Objective Although cross-sectional studies have demonstrated poor adherence to airway clearance therapy (ACT) for patients with cystic fibrosis (CF), no studies have identified longitudinal patterns of adherence. The objective was to characterize and identify predictors of ACT adherence trajectories for individuals with CF.

Methods Secondary data analyses were conducted for a randomized clinical trial examining differences in three ACTs. Participants (n = 153; M = 14.3 years, 55% male, 86% Caucasian, baseline FEV1% predicted: M = 86.7)/primary caregivers completed Daily Phone Diaries, an empirically supported adherence measure, every 4 months.

Results Group-based trajectory modeling revealed the best-fitting solution was a three-group model: low-adherence (14%), medium-adherence (49%), and high-adherence (37%) groups. ACT type was the only significant predictor of adherence trajectories.

Discussion Three trajectories of adherence to ACT for patients with CF were found. With the identification of trajectories, adherence interventions can be targeted for the subgroup at highest risk in order to prevent poor health outcomes.

Key words chest wall oscillation; compliance; developmental; Flutter; group-based models; high frequency; longitudinal; manual chest physiotherapy.

Cystic fibrosis (CF) is a progressive, multi-system pulmonary disease, affecting approximately 30,000 individuals in the United States (Cystic Fibrosis Foundation, 2009). Significant advances in medicine have resulted in increased lifespan for individuals with CF, shifting from 25 years of age in 1985 to 37.4 years in 2008 (Cystic Fibrosis Foundation, 2009). Treatment for CF has become increasingly complex in the past two decades, often taking patients several hours to complete each day. Treatment often involves taking several types of pills, including oral antibiotics, pancreatic enzymes, digestive medications, and vitamins. Because lung disease is the primary cause of morbidity and mortality in patients with CF, much of the treatment regimen is devoted to thinning and reducing mucus, as well as keeping the airways open. This is accomplished by prescribing nebulized medications (e.g., bronchodilators, domsina alpha for mucus thinning, and inhaled antibiotics) and airway clearance therapy (ACT). Evidence from several clinical trials and a recent review examining the benefits of ACT have identified improved mucus transport as one of the most prominent benefits of this treatment (see Bradley, Moran, & Elborn, 2006 for evidence-based review). Several forms of ACT are currently prescribed, including postural drainage and percussion (PD&P), Flutter, and high-frequency chest wall oscillation (HFCWO), also known as Vest therapy.
Although ACT remains a mainstay of CF treatment at this time, it is time-consuming and can be one of the most difficult to incorporate into daily routines, often taking as much as an hour a day (Abbott, Dodd, & Webb, 1996; Modi & Quittner, 2006a). Not surprisingly, several cross-sectional studies have suggested poor adherence to ACT across childhood (Modi et al., 2006; Passero, Remor, & Salomon, 1981; White, Miller, Smith, & McMahon, 2009), adolescence (Quittner et al., 2000; White et al., 2009), and adulthood (Abbott et al., 1996; Conway, Pond, Hamnett, & Watson, 1996; White, Stiller, & Haensel, 2007). For example, school-aged children demonstrated ACT adherence rates of 51–74% (Modi et al., 2006). ACT adherence has also been shown to be poor during adolescence (50%; Quittner et al., 2000) and adulthood (30–32%; Abbott et al., 1996; Myers & Horn, 2006), with increasing age associated with worse adherence (Arias Llorente, Bousono Garcia, & Diaz Martin, 2008). In addition to age, pulmonary functioning has also been associated with adherence in CF (Zindani, Streetman, Streetman, & Nasr, 2006). In contrast, studies are lacking or there are inconclusive results regarding the association between adherence and sex (Myers, 2009; Patterson, Wall, Berge, & Milla, 2008) and socioeconomic status in CF. However, it is possible that similar to other pediatric conditions (Berquist et al., 2006; Modi, Morita, & Glauser, 2008), these may be critical factors affecting ACT adherence.

