



COPD Exacerbations: The ROME Approach

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CONFLICT OF INTEREST DISCLOSURE

I have received honoraria for consultation from:

GSK, B.I., Astra Zeneca, Pfizer, Chiesi, Menarini, Sanofi Aventis, Regeneron, Medimmune, Vertx, Pulmnx.

I also declare that the contents shown are independent of commercial interests.





Why meet today
over COPD
exacerbations?

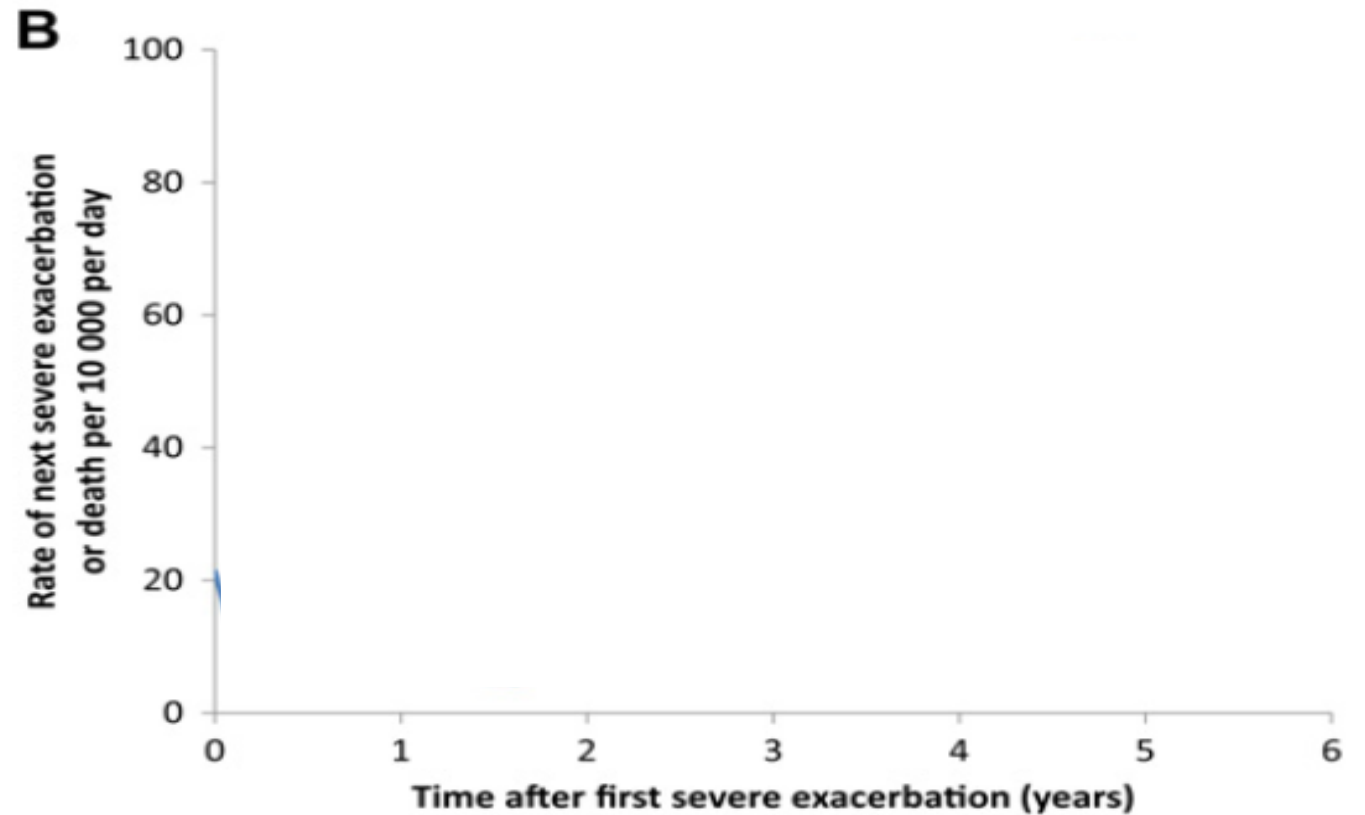
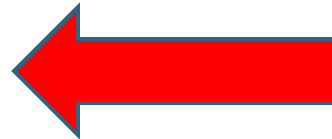
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ECOPD: TIME TO SUBSEQUENT HOSPITALISATION/DEATH

