Clinical Success in Managing CHF and COPD

February 13, 2020

Mount Sinai Health Partners

General Announcements

- Please silence your phone.
- For bathrooms, please exit to the lobby and walk out through the double doors. The bathrooms will be down the hall on your left.
- There will be two Q&A sessions throughout the presentation; one in the middle and one at the end. Please hold your questions until these sessions.

Agenda

1. Welcome and Introduction
2. Identifying and Managing Congestive Heart Failure
3. Audience Q&A Session
4. Identifying and Managing Chronic Obstructive Pulmonary Disease
5. Audience Q&A Session

Identifying and Managing Congestive Heart Failure

Sumeet Singh Mitter, MD, MSc, FACC
Director of HFpEF and Cardiac Amyloid Programs
Advanced Heart Failure and Transplant
Mount Sinai Heart

February 13, 2020

Mount Sinai Health Partners

Disclosures

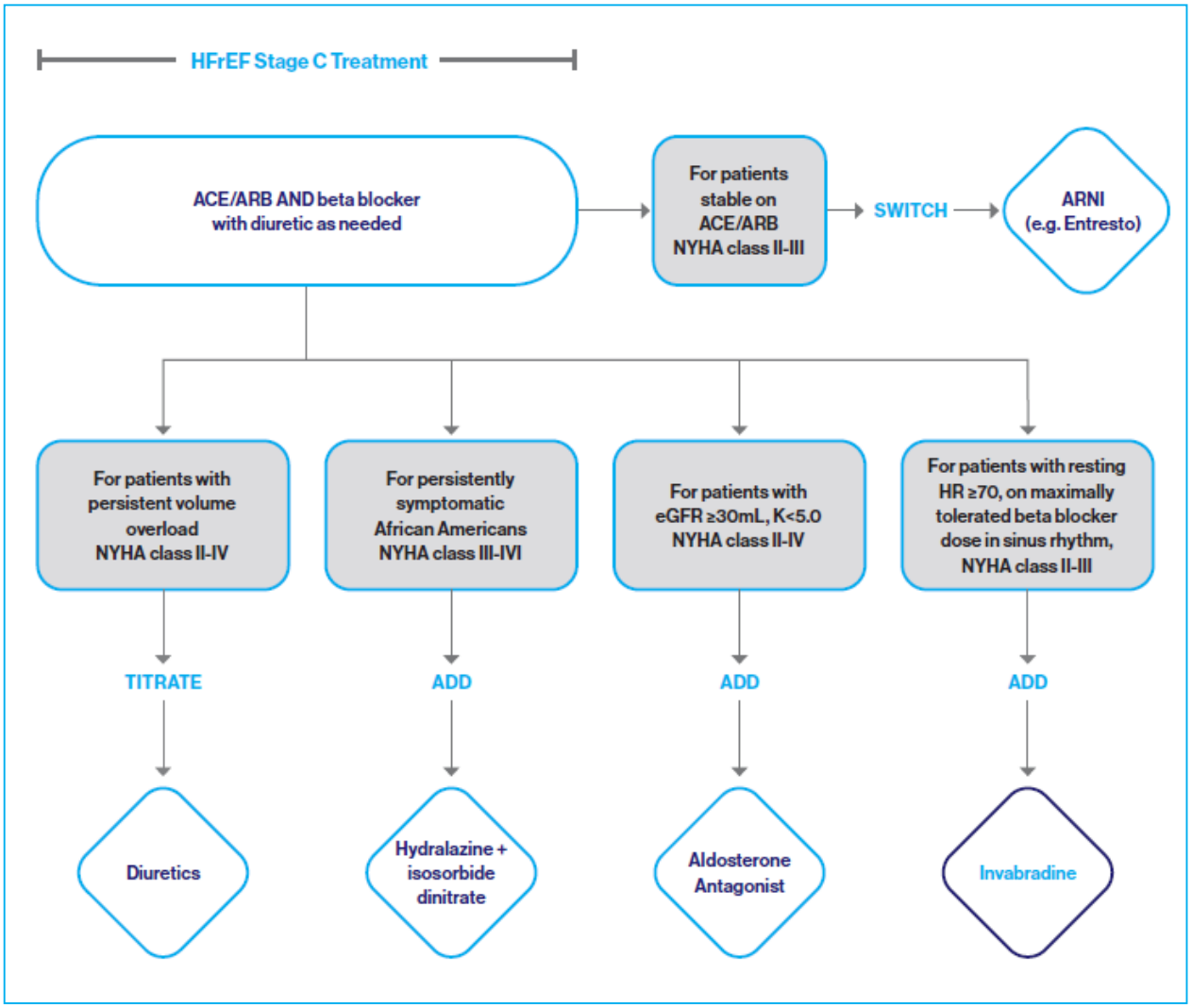
- Independent Contractor
  - Abbott Laboratories
- Honoraria for Lectures, Papers, Teaching
  - Cowen & Co

Case presentation

- A 68-year-old African American woman with hypertension, CKD-3 and T2DM presents for ongoing heart failure care
- She has a non-ischemic cardiomyopathy, LVEF 30% with Stage C HF
- She reports one-block exercise tolerance, no orthopnea or LE swelling
- Last hospitalized 3 months ago for 4 days
- Her medications are losartan 25 mg, carvedilol 3.125 mg BID, furosemide 40 mg, metformin 1000 mg bid and vitamin D
- On exam, BP 130/80, pulse 80 and regular, BMI 28. No JVD, clear lungs, regular rhythm, normal S1S2 no S3. Grade II/VI HSM. No hepatomegaly or LE edema.
- Labs: Na 138, K 4.8, BUN/Cr 28/1.4. NT-proBNP 1200 pg/mL
- EKG: NSR, LAE, LBBB, QRSd 152 msec
- CXR: cardiomegaly, clear lungs, no effusion

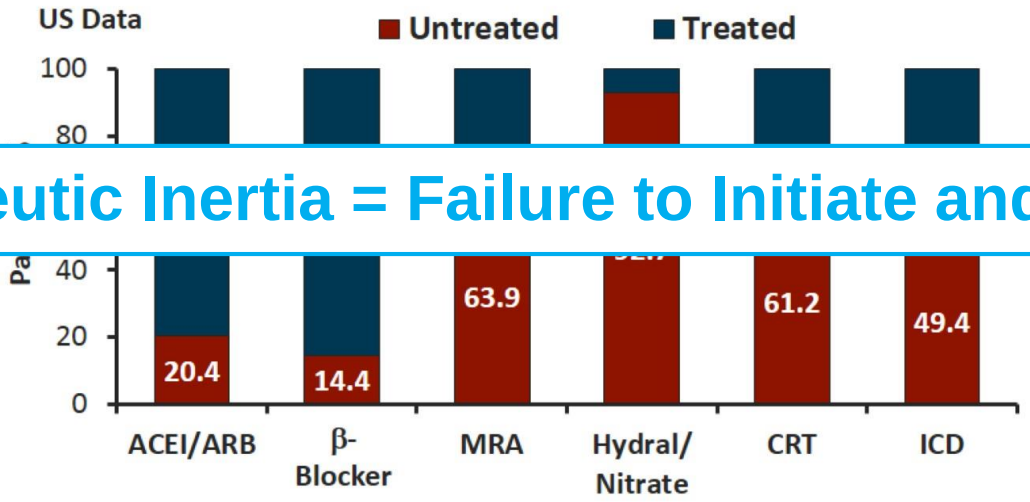
Case presentation – Cont'd

- What is the next most appropriate step in her management?
  - A. Stop losartan and start sacubitril/valsartan 24/26 mg bid
  - B. Start ISDN/hydralazine
  - C. Start spironolactone 25 mg
  - D. Add dapagliflozin 10 mg
  - E. Upgrade her ICD to a CRT-D



Heart Failure Pathway Writing Committee. J Am Coll Cardiol 2018;71(2):201-230.

A Large Number of Eligible Patients Are Untreated



	ACEI/ARB	β-Blocker	MRA	Hydral/ Nitrate	CRT	ICD
Number of Eligible Patients	2,459,644	2,512,560	603,014	150,754	326,151	1,725,732

Fonarow GC, et al. *Am Heart J*. 2011;161:1024-1030.

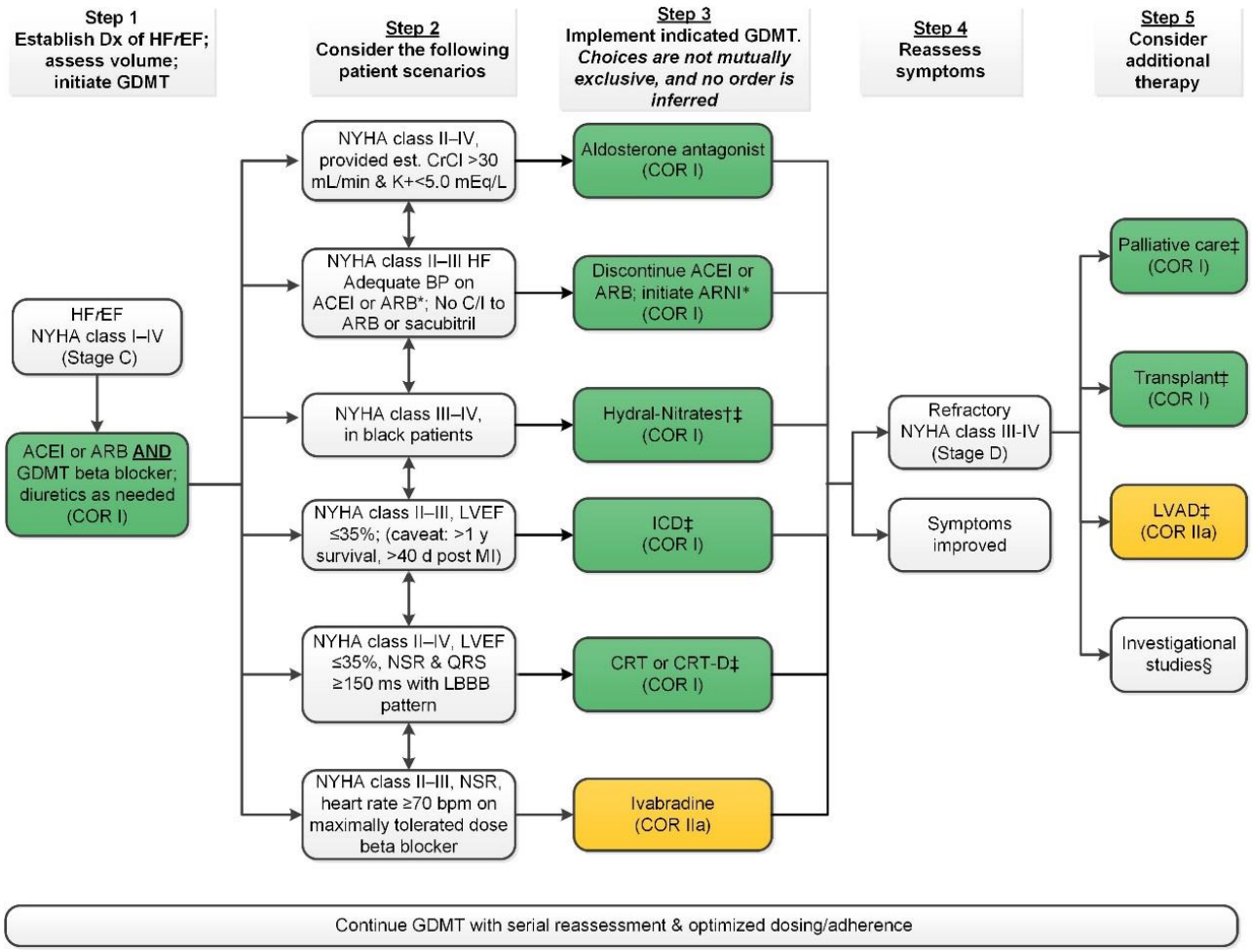
Therapeutic Inertia = Failure to Initiate and Escalate

Impact of Optimal Implementation of GDMT

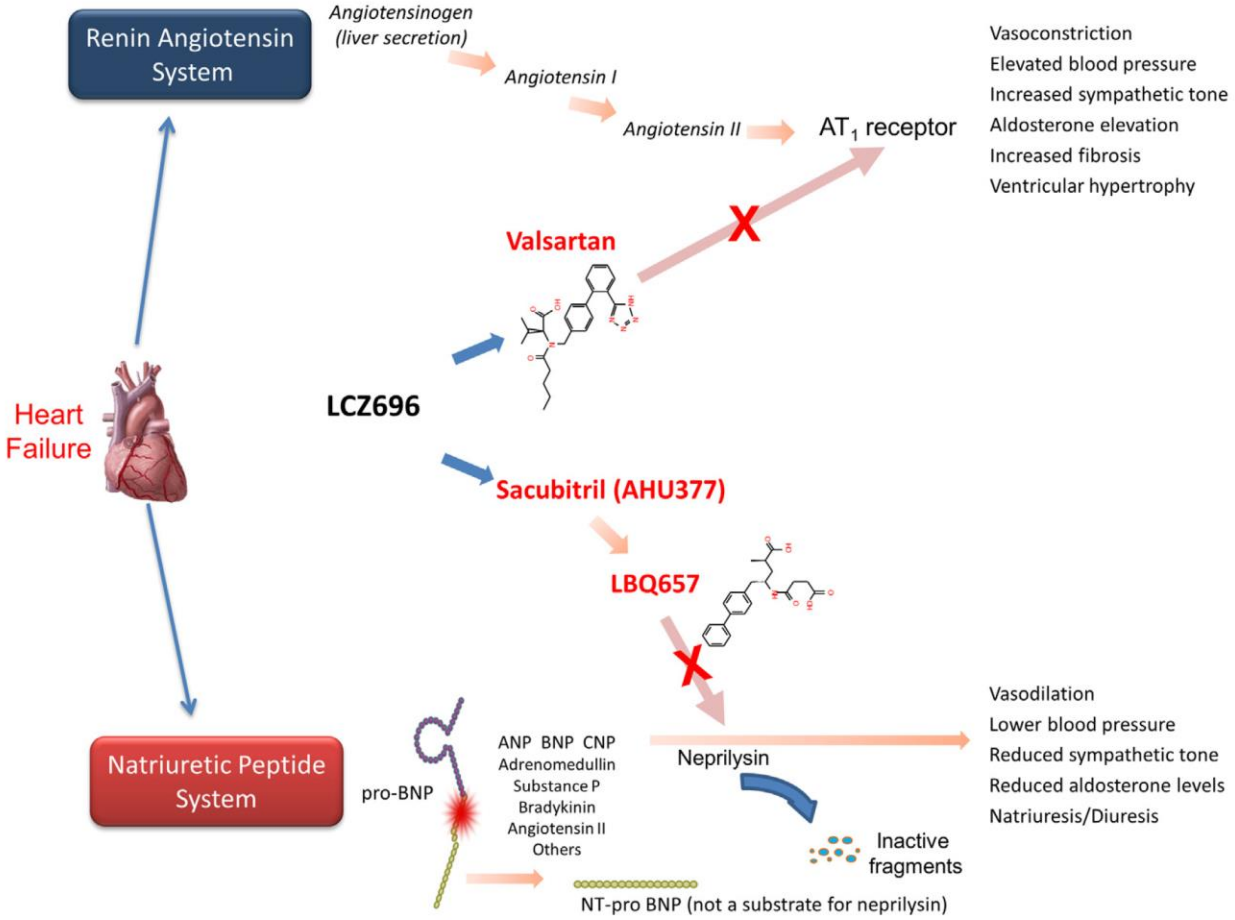
Guideline Recommended Therapy	HF Patient Population Eligible for Treatment, n*	Current HF Population Eligible and Untreated, n (%)	Potential Lives Saved per Year	Potential Lives Saved per Year (Sensitivity Range*)
ACEI/ARB	2,459,644	501,767 (20.4)	6,516	(3,336-11,260)
Beta-blocker	2,512,560	361,809 (14.4)	12,922	(6,616-22,329)
Aldosterone Antagonist	603,014	385,326 (63.9)	21,407	(10,960-36,991)
Hydralazine/Nitrate	150,754	139,749 (92.7)	6,655	(3,407-11,500)
CRT	326,151	199,604 (61.2)	8,317	(4,258-14,372)
ICD	1,725,732	852,512 (49.4)	12,179	(6,236-21,045)
Total	-	-	67,996	(34,813-117,497)
ARNI (replacing ACEI/ARB)	2,287,296	2,287,296 (100)	28,484	(18,230-41,017)

Updated from Fonarow GC, et al. *Am Heart J.* 2011;161:1024-1030. and JAMA Cardiol. 2016;1:714-17.

