

# Improving Medication Adherence in Chronic Pediatric Health Conditions: A Focus on ADHD in Youth

Anil Chacko<sup>1,2,3,\*</sup>, Jeffrey H. Newcorn<sup>3</sup>, Nicole Feirsen<sup>2</sup> and Jodi Z. Uderman<sup>2</sup>

<sup>1</sup>Department of Psychology, Queens College, City University of New York, <sup>2</sup>Neuropsychology Doctoral Program, Graduate Center of the City University of New York, <sup>3</sup>Department of Psychiatry, Mount Sinai School of Medicine,

**Abstract:** Chronic pediatric health conditions pose a significant challenge for youth, their families and professionals who treat these conditions. Long-term adherence to interventions, including and often-times, pharmacological interventions, is necessary but often problematic. Understanding factors related to poor adherence and intervening to improve adherence is essential in order to maximize long-term outcomes. Attention-deficit/hyperactivity disorder (ADHD) is one such chronic health condition requiring long-term adherence to treatment. The aims of this review are to 1) review the extant literature regarding rates of adherence to medication for youth with ADHD; 2) summarize what is known regarding factors that impede and support greater adherence to medication; 3) introduce the Unified Theory of Behavior Change as a conceptual model that may assist in developing adherence treatment packages to support medication adherence; and 4) describe several potential interventions based on the Unified Theory of Behavior Change that may improve adherence to medication for youth with ADHD. Although pharmacological interventions for youth with ADHD have been evaluated for decades, only more recently has adherence to medication been the subject of interest. However, this literature has exclusively focused on understanding factors related to adherence, with no empirical studies of interventions to improve adherence in youth with ADHD. This paper provides a rationale and research agenda for systematic study of interventions to support medication adherence in youth with ADHD.

**Keywords:** Medication, adherence, compliance, ADHD, stimulant medication, pediatric, review.

## INTRODUCTION

It is estimated that approximately 5-10% of youth throughout the world suffer from impairing, chronic health conditions [1]. These conditions require youth and often their families to manage these conditions through the administration of interventions (both psychosocial and pharmacological), management of their diet, exercise, consistent attendance to medical appointments, and coordinating treatment regimes across various settings (e.g., home - school - after-school activities). Maintaining these efforts over extended periods of time is often taxing for youth and their families. As such, it should come as no surprise that adherence to treatment is problematic, with estimates that 50% of youth are nonadherent to their treatment regimens [2]. Nonadherence to treatment is notable when one considers the impact of adherence and nonadherence. Nonadherence to treatment regimens has been shown to be related to increased hospital visits, unnecessary hospitalizations, increased symptoms of the disorder/disease, morbidity, and mortality [3-5]. Adherence to treatment regimens has been shown to be related to improved psychological functioning and overall quality of health in youth and changes in quality of life [6-9]. Given the negative consequences of nonadherence and the potential benefits of adherence to treatment regimens, understanding and improving adherence represents a significant empirical area of investigation [2].

Childhood psychiatric disorders are often chronic and lead to substantial impairments for affected youth as they enter adulthood [10]. As such, implementation of treatments over extended periods of time is often necessary for chronic psychiatric disorders of childhood. An exemplar of this issue is observed in attention-deficit/hyperactivity disorder (ADHD). Although ADHD had originally been considered a disorder of childhood [11], it is increasingly recognized as a disorder which often affects individuals well into adulthood [12], with affected individuals continuing to experience impairments in multiple areas of life functioning [12]. As such, effective, long-term interventions are often necessary. Though behavioral and pharmacological approaches have substantial evidence

for acute efficacy, compelling data do not exist that these interventions alter long-term outcomes [13, 14]. Nevertheless, as it is likely that treatment of individuals with ADHD will often require implementation of behavioral and/or pharmacologic interventions over an extended period (or periods), an issue of considerable importance is the degree to which there is adherence to long-term treatment. Although this subject has not often been the basis of empirical research in the field of ADHD, adherence is an area of considerable concern across varied chronic medical conditions (e.g., pediatric asthma, diabetes, etc) [2]. The few studies on adherence to pharmacological interventions for ADHD suggest considerable variability in short-term adherence, with generally poor adherence over the longer-term — patterns which are similar to that found in other areas of pediatric pharmacology. The objectives of this paper are to 1) review the extant literature regarding rates of adherence to medication for youth with ADHD; 2) summarize what is known regarding factors that impede and support greater adherence to medication; 3) introduce the Unified Theory of Behavior Change as a conceptual model that may assist in developing adherence treatment packages; and 4) describe several potential interventions based on the Unified Theory of Behavior Change that may improve adherence to medication for youth with ADHD.

## DEFINING AND UNDERSTANDING ADHERENCE

Adherence is a multi-faceted construct, and appreciating the various definitional issues is essential to understanding this phenomenon. The World Health Organization [2] has defined adherence as “the extent to which a person’s behaviour— e.g., taking medication, following a diet, and/or executing lifestyle changes - corresponds with agreed recommendations from a health care provider.” There are several issues in this definition that are relevant to understanding adherence to medication in youth with ADHD. First, as is likely the case for other disorders with onset during childhood, the “patient” is more broadly defined to include the parent - child dyad, as the parent is typically responsible for ensuring that the medication is administered and taken. However, this context changes rather dramatically in adolescence, as adolescents generally assume a more active role with regard to treatment decisions. The primacy of the adolescent with respect to treatment adherence complicates matters for a variety of reasons. First, there is the well de-

\*Address correspondence to this author at the Department of Psychology, Queens College, City University of New York; Tel: 718-997-3237; Fax: 718-570-0298; E-mail: anil.chacko@qc.cuny.edu

scribed and appreciated shift during adolescent development towards questioning values held by others, and the desire to take control of one's own life circumstances. More specific to the issue of adherence among adolescents with ADHD is the fact that youth with ADHD have been shown to suffer from a positive illusory bias (i.e., an overestimation of one's own performance or competence relative to an objective criterion), and therefore often underreport the impairment they experience [15]. Thus, it is likely that adolescents with ADHD and other chronic medical or psychiatric conditions will underestimate or distort the need for treatment.

