The GOLDen Path

## The 2023 GOLD Strategy & the Future of COPD

Mike Hess, MPH, RRT, RPFT
Utah Society for Respiratory Care 2023

Today's Objectives

- Identify the latest concepts in the pathogenesis and diagnosis of COPD

- Understand new treatment algorithms and their underlying evidence

- Describe future opportunities for COPD research

Same As It Ever Was?

The GOLDen Path – The 2023 GOLD Report and the Future of COPD
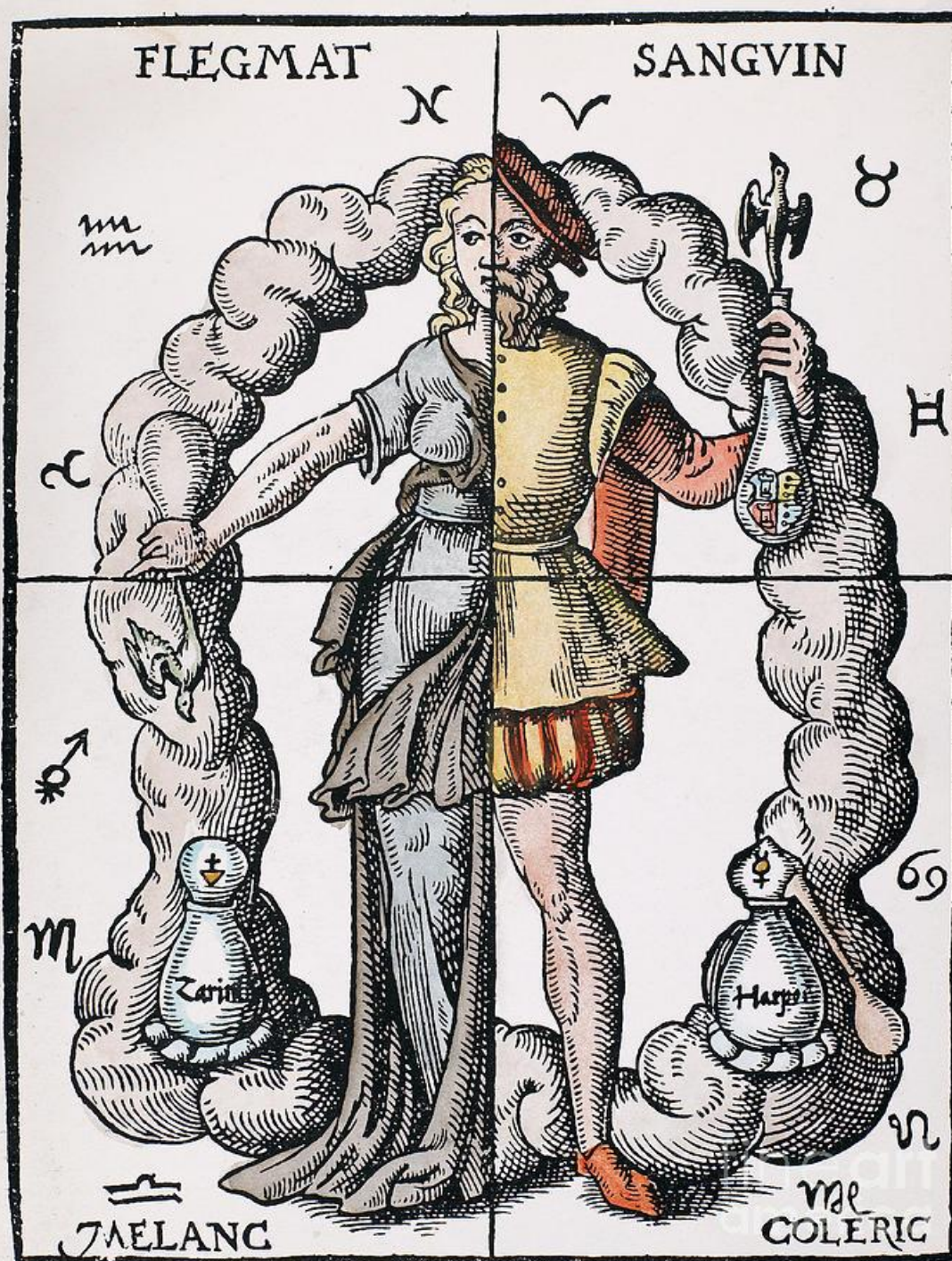
17th Century

Less Early Days

- CIBA Guest Symposium (1959)

- The "Dutch Hypothesis"

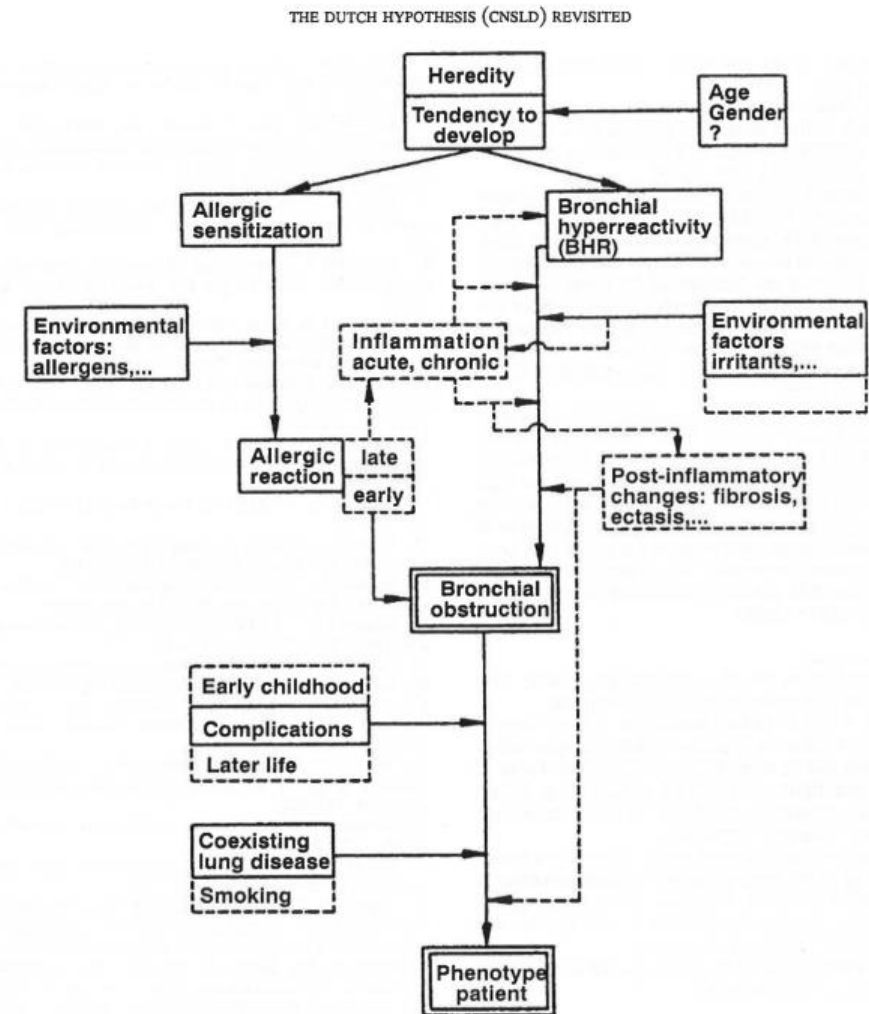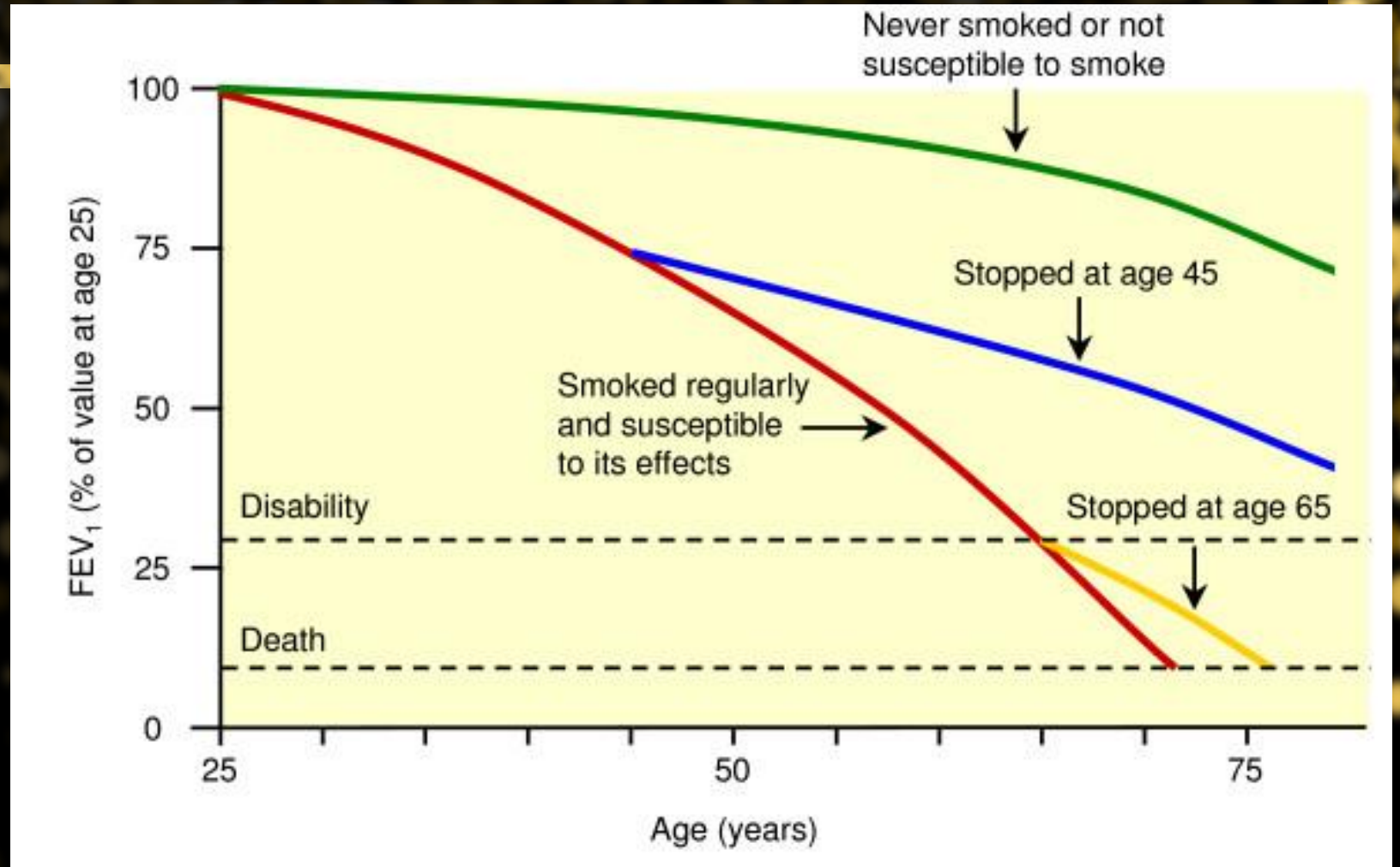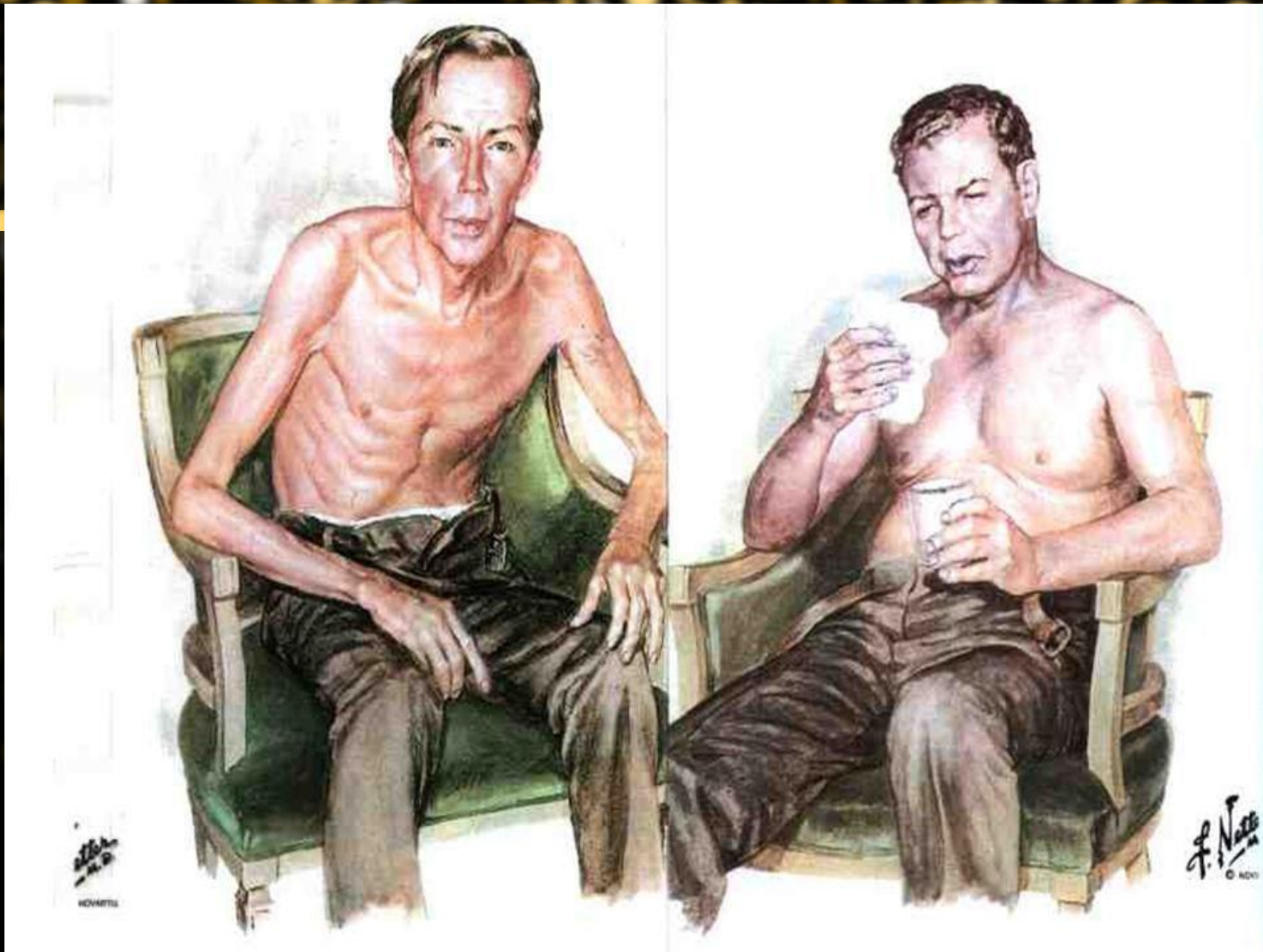THE DUTCH HYPOTHESIS (CNSLD) REVISITED   485

