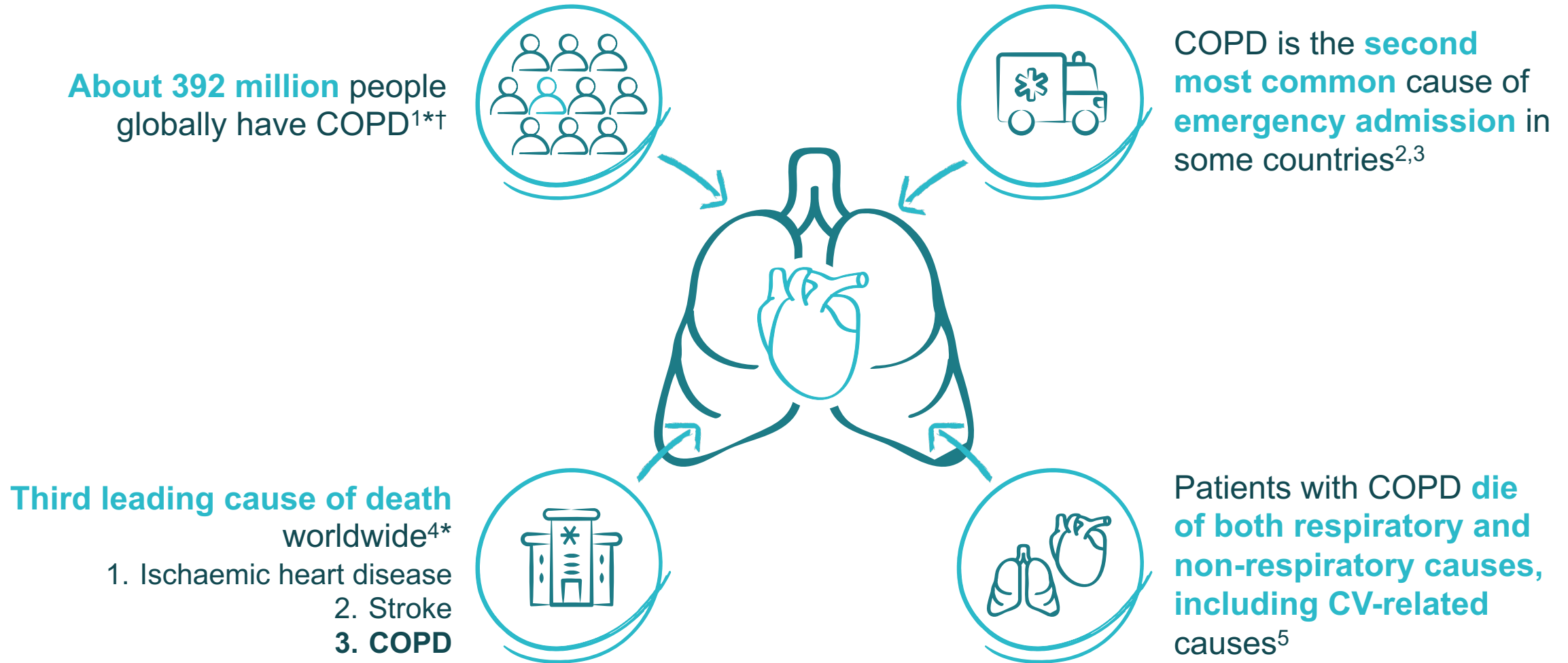


THE NEED FOR PROACTIVE, OPTIMISED MANAGEMENT OF COPD TO REDUCE THE RISK OF CARDIOPULMONARY EVENTS

FOR HEALTHCARE PROFESSIONALS ONLY

**ACT
ON
COPD**

COPD IS A MAJOR HEALTHCARE BURDEN AND CAUSE OF DEATH WORLDWIDE



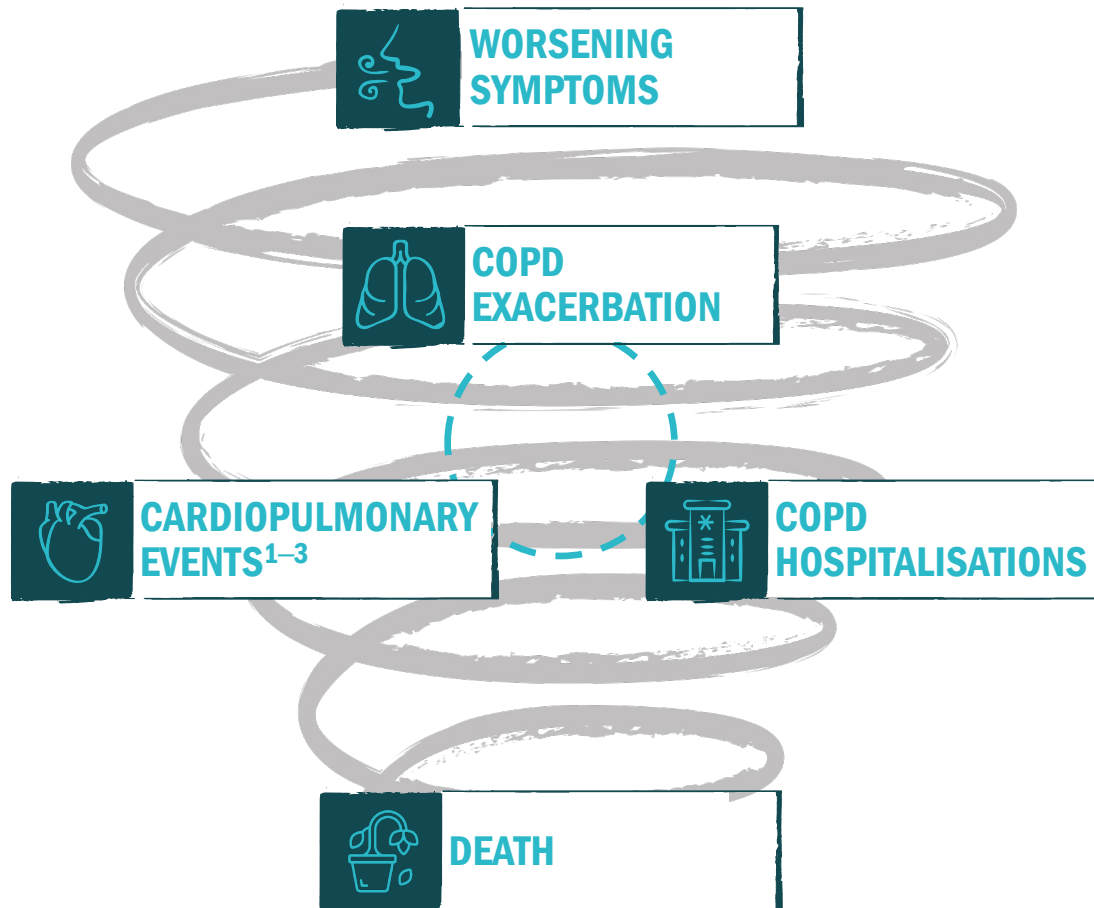
*In 2019; †among 30–79 year olds

CV, cardiovascular

1. Adeloye D, et al. Lancet Respir Med 2022;10:447–458; 2. Lane ND, et al. BMJ Open Respir Res 2018;5:e000334; 3. Nardini S, et al. Multidiscip Respir Med 2014;9:46; 4. World Health Organization (WHO).