As noted above and by others [16], the WHO definition of adherence implies that the patient has been given all pertinent information regarding the proposed treatment and has agreed to the prescribed treatment. Without agreement, failure to take the prescribed treatment cannot truly be considered non-adherence; rather, this would best be described as disagreement with a medical decision. Lastly, as with many other outcomes, adherence is not a categorical but a continuous variable. Therefore, the question is not whether the patient adhered, but to what extent the patient has adhered to the treatment recommendations [16]. Related questions of considerable importance are to what extent a patient needs to adhere to the prescribed treatment to obtain clinical benefits, and at what point non-adherence is likely to result in a clinically meaningful difference in response. This so-called "adherence threshold" is an important yet understudied area of investigation [17]. Yet, since a large number of youth with ADHD start and restart medication, sometimes repeatedly, over the course of several years [18], understanding the adherence threshold will illuminate the extent to which this pattern of behavior is seen as problematic.

#### ADHERENCE IN YOUTH WITH ADHD

A review was conducted utilizing PubMed and PsychInfo databases utilizing the following key words within three categories: 1) attention-deficit, attention-deficit/hyperactivity disorder, ADHD, ADD; 2) medication, pharmacology, treatment, psychostimulants, stimulant, nonstimulant, methylphenidate, adderall, d-amphetamine, and; 3) adherence, nonadherence, compliance, persistence, utilization, continuity, and engagement. Combination of these keywords resulted in the identification of 78 publications. Publications were further assessed to determine if they a) focused on youth (up to 18 years of age) with ADHD b) were published in peer-reviewed journals, and; c) provided empirical data on rates of adherence/ nonadherence. This resulted in a final sample of 17 empirical publications for review. Results of this review follow.

First, what little we know regarding medication adherence in youth with ADHD is principally focused on stimulant medication, given the historical place of stimulant medication in the treatment of ADHD (until recently stimulants were the only approved treatments) and the fact that the overwhelming majority of prescriptions for ADHD are still for stimulant medications. The literature suggests that only 1/3 - 2/3 of youth consistently use stimulant medication [19]. While medication use frequently continues for 2-6 years [18, 20], it is often marked by periods of inconsistent use [18, 21]. However, rates of adherence vary considerably across samples and studies. Data from community-based samples indicate that the average time to discontinuation for medication is 4 months [22], and that families are fully compliant with the treatment regimen for an average of only 2 months [23]. Approximately 20% of patients discontinue medication after their first prescription [24] and on average families do not persist in using medication beyond one year [22, 23, 25]. One exception is a community-based study which reported a high rate of adherence (46%) after three years of treatment [26]. When the comparatively large numbers of families who have relatively immediate non-adherence to medication are removed from these analyses, the average time to discontinuation typically increases [24].

The generally poor rates of adherence to medication in community samples stand in contrast to adherence figures seen in clinical research samples where considerably higher rates are reported. For example, Faraone and colleagues [27] found that up to 86% of subjects continued medication at the end of one year, and Jensen [28] and colleagues reported that up to 70% continued medication for up to three years. More typically, however, adherence rates in clinical research samples are approximately 50-80% after 1 year and 36-46% after 5 years [18, 20, 29-31]. Note that the above studies were mostly conducted with immediate release stimulants; an important but less well-studied factor is whether adherence varies as a function of the formulation used (i.e., immediate-release or extended-release). This evolving literature suggests that adherence is somewhat improved with extended-release versus immediate-release forms of medication [22, 27, 32], although extended-release forms of stimulant medication do not always result in greater adherence over extended periods of time [33].

#### WHO ADHERENCE DIMENSIONS

In order to better describe the variability in adherence rates across different disorders, studies and samples, the WHO [2] described 5 distinct dimensions - 1) health-system/healthcare-team factors, 2) condition-related factors, 3) patient-related factors, 4) therapy-related factors, and 5) SES-related factors. Below we discuss the literature on these factors as it relates to adherence to stimulant medication for youth with ADHD.

#### Health System/Healthcare Team Factors

Relatively little research has been conducted on the influence of health care-related factors on medication adherence in ADHD. However, provider training and types of services afforded may affect compliance, as parents' report that negative experiences with the healthcare system interfere with treatment acceptance [34, 35]. Lack of knowledge and training for both parents and prescribing physicians to manage ADHD as a chronic illness may be an important factor as well. Evidence suggests that training in chronic illness management [36] for ADHD may help clinicians execute strategies that support adherence, such as tracking medication usage with appropriate follow up measures [37]. However, despite training, impediments in this area include logistical efforts associated with distributing, collecting, scoring, interpreting, and filling out rating scales throughout the treatment process [38]. Further difficulties arise because clinicians often prefer to ask open-ended, non-structured questions regarding compliance, rather than using rating scales (e.g., Stimulant Adherence Measure [39]) to more properly document adherence [37]. Other management techniques that can be developed using this model include educating parents about ADHD, delineation of specific treatment goals, and working in collaboration with parents about the treatment decision, all of which may further support adherence [40]. Lastly, the cost of medication and services in the current US health care system are also quite burdensome on patients with ADHD. Cost estimates for some of the medications range from \$2,000-\$4,000 during a six month period [41], which may lead some families to discontinue medication. While cost estimates no doubt vary as a function of national regulations, practices and available treatments, it is likely that cost represents a barrier to treatment adherence in many countries, not only in the US.

#### Condition-Related Factors

Condition (Disorder)-related factors, such as greater baseline severity of inattention, hyperactive, and impulsive symptoms, are associated with prolonged use of stimulants. Children with increased symptom severity at baseline often exhibit a greater response to MPH (particularly for school behavior) suggesting that positive medication response may motivate treatment compliance [42]. Moreover, children with combined type ADHD use medication for longer periods than those with ADHD-Predominantly

Inattentive Type (ADHD-I) or ADHD-Predominantly Hyperactive/Impulsive Type (ADHD-HI [20]. Children with more severe comorbid conditions demonstrate higher stimulant use as well [43]; however, comorbid Oppositional Defiant Disorder (ODD), in particular, is associated with poor adherence in patients. Indeed, the presence/absence of ODD in school is underscored as an important moderating variable for long-term adherence, with poorer adherence observed in youth with ADHD and comorbid ODD [18, 31].