Fig. 1. – Schematic presentation of the Dutch Hypothesis 1990. The dotted lines indicate the increase in knowledge and insight in the period between 1961 and 1990.

Less Early Days

- **British Hypothesis**

- **Chronic Bronchitis vs. Emphysema**

- **More related to infections**

CHRONIC BRONCHITIS

CLINICAL DIAGNOSIS: DAILY PRODUCTIVE COUGH FOR THREE MONTHS OR MORE, IN AT LEAST TWO CONSECUTIVE YEARS

OVERWEIGHT AND CYANOTIC

ELEVATED HEMOGLOBIN

PERIPHERAL EDEMA

RHONCHI AND WHEEZING

EMPHYSEMA

PATHOLOGIC DIAGNOSIS: PERMANENT ENLARGEMENT AND DESTRUCTION OF AIRSPACES DISTAL TO THE TERMINAL BRONCHIOLE
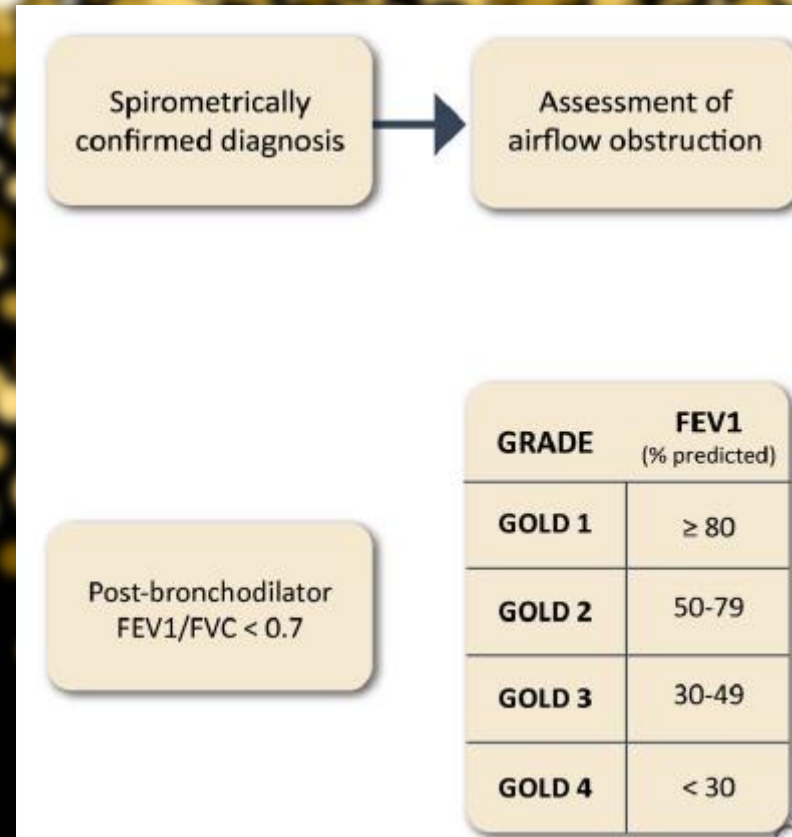
OLDER AND THIN

SEVERE DYSPNEA

QUIET CHEST

X-RAY: HYPERINFLATION WITH FLATTENED DIAPHRAGMS

Launch of GOLD (2001)

"COPD is a disease state characterized by airflow limitation that is not fully reversible. The airflow limitation is usually both progressive and associated with an abnormal inflammatory response of the lungs to noxious particles or gases."

Severity Based on Airflow

INITIAL PHARMACOLOGICAL TREATMENT

≥ 2 moderate exacerbations or ≥ 1 leading to hospitalization	**Group C** LAMA	**Group D** LAMA or LAMA + LABA* or ICS + LABA** *Consider if highly symptomatic (e.g. CAT > 20) **Consider if eos ≥ 300
0 or 1 moderate exacerbations (not leading to hospital admission)	**Group A** A Bronchodilator	**Group B** A Long Acting Bronchodilator (LABA or LAMA)
	mMRC 0-1, CAT < 10	mMRC ≥ 2, CAT ≥ 10
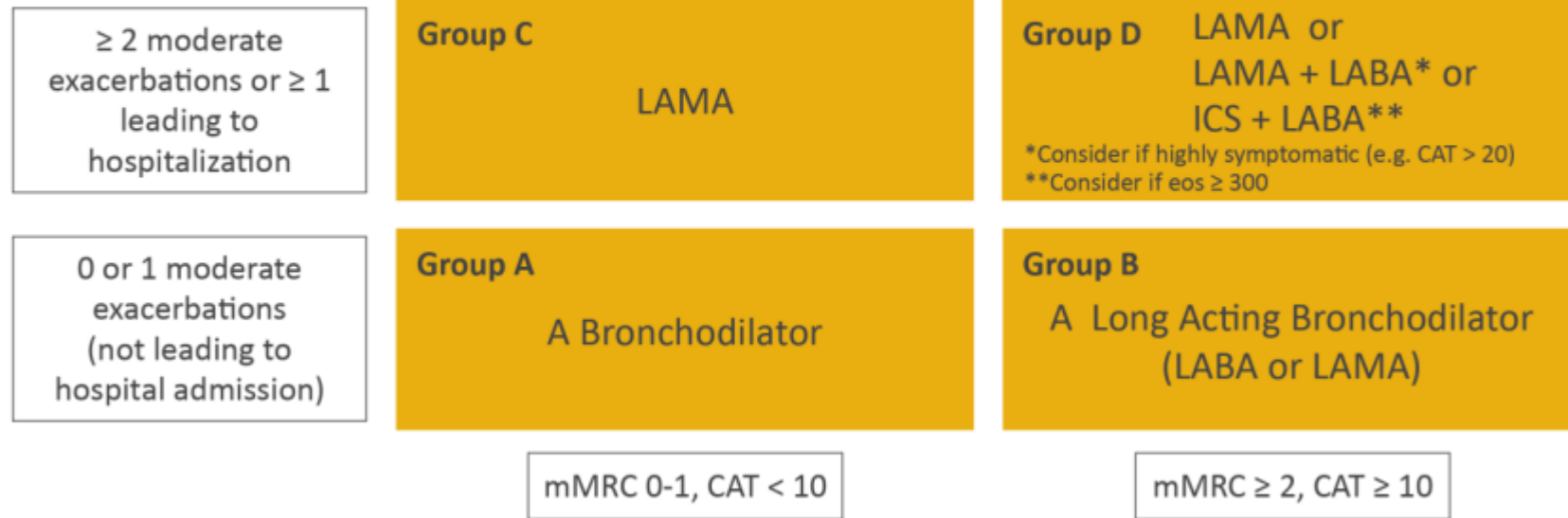
FIGURE 4.2

