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2024 Interim Results from the VAC4EU* Post-authorisation Safety Study (PASS) of the Pfizer-BioNTech COVID-19 Vaccine (COMIRNATY) in Europe

***VAccine monitoring Collaboration for Europe**

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BACKGROUND

COMIRNATY received conditional marketing authorisation in the European Union (EU), United Kingdom (UK) and United States (US) in December 2020. This non-interventional study is designated as a post-authorisation safety study (PASS) and is a commitment to the EU and US regulatory authorities. Here we describe results from the 5th interim report.

OBJECTIVES

This PASS seeks to identify if there is an increased risk of 37 prespecified adverse events of special interest (AESIs) following administration of ≥1 dose of COMIRNATY in the general European population.

METHODS

This PASS is an ongoing retrospective cohort study, with COMIRNATY vaccinated and unvaccinated individuals matched 1:1 on age, sex and other demographic and clinical factors, from six electronic health record data sources from the Vaccine monitoring collaboration for Europe (VAC4EU) in five countries: Italy (Pedianet, general practitioner, GP); Netherlands (PHARMO Data Network, GP); Norway (NHR, inpatient and outpatient); Spain (EpiChron, GP and inpatient and SIDIAP, GP and inpatient/outpatient specialist); and UK (CPRD Aurum, GP). Analyses were conducted using a common protocol, the ConcePTION common data model and common analytical programs. Propensity score-adjusted hazard ratios (HRs) were estimated for event-specific risk windows.

RESULTS

Populations

From December 2020 to March 2022 (CPRD Aurum), December 2022 (Pedianet, NHR), June 2023 (PHARMO, SIDIAP) and July 2023 (EpiChron), 12,400,847 recipients of ≥1 dose of COMIRNATY were matched with an unvaccinated individual **(Figure 1)**.

Baseline characteristics

The **mean and median age** in both the vaccinated and unvaccinated cohorts were 9 and 10 years, respectively in Pedianet. In the other data sources, these ranged from 42 and 36 years in CPRD Aurum to 50 and 48 years, respectively in EpiChron. Between 49% (Pedianet) and 53% (CPRD Aurum) of those included were **females**.

The **Charlson Comorbidity Index Score** was >1 for <2% in the Pedianet cohorts and between 8% (PHARMO) and 24% (CPRD Aurum) in the other data sources, with similar percentages in the vaccinated and unvaccinated cohorts **(Figure 2)**.

The percentage of those with ≥1 CDC risk factors ranged from 21% in CPRD Aurum to 38% in NHR, with similar percentages in the vaccinated and unvaccinated cohorts **(Figure 2)**.

The most frequent comedications recorded in the 12 months prior to inclusion were antibiotics, non-steroidal anti-inflammatory drugs, and psychotropics across the data sources.

Risk estimates for adverse events of special interest

No clear patterns of increased risk for AESIs after vaccination were identified for myocarditis, coronary artery disease, and secondary amenorrhea, except for arrhythmia and hypermenorrhoea in three data sources (PHARMO, EpiChron, and CPRD Aurum) and heart failure in PHARMO **(Figure 3)**.

