

## Temporality might matter in people with atrial fibrillation and heart failure

### Authors' reply

We thank Professor Laurent Fauchier and colleagues for their interest in our analysis.<sup>1</sup> We agree that the order in which heart failure and atrial fibrillation develop is of interest and might well be important with respect to prognosis. Previous research has reported that for people with incident atrial fibrillation, the presence of prevalent heart failure is an important predictor of all-cause mortality, whereas for people with incident heart failure, survival is similar among people with or without established atrial fibrillation.<sup>2,3</sup>

We were precluded from discussing this diagnostic order in detail in our original manuscript because of space limitations; however, we did report the results of a Cox model for survival in relation to the order in which heart failure and atrial fibrillation develop in the Article's appendix (on p 2).<sup>4</sup> The analysis was based on the first recorded date of either atrial fibrillation or heart failure diagnosis in either the primary or secondary care medical record. The model was adjusted for relevant comorbidities and demographic information and included a subgroup analysis performed considering the sex and age of the enrolled patients.

Consistent with previous research, this analysis showed that people who developed heart failure first and then atrial fibrillation were at a greater relative risk of all-cause mortality (hazard ratio [HR] 3.79, 95% CI 3.72–3.86) than people who developed atrial fibrillation first and then heart failure (HR 3.36, 95% CI 3.31–3.42), when people from both these groups were compared with people with neither heart failure nor atrial fibrillation; however, the absolute differences were minor. Of note, people who were coded as having heart failure and atrial fibrillation diagnosed on the same

day were at the greatest relative risk of death overall (HR 4.00, 95% CI 3.92–4.10). These results were largely consistent between the sexes and across different age subgroups.

Similarly, the median survival time was the shortest among people diagnosed with both heart failure and atrial fibrillation on the same day (2.63 years, IQR 0.19–7.98 years), followed by that among people diagnosed with heart failure first and then atrial fibrillation (3.01 years, IQR 0.46–8.23 years) and atrial fibrillation first and then heart failure (3.94 years, IQR 0.72–9.68 years).

Further research should include detailed investigations of specific aspects of this temporal relationship between heart failure and atrial fibrillation; one such aspect is the importance of the duration for which people have lived with one condition before developing the other. As our analysis relies on the date of diagnosis, it is possible that some people had undiagnosed heart failure or atrial fibrillation, meaning that it is not always certain that the order of diagnosis will reflect the order in which the conditions developed. Nonetheless, our results are based on a large population cohort over the period between Jan 1, 2000, and Dec 31, 2018 and show negative prognostic effects in people with heart failure who later developed atrial fibrillation.

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