MIKE HESS, MPH, RRT, RPFT – 2023 ACOI

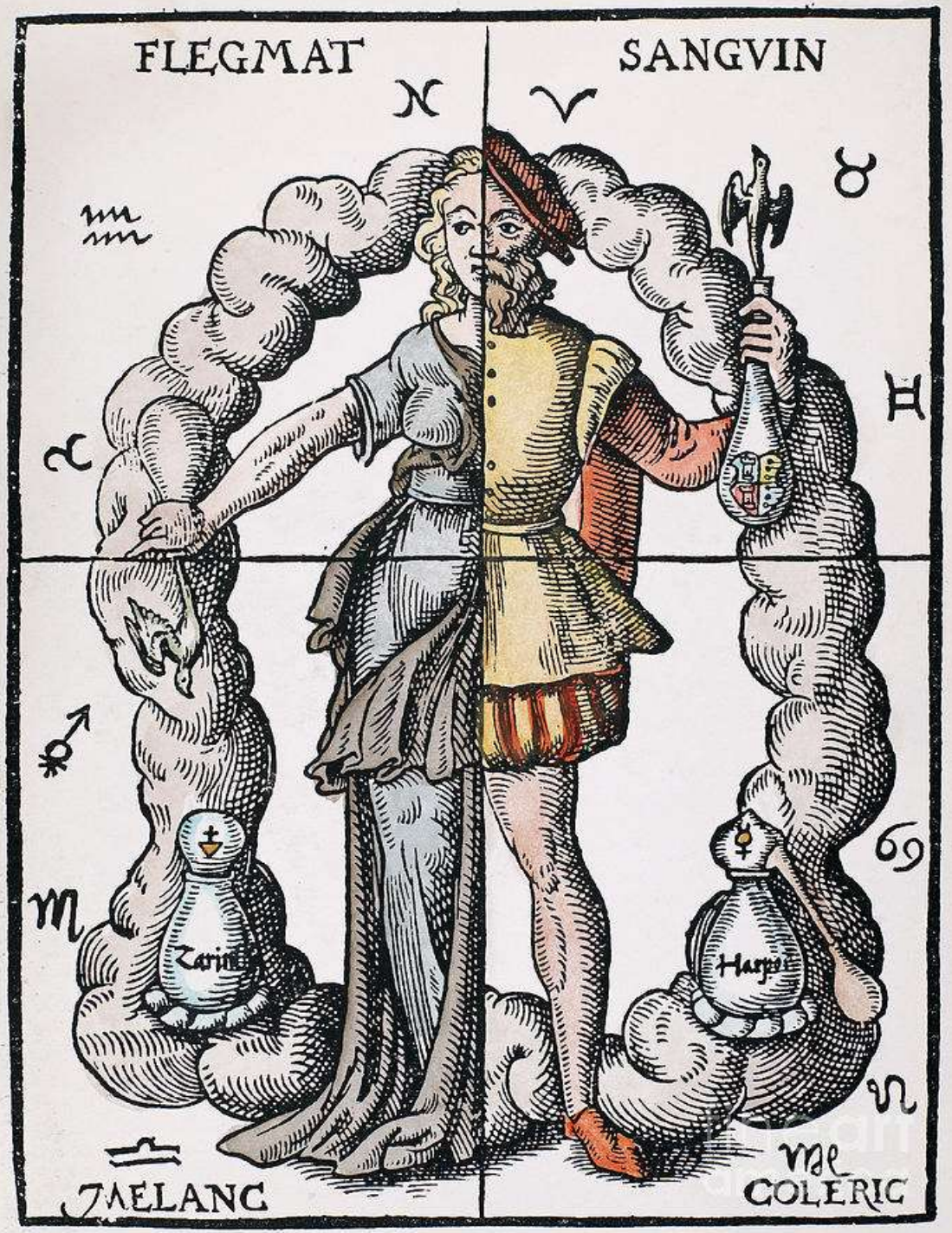
OBJECTIVES

- Identify the latest concepts in the pathogenesis and diagnosis of COPD & their relationship to previous understandings of the condition
- Understand new treatment algorithms and their underlying evidence
- Describe future opportunities for COPD research (including prevention and diagnostics)

ABOUT/DISCLOSURES

- **Senior Director, Public Outreach and Education, COPD Foundation**
- **Chronic Lung Disease Coordinator, WMed Health**

- **No industry disclosures/conflicts**


FLEGMAT
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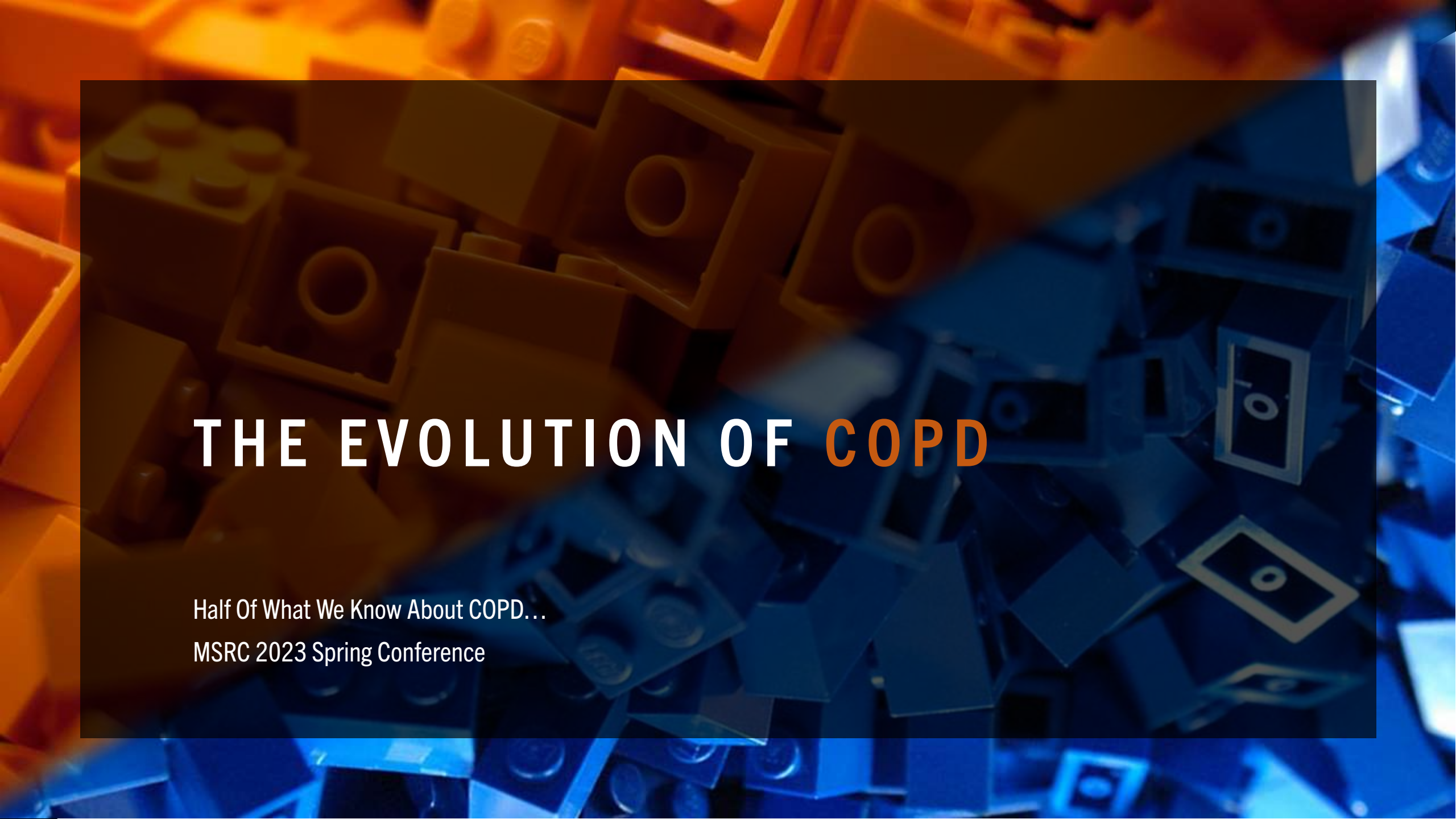
THEOPHILUS BONETUS D.M.
THEOPHILI
BONETI
MEDICINÆ DOCTORIS
SEPULCHRETUM
SIVE
ANATOMIA PRACTICA
EX
CADAVERIBUS MORBO DENATIS
HISTORIAS ET OBSERVATIONES
EDITIO ALTERA, QUAM NOVIS COMMENTARIIS
JOHANNES JACOBUS MANGETUS, MEDICINÆ DOCTOR
TOMUS PRIMUS
LUGDUNI
Sumptibus CRAMER & PERACHON
M DCC



