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.

of SARS-CoV-2 infection, it would be unwise to let the virus circulate in children, with consequent risk to their families. Reopening fully in the setting of high community transmission without appropriate safeguards risks depriving many children of education and social interaction again, worsening existing inequalities. By contributing to high community transmission, it also provides fertile ground for virus evolution and new variants.

Multi-layered mitigations can substantially reduce the risk of transmission within schools and into households.[13] In the panel we summarise a set of recommendations that are in line with guidelines from the US Centers for Disease Control and Prevention (CDC) and practised in many countries to reduce the risk of transmission in schools and mitigate the impact of COVID-19 on children and families. A detailed set of recommendations and an infographic are provided in the appendix. Making schools safer goes hand in hand with reducing community transmission and is essential to allow schools to safely reopen and remain open.

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For the **CDC's guidelines for reopening schools** see https://www.cdc.gov/coronavirus/2019-ncov/community/schools-childcare/index.html

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Effect of previous SARS-CoV-2 infection on humoral and T-cell responses to single-dose BNT162b2 vaccine

The rapid implementation of SARS-CoV-2 vaccination is now a global health-care priority. Successful phase 3 trial outcomes have been reported for numerous vaccines that induce robust humoral and cellular immune responses against the SARS-CoV-2 spike protein.[1–6] To gain rapid control of accelerating cases and maximise public health impact, the UK Government has adopted the strategy of delaying second vaccination to 12 weeks. This policy has generated controversy, particularly among health-care workers (HCWs), the majority of whom have received BNT162b2 mRNA vaccine.[7]

Limited data on immune responses to single-dose vaccination with BNT162b2 are available, and vaccine responses following previous natural infection have not been assessed in clinical trials.[2–6] We have therefore investigated immunological responses to single-dose BNT162b2 using a combination of serology, live virus neutralisation, and T-cell enzyme-linked immunospot (ELISpot) assays.

72 HCWs from Imperial College Healthcare NHS Trust, who were vaccinated between Dec 23 and Dec 31, 2020, provided blood samples at the time of receiving their first dose of BNT162b2 vaccine and 21–25 days after vaccination. Baseline samples were tested for antibodies to SARS-CoV-2 nucleocapsid and spike (anti-S) proteins using the Abbott Architect SARS-CoV-2 IgG and IgG Quant II, respectively

(Abbott, Maidenhead, UK). 21 (29%) participants had evidence of previous SARS-CoV-2 infection: 16 with positive baseline serology, and five further with strong T-cell responses to non-spike antigens post-vaccination (>100 spot forming units [SFU] per 10^6 peripheral blood mononuclear cells [PBMC]). Although baseline ELISpot data were not available for these five participants, a cohort of 30 unvaccinated, infection-naive participants did not demonstrate reactivity to these peptide pools. 51 participants had negative baseline serology and cellular responses post-vaccine limited to spike antigens; this group was defined as infection-naive.

As BNT162b2 mRNA encodes the spike glycoprotein of SARS-CoV-2, we assessed immune responses to spike protein post-vaccination. Anti-S titres were significantly higher in individuals with previous natural infection than in infection-naive individuals (median 16 353 arbitrary units [AU] per mL [IQR 4741–28 581] *vs* 615·1 AU/mL [286·4–1491], p<0·0001; figure A). The five participants with previous natural infection yet negative serology at baseline developed post-vaccination anti-S titres that were intermediate between the infection-naive and