INITIAL PHARMACOLOGICAL TREATMENT

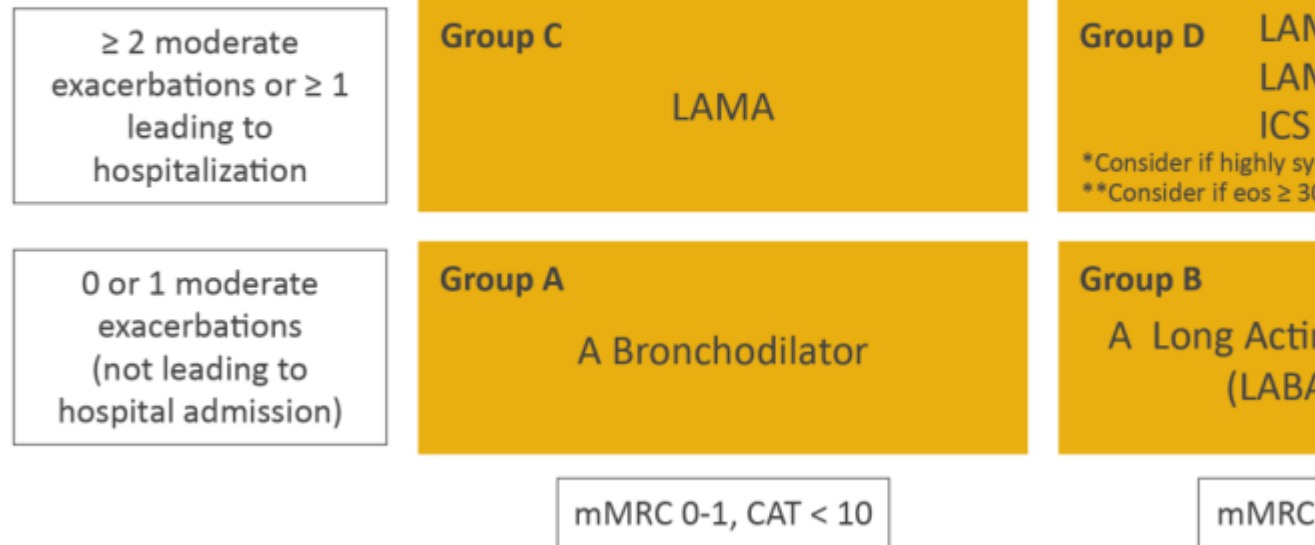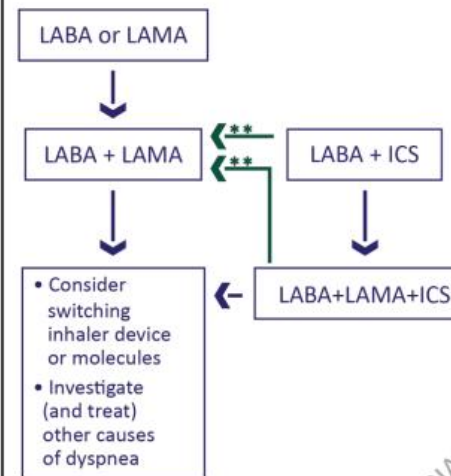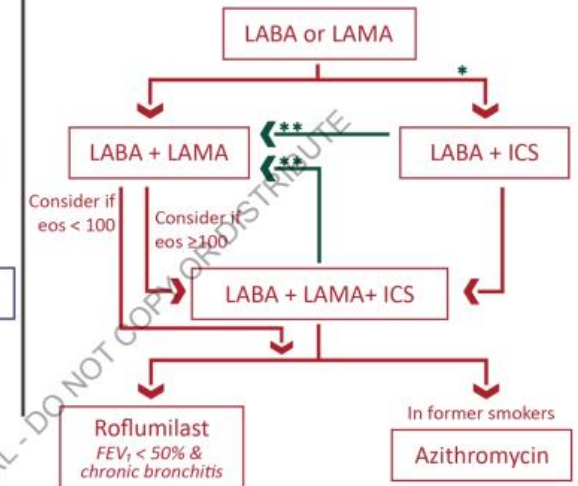| ≥ 2 moderate exacerbations or ≥ 1 leading to hospitalization	**Group C** LAMA	**Group D** LAMA or LAMA + LABA* or ICS + LABA** *Consider if highly sy[...] **Consider if eos ≥ 30[...]
0 or 1 moderate exacerbations (not leading to hospital admission)	**Group A** A Bronchodilator	**Group B** A Long Acti[...] (LABA[...]
	mMRC 0-1, CAT < 10	mMRC [...]

FIGURE 4.2

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

• DYSPNEA •

LABA or LAMA
↓
LABA + LAMA ←**← LABA + ICS
↓   ↓
• Consider switching inhaler device or molecules ← LABA+LAMA+ICS
• Investigate (and treat) other causes of dyspnea

• EXACERBATIONS •

LABA or LAMA
↓   *
LABA + LAMA ←**← LABA + ICS
Consider if eos < 100   Consider if eos ≥100
↓
LABA + LAMA+ ICS
↓   ↓
Roflumilast   In former smokers
FEV₁ < 50% &   Azithromycin
chronic bronchitis

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
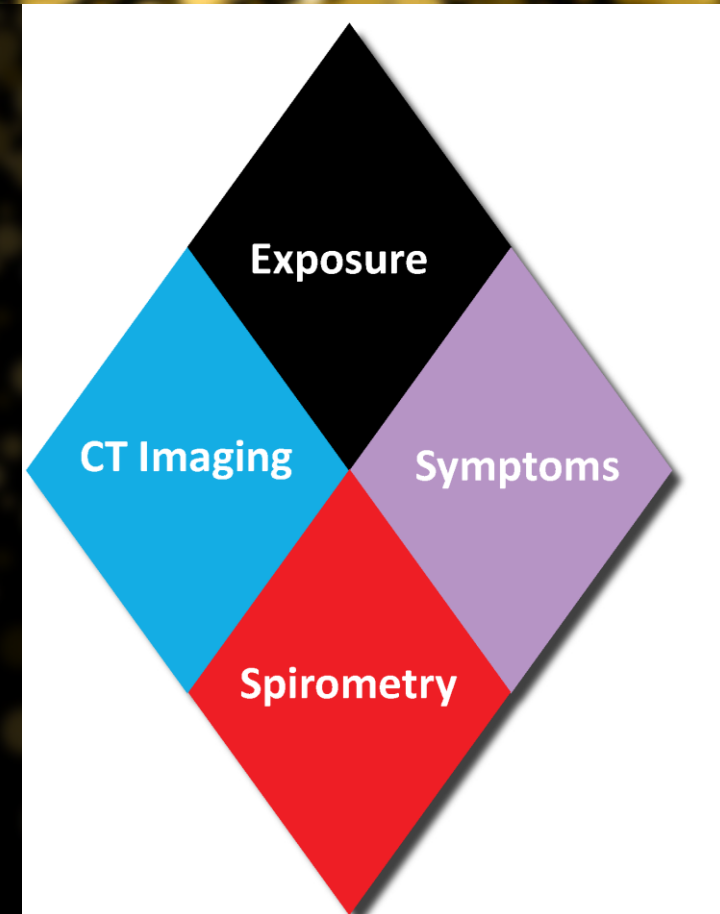
FIGURE 4.4

Big Data

Change On the Horizon – Late 2019

- >10 pack-year smoking history

- Modified Medical Research Council score ≥2 (with chronic bronchitis)

