

The Scientific and Ethical Feasibility of Immunity Passports

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Abstract: There is much debate about the use of ‘immunity passports’ in the response to the COVID-19 pandemic. Some authors have argued that immunity passports are unethical and impractical, pointing to uncertainties relating to COVID-19 immunity, issues with testing, perverse incentives, doubtful economic benefits, privacy concerns, and the risk of discriminatory effects. We first review the scientific feasibility of immunity passports. There remain significant hurdles, but increasing understanding of neutralising antibody response to COVID-19 may make it possible to identify those members of the community at low risk of contracting and transmitting SARS-CoV2. We respond to the ethical arguments against immunity passports and give the positive ethical arguments: first, a strong presumption should be in favour of preserving people’s free movement if at all feasible; second, failing to recognise the reduced infection threat immune individuals pose risks punishing people for low risk behaviour; and third, further individual and social benefits are likely to accrue from allowing people to engage in free movement. Challenges relating to immunity passport implementation ought to be met with targeted solutions so as to maximise their benefit.

Context of the Debate

At this point in the COVID-19 pandemic it is unclear how or when our lives might return to normality. One strategy proposed is the identification and documentation of immunity – so-called ‘immunity passports’. These are a potential tool for recording and sharing the immune status of an individual. Their introduction is being considered by a number of countries, including the UK, Estonia, Italy and Chile, though as yet, there is no information on the effects of their use [1-3]. Health certification for public health purposes is already used in other contexts, for example in the management of yellow fever [4]. Passports could take different forms, such as a wristband, smartphone app or certificate, and be used to confirm to others that a particular individual is at lower risk of acquiring or transmitting the SARS-CoV2. During

periods of ‘lockdown’, immunity passports could allow immune individuals to follow less stringent requirements around social distancing and travel, perhaps permitting them to return to work, care for those at risk, visit friends and relatives, or undertake other activities which expose them to the virus. Whether this strategy should be pursued depends on both scientific evidence and ethical reasoning.

The Scientific Evidence – Is an Immunity Passport Feasible?

Immunity passports could be implemented on the basis of either a laboratory test of immune response (a correlate of protection) or an immunising event (infection or vaccination). These would identify individuals less likely to get disease or transmit virus when exposed to SARS-CoV2. Important immunological issues for such passports are: i) the degree of immunity induced – an immune response might only attenuate disease severity, or might prevent any symptomatic disease and even pathogen carriage (necessary for herd-immunity); and ii) the duration of immunity.

Critics of immunity passports point to persisting uncertainties about the immune response to COVID-19 and claim that “COVID-19 immunity is a mystery” [5] and that this makes immunity passports unfeasible. Particular concerns surround whether SARS-CoV2 will generate a short-lived immune response similar to seasonal coronaviruses, or one more similar to SARS and MERS where antibody responses persisted for 2-3 years [6-8]; the sensitivity and specificity of the tests used to define immunity, especially in populations with a low incidence of previous infection; and the need for impractical numbers of tests to be undertaken to ensure a population remains immune [5, 9-11].

Infection-related immunity

To date we know that symptomatic infection with SARS-CoV2 generates a variety of T-cell, B-cell and antibody responses against components of the virus, including the spike protein (S) and the nucleoprotein (N), which could be assessed as potential correlates of protection [12-20]. For infections where reliable correlates have been established, these have been based on antibody responses which have the following advantages: they use serum or plasma that is easy to collect and store; the assays are more easily standardised and scaled for high-throughput use than cellular assays; and furthermore the assays provide a direct link to the protective immune response.

Current antibody assays for SARS-CoV2 correlates already include sensitive and specific quantitative measurements of IgG against a variety of viral proteins as well as more complex viral neutralisation assays [21-23]. Following symptomatic infection the majority of individuals develop antibody responses, with the majority of these having neutralising antibodies [12-20, 24, 25]. Although, like all antibody responses to viral infections, these wane in the weeks after infection, increasing evidence is accumulating that they appear to remain elevated above pre-infection levels over at least 4 months (the longest period that has been possible to study to date) [13, 14, 18, 24]. At present there is not a recognised level of response for any assay that has been definitively shown to protect against disease or viral

transmission. However, some progress has been made: trials of monoclonal antibodies in animal models prevent infection in a dose dependent manner [26-28]; individuals with pre-existing neutralising antibodies were less likely to get infected during an outbreak on a fishing boat [29]; and higher antibody levels were associated with lower viral loads during illness in a study of hospitalised patients in the UK [30].

