Methods to Diagnose Adherence Status

March 4, 2014

Andrew G Weinstein MD
Associate Clinical Professor Pediatrics
Jefferson Medical College
President, Adherence Management Systems
Disclosures

- President, Asthma Management Systems
- PI NIH Grant #7R44HL078252-05
- PI Merck Grant #5009
- Consultant: Merck, AmeriHealth Mercy Health Plan
- Asthma and Allergy Foundation of America
Is your patient taking the medication you prescribed?
Figure 4-5. Stepwise Approach for Managing Asthma in Youths ≥12 Years of Age & Adult

**Intermittent Asthma**

Consult with asthma specialist if step 4 care or higher is required.

Consider consultation at step 3.

Step 6

**Preferred:**

High-dose ICS + LABA + oral corticosteroid

AND

Consider Omalizumab for patients who have allergies

Step 5

**Preferred:**

High-dose ICS + LABA

AND

Consider Omalizumab for patients who have allergies

Step 4

**Preferred:**

Medium-dose ICS + LABA

Alternative:

Medium-dose ICS + either LTRA, Theophylline, or Zileuton

Step 3

**Preferred:**

Low-dose ICS + LABA

Alternative:

Low-dose ICS + either LTRA, Theophylline, or Zileuton

Step 2

**Preferred:**

Low-dose ICS

Alternative:

Cromolyn, LTRA, Nedocromil, or Theophylline

Step 1

**Preferred:**

SABA PRN

Quick-Relief Medication for All Patients

- SABA as needed for symptoms. Intensity of treatment depends on severity of symptoms: up to 3 treatments at 20-minute intervals as needed. Short course of systemic oral corticosteroids may be needed.
- Use of SABA >2 days a week for symptom relief (not prevention of EIB) generally indicates inadequate control and the need to step up treatment.

Each step: Patient education, environmental control, and management of comorbidities

Steps 2-4: Consider subcutaneous allergen immunotherapy for patients who have allergic asthma

**Key:** ICS, inhaled corticosteroid; LABA, inhaled long-acting beta₂-agonist; LTRA, leukotriene receptor antagonist; SABA, inhaled short-acting beta₂-agonist

*Guidelines for the Diagnosis and Management of Asthma (EPR-3) 2007. NIH, NHLBI. August 2007. NIH publication no. 08-4051.*
Two Different Treatment Options
Adherent vs Nonadherent

PATIENT EDUCATION OFTEN FAILS TO ACHIEVE ADHERENCE
Increasing asthma knowledge through education yields little improvement in patient adherence or asthma outcomes. Interventions that encourage patients to monitor symptoms or peak flow have shown significant but small effects on asthma morbidity. Self-management approaches, including identifying barriers to adherence, self-monitoring medication use, goal setting, and problem solving, result in fewer urgent care visits, short-term improvements in adherence, higher asthma management self-efficacy, improved quality of life, reduced asthma symptoms, and less beta-agonist use. Unfortunately, most self-management studies involve more than 5.5 hours of patient contact. Furthermore, an important limitation of both educational and self-management approaches is that they are predicated on the assumption that patients are motivated to accept treatment recommendations.

ADHERENCE MANAGEMENT MODEL
Adherence management focuses on methods to promote adherence to a prescribed medical regimen. Adherence to recommendations is a necessary component for the treatment plan to be successful. Without adherence, efforts to manage an individual’s disease and obtain desired outcomes are significantly curtailed. The 4 components of adherence management as it relates to the management of chronic asthma include: (1) objectively diagnose patient adherence status; (2) identify risk factors (barriers);...
Assessing Adherence

Direct Methods

- Observation
- Measure levels of medicine (blood/urine)
- Measure biological marker attached to the medicine
- Conduct unannounced spot check to patient’s home/clinic
- Measure clinic attendance

Cramer and Spiker Patient Compliance in Medical Practice NY Raven 1991
Assessing Adherence

Direct Methods

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- Measure biological marker attached to the medicine
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- Measure clinic attendance

Cramer and Spiker Patient Compliance in Medical Practice NY Raven 1991
Assessing Adherence

Direct Methods

Measure blood/saliva

- Theophylline 1970-1980s Maintenance Bronchodilator

- Level required because of a small therapeutic window 5-20 mcg to establish dose
  - Toxicity above 20
  - Ineffective below 5