- Data from Quebec province hospitalised ECOPD patients (1990 – 2005). Followed until 2007
- Number = 73,106 patients
- 50,580 died over 17-year follow-up
 - 50% at 3.6 years
 - 75% at 7.7 years



Agenda



- Definitions of COPD exacerbation over time
- Why change?
- Learning from the cardiologists
- A reasonable proposal?

Agenda



- Definitions of COPD exacerbation over time

Anthonisen: definition of exacerbation

Symptoms

- Dyspnea (83%)
- Sputum (82%)
- Cough (70%)

PLUS
one
of

Variables

- Preceded by upper RT infection within 5 days
- Increase in HR or RR of 20% over baseline
- Fever without another cause
- Wheezing or cough

Rodriguez Roisin: definition of exacerbation

- A sustained worsening of the patient's condition, from the stable state and beyond normal day-to-day variations, that is acute in onset and necessitates a change in regular medication in a patient with underlying COPD.
- Clinical descriptors:
 - Increased shortness of breath
 - Increased volume and purulence of sputum
 - Increased cough
 - Shallow/rapid breathing
 - Increased body temperature
 - Increased pulse/heart rate
 - Impaired mental status

Rodriguez Roisin: definition of exacerbation

Table 2—Staging of a COPD Exacerbation Based on Health-Care Utilization*

Severity	Level of Health-Care Utilization
Mild	Patient has an increased need for medication, which he/she can manage in own normal environment
Moderate	Patient has an increased need for medication and feels the need to seek additional medical assistance
Severe	Patient/caregiver recognizes obvious and/or rapid deterioration in condition, requiring hospitalization

*It is also crucial to note the severity of the underlying COPD, any comorbid conditions, and the frequency of exacerbations.

Other definitions of COPD Exacerbation

“Episodes of increasing respiratory symptoms, particularly dyspnoea, cough and sputum production, and increased sputum purulence”

Wedzicha W. et al An ERS/ATS guideline. ERJ 2017;49



“An acute worsening of respiratory symptoms that results in additional therapy”



