

## **Aim: Identify and evaluate tools to measure adherence**

Team:

**Alexandra L. Quittner, Ph.D.**  
Psychologist and Team Leader  
*USA*

**Baroukh Assael, M.D.**  
Physician  
*Italy*

**Vibsen Bregnballe**  
Nurse  
*Denmark*

**Lutz Goldbeck, Ph.D.**  
Psychologist  
*Germany*

**Martin Hug, Ph.D.**  
Pharmacist  
*Germany*

**Ulrike Pypops**  
Lawyer and adult CF patient  
*Netherlands*

## Measures of Adherence for Cystic Fibrosis

Adherence to chronic treatment regimens is a significant challenge for individuals diagnosed with cystic fibrosis (CF) (Barker & Quittner, 2010). Advances in CF care (e.g., newborn screening) and the development of new treatments have increased the time, complexity, and burden of the CF medical regimen. It is estimated that patients must now spend between two and four hours per day on treatment, which is reflected in low rates of adherence (Modi & Quittner, 2006; Tuchman et al., 2010). The negative consequences of poor adherence are significant and include: 1) more frequent symptoms, 2) increased hospitalizations, 3) greater stress and family conflict, 4) greater costs and health care utilization, and 5) greater morbidity and earlier mortality.

Research suggests that rates of adherence are influenced by a myriad of factors that change throughout development, such as child behavior, parent-child relationship, and peer influences. Several factors, such as knowledge of disease management, adequate skills in performing treatments (e.g., using a metered dose inhaler correctly), and having a written treatment plan have been shown to affect adherence behaviors (Modi et al., 2006). In addition, identifying the barriers that interfere with treatment adherence for that individual patient and family are critical (Modi & Quittner, 2006). For young children, these barriers include maternal depression, oppositional behavior, and difficulty swallowing pills. Challenges for school-age children include working with school personnel to ensure medications are dispensed (i.e. enzymes prior to lunch), wanting to be like healthy peers (i.e. not doing treatments in front of friends), confusion regarding prescribed regimen, and oppositional behavior. Adherence during adolescence decreases significantly due to less parental supervision, desire for independence and autonomy, and competing activities (Quittner et al., 2009). It is important for the CF Team to be aware of the challenges associated with adherence, the factors that influence adherence across development and interventions which have shown success in improving adherence.

Measurement of adherence in CF is challenging due to the complexity and multi-faceted nature of the CF treatment regimen. Measures of adherence include: 1) self-report, 2) daily diaries, 3) electronic monitors, and 4) pharmacy refill histories. Each method of measurement has advantages and disadvantages. For example, **self-report measures** of adherence tend to inflate estimates of adherence since patients want to “please” their health care team and appear to be following their recommendations. On the positive sides, self-report measures are inexpensive, brief to complete, and can measure each component of the treatment regimen (e.g., alterations in diet). **Daily diaries** utilize an ecological momentary assessment technique (EMA) which produce data on adherence in “real time.” These methods reduce social desirability responding (and inflated reports of adherence) because individuals are asked to recall all activities they engaged in over the past 24 hours. The Daily Phone Diary (DPD; Quittner & Pipari, 1994) is therefore, considered an “unobtrusive” measure of adherence. It was determined to be a “well-established” measure of adherence in a recent review (Quittner et al., 2008), however, this method is labor intensive and not well-suited to treatments that take less than 5 minutes to complete (i.e., oral medication). **Electronic monitors** provide the date, time and duration of treatment behaviors, and are available for oral medications, metered-dose inhalers, and some nebulized treatments (I-Neb), but are not available for all components of the CF treatment regimen, such as airway clearance. Finally, **pharmacy refill** data can be obtained from individual pharmacies or national databases and provide information on the date of refills. This yields a “medication possession ratio” (MPR) which reflects whether a prescription has been refilled, but does not indicate whether the medication has been taken. For a complete review of adherence measurement tools and issues please refer to Quittner, Modi, Lemanek, Ivers-Landis, & Rapoff, 2008.

The committee reviewed the strengths and weaknesses of each method of measurement and has proposed several recommendations for the assessment of adherence. The following is recommended:

