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Alliance and Mechanisms of Medication Adherence in Pediatric Psychiatric Practice

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Alliance and Mechanisms of Medication Adherence in Pediatric Psychiatric Practice

by

Alessandro De Nadai

A thesis submitted in partial fulfillment
of the requirements for the degree of
Master of Science
Department of Psychology
College of Arts and Sciences
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Dedication

I would like to thank my faculty mentors, Drs. Eric Storch and Marc Karver, for their remarkable support throughout my graduate training and for their incredibly generous contributions to my professional and personal development. I would also like to thank my parents for their unwavering support throughout the past three decades, for which I am exceptionally grateful. And finally, I would like to thank my wonderful wife June for her support and guidance, without which none of this work would be possible.

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Abstract

Psychiatric medications have been established as an efficacious treatment for pediatric psychopathology (Comer, Olfson, & Mojtabai, 2010), with approximately 3.9% of American children receiving psychotropic medication in a given year (Olfson, Marcus, Weissman, & Jensen, 2002). However, medication adherence for these conditions is suboptimal, with over 50% of children discontinuing treatment before the period recommended for full therapeutic benefit (e.g., Gau et al., 2006; Murray, de Vries, & Wong, 2004). This is highly problematic because pediatric psychopathology is associated with substantial functional impairment and reduced quality of life, as well as increased risk for suicidality (e.g., Bridge, Goldstein, & Brent, 2006; Kessler, Berglund, Demier, Jin, Merikangas, & Walters, 2005).

Unfortunately, few empirical data exist about variables that may relate to medication adherence in pediatric pharmacotherapy. However, the psychotherapy literature has identified several potent mechanisms of behavior change that may be related to adherence, including therapeutic alliance, motivation for behavior change, and expectancies for positive treatment outcomes. We aimed to evaluate the role of these factors in a sample of 65 outpatient youth ages 7-17 years and their families, where questionnaires evaluating these constructs were administered at patients' first session with a new psychiatric provider. Study results revealed several associations with adherence among these hypothesized predictors, with parental motivation for child behavior change being a particularly robust predictor of adherence. Results are discussed in the context of a new pathway to progress in pediatric psychiatry, where instead

of focusing predominantly on development of new pharmacological agents, identifying methods to adjust the therapeutic relationship may be indicated in order to maximize patient outcomes in pharmacotherapy.

Overview and Scope of the Problem

The purpose of this study is to address factors that may interfere with adherence to pharmacotherapy in pediatric psychopathology. While there is a dearth of research addressing factors that predict nonadherence to this treatment modality, it remains an issue with wide-ranging consequences for both research and everyday clinical practice. The central hypothesis is that therapeutic alliance, motivation for behavior change, and expectancies for treatment outcome on the part of both child and parent will predict subsequent adherence to medication treatment.

Pediatric psychopathology is associated with impaired psychosocial functioning, school interference, and even suicide (Bridge, Goldstein, & Brent, 2006; Kessler, Berglund, Demier, Jin, Merikangas, & Walters, 2005; Langley, Bergman, McCracken, & Piacentini, 2004; US Surgeon General, 1999). Such mental health difficulties are highly prevalent, with over 20% of children and adolescents having a psychological disorder at some point in their lives (Merikangas et al., 2010). Moreover, many disorders run a chronic course without intervention and have high rates of recurrence, which further compound longitudinal impairment (Birnbaum et al., 2005; Ferdinand & Verhulst, 1995; Pine, Cohen, Gurley, Brook, & Ma, 1998; Weissman et al., 1999). Pediatric psychopathology at all ages also constitutes a public health burden. For instance, annual costs attributable to attention deficit-hyperactivity disorder (ADHD) are \$42.5 billion (Pelham, Foster, & Robb, 2007), to anxiety disorders, \$42.3 billion (Greenberg et al., 1999), and to depression, \$83.1 billion (Greenberg et al., 2003).

Pharmacotherapy has been established as an efficacious treatment for a variety of pediatric psychiatric conditions (Comer, Olfson, & Mojtabai, 2010). Given evidence of efficacy and ease of dissemination relative to certain psychosocial interventions (e.g., cognitive-behavioral therapy), medication treatment has become widespread for these conditions, as approximately 3.9% of American children receive psychotropic medication in a given year (Olfson, Marcus, Weissman, & Jensen, 2002).

Despite the important role of pharmacotherapy for pediatric psychopathology, children do not always receive these treatments as intended. One substantial barrier to pharmacotherapy for pediatric psychological disorders is medication adherence, with over 50% of children with anxiety and depression discontinuing their pharmacotherapy trial before the recommended period (Murray, de Vries, & Wong, 2004; Richardson, DiGiuseppe, Christakis, McCauley, & Katon, 2004) and adherence rates for stimulants in youth with ADHD ranging as low as 35% (Gau et al., 2006). This is troublesome for multiple reasons. First, it attenuates treatment outcome, as not adhering to the proposed treatment takes an efficacious intervention and reduces its real-world effectiveness (Osterberg & Blaschke, 2005). To date, there is relatively little research into adherence for medicinal interventions in pediatric psychopathology (Weiss & Gorman, 2005). This is especially troubling since acute medication discontinuation may be associated with increased suicide risk posed by SSRIs that led to the Federal Drug Administration (FDA) imposing a “black box” warning on antidepressants (Goodman, Murphy, & Storch, 2007; Murphy, Segarra, Storch, & Goodman, 2008; Weiss & Gorman, 2005). Second, nonadherence to treatment creates additional cost and inefficiency in both clinical and research practice. For example, heterogeneous medication treatment response has been observed in research pediatric antidepressant and stimulant treatment (Vasa, Carlino, & Pine, 2006; Swanson et al., 2001),

which has made disentangling the mechanisms of treatment effect difficult. Medication adherence has been proposed as one reason for response variation in a variety of conditions (Urquhart, 1997). When incorporating a variety of associated costs (e.g., medical costs of hospitalization, missed time at work), adult antidepressant nonadherence has been associated with an additional yearly cost of ranging from \$750 to \$2,000 per nonadhering patient (Revicki, Simon, Chan, Katon & Heiligenstein, 1998; Thompson, Peveler, Stephenson, & McKendrick, 2000), and reducing antidepressant discontinuation by 40% has been associated with a reduction in medical costs of \$1,428 per patient year (Sheehan, Eaddy, Shah, & Mauch, 2005). In ADHD, the costs involved as a result of diagnosis are nearly three times that of the average medical patient, despite 41% of patients not even filling a physician's prescription for pharmacotherapy (Swenson et al. 2003). Furthermore, such nonadherence can present difficulty to practicing clinicians when they attempt to ascertain the reasons for incomplete treatment response, as it may be due to an ineffective medication, an incorrect diagnosis, or perhaps adherence is suboptimal. Such ambiguity regarding the causes of treatment response could lead to unnecessary changes in medication, as observed ineffectiveness may not be due to lack of efficacy of the antidepressant but rather attributable to patient nonadherence.

Examining Nonadherence to Medication Treatment for Pediatric Psychopathology

While medication nonadherence is a pervasive problem in pediatric psychopathology, little is known about the reasons for such poor adherence (Sanchez, Crismon, Barner, Bettinger, & Wilson, 2005; Weiss & Gorman, 2005). One focus in adherence research has been on side effects, which has been identified as a robust predictor of adherence (Osterberg & Blasckhe, 2005). Medicinal side effects have been identified as a significant concern for both youth (Cheung, Levitt, & Szalai, 2003) and

parents (Stevens et al., 2009), and adherence for tricyclic antidepressants (which are similar in efficacy to the newer SSRIs, but are associated with more substantial side effects) has been observed to be lower than that of SSRIs (Murray et al., 2004). Defining nonadherence differs among medical conditions, as varying rates of medication usage attenuate therapeutic effects differently among conditions. For example, in HAART therapy for AIDS, over 95% medication usage is necessary for medication to be efficacious (Chesney, 2003). A demarcation of 70% medication usage has been applied for antidepressants in youth (Woldu et al., 2011) and 80% adherence has been used as a criterion for adherence in youth with simulant medication (Perwien, Hall, Swensen, & Swindle, 2004). Unfortunately, suboptimal adherence for psychiatric medication with youth remains a substantial problem (Pappadopulos et al., 2009; Woldu et al., 2011). In order to understand the scope of research in adherence to pharmacotherapy for pediatric psychopathology, an overview of the existing body of research follows. Traditional patient-level models of adherence are addressed first, and then other novel models (including patient-provider interaction modeling through the therapeutic alliance) are considered.

Health beliefs model. The Health Beliefs Model (HBM; Rosenstock, 1966; Rosenstock, 1974) focuses on patient knowledge and attitudes, with a particular focus on perceived disease threat and perceived benefits of treatment in the context of perceived barriers to such treatment. Under this framework, a patient's adherence and health behavior is influenced through a process where a patient considers his/her susceptibility to a disease, the degree of threat that it poses, and the costs of a certain intervention (e.g., financial, side effects, inconvenience in dosing, etc.) in contrast to its perceived benefits. The HBM has been indicated in a variety of adherence to health behaviors, ranging from cancer screening to dental visits (Janz, Wren, Schottenfeld, &

Guire, 2003; Pine et al., 2000). However, it is limited by its reliance on individual patient-level health beliefs, and does not account for factors such as continual interpersonal dynamics between patients and others (e.g., clinicians, family members, etc.).

Theory of planned behavior. The Theory of Planned Behavior (TPB; Ajzen, 1991) is a model that stems from research in social psychology, which has more recently been introduced into research in health behavior relative to the HBM. In the context of medication adherence, TPB models adherence via perceived behavioral control and perceived social norms predicting intention to adhere to a medication regimen, which then predicts actual adherence. Thus, this model accounts to some degree for an interpersonal dynamic through perceived social norms, but does not directly account for the specific dynamic between clinician and patient (which is amorphously grouped under the larger umbrella of perceived social norms). The TPB model has been used to predict adherence to recommendations for a variety of health behaviors, including physical activity (Armitage, 2005), sexual risk behaviors (Koniak-Griffin & Stein, 2006), and substance use (Peters, Kok, & Abraham, 2008). Meta-analyses have found it to predict up to 52% of variance in intention and 34% of variance in behavior (including health behavior, but also including other constructs; Armitage & Conner, 2001; Godin & Kok, 1996; McGilligan, McClenahan, & Adamson, 2009), which is a large effect, but by no means perfectly explanatory.

Social cognitive theory. Social cognitive theory is another theory that has been implicated in adherence and health promotion behavior (Bandura, 1998). In the context of medication adherence, it focuses largely on two factors: the expectation for positive outcomes,

and expectations about the ability to actually complete the adherence behavior (i.e., perceived self-efficacy). Perceived self-efficacy is very similar to perceived behavioral control in TPB models, and expectation for positive outcomes overlaps very much with perceived benefits seen in the HBM. Social cognitive theory has also been applied in predicting increased physical activity and the effectiveness of self-management of diabetes and heart disease (Clark & Dodge, 1999; Johnston-Brooks, Lewis, & Garg, 2002). Social cognitive theory has found some success in predicting adherence in conditions such as osteoporosis, where 15% of the variance in medication adherence was explained by the model (Resnick, Wehren, & Orwig, 2003), but nevertheless it remains an imperfect predictor of adherence to pharmacotherapy. One limiting factor of this model is that it is restricted to patient-level variables, and neglects provider-level variables and patient-provider interactions.

Beyond Traditional Models of Medication Adherence

Thus, adherence to prescribed treatment for a variety of illnesses is remarkably poor despite the existence of these popular patient-level models (Osterberg & Blachke, 2005), and pediatric psychopathology is no exception (Case, 2011; Waschbusch, Pelham, Waxmonsky, & Johnston, 2009; Woldu et al., 2011). In addition to these traditional models of medication adherence, the psychotherapy literature has identified several behavioral mechanisms that logically may underlie medication adherence. In particular, therapeutic alliance has been a robust predictor of treatment outcomes in pediatric and adult psychotherapy (Karver, Handelsman, Fields, & Bickman, 2006; Shirk & Karver, 2003). In addition, motivation for behavior change and treatment expectancies have been associated with medication adherence for other medical conditions (Konkle-Parker, 2001) and treatment progress in psychotherapy (Miller & Rollnick, 2002; Wampold, 2001). Youth and parents who do not perceive their clinician as their ally, have

low motivation to change, and/or a pessimistic attitude towards treatment may be less likely to continue psychotherapeutic medication, especially given the associated costs, inconvenience of appointments, potentially long duration before clinical benefits are achieved, and the possibility of side effects. Given that one method to improve the efficacy of existing treatments is to identify and enhance their active ingredients (Shirk, 2001), and also that adherence is a necessary, moderating ingredient for medication treatment, research on these potential mechanisms underlying medication adherence for pediatric psychopathology has the implication of identifying domains where the effectiveness of these treatments can be improved on a large scale. A brief review of the evidence and logic for these mechanisms underlying medication adherence in pediatric psychiatry follows.

Therapeutic alliance. The therapeutic alliance is a concept that has its original historical roots in Freud, who highlighted the collaborative relationship between therapist and patient as a mechanism to facilitate transference, which he saw as a necessary component for therapeutic change (Meissner, 1996; Safran & Muran, 2000). The contemporary conceptualization of alliance stems from work by Bordin (1979), who divided the alliance into the components of therapist-patient bond, agreement on the tasks to be performed in therapy, and agreement on the goals to be achieved in therapy. While there may be some disagreement with this overall conceptualization for all populations (DiGiuseppe, Linscott, & Jilton, 1996), there is a general consensus that the alliance has affective (e.g., bond) and technical components (e.g., task and goals; Meissner, 1996; Safran & Muran, 2000; Shirk, Caporino, & Karver, 2010). In youth, the traditional alliance components of bond, task, and goals have been integrated into a model where therapeutic alliance is characterized by the patient perceiving the therapist as someone who can

be counted on in overcoming problems and distress (Shirk & Karver, 2006). Within this general framework, both therapists and patients bring individual characteristics that influence the development of alliance through treatment. For example, therapists who present as flexible, honest, trustworthy, confident, warm, interested, open, and respectful tend to form stronger alliances (Ackerman & Hilsenroth, 2003; Castro-Blanco & Karver, 2010), while therapist personality traits such as neuroticism, rule consciousness, independence, dominance, social control, perfectionism, and those who espouse impression management has predicted poorer alliance in child and adolescent psychotherapy (Doucette, Boley, Rauktis, & Pleczkowski, 2004). Moreover, such an alliance is not fixed at treatment onset or determined a priori, but rather can fluctuate throughout the course of treatment (Safran & Muran, 2000). The alliance has been indicated to have a robust effect throughout adult and pediatric psychotherapy, with effect sizes for adults at estimated at $r = .22$ and for children and adolescents at $r = .20$ (Martin, Garske, & Davis, 2000; Shirk, Karver, & Brown, 2011).