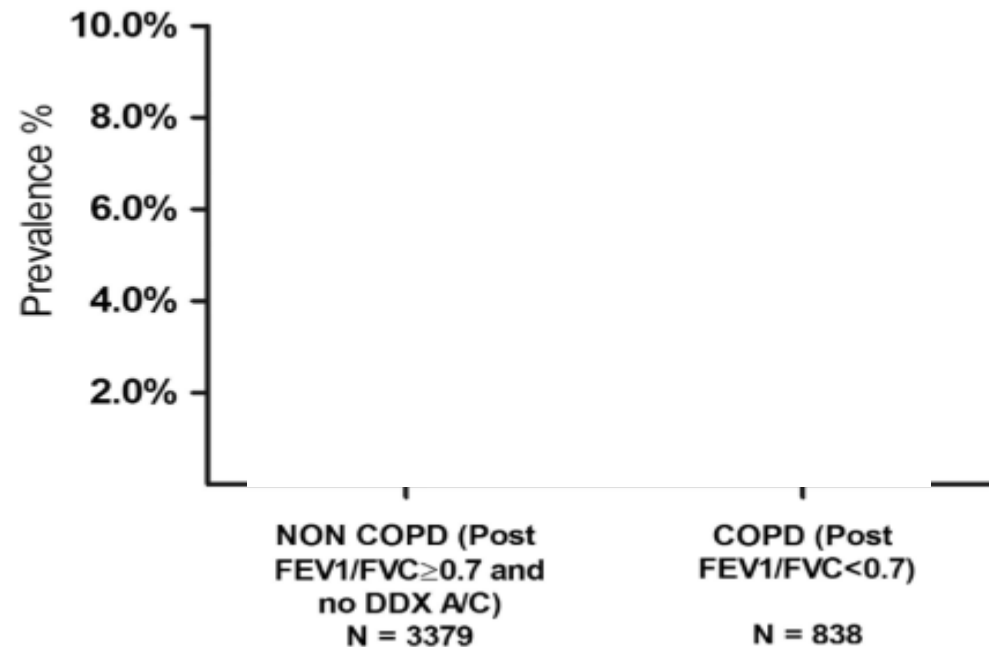
Agenda



- Why change?

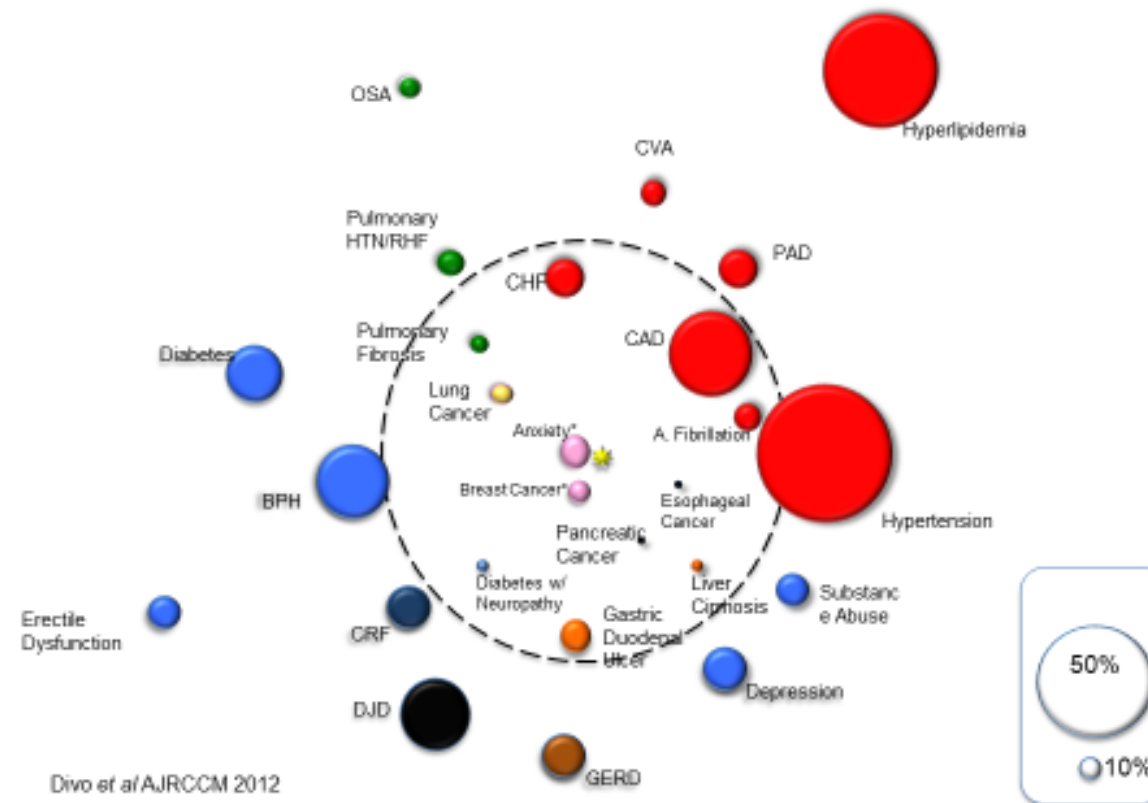
Reasons to change the ECOPD definition:

- Individuals without COPD can also present episodes of acute worsening of respiratory symptoms that are undistinguishable clinically from ECOPD.