Although these studies provide important snapshots of adherence at various developmental stages, no studies have examined adherence to ACT over time for patients at different points in their lifespan. Identifying the long-term patterns of adherence in patients with chronic disease is important because it allows us to understand their variability and potentially identify critical periods for intervention. Furthermore, it may be the first step in identifying thresholds for efficacy related to treatment. For example, what level of adherence is necessary to obtain optimal health outcomes, 75, 80, or 100%? This is especially true for patients with CF, whose treatment regimen only becomes more complex over time as a result of worsening symptoms and deterioration of health. While longitudinal ACT adherence data are unavailable, recent adherence data for nebulized medications using an adaptive aerosol delivery device indicated significant intra- and inter-patient variability in adherence (Latchford, Duff, Quinn, Conway, & Conner, 2009; McNamara, McCormack, McDonald, Heaf, & Southern, 2009), which was then used to personalize and subsequently improve adherence to this treatment (e.g., reduce treatment from twice to once daily; (McNamara et al., 2009). Overall, these studies highlight the need to examine longitudinal patterns of adherence for individuals with CF, allowing us to target individuals at highest risk during critical developmental periods.

Empirically supported treatments for adherence are behaviorally and family based, often requiring eight to 12 sessions (Kahana, Drotar, & Frazier, 2008). However, these interventions are not readily available (e.g., limited) to the populations that need them most. By identifying which patients are at highest risk, the limited resources needed to improve adherence through intervention can be better targeted across child and adult chronic disease populations. Targeting patients at highest risk may also improve health outcomes, such as pulmonary functioning, reduction in hospitalizations for pulmonary exacerbations, the likelihood of becoming infected with drug-resistant bacteria, and health-related quality of life. In addition, determining the patient-specific (e.g., age, sex) and treatment-specific (e.g., ACT type) factors that impact adherence over time will build upon prior cross-sectional, correlational studies by delineating what contributes to adherence trajectories over time. For example, if one particular ACT type is associated with the poorest adherence, clinicians may wish to prescribe other forms of ACT that patients prefer and are thus more likely to adhere to. This is clinically feasible because to date, there are no data to suggest differences in health outcomes based on which ACT is used for patients with CF (Main, Prasad, & Schans, 2005).

New statistical methods, including group-based trajectory models (GBTM), provide the ability to identify adherence sub-groups, including those with the poorest adherence (e.g., highest risk). These methods have been successfully applied to other areas and populations, including criminology (Jennings & Piquero, 2008), dental caries (Broadbent, Thomson, & Poulton, 2008), American Indian youth (Stiffman, Alexander-Eitzman, Silmere, Osborne, & Brown, 2007), and most recently dyspnea symptoms in marine transportation workers (Arrandale, Koehoorn, Macnab, & Kennedy, 2009); however, it has not been used in pediatric psychology research, which was the central goal of the current study.

The purpose of this study was 3-fold: (1) to describe rates of adherence to ACT over time for a sample of children, adolescents and adults with CF using the Daily Phone Diary (DPD), an empirically supported assessment of adherence (Quittner, Modi, Lemanek, Ievers-Landis, & Rapoff, 2008), (2) to identify and characterize adherence trajectories for individuals with CF, and (3) to identify
predictors of adherence trajectories. It was hypothesized that a minimum of two distinct adherence trajectory subgroups (e.g., high and low) would be identified and that these trajectories would be predicted from patient-specific factors such as age, sex, airway clearance treatment, baseline pulmonary functioning, and family income.

Methods
Participants
This was a secondary analysis of data collected for a randomized, prospective clinical trial examining differences in efficacy of three types of ACT (e.g., PD&P, flutter device, or Vest) on pulmonary functioning over a 3-year period. Participants for the clinical trial included individuals with CF who were 7 years of age or older across 20 CF centers. All patients had a confirmed diagnosis of CF based on either a sweat chloride or two documented CFTR mutations and forced expiratory volume in 1 s predicted (FEV₁% predicted) of at least 45%. Exclusion criterion included the following: hospitalization for a pulmonary exacerbation, episode of gross hemoptysis (>249 ml) within 60 days prior to screening, pneumothorax in the 6 months prior to screening, or unwillingness to be randomized to one of three ACTs. Although a sample size of 180 patients was expected, difficulties with recruitment resulted in a final sample of 166 participants for the larger clinical trial. Fifteen participants withdrew within the first 60 days after randomization, 11 of whom withdrew on the day of randomization. The clinical trial ended early because withdrawal rates were significantly higher in PD&P than in Flutter or HFCWO groups and in older age groups (Sontag et al., 2010).