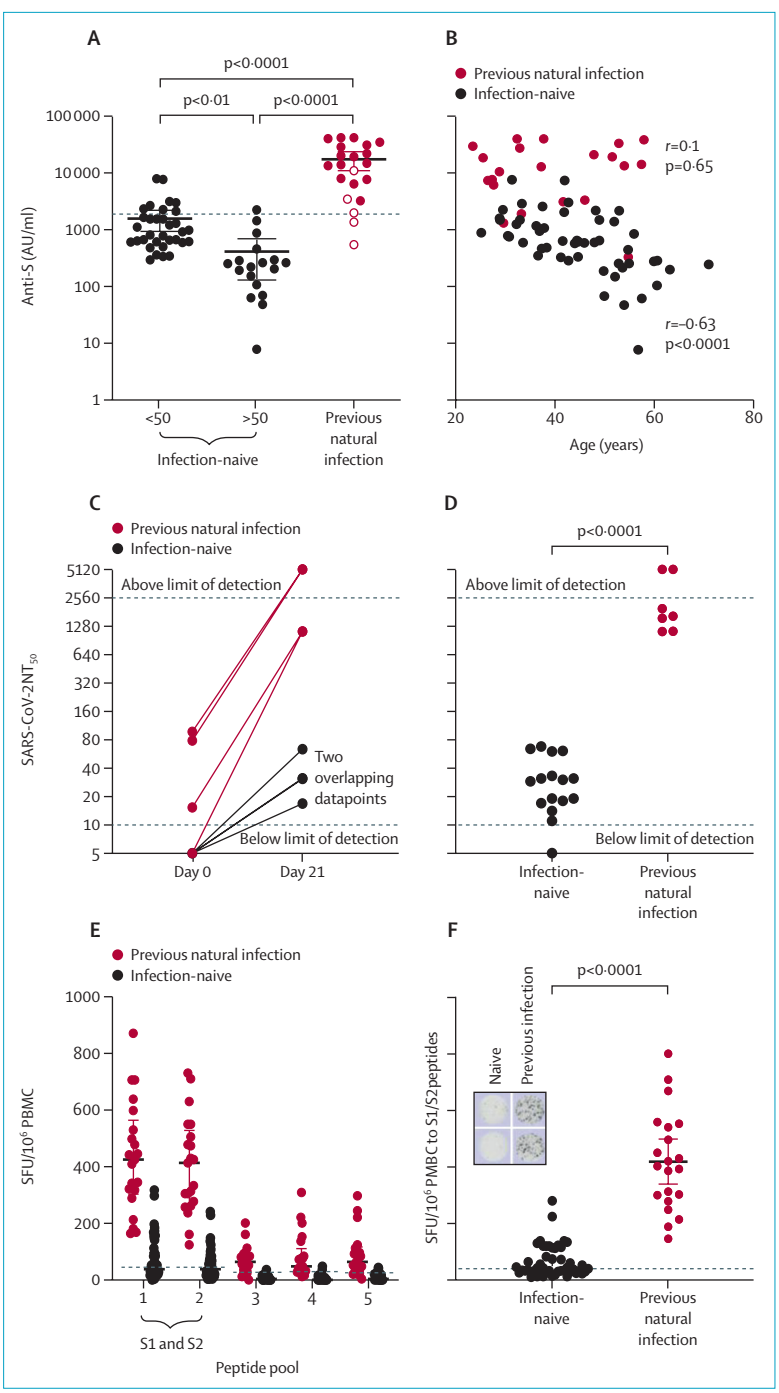

Figure: **Immunological responses to a single dose of BNT162b2 mRNA vaccine**
(A) Anti-S antibody titres 21–25 days after vaccination in individuals who were infection-naive or had evidence of previous natural infection. Datapoints with open circles represent five individuals who, despite a negative serological test at baseline, were identified as having previous infection due to reactivity to non-spike peptides on ELISpot testing post-vaccination (which could not have been induced by vaccine alone). Dotted line indicates median anti-spike titre in a cohort of health-care workers 2–8 weeks after PCR-confirmed natural infection with SARS-CoV-2 (n=23, IQR 463–3621). (B) Correlation of post-vaccination anti-spike titre with age in infection-naïve participants. (C) SARS-CoV-2 live virus neutralising antibody titres in the eight individuals with paired results available (n=4 infection-naïve, n=4 with previous natural infection. (D) SARS-CoV-2 live virus neutralising antibody titres post-vaccination in infection-naïve individuals and individuals with previous infection . (E) T-cell responses to SARS-CoV-2 peptide pools post-vaccination in infection-naïve individuals and individuals with previous infection. Peptide pool 1 and peptide pool 2 contain spike protein peptides S1 and S2. Dotted lines indicate mean plus 3 standard deviation for each peptide pool calculated from infection naïve, unvaccinated individuals (48, 43, 26, 33, and 26 SFU/10^6 PBMC for peptide pools 1–5 respectively). (F) T-cell responses to spike protein peptides of SARS-CoV-2 post-vaccination in infection-naïve and previously infected participants. Inset shows example of ELISpot for an infection-naïve and a previously infected individual for the 2 spike peptide wells. Dotted line indicates mean plus 3 standard deviation for spike peptide pool reactivity calculated from infection naïve, unvaccinated individuals. All data are median with IQR. Statistical analysis was by Kruskall-Wallis test with Dunns' post-hoc correction (A), Spearman rank correlation (B) and Mann-Whitney test (D, F). SFU=spot forming unit. PBMC=peripheral blood mononuclear cells. NT_{50}=neutralisation titres that achieved 50% neutralisation.