Reasons to change the ECOPD definition

- Patients with COPD almost invariably suffer concomitant multimorbid diseases that may precipitate, mimic and/or aggravate an ECOPD



Exacerbations rate in 3 large multicenter trials (TORCH, SUMMIT, IMPACT)

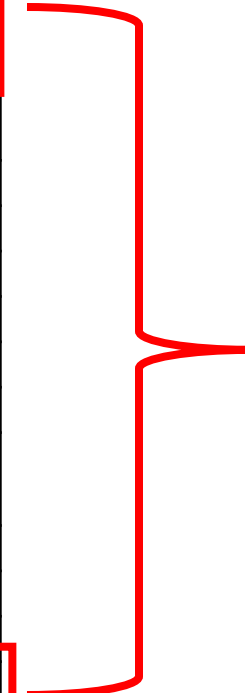
Multicenter, International trials completed over the last 2 decades

n = 29,576 patients

Different inclusion criteria

Outcome: Exacerbations

Country	Moderate+ severe exac /year	Severe exac /year	Ratio severe: total	Geographic region
UK	1.51	0.20	0.13	Western Europe
Spain	1.07	0.23	0.21	Western Europe
Canada	1.09	0.11	0.10	North America
Australia	1.09	0.21	0.20	Southern Hemisphere
RSA	0.78	0.10	0.12	Southern Hemisphere
USA	0.79	0.13	0.16	North America
Chile	1.05	0.17	0.17	South America
Austria	0.85	0.18	0.21	Central Europe
Thailand	0.69	0.35	0.51	Asia
Argentina	0.61	0.06	0.10	South America
Philippines	0.67	0.13	0.20	Asia
Czech Republic	0.44	0.05	0.12	Central Europe
Germany	0.60	0.08	0.13	Central Europe
China	0.60	0.16	0.26	Asia
Poland	0.36	0.06	0.16	Eastern Europe
Romania	0.34	0.12	0.35	Eastern Europe
Russia	0.23	0.09	0.39	Eastern Europe
Ukraine	0.19	0.04	0.21	Eastern Europe



Rates 3 fold different between certain countries

Agenda



- Learning from the cardiologists

Nomenclature and Criteria for IHD

Joint ISFC/WHO Task Force

At times, patients may have episodes of prolonged chest pain simulating myocardial infarction, but without the characteristic ECG and enzyme changes. De novo effort angina, worsening effort angina, and spontaneous angina are frequently referred to as "unstable angina." The committee prefers to use the specific terms.

3.1 Acute Myocardial Infarction

The clinical diagnosis of acute myocardial infarction is usually based on the history, the ECG, and serum enzymes.

B. ECG. Unequivocal changes in ECG are the development of abnormal, persistent Q or QS waves, and evolving injury current lasting longer than 1 day. When the ECG shows these unequivocal changes, the diagnosis may be made on the ECG alone. In other cases, the ECG may show *equivocal changes*, consisting of a) a stationary injury current, b) a symmetrical inversion of the T wave, c) a pathological Q wave in a single ECG record, or d) conduction disturbances.

C. Serum Enzymes. a) *Unequivocal change* consists of serial change, or initial rise and subsequent fall of the serum level. The change must be properly related

International diagnostic criteria for acute myocardial infarction and acute stroke

Prolonged cardiac pain: When it is characterized by pain with the following characteristics.

- (a) Occurring anywhere in the anterior chest, left arm, or jaw, which may also involve the back, shoulder, right arm, or abdomen on one or both sides.
- (b) Duration of more than 20 minutes.

ECG

- (a) *Evolving diagnostic ECG*—an evolving pattern on serial ECGs of a diagnostic ECG.