Adherence data were available for at least one time point for 153 participants; however, there were missing data (16%) for participants across the five assessment points (pre-randomization: n = 130; 4-month: n = 131; 8-month: n = 121; 12-month: n = 115; and 16-month: n = 100). Forty-three percent of participants had five complete data assessment points. Participants in the study ranged from 7 to 44 years of age at the time of enrollment (M = 14.3 years, SD = 7.9 years), and 55% were male. A majority of participants were Caucasian (86%), while 7% were Hispanic, 3% were African–American, and 2% were other. Baseline FEV₁% predicted was 86.7% (SD = 19.1), while the mean FEV₁% predicted was 85.1 (SD = 18.8) for participants at Time 5, suggesting mild disease severity at both time points. A majority of participants were either children or adolescents (80%) and the type of ACT was equally distributed across participants (PD&P = 33%, Flutter = 30%, and Vest = 37%).

Procedure
Detailed procedures and results regarding the larger randomized trial are reported elsewhere (Sontag et al., 2010); however, it is important to note that study consent was obtained from caregivers of children 7–17 years of age and adults 18 years and older while assent was obtained from adolescents. Participants were given instructions and training on their assigned ACT, which was prescribed twice daily for 20 min/session. For purposes of this secondary data analysis, adherence was the primary variable of interest. Adherence was measured at baseline and every 4 months thereafter. Because adherence data were sparse after the fifth assessment and the study was discontinued for most participants by the sixth assessment due to high drop-out rate in the adult age group (Sontag et al., 2010), data analyses were performed on the first five assessments. Institutional Review Board Approval was received from all 20 sites participating in the clinical trial.

Measures
Daily Phone Diary
The DPD, a well-established empirically supported assessment measure of adherence (Quittner et al., 2008), uses a cued recall procedure to track parents, adolescents, and adults through their activities over the past 24 hours and provides a detailed analysis of activity patterns, companions, and mood (Quittner & Opipari, 1994; Quittner, Opipari, Regoli, Jacobsen, & Eigen, 1992). For all activities lasting 5 min or longer, participants (e.g., caregivers of children 7–13 years of age, adolescents 14–18 years of age, and adults 18 years and older) reported the type of activity, duration, and who was present. The interviewer assisted participants in reconstructing their day as accurately as possible by providing prompts, such as the time of day or information about the previous activity (after you finished dinner, what did you do next?). As the phone diary was conducted, each activity was recorded by the interviewer on a computer screen with clock hands which rotated through a 24-hour clock, a set of activities, companions, and a rating of mood ranging from 1 (extremely negative) to 5 (extremely positive). A set of two DPDs (one weekday and one weekend day) was conducted by phone at each assessment point. The DPD has yielded reliable stability coefficients over a 3-week period (r = 0.61–0.71, p < .01) and high levels of inter-rater reliability (>90%) in a CF population (Quittner et al., 1992). Strong convergent validity was
found between adherence calculated through the DPD and objective measures of adherence (Modi et al., 2006; Modi & Quittner, 2006b). For the current study, time spent in ACT was extracted from the DPD to measure the duration (in minutes) each patient spent in ACT each day.

Demographic Questionnaire
A basic demographic questionnaire, which provided information about child age, sex, and family income, was obtained via a case-report form.

Health Status
Respiratory functioning was measured by pulmonary function tests (PFTs). Specifically, FEV1% predicted using equations for age, sex, and weight were performed by a trained technician at all sites.

Statistical Analyses
Data analysis proceeded in two discrete stages: a two-part descriptive phase in which we first sought to understand and describe the characteristics of the data in general, and then identified and described trajectories for specific subgroups within the broader sample of individuals with CF; and an inferential phase in which we sought to identify clinically significant predictors (e.g., age, baseline pulmonary functioning) of these adherence trajectory subgroups. All data were analyzed using SAS v9.1© (SAS Institute, Cary, NC, USA) and the PROC TRAJ Macro, a closed source module developed specifically for use with SAS software (http://www.andrew.cmu.edu/user/bjones).

Descriptive Phase (Aim 1)
Univariate statistics, including frequency counts as well as measures of central tendency, variability, and association, were used to describe sample characteristics, medical history, and patterns of adherence for this sample. Adherence rates were calculated using the number of minutes each participant engaged in airway clearance over the 2-day DPD period divided by the number of minutes prescribed for each individual (e.g., 40 min daily was prescribed for all participants). For example, if a patient conducted airway clearance for 30 min on day 1 and 20 min on day 2, the adherence rate would be as follows: [(30 + 20)/80] × 100 = 62.5%. Adherence rates were computed for each assessment point and for the entire study period.

