	114	114	114
CGAS at 6 weeks	Pearson Correlation	-.038	.059	.015
	Sig. (2-tailed)	.694	.538	.876
	N	111	111	111
CGAS at 12 weeks	Pearson Correlation	-.107	-.021	-.088
	Sig. (2-tailed)	.256	.827	.351
	N	114	114	114
CGI-I at 6 weeks	Kendall's Tau b	-.003	0.76	-.004
	Sig. (2-tailed)	.969	.297	.952
	N	110	110	110
CGI-I at 12 weeks	Kendall's Tau b	.061	.015	.025
	Sig. (2-tailed)	.381	.828	.719
	N	114	114	114
MFQ at 6 weeks	Pearson Correlation	.013	-.083	-.049
	Sig. (2-tailed)	.895	.385	.606
	N	111	111	111
MFQ at 12 weeks	Pearson Correlation	.103	-.061	.028
	Sig. (2-tailed)	.279	.524	.765
	N	113	113	113

(N = 116)

Table 19

Correlations for the Whole Sample between Total, Patient and Therapist Alliance Factors and Outcome Measures at 6 and 12 weeks Continued

		Patient Alliance	Therapist Alliance	Total Alliance
CDRS t score at 6 weeks	Pearson Correlation	.026	-.033	-.004
	Sig (2-tailed)	.784	.735	.964
	N	111	111	111
CDRS t score at 12 weeks	Pearson Correlation	.134	.017	.103
	Sig (2-tailed)	.158	.862	.276
	N	113	113	113

(N = 116)

The above tables demonstrate there were no statistically significant correlations between alliance and outcome measures in the whole sample at any time point. The same holds true at 28 weeks (follow-up outcome measure point – see Appendix C for table of results).

5.11.1 Correlations between Early Alliance and Outcome Measures by Site

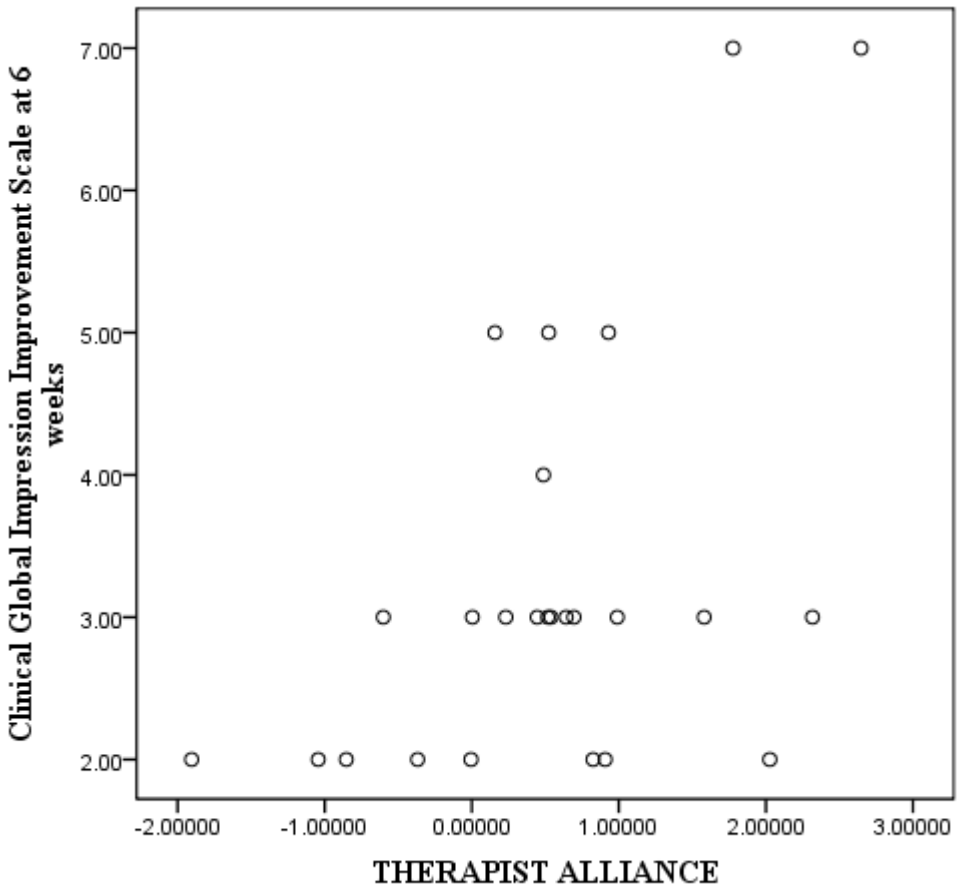
When separated by site, there are no significant correlations between early alliance and outcome at 6 and 12 weeks in Manchester or Cambridge (see Appendix C for tables).

5.11.2 Correlations between Early Alliance Factors and Outcome Measures by Treatment Group

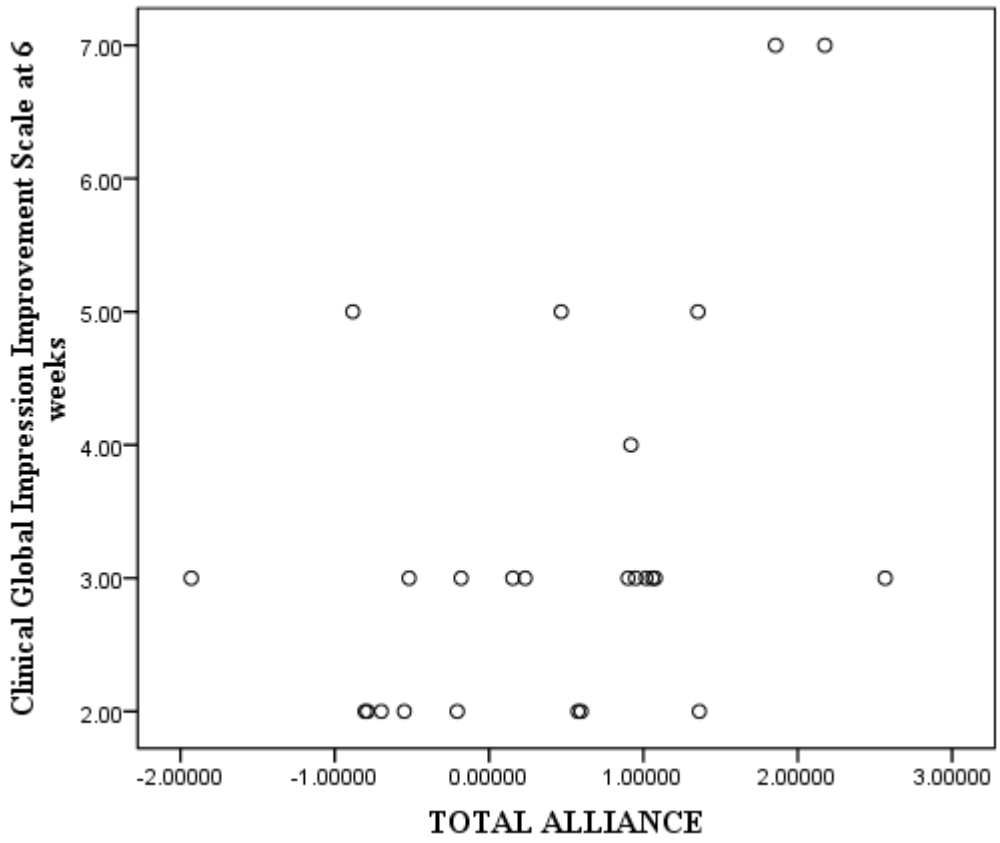
There are no significant correlations when separated by treatment group. When, however the sample is separated by site and arm of trial, Therapist (tau = .320, p value = .043) and Total alliance factors (tau = .328 p value = .038) are significantly correlated with CGI-I score at 6 weeks in the Cambridge medication only arm, but not the

combined medication and CBT arm (see Appendix C for tables of correlations by each treatment group). This implies that there is a relationship between early alliance score and clinical early improvement. This significant correlation should be seen in the context of two very influential observations (see graph below) i.e. 2 patients with high total alliance who also had improved clinically more than others.

Scatter Plot 2: Correlation between Therapist Alliance Factor and CGI-I score at 6 weeks for Cambridge Medication Arm



Scatter Plot 3: Scatter Plot to Show Correlation between Total Alliance Factor and CGI-I score at 6 weeks for Cambridge Medication Arm



5.12 Summary of Correlations between Alliance Factors and Outcome Measures

There are no significant correlations between alliance and outcome measures in the whole sample at any time point. When separated by site, there are no significant correlations between early alliance and outcome at 6 and 12 weeks in Manchester and Cambridge. When separated by treatment group, Therapist and Total alliance factors are significantly correlated with CGI-I score at 6 weeks in the Cambridge medication only arm. This implies that there is a relationship between early alliance score and clinical

early improvement in particular circumstances. This result should be seen in the context of a small number of patients with high total alliance who also had improved clinically more than others.

5.13 Predictive Effect of Early Alliance on Outcome

Linear regression was used to see if there was any predictive effect of early alliance on clinical and patient ratings of improvement (HoNOSCA, CGAS, CDRS t score, MFQ) at 6 and 12 weeks. The regressions were adjusted for baseline symptomatology as a covariate.

By total sample there is no effect on outcome scores at 6 or 12 weeks by total alliance, therapist alliance or patient alliance. Linear regressions for all outcome measures and time points are available in Appendix C. An example is included here:

Total alliance was not found to predict HoNOSCA score at 6 weeks (Beta = .025 p = .794). The overall model fit was R squared = 0.001.

5.13.1 Predictive effect of Early Alliance on Outcome at each Treatment Site

Linear regressions were repeated when the whole sample was separated by site at 6 and 12 weeks.

There is no predictive relationship between alliance and outcome measures in Manchester (see Appendix C).

At the Cambridge site alliance factors significantly predict MFQ scores at 6 weeks: MFQ by Total Alliance: Beta = .391 P value = .005 and R squared = .153 and by Therapist Alliance: Beta = .357 P value = .010 and R squared = .127. They also significantly predict at 12 weeks, the main outcome point in the original trial, as shown in the table below:

Table 20

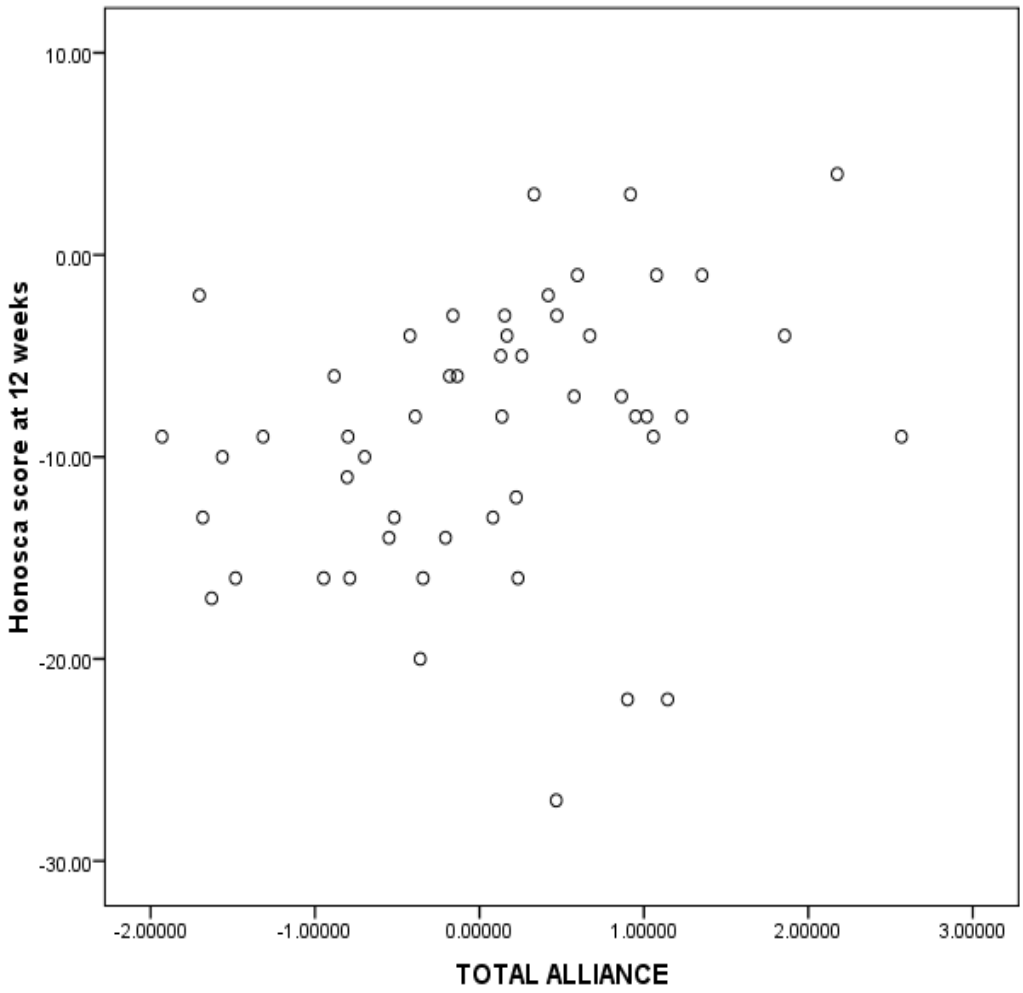
Linear Regression Analyses Where Alliance Factors Significantly Predict Outcome at 12 weeks at Cambridge Site

Alliance Factor	**Outcome Measure**	**Beta**	**P value**	**Corrected R squared**
Total Alliance	HoNOSCA	.284	.043*	.081
Total Alliance	MFQ	.348	.012*	.121
Therapist Alliance	MFQ	.305	.030*	.093
Therapist Alliance	CGAS	.286	.042*	.082
Total Alliance	CDRS	.378	.006*	.143
Therapist Alliance	CDRS	.400	.004*	.160

*(N = 52) *Significant at p value <0.05*

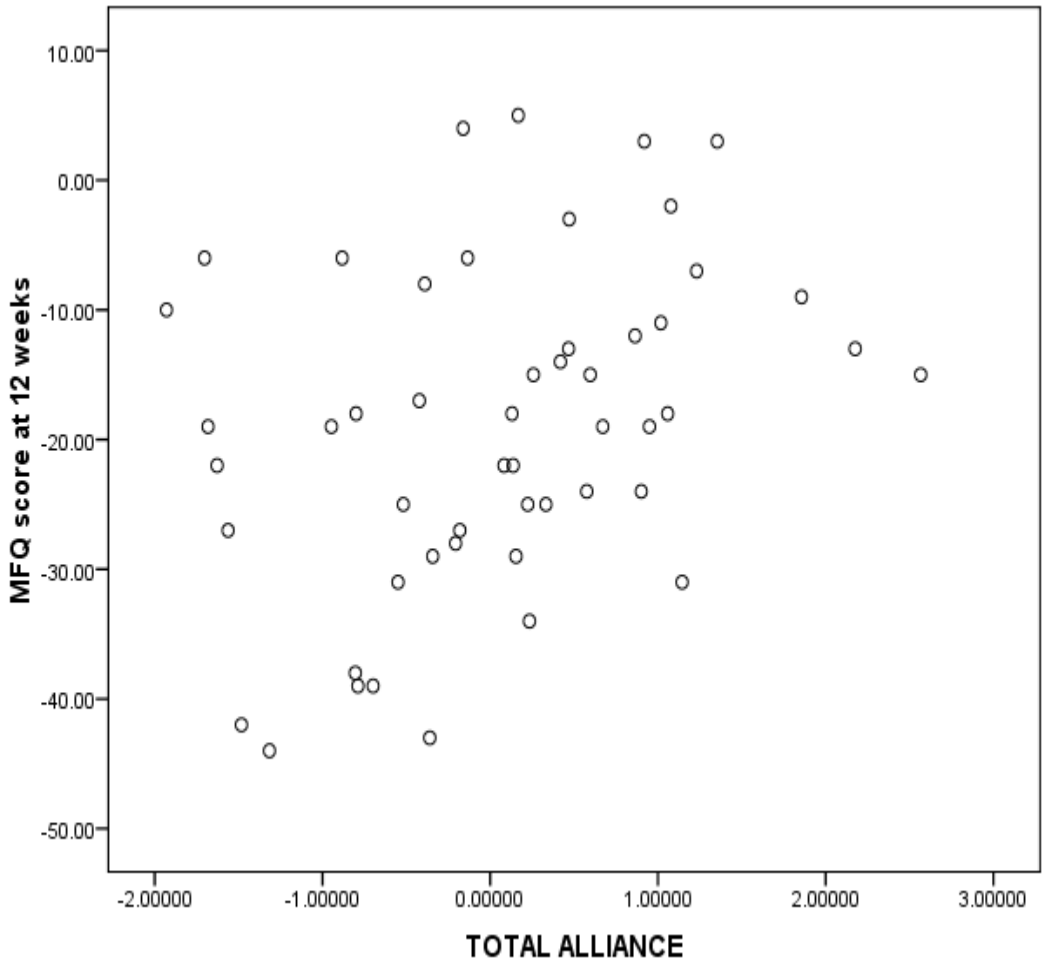
At the Cambridge site Total alliance significantly predicts HoNOSCA score at 12 weeks (Beta = .284 p value = .043 R squared = .081), the main outcome point, as shown by the following graph:

Scatter Plot 4: Prediction of HoNOSCA Score at 12 weeks by Total Alliance at Cambridge Site