The top 10 causes of death. 2020. Available from: <https://www.who.int/news-room/fact-sheets/detail/the-top-10-causes-of-death> (Accessed 12 June 2023); 5. Mannino DM, et al. Respir Med 2006;100:115–122

WORSENING COPD SYMPTOMS AND EXACERBATIONS CAN LEAD TO CARDIOPULMONARY EVENTS AND PREMATURE DEATH



Patients with **increased dyspnoea and frequent productive cough** are at higher risk of exacerbations than those without^{4,5}

Exacerbations can:

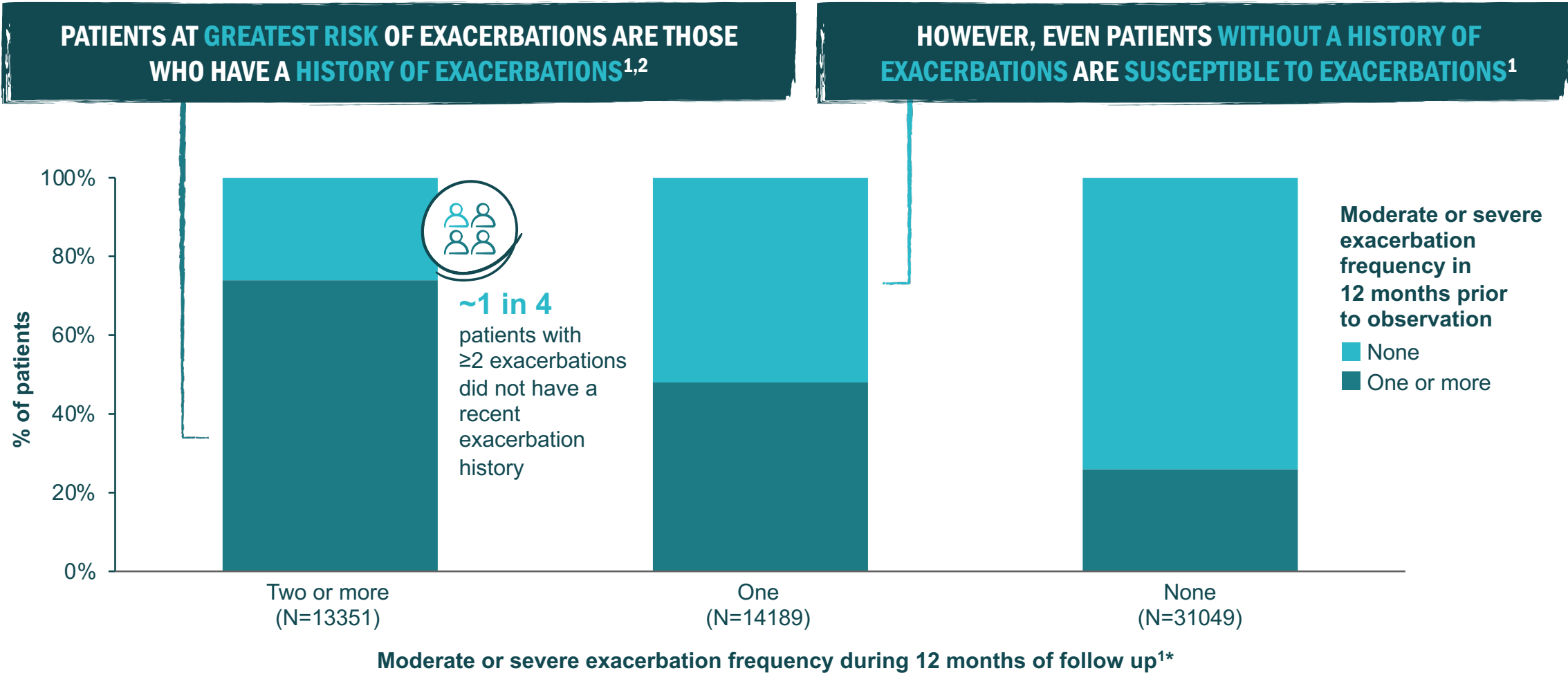
- Irreversibly reduce lung function^{6*}
- Accelerate the rate of subsequent exacerbations^{7†}
- Have an impact beyond the lungs,¹ with **280% increased risk of CV events[‡]** in the 30 days after one exacerbation compared to pre-exacerbation period^{2§¶}