THE EVOLUTION OF COPD

Half Of What We Know About COPD…

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THE FIRST THINGS WE KNEW

- **Asthma, chronic bronchitis, and emphysema are NOT separate disease states**

- **Chronic, Non-Specific Lung Disease (CNSLD) was one pathology with multiple pathways**

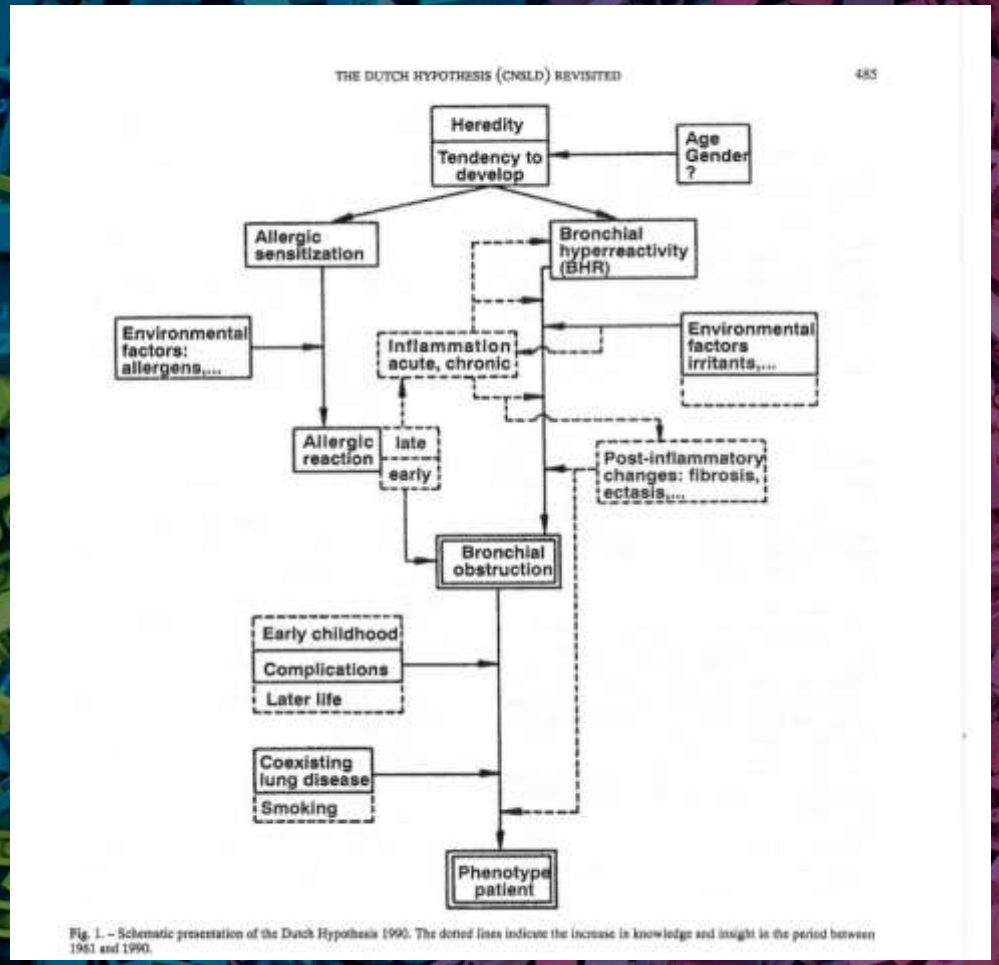
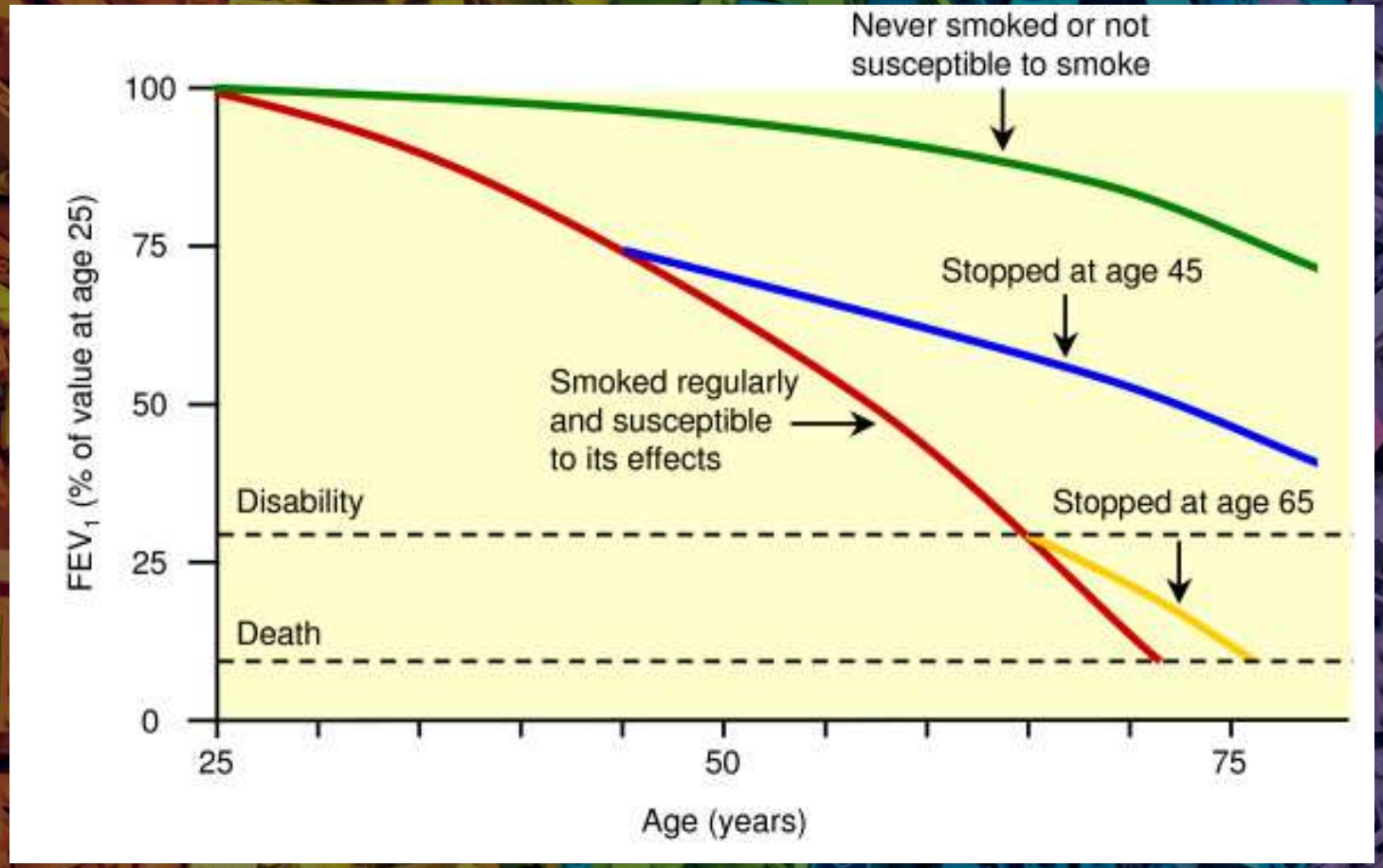
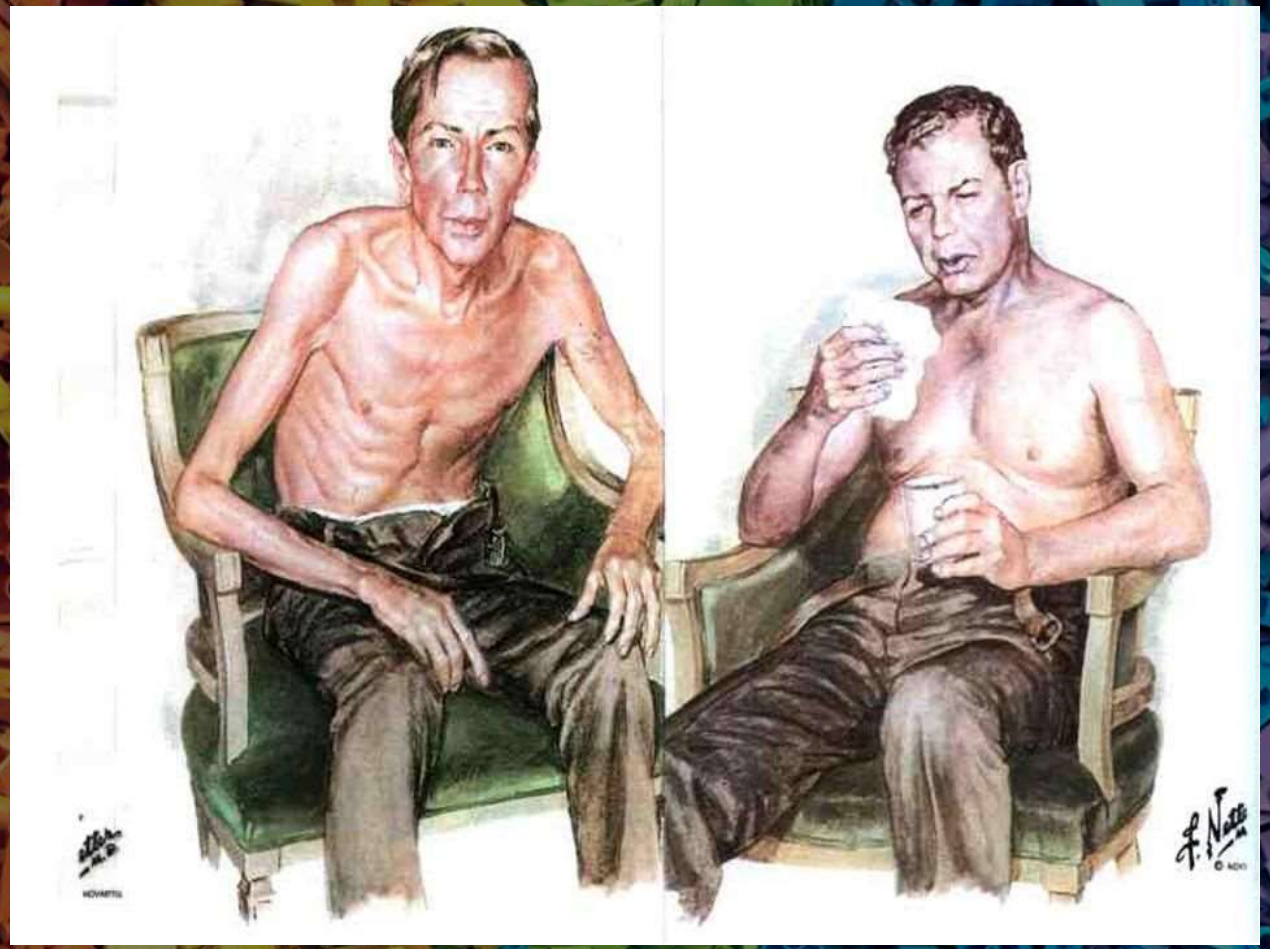