Treatment of HFrEF Stage C and D

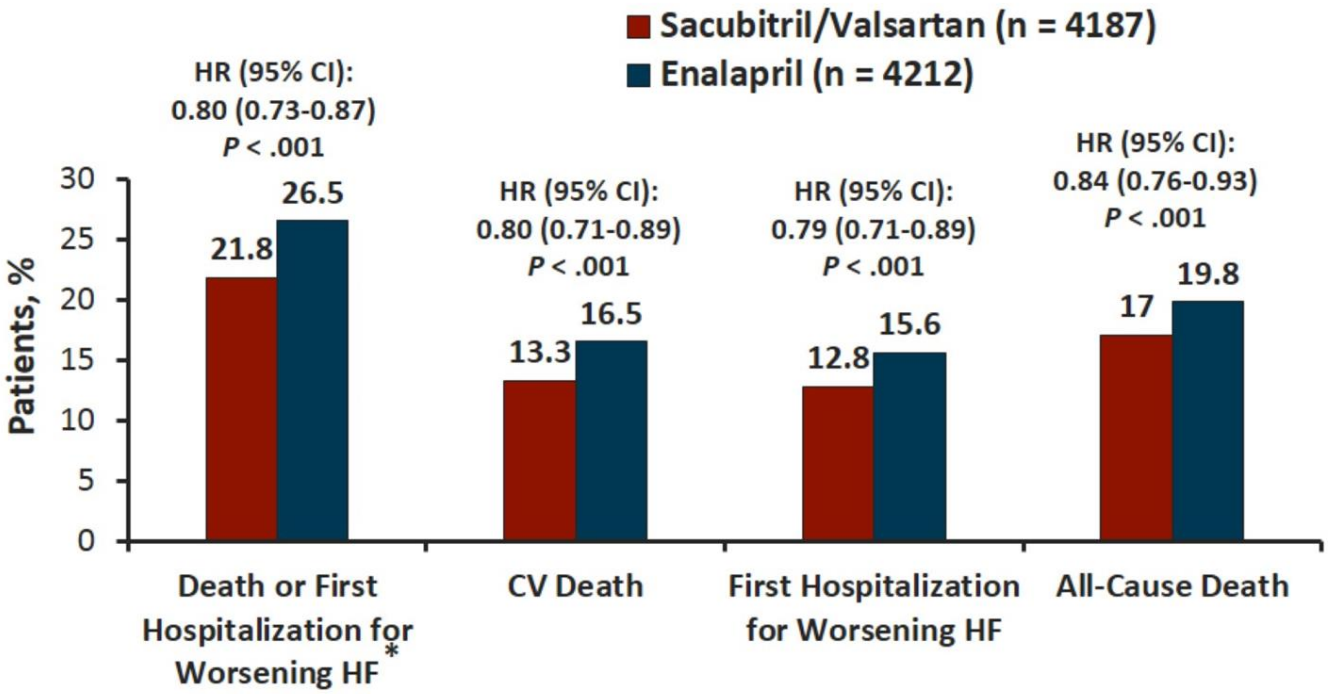


Sacubitril/Valsartan (Entresto)



Vardeney O, et al. JACC-HF 2014

PARADIGM-HF: Outcomes

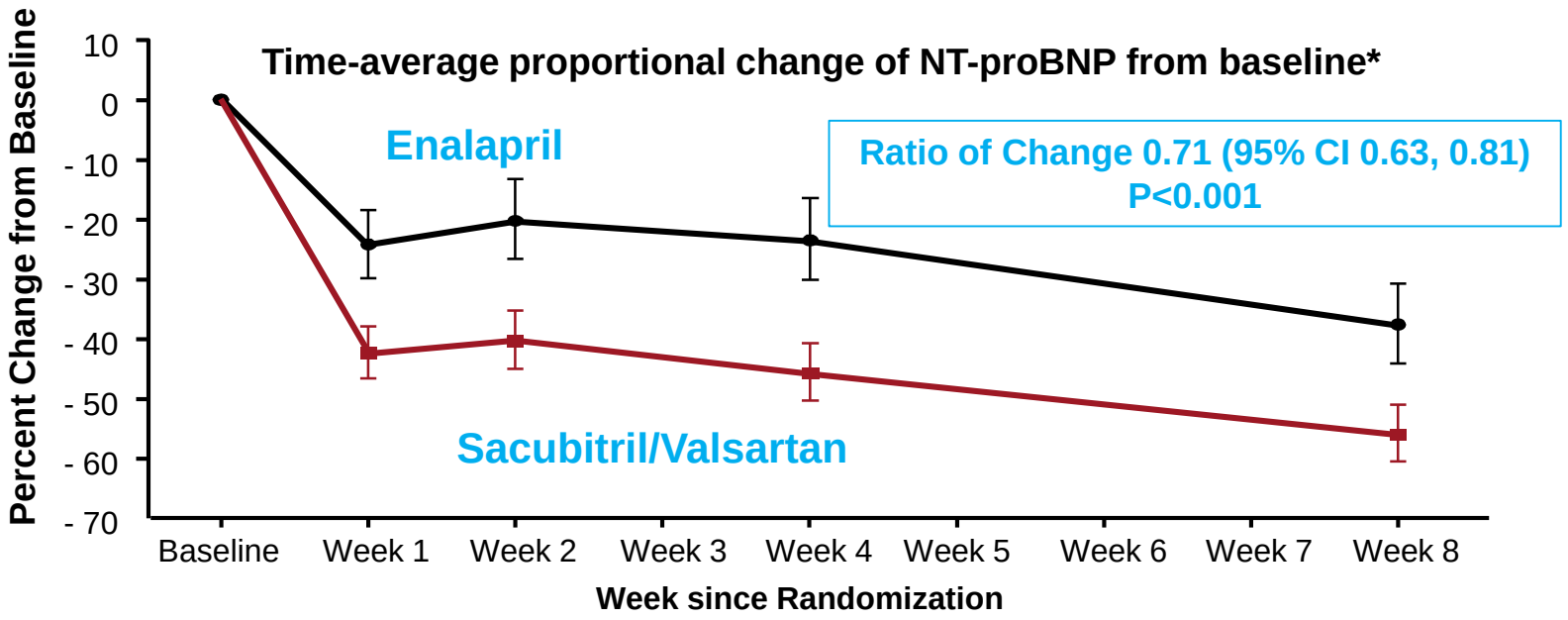


*Treatment effect was consistent across all prespecified subgroups, including NYHA Class I to II and no prior history of HF hospitalization.

McMurray JJ, et al. *N Engl J Med.* 2014;371:993-1004.

PIONEER-HF

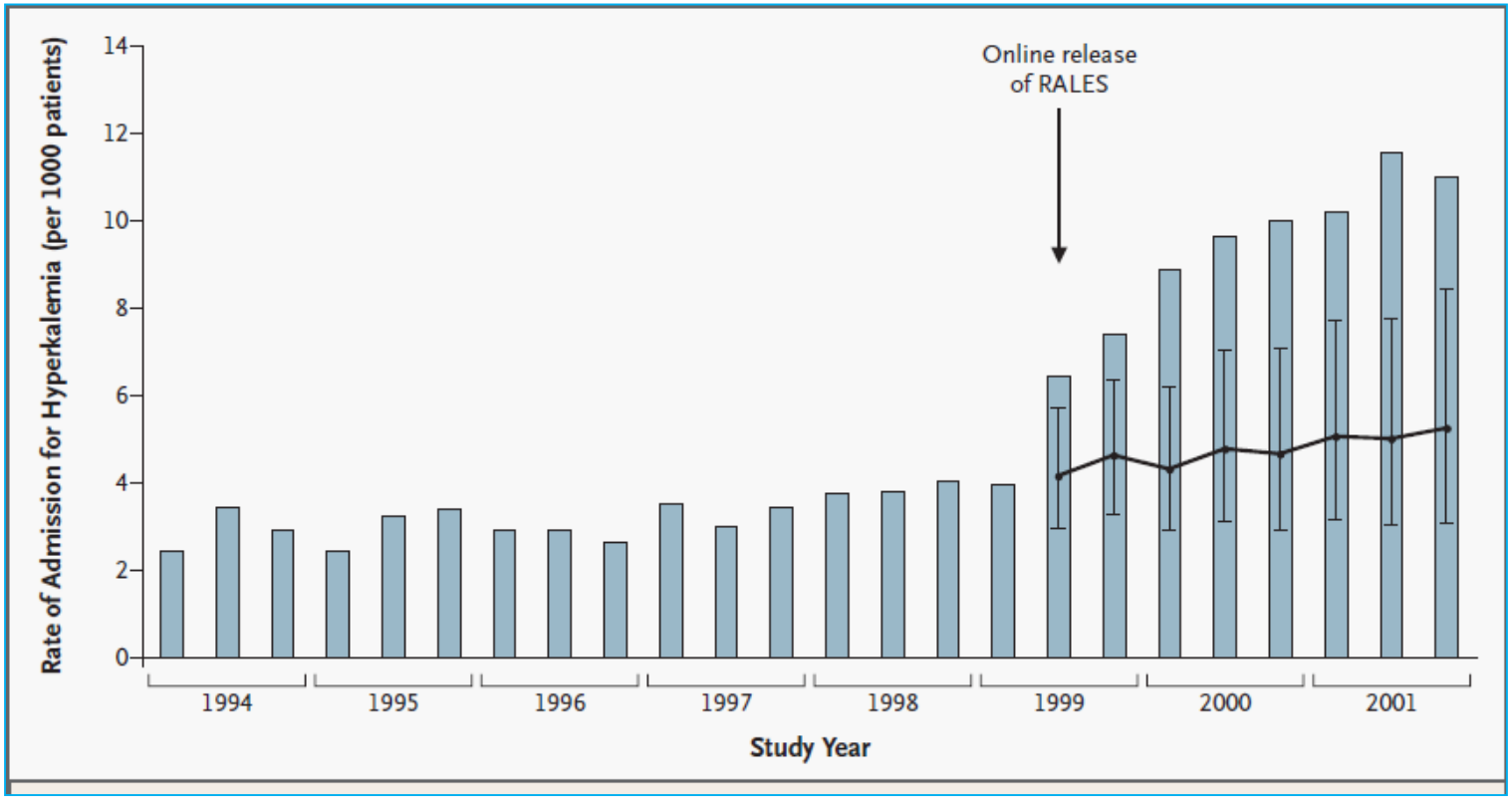
Primary Endpoint



Sacubitril/Valsartan (Entresto)

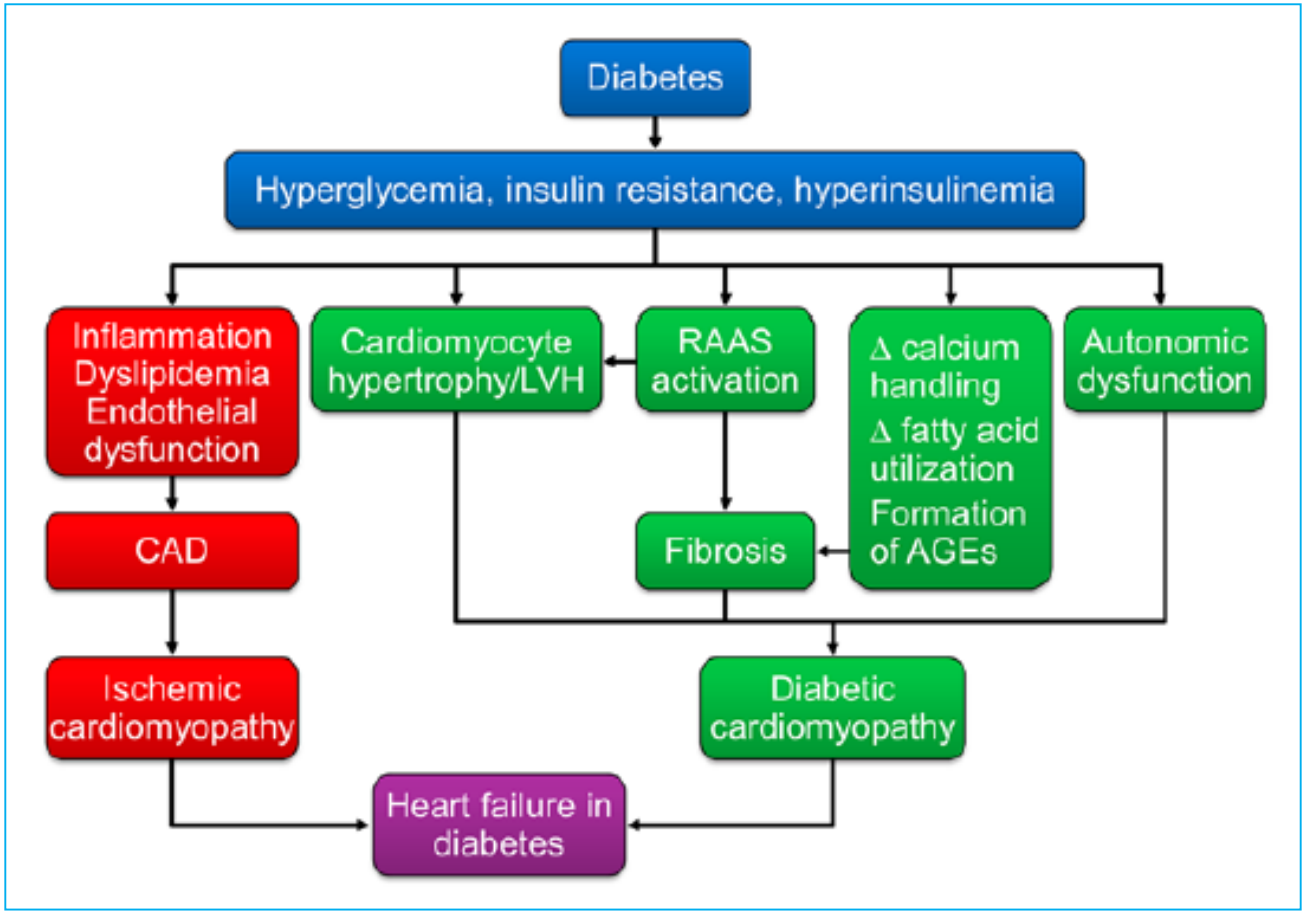
Guideline-Recommended Indications for ARNI	
Indications for Use of an ARNI • HFrEF (EF ≤40%) • NYHA class II or III HF	
Recommended Starting Dose of Sacubitril/Valsartan	
Population	**Initial Dose**
High-dose ACEI > Enolapril 10 mg total daily dose of therapeutically equivalent dose of another ACEI	**49/51 mg twice daily**
High-dose ARB > Valsartan 160 mg total daily dose of therapeutically equivalent dose of another ARB	
Low or medium dose ACEI ≤ Enalapril 10 mg total daily dose or therapeutically equivalent dose of another ACEI	**24/26 mg twice daily**
Low or medium dose ARB ≤ Valsartan 160 mg total daily dose or therapeutically equivalent dose of another ARB	
ACE/ARB naïve	
Severe renal impairment (eGFR <30 mL/min/1.73 m^2)	
Moderate hepatic impairment (Child-Pugh Class B)	
Elderly (age ≥75 years)	