An analogue to therapeutic alliance that has been considered in the medical literature is the construct of doctor-patient communication. Traditionally, it has been considered that doctor-patient communication was adequate and not particularly important for medicine (Stewart, 1995). However, over the past several decades a consensus has been established that doctor-patient interaction has a substantial impact on medical treatment with regard to adherence, satisfaction, and outcomes of interest (Zolnierek & DiMatteo, 2009). This focus is partly reflected on the contemporary term of “adherence” to medication which refers to active patient behavior in following a recommended prescribed pharmaceutical regimen, whereas the previously used term “compliance” indicated a unilateral commanding of patients. However, therapeutic alliance is somewhat more comprehensive than doctor-patient communication, which

has not been delineated into the bond, task, and goals subconstructs, but rather remains a somewhat amorphous construct with few data related to adherence.

Therapeutic alliance has also been related to a variety of outcomes, in addition to symptom reduction in psychological treatments. In the psychotherapy literature, alliance has been indicated in one study as the strongest predictor of early termination of psychotherapy (Garcia & Weisz, 2002), poor parental alliance with the therapist in particular has been indicated as a predictor of dropout (Hawley & Weisz, 2005), and conversely there are some indications of a linear relationship between positive parent-clinician alliance and pediatric psychotherapy outcomes (Karver et al., 2006; Kazdin, Marciano, & Whitley, 2005; Kazdin, Whitley, & Marciano, 2006). As a whole, attenuated alliance has been associated with premature dropout for a variety of internalizing and externalizing problems for both adults and youth (Gavin, Wamboldt, Sorokin, Levy, & Wamboldt, 1999; Johansson & Eklund, 2006; Kazdin & Whitley, 2006; Meier, Donmall, McElduff, Barrowclough, & Heller, 2006; Pereira, Lock, & Oggins, 2006). Alliance has also been indicated to be a major component of treatment engagement in youth (Green et al., 2001; Karver et al., 2006). In treatment for adult depression, substantial effects of alliance on treatment outcome have been observed for pharmacotherapy, where average alliance throughout treatment has been observed to account for 19-21% of the variance in the amelioration of depressive symptoms (Krupnick et al., 1996).

Nevertheless, research on the therapeutic relationship has been relatively neglected in medication treatment (Klein et al., 2003), with the exigent body of work in considering alliance and treatment outcome being restricted to eight studies with adults, and no studies with youth have been published (Fields, Totura, Tarquini, & Karver, under review). Given the observed relationships to a variety of outcomes, there are indications that such alliance may be a potent

mechanism to understand and improve medication adherence. Some previous research has implicated alliance as a predictor of adherence for multiple medical issues, including pediatric asthma treatment (Gavin et al., 1999) and medication treatment for schizophrenia and bipolar disorder (Adams & Scott, 2000; Frank & Gunderson, 1990; Lacro, Dunn, Dolder, Leckband, & Jeste, 2002). Additionally, desire to comply with one's psychiatrist has been indicated to be strongly related to actual adherence (Cochran & Gitlin, 1988). In the medical field as a whole, the construct of doctor-patient communication (which has some conceptual relationship with alliance) has also been associated with medication adherence. Meta-analytic estimates indicate that the odds of nonadherence are 1.47 times greater if a physician is a poor communicator, while they are 2.16 times better if a physician is a good communicator (Zolnierek & DiMatteo, 2009). However, this is a modifiable effect, as training physicians in communication skills increases the odds of adherence by 1.62, which is a larger effect than conventional pharmaceutical interventions to prevent breast cancer and serious cardiac incidents (Zolnierek & DiMatteo, 2009). Moreover, this effect of communication skills on adherence is even stronger if the provider is a pediatrician, which is hypothesized to be due to the increased skill required to communicate with both child and parent in understandable terms (Zolnierek & DiMatteo, 2009). In adult research, a chain of events has been identified where physicians' communication style influences initial beliefs about medication, which influences satisfaction, which predicts better adherence to antidepressants (Bultman & Svarstad, 2000).

The alliance may also be of importance in the context of both actual risk and fears related to the FDA-issued black box warning for antidepressant use in children and young adults (Federal Drug Administration, 2004), which may have affected overall pediatric antidepressant use. For example, paroxetine prescriptions for patients under age 18 years declined 25-34% in

the 6 months following a related FDA public health advisory (Pamer et al., 2010). While the black box warning is intended to provide adequate protection against risk, it may also result in increased barriers to treatment, and a patient who does not properly understand the risk and benefits of such medication may struggle to make an informed decision.

These observations also fit into context with previous research that indicates that parents who perceive higher risk of antidepressants are less likely to bring children for another visit in the subsequent year, whereas perceived benefits predicted the likelihood of another visit (Stevens et al., 2009). Forming a strong alliance can serve to open communication pathways, with the likely outcome of reducing fears and misperceptions of medication treatment. Unfortunately, while doctor-patient communication and therapeutic alliance have been implicated in adherence and outcome for a variety of medical and psychological conditions, there exists a gap in the literature with regard to these variables in medication treatment for pediatric psychopathology.

Motivation for behavior change. Motivation for behavior change is another potent mechanism that may underlie adherence to medication treatment for pediatric psychological disorders. This multifaceted construct addresses patient acknowledgement of problem behaviors along with the desire and willingness to change them (Miller & Rollnick, 2002). It has been most commonly conceptualized in modern research in the form of stages of patient readiness for change, where patients may have not yet considered change (precontemplation), may be considering change (contemplation), may be actively planning to change (preparation), or are taking action and/or working to maintain such change (action and maintenance, Norcross, Krebs, & Prochaska, 2011). Research with adults has indicated that lack of such motivation is associated with poorer outcomes, reduced adherence to treatment recommendations, and treatment

discontinuation (Hettema, Steele, & Miller, 2005). While originally promulgated in the treatment of alcoholism (e.g., Miller, 1983), lack of motivation for behavior change has interfered with medication adherence in a variety of conditions, such as diabetes, asthma, and AIDS (Rubak, Sandbæk, Lauritzen, & Christensen, 2005). Motivation has also been indicated to predict favorable outcomes for benzodiazepine treatment for panic disorder and generalized anxiety disorder in adults (Beitman et al., 1994; Reid, Nair, Mistry, & Beitman, 1996; Wilson, Bell-Dolan, & Beitman, 1997).

Unfortunately, there are indications that some children may be unmotivated to change in mental health treatment (Jungbluth & Shirk, 2009). Thus, given evidence indicating the importance of motivation on adherence behavior, low motivation can reduce the actual effectiveness of interventions established as efficacious. Parental motivation for change must also be considered as well, as it has been indicated to have influence on treatment attendance (Nock & Photos, 2006), and parents are the ultimate gatekeepers as far as bringing children to treatment sessions, refilling prescriptions, and often in administering doses. As a whole, parents and children are unlikely to follow through with treatment if they are unmotivated to change. This lack of motivation is particularly troubling considering the variety of barriers that exist in the use of pharmacotherapy for pediatric psychopathology, including medicinal side effects, the need to take the prescribed medication on a regular basis, and the cost of medication (Nutt, 2010). Thus, sufficient motivation for change may be necessary to fight through these barriers, and may need to be addressed by the clinician if such motivation is insufficient. While the majority of research in psychopharmacology for pediatric psychological disorders has focused on pharmacokinetics, if patients do not participate in treatment (i.e., take and refill the prescribed medication), then they cannot benefit from it (Case, 2011). Relatively little research exists in

addressing motivation in pharmacotherapy in pediatric psychopathology (Hack & Chow, 2001), but its role may differ in some instances relative to other problems. For example, alcohol use is often engaged in as a pleasurable activity (and such enjoyment may reduce motivation to change from the status quo), while anxiety and depression are often undesirable and thus patients may have some innate motivation to change, but may have difficulty making treatment a high enough priority given other demands to adhere to it successfully (Otto & Hofmann, 2010). Additionally, the relative importance of parent and child motivation for change in this situation has not been identified (e.g., must both parties be motivated, or must only parents be motivated, or if both child and parents are motivated are there enhanced outcomes, etc.). In any case, a body of evidence suggests that motivation for behavior change is related to a variety of adherence and outcome behaviors, and is likely relevant for antidepressant treatment for youth who experience psychological problems.

Treatment expectations. In addition to motivation for behavior change, another powerful predictor of a variety of behaviors is treatment expectations. Expectancies research in the context of psychological treatments has traditionally been partitioned into two major categories: role expectancies and outcome expectancies (Delsignore & Schnyder, 2007; Dew & Bickman, 2005). Role expectancies refer to the expectations patients have for their participatory role in treatment, as well as that of the clinician (e.g., should a patient spend 15 minutes or an hour with a doctor, should a doctor be expected to provide medication or psychotherapy or both, should a clinician be authoritative or collaborative, etc.). Outcome expectancies refer to expectations patients have for positive treatment outcomes (i.e., will treatment relieve the problem at hand). The majority of research in treatment expectancies has focused on outcome

expectancies, with role expectancies providing more inconsistent results in predicting overall outcome (Arnkoff et al., 2002; Delsignore & Schnyder, 2007; Halperin, Weitzman, & Otto, 2010), although such role expectations have been indicated to predict alliance (Al-Darmaki & Kivlighan, 1993; Patterson, Uhlin, & Anderson, 2008; Tokar, Hardin, Adams, & Brandel, 1996). In the psychotherapy literature, discrepancies between parental role and outcome expectancies have predicted premature treatment termination (Nock & Kazdin, 2001), and outcome expectancies at the first session have predicted parental adherence to treatment procedures as late as the seventh session (Nock et al., 2006). Furthermore, in cognitive behavioral therapy for adults with anxiety disorders, Westra, Dozois, and Marcus (2007) identified a mediational model where pretreatment expectations for anxiety change led to increased homework adherence, which in turn led to improved treatment outcome. Lack of appropriate treatment expectations may interfere with potentially efficacious treatment for children seeking psychiatric care.

Such expectations may be influential for medication treatment for pediatric psychopathology. For example, depressed adults who are skeptical towards antidepressant therapy have been associated with a 62% increased risk of premature SSRI discontinuation (Aikens, Kroenke, Swindle, & Eckert, 2005). Conversely, some patients may have unrealistic expectations of rapid and complete relief, which can lead to discouragement with the proposed treatment. Given previous research in pediatric psychiatry that indicates adherence has been related to perceived medication efficacy (e.g., RUPP Anxiety Study Group, 2003), if a patient has a negative attitude towards medication, he/she may not attribute positive effects to such medication, and then may not adhere to the proposed treatment.

Conversely, expectations are also reflected in the strong placebo effect that has been indicated in youths with ADHD, anxiety, and depression, with approximately 25-35% of patients

showing response to medication placebo (with the notable exception of OCD; Pediatric OCD Study Team, 2004; Walkup et al., 2008; Waschbusch et al., 2009). However, instead of considering this effect as solely a nuisance in research trials, perhaps this is an area to address in psychiatric treatment, where training providers to create appropriate expectancies can maximize treatment benefits. While poor expectancies may reduce treatment adherence, appropriate and optimistic expectancies can potentially maximize such adherence.

Integrating Potential Mechanisms of Medication Adherence in Pediatric Psychiatry

A conceptual model of how therapeutic alliance, motivation, and expectancies are hypothesized to work in medication adherence for pediatric psychopathology can be seen in Figure 1. Although empirical data pertaining to psychiatric practice among children is limited (Hack & Chow, 2001), given the abundance of circumstantial evidence, there is reason to believe that parent and child need to see the therapist as an ally, want to change, and expect change to happen in order to maximize adherence to medication treatment for pediatric psychopathology. Of particular note in this model is the parental role in adherence; in some cases, the parent may be even more important for achieving treatment adherence than the child, given their authority over prescription refill, medication administration, insurance/cost coverage, and child reliance on parent for attending treatment sessions. It is expected that parents and children with a stronger therapeutic alliance with the clinician, greater motivation to participate in treatment, and strong expectancies for treatment efficacy will show better medication adherence. Moreover, alliance is predicted to mediate (or partially mediate) the roles of motivation and expectancies in such adherence. Youth and parents who come in motivated and expect to

change are more likely to form a strong alliance, which leads to better adherence. However, those who come in with such strong motivation and expectations but who fail to establish a therapeutic alliance are likely to see an attenuation of their adherence rates.