Fig. 1. – Schematic presentation of the Dutch Hypothesis 1990. The dotted lines indicate the increase in knowledge and insight in the period between 1961 and 1990.

WE KNOW WE CAN DO (ALMOST) NOTHING



NOW WE KNOW THERE ARE TWO



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

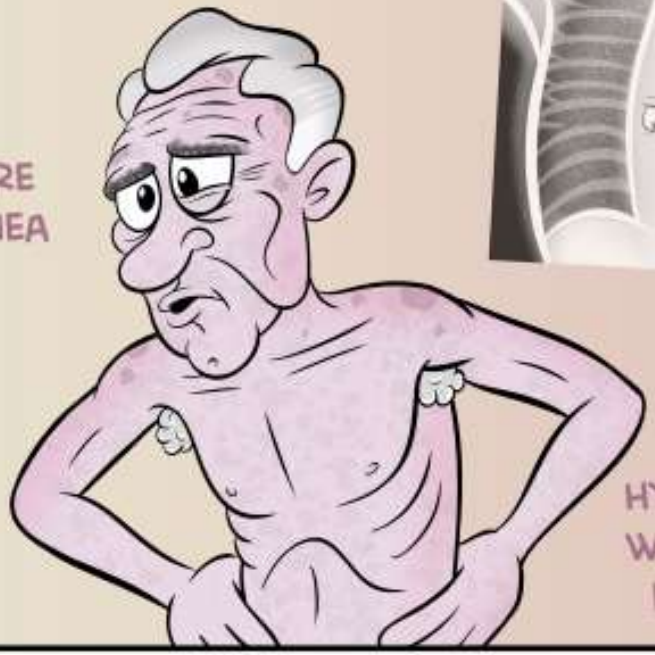
RHONCHI AND WHEEZING

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

THE GOLDEN ERA

“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.”

THE GOLDEN ERA

Spirometrically confirmed diagnosis → Assessment of airflow obstruction

Post-bronchodilator FEV1/FVC < 0.7

GRADE	FEV1 (% predicted)
GOLD 1	≥ 80
GOLD 2	50-79
GOLD 3	30-49
GOLD 4	< 30

GLOBAL INITIATIVE FOR CHRONIC OBSTRUCTIVE LUNG DISEASE™

WHY DO WE CARE WHAT WE KNOW?

Half Of What We Know About COPD…

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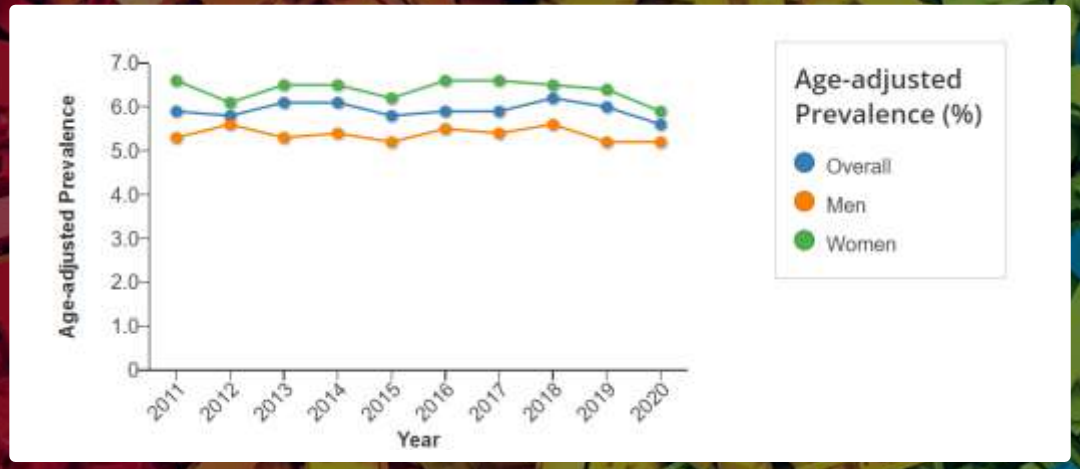
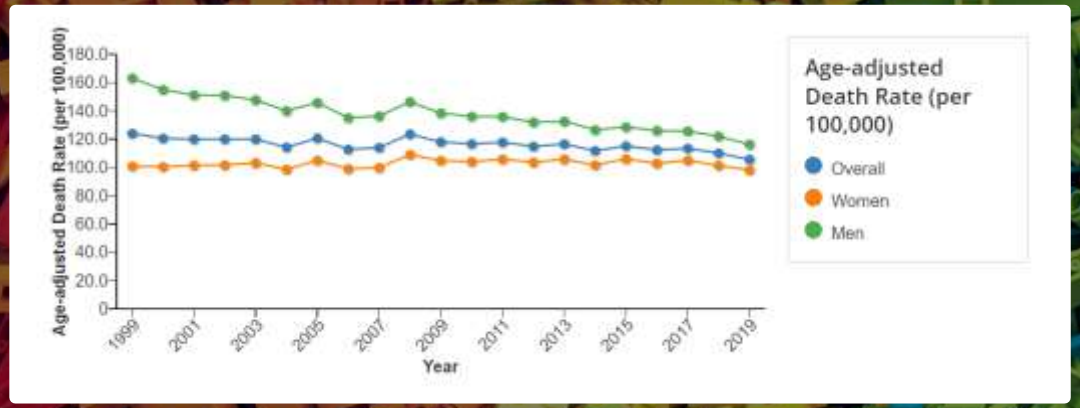
GOING NOWHERE FAST

