Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

What is the vaccine effect on reducing transmission in the context of the SARS-CoV-2 delta variant?

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COVID-19 vaccines that have obtained WHO emergency use listing appear to have high efficacy against severe disease and death, but lower efficacy against non-severe infections, and emerging evidence suggests that protection against non-severe disease declines faster following vaccination than that against severe disease and death. What is less clear is whether vaccination not only directly protects individuals but reduces the risk of infection among the contacts of vaccinated people, particularly with respect to the now dominant delta variant. Before the emergence of the delta variant, it was reported that after at least one dose of the mRNA vaccine by Pfizer or the adenoviral vector vaccine by Astra Zeneca, the risk of symptomatic cases in household contacts of vaccinated cases was about 50% lower than that among household contacts of unvaccinated cases.[1]

The now globally dominant delta variant is more transmissible[2] and associated with reduced vaccine effectiveness, particularly against mild breakthrough infections, whereas protection against severe disease is not greatly reduced.[3] Data are lacking on whether the effect of vaccination on transmission is lower for the delta variant and new insights on this are provided by a study done in the UK when the delta variant was the predominant strain, reported in *The Lancet Infectious Diseases*.[4]

Anika Singanayagam and colleagues did a carefully designed cohort study whereby 602 community contacts (household and non-household) identified via the UK contact tracing system and 471 COVID-19 index cases were enrolled through the Assessment of Transmission and Contagiousness of COVID-19 in Contacts (ATACCC) study. These participants contributed 8145 upper respiratory tract samples for up to 20 days, regardless of symptoms. The study had two study arms, with the first group enrolling contacts only, and the second group enrolling both index and contact cases at a time when the delta variant was predominant. What is unique about this study is that both vaccinated and unvaccinated contacts were included, thereby allowing for stratified analyses by vaccination status, both for the index cases and the contacts.

To address the primary study outcome to establish the secondary attack rates (SARs) in household contacts, the vaccination statuses for 232 contacts exposed to 162 epidemiologically linked delta-variant-infected index cases were analysed. The SARs in household contacts exposed to the delta variant was 25% in vaccinated and 38% in unvaccinated contacts. These results underpin the key message that vaccinated contacts are better protected than the unvaccinated. All breakthrough infections were mild, and no hospitalisations and deaths were observed. But these results also highlight that breakthrough infections continue to occur in the vaccinated, with an attack rate of 25%. Time since vaccination in fully vaccination contacts was longer for those infected than those uninfected, suggesting that waning of protection might have occurred over time, although teasing out general waning versus reduced vaccine effectiveness due to delta is challenging owing to so many confounding factors.

SAR among household contacts exposed to fully vaccinated index cases (25%; 95% CI 15–35) was similar to household contacts exposed to unvaccinated index cases (23%; 15–31). Obviously, infection might also have occurred beyond the household level with unknown exposure in the community. Indeed, genomic and virological analysis confirmed only three index-contact pairs. Owing to the small sample size, the authors were not able to establish the vaccine effectiveness against asymptomatic infections versus symptomatic infections. This limitation together with the unconfirmed source of transmission in many of these index-contact pairs, suggests that the low SAR reported here should be interpreted with caution. Nevertheless, the findings raise concern that the effect of vaccination on reducing transmission might be lower for the delta variant compared with the variants that circulated in the UK before the emergence of delta.

Infectiousness of breakthrough infections can be measured by viral densities. Higher SARS-CoV-2 viral density in the upper airways of people infected with the virus are thought to increase transmission to household members.[5,6] If vaccines reduce viral density

in those who do become infected despite vaccination, it would probably lead to lower infectiousness and less onward transmission. Hence, the authors compared the viral kinetics in breakthrough delta variant infections in vaccinated people with delta variant infections in unvaccinated people. They report that peak viral loads showed a faster decline in vaccinated compared with unvaccinated people, although peak viral loads were similar for unvaccinated and vaccinated people.

Although preventing severe disease and deaths remains the primary public health goal in the acute phase of the pandemic, and is still being achieved by available COVID-19 vaccines despite the emergence of the delta variant, addressing SARS-CoV-2 transmission is a crucial additional consideration. Reducing transmission is necessary to reduce virus circulation, reach herd immunity and end this tragic pandemic. This study confirms that COVID-19 vaccination reduces the risk of delta variant infection and also accelerates viral clearance in the context of the delta variant. However, this study unfortunately also highlights that the vaccine effect on reducing transmission is minimal in the context of delta variant circulation. These findings have immediate public health implications. Higher vaccination coverage rates need to be achieved because indirect protection from vaccinated to unvaccinated people remains suboptimal. The question of whether booster doses will improve the impact on transmission should be addressed as a top priority.[7] Research efforts should be directed towards enhancing existing vaccines or developing new vaccines that also protect against asymptomatic infections and onward transmission. Until we have such vaccines, public health and social measures will still need to be tailored towards mitigating community and household transmission in order to keep the pandemic at bay.

AWS is a member of *The Lancet* Commission on COVID-19, and a consultant to WHO. The author alone is responsible for the views expressed here and they do not necessarily represent the decisions, policies, or views of *The Lancet* Commission or WHO. I declare no competing interests.

Annelies Wilder-Smith
annelies.wilder-smith@lshtm.ac.uk

Department of Disease Control, London School of Hygiene & Tropical Medicine, London WC1E 7HT, UK

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Remdesivir, on the road to DisCoVeRy

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Despite the availability of effective SARS-CoV-2 vaccines, improving care for patients with symptomatic infection remains relevant. Strategies to blunt the hyperinflammatory state that characterises severe COVID-19 include broad-spectrum immunosuppressive drugs such as corticosteroids, targeted immunomodulatory treatments such as tocilizumab or baricitinib, and direct-acting antivirals to reduce viral load.

In *The Lancet Infectious Diseases*, Florence Ader and colleagues[1] report results of the DisCoVeRy trial, the fifth large, randomised, controlled trial with the broad-spectrum antiviral drug remdesivir.[1] In this open-label study, 857 patients admitted to hospital with severe COVID-19 (oxygen saturation SpO_2 ≤94% or in need of supplemental oxygen or respiratory support) were randomly assigned to remdesivir plus standard of care or standard of care alone. There was no significant difference in the primary outcome, the odds of better clinical status defined on the WHO ordinal scale, at day 15 (odds ratio 0·98 [95% CI 0·77–1·25]; p=0·85). This finding remained consistent across all prespecified subgroup analyses, including duration of symptoms before admission or disease severity at random assignment. There was also no significant difference in 28-day mortality (0·93 [0·57–1·52]; p=0·77), and none of the time-to-improvement analyses showed any