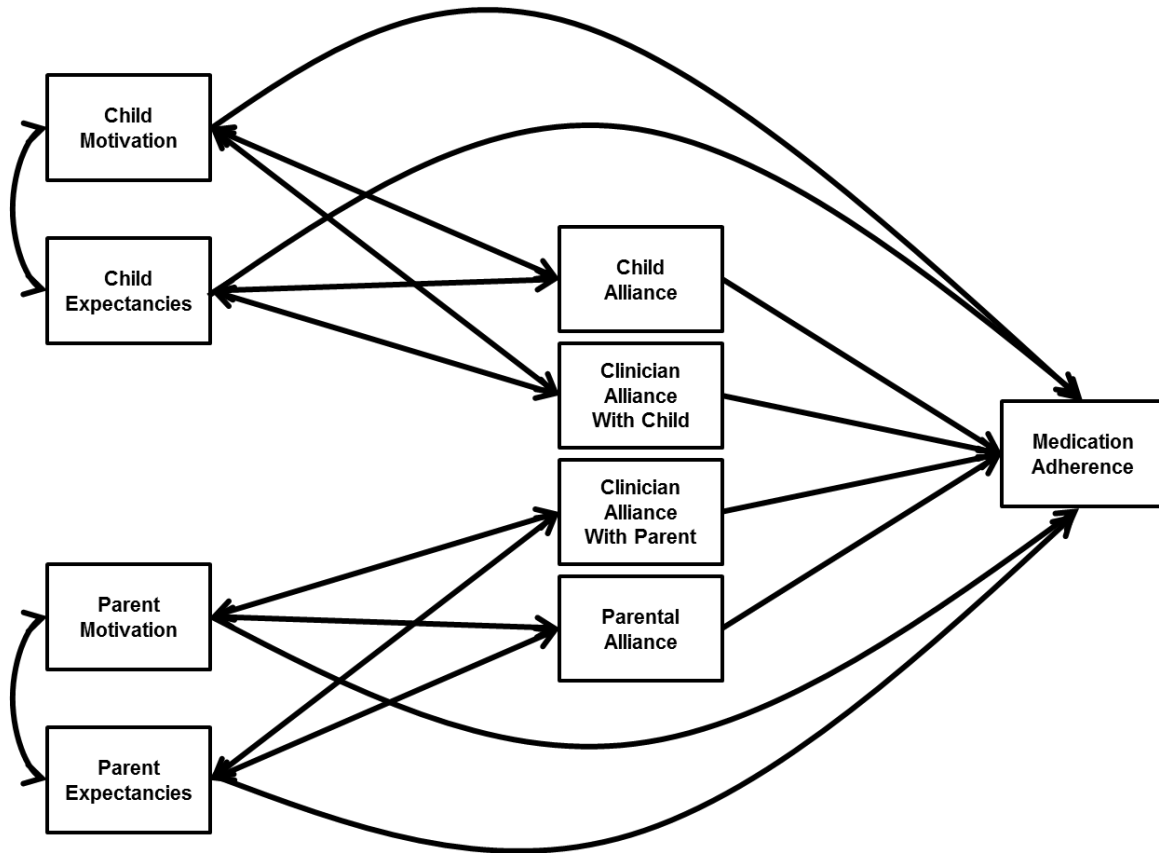


Figure 1. Conceptual model integrating the roles of therapeutic alliance, motivation for behavior change, and outcome expectancies in medication adherence for pediatric psychopathology

Summary

In the present study, therapeutic alliance, motivation for behavior change, and expectancies for behavior change are proposed as mechanisms underlying medication adherence for pediatric psychopathology. Identifying such mechanisms underlying adherence has multiple, wide-ranging implications. First, future research could be geared toward developing

interventions to address each identified mechanism underlying adherence to medication treatment (or tailoring existing ones for this purpose). For example, interventions to address motivation have been successfully employed to improve adherence rates in conditions as varied as AIDS and weight loss (Golin et al., 2006; West, DiLillo, Bursac, Gore, & Greene, 2007).

Additionally, the practice of pediatric psychiatry as a whole would be affected. For example, the didactic curriculum for physicians and other medical personnel in training (e.g., psychiatry residents, psychiatric nurses, etc.) would be indicated to include training to address these mechanisms in order to maximize the effectiveness of prescribed interventions. In this vein, healthcare insurance practice would also be affected. At present, minimal time is spent with patients given that the specific medication itself may be seen as the sole mechanism of treatment change. Thus, insurance companies may be indicated to reimburse for spending appropriate time with patients to establish an appropriate alliance, facilitate optimal motivation for change, and create appropriate expectancies for treatment, in order to reduce the costs of nonadherence. The behavior of the prescriber is important: in one study on adult depression, 7-9% of variability in outcomes were attributable to the individual psychiatrist compared to 3-6% for medication (McKay, Imel, & Wampold, 2006). Such problems with nonadherence to psychiatric medication are also not restricted to children, as adherence rates have been estimated to be below 50% for adults with a variety of psychological conditions (Keene et al., 2005; Lacro et al., 2002; Stein, Cantrell, Sokol, Eaddy, & Shah, 2006) and these principles may well be applicable to youths as well.

Furthermore, identifying these mechanisms could assist in creating an idiographic approach to patient care, where specific interventions to improve medication adherence are employed only for patients who may need them. While current indications have been to adjust the medication when symptom reduction is suboptimal, perhaps adjusting the therapeutic relationship will be a future indication in pediatric psychopharmacology. Thus, the proposed research could serve as a foundation that is applicable across a variety of settings in order to maximize outcome for a wide array of patients, who may currently not be experiencing maximal relief for these widespread and often disabling conditions.

Objectives of the Present Study

Despite the wide ranging implications of therapeutic alliance, motivation for behavior change, and outcome expectancies for pediatric psychiatric practice, almost no empirical data exist at present regarding their influence on adherence to pharmacotherapy in this setting. The proposed study serves as a preliminary trial in acquiring such evidence and to extend contemporary models of medication adherence, which have more frequently evaluated person-level predictors of adherence, but have rarely considered patient-provider predictors such as the therapeutic alliance. The aims of this study (along with associated hypotheses) are as follows:

Aim 1. To evaluate the bivariate relationships among the variables of pretreatment motivation for behavior change, pretreatment expectancy for positive treatment outcome, and therapeutic alliance at session one for both parent and child in pharmacotherapy for pediatric psychopathology.

Hypothesis 1. Pretreatment motivation for behavior change will predict therapeutic alliance for parent, child, and clinician in pharmacotherapy for pediatric psychopathology.

Hypothesis 2. Pretreatment expectancy for positive treatment outcome will predict therapeutic alliance for parent, child, and clinician in pharmacotherapy for pediatric psychopathology.

Hypothesis 3. Pretreatment motivation for behavior change and pretreatment expectancy for positive treatment outcome will show a positive correlational relationship for both parent and child in pharmacotherapy for pediatric psychopathology.

Aim 2. To examine the discrete relationships of pretreatment motivation for behavior change, pretreatment expectancy for positive treatment outcome, and therapeutic alliance at session one for parent, child, and clinician in predicting subsequent adherence to pharmacotherapy for pediatric psychopathology.

Hypothesis 4. Stronger pretreatment motivation for behavior change will predict improved adherence to pharmacotherapy for pediatric psychopathology.

Hypothesis 5. Greater pretreatment expectancies for positive treatment outcome will predict improved adherence to pharmacotherapy for pediatric psychopathology.

Hypothesis 6. Higher levels of therapeutic alliance for parent, child, and clinician will predict improved adherence to pharmacotherapy for pediatric psychopathology.

Aim 3. To simultaneously model the influence of pretreatment motivation for behavior change, pretreatment expectancy for positive treatment outcome, and parental, youth, and clinician reports of therapeutic alliance at session one in predicting adherence to pharmacotherapy for pediatric psychopathology.

Hypothesis 7. When considered simultaneously, greater pretreatment motivation for behavior change and stronger pretreatment expectancies for positive treatment outcome for both parent and child as well as higher levels of therapeutic alliance for parent, child, and clinician will each uniquely predict better subsequent medication adherence in pharmacotherapy for pediatric psychopathology.

Aim 4. To evaluate the mediating role of therapeutic alliance at session one on pretreatment motivation for behavior change and pretreatment expectancies for positive treatment outcome in predicting medication adherence in pharmacotherapy for pediatric psychopathology.

Hypothesis 8. Therapeutic alliance at session one will mediate the effects of pretreatment motivation for behavior change and pretreatment expectancies for positive treatment outcome on medication adherence in pharmacotherapy for pediatric psychopathology.

Method

Participants

Participants included 65 youth (27 females) ages 7-17 ($M = 11.66$ years, $SD = 3.25$ years) and their caregivers, who presented for a first session with a new psychiatric provider and received a prescription for a psychiatric diagnosis at one of three recruitment sites: the All Children's Hospital Pediatric Psychiatry Clinic (ACH; $n = 31$), the USF Pediatric Psychiatry Clinic (USF; $n = 30$), or the Rothman Center for Pediatric Neuropsychiatry (RCPN; $n = 4$). The ACH and USF clinics are for-profit outpatient clinics that serve youth with a broad array of psychiatric problems, whereas the RCPN is a specialty for-profit outpatient psychiatric clinic focusing on pediatric internalizing disorders (e.g., obsessive compulsive disorder). Among youth participants 89.2% were Caucasian, 3.1% were African-American, 3.1% were Hispanic, 1.5% were Native American, and 3.1% of participants did not provide their child's race/ethnicity. Among participating youths, 55.4% lived with both biological parents, 9.2% were adopted, 4.6% had parents who were separated but had shared custody, 10.8% lived with single mothers, 3.1% lived with single fathers, 1.5% lived with grandparents, 4.6% lived with mother and stepfather, 1.5% lived with father and stepmother, and 9.3% of caregivers reported their child's living situation as "other." Average grade in school for participating youths was 6.49 ($SD = 3.25$). For participating caregivers, average highest education among both caregivers was between partial college/technical school and a standard BA/BS university degree ($M = 5.69$, $SD = 0.93$; please see Appendix A for anchors). Among families who were offered participation, 26.1% of families

declined to participate (111 families consented to participate, but not all youths received a prescription for a psychiatric medication), and 16 youths did not assent to provide data for the investigation. Common reasons given for family non-participation were parent not interested in participating ($n = 20$), parent not wanting to burden child with extra questionnaires ($n = 2$), and parent not having time to complete questionnaires after the appointment ($n = 2$). Common reasons for child non-assent included a child preference to not be burdened by additional questionnaires ($n = 4$) and the child/parent not believing that the child would be able to comprehend the self-report assessments ($n = 4$). In instances of non-assent but parental consent, parents were willing to continue to provide behavioral data from themselves, but no child report was provided.

In considering child diagnoses, 33 of participating youths received an internalizing disorder diagnosis from study clinicians, 49 participants received an externalizing disorder diagnosis, and 36 youths had multiple diagnoses ($M = 0.97$ comorbid diagnoses, $SD = 1.16$ comorbid diagnoses). Common specific diagnoses given included attention deficit-hyperactivity disorder ($n = 39$), oppositional defiant disorder ($n = 9$), major depressive disorder ($n = 8$), an autism spectrum disorder ($n = 11$), a mood disorder not otherwise specified ($n = 6$), generalized anxiety disorder ($n = 6$), an anxiety disorder not otherwise specified ($n = 5$), obsessive compulsive disorder ($n = 5$), and posttraumatic stress disorder ($n = 4$). Among prescriptions written by study clinicians, 22 participants received a serotonin reuptake inhibitor, 31 participants received a stimulant medication, 12 participants were prescribed an atypical antipsychotic, 12 participants were prescribed an alpha agonist, 5 participants were prescribed an anticonvulsant medication, and 5 participants were prescribed a specific norepinephrine reuptake inhibitor. An average of 1.69 prescriptions per participant were written ($SD = 1.30$). At 1-month

follow up, 39 participating parents provided data regarding treatment seeking from other providers since starting treatment at one of the three recruiting clinics, where 17 of these participant parents (44%) reported seeking such care.

Measures

Parent and clinician rated measures.

Demographics. A basic demographics form was administered to parents to collect information on child age, gender, race/ethnicity, grade level in school, family socioeconomic status, and parent relation to child (e.g., biological mother). This demographics form takes less than 5 minutes to complete and can be found in Appendix A.

Parent and child rated measures.

University of Rhode Island Change Assessment (URICA; McConnaughy et al., 1983).

The URICA is a 32-item measure of motivation for behavior change which is rated on a 5-point Likert scale ranging from “strongly disagree” to “strongly agree,” for responses to statements such as “I am not the one with a problem. It doesn’t make much sense for me to be here.” It has four subscales (Precontemplation, Contemplation, Action, and Maintenance), with 7 items corresponding to each scale (4 URICA items stand independently from these subscales). The URICA produces a total score by subtracting the precontemplation subscale from the sum of the contemplation, action, and maintenance subscales, with higher scores reflecting greater readiness for behavior change. Acceptable internal consistency has been observed with youth ages 7-17 ($\alpha = .71$; Keeley, Geffken, Ricketts, McNamara, & Storch, unpublished data), as well as adults ($\alpha = .79$; Dozois, Westra, Collins, Fung, & Garry, 2004). Pretreatment child URICA scores have been shown to be associated with higher pretreatment child anxiety reported via the

MASC ($r = .33$, Keeley et al., unpublished data), and have been observed to predict positive outcomes in adult psychotherapy (Norcross, Krebs, & Prochaska, 2011). The URICA has explicit suggestions to be modified for different populations (Rossi, 1995), which is a technique that has been successfully used elsewhere (e.g., Dozois et al., 2004; Greenstein, Franklin, & McGuffin, 1999). In the present investigation, small modifications have been made to certain items relevant on both parent and child forms to properly address their role in treatment, with the child form focusing on child readiness for change, and the parent form also focusing on readiness for child behavior change (i.e., what is their perception of the child's problem, are parents contemplating the concept that their child needs to change, or are do they strongly believe that their child needs to change immediately). Given the previous successful use of the URICA with both adults and youth, along with its flexible design that encourages modification for specific populations, the URICA is a strong choice to use with children and adults with regard to motivation for children and parents for child behavior change. The URICA takes approximately 10 minutes to complete.

Clinician rated measures.

Therapeutic Alliance Quality Rating (TAQ-R; Bickman et al., 2010). The TAQ-R is a 1-item rating of global therapeutic alliance where the clinician rates his/her therapeutic alliance with other therapeutic parties (i.e., parent and child). Items are rated on a 5-point Likert scale with responses ranging from “very poor” to “excellent.” The TAQ-R was originally developed to reflect Bordin's (1979) conceptualization of therapeutic alliance, which consists of the elements of therapeutic bond and agreement on goals and tasks to be performed in therapy. An initial item pool of 52 items was generated, though it was determined through item response theory and classical psychometrics that single item TAQ-R ratings provided largely redundant information for clinician and parent rated alliance (Bickman, 2010). Given that the TAQ-R is a 1 item

measure, traditional reliability analyses are not available. Variability has been observed for both clinician ratings of alliance with the parent ($M = 3.94$, $SD = 0.72$) and youth ($M = 3.94$, $SD = .074$) in a large clinical sample (Bickman et al., 2010), and increases in alliance on the TAQ-R throughout treatment have been associated with improved symptom functioning in child psychotherapy (Bickman et al., 2010).

Parent rated measures.

