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.

the seeking of medical attention in some cases, until the patient was overtly sick, further increasing the death count even with appropriate treatment. A small proportion of the population might have initially visited local practitioners from alternative systems of medicine, which again could have contributed to a missed or delayed diagnosis and treatment, ultimately adding to the increased mortality.

Moreover, social issues such as reluctance to transfer older people (especially those who are staying alone with relatively poor quality of life) with respiratory symptoms to a health-care facility due to the fear or stigma associated with contracting COVID-19 might have additionally increased the mortality tally. Furthermore, lockdowns might have discouraged many people from seeking medical attention to some extent until they became overtly sick. Finally, there is an unsubstantiated perception that human and political factors might have influenced the documentation to some extent in certain countries.

In conclusion, the increased deaths in the second wave might have occurred not only due to the higher R_0 and virulence of the delta strain (B.1.617.2) and laxity in COVID-19-appropriate behaviour (the public feeling that the game is over), but also due to the inadequate anticipation of the health systems and the logistical obstacles this creates both for health-care facilities and individuals in need of care.

We declare no competing interests.

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COVID-19 vaccines in the age of the delta variant

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The clinical development and global rollout of highly effective vaccines against SARS-CoV-2 has been unprecedentedly rapid. Nevertheless, viral evolution has continued at pace to the extent that questions are being raised about the continued effectiveness of first-generation vaccines in the face of variants of concern (VOCs). In particular, the rise of the delta variant (B.1.617.2) to become the dominant virus in most of the world has spurred efforts to assess vaccine effectiveness against VOCs and to understand the associated immune mechanisms of protection.[1]

In *The Lancet Infectious Diseases*, Ramachandran Thiruvengadam and colleagues[2] report on the effectiveness of the Oxford–AstraZeneca ChAdOx1 nCoV-19 vaccine in a test-negative, case-control study done in India during the delta variant outbreak of April, 2021. The effectiveness of complete vaccination (two doses) against RT-PCR-confirmed SARS-CoV-2 infection was 63·1% (95% CI 51·5–72·1); vaccine effectiveness against moderate-to-severe COVID-19 was higher than that for mild-to-moderate COVID-19 at 81·5% (95% CI 9·9–99·0), although the smaller sample size of severe cases affects the confidence we can have in this estimate. These data are consistent with studies of ChAdOx1 nCoV-19 vaccine effectiveness against the delta variant in the UK, which estimated an effectiveness of 60–67% against PCR-confirmed infection.[3,4]

In 2020, early signals of high vaccine efficacy against both symptomatic and asymptomatic SARS-CoV-2 infection initially suggested that COVID-19 vaccines could be used to efficiently suppress viral transmission. However, with the emergence and rapid global spread of the delta variant, it now seems likely that vaccination will not provide complete protection against acquisition and onward transmission of SARS-CoV-2, which will continue to circulate for the foreseeable future.[5,6] Consequently, the goal of population-level vaccination has shifted to protecting both adults and children from developing severe disease, thereby preventing

the excess mortality and stress on health-care systems that were observed in the early phases of the pandemic. The observation that ChAdOx1 nCoV-19 remains more than 80% effective at preventing moderate-to-severe COVID-19 following breakthrough infection with the delta variant reinforces the ongoing utility and importance of this widely distributed vaccine.

Importantly, Thiruvengadam and colleagues pair these epidemiological analyses with immunological data. In a group of ChAdOx1 nCoV-19 vaccine recipients, the authors assessed neutralising antibody titres and CD4 and CD8 T-cell responses against both wild-type (ancestral) and delta viruses, in an effort to understand the immunological responses that might moderate disease severity in the event of breakthrough infection. Neutralising antibody titres, which are strong predictors of vaccine efficacy,[7] were markedly lower in ChAdOx1 nCoV-19 vaccine recipients when measured against the delta variant virus than when measured against wild-type SARS-CoV-2. Loss of neutralisation potency against the delta variant is not unique to the ChAdOx1 nCoV-19 vaccine; indeed, similar reductions have been reported using serum derived from cohorts vaccinated with mRNA vaccines.[8,9] By contrast with antibody responses, the high frequency of spike-specific CD4 and CD8 T cells elicited by ChAdOx1 nCoV-19 vaccination maintained recognition of both wild-type and delta variant spike peptides. In a comprehensive analysis, Thiruvengadam and colleagues showed that both T-cell cytokine secretion and activation were comparable following stimulation with either wild-type or delta spike peptide pools.[2]

Considering the reduced antibody neutralisation but preserved T-cell recognition of the delta variant, these data raise the intriguing question of whether even low levels of neutralising antibodies are sufficient to prevent severe disease, or whether cellular immunity is a key factor in mitigating the risk of hospital admission. Ultimately, such questions will be difficult to answer in the absence of prospective cohort studies or early immune profiling of breakthrough infections. Such data would, however, crucially inform strategies for booster vaccination and the design of next-generation vaccine candidates.

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Booster doses for inactivated COVID-19 vaccines: if, when, and for whom

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Dealing with vaccine equity and at the same time ensuring adequate protection for the most vulnerable is essential to reduce the burden of COVID-19. New questions have been challenging the scientific community and policy makers after the initial rollout of mass vaccination campaigns, particularly surrounding the potential waning of vaccine effectiveness. It is still unknown whether supplemental doses are needed, and researchers are working to determine if, when, and for whom booster doses would be helpful for the prevention of COVID-19 illness and pandemic control.

As of the time of writing, the inactivated whole-virus vaccine CoronaVac is the most widely offered COVID-19 vaccine in the world.[1] In *The Lancet Infectious Diseases*,