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The scientific and ethical feasibility of immunity passports



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There is much debate about the use of immunity passports in the response to the COVID-19 pandemic. Some 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. Considerable hurdles remain, but increasing understanding of the neutralising antibody response to COVID-19 might make identifying members of the community at low risk of contracting and transmitting COVID-19 possible. 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. Finally, further individual and social benefits are likely to accrue from allowing people to engage in free movement. Challenges relating to the implementation of immunity passports 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, how or when our lives might return to normality is unclear. One strategy proposed to help this resumption is the identification and documentation of immunity: so-called immunity passports. These passports are a potential tool for recording and sharing the immune status of an individual. The introduction of immunity passports is being considered by several countries, including the UK, Estonia, Italy, and Chile; although 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—eg, in the management of yellow fever.⁴ Passports could take different forms, such as a wristband, smartphone application, or certificate, and be used to confirm to others that a particular individual is at a low risk of acquiring or transmitting severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). During periods of lockdown, immunity passports could allow immune individuals to follow less stringent requirements around physical distancing and travel, perhaps permitting them to return to work, care for those at risk, visit friends and relatives, or undertake other activities that expose them to the virus. Whether this strategy should be pursued depends on both scientific evidence and ethical reasoning.

The scientific evidence: are immunity passports 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), which would identify individuals less likely to get disease or transmit virus when exposed to SARS-CoV-2. Important immunological issues for such passports are: (1) the degree of immunity induced (an immune response might only attenuate disease severity, or might prevent any symptomatic disease and even pathogen carriage, which is necessary for herd immunity) and (2) the duration of immunity.

Critics of immunity passports point to persisting uncertainties about the immune response to COVID-19,

claiming that “COVID-19 immunity is a mystery” and that this uncertainty makes immunity passports unfeasible.⁵ Whether SARS-CoV-2 will generate a short-lived immune response similar to those produced by seasonal coronaviruses, or one more similar to those from SARS and Middle East respiratory syndrome coronaviruses, in which antibody responses persist for 2–3 years, is unclear.⁶⁻⁹ Concerns also surround 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 done to ensure a population remains immune.^{5,10-12}

Infection-related immunity

Symptomatic infection with SARS-CoV-2 generates various T-cell, B-cell, and antibody responses against components of the virus, including the spike glycoprotein and the nucleoprotein, which could be assessed as potential correlates of protection.¹³⁻²¹ For infections that have reliable correlates, these correlates have been based on antibody responses, which have the following advantages: these tests use serum or plasma that are easy to collect and store; the assays are more easily standardised and scaled for high throughput use than are cellular assays; and the assays provide a direct link to the protective immune response.

Current antibody assays for SARS-CoV-2 correlates already include sensitive and specific quantitative measurements of IgG against various viral proteins, and complex viral neutralisation assays.²²⁻²⁴ Following symptomatic infection, most patients develop antibody responses, with the majority of these individuals having neutralising antibodies.^{13-21,25,26} Although, like all antibody responses to viral infections, responses to SARS-CoV-2 wane in the weeks after infection, increasing evidence suggests that these responses remain higher than pre-infection levels for at least 4 months (the longest period that has been possible to study).^{14,15,19,25} As of September, 2020, there is not a recognised level of response for any assay that has been definitively shown to protect against disease or viral transmission. However,

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some progress has been made: monoclonal antibodies in animal models prevented SARS-CoV-2 infection in a dose-dependent manner;²⁷⁻²⁹ individuals with pre-existing neutralising antibodies were less likely to get infected during an outbreak on a fishing boat than were individuals with either no antibody response or antibody responses that were non-neutralising when tested pre-exposure;³⁰ and higher antibody concentrations were associated with lower viral loads during illness in a study of hospitalised patients in the UK.³¹

In the absence of an immunological correlate of protection, confirmed infection itself could be used to certify immunity. In human challenge trials with seasonal coronaviruses and primate models of SARS-CoV-2 infection, disease severity was attenuated by previous infection.³² With widespread testing available and ongoing transmission occurring, there is likely to be rapid progress on quantifying the protective effect of previous infection and the duration of this effect. However, there are likely to be complexities to this approach because, for SARS-CoV-2 infection, antibody responses might be less marked in individuals with asymptomatic or mild disease than in those with severe disease.¹⁷ Furthermore, several individuals with evidence of reinfection within a short period of a first illness have been described, with at least one individual being more symptomatic with the second illness than with the first.^{33,34}

Given the scale of the pandemic and the research into COVID-19, 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 the variation in quality and duration of the subsequent immune response; the almost complete absence 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 to acquire immunity.

