Updates in COPD 2024

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We Are Better Together
Excellence and Innovation
We Seek To Advance
Diversity and Inclusion
We Value Each Other

University of Maryland Medical Center

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Disclosures

The presenter has no conflicts of interest to disclose.

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Objectives

- Review the updates on COPD management in recent guidelines, specifically Global initiative for Chronic Obstructive Lung disease (GOLD) 2024
- Understand blood eosinophil guided therapy for COPD exacerbation
- Understand the mechanism of action, efficacy and safety of biologics in COPD management and available evidence
- Discuss smoking cessation and coverage issues
- Vaccination update in COPD

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What is COPD?

A heterogeneous lung condition characterized by chronic respiratory symptoms (dyspnea, cough, expectoration, exacerbations) due to abnormalities of the airway (bronchitis, bronchiolitis) and/or alveoli (emphysema) that cause persistent, often progressive, airflow obstruction"

https://pubmed.ncbi.nlm.nih.gov/36958741

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Gold Guideline 2024: evidence category

Evidence Category	Source of Evidence
A	Randomized Controlled Trials (RCTs)
	Rich body of high quality evidence without any significant limitations or bias
B	Randomized Controlled Trials (RCTs) with important limitations
	Limited body of evidence
C	Non –Randomized trials Observational studies
D	Panel Consensus Judgement

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Risk Factors of COPD

GETomics- Gene (**G**)-environment (**E**) interactions occurring over the lifetime (**T**) of the individual that can damage the lungs and/or alter their normal development/aging process

- **G**ene- α1- antitrypsin deficiency
- Environmental-
  - Smoking History:
    - Cigarette-pack years (packs cigarettes per day x years smoking)
    - Others- e.g., pipe, cigar, water pipe and marijuana
  - Host factors
- In**T**eractions occurring over lifetime
  - Exposure
  - Infection

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Burden of COPD

- One of the **top three causes** of death worldwide
- Couse around **three million deaths annually** globally
- In the United States the costs attributable to COPD are expected to increase over the next 20 years, with projected costs **of $800.90 billion or $40 billion per year**
- In the United States, COPD is the **second leading cause of reduced DALY**, trailing only ischemic heart disease

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COPD Assessment

- **Severity** of airflow obstruction
  Spirometry
  - Forced Vital Capacity (FVC)
  - Forced Expiratory Volume in 6 seconds (FEV6)
  - Forced Expiratory Volume in 1 seconds (FEV1)
  - Ratio FEV1/FVC
- Nature and magnitude of current **symptoms**
- Previous **history** of moderate and severe exacerbations
- **Blood eosinophil count**
- Presence and type of other diseases (**multimorbidity**)
  - Alpha-1 antitrypsin screening

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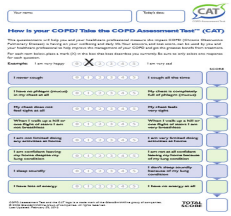
COPD Assessment tools

- COPD Assessment Test (CAT)



Modified medical research Counsel) (mMRC) dyspnea scale

Modified Medical Research Council (mMRC) dyspnea scale

Grade	Description of breathlessness
0	I only get breathless with strenuous exercise
1	I get short of breath when hurrying on level ground or walking up a slight hill
2	On level ground, I walk slower than people of the same age because of breathlessness, or have to stop for breath when walking at my own pace
3	I stop for breath after walking about 100 yards or after a few minutes on level ground
4	I am too breathless to leave the house or I am breathless when dressing

Adapted from: Fletcher CM, Elmes PC, Fairbairn AS, Wood CH. The significance of respiratory symptoms and the diagnosis of chronic bronchitis in a working population. Br Med J 1959; 2:257.