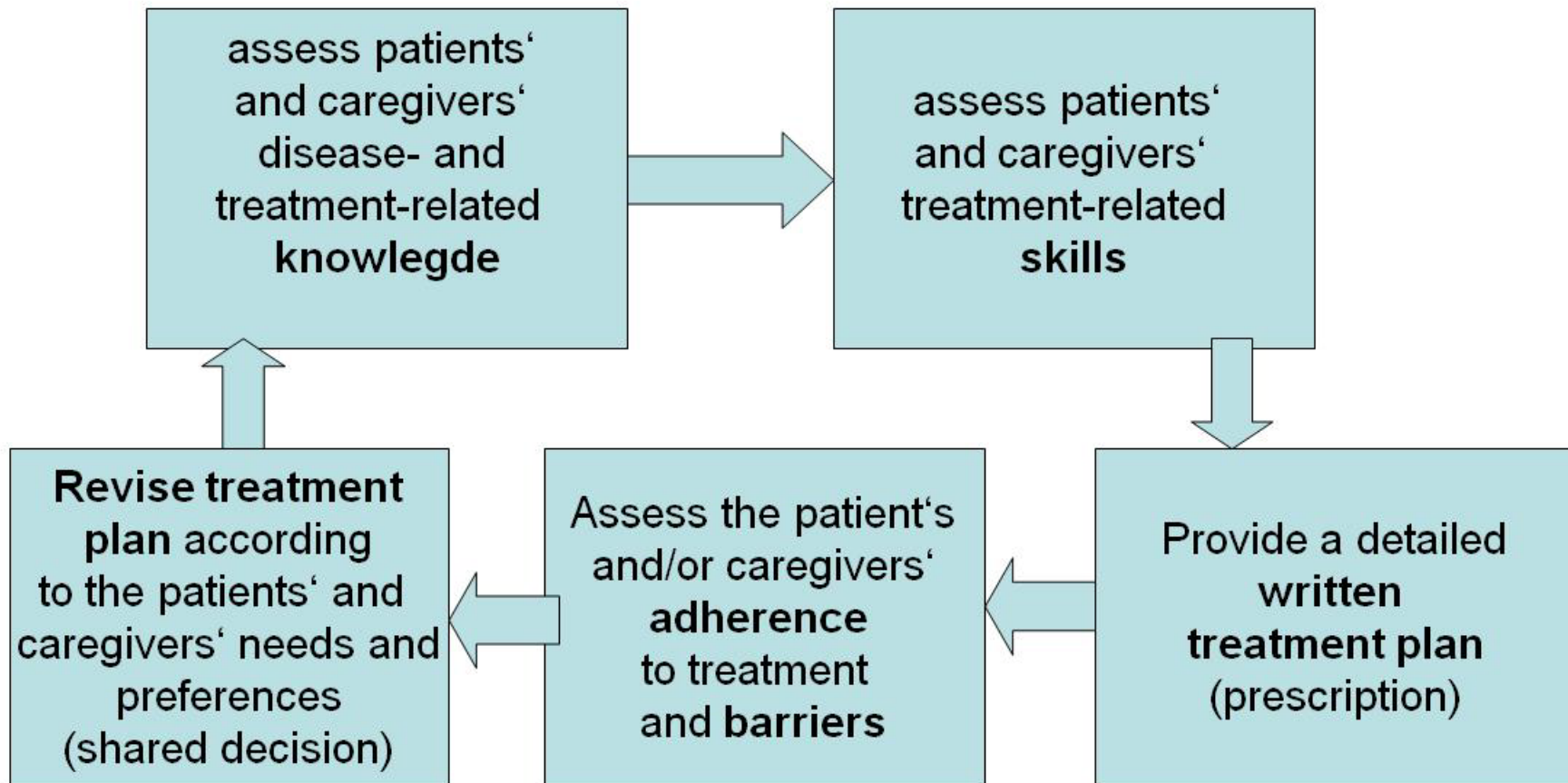
1. There should be *active engagement* of the patient and health care provider in a discussion of the treatment regimen and any challenges the patient/family may have in performing it. *Shared decision-making* between the patient/family and the provider are very important.
2. Adherence should be studied as a *process* and not just an outcome. It is reflective of communication between the patient/family and CF Team and therefore, the challenges of adhering to CF treatments must be addressed by both patients and team members (behavior change may be required for both). The provision of a written treatment plan, for example, is recommended to avoid miscommunication or misunderstandings about the treatment regimen.
3. Adherence should be measured using multi-modal method of assessment. No single measure of adherence is likely to be accurate given the complexity of the treatments and required behaviors.
4. Self-report measures of adherence are only used in conjunction with another measurement tools.
5. For large-scale studies, pharmacy refill histories are the most feasible measure of adherence.
6. Daily Phone Diaries or other EMA strategies (PDA assessment) should be utilized when possible because they have been shown to correlate well with electronic measures and provide information about the process of fitting treatments into daily life (e.g., specific barriers). These methods are time and labor-intensive and require trained personnel.

7. Electronic monitors are not yet the “gold standard” because they are expensive, may malfunction, and are not available for all CF treatments. However, when available, they provide highly accurate information that can be used in conjunction with other measures.

References:

- Barker, D.H. & Quittner, A.L. (2010). A biopsychosocial model of CF: Social and emotional functioning, adherence and quality of life. In J. Allen, H. Panitch & R. Rubenstein (Eds.) *Lung Biology in Health and Disease Series: Cystic Fibrosis*. New York: Informa Healthcare.
- Modi, A.C. & Quittner, A.L. (2006). Barriers to treatment adherence for children with cystic fibrosis and asthma: What gets in the way? *Journal of Pediatric Psychology*, 31, 846-858.
- Modi, A.C., Lim, C.S., Yu, N., Geller, D., Wagner, M.H., & Quittner, A.L. (2006). A multi-method assessment of treatment adherence for children with cystic fibrosis. *Journal of Cystic Fibrosis*, 5, 177- 185.
- Quittner, A.L., Modi, A.C., Lemanek, K.L., Ivers-Landis, C.E., & Rapoff, M.A. (2008). Evidence-based assessment of adherence to medical treatments in pediatric psychology. *Journal of Pediatric Psychology*, 33, 916-936.
- Quittner, A.L. & O'Pipari, L.C. (1994). Differential treatment of siblings: Interview and diary analyses comparing two family contexts. *Child Development*, 65, 800-814.
- Quittner, A.L., Barker, D.H., Marciel, K.K., & Grimley, M.E. (2009). Cystic fibrosis: A model for drug discovery and patient care. In M.C. Roberts and R.G. Steele (Eds). *Handbook of Pediatric Psychology* (pp. 271-286). New York: The Guilford Press.
- Tuchman, L.K., Schwartz, L.A., Sawicki, G.S. & Britto, M.T. (2010). Cystic fibrosis and transition to adult medical care. *Pediatrics*, 125, 566-573.

# Framework for approaching adherence problems



## Measures of Adherence

- Daily Phone Diary
- Electronic Measures
- Self-report Questionnaires
- Pharmacy Refill History

### **Use of Daily Phone Diary to Measure Adherence**

#### Overall Assessment of the Daily Phone Diary (Quittner et al., 2007):

- EBA classification = well-established
- Test-retest reliability = stability coefficients over a 3-week period ( $r$ 's = 0.61-0.71)
- Inter-rater reliability = high levels (>90%)
- Validity = Strong convergence (77-80%) for daily routines as measured by the DPD and Self Observation Report Technique; modest to strong convergence between the DPD and electronic monitors across CF and asthma; adolescents with HIV who perfected perfect adherence on DPD were 5x more likely to have a low viral load and DPD protease inhibitor adherence was negatively correlated with viral load (Spearman  $r = -0.48$ )