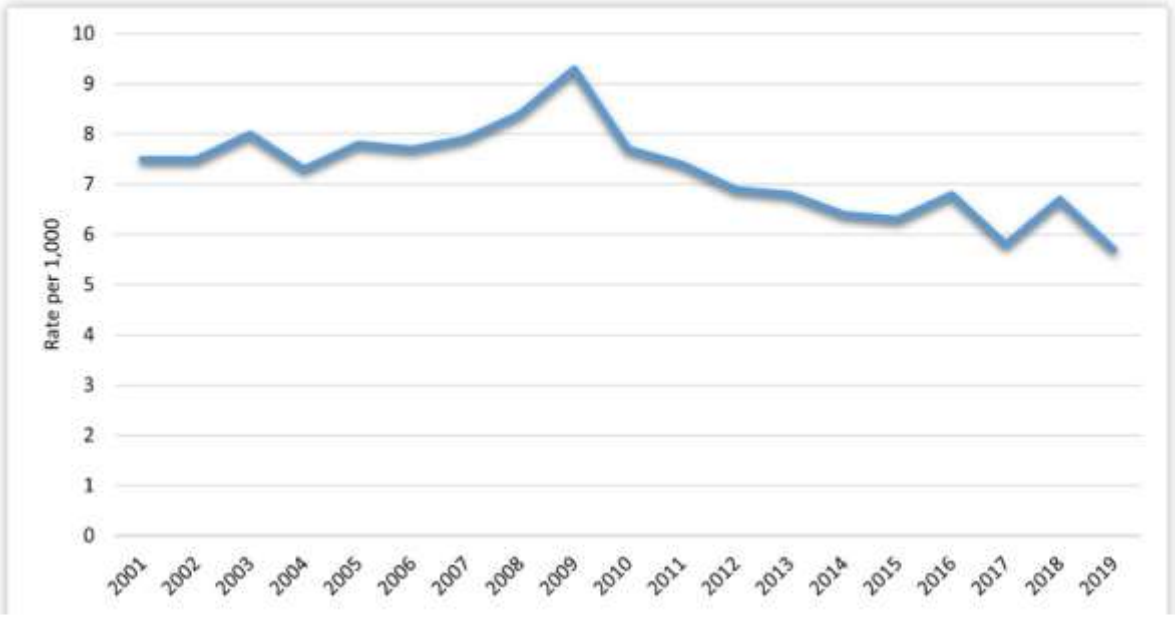


HTTPS://WWW.CDC.GOV/COPD/DATA-AND-STATISTICS/NATIONAL-TRENDS.HTML



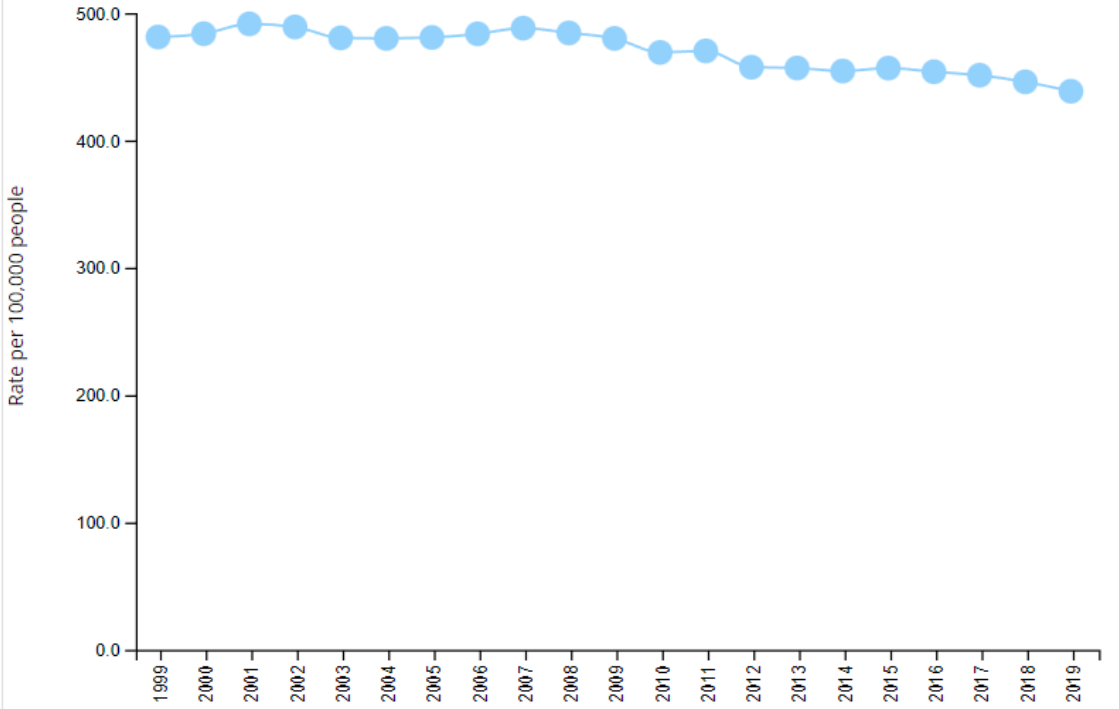
- **COPD prevalence and mortality remain essentially stagnant.**
- **Over the same time, significant progress has been made in conditions such as cancer and diabetes.**

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



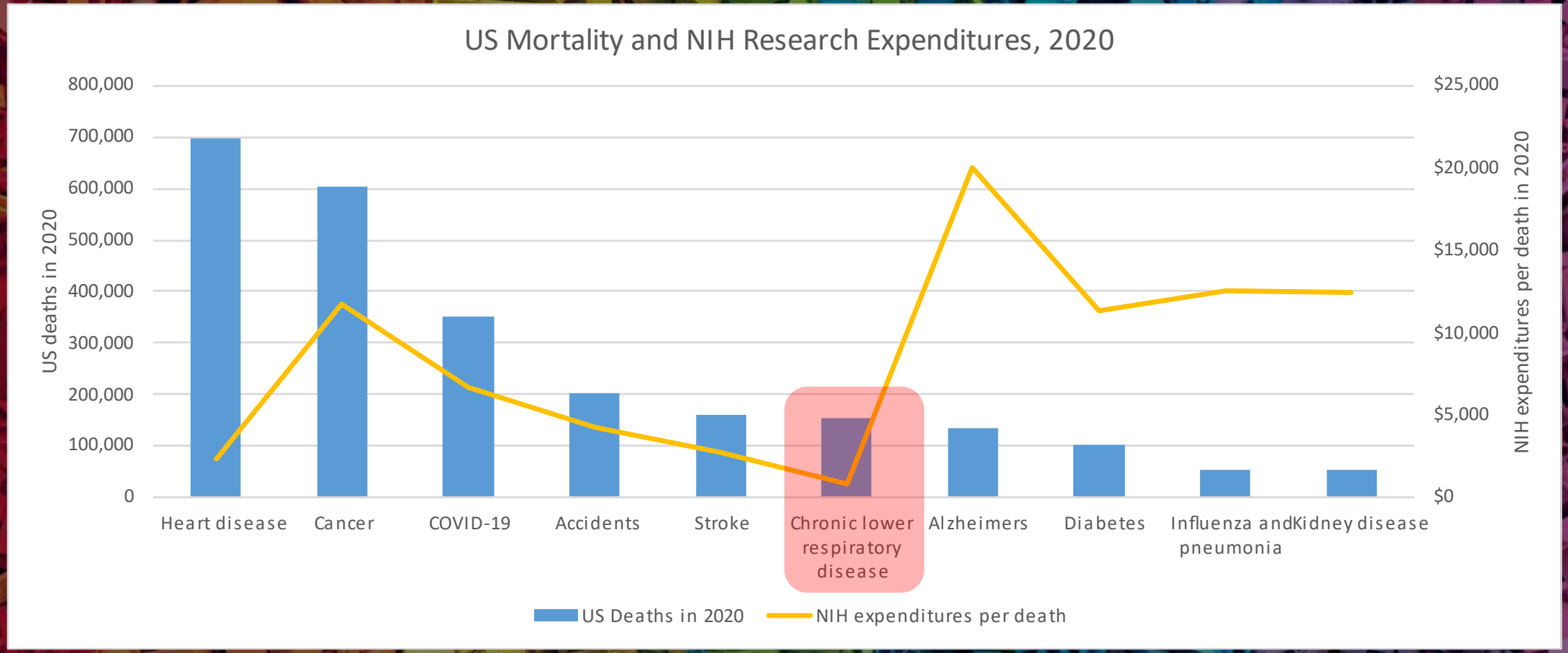
Annual Rates of New Cancers, 1999-2019

United States




GETTING WORSE GLOBALLY
212,300,000
CASES REPORTED GLOBALLY
3,300,000
DEATHS ATTRIBUTABLE TO COPD
74,400,000
DISABILITY-ADJUSTED LIFE YEARS
https://www.bmj.com/content/378/bmj-2021-069679