- Detectible emphysema on CT

- $FEV_1/FVC < 0.70$

Breaking the Cycle

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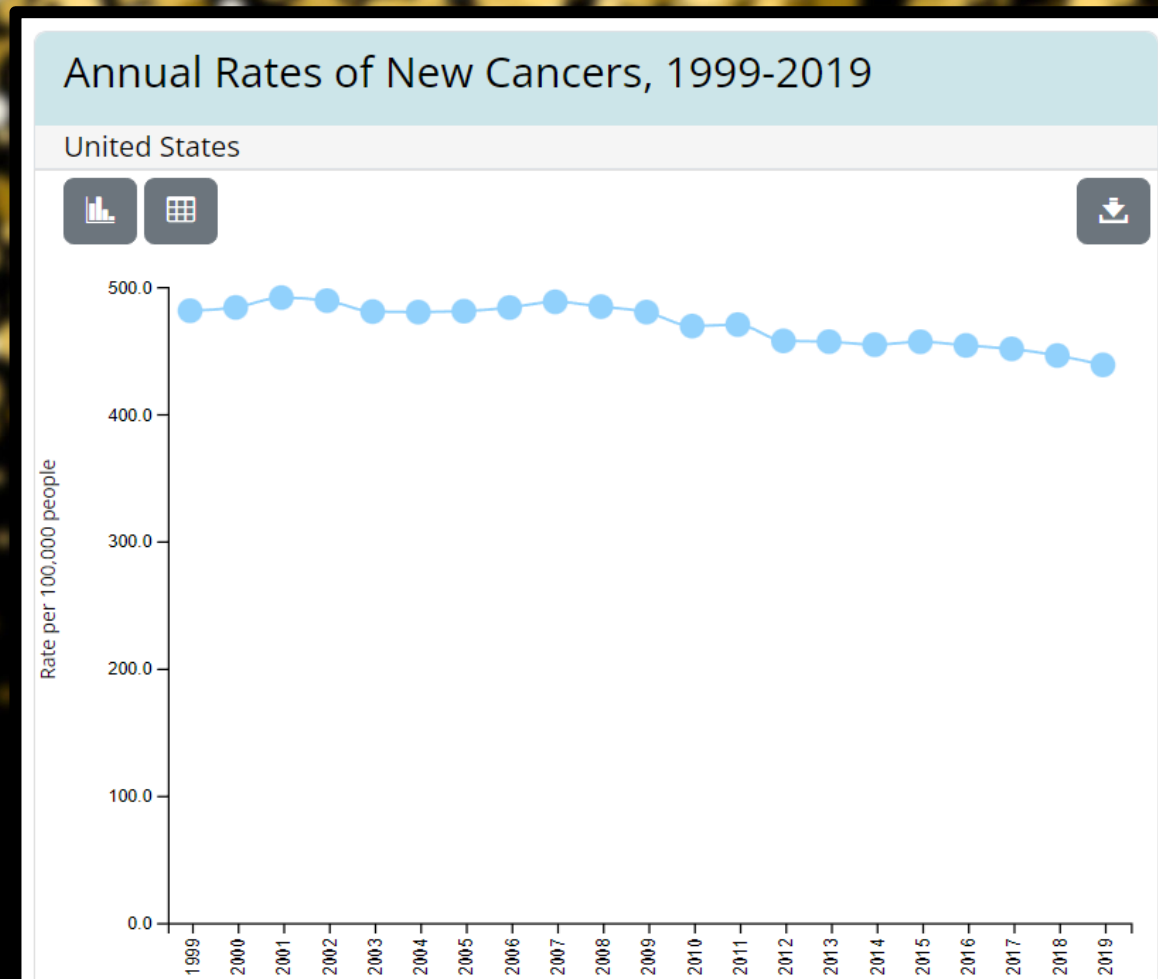
The Road to Nowhere
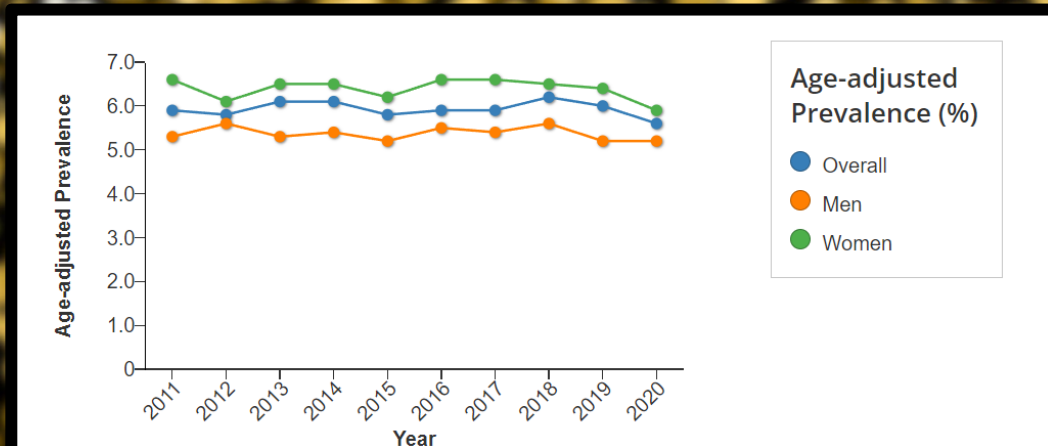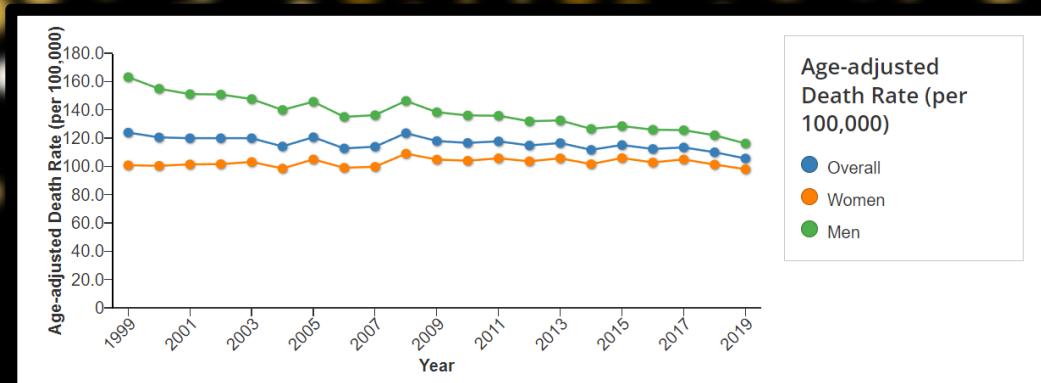
- COPD prevalence and mortality remain essentially stagnant.

- Over the same time, significant progress has been made in conditions such as cancer and diabetes.
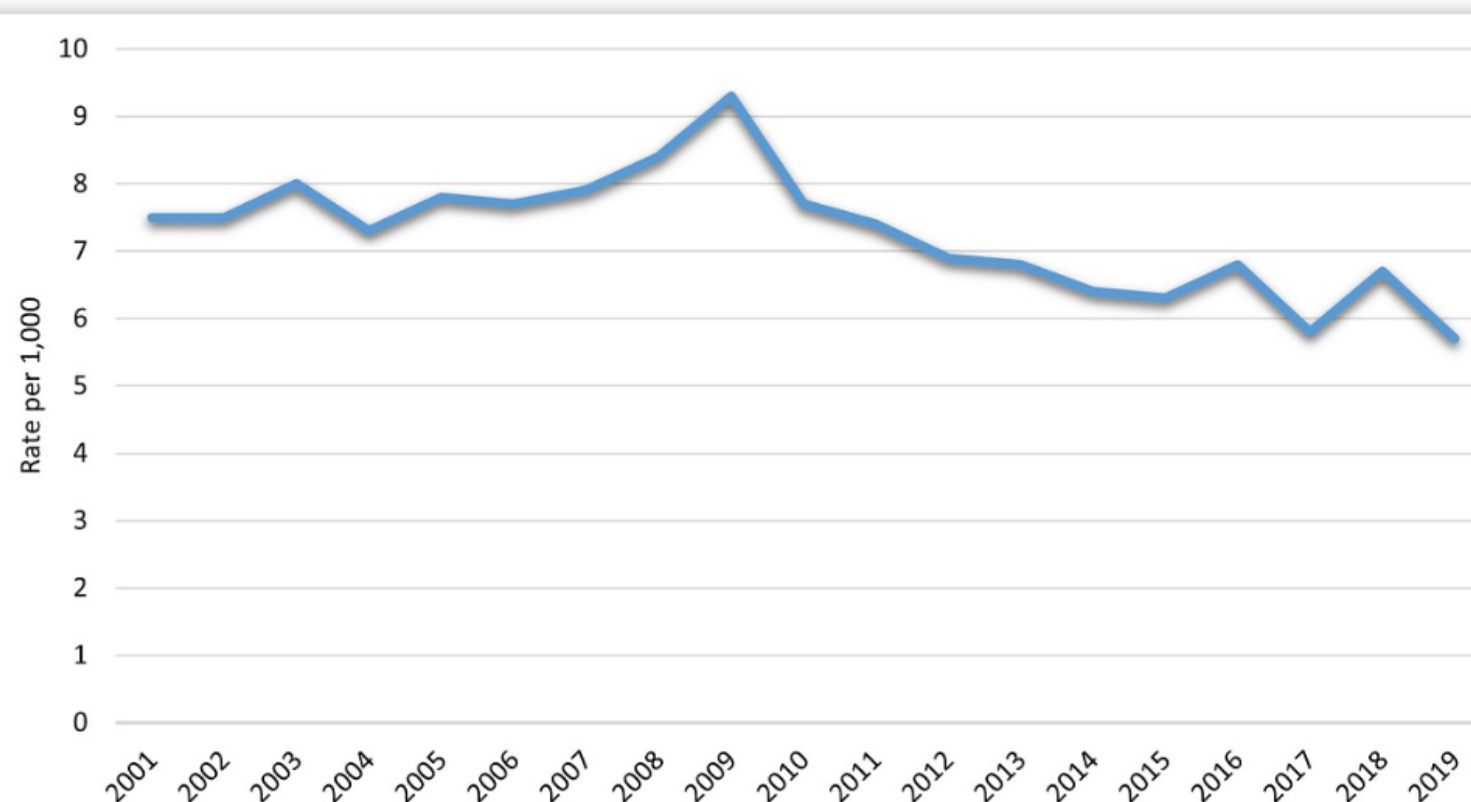
COPD Prevalence (CDC)
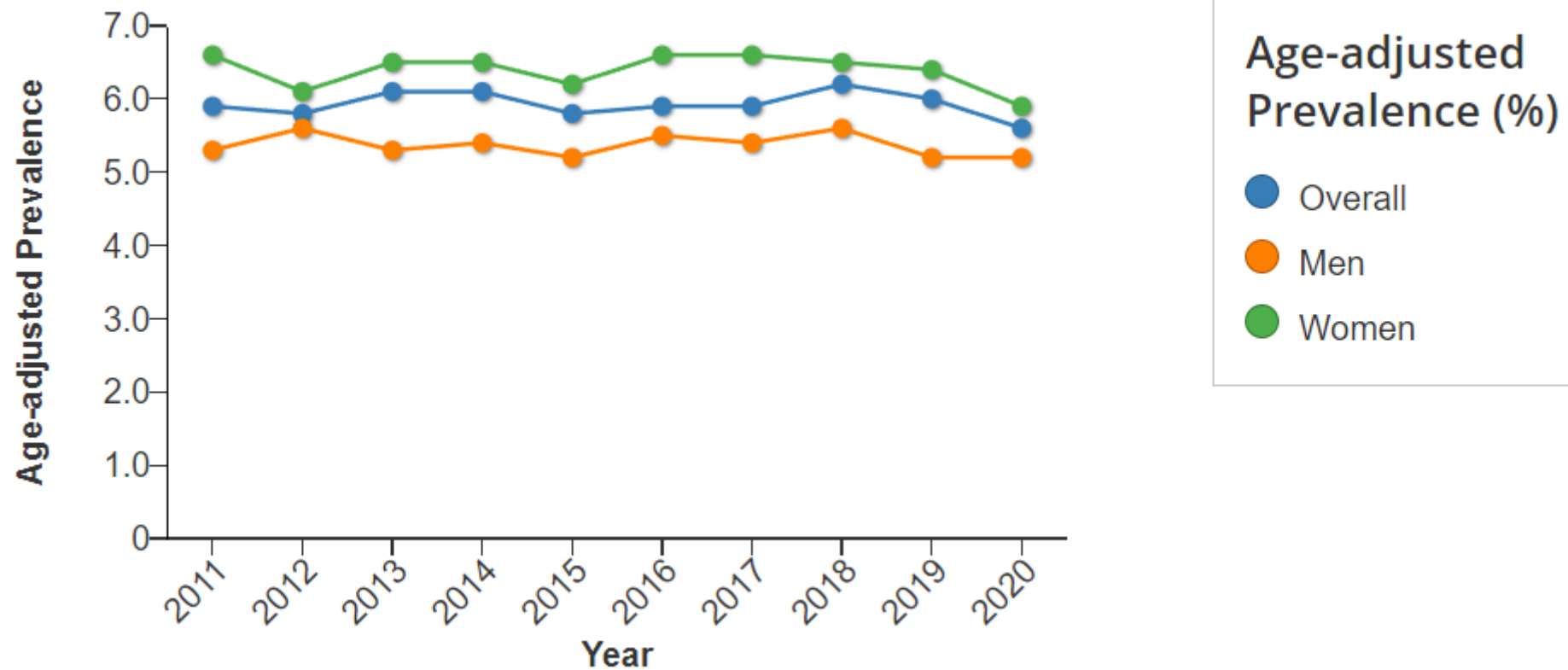
Cancer Prevalence (CDC)