### Patient-Related Factors

A variety of patient-specific characteristics - including age, patient-family relationships and histories, race, gender, and parental cognitions regarding the nature of the illness and how to best treat it (e.g., appropriateness of medication use) - may also affect medication adherence in youth with ADHD. First, evidence suggests that increased patient and parental age at the time of diagnosis is associated with lower stimulant adherence [20]. Parental influence on medication adherence in their children also decreases with the youth's age. Many adolescents who discontinue stimulants between 7th and 9th grade report the decision as their own choice; some of the individuals consult their parents before stopping, and some do not [44]. Family characteristics and family histories also moderate the consistency of medication use. Decreased adherence is predicted by strained parent-child relationships and maternal stress [45]. Two-parent families, with higher rates of perceived social support and with family histories of stimulant usage, are more likely to adhere to the medication regimen [45]. Patient race and gender also appear to moderate compliance. Parents of Caucasian boys, as compared to African-American boys and girls and Caucasian girls, are more likely to believe that boys with ADHD have a disorder requiring medication treatment [46]. This finding suggests that parents of children with ADHD perceive symptoms differently based on the child's gender and race. Further, parental and youth (particularly adolescents') cognitions and attitudes toward medication treatment for ADHD may moderate adherence as well. Parents who believe that ADHD is an organic condition with biological underpinnings, rather than a psychologically or environmentally-based condition, are more likely to encourage children to take stimulant medication [47]. Parental beliefs that the medication is safe and effective in reducing problem behavior also positively influence adherence to the medication regimen [47]. Additionally, parental knowledge about ADHD predicts initial acceptance of stimulant treatment, but this finding does not extend to stimulant use over a period of one year [48]. Not surprisingly, in the context of ADHD studies, stigma regarding psychopathology is an important factor that impedes compliance as well [19, 35, 49]. Similarly, adolescents with ADHD may not perceive ADHD as an illness, question the utility of medication as an approach to ADHD, worry about the effects of ADHD medication on changing their personality/abilities in negative ways, and are concerned with the stigma of using these medications [19]. These cognitions are likely to impact adherence in youth with ADHD, particularly adolescents, who have a heightened role in relation to decision making regarding treatment.

### Therapy-Related Factors

Medication-specific factors influence adherence as well. Christensen [50] examined self-report claims (in which 58.4% of participants were younger than age 18), finding that medication adherence was greater for patients with ADHD on stimulants compared to non-stimulants (e.g., atomoxetine), and for patients taking amphetamine vs. methylphenidate. No doubt, satisfaction with improvements from and side-effects of specific types of medications influence adherence. However, youth and parental beliefs and concerns regarding treatment effectiveness and side effects of medication are often present, and when there is limited improvement or adverse events occur, adherence to treatment generally decreases [34, 49, 51, 52]. The extent to which the extent of response, differ-

ences in onset of response across treatments, and the occurrence and nature of adverse effects no doubt vary across individuals.

Adherence rates also appear to be related to the dosing schedule used. Patients required to take multiple daily doses tend to have decreased adherence [45], mainly because they forget to take doses later in the day. For this reason, patients on long-acting medications show greater adherence compared to those using short- and intermediate-acting formulations [42, 50]. Many children also discontinue their medication regimen out of dislike for swallowing pills and embarrassment or stigma associated with medication usage [53]. Teenagers also report concerns that medication alters their personality and the way in which they experience themselves [44], which presumably might also decrease adherence. Parents often voice similar concerns regarding unwanted changes in their child's personality or demeanor; in our experience, affective blunting (even in the presence of positive behavioral change) is not well tolerated in any age group.

### SES-Related Factors

The role that socioeconomic status (SES) plays in adherence to psychostimulant treatment of ADHD is largely unknown. Findings from some studies suggest that SES is positively correlated with treatment adherence rates [54], but results of other studies indicate that medication adherence in ADHD in low-income families is not correlated with SES [51]. Thus, the relationship between medication adherence in ADHD and SES requires further investigation. This is in line with data concerning SES and adherence to medication in other disorders [2].

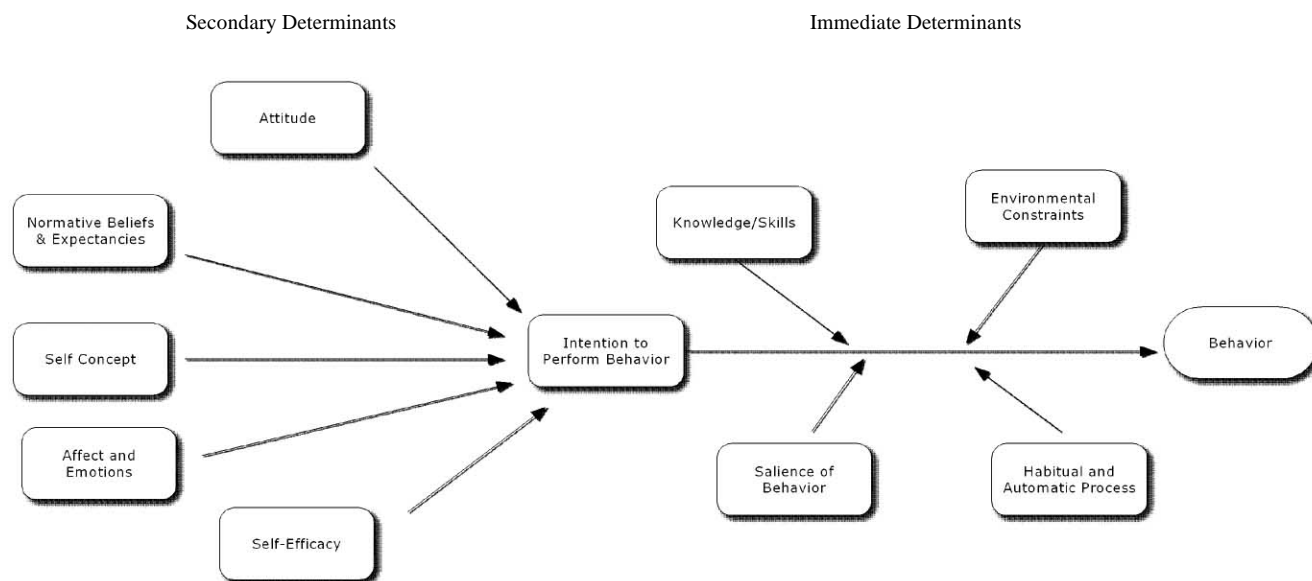
### CONCEPTUAL MODEL—THE UNIFIED THEORY OF BEHAVIOR CHANGE

Although several distinct conceptual theories may be utilized to explain adherence to medication in youth with ADHD [54], there has been growing interest in developing a more unified approach. In 2001, the National Institute of Mental Health convened a meeting focused on relevant theories of behavior change and how these impact treatment. The resultant framework, the Unified Theory of Behavior Change [55], offers an integrative model for understanding and intervening to alter behavior, including behaviors related to medication adherence, for families and youth with ADHD (see Fig. 1).