Working Alliance Inventory - Short Form (WAI-SF; Horvath & Greenberg, 1989; Tracey & Kokotovic, 1989). The WAI-SF is a 12-item measure that was originally designed to measure therapeutic alliance in adult psychotherapy. It has been adapted to assess therapeutic alliance of parents of children in psychotherapy (Hawley & Garland, 2008), where items focus on parental agreement on the tasks to be performed in their child's treatment, parental agreement on the goals of their child's treatment, and the therapeutic bond between parent and clinician. The WAI-SF is rated on a 1-7 scale, where responses range from "never" to "always." When used with parents of children in psychotherapy, it has demonstrated acceptable internal consistency ($\alpha > .93$; Hawley & Garland, 2008) as well as test-retest reliability (6-month test-retest $r = .77$; Hawley & Garland, 2008). The WAI-SF has also predicted decreases in overall youth psychopathology during psychotherapy as well as greater parent satisfaction with therapy (Hawley & Garland, 2008). The WAI-SF takes approximately 5 minutes to complete.

Credibility/Expectancy Questionnaire - Parent Version (CEQ-P; Nock, Ferriter, & Holmberg, 2006). The C/EQ-P is a 6-item scale which evaluates parental expectations for treatment success and credibility in the proposed treatment. The CEQ-P was developed as a measure of parent expectancies and credibility with the intent of being shorter than the previous

scales of parent expectancies (e.g., Parent Expectancies for Therapy Scale; Nock & Kazdin, 2001) while retaining acceptable psychometric properties for the purposes of brief use in real-world clinical settings as well as a broad array of research contexts (Nock et al., 2006). Evaluation of the factor structure of the CEQ-P has indicated a two-factor model (falling along the lines of treatment credibility and expectancies). The present study employs the expectancy subscale of the CEQ-P, which has three items that are rated on either a 9- or 11-point Likert scale that refer to expectation of positive treatment outcome. This subscale has been observed to have an internal consistency of .88 (as evaluated by Cronbach's alpha), and its test-retest reliability after 6-8 sessions of psychotherapy has been observed to be .52 (Nock et al., 2006). Scores on the CEQ-P have been associated with parent motivation to participate in treatment (Nock et al., 2006), and the CEQ-P expectancy subscale has been shown to be related to parental treatment adherence in pediatric psychotherapy (Nock et al., 2006).

Child Behavior Checklist (CBCL; Achenbach & Rescorla, 2001). The CBCL is a 118-item measure of internalizing and externalizing behavioral problems in children, which is rated on a 0-2 Likert scale. The CBCL measures a broad array of problematic childhood problems, with total scores computed for overall internalizing and externalizing behavior, along with producing eight empirically based syndrome subscales. Internal consistency (as measured by Cronbach's alpha) has been observed to be .90, .94, and .97 for the internalizing, externalizing, and total scores, respectively, and eight day test-retest reliability has been observed at .91, .92, and .94 for the internalizing, externalizing, and total scores, respectively (Achenbach & Rescorla, 2001). The CBCL has demonstrated the ability to classify children as referred or nonreferred for treatment with 85% accuracy, and a t-score of 60 or above has been found to

differentiate youth who have been referred for clinical services from their nonreferred counterparts (odds ratio = 12). The CBCL takes approximately 15 minutes to complete.

Brief Medication Questionnaire (Svarstad, Chewning, Sleath, & Claesson, 1999). The BMQ is a 7-item self-report measure of patient adherence to pharmacotherapy. The medication regimen screen portion of the BMQ was employed via phone follow up, which has been found to be related to other adherence measurement methods such as electronic monitoring (Shi et al. 2010). Additionally, it has been previously used successfully to evaluate pediatric psychiatric medication administration with caregivers (Dean, Wragg, Draper, & McDermott, 2011). Percentage of medication adherence over the prior week was calculated via the BMQ following procedures used by Curtin, Keller, & Svarstad (1999).

Service Assessment for Children and Adolescents (SACA; Stiffman et al., 2000). The SACA is a 30-item parent-interview assessment of service utilization by youths. In comparing parental report to service records, agreement with services received (as measured by Cohen's kappa) has been found to be excellent (kappa = 0.76; Hoagwood et al., 2000), and it is frequently modified to match specific patient populations (Stiffman, Horowitz, & Hoagwood, 2005). A 13-item version was used in the present investigation.

Frequency, Intensity, and Burden of Side Effects Rating/Patient Rated Inventory of Side Effects (FIBSER/PRISE; Wisniewski et al., 2006). The FIBSER is a 3-item self-report rating of the frequency, intensity, and burden of side effects experienced from taking psychiatric medication. Items are rated on a 7-point Likert scale, with response options ranging from no side effects experienced to constant/incapacitating side effects. The PRISE is a 9-item checklist which evaluates a broad array of side effects, which is intended to be used before the FIBSER in order to highlight specific side effects experienced. The FIBSER has demonstrated strong

internal consistency ($\alpha = .91-.93$; Wisniewski et al., 2006), and higher scores on the FIBSER have been associated with treatment dropout in a randomized controlled trial for adult depression (Wisniewski et al., 2006). The FIBSER and PRISE were originally designed to be administered to adults; they have been modified to be used by parents to evaluate their child's side effects experienced for the present investigation, and items have been inspected by an expert child psychiatrist (Dr. Mark Cavitt at the ACH study site) to ensure item appropriateness for the study population. When administered together, the FIBSER and PRISE take approximately 10 minutes to complete.

Child rated measures.

Therapeutic Alliance Scale for Children - Revised (TASC-R; Shirk & Saiz, 1992).

The TASC-R is a 12-item measure of youth therapeutic alliance with the therapist, which assesses bond with the therapist as well as agreement on the tasks to be performed during therapy. The TASC-R is rated on a 4-point Likert scale with responses to items such as "I felt like my therapist was on my side and tried to help me," with responses ranging from "not at all" to "very much." The original TASC (Shirk & Saiz, 1992) was intended to measure therapeutic alliance across multiple treatment sessions, while the TASC-R provides minor modifications to wording to address alliance at a specific session (e.g., the wording on the original TASC of "I like spending time with my therapist" is revised to "I liked spending time with my therapist" on the TASC-R). Acceptable levels of internal consistency for the TASC-R for children ages 7-17 years has been observed ($\alpha = .88-.92$; Creed & Kendall, 2005; Keeley, Geffken, Ricketts, McNamara, & Storch, 2011) along with acceptable levels of test-retest reliability over a period of five psychotherapy sessions ($r = .60$; Keeley et al., unpublished data). Child rated therapeutic alliance on the TASC-R at session 5 has predicted positive treatment outcome in cognitive

behavioral therapy for pediatric obsessive compulsive disorder with youth ages 7-17 years (Keeley et al., 2011). The TASC-R takes approximately 5 minutes to complete.

Credibility/Expectancy Questionnaire - Child Version (CEQ-C). The C/EQ-C is a 6-item scale created for the present investigation due to the lack of empirically validated measures of treatment expectancies for youth. The CEQ (Devilley & Borkovec, 2000) has demonstrated strong psychometric properties for adults, with a consistent factor structure composed of 2 factors (credibility and expectancies). The CEQ was developed as a modification to the Expectancies Rating Questionnaire (ERQ; Borkovec and Nau, 1972) in order to reduce the ERQ's confounding with treatment credibility. The ERQ has been successfully used with youth ages 7 years and above (Ollendick et al., 2009), and the strong similarities in content between the CEQ and the ERQ suggest its appropriateness for this age group. The present study employs the expectancy subscale of the CEQ-C, which has three items that are rated on either a 9- or 11-point Likert scale reflecting expectancies for positive treatment outcome. When used with adults, this subscale has been observed to have internal consistency values (as evaluated by Cronbach's alpha) of .79-.90, and its test-retest reliability after 1 week has been observed to be .82 (Devilley & Borkovec, 2000). The two factor structure has been supported in adults by confirmatory factor analysis, and these expectancy subscale scores have been correlated with reductions in anxiety and global distress during psychotherapy for adult anxiety disorders (Devilley & Borkovec, 2000).

Youth Self Report (Achenbach & Rescorla, 2001). The YSR is a 112-item child-report measure of internalizing and externalizing behavioral problems in children, which is rated on a 0-2 Likert scale. The YSR is intended to parallel the CBCL and also measures a broad array of problematic childhood problems, with total scores computed for overall internalizing and externalizing behavior, along with producing eight empirically based syndrome subscales. While

originally designed for youth ages 11-17 years, the YSR has demonstrated strong psychometric properties in youth ages 7 years and up, with Cronbach's alpha values in this population of .88-.89, .88-.89, and .93 for the internalizing, externalizing, and total problems scales, respectively (Ebesutani, Bernstein, Martinez, Chorpita, & Weisz, 2011). A t-score of 60 or above has been found to differentiate youths ages 11-17 years who have been referred for clinical services from their nonreferred counterparts (odds ratio = 5). For youth below age 11 (who do not have normative data available from the test manual), t-scores were created based on normative data provided by Ebesutani et al. (2011), where a t-score of 60 was used as the clinical cutoff. Items focusing on drug use and sexual behavior were not included, as it was not necessary to expose younger youth to these concepts for the purposes of the present investigation. The YSR takes approximately 15 minutes to complete.

Multidimensional Anxiety Scale for Children - Anxiety Disorders Index (MASC-ADI; March, Parker, Sullivan, Stallings, & Conners, 1997). The MASC-ADI is a 10-item child-report measure of anxiety for youth, which is rated on a 0-4 scale ranging from "never true" to "often true." The MASC-ADI consists of a subset of items from the 39-item MASC which were identified to best discriminate children with anxiety disorders from nonclinical controls. Psychometrics for youth ages 7-17 population are good, with the internal consistency for the MASC-ADI being observed at $\alpha = .74$ (Grills-Taquechel, Ollendick, & Fisak, 2008), and three month test-retest reliability has been observed at .70 (March et al., 1997). With regard to its use as a screening instrument in differentiating youth with anxiety disorders from nonclinical controls, the MASC-ADI has shown sensitivity values of .90-.95, specificity values of .84-.95, an overall correct classification rate of 87-95%, and kappa values of .74-.90 (March, 1997). The MASC-ADI has also been able to distinguish children with anxiety disorders from nonclinical

controls when using discriminant function analyses (Grills-Taquechel, Ollendick, & Fisak, 2008; Rynn et al., 2006; March, 1998). A t-score of 70 or above was used to classify youths as having an anxiety disorder. The MASC-ADI takes approximately 5 minutes to complete.

Children's Depression Inventory - 2nd Edition Short Form (CDI-2-SF; Kovacs, 2011).

The CDI-2-SF is a 12-item instrument of pediatric depressive symptomology which is appropriate for children ages 7-17. It was empirically derived from the 28 item CDI-2 long form, and covers the affective, cognitive, and neurovegetative aspects of pediatric depression. Items consist of a series of statements about the child where he/she indicates which best describe him/her; they are rated on a 0-2 scale ranging from no depressive symptoms to severe depressive symptoms, and a total score is produced indicating overall depressive severity. Internal consistency for the CDI-2-SF (as measured by Cronbach's alpha) has been observed at .82, its two week test-retest reliability has been indicated to be .77 (Kovacs, 2011), and it is strongly correlated with the CDI-2 long form ($r = .95, p < .001$; Kovacs, 2011). The CDI-2-SF has been shown to differentiate children meeting DSM-IV criteria for Major Depressive Disorder from matched controls at the $p < .01$ level, with sensitivity and specificity values of .84 and .77, respectively (with a recommended cutoff for diagnosis being a score of 6; Kovacs, 2011). The CDI-2-SF has also been shown to discriminate children with major depressive disorder from those with generalized anxiety disorder, disruptive behavior disorders (i.e., conduct disorder or oppositional defiant disorder), and attention deficit-hyperactivity disorder, with a diagnosis of major depressive disorder being associated with higher CDI-2-SF scores relative to each of these groups. For predicting clinician diagnosis, Kovacs (2011) recommends the CDI-2-SF in lieu of the complete CDI, as it has displayed stronger psychometric properties for this purpose than the

full CDI-2 form (e.g., better test-retest reliability, better discriminant validity, and improved sensitivity and specificity). Administration time for the CDI-2-SF is 5 minutes (Kovacs, 2011).

Pharmacy records.

Continuous, Multiple-Interval Measure of Medication Gaps (CMG; Steiner & Prochazka, 1997). Continuous measurement of adherence via pharmacy records was measured by the Continuous, Multiple-Interval Measure of Medication Gaps (CMG), which divides the number of days in treatment gaps (e.g., if a prescription was written for 30 days and a medication was refilled after 35 days, the treatment gap would be 5 days) by duration of treatment period of interest. The CMG has been used to predict blood serum levels of anticonvulsants (Steiner, Koepsell, Fihn, & Inui, 1988), provider assessments of adherence to prescribed beta-blockers (Steiner, Fihn, Blair, & Inui, 1991), and increased rates of hospitalization and hospital costs for those with hypertension (Maronde et al., 1989; McCombs, Nichol, Newman, & Solar, 1994). The CMG was measured at 60 days after first prescription refill.

Procedures

Clinic personnel at the ACH, USF, and RCPN clinics asked potential participants about their interest in participating in the proposed study during normal appointment scheduling for patients' first sessions. When interest existed, they immediately notified study personnel, who sought parent consent and child assent using IRB-approved documentation. Through the normal course of care, board-certified or eligible child and adolescent psychiatrists (or psychiatric residents under their supervision) established a DSM-IV diagnosis through a clinical interview, utilizing all available information (as recommended by Klein, Dougherty, & Olino, 2005 and Silverman & Ollendick, 2005). To add further support for diagnoses, a clinical level of symptomology was indicated by either child or parent via self-report (on the MASC-ADI, CDI-

2-SF, or the CBCL; please see the measures section for detail on these instruments) using a diagnostic “or” rule (Piacentini, Cohen, & Cohen, 1992). Inclusion criteria included children being of age 7-17 years, having a clinical diagnosis assigned by a clinician and corroborated by a self-report measure (the MASC-ADI, CDI-2-SF, or the CBCL), and both parent and youth being fluent in English. No specific exclusion criteria were employed above and beyond meeting inclusion criteria. After four weeks following study consent, trained research assistants called to follow up via telephone regarding side effects experienced using the FIBSER/PRISE, concurrent treatment received for mental health-related reasons via the SACA, and parent-reported adherence via the BMQ. This time period was chosen because substantial variability has been observed in medication adherence for pharmacotherapy treatment for youths at this time point (Murray et al., 2004; Richardson et al., 2004; Gau et al., 2006).

