Adult asthma management: focus on control

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Objectives

- Apply NHLBI National Asthma Education and Prevention Program (NAEPP) guidelines
  - Impairment
  - Risk
- Routine assessment of control
  - Practical tools
Evolution of the Asthma Guidelines

• 1991
  – Treatment recommendations based on consensus
• 1997
  – Evidence based treatment recommendations
• 2002
  – Further clarification of treatment of children
• 2007
  – Emphasis on assessment of control

NHLBI NAEPP EPR-3 2007

• Control
  – Degree to which the manifestations of asthma are minimized and the goals of therapy are met
• Impairment
  – Frequency and intensity of symptoms
  – Functional limitations
• Risk
  – Likelihood of exacerbations or loss of pulmonary function

### NAEPP EPR-3 2007 Guidelines

- **Asthma severity**
  - Chronic status
  - Represents potential impairment & risk
- **Asthma control**
  - Volatile status
  - Represents a point in time where impairment & risk can be evaluated & measured

### Application of EPR-3 Guidelines

- **Initial visit**
  - Classify severity
  - Determine initial therapy or adjust accordingly
- **Follow-up visit**
  - Evaluate control
  - Adjust therapy based step-wise approach
**Case: 24 year AA female presents for asthma evaluation**

- Diagnosed in childhood
- 0 hospital stays since age 16, never intubated
- ED visit last month, no other exacerbations this year
- SOB with exertion, smoke, stress, sports
- Nocturnal symptoms 1-2/week
- SABA 10-12 puffs daily (sometimes prior to sports)
- Reports SOB, cough, occ. audible wheezing

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### Components of Severity

<table>
<thead>
<tr>
<th>Impairment</th>
<th>Classification of Asthma Severity (Youths ≥12 years of age and adults)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Intermittent</td>
</tr>
<tr>
<td>Symptoms</td>
<td></td>
</tr>
<tr>
<td></td>
<td>≤2 days/week</td>
</tr>
<tr>
<td>Nighttime awakenings</td>
<td>≤2/night</td>
</tr>
<tr>
<td>Short-acting beta-agonist use for symptom control (not prevention of EIB)</td>
<td>≥2 days/week</td>
</tr>
<tr>
<td>Interference with normal activity</td>
<td>None</td>
</tr>
<tr>
<td>Lung function</td>
<td>Normal FEV\textsubscript{1} between exacerbations</td>
</tr>
<tr>
<td></td>
<td>FEV\textsubscript{1}/FVC normal</td>
</tr>
</tbody>
</table>

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**Risk**

- Exacerbations requiring oral systemic corticosteroids
  - 0-1/year (see note)
  - ≥2/year (see note)

Consider severity and interval since last exacerbation. Frequency and severity may fluctuate over time for patients in any severity category. Relative annual risk of exacerbations may be related to FEV\textsubscript{1}.

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Case: 24 year AA female presents for asthma evaluation

- Hx of GERD, allergic rhinitis
- Montelukast in past, “unsure if helped”, non-adherent to Advair
- Exam with boggy nasal turbinates, clear lungs
- CXR normal
- Spirometry with mild obstruction, reversible with albuterol

What therapy would you prescribe?
### Stepwise Approach for Managing Asthma in Youths ≥12 Years of Age and Adults

#### Components of Severity

<table>
<thead>
<tr>
<th>Impairment</th>
<th>Classification of Asthma Severity ≥12 years of age</th>
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</thead>
<tbody>
<tr>
<td>Symptoms</td>
<td>Intermittent: ≤2 days/week</td>
</tr>
<tr>
<td>Nighttime awakenings</td>
<td>&gt;2x/month</td>
</tr>
<tr>
<td>Short-acting beta2-agonist use for symptom control (not prevention of EIB)</td>
<td>≤2 days/week</td>
</tr>
<tr>
<td>Interference with normal activity</td>
<td>None</td>
</tr>
<tr>
<td>Lung function</td>
<td>Normal FEV&lt;sub&gt;1&lt;/sub&gt; between exacerbations</td>
</tr>
<tr>
<td></td>
<td>FEV&lt;sub&gt;1&lt;/sub&gt;/FVC normal</td>
</tr>
</tbody>
</table>

