



COVID vaccine mandates should recognize natural immunity exemptions

Jonathan Pugh, Julian Savulescu, Rebecca CH Brown, Dominic Wilkinson

Joint response from the UK Pandemic Ethics Accelerator Prioritisation workstream and The Oxford Uehiro Centre for Practical Ethics to the Department of Health and Social Care consultation on mandatory vaccination in the NHS – 22 October 2021.

Executive Summary

- Proof of natural immunity and vaccine induced immunity are treated equivalently for the purposes of the NHS COVID pass. However, the forthcoming vaccine mandate for care home staff (which may be extended to frontline healthcare staff following this consultation) does not recognize natural immunity exemptions to vaccine requirements.
- Vaccine mandates that do not recognize such exemptions have been heavily criticized, and subject to lawsuits in the USA.
- We currently lack clear and convincing scientific evidence that immunisation is significantly more likely to reduce spread of the virus than natural immunity.
- Vaccine requirements represent a substantial infringement of individual liberty, and could have adverse downstream effects on staff retention in healthcare, and the provision of high quality care.
- Vaccine requirements can only be justified if they are necessary to achieve a proportionate public health benefit. If we do not have clear evidence that immunisation is significantly more likely to reduce spread of the virus than natural immunity, then vaccine mandates for the immune are not necessary in this way. Instead, they would expose the immune to the non-trivial risks of vaccination without the promise of a clear and proportionate benefit.
- The high degree of exposure that frontline healthcare workers have to the vulnerable may support adopting a precautionary approach in light of scientific uncertainty about the merits of different forms of immunity. However, this precautionary strategy involves considerable moral costs, mainly due to the significance of the liberty that is infringed by professional vaccine mandates in healthcare.
- Objections to the use of 'immunity passports' prior to the advent of COVID-19 vaccination have limited force now that a large proportion of the population has been vaccinated, and public health restrictions have been relaxed. Allowing exemptions for natural immunity may now be more consistent with a concern for social justice.
- Recognising natural immunity exemptions need not undermine public health messages about the importance and benefits of having the vaccine. It is crucial to be clear about the difference between arguing that natural immunity, once acquired, confers sufficient protection, and the claim that natural immunity is a good way to acquire immunity (a claim which we do not support).

- 1.1 We are a group of academic medical ethicists at the The Oxford Uehiro Centre for Practical Ethics at the University of Oxford. As a group, and as members of the UKRI/AHRC funded UK Pandemic Ethics Accelerator Project, we have published widely on a diverse range of ethical issues raised by the pandemic. In this response to the consultation on 'making vaccination a condition of deployment in the health and wider social care sector', we shall make the case for including a natural immunity exemption in any forthcoming professional vaccine mandate. This submission is an amended and abridged version of a journal article on the topic that is currently under submission.
- 1.2 Making vaccination a condition of employment in certain industries has prompted widespread debate. Whilst some countries (such as the US) are implementing wide-reaching vaccination mandates for various kinds of employment, (The White House, 2021) the case for requiring frontline health and social care workers to have immunity to the coronavirus is particularly strong, due to the degree of exposure that such employees can be expected to have with vulnerable individuals. Nonetheless, even vaccine mandates in this sector are controversial, raising concerns about discrimination and human rights (Royal Society - Science in Emergencies Tasking – COVID, 2021). Yet, some ethicists have argued that such requirements can constitute a necessary and proportionate public health measure (Bradfield and Giubilini, 2021).
- 1.3 In this written evidence we are not concerned with the *overall* justifiability of a vaccine mandate for frontline healthcare workers. We have argued that this can be justified in at least some form (Savulescu et al., 2021). However, for this submission, we are interested in whether *if there is a mandate for healthcare workers*, this should allow an exemption for those with proof of natural immunity. The vaccination requirement for care home staff coming into force in November does not recognise testing alternatives to vaccination, and only permits tightly controlled medical exemptions. However, we believe that this is a mistake; the care home mandate and the proposed mandate for frontline health care staff should recognize natural immunity exemptions.
- 1.4 Strikingly, it is possible to obtain an NHS COVID pass with proof of natural immunity, shown by a positive PCR test result for COVID-19, lasting for 180 days from the date of the positive test and following completion of the self-isolation period. Proof of natural immunity and vaccine induced immunity are treated equivalently for the purposes of the COVID pass. We argue that they should also have parity as conditions of employment in care homes (or other health care institutions).
- 1.5 Policies that do not recognize natural immunity as a sufficient basis for exemption to vaccination requirements have attracted particular controversy in the USA. In recent months, a district court judge upheld the University of California's decision to not include an exemption for those who could provide proof of natural immunity in its COVID-19 vaccine requirement (Hals, 2021).

Conversely, according to media reports, George Mason University recently granted a medical exemption to an employee who provided proof of active antibodies following a legal challenge (Swoyer, 2021). Another pending lawsuit involves an academic bioethicist (Cook, 2021).

- 1.6 Here we address the ethical considerations at the heart of this current controversy, and make the case for recognising proof of natural immunity as an acceptable alternative to proof of vaccination. To begin, we believe that it is important to distinguish this argument from two implausible claims about natural immunity.

Two false claims about natural immunity and one true claim

- 2.1 The history of the anti-vaccination movement is replete with examples of opposition to vaccination grounded in a concern that vaccines are contrary to nature and compromise purity (Durbach, 2005). A common trope amongst the anti-vaccination movement is that natural immunity is therefore superior to ‘artificial’ vaccine-induced immunity. This is a grave mistake. It is ‘natural’ to become immune through contracting infection - but it is also natural to die from serious infections.
- 2.2 A second related claim, widely advocated amongst the anti-vaccination movement, is that it is better to *acquire* immunity through natural infection rather than through vaccination. For the vast majority of people, this is patently false, since the risks of serious illness and dying from natural infection are considerably higher than those of vaccination. It would be prudentially irrational to choose to be infected rather than to have the vaccine, for those who are vulnerable to COVID-19. A public health strategy that pursued ‘natural’ herd immunity would lead to vastly higher morbidity and mortality than one that pursued vaccine-induced herd immunity.
- 2.3 However, one need not endorse either of these claims in order to support the position that we are considering in this submission. This is the idea that, for the purposes of immunity certification, naturally acquired immunity is potentially equivalent to that obtained through vaccination. This claim does not depend on either of the problematic and logically flawed views outlined above.