To obtain pharmacy records in order to track medication adherence, participant parents were asked about which pharmacies they intended to use to refill their child’s prescriptions (similar to procedures used in Kane et al., 2003), and completed a HIPAA waiver authorizing record release to study staff of refill status of the medications prescribed during their intake visit. One national pharmacy chain declined to provide patient refill records ($n = 34$ prescriptions), despite proper release forms being signed by study participants. Because of this, pharmacy records collected were incomplete. For this reason, 56 prescriptions were tracked by the CMG, and given observed response rates during phone follow-ups, 82 dispensed medications were tracked by the BMQ. In total, 102 dispensed medications had at least one adherence measurement (with 36 prescriptions being tracked by both the CMG and BMQ simultaneously).

When the study was originally conceptualized, recruitment targeted youths with anxiety and depression, and to reduce items administered to youths only the MASC-ADI and CDI-2-SF were administered in order to corroborate clinician diagnosis. To facilitate recruitment and expand the generalizability of results, it was decided to include youth with other disorders (e.g., externalizing disorders), and the MASC-ADI and CDI-2-SF were replaced with the YSR. Thus, a certain subset of assenting youth received only the MASC-ADI and CDI-2-SF ($n = 14$), and the rest of assenting youth received the YSR.

Analytic Plan

Descriptive statistics were run on the demographic variables and each of the measures to determine the means, standard deviations, and internal consistency for study variables. Before conducting analyses to address specific study aims, distributional properties of study variables were examined; all study variables were within the recommended range of ± 2 for skewness and kurtosis (Cameron, 2004), and no substantial problems of multicollinearity among predictors was detected.

To test hypotheses 1-3, a correlation matrix was computed using the TASC-R, the WAI-SF, the TAQ-R, the URICA, the CEQ-P, the CEQ-C, as well as other study covariates (e.g., type of disorder assigned, type of medication prescribed). To test hypothesis 4, the CMG and BMQ were regressed on the URICA (for parent and child, respectively as two separate predictors). To test hypothesis 5, the CMG and BMQ were regressed on the CEQ-P and the CEQ-C. To test hypothesis 6, the CMG and BMQ were regressed on the TASC-R, the WAI-SF, as well as the TAQ-R Caregiver and Child versions. To test hypothesis 7, the CMG and BMQ were regressed on the URICA C/P, the CEQ-C/P, the TASC-R, the WAI-SF, and the TAQ-R Caregiver and Child versions. For hypotheses 4-6, moderators of exogenous effects were tested,

including child age, child diagnosis class (internalizing or externalizing), medication type, comorbid diagnostic status, and receiving concurrent treatment from another provider (as reported on the SACA at 1-month follow up). While nesting effects were possible based on treatment site, clinician, and patient (for those who received multiple medications), all design effects for each of these factors were all below 2, indicating negligible effects of hierarchical clustering on the validity of results (Muthén & Satorra, 1995). Thus, no multilevel adjustment was made to estimates.

Attrition and missing data. All inferential statistics were calculated using full-information maximum likelihood (FIML) estimation in Mplus version 7 (Muthén & Muthén, 2012). As recommended by Graham (2009), auxiliary covariates that were found to predict missing variables were employed. From evaluating bivariate correlations, frequency of side effects, child decision to assent to participation, and comorbid diagnostic status were found to be the best predictors of the CMG prior to model estimation, and these variables along with an adherence outcome (e.g., the CMG when the BMQ was the DV) were included as covariates in all estimated models. Including such covariates can make data that is normally not missing at random (NMAR) provide missing data estimates that are comparable to those estimated with data that are missing at random (Donaldson & Moïnpour, 2005). With Mplus, specific p -values are not provided for correlations, but degrees of freedom were based on amount of cases contributing to point estimates (as FIML makes use of all available data). With this approach, for $N = 65$, critical values of at the .05 and .01 levels were $r = .243$ and $r = .315$, respectively.

Results

Sample Characteristics and Evaluation of Adherence Rates

Descriptive statistics for the sample can be found in Table 1.

Table 1. *Descriptive Statistics for the Present Sample*

All Study Variables	Mean (SD)	Skewness	Kurtosis	Alpha	N ^a
CEQ-P	16.97 (4.34)	-0.60	0.40	0.77	64
URICA-P	10.06 (1.22)	-0.31	-0.47	0.75	52
CBCL Externalizing	15.46 (9.67)	0.30	-1.04	0.90	54
CBCL Internalizing	15.95 (10.81)	0.54	-0.55	0.91	55
TAQ-R-Caregiver	4.00 (0.57)	0.00	0.30	N/A ^b	57
WAI-SF	72.04 (10.03)	-0.49	-0.64	0.94	57
CEQ-C	16.82 (5.54)	-0.59	0.11	0.80	51
URICA-C	7.92 (2.29)	-1.46	3.57	0.65	43
YSR Externalizing	20.46 (9.28)	0.38	-0.24	0.88	28
YSR Internalizing	20.15 (13.22)	0.24	-1.20	0.93	34
TAQ-R-Child	3.53 (0.66)	-0.30	-0.09	N/A ^b	57
MASC-ADI	13.93 (6.67)	0.01	0.86	0.83	14
CDI-2-SF	4.38 (2.93)	0.82	-0.47	0.67	13
TASC-R	39.28 (6.41)	-1.08	1.23	0.85	46
BMQ	66.70 (43.84)	-0.78	-1.27	N/A ^b	82
CMG	0.55 (0.40)	-0.06	-1.61	N/A ^b	56

Note. CEQ-P= Credibility/Expectancy Questionnaire - Parent Version; URICA-P= University of Rhode Island Change Assessment - Parent Version; CBCL = Child Behavior Checklist; TAQ-R = Therapeutic Alliance Quality Rating; WAI-SF = Working Alliance Inventory - Short Form; CEQ-C = Credibility/Expectancy Questionnaire - Parent Version; URICA-C = University of Rhode Island Change Assessment - Child Version; YSR = Youth Self Report MASC-ADI = Multidimensional Anxiety Scale for Children - Anxiety Disorders Index; CDI-2-SF = Children's Depression Inventory - 2nd Edition Short Form; TASC-R = Therapeutic Alliance Scale for Children - Revised; BMQ = Brief Medication Questionnaire; CMG = Continuous, Multiple-Interval Measure of Medication Gaps

^aNumber of observations that were used in analyses (some participants received multiple medications, and thus could have multiple adherence measurements per participant)

^bCronbach's alpha could not be calculated for this measure because only one item is used to create the total score

Average treatment outcome expectancies were strongly positive for both parent and child (and were roughly equivalent among them). With regard to motivation, parents had stronger motivation for child behavior change than participant children. Therapeutic alliance with the treating clinician was also strong among parents and children, as assessed by the TASC and WAI. However, while clinicians also reported strong alliances with parents, clinician-rated alliance with youths was only in the “satisfactory” range (as opposed to clearly in the “good” or “excellent” ranges). Adherence as measured by the BMQ found patients to take about 67% of prescribed medication, while on the CMG adherence was found to be about 45%. Among only those patients who had both CMG and BMQ scores, medication adherence was 61% as measured by the BMQ and 42% as measured by the CMG. In considering the relationship between the BMQ and CMG, a modest correlation was found ($r = -.19$), which while nonsignificant reflected a relationship where increased adherence on the BMQ corresponded to a reduction in treatment gaps on the CMG.

Bivariate Relationships among Predictors of Adherence and Relevant Covariates

Bivariate relationships among the hypothesized behavioral predictors as well as relevant covariates can be found in Table 2. With regard to child alliance (as measured by the TASC), statistically significant relationships were found with child motivation, child expectancies, and subsequent receipt of concurrent mental health treatment from another treatment provider. These correlations reflect that children who had stronger pretreatment motivation for change and expectancies for positive treatment outcome had better alliances. However, those youth who had another treatment provider had poorer alliances

with the psychiatrists involved in this investigation. Additionally, youths who had stronger alliances were more likely to receive an SRI medication.

Table 2. Correlations among Study Predictors and Relevant Covariates

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28
1 TASC																												
2 WAI	0.20																											
3 TAQ-R-Child	0.03	0.07																										
4 TAQ-R-Caregiver	0.02	0.17	0.26*																									
5 URICA-C	0.34**	0.10	0.28*	0.18																								
6 URICA-P	0.17	0.10	0.21	0.00	0.09																							
7 CEQ-C	0.16	0.00	0.35**	-0.17	0.42**	-0.04																						
8 CEQ-P	0.41**	0.03	0.21	-0.01	-0.05	0.21	0.23																					
9 Age	0.23	-0.20	0.20	-0.13	0.06	0.18	0.04	0.23																				
10 Gender	-0.14	-0.05	-0.33**	-0.30*	-0.32**	0.09	0.00	-0.02	-0.08																			
11 Highest Parent Education	0.23	-0.03	0.02	0.07	0.03	-0.14	0.03	0.01	0.20	-0.01																		
12 Internalizing Diagnosis	0.03	-0.04	0.25*	0.18	0.14	0.39**	-0.19	0.18	0.20	-0.27*	-0.07																	
13 Externalizing Diagnosis	-0.15	0.14	-0.37**	-0.18	-0.24*	-0.09	-0.04	-0.14	-0.35**	0.32**	0.07	-0.56**																
14 Comorbid Status	-0.11	0.16	-0.26*	0.11	-0.07	-0.01	-0.12	-0.05	-0.11	0.12	-0.05	0.17	0.28*															
15 Receiving Concurrent Treatment	-0.34**	0.02	-0.04	0.02	0.11	-0.22	0.05	-0.20	-0.26*	0.24	-0.13	-0.27*	0.18	0.27*														
16 Child Assented to Participate	-0.04	-0.19	0.25*	-0.11	0.13	-0.02	0.34**	0.16	0.32**	-0.12	0.07	0.08	-0.16	-0.37**	-0.49**													
17 FIBSER - Frequency	0.18	0.23	0.27*	0.09	0.13	-0.10	0.30*	0.16	-0.18	0.09	-0.07	0.09	-0.02	0.07	0.16	-0.20												
18 FIBSER - Intensity	-0.06	-0.04	0.03	0.09	0.00	-0.18	0.21	-0.06	-0.34**	0.16	-0.17	-0.03	0.02	0.07	0.32**	-0.33**	0.78**											
19 FIBSER - Functional Impairment	0.01	0.31*	0.05	0.24	0.08	-0.02	-0.03	-0.32**	-0.26*	-0.05	-0.02	-0.01	-0.22	-0.02	0.27*	-0.28*	0.29*	0.52**										
20 Pharmacy Did Not Provide Records	-0.17	0.10	0.05	0.11	-0.07	-0.19	-0.11	-0.19	0.08	-0.13	0.09	-0.05	0.06	0.05	-0.05	0.06	0.05	-0.07	-0.04									
21 SRI Prescription	0.31*	-0.22	-0.09	0.29*	0.21	0.15	-0.27*	0.15	0.34**	-0.32**	0.00	0.44**	-0.57**	-0.01	-0.07	0.03	-0.02	-0.03	0.10	-0.08								
22 Stimulant Prescription	0.08	0.09	-0.12	0.07	-0.19	-0.40**	0.12	-0.16	-0.26*	0.18	-0.04	-0.54**	0.47**	0.05	0.07	-0.17	-0.05	-0.06	-0.09	0.14	-0.42**							
23 Atypical Antipsychotic Prescription	-0.21	-0.01	-0.29*	-0.03	0.02	-0.07	-0.30*	-0.35**	-0.09	0.00	-0.12	-0.01	0.09	0.19	0.02	-0.10	0.09	0.09	0.15	0.02	0.08	-0.14						
24 Alpha Agonist Prescription	-0.18	0.11	-0.34**	0.06	0.10	0.09	-0.17	-0.33**	-0.22	0.08	-0.24	-0.17	0.18	0.11	0.11	-0.19	-0.13	-0.08	-0.07	-0.07	-0.01	0.10	0.29*					
25 Anticonvulsant Prescription	0.10	0.03	-0.12	0.01	0.01	0.09	-0.20	-0.06	-0.02	-0.11	-0.16	-0.06	0.03	0.14	-0.18	-0.10	0.04	0.05	0.10	0.25*	0.16	-0.04	0.46**	0.16				
26 SNRI Prescription	0.07	0.08	0.16	-0.20	0.07	0.15	0.08	0.15	-0.24	0.01	-0.10	0.05	0.03	0.03	0.15	0.17	0.26*	0.20	0.29*	0.12	-0.08	-0.28*	0.01	-0.14	0.13			
27 BMQ	-0.06	0.02	-0.07	-0.03	-0.19	0.36	-0.07	-0.10	0.21	0.02	-0.06	0.16	0.04	-0.01	0.11	0.25	-0.11	-0.07	-0.12	0.09	0.10	-0.12	0.06	0.08	-0.06	0.04		
28 CMG	-0.01	-0.25	-0.15	0.08	-0.11	-0.09	-0.38	-0.08	-0.14	0.22	-0.17	0.04	0.01	0.27	-0.29	-0.09	0.03	0.09	0.04	-0.22	-0.07	-0.05	0.21	-0.01	0.19	0.00	-0.19	

Note. * $p < .05$, ** $p < .01$

Note. CEQ-P = Credibility/Expectancy Questionnaire - Parent Version; URICA-P = University of Rhode Island Change Assessment - Parent Version; TAQ-R = Therapeutic Alliance Quality Rating; WAI-SF = Working Alliance Inventory - Short Form; CEQ-C = Credibility/Expectancy Questionnaire - Parent Version; URICA-C = University of Rhode Island Change Assessment - Child Version; TASC-R = Therapeutic Alliance Scale for Children - Revised; FIBSER = Frequency, Intensity, and Burden of Side Effects Rating; BMQ = Brief Medication Questionnaire; CMG = Continuous, Multiple-Interval Measure of Medication Gaps

In considering relationships with other treatment parties, parent alliance was associated with an increase in reporting of functional interference as a result of side effects. However, parent alliance did not show other significant correlations with other study predictors. Clinician-reported alliance with youth was associated with improved clinician-reported alliance with parents and increased child motivation, as well as stronger pretreatment outcome expectancies for children. Clinicians perceived stronger alliances with internalizing youths and youths who agreed to participate in the study, but reported poorer alliances with externalizing youths and male patients. Clinician alliance with youths was also associated with subsequent parent-report of frequency of side effects, and clinicians who reported stronger alliance with youths were less likely to make prescriptions of atypical antipsychotics and alpha agonists. Clinician-reported alliance was stronger for girls, but not with other study predictors.