- Significant increase in asthma adherence studies
Blood Level

• Positives
  Identify medication within the patient

Negatives
  Intrusive
  Snap shot into medication use
  Varies with patient metabolism/diet
Assessing Adherence

Indirect Methods

- Question the patient
- Evaluate patient diaries for completeness
- Ask patient to complete questionnaire
- Assess adherence based on response to treatment
- Conduct pill counts
- Use electronic monitors
- Determine prescriptions filled at pharmacy
Indirect Methods

Question the patient

Variable results based on how you ask the question

– Closed-ended question: Response YES or NO

– Open-ended question: Allows the patient to provide more information

-- Reduce expectation of provider

“It is difficult to take medication every day. I have asked you to use your inhaler twice a day. So for one week that would be 14 times and that is a lot. Most people would use the medicine 8-10 times in a week. How are you doing?”
Question the Patient

Patient-Centered Communication Skills

• Place the patient at ease
• Make he/she an active participant
• Setting an agenda
• Assess motivation and confidence to change
• Weigh the costs and benefits of change
• Provide medical advice and feedback

S Wilson et al. Shared treatment decision making improves adherence and outcomes in poorly controlled asthma  Am J Crit Care Med 2009; 181:566-577

B Borelli et al . Brief Motivational Interviewing as a clinical strategy to promote medication adherence JACI  2007: 120:1023-1030
Question the Patient

What is the significance of a NEGATIVE response?

(When a patient says they did not take Rx)

- 286 adult Hypertensive monotherapy 3months
- Negative response by diary to anti-hypertensive regimen was consistent with
  - Pill count
  - Electronic monitor
  - Prescription refill

CONCLUSION

--95% of the time if the patient says that they are not taking the medicine, BELIEVE THEM.

--99% if the patient is symptomatic

- Choo, Rand et al. Medical Care 1999;37:846-857
Question the Patient

Positive

Inexpensive
Enhance likelihood of an accurate Hx medication use
Communications skills
Reducing expectations

Negative

History may not be truthful
Assessing Adherence

Indirect Methods

- Question the patient
- Evaluate patient diaries
- Ask patient to complete questionnaire
- Assess adherence based on response to treatment
- Conduct pill counts
- Use electronic monitors
- Determine prescriptions filled at pharmacy
Adherence with Asthma Therapy by Diary and Electronic Monitoring

Milgrom H, Bender, B, Rand, C., J Allergy Clin Immunol, 1996:1051-57
Nonadherence is associated with increased risk of disease exacerbations

Milgrom H, Bender, B, Rand, C., J Allergy Clin Immunol, 1996:1051-57
PATIENT DIARIES

• **Positive**
  – Simple to administer
  – Inexpensive

• **Negative**
  – False Positives
Assessing Adherence

Indirect Methods

- Question the patient
- Evaluate patient diaries for completeness
- **Ask patient to complete questionnaire**
- Assess adherence based on response to treatment
- Conduct pill counts
- Use electronic monitors
- Determine prescriptions filled at pharmacy
MORISKEY ADHERENCE QUESTIONNAIRES

- Adult hypertensive patients
- 4 and 8 question instruments self-administered by Pt
- Related Adherence scores to BP control

Findings
- Identify patients with adherence problems
- Monitor adherence over course of treatment
- Instrument contains treatment-related attitudinal and behavioral problems that providers can address

Moriskey Med Care 1986;24:67
Moriskey J Clin Hypertens 2008;10:348
## Table 1. Self-reported Medication-taking Scale and Item-to-total Correlation Coefficients

<table>
<thead>
<tr>
<th>Question</th>
<th>Corrected Item-to-total Correlation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Do you ever forget to take your medicine?</td>
<td>0.515</td>
</tr>
<tr>
<td>2. Are you careless at times about taking your medicine?</td>
<td>0.479</td>
</tr>
<tr>
<td>3. When you feel better do you sometimes stop taking your medicine?</td>
<td>0.527</td>
</tr>
<tr>
<td>4. Sometimes if you feel worse when you take the medicine, do you stop taking it?</td>
<td>0.561</td>
</tr>
</tbody>
</table>

Scoring: high–low; yes = 0; no = 1.  
Range: 0–4.  
Mean (weighted): n = 290; \( \bar{x} = 2.31 \).  
Cronbach alpha: 0.61.
<table>
<thead>
<tr>
<th>Predicted to be adequately controlled by (high) index score</th>
<th>Adequately Controlled at 42 months</th>
<th>Inadequately Controlled at 42 months</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Predicted to be inadequately controlled by (low) index score</td>
<td>94</td>
<td>31</td>
<td>125</td>
</tr>
<tr>
<td></td>
<td>22</td>
<td>24</td>
<td>46</td>
</tr>
<tr>
<td>Total</td>
<td>116</td>
<td>55</td>
<td>171</td>
</tr>
</tbody>
</table>

Sensitivity = \( \frac{24}{116} = 0.81 \).