Does natural immunity reduce risk of transmission?

- 3.1 Large, randomized placebo-controlled studies have clearly demonstrated that widely used vaccines have a high degree of efficacy in preventing serious morbidity and mortality from COVID-19 (Polack et al., 2020; Voysey et al., 2020). As time passes, we will continue to learn

more about the duration of vaccine-induced immunity, but data suggests that vaccine efficacy declines over time (Dolgin, 2021; Mahase, 2021).

- 3.2 We are also learning more about the effect of the vaccines on viral transmission (Hobbs and Border, 2021). There is evidence suggesting that the vaccines have some efficacy in preventing infections, as well as symptomatic disease (Hall et al., 2021; Shah et al., 2021; Voysey et al., 2021). One study suggests that full immunization with mRNA vaccines is 90% effective in preventing SARS-CoV-2 infections in real world settings, regardless of symptom status (Thompson, 2021). Infection survey data from the Office of National Statistics in the UK suggests that full vaccination reduced the risk of testing positive by 79% during the Alpha-dominant period, and by 67% during the Delta-dominant period (Office for National Statistics, 2021). These studies are consistent with the claim that the vaccines are effective in reducing transmission, but there is still a need for clinical trials and observational studies to firmly establish this. Indeed, data are beginning to emerge which suggests that the effect of the vaccines upon transmission may diminish within a matter of months (Mallapaty, 2021).
- 3.3 However, as a recent BMJ feature outlines, there is now also substantial evidence to suggest that natural immunity confers a comparable degree of protection to vaccine-induced immunity (Block, 2021). Studies have found a durable immune response in individuals eight months after infection (Dan et al., 2021), as well as low infection rates amongst those who have previously had COVID-19 (Block, 2021). Recent data also suggest that the antibodies elicited by vaccination have less potency and breadth than those generated by natural infection, although the overall neutralizing potency of plasma is greater following vaccination (Cho et al., 2021). This picture is beginning to find further support in population level data. In the same infection survey data from the UK cited above, prior infection reduced the risk of testing positive by 65% in the Alpha dominant period, and by 71% in the Delta dominant period (compared to the 79% and 69% risk reduction associated with full vaccination in the respective periods) (Office for National Statistics, 2021). Similarly, a pre-print study using a large database including the entire adult population of Israel (6.4 million people) found very similar protection (93-95%) against COVID infection, and hospitalization in those receiving COVID immunization and those who had prior COVID infection (Goldberg et al., 2021). However, further studies are needed to fully understand the strength and durability of natural immunity.
- 3.4 There are still gaps in our understanding of the differences between natural and vaccine-induced immunity, and the implications that future virus variants may have. Our aim here is not settle the scientific debates on this point. However, we believe that it is a fair reflection of the evidence base that we currently lack clear and convincing scientific evidence that immunisation is significantly more likely to reduce spread of the virus than natural immunity. We now turn to the ethical implications of this.

The case for natural immunity exemptions

- 4.1 The basic case for allowing natural immunity exemptions to vaccination requirements can be outlined straightforwardly. Vaccine requirements represent a substantial infringement of individual liberty; moreover, in professional contexts (for example, in care homes), there are real potential concerns about the downstream effects of such mandates (for example, on patient care through compromised staff numbers). Accordingly, such requirements can only be justified if they are *necessary* for achieving a proportionate public health benefit. But if we do not have clear evidence that immunisation is significantly more likely to reduce spread of the virus than natural immunity, then vaccine mandates for the immune are not necessary. It is therefore not justified to require the vaccination of those with natural immunity. Furthermore, granting freedoms to vaccinated individuals that we do not grant to those with natural immunity is discriminatory if there is no material difference in their risk of infecting others.
- 4.2 A natural immunity exemption to a vaccine requirement would mean that frontline unvaccinated health care workers could continue to be deployed in frontline services if they could provide sufficient proof of natural immunity. As detailed above, the NHS COVID pass already recognizes proof of natural immunity as providing sufficient proof of a low transmission risk. In addition to providing proof of a recent positive PCR test result to confirm natural immunity, such proof could be provided by a serological test result confirming the presence of neutralizing antibodies at the time of testing. Looking forward, it might also be possible to use T-cell testing as proof of natural immunity; indeed, the FDA has issued an emergency use authorization for a test that aims to identify an adaptive T-cell immune response to SARS-CoV-2 (Sheridan, 2021). One benefit of such testing over antibody testing is that T-cell immune responses appear to endure for longer periods than antibody responses (Sheridan, 2021).
- 4.3 It is likely that natural immunity to COVID-19 wanes over time; indeed, there is evidence to suggest that naturally acquired antibodies diminish over time, although T-Cell responses appear to be more robust (Dan et al., 2021). Because of that, an individual's proof of natural immunity should only be deemed valid for a limited period of time; this is something that is already recognised by the NHS COVID pass requirements. This would need to be regularly revisited, in light of emerging evidence about the duration of natural immunity. However, in view of the aforementioned evidence suggesting the waning of vaccine-induced immunity, the same broad point is true of vaccination; a time limit should be adopted for vaccine-induced immunity, based on the likely endurance of immunity.

Don't we need to be more precautionary in the case of frontline healthcare workers?

