

Chronic obstructive pulmonary disease and risk of incident cardiovascular disease and death: Systematic review and meta-analysis

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Introduction and Aim

Chronic obstructive pulmonary disease (COPD) is associated with adverse cardiovascular events. However, these estimates often assess disease prevalence, and pool separate cardiovascular diagnoses together.¹

Cardiopulmonary risk,^{2,3} a composite of pulmonary or cardiovascular events, or death due to any of these, includes and describes key clinical outcomes to which treatments for COPD may be targeted.

We aimed to provide a comprehensive and contemporaneous set of relative risk estimates for associations of COPD and incident cardiovascular diseases and mortality.

Methods

Medline and Embase were searched systematically from inception to May 7th 2026, for case control studies reporting associations between COPD, and cardiovascular diseases (myocardial infarction (MI), heart failure (HF), ishcaemic stroke (IS), atrial fibrillation (AF), cardiovascular mortality (CM) and all cause mortality (ACM).

Pooled estimates were obtained using random-effects models with restricted maximum likelihood estimation. Between-study heterogeneity was quantified with I². Risk of bias was assessed using the Risk Of Bias In Non-randomized Studies - of Exposures tool, and certainty of evidence assessed using . Grading of Recommendations, Assessment, Development and Evaluation(GRADE) criteria. Absolute risk difference (ARD) was calculated by the baseline rate multiplied by relative risk – 1.

Sensitivity analyses stratified studies by design, follow-up duration, region, clinical context, sample size, publication date, risk of bias, leave-one-out, COPD ascertainment method, and clinical risk. Subgroup analyses by age and meta-regression were performed.