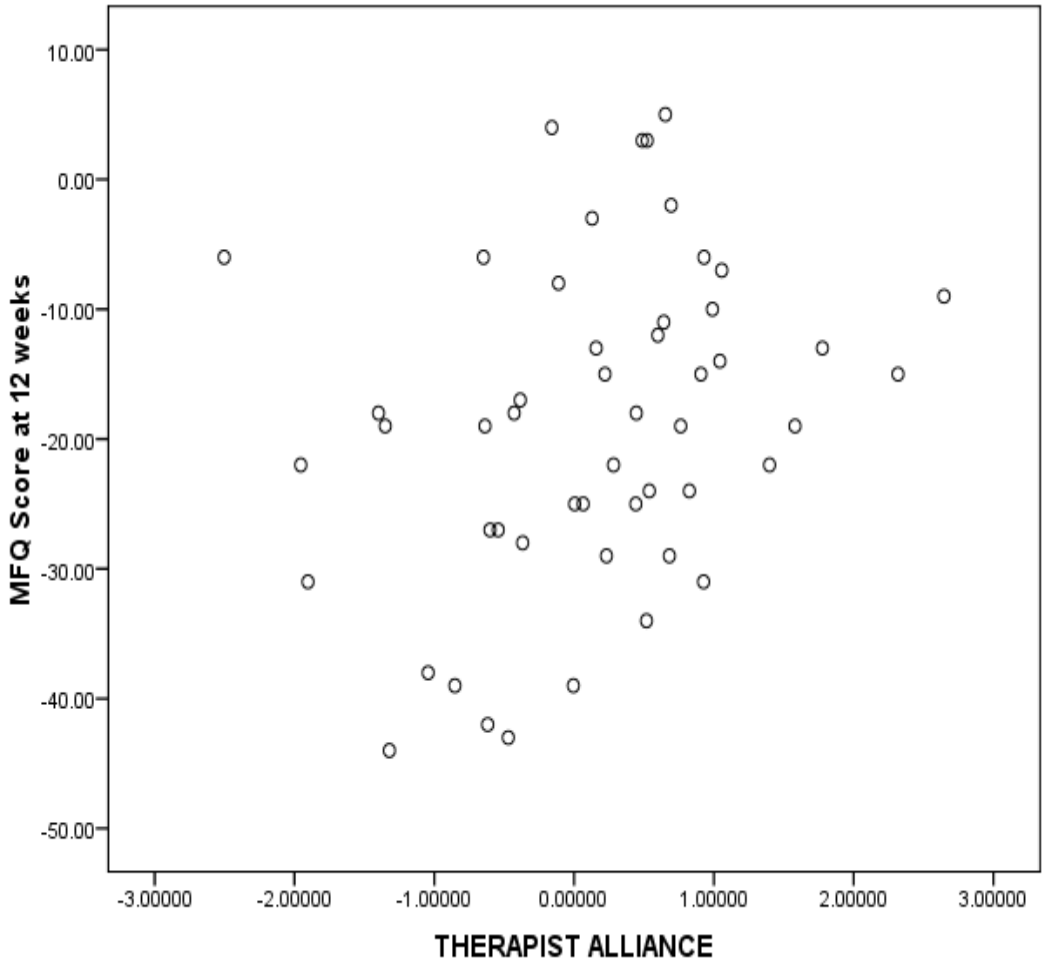
Total alliance at the Cambridge site significantly predicts measured MFQ score at 12 weeks (Beta = .348 p value = .012 R squared = .121) as shown by the following graph:

Scatter Plot 5: Prediction of MFQ Score at 12 weeks by Total Alliance at Cambridge Site

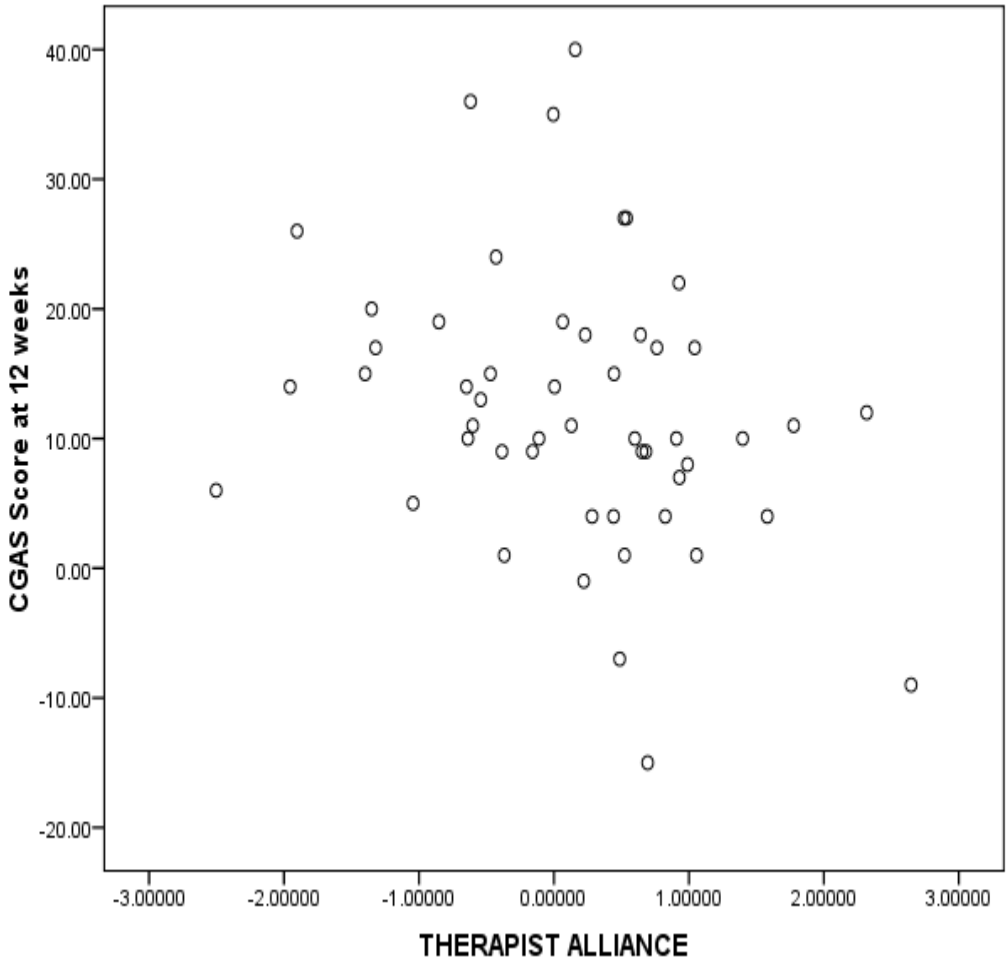


Therapist alliance also significantly predicts MFQ and CGAS scores at 12 weeks (Beta = .305 p value = .030 R squared = .093 and Beta = .286, p value = .042 R squared = .082, respectively) as shown by the following graphs:

Scatter Plot 6: Prediction of MFQ Score at 12 weeks by Therapist Alliance at Cambridge Site



Scatter Plot 7: Prediction of CGAS Score at 12 weeks by Therapist Alliance at Cambridge Site



This is not replicated however, for all outcome measures, for example there is no predictive effect of total alliance on CGAS outcome at 12 weeks (Beta = .242 p value = .087 R squared = .059).

5.13.2 Predictive effect of Early Alliance on Outcome for each Treatment Group

Linear regressions were repeated when the sample was separated by treatment allocation.

There is no effect at 6 or at 12 weeks in relation to treatment allocation, as illustrated by the linear regression below:

There is no predictive relationship between total alliance and HoNOSCA score at 6 weeks in the medication arm (Beta = .155, p value = .328, R squared = .024).

See Appendix C for complete linear regressions by treatment allocation.

5.13.3 Predictive Effect of Early Alliance on Outcome by Treatment Site and Treatment Allocation

Linear regressions were repeated when the sample was separated by treatment arm in both sites. The full set of linear regressions is available in the appendices.

There is a significantly predictive effect of early total alliance on MFQ score at week 6 (Beta = .391, p value =.005, R squared = .154) and week 12 (Beta = .463, p value = .020, R squared = .215) in Cambridge in the medication arm. Early therapist alliance also predicts significantly the outcome measured by MFQ score at 6 weeks (Beta = .357, p value =.01, R squared = .127) and 12 weeks (Beta = .543, p value = .005, R squared = .543) in the Cambridge medication arm. Therapist alliance also significantly predicts CDRS at 12 weeks (Beta = .402, p value = .004, R squared = .161).

5.14 Summary – Predictive Effect of Alliance

To summarise the results reported above, there is no predictive relationship between alliance and outcome measures in using the whole sample or when separated by site for Manchester. At the Cambridge site however, Total alliance significantly predicts HoNOSCA score at 12 weeks. Total alliance at the Cambridge site also significantly predicts measured outcome in MFQ and CDRS at 12 weeks. Therapist alliance significantly predicts MFQ, CDRS and CGAS outcomes at 12 weeks. This is not replicated by all outcome measures at 12 weeks. The Total and Therapist alliance makes a significant contribution to predicting outcome using several different (but not all) outcome measures at 12 weeks in Cambridge. 12 weeks was the main outcome point in the original trial. When the Cambridge cohort is split by treatment groups, the predictive effect of Total and Therapist alliance remains for predicting outcome as measured by MFQ score in the medication arm at weeks 6 and 12 and CDRS at week 12.

5.15 Multivariable Analysis

Analysis of covariance was carried out to look at the relationship between treatment group allocation, the alliance and outcome (where treatment group is the independent variable, outcome is the dependent variable and alliance is the co-variate). It aims to show the effect of treatment after partialling out the effect that alliance has on the outcome. The value of the treatment by alliance interaction was also analysed to make sure that the relationship between the outcome and alliance is the same in each treatment group.

5.15.1 Whole Sample Multivariable Analysis

In the whole sample there were no significant effects of alliance on outcome measures, or of treatment after controlling for the effect of alliance. There were no significant treatment by alliance interactions; therefore we can assume the relationship between alliance and outcomes at 6 and 12 weeks is the same in each treatment group. This is illustrated by the example below (see Appendix C for full list of ANCOVAS): The covariate, total alliance was not significantly related to CGAS at week 6, F (1, 108) = .088, p value = .770, r = .010. There was no significant effect of treatment on CGAS after controlling for the effect of total alliance. F (1, 108) = .479, p value = .490 R squared = .014. Treatment by alliance interaction was not significant, (p value = .500) therefore we can assume the relationship between alliance and CGAS at 6 weeks is the same in each treatment group.

5.14.2 Multivariable Analysis by Site

When separated by site, no results were significant apart from the relationship between therapist alliance, treatment and MFQ outcome at 6 weeks in Cambridge as shown by the ANCOVA below (see Appendix C for full list of ANCOVAs). The covariate, therapist alliance was significantly related to MFQ at week 6, F (1, 48) = 6.627 p value = .013 r = .049. There was no significant effect of treatment on MFQ after controlling for the effect of therapist alliance. F (1, 48) = 2.995 p value = .089. The treatment by alliance interaction, (p value = .105) was not significant, therefore we can assume the relationship between alliance and MFQ at 6 weeks is the same in each treatment group. There were no significant relationships between Total Alliance or Patient Alliance and MFQ at week 6, or MFQ and Therapist alliance at week 12.

In summary the ANCOVAS showed no relationship between alliance factors and outcome, except for the Cambridge sample where therapist alliance was significantly related to MFQ and treatment at week 6, but not for other alliance factors at 6 weeks or MFQ at other time points.

5.16 Conventional Analysis - Results Summary

In summary there is no overall correlation between baseline measures of impairment and early alliance factors for the whole sample. There is also no correlation between early total alliance and number of sessions attended at 12 weeks or 28 weeks. In the whole sample there is no association between early alliance and clinical improvement at measured outcome points (6, 12, 28 weeks) and no evidence of a predictive effect of total, therapist or patient alliance on outcome measures at 12 weeks. This linear regression is confirmed by ANCOVA. These results hold true for Manchester data when separated by site but in Cambridge there is a trend towards a negative correlation between MFQ at baseline and total early alliance score ($r = -0.258$ p value = 0.065). There are no other correlations between early alliance score and other baseline characteristics. The therapist and total alliance correlate significantly with CGI at week 6 ($r = .300$ $p = .032$ and $r = .295$ $p = .036$) in Cambridge in the medication arm of the trial but not at week 12 or 28. There are no other significant correlations

Overall there is little evidence of an effect of alliance across the sample, either in relation to baseline variables, number of sessions attended or outcome.

There is, however, an interesting site effect. In Cambridge there is a significant correlation between alliance and clinical rating of improvement at 6 weeks and there is a predictive effect of alliance on measured main outcome HoNOSCA, and MFQ and CGAS and CDRS at 12 weeks. There is no relationship between alliance and number of sessions attended at 12 weeks. In Manchester there is no alliance effect at baseline or in prediction. This implies that there is a relationship between early alliance score and clinical early improvement, but the relationship is not straightforward. The predictive effect of alliance may depend on differences in patient groups, therapist effects and the environment in which the treatment is carried out. There are no overall different treatment effects across the sites – thus in Cambridge although there is no effect on outcome by treatment allocation, there is an overall alliance effect on outcome.

Comparing the two sites, the key difference within the patient groups is that in Manchester there are significantly more patients diagnosed with comorbid behavioural problems. The data suggest that the Manchester group was also overall more disadvantaged socioeconomically, although variable amounts of socioeconomic data from the original trial are missing. There is no difference in absolute quality of alliance across sites. There is a different therapist structure between sites with one therapist in Cambridge carrying out 98% of the treatment. Higher total alliance scores were obtained in the combined group for those who had only one therapist. This perhaps indicates a therapist effect in relation to the operation of alliance.

5.17 Analysing Treatment Effect Heterogeneity

The complex nature of the effect of alliance on outcome is illustrated using the traditional statistics above. To investigate further how alliance may affect or explain

treatment effect heterogeneity, a statistical analysis was employed to investigate the following research questions:

I. Does the quality of treatment alliance influence treatment effect?
II. Does variance in baseline characteristics of the sample or other unmeasured variables which are common to both alliance and outcome account for variation in therapeutic alliance and/or its relationship to the effect of treatment?

The format of the statistical analysis is described in Analysis Plan above (page 47 onwards). Stata 10.1 was used to complete this analysis. In summary, structural mean modelling allows us to estimate the treatment effect as if everyone in the trial received all interventions. For each individual there are two potential outcomes – Yt and Yc, where Yt is their outcome if they receive one intervention (combined treatment) and Yc is the outcome if in the other arm of the trial (medication). The effect of intervention on every individual is the difference between the predicted outcome in the additional treatment group and that in the medication group i.e. the individual treatment effect (ITE) is the Yt–Yc. We can never observe both Yt and Yc in a given individual, but we can use baseline predictors of outcome under the two treatment conditions to get an estimate (imputed value) for that individual's individual treatment effect. The remaining question is then "is the individual treatment effect related to alliance under treatment"?

5.16.1 Analysis using HoNOSCA outcome at 12 weeks

HoNOSCA at 12 weeks was the primary endpoint of the original trial. The table over the page shows the result of the SMM analysis of the effect of alliance on this outcome measure at 12 weeks.

Table 21

SMM Analysis of the Effect of Alliance on HoNOSCA at 12 weeks

Variable	Reps	Observed	Bias	Standard Error	95% confidence interval (percentile method)
Alliance	1000	2.053	-.179	4.96	(-6.713, 11.970)
Average Treatment Effect (constant)	1000	-5.894	.629	13.550	(-31.636, 19.467)

Estimated effect (regression coefficient) 2.053 (SE 4.962). 95% confidence interval = (-6.713, 11.970).

The results of this analysis (tables above) suggest that treatment alliance is associated with the individual treatment effect (as alliance increases, so does the ITE). The negative estimate for the constant also implies that treatment might actually be detrimental when alliance is zero (with poor alliance, more treatment may be

detrimental). This latter result has also been found using a similar analysis within a CBT trial in schizophrenia (SOCRATES, Tarrier et al., 2004). This indicates that variations in alliance therefore do help to explain treatment effect heterogeneity in this trial.

This conclusion has to be qualified however by the large standard errors of the estimates obtained; indicating that this kind of analysis needs considerably larger sample sizes for definitive conclusions.

Table 22

SMM Analysis (HoNOSCA at 12 weeks) with No Constant

Variable	Reps	Observed	Bias	Standard Error	95% Confidence Interval (percentile method)
Alliance	1000	-.0896	-.0190	.520	(-1.098, 0.924)

When the treatment effect is constrained to zero (constant) (Table 22) then any suggestion that there is an effect of alliance vanishes. This result also has a large standard error.

Results for other outcome measures and an example of the input file for the HoNOSCA result are included in Appendix C.

CHAPTER SIX –DISCUSSION

This thesis addresses the key methodological limitations of previous studies into the impact of therapeutic alliance on the outcome of treatment in children and adolescents. The alliance literature in childhood is relatively sparse. Until recently the focus of the treatment literature was on treatment modalities and protocols rather than investigating treatment processes. Studies of alliance have often been weakened by methodological difficulties in measurement and have failed to settle the direction of causality between symptom change and alliance (Kazdin and Nock, 2003). In treatment trials, alliance is often only measured in the experimental arm; this makes analysis of its effect difficult (Dunn and Bentall, 2007, Green and Dunn, 2008).This project makes use of data collected during a large rigorous recent study in child mental health (Goodyer et al., 2007). This has enabled detailed study of the therapeutic relationship during treatment and testing the effects of this relationship on the success of treatment.

In this discussion chapter, the results are discussed in the context of the original hypotheses (page 33) and research questions and are then located in the context of the relevant literature. Strengths and limitations of the current study and the implications for future research and clinical practice are then discussed.

6.1 Discussion of Results by Hypothesis and Research Question

6.1.1 Hypothesis One

1. Alliance measured early in this trial has no relationship to baseline variables of the sample, treatment arm or characteristics of treatment (e.g. site of treatment).