FUNDING IS SCARCE, REQUIRING EFFICIENCY



COPD RESEARCH IS OFTEN DIFFICULT

- **Lack of research funding limits potential evidence base**
- **Relatively slow disease progression delays outcomes research**
- **Diagnostic uncertainty, combined with broad definition of COPD introduces many confounding factors**

ASKING THE RIGHT QUESTIONS

Half Of What We Know About COPD…

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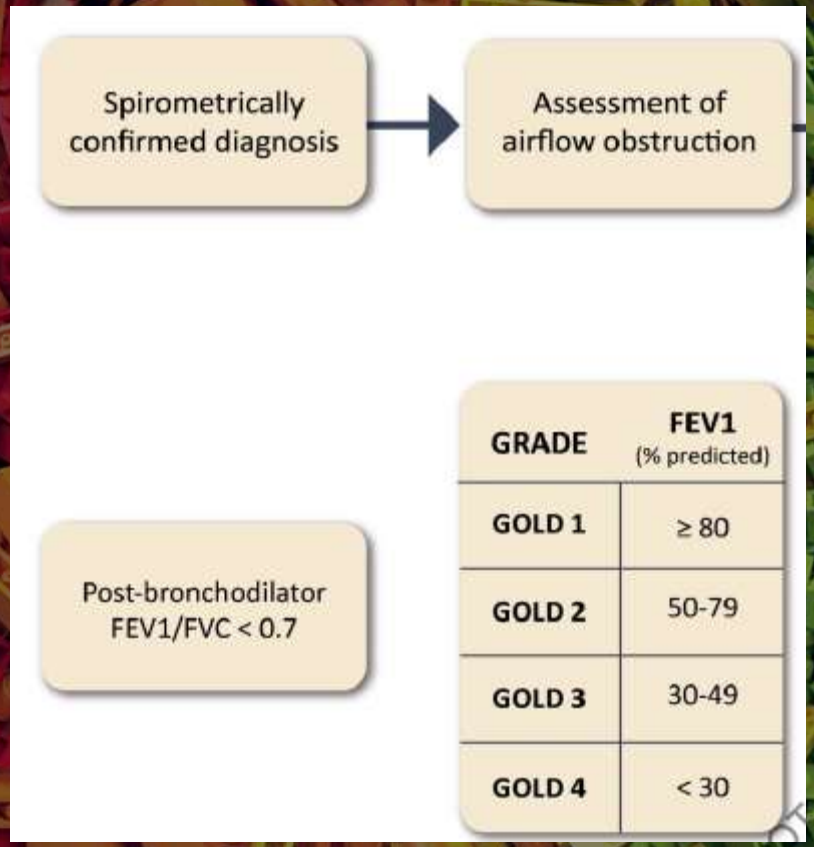
THE GOLDEN ERA REDUX

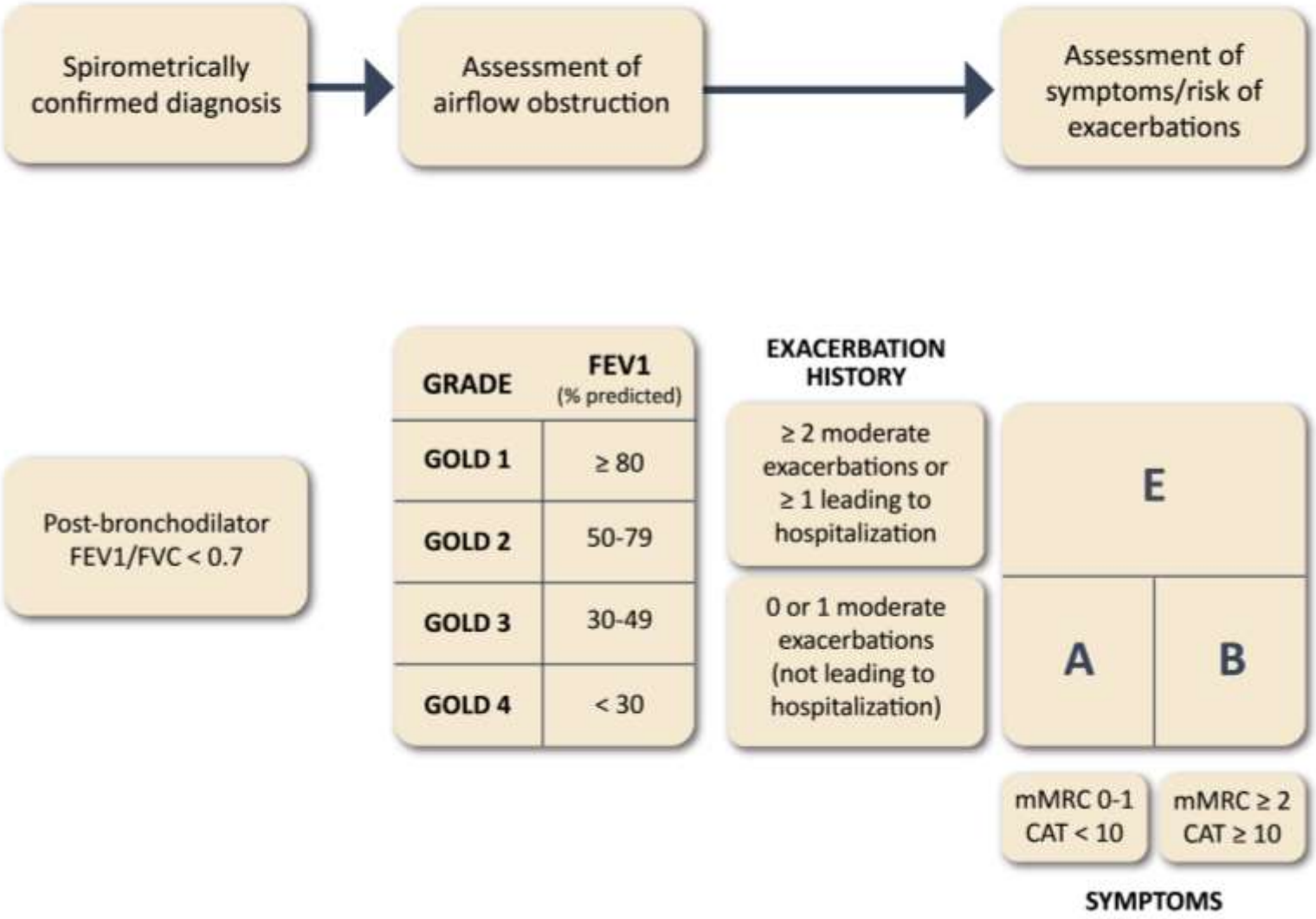


GRADE	FEV1 (% predicted)
GOLD 1	≥ 80
GOLD 2	50-79
GOLD 3	30-49
GOLD 4	< 30

GLOBAL INITIATIVE FOR CHRONIC OBSTRUCTIVE LUNG DISEASE™

GOLD ABE Assessment Tool

Figure 2.3



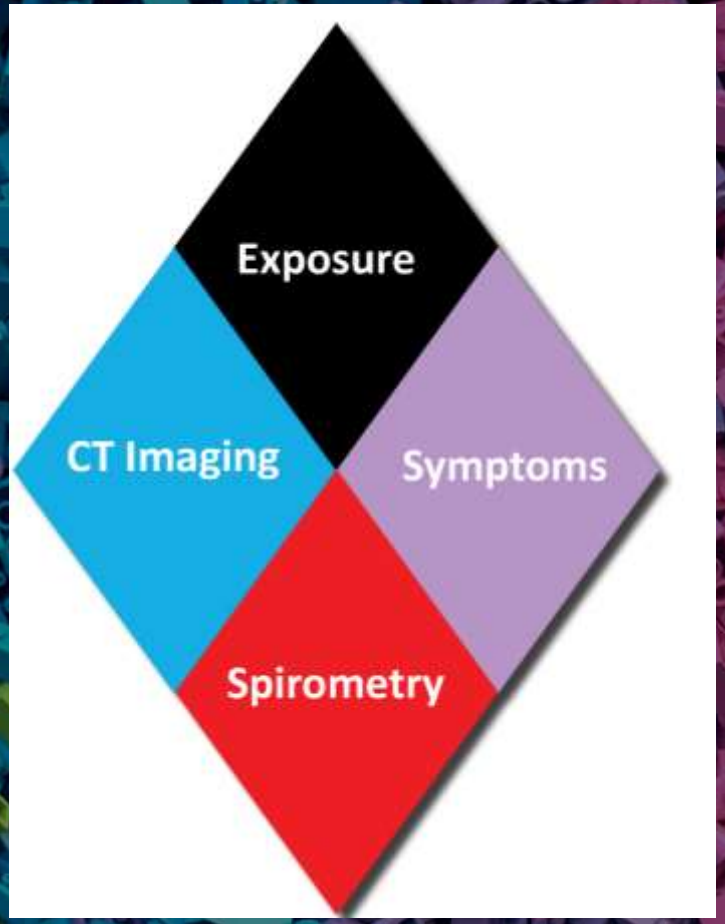
SCREENING AND DIAGNOSTICS

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?	☐	☐	☐

*COPD Assessment in Primary Care to identify Undiagnosed Respiratory Disease & Exacerbation Risk



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.).