The core variables of the model are organized into two sequences. The first sequence focuses on the immediate determinants of behavior. Behavior is influenced by five core variables. First, an individual must be willing to perform or intend to perform the behavior in question. Second, the individual must have the requisite knowledge and skills to enact the behavior. Third, there must be no environmental constraints that render behavioral performance impossible. Fourth, the behavior must be salient to the individual, so that the person does not forget to enact it. Finally, habitual and automatic processes may influence behavior.

These five variables interact in complex ways to determine behavior. Medication adherence is most likely to occur when each of the variables coalesce toward behavioral performance. For example, for medication adherence to occur, parents/youth will be most likely to utilize medication if they truly intend to use medication and have the skills to do so (e.g., can swallow a pill), if there are not environmental constraints against doing so (e.g., parent/guardian is available to administer medication; there is no stigma attached to taking the medication, there is a positive parent-child relationship), if the child and/or parent remembers to do so, and if the parent/youth have used medication successfully in the past (habitual behavior).

The second aspect of the model focuses on the determinants of an individual's willingness, intention, or decision to perform a behavior. These variables are typically influenced by six major factors that serve as the immediate psychological determinants of one's



**Fig. (1).** Determinants of intention and behavior.

decision to perform a behavior. *Attitude* refers to how favorable or unfavorable the parent/youth feels about performing the behavior (i.e., initiating and maintaining medication use). *Normative beliefs* reflect individuals' beliefs about the extent to which other people who are important to them think they should or should not perform the behaviors. *Expectancies* refer to the perceived advantages and disadvantages of performing the behavior. *Self-concept* refers to a parent/youth's conception of self and whether performing the behavior is consistent with that self-image. *Affect* refers to the fundamental affective and emotional reactions to behavioral performance. Theories of emotion emphasize two core facets, the degree of arousal and whether the affective direction of that arousal is positive or negative. In general, individuals who have a strong negative emotional reaction to a behavior will be less inclined to perform it and those who have a strong positive emotional reaction will be more inclined to perform it. Likewise affect (both parent and child) may be influenced by poor (or positive) parent-child interactions, which may further influence adherence behavior. *Self-efficacy* refers to one's perceived confidence that he or she can perform the behavior.

Importantly, the core predictors are presumed to be the primary determinants of one's decision or willingness to perform a behavior, such as adhering to medication. More distal constructs, such as personality variables, demographic variables, family variables, and media variables may influence behavior, but they do so indirectly through their influence on these primary variables. The relative importance of the constructs in Fig. (1) in influencing behavior can differ from population to population. For example, for some individuals, normative influences may be a primary determinant of the decision to perform a behavior, whereas for other individuals, such influences may be of little consequence.

To utilize the Unified Theory of Behavior Change to understand parent/youth intentions to adhere to medication, one must consider their attitudes about medication use, their expectancies about the advantages and disadvantages of medication adherence, the pressures that are being brought to bear on them with respect to medication adherence, their emotional and affective reactions to the prospects of medication adherence, and their perceptions of their abilities to adhere to medication over time.

## IMPROVING MEDICATION ADHERENCE FOR YOUTH WITH ADHD: POTENTIAL INTERVENTIONS

A theoretically well-grounded model, such as the Unified Theory of Behavior Change (UTBC), offers much to assist the field's understanding of how best to intervene to improve medication adherence for youth with ADHD. As we discuss in this final section, several types of intervention that map onto aspects of the UTBC may prove to be useful in improving medication adherence. To our knowledge, there have not been empirical studies that assess the impact of specific interventions to improve medication adherence in youth with ADHD, although several potential interventions have been discussed [35, 54]. As others have [16, 56, 57] we organize these potential interventions to improve ADHD medication adherence into key categories, including: patient education, individualized approaches to tailoring medication, behavioral strategies, and peer-support strategies. Although we provide an overview of several potential strategies across categories, it is important to take a patient-centered or personalized approach by tailoring these strategies to the particular patient's strengths and needs (youth/parent/family).

### PATIENT (YOUTH AND PARENT) EDUCATION

The UTBC suggests that targeting knowledge and skills through education may be an important strategy. Patient education regarding ADHD is likely to be critical for long-term adherence to medication - as there are often questions and concerns about the etiology of ADHD [58], the side-effects of ADHD medication (e.g., growth retardation in children [59], possible cardiovascular effects [60], increasing risk for substance abuse [61], and the long-term neuropsychological impact of continued use of medication [62]). These are relevant issues for parents and youth (depending on age) to consider when deciding to initiate and/or sustain use of medications for ADHD. However, misinformation, lack of knowledge, and inadequately crafted expectations may all work against adherence. Therefore, patient (parent and child) education is critical. As suggested by the National Council on Patient Information and Education (NCPIE [63]), the prescribing physician has a prominent role in educating patients. This includes "educating patients about the medications they are taking, why they are taking them, what the

medications look like, what time patients should take their medications, potential side effects, what to do if a patient experiences side effects, and what regular testing is necessary (pg. 15)". In particular, for patients with ADHD, it is important to address misconceptions/misinformation about ADHD and ADHD medications through psychoeducation. This type of "information" is quite prevalent and readily accessed *via* the internet. However, it is also important to note that the quality and accuracy of information on the internet may vary considerably. Therefore, it is critical that professionals direct patients and their parents to internet sites that are trusted sources to provide current, unbiased, and accurate information on ADHD and treatments for the disorder. Education can also be provided both by offering written materials to patients/parents as well as ongoing communication between the prescribing physician (as well as other key medical staff involved in patient care) and the patient (youth/parent).