Question 1

a) Does therapeutic alliance measured early in this trial vary with baseline characteristics of the sample and allocated treatment given across the trial?
b) Does therapeutic alliance vary with characteristics of treatment (e.g. treatment site, therapist variables)?
c) Is alliance in this trial stable over time?

6. 1. 1.1 Structure of alliance in adolescence

Factor analysis of the results obtained using the VTAS, as the measure of alliance in this trial, suggested that two factors were responsible for the alliance construct, a "patient" factor and a "therapist" factor. Such a two factor solution is in line with previous literature in adults (Krupnick et al, 1996). Consistent with Bordin's (1979) pan theoretical model, three facets of alliance; emotional bond, task collaboration (work), and agreements (goal consensus) are prominent in the youth literature. However, at least two studies have failed to fully support this kind of model with adolescents and produced a single factor solution, suggesting that features of the alliance may be less differentiated at younger ages (Di Giuseppe et al., 1996; Faw, Hogue, Johnson, Diamond, and Liddle, 2005). They posit that younger patients may be unable to discriminate between different aspects of the relationship. Others have shown that bond and task collaboration do represent distinct but correlated alliance dimensions (Estrada & Russell, 1999; Shirk and Saiz, 1992). The results reported in this thesis indicate that adolescents actually behave more like adults in the context of a well constructed rigorous treatment trial and that authors suggesting a one factor solution may therefore have underestimated the complexity of the alliance construct in this population.

6.1. 1.2 Relation of early alliance to patient and therapist characteristics and pre-treatment functioning

The mean and age and gender mix of the sample reflects the original trial, as does the severity of symptoms and impairment. A wide range of alliance scores were obtained over the whole sample. Scores were slightly skewed to the right, with fewer low scores. Lower scores were obtained in the medication group compared to the combined group. Slightly higher scores were obtained in the Cambridge cohort. However, these differences were not seen to be statistically significant. Some differences between sites in the selected sample have, however, been identified, in terms of both patient and therapist variables. There is a significant difference between Manchester and Cambridge in the number of patients with co-morbid behaviour disorder, with the greater number in Manchester. There were a larger number of therapists in Manchester in the original trial, from different professional disciplines. In Cambridge one therapist treated 98% of the sample. An analysis of variance did not show any significant differences in the alliance scores obtained for sessions with different therapists overall but in the combined group there was a trend for lower alliance scores in those who had more than one therapist.

There is no consistent relationship between early alliance and baseline measures of impairment and symptoms score or between early alliance and sessional attendance. Absolute therapeutic alliance in this trial does not appear to vary with baseline measures of impairment and symptom score. Absolute alliance does vary very slightly with one characteristic of treatment (treatment site), but this was not found to be statistically significant. This would indicate that the experimental hypothesis is supported.

The literature in the area of baseline impairment and its relationship to alliance is mixed. Weerasekera et al (2001) found that alliance predicted outcome independent of early mood change in depression and baseline symptomatology did not affect change in alliance in early therapy. Feeley et al. (1999) found that alliance is no longer associated with treatment outcome when previous symptom reduction is controlled for. Kazdin and Whitley (2006) reported a study in which baseline social functioning of parents explained part of the parent – therapist alliance measurement in parent management training. Other patient pre-treatment variables have been shown to predict the alliance, for example patient interpersonal styles (Kivilighan, Patton and Foote, 1998). The Study of Cognitive Realignment Therapy in Early Schizophrenia (SoCRATES trial - Tarrier et al., 2004) suggested that the strength of alliance is associated with lower baseline symptom scores. Those with lower scores were those who were better able to form a good therapeutic alliance. However, there was also a suggestion that attendance at a higher number of treatment sessions was associated with a poorer outcome, so interpretations are difficult.

In child therapy there have been very few rigorous studies on the alliance – outcome relationship which also control for pre treatment variables or early symptom change (Kazdin and Whitley, 2006, Shirk, Karver and Brown, 2011). Studies tend to focus on the age of the child, type of presenting problem or parent characteristics as the only moderators of interest. This thesis, which indicates that alliance is not related to pre treatment characteristics or symptom score in individual adolescents, therefore adds to the literature regarding adolescents in this sparse area.

6.1.1.3 Stability of alliance

The question was posited - is alliance in this trial stable over time?

There is a strong correlation between therapeutic alliance as measured early in the trial and later on in treatment, indicating that alliance established early in the relationship between patient and therapist is strongly related to the alliance as measured much later in the process of treatment. Alliance is stable throughout the process of treatment i.e. a positive alliance established early on continues to be positive towards the end of treatment. This illustrates further the significance of alliance established very early in treatment and is consistent with previously reported trials. One study in particular showed that poor early alliance predicted client drop out (Constantino et al., 2002). The NIMH collaborative treatment of depression study (Krupnick et al., 1996) found that early and mean alliance correlated and that the quality of the alliance did not differ between treatments (including pharmacotherapy), as also established in my study. The overall evidence in the literature suggests that the quality of alliance assessed by independent raters is established quite early in treatment and tends not to change radically subsequently and my study would support this view. This indicates that early relationship formation with patients is crucial.

6.1.2. Hypothesis Two

Alliance has a predictive effect on outcome in this trial

Question 2

a) Does early therapeutic alliance predict outcome in this trial?

6.1.2.1 Impact of alliance on treatment outcome

There are no significant correlations between alliance and outcome measures in the whole sample at any time point.

When separated by site, there are no significant correlations between early alliance and outcome at 6 and 12 weeks in Manchester. However, in Cambridge the Therapist and Total factor early alliance scores correlate significantly with Clinical Global Impression Improvement (CGI-I) score at week 6 but not at week 12. When separated by treatment group, Therapist and Total factor alliance scores are significantly correlated with CGI-I score at 6 weeks in the Cambridge medication only arm. This implies that there is a relationship between early alliance score and clinical early improvement in particular circumstances. This result should be seen in the context of a small number of patients with high total alliance who also had improved clinically more than others and suggests that the trial should be replicated with larger numbers to confirm this finding.

There is no predictive relationship between alliance and change in outcome measures in using the whole sample or when separated by treatment site for Manchester using linear regression. At the Cambridge site however, Total alliance factor score significantly predicts change in HoNOSCA and MFQ score at 12 weeks. Therapist alliance significantly predicts MFQ and CGAS outcomes at 12 weeks. However there is no consistent predictive effect of all alliance factors on outcome at 12 weeks.

In summary the total and therapist alliance in Cambridge makes a significant contribution to predicting outcome using several different (but not all) outcome measures at 12 weeks. 12 weeks was the main outcome point in the original trial. This indicates that there is some support for the experimental hypothesis, i.e. there is a

predictive relationship between alliance and outcome, but this relationship is not straightforward. My findings using the ADAPT trial in children and adolescents therefore do not overall replicate the equivalent trial in of depression in adults (Krupnick et al., 1996), which showed that alliance predicted outcome. My findings do indicate that, in this trial, at least, more complicated interaction effects were operating and there is an effect of alliance on outcome in certain circumstances.

The results indicate an interesting site effect. The predictive effect of alliance may depend on differences in patient groups, therapist effects and the environment in which the treatment is carried out. There are no overall different treatment effects across the sites – thus in Cambridge although there is no effect on outcome by treatment allocation, there is an overall alliance effect on outcome.

Can we learn anything about alliance processes from these site differences? The absolute quality of alliance does not differ between the sites but the operation of alliance in terms of its predictive effect on outcome does vary. At the same time these site differences are associated with important variations in both patient and therapist groups. They therefore give an opportunity to explore how such differences in patient and therapist groups may impact on the predictive effect of alliance.

Patient effects - Comparing the two sites, the key difference within the patient groups is that in Manchester there are significantly more patients diagnosed with comorbid behavioural problems (or externalising disorders). The data suggest that the Manchester group was also overall more disadvantaged socioeconomically, although variable amounts of socioeconomic data from the original trial are missing. There is no

difference in absolute quality of alliance across sites. This perhaps suggests the nature of depression is itself different in patient groups with different characteristics and this may having a bearing on whether any alliance developed is related to eventual outcome. One may hypothesise that conduct disordered young people may be able to form an alliance within session with a sympathetic therapist, but this may not act to improve their depression as their symptom profile (for example, irritability) may be very different to a young person with depression but without conduct disorder. Clinical observations have underscored the importance of the alliance in adolescent treatment (Castro-Blanco & Karver, 2010), but a recent Meta analysis suggests that the alliance is more of a robust predictor of outcomes with pre adolescent children (Shirk, Karver & Brown 2011). Furthermore, the authors suggest this may depend on the type of problem being treated as studies of externalizing disorders e.g. substance abuse, are all conducted with adolescents and these studies produce small effects. Eltz, Shirk, and Sarlin (1995) found that adolescents with relationship problems and more negative interpersonal styles had more difficulty with alliance formation than a comparable sample of young people without such problems. In contrast to this, Kendall (1994) found minimal associations between alliance and outcome in a sample of young people with anxiety disorders. This may have been because of limited variability in alliance scores that were highly positive. Martin et al., (2000) did not find alliance–outcome relations to vary as a function of problem type in their Meta analysis of studies in adults. It is possible, however, that type of problem moderates the association between therapeutic alliance and outcome in young people, or that there may be a variation in effect between internalizing and externalizing disorders. This indicates that adolescents with depression and co-morbid conduct problems are likely to form different quality alliances versus adolescents without such co-morbidity.

Therapist effects - There is a striking difference in therapist structure between sites in my study, with one therapist in Cambridge carrying out 98% of the treatment. Thus comparing site effects may allow inferences about therapist effect in relation to the operation of alliance. Comparing patients who experienced a single therapist to those who had two, the mean total alliance score was higher in the single therapist group although this difference was not significant. Possibly the consistency in approach of a single therapist effects the way alliance acts on symptoms. Some research suggests that certain therapist characteristics and behaviours may contribute to the quality of alliance (Castonguay et al., 2006). Some of these variables have also demonstrated a direct relationship to therapy outcome (Crits-Christoph et al., 2006). Howard et al. (2006), suggests that the alliance influences the relationship between patient and therapist characteristics and outcome in depression. A recent meta-analysis in adults however, looking at the contribution of therapist competence and adherence to treatment to outcome (Webb, De Rubeis & Barber, 2010) showed that neither variability in fidelity to the treatment protocol nor general therapist competence in relation to treatment delivery was found to be related to patient outcome. They account for the failure to find significant, positive relations between outcome and these therapist variables through a notion of therapist "responsiveness"; by which they mean that therapists generally do not deliver predetermined levels of particular interventions but rather adapt their behaviour to the emerging context, in particular, patient behaviours (Stiles, Honos-Webb, & Surko, 1998). For example, a therapist might adhere more to the methods of a particular intervention with patients who are not improving. The presence of enough of these cases in a study would be reflected in small or even negative correlations between process method and outcome. Adherence to CBT by therapists in the combined

treatment arm of ADAPT was found to be high (Goodyer et al., 2007) but it would therefore be interesting to further analyse my data (transcripts) to understand if any further particular techniques were being used by therapists who were adapting their behaviour to poorly responding patients. One might argue that therapist responsiveness is itself part of what is measured through the alliance concept, but this particular aspect of therapist flexibility may not be captured adequately. Barber et al., (2006) suggest that for patients with low alliance, strict adherence to the model of treatment is necessary for treatment gains whereas for those with high alliance this is not necessary for a good outcome. This applies in this instance to patients with externalizing disorders (drug misuse).

There does not appear to be any intrinsic difference in the structure of alliance scores between the sites and there is no variation in alliance scores by therapist in Manchester. It is therefore difficult to show therapist effects are working directly on alliance. However, alliance did predict outcome more strongly in Cambridge, where one therapist provided the vast majority of the sessions. In Manchester patients were more likely to have medication management and CBT provided by two different clinicians. One may posit that the consistency of a single therapist's approach helped prediction in the sample and that therefore it may be better clinically to have one therapist rather than two providing treatment for one patient. From a patient point of view, one therapist may provide a more consistent experience of therapy and thus there is a more predictable relationship with outcome. A single therapist can be thought in attachment terms to provide a 'secure base' (Bowlby, 1988) for the patient to explore and begin to control their symptoms; this may not be so straightforward with two therapists, especially over short term intervention periods.

As set out in the introduction to this thesis, it may be that in complex intervention studies there are a number of potential confounds that mask alliance effects in many treatment trials. These could include both patient and therapist effects as well as the environments in which therapy takes place. As previously explained, the traditional analysis of RCTs does not adequately account for this, which is why a more novel statistical analysis was carried out here.

6.2 Causal mediation and heterogeneity (Structural Mean Modelling analysis)

a. Does the quality of treatment alliance influence treatment effect?
b. Does variance in baseline characteristics of the sample or other unmeasured variables which are common to both alliance and outcome account for variation in therapeutic alliance and/or its relationship to the effect of treatment?

As argued in the introduction to this thesis (p.12), alliance may represent a post randomization effect, interacting with treatment. Dunn and Bentall (2007) have suggested that in considering that alliance may explain treatment effect heterogeneity, there is also the possibility of an unmeasured variable or variables between mediator and outcome, which randomisation cannot remove. Green and Dunn (2008) argue that the probable existence of this unaccounted for variable is a major challenge to valid inference from trials (that alliance affects outcome), because in most trials any such variable is assumed to be absent. Estimates of the prediction of outcome from process variables may be biased when temporal confounds are not addressed in research designs and data analyses. As noted by Feeley et al. (1999), temporal confounds have often been

ignored in studies of alliance–outcome relations. When temporal confounds have been controlled, alliance–outcome findings have been less consistent across studies (Barber, 2009; Strunk et al., 2012).

The results of the Structural Mean Modelling (SMM) analysis in this trial do suggest that when hypothesised confounds are controlled for – then indeed an effect of alliance at individual treatment level is positive (as alliance increases, so does the Individual Treatment Effect, ITE), although this effect is not statistically significant. This indicates that quality of treatment alliance does indeed therefore influence therapeutic effect.

A related analysis has recently been employed successfully in the evaluation of heterogeneity in the effects of treatment by the advisor to this project (Dunn et al., 2012) and in other complex treatment trials in medicine (Follman, 2006). Traditional approaches to the analysis of clinical trials use data from treated groups and then correlate outcome and alliance (as above). However, this approach cannot distinguish treatment–free (or different treatment) prognosis from prediction of treatment effects. My study therefore addresses these methodological difficulties by using a newer statistical approach to establish whether alliance influences treatment effect heterogeneity. The results, whilst not approaching statistical significance, do indeed suggest that alliance does influence treatment effect (outcome) at an individual level. It supports the idea that hidden confounds have led to errors in the analysis and interpretation of previous RCTs, and a bias when analysing the effects of alliance. When analysed using statistical methods which take account of hidden confounds, alliance effects are exposed. This suggests that this way of looking at complex datasets

may show up complex alliance effects and supports the use of these statistics in revealing complicated relationships between variables.

The data presented here suggests that alliance does act to explain treatment effect heterogeneity and confirms theoretical discussions that alliance may act in treatment trials in a complex relationship with other process variables. Alliance is not a straightforward predictor of outcome, but interacts with other process variables to influence outcome. This conclusion has to be qualified however by the large standard errors of the estimates obtained; indicating that this kind of analysis needs considerably larger sample sizes for definitive conclusions.

6.3 Conclusions

This study aimed to analyse the effect of alliance on outcome in adolescents with depression, using methodology superior to that previously reported in the literature. Using conventional analysis, it is found that there is no relationship between early alliance and baseline measures of impairment and symptomatology i.e. the formation of alliance is not influenced by illness severity. It is also found that there is no relationship between alliance and adherence to treatment (as measured by sessional attendance). Previous studies in this field have shown mixed results. Alliance is stable throughout the trial as found in many other previous studies. In overall terms alliance does not predict outcome in this group if we analyse the data using conventional statistical analysis. However, it can be seen that alliance does have a positive relationship with outcome in certain treatment settings and with particular characteristics of patients and therapists as discussed above. In terms of the predictive effect of alliance, three main

points can be concluded: at a patient level, that diagnosis and particularly the presence of externalising disorders may have an impact on alliance as a predictor of outcome; that therapist consistency impacts on alliance as a predictor; and that when confounds (these and others) are controlled for statistically, alliance is suggested to predict individual outcomes.

These findings have particular resonance and implications for both further research and clinical practice, as will be discussed below. The more novel statistical analysis suggests that treatment alliance is positively associated with the individual treatment effect and that treatment can actually be detrimental in the presence of poor alliance. My study therefore indicates that alliance interacts with other treatment variables in far more complex ways than previous literature, particularly that relating to children and adolescents, would suggest. The result implies that treatment might actually be detrimental when the alliance is zero (with poor alliance, more treatment may be detrimental). This latter result has also been found using a similar analysis within a CBT trial in schizophrenia (SoCRATES - Tarrier et al., 2004) in that a higher number of sessions were correlated with a poorer outcome in the presence of poorer alliance. This corroboratory finding from my trial therefore has an important implication for proponents of talking treatments. It is essential that poor therapeutic alliance is picked up and addressed (possibly with interventions designed to promote alliance) otherwise therapists may actually be causing harm to young people by continuing to provide treatment.

This study therefore corroborates certain elements of the literature e.g. stability of alliance through treatment, but is in contrast to other previously published studies,

particularly that in adults which suggests that alliance has a direct predictive effect on outcome. This could be in part explained by the more rigorous methodology that I have employed both in carrying out the trial and the statistical analysis. This has elucidated a more subtle and complicated relationship between process variables and outcome than previous studies have shown. There are also particularities of the ADAPT trial itself, such as its pragmatic nature and the nature of the participants which may have lead to differences with previously published literature. Such features and their effect on the results of this study are discussed further in the strengths and limitations section below.

