Update for 2015:
Asthma in Adults

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Instructor in Medicine, Harvard Medical School
Disclosures

• I have no disclosures.
Objectives

- Understand the importance of Pulmonary Function Testing in the diagnosis of asthma in adults
- Learn about new therapies for asthma
- Discuss how to formulate an asthma action plan
Is this asthma?

- 27 year old man presents with CC of “problems breathing.”

- He started having problems with his breathing only a few months ago. He is currently smoking about a pack of cigarettes a day. He started smoking about two years ago while in rehab for substance abuse.

- He has a chronic cough, productive of green/brown phlegm. He does notice some wheezing. No chest pain, fever, leg edema. CXR is “normal”.
Is this asthma continued…

• PMFSHx: ADHD, Depression. No history of asthma. No family history of asthma/allergies. Works in construction.

• Meds: Advair 500/50 bid, albuterol 4x/day prn, cymbalta, Vyvanse

• Exam: Normal oxygen saturation, diffuse expiratory wheezes with a prolonged expiratory phase, no evidence of pneumonia or CHF. No rashes or evidence of arthritis.

• No labs available today

• You have ordered PFTs, but they have to be done at the hospital downtown. There has been “a lot” of snow, and the earliest he can go there is in two weeks.
Is this asthma continued…

• Questions:
  - Does he have asthma? COPD? Another disease?
  - Is this an exacerbation?
  - How would you classify the severity of disease?
Adult Asthma

• 75% of patients with asthma are diagnosed before the age of 7

• Many adolescents experience a remission of asthma, but may have recurrence later in life

• Asthma may develop at any age, and 6-7% of all adults have asthma
Child and Adult Asthma Prevalence
United States, 1980-2007

Source: National Health Interview Survey; CDC National Center for Health Statistics
Definition of asthma

- Asthma is a chronic inflammatory disease of the airways.

- Diagnosis is based on:
  - Symptoms: dyspnea, cough, wheeze, chest tightness
  - Exam: Musical polyphonic wheezing when symptoms are present
  - Demonstration of variable airflow obstruction
    - Spirometry
    - Peak Expiratory Flow (PEF) over time (Note: decrease in PEF may not be caused by obstruction and should be confirmed with office spirometry when possible)

- Exclusion of alternative disorders
Inflammation and bronchoconstriction of Asthma
Is this asthma?
27 yo smoker with shortness of breath

Smokes

Pack years: 1.00

Quit Time:
BIDMC Interpretation of PFTs

- Use of FEV1/VC below your PFT lab definition of normal to define the presence of obstruction
  - Depends on age (0.7 is normal for older adults, 0.85 is normal for 20 year olds).
  - BIDMC: 95% of predicted FEV1/FVC based on age, gender, height and ethnicity
  - Other labs use “95th percentile” as the LLN

- Severity based on FEV1 values (ATS Criteria for classification):
  - Mild: >70%
  - Moderate: 60-69%
  - Moderately-severe: 50-59%
  - Severe: 35-49%
  - Very Severe: <35%
What about reversibility?

• Bronchoprovocation testing
  - Methacholine/Mannitol
  - Exercise

• Bronchodilator response

• Lung function over time
  - PEF
  - Improved spirometry with improved control
PEF Over Time: Pros and Cons

- PEF *may* be helpful to diagnose asthma
  - Highly dependent on technique
  - Useful when office spirometry is normal and patients are not symptomatic at the time of evaluation
  - Useful for occupational asthma
  - Useful for patients who are not able to tell when their asthma is not well controlled
On to management

EPR-3 (The Expert Panel Report 3, Guidelines for the Diagnosis and Management of Asthma):

- Is a comprehensive set of consensus guidelines for asthma diagnosis and management best available scientific knowledge to clinical practice

- Goals:
  - Assess disease severity
    - Intensity of exacerbations (e.g. “Zero to 60” or gradual onset of symptoms)
  - Decrease risk (future exacerbations, loss of lung function, side effects of medications)
  - Assess impairment (lung function, symptoms, reliever use)
  - Assess control (minimize symptoms, medications, and health care resources)
# Asthma severity “in a nutshell”

