Update in Medicine and Primary Care
November 11, 2017

Denitza P. Blagev, MD
Pulmonary & Critical Care Medicine
Director, Schmidt Chest Clinic
Director, Lung Cancer Screening Program
Increased mortality in asthma with LABA?

The Salmeterol Multicenter Asthma Research Trial (SMART); Chest 2006
38 yo AA M w/ asthma, poorly controlled, daily symptoms, using daily inhaled steroid and prn albuterol 3-5 times a day w/ frequent early am awakenings due to wheezing. Which do you recommend next?

1. Add LAMA (e.g. tiotropium)
2. Add ICS-LABA combination (e.g. budesonide-formoterol)
3. Add omeprazole
4. Start daily prednisone for a month and then wean as tolerated
5. Azithromycin x 5 days
Does LABA-ICS increase mortality compared with ICS alone in asthma?

26 week prospective, double-blind, multicenter RCT
ICS vs. LABA-ICS
Age 12 and older; 1-4 exacerbations in prior year
primary end point: first serious asthma-related event
• (a composite of adjudicated death, intubation, and hospitalization)
• as assessed in a time-to-event analysis.
11,693 patients randomized

A Time to First Serious Asthma-Related Event

Hazard ratio, 1.07 (95% CI, 0.70–1.65)

Cumulative Percentage of Patients

No. at Risk

<table>
<thead>
<tr>
<th>Group</th>
<th>Days since Randomization</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Budesonide-formoterol</td>
<td>5846</td>
</tr>
<tr>
<td>Budesonide</td>
<td>5847</td>
</tr>
</tbody>
</table>

A Time to First Serious Asthma-Related Event

B Time to First Asthma Exacerbation

Hazard ratio, 0.84 (95% CI, 0.74–0.94)

<table>
<thead>
<tr>
<th>Days since Randomization</th>
<th>Cumulative Percentage of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>30</td>
<td>5</td>
</tr>
<tr>
<td>60</td>
<td>8</td>
</tr>
<tr>
<td>90</td>
<td>11</td>
</tr>
<tr>
<td>120</td>
<td>14</td>
</tr>
<tr>
<td>150</td>
<td>17</td>
</tr>
<tr>
<td>180</td>
<td>20</td>
</tr>
</tbody>
</table>

No. at Risk

<table>
<thead>
<tr>
<th></th>
<th>Budesonide-formoterol</th>
<th>Budesonide</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>5846</td>
<td>5847</td>
</tr>
<tr>
<td>30</td>
<td>5589</td>
<td>5532</td>
</tr>
<tr>
<td>60</td>
<td>5406</td>
<td>5321</td>
</tr>
<tr>
<td>90</td>
<td>5257</td>
<td>5116</td>
</tr>
<tr>
<td>120</td>
<td>5117</td>
<td>4972</td>
</tr>
<tr>
<td>150</td>
<td>5011</td>
<td>4848</td>
</tr>
<tr>
<td>180</td>
<td>4863</td>
<td>4715</td>
</tr>
<tr>
<td>210</td>
<td>38</td>
<td>27</td>
</tr>
</tbody>
</table>
38 yo AA M w/ asthma, poorly controlled, daily symptoms, using daily inhaled steroid and prn albuterol 3-5 times a day w/ frequent early am awakenings due to wheezing. Which do you recommend next?

1. Add LAMA (e.g. tiotropium)
2. Add ICS-LABA combination (e.g. budesonide-formoterol)
3. Add omeprazole
4. Start daily prednisone for a month and then wean as tolerated
5. Azithromycin x 5 days
38 yo AA M w/ asthma, poorly controlled, daily symptoms, using daily inhaled steroid and prn albuterol 3-5 times a day w/ frequent early am awakenings due to wheezing. Which do you recommend next?

1. Add LAMA (e.g. tiotropium)
2. Add ICS-LABA combination (e.g. budesonide-formoterol)
3. Add omeprazole
4. Start daily prednisone for a month and then wean as tolerated
5. Azithromycin x 5 days
45 yo W w/ hx asthma on ICS-LABA developed rhinorrhea, cough and wheezing x 3 days. She is missing work and is unable to sleep because of her symptoms. Her husband, and daughter also had similar symptoms a week earlier that have now resolved. What would you recommend?