Cardiac enzymes

Total CPK has been measured and is at least twice the upper limits of normal and either LDH or SGOT has been measured and is at least twice the upper limits of normal.

Gillum R et al 1984;108:150

Nomenclature and Criteria for IHD

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Fourth Universal Definition of MI. 2018

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Universal definitions of myocardial injury and myocardial infarction

Criteria for myocardial injury

The term myocardial injury should be used when there is evidence of elevated cardiac troponin values (cTn) with at least one value above the 99th percentile upper reference limit (URL). The myocardial injury is considered acute if there is a rise and/or fall of cTn values.

Criteria for acute myocardial infarction (types 1, 2 and 3 MI)

The term acute myocardial infarction should be used when there is acute myocardial injury with clinical evidence of acute myocardial ischaemia and with detection of a rise and/or fall of cTn values with at least one value above the 99th percentile URL and at least one of the following:

- Symptoms of myocardial ischaemia;
- New ischaemic ECG changes;
- Development of pathological Q waves;
- Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality in a pattern consistent with an ischaemic aetiology;
- Identification of a coronary thrombus by angiography or autopsy (not for type 2 or 3 MIs).

Post-mortem demonstration of acute athero-thrombosis in the artery supplying the infarcted myocardium meets criteria for *type 1 MI*.

Evidence of an imbalance between myocardial oxygen supply and demand unrelated to acute athero-thrombosis meets criteria for *type 2 MI*.

Cardiac death in patients with symptoms suggestive of myocardial ischaemia and presumed new ischaemic ECG changes before cTn values become available or abnormal meets criteria for *type 3 MI*.