Specificity = \( \frac{24}{33} = 0.44 \).

\( PV_+ = 0.75 \).

\( PV_- = 0.47 \).

\( PV = 0.69 \).
FIG. 1. Blood pressure control by verbal medication-adherence index (n = 290); $r_{6\text{ me.}} = 0.43$, $P < 0.01$; $r_{42\text{ me.}} = 0.58$, $P < 0.01$. 

Source: Medical Care, Vol. 24; no. 1 (January 1986). Moritsky, Donald E., ScD; et al. Concurrent Predictive Validity of a Self-Reported Measure of Medication Adherence
<table>
<thead>
<tr>
<th>Item</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Do you sometimes forget to take your high blood pressure pills?</td>
</tr>
<tr>
<td>2. Over the past two weeks, were there any days when you did not take</td>
</tr>
<tr>
<td>your high blood pressure medicine?</td>
</tr>
<tr>
<td>3. Have you ever cut back or stopped taking your medication without</td>
</tr>
<tr>
<td>telling your doctor because you felt worse when you took it?</td>
</tr>
<tr>
<td>4. When you travel or leave home, do you sometimes forget to bring</td>
</tr>
<tr>
<td>along your medications?</td>
</tr>
<tr>
<td>5. Did you take your high blood pressure medicine yesterday?</td>
</tr>
<tr>
<td>6. When you feel like your blood pressure is under control, do you</td>
</tr>
<tr>
<td>sometimes stop taking your medicine?</td>
</tr>
<tr>
<td>7. Taking medication everyday is a real inconvenience for some people</td>
</tr>
<tr>
<td>do you ever feel hassled about sticking to your blood pressure</td>
</tr>
<tr>
<td>treatment plan?</td>
</tr>
<tr>
<td>8. How often do you have difficulty remembering to take all your</td>
</tr>
<tr>
<td>blood pressure medication?</td>
</tr>
</tbody>
</table>

**Alpha Reliability = 0.83**

### Relationship between Adherence Scale and Blood Pressure in Control

<table>
<thead>
<tr>
<th>Blood Pressure In Control*</th>
<th>No</th>
<th>Yes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low Adherence &lt; 6</td>
<td>67.2%</td>
<td>32.8%</td>
</tr>
<tr>
<td>Medium Adherence 6 - &lt; 8</td>
<td>55.2%</td>
<td>44.8%</td>
</tr>
<tr>
<td>High Adherence ≥ 8</td>
<td>43.3%</td>
<td>56.7%</td>
</tr>
</tbody>
</table>

*(χ² = 6.6; p < 0.05)*

Blood pressure in control: Systolic BP < 140 mm Hg, and Diastolic < 90 mm Hg

---

# Odds Ratios of Determinants of High Medication Adherence

<table>
<thead>
<tr>
<th>Determinant</th>
<th>Odds Ratio</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Knowledge</td>
<td>1.15</td>
<td>1.03 – 1.29*</td>
</tr>
<tr>
<td>Attitude</td>
<td>0.99</td>
<td>0.96 – 1.03</td>
</tr>
<tr>
<td>Satisfaction</td>
<td>1.07</td>
<td>1.02 – 1.11*</td>
</tr>
<tr>
<td>Social Support</td>
<td>1.06</td>
<td>1.02 – 1.37*</td>
</tr>
<tr>
<td>Coping</td>
<td>1.94</td>
<td>1.19 – 3.15*</td>
</tr>
<tr>
<td>Stress</td>
<td>0.91</td>
<td>0.86 – 0.98*</td>
</tr>
<tr>
<td>Medication Complexity</td>
<td>0.55</td>
<td>0.38 – 0.81*</td>
</tr>
</tbody>
</table>

