# Cardiovascular events after exacerbations of chronic obstructive pulmonary disease: Results from the EXAcerbations of COPD and their OutcomeS in CardioVascular diseases study in Italy

**First published:** 12/06/2025

**Last updated:** 12/06/2025

Study Finalised

## Administrative details

**EU PAS number**

EUPAS1000000622

**Study ID**

1000000622

**DARWIN EU® study**

No

**Study countries**

☐ Italy

**Study description**

Introduction: Exacerbations of chronic obstructive pulmonary disease (COPD) can increase the risk of severe cardiovascular events.

Objective: Assess the crude incidence rates (IR) of cardiovascular events and the impact of exacerbations on the risk of cardiovascular events within different time periods following an exacerbation.

Methods: COPD patients aged ≥45 years between 01/01/2015 and 12/31/2018 were identified from the Fondazione Ricerca e Salute administrative database. IRs of severe non-fatal and fatal cardiovascular events were obtained for post-exacerbation time periods (1–7, 8–14, 15–30, 31–180, 181–365 days). Time-dependent Cox proportional hazard models compared cardiovascular risks between periods with and without exacerbations.

Results: Of 216,864 COPD patients, >55 % were male, mean age was 74 years, frequent comorbidities were cardiovascular, metabolic and psychiatric.

During an average 34-month follow-up, 69,620 (32 %) patients had ≥1 exacerbation and 46,214 (21 %) experienced ≥1 cardiovascular event. During follow-up, 55,470 patients died; 4,661 were in-hospital cardiovascular-related deaths. Among 10,269 patients experiencing cardiovascular events within 365 days post-exacerbation, the IR was 15.8 per 100 person-years (95 %CI 15.5–16.1).

Estimated hazard ratios (HR) for the cardiovascular event risk associated with periods post-exacerbation were highest within 7 days (HR: 34.3, 95 %CI: 33.1–35.6), especially for heart failure (HR 50.6; 95 %CI 48.6–52.7) and remained elevated throughout 365 days (HR 1.1, 95 %CI 1.02–1.13).

Conclusions: COPD patients in Italy are at high risk of severe cardiovascular events following exacerbations, suggesting the need to prevent exacerbations and possible subsequent cardiovascular events through early interventions and treatment optimization.

**Study status**

Finalised

# Research institutions and networks

## Institutions

### Fondazione ReS (Ricerca e Salute), CINECA partner

Italy

**First published:** 05/07/2017

**Last updated:** 13/06/2025

Institution | Not-for-profit | ENCePP partner

## Contact details

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Study contact

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**Primary lead investigator**

Letizia Dondi

Primary lead investigator

## Study timelines

**Date when funding contract was signed**
Actual: 09/06/2023

**Study start date**
Actual: 23/07/2023

**Date of final study report**
Actual: 11/09/2023

## Sources of funding

- Pharmaceutical company and other private sector

## More details on funding

This study received unconditional funding from Astra Zeneca SpA.

## Regulatory

**Was the study required by a regulatory body?**

No

**Is the study required by a Risk Management Plan (RMP)?**

Not applicable

# Methodological aspects

## Study type

## Study type list

**Study topic:**

Disease /health condition

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**Study type:**

Non-interventional study

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**Scope of the study:**

Disease epidemiology

**Data collection methods:**

Secondary use of data

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**Study design:**

Observational retrospective longitudinal cohort study. Patients with COPD and aged 45 years or older were identified
between January 1st 2015 and December 31st 2018 and followed from index date to the first occurrence of a severe CV event/right censoring due to reaching 31/12/2019/loss to follow-up

**Main study objective:**

The aim of this study was to evaluate the association between time periods following an exacerbation of COPD and the occurrence of a severe CV event compared to unexposed time periods (i.e., without an exacerbation), using data from the Italian National Health Service (SSN).

# Study Design

**Non-interventional study design**

Cohort

# Study drug and medical condition

**Medical condition to be studied**

Chronic obstructive pulmonary disease

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**Additional medical condition(s)**

Exacerbations of chronic obstructive pulmonary disease, Cardiovascular events

# Population studied

**Short description of the study population**

Patients with COPD and aged 45 years or older were identified within the ReS database from 2015 to 2018. Patients with at least one day of follow-up after the index date were included. Both newly diagnosed (defined as the absence of COPD criteria within the 24-month look-back period) and previously diagnosed patients with COPD were included.

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**Age groups**

Adult and elderly population (≥18 years)

Adults (18 to < 65 years)

Adults (18 to < 46 years)

Adults (46 to < 65 years)

Elderly (≥ 65 years)

Adults (65 to < 75 years)

Adults (75 to < 85 years)

Adults (85 years and over)

# Study design details

**Setting**

Italian inhabitants or beneficiaries of the SSN which is a unversal coverage health system.

Inhospital/local outpatient settings.

Overall observation period: 2013-2019.

Patients aged ≥45 were identified as having COPD by at least one of the following criteria: at least one hospitalization with a primary/secondary diagnosis of COPD in the hospital discharge forms (ICD-9CM codes: 491.x, 492.x, 496); disease waiver claims for COPD (057); at least 4 dispensations of drugs for obstructive airway diseases (ATC code: R03) within a same 12-month period. Patients with at least one day of follow-up after the index date were included.

Patients with Alpha-1-antitrypsin deficiency (ICD-9-CM code 273.4) and patients with asthma during the accrual period were excluded.

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**Summary results**

Of 216,864 COPD patients, >55 % were male, mean age was 74 years, frequent comorbidities were

cardiovascular, metabolic and psychiatric.

During an average 34-month follow-up, 69,620 (32 %) patients had ≥1 exacerbation and 46,214 (21 %) experienced ≥1 cardiovascular event. During follow-up, 55,470 patients died; 4,661 were in-hospital cardiovascular-related deaths.

Among 10,269 patients experiencing cardiovascular events within 365 days post-exacerbation, the IR was 15.8 per 100 person-years (95 %CI 15.5–16.1). Estimated hazard ratios (HR) for the cardiovascular event risk associated with periods post-exacerbation were highest within 7 days (HR: 34.3, 95 %CI: 33.1–35.6), especially for heart failure (HR 50.6; 95 %CI 48.6–52.7) and remained elevated throughout 365 days (HR 1.1, 95 %CI 1.02–1.13).

# Documents

**Study publications**

S Calabria, G Ronconi, L Dondi, L Dondi, I Dell’Anno, C Nordon, K Rhodes, P Rog…

# Data management

## ENCePP Seal

The use of the ENCePP Seal has been discontinued since February 2025. The ENCePP Seal fields are retained in the display mode for transparency but are no longer maintained.

## Data sources

**Data source(s)**

Database of Fondazione ReS

**Data sources (types)**

Administrative healthcare records (e.g., claims)

## Use of a Common Data Model (CDM)

**CDM mapping**

No

## Data quality specifications

**Check conformance**

Yes

**Check completeness**

Yes

**Check stability**

Yes

**Check logical consistency**

Yes

## Data characterisation

**Data characterisation conducted**

Unknown