#### Risk

<table>
<thead>
<tr>
<th>Exacerbations (consider frequency and severity)</th>
<th>0–2/year</th>
<th>&gt;2/year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency and severity for patients in a severity category</td>
<td>may fluctuate over time</td>
<td>Relatively high risk of exacerbations may be related to FEV&lt;sub&gt;1&lt;/sub&gt;</td>
</tr>
</tbody>
</table>

#### Recommended Step for Initiating Treatment

(See figure 4-5 for treatment steps)

- **Step 1**
  - Preferred: Low-dose ICS
  - Alternative: Cromolyn, nedocromil, LTRA, or theophylline

- **Step 2**
  - Preferred: Low-dose ICS + LABA
  - OR
    - Medium-dose ICS

- **Step 3**
  - Preferred: Medium-dose ICS + LABA
  - OR
    - Alternative: Medium-dose ICS + either LTRA, theophylline, or zileuton

- **Step 4**
  - Preferred: Medium-dose ICS + LABA
  - AND
  - Consider omalizumab for patients who have allergies

- **Step 5**
  - Preferred: High-dose ICS + LABA + oral corticosteroid
  - AND
  - Consider omalizumab for patients who have allergies

Benefits of Inhaled Corticosteroids

- Most effective long-term controller for persistent asthma
- Improve pulmonary function
- Reduce symptom severity, rescue inhaler use, and need for oral corticosteroids
- Reduce number of exacerbations, ED visits, and hospitalizations
- May prevent airway remodeling

Take home points about LABAs

- Black box warning for LABAs
- Should NOT be used as monotherapy for asthma
- No current data supporting increased risk of adverse asthma related events if used in combination with ICS

Chowdhury at al. NEJM 2011;364:2473-2475.
Leukotriene Modifiers

- Work better than placebo
- Do NOT work as well as ICS
- Do NOT work as well as long acting beta agonists in combination with ICS


Case follow-up

- Prescribed medium dose inhaled fluticasone with spacer
- Returns 6 weeks later
-Feels asthma is “better but not great”
- Back to running & aerobics but still using SABA albuterol 4-6 puffs max/day
- Nocturnal awakenings 2-3 times/month
Case follow-up

- Allergies and post-nasal drip improved with season change
- Exam normal

Is this patient’s asthma controlled?
How Should Control Be Measured in Asthma?

- Utilization of Healthcare Resources
- Functional Status
- Daytime Symptoms
- Inflammation
  - Direct or Indirect
- Lung Function
- Missed Work and/or School
- Patient Self-Report of Control
- Nighttime Awakenings
- Use of a “Quick Relief” Inhaler and/or Nebulizer

Asthma Control


Patients Are Poor at Assessing Their Asthma Control

Patient assessment of control*

<table>
<thead>
<tr>
<th>Patients (%)</th>
<th>Europe</th>
<th>USA</th>
<th>Asia Pacific</th>
</tr>
</thead>
<tbody>
<tr>
<td>Well</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complete</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Patients with severe persistent symptoms – past 4 wk: Sx ≥ 3x/day in the daytime; Most nights/every night.


www.asthmainamerica.com

Asthma Severity: Patient Perception

NAEPP Guidelines

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Severe</th>
<th>Moderate</th>
<th>Mild</th>
<th>Intermittent</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>4.8%</td>
<td>10.4%</td>
<td>13.1%</td>
<td>48.6%</td>
</tr>
<tr>
<td>Mild</td>
<td>31.9%</td>
<td>47.2%</td>
<td>60.1%</td>
<td>42.3%</td>
</tr>
<tr>
<td>Moderate</td>
<td>41.3%</td>
<td>36.3%</td>
<td>22.1%</td>
<td>8.1%</td>
</tr>
<tr>
<td>Severe</td>
<td>21.9%</td>
<td>5.8%</td>
<td>4.5%</td>
<td>0.8%</td>
</tr>
</tbody>
</table>