*Significant at p < 0.05.
## Factors Involved in Non-Adherence

### GINA 2008

<table>
<thead>
<tr>
<th>Drug Factors</th>
<th>Non-Drug Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Difficulties with inhaler devices</td>
<td>- Misunderstanding or lack of instruction</td>
</tr>
<tr>
<td>- Awkward regimes (e.g., four times daily or multiple drugs)</td>
<td>- Fears about side-effects</td>
</tr>
<tr>
<td>- Side effects</td>
<td>- Dissatisfaction with health care professionals</td>
</tr>
<tr>
<td>- Cost of medication</td>
<td>- Unexpressed/undisclosed fears or concerns</td>
</tr>
<tr>
<td>- Dislike of medication</td>
<td>- Inappropriate expectations</td>
</tr>
<tr>
<td>- Distant pharmacies</td>
<td>- Poor supervision, training, or follow-up</td>
</tr>
<tr>
<td></td>
<td>- Anger about condition or its treatment</td>
</tr>
<tr>
<td></td>
<td>- Underestimation of severity</td>
</tr>
<tr>
<td></td>
<td>- Cultural issues</td>
</tr>
<tr>
<td></td>
<td>- Stigmatization</td>
</tr>
<tr>
<td></td>
<td>- Forgetfulness or complacency</td>
</tr>
<tr>
<td></td>
<td>- Attitudes toward ill health</td>
</tr>
<tr>
<td></td>
<td>- Religious issues</td>
</tr>
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*ASTHMA MANAGEMENT AND PREVENTION 53*
Complete Questionnaire

AsthmaPACT  www.AsthmaPACT.org

Hosted by Asthma and Allergy Foundation of America

No charge

Child and Adult

* Individuals identify areas of high-risk for non-adherence
* Survey provides written and video feedback about the significance of their selection
* Opportunity to identify how medication is actually taken versus prescribed
* Provides mechanism for preliminary validation of surveys
## Factors Involved in Non-Adherence
### Asthma PACT 2010

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*ASTHMA MANAGEMENT AND PREVENTION 53*
Complete Questionnaire

AsthmaPACT  www.AsthmaPACT.org

Preliminary Validation

Adult

Child
WAO Journal 2011:107:A41
J Allerg Clin Immunol 2012:129: A
SECTION 05 - Current Medication

Select all of the asthma medications that your doctor prescribed, how often you should take them and how often you actually take them. If less than 6 medications are used, leave the remaining fields blank.

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dosage</th>
<th>Prescribed Use</th>
<th>Actual Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alvesco (ciclesonide) 80mcg</td>
<td>1 inhalation</td>
<td>2/day</td>
<td>1/day</td>
</tr>
<tr>
<td>Please select</td>
<td>Please select</td>
<td>Please select</td>
<td>Please select</td>
</tr>
<tr>
<td>Please select</td>
<td>Please select</td>
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<td>Please select</td>
<td>Please select</td>
<td>Please select</td>
<td>Please select</td>
</tr>
</tbody>
</table>

Add a Row
SECTION 06 - Concerns About Medication/Treatment Regimen

Please answer the following questions in reference to Alvesco (ciclesonide) 80mcg.

01 I forget to take at least one dose per day
   ○ Never  ○ Sometimes  ○ Often

02 The medication I am taking doesn’t work
   ○ Never  ○ Sometimes  ○ Often

03 I don’t need this medicine
   ○ Never  ○ Sometimes  ○ Often

04 I do not like the taste of this medicine
   ○ Never  ○ Sometimes  ○ Often

05 I am concerned about medication side effects
   ○ Never  ○ Sometimes  ○ Often

06 I use this medication more than prescribed
   ○ Never  ○ Sometimes  ○ Often

07 I use this medication less than prescribed and I am fine
   ○ Never  ○ Sometimes  ○ Often

08 I use this medication less than prescribed and I am still sick
   ○ Never  ○ Sometimes  ○ Often

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Patient Questionnaire

Positive
- Inexpensive
- Easy to administer
- Accurate if NEGATIVE response

Negative
  False positive inaccuracy
Assessing Adherence

Indirect Methods

- Question the patient
- Evaluate patient diaries for completeness
- Ask patient to complete questionnaire
- Assess adherence based on response to treatment
- Conduct pill counts
- Use electronic monitors
- Determine prescriptions filled at pharmacy
Electronic Monitors

**What is the DOSER?**

**Product Description**
A Breakthrough for All Inhaler Users

**DOSER Features and Benefits Chart**

**DOSER’s Features**
- Displays the number of inhalations remaining in the inhaler. The “beep” alert informs user that fewer than 20 inhalations remain in the canister.
- Displays the number of inhalations taken during the current day.
- Stores up to 30 days usage history in a separate memory, which can be reviewed at any time, with the press of a button.