1. Add LAMA (e.g. tiotropium) to her regimen
2. Azithromycin 500mg po qday x 3 days
3. Doxycycline 100mg po BID x 7 days
4. Levofloxacin 750mg po qday x 7 days
5. Add PO prednisone and increase prn albuterol
6. Oseltamivir (tamiflu) 75mg po BID x 5 days
Azithromycin for Acute Exacerbations of Asthma

Azithromycin for Acute Exacerbations of Asthma
Azithromycin for Acute Exacerbations of Asthma

**Figure A:**

- **Mean Diary Score**
- **Mean Acute AQLQ Overall Score**

![Graph showing Acute AQLQ score over days for Active and Placebo groups.](image)

Azithromycin for Acute Exacerbations of Asthma The AZALEA Randomized Clinical Trial JAMA Intern Med. 2016
Azithromycin for Acute Exacerbations of Asthma

The AZALEA Randomized Clinical Trial


**Azithromycin for Acute Exacerbations of Asthma**

**A** Acute AQLQ score

**B** Mini AQLQ score

- **Active**
- **Placebo**
Azithromycin for Acute Exacerbations of Asthma

Acute AQLQ score

Mini AQLQ score

Time to 50% reduction in symptom scores

Mean Diary Score

Mean Acute AQLQ Overall Score

Proportion Yet to Reach 50% Reduction

Visit

Active

Placebo
Azithromycin for Acute Exacerbations of Asthma

4582 Patients assessed for eligibility

4383 Excluded
2044 Antibiotic treatment
660 Other
417 Underlying health condition
315 Discharged
259 Age
220 >48 Hours after presentation
191 Declined to participate
130 Unknown reason
110 No requirement for steroid treatment
30 Not English speaking
7 No asthma exacerbation

199 Randomized

97 Randomized to receive azithromycin
97 Received azithromycin as randomized

87 Symptom diary scores analyzed
96 Acute and Mini AQLQ scores analyzed
97 Pulmonary functions analyzed

102 Randomized to receive placebo
102 Received placebo as randomized

89 Symptom diary scores analyzed
100 Acute and Mini AQLQ scores analyzed
101 Pulmonary functions analyzed
45 yo W w/ hx asthma on ICS-LABA developed rhinorrhea, cough and wheezing x 3 days. She is missing work and is unable to sleep because of her symptoms. Her husband, and daughter also had similar symptoms a week earlier that have now resolved. What would you recommend?

1. Add LAMA (e.g. tiotropium) to her regimen
2. Azithromycin 500mg po qday x 3 days
3. Doxycycline 100mg po BID x 7 days
4. Levofloxacin 750mg po qday x 7 days
5. Add PO prednisone and increase prn albuterol
6. Oseltamivir (tamiflu) 75mg po BID x 5 days
45 yo W w/ hx asthma on ICS-LABA developed rhinorrhea, cough and wheezing x 3 days. She is missing work and is unable to sleep because of her symptoms. Her husband, and daughter also had similar symptoms a week earlier that have now resolved. What would you recommend?

1. Add LAMA (e.g. tiotropium) to her regimen
2. Azithromycin 500mg po qday x 3 days
3. Doxycycline 100mg po BID x 7 days
4. Levofloxacin 750mg po qday x 7 days
5. Add PO prednisone and increase prn albuterol
6. Oseltamivir (tamiflu) 75mg po BID x 5 days
46 yo W w/ hx asthma on ICS-LABA who recovered from her prior asthma exacerbation 1 year ago is at her baseline but still symptomatic. She uses her prn albuterol several times a day, occasionally wakes up at night due to her asthma. What treatment would you recommend that could improve her asthma-related quality of life and reduce her asthma exacerbation risk?

1. Add Omeprazole
2. Add PO prednisone at low dose
3. Add anti-IL 5 therapy (e.g. mepolizumab)
4. Add anti-IgE therapy (e.g. omalizumab)
5. Add Azithromycin 500mg po TIW
Effect of Azithromycin on asthma exacerbations and quality of life in adults with persistent uncontrolled asthma (AMAZES)

- 420 adults with symptomatic asthma despite LABA-ICS
- No hearing problems
- Normal QTc
- Azithromycin 500mg po TIW vs. placebo
- Outcome: # asthma exac/study period and asthma-related QOL
Effect of Azithromycin on asthma exacerbations and quality of life in adults with persistent uncontrolled asthma (AMAZES)