With regard to motivation for behavior change, child motivation was associated with increased child expectancies for treatment outcome. However, children were more likely to have lower pretreatment motivation for change when they had externalizing diagnoses and when patients were boys. When parents had stronger motivation for behavior change, their children were less likely to receive a stimulant prescription, but were more likely to have an internalizing diagnosis. Regarding expectancies for positive treatment outcomes, youths who had stronger expectancies were more likely have parents who reported an increased frequency of side effects at 1-month follow up, but were less likely to receive a prescription of a SRI or an atypical antipsychotic. Parents who had stronger expectancies for treatment outcome were less likely to report increased functional impairment at 1-month follow up, and their children were less likely to receive atypical antipsychotics or alpha agonists.

Regarding other study variables, older children were more likely to assent to study participation, but were less likely to have externalizing diagnoses or to be receiving concurrent treatment. Older youth also were less likely to have parents report increased intensity and functional impairment related to side effects, though they were more likely to receive an SRI and less likely to receive stimulants (which reflects a pattern of prescribed medications that have fewer side effects). Males were more likely to have externalizing diagnoses, whereas females were more likely to have internalizing diagnoses and to receive SRI prescriptions. Externalizing youth were more likely to receive comorbid diagnoses, and youth receiving concurrent treatment were more likely to have parents who reported more intense side effects and increased functional interference due to side effects. Males were more likely to provide assent, but youth who assented to participate were less likely to have comorbid diagnoses or to receive concurrent treatment in the month following study enrollment.

Evaluating the Role of Therapeutic Alliance in Predicting Adherence

In considering the simultaneous prediction of adherence by alliance as reported by youths, parents, and clinicians, child-reported alliance predicted adherence on the BMQ ($b = -.28, p = .04$), but BMQ scores were not significantly predicted by parent alliance ($b = .05, p = .69$), clinician-reported alliance with the parent ($b = .06, p = .67$), or clinician-reported alliance with the child ($b = -.18, p = .14$). On the CMG, significant prediction of alliance was not found for child-report ($b = -.14, p = .53$), parent-report ($b = -.16, p = .22$), or clinician-reported alliance with the parent ($b = -.20, p = .20$) or child ($b = .10, p = .46$). Parent alliance effects were found to be moderated by age on the BMQ (where

parent alliance had positive effects on adherence only for older youth; $b = .40, p < .01$), but not on the CMG ($b = -.16, p = .32$).

Parent alliance effects on adherence (as measured by the BMQ) were moderated by alpha agonist prescriptions ($b = .71, p < .01$), but not when the CMG was the adherence outcome ($b = .14, p = .39$). Similarly, clinician-rated alliance was also moderated by alpha agonist prescription when the BMQ was the adherence outcome ($b = -.43, p = .02$), but not when using the CMG ($b = .20, p = .20$). The directions of these effects are opposite, where alpha agonist prescriptions were associated with increased adherence when parents perceived stronger alliances, whereas such prescriptions predicted reduced adherence when clinicians perceived stronger alliances. Externalizing diagnosis moderated child alliance effects on the CMG ($b = -1.6, p < .01$), but not on the BMQ ($b = .22, p = .63$), where externalizing youth had fewer gaps in adherence relative to non-externalizing youth when they had stronger alliance in treatment. Concurrent treatment moderated the effects of child alliance ($b = 1.50, p = .02$), clinician-reported alliance with child ($b = -1.29, p = .01$), and clinician-reported alliance with parents ($b = .51, p < .01$) on the BMQ. In these instances, concurrent treatment predicted better adherence when the child perceived a stronger alliance and when the clinician perceived a better alliance with parents, but when clinicians perceived better alliances with youths, treatment with another provider was associated with reduced adherence in the presence of better clinician-reported alliance with youth. However, none of these effects were found for the CMG for child alliance ($b = -.41, p = .76$), clinician-reported alliance with child ($b = .49, p = .67$), or clinician-reported alliance with parents ($b = -.09, p = .78$). Parent alliance effects on the BMQ ($b = -.46, p = .01$) as well as clinician-reported alliance with parent on the BMQ were moderated by side effect frequency ($b = -.46, p = .01$), where side effects reduced the effects of strong alliances on adherence.

However, these effects were not replicated on the CMG for parent alliance ($b = .12, p = .59$) or clinician-reported alliance with parent ($b = .32, p = .23$). Additionally, parent alliance effects on the CMG were moderated by comorbid diagnostic status ($b = -.34, p = .04$), but not on the BMQ ($b = -.31, p = .08$); on the CMG, comorbidity in youth actually increased the effect of stronger alliances on adherence.

Evaluating the Role of Motivation for Behavior Change in Predicting Adherence

In considering simultaneous prediction of adherence from both parent and child motivation for child behavior change (via URICA scores), parent URICA scores were a significant predictor of the BMQ ($b = .36, p < .01$), but not for the CMG ($b = -.11, p = .41$), while child URICA scores did not reach the $p < .05$ level in prediction of either the BMQ ($b = -.18, p = .18$) or CMG ($b = -.26, p = .05$). Parent motivation was moderated by child age on the BMQ ($b = -.30, p = .04$), where the effects of parental motivation was actually associated with reduced adherence in older youths. However, child motivation was not moderated by age on the BMQ ($b = .06, p = .72$) and on the CMG, child age did not moderate effects for parent ($b = -.05, p = .81$) or child ($b = .24, p = .10$) URICA scores. Moderation of child URICA scores on the CMG was found for youth who received anticonvulsant medication prescription ($b = .45, p < .01$) and SNRI medication ($b = .50, p = .01$), where youths who had stronger motivation for change showed an increase in treatment gaps when taking these medications. On the BMQ, SRI prescription was found to moderate child motivation ($b = .37, p = .04$), but not on the CMG ($b = -.26, p = .34$). No other moderation of parent or child motivation effects on adherence was observed.

Evaluating the Role of Outcome Expectancies in Predicting Adherence

When evaluating the simultaneous prediction of adherence from child and parental expectancies, child expectancies for positive treatment outcome were found to predict a reduction in treatment gaps on the CMG ($b = -.51, p < .01$), but no such improvements in adherence were detected when using the BMQ as an adherence outcome ($b = .00, p = .99$), and parent expectancies were not a significant predictor of the CMG ($b = .20, p = .12$) or the BMQ ($b = -.07, p = .51$). In considering moderation of these relationships, child expectancies were moderated by use of a SRI medication ($b = .44, p < .01$) and by receiving concurrent treatment from another provider ($b = .57, p = .01$) on the CMG, where youths who had high expectancies for treatment outcome and either received an SRI medication or were receiving concurrent treatment were less likely to adhere to pharmacotherapy. On the BMQ however, neither SRI medication ($b = -.05, p = .82$) nor receiving concurrent treatment ($b = -.12, p = .63$) were found to have an interaction with child expectancy effects. On the BMQ, moderation by externalizing diagnosis was found for both child expectancies ($b = .83, p = .01$) and parent expectancies ($b = -.76, p < .01$) on adherence. In this instance a contrast was found, where youths with higher expectancies for outcome and had externalizing behavior had increased adherence, while higher parental expectancies actually predicted poorer adherence when youths had an externalizing diagnosis. Moderation was not found on the BMQ for internalizing diagnosis on either child ($b = .30, p = .32$) or parent expectancies ($b = -.16, p = .39$), and similar moderation was not found on the CMG for externalizing diagnosis on child ($b = -.04, p = .13$) or parent ($b = .03, p = .60$) expectancies, and again no moderating effects of internalizing diagnosis were observed for child ($b = .01, p = .85$) or parent ($b = .03, p = .52$) expectancies. No moderation by child age, diagnosis type, presence of comorbid diagnoses, or side effects were observed on the effects of

parent or child expectancies on the BMQ or CMG, and receiving concurrent treatment was not found to moderate any observed expectancy effects on the BMQ.

Considering Simultaneous Prediction of Adherence by Alliance, Motivation, and Expectancies

When considering all theory-based predictors in tandem (i.e., expectancies, motivation, and alliance for child, parent, and clinician), parent motivation was the only significant predictor of BMQ scores ($b = .49, p < .01$), where stronger parent motivation predicted increased adherence. For the CMG, parent motivation ($b = -.40, p < .01$) as well as parent expectancies ($b = .36, p < .01$) and child expectancies ($b = -0.76, p < .01$) were found to predict adherence. In this instance, increased parent motivation reduced treatment gaps, while increased parent and child expectancies actually predicted an increase in treatment gaps. Alliance scores were not found to predict adherence once including other variables at the $p < .05$ level. While mediational processes were originally hypothesized in Figure 1, no significant causal chains according to this model were found. That is, the only significant predictor of adherence was when simultaneously modeling alliance from all treatment parties was child alliance, and the only significant predictors of child alliance in the proposed mediational models, child motivation and parental expectancies, were not significant predictors of BMQ scores in regression models.

Discussion

The present investigation is the first known to evaluate the simultaneous roles of prominent behavioral “common factors” on pharmacotherapy for pediatric psychopathology. While employing a real-world clinical sample, a number of factors were associated with adherence, providing an alternate framework from which to conceive pharmacological interventions in pediatric psychiatry. Instead of simply seeking new chemical structures, indications may be to address the dynamic of the therapeutic relationship to maximize pharmacological outcomes. Given the limited improvement in drug development over the past 20 years (Cowen, 2011), maximizing the common factors specified in this study provide a path for the immediate improvement of contemporary pharmacotherapy.

Considerations of Sample Characteristics

While overall adherence rates were well below full compliance, they were also within the range of other adherence investigations with psychotropic medications (e.g., Gau et al., 2006; Murray et al., 2004; Richardson et al., 2004). Of note is the modest observed correlation between the two adherence measures (pharmacy records via the CMG and parent-report via the BMQ), which was nonsignificant at the $p < .05$ level. It has been reported previously that self-reported adherence rates are often higher than those found via other measurement methods (e.g., pharmacy records, blood levels, etc.) and that correlations between different adherence measurement methods are not always strong (Shi et al., 2010). However, it has also been noted that no one adherence measure is sufficient, and that different measures may capture different

aspects of adherence behavior (Otsuki, Clerisme-Beaty, Riekert, & Rand, 2008). For instance, blood levels may measure acute medicinal intake, but they are not always as useful for long-term adherence behavior due to both inconvenience as well as the limited amount of time medications can be detected via blood draw, whereas measures such as the ones used in the present investigation are well suited to track longer term adherence behavior. Thus, while there was inconsistency in results based on which adherence measure was used, different aspects of adherence behavior may be under evaluation depending on the measure employed. For instance, immediate adherence is a behavior that focuses on the consistency and accuracy in following a prescribed medical regimen, whereas the term “persistence” has been used to highlight a long term continuation of treatment (Ho, Bryson, & Rumsfeld, 2009). While the BMQ focuses solely on recent accuracy in medication adherence, the CMG is affected somewhat by persistence, as the longer refill intervals (30 days, compared to past 7 days for the CMG) reflect longer term commitments to continue to persist with therapy. Conversely, the way BMQ items are structured make them liable to be affected more by emotional and cognitive aspects of adherence (e.g., desire to comply, aversion to disclosing suboptimal adherence, effectiveness of memory) than the CMG. Given such method variance that exists in measuring adherence behavior, it has been recommended to use multiple measures in adherence investigations (Osterberg & Blaschke, 2005), and each measure provides grounding for future hypothesis testing.

In considering descriptive summaries of alliance ratings, clinician-reported alliance with youths was qualitatively lower than youth self-report with the clinician. This stands in contrast to a common problem in alliance measurement in child

psychology, where a ceiling effect of uniformly strong alliance is often observed (Bickman et al., 2012). A number of possibilities may account for this finding. First, the majority of studies only evaluate alliance with parents and youths, while many fewer evaluate the clinician's perspective on alliance (Shirk et al., 2011). One implication is that clinicians may have a different perspective on alliance that has been understudied. For instance, clinicians have much more experience in the therapy process relative to any individual youth or caregiver, and may be more aware of the possible range of therapeutic relationships and may have a different calibration of response options. However, the therapeutic relationship is quite different from normal experiences for youths and caregivers. One differentiating aspect is that they are in an environment that is much more validating than that seen in normal society (e.g., work, school), where such validation comes from a person of high socioeconomic status. Furthermore, while patients and caregivers generally receive unconditional positive regard in therapy, the clinic setting consists of a mostly one-way relationship with little direct focus on clinician interests. Thus, while clinicians may make many alliance-promoting behaviors as part of the therapeutic process, patients may not reciprocate with similar behaviors towards clinicians. In the long run, this lower clinician alliance could manifest itself as subtle clinician behaviors that may distract from clinical care. Discerning among these multiple reasons for lower clinician-reported alliance ratings is merited for future research, along with replication of this finding. However, there may be more room for improvement with clinician alliance compared to the ceiling effects observed in patient alliance, making for a more viable opportunity for therapeutic gain.

Aim 1

Implications of bivariate relationships among study predictors. While the relationships specified in Figure 1 regarding child alliance, expectancies, and motivation held

true (i.e., they were all positively related with the exception of the nonsignificant relationship between the TASC and the CEQ-C), no significant correlations were detected among these variables as reported by parents. Thus, hypotheses 1 and 3 were supported with regard to children and clinicians, but they were not supported for participating parents, and hypothesis 2 did not receive support for any reporting party. While preexisting theory would predict these relationships and other adult studies have found relationships among these variables (Westra, 2012), one study has failed to detect a relationship between parental expectancies and motivation in youth treatment (Nock et al., 2006), and some studies have failed to detect these relationships among these variables in adult treatment (e.g., Vogel, Hansen, Stiles, & Götestam, 2006). Additionally, parent motivation and expectancies were very strong, and perhaps a ceiling effect was observed where most of the parents who brought youths in for treatment came to a psychiatric clinic because they expected positive outcomes and were motivated for child behavior change. Thus, while these constructs show interrelationships in a number of settings, the consistency with which they are detected at a significant level among adults is not uniform. How they play a role with regard to adult participation in pediatric psychiatric treatment is an open question, as the present study did not support their interrelationships for caregivers. Nevertheless, this pattern of findings indicates that psychiatric physicians may wish to be particularly attentive to children when it comes to expectancies and motivation, as these factors were more likely to accurately model the therapeutic process for them.