- 5.1 There remains some uncertainty about the relative protection (including particularly the duration of protection) afforded by natural and vaccine-induced immunity to COVID-19. A key ethical question is how we should respond to that uncertainty and what evidence we take as being sufficient. We have suggested that in the absence of clear evidence that vaccine-induced immunity is superior, governments should provide an exemption for those with natural immunity. However, it might be argued that this standard is too low; someone could instead claim that exemptions are only justified if we can prove that vaccinating those with natural immunity is *not* necessary. This is a subtle change but a crucial one. Although we believe that the evidence base cannot establish that a vaccine mandate is necessary in those with natural immunity, we do not yet have sufficient evidence about the differences between natural and vaccine-induced immunity to prove that vaccines in this group are definitely *not* necessary.
- 5.2 Of course, frontline healthcare workers have a high degree of exposure to individuals who remain highly vulnerable to COVID-19; as such, it might be argued the higher standard of proof is more appropriate in the context of frontline health care workers. Given the clear need to protect the vulnerable, it might be argued that we should exercise precaution by invoking the higher standard of proof. The problem with this argument is that it overlooks the significant harms that precaution has in this context. When unwilling individuals are subject to a vaccine mandate, their liberties are being significantly restricted – when that mandate prevents them from exercising a particularly important liberty, such as their freedom to work in a particular profession, then that restriction carries considerable moral weight. In the case of professional mandates, people's employment and income are at stake. So, whilst the risk to the vulnerable is higher in the healthcare context than in the context of using the NHS COVID pass to enter other public events and venues, we submit that the liberty that is infringed by a vaccine requirement in the former context carries far more moral weight than the liberty that is infringed by a vaccine requirement in the latter. Lacking the freedom to continue in one's profession is a more serious infringement on an individual's liberty than lacking the freedom to attend a public venue or event.
- 5.3 This is not to say that vaccine requirements cannot be justified. Rather, the point we are making here is that to assume that the higher standard of proof is correct in the healthcare context is to assume that avoiding an uncertain (but very likely low) risk of increased viral transmission should take precedence over avoiding the known and quantifiable harms of restricting individual liberties in this context. But that seems ethically fraught. In the absence of compelling evidence that vaccine-induced immunity is significantly more likely to reduce spread of the virus than natural immunity, we believe that the case for ethical necessity cannot be

convincingly made. The burden lies with those claiming there is increased risk associated with exemptions for naturally immune individuals to show that this is the case.

- 5.4 Indeed, although restrictions of individual liberty are amongst the most significant harms involved in vaccine requirements, there are also others. As critics of the care home mandate have pointed out, implementing professional mandates may have considerable downstream effects on staff retention – in the case of both care home workers and frontline health care workers, the loss of staff is likely to translate to lower standards of care. There are also non-trivial risks associated with vaccination, and vaccines also continue to be scarce in some countries, where some citizens who are highly vulnerable to COVID-19 have not yet been able to access a dose.

Pragmatic issues

- 6.1 Even if the case for necessity is not convincing, it might be argued that there are some important practical reasons for refraining from allowing natural immunity exemptions. Earlier in the pandemic, critics of immunity passports raised the concern that they could incentivize people to intentionally become infected with the coronavirus, and that they could have particularly disadvantageous effects on the most vulnerable groups in society (Kofler and Baylis, 2020). Second, proof of vaccination status is simple, binary and verifiable, whilst natural immunity exemptions measures could be more complex and require additional resources. Third, the positive predictive value of the tests we might accept as proof of natural immunity may vary, depending on both the tests employed and the prevalence of infections at the time and place they are deployed (Brownstein and Chen, 2021).
- 6.2 We believe that these objections have limited force. With respect to the first objection, Brown et al., have argued previously against the empirical assumption underlying this argument (Brown et al., 2021, 2020). It is also important to acknowledge that we are now at a very different stage of the pandemic. Billions of people have now been vaccinated and would have no need for a natural immunity exemption. In many places at least, unvaccinated people in 2021 are afforded far more freedoms today than they were afforded in 2020.
- 6.3 Furthermore, allowing exemptions for natural immunity might be more consistent with a concern for social justice. Data suggest that vaccine uptake is lower in marginalized groups (Office for National Statistics, 2021; Razai et al., 2021), and they will be disadvantaged by requirements that recognize only vaccine-induced immunity. In addition, as Patel et al. have highlighted, a number of factors led low SES (socioeconomic status) groups to have greater exposure to the virus over the course of the pandemic, (Patel et al., 2020) and there are data

to suggest that deprived areas have seen more confirmed cases of COVID-19. (Sa, 2020) Denying the protective effect of natural immunity puts lower SES groups at a disadvantage.

- 6.4 With respect to the second objection, it is clearly important to ensure that the standards of proof that we accept for natural immunity are sufficiently robust. That means we should only accept positive test results as proof if the tests meet acceptable levels of sensitivity and specificity, and have an acceptable positive predictive value given prevalence at the time. It may also be possible to ensure more robust protection against false positive results by adopting serial testing regimes. In any case though, the practicality of using natural immunity as sufficient proof of a low transmission risk has already been demonstrated by the NHS COVID pass, as detailed above.
- 6.5 One significant reason, we suspect, for not considering natural immunity as equivalent to vaccine-acquired immunity for the purposes of vaccine certification is the concern that this would provide support for those opposed to vaccination, or undermine public health messages about the importance and benefits of having the vaccine (Gerussi et al., 2021). It is possible that natural immunity exemptions would embolden anti-vaccination movements. However, we suggest that being clear (as we have tried to do at the start of this submission) about the different types of natural immunity claim would help redress any misinformation or misunderstanding. There is an important distinction between arguing that natural immunity, once acquired, confers sufficient protection (which we have made) and the claim that natural immunity is a good way to acquire immunity (which we do not support, and have not made). Second, even if it were the case that public health messages could be misinterpreted (if they allowed exemption), we would argue that it would be deeply ethically problematic to mandate vaccination (of the immune) for that reason. It would imply that (for example) aged care workers with natural immunity who are not at serious risk of passing on COVID were being used as a means to prevent wider misunderstanding in the community.
- 6.6 Throughout the pandemic there has been reluctance to consider natural immunity as protective against COVID-19, perhaps partly due to concerns about incentivising deliberate infection, and uncertainty about the strength and durability of natural immunity. However, legislators now cannot avoid the issue for two reasons: there is less reason to believe people will flood to be infected when there is a safer alternative: vaccination, and there is now evidence to suggest that those with immunity from natural infection appear to pose a low risk to others, comparable to individuals with immunity from vaccination.

