

Association between hospitalized vaso-occlusive crises and mortality in sickle cell disease patients aged 16 years and older using the French National Health Insurance Database (SNDS)

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KEY FINDINGS & CONCLUSION

Interpretation

We can infer that the annual hospitalised VOC rate has a significant effect on the risk of death.

The effect of having ≥3 hospitalised VOCs per year is stronger in older age groups.

VOC recurrence was within 83 days of a priori hospitalized VOC for 50% of the patients with more than one VOC.

The effect of having more than 1 hospitalised VOC is significant for at least one category among all the age groups (lack of power for age ≥40 years); therefore, it is a true VOC effect, and not an age effect.

Limitations

Patients admitted to emergency room for VOC and requesting only intravenous morphine and not hospitalized are not studied leading to underestimation of VOCs when compared to other studies.

A better monitoring of women during pregnancy and also an increase prevalence of sickle crisis during pregnancy could explain the over representation of women. A miscoding of SCD by obstetricians at time of pregnancy, with coding of SC Trait as having SCD with crisis could also be anticipated.

Conclusion

Our study confirms, in a nationwide cohort in France, in a real-life setting, that patients frequently experiencing hospitalised VOCs are at higher risk of death compared to patients seldom experiencing VOCs.

Despite the proportion of VOC was lower in older age categories, the risk of death is still a concern for older patients. The combination with organ damage could explain this.

The recurrence of hospitalised VOC happen in a short time interval after the first hospitalised VOC (within 83 days of a prior hospitalised VOC for 50% of the patients with a recurrent VOC). Therefore, hydroxyurea therapy should be reinforced in patients with recurring VOCs. These patients are also at greatest need for innovative therapies that could reduce or prevent these events.

Patients who are able to reduce their annual number of hospitalised VOCs may live longer.

INTRODUCTION

Patients with sickle cell disease (SCD) experience a wide range of complications thought to be due to the systemic impact of chronically inflamed vasculature, ongoing haemolysis, multi-cellular adhesion and ischemic damage.

The hallmark of SCD is the vaso-occlusive crisis (VOC). An early study suggested a relationship between VOC occurrence and increased mortality^{1,2}. Reviewing this possible relationship, now that SCD management has improved, is important.

To assess the association between hospitalised VOCs and mortality, in SCD patients.

METHODS

Study overview and data sources

This study was a **retrospective observational cohort study** using the French national health insurance's claims database (SNDS, Système National des Données de Santé)³. This database gathers information on hospital records, primary and secondary care, and death.