- 420 adults with symptomatic asthma despite LABA-ICS
- No hearing problems
- Normal QTc
- Azithromycin 500mg po TIW vs. placebo
- Outcome: # asthma exac/study period and asthma-related QOL

Effect of azithromycin on asthma exacerbations and quality of life in adults with persistent uncontrolled asthma (AMAZES) Gibson et al. Lancet 2017
Effect of Azithromycin on asthma exacerbations and quality of life in adults with persistent uncontrolled asthma (AMAZES)

- 420 adults with symptomatic asthma despite LABA-ICS
- No hearing problems
- Normal QTc
- Azithromycin 500mg po TIW vs. placebo
- Outcome: # asthma exac/study period and asthma-related QOL

Effect of azithromycin on asthma exacerbations and quality of life in adults with persistent uncontrolled asthma (AMAZES) Gibson et al. Lancet 2017
Effect of Azithromycin on asthma exacerbations and quality of life in adults with persistent uncontrolled asthma (AMAZES)

- 420 adults with symptomatic asthma despite LABA-ICS
- No hearing problems
- Normal QTc
- Azithromycin 500mg po TIW vs. placebo
- Outcome: # asthma exacerbation/study period and asthma-related QOL

### Table: Azithromycin Effect on Asthma Exacerbations and QOL

<table>
<thead>
<tr>
<th>Condition</th>
<th>Placebo</th>
<th>Azithromycin</th>
<th>Incidence Rate Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-eosinophilic asthma</td>
<td>1.74</td>
<td>1.15</td>
<td>0.66 (0.47-0.93)</td>
</tr>
<tr>
<td>Eosinophilic asthma</td>
<td>1.98</td>
<td>0.96</td>
<td>0.52 (0.29-0.94)</td>
</tr>
<tr>
<td>Inhaled corticosteroid dose adj.</td>
<td>1.86</td>
<td>1.07</td>
<td>0.58 (0.46-0.74)</td>
</tr>
<tr>
<td>Frequent exacerbators</td>
<td>2.79</td>
<td>1.47</td>
<td>0.55 (0.41-0.73)</td>
</tr>
<tr>
<td>Cough and sputum VAS</td>
<td>1.72</td>
<td>0.79</td>
<td>0.49 (0.26-0.95)</td>
</tr>
<tr>
<td>Bacteria-negative</td>
<td>1.85</td>
<td>1.18</td>
<td>0.61 (0.52-0.72)*</td>
</tr>
<tr>
<td>Bacteria-positive</td>
<td>2.64</td>
<td>1.21</td>
<td>0.39 (0.22-0.69)*</td>
</tr>
</tbody>
</table>

Favours azithromycin  
Favours placebo
46 yo W w/ hx asthma on ICS-LABA who recovered from her prior asthma exacerbation 1 year ago is at her baseline but still symptomatic. She uses her prn albuterol several times a day, occasionally wakes up at night due to her asthma. What treatment would you recommend that could improve her asthma-related quality of life and reduce her asthma exacerbation risk?

1. Add Omeprazole
2. Add PO prednisone at low dose
3. Add anti-IL 5 therapy (e.g. mepolizumab)
4. Add anti-IgE therapy (e.g. omalizumab)
5. Add Azithromycin 500mg po TIW
45 yo W w/ hx asthma on ICS-LABA who recovered from her prior asthma exacerbation 6 months ago is at her baseline and still symptomatic. She uses her prn albuterol several times a day, occasionally wakes up at night due to her asthma. What treatment would you recommend that could reduce improve her asthma-related quality of life and reduce her asthma exacerbation risk.

1. Add Omeprazole
2. Add PO prednisone at low dose
3. Add anti-IL 5 therapy (e.g. mepolizumab) frequent exacerbation, PO pred, obstruction on PFTs
4. Add anti-IgE therapy (e.g. omalizumab) frequent exacerbation, PO pred, obstruction on PFTs
5. Add Azithromycin 500mg po TIW
6. Add LAMA (e.g. tiotropium) to her regimen
7. Add leukotriene receptor antagonist (e.g. montelukast)
67 yo M w/ hx COPD on LABA-LAMA-ICS s/p admission to hospital for COPD exacerbation presents for post-hospital follow up 3 weeks after his hospitalization. Reports he is back to baseline. Which of the following interventions has not been shown to reduce COPD-related hospitalizations?

