

## Proportionality, Wrongs, and Equipose for Natural Immunity Exemptions – Response To Commentators

We would like to thank each of the commentators on our feature article for their thoughtful engagement with our arguments. All the commentaries raise important questions about our proposed justification for natural immunity exemptions to COVID-19 vaccine mandates. Thankfully, for some of the points raised, we can simply signal our agreement. For instance, Reiss is correct to highlight that our article did not address the important US-centric considerations she helpfully raises and fruitfully discusses. We also agree with Williams about the need to provide a clear rationale for mandates, and to obtain different kinds of data in support of possible policies.

Unfortunately, we lack the space to directly engage with every one of the more critical comments raised in this rich set of commentaries; as such, in this response, we shall focus on a discussion of hybrid immunity, which underlies a number of different arguments evident in the commentaries, before concluding with some reflections responding to Lipsitch's concern about the appropriate standard of proof in this context.

### Proportionality and Hybrid Immunity

Each of the commentators highlight evidence to suggest that vaccination enhances protection against severe disease for those with prior infection; this means that would be some benefit in mandating vaccination in such individuals. Lipsitch highlights this point in suggesting that we address the 'wrong question' in our article because he suggests that our comparison between vaccine-induced immunity and natural immunity is not the relevant one to draw in this context. Ferguson raises this evidence when suggesting that we mostly ignore the consequences of natural immunity exemptions for unvaccinated individuals who lack prior immunity, noting that our proposal would reduce rates of such 'hybrid immunity'. He also goes on to note that a principle of justified paternalism would probably support mandating the vaccination of those with natural immunity. Reiss similarly discusses the benefits of hybrid immunity in support of her case for giving officials discretion on the matter of natural immunity exemptions.

Crucially, as Williams rightly acknowledges in her commentary, we also highlighted evidence about hybrid immunity in our original article, and noted that maximal protection against

COVID-19 might be best achieved by such hybrid immunity. Williams also astutely captures our thoughts on the moral significance of this, noting that the absolute risk reduction achieved by hybrid immunity may not be sufficient to justify a mandate in the general population for those with natural immunity. However, in order to adequately explain how this view can be invoked in response to some of the objections above, it will be useful for us to more explicitly detail why we believe this is the case.

As stated in the initial article, we believe that vaccine requirements can only be justified if they are necessary for achieving a proportionate public health benefit. We were mainly interested in defending the claim that there is not a strong evidential basis in support of the necessity of vaccinating those with natural immunity. However, in light of the evidence about hybrid immunity, one might be tempted claim that in order to achieve the additional public health benefits of hybrid immunity, it is clearly necessary to subject those with natural immunity to a vaccine mandate. That may be true; however, in our view, the issue with a mandate to achieve hybrid immunity is one of proportionality rather than necessity. Whilst acknowledging the fluid nature of the evidence-base, we remain unconvinced that magnitude of the public health benefit of achieving high levels of hybrid immunity (rather than natural or vaccine-induced immunity alone) would be sufficient to justify a mandate for that purpose.

To illustrate the point, consider the data we quoted in the initial article, suggesting that 767 individuals with natural immunity would need to be vaccinated to prevent one reinfection during follow-up. Although this is only one study, suppose that this number is a reasonable reflection of the number needed to vaccinate; in our view, to claim that it would be proportionate to subject this many people to a mandate to prevent just one case of infection is to significantly underplay the moral significance of the restriction of liberty involved in mandating unwilling individuals to undergo vaccination.

That said, Williams is right to acknowledge that there may be some circumstances in which we might have much stronger moral reasons than usual to prevent even a small number of infections, such as when healthcare systems are on the point of collapse. Whether or not exemptions should be permitted in such cases will depend on (i) just how beneficial it is to prevent low numbers of cases in that context, and (ii) how many people's liberties must be restricted to achieve that benefit, and how severe those restrictions must be. In general though, our view is that, on the evidence we have available, the value of (i) will seldom be sufficient to outweigh the disvalue of (ii).