<table>
<thead>
<tr>
<th>Age 0-4</th>
<th>Age 5-11</th>
<th>Age 12 and older</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Components of Severity</strong></td>
<td><strong>Classification of Asthma Severity ≥ 12 years of age</strong>&lt;br&gt;(Not currently taking long-term control medication)</td>
<td></td>
</tr>
<tr>
<td><strong>Impairment</strong></td>
<td><strong>Intermittent</strong></td>
<td><strong>Mild</strong></td>
</tr>
<tr>
<td>Symptoms</td>
<td>≤2 days/week</td>
<td>&gt;2 days/week but not daily</td>
</tr>
<tr>
<td>Nighttime awakenings</td>
<td>≤2x/month</td>
<td>3-4x/month</td>
</tr>
<tr>
<td>Short-acting beta2-agonist use for symptom control (not prevention of EIB)</td>
<td>≤2 days/week</td>
<td>&gt;2 days/week but not daily, and not &gt;1x/on any day</td>
</tr>
<tr>
<td>Interference with normal activity</td>
<td>None</td>
<td>Minor limitation</td>
</tr>
<tr>
<td>Lung function</td>
<td>Normal FEV1 between exacerbations</td>
<td>FEV1&gt;80% predicted</td>
</tr>
<tr>
<td><strong>Risk</strong></td>
<td><strong>Exacerbations requiring oral systemic corticosteroids</strong></td>
<td>0-1/year (see note)</td>
</tr>
<tr>
<td></td>
<td>Consider severity and interval since last exacerbation. Frequency and severity may fluctuate over time for patients in any severity category.</td>
<td></td>
</tr>
<tr>
<td><strong>Recommended Step for Initiating Therapy</strong>&lt;br&gt;(See figure 4-1b for treatment steps.)</td>
<td><strong>Step 1</strong></td>
<td><strong>Step 2</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td>and consider short course of oral systemic corticosteroids</td>
</tr>
</tbody>
</table>

**Key:** FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity; ICU, intensive care unit.

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**Notes**
Take the ACT!  
(Asthma Control Test)

It’s simple, easy to use, and all you need to know!

- 5 simple questions in under 2 minutes (goal ≥ 20/25 points)
- “In the last four weeks, on average…”
  1. How many **nights** have you had asthma symptoms
  2. How many times a week have you used your **rescue meds**
  3. How many times a week have you felt **short of breath**
  4. How much has your asthma affected **work/school/etc**.
  5. Control: **Completely**…Well…Somewhat…Poor…Not at all

- Answers other than **“Never”** or **“Completely”** get one or more points.
- Five or more points: consider step up therapy
- Five or fewer points: consider step down therapy
# Asthma severity “in a nutshell”

## Components of Severity

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<thead>
<tr>
<th>Age 0-4</th>
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<th>Age 12 and older</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Impairment</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nighttime awakenings</td>
<td>≤2/night</td>
<td>≥3-4/night</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Interference with normal activity</strong></td>
<td>None</td>
<td>Minor limitation</td>
</tr>
<tr>
<td>Lung function</td>
<td>Normal FEV₁ between exacerbations, FEV₁ &gt;80% predicted, FEV₁/FVC normal</td>
<td>FEV₁ &gt;60% but ≤80% predicted, FEV₁/FVC reduced 5%</td>
</tr>
</tbody>
</table>

## Classification of Asthma Severity ≥ 12 years of age

<table>
<thead>
<tr>
<th></th>
<th>Intermittent</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Risk</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exacerbations requiring oral systemic corticosteroids</td>
<td>0-1/year (see note)</td>
<td>≥2/year (see note)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Consider severity and interval since last exacerbation. Frequency and severity may fluctuate over time for patients in any severity category.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Relative annual risk of exacerbations may be related to FEV₁</td>
<td></td>
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<td></td>
<td></td>
</tr>
</tbody>
</table>

## Recommended Step for Initiating Therapy

(See figure 4-1b for treatment steps.)

- **Step 1**: Evaluate level of asthma control that is achieved and adjust therapy accordingly.
- **Step 2**: And consider short course of oral systemic corticosteroids.

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**Key**: FEV₁, forced expiratory volume in 1 second; FVC, forced vital capacity; ICU, intensive care unit.
Stepwise Approach for Managing Asthma (Youths ≥12 years of age)

**Intermittent Asthma**
Consult with asthma specialist if step 4 care or higher is required. Consider consultation at step 3.

**Step 1**
Preferred: SABA PRN
Alternative: Cromolyn, LTRA, Nedocromil, or Theophylline

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

**Step 3**
Preferred: High-dose ICS + LABA
Alternative: Medium-dose ICS + either LTRA, Theophylline, or Zileuton

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

**Step 5**
Preferred: Oral systemic corticosteroid AND
Consider Omalizumab for patients who have allergies

**Step 6**
Prefered: High-dose ICS + LABA + oral systemic corticosteroid AND
Step up if needed
(first, check adherence, environmental control, and comorbid conditions)

Assess Control
Step down if possible
(and asthma is well controlled at least 3 months)

Each step: Patient education, environmental control, and management of comorbidities.
Steps 2-4: consider subcutaneous allergen immunotherapy for patients who have allergic asthma (see notes).