Hospitalizations for Hyperkalemia



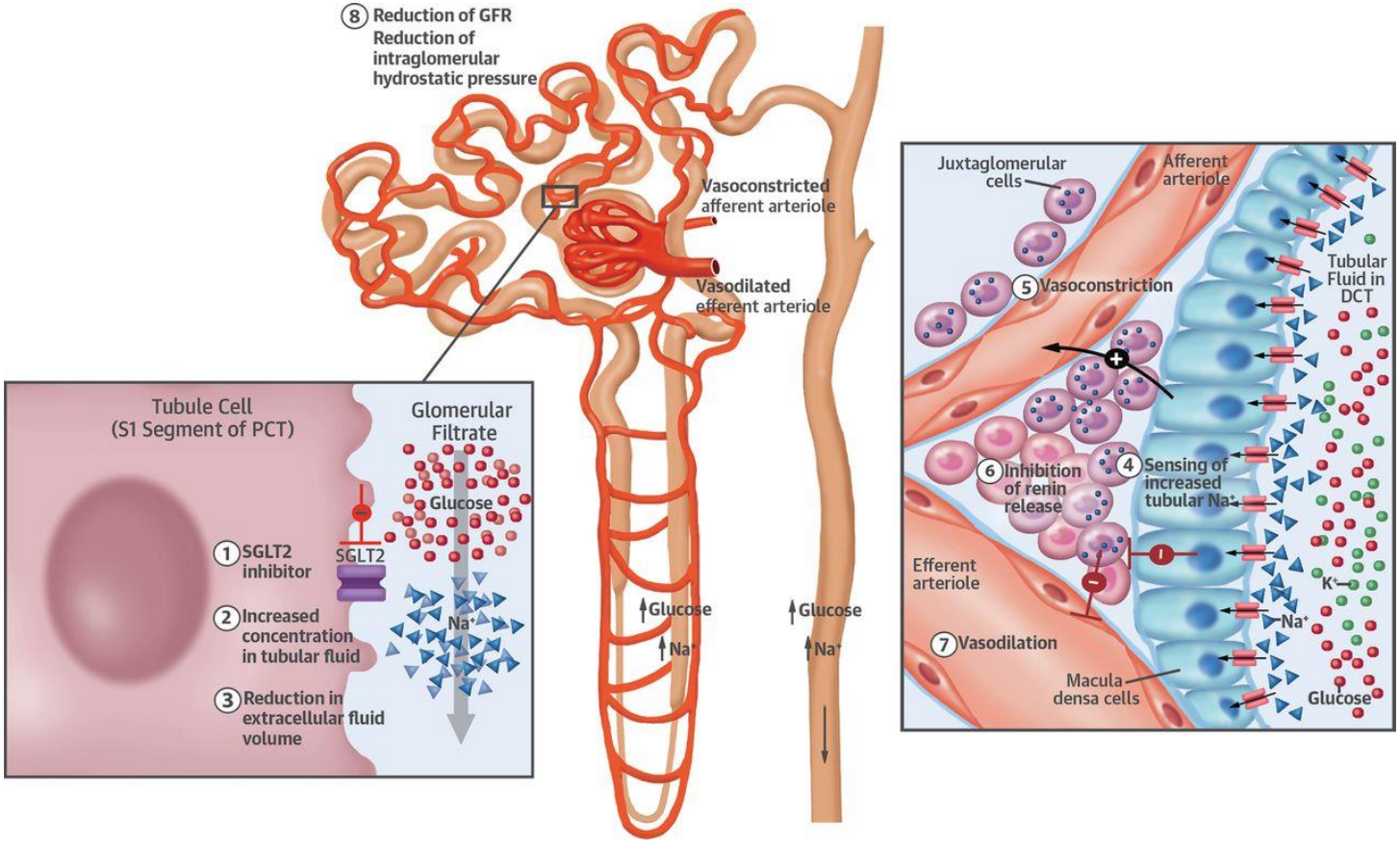
Juurlink DN et al. *N Engl J Med* 2004;351:543.

Pathophysiology of HF in Diabetes



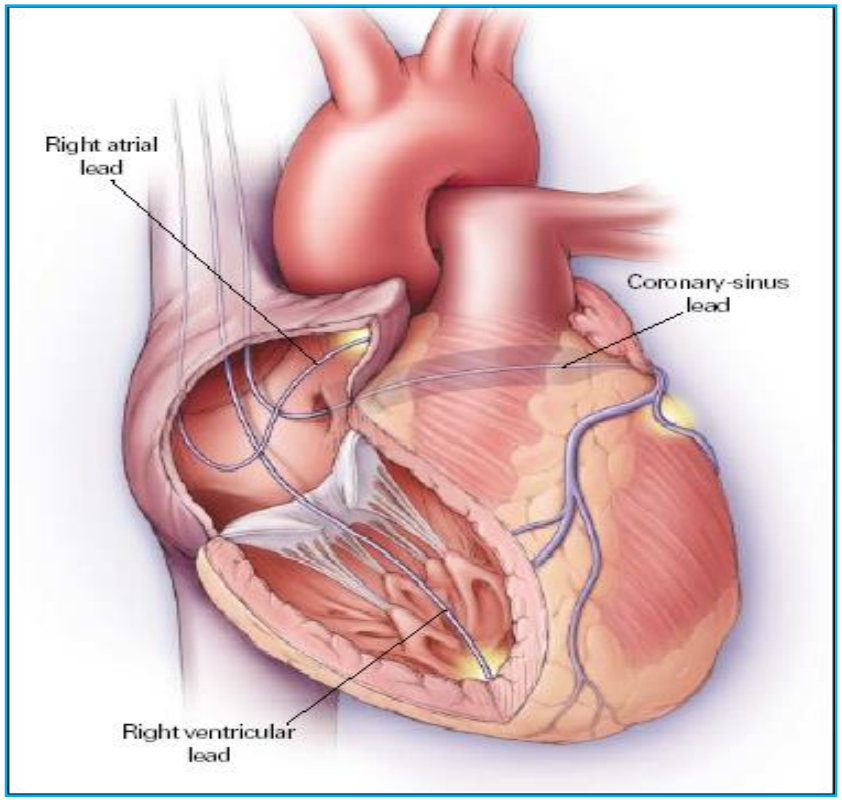
Dunlay SM et al. Circulation 2019;139:

Mechanism of SGLT2-i



Zelniker TA, Braunwald E. J Am Coll Cardiol 2018;72:1845-55.

Cardiac Resynchronization Therapy



- Reduces LV volumes, improves LVEF and produces sustained reductions in MR[1]
- Acutely reduces MR by increasing closing forces[2]
- Class I recommendation in appropriate patients: LBBB, QRSd > 150 msec, NYHA II-IV

1. St John Sutton MG et al. *Circulation* 2003;107:1985.
2. Breithardt OA et al. J Am Coll Cardiol 2003;41:765.

Hypertension

Treating Hypertension in Stage C HFrEF

COR	LOE	Recommendations	Comment/ Rationale
I	C-EO	Patients with HF*r*EF and hypertension should be prescribed GDMT titrated to attain systolic blood pressure less than 130 mm Hg.	**NEW:** Recommendation has been adapted from recent clinical trial data but not specifically tested per se in a randomized trial of patients with HF.

Case presentation – continued

- What is the next most appropriate step in her management?
  - A. Stop losartan and start sacubitril/valsartan 24/26 mg bid √
  - B. Start ISDN/hydralazine √
  - C. Start spironolactone 25 mg √
  - D. Add dapagliflozin 10 mg √
  - E. Upgrade her ICD to a CRT-D √

10 Principles to Guide HFrEF Care

Principle 1: Target doses are associated with best outcomes

Principle 2: When facing clinical scenarios that limit the ability to use target doses of all relevant therapies, a top priority should be to address the factor(s) limiting GDMT.

Principle 3: Optimal SNS modulation with target doses of beta blocker appears to have the best effect on HFrEF outcomes (cardiovascular mortality, pump failure mortality, and sudden cardiac death).

Principle 4: Although high heart rate is associated with worse outcomes, not all medications that lower heart rate impact outcomes equally.

Principle 5: African-American patients experience further benefit from the use of HYD/ISDN therapy.

Principle 6: Primary prevention device therapy and cardiac resynchronization therapy should only be considered after consistent use of optimal doses of all medications for 3 to 6 months.

Principle 7: Symptomatic congestion should be treated with diuretics irrespective of other therapies.

Principle 8: Optimize team-based care.

Principle 9: Tolerability and side effects in part depend on how and when the therapy is prescribed.

Principle 10: Focus on both the patients' symptoms and functional capacity as well as improving cardiac function.

Heart Failure Pathway Writing Committee. J Am Coll Cardiol 2018;71(2):201-230.

Studies to Order

- BNP/NT-proBNP
- CBC
- Basic metabolic panel
- EKG
- Chest X-ray
- Echocardiogram

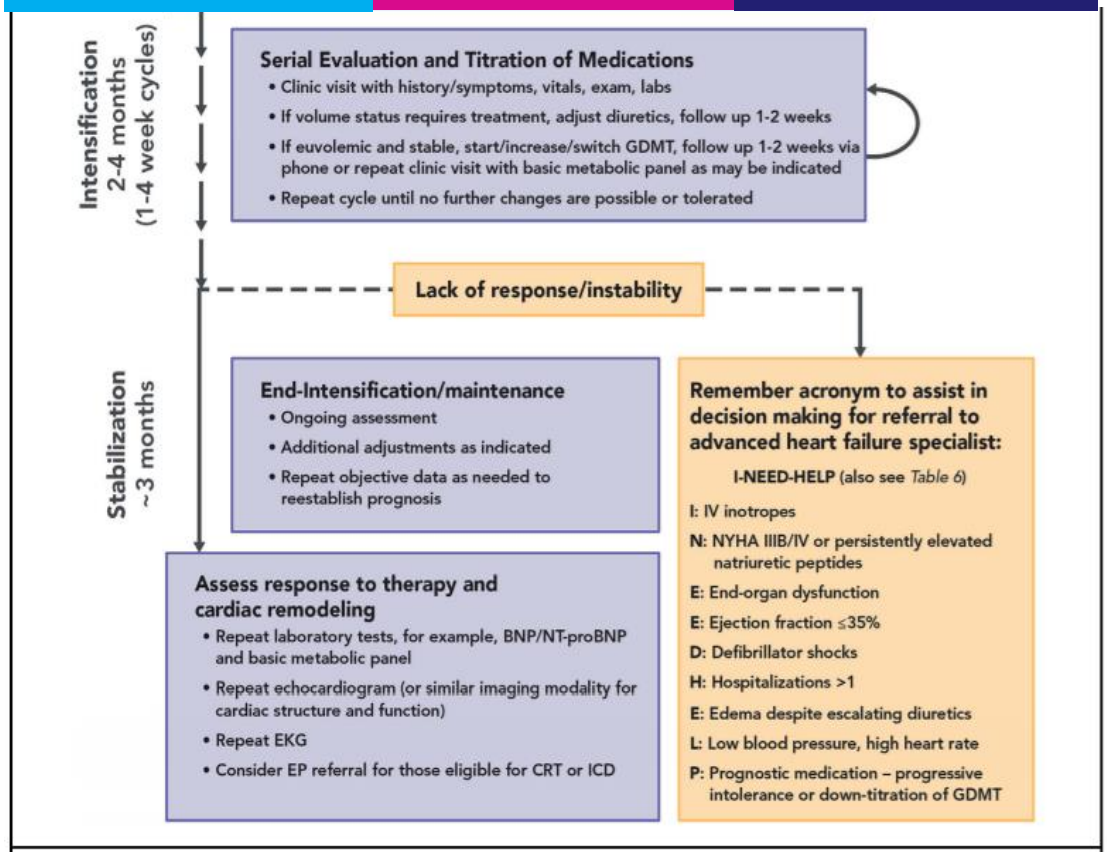
Studies to Consider

- Liver function
- Iron studies
- HbA1c
- Coronary angiogram
- Cardiac MRI

If No Cause Is Found

Consider contributing etiologies:

- Alcoholism, Substance Abuse, Cocaine
- Pulmonary disease



Triggers for HF Patient Referral to a Specialist/Advanced heart failure program
Chronic HF with high-risk features, such as development of 1 or more of the following risk factors: • Persistent NYHA functional class III-IV symptoms of congestion or profound fatigue • 2 or more emergency department visit or hospitalizations for HF in prior 12 months • Clinical deterioration as indicated by worsening edema, rising biomarkers (BNP) • Inability to tolerate GDMT – needing to reduce or withdrawal GDMT due to blood pressure or worsening renal function. • Systolic blood pressure ≤90 mm Hg or symptomatic hypotension • Creatinine ≥1.8 mg/dl or BUN ≥43 mg/dl • Onset of atrial fibrillation or ventricular arrhythmias or repetitive ICD shocks
To assist with management of GDMT, including replacement of ACEI or ARB therapy with ARNI for eligible patients, or to address comorbid conditions such as chronic renal disease or hyperkalemia, which may complicate treatment.
Annual review for patients with established advanced HF in which patients/caregivers and clinicians discuss current and potential therapies for both anticipated and unanticipated events, possible HF disease trajectory and prognosis, patient preferences, and advanced are planning.
Persistent reduced LVEF ≤35% despite GDMT for ≥3 months for consideration of device therapy in those patients without prior placement of ICD or CRT, unless decide therapy contraindicated.
Second option regarding etiology of HR; for examples • Evaluation for potential ischemic etiology • Suspected myocarditis • Established or suspected specific cardiomyopathies, e.g., hypertrophic cardiomyopathy, arrhymogenic right ventricular dysplasis, Chagas disease, restrictive cardiomyopathy, cardiac sarcoidosis, amyloid, aortic stenosis. • Valvular heart disease with or without HF symptoms.

Referral Options for Patients with HF

- **Care Management**
  - Email mshpcmreferral@mountsinai.org, call **212-241-7228**, or use the **MSHP Care Management Referral in Epic (order #391414)**
  - Prompt and efficient processing of your referral
  - Communication about assignment through Epic In-Basket
  - Follow up from clinical staff within 1 week of assignment

- **Behavioral Health**
  - Screen patients annually for depression using the PHQ-2/PHQ-9 and refer to psychiatric services

- **Palliative Care**
  - NYHA class III/IV symptoms with frequent readmissions
  - Anxiety/depression adversely affecting quality of life or ability to manage illness
  - Assistance with decision making regarding advanced therapies
  - Martha Stewart Center for Living, 1440 Madison Avenue, **212-241-1446**
  - Martha Stewart Center for Living Downtown, Union Square, **212-844-1712**

HFrEF Guideline Directed Medical Therapy

	Starting dose	Target dose
Beta Blockers		
Bisoprolol	1.25 mg once daily	10 mg once daily
Carvedilol	3.125 mg twice daily	25 mg twice daily for weight <85 kg and 50 mg twice daily for weight ≥85 kg
Metoprolol succinate	12.5-25 mg/d	200 mg daily
ARNI		
Sacubitril/valsartan	24/26 mg-49/51 mg twice daily	97/103 mg twice daily
ACEI		
Captopril	6.25 mg 3× daily	50 mg 3x daily
Enalapril	2.5 mg twice daily	10-20 mg twice daily
Lisinopril	2.5-5 mg daily	20-40 mg daily
Ramipril	1.25 mg daily	10 mg daily
ARB		
Candesartan	4-8 mg daily	32 mg daily
Losartan	25-50 mg daily	150 mg daily
Valsartan	40 mg twice daily	160 mg twice daily

	Starting dose	Target dose
Aldosterone antagonists		
Eplerenone	25 mg daily	50 mg daily
Spironolactone	12.5-25 mg daily	25-50 mg daily
Vasodilators		
Hydralazine	25 mg 3× daily	75 mg 3× daily
Isosorbide dinitrate*	20 mg 3× daily	40 mg 3× daily
Fixed-dose combination isosorbide dinitrate/ hydralazine†	20 mg/37.5 mg (one tab) 3× daily	2 tabs 3× daily
Ivabradine		
Ivabradine	2.5-5 mg twice daily	Titrate to heart rate 50-60 bpm. Maximum dose 7.5 mg twice daily