The Lancet Commissions

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

A HOLISTIC VIEW…

- **COPD has “complex interactions” with physiology, concurrent conditions, and exacerbations.**
- **We fail to optimally describe or even identify early stages of COPD.**
- **Defining it as a single “disease” is inherently limiting and possibly inaccurate.**

...WITH SYSTEMIC BARRIERS

- We fail to limit exposures to risk factors (tobacco products, environmental pollutants, etc).
- We have insufficient screening and diagnostic approaches.
- We need a heterogenous approach for a heterogenous condition.
- We fail to invest in research for diagnostics and therapeutics.

COPD REDEFINED

- **“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)**

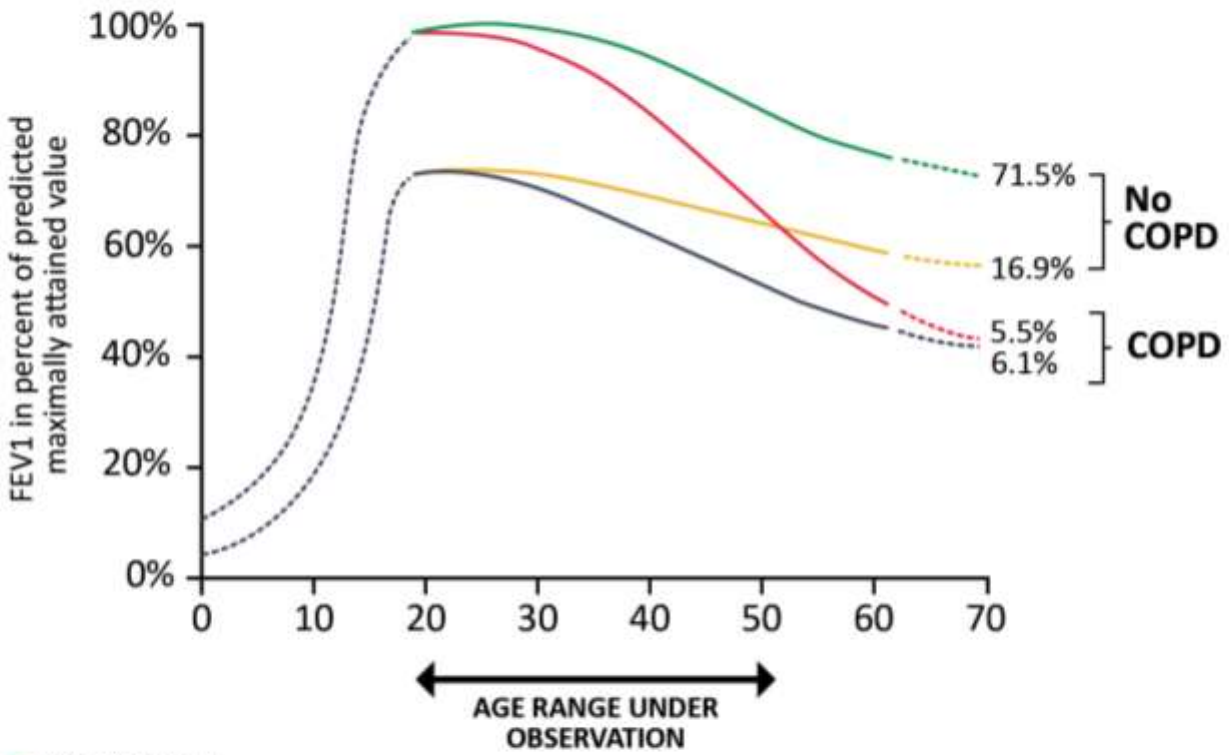
- **“COPD is a heterogenous lung condition characterized by chronic respiratory symptoms (dyspnea, cough, sputum production) due to abnormalities of the airways (bronchitis, bronchiolitis) and/or alveoli (emphysema) that cause persistent, often progressive airflow obstruction.” (2023)**

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

FEV1 Trajectories (TR) Over the Life Course

Figure 1.1



- 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].

NEW TAXONOMIES

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

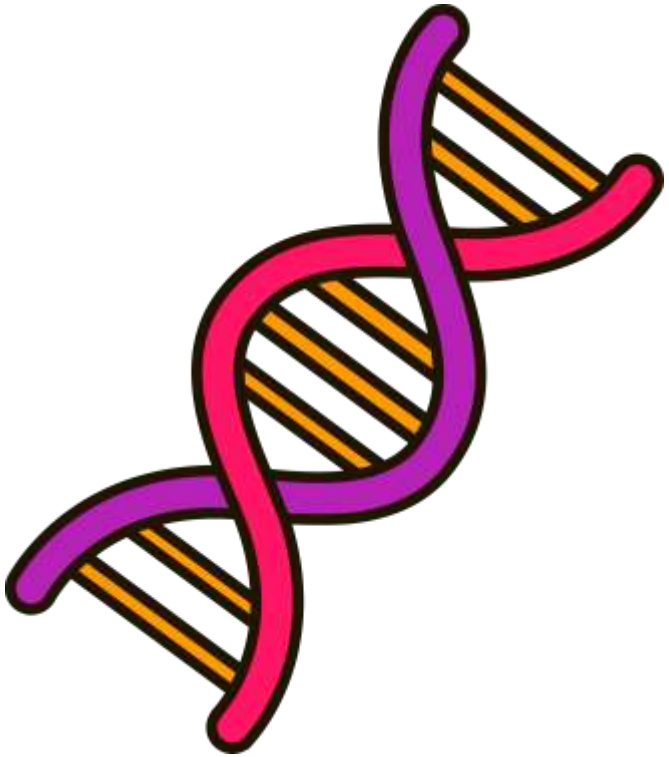
- **Etiotype:** Clinical traits based on the etiology of a particular disease process

COPD-C

- **COPD due to cigarette smoking**
- **May potentially include ENDS and cannabis**
- **Also includes secondhand smoke**

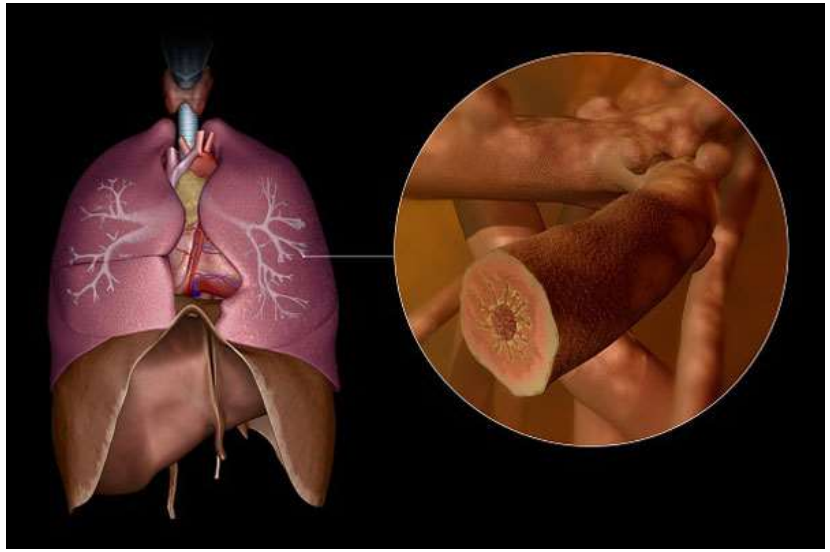
COPD-G

- **Genetically determined**
- **Includes alpha-1 antitrypsin deficiency (AATD)**
- **Potentially other genetic variants**



COPD-A

- COPD associated with asthma
- Particularly childhood/poorly controlled cases
- May include asthma-COPD overlap



COPD-P

- **COPD from pollution exposure**
- **Biomass fuel smoke**
- **Ambient air pollution (natural or anthropogenic)**
- **Occupational exposures**

COPD-D

- **COPD secondary to abnormal lung development**
- **Prenatal issues, premature birth, neonatal lung problems**
- **Adverse childhood events (ACEs)/ social determinants of health (SDHs) limiting lung maturity**

COPD-I

- COPD related to infections
- May include childhood illnesses
- TB-associated COPD
- HIV-associated COPD

TAXONOMY TAKEAWAYS

- No long a single “disease,” but more of a syndrome (especially considering certain overlaps)
- Impact on current practice likely limited
- Tremendous potential for future research (validation & treatment)
- A reminder that ANYONE can get COPD

WHAT DO WE KNOW NOW ?