In the absence of an immunological correlate of protection, confirmed infection itself could be used to certify immunity. In human challenge with seasonal coronaviruses and primate models of SARS-CoV2, infection disease severity is attenuated by previous infection [31]. With widespread testing available and ongoing transmission occurring there is likely to be rapid progress on quantifying the protective effect of previous infection and its duration. However, it is already clear that there are likely to be complexities to this approach since, for SARS-CoV2 infection, antibody responses may be less marked in individuals with less severe or asymptomatic disease [16]. Furthermore, several individuals have recently been described with evidence of reinfection within a short period of a first illness, with at least one being more symptomatic with the second illness [32, 33].

Given the scale of the pandemic and the research into it there is likely to be rapid progress in understanding the nature of infection and immunity such that clinical infection with or without a measurement of antibody response might form the basis of a time-limited immunity passport. Challenges for this approach include the heterologous nature of the initial infection reflected in variation in quality and duration of the subsequent immune response; almost complete lack of information about an individual's ability to still transmit virus to others even if protected from disease; and the need to undergo the 'risk' of infection in order to acquire immunity.

A recurrent criticism of immunity passports using correlates of infection has referred to the use of serosurveys of populations with a low incidence of infection. For instance a recent Cochrane review suggested that the number of false positives produced in a setting with a 5% seroprevalence would be around 21% [34]. However, an assessment of individual immunity is not likely to be derived from serosurveys of whole populations with a low incidence of infection – such approaches are also unattractive given that asymptomatic infections may lead to less functional and less persistent antibody. If a surveillance approach was considered in a higher-risk group such as exposed health-care, workers a two stage testing process could be considered whereby those with a positive antibody test underwent second-line testing with neutralisation assays. At least one study has demonstrated that antibody positive, neutralising antibody negative individuals were susceptible to infection reinforcing the need for a two-stage approach in some settings especially where there is no documented infection as the known origin of the antibody [29].

Vaccine-induced immunity

There has been rapid progress with vaccine development and emerging evidence that vaccines can provide protection in animal models [31, 35, 36]. Given ongoing clinical efficacy trials with widespread serological and cellular sampling there will be more data emerging as to whether vaccination could form the basis of an immunity passport and, if so, whether there are any assays that provide correlates of protection. A vaccine has advantages as the basis for an immunity passport, since the stimulus is uniform and therefore likely to have a more predictable pattern and duration of immunity than infection, and vaccination further makes immunity available to the whole population. The ethical issue then becomes one of timely access to vaccination. In the setting of routine immunisation in a population the duration of immunity can be estimated from efficacy and effectiveness studies together with serological surveys and this used as a basis for booster doses rather than burdensome continual reassessment of immunity in each individual. Hepatitis B infection for occupational health reasons provides some parallels for considering immunity passports in SARS-CoV2 infection. Whilst health workers with low responses to hepatitis B vaccine are not usually restricted in the activities that they can undertake, given effective means of preventing transmission of infection, there are more onerous schedules of monitoring for seroconversion related to infection.

Transmission

A neglected issue in discussions of immunity passports is that of individual protection versus community protection. Perhaps the most important issue for immunity passports is whether an individual can transmit infection to others. This is likely a more stringent test as evidence from previous work with seasonal coronaviruses and SARS-CoV2 vaccine studies in macaques [16, 31, 37, 38] suggests previous infection or vaccination may protect from severe disease but an individual may nevertheless carry the virus at similar levels and for a similar duration to those previously uninfected, with an unchanged potential for transmission. This fact provides the greatest challenge to the assurance immunity passports provide of a reduced risk to others.

There are significant challenges in measuring and inferring immunity to SARS-CoV2. However, many of those challenges could potentially be overcome in the coming months. As information regarding these questions continues to accumulate, it is important to consider whether we should use immunity passports *if it were possible* to reliably identify immune individuals.

Ethical Arguments: Would Immunity Passports Be Ethical?