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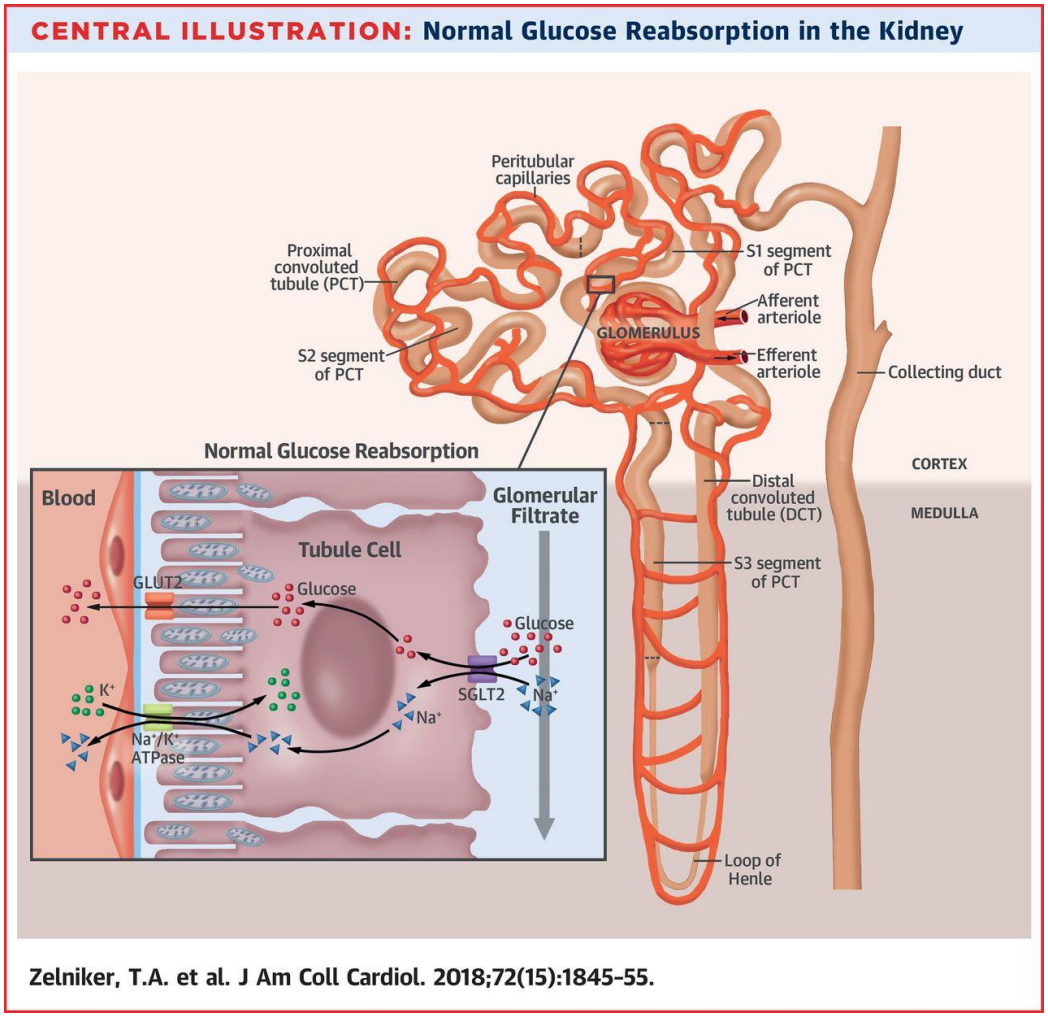


- 180 gm glucose filtered per day
- ~ 90% reabsorbed S1 segment of PCT by SGLT-2
- ~ 10% reabsorbed S2/S3 segments of PCT by SGLT-1
- Virtually no glucose excreted in the urine

Thank You!

Questions?

Management of COPD

Stacey-Ann Brown, MD MPH

Assistant Professor

Division of Pulmonary, Critical Care and Sleep Medicine

February 13, 2020

Mount Sinai Health Partners

Table of Contents

COPD: Definition and Classification

“COPD is a common, preventable and treatable disease that is characterized by *persistent respiratory symptoms* and *airflow limitation* that is due to airway and/or alveolar abnormalities *usually caused by significant exposure* to noxious particles or gases.”

-GOLD definition

COPD Epidemiology

- **14 million** patients have COPD in the US [1].
- **Third (3rd)** leading cause of death [2].
- May be underdiagnosed; **24 million** have obstruction on spirometry in a population-based survey [3].
- **High cost-burden**: 8 million office visits, 1.5 million ED visits, 715,000 hospitalizations, $50 billion annually in spending [4,5].

1. Ford E et al. Chest, 2013. 144(1): p. 284-305.
2. Hoyert et al. Natl Vital Stat Rep 2011; 61(6): 1-65.
3. Mannino DM et al. MMWR Surveill Summ . 2002 ; 51(6):1–16
4. Centers for Disease Control and Prevention; National Center for Health Statistics . 2010
5. Guarascio AJ et al. CEOR 2013; 5: 235-45.

COPD Pathogenesis

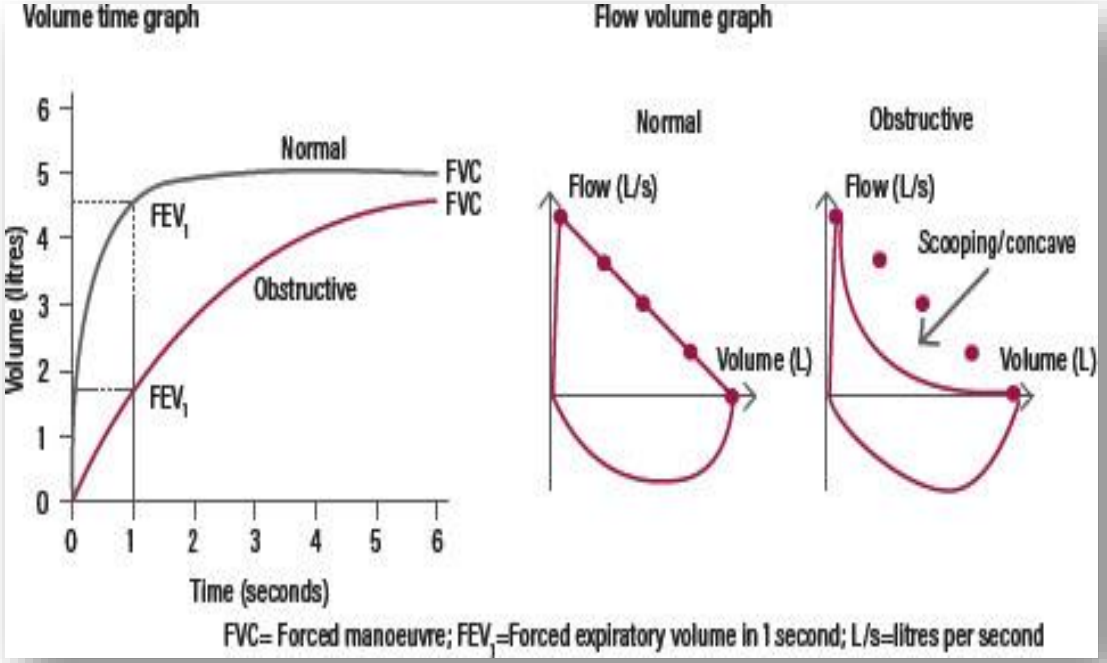
- Tobacco smoke results in airway inflammation involving innate (neutrophils, macrophages) and adaptive immune responses (Th1 mediated).

- Some patients have eosinophilic inflammation (Th2 mediated) which may lead to increased steroid responsiveness.

- Pro-inflammatory mediators and oxidative stress lead to:
  - Small airway narrowing:
    - Peribronchiolar fibrosis
    - Mucosal/submucosal thickening from smooth muscle
    - Hypertrophy and mucus gland enlargement
    - Intraluminal exudate/mucus
  - Proteolytic destruction of the lung (emphysema)

COPD: Spirometric Assessment

- Persistent airflow limitation: post-bronchodilator FEV1/FVC ratio < 70%
- Only 31-42% received spirometrically-confirmed diagnosis in 2018 [1].



1. National Committee for Quality Assurance. http://www.ncqa.org/ReportCards/HealthPlans/StateofHealthCareQuality.aspx. Accessed February 5, 2020.
2. Rush. Primary Health Care. 2017 (28)2, 34-41. Imaged Accessed at https://dm3omg1n1n7zx.cloudfront.net/rcni/static/journals/phc/28/2/phc.2018.e1367/graphic/phc_v28_n2_21_0005.jpg Accessed February 5, 2020

COPD: Spirometric Stage

CLASSIFICATION OF AIRFLOW LIMITATION SEVERITY IN COPD (BASED ON POST-BRONCHODILATOR FEV_1)		
In patients with FEV1/FVC < 0.70:		
GOLD 1:	Mild	$FEV_1 \geq 80\%$ predicted
GOLD 2:	Moderate	$50\% \leq FEV_1 < 80\%$ predicted
GOLD 3:	Severe	$30\% \leq FEV_1 < 50\%$ predicted
GOLD 4:	Very Severe	$FEV_1 < 30\%$ predicted

TABLE 2.4

COPD: Beyond Spirometry

- COPD severity is an interplay of **lung function, symptom burden** and **exacerbation history.**
- Lung function correlates weakly with symptom burden [1].
- Dyspnea and high symptom burden are independent risk factor for mortality [2-3].

1. Mahler DA. Chest 1984;85:751-758
2. Nishimura K. Chest 2002;121:1434-1440
3. Domingo-Salvany A. Am J Respir Crit Care Med 2002;166:680-685

MODIFIED MRC DYSPNEA SCALE[a]

PLEASE TICK IN THE BOX THAT APPLIES TO YOU | ONE BOX ONLY | Grades 0 - 4

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

[a] Fletcher CM. BMJ 1960; 2: 1662.

TABLE 2.5

CAT™ ASSESSMENT

For each item below, place a mark (x) in the box that best describes you currently.
Be sure to only select one response for each question.

EXAMPLE: I am very happy	0 (X) 2 3 4 5	**I am very sad**	**SCORE**
I never cough	0 1 2 3 4 5	I cough all the time	
I have no phlegm (mucus) in my chest at all	0 1 2 3 4 5	My chest is completely full of phlegm (mucus)	
My chest does not feel tight at all	0 1 2 3 4 5	My chest feels very tight	
When I walk up a hill or one flight of stairs I am not breathless	0 1 2 3 4 5	When I walk up a hill or one flight of stairs I am very breathless	
I am not limited doing any activities at home	0 1 2 3 4 5	I am very limited doing activities at home	
I am confident leaving my home despite my lung condition	0 1 2 3 4 5	I am not at all confident leaving my home because of my lung condition	
I sleep soundly	0 1 2 3 4 5	I don't sleep soundly because of my lung condition	
I have lots of energy	0 1 2 3 4 5	I have no energy at all	

TOTAL SCORE: ◯

Reference: Jones et al. ERJ 2009; 34 (3); 648-54.

FIGURE 2.3

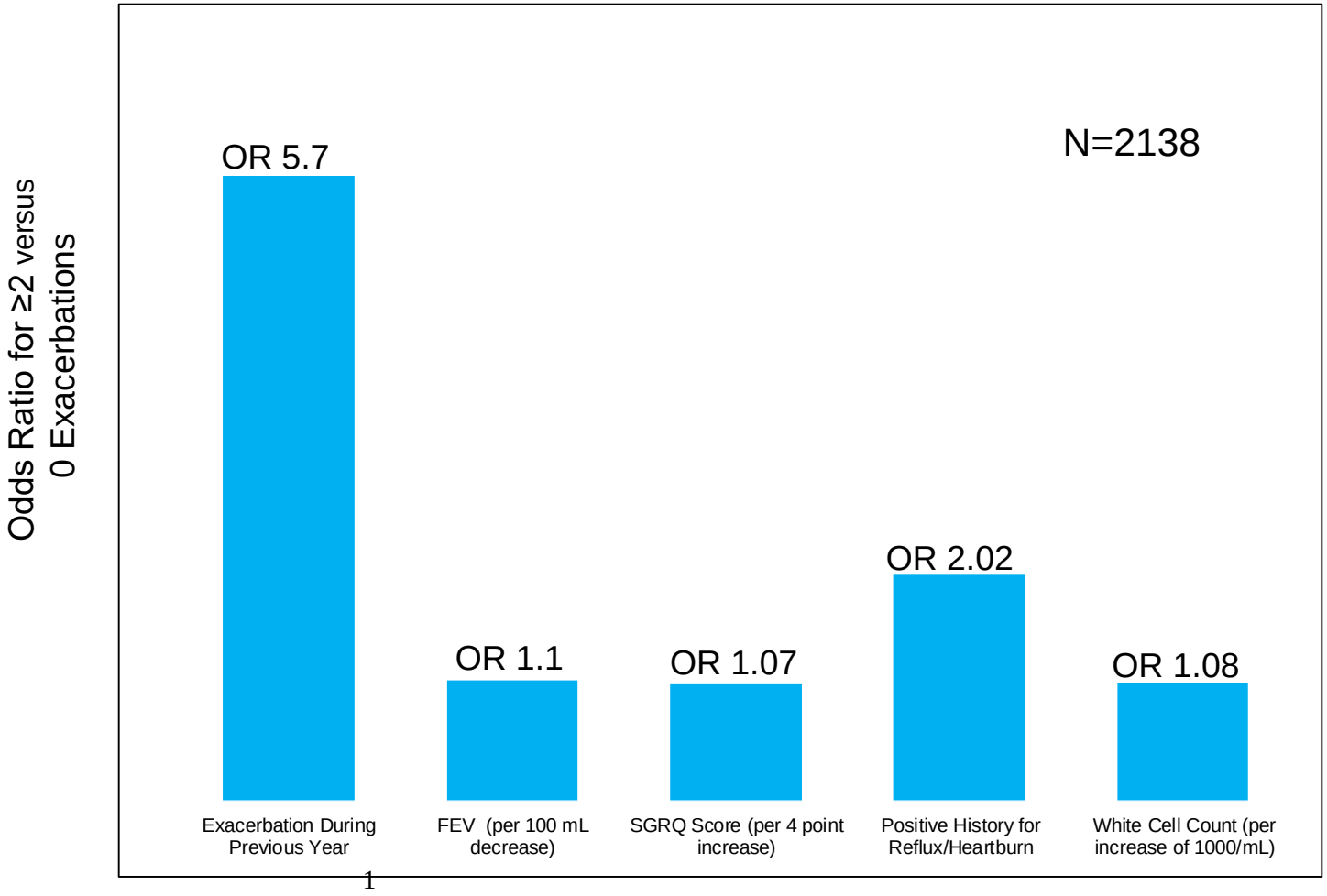
COPD: Exacerbations

- Defined as any change in symptoms requiring additional therapy [1].
- At least 2 consecutive days of at least 2 major criteria, or 1 major and 1 minor criteria [2].
  - **Mild exacerbation**: treated with bronchodilators only
  - **Moderate exacerbation**: treated with steroids and antibiotics
  - **Severe exacerbation**: any exacerbation requiring ED visit or hospitalization.

Major Criteria	Minor Criteria
Increased sputum volume	Wheezing
Sputum purulence	Sore throat
Dyspnea	Nasal congestion
	Cough

1. Global Initiative for Chronic Obstructive Lung Diseases. 2020.
2. Seemungal TA et al. Am J Respir Crit Care Med, 2000.161(5): 1608-13.

Factors Associated With Increased Exacerbation Frequency



Hurst JR, et al. N Engl J Med. 2010;363:1128-1138.

