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Symptom study app provides real-world data on COVID-19 vaccines

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Vaccines offer the best opportunity for bringing the COVID-19 pandemic under control. Several vaccines have now been authorised in multiple countries on the basis of demonstrated safety and efficacy in large-scale phase 3 trials.[1,2] On Dec 8, 2020, the COVID-19 vaccine programme kicked off in the UK with the introduction of the Pfizer-BioNTech mRNA vaccine (BNT162b2). Within a month, the Oxford-AstraZeneca ChAdOx1 nCoV-19 (AZD1222) adenoviral vector vaccine had also been deployed. Compelling evidence from large-scale post-implementation observation studies has shown that COVID-19 vaccination programmes have substantially reduced COVID-19-related hospitalisation in the UK and Israel.[3,4] Furthermore, BNT162b2 and ChAdOx1 nCoV-19 appear to offer greater protection against severe disease than symptomatic disease—the primary endpoint used in the phase 3 trials.[5] Rapid and detailed post-marketing surveillance of COVID-19 vaccine safety and effectiveness is now required to enable assessment of the real-world impact of COVID-19 vaccination programmes,[1,2] particularly in light of the emergence of SARS-CoV-2 variants of concern.[6]

In *The Lancet Infectious Diseases*, Cristina Menni and colleagues[7] describe real-world data on COVID-19 vaccine reactogenicity and SARS-CoV-2 infection in users of the COVID Symptom Study app. This app is a community-led initiative designed to capture longitudinal data relating to the COVID-19 pandemic, with more than 4·5 million contributors. The app is freely available to the UK public and involves users logging their daily health status, COVID-19 test results, and COVID-19 vaccine status, alongside their demographic information and comorbidities.[8] App users logging COVID-19 vaccinations are asked about a list of systemic and local reactions for 8 days following vaccination. In this study, 627 383 UK app users logged a COVID-19 vaccine between Dec 8, 2020, and March 10, 2021. 345 280 (55%) vaccinees received ChAdOx1 nCoV-19, whereas 282 103 (45%) received BNT162b, 28 207 (10%) of whom logged a second dose. No ChAdOx1 nCoV-19 second dose data were available.

Across both vaccines, local adverse events (eg, injection-site pain and swelling) were common, occurring in 257 209 (66·2%) of 388 430 individuals. Systemic adverse events were less common, with 159 101 (25·4%) of 627 383 experiencing at least one systemic adverse event. The most frequent systemic adverse events were fatigue and headache, peaking 24 h after vaccination. Notably, local and systemic reactions were less common in this community-based cohort than in phase 3 trial reports.[1,2] Possible explanations for this discrepancy include differences in study populations (eg, demographic data such as age), psychological differences in symptom reporting behaviour between clinical trial participants and those receiving an authorised vaccine, and study dropout—data could be more complete in clinical trials, in which follow up is typically fastidious.[9]

In keeping with the phase 1–3 vaccine trial data of both vaccines,[1,2] systemic adverse events were more common in individuals aged 55 years or younger than in those older than 55 years and in women than in men. Consistent with the phase 3 trial,[2] systemic reactions were more common after the second dose than after the first dose of BNT162b2. Curiously, previous documented SARS-CoV-2 infection was associated with increased incidence of adverse events. In BNT162b2 recipients, 5148 (35·8%) of 14 369 who had previously been infected with SARS-CoV-2 had a systemic reaction compared with 33 007 (12·3%) of 267 734 without previous documented infection. This finding was also true in ChAdOx1 nCoV-19 vaccinees: 7551 (53·1%) of 14 231 with past infection reported a systemic reaction compared with 108 922 (32·9%) of 331 049 without. These findings potentially implicate pre-existing immunity in vaccine reactogenicity.

Analysis of SARS-CoV-2 test positivity in vaccinated and unvaccinated app users showed that protection against SARS-CoV-2 infection appears as early as 12 days after vaccination. A single dose of BNT162b2 reduced the risk of infection compared with unvaccinated controls by 58% (95% CI 54–62) at 12–20 days, 69% (66–72) at 21–44 days, and 72% (63–79) at 45–59 days after vaccination. Similarly, the risk of infection was reduced after ChAdOx1 nCoV-19 vaccination compared with unvaccinated controls, with a risk reduction of 39% (21–53) at 12–20 days and 60%

(49–68) at 21–44 days after vaccination. These findings support vaccination strategies opting to delay a second dose in favour of maximising first-dose rollout.[4,5,10]

Overall, this study provides valuable information to health-care professionals and the general public on vaccine reactogenicity and effectiveness in the community setting. In this era of rapid dissemination of information, good science communication has a crucial role to play in strengthening public confidence in vaccines and thus maximising vaccine uptake. The independent, community-led nature of this study might provide reassurance to members of the public who are reticent to trust the findings of pre-licensure vaccine studies involving large pharmaceutical companies. As a final point, this study is also a great example of the fruitfulness of engaging the public—as major stakeholders—in scientific research.

RED and DO'C are members of the Oxford COVID Vaccine Trial Group that conducted phase 1–3 trials of the Oxford-AstraZeneca ChAdOx1 nCoV-19 vaccine (AZD1222).

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Adjuvantation helps to optimise COVID-19 vaccine candidate

As of Feb 6, 2021, the global COVID19 pandemic, caused by SARS-CoV-2, has resulted in over 103 million confirmed cases and 2·22 million deaths worldwide, and the situation is getting worse.[1] To date, eleven COVID-19 vaccines have been approved for emergency use or conditional licensure by at least one country. However, the production and supply of these vaccines are still inadequate, as they will not be available to cover the global population within a short period of time. Developed countries have purchased approximately 70% of the authorised novel COVID-19 vaccines, which could skew the epidemics further toward low-income and middle-income countries and exacerbate overburdened public health-care resources. COVID-19 vaccines from multiple manufacturers will be needed to address the global need.

BBV152 is a whole-virion inactivated SARS-CoV-2 vaccine, formulated with a toll-like receptor (TLR) 7/8 agonist molecule (IMDG) adsorbed to alum (Algel), and manufactured and produced by Bharat Biotech (India).[2] In *The Lancet Infectious Diseases*, Raches Ella and colleagues[3] report on the safety and immunogenicity of BBV152 in a double-blind, randomised, multicentre, phase 2 trial, and describe the persistence of immune responses at 3 months follow-up from the double-blind, randomised, phase 1 trial.[2] The results showed that two intramuscular injections of 6 µg BBV152 with Algel-IMDG administered 4 weeks apart induced seroconversion (plaque-reduction neutralisation test [$PRNT_{50}$]) in 174 (98·3% [95% CI 95·1–99·6]) of 177 participants, and geometric mean titres (GMT; microneutralisation assay [MNT_{50}]) of neutralising antibodies of 160·1 (95% CI 135·8–188·8) on day 56 (4 weeks after the second dose). BBV152 was also found to induce a persistent immune response, with high neutralising antibody titres observed in phase 1 participants at 3 months after the


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