

A self controlled case series approach to assess NIV effects on cardiovascular risk after COPD exacerbations

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BACKGROUND

The self-controlled case series (SCCS) design uses each patient as their own control, enabling assessment of treatment effects within individuals while adjusting for fixed confounders. This approach strengthens causal inference when exposure varies over time.
In the context of increased risk of cardiovascular events after chronic obstructive pulmonary disease exacerbations (AECOPD) which more and more recognized, it seemed interesting to assess the impact of being treated by long term non-invasive ventilation (NIV) on subsequent cardiovascular events occurring after an AECOPD has never been studied. This of special interest in a severe COPD population at the stage of chronic respiratory failure and as a consequence exhibiting a high annual rate of severe hospitalized AECOD.

OBJECTIVE

The objective of this study was to determine whether the risk of developing a cardiovascular event (CVE) during the month after an COPD exacerbation differs between periods with Non-Invasive Ventilation (NIV) and after a stop of NIV. The research question that we want to answer was : What is the impact of Long-term domiciliary noninvasive ventilation (NIV) on incident Subsequent Cardiovascular Events after Acute Exacerbations of COPD?

METHODS

Data source

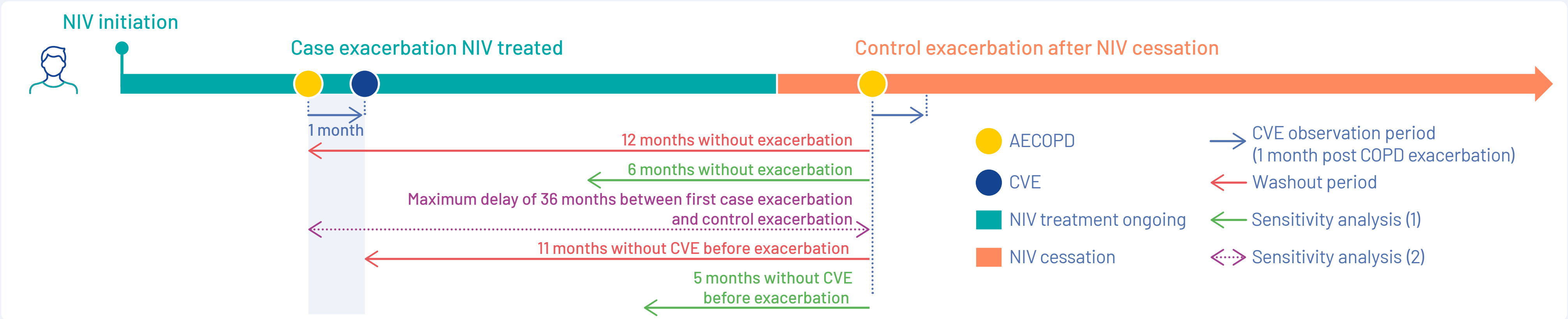
Data were extracted from the French National Healthcare Database, entitled SNDS, which includes socio-demographic data (age, sex, area), all healthcare expenses (including outpatient visits, reimbursed medication, medical procedures, hospital admission diagnoses and procedures) and date of death.

Study population and period

Individuals aged ≥40 years who had at least one reimbursement for domiciliary NIV between 1st January 2015 and 31 December 2019 with COPD as the primary cause for initiating NIV were identified based on ICD-10 codes, treatment with COPD medications and the occurrence of COPD-related hospitalizations. Claims data from the 5 years preceding domiciliary NIV initiation (ICD-10 codes and medications) were used to identify comorbidities and relevant medical history including previous cardiovascular events. Cessation of long-term NIV was deemed to have occurred when there were no longer any reimbursement codes for this therapy.

Study design

This is a self-controlled serie1. The study population included individuals in the MONTANA cohort that have first initiated NIV and stopped treatment during follow-up (death excluded) and exhibited AECOPDs at least once during these two conditions [Figure 1]. For each COPD patient included at least two periods were considered: AECOPD occurring under NIV ("case exacerbation") versus AECOPD occurring after NIV cessation ("control exacerbation"). Patients can have experienced more than 1 case/control period.