Half Of What We Know About COPD…

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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

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

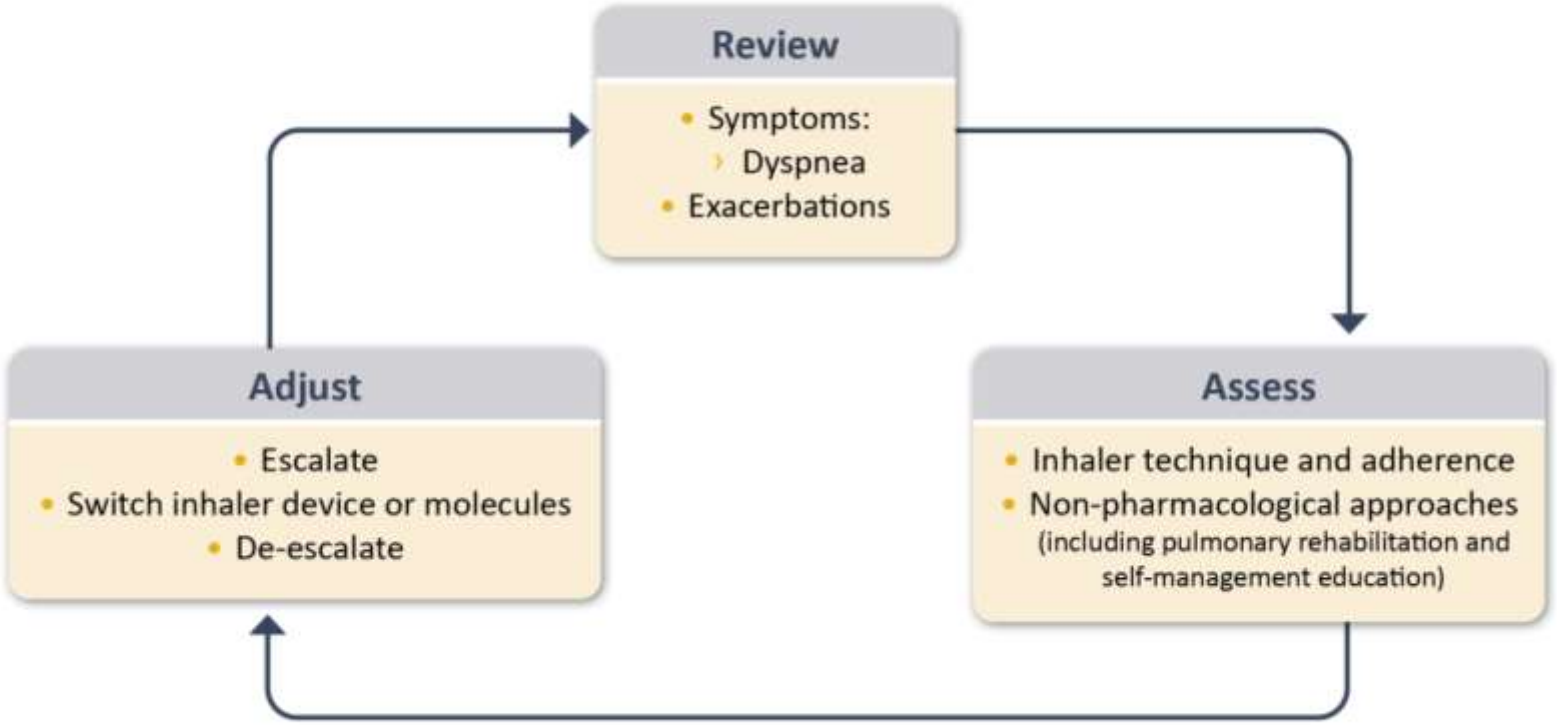
LABA + LAMA*

mMRC ≥ 2, CAT ≥ 10

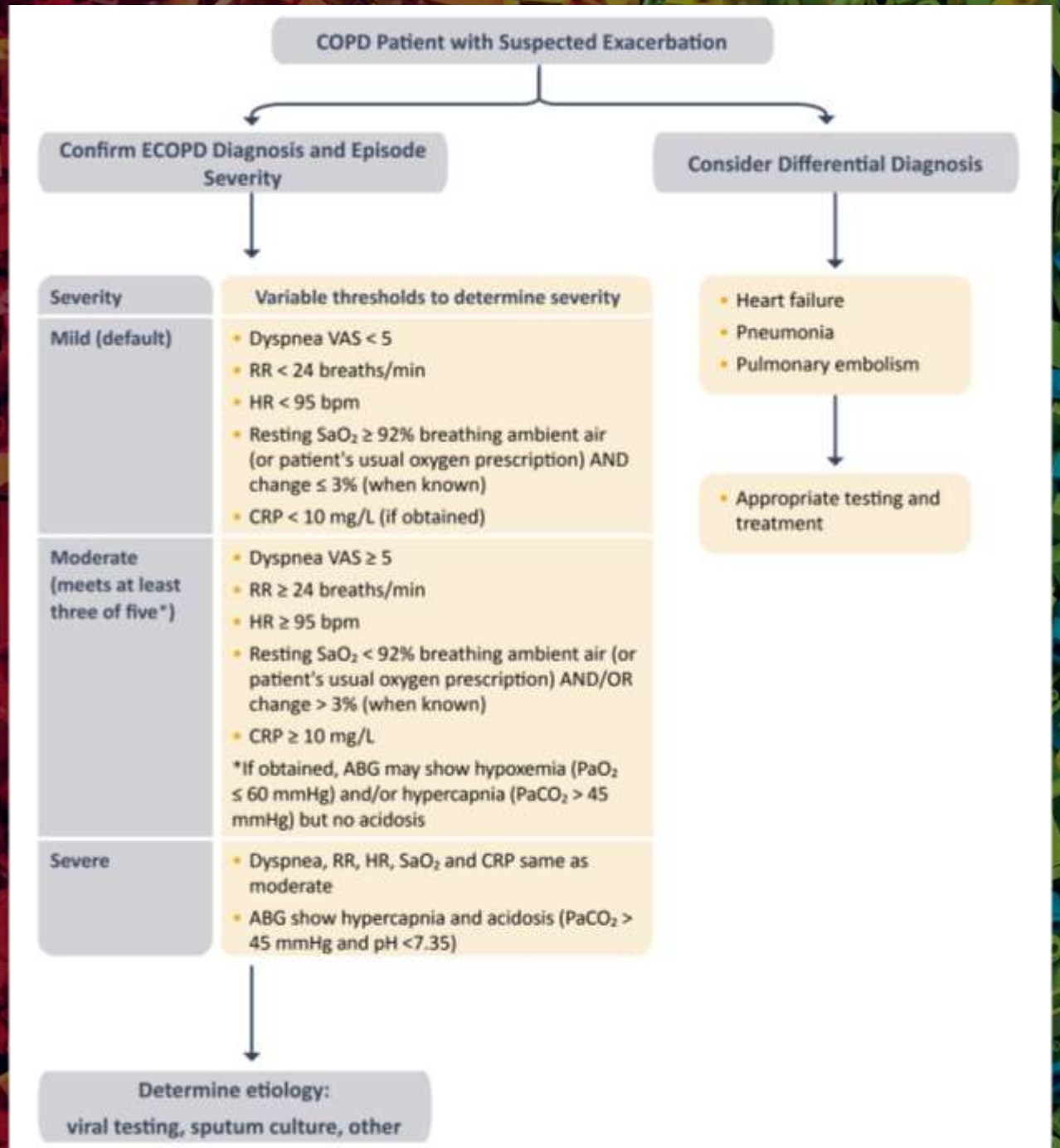
*single inhaler therapy may be more convenient and effective than multiple inhalers

Management Cycle

Figure 4.3



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.

