Introduction to the Special Issue on Adherence in Pediatric Medical Conditions

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Research with a wide range of chronic health conditions in children and adolescents has indicated that nonadherence to medical treatment is pervasive, estimated to be as high as 50% for some conditions (Drotar, 2000; Rapoff, 2010). Nonadherence can take many forms including not filling prescriptions to skipping or missing doses and can be intentional (e.g., deciding not to take a medication because of side effects) or unintentional (e.g., forgetting). Poorer adherence has been documented for regimens that are more time-consuming and complex, and rates of nonadherence in pediatric chronic illness populations, especially among adolescents, are even higher than those in adult populations (Rapoff, 2010). Potentially serious health consequences can result from nonadherence. For example, incomplete adherence to immunosuppressive drugs has been linked to heart, kidney, and liver transplant failures (Ettenger et al., 1991). Nonadherence can influence clinical decisions about care, resulting in increases or changes in medication when none are needed. Nonadherence has been estimated to result in billions of dollars of excess medical care annually (The Task Force for Compliance, 1994). Despite the clinical importance of nonadherence and the significance of its impact on health care delivery, assessment of adherence is not routinely or systematically done in clinical practice, and treatments for adherence problems in pediatric chronic diseases continue to be limited (Rapoff, 2010). Moreover, few studies have evaluated the impact of interventions designed to promote adherence to medical treatment in childhood chronic diseases using randomized controlled trials (Rapoff, 2010).

Many of the provisions of Affordable Care Act (ACA; Public Law No: 111–148, March 23, 2010) seek to align the incentives to health care providers to deliver improved patient health outcomes and reduce costs through the creation of accountable care organizations (ACO) and Patient Centered Medical Home (Berwick, 2011; Rittenhouse, Shortell, & Fisher, 2009). As noted by Rozensky and Janicke (2012), the recognition that these aims can best be achieved through interprofessional care that integrates mental and physical health care is an opportunity for pediatric psychologists to capitalize on our multi-disciplinary roots and, for many, our every day practice (Roberts, Canter, & Odar, 2012). Addressing adherence is one primary example of where and how pediatric psychologists can bring improved outcomes and value to the health care system. In a recent meta-analytic review of the efficacy of adherence interventions for children with chronic diseases across 71 studies, Graves, Roberts, Rapoff, and Boyer (2010) reported medium effect sizes for adherence interventions and health outcomes pre to post-treatment and at follow-up, with larger improvements in health outcomes for studies that combined education and behavioral intervention. Although many of these studies did not have the rigor of being randomized control trials, the effect sizes are encouraging.

The purpose of the Special Issue of the Journal of Pediatric Psychology on Adherence is to highlight innovative approaches to the treatment or assessment of adherence or to understanding factors associated with adherence that can inform the development of more effective interventions to improve adherence in children with chronic medical conditions. Ultimately, we are most interested in improving adherence with the goal of improving health outcomes and child functioning and well-being.

Special Issue

The Special Issue includes eight articles and a commentary by Michael Rapoff. The majority of the articles are
intervention with five articles describing pilot studies of novel and innovative interventions and one describing the effects of established, evidence-based interventions in the context of clinical care via a series of case studies. Two additional articles describe factors associated with nonadherence with the goal of elucidating target behaviors for subsequent intervention development.

The issue leads off with a survey study conducted by a subcommittee of the Adherence Special Interest Group of the Society of Pediatric Psychology (SPP) assessing the use of evidence-based assessment and intervention for nonadherence in pediatric populations (Wu et al., 2013). As noted earlier in the text, there are a number of interventions that have been found to improve adherence (Graves, Roberts, Rapoff, & Boyer, 2010) and tools for assessing adherence (Kahana, Drotar, & Frazier, 2008; Quitmier, Modi, Lemanek, Ievers-Landis, & Rapoff, 2008). Wu and colleagues invited SPP members who subscribed to the SPP listserv to participate in a survey on clinical practice in the assessment and treatment of adherence. Of the 113 completers, 108 were engaged in clinical care or supervision of clinical care, with 62% being licensed psychologists and 48% being a trainee (graduate student, intern, or fellow) providing care across 23 different pediatric conditions. The findings with regard to assessment of adherence are discouraging but perhaps not unexpected as the majority of respondents reported using a clinical interview to assess adherence, and only a small minority used more objective assessments such as electronic monitoring [e.g., Medication Event Monitoring Systems (MEMS)], pill counts or drug assays. Discouraging because studies have shown that self-report of adherence is inflated when compared with more objective assessments (Bender et al., 2000). Not unexpected because the cost and availability of objective measures such as MEMS caps likely place them outside of the feasibility of routine clinical care at this time. But as shown in Table 2 of Wu et al. (2013), even where there are well-established and approaching well-established assessment inventories/scales, these are rarely used, and daily diaries, which need no special equipment, are only used by a third of the respondents. Perhaps most surprising is that almost 42% of respondents cited unfamiliarity with available adherence assessment/interventions as a barrier.

