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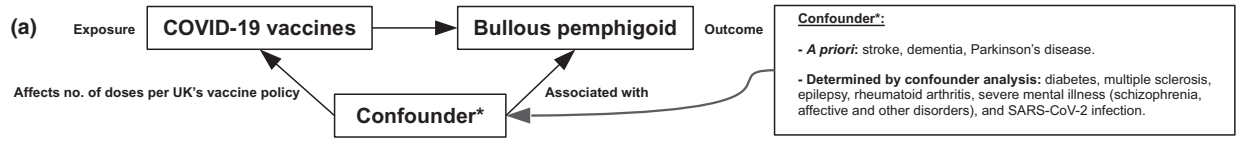
LETTER TO THE EDITOR

The association between COVID-19 vaccines and bullous pemphigoid risk: A UK population-based study

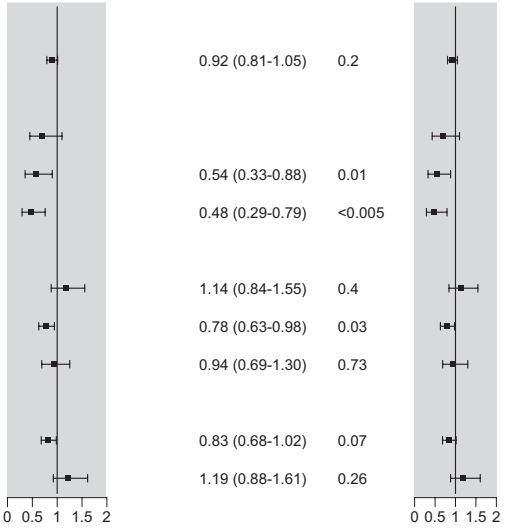
Dear Editor,

Bullous pemphigoid (BP) is a rare autoimmune blistering disease mostly affecting older people.[1] Previous studies reported varied BP risk following COVID-19 vaccines, but were either hospital-based or sampled from ethnically homogeneous populations not representative of the United Kingdom.[2–4] Accurate BP risk estimates following COVID-19 vaccination could help GPs and patients consider routine vaccinations. Earlier BP recognition may result in less severe symptoms and a need for aggressive treatments. We conducted a population-based nested case–control study (2021–2023) using the Clinical Practice Research Datalink (CPRD) GOLD and Aurum and linked hospital data. People (cases ≥18 years old) with the earliest BP record (validated Read/ICD-10 code)[5] were matched up to four controls by age, sex and general practice. COVID-19 vaccine exposure (general, product: AstraZeneca®/Pfizer®/Spikevax®; technology: vector/mRNA) was the latest vaccination within 3 months prior to the index date. The period was chosen based on previous studies on BP onset[6]



(b)

Exposure (a)	Cases, n (%)	Controls, n (%)	Crude (c) OR (95% CI)	Crude (c) p (b)	Fully adjusted (c,d) OR (95% CI)	Fully adjusted (c,d) p (b)
General						
Vaccine (GOLD and Aurum)	1157 (40.91)	4668 (42.18)	0.89 (0.79-1.01)	0.07	0.92 (0.81-1.05)	0.2
Doses (GOLD and Aurum) (e)						
1	252 (8.91)	935 (8.45)	0.70 (0.45-1.10)	0.12		
2	627 (22.17)	2393 (21.62)	0.57 (0.36-0.90)	0.02	0.54 (0.33-0.88)	0.01
>=3	1851 (65.45)	7403 (66.89)	0.47 (0.29-0.76)	<0.005	0.48 (0.29-0.79)	<0.005
Vaccine products (Aurum)						
AstraZeneca	216 (9.06)	712 (7.63)	1.17 (0.88-1.55)	0.28	1.14 (0.84-1.55)	0.4
Pfizer	335 (14.06)	1526 (16.36)	0.77 (0.63-0.94)	0.01	0.78 (0.63-0.98)	0.03
Spikevax	94 (3.94)	358 (3.84)	0.93 (0.69-1.25)	0.63	0.94 (0.69-1.30)	0.73
Vaccine types (Aurum)						
mRNA (Pfizer, Spikevax)	429 (18.00)	1884 (20.20)	0.82 (0.68-0.98)	0.03	0.83 (0.68-1.02)	0.07
Vector (AstraZeneca)	216 (9.06)	712 (7.63)	1.22 (0.92-1.61)	0.16	1.19 (0.88-1.61)	0.26



a - Not vaccinated was the baseline category. Exposure was defined as latest COVID-19 vaccination within three months prior to BP diagnosis. The exposure in the doses category was defined as the number of doses prior to BP diagnosis.
b - statistically significant results when p<0.005.
c - adjusted a priori for dementia, Parkinson's diease and stroke.
d - additionally adjusted for gliptins, antiepileptic drugs, azathioprine, dapsone, doxycycline, prednisolone, methotrexate, mycophenolate, dupilumab.
e - additionally adjusted for the multiple sclerosis and SARS-CoV-2 diagnoses in the fully adjusted analysis.