6.4 Strengths of the Study

There are particular strengths of the current study. This is to my knowledge the largest data set available in childhood depressed populations that has been analysed in terms of therapeutic alliance. The original RCT used rigorous methodology and the baseline and outcome data collected were robust. The quality and range of baseline measures available was high. The tape sampling strategy used in this study was particularly rigorous. We did not use a random sample as we would expect those who are less likely to have a tape to differ systematically from those who are highly likely. We therefore used a propensity score to select tapes of sessions to transcribe which removes the confounding effect of the likelihood of having a tape.

An observer measure of alliance was used (VTAS) in order to minimise the effects of common method errors due to non independent information sources (e.g. therapists reporting both alliance and symptom change) and as previous literature suggested that observer measures may be more reliable than self report. The VTAS has been used in a

number of previous studies and has been shown to be reliable and valid. It was slightly modified to reflect an adolescent population (Krupnick et al., 1996). Three raters analysed a selection of tapes and the interrater reliability was high.

Much in the published literature indicates that alliance predicts outcome, as we have seen. However the apparent direction of causality may be an artefact due to subtle symptom change early in treatment influencing alliance formation. I used an alliance measure particularly early in treatment (week 3).

Within randomized trials, alliance is commonly only studied in the experimental treatment group. However, factors measured at the time of randomisation such as severity of symptoms were thought from previous literature to be predictors of both alliance and outcome. Solely looking at associations between alliance and outcome in the treated group would reflect a mix of selection and treatment effects. Treatment effect heterogeneity is not often accounted for in traditional investigations into the effect of alliance on outcome i.e. the effect of alliance on efficacy of treatment in the presence of hidden confounders (hidden common causes of alliance and clinical outcome). The more novel statistical methods employed in the current study which look at individual treatment effects, alongside conventional statistics, are therefore a particular strength of the methodology, and as we have seen, yield some interesting results. To my knowledge, this is the first complex treatment trial in childhood in which alliance has been analysed in this particular way. These factors may help explain why the relationship between alliance and outcome is found to be different to that reported in previous trials, particularly in an equivalent depression trial in adults (Krupnick et al., 1996).

My results take the field forward in the following ways: Alliance has been shown to be a subtle influencer of individual treatment effects, interacting in various ways with other measured and non measured factors. This study adds to our knowledge of how alliance may operate in childhood treatment trials and suggests that alliance should not continue to be looked at as a straightforward predictor or mediator of treatment. To approach the concept of alliance with such rigour may puncture convenient illusions that alliance acts in a straightforward manner, but helps both researchers and clinicians move forward with the complex reality. Both therapist and patient factors may influence how alliance operates within treatment, as does the environment in which the therapy takes place. My study is also among the first to suggest, in a childhood population, that continued treatment in the presence of poor alliance may actually be detrimental. Further trials aiming to investigate alliance should take account of new developments both in the methodology of complex treatment trials (as shown by ADAPT) and in the statistical analysis of such trials, as we have seen in my study.

6.5 Limitations of the Current Study

There are some limitations of the current study which may help explain differences between my trial and previous published data, but identification of which may also help to move the research field forwards.

ADAPT was essentially a “null” trial, showing no difference in outcome for depression following different treatments. A simple mediation or prediction effect of alliance would therefore be difficult to identify in these circumstances (where the treatment effect was nil) – but not impossible (MacKinnon et al., 2007). The patients in ADAPT

received an initial brief intervention and were not included in the trial if they responded to this. The researchers may therefore have selected out good alliance / treatment responders at an early stage, thus reducing the effect of alliance as a non-specific predictor of outcome.

Alliance in the ADAPT trial was not related to baseline characteristics of the patients or their symptom score. Again, this may indicate there was something slightly different about the patients who met criteria to be entered into the full trial in ADAPT – patients with a "straightforward" response to treatment, where perhaps alliance would have been related to severity of symptoms, for example, were selected out. However, my data does replicate previous literature outlining the independence of alliance from pre-treatment characteristics (Klein et al., 2003), although the evidence from the literature is mixed as discussed above.

The VTAS was scored in this trial using audiotapes, rather than videotapes. The original VTAS was devised using videotapes, but these were not available to me for ADAPT. It might on the face of it be argued that it is more difficult to pick up subtle variations in alliance through audiotape, where non-verbal cues cannot obviously be observed but may be implied, for example.

Depression is a heterogeneous concept, particularly in childhood. Symptoms in children may be more diffuse and subtle than in adult populations and the distinction between clinical symptoms and personality development is not always well defined in childhood samples (Griffiths, 2011). Although diagnoses in ADAPT were made in the most robust manner (by the Kiddie Schedule for affective disorders and schizophrenia present and

lifetime version - KSADS-PL - Kaufman et al., 1987), diagnostic groupings are not always homogeneous. It follows, therefore, that clinical samples may well include children and adolescents who suffer from quite different syndromes. This may obviously have an effect both on treatment response and the ability of the patient and therapist to form a positive alliance. Co-morbidity appears to have an effect on the predictive nature of alliance in this study. Children and young people with behavioural problems alongside depression are probably a very different group to children without this extra difficulty. Behaviour that is not thought to be socially acceptable in a child or young person has obvious implications for conventional treatment response and alliance formation. What is interesting in this study is that there was not an overall poorer alliance in the sample which contained more children with behaviour problems, but that alliance in this context did not predict outcome. This suggests that more complex interactions are taking place when one is not treating "pure" clinical syndromes. It is possible that personal alliances were developed very well in sessions with children with behavioural problems, but for example, there was less focus on the tasks or goals of the therapy and therefore outcomes were different. ADAPT was designed to be a pragmatic treatment trial and thus my study probably represents something closer to what happens in "real life" mental health treatment sessions than in some RCTs. My study may therefore have greater validity in this context.

6.6 Implications for Future Alliance Research

This thesis forms an original contribution to the literature around alliance in adolescence. It asks some central questions and highlights some deficiencies in the extant literature. In particular, it highlights the difficulties of the alliance concept in

childhood, which is not well defined or agreed upon by all commentators. It also implies that alliance interacts in a more complex manner with other variables, both patient and therapist, to predict outcome than previously thought. It suggests that continued treatment may be actually detrimental in some circumstances. The rigour and creativity with which the methodology of this trial was approached would indicate that these findings could be considered more robust than those of some earlier trials in adolescence in this field.

This study generates some important new leads in the alliance research in terms of new questions and new methods to consider. Given that the results indicate that poor alliance can make treatment harmful, it is particularly important that poor alliance can be identified quickly. Alliance measures should be used as routine early in treatment trials and their use designed prospectively to avoid difficulties with for example, poor quality recordings. The form of the recording can also be thought about in advance in terms of measuring alliance (i.e. using videotapes). Alliance modifying treatments should be investigated further in this context and could form the basis of an RCT into their effect on outcome. Motivational Interviewing techniques could be a candidate treatment.

My results indicate that further work should be undertaken into both patient characteristics and therapist variables. ICD-11 and DSM-V are shortly due to be published and hopefully will remove some of the heterogeneity in current diagnostic categories. RCTs should be taken forward on this basis with good identification of co-morbidity; particularly externalising disorders in adolescence, and the ability to examine their effect on both the presentation of clinical syndromes, such as depression, and on outcome. Previous trials in adolescence have been hampered by small numbers and it is

important that large well designed trials are carried out in future. Large scale trials could enable the methodology I have used here to be repeated with a larger sample in order to confirm my findings.

Interesting findings are likely to result from studies examining the interaction between multiple process variables across several time points (Barber, 2009). Such trials are likely to provide a more accurate picture of how these variables change and interact with one another over time to account for variability in outcome. This may help move the field beyond overly simplistic ways of looking at how alliance operates in treatment. In order to strengthen causal inferences researchers should conduct more experimental studies into the process of therapy, in which one therapy process variable is manipulated, while all others are held constant and patients are randomly assigned to conditions (e.g., Høglend et al., 2008). The continued difficulty is in identifying all such variables, but this thesis helps to identify candidates such as therapist consistency.

6.7 Clinical Implications

My study implies that continued treatment may well be detrimental in the presence of poor alliance in childhood depression. This is extremely important in clinical practice as well as in research terms, and therefore, measurement of the quality of alliance should be undertaken in treatment sessions, particularly early in treatment, in order to identify where poor alliance exists. Interventions to improve alliance could be instituted and potential reasons for poor alliance elucidated.

Alliance may well operate differently (i.e. less straight forwardly predictive of outcome) in treatment with children with more than one clinical diagnosis, particularly behavioural problems, as implied by my study. This may have implications as to which populations alliance interventions are best directed. If research can help further elucidate the mechanism of action of alliance in different populations and different environments, clinicians may be able to maximise response to treatment. This will be particularly important as the NHS moves towards a different way of commissioning services and the onus is on providers to demonstrate value for money. The provision of robust outcome data and demonstrating improvement in clinical services is vital in this regard. Child and Adolescent Mental Health Services (CAMHS) are moving more towards brief interventions and focussing on patient choice (for example, CAPA, the Choice and Partnership Approach). It is vital that the quality of alliance with patients and families can firstly be identified and secondly manipulated to improve outcomes where contact with services is limited, or patients are asked to opt-in or make choices about services very early in their contact.

Therapist consistency appears to be important in the predictive effect of alliance on outcome. It may therefore be essential for single therapists to be able to provide treatment across a time period for one child or family and for this not to be disrupted. Again, in an NHS moving more towards brief interventions and "patient pathways" it will be important to ensure that care even across mental health disciplines should be provided by a single clinician able to call on a range of skill sets.

My study indicates an important point for continuing professional development and in the context of revalidation for psychiatrists. Clinicians should be made more aware of

not just the importance of alliance in therapy (including pharmacotherapy), but the complexity of the concept and interaction with other variables in treatment, particularly therapist variables, so that they are able to reflect on their practice in an informed manner.

6.8 Closing Summary

My thesis has successfully demonstrated the complexity of analysing alliance in treatment trials. It has produced some very suggestive results, in terms of both patient and therapist effects in trials and using a newer and creative methodology that significantly improves on previous studies. This is an original contribution to the literature and raises some important new questions in the alliance field.

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APPENDIX A – ETHICAL APPROVAL

- **Ethical approval:** ADAPT was given approval by Multi-centre research ethics committee and all relevant local research ethics committees (Goodyer et al 2007), including permission for audiotape recording of sessions.

- The ADAPT steering committee gave additional permission for sessional audiotapes to be transcribed and rated for therapeutic alliance for the purposes of this study (see copies of emails below):

-----Original Message-----
From: Ian Goodyer [mailto:ig104@hermes.cam.ac.uk] On Behalf Of Ian Goodyer
Sent: 12 March 2006 19:11
To: Dr Jonathan Green
Cc: bernadka.dubicka@manchester.ac.uk
Subject: Re: ADAPT process study

John

I confirm that the analysis lies within the favourable ethics apporval
given to adapt. Indeed i believe we have a responsibility to undertake
process analysis and your contributions to the anonymised tapes will be the
most incisive availbale. Good luck with this John and i look forward to
your reports.

Best Wishes

Ian

On Mar 11 2006, Dr Jonathan Green wrote:

>
>
>ACADEMIC DEPARTMENT OF CHILD & FAMILY PSYCHIATRY
> Booth Hall Children's Hospital, Charlestown Road,
>Blackley, Manchester, M9 7AA
>
>Email: jonathan.green@manchester.ac.uk
>JG/JM Direct Tel: 0161
>918 5322
>
>
>27 February 2006

>
>Professor Ian Goodyer Dr Bernadka
>Dubicka
>Brookside Family Consultation Clinic Child & Adolescent
>Psychiatry
>Developmental Psychiatry Section RMCH
>Douglas House
>18d Trumpington Road
>Cambridge
>CB2 2AH
>
>Dear Ian & Bernadka
>
>Re: Therapeutic Process in ADAPT
>
>Just to update you on progress in this project.
>
>1. Two good MSc students are going to work on this. Bernadka has
>met both.
>2. Inventory of the audio tapes is underway and should be completed
>in the next week or two. This will enable me to commission appropriate
>transcriptions (I have a budget for this).
>3. Ethics. Please see the enclosed note below from the lead of the
>University Ethics Committee. You will see that he notes, I guess
>sensibly, that the wording of the existing consent is most likely to
>cover this and he is happy to sanction the project on that basis.
>I'm sorry that my previous mail on this (26/2) went somewhat haywire
>without my realising and I think didn't actually get to you Ian.
>Bernadka's response was that: "I think we could say that the new study
>falls into a similar remit as we had in ADAPT, ie analysis of the tapes
>to study the therapy being given, which also includes analysis of the
>therapeutic relationship as part of the therapeutic process". Can I
>assume that, Ian, you are in agreement with this? If so I think we're
>clear to proceed.
>
>Best wishes
>
>Yours sincerely
>
>
>Dr Jonathan Green
>Reader in Child & Adolescent Psychiatry &
>Acting Head of Department
>
>
>Enc:
>
>-----Original Message-----
>From: Timothy Stibbs [mailto:Timothy.Stibbs@manchester.ac.uk]
>Sent: 24 February 2006 11:23

>To: 'Dr Jonathan Green'
>Subject: RE: Ethical question
>
>Dear Dr Green,
>
>I think the essential points in this issue are: (1) That the data being
>used is anonymous and (2) that the new analysis does not lie outside
>what the participants originally consented to. The answer to (1) is
>straightforward, but I would leave it your judgment about (2). However,
>it seems unlikely to me that the original consent forms were drafted so
>precisely that such a closely related analysis was excluded.
>
>In my view the new analysis should go ahead, subject to you judgement on
>(2) and that this be noted on your files for the ADAPT trial.
>
>I hope this is helpful
>
>Best wishes
>
>Timothy Stibbs
>

APPENDIX B: MATERIALS

The Vanderbilt Therapeutic Alliance Scale

Study 979

NATIONAL INSTITUTE OF MENTAL HEALTH

TREATMENT OF DEPRESSION COLLABORATIVE RESEARCH PROGRAMME

Form 60

Vanderbilt Therapeutic Alliance Scale (VTAS)

Site: _____ (1)

Patient Number: ___ ___ ___ (2-4)

Rater: _____ (5)

Rating Date: _____ _____ _____ (6-11)
Mo Day Yr

Treatment Hour: _____ (12-13)

Type of Treatment: _____ (14)

Treatment Outcome: _____ (15)

VANDERBILT THERAPEUTIC ALLIANCE SCALE

A. To what extent did the therapist:

	Not at all					Great deal
1. Convey the idea that he is competent to help with patient's problems? _____	0	1	2	3	4	5
2. Express hope and encouragement, a belief that the patient is making (or can make) progress _____	0	1	2	3	4	5
3. Commit himself and his skills to help the patient to the fullest extent possible. _____	0	1	2	3	4	5
4. Show respect, acceptance, and compassion for the patient and his problems. _____	0	1	2	3	4	5
5. Acknowledge the validity of the patient's feelings, thoughts and behaviour. _____	0	1	2	3	4	5
6. Make sure that the patient understood the procedures of therapy and their rationale, what was asked of him and why? _____	0	1	2	3	4	5
7. Make his interventions in a way that preserved the patient's self-esteem and dignity. _____	0	1	2	3	4	5
8. Intrude in his own life story, ideas, or values on the patient. _____	0	1	2	3	4	5
9. Express his own reactions, assets, and liabilities in appropriate ways. _____	0	1	2	3	4	5

10. Foster undue dependency. 0 1 2 3 4 5

_____

11. Make irrelevant or uncalled for comments. 0 1 2 3 4 5

_____

12. Build a sense of mutuality by using "we" and "us" 0 1 2 3 4 5

_____

13. Miss interventions where they appeared needed 0 1 2 3 4 5

_____

B. <u>To what extent did the patient:</u>

	Not at all					Great deal
14. Express that he feels better since Beginning therapy?	0	1	2	3	4	5
15. Indicate that he experiences the therapeutic as understanding and supporting him	0	1	2	3	4	5
16. Seems to identify with the therapists method of working, so that he assumed part of the therapeutic task himself	0	1	2	3	4	5
17. Expect the therapist to change him without accepting his own responsibility for the session	0	1	2	3	4	5
18. Make an effort to carry out therapeutic procedures suggested by the therapist.	0	1	2	3	4	5
19. Acknowledge that he had problems which the therapist could help him deal with.	0	1	2	3	4	5
20. Indicate a strong desire to overcome his problems.	0	1	2	3	4	5

21 Talk freely, openly, and honestly with the therapist about his thoughts, feelings and behaviour. 0 1 2 3 4 5

_____

22 Act in a hostile, attacking or critical manner towards the therapist. 0 1 2 3 4 5

_____

23 Act in a mistrustful or defensive manner towards the therapist. 0 1 2 3 4 5

_____

24 Become so anxious in the session that it interfered with the therapeutic task. 0 1 2 3 4 5

_____

25 Show evidence that he missed an appointment came late to sessions, or hesitates to make the next appointment 0 1 2 3 4 5

_____

C. <u>The therapist and patient together:</u>

	Not at all					Great deal
26. Show enthusiasm which made the session seem alive and energetic	0	1	2	3	4	5

_____

27. Work together in a joint effort to deal with the patient's problems. 0 1 2 3 4 5

_____

28. Share a common viewpoint about the definition, possible causes, and potential alleviation of the patient's problems. 0 1 2 3 4 5

_____

29. Relate in a realistic, honest, straightforward way, within the bounds of reasonable human interaction. 0 1 2 3 4 5

_____

30 Agree upon the goals and tasks for the session. 0 1 2 3 4 5
_____

31. Focus on the therapeutic task throughout the session, without excessive superficiality. 0 1 2 3 4 5
_____

32. Seems to be engaged in a power struggle. 0 1 2 3 4 5
_____

21 Express directly or indirectly the possibility of premature termination. 0 1 2 3 4 5
_____

22 Allow the session to become ruminative, empty, or boring, without a clear trend or theme. 0 1 2 3 4 5
_____

23 Accept their different roles and responsibilities as part of heir relationship. 0 1 2 3 4 5
_____

24 Refer back to experiences they have been through together. 0 1 2 3 4 5
_____

25 Have awkward silences or pauses in their conversation. 0 1 2 3 4 5
_____

Vanderbilt University Therapeutic Alliance Scale
Decision Rule Manual

General Rules

1. When the scale and the manual do not fit together, rely on annual definitions.

2. In rating patient items and interaction items, do not take level of patient difficulty into consideration, for example, thinking that a patient may be doing well after his/her level of pathology.