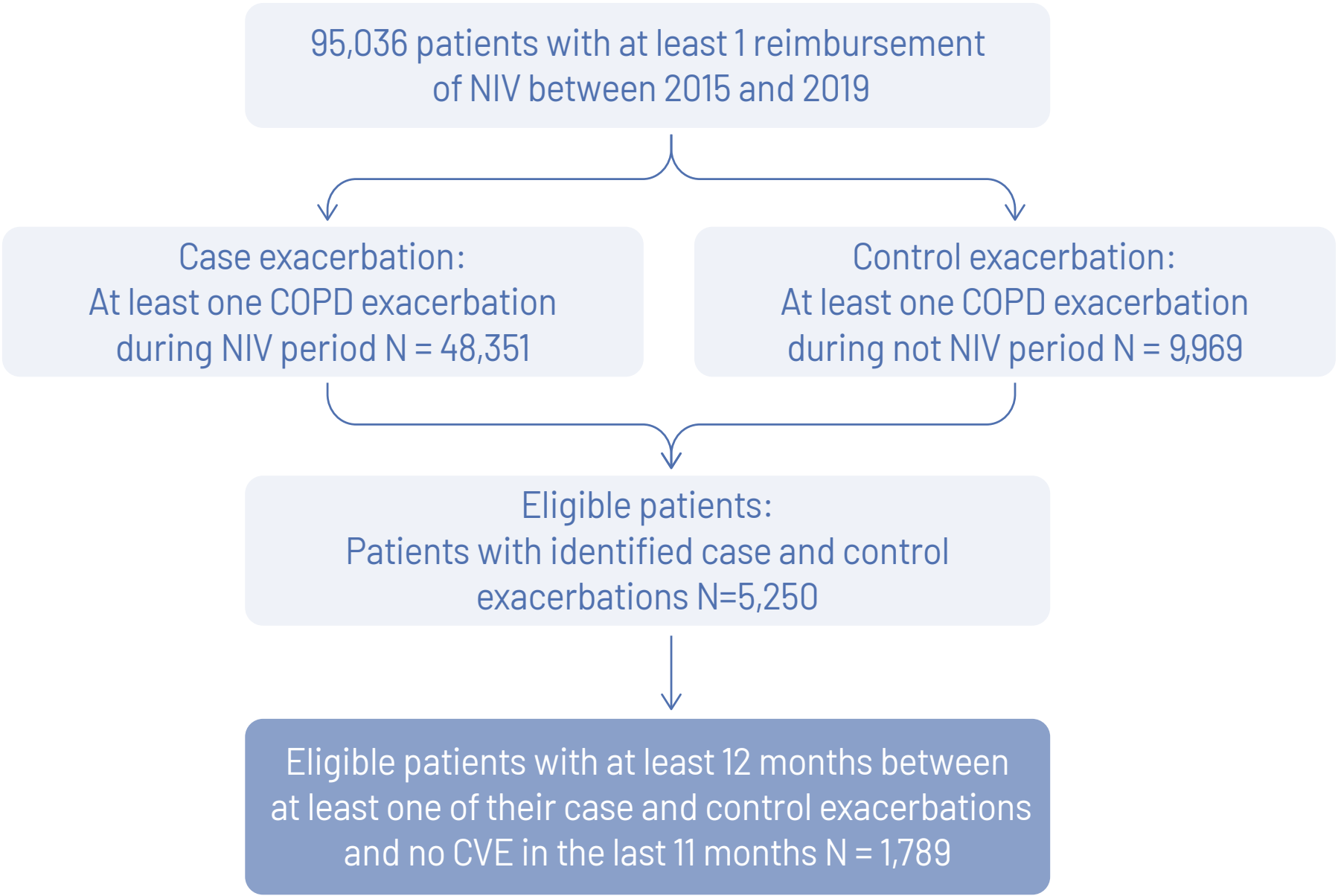
Statistical analysis

CVE occurrence was assessed using stratified logistic regression.

RESULTS

Selection of the study population

A total of 1,789 individuals were considered as eligible patients, i.e. with at least 12 months between at least one of their case and control exacerbations and no CVE in the last 11 months.



Baseline characteristics

Table with 2 columns: Baseline characteristics and N=1,789. Rows include Mean length of follow-up, Median age, % men, Diabetes, Previous hypertension or cardiovascular disease, Morbid obesity, Obstructive sleep apnea, Depression / anxiety / psychiatric treatments, Charlson score of comorbidities, and Bronchodilator / Corticoids / LABA / LAMA.

