

## Immune evasion means we need a new COVID-19 social contract

The collective benefits of herd immunity have become similar to a mantra in mass vaccination strategies, repeated by governments and researchers. However, the prominence of herd immunity being touted as a solution to the pandemic might be about to change with the emergence of immune evasion, a virological game changer that is as important as the arrival of SARS-CoV-2 variants. Dealing with immune evasion will require a re-evaluation of public health strategies, and the creation of a new, evidence-based social contract.

Studies suggest that the emergence and spread of SARS-CoV-2 variants is correlated with the absence of robust immune protection after first exposure to previous (wild-type) viruses, or even to a vaccine.<sup>1,2</sup> This evolution, associated with the emergence of immune escape mutants, has not only been observed with SARS-CoV-2, but also with other viruses.<sup>3</sup> Such evolution might be assisted by the waning of the immune response and notably the antibody response. The rapid arrival of SARS-CoV-2 variants such as the variants first identified in South Africa and Brazil suggests a so-called natural immune evasion.<sup>2</sup> Also, the dynamics of natural or vaccinal collective immunity in the regions where these variants emerged might have placed substantial pressure on the viral ecosystem, facilitating the emergence of a variant with enhanced transmissibility.

If substantial immune evasion occurs, current vaccines are likely to still offer some benefit to individuals. At the population level, however, they could induce viral selection and escape, making the prospect of achieving herd immunity increasingly remote.

This virological game changer has numerous consequences, not only for vaccines and treatment, but also for prevention and control strategies. The fervently awaited end of this global

health crisis might be continually postponed, as new variants emerge and immune evasion reduces vaccination effectiveness in the short and medium term.

Hence, it is time to abandon fear-based approaches based on seemingly haphazard stop-start generalised confinement as the main response to the pandemic; approaches which expect citizens to wait patiently until intensive care units are re-enforced, full vaccination is achieved, and herd immunity is reached.

Populations have so far been relatively complacent, but their doubts and distrust are visible in protest movements in several countries. The impact of general confinement on entire economies has been devastating, with worse still to come in levels of unemployment and national debt.<sup>4,5</sup> Social and health (including mental health) consequences are also colossal, in particular for the younger generations, despite them being at low risk in terms of morbidity and mortality from SARS-CoV-2 infection.

To best ensure the success of mass vaccination—whatever its hoped-for impact on transmission—and to slow the emergence of new variants, while avoiding general confinement, governments need to integrate and apply available measures in a way that is much more targeted to different generational groups. Different age groups are not affected similarly by the virus; from March to June, 2020, 96% of additional deaths related to COVID-19 in Europe occurred in patients aged older than 70 years.<sup>6,7</sup>

Crucially, the new approach should be based on a social contract that is clear and transparent, rooted in available data, and applied with precision to its range of generational targets. Under this social contract, younger generations could accept the constraint of prevention measures (eg, masks, physical distancing) on the condition that the older and more vulnerable groups adopt not only these measures, but also more specific steps

(eg, voluntary self-isolation according to vulnerability criteria) to reduce their risk of infection. Measures to encourage adherence of vulnerable groups to specific measures must be promoted consistently and enforced fairly. Implementation of such an approach must be done sensitively and in conjunction with the deployment of vaccination across the various population targets, including all generations of society.

Using stop-start general confinement as the main response to the COVID-19 pandemic is no longer feasible. Though attractive to many scientists, and a default measure for political leaders fearing legal liability for slow or indecisive national responses, its use must be revisited, only to be used as a last resort.

We scientists working against COVID-19 must have the courage to address those in power, who bear ultimate responsibility for the policies chosen and their consequences. If this responsibility is shirked or delayed, the inevitable day of reckoning might be terrible.

We are members of the French COVID-19 Scientific Council.

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Lancet Public Health 2021

Published Online  
February 18, 2021  
[https://doi.org/10.1016/S2468-2667\(21\)00036-0](https://doi.org/10.1016/S2468-2667(21)00036-0)

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