Asthma in America, 2001

Asthma Symptoms Correlate Poorly With FEV\textsubscript{1}

Monitoring Asthma Control: Asthma Control Test™

1. In the past 4 weeks, how much of the time did your asthma keep you from getting as much done at work, school or at home?  
   - All of the time  
   - Most of the time  
   - Some of the time  
   - A little of the time  
   - None of the time  

2. During the past 4 weeks, how often have you had shortness of breath?  
   - More than once a day  
   - Once a day  
   - 2 to 6 times a week  
   - 2 times a week  
   - Not at all  

3. During the past 4 weeks, how often did your asthma symptoms (wheezing, coughing, shortness of breath, chest tightness or pain) wake you up at night or earlier than usual in the morning?  
   - 4 or more nights a week  
   - 3 or 3 nights a week  
   - Once a week  
   - Once or twice  
   - Not at all  

4. During the past 4 weeks, how often have you used your rescue inhaler or nebulizer medication (such as albuterol)?  
   - 3 or more times per day  
   - 2 or 3 times per week  
   - 1 or 2 times per day  
   - Once or twice a week  
   - Not at all  

5. How would you rate your asthma control during the past 4 weeks?  
   - Not controlled at all  
   - Poorly controlled  
   - Somewhat controlled  
   - Well controlled  
   - Completely controlled  

Level of Control Based on Composite Score  
20-25 = Controlled  
14-19 = Suboptimal  
<14 = Poorly Controlled  

Regardless of patient's self assessment of control in Question 5


Asthma Therapy Assessment Questionnaire (ATAQ)

1. In the past 4 weeks did you miss any work, school, or normal activities due to your asthma? (1 point for yes)
2. In the past 4 weeks, did you wake up at night because of your asthma? (1 point for yes)
3. Do you believe your asthma was well controlled in the past 4 weeks? (1 point for no)
4. Do you use an inhaler for quick relief of asthma symptoms? If yes, in the past 4 weeks, what was the highest number of puffs you used in one day? (1 point for >12)

Level of Control Based on Composite Score  
1-2 = not well controlled, 3-4 = very poorly controlled

Simple Rules of Thumb

• Rules of Two®
  – one should be on maintenance asthma therapy if any of the following apply:
    • rescue inhaler use more than TWICE a week
    • nighttime symptoms more than TWICE a month
    • refill of rescue inhaler prescription TWICE a year

© Baylor Health System

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**Classification of Asthma Control (Youths ≥12 years of age and adults)**

<table>
<thead>
<tr>
<th>Components of Control</th>
<th>Well-CONTROLLED</th>
<th>Not Well-CONTROLLED</th>
<th>Very Poorly CONTROLLED</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Symptoms</strong></td>
<td>≤2 days/week</td>
<td>&gt;2 days/week</td>
<td>Throughout the day</td>
</tr>
<tr>
<td><strong>Nighttime awakening</strong></td>
<td>≤2x/month</td>
<td>1–3x/week</td>
<td>≥4x/week</td>
</tr>
<tr>
<td><strong>Interference with normal activity</strong></td>
<td>None</td>
<td>Some Limitation</td>
<td>Extremely Limited</td>
</tr>
<tr>
<td><strong>Short-acting beta-agonist use for symptoms control (not prevention of EIB)</strong></td>
<td>≤2 days/week</td>
<td>&gt;2 days/week</td>
<td>Several times per day</td>
</tr>
<tr>
<td><strong>FEV1, or peak flow</strong></td>
<td>&gt;80% predicted/ personal best</td>
<td>60–80% predicted/ personal best</td>
<td>&lt;60% predicted/ personal best</td>
</tr>
<tr>
<td><strong>Impairment</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Validated Questionnaires</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ATAQ</td>
<td>0</td>
<td>1–2</td>
<td>3–4</td>
</tr>
<tr>
<td>ACQ</td>
<td>≤0.75*</td>
<td>≥1.5</td>
<td>N/A</td>
</tr>
<tr>
<td>ACT</td>
<td>≥20</td>
<td>15–19</td>
<td>≤15</td>
</tr>
<tr>
<td><strong>Exacerbations</strong></td>
<td>0–1/year</td>
<td>≥2/year (see note)</td>
<td></td>
</tr>
<tr>
<td><strong>Risk</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Progressive loss of lung function</strong></td>
<td>Evaluation requires long-term followup care</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Treatment-related adverse effects</strong></td>
<td>Medication side effects can vary in intensity from none to very troublesome and worrisome. The level of intensity does not correlate to specific levels of control but should be considered in the overall assessment of risk.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Case follow-up