1. Pulmonary Rehab referral
2. Tobacco cessation
3. Action plan: e.g. pred 40 x 5 days +/- abx
4. Chronic azithromycin
5. home noninvasive ventilation (NIV) if PCO2 >52
6. Roflumilast therapy
7. Perform spirometry if not previously done
COPD patients s/p admission for acute COPD exacerbation

- 116 pts randomized to Noninvasive ventilation vs. Oxygen alone
- Exclude OSA, BMI>35, other causes of resp failure
- Primary outcome: time to readmission or death within 12 months
- PCO2 >52 at 2-4 weeks post-exac
NIV for COPD patients

- 2021 patients screened to find 124 eligible patients
- Median IPAP 24 (IQR 22-26)
- Medial EPAP 4 (IQR 4-5)
- Backup rate of 14 (IQR, 14-16) breaths/minute.
- Exclude OSA, BMI>35, other causes of respiratory failure
- PCO2 >52 at 2-4 weeks post-exac
67 yo M w/ hx COPD on LABA-LAMA-ICS s/p admission to hospital for COPD exacerbation presents for post-hospital follow up 3 weeks after his hospitalization. Reports he is back to baseline. Which of the following interventions has not been shown to reduce COPD-related hospitalizations?

1. Pulmonary Rehab referral
2. Tobacco cessation
3. Action plan: e.g. pred 40 x 5 days +/- abx
4. Chronic azithromycin
5. home noninvasive ventilation (NIV) if PCO2 >52
6. Roflumilast therapy
7. Perform spirometry if not previously done
69 yo M with 50p-y tobacco use, quit 10 yrs ago, presents with a new diagnosis of COPD. He has daily symptoms and is currently using his prn albuterol 3-4 times a day. What inhaler treatment do you NOT recommend?

1. LABA (e.g. salmeterol)
2. LAMA (e.g. tiotropium)
3. LABA-ICS (e.g. budesonide-formoterol)
4. LAMA-LABA (e.g. indacaterol-glycopyrronium)
5. ICS (e.g. mometasone)
COPD Therapy

- 3362 patients
- Randomized to LABA-ICS vs. LAMA-LABA
- Primary outcome: annual rate of COPD exacerbations
COPD: LABA vs. LAMA

Hazard ratio, 0.83 (95% CI, 0.77–0.90)
P < 0.001 by log-rank test

No. at Risk
Tiotropium 3707 3369 3136 2955 2787 2647 2561 2455 2343 2242 2169 2107 1869
Salmeterol 3669 3328 3028 2802 2605 2457 2351 2251 2137 2050 1982 1915 1657

LAMA vs. LABA-ICS: no difference

More short of breath

Less short of breath

Wedzicha et al. AJRCCM 2007
COPD Therapy: Do ICS help?

A Moderate or Severe COPD Exacerbation

Hazard ratio, 1.06 (95% CI, 0.94–1.19)
P = 0.35 by Wald’s chi-square test

No. at Risk

<table>
<thead>
<tr>
<th></th>
<th>IGC continuation</th>
<th>IGC withdrawal</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1243</td>
<td>1242</td>
</tr>
<tr>
<td>6</td>
<td>1059</td>
<td>1090</td>
</tr>
<tr>
<td>12</td>
<td>927</td>
<td>965</td>
</tr>
<tr>
<td>18</td>
<td>827</td>
<td>825</td>
</tr>
<tr>
<td>24</td>
<td>763</td>
<td>740</td>
</tr>
<tr>
<td>30</td>
<td>694</td>
<td>688</td>
</tr>
<tr>
<td>36</td>
<td>646</td>
<td>646</td>
</tr>
<tr>
<td>42</td>
<td>615</td>
<td>607</td>
</tr>
<tr>
<td>48</td>
<td>581</td>
<td>570</td>
</tr>
<tr>
<td>54</td>
<td>14</td>
<td>19</td>
</tr>
</tbody>
</table>
69 yo M with 50p-y tobacco use, quit 10 yrs ago, presents with a new diagnosis of COPD. He has daily symptoms and is currently using his prn albuterol 3-4 times a day. What inhaler treatment do you NOT recommend?

1. LABA (e.g. salmeterol)
2. LAMA (e.g. tiotropium)
3. LABA-ICS (e.g. budesonide-formoterol)
4. LAMA-LABA (e.g.indacaterol-glycopyrronium)
5. ICS (e.g. mometasone)
69 yo M with 50p-y tobacco use, quit 10 yrs ago, presents with a new diagnosis of COPD. He has daily symptoms and is currently using his prn albuterol 3-4 times a day. What inhaler treatment do you NOT recommend?