In this bivariate context, several other findings stand out when considering relationships among the hypothesized predictors of adherence. First, agreement was low

among reporting parties regarding the quality of the alliance. This finding is in accord with others (e.g., Bickman et al., 2012) which have found inconsistent agreement among alliance reporting parties in youth psychotherapy. In fact, it appears that while alliance is a critical component influencing a variety of treatments (Shirk et al., 2011) it is not reflected by uniform agreement of therapy participants. In considering demographic factors that influence the alliance, the clinician-reported alliance with youths was most notable for having stronger alliances with youths who had internalizing disorders but poorer alliances with externalizing disorders, which is consistent with other reports of pediatric externalizing behavior (Gallagher, Kurtz, & Blackwell, 2010). In this instance, alliance was quite high overall for parents and youths across disorders, but the clinician-reported alliance had a unique relationship with child symptom presentation. This finding may give clinicians increased insight into a possible error in clinical judgment, as while they may perceive a poorer alliance with more interpersonally difficult youth (i.e., those with externalizing disorders), parents and youths with more difficult symptoms may be grateful for a therapeutic relationship. While a clinician may think the alliance is poorer in this circumstance, youths and parents in fact may still have stronger alliances and subsequent improvements in adherence. A possible remedy to this situation would be for clinicians to collect quantitative data from patients regarding the alliance in order to adjust their clinical judgment. However, the quality of the information reported may be limited, given that ceiling effects have been observed for a number of alliance investigations (Chu et al., 2004). In this case, parents and youths may be overestimating the quality of the therapeutic relationship given that they do not know the entire distribution of relationship possibilities. A contrast was also found where these effects of diagnosis class did not extend to parents, youths, or clinician reports of their relationships with parents. While some differences have been observed with regard to the

predictive value of internalizing/externalizing diagnoses and the alliance-outcome relationship in youths, the differences are fairly small (where alliance accounts for only 2.9% more outcome variance for youths with externalizing diagnoses relative to those with internalizing diagnoses; Shirk & Karver, 2011). Given the present sample size as well as possible ceiling effects in measurement, differences in alliance based on disorder class may exist but are too small to be detected in the present investigation.

Interestingly, higher parent alliances coincided with increased reporting of side effects, where parents who perceive a stronger connection with the clinician possibly may be more attentive to side effects and are more forthcoming in reporting them. Given the “black box” warning as well as other potential side effects associated with SSRI antidepressants (Goodman, Murphy, & Storch, 2007; Murphy, Segarra, Storch, & Goodman, 2008; Weiss & Gorman, 2005), fostering the identification and communication of adverse effects is a critical factor that may be facilitated by a strong parental alliance. In this context, children receiving concurrent treatment were more likely to have side effects of medications reported, whereas older youth were less likely to have side effects reported. Perhaps youths with multiple providers may be having more professional focus on symptoms that helps to identify side effects, and older youths may communicate less with parents regarding side effects experiences. While the caveat exists that older youths had a prescription pattern that is associated with fewer side effects (i.e., more SRIs and fewer stimulants), indications may be for more frequent contact in the first month of pharmacotherapy to assist in identification of side effects, and for parents to be particularly fastidious in inquiring about side effects with older youth.

Another finding of note was that parents who had poorer pretreatment motivation for youth behavior change had children who were more likely to be prescribed stimulants during their initial clinic session. While other work has found strong parental motivation for youth behavior change for youth with externalizing disorders (Nock & Photos, 2006), perhaps these parents have been particularly frustrated with seemingly intractable behavior problems that are disrupting at home and school, and may be seeking external help through pharmacotherapy as opposed to focusing on behavioral change. Further research investigating parental locus of control (Kormanik & Rocco, 2009) relative to child behavior problems may further illuminate this issue.

Aim 2

Considering alliance and adherence. When considering all reported therapeutic alliances in treatment, the only significant main effect was child-reported alliance being surprisingly associated with poorer adherence on the BMQ. However, a number of specific circumstances were found with regard to moderation in the prediction of adherence by alliance. For instance, if youths participated in outside treatment in addition to their study clinician, then stronger youth alliances corresponded to increased adherence on the BMQ. Perhaps those youths with low alliances and who have a study clinician as their only provider are likely to have poor adherence, whereas improved adherence is found by those with strong alliances or for those who have low alliance but also have multiple providers. Parents of youths who have multiple providers have actually created a personal system of multiple mental health providers, which has been recommended by the Institute of Medicine (2006); given the diverse nature of psychopathology and because such disorders are often complex, multiple professionals of varying expertise are frequently required in order to provide quality care. Perhaps then,

incorporating other mental health professionals in a system of coordinated care can help to ameliorate the impact of poor alliance with any one provider. It appears then that youths who have poor alliance and do not see multiple providers drag the overall main effect downwards, but other youths may still have an association between increased alliance and increased adherence.

In further considering the nature of child alliance and its relationship with adherence, an interaction was also found on the CMG between child alliance and externalizing diagnoses. In this instance, treatment gaps were reduced for children who had strong alliances but also had externalizing diagnoses. Stronger alliance made a larger difference with externalizing youths, but trended downwards for these youths when alliance was poorer. Perhaps in these cases, if one can form an alliance with these more difficult youth, it is an especially strong protective factor, whereas alliance may come more easily with non-externalizing youths (as also reported by DiGiuseppe et al., 1996) and differentiate outcomes less with them, as has been found in meta-analysis (Shirk & Karver, 2011).

When considering factors affecting parent-provider relationships, parental alliance and comorbid youth diagnostic status resulted in a reduction in treatment gaps on the CMG, where perhaps alliance only makes a clear distinction with these more difficult-to-treat youth, and it may not be as distinguishing a factor in more straightforward cases. Increases in morbidity have been related to poorer parental attitudes towards therapy in other conditions such as asthma (Conn et al., 2005), and given that parents are responsible for a number of aspects of medication adherence in youth (e.g., refilling medication, physical transport to appointments, etc.), data from the present investigation

are consistent with the notion that parents of youth who have increased symptom presentations are particularly important to engage more strongly with. Another interaction effect was found where concurrent outside treatment moderated the effects of child and parent alliance on the BMQ (where concurrent treatment increased the effects of alliance on adherence), but this moderation was reversed for clinician-perceived alliance with youth on the BMQ. Perhaps outside treatment helps overall in fostering child alliances with multiple providers due to increased comfort in professional treatment for psychopathology (as increased service use has been associated with comfort in treatment; Gonzalez, Alegría, Prihoda, Copeland, & Zeber, 2011). Conversely, these youths may be seeking multiple providers due to a multitude of problems (as youths in concurrent treatments were found to be more likely to have comorbid issues in bivariate relationships in the present dataset, and youths with comorbid disorders have been found to seek an increase in service visits; Merikangas et al., 2011), and clinicians may perceive more difficulty in forming an alliance with these more troubled youth. Intriguingly, parent alliance was related to increased adherence even more when youths were prescribed alpha agonists, but clinician-reported alliance with parents was actually associated with reduced adherence to these medications. One explanation of this finding involves the role of alpha agonists, which are often given to youths who are inappropriate candidates for stimulants (for reasons such as past failed trials of stimulants, stimulants increasing undesired behavior in aggressive youth, etc.; Scahill, 2009; Scahill & Pachler, 2007). In this instance, parents may be pleased to have a more tolerable alternative to stimulants (i.e., finding a more palatable intervention can maximize the task agreement component of alliance) and be more likely to facilitate adherence. However, despite increased adherence for this reason, clinicians may still perceive poorer alliances when working with these treatment-resistant externalizing youth. This

highlights a possible incongruence among components of the alliance construct that can actually work in the favor of outcomes: while the bond component (which the central component of the clinician-rated TAQ-R-C) may be reduced, the task component can still be maximized (which has greater focus in the parent-rated WAI-SF). Thus, even if the bond is not maximized, perhaps shifting to agreement on task and goals can continue to improve outcomes.

Considering motivation and adherence. Limited support was found for hypothesis 4, where parent motivation predicted better adherence on the BMQ (but not on the CMG), and child motivation did not predict either the BMQ or CMG. Additionally, an interaction was found where increased motivation in parents with older youth decreased adherence (as measured by the BMQ). Perhaps parents who are more motivated to change child behavior may be overzealous in pushing older youth to change, who may want to feel a sense of autonomy and not be constrained by parents. Indeed, it has been found that parents and clinicians both underestimate the amount of health-related knowledge held by adolescents (Erickson, Gerstle, & Feldstein, 2005) and thus it would be easy to become patronizing and overmanage care. For these youth, parents can work to foster intrinsic motivation for change in their children and take more of a supporting role while being conscientious of not being overbearing. In contrast, parents of younger children are more responsible for medication administration (and thus their active intervention is more necessary), but as youths age, they have greater control over medication administration and often rely less on parental support for adherence (Hsin, La Greca, Valenzuela, Moine, & Delamater, 2010).

An inspection of moderators revealed that increased child motivation was associated with a stronger increase in adherence to SRI medication on the BMQ, and another interaction effect was found where increased motivation predicted a relative increase in treatment gaps for SNRI and anticonvulsant medication on the CMG. Perhaps youth who receive an SRI have less severe symptoms as given that SRIs are often used as first-line pharmacological agents (e.g., Geller, March, & the AACAP Committee on Quality Issues, 2012). Thus, they may be more treatment naïve, and thus are more likely to have increased motivation affect their clinical care. In contrast, SNRIs and anticonvulsants are often used as augmenting agents to other ineffective medicinal interventions (e.g., Shelton, Osuntokun, Heinloth, & Corya, 2010; Vigo & Baldessarini, 2009). Perhaps the effects of increased motivation matter more for patients who do not have such intractable symptoms, whereas the effects of motivation on adherence do not matter as much with patients who are more treatment-refractory.

Considering outcome expectancies and adherence. Hypothesis 5 also received partial support, where child expectancies for positive treatment outcome predicted a reduction in treatment gaps on the CMG, but such expectancies were not a predictor of the BMQ, and parent expectancies did not significantly predict the CMG or the BMQ. However, interactions effects were observed with child expectancies, where SRI medication administration and concurrent treatment with another provider and resulted in even further increases BMQ scores for youth with high treatment expectancies. With regard to the interaction with SRI administration, placebo effects (which are often strongly tied to expectancies; Kirsch, 2009) have been found to have particularly strong effects on a number of disorders these medications are used for (e.g., depression and non-OCD anxiety disorders; Bridge, Birmaher, Iyengar, Barbe, & Brent, 2009; In-Albon & Schneider, 2007). Thus, perhaps these youth will have symptoms begin to resolve on

their own without medicinal intervention, and find it less necessary to keep taking medication given that symptoms improve whether they take medication or not. With regard to the finding of moderation by concurrent treatment with another provider, it has been found that youth who seek treatment with multiple providers often have increased levels of psychopathology (Merikangas et al., 2011) and they were also more likely to have comorbid diagnoses in the present sample. Thus, perhaps expectancies make a bigger difference for youth who are less impaired, whereas with more difficult youth, the overall effects of expectancies are reduced to overall lower adherence levels.

Interestingly, youth who presented with externalizing psychopathology had increased adherence in the presence of high expectancies, whereas these same externalizing youths had poorer adherence relative to non-externalizing youths when parents had higher outcome expectancies. Perhaps because youth with externalizing disorders had lower expectancies for treatment outcome (as found in bivariate relationships), the subset who have strong expectancies for change may be particularly fastidious in adherence relative to their counterparts who expect little change. Conversely, perhaps some parents have overly optimistic expectations for reduction in child externalizing behaviors (as they have shown strong expectancies for psychological treatments with child externalizing disorders; Nock et al., 2007), and do not follow through on assisting in adherence if pharmacotherapy does not serve as an adequate remedy. Or, perhaps parental expectancies do not matter as much with externalizing behaviors (as no matter how strong the parent expects change, the youth will be recalcitrant in participating in adherence), whereas with non-externalizing youth, the strength of parental expectancies may make an actual difference in adherence.

Aims 3 and 4

Considering simultaneous prediction of adherence by alliance, motivation, and outcome expectancies. When considering all reporting parties (hypothesis 7), therapeutic alliance did not predict unique variance in treatment adherence in simultaneous modeling. However, increased child expectancies continued to predict a reduction treatment gaps (as it did when addressing hypothesis 5), and interestingly an effect emerged where stronger parent expectancies actually predicted an increase in treatment gaps (that was not found when testing hypothesis 5). This is evidence of a statistical suppressor effect (Meyers, Gamst, & Guarino, 2005), which can occur when predictors share facets with other predictors that they do not share with a criterion variable. In this case, it may generate from the fact that in some instances, increased parental expectancies can have both facilitate and detract from adherence, as it has been observed that parental expectations that are incongruent with treatment processes have been related to lower adherence to psychological treatments (such as expecting strong symptom reduction in 1-2 sessions; Morrissey-Kane & Prinz, 1999). In this instance, perhaps the adherence-facilitating variance of parental expectancies were claimed by other variables (i.e., increased alliance, increased motivation), but the adherence-deteriorating variance remained as a residual and was a significant predictor of adherence. Additionally, the negative coefficient could be an artifact resulting from the matrix inversion process when estimating beta weights (Cohen, Cohen, Aiken, & West, 2003). Nevertheless, while a body of work has focused on the adherence-promoting effects of expectancies, these results may expose a potential downside to strong outcome expectancies that merits further investigation.