### Daily Phone Diary (DPD)

Authors, Date	Sample	Study Design	Measures	Outcomes
<sup>1</sup> Smith, Modi, Quittner, & Wood, under review ( <i>Pediatric Pulmonology</i> )	-CF -N = 39 children and caregivers -n =19 children ages 7 -11 years -n = 20 adolescents 12 – 17 years -Mean FEV1 % predicted = 84%	- cross- sectional -estimated prevalence of depression in patients with CF (ages 7 – 17) and their caregivers -determine association between depressive symptoms and poor adherence	-Center for Epidemiological Studies (CES-D) -Hospital Anxiety and Depression Scale (HADS) -Child Depression Inventory (CDI) - <u>Daily Phone Diary (DPD)</u> -Health status (FEV1 % predicted)	- <b>DPD measured adherence</b> - <b>increase in child depressive symptoms → decrease in adherence (<math>r = -0.34, p = 0.02</math>)</b> -children's depression scores significantly predicted adherence after controlling for child age (older children had worse adherence) and parent education (parents with more education had children with better adherence) -mothers with more depressive symptoms had adolescents with better adherence ( $r = 0.62, p = 0.01$ ) -trend for fathers in same direction
<sup>2</sup> Modi, Marciel, Slater, Drotar, & Quittner, 2008	-CF -N = 103 families -Mean age = 13.4 years -% female = 47% -FEV1 % predicted = 82.1%	-cross-sectional data from a longitudinal study -evaluated relationships between parental supervision and adherence	-Prescribed Treatment Plan - <u>Daily Phone Diary</u> : time in various activities grouped according to companions (activities spent along and activities with parents) and activity type (medical vs. non-medical) -Electronic monitoring (nebulizer) -health status	-according to DPD, preadolescents spent more time with parents in medical activities than older adolescents -parental supervision decreased around age 15 -time spent with mother supervising treatments was a significant predictor of better adherence - <b>DPD allowed information regarding activities and supervision to be collected</b>
<sup>3</sup> Quittner, Modi, Lemanek, Levers-Landis, & Rapoff, 2007	-N/A -Review article	-N/A -Review article	Empirical evidence for 18 measures using 3 assessment methods: 1)self-report or structured interviews 2) <u>daily diary methods</u> 3)electronic monitors	-DPD uses day reconstruction method to assess daily activity patterns and reduce problems with memory and recall -DPD data is collected in real-time over a 24 hour recall period - <b>DPD closely converges with electronic measures</b> - <b>DPD identifies barriers and is an unobtrusive method</b> - <b>DPD developed for parents of children/adolescents with CF and adolescents with CF</b> - <b>DPD: stability over 3 weeks, high inter-rater agreement, strong convergence with electronic measures</b> - <b>DPD adapted for HIV and asthma with strong relationship between DPD and electronic measures and health variables → well-established measure</b>
<sup>4</sup> Modi & Quittner, 2006	-CF, asthma -N = 73 children and their parents -n = 37 children (CF) -n = 36 children asthma -Mean age = 9.9	-longitudinal design (3 months) -identify most frequent barriers to adherence for children and their parents	-Prescribed Treatment Plan -Disease Management Interview -Prescription refill data - <u>Daily Phone Diary</u> (CF and adapted for parents of children with asthma) -electronic monitoring -Barriers to Adherence Interview	-modest negative correlations between barriers for pulmozyme and adherence measured by DPD - <b>patients and parents experience disease specific barriers → need for disease-specific measures and interventions</b>

	years -% male = 58%		-Cystic Fibrosis Knowledge Questionnaire -Asthma Questionnaire -health status	
--	------------------------	--	---	--

Authors, Date	Sample	Study Design	Measures	Outcomes
<sup>5</sup> Modi, Lim, Yu, Geller, Wagner, & Quittner, 2006	-CF -N = 37 -Mean age = 10.1 years -Average FEV1 % predicted = 79.6	-longitudinal design (3 months) -4 methods to measure adherence to enzymes, airway clearance, nebulized medications and vitamins	-Prescribed Treatment Plan -Disease Management Interview-CF -Prescription refill data - <u>Daily Phone Diary (DPD)</u> -Medication Event Monitoring Systems (MEMS) -Pulmonary function tests (FEV1 % predicted)	-51% adherent to frequency and 64% for duration of airway clearance treatment per DPD <b>-DPD and pharmacy refill data comparable to electronic measures (“gold standard”)</b> <b>-DPD is advantageous since it is obtained in an unobtrusive manner</b> <b>-self-report measure but provides more accurate estimates of adherence than traditional self-report methods</b> <b>-DPD offered most comprehensive method for measuring all treatment components; electronic monitors cannot capture all components of Tx</b>
<sup>6</sup> Marhefka, Tepper, Farley, Sleasman, & Mellins, 2006	-caregivers of children with HIV (ages 2-12) -N = 51	-Cross-sectional -2 methods to measure adherence	-24-Hour Recall Interview (frequency adherence, dietary adherence, interval adherence) -Pharmacy refill data -clinical interview with a focus on barriers to adherence	-Frequency adherence was 93% -Dietary adherence was 7% -37% missed $\geq 1$ dose of medication over the 3 days of the recall procedure -52% of caregivers reported barriers -diary report of frequency and interval adherence did not correspond to viral load or pharmacy refill
<sup>7</sup> Weiner, Riekert, Ryder, & Wood, 2004	-HIV -N = 35 -Mean age = 15.4 -% male = 22	-Cross-sectional -3 different measures of adherence completed for anti-retroviral medications: -protease inhibitors (PI) -nucleoside reverse transcriptase inhibitors (NRTI) -non- nucleoside reverse transcriptase inhibitors (NNRTI)	-Clinic Nurse Rating -Retrospective Self-Report Interview of Medication Use - <u>Daily Phone Diary (DPD)</u> -Viral load (HIV-1 RNA levels)	-on DPD 50% participants reported to be completely adherent to PI -on DPD 44% participants reported to be completely adherent across all anti-retroviral medications <b>-DPD PI adherence was negatively correlated with viral load</b> <b>-DPD may help identify barriers that teen is unaware of → benefit in research context</b> -disadvantages of DPD in clinical context
<sup>8</sup> Quittner, Espelage, levers-Landis & Drotar, 2000	-NA -Review article	-NA -Review article	-Self-Report Measures -Diary methods -Electronic monitors	<b>-DPD advantages include:</b> <b>-ability to assess behaviors and activities that cannot be evaluated via observation</b> <b>-reduce problems with memory and recall</b> <b>-temporal precision</b> <b>-identifies barriers to adherence</b> <b>-available for multiple informants</b> <b>-unobtrusive measure which may reduce tendency to “fake good”</b>