Results

Figure 1: Forest plot of investigated outcomes

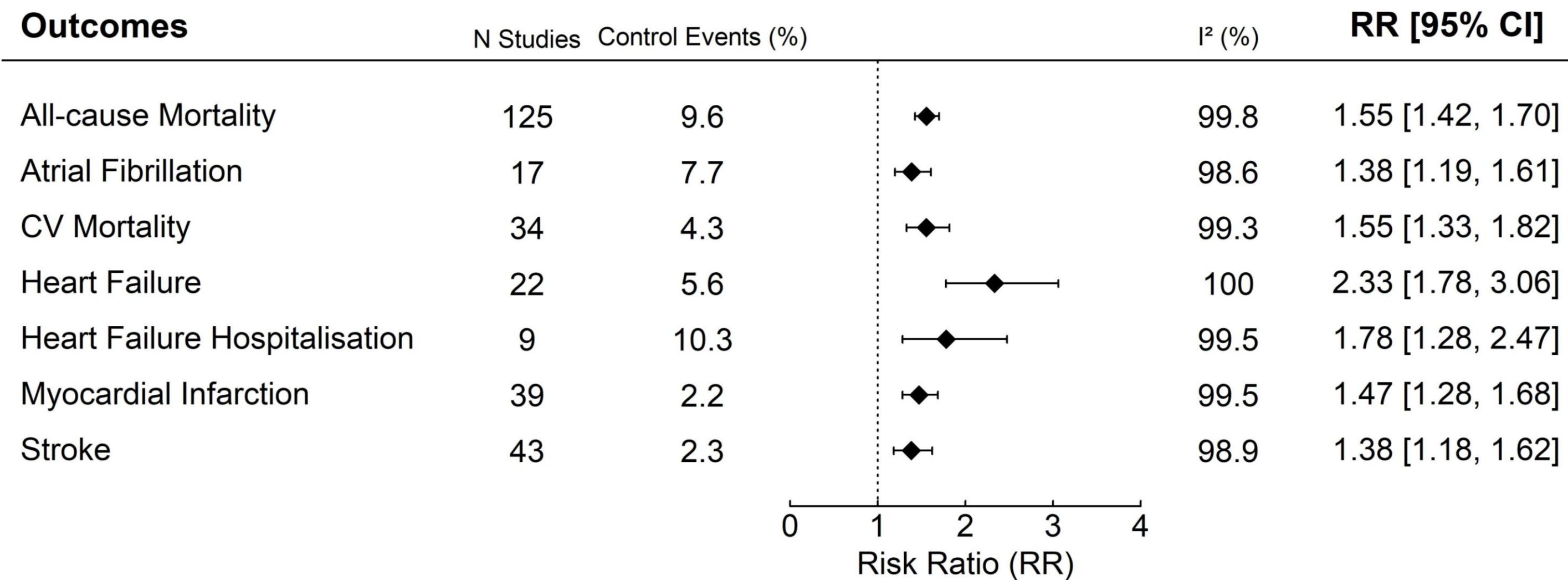


Figure 2: Results from 10 sensitivity analyses

Outcome	Design	RoB removed	Sample size	Region	Publication date	COPD method	Context	F/U	Risk	Leave-one-out
ACM	S	S	S	S	S	S	NS	S	S	S
AF	S	S	S	S	S	S	S	NS	S	S
CM	S	S	S	S	S	S	S	S	S	S
HF	S	S	S	S	S	S	S	S	S	S
HHF	S	S	S	S	S	S	S	S	S	S
MI	S	S	S	S	S	S	S	S	S	S
IS	S	S	S	S	S	S	NS	S	S	S

16299 studies from searches, with 442 full texts searched to include 140 case-control studies spanning 30 144 481 patients (3 062 712 with COPD) from 25 countries, with median follow -up duration 3·0 years (IQR 1·0 - 5·2 years). 38.5% of studies at high risk of bias.

COPD was associated with a significantly increased risk for all investigated outcomes (Figure 1).

The ARD (%) was elevated for all outcomes:

ACM 5.30 ((95%CI) 4.16 – 6.70)

AF – 2.95 (1.77 – 4.81)

CM – 2.4 (1.38 – 4.10)

HF – 7.45 (4.63 – 11.83)

HHF – 8.02 (3.95 – 15.4)

MI – 1.04 (0.74 – 1.45)

IS - 0.86 (0.66 – 1.14).

Despite substantial heterogeneity for all outcomes, associations between COPD and outcomes were broadly consistent across all sensitivity analyses (Figure 2).

Certainty of evidence was moderate for all outcomes. No outcome demonstrated dissemination bias.

Univariate and multivariate meta-regression identified covariates associated with individual outcomes, but did not explain the substantial heterogeneity

Conclusion

- COPD is associated with incident cardiovascular disease, including AF, HF, MI, stroke and cardiovascular death, with the greatest magnitude of effect for HF, HHF and both CM and ACM, in relative and absolute terms.
- Individuals with COPD warrant holistic cardiovascular risk assessment and treatment to reduce the risk of adverse events
- The impact of current and novel treatments on a broader range of cardiovascular outcomes in COPD warrants assessment.

References

1. Chen W, Thomas J, Sadatsafavi M, FitzGerald JM. Risk of cardiovascular comorbidity in patients with chronic obstructive pulmonary disease: a systematic review and meta-analysis. *Lancet Respir Med* 2015;3(8):631-9. 2. Gale CP, Hurst JR, Hawkins NM, et al. Identification and management of cardiopulmonary risk in patients with COPD: a multidisciplinary consensus and modified Delphi study. *Eur J Prev Cardiol* 2025 3. Uysal OF, Joseph T, Alharbi AM, et al. Methods to assess atherosclerotic cardiovascular risk in chronic respiratory diseases: a systematic review. *Eur Respir Rev* 2025;34(178)

Abbreviations

ACM – all-cause mortality
AF – atrial fibrillation
COPD – chronic obstructive pulmonary disease
CM – cardiovascular death

HHF – hospitalization for heart failure
IQR – interquartile range
IS – ischaemic stroke
MI – myocardial infarction

S – significant across all analyses
NS – not significant across all analyses