On the promising side, almost 70% reported using at least one intervention that had empirical support and used an established theoretical approach to guide their conceptualization to intervention. Also promising in the context of the ACA and ACO is that the majority of the respondents (86.8%) reported being part of a multidisciplinary team; unfortunately, only 36.5% reported “always” discussing adherence with the other providers, whereas 61% reported they “sometimes” did. Based on this small sample of members of the SPP listserv, it appears that we have the potential to be an important part of the interdisciplinary health care team, but we will need to find effective and efficient ways to integrate evidence-based assessment and treatment into the clinical realm and, perhaps equally important, communicate across disciplines to maximize efficacy of the intervention by inclusion of all team members.

The next study by Modi and colleagues (Modi, Guilfoyle, & Rausch, 2013) describes an innovative model for integrating pediatric psychology within a medical team and systematically assessing and intervening on adherence. This pilot randomized control trial (RCT) examines the feasibility, acceptability, and potential efficacy of a tailored education and problem-solving intervention for children newly diagnosed with epilepsy and their families, a disorder in which adherence has rarely been studied, but for which the health consequences of nonadherence can be severe. The novel aspects of this study were the assessment of adherence of all newly diagnosed children—not waiting until adherence was identified as a problem, use of objective measure of adherence (MEMS caps), a 30-day baseline assessment period, and only intervening with children who met a defined level of nonadherence early on in their treatment. The intervention also addressed the primary barrier identified in the Wu et al. (2013) survey—time, as it was a brief four-session treatment that tailored the specific intervention adopted by the family via problem-solving. The results were encouraging with notable improvements in adherence in the intervention group, high satisfaction ratings from the families, and 100% retention through out treatment. That families were willing and preferred being seen in Behavioral Medicine and Clinical Psychology over Neurology indicates that families may be willing to spend the time and be seen outside of the medical clinic when the intervention seems relevant and useful.

The next study by Duncan et al. (2013) addresses adherence in children and teens aged 9–15 years by explicitly addressing parental involvement (Teamwork Intervention) in management of the asthma medication Fluticasone (delivered via a metered dose inhaler) to improve adherence in another pilot RCT. In contrast to the Modi, Guilfoyle, & Rausch (2013) study, Duncan and colleagues approached children with a diagnosis of persistent asthma for 6 months and their families for participation without regard to suspected adherence issues because, based on the literature, this is the age range during which children with asthma have been found to be taking on more responsibility for their asthma management and presumably places them at increased risk of nonadherence. Similar to the Modi,
Guilfoyle, & Rausch (2013) study, monitoring of adherence was done via electronic monitoring, and the intervention was a brief four-session treatment for 8 weeks. The issue of responsibility for asthma treatment management was explicitly addressed in the intervention, which involve identifying shared responsibilities for asthma management across parents and their child or teen and methods for managing conflicts around asthma management including problem-solving.

A novel aspect of the intervention was that it started out with maximal parental involvement and gradually allowed the child/teen to earn more independence contingent on achieving predetermined adherence goals that gradually increased across sessions. Intervention was compared with Education alone and Standard Care. The results were impressive. Children assigned to Education and Standard Care demonstrated adherence rates typically reported in the literature of ~30–60% in the initial weeks of monitoring (Week 2 and 4) that coincided with the intervention for those assigned to Education and Teamwork treatments. However, by Week 8, adherence for the children in both the Education and Standard Care conditions plummeted to the range of 30–40% adherence. In contrast, children assigned to the Teamwork Intervention, while showing some decline in adherence, demonstrated >80% adherence across all time points including at 20 weeks, the time point that would coincide with being 12 weeks out from the end of treatment. No differences were found on the physiological variable of FEF25–75 as measured by Spirometry, but the Teamwork group did report significantly less asthma symptoms. Similar to Modi, Guilfoyle, & Rausch (2013), both parents and children reported a high level of satisfaction with treatment. However, although parents rated the electronic monitor (MDIlog-II) and supervision charts useful, they also rated them high on difficulty to use and had an average of 47% errors in making changes in the level of parental supervision earned based on child adherence.