Authors, Date	Sample	Study Design	Measures	Outcomes
<sup>9</sup> Quittner, Espelage, Opiari, Carter, & Eid, 1998	-CF, HC -N = 66 married couples -n = 33 couples had a child with CF -n = 33 couples had a healthy control child	-mixed between subjects (CF vs. comparison) -within-subject (husband vs. wife) repeated measure	-home interviews (demographic and medical information) -card sort procedure (division of labor) -Family Stress Scale, Marital Satisfaction Inventory - <u>Daily Phone Diary (DPD)</u>	- couples in CF group reported greater number of child-care tasks on the DPD -DPD indicated couples in CF group spent more time in medical care and child-focused play -wives in CF group spent 2X as much time as husbands on medical care tasks per DPD -DPD results indicated that CF group couples spent less time in recreational activities overall with the largest difference in in-home recreational activities -no mood rating differences on DPD <b>-utility and validity of daily diary approach → information gathered about processes that underlie adaptation to stress, reduce recall biases, provide information about changes, reveal family life</b>
<sup>10</sup> Quittner & Opiari, 1994	-CF, HC -N = 40 mothers with ≥ 2 children -n = 20 families younger child had CF -n = 20 families neither child had any illness or disability	-between-group comparison (CF vs. controls) -within-family comparison (older vs. younger child)	-home interviews (demographic and medical information; ratings of differential treatment of younger vs. older sibling; ratings of positive and negative disciplinary behaviors) -nightly phone ratings (differential treatments; disciplinary behaviors) - <u>Daily Phone Diary (DPD)</u> ; how mother spent time during the day)- phoned on 6 evenings and reported each activity they did from the start of their day to the point of the phone call -4 outcome variables: activity type, duration, companions and quality of interaction	<b>-DPD showed sufficient stability in terms of quantity and pattern of spending time with each child across 2 time periods</b> <b>-convergence found between differential treatment measured in DPD and home and nightly phone measures</b> -CF mothers spent more time with younger child than older child and rated time with older child as more negative; pattern was not as dramatic for control group -younger child with CF spends more time with mom individually than healthy control <b>-measurement of parental differential treatment through DPD was advantageous to other methods: less obtrusive, flexible means of measuring variables as they may change across the lifespan</b>



## References:

- <sup>1</sup>Smith, B.A., Modi, A.C., Quittner, A.L., & Woods, B.L. (under review). Depression in children with cystic fibrosis and parent caregivers and its effect on adherence. *Pediatric Pulmonary*.
- <sup>2</sup>Modi, A.C., Marciel, K.K., Slater, S.K., Drotar, D., & Quittner, A.L. (2008). The influence of parental supervision on medical adherence in adolescents with cystic fibrosis: Developmental shifts from pre to late adolescence. *Children's Health Care, 37*, 78-92.
- <sup>3</sup>Quittner, A.L., Modi, A.C., Lemanek, K.L., Ievers-Landis, C.E., & Rapoff, M.A. (2007). Evidence-based assessment of adherence to medical treatments in pediatric psychology. *Journal of Pediatric Psychology, 33*, 1-21.
- <sup>4</sup>Modi, A.C. & Quittner, A.L. (2006). Barriers to treatment adherence for children with cystic fibrosis and asthma: What gets in the way? *Journal of Pediatric Psychology, 31*, 846-858.
- <sup>5</sup>Modi, A.C., Lim, C.S., Yu, N., Gellar, D., Wagner, M.H., & Quittner, A.L. (2006). A multi-method assessment of treatment adherence for children with cystic fibrosis. *Journal of Cystic Fibrosis, 5*, 177- 185.
- <sup>6</sup>Marhefka, S.L., Tepper, V.J., Farley, J.J., Sleasman, J.W., & Mellins, C.A. (2006). Brief report: Assessing adherence to pediatric antiretroviral regimens using the 24-hour recall interview. *Journal of Pediatric Psychology, 31*, 989-994.
- <sup>7</sup>Wiener, L., Riekert, K., Ryder, C., & Wood, L.V. (2004). Assessing medication adherence in adolescents with HIV when electronic monitoring is not feasible. *AIDS Patient Care and STDs, 18*, 527-538.
- <sup>8</sup>Quittner, A.L., Espelage, D.L., Ievers-Landis, C., & Drotar, D. (2000). Measuring adherence to medical treatments in childhood chronic illness: Considering multiple methods and sources of information. *Journal of Clinical Psychology in Medical Settings, 7*, 41- 54.
- <sup>9</sup>Quittner, A.L. Espelage, D.L., Opiari, L.C., Carter, B., Eid, N., & Eigen, H. (1998). Role strain in couples with and without a child with a chronic illness: Associations with marital satisfaction, intimacy, and daily mood. *Health Psychology, 17*, 112-124.
- <sup>10</sup>Quittner, A.L. & Opiari, L.C. (1994). Differential treatment of siblings: Interview and diary analyses comparing two family contexts. *Child Development, 65*, 800-814.

## Electronic Measures of Adherence

### Overall assessment of common electronic monitors

(electronic monitors reviewed in Quittner, Modi, Lemanek, Ievers-Landis & Rapoff, 2008<sup>1</sup>)

#### 1) Medication Management System (MEMS):

- MEMS bottle cap records the date and time of pill bottle opening
- Have been used with pediatric patients: HIV-AIDS, CF, TB
- Accurate in benchmarking studies
- Convergent and predictive validity
- Convergence with pharmacy refill data and daily diary data (CF); urine assays (TB); viral load (HIV-AIDS)

#### 2) Metered Dose Inhaler (MDI) Monitors (MDILog, Nebulizer Chronolog, Doser CT)

- Doser CT and Nebulizer Chronolog are no longer used for research or clinical purposes
- Currently used is the MDILog: can identify errors in administration of medications for actuation (accuracy 97-100%), inhalation (accuracy 86-95%), late inhalation/multiple actuation (accuracy 97-99%)
- No artificial recordings
- Rates of adherence on MDILog correlated with other measures of adherence

#### 3) Halolite Nebulizer Monitor

- Adaptive aerosol delivery system that releases aerosol medication when inhalation is detected
- Shortens treatment time by 40%
- Records date, time and duration of each nebulized treatment
- Converges well with other measures of adherence
- More accurate estimates than traditional nebulizer monitors