There are a number of key ethical advantages to immunity passports.

First, the justification for requiring people to remain in lockdown is the risk their free movement poses to themselves and others, since they may acquire and pass on the virus. Those who are immune are at a

vastly reduced risk, and so this justification for the removal of basic civil liberties is absent. It is unethical to require someone to avoid contact with others if they pose no or minimal risk of spreading the virus.

Second, people will know this, and are likely to become less compliant with lockdown restrictions if they believe themselves to be immune anyway [39]. Consider Neil Ferguson, who resigned from his role as UK government adviser after breaking lockdown guidelines, stating “I acted in the belief that I was immune” [40]. By refusing to formalise the permissibility of such actions, we make inevitable low-risk behaviour *rule-breaking*, and may even subject people to fines and punishments which do not track the harm their behaviour causes.

Third, as well as benefits that accrue to immune individuals, there will be broader benefits to society from allowing people to return to work and care obligations. The lonely and isolated could be visited by immune friends and relatives; small businesses may be reopened by immune staff who won’t risk the health of colleagues and customers; immune healthcare staff can care for COVID-positive patients; and immune care workers can protect vulnerable people in residential homes.

Ethical Objections

Despite these advantages, some have strongly opposed immunity passports. In a number of articles, ethicists Natalie Kofler and Françoise Baylis have claimed that immunity passports are “the height of folly” and should be fought against “tooth and nail” [41, 42]. They point to how, in nineteenth century New Orleans, presumed immunity to yellow fever “was weaponised to justify white supremacy” [5], and warn that immunity passports threaten similar effects in the modern day. The World Health Organisation has also expressed concerns about immunity passports [43], as has Alexandra Phelan writing in *The Lancet* [10] as well as numerous news outlets [44-48]. A rapid policy briefing by the Nuffield Council on Bioethics emphasises the ethical risks of immunity passports, speculating that they could “create coercive and stigmatising work environments” and are “more likely to compound than redress... structural disadvantages and... social stigmatisation” [49]. However, the strength of much of this opposition does not seem justified by the strength of the arguments opposing immunity passports.

Undermining solidarity and creating perverse incentives

Critics warn that immunity passports create a “perverse incentive for individuals to seek out infection”, or choose to fraudulently acquire passports [10]. We currently lack much evidence regarding how likely this is, or an idea of how damaging it would be to efforts to maintain control over the virus (one survey suggest people are very unlikely to intentionally seek infection [50] and reporting of so-called ‘covid parties’ may be overblown [51]). This is one area where additional evidence would greatly help to judge the risk, and how this can be traded off against the benefits of immunity passports.

Behavioural scientists have also gestured towards research on ‘in-groups’ and ‘out-groups’ psychology to claim that permitting those who are immune to exercise more freedoms would undermine

the message that we're "all in this together" [11]. We are not aware of published research which presents clear and compelling evidence that this is the case. There has been some exploration of how various theories and findings from social and behavioural science can be applied to the pandemic response [52]. At this stage, however, extrapolation from theories supported by evidence of variable quality (often based on lab experimentation or very different situational contexts) is risky. It is often unclear what, exactly, the implications of behavioural science research are for how different policy options will be received and what their downstream effects on people's behaviour will be. A number of behavioural scientists have raised concerns about the robustness and generalisability of claims from behavioural science and caution against using them to inform major policy decisions [53].

Minimal economic benefits

The baseline rates of immunity vary from place to place – in some cities (London, New York, Stockholm) it may be as high as a fifth [54-56] whilst elsewhere it is likely to be much lower. Economic analyses are needed to tell us how much economic benefit would be generated if some proportion of the population experienced fewer restrictions on their movement. We are not aware of published work to inform this argument. But it would be a mistake for ethicists, in the absence of such evidence or expertise, to dismiss immunity passports on the assumption that there will be "Too few survivors to boost the economy" [5]. In addition, immunity passports may deliver important non-economic benefits, even if they affect a relatively small proportion of people.