Since comparisons of (i) and (ii) may require knowledge of local contextual pragmatic factors, we accept Reiss' point that there could be grounds for giving officials some discretion

about whether exemptions should apply. However, notwithstanding the issue of whether paternalistic principles are an appropriate basis for vaccine policy, contra Ferguson, we believe that only an implausibly strong paternalistic principle could provide support for a mandate in those with natural immunity.

These considerations also explain why we respectfully disagree with Lipsitch when he suggests that our article addresses the wrong question. Lipsitch writes:

The relevant comparison, *if one is trying to maximise protection in the population*, is not vaccination vs prior infection, but (vaccination plus prior infection) vs prior infection alone (emphasis added).

We agree that this is the relevant comparison to draw for the purpose emphasised; however, assuming that a simple maximising approach to public protection is the appropriate goal of public health policy begs an important question. A maximising approach may sometimes support policies that achieve only incremental increases in benefit at significant cost. Such a maximising approach may thus support disproportionate policies which are unjustified on the approach that we adopted in the original article; as Williams notes, such policies can also raise issues of fairness. In our view then, Lipsitch's suggested comparison is relevant, but largely because it suggests that mandating the naturally immune only in order to achieve the benefit of hybrid immunity would likely be a disproportionate measure.

We also maintain that the comparison we did draw in the paper addresses a question that it is important to ask. We assumed, for the sake of argument, that a vaccine mandate is justified for those who lack natural immunity; we therefore assumed both that increasing the number of people with the level of protection conferred by vaccination is a proportionate benefit to the harms involved in a mandate, and that it can generally be necessary to impose the harms of mandate to achieve this benefit. In debating the moral justification of natural immunity exemptions however, we must consider how generally this necessity obtains; and in order to do that, we must compare the level of protection afforded by vaccine-induced immunity and natural immunity. This is the relevant comparison for those who maintain, like we do, that a mandate must be necessary if it is to be justified.

Our assumption that a general mandate is justified also explains a feature of our article that Ferguson objects to in his commentary. Ferguson claims that we mostly ignore the unvaccinated without natural immunity in our arguments, and he writes:

We should evaluate a pragmatic argument by carefully assessing the consequences we expect to follow from the policy.

We agree that consequences matter for moral evaluation, but Ferguson's consequentialist approach here is too narrow; it also matters whether or not policies with good overall consequences wrong certain individuals, as opposed to merely harming them.(1) Crucially, when unvaccinated individuals lacking natural immunity are subject to a (*ex hypothesi*) justified mandate, they are harmed, but not wronged by having their liberty justifiably restricted. In contrast, if a mandate is *not* justified for those with natural immunity (as we have argued), then the restriction of liberty doesn't just harm them; it wrongs them by violating (rather than merely infringing) their rights (2). This matters, because on both deontological and suitably constrained consequentialist approaches in public health ethics, we should not pursue policies that plausibly violate rights or wrong individuals in this way, even if the policy would lead to the best overall consequences (3). So, whilst we agree that we should attend to the potential effects of natural immunity exemptions for unvaccinated individuals, and identify ways to potentially avert bad consequences of a natural immunity exemption for this group (as we did in the article), it is still an open question as to whether it would be permissible to avert any potential bad consequences for this group by perpetuating a policy that potentially wrongs another.

### Equipoise and Standards of Proof

We shall conclude with some reflections about Lipsitch's concerns regarding the standard of proof we invoke in our defence of natural immunity exemptions. We agree with Lipsitch on some crucial points - there are a number of challenges in obtaining evidence about vaccine-induced immunity and natural immunity in the course of a global pandemic. We also agree with the perils of invoking a strict evidence-based medicine position regarding the hierarchy of evidence in this context; observational studies can offer a valuable evidential avenue in these circumstances.

In the article, we highlighted two salient possibilities for when our evidence base might be deemed sufficient to justify a natural immunity exemption to a vaccine mandate; either we may change policy when we lack a clear evidential basis for believing that vaccine-induced immunity is superior to natural immunity (i.e. absence of sufficient evidence of superiority), or we change policy when we have evidence that natural immunity is not inferior (i.e. presence of sufficient evidence of non-inferiority). We supported the first standard, but Lipsitch objects that

this would lead to an unattainable standard for public health action, and notes that ‘waiting for certainty is a sure recipe for doing too little’.