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Gold Grades and Severity of Airflow Obstruction in COPD (Based on post-bronchodilator FEV1)

GOLD 1:	**Mild**	**FEV1/FVC <0/7** **FEV1 ≥ 80% predicted**
GOLD 2:	Moderate	FEV1/FVC <0/7 ≤50% FEV1 < 80% predicted
GOLD 3:	Severe	FEV1/FVC <0/7 ≤30% FEV1 < 50% predicted
GOLD 4:	Very severe	FEV1/FVC <0/7 FEV1 <30% predicted

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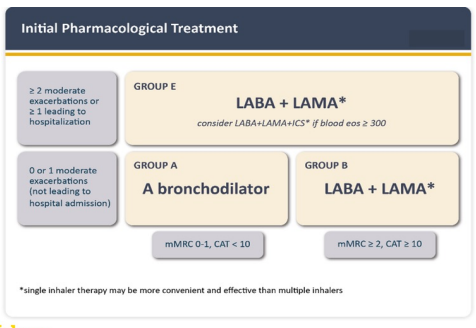

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Prevention & Management of COPD: Group A

mMRC 0-1, CAT <10 and 0-1 **Minimal symptoms moderate exacerbations and no hospitalization**

Short- or a long-acting bronchodilator

- SABA
  - AccuNeb, Proair HFA, Proventil HFA, Ventolin HFA (albuterol), Xopenex HFA® (Levalbuterol)
- SAMA
  - Atrovent ®(Ipratropium)
- SAMA-SABA
  - Combivent®(Ipratropium/albuterol-)
- LABA
  - Serevent ®(salmeterol), Foradil® (formoterol), Striverdi® (olodaterol).
- LAMA
  - Genuair ® (aclidinium), Breezhaler ® (glycopyrronium), Spiriva ® HandiHaler, Respimat (tiotropium), Incruse Ellipta ® (umeclidinium)

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Prevention & Management of COPD: COPD: Group B

mMRC ≥2 or CAT ≥ 10, and **with ≤ 1 moderate exacerbation in the year and no hospitalization**

- LAMA+LABA
  - Anoro® (umeclidinium and vilanterol), Stiolto® (olodaterol and tiotropium), Utibron® (indacaterol and glycopyrrolate)
- LAMA
  - Genuair® (aclidinium), Breezhaler ® (glycopyrronium), Spiriva® HandiHaler, Respimat (tiotropium), Incruse Ellipta® (umeclidinium)
- LABA
  - Serevent ®(salmeterol), Foradil® (formoterol), Striverdi® (olodaterol).

LABAs and LAMAs significantly improve lung function, dyspnea, health status, and reduce exacerbation rates (Evidence A)

LAMAs Have a greater effect on exacerbation reduction compared with LABAs and decrease hospitalizations (Evidence A)

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Prevention & Management of COPD: Group E

≥2 moderate exacerbations or ≥1 leading to hospitalization

- LAMA+LABA Plus SABA
- LABA+LAMA+ICS - if eos ≥ 300 cells/µL (practical recommendation)
  - Trelegy Ellipta® (fluticasone-furoate/vilanterol/umeclidinium)
  - Breztri Aerosphere® (budesonide/glycopyrronium/formoterol)
  - Trimbow®(beclometasone dipropionate, formoterol fumarate dihydrate and glycopyrronium bromide)*
- Roflumilast (Daliresp®, Zoryve®)
- Azithromycin

For patients with COPD and asthma, treatment protocol for asthma should followed.

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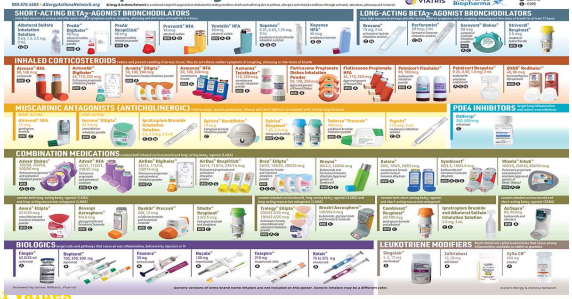
Respiratory Treatments