### INDIVIDUALIZED APPROACHES FOR TAILORING MEDICATION

Tailoring ADHD medication treatment to the profile of the youth and family in such a way as to minimize environmental constraints (e.g., reducing the number of adults needed to implement/monitor medication regimen) while maximizing salience and habitual/automatic processes is an essential component of addressing adherence. Prescribing physicians should consider optimizing the benefit/adverse event profile such that patients obtain maximal therapeutic benefit and minimal adverse effects. Medication titration that systematically assesses the effects of different medications and medication doses across multiple key domains of functioning (e.g., home, school, after-school, recreational) while systematically measuring the level of adverse events will provide the prescribing physician important information regarding response and tolerability. Given that the occurrence of significant adverse events predicts discontinuation of stimulant medication [53], minimizing adverse events is often equally important as symptom reduction in achieving longer-term adherence. The immediate benefit of medication early in treatment is likely to promote long-term adherence [42], so if a medication is less likely to achieve response immediately (e.g., atomoxetine or other non-stimulants), the family must be educated about this so expectations can be adjusted. The balance between maximizing initial therapeutic response while minimizing side-effects is likely to vary across individuals/families. For some, the highest priority is to attain the most robust response as quickly as possible, and they are willing to endure some tolerability problems in achieving this response. For others, tolerability is more important than early response, so the titration approach should necessarily be slower.

Another important perspective is to simplify the medication regimen as much as possible. This means utilizing long-acting formulations that provide full-day coverage, and which can be used once-daily. This is likely to minimize the impact of embarrassment/stigma or forgetting to take or administer medication, all of which have been associated with poorer adherence [19, 35, 45, 49, 53]. It may be best to consider a tiered approach to prescribing, starting off with a single long-acting medication and subsequently tailoring if response and/or tolerability are inadequate (note: here we have offered the approach favored by experts in the US; however, guidelines with regard to this approach may differ across countries). The range of therapeutic options includes switching to a different medication formulation or class, adding a short-acting agent to a longer-acting agent to augment duration of response, and implementing strategies for managing adverse events. Perhaps, as the field continues to develop an understanding of which patients (youth) and parents will have considerable adherence issues to ADHD medications, we will be able to determine, a priori, which families may be best candidates for an initial tailored approach to optimizing treatment. Importantly, regardless of the approach taken,

decisions about a medication regimen must be made in full partnership with the patient and his/her family.

### BEHAVIORAL STRATEGIES

Behavioral strategies focus on applied behavioral methods (e.g., tailoring medication to the profile of the youth and family, technology-based interventions, parent-training, etc. [56]). In line with the UTBC model, these interventions target environmental constraints to adherence, improve the salience of taking medication, address habitual and automatic processes that may influence adherence behavior, and improve patient self-efficacy in taking medication. These strategies have been found to be most effective in improving medication adherence relative to education and support strategies [56]. The utility of applied behavioral strategies is likely particularly important for families of youth with ADHD for several reasons. First, youth with ADHD often present with oppositional behavior and as such there is considerable parent-child conflict [64]. Therefore, the parent's ability to obtain their child's assent to take medication may be compromised. For adolescents, as discussed earlier, cognitive processes such as positive illusory bias may further interfere with the perceived need to take medication for ADHD. As predicted by the UTBC, taking ADHD medication may not fit the adolescent's self-concept (e.g., being independent and/or invulnerable), thereby reducing the chances for adherence. Moreover, parents of youth with ADHD are at higher risk for having ADHD themselves, as well as depression [65], both of which may interfere with the parents' ability to administer medication. In the examples given above, it is unlikely that *education alone* could achieve the change in attitude or behavior that would be required to embrace medication treatment and implement an effective method for taking the medication regularly. Therefore, utilizing behavioral strategies in combination with psychoeducation will often be necessary to affect change in attitude and behavior.

Technology-based interventions may also be utilized to reduce the impact of environmental constraints to adherence and improve the salience of administering or taking medication. For instance, automatic messages to refill prescriptions *via* home/cell phones and reminders to take medication *via* pill reminder boxes, beepers or other handheld devices can be used to remind parents/youth to take medication. Although yet to be studied, for families in which multiple members have ADHD, where the ability to organize and complete tasks may be impaired (for both youth and parent), these methods may be highly effective.

Parent-training may be necessary to assist parents in developing specific behavioral skills which support adherence. This can be as discrete as teaching parents how to perform pill-swallowing training procedures, in which children learn to swallow very small pills (starting with sprinkle size) *via* positive reinforcement until they are able to swallow their prescribed medication, to more complicated skills such as supporting parents in learning how to utilize rewards and consequences in order to maximize medication adherence from their child. Given that many youth with ADHD have significant oppositional problems, supporting parents in learning skills to improve overall behavioral compliance should have clear benefits on adherence. We are unaware of any studies that have assessed the benefits of utilizing a parent training approach to teach skills to parents to enhance medication adherence in children. This would be a potentially important area of investigation.

### PEER SUPPORT STRATEGIES

Although family support provided by professionals *via* scheduled treatment appointments has been the traditional method to support adherence, there has been a growing trend to utilize peers to increase treatment adherence [66] and manage chronic illnesses [67]. Peer-delivered models have also been utilized within the mental health field to facilitate use of services [68]. Peers are often effective at engaging similarly-situated individuals into services be-

cause they are viewed as credible role models who provide hope, empower participants and enhance satisfaction with services. Further, peer-delivered services decrease isolation, normalize feelings of distress, and de-stigmatize views about mental illness and seeking treatment.

In the broader field of children's mental health, peer models using Family Advocates [69] have been introduced in several communities in the United States [70]. For instance, New York State's Office of Mental Health created a network of Family Advocates to connect parents of children with mental health needs to mental health service systems. These Family Advocates are typically parents of children who have special needs or have been involved in the mental health system themselves. As such, the Family Advocates' first-hand knowledge of the mental health system provides a unique perspective that adds credibility to these individuals as peers to model, coach, and support parents in their efforts to navigate the mental health system. In particular, these Family Advocates are considered prime agents to empower parents. Importantly, the underlying conceptual approach to training Family Advocates has been *via* the UTBC model [69]. Family Advocates focus on four primary constructs within this model (beliefs and expectancies, social norms, attitudes, and self-efficacy) in order to support and empower parents to fully engage in and become active participants in their child's mental health services. Although the value of such interventions has not been specifically studied, it is likely that Family Advocates can play a prominent role in enhancing adherence to ADHD medication. In addition, there may also be a role for youth advocates, particularly young adults, who can serve as older peer-mentors to adolescents with ADHD *via* one-to-one or group formats as these youth contemplate decisions regarding ADHD medication.