THE REFINED ABCD ASSESSMENT TOOL

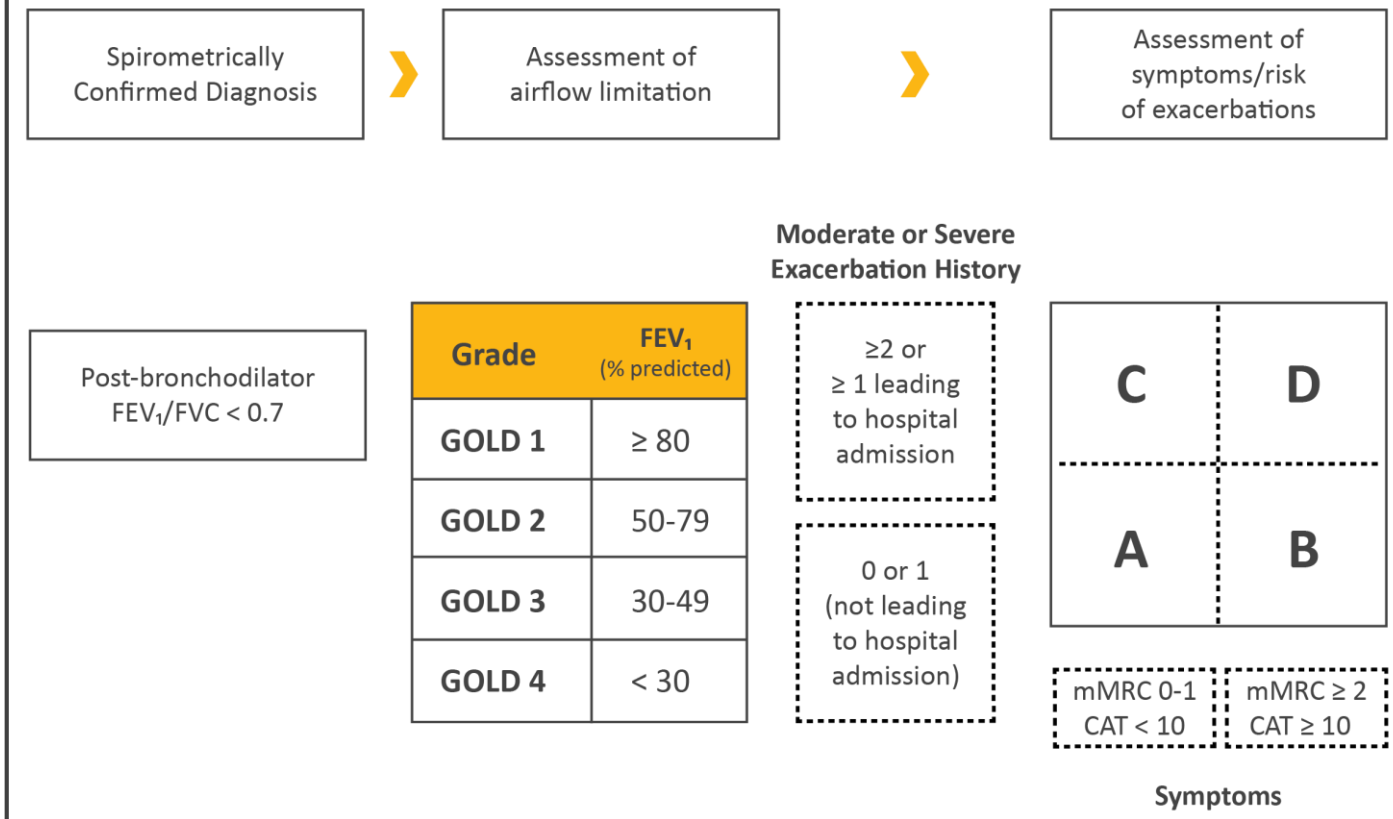


FIGURE 2.4

A Personalized Approach to Diagnosing COPD

- A COPD patient with a post-bronchodilator FEV1 of 40% who was very symptomatic (CAT score=15) with only 1 moderate exacerbation in the past year (without hospitalization) would be GOLD stage 3, Group B.

- Management is determined by ABCD group, not spirometric stage.

COPD: Pharmacologic Management

Key Principles

1. Modes of Delivery of Inhaled Devices
2. Initial Pharmacologic Delivery
3. Dose Escalation
4. De-escalating Therapy if Appropriate
5. Oral Medications

Pharmacologic Therapy

- 4 Types of Inhaled Devices:
  - Pressurized Metered Dose Inhaler (MDI)
  - Soft Mist Inhaler (SMI)
  - Dry Powder Inhaler (DPI)
  - Nebulizer

- 3 Classes of Drugs:
  - Beta-Agonists
  - Muscarinic Antagonists
  - Inhaled corticosteroids

Types of Inhalers Devices

- MDI
  - Advantages: Multiple doses (≥100/inhaler), compact, portable, available for most inhaled medicines, short administration time, low cost, and can be used with a “spacer”
  - Disadvantages: Requires coordination and sufficient hand strength, propellant causes some patients to stop inhaling when the medicine hits the back of the throat (**the “cold freon” effect**), needs to be shaken prior use

- DPI
  - Advantages: Does not require coordination of inhalation and actuation, does not contain propellant, compact, and portable
  - Disadvantages: Requires patient to generate sufficient inspiratory force **(PIF rate >30 mL/min)**, generally not suitable for young children or elderly

Types of Inhalers Devices (Continued)

- SMI
  - Advantages: No propellant, easy to use for patients with impaired dexterity, high lung deposition, and does not require coordination
  - Disadvantages: Requires dose loading into device and priming

- Nebulizer
  - Advantages: No coordination, propellant free, and high patient adherence
  - Disadvantages: Long administration time, bulky, much less portable compared to all other inhalers, needs power source, and requires daily cleaning

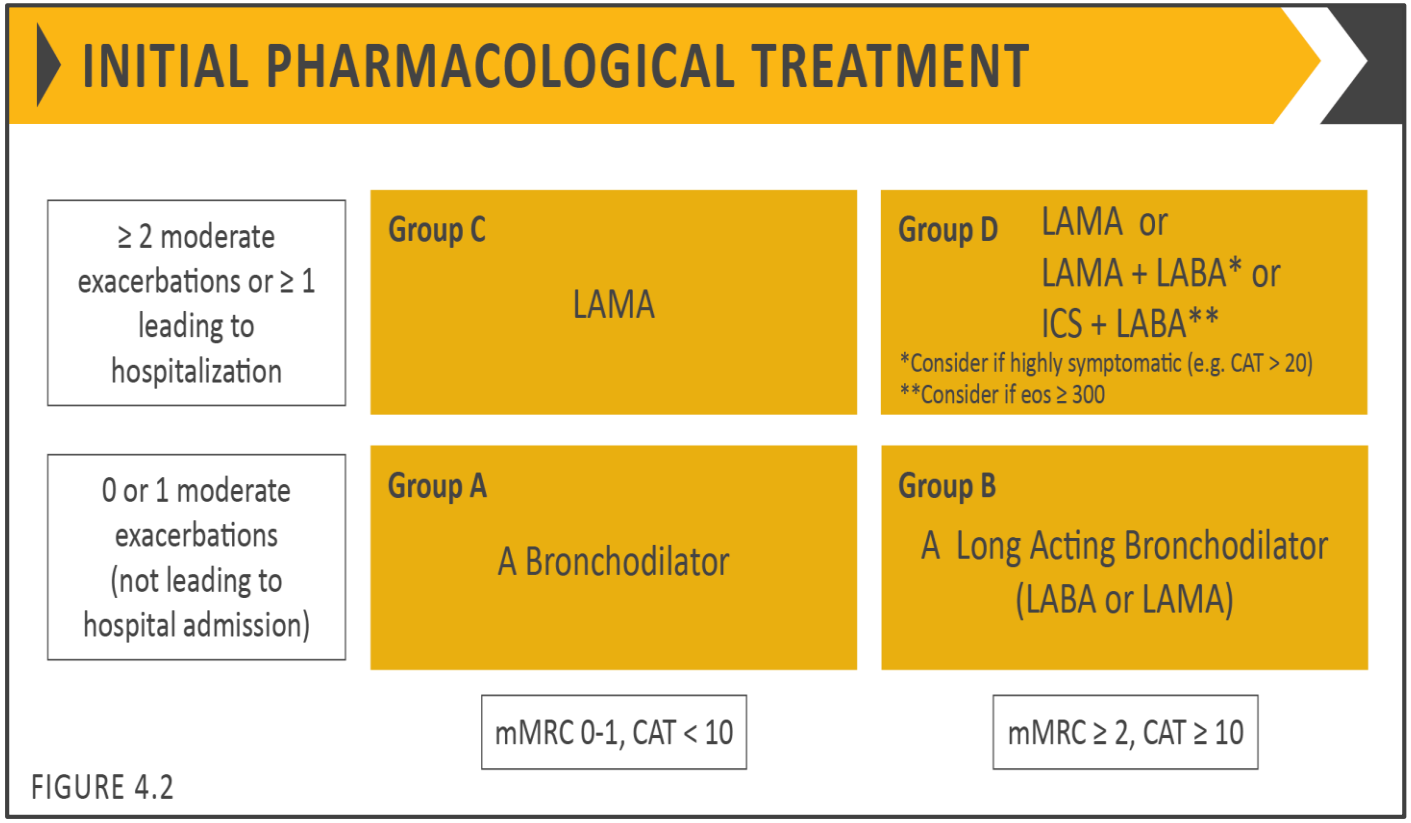
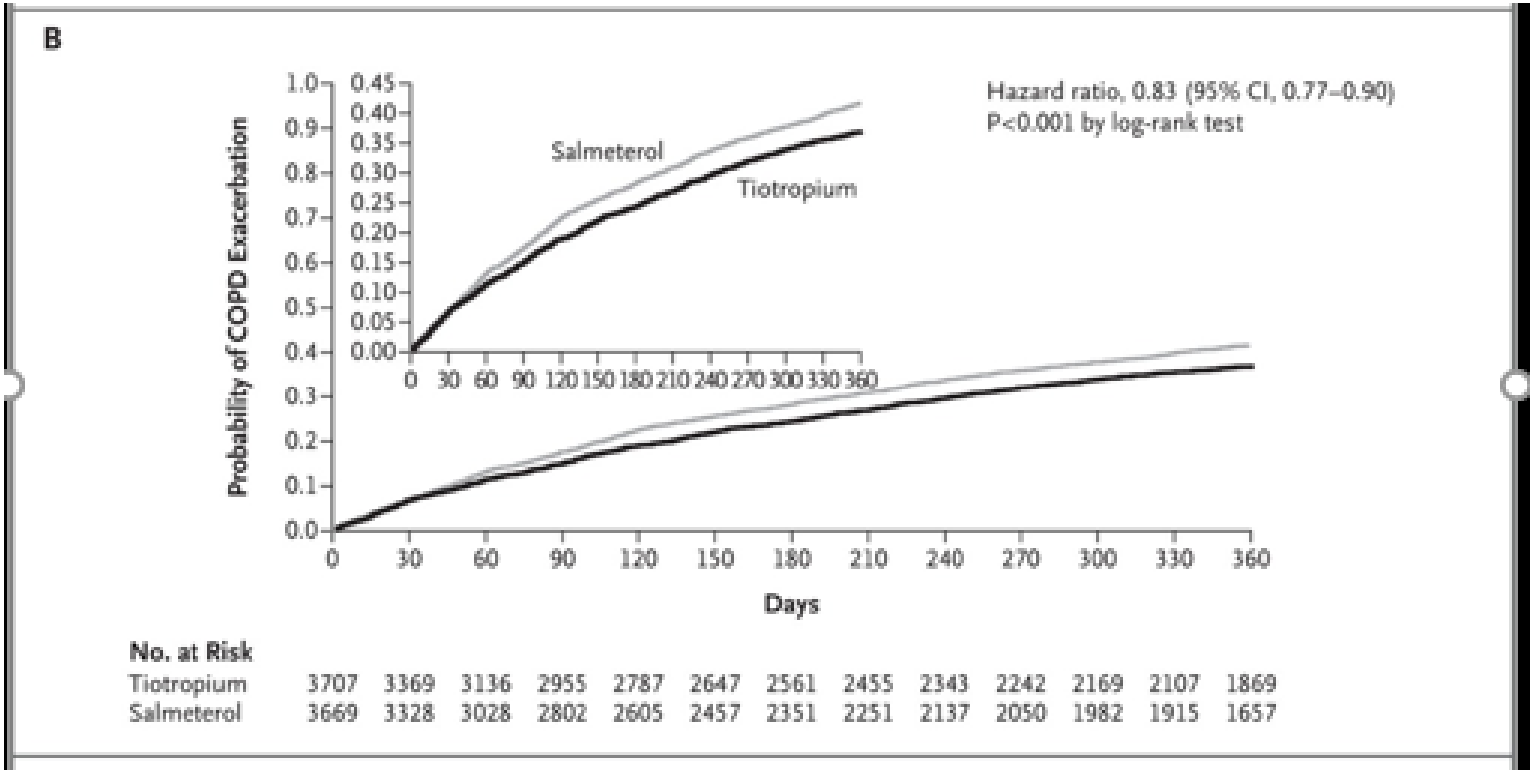


FIGURE 4.2

Efficacy of LAMA vs. LABA in Reducing Exacerbations (Groups C-D)



Vogelmeier C et al. N Engl J Med 2011;364:1093-1103.

Use of Combined LAMA/LABA for Symptomatic COPD Patients

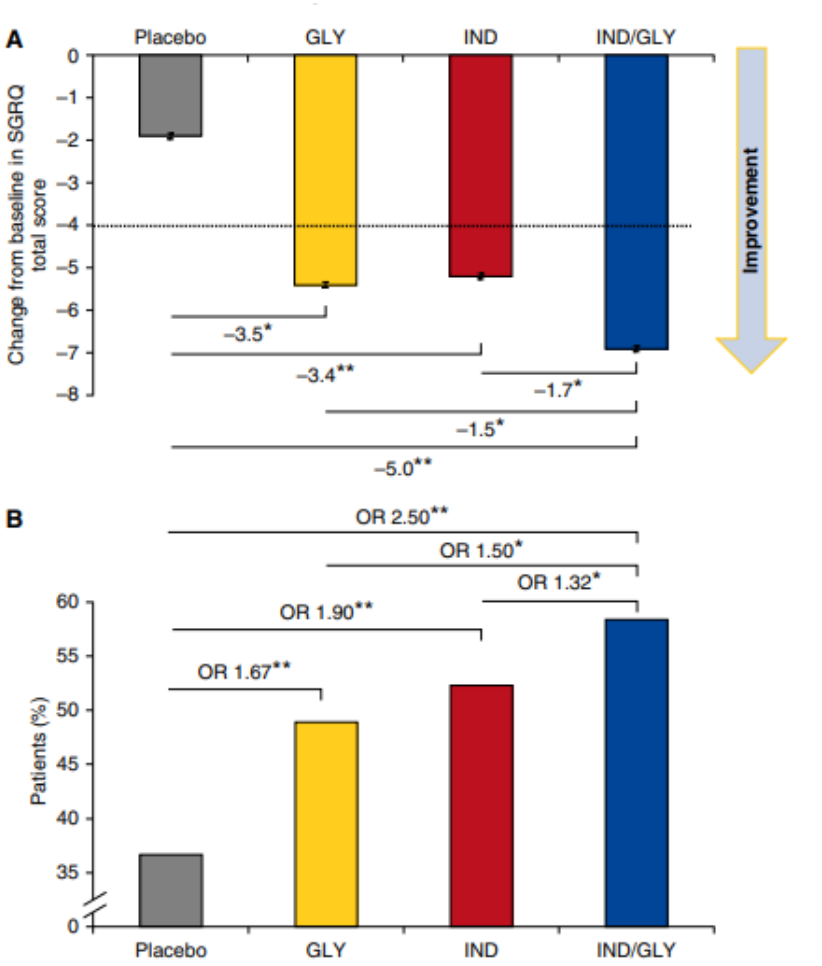
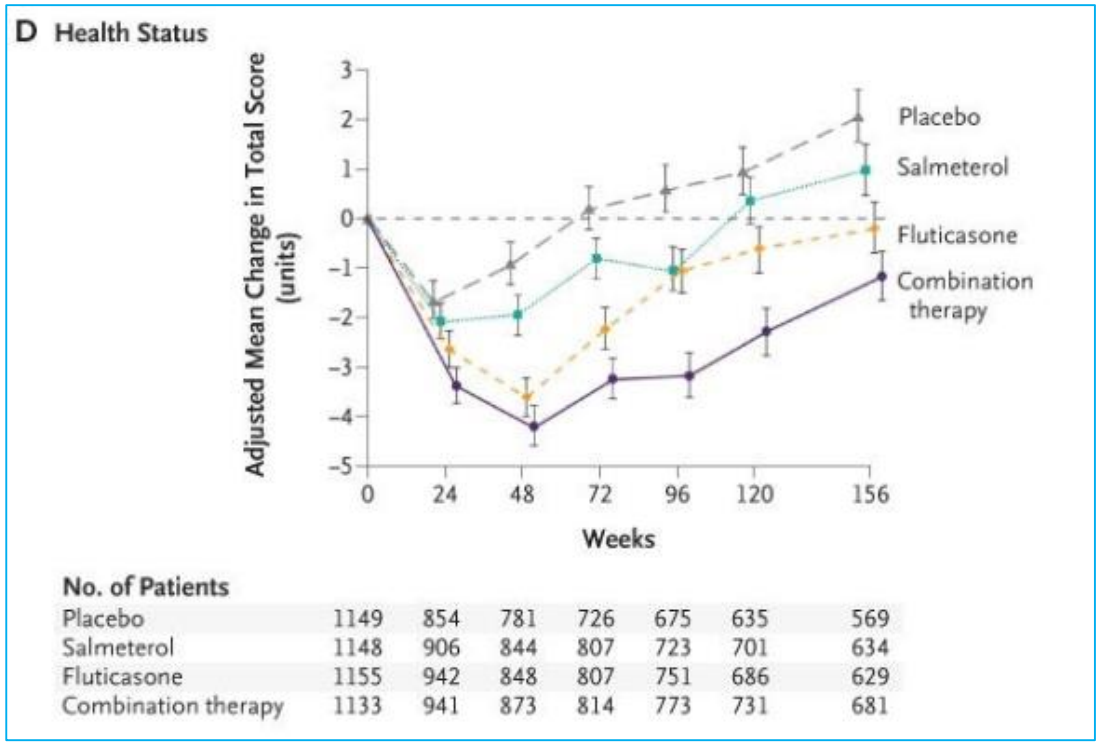