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Select the correct answer

- For patient with Asthma and COPD, pharmacotherapy for Asthma should be followed
  - ○True
  - ○False

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Select the correct answer

- For patient with Asthma and COPD, pharmacotherapy for Asthma should be followed
  - ○True
  - ○False

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COPD Exacerbation

- Mild
  - SABA (Increased frequency)
  - LABA+LAMA
  - LABA+LAMA+ICS (if blood eosinophil counts ≥ 100 cells/µL)
  - Macrolide Antibiotics (e.g. azithromycin)
- Moderate
  - LABA+LAMA
  - LABA+LAMA+ICS (if blood eosinophil counts ≥ 100 cells/µL)
  - Roflumilast (if at least one hospitalization for AECOPD in a year)
  - Macrolide Antibiotics (e.g. azithromycin)
  - Antivirals
  - Prednisone 40mg daily x 5 days

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COPD Exacerbation : Severe

- LABA+LAMA
- LABA+LAMA+ICS (if blood eosinophil counts ≥ 100 cells/µL)

Others-

- Roflumilast (if at least one hospitalization for AECOPD in a year)
- Macrolide Antibiotics (e.g. azithromycin)
- Antivirals
- Prednisone 40mg daily x 5 days
- Opioids
- α- antitrypsin

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COPD Exacerbation : Considerations for ICS

Strongly favors	• History of Hospitalization • ≥ 2 moderate exacerbations per year • Blood eos ≥ 300 cells/µl • History of, or concomitant asthma
Favors	• 1 moderate exacerbation per year • Blood eos 100 to ≤ 300 cells/µl
Oppose	• Pneumonia or other side effects • Blood eos ≤ 100 cells/µl • History of mycobacterial infection

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Select the correct answer

- LABAs has greater effect on exacerbation reduction compared with LAMAs
- LAMAs has greater effect on exacerbation reduction compared with LABAs
- Short acting agents are preferred over LAMAs and LABAs except for patients only with occasional dyspnea
- Combination with a treatment of a LABA and a LAMA does not increase FEV1 or reduce symptoms compared with monotherapy

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Select the correct answer

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Role of Eosinophil in COPD

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COPD and Biomarkers

- Type-1 COPD
  - Neutrophils
- Type-2 COPD
  - Eosinophils
    - Sustained inflammation and possible tissue damage
    - Increased exacerbations

Recently GOLD has introduced the blood eosinophil count as a biomarker for estimating the efficacy of inhaled corticosteroids (ICS) for the prevention of exacerbations.

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COPD and Role of Eosinophils

- Eosinophil, key immuno-effector and inflammatory cell
- Infiltration into airways occur with inflammatory signals and recruitment
  - T Helper type-2 Cells
    - IL-5 and other chemoattractant secretion
  - Locally produced
    - IL-4 and IL-13 increase adhesives

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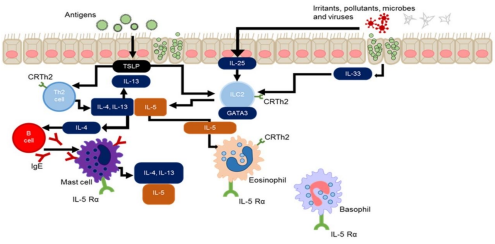
Role of Eosinophils on COPD



David B, Bafadhel M, Koenderman L, *et al*. Eosinophilic inflammation in COPD: from an inflammatory marker to a treatable trait. *Thorax* 2021;76:188-195.