### Electronic Monitors of Adherence- Cystic Fibrosis

Authors, Date	Sample	Study Design	Measures	Outcomes
<sup>2</sup> Quittner, Barker, Geller, Butt, & Gondor, 2007	-N = 92 children ages 1 – 12 and their parents -Mean age = 6.36 years	-longitudinal study (3 months)	-CES-D (parent) -Disease Management Interview - <u>electronic monitor</u> (record the date and time of each bottle opening) - health status (weight)	-rates of adherence were 42% at home and 88% at school <b>-caregiver depression was negatively associated with adherence</b> -caregivers who endorsed more depressive symptoms were less likely to give enzymes to their child -enzyme adherence was associated with changes in weight -rate of adherence decreased with age
<sup>3</sup> Modi, Lim, Yu, Geller, Wagner, & Quittner, 2006	-37 children with CF ages 6 – 11 and their primary caregivers	-longitudinal study (3 months)	-Prescribed Treatment Plan -Disease Management Interview -Prescription refill data -Daily Phone Diary - <u>electronic monitor</u> (adherence to enzymes) -Medication Event Monitoring Systems (MEMS®): stores dates and times for over 200 doses -MEMS cap did not account for number of capsules taken -health status (FEV1 % predicted)	-significant variability in adherence rates for enzymes (27% adherent per diary data, 42.5% per electronic monitoring, 90% per child self-report) -overall mean rate of adherence for CF using objective measures (e.g., pharmacy refill history, diary data, and electronic monitoring) was below 50% -parents reported higher rates of adherence compared to electronic monitoring, pharmacy refill history, and diary data <b>-pharmacy refill history and diary data were comparable to electronic measures</b>

Authors, Date	Sample	Study Design	Measures	Outcomes
<p><sup>4</sup>Modi &amp; Quittner, 2006</p>	<p>-N = 73 children with CF or asthma            -CF (n= 37)            -asthma (n= 36)            -mean age = 9.9 years</p>	<p>-longitudinal study (3 months)</p>	<p>-Prescribed Treatment Plan            -Disease Management Interview            -Prescription refill data            -Daily Phone Diary            -<u>electronic monitoring for enzyme medications and MDIs</u>              -Electronic Drug Exposure Monitor (eDEM®) monitored enzymes              -MDILog II® recorded date and time inhaled medications were taken, whether canister was shaken appropriately and whether medication was properly inhaled            -barriers to adherence interview            -CF Knowledge Questionnaire            -Asthma Questionnaire            -health status (FEV1 % predicted)</p>	<p>-greater number of barriers were moderately associated with poorer adherence (as measured by electronic monitors)            -although electronic monitors are often viewed as “gold-standard”, 77% of MDILog failed, did not fit properly or were lost            -electronic monitors were not available for all parts of treatment regimen</p>

**Electronic Measures of Adherence (non-CF populations)**

Authors, Date	Sample	Study Design	Measures	Outcomes
<sup>5</sup> McClellan, Schatz, Puffer, Sanchez, Stancil, & Roberts, 2009	-19 patients with sickle cell disease ages 9 – 20 who experience vaso-occlusive pain	-longitudinal study (8 week intervention) -intervention group and waitlist group	-handheld wireless electronic device to guide skills practice and monitor daily pain -1 CBT coping skills session -data from monitor was sent immediately after a participant completed a pain diary entry or a skills practice session	-high rates of consumer satisfaction -diaries completed 76% of the days -self report of practicing CBT skills with the device was 1.7 times per day
<sup>6</sup> Bogen & Apter, 2004	-individuals who use a dry powder inhaler	-development of the Diskus Adherence Logger (DAL)	-DAL detects and records the motion of the drug delivery lever in the inhaler with a magnetic sensor -data uploaded to a computer	-system verification results: every simulated dose was recorded by the device, no missed doses or extra doses recorded -device is small, non-interfering operation, external attachment, extended battery life, simplistic, low cost
<sup>7</sup> Kumar, Wentzell, Mikkelsen, Pentland, & Laffel, 2004	- 40 children ages 8 – 18 with diabetes	-Game group and control group -longitudinal study (4 weeks)	-Daily Automated Intensive Log for Youth -facilitate blood glucose monitoring and help optimize glycemic control with a motivational game	-game group transmitted more BG values than control group -game group had significantly less hyperglycemia -game group had significant increase in diabetes knowledge

Authors, Date	Sample	Study Design	Measures	Outcomes
<sup>8</sup> Finklestein, Synder, Edin-Stibbs, Chlan, Dutta, Lindgren, Wielinski, & Hertz, 1996	-lung transplant patients -n = 53	-longitudinal study (data reported on one year)	-electronic spirometer/diary instrument to be used at home -electronic spirometer measures FVC, FEV1, FEF, peak flow -vital signs collected include body weight, resting pulse, temperature, blood pressure -symptoms information include frequency of coughing and wheezing, presence and color of sputum, shortness of breath at rest and after exercise, type and duration of exercise, emotional well being and stress level -1 time per week data downloaded and sent to research team	-participants received weekly phone call by nursing team members to review data, quarterly graphs of their own data and tips from clinic tea -subject adherence was 90% for first 8 weeks, 82% for the entire year, only fell below 5% for 4 weeks -ultimate goal is early detection of infection

## References:

- <sup>1</sup>Quittner, A.L., Modi, A.C., Lemanek, K.L., Iever-Landis, C.E., & Rapoff, M.A. (2008). Evidence-based assessment of adherence to medical treatments in pediatric psychology. *Journal of Pediatric Psychology*, 33, 916-936.
- <sup>2</sup>Quittner, A.L., Barker, D.H., Geller, D., Butt, S., & Gondor, M. Effects of Maternal Depression on self reported and electronically monitored enzyme adherence and changes in weight for children with CF. Presented at the North American Cystic Fibrosis Conference, 2007 Oct 4-6; Anaheim, CA.
- <sup>3</sup>Modi, A.C., Lim, C.S., Yu, N., Geller, D., Wagner, M.H., & Quittner, A.L. (2006). A multi-method assessment of treatment adherence for children with cystic fibrosis. *Journal of Cystic Fibrosis*, 5, 177-185.
- <sup>4</sup>Modi, A.C. & Quittner, A.L. (2006). Barriers to treatment adherence for children with cystic fibrosis and asthma: What gets in the way? *Journal of Pediatric Psychology*, 31, 846-858.
- <sup>5</sup>McClellan, C.B., Schatz, J.C., Puffer, E., Sanchez, C.E., Stancil, M.T., & Roberts, C.W. (2009). Use of handheld wireless technology for a home-based sickle cell pain management protocol. *Journal of Pediatric Psychology*, 34, 564-573.
- <sup>6</sup>Bogen, D. & Apter, A.J. (2004). Adherence logger for a dry powder inhaler: A new device for medical adherence research. *American Academy of Allergy, Asthma and Immunology*, 10, 863-868.
- <sup>7</sup>Kumar, V.S., Wentzel, K.J., Mikkelsen, T., Pentland, A., & Laffel, L.M. (2004). The DAILY (Daily Automated Intensive Log for Youth) trial: A wireless, portable system to improve adherence and glycemic control in youth with diabetes. *Diabetes Technology & Therapeutics*, 6, 445-453.
- <sup>8</sup>Finkelstein, S.M., Snyder, M., Edin-Stibbe, C., Chlan, L., Prasad, B., Dutta, P., Lindgren, B., Wielinski, C., & Hertz, M.I. (1996). Monitoring progress after lung transplantation from home-patient adherence. *Journal of Medical Engineering & Technology*, 20, 203-210.