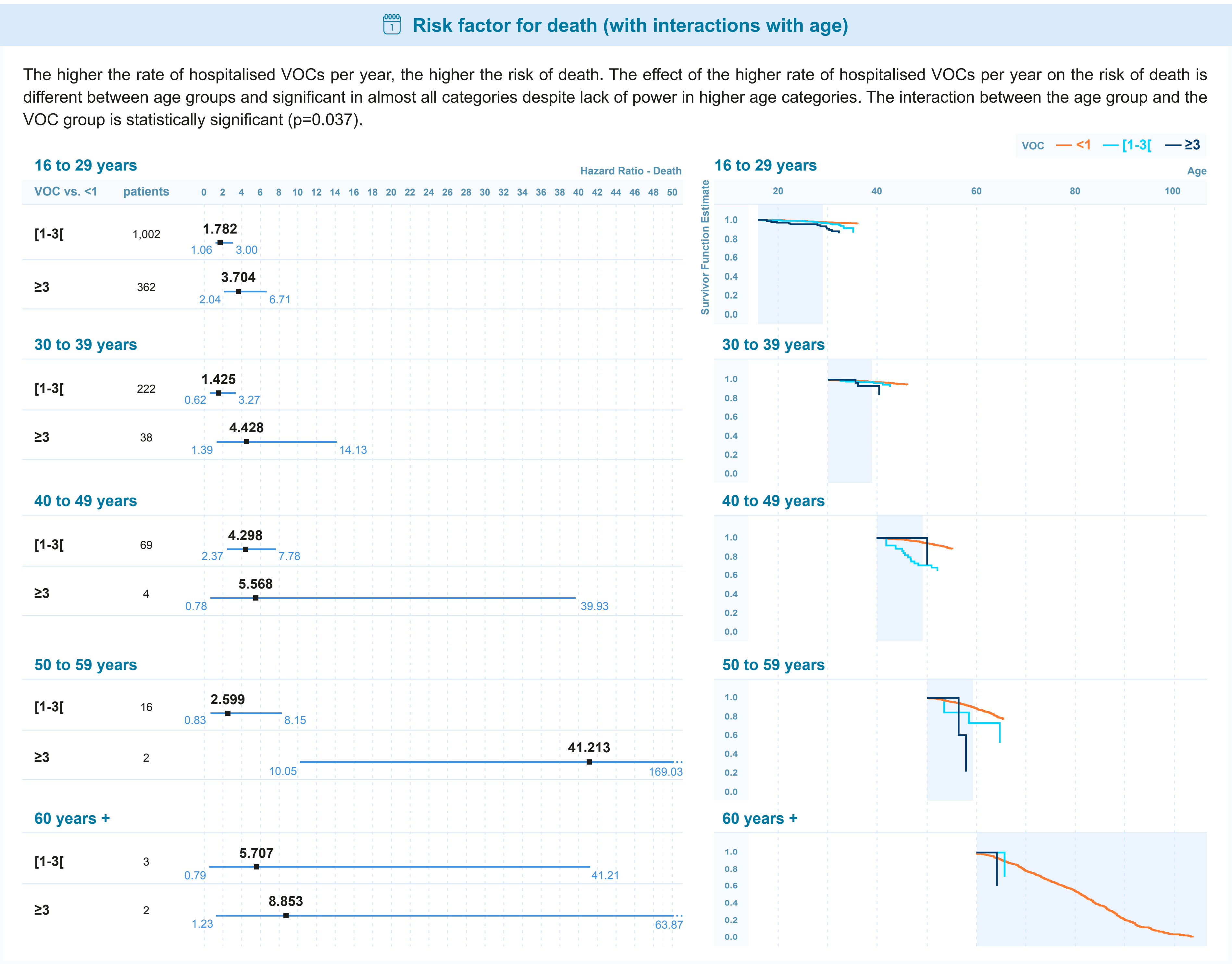
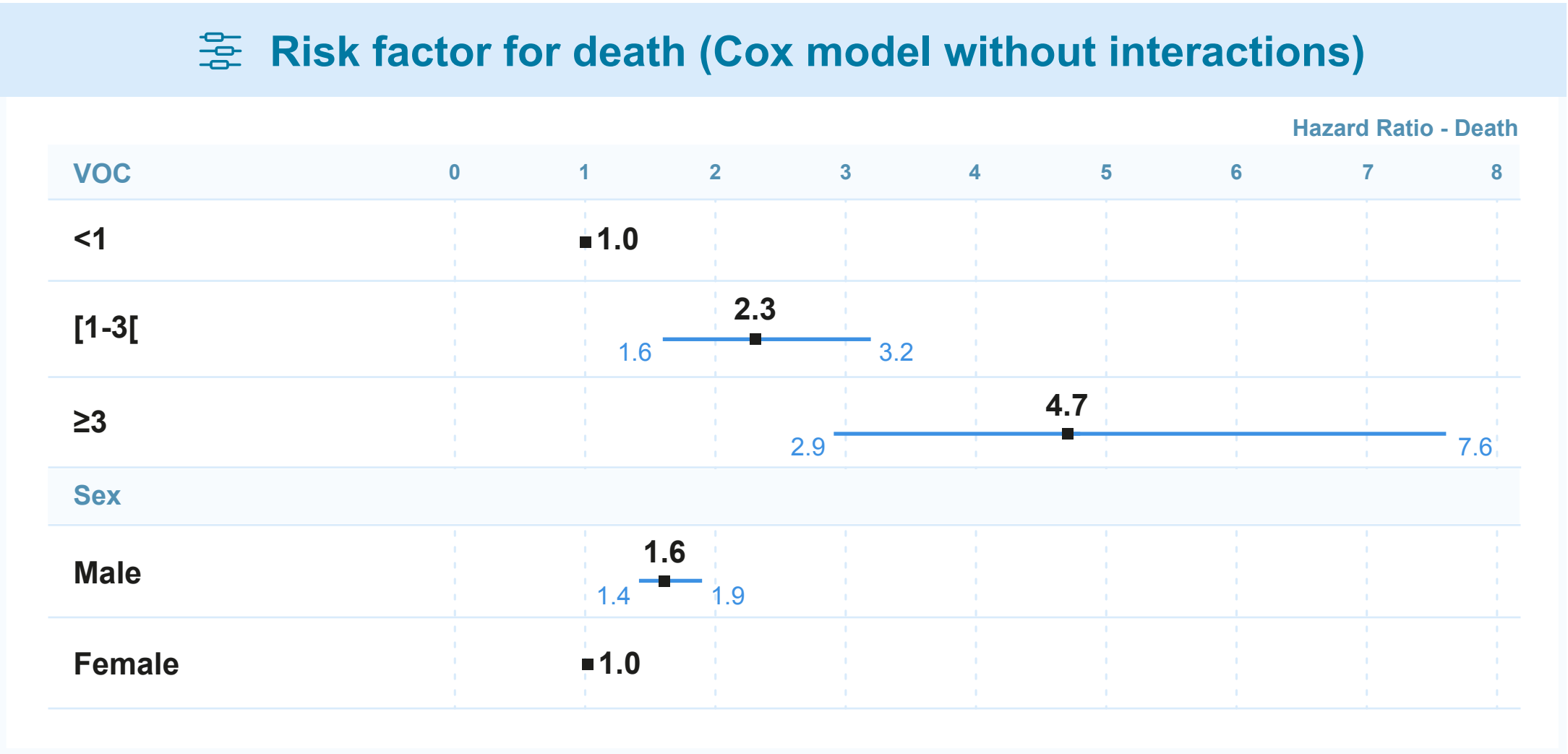