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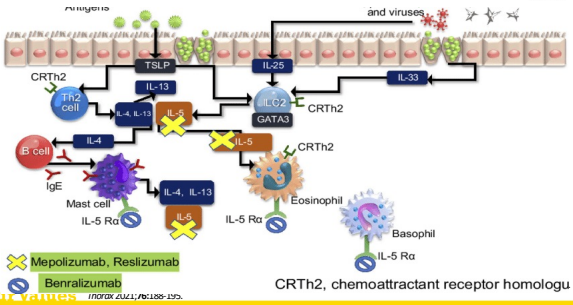

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COPD and Role of Eosinophils

- Diagnosis
  - Blood Eosinophils: ≥ 300 cells/µL
  - Sputum Eosinophils: ≥ 3%
- Treatment
  - ICS
  - Biologics (under study)
    - ADCC pathway. E.g. Benralizumab (Fasenra)
    - Anti-IL 5 e.g. Mepolizumab (Nucala), Resilizumab (Cinqair)
    - Anti-IL 4 and IL- 13 e.g. Dupilumab (Dupident)
    - Anti-TSLP e.g. Tezepelumab (Tezspire)

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COPD and Role of Eosinophils

Few studies on biologics-

- Benralizumab – GALATHEA, TERRANOVA
- Mepolizumab- METREX and METREO
- Dupilumab- BOREAS

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What Gold states on biologics

BOREAS showed clear clinical effects of dupilumab in a selected subgroup of COPD patients.

GOLD 2024 acknowledges the results of the BOREAS study pending confirmation studies.

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BOREAS Trial

- Phase 3 trial:
  - Dupilumab 300mg every 2 weeks add on therapy vs placebo
- Patient selection:
  - Physician diagnosed COPD ≥ 12 months
  - Current (30% cap) or former smokers
  - 40 to 80 years of age
  - FEV1/FVC <0.70
  - FEV1- 30% to 70% or predicted value
  - Triple therapy ≥ 3 months (stable dose x 1 month)
  - Eos ≥ 300 cells/μL
  - 2 moderate exacerbations or 1 severe exacerbation in the past year
  - Exclusion: Asthma
- Baseline characteristics were similar

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BOREAS Trial

- Primary end point
  - Annualized rate of moderate of severe exacerbations
- Secondary
  - Change in FEV1 at 12 and 52 weeks
  - Change in FEV1 in patients with FeNO level of ≥ 20 ppb
  - Change in St. George's Respiratory Questionnaire (SGRQ) total score at 52 weeks
    - Minimum clinically important difference of 4
  - Evaluating Respiratory Symptoms in COPD (E-RS–COPD) total score
  - Annualized rate of moderate or severe COPD exacerbations among the patients who had a FeNO level ≥ 20 ppb

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BOREAS Trial

- Statistics
  - Intent to treat population (ITT)
  - 924 patients to reach a power of 90% to detect difference in annualized rate of COPD exacerbations of 2% at week 52 with 2sided alpha of 0.049
  - Primary endpoint analyzed with negative binomial model
  - Secondary end points were evaluated with mixed effects model

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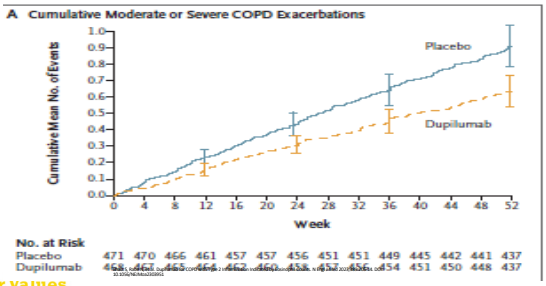
BOREAS Trial



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BOREAS Trial

	Placebo	Dupilumab	P-Value
Annualized COPD moderate to severe exacerbation	1.10 (0.93 to 1.30)	0.78 (0.64 to 0.93)	<0.001
Change in prebd FEV1 at week 12	0.077 (0.042 to 0.112)	0.160 (0.126 to 0.195)	<0.001
Change in prebronchodilator FEV1 from baseline to wk 52	0.070 (0.033 to 0.107)	0.153 (0.116 to 0.189)	<0.001
Change in prebronchodilator FEV1 from baseline to wk 12 among patients with a baseline FeNO ≥20 ppb	0.108 (0.038 to 0.177)	0.232 (0.164 to 0.299)	0.002
Change in prebronchodilator FEV1 from baseline to wk 52 among patients with a baseline FeNO ≥20 ppb	0.120 (0.047 to 0.192)	0.247 (0.176 to 0.318)	0.003