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 oral systemic corticosteroids may be needed.
- Use of SABA or use >2 days a week for symptom relief (not prevention if EIB) generally indicates inadequate control and the need to step up treatment.

Key: Alphabetical order is used when more than one treatment option is listed within either preferred or alternative therapy. EIB, exercise-induced bronchospasm; ICS, inhaled corticosteroid; LABA, inhaled long-acting beta2-agonist; LTRA, leukotriene

**Notes**
Figure 1. Stepped-Care Approach to Asthma Treatment.
Goal of Therapy – Asthma Control

Reduce Impairment:

• Prevent chronic and troublesome symptoms
• Require infrequent use (≤2 days per week) of inhaled SABA for quick relief of symptoms (not including prevention of exercise-induced bronchospasm (EIB))
• Maintain (near) normal pulmonary function
• Maintain normal activity levels (exercise and attendance at work or school)
• Patient satisfaction
<table>
<thead>
<tr>
<th>Age 0-4</th>
<th>Age 5-11</th>
<th>Age 12 and older</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Components of Control</strong></td>
<td><strong>Classification of Asthma Control (≥ 12 years of age)</strong></td>
<td></td>
</tr>
<tr>
<td>Symptoms</td>
<td>Well Controlled</td>
<td>Not Well Controlled</td>
</tr>
<tr>
<td>≤2 days/week</td>
<td>&gt;2 days/week</td>
<td>Throughout the day</td>
</tr>
<tr>
<td>Nighttime awakenings</td>
<td>≤2×/month</td>
<td>1-3×/week</td>
</tr>
<tr>
<td>Interference with normal activity</td>
<td>None</td>
<td>Some limitation</td>
</tr>
<tr>
<td>Short-acting beta2-agonist use for symptom control (not prevention of EIB)</td>
<td>≤2 days/week</td>
<td>&gt;2 days/week</td>
</tr>
<tr>
<td><strong>Impairment</strong></td>
<td><strong>Exacerbations</strong></td>
<td><strong>Risk</strong></td>
</tr>
<tr>
<td>FEV1 or peak flow</td>
<td>0-80% predicted/ personal best</td>
<td>60-80% predicted/ personal best</td>
</tr>
<tr>
<td>Validated Questionnaires</td>
<td>ATAQ</td>
<td>ACQ</td>
</tr>
<tr>
<td>0</td>
<td>≤0.75*</td>
<td>≥20</td>
</tr>
<tr>
<td>0-1/year</td>
<td>≥2/year (see note)</td>
<td>Consider severity and interval since last exacerbation.</td>
</tr>
<tr>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Progressive loss of lung function</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment-related adverse effects</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| | | | - Maintain current step 
| | | | - Regular followup every 1-6 months to maintain control. 
| | | | - Consider step down if well controlled for at least 3 months |
| | | | - Step up 1 step and 
| | | | - Reevaluate in 2-6 weeks. 
| | | | - For side effects: consider alternative treatment options. |
| | | | - Consider short course of oral systemic corticosteroids. 
| | | | - Step up 1-2 steps, and 
| | | | - Reevaluate in 2 weeks. 
| | | | - For side effects, consider alternative treatment options. |

*ACQ values of 0.76-1.4 are indeterminate regarding well-controlled asthma. 
**Key:** EIB, exercise-induced bronchospasm; FEV1, forced expiratory volume in 1 second. See notes for full name and sources of ATAQ, ACQ, ACT.
Back to our case

• 27 year old man with severe obstruction

• He is still smoking

• His PFTs have not improved after prednisone, antibiotics and adding LTM/LAMA

• Still not sure if he has asthma or another diagnosis
“The Zebras”

Differential of Severe Persistent Asthma

- Vasculitis/Churg Strauss:
- ABPA
- Cystic Fibrosis
- Bronchiectasis
- COPD
- Vocal Cord Dysfunction
- CHF
- Tracheobronchomalacia
Are we missing something?

**Figure 4-5. Stepwise Approach for Managing Asthma in Youths ≥12 Years of Age and Adults**

**Persistent Asthma: Daily Medication**
Consult with asthma specialist if step 4 care or higher is required.
Consider consultation at step 3.