WHAT COMES NEXT ?

Half Of What We Know About COPD…

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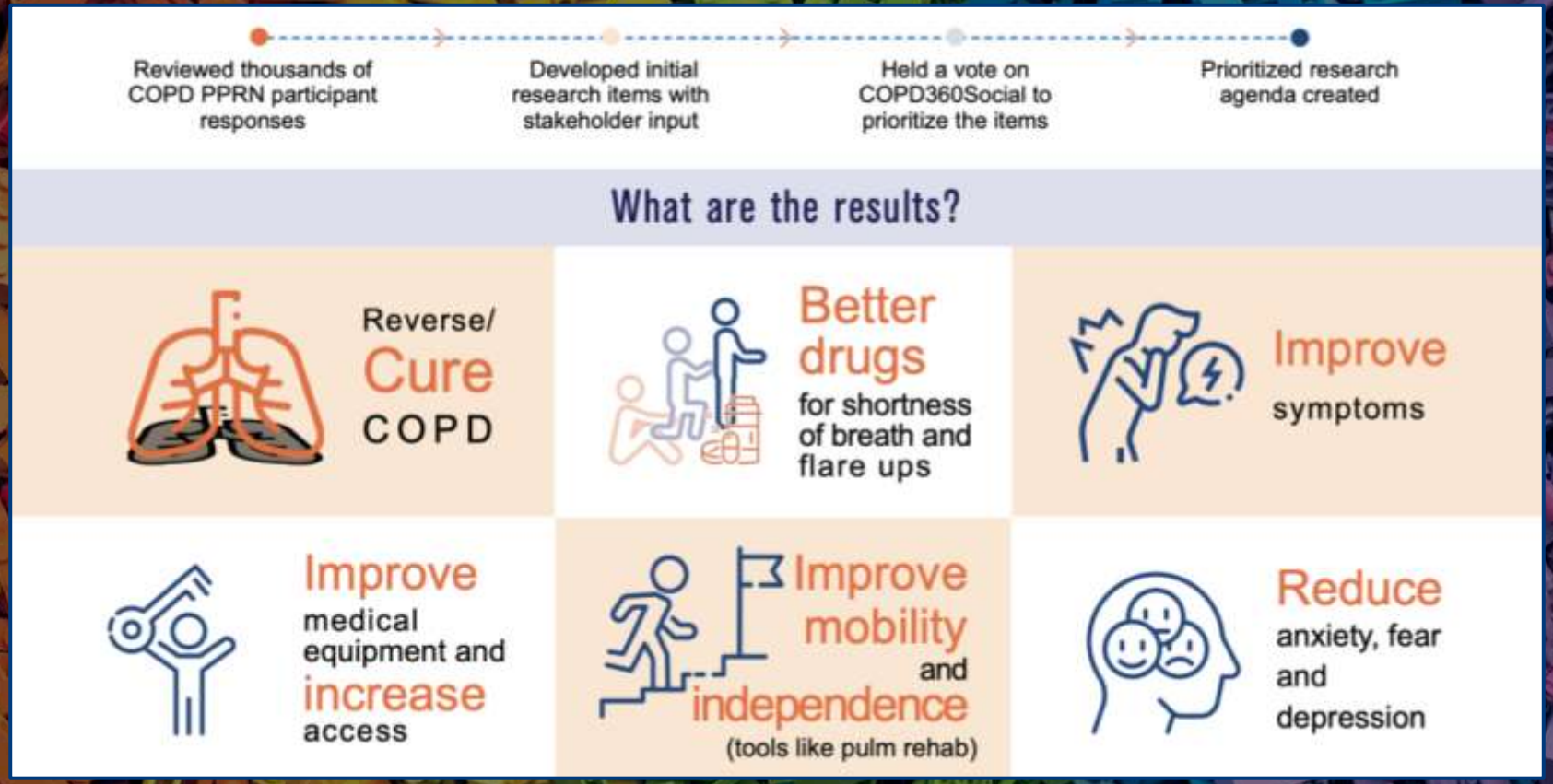
EMERGING RESEARCH PRIORITIES

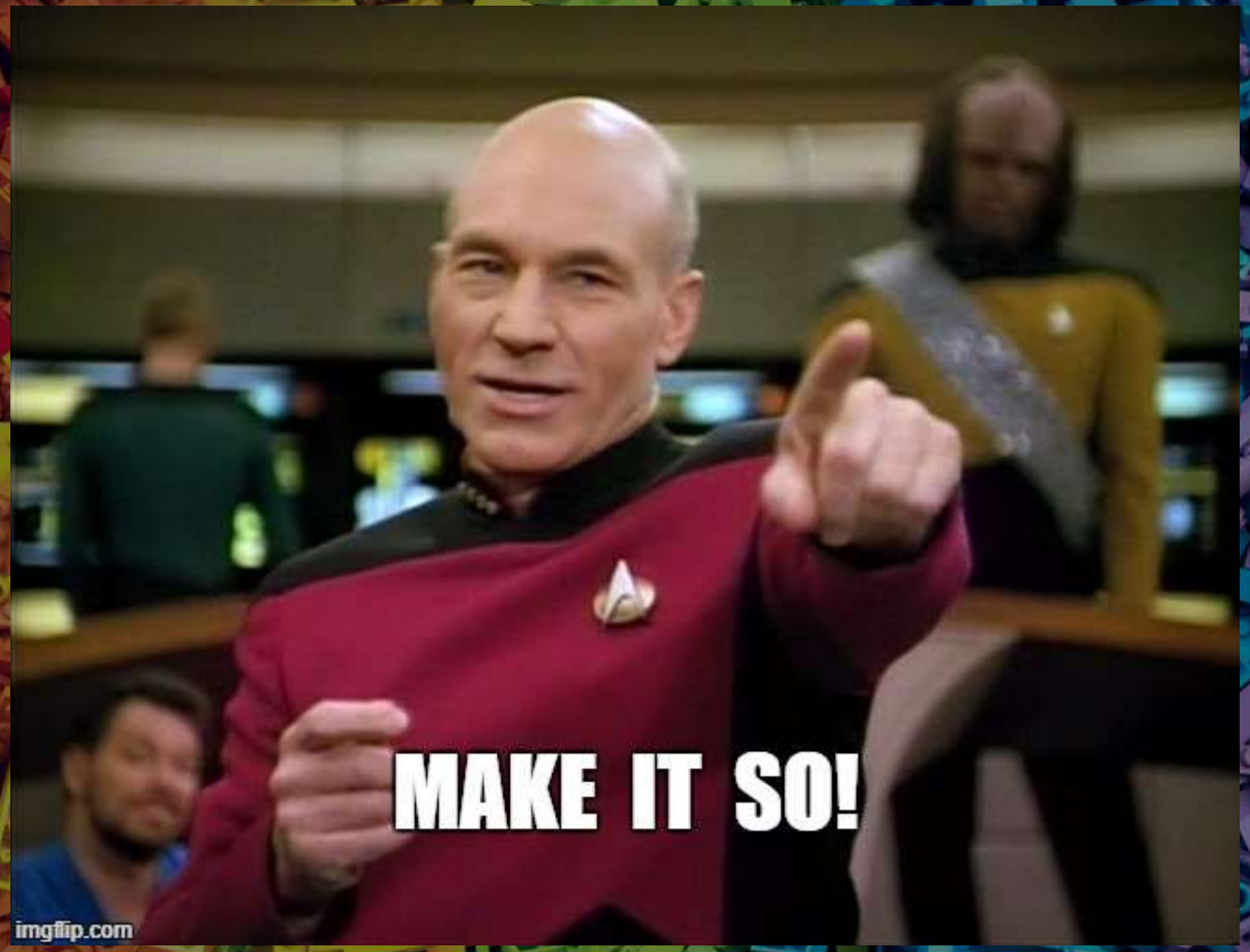


1 Gruß, I., McCreary, G.M., Ivlev, I. *et al.* Developing a patient-driven chronic obstructive pulmonary disease (COPD) research agenda in the U.S.. *J Patient Rep Outcomes* **5**, 126 (2021). https://doi.org/10.1186/s41687-021-00399-7

EMERGING RESEARCH PRIORITIES

- **Telehealth (including remote pulmonary rehab)**
- **Screening/case-finding**
- **Improvements in inhaled medication delivery**
- **New treatment pathways (long-term lung fitness?)**

IT'S UP TO ALL OF US TO...



THANK YOU!

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