Diabetes Prevalence (CDC)

Figure 1. Trends in Incidence of Diagnosed Diabetes Among Adults Aged 18 Years or Older, United States, 2001–2019

A Global Burden

212,300,000

CASES REPORTED GLOBALLY

3,300,000

DEATHS ATTRIBUTABLE TO COPD

74,400,000

DISABILITY-ADJUSTED LIFE YEARS

PULMONARY PERSPECTIVE

Definition and Nomenclature of Chronic Obstructive Pulmonary Disease
Time for Its Revision

Bartolome Celli[1], Leonardo Fabbri[2], Gerard Criner[3], Fernando J. Martinez[4], David Mannino[5], Claus Vogelmeier[6], Maria Montes de Oca[7], Alberto Papi[2], Don D. Sin[8], MeiLan K. Han[9], and Alvar Agusti[10]

[1]Pulmonary Division, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts; [2]Department of Translational Medicine, University of Ferrara, Ferrara, Italy; [3]Department of Thoracic Medicine and Surgery, Lewis Katz School of Medicine at Temple University, Philadelphia, Pennsylvania; [4]Joan and Sanford I. Weill Department of Medicine, Weill Cornell Medicine, New York, New York; [5]Division of Pulmonary, Critical Care, and Sleep Medicine, University of Kentucky College of Medicine, Lexington, Kentucky; [6]Pulmonary and Critical Care Medicine, Department of Medicine, University Medical Center University of Marburg, German Center for Lung Research (DZL), Philipps University Marburg, Marburg, Germany; [7]Hospital Universitario de Caracas, Universidad Central de Venezuela and Centro Médico de Caracas, Caracas, Venezuela; [8]Division of Respiratory Medicine, Centre for Heart Lung Innovation, St. Paul's Hospital, University of British Columbia, Vancouver, British Columbia, Canada; [9]University of Michigan Health System, Ann Arbor, Michigan; and [10]Cátedra Salud Respiratoria, Universitat de Barcelona; Respiratory Institute, Hospital Clinic, Barcelona; IDIBAPS, CIBERES, Barcelona, Spain

ORCID IDs: 0000-0002-7266-8371 (B.C.); 0000-0001-8894-1689 (L.F.).

Why the Plateau?

- "Complex interactions" with physiology, concurrent conditions, and exacerbations

- Failure to optimally describe/identify early stages of the disease

- Identity as a "disease" in inherently limiting

Towards the elimination of chronic obstructive pulmonary disease: a *Lancet* Commission

Daiana Stolz, Takudzwa Mkorombindo, Desiree M Schumann, Alvar Agusti, Samuel Y Ash, Mona Bafadhel, Chunxue Bai, James D Chalmers, Gerard J Criner, Shyamali C Dharmage, Frits M E Franssen, Urs Frey, MeiLan Han, Nadia N Hansel, Nathaniel M Hawkins, Ravi Kalhan, Melanie Konigshoff, Fanny W Ko, Trisha M Parekh, Pippa Powell, Maureen Rutten-van Mölken, Jodie Simpson, Don D Sin, Yuanlin Song, Bela Suki, Thierry Troosters, George R Washko, Tobias Welte, Mark T Dransfield

System Failures

- Failure to limit exposure to risk factors (tobacco products, environmental pollutants, etc.)

- Failure to develop better diagnostic approaches

- Failure to create heterogeneous approaches to a heterogeneous disease

- Failure to invest
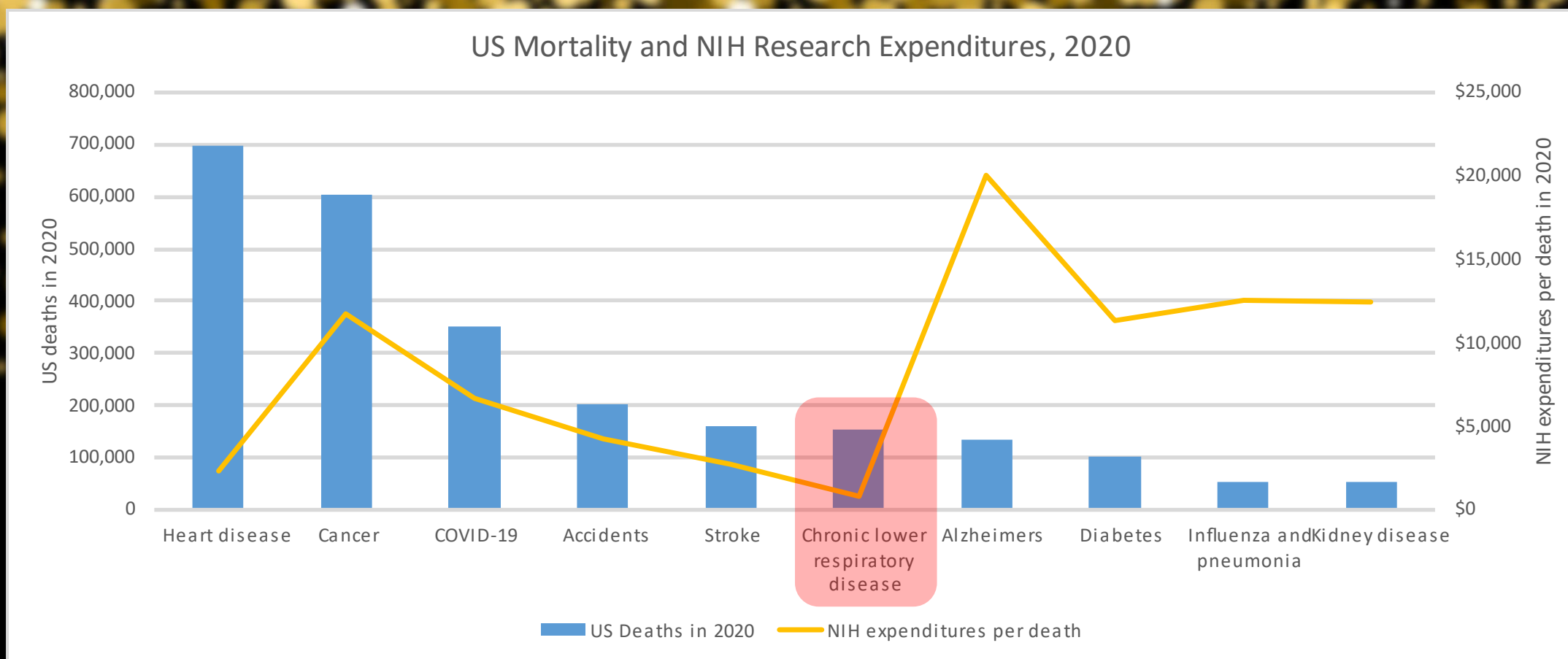
The Beginning of Wisdom

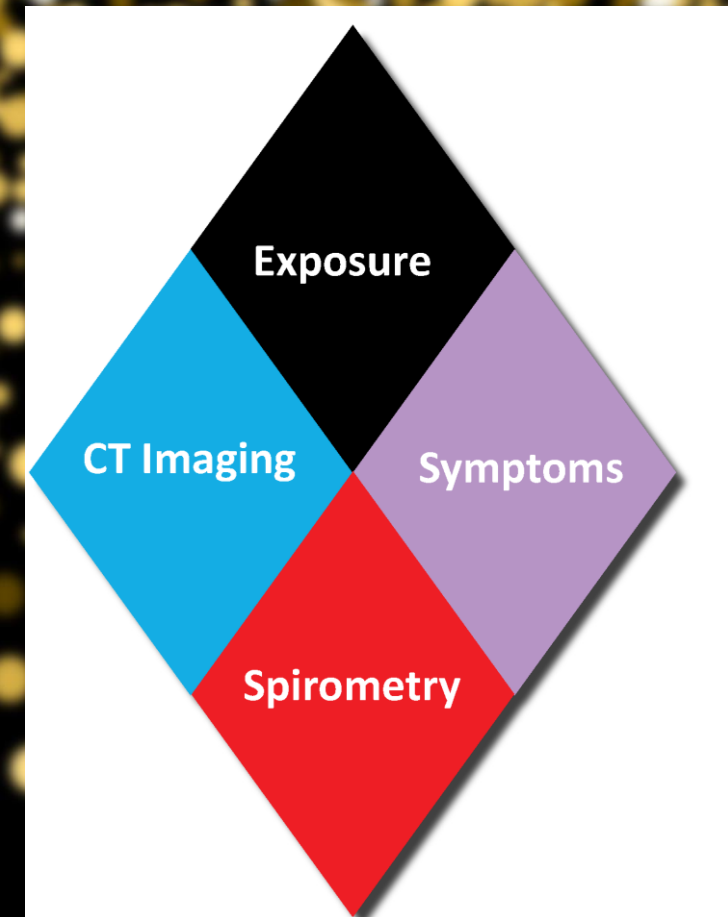The GOLDen Path – The 2023 GOLD Report and the Future of COPD

A New Definition

- "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 and influenced by host factors including abnormal lung development." (2017)

- "COPD is a heterogenous lung condition characterized by chronic respiratory symptoms (dyspnea, cough, sputum production) due to abnormalities of the airways (bronchitis, bronchiolitis) and/or alveoli (emphysema) that cause persistent, often progressive airflow obstruction." (2023)

Screening and Diagnostics

CAPTURE*™

For each question, place an X in the box with the answer that is best for you.
There are no right or wrong answers, only answers which are right for you.