- Prescribed medium dose inhaled fluticasone with spacer
- Returns 6 weeks later
- Feels asthma is “better but not great”
- Back to running & aerobics still with albuterol 4-6 puffs max/day
- Nocturnal awakenings 2-3 times/month

ATAQ Questionnaire for case

1. In the past 4 weeks did you miss any work, school, or normal activities due to your asthma? (0 points)
2. In the past 4 weeks, did you wake up at night because of your asthma? (1 point)
3. Do you believe your asthma was well controlled in the past 4 weeks? (1 point)
4. Do you use an inhaler for quick relief of asthma symptoms? If yes, in the past 4 weeks, what was the highest number of puffs you used in one day? (0 points)

ATAQ 2/4 not well controlled

Level of Control Based on Composite Score
1-2 = not well controlled, 3-4 = very poorly controlled

What would you do next for this patient?

Stepwise Approach for Managing Asthma in Youths ≥12 Years of Age and Adults

<table>
<thead>
<tr>
<th>Step 1</th>
<th>Preferred: SABA PRN</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Intermittent</td>
</tr>
<tr>
<td></td>
<td>Persistent</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Step 2</th>
<th>Preferred: Low-dose ICS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Alternative: Cromolyn, nedocromil, LTRA, or theophylline</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Step 3</th>
<th>Preferred: Low-dose ICS + LABA</th>
</tr>
</thead>
<tbody>
<tr>
<td>OR</td>
<td>Medium-dose ICS</td>
</tr>
<tr>
<td>Alternative: Low-dose ICS + either LTRA, theophylline, or zileuton</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Step 4</th>
<th>Preferred: Medium-dose ICS + LABA</th>
</tr>
</thead>
<tbody>
<tr>
<td>OR</td>
<td>Alternative: Medium-dose ICS + either LTRA, theophylline, or zileuton</td>
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</tbody>
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<table>
<thead>
<tr>
<th>Step 5</th>
<th>Preferred: High-dose ICS + LABA</th>
</tr>
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<tbody>
<tr>
<td>AND</td>
<td>Consider omalizumab for patients who have allergies</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Step 6</th>
<th>Preferred: High-dose ICS + LABA + oral corticosteroid</th>
</tr>
</thead>
<tbody>
<tr>
<td>AND</td>
<td>Consider omalizumab for patients who have allergies</td>
</tr>
</tbody>
</table>

ICS vs ICS + LABA

• “Studies of adults in whom the dose of ICS was at least doubled demonstrate some improvements in lung function...although these results are generally less effective than adding a LABA (Ind et al. 2003).”

