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Elimination versus mitigation of SARS-CoV-2 in the presence of effective vaccines



Miquel Oliu-Barton, Bary S R Pradelski, Yann Algan, Michael G Baker, Agnes Binagwaho, Gregory J Dore, Ayman El-Mohandes, Arnaud Fontanet, Andreas Peichl, Viola Priesemann, Guntram B Wolff, Gavin Yamey, Jeffrey V Lazarus



There is increasing evidence that elimination strategies have resulted in better outcomes for public health, the economy, and civil liberties than have mitigation strategies throughout the first year of the COVID-19 pandemic. With vaccines that offer high protection against severe forms of COVID-19, and increasing vaccination coverage, policy makers have had to reassess the trade-offs between different options. The desirability and feasibility of eliminating SARS-CoV-2 compared with other strategies should also be re-evaluated from the perspective of different fields, including epidemiology, public health, and economics. To end the pandemic as soon as possible—be it through elimination or reaching an acceptable endemic level—several key topics have emerged centring around coordination, both locally and internationally, and vaccine distribution. Without coordination it is difficult if not impossible to sustain elimination, which is particularly relevant in highly connected regions, such as Europe. Regarding vaccination, concerns remain with respect to equitable distribution, and the risk of the emergence of new variants of concern. Looking forward, it is crucial to overcome the dichotomy between elimination and mitigation, and to jointly define a long-term objective that can accommodate different political and societal realities.

Introduction

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During the first year of the COVID-19 pandemic, countries adopted a wide range of approaches including elimination, mitigation, or no substantive strategy at all.¹ In a recent Comment in *The Lancet*, we argued that strategies to eliminate SARS-CoV-2 (ie, elimination of community transmission by maximum action to control the spread of the pathogen) produced better outcomes for public health, the economy, and civil liberties during the first year of the pandemic than did mitigation (ie, increased action in a stepwise, targeted way to reduce cases so as not to overwhelm health-care systems).²

The situation has changed. Effective vaccines are being widely deployed in high-income countries, whereas some low-income and middle-income countries (LMICs) are disproportionately unprotected due to limited access. However, increasingly transmissible variants (eg, delta [B.1.617.2]) are proliferating, and the risk of new, immunity-escaping variants is largest when populations are only partially vaccinated.³

It is thus important to reassess the different strategies. Is elimination still preferable, or has the balance shifted towards other strategies, notably mitigation? The COVID-19 pandemic has had implications for almost everyone around the world, and thus needs to be considered from different viewpoints, ranging from virological and epidemiological perspectives, to views from the public health, economics, and political sciences communities. We have gathered scholars from around

the world and from this wide range of fields, who have all actively contributed to the analysis and discussion of the COVID-19 pandemic through scientific publications, public outreach, and policy advice. Each contributor was asked to address the question of whether elimination or mitigation is preferable in the presence of widespread vaccine availability, and what other factors will be key to manage the ongoing pandemic.

The early dichotomy between elimination and mitigation has been largely replaced by nuanced analyses. Although there is consensus that the costs associated with mitigation are substantially reduced by vaccines, there is no agreement over the desirability, and more importantly feasibility, of eliminating SARS-CoV-2, given its high prevalence and transmissibility. Shared concerns and recommendations to leave the pandemic behind centre around the key role played by coordination, and the importance of fast and equitable vaccine distribution.

The first section of this Viewpoint critically discusses why coordination, both locally and internationally, is important and whether it can be expected. The second section examines how vaccines have altered the balance between different interventions and how vaccine equity is lacking. The third section then asks how the pandemic might end and what risks and uncertainties we still face. Finally, the fourth section concludes with an outlook.

The capacity to deliver a coordinated response

Trust in science and government has a key role

Yann Algan (Professor of Economics, Associate Dean of Pre-experience Programs at HEC, France)

Elimination seems to have caused better health and economic outcomes than mitigation.² So why has this strategy not been followed by all countries? To provide a rationale for this puzzle, we need to understand not only the technological and geographical realities faced by governments, but also the social hurdles. The COVID-19