### Self-Report Measures of Adherence (CF-Specific)

Measures	Ages	Details of Measures	Psychometrics: Reliability	Psychometrics: Validity	Outcomes/Clinical Relevance
Disease Management Interview- CF (formerly Treatment Adherence Questionnaire) ( <sup>1</sup> Quittner, Modi, Lemanek, levers-Landis, & Rapoff, 2008; <sup>2</sup> Modi, Lim, Yu, Gellar, Wagner, & Quittner, 2006; <sup>3</sup> Quittner, Espelage, levers-Landis, & Drotar, 2000)	-children 10+ -parents of children with CF (all ages)	-51 items -instructions normalize challenges of managing treatment regimen - 2 week recall -consider use over past 3 months for oral antibiotics and aerosolized antibiotics	-internal consistency not appropriate - test-retest reliability adolescent report: $r$ 's 0.62 to .73 -test- retest reliability parent report: $r$ 's =0.76 to 0.88 -inter-rater reliability nebulized medications (parent- teen): $r = 0.55$ - inter-rater reliability CPT (parent- teen): $r = 0.78$ - inter-rater reliability nebulized medications (parent- child): $r = 0.69$ - inter-rater reliability CPT (parent- child): $r = 0.88$	- greater number of barriers for pulmozyme associated with reduced adherence per parent self-report (moderate negative correlation)	- associations found between adherence and knowledge of treatment regimen
Treatment Adherence Questionnaire Modified (TAQ-CFM; <sup>4</sup> Masterson, Wilderman, Newberry, Omior, Bryson & Kukay, 2008)	-not reported	-patient, parent, and physician versions -self-report questionnaire/interview (interview form for children and adults with CF; questionnaire format for parents and physicians) -assesses compliance with and knowledge of airway clearance, aerosol medications, inhalers, antibiotic aerosols, oral antibiotics, steroids, enzymes, nutritional supplements	-no formal studies on TAQ-CFM, but TAQ-CF demonstrated moderate to high agreement between parent and patient report -test-retest of TAQ-CF for one year ranges from 0.62 to 0.73	-not reported	-compliance with medical treatment was based on TAQ-CFM responses -medical noncompliance was defined as compliance with less than 50% of health professional recommendations on two or more of the treatment recommendations



Measures	Ages	Details of Measures	Psychometrics: Reliability	Psychometrics: Validity	Outcomes/Clinical Relevance
Treatment Adherence Rating Scale (TARS; <sup>5</sup> Delambo, Levers-Landis, Drotar & Quittner, 2004)	-children, adolescents, parents	-16 items	-internal consistency for airway clearance/aerosolized medications = .82-.84 -inter-rater reliability among informants (.42 - .57)	-not assessed	
Barriers to Adherence Interview <sup>6</sup> Modi & Quittner, 2006)	-children ages 10+ and parent	-interview format -for each component of treatment regimen, open ended questions re: taking medications and why doing treatments can be difficult -participants given list of 25 common barriers and asked to chose any additional barriers that were relevant -participants rated frequency of barriers	-NA	-more barriers were associated with worse adherence	-important to evaluate barriers within the context of each treatment group
Prescribed Treatment Plan ( <sup>3</sup> Quittner, Espelage, levers-Landis, & Drotar, 2000)	-all ages	-form that treatment team completes after clinic visit so patient and family know recommended treatments	-NA	-NA	-attempt to remediate differences in CF team member recommendations and children and families recall of treatment regimen
CF My Way ( <sup>7</sup> Novartis in consultation with Quittner, A.L., Nasr, S.Z., Bryson, E.A., & Thrasher, S., 2008)	-children, adolescents, parents	-3 step process -self-report questionnaire -group problem solving activity (child/adolescent, parent and member of CF team)	-currently being studied	-currently being studied	-includes a prescribed treatment plan (see below), barrier assessment and problem solving session to be done at a clinic visit

Measures	Ages	Details of Measures	Psychometrics: Reliability	Psychometrics: Validity	Outcomes/Clinical Relevance
Project on Adult Care in Cystic Fibrosis, Treatment Activity Survey (PAC-CF; <sup>8</sup> Sawicki, Sellers & Robinson, 2009)	-adults with CF	- treatment activities assessed through a series of survey questions: report the medications and therapies that they took on the day prior to the survey -reported on treatment activity, whether treatment was comparable to a typical treatment, and why there was a difference	-not reported	-not reported	-allowed for responses that indicated whether a decision about a therapy on a particular day was part of their overall disease management strategy
Living with Cystic Fibrosis Questionnaire (LCFQ; <sup>9</sup> Patterson, Wall, Berge & Milla, 2008, <sup>10</sup> 2009)	-ages 10 -21 with CF	-36 item self-report -measure different family, peer, and personal factors expected to be associated with CF -for each question respondents indicate how often the item occurred -8 scales (parent-youth strains, parental support, peer relationship status, peer relationship strains, risk taking behaviors, seeking support) -3 single items (friend support, self-care motivation, self-care discouragement) -index addressing non-adherence with treatment (5 questions)	-acceptable alphas for parent-youth strains and illness strains/worries (.73 - .85), emotional strain (.84) -lower alphas for physical strains (.64) and appearance worries (.55) -no alpha reported for non-adherence index	-gender differences found across scales -girls reported more illness related strains and worries, as well as greater treatment discouragement, lower self-esteem, and lower adherence	-nine factors confirmed through confirmatory factor analysis -psychological strains at the personal, family, and friend level were associated with reduced treatment adherence -questionnaire offers promise in assessing and understanding gender differences with respect to CF morbidity and mortality