Figure 3. *Adjusted hazard ratios (HR) for selected AESIs*

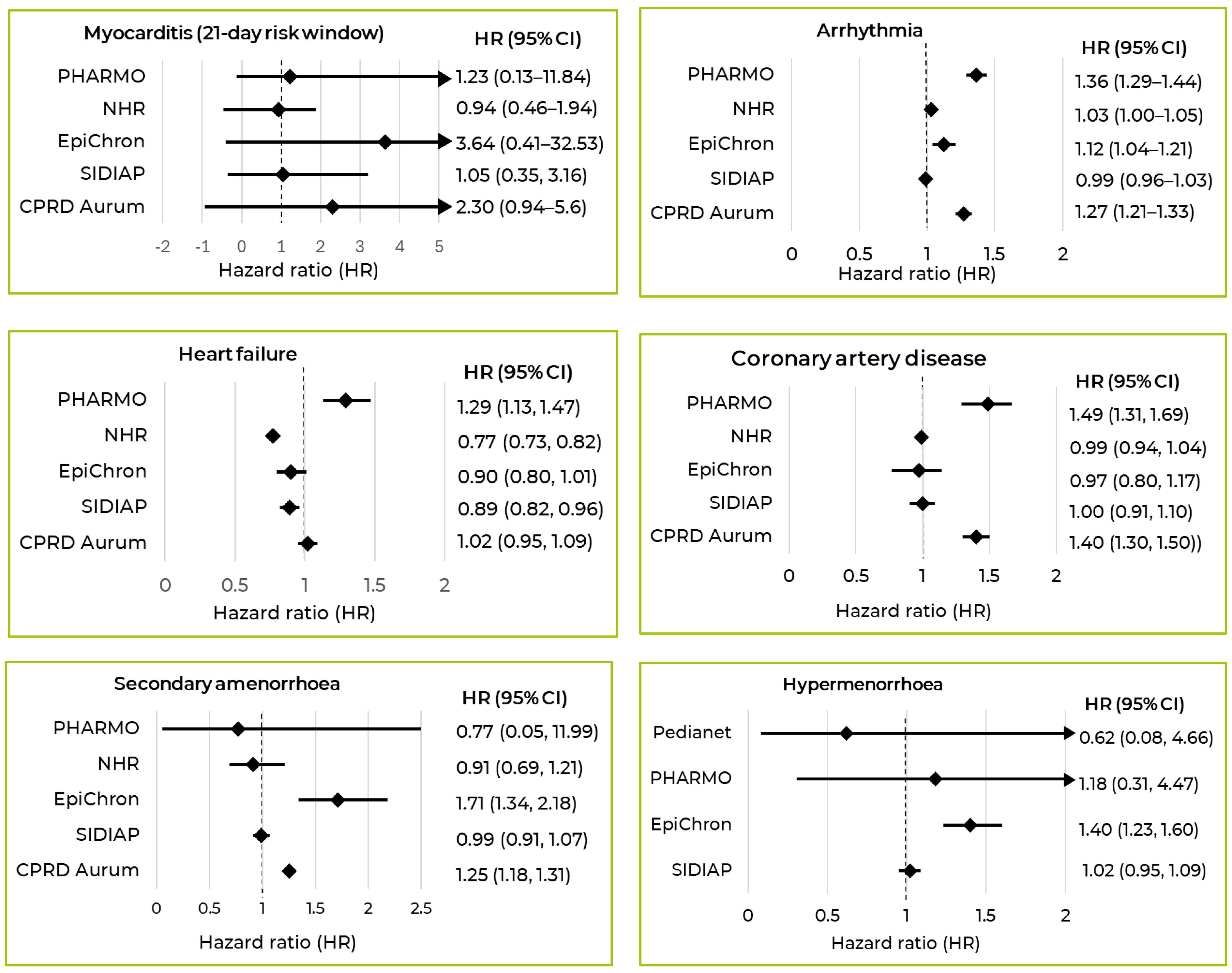


Figure 1. Location and number