Continuous Monitoring and Reevaluation Is Essential to Achieve Control

Presentation With Asthma

Assess Asthma Control
• Symptoms
• Activity
• Patient assessment
• PFTs
• Exacerbations

Periodic Assessment of Asthma
• Adherence
• Action plan
• Comorbidities
• ? Correct diagnosis

Asthma Well Controlled

Yes

Maintain or Step Down Therapy

No

• Assessment
• Optimize therapy

Adapted with permission from Li JT et al. J Allergy Clin Immunol. 2005;116(suppl):S5-S11.)
## Conclusions

- Characterization of impairment & risk
  - Severity
  - Control
- Assessment of risk
  - Continuous & routine
  - Multiple methods

## Asthma: Pediatric Nuances and Call to Action (Plans)

Elizabeth D. Allen, MD  
Pediatric Pulmonary Medicine  
Nationwide Children’s Hospital
Case #1 – Inhaler Failure

- 12 yo with on low dose ICS therapy for asthma
- Presents for sore throat
- Asthma Control Test score is only 15 (<20 suggests poor control)

Case #1: More Detail

- You started this 12 yo on low dose ICS 6 months ago
- He stopped having bad attacks, so family hasn’t followed up
- But he’s still having day to day symptoms
- Parent report (and pharmacy fill check) suggest good compliance, and they swear they use a spacer
### Why Do Asthma Therapies Fail?

- Compliance issues
- Ongoing “trigger” exposures
- Co-morbidities
- Wrong diagnosis
- Inadequate medication issues

### Ongoing “Trigger” Issues

- Second hand (or first hand) smoke
- Allergens
  - Pets
  - Indoor mold/dust
  - Outdoor allergens
- General airway irritants
  - Perfumes, candles, cleaning agents . . .
Co-Morbidities

- Chronic sinus disease
- Obesity
- Gastroesophageal reflux
- Vocal Cord Dysfunction
- Obstructive Sleep Apnea (?)

Case #2: Further History

- No smokers, no pets
- No nasal drainage
- No heartburn or other GER like symptoms
- No snoring
- Not obese
Case #1: Not Asthma?

- Still reports typical symptoms
- When he takes his albuterol, it helps
- Otherwise healthy
- Exam is normal
- Spirometry?

Pulmonary Function Tests and Kids

- Obtaining quality spirometry tests prior to age 6 yrs is challenging!
- Most asthmatics develop symptoms prior to age 5 yrs
- "Well" asthmatics often have normal spirometry
- Minimally symptomatic patients may have very abnormal spirometry!
**Case #1: Spirometry**

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<table>
<thead>
<tr>
<th></th>
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<tbody>
<tr>
<td>FVC</td>
<td>82% pred</td>
<td></td>
</tr>
<tr>
<td>FEV1</td>
<td>69% pred</td>
<td></td>
</tr>
<tr>
<td>FEV1/FVC</td>
<td>75.7 %</td>
<td></td>
</tr>
<tr>
<td>FEF25-75</td>
<td>43 % pred</td>
<td></td>
</tr>
</tbody>
</table>

Change post albuterol
- FEV1 - 19% increase
- FEF 25-75 - 53% increase

Moderate Obstruction with (+) bronchodilator response

**Case #1: What Next?**

- Child’s asthma is not controlled on current therapy (low dose ICS)
- Compliance & inhaler technique appear good
- Nothing to suggest ongoing major trigger or co-morbidity
- Symptom description and PFT’s confirm asthma IS the problem
- Time to Step Up Therapy
Options for Stepping Up Therapy

- Double ICS
- Add Montelukast
- Add LABA

Step-Up Therapy for Children . . .

- N=182, 6-17 yo’ s, uncontrolled on 100 µg BID fluticasone
- Triple cross-over between:
  - 250 µg fluticasone BID
  - 100 µg fluticasone BID & leukotriene
  - 100 µg fluticasone & 50 µg LABA BID
- Based on exacerbation & control score & FEV$_1$:
  - Added LABA most likely to produce best response
  - Some children, however, responded best to moderate dose ICS, or to ICS & leukotriene