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BOREAS Trial

Change in SGRQ total score from baseline to wk 52	−6.4 (−8.0 to −4.8) −9.7	(−11.3 to −8.1)	0.002
SGRQ total score improvement ≥4 points at wk 52	43.1 (38.6 to 47.7)	51.5 (46.9 to 56.1)	0.009
Change in E-RS–COPD total score from baseline to wk 52	−1.6 (−2.1 to −1.1)	−2.7 (−3.2 to −2.2)	0.001
Annualized rate of moderate or severe exacerbations of COPD among patients with a baseline FeNO ≥20 ppb	1.12 (0.83 to 1.50)	0.70 (0.51 to 0.96)	0.005

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BOREAS Trial

Table 3. Adverse Events (Safety Population).*

Event	Placebo (N = 470)	Dupilumab (N = 469)
	no. of patients (%)	
Any adverse event	357 (76.0)	363 (77.4)
Any serious adverse event	73 (15.5)	64 (13.6)
Any adverse event leading to death	8 (1.7)	7 (1.5)
Any adverse event leading to permanent discontinuation of placebo or dupilumab	16 (3.4)	14 (3.0)
Adverse events occurring in ≥5% of patients in either group		
Nasopharyngitis	45 (9.6)	44 (9.4)
Upper respiratory tract infection	46 (9.8)	37 (7.9)
Headache	32 (6.8)	38 (8.1)
COPD	28 (6.0)	27 (5.8)
Covid-19	27 (5.7)	19 (4.1)
Hypertension	28 (6.0)	17 (3.6)
Diarrhea	17 (3.6)	25 (5.3)
Back pain	16 (3.4)	24 (5.1)
Major adverse cardiovascular event†	9 (1.9)	4 (0.9)

Bhatt S, Rabe K, et al. Dupilumab for COPD with Type 2 Inflammation Indicated by Eosinophil Counts. N Engl J Med 2023;389:205-14. DOI: 10.1056/NEJMoa2303951

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BOREAS Trial

- Strengths
  - Adequately powered
  - International trial
  - Low drop-out rate
  - Similar adverse effects
- Limitations
  - COVID during trial
  - Randomization not stratified based on smoking status

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BOREAS Trial

- Dupilumab showed reduction in moderate to severe COPD exacerbations
  - EXACT defined exacerbations
- Need addition trials, unsure of place in therapy at this time

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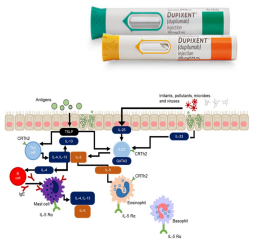
Dupilumab (Dupixent®)

- Interleukin- 4 receptor antagonist
  - Inhibits IL-4 and IL- 13
- Binds to IL-4 receptor alpha subunit →inhibiting IL-4 and IL-13 cytokine induced responses



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Dupilumab (Dupixent®)

- SC injection
- Thigh, lower abdomen, or upper arm (rotating inj. sites)
- Primarily degraded into peptides and amino acids by catabolism
- Approx 1 week to peak conc.

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Dupilumab (Dupixent®)

Common S.E

- injection site reactions
- eye and eyelid Inflammation, including redness, swelling, and itching, sometimes with blurred vision
- cold sores in your mouth or on your lips
- high count of a certain white blood cell (eosinophilia)

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Select the correct answer

- There is evidence of beneficial role of antitussives in people with COPD
- Vasodilators improve outcome and oxygenation
- Low dose long acting oral and parenteral opioids may be considered for treating dyspnea in COPD patients with severe diseases
- Intravenous augmentation therapy does not slow down the progression of emphysema

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Select the correct answer

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- Vasodilators improve outcome and oxygenation
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Non-Pharmacological Management of COPD