Figure 5. Pooled analysis of SGRQ total score (*A*) and percentage responders (*B*) at Week 12. $^{**}P < 0.001$; $^{*}P < 0.05$; data are least-squares mean ± SE; *dotted line* represents clinically meaningful improvement in SGRQ total score. GLY = glycopyrrolate; IND = indacaterol; OR = odds ratio; SGRQ = St. George's Respiratory Questionnaire.

Mahler et al. Am J Respir Crit Care Med 1921068-1079.

Use of Inhaled Corticosteroids in COPD

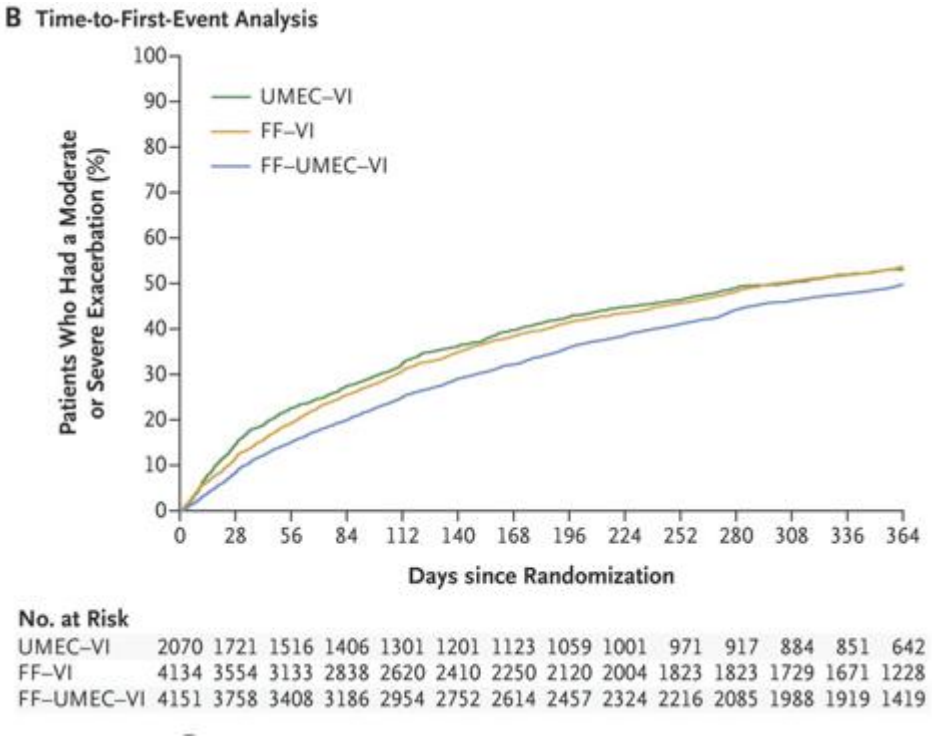


No. of Patients							
Placebo	1149	854	781	726	675	635	569
Salmeterol	1148	906	844	807	723	701	634
Fluticasone	1155	942	848	807	751	686	629
Combination therapy	1133	941	873	814	773	731	681

Moderate to Severe Exacerbations	
	Rate Ratio (95% CI)
Combination therapy vs. placebo	0.75 (0.69-0.81)
Combination therapy vs. salmeterol	0.88 (0.81-0.95)
Combination therapy vs. fluticasone	0.91 (0.84-0.99)

Calverley PM. N Engl J Med. 2007 Feb 22;356(8):775-89.

Inhaled Corticosteroids in Escalating Therapy for Severe COPD (Group D)



- LAMA/LABA/ICS reduced risk of severe exacerbation
  - 15% compared to LABA/ICS
  - 25% compared to LAMA/ICS

DA Lipson et al. N Engl J Med 2018;378:1671-1680.

Inhaled Corticosteroids: Risk of Pneumonia and Role of Eosinophilia

- Inhaled corticosteroids (ICS) increased the risk of pneumonia relative to LAMA/LABA (HR, 1.53; 95% CI, 1.22 to 1.92)
  - Consistent with a Cochrane meta-analysis of ICS in COPD (OR 1.62-1.78) [1].

- There was effect modification by eosinophil count.
  - Eosinophil count <150 cells/µL, rate reduction was 12% relative to LAMA/LABA
  - Eosinophil count>150 cells/µL, rate reduction was 44% relative to LAMA/LABA

- Post-hoc analysis demonstrated efficacy of ICS-LABA at an eosinophilic cutoff of 100 cells/µL [2].

1. Kew KM et al. Cochrane Database Syst Rev, 2014 (3): p.Cd010115.
2. Bafadhel M et al. Lancet Respir Med. 2018 6(2):117-126

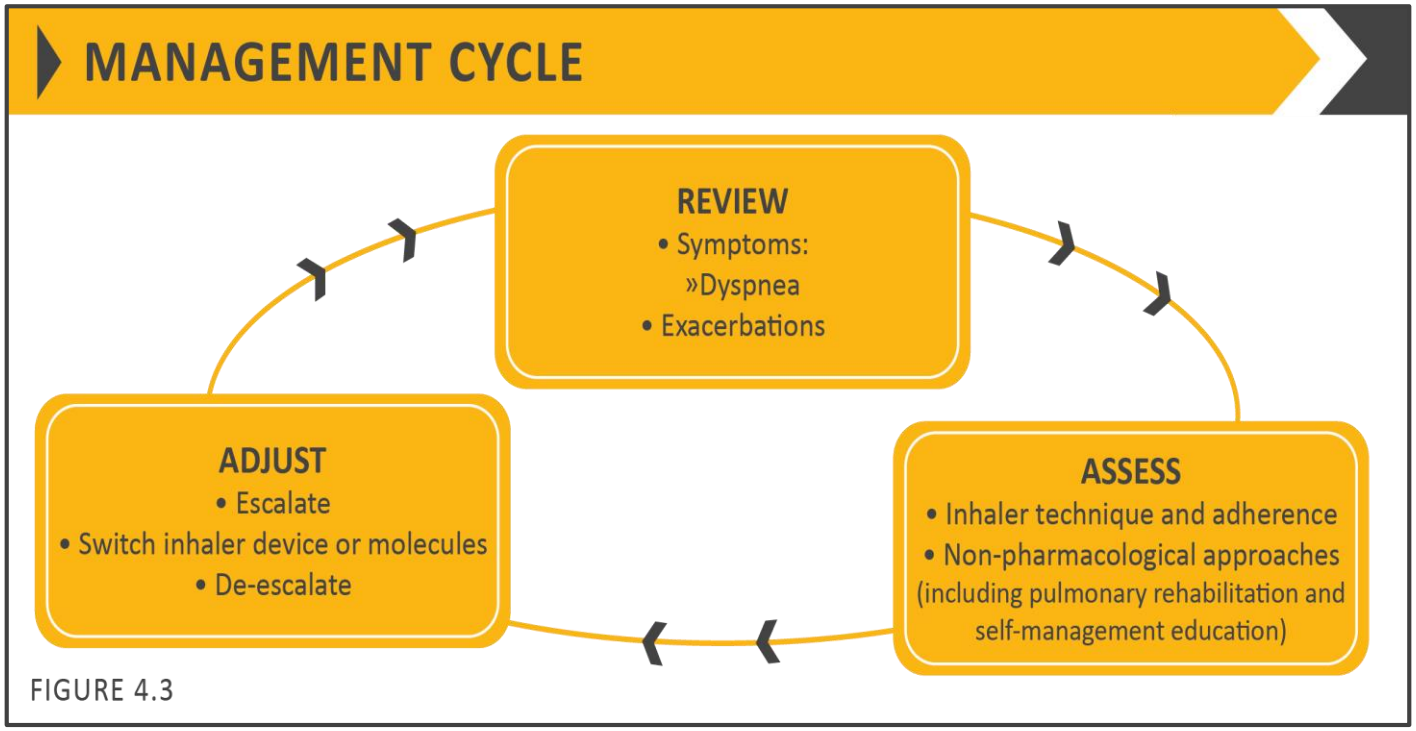
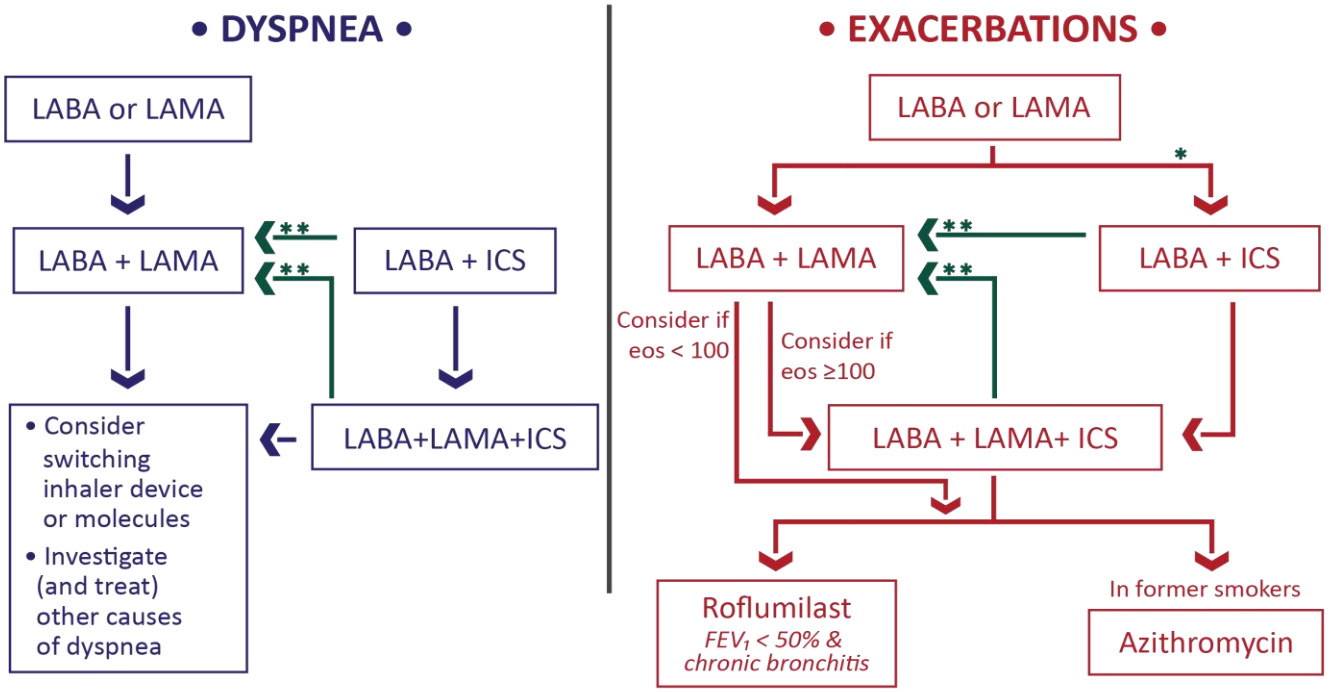


FIGURE 4.3

FOLLOW-UP PHARMACOLOGICAL TREATMENT

1. **IF RESPONSE TO INITIAL TREATMENT IS APPROPRIATE, MAINTAIN IT.**
2. **IF NOT:**
   - ✓ Consider the predominant treatable trait to target (dyspnea or exacerbations)
     - Use exacerbation pathway if both exacerbations and dyspnea need to be targeted
   - ✓ Place patient in box corresponding to current treatment & follow indications
   - ✓ Assess response, adjust and review
   - ✓ These recommendations do not depend on the ABCD assessment at diagnosis



eos = blood eosinophil count (cells/µL)
** Consider if eos ≥ 300 or eos ≥ 100 AND ≥2 moderate exacerbations / 1 hospitalization*
*** Consider de-escalation of ICS or switch if pneumonia, inappropriate original indication or lack of response to ICS*

FIGURE 4.4

Oral Therapies for COPD

- **Systemic corticosteroids** are not recommended and may be associated with an increased risk of death, HR 1.73 (p=0.0001) [1].

- **Azithromycin** is associated with reduced exacerbations in frequent exacerbators (HR=0.73; 95%CI 0.63-0.84) [2].
  - Azithromycin also resulted in better symptom burden as assessed by the SGRQ.
  - There was a small increase in hearing loss (25% vs. 20%, p=0.04)
  - Post hoc analysis showed the benefit was shown in non-smokers only [3].
  - The long-term effects (cardiovascular events and bacterial resistance) are unknown.

1. Horita, N. Respir Res, 2014. 15: 37.
2. Albert RK et al. N Engl J Med, 2011. 365(8):689-98.
3. Han MK et al. Am J Respir Crit Care Med, 2014. 189(12):1503-8

Oral Therapies for COPD

- **Roflumilast** is a phosphodiesterase-4 inhibitor which reduces airway inflammation.
- Reduces exacerbations and improves lung function in patients with an FEV1<50% and history of chronic bronchitis [1,2].
- Side effects include weight loss and diarrhea
- Caution should be employed in patients with depression or suicidality.

- **Theophylline** is a methylxanthine that results in bronchodilator through unclear mechanisms.
- Improves lung function and symptoms when added to long-acting bronchodilators [3].
- No benefit when added to inhaled corticosteroids in reducing exacerbations [4].
- Given toxicity and narrow therapeutic window, theophylline is no longer first line for adjunctive therapy.

1. Fabbri LM et al. Lancet, 2009. 374(9691):695-703.
2. Martinez FJ et al. Lancet, 2015. 385(9971):857-66.
3. ZuWallack RL et al. Chest. 2001;119(6):1661-70.
4. Devereux G et al. JAMA. 2018 320(15):1548-1559.