#### FUTURE DIRECTIONS

ADHD is a complex disorder that is often chronic and can lead to substantial long-term impairments for affected individuals. Interventions delivered acutely to youth affected with ADHD, regardless of how intensive, have not proven to alter these poor outcomes for a majority of youth with ADHD [13, 14]. Best practice suggests that application of evidence-based interventions, including medication, may offer youth with ADHD the best opportunity for long-term success. As such, adherence to these interventions is critical; however, the field is just beginning to tackle the critical questions that can help support families of youth with ADHD to maximize adherence to ADHD medications. Empirical investigation in several key areas is needed to further advance the science in this area. First, as argued by others [54], a universal definition of adherence is needed. Currently, the field is awash with a multitude of definitions, making comparisons between studies extremely challenging. It is also important to go beyond identifying predictors and processes of categorical (yes/no) or continuous (mean numbers of months) adherence outcomes, and begin to look at individualized predictors and processes in families who have different patterns of adherence (e.g., consistently high, intermittent adherence, those that never initiate medication and those that initially take medication but discontinue very early-on; [18, 24]). This will assist in determining the most effective strategy for these different "adherence typologies".

Although our understanding of the problem of non-adherence to medication for youth with ADHD is not yet complete, the field does recognize this as a major issue. As leading international experts have recently argued [71], it is important to focus our efforts on improving adherence rather than just explaining it. To date, however, approaches to improving medication adherence for youth with ADHD have more often been based on conjecture than on systematic, theory-driven methods. To our knowledge, there has not been a single empirical investigation to determine the effects of adherence interventions for improving medication adherence for youth with ADHD. However, we do know that, based on the extant literature on intervening to improve medication adherence for a variety of

chronic childhood conditions, it is possible to improve medication adherence for youth with ADHD. As Haynes [72] argues, adherence is a problem for the majority of chronic health conditions, and it is important to understand adherence to treatment in ADHD in that context. Yet, despite the commonalities across conditions, adherence research is often fragmented - each field discovers anew the problem of adherence, then reinvents approaches to it. When research is conducted, it tends to be non-cumulative, in that it does not build on earlier research and does not attempt to move the field of adherence research forward.

Furthermore, research often focuses on interventions that are either impractical (i.e., unsustainable in real world practice) or unimaginative and therefore unlikely to succeed (e.g., relying upon pamphlets, logic, and "scaring the patient to death"). Lastly, interventions have tended to be atheoretical. A more effective approach would synthesize the available literature and utilize theory-driven approaches to systematically evaluate interventions to improve medication adherence. We have argued here that the Unified Theory of Behavior Change offers a strong conceptual model that can guide intervention efforts, several of which have been described in this paper. Importantly, adherence interventions need to target multiple factors [72], and therefore require combinations of interventions [56], delivered by various individuals, over extended periods of time, in order to maximize adherence and beneficial outcomes for youth with ADHD. Although we have focused here on strategies for improving adherence to medication treatment for ADHD, we also believe the model that we have advanced is applicable to other chronic health conditions in children and adolescents.

#### REFERENCES

References 73-75 are related articles recently published.

- [1] Newacheck PW, McManus M, Fox HB. Access to health care for children with special health care needs. *Pediatrics* 2000; 105: 760-6.
- [2] World health organization. Adherence to long term therapies: A call to action. World health organization: Switzerland 2003.
- [3] Milgrom H, Bender B, Ackerson L. Noncompliance and treatment failure in children with asthma. *J Allergy Clin Immunol* 1996; 98: 1051-7.
- [4] Kennard BD, Stewart SM, Olvera R. Nonadherence in adolescent oncology patients: Preliminary data on psychological risk factors and relationships to outcome. *J Clin Psychol Med Settings* 2004; 11: 31-9.
- [5] Rapoff M. Adherence to pediatric medical regimens. Issues in Clinical Child Psychology. 2<sup>nd</sup> ed. New York: Springer 2009.
- [6] Drotar D, Greenley RN, Demeter CA. Adherence to pharmacological treatment for juvenile bipolar disorder. *J Am Acad Child Adol Psychiatry* 2007; 46: 831-9.
- [7] Ekberg H, Kyllonen L, Madsen S. Clinicians underestimate gastrointestinal symptoms and overestimate quality of life in renal transplant recipients: A multinational survey of nephrologists. *Transplantation* 2007; 84: 1052-954.
- [8] Fredericks EM, Magee JC, Opiari-Arrigan L. Adherence and health-related quality of life in adolescent liver transplant recipients. *Pediatr Transplant* 2008; 12: 289-99.
- [9] Hommel KA, Davis CM, Baldassano RN. Medication adherence and quality of life in pediatric inflammatory bowel disease. *J Pediatr Psychol* 2008; 33: 867-74.
- [10] Kessler R, Berglan P, Demler O. Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication. *Arch Gen Psychiatry* 2005; 62: 593-603.
- [11] American Psychiatric Association. Diagnostic and Statistical Manual of Mental Health Disorders, IV-TR. Washington: APA 2000.
- [12] Kessler R, Adler L, Barkley R. The Prevalence and Correlates of Adult ADHD in the United States: Results from the National Comorbidity Survey Replication. *Am J Psychiatry* 2006; 163: 716-23.
- [13] Molina B, Flory K, Hinshaw S. Delinquent behavior and emerging substance use in the MTA at 36 months: prevalence, course, and treatment effects. *J Am Acad Child Adol Psychiatry* 2007; 46: 1028-40.