3. On the interaction items, if the patient and therapist are not "in sync", for example, if the therapist is effective in providing an alliance but the patient is

resistant, score low. For ratings of 4 or 5, both the therapist and patient should be actively engaged and working well together.

4. In some cases where the therapist withdraws a patient from treatment, rate the alliance based on the level of consensus, agreement and respect between the two.

Rules regarding individual items.

1. Therapist conveys competence to help patients usually through indirect means. These may include a sense that the therapist is knowledgeable about the problems presented by the patient, a self-confident manner in pursuing questions or making interpretations, a relatively low level of anxiety. While a therapist may occasionally give direct assurance in more subtle ways.

   DR: This does not reflect the therapist's actual competence, but rather the therapist's sir of authority and a quality of confidence and decisiveness. For a rating of 5, the therapist should clearly convey the message that s/he is experienced, knowledgeable and knows what s/he is doing.

2. The therapist may with express his own sense of hope or point out progress by the patient, or agree with and support the patient's expression of optimism and/or change.

   DR: Rate the degree of explicitly encouragement.
   0 = not at all
   1-2 = implicit encouragement.
   3 = mildly explicit encouragement.
   4-5 = Greater explicit encouragement.

   In cases where the therapist withdraws the patient from treatment, rate 0 if the therapist is hopeless about this treatment and offers no alternatives, rate 1 or 2 if the therapist is negative about this treatment but offers the possibility of hope with another treatment and 3 if the therapist is extremely hopeful about the patient making progress with another treatment.

3. The therapist is actively attentive, pursuing leads in the patient's productions, applying his skills in the patient's interests. Qualities which are in the negative direction on this item include indifference, withdrawal, passivity, or an attitude of "just doing a job". The therapist is not put off by the patient's responses to interventions and does not let resistances interfere with his/her pursuit of therapeutic goals.

4. The therapist is gentle and non-critical in his/her interventions, coveys a genuine respect for the health striving parts of the patient's personality and also an understanding of how and why the patient developed the particular problems presented.

DR: If the therapist is infantilising, patronising, and/or controlling, score 1 or 2.

This is the opposite of being judgemental.

Note that in CBT and pharmacotherapy, the therapist may come across as more active and directive. This, in itself, should not be construed as a lack of respect or compassion. If the therapist interrupts the patient or does not allow him/her to express what is on her/his mind, this may seem as disrespectful.

5. The therapist's stance toward the patient's subjective representation of his/her experiences is one of I can understand how it would be that way, given…." Low ratings thus would indicate active, direct challenges to the patient's construction of events, while in the mid range, the patient's experience is not questioned, and the higher end of the scale, the therapist demonstrates empathic and cognitive understanding of the patient's reactions.

   DR: This item refers to the manner in which the challenge is made. If the therapist is good enough in this regard, score 3. If the therapist is implicitly quite validating, score 4.

   In CBT, it is appropriate for the therapist to challenge the validity of the patient's thoughts and challenges might be perceived as quite direct, e.g., with the therapist asking the patient for evidence for a particular conclusion. Nevertheless, there should be a sense of collaboration with the patient, with the sense that the therapist is challenging the patient in order to help rather than criticise or demean him/her.

6. The therapist makes sure the patient understands the nature of the treatment contract or framework, and intervenes as necessary to educate the patient about his/her responsibility in the treatment, or to explain why certain requests are made.

   DR: If the patient seems to understand and the therapist is not doing too much explaining, rate 3.

7. Low ratings on this item indicate that the therapists are careless about or insensitive to the import of interventions on the patient's self-esteem. Mid range ratings should be used for a "good enough" level of sensitivity, and high ratings for extremely well phrased interventions which clearly support self-esteem while making an important point

   DR: If the therapist seems well intentioned but infantilising, patronising and/or controlling, rate 2.

8. This item measures such therapist behaviours as using the patient for gratification of the therapist needs (e.g.,. to be superior, to have others be dependent, etc), ignoring the patient's goals for the therapy and imposing ones

own, pushing the patient to conform to pre-conceived norms of "healthy" behaviour, or disclosing unnecessary information about oneself to the patient.

9. This item refers to the therapist's expression of his own immediate reaction, feelings or attitudes towards the patient. Appropriate as used here means genuine and sincere, as well as done in a way that facilitates the progress of the therapy. The therapist is judicious in the use of such self-disclosure, neither rigid and withholding nor excessive and falsely supportive.

    DR: If the therapist is infantilising, patronising or controlling score 1 or 2.

    If the therapist is seductive, score 1 or 2.

    If there are no expressions and that is appropriate score 3.
    4-5 = therapist expresses self appropriately and it is done skilfully.

10. The therapist allows or encourages the patient to be more dependent that necessary in the relationship by undermining the patient's attempts at independence or mutuality, by giving unneeded advice or encouragement, by taking excessive responsibility for the progress of the therapy, or by going "above and beyond duty".

    DR: Note that in pharmacotherapy, the doctor may take more responsibility for the treatment, conveying the sense that the therapist will be in charge and will help the patient. The therapist might take control of the situation in order to convey a sense of competence and authority. Moreover phone calls in between sessions, which would not be encouraged in psychotherapy, would be appropriate in pharmacotherapy. Undue dependency in pharmacotherapy might be seen as a doctor who refuses to hear and/or attend to the patient's questions. S/he might actively discourage the patient from choosing when to take medication or refuse to provide information about the medication or side effects.

11. The therapist interjects comments which at least temporarily interrupt the development of the patient's material, which seem to reflect the therapist's own interests or problems rather than the needs of the patient, or which are simply not productive.

12. A sense of mutuality may be conveyed by the direct use of "we" or "us" by references to the working relationship, or by using "you" and "I" in the same sentence.

    DR: If the "we's" focus on administrative issues only, score 1 or 2.

13. High ratings on this item would indicate that the patient seems to be floundering, needing some structuring of material or of the therapy relationship from the therapist, and that the therapist does not respond to this need.

    DR: Look for tracking and following of patient. Note, for example, that in pharmacotherapy a missed intervention, may in clued missing

opportunities to make important transitions e.g.,. If a patient is talking about problems in a relationship, the therapist can say that things will likely improve when the patient feels less depressed. Efforts should be made to refocus the patient to reporting on clinical change rather than allowing him/her to ramble. Tracking effect = 0.

14. The patient should specifically refer to feeling/doing better. For ratings of 4 or 5, the patient should explicitly link the improvement to therapy.

    DR: If the patient says s/he feels better now, but not great, score 1.

15. The patient may explicitly refer to the therapist's understanding and support, or may implicitly express this experience by, for example, agreeing with the therapist's intervention or elaborating further on the therapist's remarks.

    DR: If the patient expresses neither t hat the therapist is very "in tune", nor that the therapist is really "off bade", score 3. If the patient expresses/implies that the therapist doesn't appreciate the severity of the illness score 1 or 2.

16. The patient actively joins in working and collaborating with the therapist within the therapeutic framework. For ratings of 4 or 5, the process should reflect acceptances of the framework as the patient's own not just compliance with the therapist's guidelines.

    DR: In pharmacotherapy, give a low rating if the patient demonstrates resistance to taking the medication.

    Regarding cases where the therapist withdraws a patient from treatment, consider whether the patient can engage with the therapist in thinking about the alternatives to the current treatment. Score low if the patient acts helpless.

17. The emphasis here is on the patient's accepting responsibility for making the wished for changes which led him or her to seek therapy. High ratings indicate that the patient expects to acted upon, provided with answers, or told what to do, without active involvement in the therapy process, in terms of either self exploration or behavioural experimentation.

    DR: Change to read "The emphasis here is on the patient's accepting responsibility for treatment". This refers to "in-session" behaviour. If necessary, rely on inference, e.g. evidence of resistance, passivity and/or lack of motivation to change. If the patient expresses a direct request for help or advice, rate 3.

18. The patient is willing (1) to work within the therapeutic framework and carry out the procedures of the therapy. (2) to consider the implications of the therapist's suggestions or interpretations for how he or she views the world and (3 to use the therapy and the therapist in understanding and resolving problems.

DR: For pharmacotherapy tapes, use only part 1 of the manual definition. For IPT and CBT, also consider part 2. Do not use part 3. If somebody doesn't do their homework or take their meds give 1 or 2.

In withdrawal cases, rate on the basis of the patient's willingness to go along with the therapist's advice to seek alternative treatment.

19. This item includes both the patient's openness in acknowledging what the problems are and willingness to accept the therapist's help. Both elements must be present for ratings in the 4-5 range.

DR: Mot "to seek therapist's help" in definition. For pharmacotherapy, the therapist's help may influence the patient's attitude toward the medication the therapist is offering. If the patient is open in acknowledging problems, but closed to accepting help, score 2.

In cases where a therapist withdraws a patient from treatment rate on the basis of the degree to which the patient acknowledges that he has problems and his willingness to accept the therapist's help even if that help consists of accepting advice to try another form of treatment.

20. The patient expresses a strong feeling that his difficulties interfere with the achievement of important life goals, that they are experienced as ego-alien, or that for some other reason (s) they cause distress.

DR: Include a strong desire to get better, as reflected by in session behaviour as reports of what goes on between sessions. Patients who assume a "yes but…." Attitude across the board or who deriving considerable secondary gain from their "sick role" should get low ratings. Those who intellectually recognise a need for change but are having trouble motivating themselves because of their depression should be scored 3.

21. High ratings on this item reflect evidence of all three criteria. freely, openly, honestly, in such a way that here is a relatively smooth flow of information about whatever is in the patient's mind.

DR: Do not score high if the patient is intellectualising.

Low ratings indicate the absence of some aspect of the patient's experience which would reasonably be expected, or difficulty in sharing thoughts or communicating with the therapist.

22. The patient is negativistic or overtly hostile toward the therapist, and at higher levels of the scale, is unwilling to explore the meaning of these feelings. This item can also be used to rate derogatory attitudes toward the therapy process or active interference with the therapist's efforts.

DR: Hostility towards the treatment or treatment package may be seen as equal to hostility toward the therapist. Devaluation of the therapy 4.

23. This item refers to less overt (covert, hostile, provocative, and defensive), mistrust or negative feelings about the therapist, including defensiveness that does not seem to be motivated by conscious evasiveness. Defensiveness may include an overly positive or compliant attitude toward the therapist.

24. The patient's level of anxiety leads to interference with communication, e.g. periods of silence, abrupt shifts of topic, uncontrolled crying.

    DR: If patient reports feeling in the session or in anticipation thereof score 1.

25. This item refers to the patient's acting on ambivalence about carrying out the therapeutic contract by violating agreements about time.

    DR: If a patient does not act on this ambivalence, rate 0, if the patient seems hesitant to make the next appointment, score from 1-5 based on the degree of hesitation. Consider why an appointment was cancelled and score low if the cancellation was not related to feelings about therapy.

    In withdrawal cases, rate on the basis of the patient's reluctance to continue with the present treatment and reluctance to accept subsequent treatment recommendations.

26. This item involves a sense of activity engagement and mutual investment of energy in the work of therapy

27. The patient and therapist are "tracking" each other's comments, and are not being tangential or superficial.

    DR: Focus on tracking but do not evaluate how meaningful the dialogue is. Given reasonable tracking, score 3. Do not rate comprehension. The goals here are for the session not for treatment.

28 This item measures the extent to which the patient come to genuinely share the therapist's understanding of the patient's problems, as well as the therapist's understanding and communicating within the patient's subjective world. At the higher end of the scale, there should be evidence of positive identification with the therapist, as distinguished from compliance.

    DR: This does not measure tracking, but is a belief system item. Use inference to rate this item. If patient and therapist are moving along in an average way, rate 3. If they express enthusiasm about this treatment and its match with this patient and/or the observation that the patient is unreservedly engaging in treatment score 4 or 5, in the absence of info rate 5.

    Enthusiasm about this treatment and its match with this patient and/or the observation that the patient is unreservedly engaging in the treatment

should be construed as evidence of sharing a common viewpoint with the therapist.

Patients, who openly complain about the treatment received, express open dissatisfaction with their treatment or an overt wish for another type of treatment should get low ratings.

29 This item refers to the maintenance of a friendly but professional working relationship, neither too distant nor too involved. A high score indicates that the working relationship is firmly established and maintained even through periods when the patient experiences intense positive or negative feelings toward the therapist.

30 Either the patient or the therapist may explicitly state a purpose for this particular session, or there may be implicit evidence that both sense themselves as "picking up where they left off" and continuing to work towards mutually understood goals.

DR: For ratings of 4 or 5, there should be evidence of a mutual willingness to focus on a particular issue. If the therapist or the patient seems to be pulling the other along, give a low rating.

31 The rater should be able to discern a task or theme in a session and then to rate the degree to which it was followed. If none can be identified, the session is assumed to relatively fragmented and superficial.

DR: If a particular theme is followed rate 4 or 5. For pharmacotherapy tapes, the therapeutic task may be a more thorough review of symptoms and side effects.

32 More subtle engagement in control issues would be rated 2-3. If there is explicit struggle around issues of power and control then rating should be higher.

33 Premature termination may be discussed explicitly or there may be an accumulation of indirect evidence such as a wish to end, a feeling of hopelessness about reaching goals, or strong dissatisfaction with the process of therapy.

DR: Score high for comments like or sense of "this isn't getting anywhere". In withdrawal cases, give high scores for the likelihood of premature termination (probably a 5 if both parties agree that treatment should end immediately.

34. The patient and therapist seem to be repeating old material or unable to focus their efforts, in a way that neither acts to correct.

DR: Note. Whether the interaction is or is not moving. If the discussion seems like a broken record, rate 4.

In pharmacotherapy, there may be a repetitive quality to reviewing symptoms. Nevertheless for ratings of 1 or 2 there should be a sense progress in moving through the required areas, e.g. in reviewing symptoms, issues of compliance and general clinical picture.

35. Both patient and therapist are clear about what their responsibilities are for the particular therapy they have undertaken, and act in accordance with the framework.

    DR: Take into consideration what the particular roles and responsibilities should be for the particular treatment condition being rated.

36. Referring to earlier sessions or to previously discussed experiences gives in this session the sense of continuity and progress to the work.

    DR: Look for concrete references, not implicit comparisons. If the issue is explicitly stated score 3 or 4. Score their mutual past in therapy, not the past symptomatically.

37. This item refers not to thoughtful silences, but to those which come about because the participants seem anxious, uncomfortable with each other, or at an impasse.

    DR: Even if a pause is very brief, followed by an awkwardness and then change of topic score 2.