previously infected groups (figure A). Infection-naive individuals showed an inverse correlation between post-vaccination anti-S titre and age (figure B), with individuals older than 50 years generating a significantly weaker serological response than those younger than 50 years (median 230·1 AU/mL *vs* 888·9 AU/mL, p<0·0001; figure A). This correlation was not seen in the group with previous natural infection (figure B).

Anti-S titre is reported to correlate with in-vitro virus neutralisation. We therefore used a subset of samples for live SARS-CoV-2 virus (SARS-CoV-2/England/IC19/2020) neutralisation assays on Vero cells.[8] Eight paired sera (n=4 infection-naive, n=4 previous natural infection) and a further 15 post-vaccination samples were included (n=12 infection-naive, n=3 previous natural infection). In individuals with previous exposure, vaccine induced very strong neutralising antibody titres even in those without detectable or very low virus neutralisation titres (NT) at baseline (median NT that achieved 50% neutralisation [NT_{50}] 1/1635, range 1/1123·1 to beyond the 1/2560 upper limit; figure C, D). In infection-naive individuals, vaccination induced detectable neutralising antibodies in 15 of 16 sera, but titres were all lower than for previously infected individuals (median NT_{50} 1/29·50, range from below lower limit of detection to 1/68; figure C, D).

We next assessed post-vaccination T-cell responses using the T-SPOT Discovery SARS-CoV-2 (Oxford Immunotec, Oxford, UK), which includes a panel of five SARS-CoV-2 peptide pools. Post-vaccination, participants with evidence of previous SARS-CoV-2 infection at baseline (n=21) mounted very strong T-cell responses to spike peptides (median 400 SFU/10^6 PBMC [IQR 287–544]; figure E, F). In the infection-naive group, post-vaccination T-cell responses to spike peptides were significantly weaker than in individuals with previous infection (38 SFU/10^6 PBMC [IQR 26–110], p<0·0001; figure E, F), and 24 (50%) of 48 participants generated T-cell responses that could be considered negative (<40 SFU/10^6 PBMC). Unlike humoral responses, there was no correlation between age and degree of T-cell response.

In summary, we show that individuals with previous SARS-CoV-2 infection generate strong humoral and cellular responses to one dose of BNT162b2 vaccine, with evidence of high titres of in-vitro live virus neutralisation. In contrast, most individuals who are infection-naive generate both weak T-cell responses and low titres of neutralising antibodies.