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Non-Pharmacological Management of COPD

- Vaccinations
- Smoking Cessation
- Self Management Education and Physical Activity
- Pulmonary Rehabilitation

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Non-Pharmacological Management of COPD: Vaccination

- Influenza
- Covid-19 (SARS-CoV-2)
- Pneumococcal: (PCV20 or PCV15 and PPSV23)
- Pertussis (Tdap -dTap/dTPa)
- Shingles
- RSV*

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Non-Pharmacological Management of COPD: Smoking Cessation

Patient group A, B and E
- Smoking Cessation Essential
- Can include pharmacological treatment
- Counselling should be delivered with 5A (Ask, Advise, Assess, Assist, Arrange) strategy in mind

Available pharmacological products:
- Varenicline (Chantix®)
- Nicotine replacement products (Nasal spray, Patch, Lozenzes, Gums)
- Bupropion sustained release (Zyban®)
- Nortriptyline

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Non-Pharmacological Management of COPD: Smoking Cessation

- Nicotine Replacement Therapy (NRT)
  - Nicotine patch 21mg, 14mg, 7mg
    - > 10 cigarettes per day → 21mg
    - ≤ 10 cigarettes per day → 14mg
  - Nicotine Gum 2mg and 4mg
    - 1 piece every hour as needed
    - Instruct on appropriate administration (chew and park)
    - Trouble for people with poor dentition
  - Nicotine Lozenge 2mg and 4mg
    - 1 lozenge every hour as needed
    - DO NOT CHEW

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Non-Pharmacological Management of COPD: Smoking Cessation -Coverage

- Nicotine Inhaler
  - 10mg cartridge
  - Quick breaths holding in mouth
- Nicotine Nasal Spray
  - 1 spray each nostril every 1 to 2 hours

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Non-Pharmacological Management of COPD: Smoking Cessation

- Medicare does cover Rx only (NOT OTC products)
  - Medicare/Medicaid plans
  - Advantage Plans
- **Maryland Medicaid (Not MCOs) covers OTC and Rx products**
- Commercial Plans
- 1-800-QUIT NOW
- Midtown Pulmonary Clinic

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Non-Pharmacological Management of COPD: Smoking Cessation -Coverage

- Medicare will cover as inhaler and nasal spray as Rx -not OTC
- MD Medicaid: Requires prior authorization for coverage of NRT
- Commercial plans: Increased cost

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Non-Pharmacological Management of COPD: Smoking Cessation

- Buproprion
  - 150 mg/day for 3 days, then 150 mg twice a day
  - Initiate 1 to 2 weeks prior to quite date
    - Lowers seizure threshold
- Varenicline
  - 0.5 mg/day for 3 days, then 0.5 mg twice a day for 4 days, then 1 mg twice a day
  - Initiate 1 to 2 weeks prior to quite date
    - Insomnia, vivid dreams, "neuropsychiatric symptoms"

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Non-Pharmacological Management of COPD: Smoking Cessation -Coverage

- Bupropion
  - Medicare
  - MD Medicaid
  - Commercial Plans
- Varenicline
  - Medicare
  - MD Medicaid: Prior authorization
  - Commercial Plans

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Non-Pharmacological Management of COPD: Pulmonary Rehabilitation

- **Patient Group B and Group E only**
- **Facilities in our area**
  - UMMC Midtown
  - UM BWMC
  - Johns Hopkins Howard Country General Hospital
  - Medstar
  - St. Agnes
  - Lifebridge Carol hospital

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Select the correct answer

- **Which group should get RSV vaccine per new recommendation?**
  - Individuals over 60 years and/or with chronic heart or lung disease
  - Individuals over 65 years and or with chronic heart or lung disease
  - Individuals over 60 years and with chronic lung disease
  - Individuals over 65 years and with chronic lung disease

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Select the correct answer

Which group should get RSV vaccine per new recommendation?

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