Science Letter

Hospital admission for symptomatic COVID-19 and impact of vaccination: analysis of linked data from the Coronavirus Clinical Information Network and the National Immunisation Management Service

SARS-CoV-2 vaccines administered in the UK are highly effective in preventing hospitalisation and death from COVID-19 [1]. Patients with immunocompromise are less likely to be able to mount a satisfactory immunological response to the vaccine and therefore may remain at higher risk of moderate-to-severe COVID-19 [2]. Understanding the reasons and risk-factors for admission will provide insight into strategies for future vaccination. This study aimed to characterise the hospitalised vaccinated population and identify the effect of the relationship between vaccination status and immunocompetence on hospital mortality using the prospective observational cohort recruited from the UK Coronavirus Clinical Information Network (CO-CIN).

ISARIC4C/CO-CIN collected data on hospitalised patients with COVID-19 in the UK since February 2020 [3]. The National Immunisation Management Service contains vaccine type and date of first and/or second vaccination since the COVID-19 vaccination programme started in the UK on 8 December 2020. We linked data in CO-CIN and the National Immunisation Management Service and restricted our population to adults admitted to hospital with symptomatic polymerase chain reaction (PCR)-positive SARS-CoV-2 infection with at least 28 days of follow-up. This is a complete case analysis. Patients with re-infection were removed from this analysis. We categorised patients into the following three groups: no virus immunity – unvaccinated patients and patients experiencing symptoms ≤ 20 days after first vaccination dose [4]; first dose failure – patients experiencing symptoms ≥ 21 days after first vaccination dose or patients experiencing symptoms ≤ 13 days after second vaccination dose; and second dose failure – patients experiencing symptoms ≥ 14 days after second vaccination dose. Immunocompromise was defined as pre-existing immunological or metabolic disorder (e.g. severe combined immunodeficiency or common variable immunodeficiency); solid organ transplant; HIV/AIDS; cancer on active treatment with chemotherapy or immune modifying drugs; or receipt of immunosuppressing drugs. We assessed the association between immunocompromise, vaccine failure status and 28-day mortality, adjusting for age, sex, ethnicity, socio-economic status and comorbidity using logistic regression with an interaction between immunocompromise and vaccine failure status.

There were 40,870 patients recruited to ISARIC4C/CO-CIN between 8 December 2020 and 15 August 2021 with symptomatic PCR-positive COVID-19. At the time of admission, 33,856 (82.8%) patients were unvaccinated; 5332 (13.0%) had received their first vaccination; and 1682 (4.1%) had received their second vaccination. Of the 7014 patients who had received a vaccination, 3606 (51.4%) had no virus immunity; 1941 (27.7%) had first dose failure; and 1467 (20.9%) had second dose failure (see online Supporting Information Figure S1), proportions which persisted when restricting to patients with at least 60 days of follow-up (see online Supporting Information Figure S2). Despite lower absolute values, the relative proportion of immunocompromised patients increased from no virus immunity (12.4%) to first dose failure (17.5%) to second dose failure (20.6%) (Table 1).

After adjustment, vaccination reduced the odds of mortality in patients admitted to hospital (Fig. 1 and online Supporting Information Figure S3). Immunocompromised patients had consistently higher odds of mortality compared with immunocompetent patients (Fig. 1), and there was a significant interaction between vaccination status and immunocompromise ($p = 0.001$).

Most patients hospitalised with symptomatic COVID-19 since the vaccination programme began in the UK have not been vaccinated, and for those who have received a vaccine, most admissions occurred within 3 weeks of the first dose before the vaccine would be expected to be effective (see online Supporting Information Figure S1). It is important to highlight to the general population that there is a lag between receiving a vaccination and developing the immunity required to prevent hospitalisation or death, as awareness may alter post-vaccination behaviour. We found that vaccination generally

Table 1 Patient characteristics stratified by immunocompetency. Values are number (proportion) or number