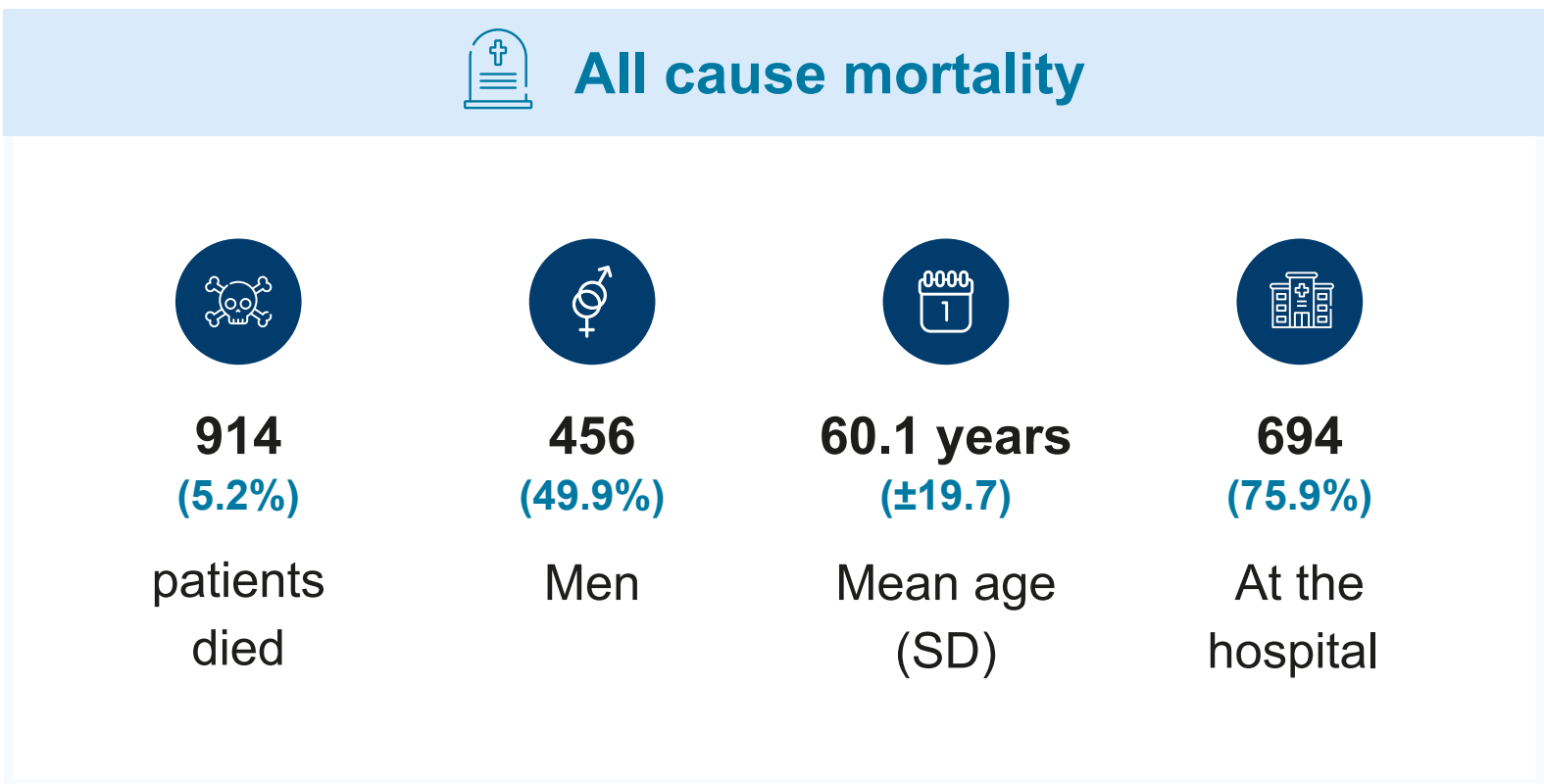
