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Severe acute respiratory coronavirus virus 2 (SARS-CoV-2) delta variant of concern breakthrough infections: Are vaccines failing us?

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To the Editor—The severe acute respiratory coronavirus virus 2 (SARS-CoV-2) delta (formerly B.1.617.2) variant of concern (VOC) has become or is becoming the most prevalent type of SARS-CoV-2 in many countries.¹ Whether available vaccines can protect people against this variant as effectively as against other common variants is yet unknown.

Most countries have already started public vaccination against coronavirus disease 2019 (COVID-19), and the share of people who have received at least 1 vaccine dose reaches as high as 70% in some regions.² The effect of vaccination is evident in the pattern of daily new cases and deaths in countries with high vaccination rates.³ However, many of these nations are experiencing a surge in COVID-19 cases³ possibly attributable to novel SARS-CoV-2 variants, especially the delta VOC. On the other hand, number of deaths has not increased significantly,³ which might be due to the effect of vaccines against serious illness or the relatively short time since the dominance of the new variant. Whether currently available vaccines stand the test of time and limit the COVID-19 burden on communities remains to be seen.

Although several studies have indicated reduced neutralizing antibody activity (ie, vaccine effectiveness) against the delta VOC compared with the B.1.17 lineage and the wild-type virus,⁴ only 2 Medline-indexed studies^{5,6} have assessed vaccine efficacy against this variant. Using data from registries in Scotland, Sheikh *et al*⁵ estimated vaccine efficacy against symptomatic delta VOC infection 14 days after the second dose for BNT162b2 (Pfizer-BioNTech) and ChAdOx1 (Oxford-AstraZeneca) at 83% and 61%, respectively. Efficacy regardless of symptom presence was 79% for BNT162b2 and 60% for ChAdOx1. Another study

in the United Kingdom⁶ indicated 67.0% efficacy for ChAdOx1 and 88.0% for BNT162b2 vaccines against symptomatic delta VOC infection, 2 weeks after the second injection. Vaccine efficacy 21 days after the first dose was low for both ChAdOx1 and BNT162b2 (30.0% and 35.6%, respectively).

Although these are the only published studies, promising results have also been found in unpublished investigations. A preprint study by Nasreen *et al*,⁷ conducted in Canada, showed 56%, 72%, and 67% efficacy against symptomatic delta VOC infection for BNT162b2, mRNA-1273 (Moderna), and ChAdOx1, respectively, 2 weeks after the first dose, and 87% efficacy 7 days after the second dose of BNT162b2. The vaccines demonstrated 78%–96% protection against serious illness, 14 days after their first dose, which will most likely be even higher after full vaccination.

Most healthcare personnel in Iran have been vaccinated with either ChAdOx1, Gam-COVID-Vac (Sputnik V, Gamaleya), BBIBP-CorV (Sinopharm), or BBV152 (Bharat) vaccine. However, as the country experiences the fifth wave of COVID-19,³ there are many reports of infection, serious respiratory involvement, hospitalization, and even death among vaccinated persons.⁸ As indicated in phase 3 trials,⁹ none of the currently available vaccines have 100% protection against infection, and community protection against serious illness is expected to differ from those of clinical trials. The incidence and severity of breakthrough infections cases is concerning and raises doubts regarding the efficacy of the vaccines utilized against the delta VOC. The proper way of addressing this issue is by conducting studies to assess the efficacy of vaccines against this variant and other VOCs. Unfortunately, to the best of our knowledge, no published or preprint studies have investigated the efficacy of the 4 mentioned vaccines against the delta VOC, except for ChAdOx1. Nonetheless, vaccine producers claim that their vaccines are effective to some degree against the mentioned variant (eg, 90% for Gam-COVID-Vac and 65.2% for BBV152).^{10,11}

We encourage the scientific community to further evaluate the vaccines that have limited data on their effectiveness (eg,

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those mentioned in this letter) by conducting randomized clinical trials and assessing protection against infection, rather than the ability to produce neutralizing antibodies because the former reflects the real-world effects of the vaccine more accurately. Governments and healthcare organizations must implement registry systems for breakthrough infections, to better understand the ongoing pandemic and outcomes of vaccination in the community. Finally, vaccines might be less effective against novel SARS-CoV-2 variants. Research institutes and vaccine producers should be prepared for such conditions and should develop new strategies to increase effectiveness against resistant lineages, such as introducing additional booster doses or reformulating the vaccines.

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SARS-CoV-2 vaccine breakthrough infections among healthcare workers in a large Belgian hospital network

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To the Editor—Since the first occurrence of SARS-CoV-2, different vaccines have been produced, tested, and approved in record time. However, the exact vaccination effect has yet to be determined in the ever-changing landscape of SARS-CoV-2 variants.^{1,2}

Breakthrough infections

As of June 15, 2021, the overall vaccination rate in Belgium was 62.8% having received 1 dose (adult population), of whom 35.2% had fully completed their vaccination scheme.³ Belgian healthcare workers (HCWs) have a high exposure to COVID-19: the estimated percentage of confirmed Belgian COVID-19 cases is significantly higher among those working in healthcare facilities than among employees in other industries as well as the national average.⁴

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Because HCWs were prioritized in the vaccination strategy, studying this population provided early data with which to analyze its effect. Vaccination in Belgium is not mandatory.

Vaccination of HCWs in ZNA started on January 18, 2021. ZNA is a 2,500-bed, public, multiple-site, hospital network in the Antwerp region. It comprises 3 acute-care hospitals, a children's hospital, and 5 chronic care facilities. Depending on their availability, 3 different vaccines were used: BNT162b2 (Comirnaty, BioNTech/Pfizer, Mainz, Germany), mRNA-1273 (COVID-19 Vaccine Moderna, Moderna, Cambridge, MA) and AZD1222 (Vaxzevria, Astra Zeneca, Cambridge, UK). The impact of vaccinations on the positive test ratio was evaluated from March 1 through April 30, 2021, a period with continuing and substantial viral circulation in the Belgian population.³ Tests were performed for contact tracing or COVID-like symptoms. Among 3,491 fully vaccinated ZNA HCWs, 9 (0.3%) tested positive for SARS-CoV-2 (RT-PCR, Cobas 6800, Roche). After excluding 1 case, following CDC guidelines on persistent shedding,⁵ 22 (1.0%) of 2,215 unvaccinated HCWs (n = 584) or partially vaccinated HCWs (n = 1,631) tested