**DOSER’s Benefits**
- Those with respiratory conditions, and the parents of asthmatic children, can avoid being caught without medication.
- Enables easy monitoring for better self care. Minimizes following doctors’ instructions easier, especially for those on daily medication.
- Parents can better monitor children’s medication usage.
- Healthcare professionals are able to accurately monitor their patients’ compliance with preventative medication and the over/under use of rescue medication.

The DOSER works in conjunction with most Rx* inhalers (and may be transferred from inhaler to inhaler).

* Except Abruvent and Tilade.

[Top]
Smartinhaler
www.smartinhaler.com

SmartTrack
Price: US $195 per device (Higher Education Price*)
Source: SmartInhaler Live
MEASURE ADHERENCE

1) Diagnose Adherence Status
2) Strategy to Improve adherence - FEEDBACK
## Asthma Outcomes When Theophylline Monitoring Severe Asthmatic Children After Intensive Rehabilitation

<table>
<thead>
<tr>
<th></th>
<th>1 Year Prior Median (5-95 Pctl.) n=59</th>
<th>1 Year Post Median (5-95 Pctl.) n=59</th>
<th>2nd Year Post Median (5-95 Pctl.) n=59</th>
<th>3rd Year Post Median (5-95 Pctl.) n=57</th>
<th>4th Year Post Median (5-95 Pctl.) n=51</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total Cost (dollars)</strong></td>
<td>$10,240 (1,874-27,964)</td>
<td>$4,036 (1,696-13,450)</td>
<td>$2,801 (940-8,625)</td>
<td>$2,316 (450-8,425)</td>
<td>$1,936 (340-7,311)</td>
</tr>
<tr>
<td><strong>Inpatient Days</strong></td>
<td>7 (0-25)</td>
<td>0 (0-6)*</td>
<td>0 (0-4)*</td>
<td>0 (0-4)*</td>
<td>0 (0-4)*</td>
</tr>
<tr>
<td><strong>Emergency Care</strong></td>
<td>4 (1-11)*</td>
<td>0 (0-5)*</td>
<td>0 (0-5)**</td>
<td>0 (0-2)*</td>
<td>0 (0-2)*</td>
</tr>
<tr>
<td><strong>Corticosteroid Bursts</strong></td>
<td>2 (0-9)</td>
<td>2 (0-8)</td>
<td>1 (0-5)*</td>
<td>1 (0-4)*</td>
<td>1 (0-5)*</td>
</tr>
<tr>
<td><strong>Physician Visits</strong></td>
<td>2 (3-24)</td>
<td>2 (0-11)</td>
<td>1.5 (0-8)</td>
<td>2 (0-8)</td>
<td>2 (0-8)</td>
</tr>
</tbody>
</table>

*P<0.001 **P<0.01

beclomethasone Log Daily Dispenses for Patient Name

- Computed date range: 09/04/2005 to 10/05/2005
SpiroLog PEFR for Corn, D. (0101CC9261)
- Computed date range: 09/04/2005 to 10/03/2005
Electronic Monitor

Positive
- Records usage over extended time
- Accurate
- Identify patterns of use

Negative
- Cost
- Infers use
Assessing Adherence

Indirect Methods

- Question the patient
- Evaluate patient diaries for completeness
- Ask patient to complete questionnaire
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- Determine prescriptions filled at pharmacy

Cramer and Spiker Patient Compliance in Medical Practice NY Raven 1991
Adherence/Persistence

Adherence refers to how well a patient follows physician orders within a designated timeframe (number of days supplied/observable period PDC)

Persistence addresses how long a patient remains on therapy. Persistence introduces chronology into the assessment while adherence does not.
Definitions of Compliance and Persistence

Fig. 1: Definitions of Compliance and Persistence

Prescription Refill

Defining Adherence is related to the definition of persistence

Grace Period

30 day “retail prescription” Allows 60 days

90 day “mail away” prescription Allows 60 days

Shorter the grace period the greater chance for a decrease in persistence and adherence
Such data can form the basis for establishing more aggressive patient-education, compliance, and/or monitoring programs for specific patient populations. The data also can
Prescription Refill

Positive
Administrative pharmaceutical-claims data bases
- Inexpensive
- Unobtrusive
- Track chronic diseases

Negative
Infers ingestion