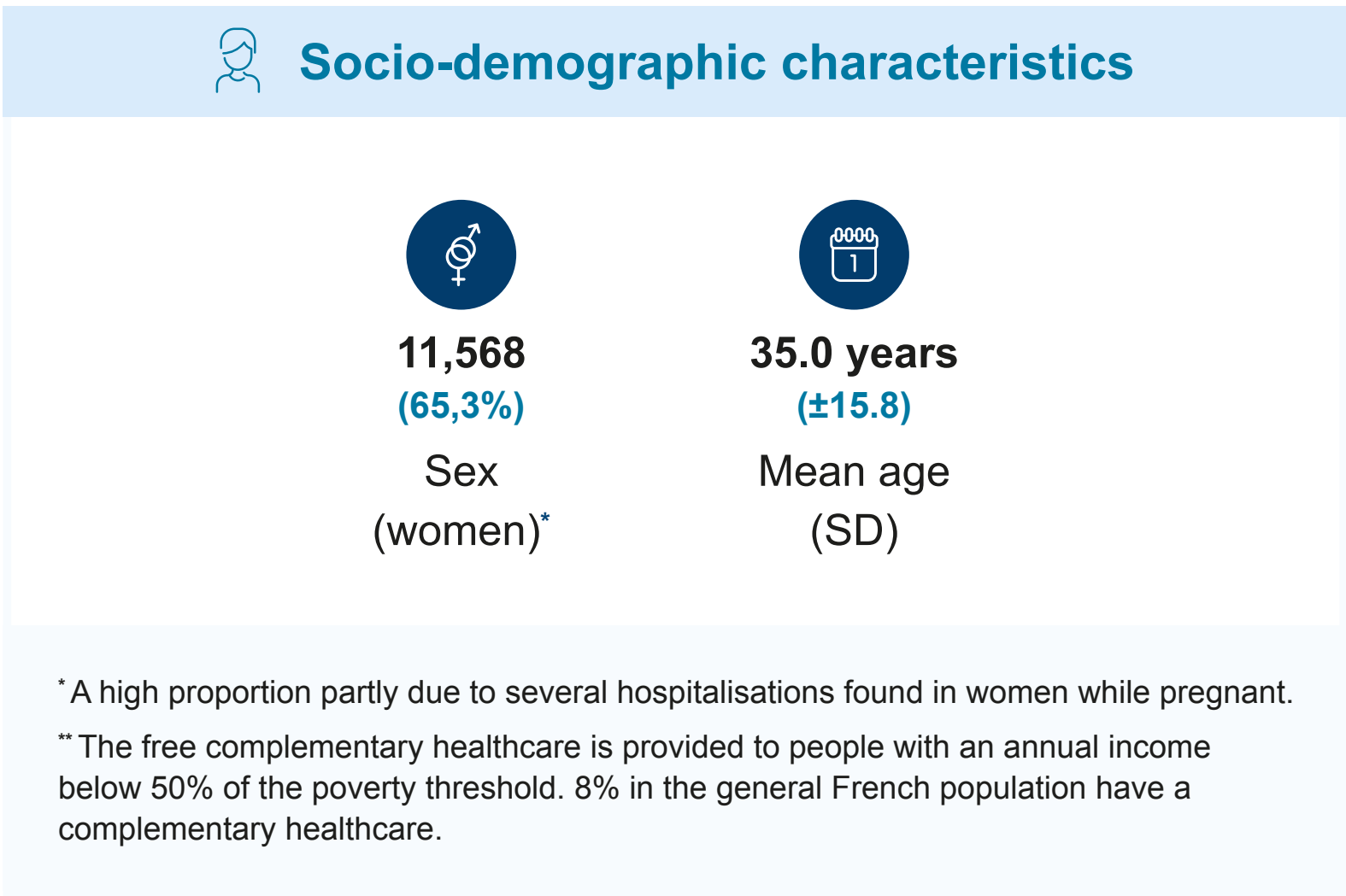