1. LABA (e.g. salmeterol)
2. LAMA (e.g. tiotropium)
3. LABA-ICS (e.g. budesonide-formoterol)
4. LAMA-LABA (e.g. indacaterol-glycopyrronium)
5. ICS (e.g. mometasone)
Reduced Lung-Cancer Mortality with Low-Dose Computed Tomographic Screening

The National Lung Screening Trial Research Team*

ABSTRACT

BACKGROUND
The aggressive and heterogeneous nature of lung cancer has thwarted efforts to reduce mortality from this cancer through the use of screening. The advent of low-dose helical computed tomography (CT) altered the landscape of lung-cancer screening, with studies indicating that low-dose CT detects many tumors at early stages. The National Lung Screening Trial (NLST) was conducted to determine whether screening with low-dose CT could reduce mortality from lung cancer.

METHODS
From August 2002 through April 2004, we enrolled 53,454 persons at high risk for lung cancer at 33 U.S. medical centers. Participants were randomly assigned to undergo three annual screenings with either low-dose CT (26,722 participants) or single-view posteroanterior chest radiography (26,732). Data were collected on cases of lung cancer and deaths from lung cancer that occurred through December 31, 2009.

The members of the writing team (who are listed in the Appendix) assume responsibility for the integrity of the article. Address reprint requests to Dr. Christine D. Berg at the Early Detection Research Group, Division of Cancer Prevention, National Cancer Institute, 6130 Executive Blvd., Suite 3112, Bethesda, MD 20892-7346, or at bengc@mail.nih.gov.

*A complete list of members of the National Lung Screening Trial research team is provided in the Supplementary Appendix, available at NEJM.org.

This article (10.1056/NEJMoa1102873) was published on June 29, 2011, at NEJM.org.
A Lung Cancer

Cumulative No. of Lung Cancers

Low-dose CT

Chest radiography

Years since Randomization

0 1 2 3 4 5 6 7 8
USPSTF Recommends Lung Cancer Screening

Lung Cancer: Screening
Release Date: December 2013

Recommendation Summary

Summary of Recommendation and Evidence

<table>
<thead>
<tr>
<th>Population</th>
<th>Recommendation</th>
<th>Grade (What’s This?)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults Aged 55-80, with a History of Smoking</td>
<td>The USPSTF recommends annual screening for lung cancer with low-dose computed tomography (LDCT) in adults aged 55 to 80 years who have a 30 pack-year smoking history and currently smoke or have quit within the past 15 years. Screening should be discontinued once a person has not smoked for 15 years or develops a health problem that substantially limits life expectancy or the ability or willingness to have curative lung surgery.</td>
<td>B</td>
</tr>
</tbody>
</table>

http://www.uspreventiveservicestaskforce.org/uspstf/uspslung.htm
USPSTF Grade recommendation

Breast Cancer Screening

| Women, Age 50-74 Years | The USPSTF recommends biennial screening mammography for women 50-74 years. | B |

Colorectal Cancer Screening

| Adults, beginning at age 50 years and continuing until age 75 years | The USPSTF recommends screening for colorectal cancer using fecal occult blood testing, sigmoidoscopy, or colonoscopy in adults, beginning at age 50 years and continuing until age 75 years. The risks and benefits of these screening methods vary. | A |

Cervical Cancer Screening

| Women 21 to 65 (Pap Smear) or 30-65 (in combo with HPV testing) | The USPSTF recommends screening for cervical cancer in women age 21 to 65 years with cytology (Pap smear) every 3 years or, for women age 30 to 65 years who want to lengthen the screening interval, screening with a combination of cytology and human papillomavirus (HPV) testing every 5 years. See the Clinical Considerations for discussion of cytology method, HPV testing, and screening interval. | A |

Prostate Cancer Screening

| Men, Screening with PSA | The U.S. Preventive Services Task Force (USPSTF) recommends against prostate-specific antigen (PSA)-based screening for prostate cancer. | D |
Who pays? CMS
Center for Medicare and Medicaid Services

- Age 55-77
- 30 pack-years of smoking history
- Currently smoking or quit within 15 years
- Asymptomatic (no signs/symptoms of lung cancer)
- 1:1 dedicated Shared Decision-Making Visit
- ShouldI-screen.com

Compared to other people like you, there will be 7 fewer deaths out of 1000 in the next 6 years if you get screened.