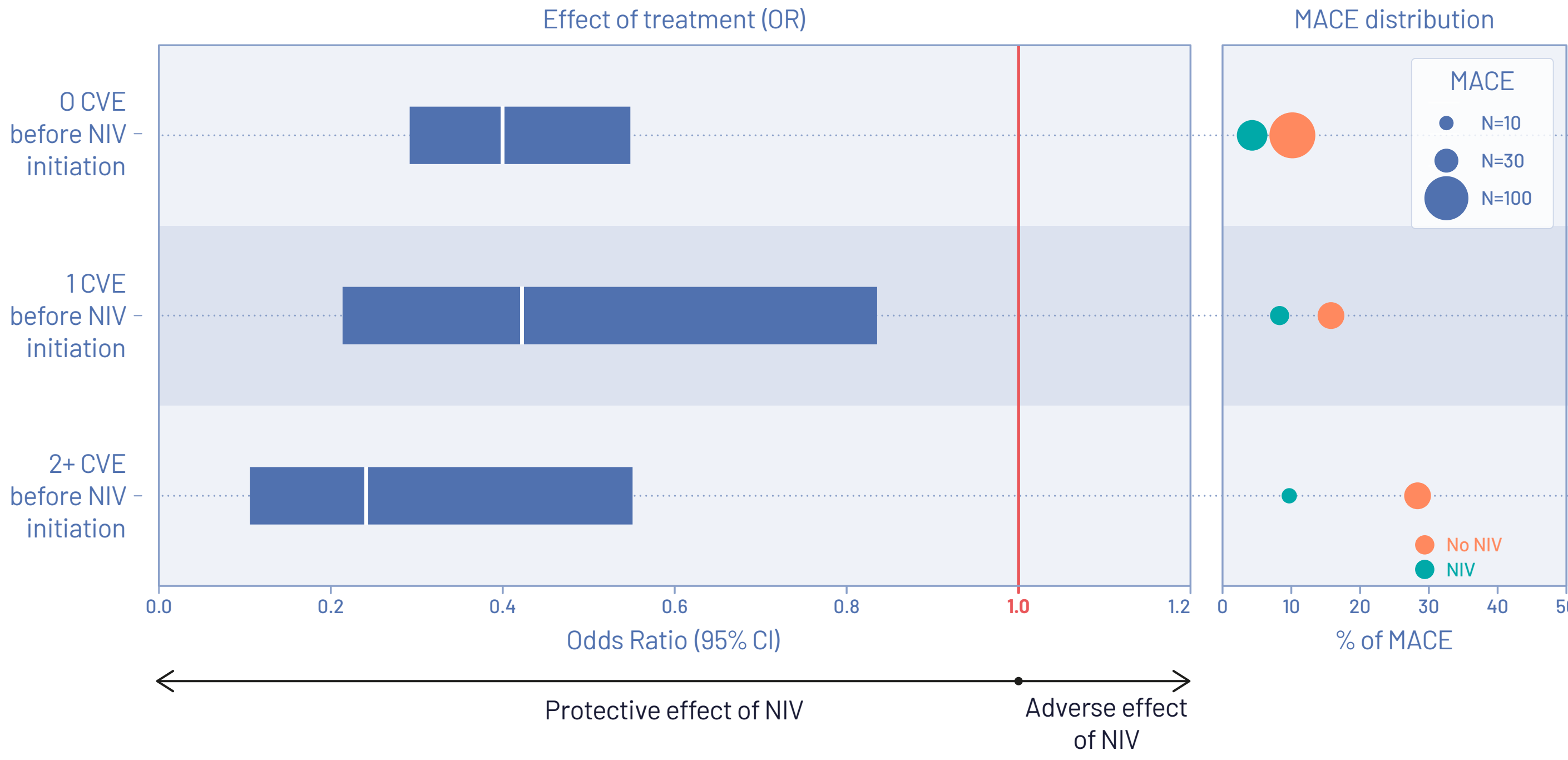
Description of cardiovascular MACEs incidence in the month following AECOPDs in case and control groups.

Overall, 5.3% of the population exhibited an incident CVE in the month following an AECOPD. Results are presented stratified by the number of cardiovascular events occurring in the previous 5 years preceding the first AECOPD to account for level or cardiovascular risk NIV exposure was associated with a 6.8% reduction of incident CVEs with a dose response effect depending upon cardiovascular risk (from -5.7% to -16.6%).

Table with 6 columns: Number of CVE during 5 years before the first, Variable, Indicator, Exacerbation s during NIV period (case), Exacerbations during no NIV period (control), and Difference between NIV and no NIV period within patients. Rows show data for Total, 0, 1, and 2+ CVEs.

Impact of NIV on incident subsequent cardiovascular events after acute exacerbations of COPD

Protective effect observed in the group treated by NIV compared to patients not under NIV. It is true across the range of previous CVE before the first exacerbation.



CONCLUSION

The SCCS method highlighted the strong protective effect of NIV on the occurrence of CVE after a COPD exacerbation. As the independence of events and the stability of confounders may influence results, sensitivity analyses are essential to confirm these assumptions.
The results suggest that AECOPDs occurring without NIV treatment are associated with an increased risk of incident cardiovascular events. Close monitoring, especially at the initial phase following AECOPD presents a critical opportunity for clinical intervention and treatment optimization to prevent future cardiovascular events

Sensitivity analysis

Sensitivity analyses were designed to confirm the robustness of the findings across several washout periods:
1. Variation of washout windows
• Washout period of 6 months between exacerbations compared to 12 months in the main analysis
• Washout of 5 months without CVE before exacerbation compared to 11 months in the main analysis
2. Maximum time delay between the two exacerbations periods:
As the risk of incident CVE might evolve with the delay between evaluation periods, we have conducted sensitivity analysis evaluating a delay of < 36 months

Table with 5 columns: Variable, Indicator, Main study population, Eligible patient's lower washout window, and Eligible patient's different window for previous CVE. Rows show data for N, Number of exacerbations (case), and Number of exacerbations (control) under Sensitivity analysis (1) and (2).

Regulatory aspects

This project was approved by the Comité éthique et scientifique pour les recherches, les études et les évaluations dans le domaine de la santé (CESREES; ref: 3904033) and the French information technology and personal data protection authority ("Commission Nationale Informatique et Liberté" [CNIL]; DR 2021 162 and n° 921198).

Acknowledgment

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References

1 Bots SH, Brown J, Wong AYS, Martin I, Douglas I, Klungel OH, et al. Core Concepts: Self-Controlled Designs in Pharmacoepidemiology. Pharmacoepidemiol Drug Saf. janv 2025;34(1):e70071. doi:10.1002/pds.70071 PubMed PMID: 39805806; PubMed Central PMCID: PMC11729261.