FIGURE 1 Directed acyclic graphs for examined confounders (a) and estimates (odds ratios) of the association between COVID-19 vaccines and bullous pemphigoid in the main analysis (b).

and because it is likely that after 3 months, vaccine efficacy drops, potentially decreasing the risk of a dysregulated immune response.[7] Doses (0/1/2/≥3) were the number of vaccinations prior to the index date. To estimate BP risk (odds ratio [OR]) following vaccine exposures, we used conditional logistic regression. We adjusted a priori for confounders: stroke, dementia and Parkinson's disease, previously associated with BP[1], which qualified people for more vaccine doses per the UK vaccination policy.[8] Analogically, we tested if diabetes, multiple sclerosis, epilepsy, rheumatoid arthritis, severe mental illness (schizophrenia, affective and other disorders) and SARS-CoV-2 infection were cofounders (Figure 1a).[1,3,9,10] Multivariable analysis adjusted for the latest prescription of drugs previously associated with BP, namely DPP-4 inhibitors and antiepileptics, issued within 1 year before BP diagnosis and anti-inflammatory drugs within 3 months, as this exposure window qualified for additional vaccine doses.[6,8] We performed Charlson Comorbidity Index (CCI: 0–2 vs. ≥3) subgroup analysis to inform risk–benefit assessment of vaccinations. Sensitivity analyses included: (i) adjusting for ethnicity and deprivation to examine sociodemographic inequalities, (ii) a reduced 2-month exposure window to assess temporal delay between vaccination and BP onset. Post hoc mediation analysis proposed SARS-CoV-2 infection could mediate the vaccine–BP association, as additional doses may reduce infection and, indirectly, BP risk. We included 2828 cases (median age 80 [IQR: 72–86], 50.5% women) and 11,067 controls (Table 1). There was no evidence of increased BP risk after COVID-19 vaccines. Individuals after ≥3 doses had an observed lower odds of BP (adjusted OR: 0.48; 95% CI: 0.29–0.79; $p < 0.005$, Figure 1b). Sensitivity, subgroup and mediation analyses had similar results. The results were consistent with previous studies, which found no association between COVID-19 vaccines and BP and a lower risk following a third dose.[2–4] However, these results should not be interpreted as evidence of a causal relationship. Our study's strengths include a large sample drawn from >2000 UK practices. We adjusted for confounders with reliable data, and our design aligns with UK vaccination policy and BP research.[1,3,6,8–10] However, residual confounding may persist, as SARS-CoV-2 infections were likely under-ascertained in CPRD. Despite using validated codes,[5] misclassification is possible due to coding delays, mild/atypical cases and no BP severity data. Missing ethnicity and deprivation data limited the interpretation of vaccine uptake inequalities. Surveillance bias may have affected estimates for ≥3 doses, as conditions that often require regular consultations qualified for additional doses.[8] Furthermore, as BP is a condition of older people, our results are also not generalisable to younger people. Our study found no association between COVID-19 vaccines and BP, which may reassure healthcare professionals and patients about vaccine safety. However, any skin manifestations in people at high risk of BP, that is, the elderly and/or with neurological comorbidities, should be addressed promptly.

TABLE 1 Study population characteristics.

Total, $N = 13{,}895$[a]	Cases, $N = 2828$[a]	Controls, $N = 11{,}067$[a]
Characteristic	**Cases *N* (%)**[b]	**Controls *N* (%)**[b]
Sex		
Male	1401 (49.54)	5475 (49.47)
Female	1427 (50.46)	5592 (50.53)
Median age (IQR)	80 (72–86)	79 (71–85)
Age		
<60	279 (9.87)	1116 (10.08)
60–69	325 (11.49)	1300 (11.75)
70–79	807 (28.54)	3217 (29.07)
80–89	1047 (37.02)	4139 (37.40)
≥90	370 (13.08)	1295 (11.70)
Comorbidities		
Dementia	286 (10.11)	492 (4.45)
Parkinson's disease	67 (2.37)	107 (0.97)
Stroke	401 (14.18)	1216 (10.99)
Diabetes	874 (30.91)	2384 (21.54)
Multiple Sclerosis	36 (1.27)	36 (0.33)
Epilepsy	80 (2.83)	155 (1.40)
Rheumatoid Arthritis	76 (2.69)	215 (1.94)
Severe Mental Illness	50 (1.77)	120 (1.08)
SARS-CoV-2	126 (4.46)	335 (3.03)
Charlson Comorbidity Index		
0	865 (30.59)	4742 (42.85)
1	497 (17.57)	1764 (15.94)
2	477 (16.87)	1785 (16.13)
≥3	989 (34.97)	2776 (25.08)
Ethnicity		
Asian	147 (5.20)	435 (3.93)
Black	40 (1.41)	160 (1.45)
White	2087 (73.80)	7976 (72.07)
Other	32 (1.13)	97 (0.88)
Unknown	522 (18.46)	2399 (21.68)
Index of Multiple Deprivation		
1 (most affluent)	444 (15.70)	1795 (16.22)
2	448 (15.84)	1621 (14.65)
3	392 (13.86)	1521 (13.74)
4	328 (11.60)	1221 (11.03)
5 (most deprived)	262 (9.26)	959 (8.67)
Unknown	954 (33.73)	3950 (35.69)

[a]Aurum only study population – Total: $N = 11{,}710$, Cases: $N = 2383$, Controls: $N = 9327$.

[b]Percentages might not total 100%.

KEYWORDS
bullous pemphigoid, case–control study, COVID-19 vaccine, epidemiology, population-based

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CONFLICT OF INTEREST STATEMENT

The authors have nothing to declare.

DATA AVAILABILITY STATEMENT

This study 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. Copyright© (2026), re-used with the permission of The Health & Social Care Information Centre. All rights reserved. The data is available by applying to CPRD directly via www.cprd.com. Results of the additional analyses and supplementary material are available upon request.

ETHICAL APPROVAL

The study and its protocol were approved by the CPRD (ID: 23_003023).

ETHICS STATEMENT

This study does not raise any ethical issues. Data in the CPRD are anonymised and provided to the researchers by the Medicines and Healthcare products Regulatory Authority after external peer review and approval by their Independent Scientific Advisory Committee.

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