COPD: Non-Pharmacologic Management

Key Principles

1. Vaccination
2. Smoking Cessation
3. Pulmonary Rehabilitation
4. Self-Management Strategies
5. Supplemental Oxygen
6. Non-Invasive Positive Pressure Ventilation
7. Comorbidities

GOLD guidelines for Non-Pharmacologic Management by Gold Group

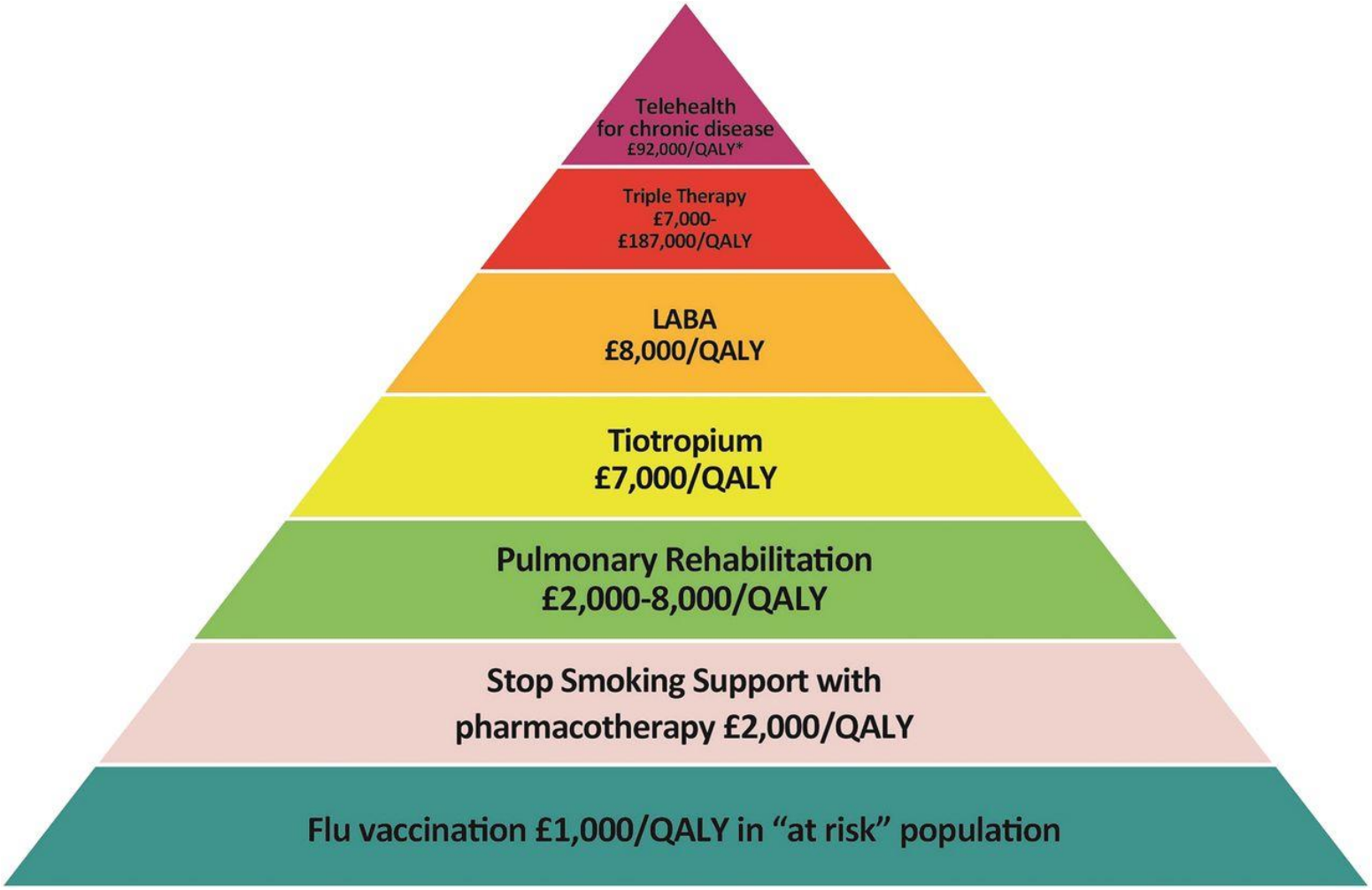
NON-PHARMACOLOGIC MANAGEMENT OF COPD*

PATIENT GROUP	ESSENTIAL	RECOMMENDED	DEPENDING ON LOCAL GUIDELINES
A	Smoking Cessation (can include pharmacologic treatment)	Physical Activity	Flu Vaccination Pneumococcal Vaccination
B, C and D	Smoking Cessation (can include pharmacologic treatment) Pulmonary Rehabilitation	Physical Activity	Flu Vaccination Pneumococcal Vaccination

*Can include pharmacologic treatment.

TABLE 4.8

COPD Pyramid of Value



Smoking Cessation

- US Public Health Service Clinical Practice Guidelines recommend 5 A's [1]:
  - **Ask** about active smoking
  - **Advise** against smoking
  - **Assess** readiness
  - **Assist** (strongly consider pharmacologic aids unless contraindications exist)
  - **Arrange** follow-up visits.

- For the busy practitioner **AAR** (ask, advise, refer to smoking cessation) and **AAC** (ask, advise, connect to smoking cessation electronic resources/quitlines) is reasonable.

Pharmacologic Smoking Cessation Aids

- Combination of pharmacologic aids and behavioral therapy is more effective [1].
- First line therapies include: combination NRT or varenicline
  - Varenicline is superior to bupropion (OR 1.59; 95% CI 1.29–1.96) and single forms of NRT (OR 1.57; 95%CI 1.29–1.91) [2]
  - Not more effective than combination NRT (OR1.06; 95% CI 0.75–1.48) [2]
- E-cigarettes are not recommended at this time given safety concerns, though a recent RCT demonstrated superiority compared to other NRT (RR 1.83; 95%CI 1.30-2.58) [3].

1. Patel, M. et al. *Ann Intern Med.* 2016;164(5):ITC33-ITC48.
2. Cahill,K. et al.Cochrane Database Syst Rev 2013;5:Cd009329
3. Hajek, P et al. N Engl J Med. 2019 Feb 14;380(7):629-637

Pulmonary Rehabilitation

- A comprehensive program of **supervised exercise training** and **behavioral therapy**, including breathing exercises, smoking cessation counseling and self-management.

- Benefits include improved exercise capacity and health-related QoL [1].
  - Improved 6MWD
  - Improved symptom burden assessed by SGRQ

- When initiated within 3 weeks of discharge after a COPD exacerbation, readmissions were reduced by 66% (OR 0.44, 95%CI 0.21-0.91)[2].

1. McCarthy B. et al. Cochrane Database Syst Rev. 2015 Feb 23;(2):CD003793
2. Puhan MA, Cochrane Database Syst Rev. 2016 Dec 8;12:CD005305.

Self Management Strategies

- "A COPD self-management intervention is structured but personalized and often multi-component, with goals of motivating, engaging and supporting the patients to positively adapt their health behavior(s) and develop skills to better manage their disease." [1]

- What it is not: a blank script for prednisone and antibiotics when symptoms worsen.

- Meta-analysis demonstrated reduction in respiratory hospitalizations (OR 0.69, 95%CI 0.51-0.94) and improvement in dyspnea.

- Very small, statistically significant increase in respiratory deaths (RD 0.028, 95% CI 0.0049-0.0511)

1. Effing TW et al. Eur Respir J. 2016 Jul;48(1):46-54.
2. Lenferink, A., et al. Cochrane Database Syst Rev, 2017. **8**: p. Cd011682.

FOLLOW-UP OF NON-PHARMACOLOGICAL TREATMENT

1. IF RESPONSE TO INITIAL TREATMENT IS APPROPRIATE, MAINTAIN IT AND OFFER:

- Flu vaccination every year and other recommended vaccinations according to guidelines
- Self-management education
- Assessment of behavioral risk factors such as smoking cessation (if applicable) and environmental exposures

Ensure

- Maintenance of exercise program and physical activity
- Adequate sleep and a healthy diet

2. IF NOT, CONSIDER THE PREDOMINANT TREATABLE TRAIT TO TARGET

• DYSPNEA •

- Self-management education (written action plan) with integrated self-management regarding:
  - Breathlessness and energy conservation techniques, and stress management strategies
- Pulmonary rehabilitation (PR) program and/or maintenance exercise program post PR

• EXACERBATIONS •

- Self-management education (written action plan) that is personalized with respect to:
  - Avoidance of aggravating factors
  - How to monitor/manage worsening of symptoms
  - Contact information in the event of an exacerbation

All patients with advanced COPD should be considered for end of life and palliative care support to optimize symptom control and allow patients and their families to make informed choices about future management

TABLE 4.9

Supplemental Oxygen

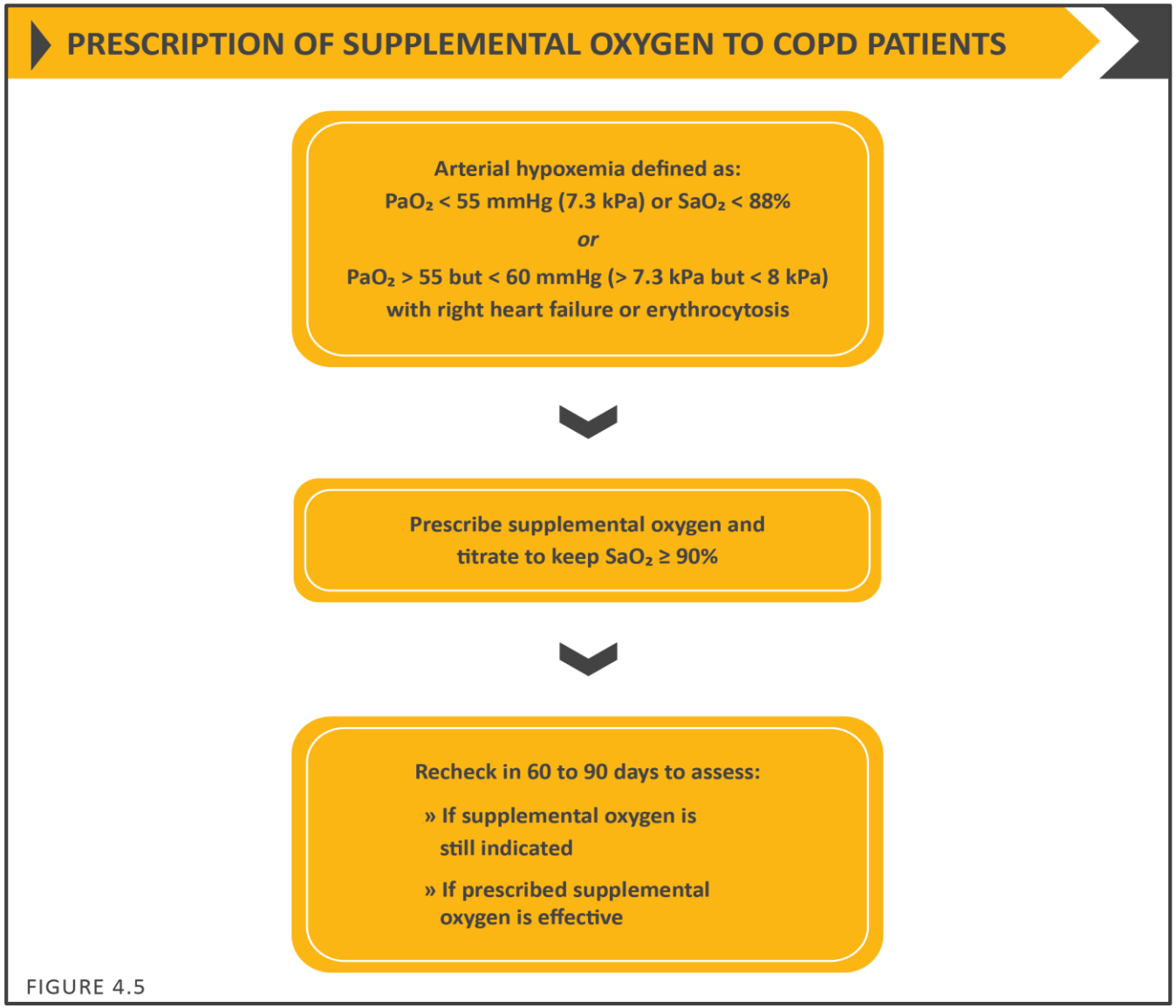
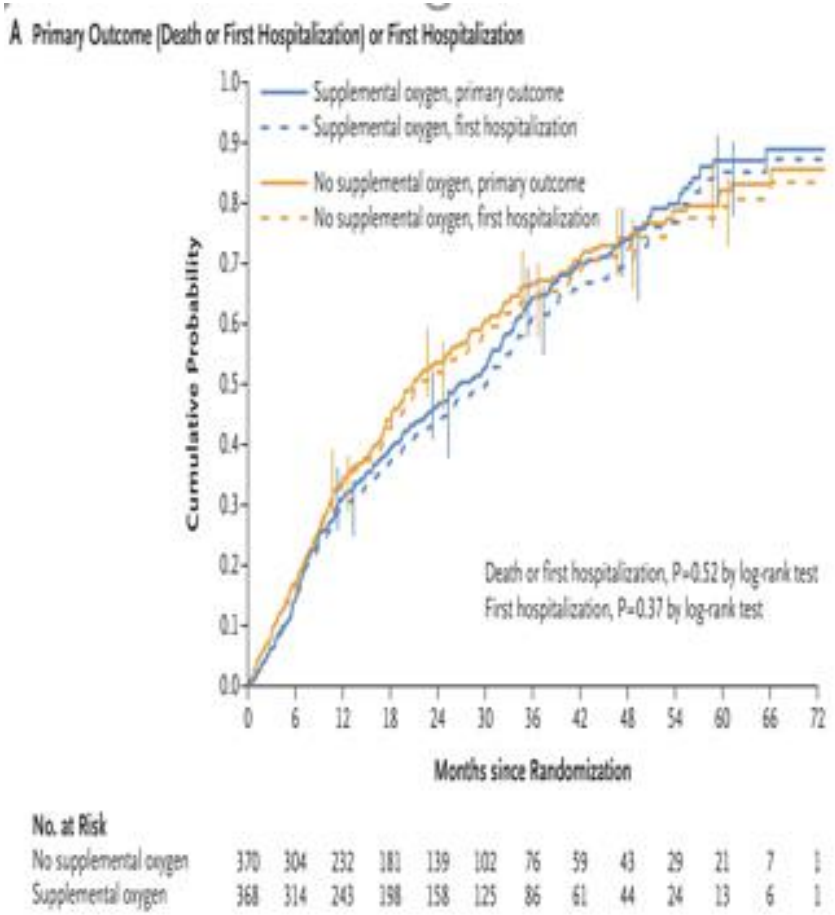


FIGURE 4.5

Oxygen Supplementation for Mild Exertional Hypoxemia

- LTOT is not beneficial in those with mild to moderate exertional hypoxemia:
  - Resting saturation between 89-93% and moderate desaturation to 80% with exertion.



Albert, R.K., et al. N Engl J Med, 2016. **375**(17): p. 1617-1627.

Non-Invasive Positive Pressure Ventilation

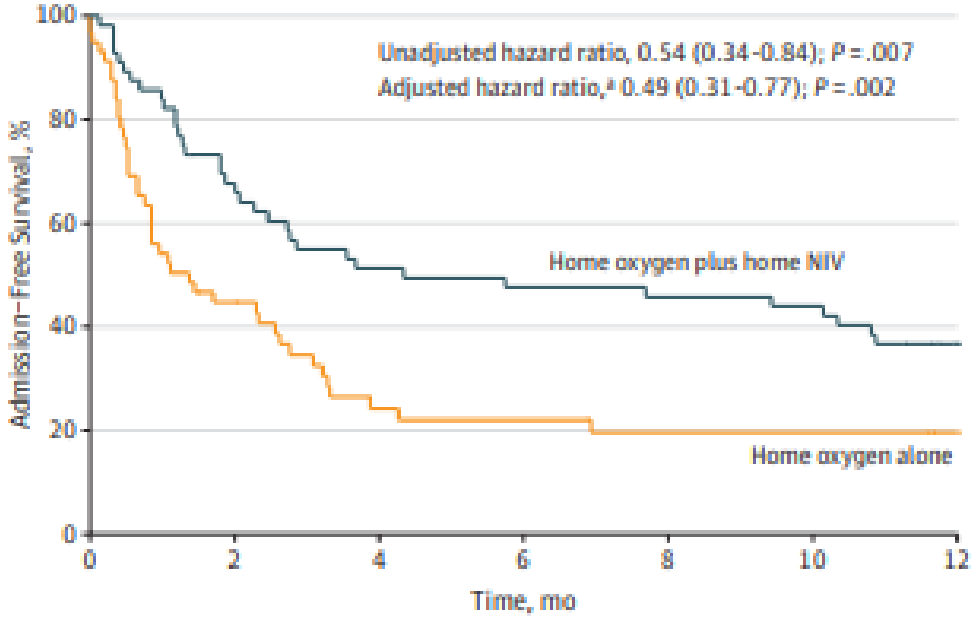
- NIPPV in stable patients with severe COPD and chronic hypercapneic respiratory failure is associated with improved mortality (OR 0.66; 95%CI 0.51-0.87) and decreased hospital admission, but no change in quality of life [1].
  - Settings matter: High-intensity (high pressure) Bilevel titrated to reduce pCO2 is most beneficial.