Out of 100 people like you, 6 will avoid a lung cancer death over 6 years because of screening.
57 yo M active smoker w/ hx 35p-y tobacco use has had scant hemoptysis for a few months and presents for evaluation.

Which ONE option of these below is appropriate as part of the evaluation and treatment of this patient?

1. Lung cancer screening with Low Dose Chest CT
2. Spirometry
3. Tobacco Cessation counseling
4. Positron Emission Tomography-CT (PET-CT)
57 yo M active smoker w/ hx 35p-y tobacco use has had scant hemoptysis for a few months and presents for evaluation.

Which ONE option of these below is appropriate as part of the evaluation and treatment of this patient?

1. Lung cancer screening with Low Dose Chest CT
2. Spirometry
3. Tobacco Cessation counseling
4. Positron Emission Tomography-CT (PET-CT)
Questions?
Learning objectives

1. Understand the safety profile of asthma inhalers
2. Understand the role of azithromycin therapy in treatment of asthma – acute exacerbations and chronic prevention of exacerbations
3. Understand the options of using different classes of inhalers in treating COPD
4. Understand the role of noninvasive ventilation in COPD patients
5. Understand the criteria for lung cancer screening using low-dose Chest CT
MOC questions
45 yo W w/ hx asthma on ICS-LABA developed rhinorrhea, cough and wheezing x 3 days. She is missing work and is unable to sleep because of her symptoms. Her husband, and daughter also had similar symptoms a week earlier that have now resolved. What would you recommend?

1. Add LAMA (e.g. tiotropium) to her regimen
2. Azithromycin 500mg po qday x 3 days
3. Doxycycline 100mg po BID x 7 days
4. Levofloxacin 750mg po qday x 7 days
5. Add PO prednisone and increase prn albuterol
6. Oseltamivir (tamiflu) 75mg po BID x 5 days
MOC questions

The patient described has an acute asthma exacerbation. Standard of care for acute asthma exacerbation is prednisone burst (answer 5).

Numbers 2, 3 and 4 are antibiotics for asthma exacerbation. The study most recently answering the question of whether antibiotics (azithromycin) improve asthma outcomes when used for asthma exacerbation showed no difference in any asthma outcome (Azithromycin for Acute Exacerbations of Asthma The AZALEA Randomized Clinical Trial JAMA Intern Med. 2016) . For preventing future exacerbations chronic azithromycin was effective. (http://thorax.bmj.com/content/68/4/322.short).

Oseltamivir (number 5) would be appropriate treatment for acute influenza. But the vignette does not mention acute onset, myalgias, or fevers and is not typical of influenza syndrome.

Finally, tiotropium is a reasonable add on therapy to prevent future asthma exacerbations in patients already treated with first line therapy, but would not be adequate therapy for an acute asthma exacerbation.

http://www.nejm.org/doi/full/10.1056/nejmoa1008770#t=article
67 yo M w/ hx COPD on LABA-LAMA-ICS s/p admission to hospital for COPD exacerbation presents for post-hospital follow up 3 weeks after his hospitalization. Reports he is back to baseline. Which of the following interventions has not been shown to reduce COPD-related hospitalizations?

1. Pulmonary Rehab referral
2. Tobacco cessation
3. Action plan: e.g. pred 40 x 5 days +/- abx
4. Chronic azithromycin
5. home noninvasive ventilation (NIV) if PCO2 >52
6. Roflumilast therapy
7. Perform spirometry if not previously done
MOC questions

Spirometry, while recommended and should be performed when the patient is not in an acute exacerbation and is the most important diagnostic test for COPD, does not, by itself, reduce COPD exacerbations.

All of the other options listed have been shown to reduce COPD exacerbation frequency.


1. Pulmonary Rehab referral
2. Tobacco cessation
3. Action plan: e.g. pred 40 x 5 days +/- abx
4. Chronic azithromycin

http://www.nejm.org/doi/full/10.1056/nejmoa1104623#t=article

1. home noninvasive ventilation (NIV) if PCO2 >52


1. Roflumilast therapy

68 yo W smoking 1ppd x 50 years was recently hospitalized for COPD exacerbation and pneumonia. She is on prn albuterol. Her room air saturation at rest is 89% and drops to 85% with exertion. You recommend which of the following to reduce her MORTALITY RISK?