Stanger and colleagues (Stanger et al., 2013) tested a two-session computer delivered MI intervention to improve adherence to antiretroviral treatment (ART) in youth aged 16–24 years diagnosed as HIV positive in a pilot RCT. The control group received computer-delivered information targeting nutrition and physical activity. The computerized intervention, Motivational Enhancement System for Adherence (MESA), was both novel and innovative, as it uses the principles of MI to deliver messages via an avatar, chosen among seven possible avatars by participants, personalized health feedback, ART, and activities to increase youth motivation and confidence around their treatment management. Although viral load, an important health outcome measure for HIV positive patients, was collected, adherence was measured by self-reported adherence rather than electronic monitoring. This pilot study was not powered to detect significant differences; however, the results were promising in that the viral load for youth randomized to MESA showed a greater, although not significantly greater, decrease in viral load at both 3 months and 6 months post-treatment. The self-report of adherence was also greater for MESA participants than the control group. Clearly a two-session intervention that is delivered...
via computer holds much promise for integrating adherence promoting strategies into routine medical care. As with all the pilot intervention studies included in the special edition, a fully powered RCT appears warranted to evaluate this approach to improve adherence.

The last intervention article in the special issue is a series of case studies by Cortina and colleagues (Cortina, Somers, Rohan, & Drotar, 2013) describing the implementation of evidence-based adherence interventions for oral medication in the context of clinical care through an outpatient adherence service for six children and teens aged 10–17 years referred by their medical providers for nonadherence to oral medication. These referrals represent five chronic diseases and included patients covered by both private insurance and Medicaid. Notably, and uniquely for a clinical service, adherence was measured by electronic monitoring using MEMS caps for all patients. The interventions described were tailored to the individual patient, but all meet the criteria for being evidence-based. Unlike the pilot RCTs in the issue, the number of treatment sessions and length of the sessions varied across and within patients, with breaks in treatment seen for two of the six patients. These data indicate that children with adherence issues in the real world of clinical care are often more complex and require greater flexibility in the provision of treatment than children with chronic conditions recruited for a research study. As noted by the authors, half the sample had scores in the clinical range on the Child Depression Inventory and scored above the cutoff for post-traumatic stress. Using time series analysis, Cortina, Somers, Rohan, & Drotar (2013) show that four of the six patients increased their adherence to oral medication, but these improvements were highly variable both across and within patients and most patients either returned to baseline levels of adherence (N = 3) or declined below baseline levels (N = 2) after treatment ended. Cortina, Somers, Rohan, and Drotar (2013) do an excellent job of discussing the possible reasons for the differences between adherence outcomes in research studies compared with clinical care including co-morbid psychological conditions that are often excluded from clinical research studies but are frequently present in real world clinical care. This study highlights the importance of dissemination studies as well as RCTs in the area of adherence.

The last two studies in the Special Edition focus on understanding factors that are related to adherence. Naar-King et al. (2013a) use the social ecological model to examine psychological factors of associated with ART in youth aged 8–18 years old who were infected with HIV perinatally. Using multivariate analysis, they found that youth awareness of their HIV status, those who had caregivers who were not fully responsible for medications, and whose caregivers were not well themselves, as well as youth perception of poor caregiver–youth relations, African-American ethnicity, and caregiver perception of low social support were associated with caregiver report of poor youth adherence to ART (“adherent” was defined as no missed doses in past month) across three time points: baseline, 24 weeks, and 48 weeks. The authors report significant associations between some of these variables such that teens who did not know their HIV status had caregivers who reported being fully responsible for the teens medication. O’Hara and Holmbeck (2013) examined the association between executive functioning and parenting behaviors and adherence in 140 youth aged 8–15 years of age with spina bifida. It is notable that parenting behaviors were based on direct observation using a coding system across four family interaction tasks. Adherence across several treatment dimensions including bowel control and medication was assessed with a validated parent report measure for spina bifida, and executive functioning was assessed using several neurocognitive tests including the Behavior Rating Inventory of Executive Functions via parent and teacher report. These investigators found that executive functioning as measured by the Behavior Rating Inventory of Executive Function, but not gross motor functioning, was associated with higher adherence levels. They also found that higher levels of maternal acceptance and behavioral control were associated with better adherence and that maternal behavioral control appeared to buffer the relationship between lower executive functioning and lower adherence. This study was unique in that is also assessed parental parenting style and interestingly found no association between parental parenting style and adherence.