Please answer each question	No	Yes
1. Have you ever lived or worked in a place with dirty or polluted air, smoke, second-hand smoke, or dust?	☐	☐
2. Does your breathing change with seasons, weather, or air quality?	☐	☐
3. Does your breathing make it difficult to do things such as carry heavy loads, shovel dirt or snow, jog, play tennis, or swim?	☐	☐
4. Compared to others of your age, do you tire easily?	☐	☐

	0	1	2 or more
5. In the past 12 months, how many times did you miss work, school, or other activities due to a cold, bronchitis, or pneumonia?	☐	☐	☐

*__C__OPD __A__ssessment in __P__rimary Care __t__o identify __U__ndiagnosed __R__espiratory Disease & __E__xacerbation Risk

Exposure

CT Imaging

Symptoms

Spirometry

Words Matter!

Early COPD	Mild COPD	Young COPD	Pre-COPD	PRISm
Related to the beginning of the process	Sometimes used to describe early phases of disease progression	May include patients who never achieved peak lung function	Represents patients of any age with regular symptoms or abnormalities, but no airflow obstruction	Indicates patients with normal FEV_1/FVC ratio but FEV_1 < 80% predicted
Biological "early" may be different from clinical "early"	Can occur at any age, does NOT indicate initial phases of disease	May still represent severe disease, not just initial stages	Treatment should still be provided to manage symptoms	Patients may oscillate between PRISm and obstructed spirometry
Term should generally be avoided, unless discussing specifically biological "early"	Term should be used to represent only spirometrically measured airflow obstruction of 80-99% predicted value	Term should be used to describe patients diagnosed with COPD between 20-50 years of age	Additional research is needed to better elucidate optimal treatment options	Additional research is needed to better elucidate optimal treatment options

Taxonomy: Etiotype vs. Phenotype

- Phenotype: Observable clinical traits based on interaction between physiology, genetics, and environment

- Etiotype: Clinical traits based on the etiology of a particular disease process

COPD-C

- COPD due to cigarette smoking

- May potentially include ENDS and cannabis

- Also includes secondhand smoke

COPD-G

- Genetically-determined COPD

- Includes alpha-1 antitrypsin deficiency
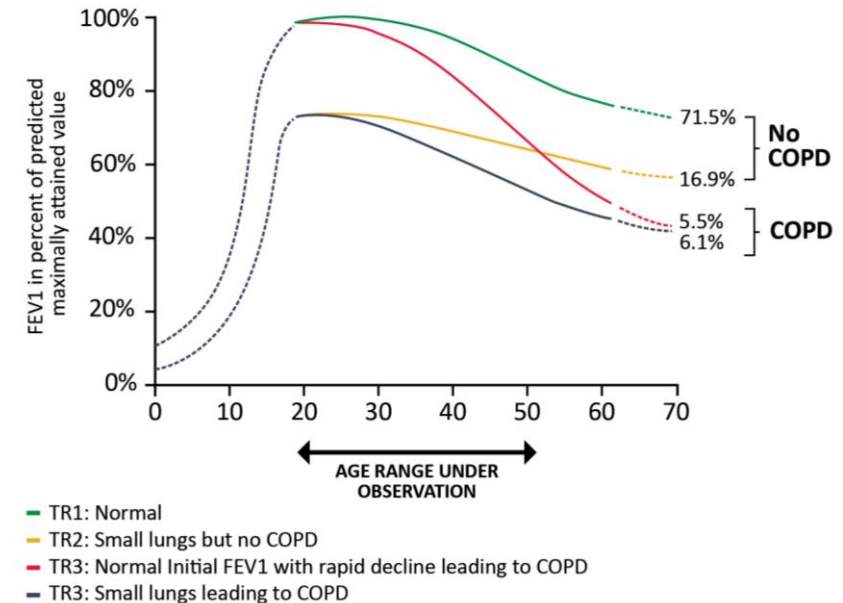
- Potentially other genetic variants

COPD-D

- COPD secondary to abnormal lung development

- Prenatal conditions, premature birth

- Adverse Childhood Events (ACEs), social determinants of health limiting lung development

FEV1 Trajectories (TR) Over the Life Course

Figure 1.1

FEV1 in percent of predicted maximally attained value

- 71.5% } No COPD
- 16.9%
- 5.5% } COPD
- 6.1%

AGE RANGE UNDER OBSERVATION

- TR1: Normal
- TR2: Small lungs but no COPD
- TR3: Normal Initial FEV1 with rapid decline leading to COPD
- TR3: Small lungs leading to COPD

Note: This is a simplified diagram of FEV1 progression over time. In reality, there is heterogeneity in the rate of decline in FEV1 owing to the complex interactions of genes with environmental exposures and risk factors over an individual's lifetime [adapted from Lange et al. NEJM 2015;373:111-22].

COPD-P

- COPD from pollution exposure

- Biomass fuel smoke

- Ambient air pollution (natural or anthropogenic)
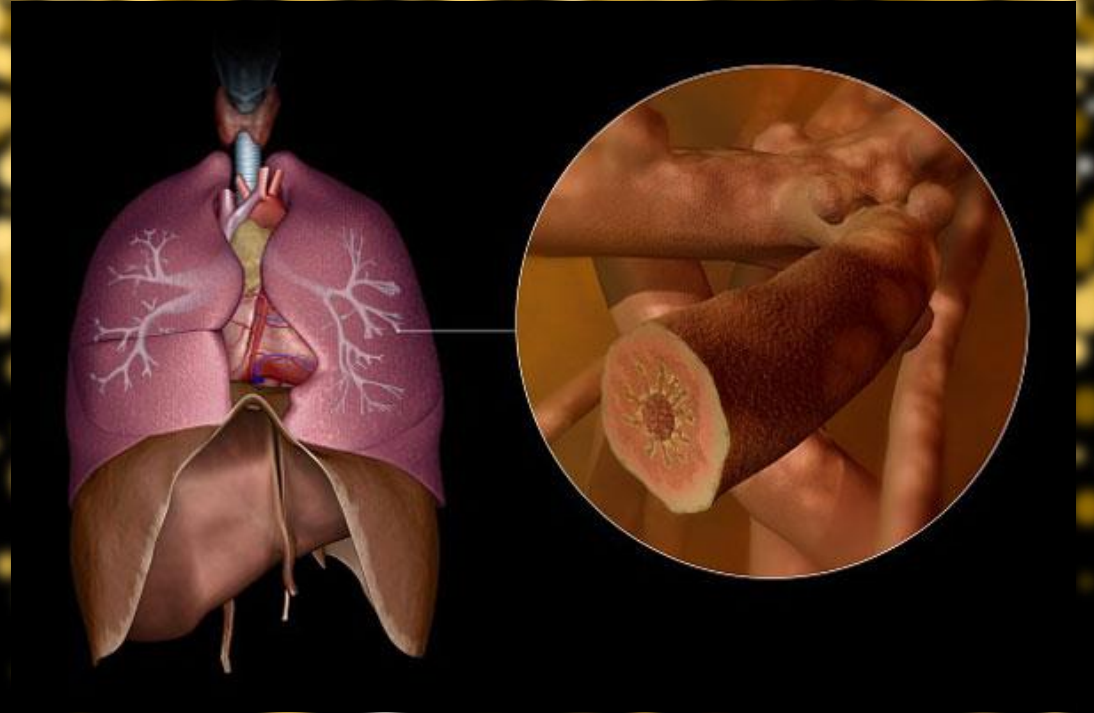
- Occupational exposures

COPD-I

- COPD related to infections

- Can include childhood illness

- TB-associated COPD

- HIV-associated COPD

COPD-A

- COPD associated with asthma

- Particularly childhood/ poorly controlled cases

Taxonomy Takeaways

- No long a single "disease," but more of a syndrome

- Impact on current practice likely limited

- Tremendous potential for future research (validation & treatment)

- A reminder that ANYONE can get COPD

Classification & Treatment

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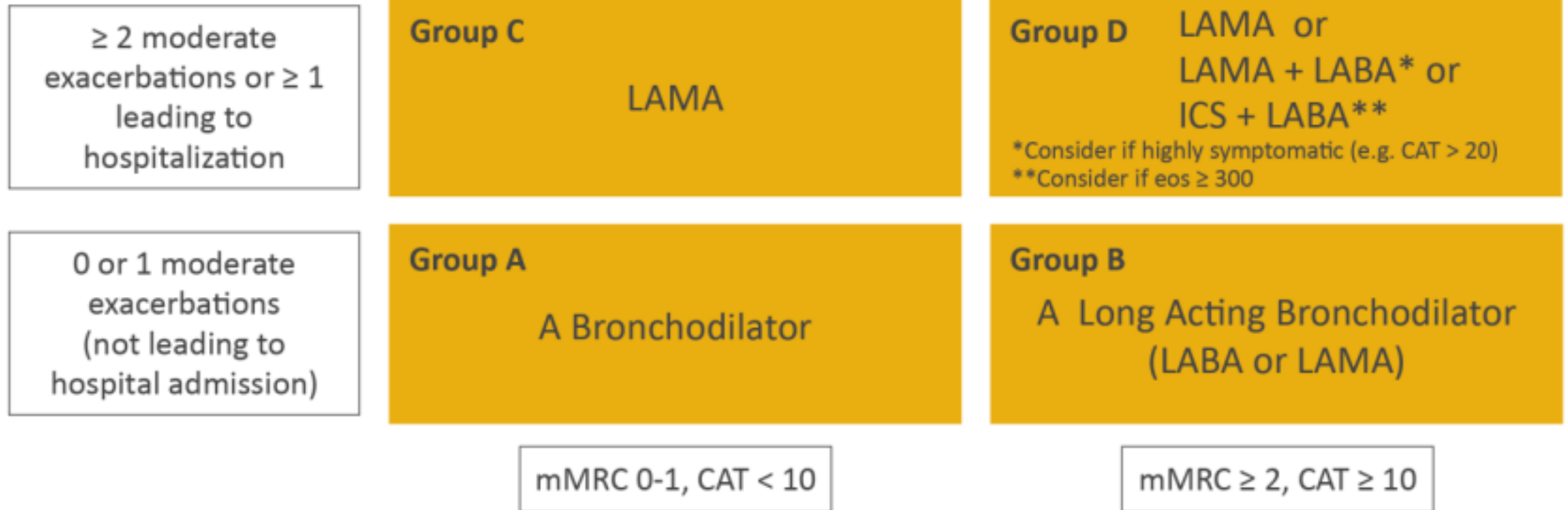
INITIAL PHARMACOLOGICAL TREATMENT

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0 or 1 moderate exacerbations (not leading to hospital admission)	**Group A** A Bronchodilator	**Group B** A Long Acting Bronchodilator (LABA or LAMA)
	mMRC 0-1, CAT < 10	mMRC ≥ 2, CAT ≥ 10

FIGURE 4.2

Honest ABE

- Exacerbations are the single greatest factor affecting lung function decline & disease progression!

