

## 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, based on safety and efficacy in large-scale phase 3 trials<sup>1,2</sup>. On 8<sup>th</sup> December 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 have shown COVID-19 vaccination programmes have substantially reduced COVID-19 related hospitalisation in the UK and Israel<sup>3,4</sup>. Furthermore, BNT162b2 and ChAdOx1 nCoV-19 appear to offer greater protection against severe disease than symptomatic disease — primarily the endpoint used in the phase 3 trials<sup>5</sup>. Rapid and detailed post-marketing surveillance of COVID-19 vaccine safety and efficacy is now required to enable assessment of the real-world impact of COVID-19 vaccination programmes<sup>1,2</sup>, particularly in light of the emergence of SARS-CoV-2 variants of concern<sup>6</sup>.

In *The Lancet Infectious Diseases* Cristina Menni and colleagues<sup>7</sup> describe “real-world” data on COVID-19 vaccine reactogenicity and SARS-CoV-2 infection amongst 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 over 4.5 million contributors. This free app is open 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 co-morbidities<sup>8</sup>. 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 8<sup>th</sup> December 2020 to the 10<sup>th</sup> March 2021. Fifty-five percent of vaccinees received ChAdOx1 nCoV-19, whilst 45% received BNT162b, 10% of whom logged a second dose. No ChAdOx1 nCoV-19 second dose data were available.

Across both vaccines, local adverse events (e.g. injection-site pain and swelling) were common, occurring in 66.2% of individuals. Systemic adverse events were less common, with 25.4% experiencing at least one systemic adverse event. The most frequent of which were fatigue and headache, peaking 24 hours after vaccination. Interestingly, local and systemic reactions were less common in this community-based cohort than in phase 3 trial reports. Possible explanations for this discrepancy include differences in study populations (e.g. demographic data such as age), psychological differences in symptom reporting behaviour between clinical trial participants versus those receiving an authorised vaccine,

and study dropout — data may be more complete in clinical trials where follow up is typically more fastidious<sup>9</sup>.

In keeping with the phase 1-3 vaccine trial data of both vaccines, systemic adverse events were more common in those under 55 versus those over 55 years of age, and in women compared with men. Consistent with the phase 3 trial, systemic reactions were more common after a second dose of BNT162b2. Curiously, previous documented SARS-CoV-2 infection was associated with increased incidence of adverse events. Amongst BNT162b2 recipients, 36.2% of those who had previously been infected with SARS-CoV-2 had a systemic reaction compared with 12.7% of those without prior documented infection; this was also true in ChAdOx1 nCoV-19 vaccinees, 53.1% versus 32.9%, respectively. 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%, 69% and 72% at 12-20 days, 21-44 days and 45-59 days post-vaccination, respectively. Similarly, the risk of infection was also lower after ChAdOx1 nCoV-19 vaccination compared with controls; with a risk reduction of 39% at 12–20 days and 60% at 21–44 days after vaccination. These findings support vaccination strategies opting to delay a second dose in favour of maximising first dose rollout<sup>4,5,10</sup>.

Overall, this study provides valuable information to healthcare 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 is critical to ensuring uptake of vaccines, and part of this requires reinforcing confidence in vaccines. The independent — community-led — attribute of this study may 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.

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