Concluding remarks

- 7.1 There still some gaps in our understanding of the differences between natural and vaccine-induced immunity. For some, this uncertainty might lend support to a 'belt and braces' approach of ensuring that those with natural immunity also acquire vaccine-induced immunity. However, as we have argued, there are significant ethical costs with a precautionary strategy of *mandating* this. Our argument in this paper is based on a claim about the current evidence of the relative protection of vaccine-induced versus naturally acquired immunity against COVID, as it pertains to vaccine requirements that will come into force in 2021. This means that if the evidence changes, our conclusions will also change. For example, if further studies are published that clearly show that vaccination is superior for reducing transmission of the virus, or that naturally acquired immunity wanes substantially over time, then that would (other things being equal) support a vaccine mandate in this group (potentially at least after a certain period following infection). With some studies estimating that reinfection is likely to become increasingly common as the pandemic continues (Townsend et al., 2021), it is crucial that infections amongst those with both natural and vaccine-induced immunity are closely monitored.
- 7.2 At the present time however, it appears that we lack the data to establish that vaccinating those with natural immunity is necessary. It follows that it is discriminatory to treat natural immunity differently to vaccine mediated immunity, and this is something that ethical, evidence-based public health policy should reflect. This argument implies that the UK government should allow care home workers and frontline healthcare staff with sufficient proof of natural immunity to continue working for as long as that immunity can reasonably be expected to endure. Such an exemption would prevent the unnecessary loss of valuable employees who do not pose an increased risk of transmitting coronavirus to vulnerable individuals.

About this evidence submission

Jonathan Pugh, Julian Savulescu and Dominic Wilkinson are supported by the UK Pandemic Ethics Accelerator, grant number AH/V013947/1. Julian Savulescu also receives funding from the Uehiro Foundation on Ethics and Education, NHMRC, Wellcome Trust, Australian Research Council and WHO. He is a Partner Investigator on an Australian Research Council Linkage award (LP190100841, Oct 2020-2023) which involves industry partnership from Illumina. He does not personally receive any funds from Illumina. For further details contact Jonathan Pugh via email at jonathan.pugh@philosophy.ox.ac.uk.

The UK Pandemic Ethics Accelerator is a UKRI/AHRC-funded initiative that aims to bring UK ethics research expertise to bear on the multiple, ongoing ethical challenges arising during pandemics. We provide rapid evidence, guidance, and critical analysis to decision-makers across science, medicine, government and public health. We also support public debate on key ethical challenges. See <https://ukpandemicethics.org>.

October 2021.

Bibliography

Block, J., 2021. Vaccinating people who have had covid-19: why doesn't natural immunity count in the US? *BMJ* 374, n2101. <https://doi.org/10.1136/bmj.n2101>

Bradfield, O.M., Giubilini, A., 2021. Spoonful of honey or a gallon of vinegar? A conditional COVID-19 vaccination policy for front-line healthcare workers. *Journal of Medical Ethics*. <https://doi.org/10.1136/medethics-2020-107175>

Brown, R.C.H., Kelly, D., Wilkinson, D., Savulescu, J., 2021. The scientific and ethical feasibility of immunity passports. *The Lancet infectious diseases* 21, e58–e63. [https://doi.org/10.1016/S1473-3099\(20\)30766-0](https://doi.org/10.1016/S1473-3099(20)30766-0)

Brown, R.C.H., Savulescu, J., Williams, B., Wilkinson, D., 2020. Passport to freedom? Immunity passports for COVID-19. *Journal of Medical Ethics* 46, 652–659. <https://doi.org/10.1136/medethics-2020-106365>

Brownstein, N.C., Chen, Y.A., 2021. Predictive values, uncertainty, and interpretation of serology tests for the novel coronavirus. *Sci Rep* 11, 5491. <https://doi.org/10.1038/s41598-021-84173-1>

Cho, A., Muecksch, F., Schaefer-Babajew, D., Wang, Z., Finkin, S., Gaebler, C., Ramos, V., Cipolla, M., Mendoza, P., Agudelo, M., Bednarski, E., DaSilva, J., Shimeliovich, I., Dizon, J., Daga, M., Millard, K., Turroja, M., Schmidt, F., Zhang, F., Tanfous, T.B., Jankovic, M., Oliveria, T.Y., Gazumyan, A., Caskey, M., Bieniasz, P.D., Hatzioannou, T., Nussenzweig, M.C., 2021. Anti-SARS-CoV-2 receptor binding

domain antibody evolution after mRNA vaccination. *Nature* 1–9. <https://doi.org/10.1038/s41586-021-04060-7>

Cook, M., 2021. BioEdge: Bioethicist refuses to comply with vaccine mandate. BioEdge.

Dan, J.M., Mateus, J., Kato, Y., Hastie, K.M., Yu, E.D., Faliti, C.E., Grifoni, A., Ramirez, S.I., Haupt, S., Frazier, A., Nakao, C., Rayaprolu, V., Rawlings, S.A., Peters, B., Krammer, F., Simon, V., Saphire, E.O., Smith, D.M., Weiskopf, D., Sette, A., Crotty, S., 2021. Immunological memory to SARS-CoV-2 assessed for up to 8 months after infection. *Science* 371. <https://doi.org/10.1126/science.abf4063>

Dolgin, E., 2021. COVID vaccine immunity is waning — how much does that matter? *Nature*. <https://doi.org/10.1038/d41586-021-02532-4>

Durbach, N., 2005. *Bodily matters: the anti-vaccination movement in England, 1853-1907, Radical perspectives*. Duke University Press, Durham, N.C. ; London.