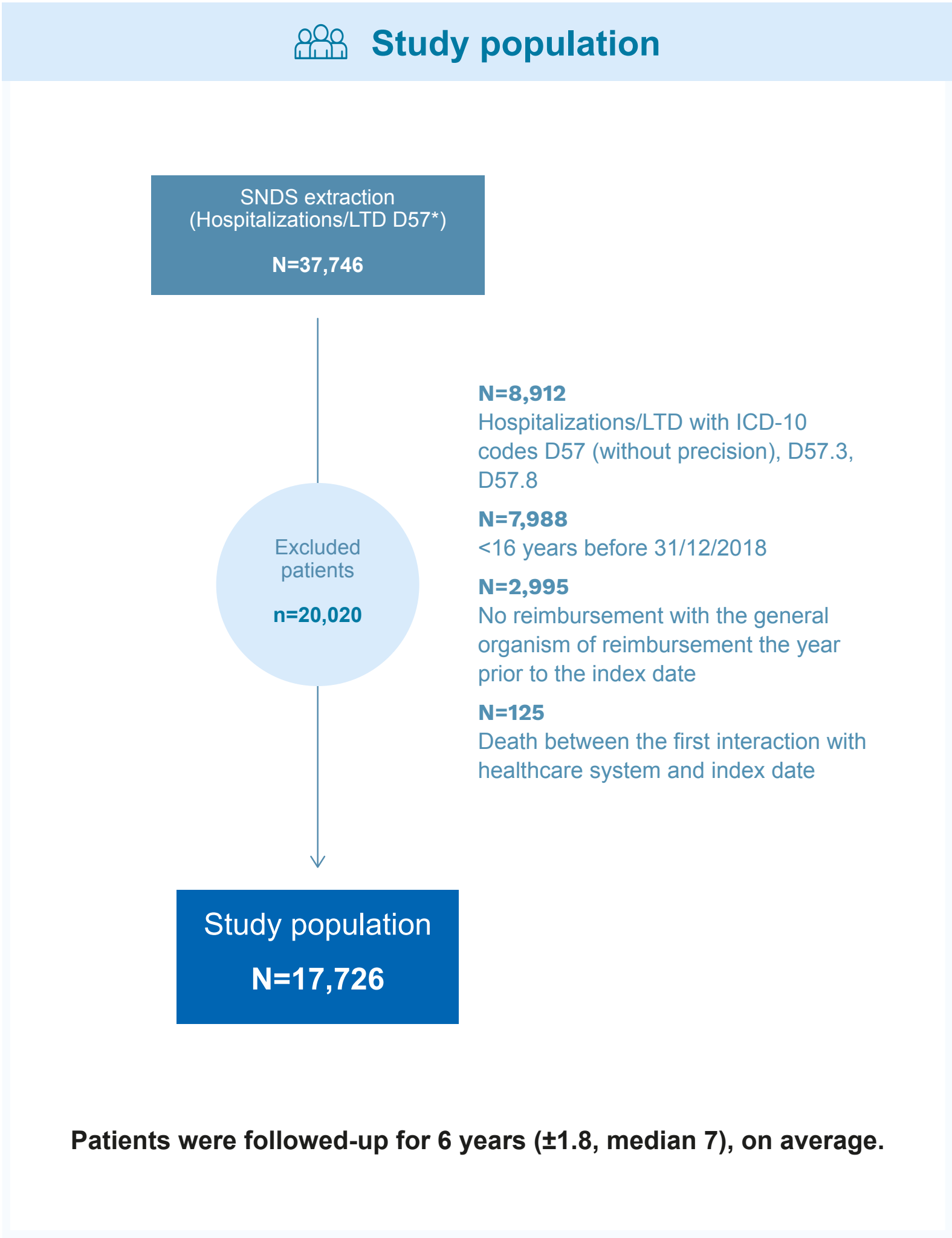
Inclusion period and inclusion criteria