**Comments and Conclusions**

In the upcoming age of the ACA with an emphasis on improved outcomes and lower cost, the issue of adherence to medical treatment will be significant. One of the “take away” messages listed in 2003 the World Health Organization (WHO) report on medication adherence (Sabaté, 2003) was a quote by Haynes that “increasing the effectiveness of adherence interventions may have a far greater impact on the health of the population than any improvement in specific medical treatments” (Haynes, McDonald, Garg, & Montague, 2001). The articles in the Special Issue highlight several important aspects of moving the field forward. Although adherence is complex, it will be incumbent on pediatric psychologists to develop interventions that can be implemented in the
context of an interprofessional care system. This by necessity will mean that adherence assessment and intervention will need to be universal and brief. Although the article by Cortina, Somers, Rohan, & Drotar (2013) highlights the improvement that can be achieved by the systematic implementation of evidence-based adherence interventions in the clinical setting, clearly, the results achieved do not match the effects reported for research studies in the adherence literature (Graves, Roberts, Rapoff, & Boyer, 2010) or the pilot RCTs in this special edition.

One reason for these differences may be that the clinical cases represent the difference in the co-morbidities of patients in the clinical setting verses a research study. Another reason may be that the patients in the clinical setting were not referred for treatment until well after patterns of non-adherence were formed, making it more difficult to treat than adherence issues identified shortly after diagnosis or treated by universal intervention to an entire population. The article by Modi, Guilfoyle, and Rausch (2013) indicates that the use of electronic monitoring to identify those families in need of intervention immediately after diagnosis may allow the intervention to be brief and targeted and that those families in need of treatment would be agreeable to treatment outside of the medical visit. If monitoring were an ongoing part of medical care, families could be identified and targeted whenever adherence fell below a specified criteria, which is exactly what Modi and colleagues have proposed in their larger RCT of the adherence intervention for new onset epilepsy (Modi, 2013). Conversely, based on the literature on self-management and asthma, Duncan et al. (2013) implemented a universal intervention with the assumption that all children with asthma, and their families would struggle with adherence during the age that self-management transitions from parent to child. Similar to the epilepsy intervention, the asthma intervention was brief. The articles by Duncan et al. (2013) and Stanger et al. (2013) highlight the importance of parental involvement. Stanger et al. (2013) introduced a novel concept of contingently rewarding parents for implementing monitoring of their teens BGM and rewarding the teen when they achieved their BGM goal.

Many of these approaches (e.g., routine electronic monitoring and use of data in clinical care) are not feasible in our current fee for service health care system. In the context of an ACO, where the health care system will be paid a set fee per member per month, there will be greater incentive to ensure patients are following their treatment regimen and therefore using less health care resources. Under an ACO model providing electronic monitoring devices to all patients, identifying personnel, such as nurses, to download the data from these devices, and targeting nonadherence in the context of routine clinical intervention will likely be necessary to reduce other high cost medical services such as inpatient or emergency room care.

In an ACO model, it may not be unreasonable to reward both parents and children with the disease for their work as partners with the medical team to achieve optimal outcomes. One aspect that appears clear across all the intervention articles is that a one-time intervention is likely not sufficient to ensure long lasting, optimal adherence, and that intervention boosters will be needed. The timing and dose of such boosters has not been explored and is therefore worthy of attention in future research. The intervention articles in the special issue were all pilot studies but clearly show promise and are worthy of being tested within the context of large RCTs. These future trials should not only have power to demonstrate improvements in adherence, but on health outcomes.

References