	Immunocompetent n = 35,581	Immunocompromised n = 5289	Overall n = 40,870
Sex			
Female	15,662 (86.4%)	2456 (13.6%)	18,118
Male	19,885 (87.6%)	2823 (12.4%)	22,708
Missing	34 (77.3%)	10 (22.7%)	44
Ethnicity			
White	24,414 (86.1%)	3934 (13.9%)	28,348
South Asian	2220 (88.6%)	285 (11.4%)	2505
Black	909 (88.9%)	114 (11.1%)	1023
East Asian	181 (91.9%)	16 (8.1%)	197
Other	2380 (88%)	324 (12%)	2704
Missing	5477 (89.9%)	616 (10.1%)	6093
Vaccination tier			
Tier 2	9274 (88.5%)	1209 (11.5%)	10,483
Tier 3	3454 (82.7%)	725 (17.3%)	4179
Tier 4	3655 (66.4%)	1848 (33.6%)	5503
Tier 5	2850 (90.7%)	291 (9.3%)	3141
Tier 6	6241 (83.7%)	1216 (16.3%)	7457
Tier 7	1632 (100%)	0	1632
Tier 8	1850 (100%)	0	1850
Tier 9	1711 (100%)	0	1711
Tier 10	4914 (100%)	0	4914
IMD quintile			
1 (most deprived)	9438 (88.5%)	1231 (11.5%)	10,669
2	7353 (86.9%)	1110 (13.1%)	8463
3	6528 (87.2%)	958 (12.8%)	7486
4	6008 (86.3%)	953 (13.7%)	6961
5 (least deprived)	5472 (85.6%)	920 (14.4%)	6392
Missing	782 (87%)	117 (13%)	899
Comorbidities			
Chronic kidney disease	4176 (81.7%)	937 (18.3%)	5113
Solid organ transplant	0	324 (100%)	324
Chronic cardiac disease	7905 (84.1%)	1491 (15.9%)	9396
Chronic pulmonary disease	4187 (75.3%)	1374 (24.7%)	5561
Diabetes	4692 (85.6%)	789 (14.4%)	5481
Obesity	5101 (86.2%)	820 (13.8%)	5921
Chronic neurological disorder	3106 (87.2%)	457 (12.8%)	3563
Dementia	2922 (89.8%)	331 (10.2%)	3253
Vaccine failure			
No information on the date of symptom onset	75 (92.6%)	6 (7.4%)	81
No virus immunity	32,740 (87.6%)	4641 (12.4%)	37,381
First dose failure	1601 (82.5%)	340 (17.5%)	1941
Second dose failure	1165 (79.4%)	302 (20.6%)	1467

IMD, index of multiple deprivation.

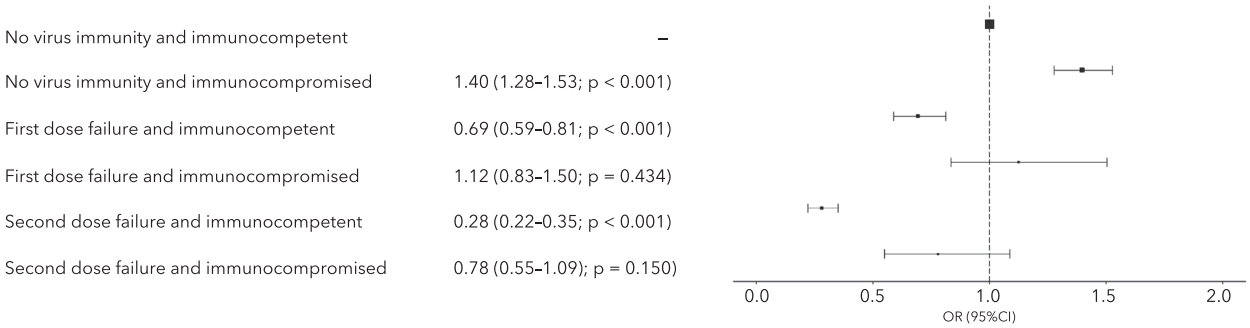

Figure 1 Logistic regression odds of 28-day mortality for immunocompetent vs. immunocompromised patients, stratified by vaccine group: no virus immunity; first dose failure; and second dose failure. Odds adjusted for age; sex; ethnicity; socio-economic status; and comorbidity

reduced the odds of in-hospital mortality in both immunocompetent and immunocompromised patients; however, this effect was reduced in immunocompromised patients. This is consistent with previous study findings that although patients with weakened immune systems mount a response to COVID-19 vaccines, the rates of seroconversion and antibody generation are lower [2, 5, 6, Kearns et al., preprint, https://doi.org/10.2139/ssrn.3910058].

This analysis was undertaken before the emergence of the omicron variant and before third booster doses were available to all adults, and should be repeated in the context of omicron to examine the effect of third doses on outcomes for patients admitted to hospital with COVID-19. Public health messaging regarding booster vaccine doses and non-pharmaceutical interventions should target this vulnerable immunocompromised group. Alternative strategies such as prophylactic or therapeutic administration of high potency monoclonal antibodies should also be considered.

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Supporting Information

Additional supporting information may be found online via the journal website.

Figure S1. Time between first and second vaccination and onset of symptoms, up to 150 days.

Figure S2. Time between first and second vaccination and onset of symptoms, up to 60 days.

Figure S3. Full model for 28-day in-hospital mortality.