Parent motivation was also a consistent predictor of both the BMQ and CMG in this model. This more robust pattern of results reflects that in the current investigation, parental

motivation for change was found to be the most consistent predictor of adherence outcomes when considering other common factors. However, a similar suppressor effect was found for parent motivation on the CMG, where adding alliance/expectancy predictors led to a previously nonsignificant coefficient becoming significant. While individual alliance/expectancy variables did not show significant correlations with parent motivation in bivariate relations, it appears that by including this constellation of variables into the model, variance in parent motivation that was not related to adherence was accounted for by this group of variables. While a wide array of unobserved factors may contribute to this (and there is no a priori reason indicated in the research base to indicate variance in motivation claimed by alliance/expectancies that would not be claimed in adherence), one possible explanation centers around a state/trait distinction (e.g., Spielberger & Reheiser, 2009) of reporting. While motivation for behavior change is a construct that is intended to be relatively stable (i.e., it is not impacted as strongly by immediate emotional states, resembling a trait in the state/trait model), responses could be subtly affected by differences in state affect (e.g., the participating parent had a lot of frustration with insurance paperwork before the session, which could make them more pessimistic than they would otherwise be in their desire for change). However, alliance is intended to directly capture these state-based fluctuations, as it directly reflects behavior from the specific day of report. Incorporating alliance variables into the model may then suppress error in measuring motivation due to state-based factors), making for a more “pure” measurement of the trait of motivation.

Relationships among predictors were also likely responsible for child alliance becoming a nonsignificant predictor of the CMG in simultaneous modeling. Alliance was

very close to the $p = .05$ level in terms of significance before considering modeling of all predictors, and given the conceptual overlap in motivation, alliance, and expectancies (De Nadai & Karver, 2013), only a small portion of alliance variance would have to be accounted for by other variables to render it nonsignificant. Additionally, the effect size of alliance in child therapy is small to medium (Shirk et al., 2011), and the limited sample size and inclusion of other predictors that introduce model multicollinearity could have limited detection of significant alliance effects. Given debates focusing on the conceptualization of child alliance (Shirk & Karver, 2006), in future studies perhaps administering multiple alliance measures that evaluate different alliance components (i.e., goal, task, bond) may help in ascertaining certain parts of alliance that are differentiated from motivation and outcome expectancies.

No potential mediational pathways through were identified, as was originally posited in hypothesis 8. This could be for several reasons. First, perhaps alliance functions in a different role than was specified. While alliance was conceptualized as a mediator, it has been observed to moderate treatment outcomes in psychotherapy (Barber, Khalsa, & Sharpless, 2010), and it possibly may play a moderating role in adherence in pediatric psychiatry also as opposed to being solely a mediator in a causal chain. Secondly, while alliance, motivation, and expectancies were modeled as separate variables, perhaps they are better conceptualized as a dynamic process using models such as the actor-partner interdependence model (Kenny, Kashy, & Cook, 2006) as opposed to being characterized as discrete variables. Finally, the specified mediational pathways could still be viable, but the effects observed may have been too small to be detected by the present sample. While no possible mediational pathways were observed at the $p < .05$ level, perhaps a study with greater power would detect them.

Limitations

A number of limitations of the present investigation are to be noted. First, the study relied on a correlational design, limiting causal inference for observed relationships. While these data provide the first quantitative support for a number of the proposed hypotheses, conclusions are tempered by the lack of an experimental design. Second, during phone follow-ups, only parental reports were obtained. While child report would have provided additional valuable information, pilot testing of the protocol found that parents felt that attempting to get children involved in phone follow-ups was burdensome. In an attempt to find a compromise between participant burden and obtaining valuable data via follow up, psychometrically strong measures were employed with parents only. Additionally, a measure of adherence was employed to corroborate this parent report (pharmacy records) that is independent of parent report for our central study outcome, which along with a large degree of non-overlapping variance between the employed adherence measures mitigates this method effect somewhat. Third, we did not use semi-structured assessment for patient diagnosis, which is the contemporary gold standard in clinical trials for pediatric psychopathology (Klykylo & Kay, 2012). However, all clinicians were either board-certified or directly consulted with a board-certified psychiatrist with at least 10 years of experience during diagnosis, and diagnoses were corroborated by parent and child self-reports. Fourth, a substantial amount of data were missing, especially on the CMG and BMQ in particular. While this is undesirable, as long as the assumptions for missing data at random are met, this proportion of data can still yield unbiased population estimates with modern missing data estimation (Lee, 2011). A comprehensive plan to address missing data was used where useful predictors of

missingness were used in all estimation models, with particular use of multiple measures of the dependent variable in all models (e.g., the CMG was an auxiliary covariate in all models where the BMQ was the DV), which is noted as the best type of covariate for such use of auxiliary variables (Graham, 2009). Further supporting the validity of results is that there is no a priori hypothesis that patients whose pharmacies refused to provide refill data differ substantially from those of other common pharmacies used in the investigation, and no group differences were found on main predictor variables or on the BMQ regarding pharmacies that did not provide records. While other investigations have used centralized databases to evaluate pharmacy records (e.g., Murray et al., 2004), which can result in fewer missing data as there will be no heterogeneity in pharmacy cooperation, such databases only include patients who have a certain insurance provider (e.g., Medicare, Kaiser Permanente, etc.). In contrast, the current study population may be more representative relative to this centralized approach, given that different characteristics of insurance usage can make populations less representative of adherence behavior (such as varying likelihood of insurers creating barriers to refills or the differing socioeconomic status of those using a high-cost insurance plan relative to a lower-cost plan; Chen, 2004; Lanouette, Folsom, Sciolla, & Jeste, 2009; Mulvale & Hurley, 2008). As part of this missing data approach, child assent status was also used as an auxiliary covariate in all estimated models. While a number of youths did not assent to participate in this study, their parents were willing to participate provided that youths were not burdened by questionnaires. Fifth, systematic information was not collected regarding why participants discontinued medications. Indeed, it could be attributable to several causes, such as poor treatment response, or undesirable adverse effects. However, the recommended trial period for medications in clinical trials for these medications is at minimum 6 weeks (American Academy of Child and Adolescent Psychiatry,

2001; Geller et al., 2012, Pliszka and the AACAP Work Group on Quality Issues, 2007), with adverse effects occurring at a low enough rate to complete the trial. Thus, patients not being able to maintain adherence during the duration of the study would reflect patients not adhering to clinical recommendations, and the present study has evaluated factors that may influence this deviation from recommended clinical practice, such as reduced parental motivation for child behavior change. Furthermore, such increases in parental motivation may make families more willing to tolerate minor side effects or other inconveniences of cost, effort in refilling, etc. Sixth, while the sample was largely Caucasian, a diverse range of family situations (single parents, adoptive families, etc.) was observed. This limits generalizability somewhat from this first investigation into this population. Subsequent studies would be improved by expanded recruitment of racial and ethnic minority populations, as some of them may display increased barriers to doctor-patient communication (Schouten & Meeuwesen, 2006) and thus such common factors may be even more critical. Seventh, when considering bivariate relationships, many of the correlations were modest in size. While alliance correlations with psychotherapy outcome have also been in a similar range (McLeod, 2011; Shirk et al., 2011), these factors have been underexplored in psychiatry and may open up an avenue to magnifying effects in current psychiatric practice. Eighth, internal consistency was slightly below the accepted convention of .70 (Nunnally & Bernstein, 1994) for the URICA-C and the CDI-2-SF (which were .65 and .67, respectively). While the CDI-2-SF was used only for diagnostic purposes and not in analyses, correlational relationships with the URICA-C may have been attenuated due to this reduction in reliability. For this reason, all analyses including this variable should be considered at additional risk for type II error. Finally,

while this is the largest investigation of behavioral predictors of adherence in pediatric psychiatry, the sample size is modest. While FIML estimation along with choice auxiliary covariates are the best contemporary practice to address missing data, and such estimation serves to retain many cases which would be discarded with older missing data methods, the present results are to be considered exploratory and meriting further replication and extension given the amount of missing data. This sample size also reduces the power to detect the effect of moderators (e.g., different types of medications, different types of diagnoses, etc.), limiting the ability to detect these influences on common therapy factors. To maintain power, no correction for type I error was made; the present investigation is the first of its kind with regard to evaluating the effects of therapeutic alliance in pediatric psychiatry, and it provides hypothesis-generating data for future investigations.

Conclusion

Given that psychiatry has shown heavy influence on what has been derided as a “bio-bio-bio” model (Sharfstein, 2005), these findings provide a novel way forward in pediatric psychiatric treatment. Given this study’s innovative investigation of the role of common factors in predicting medication adherence, a number of subsequent steps logically follow. First, a replication and extension of this investigation with semi-structured diagnosis as well as clinician-rated evaluation of subsequent symptom outcomes would improve internal validity and permit the evaluation of how such adherence affects clinical outcomes. Second, interventions exist to improve these common factors, which could be employed in the context of a pilot trial focused on improving subsequent adherence. For instance, motivational interviewing can improve motivation for behavior change even with treatment resistant populations (Lundahl, Kunz, Brown, Tollefson, & Burke, 2010), and alliance skills training has shown to be a promising

intervention to improve the alliances formed by physician treatment providers (Meystre, Bourquin, Deplaned, Stiegel, & de Rotten, 2013). Third, identifying specific aspects of clinical care that contribute to improved expectancies, motivation, and alliance (e.g., clinician experience, specific clinician behaviors in-session, etc.) would provide further information about how to maximize the role of these common factors. Other considerations for future work include integrating all of these factors into comprehensive model testing (e.g., a structural equation model) that could further integrate all aspects of the specified model, along with directly comparing model fit with other contemporary adherence models (e.g., health beliefs model, theory of planned behavior, social cognitive theory). While the specified model includes many constructs used in these models, it does not fully incorporate every facet of each model (e.g., perceived disease threat in the health beliefs model), and a model comparison would permit evaluation of what is unique and what is shared among models. In addition, systematically collecting reasons patients attribute for discontinuation would permit investigation of the moderating effects of these attributions on observed effects. Despite these limitations, the present investigation provides the first quantitative data regarding several behavioral predictors of medication adherence in pediatric psychiatric practice, which provides several potential avenues to directly impact clinical care for millions of youth with disabling psychopathology.

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Appendix A

Patient Demographics Form

Patient: _____ **Date:** _____

Person filling out this form: Mother Father Grandmother Grandfather
 Other: _____

1. Child's Date of Birth:

<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
Month	Day	Year					

2. Child's Grade in School: _____

3. Child's Gender: (1 = Female, 2 = Male)

4. Your Gender: (1 = Female, 2 = Male)

5. Child's Ethnicity:

1 = White (non-Hispanic)

2 = African-American (non-Hispanic)

3 = Hispanic/Latin American

4 = Asian

5 = Native American

6 = Pacific Islander

7 = Middle Eastern

8 = Other (specify): _____

6. Your Ethnicity:

1 = White (non-Hispanic)

2 = African-American (non-Hispanic)

3 = Hispanic/Latin American

4 = Asian

5 = Native American

6 = Pacific Islander

7 = Middle Eastern

8 = Other (specify): _____

7. Child's Living Situation:

1 = Lives with both biological parents (same residence)

2 = Lives with both biological parents (different residences – shared custody)

3 = Lives with single parent: Mother

- 4 = Lives with single parent: Father
- 5 = Lives with Mother and Stepfather
- 6 = Lives with Father and Stepmother
- 7 = Lives with Grandparents
- 8 = Other (specify): _____

8. Father's highest education received Mother's highest education received

- 1 = less than 7 years of schooling
- 2 = junior high/middle school
- 3 = partial high school
- 4 = high school graduate/GED
- 5 = partial college/technical school
- 6 = standard college/university graduate (BA/BS)
- 7 = graduate professional training (MA/MS/PhD/MD)

9. Father's current occupation Mother's current occupation

- 1 = Never worked/on welfare
- 2 = Unskilled labor
- 3 = Semi-skilled/armed services enlisted
- 4 = Small business/Skilled worker/Craftsman/NCO
- 5 = Clerical/Sales/Bank teller/Clerk/Telephone/Officer
- 6 = Technician/Semiprofessional
- 7 = Managers/Entertainers/Artists
- 8 = Administrators
- 9 = Executive/Professional
- 10 = Student/Homemaker
- 11 = Other – Mother:
- 12 = Other – Father:

Father's Job/Occupation: _____

Mother's Job/Occupation: _____

Appendix B

Documentation of Institutional Review Board Approval

Institutional Review Board
All Children's Hospital
ACH Box #9496
FWA# 00000977
IRB# 00001642

Gary Cames, CEO
All Children's Health
System, Inc.
FWA Signatory Official

E. Verena Jorgensen, M.D.
Chair

Holly Pageau, CIP
Administrative
Coordinator
727.767.4275
pageauh@allkids.org

Sue Ellie
IRB Coordinator
727.767.4275
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November 21, 2011

Alessandro De Nadai

Dear Alessandro De Nadai:

Your new protocol entitled, "Alliance and Mechanisms of Medication Adherence in Pediatric Psychiatric Practice" IRB# 11-0431, Ref# 105931 was approved under the expedited review process and will be reported at the 12/14/2011 meeting of the All Children's Hospital Institutional Review Board. This protocol meets the criteria 45 CFR 46.404, research not involving greater than minimal risk. This action fits the criteria for expedited review under research category 45 CFR 46.110 (b) (1).

The initial approval period is for a maximum of one year. The IRB approval for this protocol will expire on 11/20/2012. Please submit your continuation request by 10/15/2012 in order to avoid lapses in approval of your research and possible suspension of subject enrollment. If during the course of the study, there are any changes or amendments, or you decide to terminate the study, please notify the All Children's Hospital Institutional Review Board.

As Principal Investigator of this protocol, it is your responsibility to keep the necessary documentation, and not add further responsibility to the role of nurses, pharmacists or other healthcare providers not directly involved with this study.

Per Hospital Administrative Policy No. 014-0024-9581-000-A *Research Administrative Review Process*, your protocol must receive administrative approval prior to commencing the study. For administrative review questions, please contact the Department of Research Administration at (727) 767-4813.

Thank you for your participation in the All Children's Institutional Review Board process. If you have any questions, please contact the office of the ACH Institutional Review Board at (727) 767-4275.

Sincerely,

Denise Maguire

Wed Nov 11 02:08:03 2011

Signature applied by Denise Maguire on 11/21/2011 02:08:03 PM EST

Denise Maguire, PhD, RN-BC
Member, ACH Institutional Review Board

DM:se