Lipsitch somewhat misconstrues our position; uncertainty admits of degrees, and the standard we invoke does not entail that we can only act in public health once we achieve an unattainable *certainty* about the benefits of doing so; the standard merely invokes the absence of a clear evidential basis for a belief. [Notably, this clarification is also important for the opponent of our view, since the alternative standard we highlighted invokes the *presence* of clear evidence (albeit of non-inferiority in this case), rather than its absence. So, if our opponent were correct to claim that our proposed standard requiring the absence of clear evidence would lead to an unattainable standard for public health action, then the alternative standard we highlight would be even more susceptible to the objection that it would lead to an unattainable standard for endorsing less restrictive public health interventions over restrictive interventions that have some evidence of benefit.]

With this in mind, we believe that the standard we invoked is attainable, and has in fact been obtained for large parts of the pandemic; we *did* have a good evidential basis for the belief that vaccine-induced immunity was superior to natural immunity at earlier points in the pandemic. Researchers were able to perform rigorous RCTS of the protective effect of vaccine immunity, before large numbers of suitably powered observational studies of the protective effect of natural immunity were published. Our suggestion though, is that our evidential basis for the comparative claim is now weaker given the growth in the evidence base for the protective effect of natural immunity.

Lipsitch is correct to point out that we did not fully explain when we it is appropriate to say that we no longer have a clear evidential basis for the claiming that vaccine-induced superiority is superior. This is a fair criticism, and it raises deep questions in the philosophy of science and epistemology that we cannot hope to settle here. However, it may be helpful to draw on an adapted version of the concept of clinical equipoise, which is commonly invoked in response to a comparable problem in research ethics (4). Clinical equipoise is often invoked as a condition of morally permissible research trials, and may be said to obtain when there is “a state of disagreement or uncertainty in the informed, expert medical community about the relative clinical merits of the intervention arms in a trial”. We suggest that when there is an analogous state of disagreement with respect to the protective effect of vaccine-induced and natural immunity, then we may plausibly say that we no longer have a clear evidential basis for the belief that vaccine induced immunity is superior. What we referred to as compelling evidence in the original article is that which would be sufficient to disrupt this state of equipoise. Of course, whether or

not this sort of ‘immunity equipoise’ obtains in the relevant community is itself an empirical question; however, the varied expert views evident in Block’s report on the question in the *BMJ* is at least sympathetic to the view that it might.<sup>(5)</sup>

Clinical equipoise is typically invoked in the research context to ensure that the use of an experimental intervention is compatible with the demands of beneficence. If equipoise obtains, then we have good reasons to think that putting a participant in either arm of the trial is compatible with acting in their best interests; either action would be justifiable. In contrast, when immunity equipoise obtains, then *we no longer have* good reasons for thinking that that it is necessary (and therefore) justifiable to impose the significant restrictions of liberty on a particular group. As noted in the original article, we can choose to respond to this uncertainty with precaution, and to prioritise the maximisation of public protection. However, this approach sails very close to the simplistic consequentialist winds that can easily blow us towards an unreflective acceptance of the moral wrongs that we might perpetuate in the name of single-mindedly seeking to maximise benefits in public health policy. Our own view is that we should be more nuanced in our approach to the goals of public health ethics.

1. Feinberg J. *The Moral Limits of the Criminal Law Volume 1: Harm to Others*. New York: Oxford University Press; 1987.
2. Thomson JJ. *The realm of rights*. Cambridge, Mass ; London: Harvard University Press; 1990. viii+383.
3. Pugh J, Douglas T. Justifications for Non-Consensual Medical Intervention: From Infectious Disease Control to Criminal Rehabilitation. 2016 Sep 1;205-29.
4. Freedman B. Equipoise and the ethics of clinical research. 1987 Jul 16;141-5.
5. Block J. Vaccinating people who have had covid-19: why doesn’t natural immunity count in the US? *BMJ*. 2021 Sep 13;374:n2101.