Gerussi, V., Peghin, M., Palese, A., Bressan, V., Visintini, E., Bontempo, G., Graziano, E., De Martino, M., Isola, M., Tascini, C., 2021. Vaccine Hesitancy among Italian Patients Recovered from COVID-19 Infection towards Influenza and Sars-Cov-2 Vaccination. *Vaccines (Basel)* 9, 172. <https://doi.org/10.3390/vaccines9020172>

Goldberg, Y., Mandel, M., Woodbridge, Y., Fluss, R., Novikov, I., Yaari, R., Ziv, A., Freedman, L., Huppert, A., 2021. Protection of previous SARS-CoV-2 infection is similar to that of BNT162b2 vaccine protection: A three-month nationwide experience from Israel. <https://doi.org/10.1101/2021.04.20.21255670>

Hall, V.J., Foulkes, S., Saei, A., Andrews, N., Oguti, B., Charlett, A., Wellington, E., Stowe, J., Gillson, N., Atti, A., Islam, J., Karagiannis, I., Munro, K., Khawam, J., Chand, M.A., Brown, C.S., Ramsay, M., Lopez-Bernal, J., Hopkins, S., SIREN Study Group, 2021. COVID-19 vaccine coverage in health-care workers in England and effectiveness of BNT162b2 mRNA vaccine against infection (SIREN): a prospective, multicentre, cohort study. *Lancet* 397, 1725–1735. [https://doi.org/10.1016/S0140-6736\(21\)00790-X](https://doi.org/10.1016/S0140-6736(21)00790-X)

Hals, T., 2021. U.S. Judge upholds COVID-19 vaccine requirement for those with “natural immunity.” *Reuters*.

Hobbs, A., Border, P., 2021. COVID-19 vaccines and virus transmission.

Kofler, N., Baylis, F., 2020. Ten reasons why immunity passports are a bad idea. *Nature* 581, 379–381. <https://doi.org/10.1038/d41586-020-01451-0>

Mahase, E., 2021. Covid-19: Pfizer vaccine’s efficacy declined from 96% to 84% four months after second dose, company reports. *BMJ* 374, n1920. <https://doi.org/10.1136/bmj.n1920>

Mallapaty, S., 2021. COVID vaccines cut the risk of transmitting Delta — but not for long. *Nature*. <https://doi.org/10.1038/d41586-021-02689-y>

Office for National Statistics, 2021. Coronavirus (COVID-19) Infection Survey Technical Article: Impact of vaccination on testing positive in the UK.

Office for National Statistics, 2021. Coronavirus and vaccine hesitancy, Great Britain.

Patel, J.A., Nielsen, F.B.H., Badiani, A.A., Assi, S., Unadkat, V.A., Patel, B., Ravindrane, R., Wardle, H., 2020. Poverty, inequality and COVID-19: the forgotten vulnerable. *Public Health* 183, 110–111. <https://doi.org/10.1016/j.puhe.2020.05.006>

Polack, F.P., Thomas, S.J., Kitchin, N., Absalon, J., Gurtman, A., Lockhart, S., Perez, J.L., Pérez Marc, G., Moreira, E.D., Zerbini, C., Bailey, R., Swanson, K.A., Roychoudhury, S., Koury, K., Li, P., Kalina, W.V., Cooper, D., Frenck, R.W., Hammitt, L.L., Türeci, Ö., Nell, H., Schaefer, A., Ünal, S., Tresnan, D.B., Mather, S., Dormitzer, P.R., Şahin, U., Jansen, K.U., Gruber, W.C., 2020. Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine. *New England Journal of Medicine* 0, null. <https://doi.org/10.1056/NEJMoa2034577>

Razai, M.S., Osama, T., McKechnie, D.G.J., Majeed, A., 2021. Covid-19 vaccine hesitancy among ethnic minority groups. *BMJ* 372, n513. <https://doi.org/10.1136/bmj.n513>

Royal Society - Science in Emergencies Tasking – COVID, 2021. Twelve criteria for the development and use of COVID-19 vaccine passports.

Sa, F., 2020. Socioeconomic Determinants of COVID-19 Infections and Mortality: Evidence from England and Wales.

Savulescu, J., Pugh, J., Wilkinson, D., 2021. Balancing incentives and disincentives for vaccination in a pandemic. *Nat Med* 27, 1500–1503. <https://doi.org/10.1038/s41591-021-01466-8>

Shah, A.S.V., Gribben, C., Bishop, J., Hanlon, P., Caldwell, D., Wood, R., Reid, M., McMenamin, J., Goldberg, D., Stockton, D., Hutchinson, S., Robertson, C., McKeigue, P.M., Colhoun, H.M., McAllister, D.A., 2021. Effect of Vaccination on Transmission of SARS-CoV-2. *New England Journal of Medicine* 0, null. <https://doi.org/10.1056/NEJMc2106757>

Sheridan, C., 2021. COVID-19 testing turns to T cells. *Nature Biotechnology* 39, 533–534. <https://doi.org/10.1038/s41587-021-00920-9>

Swoyer, A., 2021. George Mason grants professor COVID vaccine mandate exemption after ‘natural immunity’ lawsuit. *The Washington Times*.

The White House, 2021. President Biden’s COVID-19 Plan [WWW Document]. The White House. URL <https://www.whitehouse.gov/covidplan/> (accessed 10.14.21).