Initial Pharmacological Treatment

Figure 4.2

≥ 2 moderate exacerbations or ≥ 1 leading to hospitalization	**GROUP E** **LABA + LAMA*** *consider LABA+LAMA+ICS* if blood eos ≥ 300*	
0 or 1 moderate exacerbations (not leading to hospital admission)	**GROUP A** **A bronchodilator** mMRC 0-1, CAT < 10	**GROUP B** **LABA + LAMA*** mMRC ≥ 2, CAT ≥ 10
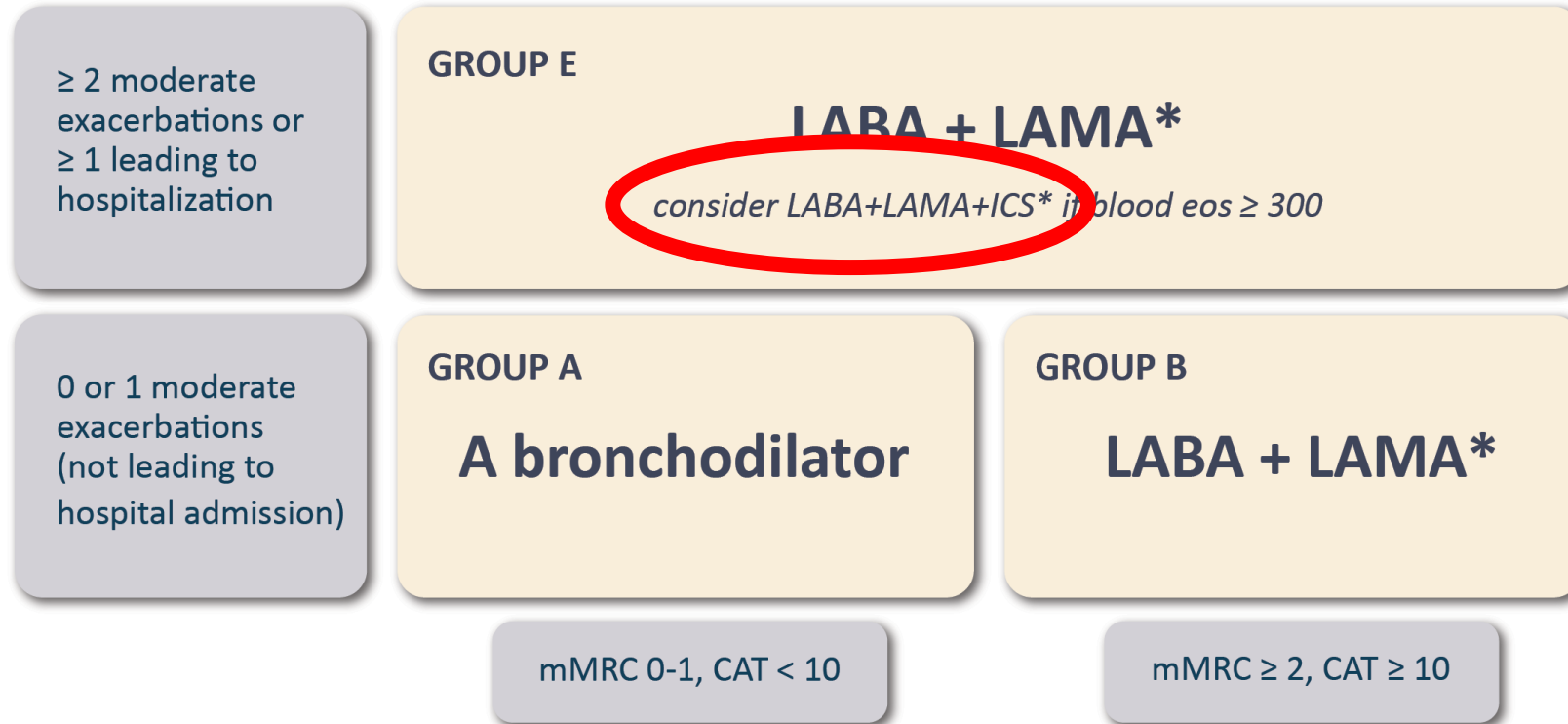
*single inhaler therapy may be more convenient and effective than multiple inhalers

Goals for Treatment of Stable COPD

Table 4.1

- Relieve Symptoms
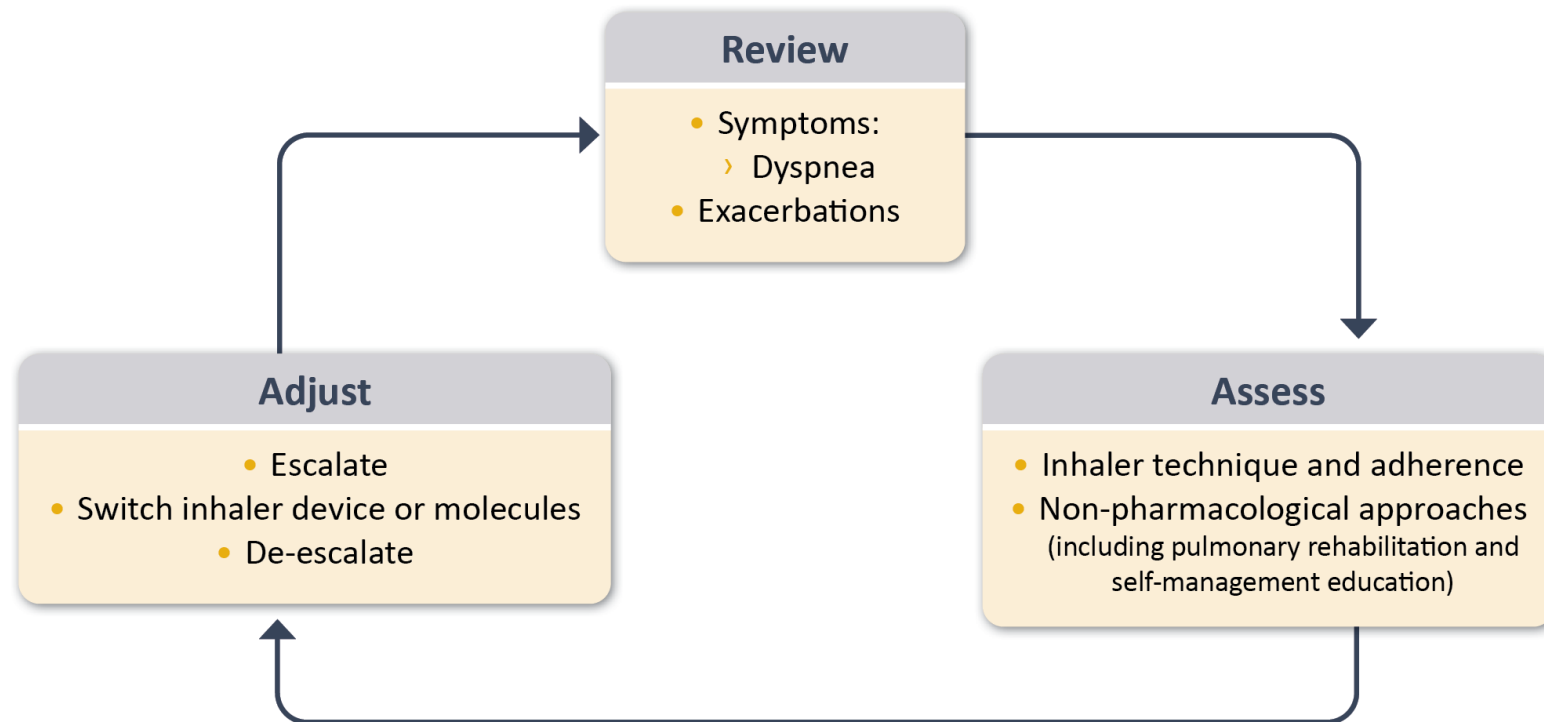- Improve Exercise Tolerance
- Improve Health Status

▶ **REDUCE SYMPTOMS**

AND

- Prevent Disease Progression
- Prevent and Treat Exacerbations
- Reduce Mortality

▶ **REDUCE RISK**
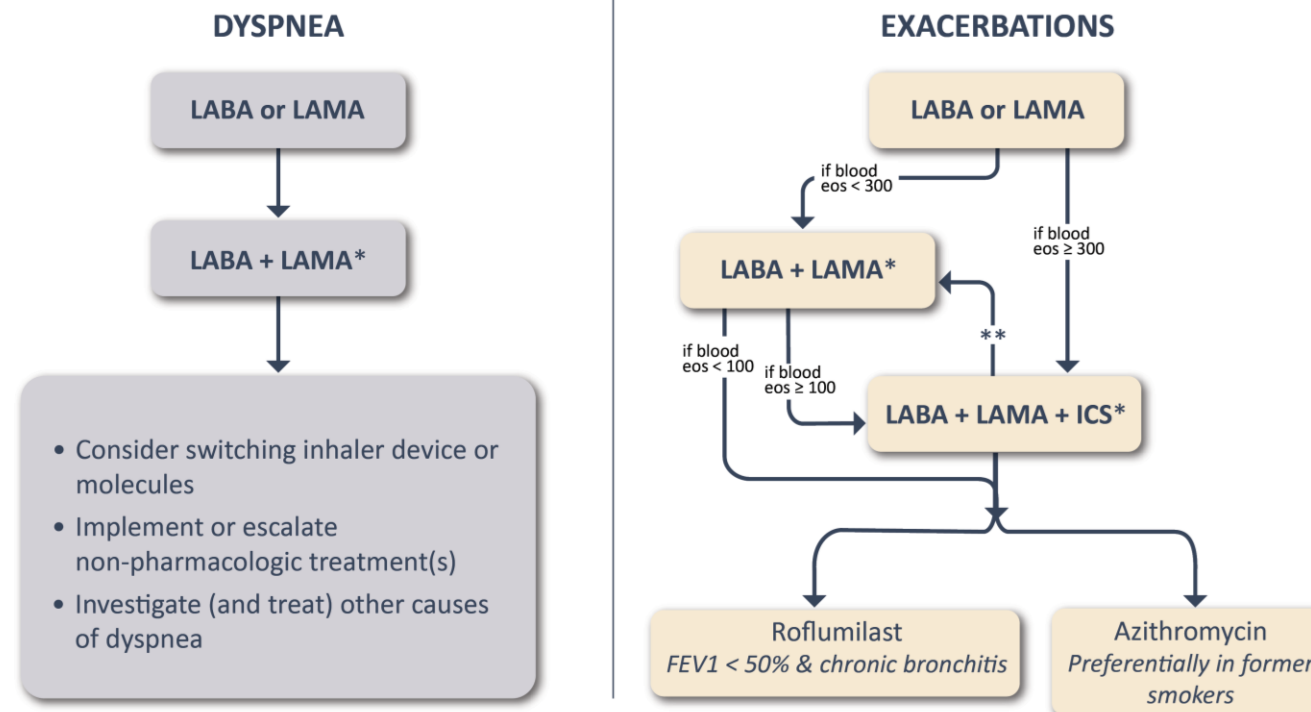
Management Cycle

Figure 4.3

Follow-up Pharmacological Treatment

Figure 4.4

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

② IF NOT:
- Check adherence, inhaler technique and possible interfering comorbidities
- 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 ABE assessment at diagnosis