of matched individuals in each data source

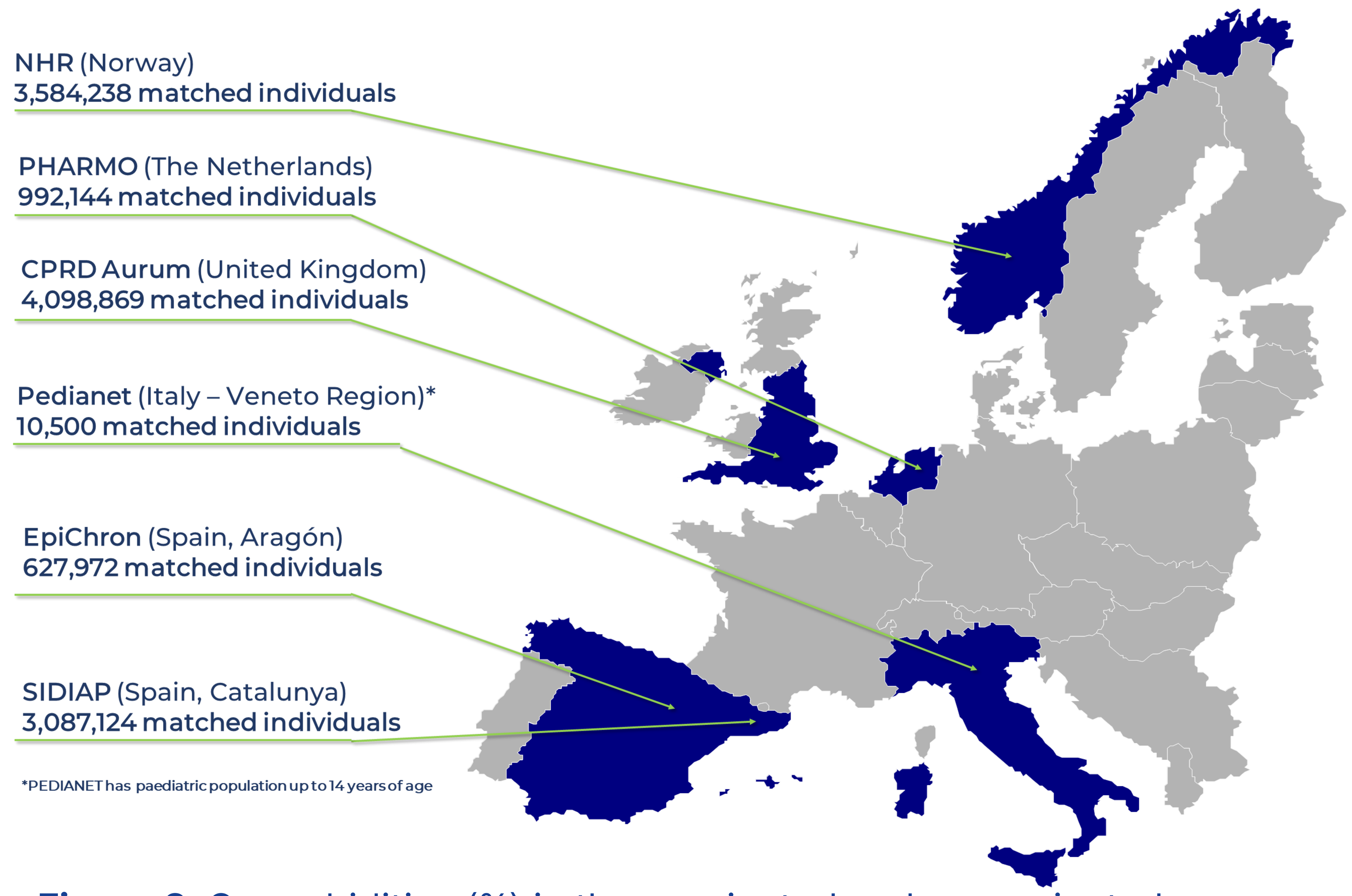
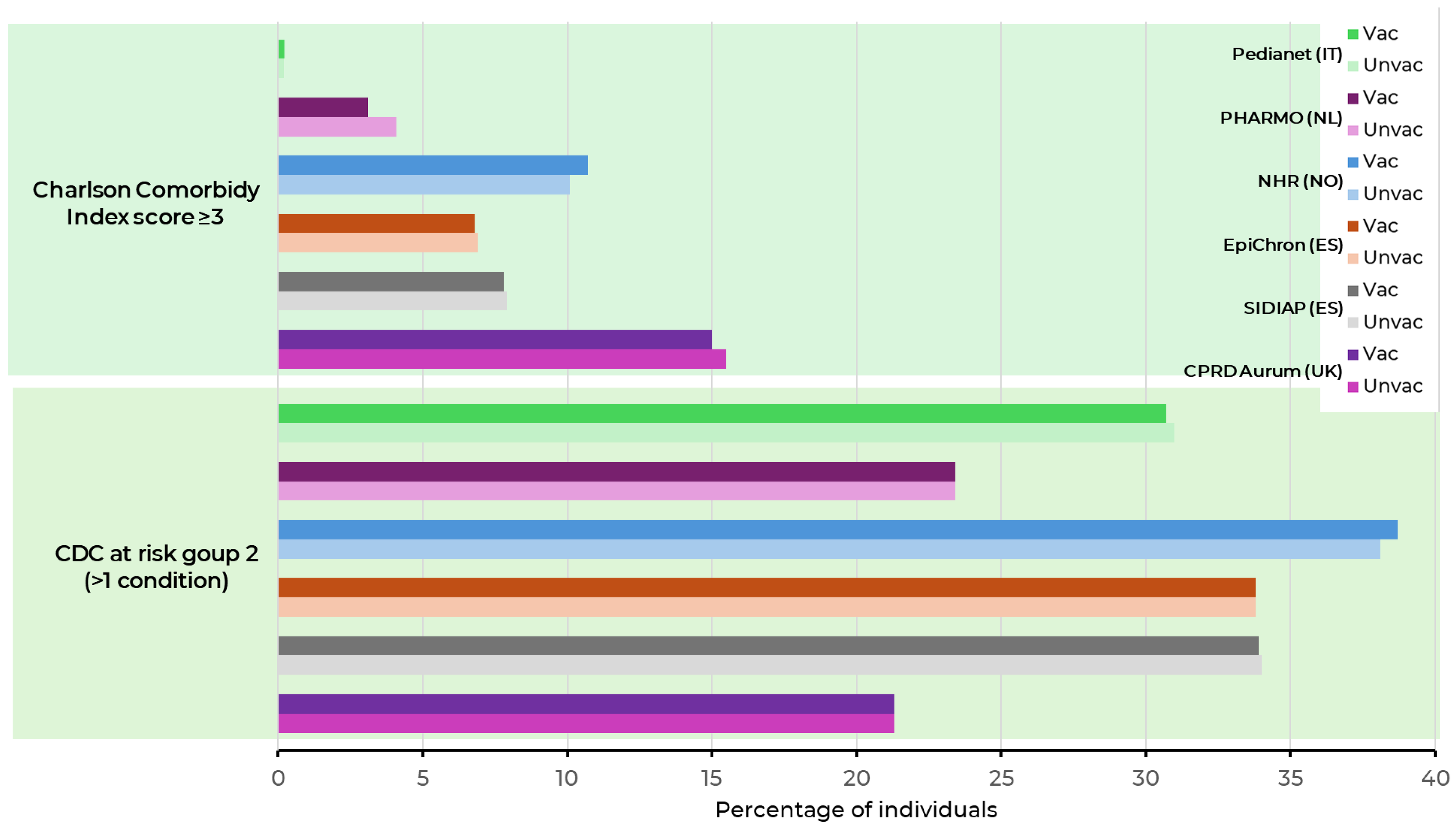