Existing studies predicting risk of re-infection based on neutralising antibody titres, or longevity of immunological responses, are highly heterogeneous.[9–13] Evidence for the longevity and protective effect of T-cell responses is particularly limited. In particular, peptide pool selection might affect T-cell responses, meaning results cannot be compared between studies. We use S1 and S2 peptide pools, rather than peptides spanning the whole spike glycoprotein, which might underestimate the true magnitude of T-cell responses. Despite the difficulty of extrapolating immunological data to clinical protection, our findings raise important issues that warrant consideration when determining optimal use of vaccine supplies. Firstly, those with serological evidence of previous disease at baseline mount robust antibody and T-cell responses after a single dose of vaccine. Conversely, some infection-naive individuals mount very little demonstrable response to single-dose vaccination, which might not provide sufficient immunity to protect from clinical disease or viral shedding, and might not persist for a 12-week delay until second vaccine is administered. One infection-naive individual included in our study developed symptomatic, PCR-proven infection 5 weeks after one dose of vaccine; notably, their anti-S titre post-vaccination was 61·8 AU/mL.

In keeping with published reports of other vaccines, serological response to BNT162b2 inversely correlates with age.[14] We found median anti-S titres post-vaccination in the infection-naive cohort to be lower than those seen 2–8 weeks after natural infection alone, and this difference was particularly striking in those older than 50 years. Two participants did not seroconvert, and eight participants generated antibody titres less than 250 AU/mL, which might not be sufficient for any virus neutralisation based on correlation of virus neutralisation and anti-S titre in our study. All ten of these individuals were older than 50 years. In a setting where prioritisation of groups of HCWs for second vaccination might be necessary, consideration must be given to protocolised vaccination of infection-naive individuals or those over the age of 50 (who are at increased risk of both severe COVID-19 and minimal vaccine response). These results also highlight the need for continuing rigorous use of personal protective equipment after vaccination to prevent both infection and asymptomatic spread of disease.

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COVID-19, cults, and the anti-vax movement

Rochelle Burgess and colleagues[1] eloquently described participatory community engagement as essential for successful COVID-19 vaccination, which involves appreciating the heterogeneous public and working with communities and their leaders to enable bottom-up approaches. They suggested that COVID-19 has drawn attention to the structural violence that is embedded within society, with the pandemic furthering the marginalisation of historically oppressed and excluded groups. Burgess and colleagues[1] drew attention to how people who might have suffered disproportionate economic and health consequences from COVID-19 are now being asked "to trust the same structures"[1] that failed to provide adequate resources and social protection during the pandemic. Failure to address these contextual dimensions can worsen mistrust, damaging vaccine uptake. However, Burgess and colleagues make a distinction between "people wholly opposed to vaccinations (anti-vaxxers) and…vaccine hesitancy",[1] and imply participatory community engagement as a means to engage only people with vaccine hesitancy.

Lessons from studying cults (which are less pejoratively called new religious movements, describing movements that emerged in the late 20th century) can inform approaches to the anti-vax movement. A cult has come to mean a non-conforming ideology, or a religion that is disliked, with beliefs that are unacceptable to mainstream society. Just as cults are grouped together as sinister, bad, or wrong, the discourse surrounding anti-vaxxers in both academic and popular circles can be dismissive and derogatory. The pejorative label and negative attitudes towards cults promote an us-and-them viewpoint, creating martyrs[2,3] and extending the length of time that members hold the new beliefs, thus encouraging further involvement in the movement and radicalisation.[4]

Learning from these consequences, a more constructive perspective could view the anti-vax movement as a religious phenomenon, involving a whole spectrum of ideas, and focus on the essential need to understand the beliefs that are involved to avoid further marginalisation. Hence, implying that anti-vaxxers are beyond the reach of community engagement activities could result in increased anti-vax activities. We suggest a more inclusive approach, where the same inquisitive dialogue and contextual understanding that was suggested for vaccine hesitancy should be extended to members of the anti-vax movement.

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Health systems in the ACT-A

The attention to health systems in the headline of Ann Usher's World Report[1] about the Access to COVID-19 Tools Accelerator (ACT-A) is most welcome. However, we were disappointed that the World Report focused on medical oxygen and personal protective equipment (PPE), interventions that, although important, are better described as components of clinical