A recurrent criticism of immunity passports based on correlates of infection is the use of serosurveys of populations with a low incidence of infection. For instance, a Cochrane review suggested that the number of false positives produced in a setting with a 5% SARS-CoV-2 seroprevalence would be around 21%.³⁵ 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 might lead to less functional and less persistent antibody than might symptomatic infections. If a surveillance approach was considered in a group at high risk of infection, such as exposed health-care workers, a two-stage testing process could be implemented whereby individuals with a positive antibody test undergo second-line testing with neutralisation assays. At least one study

has shown that individuals positive for antibodies against SARS-CoV-2 but negative for neutralising antibodies were susceptible to SARS-CoV-2 infection, reinforcing the need for a two-stage approach in some settings, especially where there is no infection documented as the origin of the antibodies.³⁰

Vaccine-induced immunity

There has been rapid progress in vaccine development and emerging evidence that vaccines can provide protection from SARS-CoV-2 in animal models.^{32,36,37} Given the ongoing clinical efficacy trials that use 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. Basing immunity passports on a vaccine has advantages: the stimulus is uniform and is therefore likely to have a more predictable pattern and duration of immunity than is infection, and vaccination makes immunity potentially available to the whole population. The ethical issue then becomes one of timely access to vaccination for everyone. In the setting of routine immunisation in a population, the duration of immunity can be estimated from efficacy studies, together with serological surveys, and these data can support booster doses rather than continually reassessing immunity in individuals.

Transmission

A neglected issue in discussions of immunity passports is that of individual protection versus community protection. Perhaps the most important consideration for immunity passports is whether an individual can transmit the infection to others. Evidence from previous work with seasonal coronaviruses and studies of SARS-CoV-2 vaccines in macaques suggests that previous infection or vaccination might protect from severe disease but an individual might nevertheless carry the virus at similar levels, and for a similar duration, to those previously uninfected, with an unchanged potential for transmission.^{17,32,38,39} This fact provides the greatest challenge to the assurance that individuals who carry immunity passports would have a reduced risk to others. There are considerable challenges in measuring and inferring immunity to SARS-CoV-2. However, many of those challenges could potentially be overcome in the coming months. As information continues to accumulate, it is important to consider whether immunity passports should be used to reliably identify immune individuals, if this identification were possible.

Ethical arguments: are immunity passports ethical?

There are several key ethical advantages to immunity passports. First, the justification behind requiring people to remain in lockdown is the risk their free movement

poses to themselves and others as they could acquire and pass on the virus. Individuals who are immune to SARS-CoV-2 are expected to be at a vastly reduced risk of getting and transmitting the virus, and so removing their civil liberties would be unjustified. 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 the reduced risks, and are likely to become less compliant with lockdown restrictions if they believe themselves to be immune anyway.⁴⁰ Consider Neil Ferguson, who resigned from his role as an adviser to the UK Government after breaking lockdown guidelines, stating “I acted in the belief that I was immune”.⁴¹ By refusing to formalise the permissibility of such actions, inevitable low-risk behaviour is classified as rule breaking, and could even subject people to fines and punishments that do not correspond to the harm their behaviour causes.

Finally, there will be benefits for immune individuals and broader benefits to society from allowing people to return to work and care obligations. Lonely and isolated individuals could be visited by immune friends and relatives; small businesses can be reopened by staff who are immune and will not risk the health of colleagues and customers; immune health-care staff can care for patients with COVID-19; and immune care workers can protect vulnerable people in residential homes.

Ethical objections

Despite these advantages, some people have strongly opposed immunity passports. In numerous 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”.^{42,43} Kofler and Baylis have highlighted how, in 19th century New Orleans, LA, USA, presumed immunity to yellow fever “was weaponised to justify white supremacy”,⁵ and have warned that immunity passports could cause similar effects in modern day. WHO have also expressed concerns about immunity passports,⁴⁴ as has Alexandra Phelan writing in *The Lancet*,¹¹ and numerous news outlets.⁴⁵⁻⁴⁹ A rapid policy briefing by the Nuffield Council on Bioethics emphasised the ethical risks of immunity passports, speculating that these passports could “create coercive and stigmatising work environments” and are “more likely to compound than redress...structural disadvantages and...social stigmatisation”.⁵⁰ 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.¹¹ How likely these scenarios would be is largely unknown. One survey

suggested that people are very unlikely to intentionally seek infection, and Gilad Edelman, writing in *Wired*, has proposed that the reporting of so-called COVID parties might be overblown.^{51,52} This area is one for which additional evidence would greatly help to judge risk and how this risk can be traded off against the benefits of immunity passports.