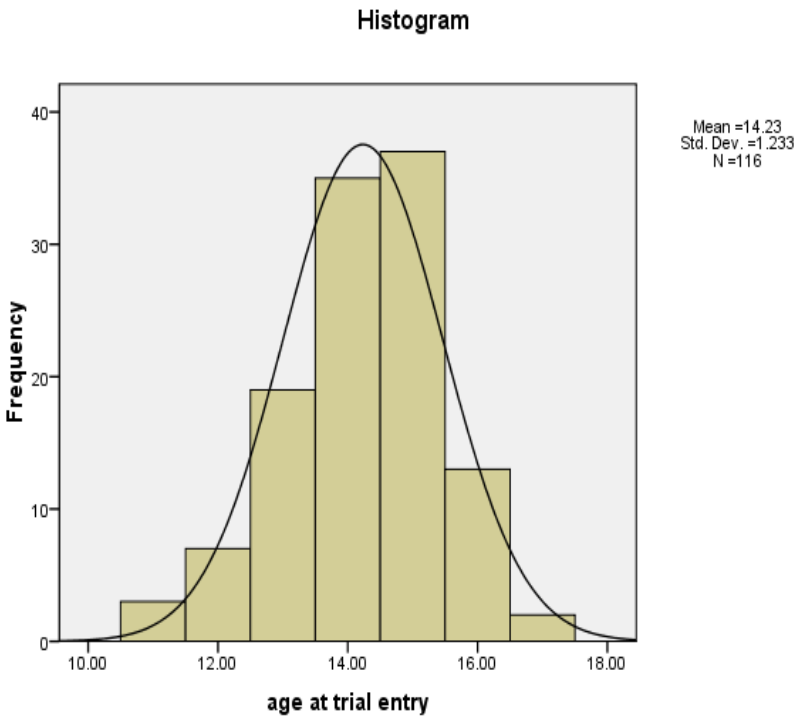
APPENDIX C: RESULTS

Table C1

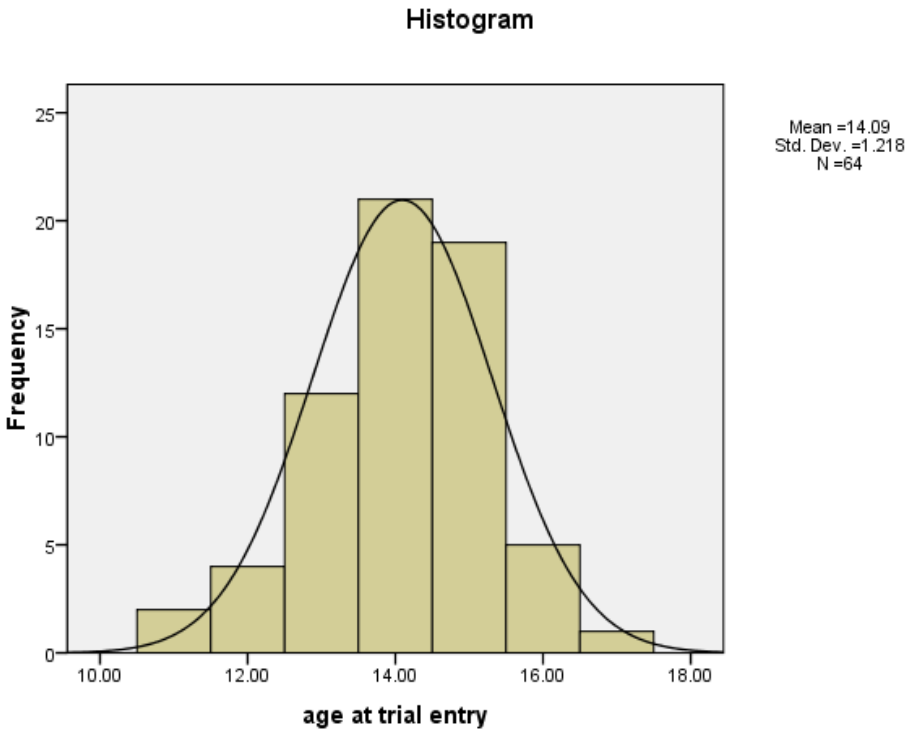
Whole Sample Age at Trial Entry

Age (years)	Frequency	Percentage (%)
11	3	2.6
12	7	6.0
13	19	16.4
14	35	30.2
15	37	31.9
16	13	11.2
17	2	1.7
Total	116	100.0

Histogram C1: Histogram to Show Whole Sample Age at Trial Entry



Histogram C2: Histogram to Show Manchester Sample Age at Trial Entry



Histogram C3: Histogram to Show Cambridge Sample Age at Trial Entry

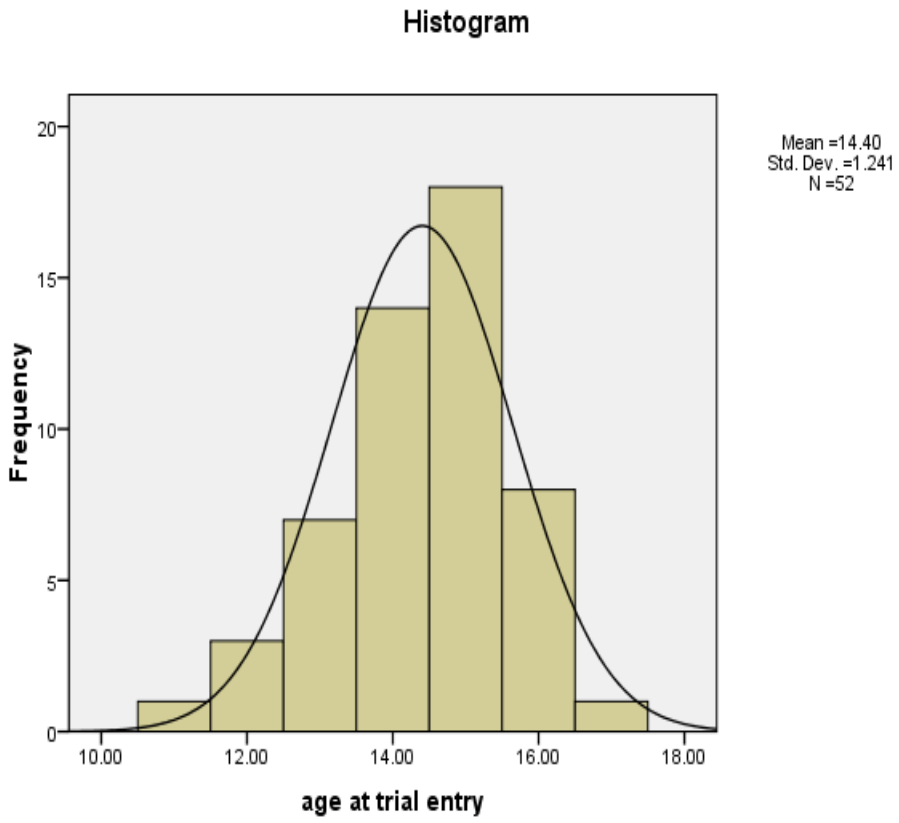


Table C2

Correlations in Cambridge between Baseline Factors and Alliance Scores

(CBT and Medication arm - Combined Treatment)

		Total Alliance	Patient Alliance	Therapist Alliance
HoNOSCA	Pearson Correlation	-.079	.045	-.140
	Sig. (2-tailed)	.700	.829	.495
CGAS	Pearson Correlation	.102	.176	.006
	Sig. (2-tailed)	.621	.391	.978
MFQ	Pearson Correlation	-.325	-.355	-.173
	Sig. (2-tailed)	.105	.075	.399
CDRS t score	Pearson Correlation	-.154	-.099	-.133
	Sig. (2-tailed)	.452	.629	.516

(N=26)

Table C3

Correlations in Cambridge between Baseline Factors and Alliance Scores (Medication arm)

		Total Alliance	Patient Alliance	Therapist Alliance
HoNOSCA	Pearson Correlation	.104	.087	.053
	Sig. (2-tailed)	.615	.672	.798
CGAS	Pearson Correlation	.011	.033	-.021
	Sig. (2-tailed)	.958	.872	.920
MFQ	Pearson Correlation	-.191	-.012	-.259
	Sig. (2-tailed)	.351	.955	.201
CDRS t score	Pearson Correlation	-.028	-.009	-.029
	Sig. (2-tailed)	.893	.965	.886

(N=26)

Table C4

Correlations between Number of Sessions Attended and Alliance Factor Scores in Manchester

		total sessions (12 weeks)	total sessions (week 28)
Total Alliance	Pearson Correlation	.088	.120
	Sig. (2-tailed)	.489	.346
Patient Alliance	Correlation	.115	.219
	Sig. (2-tailed)	.364	.082
Therapist Alliance	Correlation	.001	-.068
	Sig. (2-tailed)	.992	.596

(N = 64)

Table C5

Correlations between Number of Sessions Attended and Alliance Factor Scores in Cambridge

		total sessions (12 weeks)	total sessions (week 28)
Total Alliance	Correlation	.127	-.001
	Sig. (2-tailed)	.368	.992
Patient Alliance	Correlation	-.051	-.062
	Sig. (2-tailed)	.718	.664
Therapist Alliance	Correlation	.220	.053
	Sig. (2-tailed)	.117	.710

(N = 52)

Table C6

Whole Sample Correlations between Alliance Scores and Outcome Measure at 28 Weeks

		Total Alliance	Patient Alliance	Therapist Alliance
HoNOSCA	Pearson Correlation	-.044	-.057	-.008
	Sig. (2-tailed)	.641	.551	.936
CGAS	Pearson Correlation	.051	.028	.046
	Sig. (2-tailed)	.592	.770	.631
CGI-I	Kendall's Tau	-.090	-.077	-.054
	Sig. (2-tailed)	.344	.422	.572
MFQ	Pearson Correlation	-.008	-.005	-.007
	Sig. (2-tailed)	.933	.959	.944
CDRS t	Pearson Correlation	-.076	-.065	-.044
	Sig. (2-tailed)	.428	.495	.644

(N = 112)

Table C7

Correlations between Alliance and Outcome Measures at 6 Weeks in Cambridge

		Total Alliance	Patient Alliance	Therapist Alliance
HoNOSCA	Pearson Correlation	-.106	-.050	-.102
	Sig. (2-tailed)	.420	.706	.437
CGAS	Pearson Correlation	.099	.056	.084
	Sig. (2-tailed)	.453	.671	.522
MFQ	Pearson Correlation	-.213	-.013	-.303*
	Sig. (2-tailed)	.102	.922	.019
CDRS t	Pearson Correlation	-.091	-.033	-.098
	Sig. (2-tailed)	.491	.803	.456

(N=52)

Table C8

Correlations between Alliance and Outcome Measures at 12 Weeks in Cambridge

		Total Alliance	Patient Alliance	Therapist Alliance
HoNOSCA	Pearson Correlation	-.051	.084	-.165
	Sig. (2-tailed)	.692	.514	.196
CGAS	Pearson Correlation	-.059	-.158	.079
	Sig. (2-tailed)	.647	.217	.540
MFQ	Pearson Correlation	-.017	.140	-.175
	Sig. (2-tailed)	.897	.277	.173
CDRS t	Pearson Correlation	.047	.156	-.096
	Sig. (2-tailed)	.717	.225	.458

(N = 52)

Table C9

Correlations between Alliance and Outcome Measures at 6 Weeks in Manchester

		Total Alliance	Patient Alliance	Therapist Alliance
HoNOSCA	Pearson Correlation	.168	.146	.104
	Sig. (2-tailed)	.238	.307	.466
CGAS	Pearson Correlation	-.089	-.121	-.016
	Sig. (2-tailed)	.536	.399	.910
MFQ	Pearson Correlation	.109	.062	.096
	Sig. (2-tailed)	.448	.666	.503
CDRS t	Pearson Correlation	.101	.118	.035
	Sig. (2-tailed)	.482	.411	.805

(N = 63)

Table C10

Correlations between Alliance and Outcome Measures at 12 Weeks in Manchester

		Total Alliance	Patient Alliance	Therapist Alliance
HoNOSCA	Pearson Correlation	.187	.161	.112
	Sig. (2-tailed)	.190	.259	.433
CGAS	Pearson Correlation	-.149	-.003	-.205
	Sig. (2-tailed)	.296	.984	.149
MFQ	Pearson Correlation	.087	.047	.078
	Sig. (2-tailed)	.545	.743	.589
CDRS t	Pearson Correlation	.192	.073	.200
	Sig. (2-tailed)	.178	.613	.159

(N = 62)

Table C11

Correlations between Alliance and Outcome Measures at 6 Weeks in Medication Arm

		Total Alliance	Patient Alliance	Therapist Alliance
HoNOSCA	Pearson Correlation	.130	.130	.077
	Sig. (2-tailed)	.411	.413	.626
CGAS	Pearson Correlation	-.053	-.112	.028
	Sig. (2-tailed)	.739	.481	.860
MFQ	Pearson Correlation	-.094	.050	-.200
	Sig. (2-tailed)	.554	.751	.204
CDRS t	Pearson Correlation	.022	.147	-.113
	Sig. (2-tailed)	.891	.355	.478

(N =43)

Table C12

Correlations between Alliance and Outcome Measures at 12 Weeks in Medication Arm

		Total Alliance	Patient Alliance	Therapist Alliance
HoNOSCA	Pearson Correlation	.151	.293	-.055
	Sig. (2-tailed)	.332	.057	.727
CGAS	Pearson Correlation	-.222	-.308	-.043
	Sig. (2-tailed)	.152	.054	.786
MFQ	Pearson Correlation	-.008	.136	-.151
	Sig. (2-tailed)	.959	.385	.335
CDRS t	Pearson Correlation	.122	.233	-.040
	Sig. (2-tailed)	.434	.133	.797

(N = 43)

Table C13

Correlations between Alliance and Outcome Measures at 6 and 12 weeks in Combined Arm

		Total Alliance	Patient Alliance	Therapist Alliance
HoNOSCA 6 weeks	Pearson Correlation	-.069	-.014	-.078
	Sig. (2-tailed)	.575	.911	.525
CGAS 6 weeks	Pearson Correlation	.083	.015	.097
	Sig. (2-tailed)	.496	.905	.430
MFQ 6 weeks	Pearson Correlation	-.039	-.017	-.035
	Sig. (2-tailed)	.750	.887	.778
CDRS t 6 weeks	Pearson Correlation	-.050	-.060	-.007
	Sig. (2-tailed)	.682	.625	.956
HoNOSCA 12 weeks	Pearson Correlation	-.008	.041	-.051
	Sig. (2-tailed)	.944	.734	.673
CGAS 12 weeks	Pearson Correlation	-.001	-.001	.000
	Sig. (2-tailed)	.991	.992	.996
MFQ 12 weeks	Pearson Correlation	.027	.069	-.031
	Sig. (2-tailed)	.824	.572	.800
CDRS 12 weeks	Pearson Correlation	.049	.049	.018
	Sig. (2-tailed)	.687	.689	.884

(N = 73)

Table C14

Correlations between Alliance and Outcome Measures at 6 and 12 weeks in Medication Arm in Cambridge

		Total Alliance	Patient Alliance	Therapist Alliance
HoNOSCA 6 weeks	Pearson Correlation	.132	.222	-.044
	Sig. (2-tailed)	.625	.408	.871
CGAS 6 weeks	Pearson Correlation	-.047	-.173	.146
	Sig. (2-tailed)	.862	.522	.590
MFQ 6 weeks	Pearson Correlation	-.160	.140	-.515
	Sig. (2-tailed)	.555	.605	.051
CDRS t score	Pearson Correlation	.013	.182	-.227
	Sig. (2-tailed)	.961	.500	.399
HoNOSCA 12 weeks	Pearson Correlation	.198	.379	-.136
	Sig. (2-tailed)	.447	.134	.603
CGAS 12 weeks	Pearson Correlation	-.326	-.517*	.071
	Sig. (2-tailed)	.201	.034	.786
MFQ 12 weeks	Pearson Correlation	-.012	.273	-.410
	Sig. (2-tailed)	.963	.289	.102
CDRS 12 weeks	Pearson Correlation	.134	.369	-.250
	Sig. (2-tailed)	.607	.145	.334

(N = 26)

Table C15

Correlations between Alliance and Outcome Measures at 6 and 12 weeks in Combined Arm in Cambridge

		Total Alliance	Patient Alliance	Therapist Alliance
HoNOSCA 6 weeks	Pearson Correlation	-.271	-.209	-.140
	Sig. (2-tailed)	.076	.173	.364
CGAS 6 weeks	Pearson Correlation	.247	.238	.079
	Sig. (2-tailed)	.106	.119	.612
	N	44	44	44
MFQ 6 weeks	Pearson Correlation	-.295	-.128	-.257
	Sig. (2-tailed)	.052	.409	.092
CDRS 6 weeks	Pearson Correlation	-.210	-.193	-.077
	Sig. (2-tailed)	.171	.208	.620
HoNOSCA 12 weeks	Pearson Correlation	-.182	-.067	-.178
	Sig. (2-tailed)	.226	.660	.237
CGAS 12 weeks	Pearson Correlation	.084	.029	.084
	Sig. (2-tailed)	.578	.847	.580
MFQ 12 weeks	Pearson Correlation	-.065	.036	-.120
	Sig. (2-tailed)	.672	.812	.431
CDRS 12 weeks	Pearson Correlation	-.044	-.007	-.052
	Sig. (2-tailed)	.773	.961	.737

(N = 26)

Table C16

Correlations between Alliance and Outcome Measures at 6 and 12 weeks in Combined Arm in Manchester

		Total Alliance	Patient Alliance	Therapist Alliance
HoNOSCA 6 weeks	Pearson Correlation	.131	.037	.148
	Sig. (2-tailed)	.524	.857	.469
CGAS 6 weeks	Pearson Correlation	-.058	-.033	-.054
	Sig. (2-tailed)	.778	.874	.794
MFQ 6 weeks	Pearson Correlation	-.030	-.042	-.010
	Sig. (2-tailed)	.883	.839	.963
CDRS t 6 weeks	Pearson Correlation	.037	.123	-.042
	Sig. (2-tailed)	.857	.550	.839
HoNOSCA 12 weeks	Pearson Correlation	.115	.217	-.008
	Sig. (2-tailed)	.578	.287	.970
CGAS 12 weeks	Pearson Correlation	-.112	-.024	-.133
	Sig. (2-tailed)	.587	.909	.518
MFQ 12 weeks	Pearson Correlation	-.007	.010	-.017
	Sig. (2-tailed)	.973	.960	.934
CDRS t 12 weeks	Pearson Correlation	.112	.071	.097
	Sig. (2-tailed)	.587	.731	.636

(N = 47)

Table C17

Correlations between Alliance and Outcome Measures at 6 and 12 weeks in Medication Arm in Manchester

		Total Alliance	Patient Alliance	Therapist Alliance
HoNOSCA 6 weeks	Pearson Correlation	.310	.259	.168
	Sig. (2-tailed)	.132	.211	.423
CGAS 6 weeks	Pearson Correlation	-.188	-.192	-.065
	Sig. (2-tailed)	.368	.359	.757
MFQ 6 weeks	Pearson Correlation	.233	.123	.204
	Sig. (2-tailed)	.262	.558	.328
CDRS t 6 weeks	Pearson Correlation	.228	.140	.178
	Sig. (2-tailed)	.274	.504	.395
HoNOSCA 12 weeks	Pearson Correlation	.315	.149	.293
	Sig. (2-tailed)	.125	.478	.156
CGAS 12 weeks	Pearson Correlation	-.209	.001	-.308
	Sig. (2-tailed)	.315	.995	.134
MFQ 12 weeks	Pearson Correlation	.246	.092	.255
	Sig. (2-tailed)	.237	.663	.218
CDRS t 12 weeks	Pearson Correlation	.284	.078	.327
	Sig. (2-tailed)	.169	.711	.110

(N = 17)

Table C18

Correlations between Alliance Measures and Clinical Global Impression Improvement Scale at 6 and 12 weeks for Whole Sample

			CGI -I at 6 weeks	CGI-I at 12 weeks
Kendall's tau	Total Alliance	Correlation Coefficient	-.004	.025
		Sig. (2-tailed)	.952	.719
		N	110	114
	Patient Alliance	Correlation Coefficient	-.003	.061
		Sig. (2-tailed)	.969	.381
		N	110	114
	Therapist Alliance	Correlation Coefficient	.076	.015
		Sig. (2-tailed)	.297	.828
		N	110	114