Measures	Ages	Details of Measures	Psychometrics: Reliability	Psychometrics: Validity	Outcomes/Clinical Relevance
Cystic Fibrosis Treatment Questionnaire (CFTQ; <sup>11</sup> Bucks, Hawkins, Skinner, Horn, Seddon & Horne, 2009; <sup>12</sup> Myers & Horn, 2006)	-not reported	-adapted from the Living with Cystic Fibrosis Questionnaire -patients asked to rate level of adherence to CPT, ES, antibiotics according to how often they do treatment, whether they see treatment as part of their daily routine, how often they miss the treatment	-good internal consistency across scales: physiotherapy (.91), ES (.85), antibiotics (.81)	-not reported	-attempts to reduce over reporting by normalizing the process of modifying treatment to fit lifestyle
Revised Illness Perception Questionnaire (IPQ-R; <sup>13</sup> Moss-Morris, Weinman, Petrie, Horne, Cameron, & Buik, 2002; <sup>11</sup> Bucks, Hawkins, Skinner, Horn, Seddon & Horne, 2009)	-not reported	-several subscales assessing: illness identity (presence or absence of 14 general symptoms and 5 CF related symptoms); timeline (10 items regarding views about the chronic or episodic nature of CF); consequences (6 items assessing beliefs about impact of CF); personal and treatment control (11 items assessing how amenable CF is to personal actions and treatment); cause (18 items assessing attributions about possible causes); emotional representations (6 items regarding emotional responses to illness)	-no previous studies using tool with CF, but has been shown to have good reliability in other populations -internal consistency was adequate to good for all scales (alpha = 0.66 to 0.84)	-construct, content and predictive validity shown in other chronic illnesses -identity, time-line, and consequences used in 4 studies of 11-18 year olds with type 1 diabetes	- measure can help determine whether personal models of CF are predictive of adherence to CF treatment -personal models of CF accounted for approximately 50% of variance in self-reported adherence behavior

Measures	Ages	Details of Measures	Psychometrics: Reliability	Psychometrics: Validity	Outcomes/Clinical Relevance
Confidential CF Management Profile ( <sup>14</sup> White, Miller, Smith & McMahon, 2009)	-parent questionnaire -youth questionnaire -team report questionnaire	-3 part questionnaire that evaluates level of adherence to medical management -parent and youth questionnaires have 57 items each -team report has 37 questions -sub-scores measure adherence in diet, pulmonary care, medication management -questions focus on duration and frequency of treatments compared to duration and frequency prescribed by the team -divided into parent/patient reported non-adherence and non-adherence related to a mismatch with teams recommendations	-moderate, statistically significant correlation between youth and parent report for pulmonary treatments ( $r = 0.44$ )	-not reported	-for youth report 67% of non-adherence was due to missing or shortening of treatments-33% of non-adherence attributed to a mismatch with the CF team's recommendations -higher levels of family cohesion were linked with high rates of youth-reported adherence and higher rates of parent reported adherence -families with overly rigid or overly flexible patterns of family function had lower rates of adherence
Medication Adherence Report Scale ( <sup>15</sup> Horne & Weinman, 2002; <sup>11</sup> Bucks, Hawkins, Skinner, Horn, Seddon & Horne, 2009)	-not reported	-generic questionnaire -rate how frequently non-adherent behaviors occur	-non-CF sample had good reliability and internal consistency; results replicated in CF sample -alphas: physiotherapy (.88), antibiotic (.75), ES (.51)	-not reported	-questionnaire preceded by a statement assuring that many people follow treatment in a way that suits them and may differ from recommendations by health care teams -diminish social pressure to over-estimate adherence

## References:

- <sup>1</sup>Quittner, A.L., Modi, A.C., Lemanek, K.L., Iever-Landis, C.E., & Rapoff, M.A. (2008). Evidence-based assessment of adherence to medical treatments in pediatric psychology. *Journal of Pediatric Psychology*, 33, 916-936.
- <sup>2</sup>Quittner, A.L., Espelage, D.L., Iever-Landis, C., & Drotar, D. (2000). Measuring adherence to medical treatments in childhood chronic illness: Considering multiple methods and sources of information. *Journal of Clinical Psychology in Medical Settings*, 7, 41-54.
- <sup>3</sup>Modi, A.C., Lim, C.S., Yu, N., Gellar, D., Wagner, M.H., & Quittner, A.L. (2006). A multi-method assessment of treatment adherence for children with cystic fibrosis. *Journal of Cystic Fibrosis*, 5, 177-185.
- <sup>4</sup>Masterson, T., Wildman, B.G., Newberry, B., Omlor, G., Bryson, E., & Kukay, A. (2008). Compliance in cystic fibrosis: An examination of infection control guidelines. *Pediatric Pulmonology*, 43, 435-442.
- <sup>5</sup>DeLambo, K.E., Iever-Landis, C.E., Drotar, D., & Quittner, A.L. (2004). Association of observed family relationship quality and problem-solving skills with treatment adherence in older children and adolescents with cystic fibrosis. *Journal of Pediatric Psychology*, 29, 343-353.
- <sup>6</sup>Modi, A.C. & Quittner, A.L. (2006). Barriers to treatment adherence for children with cystic fibrosis and asthma: What gets in the way? *Journal of Pediatric Psychology*, 31, 846-858.
- <sup>7</sup>The CF My Way program was developed by Novartis in consultation with A.L. Quittner, S.Z. Nasr, E.A. Bryson, & S. Thrasher. (2008).
- <sup>8</sup>Sawicki, G.S., Sellers, D.E., & Robinson, W.M. (2009). High treatment burden in adults with cystic fibrosis: Challenges to disease self-management. *Journal of Cystic Fibrosis*, 8, 91-96.
- <sup>9</sup>Patterson, J.M., Wall, M., Berge, J., & Milla, C. (2009). Associations of psychological factors with health outcomes among youth with cystic fibrosis. *Pediatric Pulmonology*, 44, 46-53.
- <sup>10</sup>Patterson, J.M., Wall, M., Berge, J., & Milla, C. (2008). Gender differences in treatment adherence among youth with cystic fibrosis: Development of a new questionnaire. *Journal of Cystic Fibrosis*, 7, 154-164.
- <sup>11</sup>Bucks, R.S., Hawkins, K., Skinner, T.C., Horn, S., Seddon, P., & Horne, R. (2009). Adherence to treatment in adolescents with cystic fibrosis: The role of illness perceptions and treatment beliefs. *Journal of Pediatric Psychology*, 34, 893-902.
- <sup>12</sup>Myers, L.B. & Horn, S.A. (2006). Adherence to chest physiotherapy in adults with cystic fibrosis. *Journal of Health Psychology*, 11, 915-926.
- <sup>13</sup>Moss-Morris, R., Weinman, J., Petrie, K., Horne, R., Cameron, L., & Buick, D. (2002). The revised illness perception questionnaire (IPQ-R). *Psychology & Health*, 17, 1-16.
- <sup>14</sup>White, T., Miller, J., Smith, G.L., & McMahon, W.M. (2009). Adherence and psychopathology in children with cystic fibrosis. *European Journal of Child and Adolescent Psychiatry*, 18, 96-104.
- <sup>15</sup>Horne, E. & Weinman, J. (2002). Self-regulation and self-management in asthma: Exploring the role of illness perceptions and treatment beliefs in explaining non-adherence to preventer medication. *Psychology & Health*, 17, 17-32.