80% increase in risk of death in patients with COPD who had two moderate exacerbations in the previous year^{8**}

Reprinted from Eur J Intern Med, 73, Hurst JR, Skolnik N, Hansen GJ, Anzueto A, Donaldson GC, Dransfield MT, Varghese P, Understanding the impact of chronic obstructive pulmonary disease exacerbations on patient health and quality of life, 1–6, Copyright (2020), with permission from Elsevier on behalf of the European Federation of Internal Medicine.⁹ *In some patients, lung function did not recover to pre-exacerbation levels by eight weeks after the start of the moderate exacerbation; †following a severe exacerbation, the rate of severe exacerbation increased and the time to subsequent exacerbations decreased; ‡CV death, MI, stroke, unstable angina and transient ischaemic attack; §moderate or severe exacerbation, in patients with existing or risk factors for CV disease; ¶Post-hoc analysis of the SUMMIT trial (n=16485) was performed to determine whether the risk for CV events increases after a moderate/severe COPD exacerbation; **based on adjusted ORs for comparison of exacerbation frequency in the prior 12 months versus those with no exacerbations in the prior 12 months (OR 1.80; 95% CI 1.19 to 2.70). CV, cardiovascular; MI, myocardial infarction

1. Donaldson GC, et al. Chest 2010;137:1091–1097; 2. Kunisaki KM, et al. Am J Respir Crit Care Med 2018;198:51–57; 3. Goto T, et al. J Gen Intern Med 2018;33:1461–1468; 4. Müllerová H, et al. BMJ Open 2014;4:e006171; 5. Hughes R, et al. Respir Med 2022;200:106921; 6. Watz H, et al. Respir Res 2018;19:251; 7. Suissa S, et al. Thorax 2012;67:957–963; 8. Rothnie KJ, et al. Am J Respir Crit Care Med 2018;198:464–471; 9. Hurst JR, et al. Eur J Int Med 2020;73:1–6

PATIENTS WITH COPD ARE SUSCEPTIBLE TO EXACERBATIONS, EVEN WITHOUT A HISTORY OF EXACERBATIONS¹



Reproduced from BMJ Open, Müllerová H, Shukla A, Hawkins A, Quint J, 4, e006171, 2014 with permission from BMJ Publishing Group Ltd
*Retrospective observational cohort study that evaluated risk factors associated with exacerbation frequency in 58589 patients with COPD identified in the UK Clinical Practice Research Datalink
1. Müllerová H, et al. BMJ Open 2014;4:e006171; 2. Hurst JR, et al. N Engl J Med 2010;363:1128–1138

PATIENTS WITH INCREASED SYMPTOMS AND FREQUENT PRODUCTIVE COUGH ARE AT HIGH RISK OF EXACERBATIONS



**INCREASING DYSPNOEA (BASED ON MRC SCALE)
WAS ASSOCIATED WITH AN
INCREASED RISK OF EXACERBATIONS^{1*}**

~1 in 2

patients who have an MRC grade of $\geq 3^{\dagger}$ had an exacerbation in the following 12 months¹



**FREQUENT PRODUCTIVE COUGH[‡]
WAS AN INDICATOR OF RISK
OF EXACERBATIONS^{2§}**

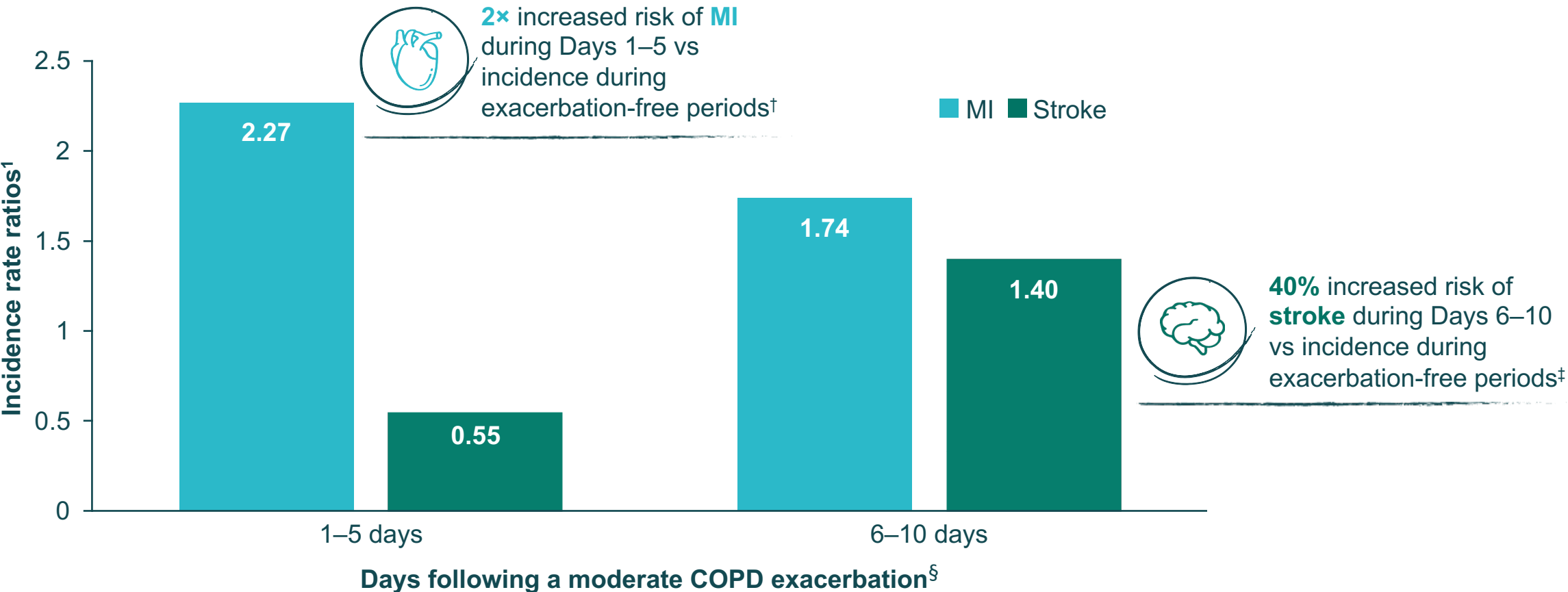
Patients having frequent productive cough at baseline were associated with a
~2× greater risk of hospital admission for exacerbation[¶] in the next 12 months²