- [14] Molina B, Hinshaw S, Swanson J. The MTA at 8 years: prospective follow-up of children treated for combined-type ADHD in a multisite study. *J Am Acad Child Adolesc Psychiatry* 2009; 48: 484-500.
- [15] Owens JS, Hoza B. The role of inattention and hyperactivity/impulsivity in the positive illusory bias. *J Consult Clin Psychol* 2003; 71: 680-91.
- [16] Shemesh E, Drotar D. Treatment Adherence. In: *Textbook of Pediatric Psychosomatic Medicine*. In press.
- [17] Stuber ML, Shemesh E, Seacord D. Evaluating nonadherence to immunosuppressant medications in pediatric liver transplant recipients. *Pediatr Transplant* 2008; 12: 284-8.
- [18] Charach A, Ickowicz, Schachar R. Stimulant treatment over five years' adherence, effectiveness, and adverse effects. *J Am Acad Child Adolesc Psychiatry* 2004; 43: 559-67.
- [19] Charach A, Volpe T, Boydell KM. A theoretical approach to medication adherence for children and youth with psychiatric disorders. *Harv Rev Psychiatry* 2008; 16: 126-35.
- [20] Barbaresi W, Katusic S, Colligan R. Long-term stimulant medication treatment of attention-deficit/hyperactivity disorder: results from a population study. *J Dev Behav Pediatr* 2006; 27: 1-10.
- [21] Winterstein AG, Gerhard T, Shuster J, *et al.* Utilization of pharmacologic treatment in youth with attention deficit/hyperactivity disorder in Medicaid database. *Ann Pharmacother* 2008; 42(1): 24-31.
- [22] Marcus SC, Wan GJ, Kemner JE, *et al.* Continuity of methylphenidate treatment for attention-deficit/hyperactivity disorder. *Arch Pediatr Adolesc Med* 2005; 159(6): 572-8.
- [23] Perwien AR, Hall J, Swensen A, *et al.* Stimulant treatment patterns and compliance in children and adults with newly treated attention-deficit/hyperactivity disorder. *J Manag Care Pharm* 2004; 10(2): 122-9.
- [24] Miller AR, Ialonde CE, McGrail KM. Children's persistence with methylphenidate therapy: a population based study. *Can J Psychiatry* 2004; 49: 761-8.
- [25] Firestone P. Factors associated with children's adherence to stimulant Medication. *Am J Orthopsychiatry* 1982; 52: 447-57.
- [26] Atzori P, Usala T, Carucci S. Predictive Factors for Persistent Use and Compliance of Immediate-Release Methylphenidate: A 36-Month Naturalistic Study. *J Child Adolesc Psychopharm* 2009; 19: 673-81.
- [27] Faraone SV, Biederman J, Zimmerman B. An analysis of patient adherence to treatment during a 1-year, open-label study of OROS methylphenidate in children with ADHD. *J Atten Disord* 2007; 11: 157-66.
- [28] Jensen P, Arnold E, Swanson J. Three-year follow-up of the NIMH MTA study. *J Am Acad Child Adolesc Psychiatry* 2007; 46: 989-1002.
- [29] McBride MC. An individual double-blind crossover trial for assessing methylphenidate response in children with attention deficit disorder. *J Pediatr* 1988; 113: 137-45.
- [30] Barkley RA, McMurray MB, Edelbrock CS, *et al.* Side effects of methylphenidate in children with attention deficit hyperactivity disorder: A systemic, placebo-controlled evaluation. *Pediatrics* 1990; 86: 184-92.
- [31] Thiruchelvam D, Charach A, Schachar RJ. Moderators and mediators of long-term adherence to stimulant treatment in children with ADHD. *J Am Acad Child Adolesc Psychiatry* 2001; 40: 922-8.
- [32] Olfson M, Marcus SC, Zhang HF, *et al.* Continuity of methylphenidate treatment of adults with attention-deficit/hyperactivity disorder. *J Manag Care Pharm* 2007; 13(7): 570-7.
- [33] Chou WJ, Chou MC, Tzang RF, *et al.* Better efficacy for the osmotic release oral system methylphenidate among poor adherents to immediate-release methylphenidate in the three ADHD subtypes. *Psychiatry Clin Neurosci* 2009; 63(2): 167-75.
- [34] Bussing R, Gary FA. Practice guidelines and parental ADHD treatment evaluations: friends or foes? *Harv Rev Psychiatry* 2001; 9: 223-33.
- [35] Charach A, Skyba A, Cook L. using stimulant medication for children with ADHD: what do parents say? A brief report. *J Can Acad Child Adolesc Psychiatry* 2006; 15: 75-83.
- [36] Bodenheimer T, Wagner EH, Grumbach K. Improving primary care for patients with chronic illness. *JAMA* 2002; 288: 1775-9.
- [37] Epstein JN, Langberg JN, Lichtenstein PK. Community-wide intervention to improve the attention-deficit/hyperactivity assessment and treatment practices of community physicians. *Pediatrics* 2008; 122: 19-27.
- [38] Tsai AC, Morton SC, Mangione CM. A meta-analysis of intervention to improve chronic care for chronic illness. *Am J Manag Care* 2005; 11: 478-88.
- [39] Charach A, Gajaria A, Skyba A, *et al.* Documenting adherence to psychostimulants in children with ADHD. *J Can Acad Child Adolesc Psychiatry* 2008; 17: 131-6.
- [40] Wolraich ML. Attention-deficit hyperactivity disorder. *Semin Pediatr Neurol* 2006; 13: 279-85.
- [41] Wu EQ, Birnbaum HG, Zhang HF. Health care costs of adults treated for attention-deficit/hyperactivity disorder who received alternative drug therapies. *J Manag Care Pharm* 2007; 13: 561-9.
- [42] Denney, Colin B, Rapport, *et al.* Predicting methylphenidate response in children with ADHD: Theoretical, empirical, and conceptual models. *J. Am Acad Child Adolesc Psychiatry* 1999; 38: 393-401.
- [43] Swanson JM, Hinshaw SP, Arnold LE. Secondary evaluations of the MTA 36-month outcomes: propensity score and growth mixture model analyses. *J Am Acad Child Adolesc Psychiatry* 2007; 46: 1003-14.
- [44] Meaux JB, Hester C, Smith B. Stimulant medications: a trade-off? The lived experience of adolescents with ADHD. *J Spec Pediatr Nurs* 2006; 11: 214-26.
- [45] Gau SF, Shen H, Chou M. Determinants of adherence to methylphenidate and the impact of poor adherence on maternal and family measures. *J Child Adolesc Psychopharm* 2006; 16: 286-97.
- [46] Bussing R, Koro-Ljungberg ME, Gary F. Exploring help-seeking for ADHD symptoms: a mixed methods approach. *Harv Rev Psychiatry* 2005; 13: 85-101.
- [47] Johnston C, Seipp C, Hommersen P. Treatment choices and experiences in attention deficit hyperactivity disorder: relations to parents' beliefs and attributions. *Child Care Health Dev* 2005; 31: 669-77.
- [48] Corkum P, Rimer P, Shachar R. Parental knowledge of attention-deficit hyperactivity disorder and opinions of treatment options: impact on enrollment and adherence to 12-month treatment trial. *Can J Psychiatry* 1999; 44: 1043-8.
- [49] Hansen DL, Hansen EH. Caught in a balancing act: parents dilemmas regarding their ADHD child's treatment with stimulant medication. *Qual Health Res* 2006; 16: 1267-85.
- [50] Christensen L, Sasané R, Hodgkins P. Pharmacological treatment patterns among patients with attention-deficit/hyperactivity disorder: retrospective claims-based analysis of a managed care population. *Curr Med Res Opin* 2010; 26: 977-89.
- [51] Rieppi R, Greenhill L, Ford R. Socioeconomic status as a moderator of ADHD treatment outcomes. *J Am Acad Child Adolesc Psychiatry* 2002; 41: 269-77.
- [52] Leslie LK, Plemmons D, Monn AR. Investigating ADHD treatment trajectories: listening to families' stories about medication use. *J Dev Behav Pediatr* 2007; 28: 179-88.
- [53] Dosreis S, Zito JM, Safer DJ. Parental perceptions and satisfaction with stimulant medication for attention-deficit hyperactivity disorder. *J Dev Behav Pediatr* 2003; 24: 155-62.
- [54] Charach A, Gajaria A. Improving psychostimulant adherence in children with ADHD. *Expert Rev Neurother* 2008; 8: 1563-71.
- [55] Fishbein M, Triandis H, Kanfer F, *et al.* Factors influencing behavior and behavior change. In: Baum A, Revenson T, Singer J, Eds. *Handbook of health psychology*. Mahwah, NJ: Erlbaum 2001.
- [56] Kahana S, Drotar D, Frazier T. Meta-analysis of psychological interventions to promote adherence to treatment in pediatric chronic conditions. *J Pediatr Psychol* 2009; 33: 590-611.
- [57] Lemanek KL, Kamps J, Chung NB. Empirically supported treatments in pediatric psychology: Regimen adherence. *J Pediatr Psychol* 2001; 26: 253-75.
- [58] Chacko A, Wakschlag L, Hill C. Viewing preschool disruptive behavior disorders and ADHD through a developmental lens: what we know & what we need to know. *Child Adolesc Psychiatric Clin N Am* 2009; 18(3): 627-43.
- [59] Swanson JM, Elliott GR, Greenhill LL. Effects of stimulant medication on growth rates across 3 years in the MTA follow-up. *J Am Acad Child Adolesc Psychiatry* 2007; 46: 1015-27.
- [60] American Academy of Pediatrics/American Heart Association. American Academy of Pediatrics/American Heart Association clarification of statement on cardiovascular evaluation and monitoring of children and adolescents with heart disease receiving medications for ADHD. *J Dev Behav Pediatr* 2008; 29: 335.