## **Pharmacy Refill History to Measure Adherence**

### Overall assessment of pharmacy refill data

- Beneficial for large scale studies
- Serve as an estimate of adherence in epidemiology and health outcomes research
- Strongly correlated with other objective measures of adherence (i.e. electronic monitors, Daily Phone Diary)
- Pharmacy refill history cannot reveal whether medication is in fact taken or whether prescription guidelines in terms of dose and time are adhered to
- Refill history does not capture medicine obtained at physician offices or emergency rooms

### Pharmacy Refill History- Cystic Fibrosis

Authors, Date	Sample	Study Design	Measures	Outcomes
<sup>1</sup> Modi, Lim, Yu, Gellar, Wagner & Quittner, 2006	-N = 37 children ages 6 – 13 years and their primary caregivers	-longitudinal study (3 months)	-Prescribed Treatment Plan -Disease Management Interview - <u>Prescription refill data</u> : rates of adherence calculated for individual medications taken continuously; medication obtained during 3 month interval was divided by the total # of days in the time period (90 days) -Daily Phone Diary -electronic monitor_(adherence to enzymes) -health status (FEV1 % predicted)	-overall rates of adherence using objective measures, including pharmacy refill history, was below 50% -pharmacy refill history and diary data were consistent with electronic measures of adherence -multi-method measurement approach of adherence results in unique information for different treatment types
<sup>2</sup> Burrows, Bunting, Masel, & Bell, 2002	-90 individuals with CF	-longitudinal study (3 years)	-Patient interview -self-reported adherence -pharmacy dispensing records	-significant differences between self-reported rates of adherence and pharmacy refill history -refill data provides an indirect but objective measure of adherence
<sup>3</sup> Modi & Quittner, 2006	-73 children with asthma or CF and their caregivers -mean age = 9.9 years -58% males	-longitudinal study (3 months)	-Background information form -Prescribed Treatment Plan -Disease Management Interview -Prescription Refill Data -Daily Phone Diary -Electronic Monitoring -Barriers to Adherence Interview -Cystic Fibrosis Knowledge Questionnaire (CFKQ) -Asthma Questionnaire (AQ) -Health Status	-no statistical relationship between barriers and adherence -greater number of barriers were moderately related to poorer adherence through objective measures -difficult to calculate rates of adherence due to incomplete prescriptions in medical charts prior to study -challenges to pharmacy refill data include use of multiple pharmacies, dispensing of free samples, and use of online pharmacies

**Pharmacy Refill History- (non-CF populations)**

Authors, Date	Sample	Study Design	Measures	Outcomes
<sup>4</sup> Choo, Rand, Inui, Lee, Cain, Corderior-Breault, Canning, Platt, 1999	-N = 286 member of Harvard Pilgrim Health Care -at least 18 years of age, on monotherapy for hypertension, and had prescription drug coverage	-longitudinal study (12 months prescription refill, 3 month electronic monitoring)	-patient reported adherence through telephone administered questionnaire (3 questions taken from the Brief Medication Questionnaire) -SF-36 -social support -automated pharmacy records -Medication Management System – 4 (MEMS-4)	-pharmacy refill history demonstrates predictive validity (exposure and gaps in medication supply) -refill history correlates more closely with quantity of medication than timing of dose from MEMS-4
<sup>5</sup> Mudd, Bollinger, Hsu, Donithan, & Butz, 2006	-N = 175 children ages 2 – 9 years with persistent asthma -children enrolled in a nebulizer education intervention clinical trial -mean age = 5.15 years	-cross-sectional analysis of pharmacy refill data over 6 months	-interviews regarding measurements of asthma control (i.e. asthma-related healthcare utilization and activity restriction) -pharmacy refill data -health status -sociodemographic information	-asthma medication use and activity restriction are incongruent -unable to determine temporal relationship between rescue prescription refills and controller fills -children with no/low rescue medication fills were less likely to fill controllers compared to those with high rescue medications fills (this finding was contrary to apriori expectations)



References:

- <sup>1</sup>Modi, A.C., Lim, C.S., Yu, N., Gellar, D., Wagner, M.H., & Quittner, A.L. (2006). A multi-method assessment of treatment adherence for children with cystic fibrosis. *Journal of Cystic Fibrosis*, 5, 177-185.
- <sup>2</sup>Burrows, J.A., Bunting, J.P., Masel, P.J., & Bell, S.C. (2002). Nebulised dornase alpha: adherence in adults with cystic fibrosis. *Journal of Cystic Fibrosis*, 1, 255-259.
- <sup>3</sup>Modi, A.C. & Quittner, A.L. (2006). Barriers to treatment adherence for children with cystic fibrosis and asthma: What gets in the way? *Journal of Pediatric Psychology*, 31, 846-858.
- <sup>4</sup>Choo, p., Rand, C.S., Inui, T.S., Lee, M.L., Cain, E., Cordeiro-Breault, M., Canning, C., & Platt, R. (1999). Validation of patient reports, automated pharmacy records, and pill counts with electronic monitoring of adherence to antihypertensive therapy. *Medical Care*, 37, 846-857.
- <sup>5</sup>Mudd, K., Bollinger, M.E., Hsu, V.D., Donithan, M & Butz, A. (2006). Pharmacy fill patterns in young urban children with persistent asthma. *Journal of Asthma*, 43, 597-600.