Between January 1st, 2012 and December 31st, 2018

- **Patients with SCD** (with either a hospital record or Long-Term Disease status with diagnostic ICD-10 codes D57.0-2)
- **16 years and older**

The index date was defined as the first interaction with the healthcare system (whether it was related to their SCD or not). Participants were followed-up for at least one year and until the end of the study (December 31st, 2018).

RESULTS



Study outcomes

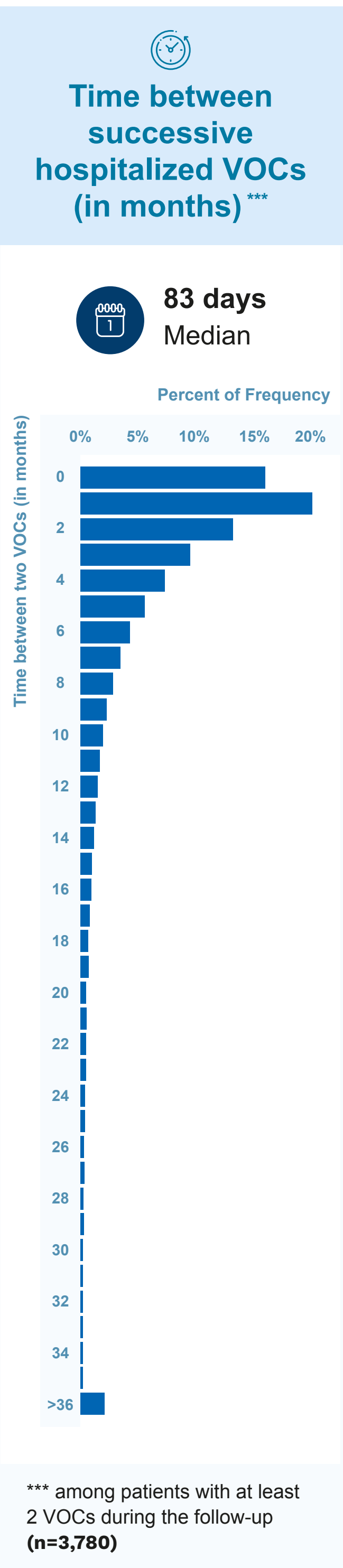
A **hospitalised VOC** was defined as a hospital stay of at least one night with a primary or related diagnosis of sickle-cell anaemia with crisis (D57.0), preceded by a transit through the emergency room (to avoid capturing SCD-related hospital stays for reasons other than VOCs).

Time between successive hospitalised VOCs was studied

The hospitalized VOC annual rate was defined as the total number of hospitalized VOCs during the follow-up divided by the number of follow-up years. Patients were categorised by the annual rate of VOCs they experienced into three groups: <1; 1 to <3; ≥3 VOCs per year.

Statistical analyses

Cox proportional hazards models, with age as the time scale, were used to study the effect of the cumulative rate of hospitalised VOCs on the risk of death, adjusted for sex.



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Disclosures

Hannah Lennon, Eleonore Herquelot, Ludovic Lamarsalle and Fanny Raguideau are employees of HEVA, a company contracted by Novartis to carry out the study.

Miranda Bailey is employed by Novartis.

Pr. Jean-benoît Arlet and Pr. Pablo Bartolucci reports consultancy fees from Novartis.

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