Group-based Trajectories (Aim 2)
A semi-parametric, group-based approach to model estimation was used to identify and characterize ACT adherence rates over time. This technique, known as GBTM, draws from a broader class of mixture models in which a finite number of subgroups within a broader population are allowed to have different patterns (or trajectories) of change over time (Nagin, 2005). GBTM is particularly useful when the number of subgroups and shapes of the respective trajectories are unknown. To this extent, a two-step approach for model estimation was used. First, two-, three-, and four-group solutions were compared to identify the optimal number of trajectories based on model Bayesian Information Criterion (BIC) values, where the value closest to zero value indicates the best fit. Second, parameter estimates and Wald-statistics for intercept-only, linear, quadratic, and cubic polynomials were compared to determine the preferred model. In this case, the preferred model included three separate trajectories, which were then plotted for visual inspection. Assignment of individuals to the three trajectory subgroups was based on the highest posterior probability estimate for the final, best-fitting model. A censored normal probability distribution served as the reference distribution for all three curves analyzed here. For linear trajectories, a mixed model was tested to examine the slope of adherence over time.

Inferential Phase (Aim 3)
In addition, five cumulative logistic regression models (i.e., ordinal logistic regression) were specified and tested to identify patient-specific factors capable of distinguishing the three adherence trajectory subgroups. Cumulative logistic regression was chosen due to the ordinal nature of the adherence groups. Although the specific number of adherence groups was initially unknown, it was reasonable to assume that the groups would be ordinal in nature (e.g., low, medium, high adherence). The proportional odds model of cumulative logistic regression has the added advantage of offering summary odds ratios for each of the predictors rather than multiple odds ratios for each pair of outcomes (Gameroff, 2005). The outcome of interest was trajectory group membership. Testable covariates included patient sex, age, randomized ACT type, baseline FEV1% predicted, and household income.

Results
Descriptive Phase (Aims 1 and 2)
Descriptive data, including means and standard deviations for adherence rates across the five time points, are as follows: pre-randomization: $M = 36.1$ ($SD = 30.4$);
4-month: $M = 57.5$ ($SD = 37.2$); 8-month: $M = 54.5$ ($SD = 41.5$); 12-month: $M = 58.0$ ($SD = 42.8$); 16-month: $M = 55.9$ ($SD = 35.6$). Average adherence rates across all time points were slightly better than 50% (range 36–58%), and were consistently better than 50% after randomization. A spaghetti plot of adherence data is presented in Figure 1A to demonstrate inter and intra-patient variability.

GBTM analyses were conducted on two-, three-, and four-group models, with time as the only covariate representing the five different observation periods. All five time points were used, including baseline values, specifically to obtain a more complete description of adherence patterns over time for individuals with CF. All three models are presented in Table 1 to illustrate why the three-group model was preferred. Results indicated that a three-group model best explained the data compared with a two- and four-group model using BIC values as our criterion for statistical significance. Table II demonstrates the best-fitting solution for a three-group model included a linear trajectory that assigned 14% of patients to a low-adherence group (Group 1), a cubic trajectory for the medium-adherence group (Group 2 accounting for 49% of the total sample), and a quadratic trajectory for the

![Figure 1](image-url)
high-adherence group (Group 3 accounting for 37% of the total sample). Group membership for each trajectory can be found in Figures 1B through D. Individual trajectories for the high-adherence Figure 1B, medium-adherence Figure 1C, and low-adherence Figure 1D groups are plotted. Final estimates of the trajectories are presented in Figure 1E. Results indicated a significant negative slope for the low-adherence group \[ F(4, 94) = 3.22; p < .05 \].

Predictors of Adherence Trajectories (Aim 3)

Using the newly created adherence trajectories (low, medium, and high), patient-specific factors that predicted group membership were examined. Of the five cumulative single covariate logistic regression models specified, only ACT type emerged as a statistically significant predictor of adherence group membership (Table III). Specifically, we found significantly more participants using the Flutter device in the medium-adherence group (see Table IV). A trend was also noted for family income, in which patients with a family income greater than $50,000 were 1.87 times more likely to be in the high-adherence trajectory group. Similarly, a positive trend was noted for pulmonary functioning, in which patients with better FEV1% predicted were slightly more likely to be in the high adherence group.

