PUBLIC HEALTH

Protecting the population with immune individuals

Modeling an approach in which people who have recovered from COVID-19 are returned to society to reduce interactions between infected people and vulnerable people indicates the effectiveness of such an approach in reducing deaths.

Ole F. Norheim

The COVID-19 outbreak was declared a pandemic by the World Health Organization on 12 March 2020, and the causative coronavirus has now spread to most countries of the world. Although the disease can be fatal, the majority of those afflicted recover and could be rendered immune. Widespread serological testing can identify people who are virus negative and antibody positive and are thought to have some immunity. One pathway out of the lockdown for many of the hardest-hit countries is to protect the general population and reduce the spread of COVID-19 with such immune people. The idea is that these recovered people can work at the front line in hospitals, nursing homes, pharmacies, grocery stores and other critical institutions in which the infection spreads easily, to lower the number of interactions between susceptible people and infected people. In a recent study in *Nature Medicine*, Weitz et al. model this strategy and find that the immunity strategy can substantially reduce the impact of COVID-19 on deaths and the need for beds in intensive care units[1].

The authors build on and improve a standard age-structured epidemiological, mathematical intervention model (the susceptible–infectious–recovered model) to estimate how interaction substitution — that is, substituting vulnerable and potentially infected people with recovered people — could reduce epidemic spread (Fig. 1). The model allows modification of how infectious the disease is, how immune people can replace others in interactions, and the age distribution of the population. The authors find that the impact of the intervention (that is, the reduction in deaths) increases with the reproduction number R_0 (the number of people that an individual person infects on average), when more susceptible people are replaced with recovered people, and in populations with higher proportions of elderly people. Interestingly, the authors also find that interaction-substitution protection works synergistically with other public-health interventions such as social distancing. This is important because existing measures, such as school and workplace shutdown and restrictions on social gatherings, affect the income and welfare of millions of people, especially those who are already disadvantaged. Protecting the population with recovered people may therefore gradually replace other and more-costly interventions.

Although it is promising and not yet proven effective, the strategy of having recovered people interact with those at risk faces substantial implementation issues. First, are the serological tests accurate enough? A specificity below 100% will give some false-positive results; i.e., people are informed that they are immune, while this is actually not correct, which results in some falsely thinking they are able to interact with vulnerable people without risk. In the USA, the first antibody test approved by the Food and Drug Administration has 96% specificity and 94% sensitivity. This sounds good, but when the true prevalence of infection is low, even a specificity of 96% will lead to a substantial number of false-positive results. This is because the positive predictive value of a test decreases with prevalence. Second, the strength and duration of immunity after infection is still uncertain for COVID-19, and if it is weak or short, this may undermine the whole strategy. Indeed the authors' model indicates that the interaction-substitution approach is more effective if the duration of immunity is longer.

There are also ethical issues with this approach, which can be divided into two groups. The first concerns the right to privacy. For the strategy to work, recovered antibody-positive people must be issued some sort of 'corona certificate' or, as some have suggested, a 'corona passport'. This means informing others, including employers, about a person's status as

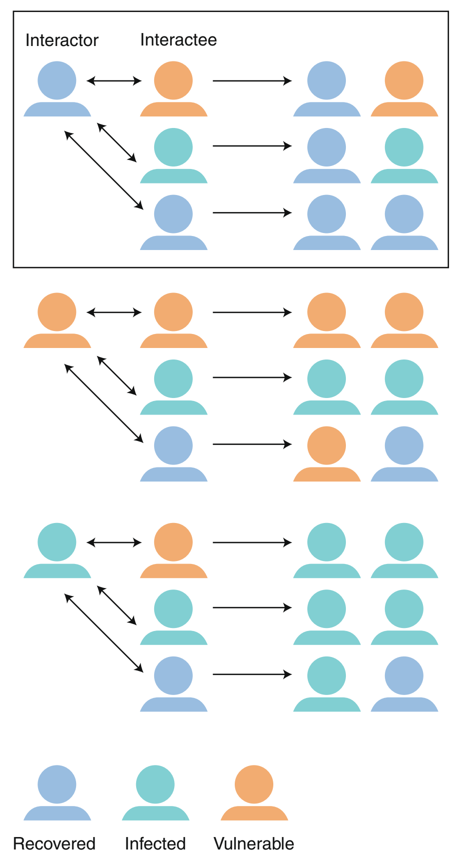

Fig. 1 | Interaction substitution to prevent the spread of COVID-19. Wietz et al.[1] carry out modeling to test the principle that deploying recovered people (blue) who carry antibodies will reduce viral transmission. Those people would be returned to society and would be the main interactors (top box). Their interaction with either infected people (green) or vulnerable people (orange) does not result in the propagation of infection. This is in contrast to interactions in which either infected people (bottom) or vulnerable people (middle) are the main interactors.