Figure 2. Comorbidities (%) in the vaccinated and unvaccinated cohorts by data source



CONCLUSION

This 5th interim report analysed data from >12 million individuals who received ≥1 dose of COMIRNATY. For most of the 37 AESIs there was no suggestion of an association between the vaccine and the AESIs. Six AESIs were presented due to their special attention from Pharmacovigilance Risk Assessment Committee (PRAC) or study findings. Myocarditis is very rare and there was no apparent increased risk in vaccinated individuals, although estimates were imprecise. The adjusted HR for a few cardiac events and menstrual disorders were heterogeneous across data sources. Potential explanations for these results include differences in the composition of unvaccinated cohorts over time, driven by progressive vaccine uptake and the divergence of cumulative incidence of cardiac events with long risk windows. The identification and differentiation of secondary amenorrhoea and hypermenorrhoea was challenging in electronic healthcare data sources. The final study report (expected in September 2025) may further elucidate these findings.

Conflicts of interest: This study is funded by Pfizer Inc. CD and HR are employees of Pfizer Inc, and hold Pfizer stock. DW, ACR, OR, TV, EP, MH, BP, AGM, ASM, EB, EC, LS, TL,JG, JO, RH, DR, SL, CF, DM, AL, AAD, FV, CAB declare no conflict of interest. JA, JM, XG, RW, and AA are employed at RTI Health Solutions, an independent, non-profit organisation that conducts work for government, public, and private organisations, including pharmaceutical companies. EM and EP provided consultancy services for protocol preparation. GH and AG are consultants for a public research institution that conducts or participates in pharmacoepidemiology studies compliant with the ENCePP Code of Conduct and whose budget is partially sustained by such studies. MCJMS coordinates a department that conducts studies for EMA and pharmaceutical companies (Pfizer, AstraZeneca, Janssen) using the ENCePP Code of Conduct.

This study, protocol number 21_000535, is based in part on data from the Clinical Practice Research Datalink obtained under licence from the UK Medicines and Healthcare products Regulatory Agency. The data is provided by patients and collected by the NHS as part of their care and support. The interpretation and conclusions contained in this study are those of the author/s alone.

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