Discussion

Results from the current study build upon prior cross-sectional research examining adherence to ACT for patients with CF and suggest significant inter-patient variability. Prior to randomization for the ACT clinical trial, adherence to this treatment was quite low at ~36% for the entire sample. This translates into patients performing 14 min of ACT each day compared to the recommended 40 min per day. However, as expected, adherence to ACTs increased with enrollment in a clinical trial to 58%.

Although this rate is still low, it is consistent with prior studies (Abbott et al., 1996; Modi et al., 2006; Myers & Horn, 2006; Quittner et al., 2000) and suggests that patients with CF have poor adherence to this critical aspect of their treatment regimen. Longitudinal results also indicated that rates of adherence remained relatively stable over the 16-month study period, indicating that patients with CF who enroll and remain in a randomized, clinical trial are able to consistently engage in ACT ~50% of the recommended time.

One novel aspect of this study was its examination of trajectories of adherence over time in a large cohort of patients with CF. Data indicated three distinct groups, including a low, medium, and high adherence group. Specifically, it appears that patients whose initial adherence was lowest (e.g., 17%) remained low over time. In contrast, patients who exhibited the highest rate of adherence initially maintained higher levels of adherence over time. The medium adherence group, which encompassed the largest proportion of individuals with CF (49%), displayed the most variability in adherence. As suggested by prior studies, this is likely due to ACT barriers, such as competing activities and forgetting (Abbott et al., 1996; Modi & Quittner, 2006a), which interfere at various

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**Table II. Final three-group model for adherence trajectories**

<table>
<thead>
<tr>
<th>Group</th>
<th>Parameter</th>
<th>Estimate (SE)</th>
<th>T</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>Intercept</td>
<td>17.73 (11.22)</td>
<td>1.58</td>
<td>0.11</td>
</tr>
<tr>
<td></td>
<td>Linear model</td>
<td>–8.58 (4.13)</td>
<td>–2.08</td>
<td>0.03</td>
</tr>
<tr>
<td>Medium</td>
<td>Intercept</td>
<td>–43.82 (25.06)</td>
<td>–1.75</td>
<td>0.08</td>
</tr>
<tr>
<td></td>
<td>Cubic model</td>
<td>3.61 (1.28)</td>
<td>2.82</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>High</td>
<td>Intercept</td>
<td>0.73 (11.42)</td>
<td>0.06</td>
<td>0.94</td>
</tr>
<tr>
<td></td>
<td>Quadratic model</td>
<td>–8.22 (1.49)</td>
<td>–5.33</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

**Table III. Logistic regression: patient predictors of adherence trajectories**

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR</th>
<th>CI 95%</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (male as reference category)</td>
<td>1.26</td>
<td>0.69, 2.31</td>
<td>0.46</td>
</tr>
<tr>
<td>Age</td>
<td>0.99</td>
<td>0.96, 1.03</td>
<td>0.72</td>
</tr>
<tr>
<td>ACT type</td>
<td>0.04</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PD&amp;P (reference group)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Flutter</td>
<td>2.46</td>
<td>1.13, 5.36</td>
<td>0.02</td>
</tr>
<tr>
<td>Vest</td>
<td>1.08</td>
<td>0.52, 2.23</td>
<td>0.84</td>
</tr>
<tr>
<td>Baseline FEV1% predicted</td>
<td>1.05</td>
<td>0.99, 1.03</td>
<td>0.06</td>
</tr>
<tr>
<td>Household income (&lt;$50,000 as reference category)</td>
<td>1.87</td>
<td>0.92, 3.80</td>
<td>0.08</td>
</tr>
</tbody>
</table>

Note. All models tested met the score test for the proportional odds assumption.

*Multiple iterations were used to examine household income differences, including a four- and a seven-category income variable with results indicating no statistically significant relationship.

**Table IV. ACT type by adherence trajectory subgroup**

<table>
<thead>
<tr>
<th>Group</th>
<th>PD&amp;P</th>
<th>Flutter</th>
<th>Vest</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low adherence (n = 22)</td>
<td>7 (14%)</td>
<td>7 (15%)</td>
<td>8 (14%)</td>
</tr>
<tr>
<td>Medium adherence (n = 75)</td>
<td>20 (40%)</td>
<td>31 (67%)</td>
<td>24 (42%)</td>
</tr>
<tr>
<td>High adherence (n = 56)</td>
<td>23 (46%)</td>
<td>8 (17%)</td>
<td>25 (44%)</td>
</tr>
</tbody>
</table>