(N = 116)

Table C19

Correlations between Alliance Factors and CGI-I at 6 and 12 weeks in Manchester

			CGI-I at 6 weeks	CGI-I at 12 weeks
Kendall's tau	Total Alliance	Correlation Coefficient	-.147	-.039
		Sig. (2-tailed)	.140	.679
	Patient Alliance	Correlation Coefficient	-.120	.028
		Sig. (2-tailed)	.230	.761
	Therapist Alliance	Correlation Coefficient	-.003	-.033
		Sig. (2-tailed)	.978	.724
		N	49	53

(N = 64)

Table C20

Correlations between Alliance Factors and CGI-I at 6 and 12 weeks in Cambridge

			CGI-I at 6 weeks	CGI-I at 12 weeks
Kendall's tau	Total Alliance	Correlation Coefficient	.157	.110
		Sig. (2-tailed)	.150	.300
	Patient Alliance	Correlation Coefficient	.119	.070
		Sig. (2-tailed)	.277	.507
	Therapist Alliance	Correlation Coefficient	.178	.094
		Sig. (2-tailed)	.102	.377

(N = 51)

Table C21

Correlations between Alliance Factors and CGI-I at 6 and 12 weeks in Combined Arm

			CGI-I at 6 weeks	CGI-I at 12 weeks
Kendall's tau	Total Alliance	Correlation Coefficient	-.057	.094
		Sig. (2-tailed)	.636	.409
	Patient Alliance	Correlation Coefficient	-.029	.099
		Sig. (2-tailed)	.813	.385
	Therapist Alliance	Correlation Coefficient	-.072	.035
		Sig. (2-tailed)	.554	.756

(N = 73)

Table C22

Correlations between Alliance Factors and CGI-I at 6 and 12 weeks in Medication Arm

			CGI-I at 6 weeks	CGI-I at 12 weeks
Kendall's tau	Total Alliance	Correlation Coefficient	.012	-.008
		Sig. (2-tailed)	.893	.930
	Patient Alliance	Correlation Coefficient	-.009	.054
		Sig. (2-tailed)	.920	.545
	Therapist Alliance	Correlation Coefficient	.133	.006
		Sig. (2-tailed)	.153	.946

(N = 43)

Table C23

Correlations between Alliance Factors and CGI-I at 6 and 12 weeks at Manchester Medication Only Arm

			CGI-I at 6 weeks	CGI-I at 12 weeks
Kendall's tau	Total Alliance	Correlation Coefficient	-.049	.137
		Sig. (2-tailed)	.810	.469
	Patient Alliance	Correlation Coefficient	-.069	.137
		Sig. (2-tailed)	.736	.469
	Therapist Alliance	Correlation Coefficient	-.088	.056
		Sig. (2-tailed)	.664	.765

(N = 17)

Table C24

Correlations between Alliance Factors and CGI-I at 6 and 12 weeks at Manchester Combined Arm

			CGI-I at 6 weeks	CGI-I at 12 weeks
Kendall's tau_b	Total Alliance	Correlation Coefficient	-.201	-.099
		Sig. (2-tailed)	.090	.371
	Patient Alliance	Correlation Coefficient	-.172	.047
		Sig. (2-tailed)	.147	.673
	Therapist Alliance	Correlation Coefficient	.017	-.060
		Sig. (2-tailed)	.885	.589

(N = 47)

Table C25

Correlations between Alliance Factors and CGI-I at 6 and 12 weeks at Cambridge Medication Only Arm

			CGI-I at 6 weeks	CGI-I at 12 weeks
Kendall's tau	Total Alliance	Correlation Coefficient	.328*	.181
		Sig. (2-tailed)	.038	.256
	Patient Alliance	Correlation Coefficient	.210	.132
		Sig. (2-tailed)	.185	.405
	Therapist Alliance	Correlation Coefficient	.320*	.165
		Sig. (2-tailed)	.043	.300

*(N = 26)*p is significant at <0.05*

Table C26

Correlations between Alliance Factors and CGI-I at 6 and 12 weeks at Cambridge Combined Arm

			CGI-I at 6 weeks	CGI-I at 12 weeks
Kendall's tau	Total Alliance	Correlation Coefficient	-.089	.045
		Sig. (2-tailed)	.572	.765
	Patient Alliance	Correlation Coefficient	-.027	-.003
		Sig. (2-tailed)	.864	.982
	Therapist Alliance	Correlation Coefficient	-.074	.038
		Sig. (2-tailed)	.641	.800

(N = 26)

Table C27

Linear Regressions for Whole Sample

Outcome Measure	Alliance Factor	Beta	P Value	R Squared
MFQ 6 weeks	Total	.056	.562	.003
	Therapist	.107	.263	.011
	Patient	.028	.774	.001
MFQ 12 weeks	Total	.132	.163	.017
	Therapist	.084	.374	.007
	Patient	.107	.261	.011
CGAS 6 weeks	Total	.065	.501	.004
	Therapist	.049	.611	.002
	Patient	.043	.652	.002
CGAS 12 weeks	Total	.242	.087	.059
	Therapist	.286	.042	.082
	Patient	.055	.700	.003
CDRS 6 weeks	Total	.030	.757	.001
	Therapist	.036	.705	.001
	Patient	.007	942	.000
CDRS 12 weeks	Total	.160	.091	.026
	Therapist	.081	.392	.007
	Patient	.150	.112	.023
HoNOSCA 6 weeks	Total	.025	.794	.001
	Therapist	.034	.722	.001
	Patient	.070	.465	.005
HoNOSCA 12 weeks	Total	.284	.043	.081
	Therapist	.261	.065	.068
	Patient	.147	.304	.022

(N = 116)

Table C28

Linear Regressions – Manchester

Outcome Measure	Alliance Factor	Beta	P Value	R Squared
MFQ 6 weeks	Total	.226	.083	.051
	Therapist	.114	.387	.013
	Patient	.199	.128	.040
MFQ 12 weeks	Total	.011	.933	.000
	Therapist	.020	.876	.000
	Patient	.034	.790	.001
CGAS 6 weeks	Total	.273	.035	.075
	Therapist	.125	.342	.016
	Patient	.252	.052	.063
CGAS 12 weeks	Total	.039	.759	.002
	Therapist	.167	.191	.028
	Patient	.102	.427	.010
CDRS 6 weeks	Total	.112	.392	.013
	Therapist	.072	.587	.005
	Patient	.086	.516	.007
CDRS 12 weeks	Total	.040	.760	.002
	Therapist	.089	.494	.008
	Patient	.139	.282	.019
HoNOSCA 6 weeks	Total	.192	.142	.037
	Therapist	.078	.536	.006
	Patient	.186	.156	.034
HoNOSCA 12 weeks	Total	.131	.308	.017
	Therapist	.164	.199	.027
	Patient	.030	.815	.001

(N = 64)

Table C29

Linear Regressions – Cambridge

Outcome Measure	Alliance Factor	Beta	P Value	R Squared
MFQ 6 weeks	Total	.391*	.005	.153
	Therapist	.357*	.010	.127
	Patient	.210	.139	.044
MFQ 12 weeks	Total	.348*	.012	.121
	Therapist	.305*	.030	.093
	Patient	.196	.167	.039
CGAS 6 weeks	Total	.155	.277	.024
	Therapist	.052	.715	.003
	Patient	.184	.196	.059
CGAS 12 weeks	Total	.242	.087	.059
	Therapist	.286*	.042	.082
	Patient	.055	.700	.003
CDRS 6 weeks	Total	.210	.139	.044
	Therapist	.152	.287	.023
	Patient	.157	.271	.025
CDRS 12 weeks	Total	.378*	.006	.143
	Therapist	.400*	.004	.160
	Patient	.137	.339	.019
HoNOSCA 6 weeks	Total	.211	.138	.044
	Therapist	.202	.156	.041
	Patient	.103	.474	.011
HoNOSCA 12 weeks	Total	.284*	.043	.081
	Therapist	.261	.065	.068
	Patient	.147	.304	.022

*(N = 52)*significant at p = <0.05*

Table C30

Linear Regressions - Medication Only Arm

Outcome Measure	Alliance Factor	Beta	P Value	R Squared
MFQ 6 weeks	Total	.193	.220	.037
	Therapist	.092	.562	.008
	Patient	.215	.172	.046
MFQ 12 weeks	Total	.234	.131	.055
	Therapist	.099	.527	.010
	Patient	.271	.078	.074
CGAS 6 weeks	Total	.016	.918	.000
	Therapist	.027	.865	.001
	Patient	.053	.740	.003
CGAS 12 weeks	Total	.058	.242	.119
	Therapist	.062	.694	.004
	Patient	.320	.037	.102
CDRS 6 weeks	Total	.080	.613	.006
	Therapist	.000	.998	.000
	Patient	.128	.420	.016
CDRS 12 weeks	Total	.212	.173	.045
	Therapist	.074	.630	.005
	Patient	.261	.091	.068
HoNOSCA 6 weeks	Total	.155	.328	.024
	Therapist	.211	.180	.044
	Patient	.035	.825	.001
HoNOSCA 12 weeks	Total	.185	.236	.034
	Therapist	.053	.735	.003
	Patient	.238	.124	.057

(N = 43)

Table C31

Linear Regressions for Combined Treatment Arm

Outcome Measure	Alliance Factor	Beta	P Value	R Squared
MFQ 6 weeks	Total	.022	.860	.000
	Therapist	.004	.432	.009
	Patient	.124	.310	.015
MFQ 12 weeks	Total	.056	.643	.003
	Therapist	.060	.624	.004
	Patient	.016	.896	.000
CGAS 6 weeks	Total	.147	.228	.022
	Therapist	.090	.462	.008
	Patient	.106	.388	.011
CGAS 12 weeks	Total	.033	.788	.001
	Therapist	.020	.870	.000
	Patient	.024	.842	.001
CDRS 6 weeks	Total	.032	.792	.001
	Therapist	,023	.850	.001
	Patient	.066	.592	.004
CDRS 12 weeks	Total	.088	.466	.008
	Therapist	.048	.691	.006
	Patient	.071	.558	.005
HoNOSCA 6 weeks	Total	.151	.216	.023
	Therapist	.067	.586	.004
	Patient	.133	.274	.018
HoNOSCA 12 weeks	Total	.062	.610	.004
	Therapist	.031	.799	.001
	Patient	.053	.663	.003

(N = 73)

Table C32

Linear Regressions – Manchester Medication Arm

Outcome Measure	Alliance Factor	Beta	P Value	R Squared
MFQ 6 weeks	Total	.227	.083	.052
	Therapist	.114	.387	.013
	Patient	.199	.128	.040
MFQ 12 weeks	Total	.011	.933	.001
	Therapist	.020	.876	.000
	Patient	.035	.790	.001
CGAS 6 weeks	Total	.115	.352	.075
	Therapist	.125	.342	.016
	Patient	.252	.052	.063
CGAS 12 weeks	Total	.037	.759	.002
	Therapist	.168	.191	.028
	Patient	.102	.427	.010
CDRS 6 weeks	Total	.113	.392	.015
	Therapist	.072	.587	.005
	Patient	.084	.516	.007
CDRS 12 weeks	Total	.040	.761	.002
	Therapist	.090	.494	.009
	Patient	.140	.282	.019
HoNOSCA 6 weeks	Total	.192	.142	.037
	Therapist	.079	.536	.007
	Patient	.186	.156	.034
HoNOSCA 12 weeks	Total	.131	.308	.017
	Therapist	.164	.199	.028
	Patient	.030	.815	.002

(N = 17)

Table C33

Linear Regressions - Manchester Combined Arm

Outcome Measure	Alliance Factor	Beta	P Value	R Squared
MFQ 6 weeks	Total	.195	.220	.038
	Therapist	.092	.562	.006
	Patient	.215	.172	.046
MFQ 12 weeks	Total	.234	.132	.055
	Therapist	.100	.527	.011
	Patient	.269	.078	.074
CGAS 6 weeks	Total	.016	.919	.000
	Therapist	.027	.865	.001
	Patient	.053	.740	.003
CGAS 12 weeks	Total	.057	.242	.119
	Therapist	.062	.695	.004
	Patient	.320	.037	.102
CDRS 6 weeks	Total	.081	.615	.006
	Therapist	.003	.998	.001
	Patient	.128	.420	.016
CDRS 12 weeks	Total	.212	.174	.045
	Therapist	.074	.630	.006
	Patient	.261	.091	.068
HoNOSCA 6 weeks	Total	.156	.328	.024
	Therapist	.211	.180	.045
	Patient	.035	.825	.001
HoNOSCA 12 weeks	Total	.185	.236	.034
	Therapist	.053	.735	.003
	Patient	.238	.124	.057

(N = 47)

Table C34

Linear Regressions – Cambridge Medication Arm

Outcome Measure	Alliance Factor	Beta	P Value	R Squared
MFQ 6 weeks	Total	.391*	.005	.154
	Therapist	.357*	.010	.127
	Patient	.212	.139	.044
MFQ 12 weeks	Total	.463*	.020	.215
	Therapist	.543*	.005	.543
	Patient	.196	.167	.039
CGAS 6 weeks	Total	.155	.278	.024
	Therapist	.052	.715	.004
	Patient	.184	.196	.059
CGAS 12 weeks	Total	.243	.087	.059
	Therapist	.245	.082	.082
	Patient	.055	.700	.004
CDRS 6 weeks	Total	.210	.139	.044
	Therapist	.149	.287	.023
	Patient	.158	.271	.025
CDRS 12 weeks	Total	.053	.700	.143
	Therapist	.402*	.004	.161
	Patient	.137	.339	.019
HoNOSCA 6 weeks	Total	.211	.139	.044
	Therapist	.202	.156	.041
	Patient	.103	.474	.011
HoNOSCA 12 weeks	Total	.270	.053	.081
	Therapist	.261	.065	.068
	Patient	.145	.304	.024

*(N = 26) * Significance at p = <0.05*

Table C35

Linear Regressions for Cambridge Combined Treatment Arm

Outcome Measure	Alliance Factor	Beta	P Value	R Squared
MFQ 6 weeks	Total	.021	.860	.002
	Therapist	.004	.432	.009
	Patient	.124	.311	.015
MFQ 12 weeks	Total	.056	.643	.003
	Therapist	.061	.624	.003
	Patient	.014	.896	.000
CGAS 6 weeks	Total	.147	.228	.022
	Therapist	.090	.462	.008
	Patient	.107	.389	.011
CGAS 12 weeks	Total	.033	.779	.001
	Therapist	.019	.870	.000
	Patient	.024	.842	.001
CDRS 6 weeks	Total	.032	.792	.002
	Therapist	.024	.850	.001
	Patient	.067	.593	.005
CDRS 12 weeks	Total	.088	.466	.009
	Therapist	.048	.691	.006
	Patient	.071	.558	.005
HoNOSCA 6 weeks	Total	.151	.216	.024
	Therapist	.069	.586	.004
	Patient	.133	.274	.018
HoNOSCA 12 weeks	Total	.062	.610	.004
	Therapist	.031	.799	.002
	Patient	.053	.663	.003

(N = 26)

Table C36

Logistic Regressions for CGI-I

Outcome Measure	Alliance Factor	Beta	P Value	R Squared (Cox and Snell)
Whole Sample 6 weeks	Total	.022	.861	.002
	Therapist	.004	.432	.008
	Patient	.125	.311	.016
Whole Sample 12 weeks	Total	.147	.228	.022
	Therapist	.090	.462	.008
	Patient	.107	.389	.011
Manchester 6 weeks	Total	.056	.643	.003
	Therapist	.061	.624	.003
	Patient	.014	.896	.000
Manchester 12 weeks	Total	.034	.779	.001
	Therapist	.019	.870	.000
	Patient	.024	.842	.001
Cambridge 6 weeks	Total	.031	.794	.002
	Therapist	.024	.851	.001
	Patient	.067	.594	.005
Cambridge 12 weeks	Total	.090	.466	.009
	Therapist	.048	.691	.007
	Patient	.072	.549	.006
Combined 6 weeks	Total	.152	.217	.025
	Therapist	.069	.587	.004
	Patient	.133	.274	.018
Medication 12 weeks	Total	.062	.610	.004
	Therapist	.031	.799	.002
	Patient	.054	.663	.004

Table C36

Logistic Regressions for CGI-I Continued

Outcome Measure	Alliance Factor	Beta	P Value	R Squared (Cox and Snell)
Man Med 6 weeks	Total	.021	.860	.001
	Therapist	.004	.429	.009
	Patient	.124	.311	.015
Man Med 12 weeks	Total	.056	.644	.003
	Therapist	.062	.625	.003
	Patient	.067	.593	.005
Man Comb 6 weeks	Total	.089	.466	.009
	Therapist	.048	.691	.006
	Patient	.071	.559	.005
Man Comb 12 weeks	Total	.151	.216	.024
	Therapist	.069	.587	.004
	Patient	.133	.269	.018
Cambridge Med 6 weeks	Total	.062	.610	.004
	Therapist	.031	.799	.002
	Patient	.053	.663	.003
Cambridge Med 12 weeks	Total	.014	.896	.000
	Therapist	.147	.228	.022
	Patient	.090	.462	.008
Cambridge Comb 6 weeks	Total	.107	.389	.011
	Therapist	.033	.779	.001
	Patient	.019	.870	.000
Cambridge Comb 12 weeks	Total	.024	.842	.001
	Therapist	.032	.792	.002
	Patient	.024	.850	.001