**Step 1**
**Preferred:** Low-dose ICS
**Alternative:** Cromolyn, LTRA, Nedocromil, or Theophylline

**Step 2**
**Preferred:** Medium-dose ICS + LABA
**Alternative:** Medium-dose ICS + either LTRA, Theophylline, or Zileuton

**Step 3**
**Preferred:** High-dose ICS + LABA
**AND**
Consider Omalizumab for patients who have allergies

**Step 4**
**Preferred:** Medium-dose ICS + either LTRA, Theophylline, or Zileuton

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

**Step 6**
**Preferred:** Step up if control is not reached (first, check adherence, environmental control, and comorbid conditions)
**Assess Control**
Step down if possible (and asthma is well controlled at least 3 months)

Each step: Patient education, environmental control, and management of comorbidities.
Steps 2-4: Consider subcutaneous allergen immunotherapy for patients who have allergic asthma (see notes).

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 oral systemic 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.

From: NHLBI EPR3 Guidelines on Asthma, 2007
Treating Smokers in the Health Care Setting

Michael C. Fiore, M.D., M.P.H., M.B.A., and Timothy B. Baker, Ph.D.
Smoking Cessation (at every visit)

US Public Health Service 5 step program

1. ASK
2. ADVISE
3. ASSESS
4. ASSIST
5. ARRANGE

JAMA 2000; 28:3244-54
NEJM 2011;365:1222-31
Fiore M, et al. NEJM 2011

- For patients who are not ready to quit...

- **Motivational Interviewing** to discuss the “5 R’s”
  - personally **relevant** reasons to quit
  - **risks** associated with continued smoking
  - **rewards** for quitting
  - **roadblocks** to successful quitting
  - **repetition** of the counseling at subsequent clinic visits
Electronic cigarettes?

“freedom to have a cigarette without the guilt.”
— Jenny McCarthy

Find a blu Retailer Near you!

Check out Stephen Dorff in “Chase It”

Beth Israel Deaconess
CARE ORGANIZATION LLC
How much SABA is “too much?”

- Use greater than 2 days per week
- Use of more than one canister per month: marker for increased risk of exacerbation

***Step up to controller medications if your patient is taking “too much” albuterol***
Is it a “rescue” inhaler or just a way to improve/monitor asthma control?
Controller Medication: First Choice

- Inhaled steroids are (almost) always the answer
Inhaled Steroids Work.

**Figure 1.** Fitted Rate Ratio for Death from Asthma as a Function of the Number of Canisters of Inhaled Corticosteroids Used during the Year before the Index Date.

The index date for case patients and matched controls was the date of each case patient’s death from asthma. The rate ratio is adjusted for the age and sex of the patient; the number of prescriptions for theophylline, nebulized and oral β-adrenergic agonists, and oral corticosteroids in the year before the index date; the number of canisters of inhaled β-adrenergic agonists dispensed in the year before the index date; and the number of hospitalizations for asthma during the two years before the index date.

From: Suissa et al, NEJM, 2000
Inhaled Steroids Work.

From: Donahue et al, JAMA, 1997
Inhaled Steroids: Which one and how much?
<table>
<thead>
<tr>
<th>Drug</th>
<th>Brand Name</th>
<th>Formulation</th>
<th>Dose per Inhalation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beclomethasone</td>
<td>Qvar (Teva)</td>
<td>MDI–HFA</td>
<td>40 or 80</td>
</tr>
<tr>
<td>Budesonide</td>
<td>Pulmicort</td>
<td>DPI or suspension for nebulization</td>
<td>DPI: 90 or 180; suspension for nebulization: 250 or 500</td>
</tr>
<tr>
<td>Ciclesonide</td>
<td>Alvesco (Sepracor)</td>
<td>MDI–HFA</td>
<td>80 or 160</td>
</tr>
<tr>
<td>Flunisolide</td>
<td>Aerobid (Forest Laboratories)</td>
<td>MDI–CFC</td>
<td>250</td>
</tr>
<tr>
<td>Fluticasone</td>
<td>Flovent (GlaxoSmithKline)</td>
<td>MDI–HFA or DPI</td>
<td>MDI–HFA: 44, 110, or 220; DPI: 50 or 100</td>
</tr>
<tr>
<td>Mometasone</td>
<td>Asmanex (Schering-Plough)</td>
<td>DPI</td>
<td>110 or 220</td>
</tr>
<tr>
<td>Triamcinolone</td>
<td>Azmacort (Abbott)</td>
<td>MDI–CFC</td>
<td>75</td>
</tr>
</tbody>
</table>

From: Fanta, NEJM, 2009
Figure 1. Stepped-Care Approach to Asthma Treatment.