Thompson, M.G., 2021. Interim Estimates of Vaccine Effectiveness of BNT162b2 and mRNA-1273 COVID-19 Vaccines in Preventing SARS-CoV-2 Infection Among Health Care Personnel, First Responders, and Other Essential and Frontline Workers — Eight U.S. Locations, December 2020–March 2021. *MMWR Morb Mortal Wkly Rep* 70. <https://doi.org/10.15585/mmwr.mm7013e3>

Townsend, J.P., Hassler, H.B., Wang, Z., Miura, S., Singh, J., Kumar, S., Ruddle, N.H., Galvani, A.P., Dornburg, A., 2021. The durability of immunity against reinfection by SARS-CoV-2: a comparative evolutionary study. *The Lancet Microbe* 0. [https://doi.org/10.1016/S2666-5247\(21\)00219-6](https://doi.org/10.1016/S2666-5247(21)00219-6)

Voysey, M., Clemens, S.A.C., Madhi, S.A., Weckx, L.Y., Folegatti, P.M., Aley, P.K., Angus, B., Baillie, V.L., Barnabas, S.L., Bhorat, Q.E., Bibi, S., Briner, C., Cicconi, P., Collins, A.M., Colin-Jones, R., Cutland, C.L., Darton, T.C., Dheda, K., Duncan, C.J.A., Emary, K.R.W., Ewer, K.J., Fairlie, L., Faust, S.N., Feng, S., Ferreira, D.M., Finn, A., Goodman, A.L., Green, C.M., Green, C.A., Heath, P.T., Hill, C., Hill, H., Hirsch,

I., Hodgson, S.H.C., Izu, A., Jackson, S., Jenkin, D., Joe, C.C.D., Kerridge, S., Koen, A., Kwatra, G., Lazarus, R., Lawrie, A.M., Lelliott, A., Libri, V., Lillie, P.J., Mallory, R., Mendes, A.V.A., Milan, E.P., Minassian, A.M., McGregor, A., Morrison, H., Mujadidi, Y.F., Nana, A., O'Reilly, P.J., Padayachee, S.D., Pittella, A., Plested, E., Pollock, K.M., Ramasamy, M.N., Rhead, S., Schwarzbald, A.V., Singh, N., Smith, A., Song, R., Snape, M.D., Sprinz, E., Sutherland, R.K., Tarrant, R., Thomson, E.C., Török, M.E., Toshner, M., Turner, D.P.J., Vekemans, J., Villafana, T.L., Watson, M.E.E., Williams, C.J., Douglas, A.D., Hill, A.V.S., Lambe, T., Gilbert, S.C., Pollard, A.J., Aban, M., Abayomi, F., Abeyskera, K., Aboagye, J., Adam, M., Adams, K., Adamson, J., Adelaja, Y.A., Adlou, S., Ahmed, K., Akhalwaya, Y., Akhalwaya, S., Alcock, A., Ali, A., Allen, E.R., Allen, L., Almeida, T.C.D.S.C., Alves, M.P.S., Amorim, F., Andritsou, F., Anslow, R., Appleby, M., Arbe-Barnes, E.H., Ariaans, M.P., Arns, B., Arruda, L., Awedetan, G., Azi, P., Azi, L., Babbage, G., Bailey, C., Baker, K.F., Baker, M., Baker, N., Baker, P., Baldwin, L., Baleanu, I., Bandeira, D., Bara, A., Barbosa, M.A.S., Barker, D., Barlow, G.D., Barnes, E., Barr, A.S., Barrett, J.R., Barrett, J., Bates, L., Batten, A., Beadon, K., Beales, E., Beckley, R., Belij-Rammerstorfer, S., Bell, J., Bellamy, D., Bellei, N., Belton, S., Berg, A., Bermejo, L., Berrie, E., Berry, L., Berzenyi, D., Beveridge, A., Bewley, K.R., Bexhell, H., Bhikha, S., Bhorat, A.E., Bhorat, Z.E., Bijker, E., Birch, G., Birch, S., Bird, A., Bird, O., Bisnauthsing, K., Bittaye, M., Blackstone, K., Blackwell, L., Bletchly, H., Blundell, C.L., Blundell, S.R., Bodalia, P., Boettger, B.C., Bolam, E., Boland, E., Bormans, D., Borthwick, N., Bowring, F., Boyd, A., Bradley, P., Brenner, T., Brown, P., Brown, C., Brown-O'Sullivan, C., Bruce, S., Brunt, E., Buchan, R., Budd, W., Bulbulia, Y.A., Bull, M., Burbage, J., Burhan, H., Burn, A., Buttigieg, K.R., Byard, N., Puig, I.C., Calderon, G., Calvert, A., Camara, S., Cao, M., Cappuccini, F., Cardoso, J.R., Carr, M., Carroll, M.W., Carson-Stevens, A., Carvalho, Y. de M., Carvalho, J.A.M., Casey, H.R., Cashen, P., Castro, T., Castro, L.C., Cathie, K., Cavey, A., Cerbino-Neto, J., Chadwick, J., Chapman, D., Charlton, S., Chelysheva, I., Chester, O., Chita, S., Cho, J.-S., Cifuentes, L., Clark, E., Clark, M., Clarke, A., Clutterbuck, E.A., Collins, S.L.K., Conlon, C.P., Connarty, S., Coombes, N., Cooper, C., Cooper, R., Cornelissen, L., Corrah, T., Cosgrove, C., Cox, T., Crocker, W.E.M., Crosbie, S., Cullen, L., Cullen, D., Cunha, D.R.M.F., Cunningham, C., Cuthbertson, F.C., Guarda, S.N.F.D., Silva, L.P. da, Damratoski, B.E., Danos, Z., Dantas, M.T.D.C., Darroch, P., Dattoo, M.S., Datta, C., Davids, M., Davies, S.L., Davies, H., Davis, E., Davis, Judith, Davis, John, Nobrega, M.M.D.D., Kalid, L.M.D.O., Dearlove, D., Demissie, T., Desai, A., Marco, S.D., Maso, C.D., Dinelli, M.I.S., Dinesh, T., Docksey, C., Dold, C., Dong, T., Donnellan, F.R., Santos, T.D., Santos, T.G. dos, Santos, E.P.D., Douglas, N., Downing, C., Drake, J., Drake-Brockman, R., Driver, K., Drury, R., Dunachie, S.J., Durham, B.S., Dutra, L., Easom, N.J.W., Eck, S. van, Edwards, M., Edwards, N.J., Muhanna, O.M.E., Elias, S.C., Elmore, M., English, M., Esmail, A., Essack, Y.M., Farmer, E., Farooq, M., Farrar, M., Farrugia, L., Faulkner, B., Fedosyuk, S., Felle, S., Feng, S., Silva, C.F.D., Field, S., Fisher, R., Flaxman, A., Fletcher, J., Fofie, H., Fok, H., Ford, K.J., Fowler, J., Fraiman, P.H.A., Francis, E., Franco, M.M., Frater, J., Freire, M.S.M., Fry, S.H., Fudge, S., Furze, J., Fuskova, M., Galian-Rubio, P., Galiza, E., Garland, H., Gavrilu, M., Geddes, A., Gibbons, K.A., Gilbride, C., Gill, H., Glynn, S., Godwin, K., Gokani, K., Goldoni, U.C., Goncalves, M., Gonzalez, I.G.S., Goodwin, J., Goondiwala, A., Gordon-Quayle, K., Gorini, G., Grab, J., Gracie, L., Greenland, M., Greenwood, N., Greffrath, J., Groenewald, M.M., Grossi, L., Gupta, G., Hackett, M., Hallis, B., Hamaluba, M., Hamilton, E., Hammersley, D., Hanrath, A.T., Hanumunthadu, B., Harris, S.A., Harris, C., Harris, T., Harrison, T.D., Harrison, D., Hart,