- [61] Lambert NM, Hartsough CS. Prospective study of tobacco smoking and substance dependencies among samples of ADHD and non-ADHD participants. *J Learn Disabil* 1998; 31: 533-44.
- [62] Berman SM, Kuczenski R, McCracken JT. Potential adverse effects of amphetamine treatment on brain and behavior: a review. *Mol Psychiatry* 2009; 14: 123-42.
- [63] National Council on Patient Information and Education. Enhancing prescription medication adherence: a national action plan. Bethesda: National Council on Patient Information and Education 2007.
- [64] Johnston C, Mash E. Families of children with attention-deficit/hyperactivity disorder: review and recommendations for future research. *Clin Child Fam Psychol Rev* 2001; 4: 3, 183-207
- [65] Chronis AM, Lahey BB, Pelham WE. Psychopathology and substance abuse in parents of children with attention-deficit/hyperactivity disorder. *J Am Acad Child Adolesc Psychiatry* 2003; 42: 1424-32.
- [66] Deering KN, Shannon K, Sinclair H. Piloting a peer-driven intervention model to increase access and adherence to antiretroviral therapy and HIV care among street-entrenched HIV-positive women in Vancouver. *AIDS Patient Care STDs* 2009; 23: 603-9.
- [67] Heisler M, Halasyamani L, Resnicow K. "I am not alone": the feasibility and acceptability of interactive voice response-facilitated telephone peer support among older adults with heart failure. *Congest Fail* 2007; 13: 149-57.
- [68] Sells D, Davidson L, Jewell C. The treatment relationship in peer-based and regular case management for clients with severe mental illness. *Psychiatr Serv* 2006; 57: 1179-84.
- [69] Olin SS, Hoagwood KE, Rodriguez J. The application of behavior change theory to family-based services: Improving parent empowerment in children's mental health. *J Child Fam Stud* 2009; 45: 1062-24.
- [70] Hoagwood KE, Green E, Kelleher K. Family advocacy, support and education in children's mental health: Results of a national survey. *Adm Policy Men Health* 2008; 35: 73-83
- [71] van Dulmen S, Sluijs E, van Dijk L. Furthering patient adherence: A position paper of the international expert forum on patient adherence based on an internet forum discussion. *BMC Health Serv Res* 2008; 8: 47.
- [72] Haynes RB, Ackloo E, Sahota N. Interventions for enhancing medication adherence. *Cochrane Database Syst Rev* 2008; Issue 2. Art. No.: CD000011.
- [73] Berenguer B, La CC, de la Matta MJ, Martin-Calero MJ. Pharmaceutical care: past, present and future. *Curr Pharm Des* 2004; 10(31): 3931-3946.
- [74] Guilloteau D, Chalon S. PET and SPECT exploration of central monoaminergic transporters for the development of new drugs and treatments in brain disorders. *Curr Pharm Des* 2005; 11(25): 3237-3245.
- [75] Kirchheiner J, Seeringer A, Viviani R. Pharmacogenetics in psychiatry--a useful clinical tool or wishful thinking for the future? *Curr Pharm Des* 2010; 16(2): 136-144.