- **SABA, as needed**
- Inhaled steroid (or LTRA)
- Inhaled steroid + LABA (or inhaled steroid + LTM)
- Inhaled steroid + LABA + LTM
- Add anti-IgE monoclonal antibody (omalizumab)

**Step up treatment to achieve asthma control**

**Step down treatment to minimize short- and long-term side effects, cost, and inconvenience**
Next Up: Long Acting Beta Agonists (LABAs)

### Table 3. Inhaled Long-Acting β-Agonist Bronchodilators.*

<table>
<thead>
<tr>
<th>Drug</th>
<th>Brand Name</th>
<th>Formulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arformoterol</td>
<td>Brovana (Sepracor)</td>
<td>Liquid for aerosolization</td>
</tr>
<tr>
<td>Formoterol</td>
<td>Foradil (Schering-Plough)</td>
<td>Single-dose DPI</td>
</tr>
<tr>
<td></td>
<td>Perforomist (Dey)</td>
<td>Liquid for aerosolization</td>
</tr>
<tr>
<td>Salmeterol</td>
<td>Serevent (GlaxoSmithKline)</td>
<td>DPI (60 doses per device)</td>
</tr>
</tbody>
</table>

*From: Fanta, NEJM, 2009*
LABAs: A Word of Caution

From: Nelson, Chest, 2006
LABAs

- Should always be used if possible as a combination drug with inhaled glucocorticoid
  - Fluticasone propionate/Salmeterol (Advair)
  - Budesonide/Formoterol (Symbicort)
  - Mometasone/Formoterol (Dulera)
  - Fluticasone furoate/vilanterol (Breo Ellipta) **

** New, Once daily low dose IC only (fluticasone 100mcg)
Figure 1. Stepped-Care Approach to Asthma Treatment.

Step up treatment to achieve asthma control.

- SABA, as needed
- Inhaled steroid (or LTRA)
- Inhaled steroid + LABA (or inhaled steroid + LTM)
- Inhaled steroid + LABA + LTM
- Add anti-IgE monoclonal antibody (omalizumab)

Step down treatment to minimize short- and long-term side effects, cost, and inconvenience.
Leukotriene Modifiers

From: Reiss et al, Arch Intern Med, 1998
Figure 1. Stepped-Care Approach to Asthma Treatment.

Step up treatment to achieve asthma control.

- SABA, as needed
- Inhaled steroid (or LTRA)
- Inhaled steroid + LABA (or inhaled steroid + LTM)
- Inhaled steroid + LABA + LTM
- Add anti-IgE monoclonal antibody (omalizumab)

Step down treatment to minimize short- and long-term side effects, cost, and inconvenience.
Omalizumab: Anti-IgE Monoclonal Antibody

- For patients refractory to usual therapies
- IgE is a marker of allergy
- Allergic “flavor” of asthma
- High IgE (but not too high)
Off the beaten path…

- Long acting anti-muscarinic agents
- Bronchial Thermoplasty
Use of Tiotropium? (Off-Label...for now)

From: Peters et al., NEJM, 2010

From: Kerstjens al., NEJM, 2012
What is new? (And...Is “New” better?)

- LABA monotherapy *** Don’t Use This Without Inhaled Steroid!***
  - Striverdi Respimat (olodaterol 2.5mcg two inhalations QD: $186)
  - Arcapta Neohaler (indacaterol 75mcg one inhalation daily: $242)

- LAMA monotherapy:
  - Spiriva Respimat (tiotropium 2.5mcg two inhalations QD: $357)
  - Tudorza Pressair (aclidinium 400mcg inhaled BID: $285)
  - Incruse Ellipta (umeclidinium 62.5mcg inhaled QD: $270)

- IC/LA-beta agonist combination therapy:
  - Breo Ellipta (fluticasone-vilanterol 100mcg-25 one inhalation QD: $321)
  - Compare with Advair 500/50 BID ($422) or Symbicort 160/4.5 BID ($283)

- LA-antimuscarinic/LA-beta agonist combination therapy:
  - Anoro Ellipta (umeclidinium-vilanterol 62.5 mcg-25mcg inhaled QD: $337)
Finally...What’s Next Coach?
Asthma Action Plan
Asthma Action Plan (V.2.DMB)

• Do you know you have asthma?

• Are you using your controller medications regularly?

• Do you know how to use your inhalers?

• Are you treating your asthma exacerbating disorders (smoking, GERD, allergies, dust, mold, hand hygiene..)?

• How do you know when your asthma is out of control? (Symptoms, PEF, increase in medication use)?

• What should you do when your asthma is not well controlled?

If the answer is “no” to any of the above, talk to your doctor!!
Thanks!

- Questions?
- dbeach@bidmc.harvard.edu
- 617-667-LUNG (5864)