Agenda



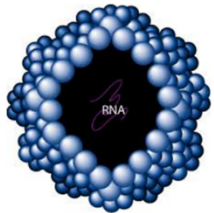
- A reasonable proposal

Pathophysiology of an Exacerbation: Conceptual model

Exacerbation
Causes



Bacteria



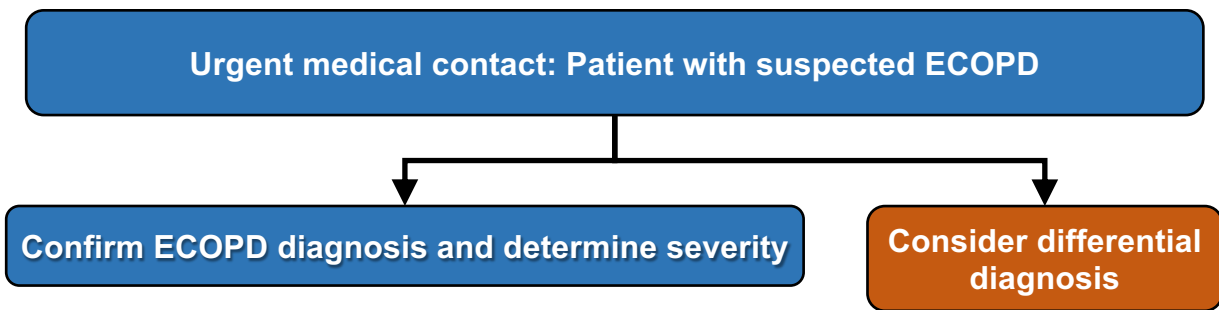
Virus



Pollution



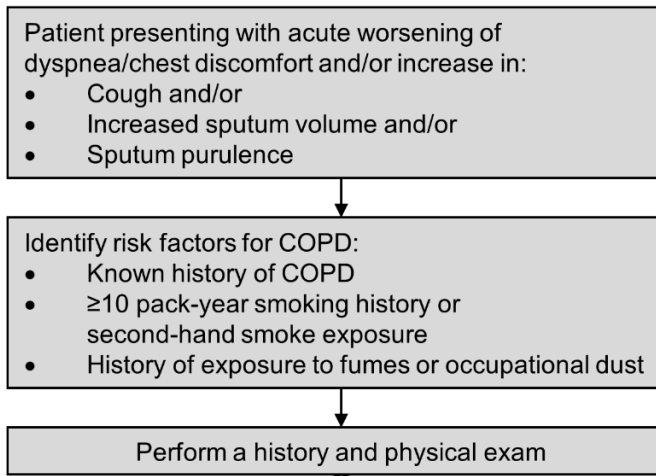
Other

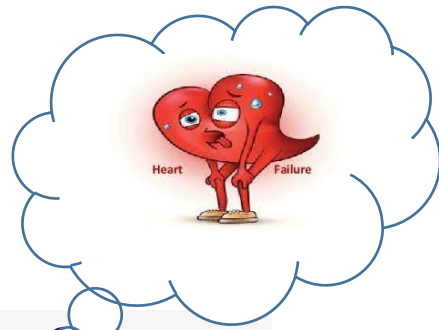




Patient with confirmed or suspected COPD and unexplained worsening of respiratory symptoms







Determine pre-test probability by history and physical examination

Diagnostic tests

Ancillary tests

Likely diagnosis

Treatment

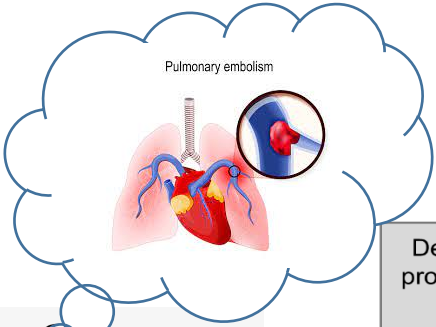
Patient with COPD presenting with:
acute worsening of dyspnea/chest discomfort,
and suspected acute heart failure

History of COPD
Cough, sputum

History of HF and/or
heart disease
PND, JVD, HJ reflux
3rd heart sound



Patient with COPD presenting with:
acute worsening of dyspnea/chest discomfort,
and suspected pulmonary embolism



Determine pre-test
probability by history
and physical
examination



Diagnostic tests

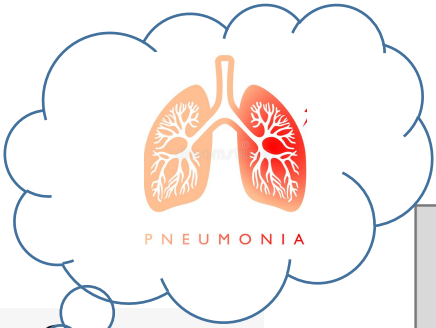
Ancillary tests

Likely diagnosis

Treatment



Patient with COPD presenting with:
acute worsening of dyspnea/chest discomfort,
and suspected pneumonia



Determine pre-test
probability by history
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examination

Diagnostic tests

Ancillary tests

Likely diagnosis

Treatment

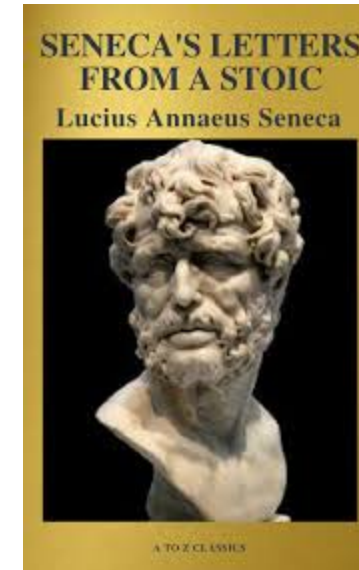


Conclusions



- The current definition has been useful
- It is difficult to move the field forward with the current definition based only on subjective variables
- Lessons from other fields provide a guide
- The Rome definition and severity classification needs to be tested, but it proposes the measuring of objective clinical markers to complement the subjective elements of the current definition

Thank You



“Every new beginning comes from some other beginning’s end”

Lucius Annaeus Seneca

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