Behavioural scientists have also highlighted research on the psychology of in-groups, social groups with which people identify, and out-groups, social groups with which people do not identify, suggesting that permitting immune individuals to exercise more freedoms than those who are not immune would undermine the message that we are “all in this together”.¹² We are not aware of any published research that presents clear and compelling evidence supporting this assertion. There has been some exploration as to how various theories and findings from social and behavioural science can be applied to the pandemic response.⁵³ At this stage, however, extrapolation from theories supported by evidence often based on laboratory experimentation or very different situational contexts is risky. Several behavioural scientists have raised concerns about the robustness and generalisability of claims from behavioural science and caution against the use of these claims to inform major policy decisions.⁵⁴

Minimal economic benefits

The baseline prevalence of immunity varies from place to place. In some cities (ie, London [UK], New York [NY, USA], and Stockholm [Sweden]), the prevalence of immunity could be as high as a fifth;⁵⁵⁻⁵⁹ elsewhere, prevalence is likely to be much lower. Economic analyses are needed to find out how much economic benefit would be generated if some proportion of the population had fewer restrictions on their movement. We are not aware of any published work that informs this argument. However, 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 might deliver important non-economic benefits, such as regaining the ability to operate small businesses, to a small proportion of people.

Privacy

There is suspicion that immunity passports could provide a way in to more troublesome monitoring of people’s movements and health statuses.⁶⁰ Some have claimed that “the whole point of immunity passports is to control movement”.⁵ However, this claim is a gross mischaracterisation: the point of immunity passports is to facilitate movement when it is safe to do so. Of course, steps must be taken to avoid the production of fraudulent immunity passports, and careful attention must be given to privacy concerns and information governance. These problems are not unique to immunity passports (conventional passports and contact tracing measures

also encounter such problems) and are not insurmountable.

Marginalised groups and discrimination

Immunity passports have been frequently objected to on the basis that their introduction would exacerbate existing inequalities.^{5,11,47,50} The main concerns are that, if immunity passports were introduced, marginalised groups would be subject to more scrutiny because of existing inequities and racism (eg, police checks for lockdown regulations) and would be less likely to access testing (and establish immunity) than non-marginalised groups would be. Furthermore, the advantages accruing to those with immunity (and immunity passports) would persist into the future. Although 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 published responses⁴² of some prominent critics of immunity passports do not include suggestions of ways to mitigate resultant inequalities.

As frequently noted, such unequal experiences are not new. Factors, such as race and socioeconomic status, influence the health care that people access and the treatment they receive.^{61–63} Yet, this issue is rarely interpreted as a reason to remove health-care treatments or refuse to introduce new ones, assuming these therapies are considered cost-effective and net beneficial. Instead, such patterns point us to areas in which 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. Furthermore, as some have highlighted, the advantages of COVID-19 immunity might not entrench existing inequalities in the way often assumed.⁴⁰

Concluding remarks

Lockdown measures considerably curtail people's freedom. Immunity passports would potentially allow some proportion of the population to access more freedoms during lockdown periods. It is unethical to restrict freedom unless there is a real risk to other people. If we have the technology to decide who is not a risk, 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 for immunity passports to record individuals, especially those who have pre-existing vulnerabilities, who have been identified as having a correlate of immunity that reliably indicates that they will not contract severe disease in the future. 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.

Although there remains considerable uncertainty regarding the nature, degree, and duration of immunity to

SARS-CoV-2, the world's intense research focus on this infection will potentially yield useful answers in a practicable timeframe 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 might not be necessary for policy in the medium term.⁶⁴ Assuming that developing scientific evidence supports the use of immunity passports, safety nets must be put in place to protect individuals who remain in lockdown and are the most disadvantaged by lockdown (eg, those who are unable to work, socially isolated, or at risk from domestic violence). Similarly, we must take seriously the need to ensure fair access to testing and to address inequality that arises in the context of COVID-19 through targeted solutions.

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, the choice is between periodic lockdowns, attempting to emerge from lockdowns with immunity passports, and attempting to emerge from lockdowns without immunity passports. Immunity passports are a potentially valuable and ethical tool. As further evidence relating to the immune response to COVID-19 accumulates, and the capacity to reliably identify immune individuals develops, immunity passports could be appropriately adopted. In such an event, the freedoms these passports confer must be subject to amendments and cancellations, and integrated with other measures, such as contact tracing and physical distancing, to keep people safe while maintaining quality of life.

Contributors

RCHB produced the initial draft of the manuscript. DK drafted the sections relating to scientific knowledge of SARS-CoV-2 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.

Declaration of interests

We declare no competing interests.

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