*Retrospective observational cohort study that evaluated risk factors associated with exacerbation frequency in 58589 patients with COPD identified in the UK Clinical Practice Research Datalink; [†]equivalent to mMRC ≥ 2 ; [‡]Frequent productive cough was defined as cough and sputum production several or most days a week (SGRQ cough and sputum scores ≥ 3) in the past 3 months; [§]analysis of 7125 patients from the prospective, observational study, NOVELTY, to describe the relationship between frequent productive cough and disease characteristics, disease burden and exacerbation risk; [¶]physician-reported exacerbations were defined based on ATS/ERS recommendations as beyond the patient's usual day-to-day variance. ATS/ERS, American Thoracic Society / European Respiratory Society; MRC, Medical Research Council; mMRC, modified Medical Research Council; SGRQ, St George's Respiratory Questionnaire

1. Müllerová H, et al. BMJ Open 2014;4:e006171; 2. Hughes R, et al. Respir Med 2022;200:106921

THE IMPACT OF COPD EXACERBATIONS GOES BEYOND THE LUNGS ...

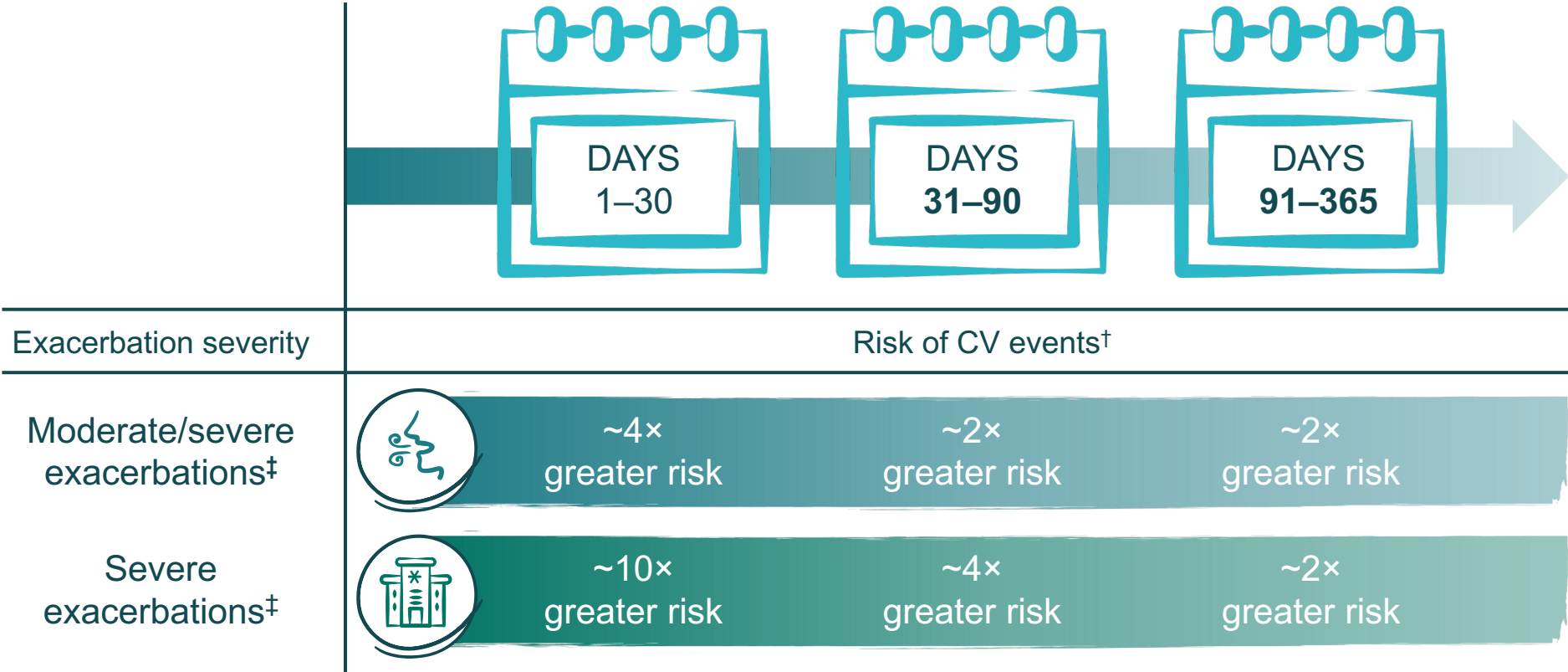
MI AND STROKE RISK INCREASED IN THE FIRST 10 DAYS FOLLOWING A MODERATE EXACERBATION*



*Although the definition and classification of exacerbations have been updated in the 2023 GOLD report, exacerbations severity refers to an earlier definition and classification to align with the published data; [†]risk of MI doubled within 5 days (P=0.03) and returned to baseline over time; [‡]incidence rate ratio for MI on Days 6–10 and for stroke on Days 1–10 were not statistically significant; [§]a self-controlled case-series study conducted in 25857 patients with COPD to assess the magnitude and timing of the risk of MI and stroke following a COPD exacerbation compared with exacerbation-free periods. GOLD, Global Initiative for Chronic Obstructive Lung Disease; MI, myocardial infarction
Donaldson GC, et al. Chest 2010;137:1091–1097