### The LABA Controversy

- LABA’s used alone are a bad idea
- Used as intended (combined with ICS) there’s been no clear signal of trouble
- Decision to use should factor in:
  - Higher ICS doses increase risk of side effects
  - Leukotrienes can (uncommonly) have behavioral side effects
  - Most LABA combinations are only FDA approval for $\geq$ 12 year olds

### ICS Side Effects - Kids

- Mild side effects – low-medium dose
  - Thrush
  - Growth velocity decrease
    - Related to dose/weight
    - CAMP study found 400 mcg budesonide/day led to mean 1.2 cm decrease in adult height *
    - Effect occurred within first 2 years; not cumulative
- Serious side effects - rare, high doses
  - Adrenal suppression

*NEJM 2000;343:1054-1063*
Balancing Medication Risk and Asthma Risk

Balancing Medication Risk and Asthma Risk
Stepping Up Therapy Recs

- In the pre-school set, first step-ups usually involve ↑ ICS dosing, or adding a leukotriene
- Consider LABA’s as a first step up if:
  - Older child
  - Frequent low grade symptoms
  - Exercise intolerance
- Regardless, follow-up (6-8 weeks) needed to make sure change worked

NHLBI 2007 EPR-3 Asthma Guidelines

Case #1: Conclusions

- Asthma therapy can fail for a variety of reasons
- Spirometry can sometimes uncover severity of asthma that is not suspected from history
- Stepping up from low dose ICS therapy can be done in a variety of ways: different approaches work better for different kids
- Recheck progress!
Case #2: Ambulance Again

- 6 yo with h/o asthma for 3 years, 2 previous hospital stays, multiple ED visits
- Presented in severe distress, $O_2$ sat 85%

Case #2: More Story

- Mom reports
  - Runny nose began 3 days ago
  - Frequent coughing began 2 days ago
  - Last night wheezing started - albuterol nebs begun
  - This morning 3 back-to-backs didn’t help . . .
  - Mom called 911!
- Now improving with aggressive inpatient therapy
How does this scenario compare to what you want your parents/patients to do in response to an asthma event?

Asthma Mortality & Morbidity

- Of 298 children admitted to PICU for status asthmaticus at Connecticut Children’s Medical Center, 55% were classified pre admission as “mild asthma”
- Of 20 children who died of asthma in UK Eastern Region between 2001-2006, 9 had “mild to moderate” asthma

* J Asthma 2008: 45(6);513-7
** Prim Care Respir J 2012; 21(1);71-7
**Written Asthma Action Plans**

- Reduce acute asthma visits & hospitalizations
- Work well based on symptoms alone (for kids); can also include peak flow readings
- List control medication
- Advise SABA therapy for asthma symptoms
- *Indicate steps to take if albuterol isn’t working*
- Need to be reviewed regularly!

**Acute Asthma: What Parents Should Know**

- During acute flares, 3 things happen:
  - Smooth muscle constriction
  - Airway swelling
  - Mucus overproduction/plugging
- Albuterol ONLY helps the first issue!
- If albuterol is failing, oral steroids – quickly – are the next step in treatment
- Viral infection (esp. rhinovirus!) is the most common cause of severe asthma attacks
Acute Asthma: Reminders for Providers

- Home supply of oral steroids can be an important tool for educated patients
- Not helpful:
  - Antihistamines
  - Cough medications
  - Antibiotics (unless a bacterial infection is trigger)
  - Doubling ICS therapy

Case #2: Conclusions

- Good asthma care includes educating patients and families of even mild asthmatics about how to respond to acute flares
- Written plans help – and are standard of care
- Instruction regarding next steps if albuterol isn’t working – especially during colds! – particularly important
### AAP’s on the Web

- [https://www.aaaai.org/Aaaai/media/MediaLibrary/PDF%20Documents/Libraries/NEW-WEBSITE-LOGO-asthma-action-plan_HI.pdf](https://www.aaaai.org/Aaaai/media/MediaLibrary/PDF%20Documents/Libraries/NEW-WEBSITE-LOGO-asthma-action-plan_HI.pdf)