Privacy

There is suspicion that immunity passports could provide a 'way in' to more troublesome monitoring of people's movement and health status [57]. Some have claimed that "the whole point of immunity passports is to control movement" [5]. However, this seems a gross mischaracterisation: their point is to *facilitate* movement when it is safe to do so. It is true, of course, that steps must be taken to avoid the production of fraudulent immunity passports, and there must be careful attention to privacy concerns and information governance. But these are not problems unique to immunity passports (conventional passports and contact tracing measures encounter such problems as well), and are not insurmountable.

Marginalised groups and discrimination

There have been a number of objections on the basis that the introduction of immunity passports would exacerbate existing inequalities [5, 10, 46, 49]. The main concerns are that, if immunity passports were introduced, marginalised groups would be subject to more scrutiny due to existing inequities and racism, such as facing more police checks to ensure they were not breaking lockdown requirements; that more vulnerable groups would be less likely to access testing (and establish immunity); and that the advantages accruing to those with immunity (and immunity passports) would persist into the future. Whilst we

recognise the deep existing inequalities in all countries, and the ways in which COVID-19 has increased the hardships for the worst off, we are surprised that the response of some of those concerned by such patterns has been to argue that immunity passports must not be permitted, rather than seeking to explore ways to directly mitigate such inequalities.

As frequently noted, such unequal experiences are nothing new. Factors such as race and socioeconomic status influence the healthcare that people access and treatment they receive [58-60]. Yet this is rarely interpreted as a reason to remove healthcare treatments, or refuse to introduce new ones, assuming they are considered cost-effective and net beneficial. Instead, such patterns point us to areas where more effort must be made to improve the care of the most deprived, to look for solutions to the inequitable distribution of resources, and to tackle the upstream causes of inequality. This same reasoning should be applied to immunity passports. Further, as some point out, the advantages of COVID-19 immunity may not entrench existing inequalities in the way often assumed [39].

Concluding Remarks

Lockdown measures significantly curtail people's freedom. Immunity passports would potentially allow some proportion of people to access more freedoms during lockdown periods. It is unethical to restrict freedom unless there is a real threat to other people. If we have the technology to decide who is not a threat, we should use it.

The specific scenarios in which immunity passports can be used will depend on the nature of the immunity generated. It might be desirable to document that front-line health care workers are unlikely to become unwell, especially for those with pre-existing vulnerability; for this we might require a correlate indicating reliable protection from severe disease. Alternatively, if immunity passports certify that individuals can move around freely and interact for business or leisure without increasing the risk of transmission, we might wish to certify only those who are unlikely to transmit the virus.

Whilst there remains significant uncertainty regarding the nature, degree and duration of immunity to SARS-CoV2, the intense research focus that has been brought to bear across the world on this infection will potentially yield useful answers in a practicable time frame that could be translated into some form of immunity passport. Even after a correlate of protection is established there will still be uncertainty around the duration of protection or whether the correlate can be applied across all ages and clinical scenarios, but complete certainty may not be necessary for medium term policy [61]. Assuming developing scientific evidence supports immunity passport use, it would be essential to ensure safety nets are in place to protect those who remain in lockdown and are most disadvantaged by it (those unable to work, socially isolated, or at risk from domestic violence, for instance). Similarly, we must take seriously the need to ensure fair access to testing and to tackle inequality that arises in the context of COVID-19, through targeted solutions rather than the blanket abandonment of useful tools.

We must be clear about what the alternatives are when evaluating the merits of different ways of tackling this pandemic. The choice is not between returning to a ‘normal’ life versus issuing immunity passports. Instead, it is between periodic lockdowns, attempting to emerge from lockdowns *with* immunity passports, and attempting to emerge from lockdowns *without* them. Immunity passports are a potentially valuable and ethical tool. As further evidence relating to people’s immune response to COVID-19 accumulates, and the capacity to reliably identify immune individuals develops, immunity passports may be appropriately adopted. In such an event, the freedoms they confer must be subject to amendments and cancellation, and integrated into a package of measures such as contact tracing and social distancing in order to keep people safe whilst maintaining quality of life.

Contributors

RB produced the initial manuscript draft; DK drafted sections relating to scientific knowledge of SARS-CoV2 immunity, and provided comments on the rest of the manuscript; DW and JS provided input into the initial preparation of the manuscript and edited the full manuscript.

Conflicts of Interest

We declare that we have no conflicts of interest.

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