Supplementary Online Content

Andrews N, Stowe J, Miller E, Ramsay M. BA1 bivalent COVID-19 vaccine use and stroke in England. *JAMA*. Published online June 15, 2023. doi:10.1001/jama.2023.10123

eTable. Selection of Study Participants

eAppendix 1. Influenza Vaccine Eligibility and Types of Vaccine Used

eAppendix 2. Statistical Methods

This supplementary material has been provided by the authors to give readers additional information about their work.

eTable. Selection of study participants

<i>ICD-10</i> codes in the first diagnostic field:			
Acute ischemic strokes (including TIA)	163*	G458	G459
Single stroke due to hemorrhage	160*	l61*	162*
Exclusions were as follows:			
A prior occurrence of any of the above codes in the first 3 diagnostic fields recorded in			
SUS since January 2019.			
A prior admission in SUS for atrial fibrillation admission (ICD codes I48) sickle-cell			
disorders (D57) or primary thrombophilia (D68.5) in the first 3 diagnostic fields.			
A prior admission in the 28 days before the stroke admission for a myocardial infarction			
ICD I21* in the primary diagnostic field.			
A prior admission in the day before the stroke admission for S15* injury of blood			
vessels at neck level or I74* arterial embolism and thrombosis in the primary diagnostic			
field.			

eAppendix 1. Influenza vaccine eligibility and types of vaccine used

The national recommendations for influenza vaccine in England for the study population for the 2022/2023 influenza season were that all those aged 65+ years should receive an adjuvanted influenza vaccine either quadrivalent (QIV) or trivalent (TIV), and all those aged 50-64 years should receive an egg or cell based quadrivalent vaccine.[1] For those invited for an mRNA booster vaccination at the time their seasonal influenza vaccine was due, it was recommended that both vaccines can be given on the same day. High dose influenza vaccines were not used in the study population during the 2022/23 season. The influenza vaccines given to the study population on the same day as a COVID-19 vaccine were consistent with the national recommendations. Of those aged 65+ years, 94.59% received an adjuvanted vaccine compared with 7.89% of those aged 50-64 years.

eAppendix 2. Statistical methods

The statistical analysis was carried out using the self-controlled case-series method. The specific implementation of the method in this paper uses only vaccinated cases and only person time after vaccination. Cases are ascertained independent of vaccine history and comparison is made within cases of the incidence in the period 1-21 days to >=22 days (to end of follow-up) after vaccination using a conditional Poisson model to give a relative incidence. Each individual contributes an event to one of the intervals (risk or control) and person time to these intervals. Person time was also stratified by period in 2-weekly intervals to allow adjustment for changes in stroke incidence by calendar time when fitting the model. As this is an in-person comparison it automatically adjusts for within individual confounding variables such as clinical risk group. Although stroke has a high associated mortality this specific implementation of the method in which there is only one exposure, and all individuals are censored at the end of follow up rather than death is not affected by this as detailed in section 3.2.1 of reference [1]. Stata version 15 was used for the analysis.

[1] <u>https://www.england.nhs.uk/wp-content/uploads/2019/12/B1868_Reimbursable-vaccines-and-eligible-cohorts-for-the-2022-23-NHS-Seasonal-Influenza-flu-Vaccination-Progra.pdf</u>

[2] Whitaker H, Ghebremichael-Weldeselassie Y. Self-Controlled Case Series Methodology. Annu. [1] Rev. Stat. Appl. 2019. 6:241–61.