Analysis of Covariance

Table C37

ANCOVA Analysis – Whole Sample CGAS at 6 Weeks by Treatment and Alliance

	F	df	Sig	R squared
Total	0.088	1, 108	0.770	0.014
Alliance				
Treatment	0.479		0.490	
Alliance x Treatment Interaction	0.469	1, 107	0.500	0.019
Therapist	0.551	1, 108	0.460	0.009
Alliance				
Treatment	0.587		0.445	
Alliance x Treatment Interaction	0.065	1, 107	0.799	0.018
Patient	0.100	1, 108	0.752	0.014
Alliance				
Treatment	0.361		0.549	
Alliance x Treatment Interaction	0.488	1, 107	0.487	0.019

Table C38

ANCOVA Analysis – Whole Sample CGAS at 12 Weeks by Treatment and Alliance

	F	df	Sig	R squared
Total Alliance	0.721	1, 111	0.398	0.009
Treatment	0.085		0.772	
Alliance x Treatment Interaction	1.104	1, 110	0.296	0.008
Therapist Alliance	0.021	1, 111	0.884	0.016
Treatment	0.205		0.651	
Alliance x Treatment Interaction	0.045	1, 110	0.833	0.025
Patient Alliance	1.159	1, 111	0.284	0.005
Treatment	0.097		0.755	
Alliance x Treatment Interaction	2.395	1, 110	0.125	0.007

Table C39

ANCOVA Analysis – Whole Sample HoNOSCA at 6 Weeks by Treatment and Alliance

	F	DF	Sig	R squared
Total Alliance	0.019	1, 108	0.890	0.017
Treatment	0.078		0.780	
Alliance x Treatment Interaction	1.086	1, 107	0.300	0.017
Therapist Alliance	0.044	1, 108	0.835	0.017
Treatment	0.121		0.729	
Alliance x Treatment Interaction	0.605	1, 107	0.438	0.021
Patient Alliance	0.162	1, 108	0.688	0.016
Treatment	0.070		0.792	
Alliance x Treatment Interaction	0.663	1, 107	0.417	0.019

Table C40

ANCOVA Analysis – Whole Sample HoNOSCA at 12 Weeks by Treatment and Alliance

	F	DF	Sig	R squared
Total Alliance	0.307	1, 111	0.581	0.015
Treatment	0.000		0.999	
Alliance x Treatment Interaction	0.656	1, 110	0.420	0.018
Therapist Alliance	0.302	1, 111	0.584	0.015
Treatment	0.041		0.840	
Alliance x Treatment Interaction	0.004	1, 110	0.951	0.024
Patient Alliance	1.872	1, 111	0.174	0.001
Treatment	0.008		0.927	
Alliance x Treatment Interaction	1.899	1, 110	0.171	0.007

Table C41

ANCOVA Analysis – Whole Sample MFQ at 6 Weeks by Treatment and Alliance

	F	Df	Sig	R squared
Total Alliance	0.402	1,108	0.527	0.012
Treatment	0.389		0.534	
Alliance x Treatment Interaction	0.098	1, 107	0.754	0.021
Therapist Alliance	0.947	1, 108	0.333	0.007
Treatment	0.444		0.506	
Alliance x Treatment Interaction	0.987	1, 107	0.323	0.007
Patient Alliance	0.005	1, 108	0.944	0.016
Treatment	0.239		0.626	
Alliance x Treatment Interaction	0.130	1, 107	0.719	0.024

Table C42

ANCOVA Analysis – Whole Sample MFQ at 12 Weeks by Treatment and Alliance

	F	df	Sig	R squared
Total Alliance	0.018	1, 110	0.892	0.013
Treatment	0.515		0.475	
Alliance x Treatment Interaction	0.531	1, 109	0.468	0.022
Therapist Alliance	0.596	1, 110	0.442	0.007
Treatment	0.778		0.380	
Alliance x Treatment Interaction	0.506	1, 109	0.479	0.012
Patient Alliance	0.959	1, 110	0.330	0.004
Treatment	0.372		0.543	
Alliance x Treatment Interaction	0.196	1, 109	0.659	0.011

Table C43

ANCOVA Analysis – Whole Sample CDRS at 6 Weeks by Treatment and Alliance

	F	df	Sig	R squared
Total Alliance	0.043	1, 108	0.836	0.013
Treatment	0.605		0.438	
Alliance x Treatment Interaction	0.126		0.723	0.021
Therapist Alliance	0.032		0.724	0.012
Treatment	0.624		0.410	
Alliance x Treatment Interaction	0.187		0.699	0.022
Patient Alliance	0.045		0.0832	0.015
Treatment	0.618		0.400	
Alliance x Treatment Interaction	0.120		0.586	0.016

Table C44

ANCOVA Analysis – Whole Sample CDRS at 12 Weeks by Treatment and Alliance

	F	df	Sig	R squared
Total Alliance	0.690	1, 110	0.408	0.004
Treatment	1.207		0.274	
Alliance x Treatment Interaction	0.172	1, 109	0.679	0.004
Therapist Alliance	0.524	1, 110	0.514	0.005
Treatment	1.309		0.215	0.003
Alliance x Treatment Interaction	0.184	1, 109	0.624	0.005
Patient Alliance	0.710	1, 110	0.399	0.006
Treatment	1.230		0.299	0.004
Alliance x Treatment Interaction	0.186	1, 109	0.620	0.005

ANCOVA ANALYSIS BY SITE – CAMBRIDGE

Table C45

ANCOVA Analysis – CGAS at 6 Weeks by Treatment and Alliance

	F	df	Sig	R squared
Total Alliance	0.883	1, 48	0.352	0.11
Treatment	1.082		0.304	
Alliance x Treatment Interaction	0.117	1, 47	0.734	0.032
Therapist Alliance	0.175	1, 48	0.678	0.026
Treatment	0.742		0.393	
Alliance x Treatment Interaction	0.003	1, 47	0.956	0.047
Patient Alliance	0.901	1, 48	0.347	0.010
Treatment	0.769		0.385	
Alliance x Treatment Interaction	0.176	1, 47	0.677	0.028

Table C46

ANCOVA Analysis – CGAS at 12 Weeks by Treatment and Alliance

	F	df	Sig	R squared
Total Alliance	1.436	1, 48	0.237	0.010
Treatment	0.401		0.530	
Alliance x Treatment Interaction	0.158	1, 47	0.693	0.028
Therapist Alliance	2.781	1, 48	0.102	0.017
Treatment	0.714		0.402	
Alliance x Treatment Interaction	0.591	1, 47	0.446	0.008
Patient Alliance	0.002	1, 48	0.964	0.040
Treatment	0.069		0.794	
Alliance x Treatment Interaction	0.008	1, 47	0.930	0.062

Table C47

ANCOVA Analysis – HoNOSCA at 6 Weeks by Treatment and Alliance

	F	df	Sig	R squared
Total Alliance	2.470	1, 48	0.123	0.022
Treatment	1.682		0.201	
Alliance x Treatment Interaction	0.178	1, 47	0.675	0.005
Therapist Alliance	1.217	1, 48	0.275	0.003
Treatment	1.317		0.257	
Alliance x Treatment Interaction	0.002	1, 47	0.967	0.024
Patient Alliance	1.292	1, 48	0.261	0.001
Treatment	0.874		0.354	0.001
Alliance x Treatment Interaction	0.232	1, 47	0.632	0.018

Table C48

ANCOVA Analysis – HoNOSCA at 12 Weeks by Treatment and Alliance

	F	df	Sig	R squared
Total Alliance	2.535	1, 48	0.118	0.017
Treatment	1.070		0.306	
Alliance x Treatment Interaction	0.383	1, 47	0.539	0.004
Therapist Alliance	1.109	1, 48	0.298	0.012
Treatment	0.785		0.380	0.012
Alliance x Treatment Interaction	1.073	1, 47	0.305	0.010
Patient Alliance	1.427	1, 48	0.238	0.005
Treatment	0.436		0.512	
Alliance x Treatment Interaction	0.255	1, 47	0.616	0.021

Table C49

ANCOVA Analysis – MFQ at 6 Weeks by Treatment and Alliance

	F	df	Sig	R squared
Total Alliance	0.737	1, 48	0.395	0.025
Treatment	0.182		0.672	
Alliance x Treatment Interaction	0.818	1, 47	0.370	0.029
Therapist Alliance	6.627*	1, 48	0.013	0.049
Treatment	2.995		0.089	
Alliance x Treatment Interaction	2.709	1, 47	0.105	0.133
Patient Alliance	0.203	1, 48	0.654	0.037
Treatment	0.039		0.845	
Alliance x Treatment Interaction	0.252	1, 47	0.618	0.053

Table C50

ANCOVA Analysis – MFQ at 12 Weeks by Treatment and Alliance

	F	df	Sig	R squared
Total Alliance	0.662	1, 48	0.420	0.022
Treatment	0.555		0.460	
Alliance x Treatment Interaction	0.553	1, 47	0.461	0.032
Therapist Alliance	0.602	1, 48	0.442	0.023
Treatment	0.570		0.454	
Alliance x Treatment Interaction	0.716	1, 47	0.402	0.029
Patient Alliance	0.143	1, 48	0.707	0.033
Treatment	0.295		0.590	
Alliance x Treatment Interaction	0.027	1, 47	0.869	0.054

Table C51

ANCOVA Analysis – CDRS at 6 Weeks by Treatment and Alliance

	F	df	Sig	R squared
Total Alliance	0.043	1, 48	0.834	0.012
Treatment	0.615		0.428	
Alliance x Treatment Interaction	0.126	1, 47	0.723	0.021
Therapist Alliance	0.032	1, 48	0.724	0.015
Treatment	0.604		0.434	
Alliance x Treatment Interaction	0.177	1, 47	0.689	0.022
Patient Alliance	0.045	1, 48	0.0832	0.016
Treatment	0.618		0.400	
Alliance x Treatment Interaction	0.122	1, 47	0.596	0.015

Table C52

ANCOVA Analysis – CDRS at 12 Weeks by Treatment and Alliance

	F	df	Sig	R squared
Total Alliance	0.599	1, 48	0.408	0.003
Treatment	1.207		0.274	
Alliance x Treatment Interaction	0.183	1, 47	0.679	0.004
Therapist Alliance	0.532	1, 48	0.514	0.005
Treatment	1.319		0.205	0.002
Alliance x Treatment Interaction	0.184	1, 47	0.624	0.005
Patient Alliance	0.710	1, 48	0.399	0.006
Treatment	1.230		0.299	0.004
Alliance x Treatment Interaction	0.186	1, 47	0.620	0.005

ANCOVA ANALYSIS BY SITE – MANCHESTER

Table C53

ANCOVA Analysis – CGAS at 6 Weeks by Treatment and Alliance

	F	df	Sig	R squared
Total Alliance	0.821	1, 57	0.369	0.001
Treatment	1.512		0.224	
Alliance x Treatment Interaction	0.993	1, 56	0.323	0.001
Therapist Alliance	0.524	1, 57	0.472	0.004
Treatment	1.366		0.247	
Alliance x Treatment Interaction	0.265	1, 56	0.609	0.017
Patient Alliance	0.301	1, 57	0.585	0.008
Treatment	1.374		0.246	
Alliance x Treatment Interaction	2.223	1, 56	0.142	0.014

Table C54

ANCOVA Analysis – CGAS at 12 Weeks by Treatment and Alliance

	F	df	Sig	R squared
Total Alliance	0.182	1, 60	0.672	0.029
Treatment	0.031		0.862	
Alliance x Treatment Interaction	2.144	1, 59	0.148	0.010
Therapist Alliance	0.386	1, 60	0.537	0.026
Treatment	0.071		0.791	
Alliance x Treatment Interaction	0.001	1, 59	0.973	0.043
Patient Alliance	1.472	1, 60	0.230	0.008
Treatment	0.001		0.975	
Alliance x Treatment Interaction	3.838	1, 59	0.055	0.038

Table C55

ANCOVA Analysis – HoNOSCA at 6 Weeks by Treatment and Alliance

	F	df	Sig	R squared
Total Alliance	0.877	1, 57	0.353	0.004
Treatment	1.008		0.301	
Alliance x Treatment Interaction	0.239	1, 56	0.627	0.016
Therapist Alliance	0.717	1, 57	0.401	0.007
Treatment	0.975		0.328	
Alliance x Treatment Interaction	0.035	1, 56	0.852	0.024
Patient Alliance	0.230	1, 57	0.634	0.016
Treatment	0.948		0.334	0.016
Alliance x Treatment Interaction	2.458	1, 56	0.123	0.010

Table C56

ANCOVA Analysis – HoNOSCA at 12 Weeks by Treatment and Alliance

	F	df	Sig	R squared
Total Alliance	0.191	1, 60	0.663	0.029
Treatment	0.097		0.756	
Alliance x Treatment Interaction	1.937	1, 59	0.169	0.13
Therapist Alliance	1.713	1, 60	0.196	0.004
Treatment	0.093		0.761	
Alliance x Treatment Interaction	0.000	1, 59	0.995	0.021
Patient Alliance	0.381	1, 60	0.539	0.026
Treatment	0.020		0.888	
Alliance x Treatment Interaction	2.411	1, 59	0.126	0.002

Table C57

ANCOVA Analysis – MFQ at 6 Weeks by Treatment and Alliance

	F	df	Sig	R squared
Total Alliance	3.600	1, 57	0.063	0.062
Treatment	3.053		0.086	
Alliance x Treatment Interaction	0.191	1, 56	0.663	0.049
Therapist Alliance	0.600	1, 57	0.442	0.028
Treatment	0.172		0.680	
Alliance x Treatment Interaction	0.574	1, 56	0.452	0.038
Patient Alliance	0.066	1, 57	0.798	0.004
Treatment	2.240		0.140	
Alliance x Treatment Interaction	0.938	1, 56	0.337	0.003

Table C58

ANCOVA Analysis – MFQ at 12 Weeks by Treatment and Alliance

	F	df	Sig	R squared
Total Alliance	0.035	1, 59	0.715	0.006
Treatment	2.345		0.131	
Alliance x Treatment Interaction	0.048	1, 58	0.828	0.010
Therapist Alliance	2.170	1, 59	0.146	0.039
Treatment	2.528		0.117	
Alliance x Treatment Interaction	1.312	1, 58	0.257	0.044
Patient Alliance	0.740	1, 59	0.393	0.016
Treatment	1.771		0.188	
Alliance x Treatment Interaction	0.540	1, 58	0.465	0.008

Table C59

ANCOVA Analysis – CDRS at 6 Weeks by Treatment and Alliance

	F	df	Sig	R squared
Total Alliance	0.043	1, 57	0.834	0.011
Treatment	0.617		0.428	
Alliance x Treatment Interaction	0.126	1, 56	0.723	0.022
Therapist Alliance	0.032	1, 57	0.724	0.016
Treatment	0.604		0.436	
Alliance x Treatment Interaction	0.178	1, 56	0.679	0.032
Patient Alliance	0.045	1, 57	0.0832	0.017
Treatment	0.618		0.400	
Alliance x Treatment Interaction	0.123	1, 56	0.587	0.016

Table C60

ANCOVA Analysis – CDRS at 12 Weeks by Treatment and Alliance

	F	df	Sig	R squared
Total Alliance	0.601	1, 57	0.409	0.004
Treatment	1.019		0.276	
Alliance x Treatment Interaction	0.183	1, 56	0.679	0.003
Therapist Alliance	0.532	1, 57	0.514	0.005
Treatment	1.319		0.205	0.002
Alliance x Treatment Interaction	0.184	1, 56	0.624	0.005
Patient Alliance	0.710	1, 57	0.399	0.006
Treatment	1.229		0.299	0.004
Alliance x Treatment Interaction	0.187	1, 56	0.620	0.005

SMM Analysis

Example of Stata v.10 Input file

Honosca

```
. do ADAPT_alliance_smm4b

. program smm_adapt_alliance4b
  1.
. xi: regress totalalliance i.mancam  age i.gender honosc_1  if
treat==2
  2. predict alliance
  3.
. xi: regress honosc_ch i.mancam  age i.gender honosc_1  if treat==2
  4. predict htreat
  5.
. xi: regress honosc_ch i.mancam  age i.gender honosc_1  if treat==1
  6. predict hcontrol
  7.
. gen ite=htreat-hcontrol
  8.
. reg ite alliance
  9.
. drop alliance htreat hcontrol ite
 10.
. end

.
end of do-file

. bootstrap "smm_adapt_alliance4b" _b, reps(1000) dots
```

Table C61

SMM Analysis CGAS score at 12 weeks

Variable	Reps	Observed	Bias	Standard Error	95% CI
Alliance	1000	11.147	-3.774	9.198	(-6.903, 29.197) (N) (-9.454, 26.216) (P) (-0.917, 44.167) (BC)
Average Treatment Effect	1000	-4.471	.9767	3.284981	(-10.917, 1.975) (N) (-9.936, 3.131) (P) (-13.231, 0.644) (BC)

Note: N = normal
P = percentile
BC = bias-corrected

Table C62

SMM Analysis CDRS t score at 12 weeks

Variable	Reps	Observed	Bias	Standard Error	95% CI
Alliance	1000	5.761	-1.280	10.036	(-13.931, 25.454) (N) (-11.889, 25.098) (P) (-7.544, 33.962)
Average Treatment Effect	1000	-18.245	3.753	27.854	(-72.905, 36.413) (N) (-73.045, 33.528) (P) (-95.786, 20.002) (BC)

Table C63

SMM Analysis MFQ score at 12 weeks

Variable	Reps	Observed	Bias	Standard Error	95% CI
Alliance	1000	-14.169	7.594	14.011	(-41.666, 13.326) (N) (-35.840, 22.688) (P) (-67.807, 0.40783) (BC)
Average Treatment Effect	1000	5.099	-1.578	4.469	(-3.670, 13.869) (N) (-4.528, 12.507) (P) (-1.365, 22.918) (BC)