T.C., Hartnell, B., Hassan, S., Haughney, J., Hawkins, S., Hay, J., Head, I., Henry, J., Herrera, M.H., Hettle, D.B., Hill, J., Hodges, G., Horne, E., Hou, M.M., Houlihan, C., Howe, E., Howell, N., Humphreys, J., Humphries, H.E., Hurley, K., Huson, C., Hyder-Wright, A., Hyamns, C., Ikram, S., Ishwarbhai, A., Ivan, M., Iveson, P., Iyer, V., Jackson, F., Jager, J.D., Jaumdally, S., Jeffers, H., Jesudason, N., Jones, B., Jones, K., Jones, E., Jones, C., Jorge, M.R., Jose, A., Joshi, A., Júnior, E.A.M.S., Kadziola, J., Kailath, R., Kana, F., Karampatsas, K., Kasanyinga, M., Keen, J., Kelly, E.J., Kelly, D.M., Kelly, D., Kelly, S., Kerr, D., Kfourri, R. de Á., Khan, L., Khozoe, B., Kidd, S., Killen, A., Kinch, J., Kinch, P., King, L.D.W., King, T.B., Kingham, L., Klenerman, P., Knapper, F., Knight, J.C., Knott, D., Koleva, S., Lang, M., Lang, G., Larkworthy, C.W., Larwood, J.P.J., Law, R., Lazarus, E.M., Leach, A., Lees, E.A., Lemm, N.-M., Lessa, A., Leung, S., Li, Y., Lias, A.M., Liatsikos, K., Linder, A., Lipworth, S., Liu, S., Liu, X., Lloyd, A., Lloyd, S., Loew, L., Ramon, R.L., Lora, L., Lowthorpe, V., Luz, K., MacDonald, J.C., MacGregor, G., Madhavan, M., Mainwaring, D.O., Makambwa, E., Makinson, R., Malahleha, M., Malamatsho, R., Mallett, G., Mansatta, K., Maoko, T., Mapetla, K., Marchevsky, N.G., Marinou, S., Marlow, E., Marques, G.N., Marriott, P., Marshall, R.P., Marshall, J.L., Martins, F.J., Masenya, M., Masilela, M., Masters, S.K., Mathew, M., Matlebjane, H., Matshidiso, K., Mazur, O., Mazzella, A., McCaughan, H., McEwan, J., McGlashan, J., McInroy, L., McIntyre, Z., McLenaghan, D., McRobert, N., McSwiggan, S., Megson, C., Mehdipour, S., Meijs, W., Mendonça, R.N.Á., Mentzer, A.J., Mirtorabi, N., Mitton, C., Mnyakeni, S., Moghaddas, F., Molapo, K., Moloi, M., Moore, M., Moraes-Pinto, M.I., Moran, M., Morey, E., Morgans, R., Morris, Susan, Morris, Sheila, Morris, H.C., Morselli, F., Morshead, G., Morter, R., Mottal, L., Moultrie, A., Moya, N., Mpelembue, M., Msomi, S., Mugodi, Y., Mukhopadhyay, E., Muller, J., Munro, A., Munro, C., Murphy, S., Mweu, P., Myasaki, C.H., Naik, G., Naker, K., Nastouli, E., Nazir, A., Ndlovu, B., Neffa, F., Njenga, C., Noal, H., Noé, A., Novaes, G., Nugent, F.L., Nunes, G., O'Brien, K., O'Connor, D., Odam, M., Oelofse, S., Oguti, B., Olchawski, V., Oldfield, N.J., Oliveira, M.G., Oliveira, C., Oosthuizen, A., O'Reilly, P., Osborne, P., Owen, D.R.J., Owen, L., Owens, D., Owino, N., Pacurar, M., Paiva, B.V.B., Palhares, E.M.F., Palmer, S., Parkinson, S., Parracho, H.M.R.T., Parsons, K., Patel, D., Patel, B., Patel, F., Patel, K., Patrick-Smith, M., Payne, R.O., Peng, Y., Penn, E.J., Pennington, A., Alvarez, M.P.P., Perring, J., Perry, N., Perumal, R., Petkar, S., Philip, T., Phillips, D.J., Phillips, J., Phohu, M.K., Pickup, L., Pieterse, S., Piper, J., Pipini, D., Plank, M., Plessis, J.D., Pollard, S., Pooley, J., Pooran, A., Poulton, I., Powers, C., Presa, F.B., Price, D.A., Price, V., Primeira, M., Proud, P.C., Provstgaard-Morys, S., Pueschel, S., Pulido, D., Quaid, S., Rabara, R., Radford, A., Radia, K., Rajapaska, D., Rajeswaran, T., Ramos, A.S.F., Lopez, F.R., Rampling, T., Rand, J., Ratcliffe, H., Rawlinson, T., Rea, D., Rees, B., Reiné, J., Resuello-Dauti, M., Pabon, E.R., Ribiero, C.M., Ricamara, M., Richter, A., Ritchie, N., Ritchie, A.J., Robbins, A.J., Roberts, H., Robinson, R.E., Robinson, H., Rocchetti, T.T., Rocha, B.P., Roche, S., Rollier, C., Rose, L., Russell, A.L.R., Rossouw, L., Royal, S., Rudiansyah, I., Ruiz, S., Saich, S., Sala, C., Sale, J., Salman, A.M., Salvador, N., Salvador, S., Sampaio, M., Samson, A.D., Sanchez-Gonzalez, A., Sanders, H., Sanders, K., Santos, E., Guerra, M.F.S.S., Satti, I., Saunders, J.E., Saunders, C., Sayed, A., Loeff, I.S. van der, Schmid, A.B., Schofield, E., Screatton, G., Seddiqi, S., Segireddy, R.R., Senger, R., Serrano, S., Shah, R., Shaik, I., Sharpe, H.E., Sharrocks, K., Shaw, R., Shea, A., Shepherd, A., Shepherd, J.G., Shiham, F., Sidhom, E., Silk, S.E., Moraes, A.C. da S., Silva-Junior, G., Silva-Reyes, L., Silveira, A.D., Silveira, M.B.V., Sinha, J., Skelly, D.T., Smith, D.C., Smith, N., Smith, H.E., Smith, D.J., Smith, C.C., Soares, A., Soares, T., Solórzano, C., Sorio,