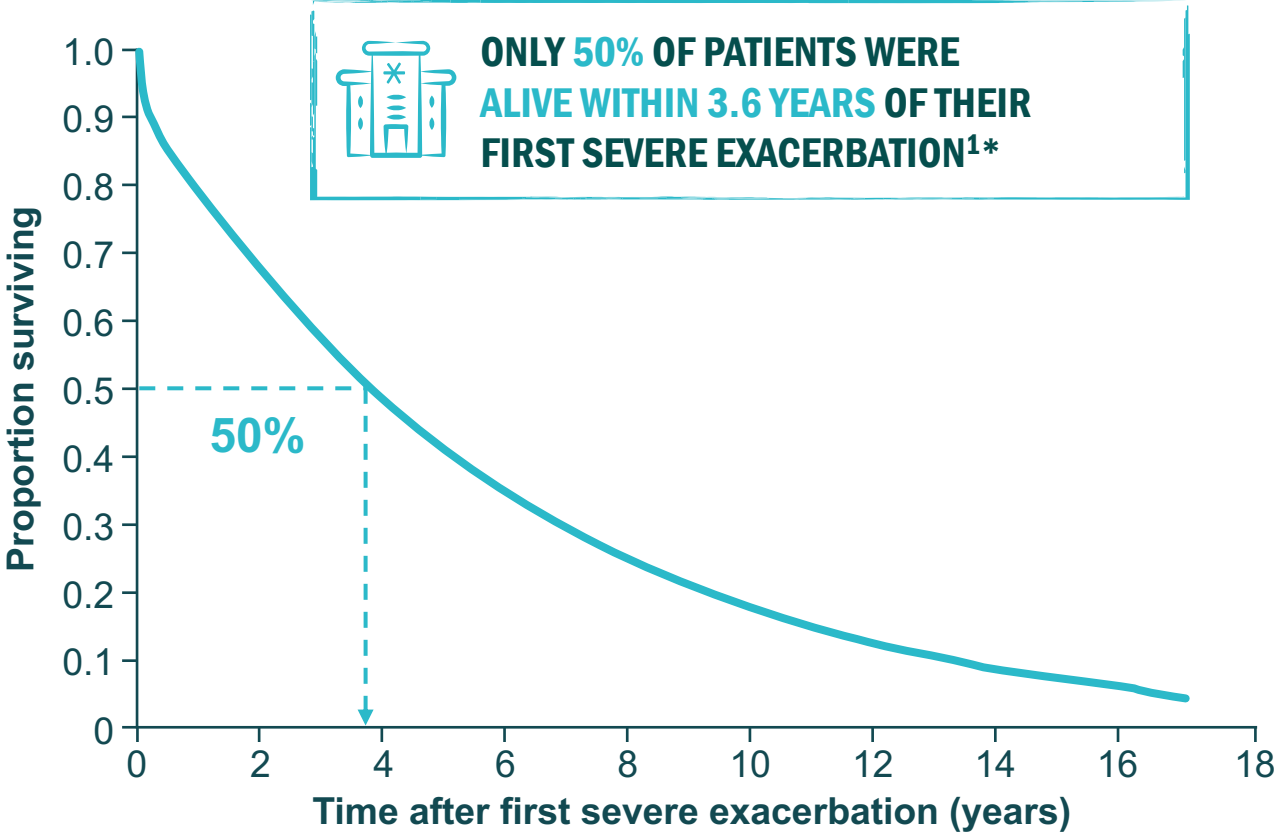
... WITH AN INCREASED RISK OF CV EVENTS THAT MAY PERSIST FOR UP TO A YEAR AFTER AN EXACERBATION

IN PATIENTS WITH COPD AND EXISTING OR RISK FACTORS FOR CVD,
THE RISK OF CV EVENTS WAS ELEVATED IN THE DAYS FOLLOWING AN EXACERBATION*



*Post-hoc analysis of the SUMMIT trial (n=16485) was performed to determine whether the risk for CV events increases after a moderate/severe COPD exacerbation; †Cox proportional hazards models compared the hazard for CVD events prior to an exacerbation versus after an exacerbation; ‡moderate exacerbation refers to exacerbations requiring treatment with antibiotics and/or systemic corticosteroids and severe exacerbation refers to exacerbations requiring hospitalisation. CV, cardiovascular; CVD, cardiovascular disease
Kunisaki KM, et al. Am J Respir Crit Care Med 2018;198:51-57

EXACERBATIONS INCREASE THE RISK OF DEATH, INCLUDING CV-RELATED DEATH



EVEN ONE MODERATE EXACERBATION INCREASES THE RISK OF CARDIOPULMONARY-RELATED DEATH²

RISK OF COPD-RELATED DEATH WAS INCREASED BY:

(Adjusted IRR 1.17 [95% CI 1.04, 1.33])^{2†}

17%

RISK OF CV-RELATED DEATH WAS INCREASED BY:

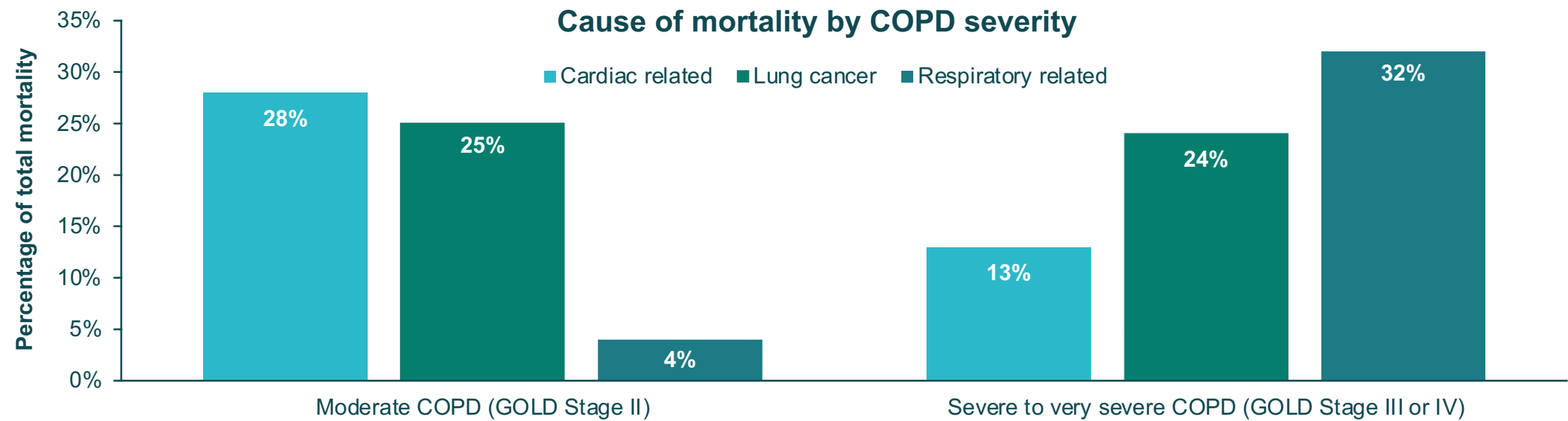
(Adjusted IRR 1.23 [95% CI 1.07, 1.42])^{2†}

23%

Reproduced from Thorax, Suissa S, Dell’Aniello S, Ernst P, 67, 957–963, 2012 with permission from BMJ Publishing Group Ltd
Moderate exacerbations defined as those managed outside hospital and severe exacerbations as those requiring hospitalisation
*Cohort study that evaluated severe COPD exacerbations and their association with mortality in 73106 patients with their first severe COPD exacerbation requiring hospitalisation. Patients with data available between 1990 and 2005 were identified and followed until death or 31 March 2007; †observational analysis of 340,515 patients with COPD in the Clinical Practice Research Datalink database from 2004 to 2019.
CI confidence interval; CV, cardiovascular; IRR, incidence risk ratio;
1. Suissa S, et al. Thorax 2012;67:957–963; 2. Whittaker H, et al. Int J Chron Obstruct Pulmon Dis 2022;17:427–437

CARDIOPULMONARY CAUSES ARE A COMMON REASON FOR DEATH IN PATIENTS WITH COPD

THE UNDERLYING CAUSES OF MORTALITY VARY ACROSS DIFFERENT SEVERITIES OF COPD

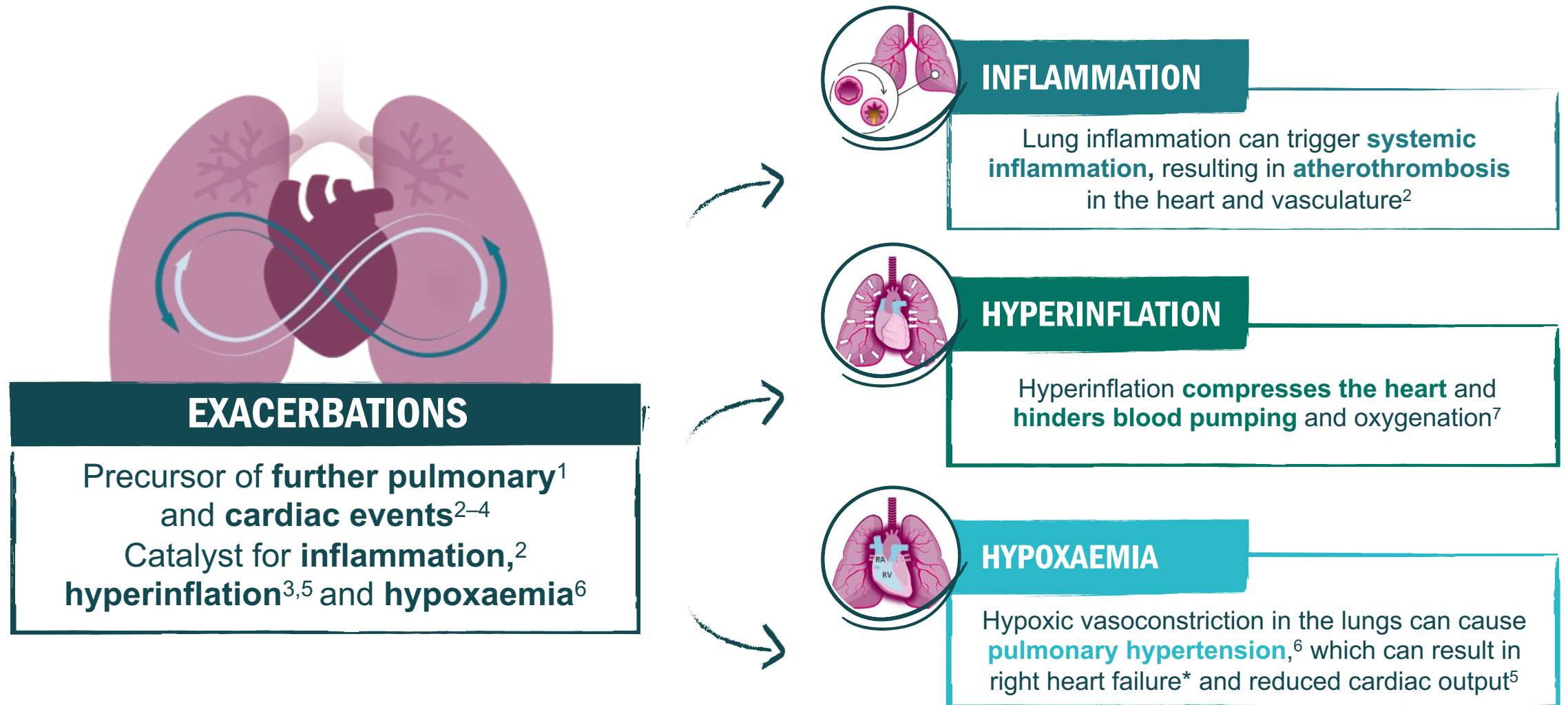


	GOLD Stage II	GOLD Stage III or IV
n	1484	271
Deaths, n (%)	232 (15.6)	92 (34.0)
Cardiac related, n	64	12
Lung cancer, n	59	22
Respiratory related, n	8	29