immune or not. Since there is no or little stigma attached to COVID-19 status, giving up the right to privacy in this case may be a small cost relative to the substantial gains for others. In many countries, this issue is already regulated by legislation related to infection control. However, if a proportion of patients suffer long-term complications as a result of COVID-19, protecting privacy against employers and insurance agencies will be much more important. Whether giving up the right to privacy in a crisis could lead to an erosion of this right to privacy for health-related data forever needs to be considered carefully. For these reasons, the 'recovered-individuals' strategy should not be mandatory, it should last for a short period, and there must be an opt-out mechanism in place.

Furthermore, since a recovered status may provide additional benefits, such as employment, the strategy of allowing only those previously infected back into society can create perverse incentives such that some people might try to become infected in order to go back to work. A 'corona certificate' may also create a new social stratification. Social stratification may be a challenge, but again, since there is currently little known stigma attached, the cost is most likely small relative to the health gains and reduced burdens on everyone.

The second and most important set of ethical issues concerns the distribution of benefits and burdens within this proposed strategy. Scientists, infectious-disease specialists, mathematical modelers and economists all over the world are trying to predict the course of the COVID-19 pandemic and evaluate the best courses of action. For all options, hard trade-offs must be made between the benefits gained in terms of lives saved versus the economic, emotional and social costs of lockdown imposed on everyone: children, students, prisoners, employees, employers, small businesses and large organizations. Decision-makers must therefore make ethical choices under uncertainty, and they must weigh benefits to and burdens on different people. COVID-19 seems to take lives mostly among the elderly and frail with comorbidities, while current measures to curb the pandemic impose a burden on everyone, especially the very young and the worst-off groups in society.

Can it ever be ethical to sum up and weigh the number of life-years saved against the loss of welfare for all others, including those already disadvantaged? Ethics as a discipline and theories of distributive justice in health and society try to answer precisely this question[2–5]. Whatever we do to curb the epidemic, we have to set priorities and rank policies by looking at the pattern of harms and benefits, taking into account our deepest values and choosing options that can gain wide social acceptance. A recent report on priority setting from a group of ethicists published by the World Health Organization provides three guiding principles that are relevant here: choose policies that maximize health in the population, give extra priority to the worst-off, and provide financial risk protection[6]. Making fair choices built on these principles must be based on careful consideration of policy options and should rest on the best available evidence.

Societies over the next few months will face the choice between continued lockdown with huge economic and social costs for everyone, versus lifting restrictions and replacing them with effective public-health interventions, including advice on social distancing, hygiene, protection of high-risk groups and widespread testing. The immunity strategy will have a place in this mix of policies if we find the mathematical models convincing — and this is all we have just now — and it can be combined with an accurate test. Protection with potentially immune people can avert a large number of deaths at a much lower cost for everyone, including the worst-off, relative to the continued lockdown currently being experienced by many countries. If followed up with financial-protection mechanisms, it may be part of the best long-term solution until a vaccine or treatment is developed.

Ultimately, decision-makers must take a stand on whether to embrace the immunity strategy or not. As scientific understanding improves the safety and efficacy of this strategy, and even if there are some valid counterarguments, I foresee wide acceptance of this strategy on ethical grounds: it will maximize lives saved at a lower cost and with burdens more fairly distributed, relative to most other alternative policies. ❐

Ole F. Norheim ✉
Bergen Centre for Ethics and Priority Setting, Department of Global Public Health and Primary Care, University of Bergen, Bergen, Norway.
✉*e-mail:* Ole.Norheim@uib.no

Published online: 07 May 2020
https://doi.org/10.1038/s41591-020-0896-2

References

1. Weitz, J.S. & et al. *Nature Medicine* https://doi.org/10.1038/s41591-020-0895-3 (2020).
2. Daniels, N. *Just Health: Meeting Health Needs Fairly* (Cambridge University Press, Cambridge, 2008).
3. Adler, M. *Measuring Social Welfare: An Introduction* (Oxford University Press, New York, 2019).
4. Parfit, D. *On What Matters* (Oxford University Press, Oxford, 2011).
5. Emanuel, E.J. et al. *N. Engl. J. Med.* https://doi.org/10.1056/NEJMsb2005114 (2020).
6. World Health Organization. *Making Fair Choices on the Path to Universal Health Coverage. Final report of the WHO Consultative Group on Equity and Universal Health Coverage* (World Health Organization, Geneva, 2014).

Competing interests

The author declares no competing interests.