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times and occur inconsistently. It is possible that individuals in the high adherence group are better able to problem solve their barriers to ACT adherence and incorporate these strategies into daily routines compared to individuals in the medium adherence group. Overall, these adherence trajectories allowed for identification of patients who are highest risk for poor adherence by demonstrating that patients who exhibit adherence rates below 25% are likely to maintain these levels over time, placing them at risk for increased morbidity (e.g., pulmonary exacerbations, acquisition of drug-resistant microorganisms). It is this subgroup that would benefit from the most intensive intervention to improve adherence. However, even the high and medium groups are below 50% and thus would benefit from adherence interventions. Specifically, adherence interventions that focus on providing education to fill gaps in knowledge, teaching and ensuring that patients have the skills to conduct the therapy, identifying and problem solving around barriers to adherence, and matching the type of therapy that best suits the needs of the patient and their family are likely the most beneficial (Homnick, 2007; Kahana et al., 2008).

Interestingly, ACT was the only significant patient-specific predictor of adherence trajectories. Patients prescribed Flutter were more likely to be in the medium adherence group compared to PD&P and Vest. The Flutter can be completed independently once the technique has been mastered, which is likely desirable for adolescents and adults. However, because the Flutter requires active participation (versus passive with Vest), patients may become bored or disinterested in the therapy for the full prescribed duration. These findings suggest that patients prescribed the Flutter device are not likely to have high rates of adherence overall. If, in contrast, patients prescribed PD&P or Vest are more likely to be in the high-adherence trajectory, it is important to incorporate patient preference when making decisions about ACTs, especially given lack of evidence regarding efficacy differences between the three ACT methods (Main et al., 2005). Homnick (2007) has suggested the need to adapt ACTs based on disease severity and patient preference to encourage optimal adherence, with frequent monitoring to ensure health status does not decline.

While age and sex were not associated with adherence trajectories, a trend was noted for both family income and baseline pulmonary functioning. Specifically, patients with CF were almost twice as likely to be in the high adherence group if their family income was greater than $50,000. These results are similar to studies in pediatric epilepsy (Modi et al., 2008) and liver transplant (Berquist et al., 2006) suggesting a positive association between adherence and socioeconomic status. In addition, patients with CF with higher pulmonary functioning trended toward being in the high adherence group compared to the low adherence group. Future studies with more variability in pulmonary functioning (e.g., patients with more severe disease) would better elucidate these findings.

While this study is the first to examine longitudinal adherence to ACT for children, adolescents, and adults with CF, several limitations exist that provide directions for future research. The identification of adherence trajectories and predictors of these trajectories represented the first step in understanding adherence behaviors over time. An important next step is to examine the relations between adherence trajectories and health outcomes, including pulmonary functioning, nutritional status, and health-related quality of life. With this information, clinical researchers may be able to identify optimal levels of adherence, which promote the best outcomes. Future studies should also include a larger cohort of adults with CF to elucidate developmental differences in adherence. Although the use of GBTM techniques was a major strength of this study, research from other fields has suggested that large sample sizes are necessary to identify trajectories. While our sample size fell below the suggested 200 cases, studies have successfully used sample sizes consistent with ours (Conklin et al., 2005; Mulvaney, Lambert, Garber, & Walker, 2006). An important area for future research is a confirmatory analysis of the low, medium, and high adherence trajectories we identified. Finally, these data are a secondary analysis of a randomized clinical trial examining differences between three ACT types and thus must be considered within this context. Sontag et al. (2010) have reported lessons learned from this trial, including early termination due to differential drop-out in the adult PD&P study arm, which contributed to inadequate power to detect group differences. While the early termination of the trial has important implications for adherence, because adherence was the primary outcome variable, we had sufficient longitudinal data to compute our results.

Overall, this is the first study to use GBTM to examine adherence behaviors in individuals with a chronic illness that requires a time-consuming and complex treatment regimen. Adherence trajectories, such as the ones identified in this study, are likely to generalize to other chronic illness populations with complex treatment regimens, including diabetes, sickle cell disease, and asthma and
should be evaluated in these populations. Examining adherence trajectories holds promise for identifying the level of adherence necessary to obtain the best health outcomes and quality of life.

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Conflict of interest: American Biosystems provided one of the three ACT methods used in the larger randomized clinical trial. Dr. Accurso has served on the advisory board for American Biosystems.

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