DYSPNEA

LABA or LAMA

↓

LABA + LAMA*

↓

- Consider switching inhaler device or molecules
- Implement or escalate non-pharmacologic treatment(s)
- Investigate (and treat) other causes of dyspnea

EXACERBATIONS

LABA or LAMA

if blood eos < 300

if blood eos ≥ 300

LABA + LAMA*

if blood eos < 100   if blood eos ≥ 100

**

LABA + LAMA + ICS*

Roflumilast
FEV1 < 50% & chronic bronchitis

Azithromycin
Preferentially in former smokers

*Single inhaler therapy may be more convenient and effective than multiple inhalers

**Consider de-escalation of ICS if pneumonia or other considerable side-effects. In case of blood eos ≥ 300 cells/μl de-escalation is more likely to be associated with the development of exacerbations

Exacerbations

Adapted from: The ROME Proposal, Celli et al. (2021) Am J Respir Crit Care Med. 204(11): 1251-8. Abbreviations: VAS visual analog dyspnea scale; RR respiratory rate; HR heart rate; SaO_2 oxygen saturation; CRP C-reactive protein; ABG arterial blood gases; PaO_2 Arterial pressure of oxygen.
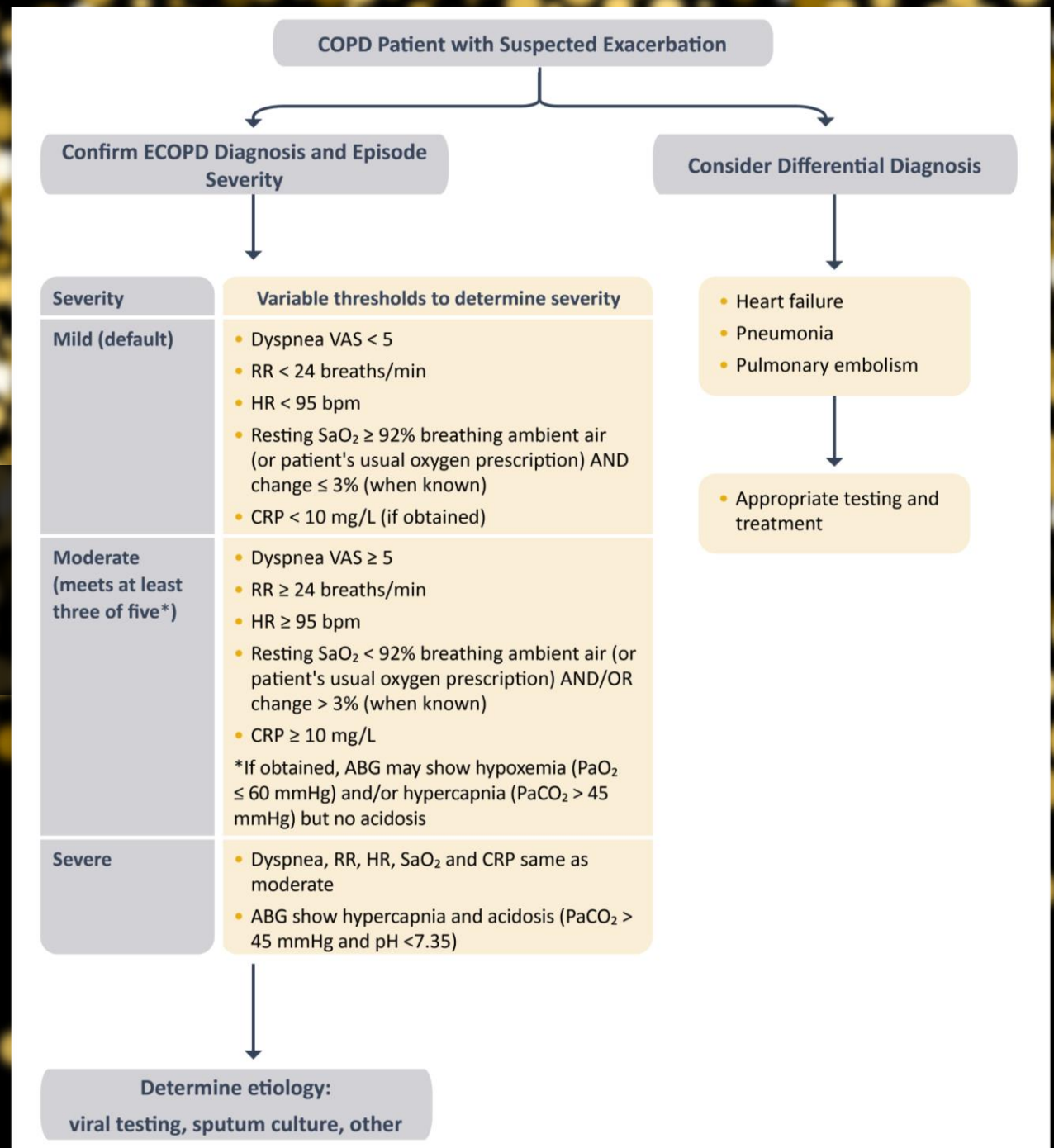
Emerging Research Priorities
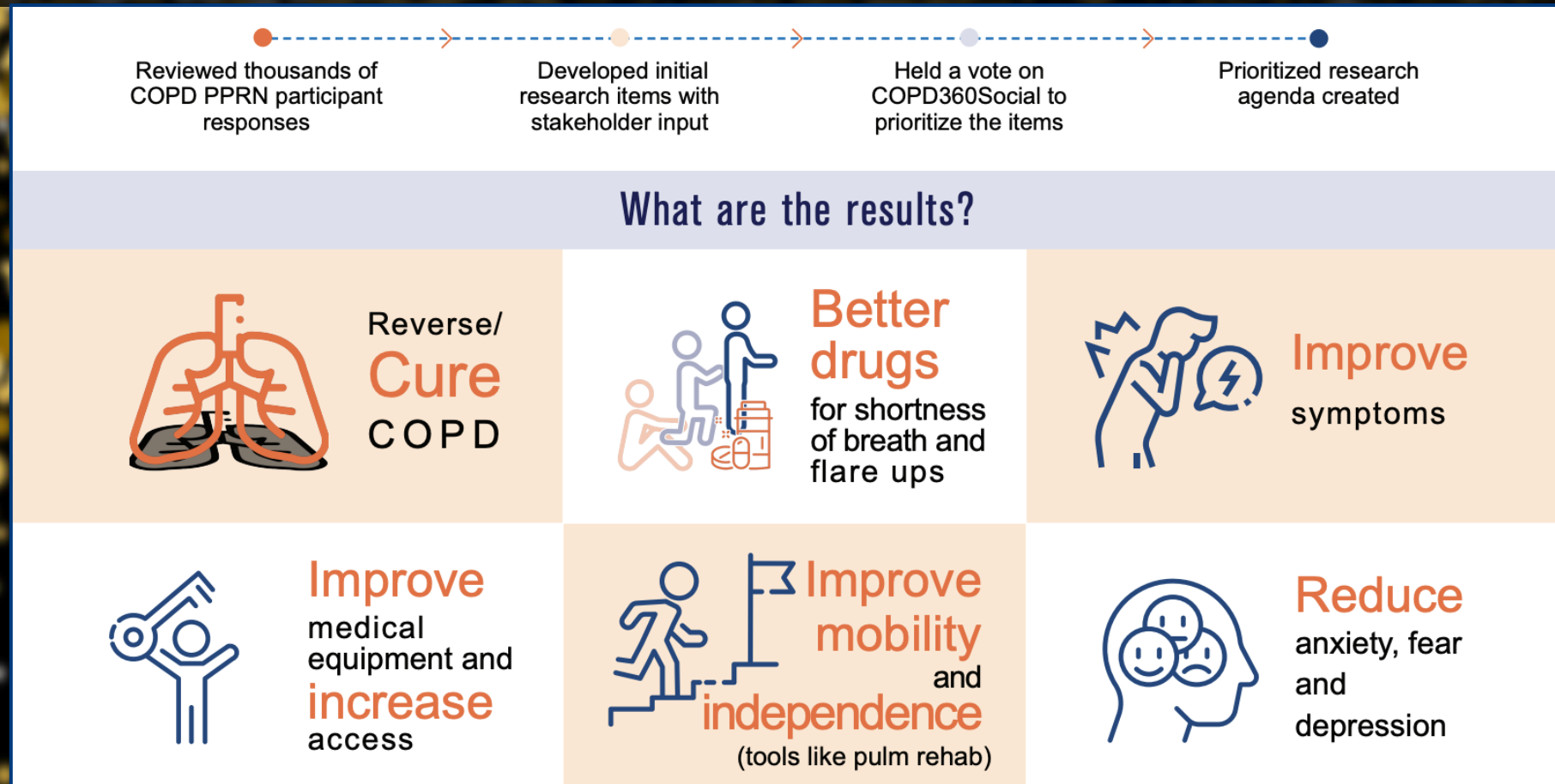
1 Gruß, I., McCreary, G.M., Ivlev, I. *et al.* Developing a patient-driven chronic obstructive pulmonary disease (COPD) research agenda in the U.S.. *J Patient Rep Outcomes* 5, 126 (2021). https://doi.org/10.1186/s41687-021-00399-7

Emerging Research Priorities

- Telehealth (including remote pulmonary rehab)

- Screening/case-finding

- Improvements in inhaled medication delivery

- New treatment pathways

Thank You!

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