- NIPPV reduces readmissions in those carefully selected with chronic hypercapneic respiratory failure [2].

1. Wilson ME et al. JAMA 2020. 323(5):455-465.
2. Murphy, P.B., et al. JAMA 2017. **317**(21): 2177-2186**.**

Non-Invasive Positive Pressure Ventilation following a Hospitalization for COPD exacerbation

Figure 2. Kaplan-Meier Survival Plot of Time to Readmission or Death From Randomization to the End of Trial Follow-up at 1 Year



No. at risk							
Home oxygen plus home NIV	57	37	28	26	25	24	16
Home oxygen alone	59	23	11	10	8	8	6

Murphy, P.B., et al. JAMA 2017. 317(21): 2177-2186.

CMS criteria for BiPAP

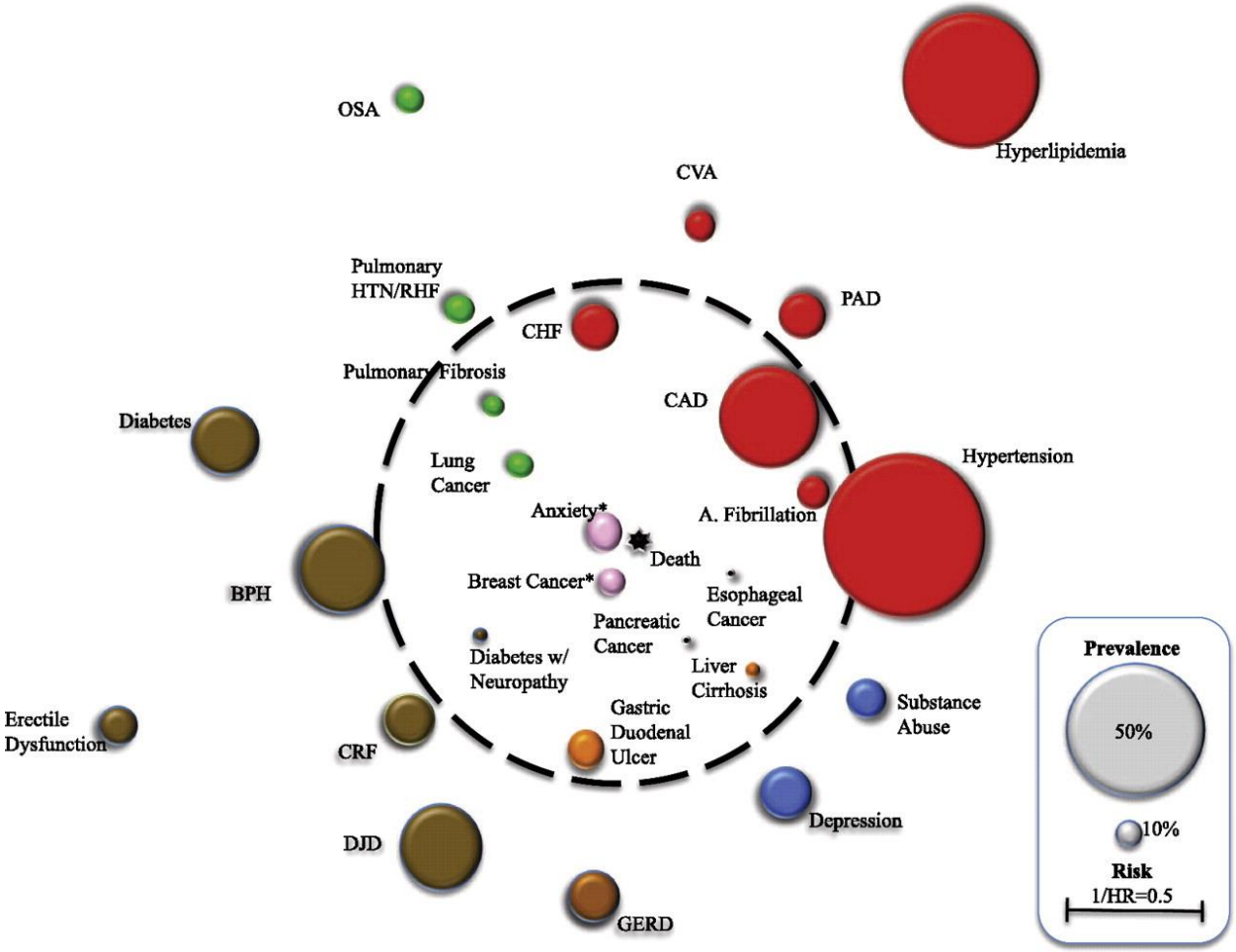
- The Centers for Medicare and Medicaid Services criteria for initiation of NIPPV for chronic respiratory failure without a back-up rate include:
  - Arterial blood gas while awake and on prescribed O2 with pCO2>52 mmHg and
  - Overnight oximetry <88% for over 5 minutes with a minimum of 2 hours of nocturnal recording on 2L via nasal cannula or the patient's prescribed oxygen rate (whichever is higher)

- Of note, this excludes patients with OSA/OHS.

- To qualify for a back-up rate, patients must have evidence of persistent hypercapnia 60 days after bilevel initiation with demonstrated compliance.

- Criteria for non-invasive ventilator systems are less stringent in demonstrable cases of severe chronic hypercapneic respiratory failure.

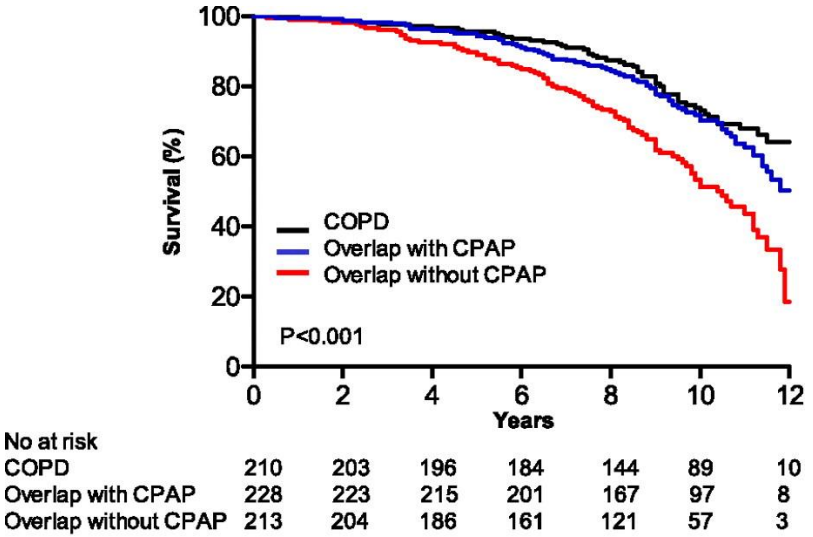
The Comorbidome in COPD

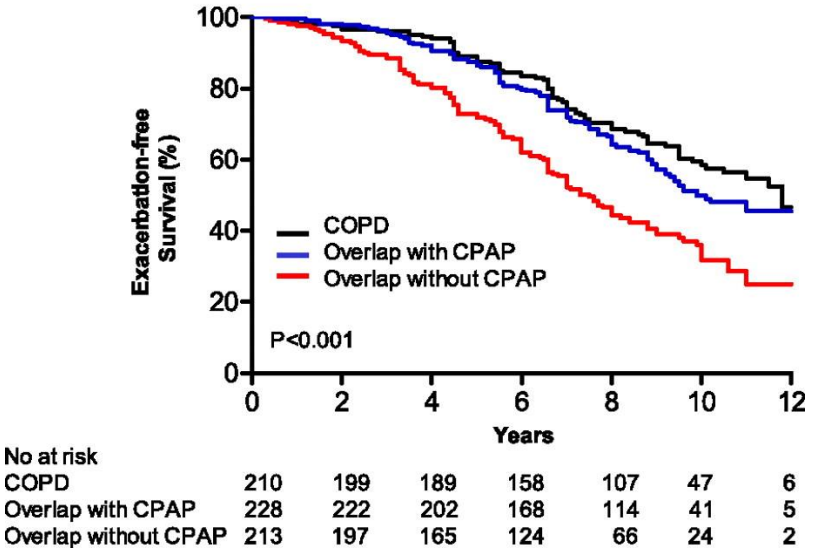


Divo M. Am J Respir Crit Care Med. 2012 186(2):155-61

Comorbidities: OSA

- Patients tend to have more severe hypercapnia (out of proportion to lung function) and increased risk of pulmonary hypertension [1].
- Untreated COPD-OSA overlap have higher mortality relative to COPD alone (RR 1.79; 95% CI, 1.16-2.77) [2].
- Screen patients with the Stop-Bang questionnaire
- Refer for sleep study with titration.





1. McNicholas WT et al. Chest. 2017 Dec;152(6):1318-1326
2. Marin, JM et al. Am J Respir Crit Care Med, 182 (2010), pp. 325-331

Comorbidities: Lung Cancer

- Lung cancer accounts for nearly 25% of all deaths in patients with COPD [1].

- Currently, LDCT is reimbursed according to the following CMS criteria based on the National Lung Screening Trial [3]:
  - Age 55-77
  - At least 30 pack-year smoking
  - Current smoker or quit within 15 years.

1. McGarvey LP et al. *Respiratory medicine* 2012; 106: 515-521.
2. Aberle DR et al. N Engl J Med. 2011 Aug 4;365(5):395-409

Comorbidities: Frailty and Mood Disturbances

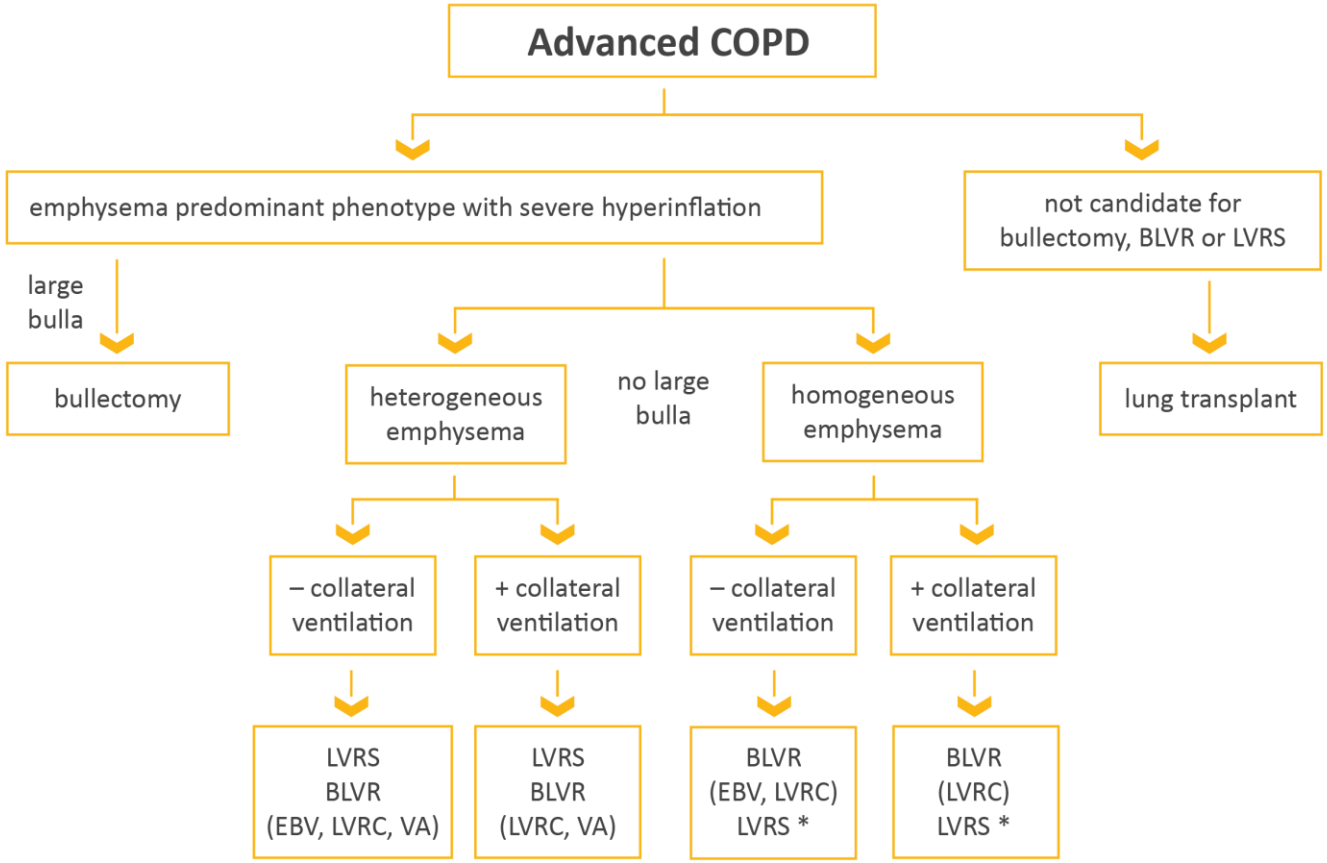
- Patients with COPD should be assessed for frailty and low BMI is independently associated with mortality [1].
  - Referral to nutrition services and pulmonary rehabilitation is essential.

- Patients with COPD should be screened for anxiety and depression using validated questionnaires; the Generalized Anxiety Disorder (GAD)-7 and the Patient Health Questionnaire (PHQ)-9 depression scale [2,3].
  - Those with positive screens for anxiety (GAD-7 score>10) and depression (PHQ-9>15) should have a palliative care and pulmonary rehabilitation referral for symptom management.

1. Celli BR et al. N Engl J Med. 2004 Mar 4; 350(10):1005-12
2. Lowe B et al. *Medical care* 2008; 46: 266-274.
3. Kroenke K *Journal of general internal medicine* 2001; 16: 606-613.

INTERVENTIONAL BRONCHOSCOPIC AND SURGICAL TREATMENTS FOR COPD

Overview of various therapies used to treat patients with COPD and emphysema worldwide. Note that all therapies are not approved for clinical care in all countries. Additionally, the effects of BLVR on survival or other long term outcomes or comparison to LVRS are unknown.



Definition of Abbreviations: BLVR, Bronchoscopic Lung Volume Reduction, EBV, endobronchial Valve, LVRS, Lung volume reduction surgery, LVRC, Lung volume reduction coil, VA, Vapor ablation

*at some but not all centers

FIGURE 4.6

Summary

- Management of COPD involves a personalized approach of characterizing exacerbation history, symptom burden and eosinophilic phenotype.
- Pharmacologic interventions can improve quality of life, lung function and exacerbations.
- The most cost-effective interventions are non-pharmacologic: vaccination, smoking cessation and pulmonary rehabilitation.
- Assess for common and lethal comorbidities.
- Ensure patients have undergone a complete evaluation, including pulmonary rehabilitation and advanced therapies, before prognosticating if COPD is the main life-limiting disease.

Thank You!

Questions?