G.L., Sorley, K., Sosa-Rodriguez, T., Souza, C.M.C.D.L., Souza, B.S.D.F., Souza, A.R., Spencer, A.J., Spina, F., Spoor, L., Stafford, L., Stamford, I., Starinskij, I., Stein, R., Steven, J., Stockdale, L., Stockwell, L.V., Strickland, L.H., Stuart, A.C., Sturdy, A., Sutton, N., Szigeti, A., Tahiri-Alaoui, A., Tanner, R., Taoushanis, C., Tarr, A.W., Taylor, K., Taylor, U., Taylor, I.J., Taylor, J., Naude, R. te W., Themistocleous, Y., Themistocleous, A., Thomas, M., Thomas, K., Thomas, T.M., Thombrayil, A., Thompson, F., Thompson, Amber, Thompson, K., Thompson, Aameeka, Thomson, J., Thornton-Jones, V., Tighe, P.J., Tinoco, L.A., Tiongson, G., Tladinyane, B., Tomasicchio, M., Tomic, A., Tonks, S., Tran, N., Tree, J., Trillana, G., Trinh, C., Trivett, R., Truby, A., Tsheko, B.L., Turabi, A., Turner, R., Turner, C., Ulaszewska, M., Underwood, B.R., Varughese, R., Verbart, D., Verheul, M., Vichos, I., Vieira, T., Waddington, C.S., Walker, L., Wallis, E., Wand, M., Warbick, D., Wardell, T., Warimwe, G., Warren, S.C., Watkins, B., Watson, E., Webb, S., Webb-Bridges, A., Webster, A., Welch, J., Wells, J., West, A., White, C., White, R., Williams, P., Williams, R.L., Winslow, R., Woodyer, M., Worth, A.T., Wright, D., Wroblewska, M., Yao, A., Zimmer, R., Zizi, D., Zuidewind, P., 2020. Safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARS-CoV-2: an interim analysis of four randomised controlled trials in Brazil, South Africa, and the UK. *The Lancet* 0. [https://doi.org/10.1016/S0140-6736\(20\)32661-1](https://doi.org/10.1016/S0140-6736(20)32661-1)

Voysey, M., Costa Clemens, S.A., Madhi, S.A., Weckx, L.Y., Folegatti, P.M., Aley, P.K., Angus, B., Baillie, V.L., Barnabas, S.L., Bhorat, Q.E., Bibi, S., Briner, C., Cicconi, P., Clutterbuck, E.A., Collins, A.M., Cutland, C.L., Darton, T.C., Dheda, K., Dold, C., Duncan, C.J.A., Emary, K.R.W., Ewer, K.J., Flaxman, A., Fairlie, L., Faust, S.N., Feng, S., Ferreira, D.M., Finn, A., Galiza, E., Goodman, A.L., Green, C.M., Green, C.A., Greenland, M., Hill, C., Hill, H.C., Hirsch, I., Izu, A., Jenkin, D., Joe, C.C.D., Kerridge, S., Koen, A., Kwatra, G., Lazarus, R., Libri, V., Lillie, P.J., Marchevsky, N.G., Marshall, R.P., Mendes, A.V.A., Milan, E.P., Minassian, A.M., McGregor, A., Mujadidi, Y.F., Nana, A., Padayachee, S.D., Phillips, D.J., Pittella, A., Plested, E., Pollock, K.M., Ramasamy, M.N., Ritchie, A.J., Robinson, H., Schwarzbald, A.V., Smith, A., Song, R., Snape, M.D., Sprinz, E., Sutherland, R.K., Thomson, E.C., Török, M.E., Toshner, M., Turner, D.P.J., Vekemans, J., Villafana, T.L., White, T., Williams, C.J., Douglas, A.D., Hill, A.V.S., Lambe, T., Gilbert, S.C., Pollard, A.J., Oxford COVID Vaccine Trial Group, 2021. Single-dose administration and the influence of the timing of the booster dose on immunogenicity and efficacy of ChAdOx1 nCoV-19 (AZD1222) vaccine: a pooled analysis of four randomised trials. *Lancet* 397, 881–891.

[https://doi.org/10.1016/S0140-6736\(21\)00432-3](https://doi.org/10.1016/S0140-6736(21)00432-3)