1. LAMA alone (e.g. tiotropium)
2. Supplemental oxygen
3. LABA-LAMA combination (e.g. indacaterol-glycopyrronium)
4. Tobacco cessation
5. LABA-ICS combination (e.g. salmeterol-fluticasone)
COPD and oxygen: LOTT trial

Stable COPD
SpO$_2$ at rest, 89 to 93%
OR during the 6-minute walk test, SpO$_2$ $\geq$80% for $\geq$5 minutes and $<$90% for $\geq$10 seconds
Oxygen 24/7 if resting SpO$_2$ 89 - 93%
Oxygen with sleep and exertion if only desat with exercise

Blagev 2017

COPD Therapy: Supplemental Oxygen?

A Primary Outcome (Death or First Hospitalization) or First Hospitalization

- Supplemental oxygen, primary outcome
- Supplemental oxygen, first hospitalization
- No supplemental oxygen, primary outcome
- No supplemental oxygen, first hospitalization

No. at Risk
No supplemental oxygen 370 304 232 181 139 102 76 59 43 29 21 7 1
Supplemental oxygen 368 314 243 198 158 125 86 61 44 24 13 6 1

Death or first hospitalization, P=0.52 by log-rank test
First hospitalization, P=0.37 by log-rank test

Blagev 2017

COPD Therapy: Supplemental Oxygen?

A Primary Outcome (Death or First Hospitalization) or First Hospitalization

B Death

No. at Risk
No supplemental oxygen 370 366 362 319 295 242 210 177 152 120 88 33 10
Supplemental oxygen 368 366 358 321 294 245 216 184 149 116 88 33 8

P=0.53 by log-rank test
## Oxygen Related Adverse Events

<table>
<thead>
<tr>
<th>Event</th>
<th>No. of reports</th>
<th>Reports per 100 person-years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fires related to oxygen use</td>
<td>2</td>
<td>0.08</td>
</tr>
<tr>
<td>Burn from smoking around oxygen equipment</td>
<td>3</td>
<td>0.12</td>
</tr>
<tr>
<td>Burn from using oxygen equipment around open flame</td>
<td>1</td>
<td>0.04</td>
</tr>
<tr>
<td>Burn from liquid oxygen frost</td>
<td>4</td>
<td>0.16</td>
</tr>
<tr>
<td>Nosebleed</td>
<td>9</td>
<td>0.35</td>
</tr>
<tr>
<td>Tripping/falling over oxygen equipment</td>
<td>23*</td>
<td>0.90</td>
</tr>
</tbody>
</table>

**Total no. of expected, related events**

<table>
<thead>
<tr>
<th></th>
<th>No. of reports</th>
<th>Reports per 100 person-years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total no. of expected, related events</td>
<td>42</td>
<td>1.64</td>
</tr>
</tbody>
</table>

**Total no. of patients ever using supplemental oxygen during follow-up**

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Total no. of patients ever using supplemental oxygen during follow-up</td>
<td>490</td>
</tr>
</tbody>
</table>

**No. (%) reporting at least 1 related adverse event**

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>No. (%) reporting at least 1 related adverse event</td>
<td>42 (8.6%)</td>
</tr>
</tbody>
</table>

*Two of these events involved hospitalization: overnight hospitalization with humerus fracture and 6-day hospitalization with rib fractures.*
68 yo W smoking 1ppd x 50 years was recently hospitalized for COPD exacerbation and pneumonia. She is on prn albuterol. Her room air saturation at rest is 89% and drops to 85% with exertion. You recommend which of the following to reduce her MORTALITY RISK?

1. LAMA alone (e.g. tiotropium)
2. Supplemental oxygen
3. LABA-LAMA combination (e.g. indacaterol-glycopyrronium)
4. Tobacco cessation
5. LABA-ICS combination (e.g. salmeterol-fluticasone)
68 yo W smoking 1ppd x 50 years was recently hospitalized for COPD exacerbation and pneumonia. She is on prn albuterol. Her room air saturation at rest is 89% and drops to 85% with exertion. You recommend which of the following to reduce her MORTALITY RISK?

1. LAMA alone (e.g. tiotropium)
2. Supplemental oxygen
3. LABA-LAMA combination (e.g. indacaterol-glycopyrronium)
4. Tobacco cessation
5. LABA-ICS combination (e.g. salmeterol-fluticasone)