GOLD, Global Initiative for Chronic Obstructive Lung Disease
Mannino DM, et al. Respir Med 2006;100:115–122



POTENTIAL MECHANISMS OF COPD-DRIVEN CARDIOPULMONARY RISK



*In a minority of cases

1. Müllerová H, et al. BMJ Open 2014;4:e006171; 2. Van Eeden S, et al. Am J Respir Crit Care Med 2012;186:11–16; 3. Crisan L, et al. Front Cardiovasc Med 2019;6:79; 4. Calderón Montero A. Semergen 2023;49:101928; 5. Rabe KF, et al. Eur Respir Rev 2018;27:180057; 6. Kent BD, et al. Int J Chron Obstruct Pulmon Dis 2011;6:199–208; 7. Aisanov Z, et al. J Thorac Dis 2020;12:2791–2802

TIME TO RAISE THE STANDARDS OF CARE FOR PATIENTS WITH COPD¹⁻³

1

IDENTIFY AT-RISK PATIENTS^{1,2*}

Symptomatic patients regardless of a recent history of exacerbations:⁴

- Increased dyspnoea (mMRC ≥ 2)^{3†}
- Frequent productive cough^{5‡}

Patients with recent history of exacerbations⁴

2

OPTIMISE MANAGEMENT^{2,3}

Prevent exacerbations, CV complications and decrease risk of mortality:²

- Non-pharmacological interventions³
- Appropriate initiation and escalation of pharmacological treatments³

THERAPEUTIC INERTIA[¶] CONTRIBUTES TO POOR MANAGEMENT OF COPD EXACERBATIONS¹

*Including patients at-risk of cardiopulmonary events; †GOLD considers mMRC ≥ 2 (equivalent to MRC ≥ 3) a threshold for separating "less breathlessness" from "more breathlessness"; ‡defined as cough and sputum production several or most days a week (SGRQ cough and sputum scores ≥ 3) in the past 3 months; §compared with LAMA alone, LAMA/LABA or ICS/LABA; ¶defined as a failure to change therapy when treatment goals are not met

GOLD, Global Initiative for Chronic Obstructive Lung Disease; ICS, inhaled corticosteroid(s); LABA, long-acting beta₂-agonist; LAMA, long-acting muscarinic antagonist; MRC, Medical Research Council; mMRC, modified Medical Research Council; SGRQ, St George's Respiratory Questionnaire

1. Singh D, et al. Int J Chron Obstruct Pulmon Dis 2021;16:2301–2322; 16:3009-3016; 3. Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global strategy for prevention, diagnosis and management of COPD. 2023. Available from: <https://goldcopd.org/2023-gold-report-2/#> (Accessed 12 June 2023); 4. Müllerová H, et al. BMJ Open 2014;4:e006171; 5. Hughes R, et al. Respir Med 2022;200:106921

ACT ON COPD PROGRAMME



**TOGETHER, WE CAN EMBED A 'PREVENTATIVE' MINDSET
AMONG PATIENTS AND HCPs, AND
TRANSFORM THE COPD CLINICAL CARE PATHWAY**

ACT ON COPD OVERALL AMBITION

BY 2030 ACT ON COPD AIMS TO:

PREVENT
>80M
EXACERBATIONS



REDUCE
CARDIOPULMONARY
RISK

BEND THE
MORTALITY
CURVE

IN ORDER TO DOWNGRADE COPD AS A LEADING CAUSE OF DEATH

TOGETHER, WE WILL:

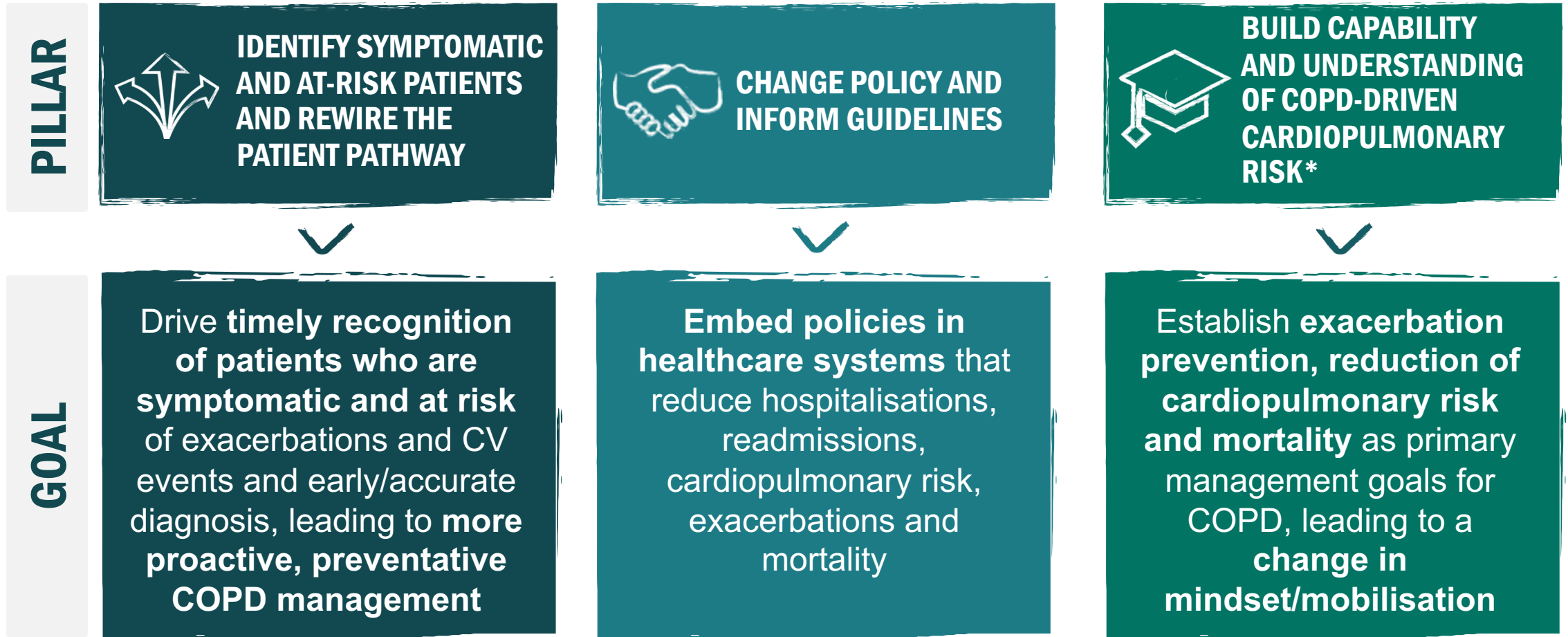


Enable early, proactive, accurate diagnosis and **identification of symptomatic and at-risk patients**,* triggering a **review and optimisation** of care



Embed **exacerbations and mortality targets** in healthcare system policies and raise awareness of **COPD-driven cardiopulmonary risk**[†]

THE ACT ON COPD STRATEGIC PILLARS WILL HELP US TO ACHIEVE OUR AMBITION



*Risk of events including exacerbations, MI, stroke and CV death
CV, cardiovascular; MI, myocardial infarction

IT'S TIME TO ACT

**TO PREVENT EXACERBATIONS, POTENTIALLY REDUCE
CARDIOPULMONARY EVENTS AND PREVENT PREMATURE
MORTALITY**

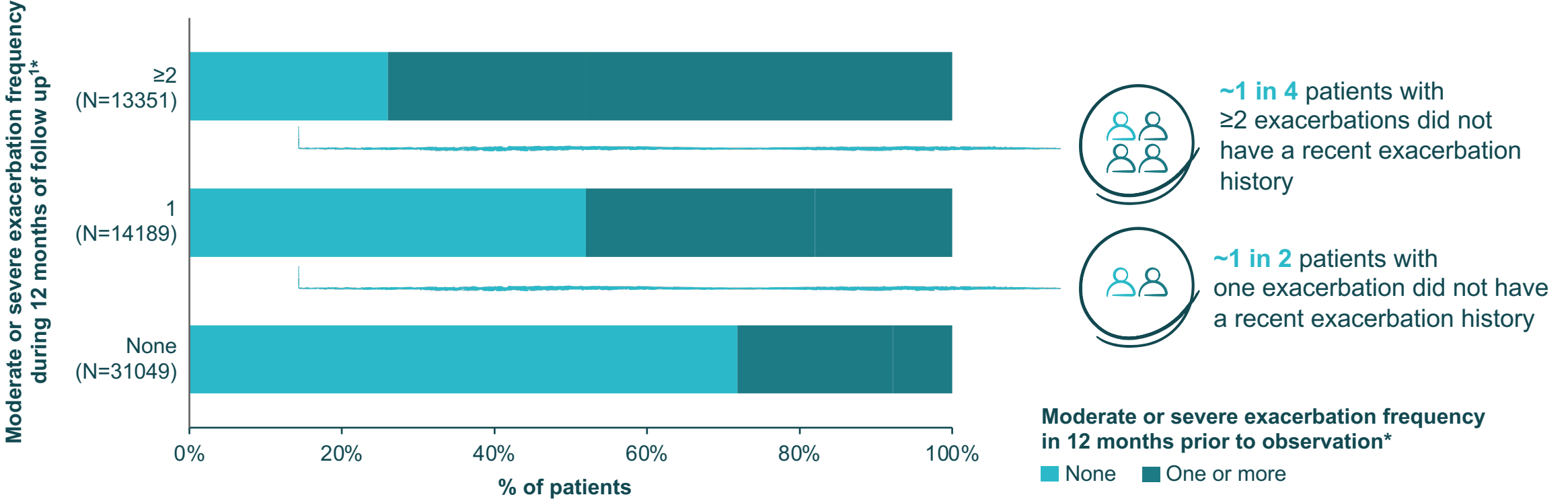
**ACT
ON
COPD**

BACKUP

PATIENTS WITH COPD ARE SUSCEPTIBLE TO EXACERBATIONS, EVEN WITHOUT A HISTORY OF EXACERBATIONS¹

PATIENTS AT **GREATEST RISK OF EXACERBATIONS ARE THOSE WHO HAVE A HISTORY OF EXACERBATIONS^{1,2}**

HOWEVER, EVEN PATIENTS WITHOUT A HISTORY OF EXACERBATIONS ARE SUSCEPTIBLE TO EXACERBATIONS¹



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Prevent exacerbations, CV complications and decrease risk of mortality:²

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- Appropriate initiation and escalation of pharmacological treatments³

3

IMPROVE OUTCOMES¹⁻³

Non-pharmacological therapy with evidence supporting mortality reduction include smoking cessation and pulmonary rehabilitation³

Pharmacotherapy (monotherapy, dual therapy or triple therapy as appropriate)

THERAPEUTIC INERTIA[¶] CONTRIBUTES TO POOR MANAGEMENT OF COPD EXACERBATIONS¹

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