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crisis has not been just a health crisis, but a total social fact (ie, it has had implications on the social, economic, legal, political, and religious spheres) thus requiring a high level of cooperation between citizens, governments, and experts. Research has shown that trust in government⁴ and trust in scientists⁵ have been the main drivers for citizens' compliance with public health measures throughout the COVID-19 pandemic, including vaccination uptake. Using a large-scale, longitudinal, and representative survey in 12 countries from March to December, 2020, combined with experimental data, we have shown that trust levels, and in particular trust in scientists, have changed dramatically for individuals and within countries.⁶ Countries and individuals for whom trust in scientists has declined during the crisis, such as France, have experienced a dramatic erosion of the support for and compliance with non-pharmaceutical interventions during the crisis.⁶ Moreover, distrust in scientists has emerged in countries where the level of trust in government was very low at the initial stage of the pandemic.⁶

Since elimination requires temporary but strict and coercive policies affecting people's behaviour and liberties, countries with low levels of civic solidarity and government trust will have to protect the independence of scientific institutions in the short run to get citizens to adhere to this strategy. This situation is comparable to the central bank independence in the economic literature, in which independence of monetary institutions has been a crucial tool against inflation in a low-trust environment. In the face of future pandemics, the independence of scientific research and communication will be crucial to obtain the support of public opinion for elimination policies and to maintain citizens' resilience in countries where trust in government is low.

International coordination and swift responses remain key to controlling SARS-CoV-2

Viola Priesemann (Physicist, Research Group Leader in Neural Systems Theory, Max Planck Institute for Dynamics and Self-Organization, Germany)

Researchers from a wide range of disciplines have argued that a low incidence of SARS-CoV-2 infection has clear advantages for society, public health, and the economy.^{2,7} The question is how to reach it. At a national level, a core mathematical principle is that pushing the effective reproductive number (R) substantially below 1 reduces case numbers very fast compared with an R-value slightly below 1.⁸ Hence, a quick and decisive response to an outbreak will re-establish control much faster than implementing more lenient strategies to reduce transmission (ie, a so-called lockdown-light), thus allowing for the subsequent lifting of restrictions sooner. Once case numbers are low, health authorities can concentrate all their capacities on stopping the remaining infection chains locally and thereby contribute efficiently to local elimination. But to maintain low incidences in a populous and integrated region such as Europe, for

example, coordination is key.⁹ If all European countries aim for low incidence, then reaching this goal is much easier for each of them. Otherwise, a promising low-incidence strategy in one country is put at risk by shared mobility with regions of high incidence. Mobility is necessary, and it is one of the core pillars of European cohesion.¹⁰ However, during the pandemic, it also enables the virus and its variants to spread, potentially leading to lockdowns, and putting the economy, the prosperity of individuals, and society at risk. Thus, to secure low incidence, either a joint, pan-European control strategy must be adopted, or the mobility of the virus needs to be reduced. A reduction in the mobility of the virus can be achieved by efficient test, trace, and isolate measures, and a test and quarantine strategy for long-distance travellers, rather than enforcing blanket border closures.^{10,11}

Elimination of SARS-CoV-2: an impossible coordination task

Andreas Peichl (Professor of Economics, Director of the IFO Centre for Macroeconomics and Surveys, Germany)

Although elimination is preferable for health, the economy, and civil liberties,^{2,12} optimal policies might differ from one country to another due to context-specific circumstances. In particular, although islands can opt for elimination without coordinating with neighbouring countries, this strategy is much more difficult in an integrated region such as Europe, where a coordinated effort is needed.¹³ The coexistence of countries focused on either elimination or mitigation imposes externalities on countries that have adopted an elimination strategy, because these countries need to impose stricter rules to prevent cross-border entries of the virus than do those with a mitigation strategy, resulting in higher costs. Hence, unilaterally opting for elimination does not seem to be fully preferable to a mitigation strategy (let alone feasible).

Moreover, the waves of infections within highly vaccinated countries reported since July, 2021, and the risk of further virus variants highlight the need for public health measures to prevail even after a large proportion of the population is vaccinated. These measures are especially important for countries with high mobility and many neighbouring countries, making pan-national action necessary.^{7,9} This approach does not seem politically feasible at the moment, given that European countries continue to adopt unilateral public health measures including varying travel restrictions.

Cost-benefit considerations of vaccination

Vaccines are increasingly replacing non-pharmaceutical interventions and could achieve elimination of severe COVID-19

Arnaud Fontanet (Professor of Epidemiology and Public Health, Director of the Epidemiology of Emerging Diseases Unit at the Institut Pasteur, France)

Highly efficacious vaccines have raised expectations regarding the feasibility of elimination, while gradually

shifting the weight of epidemic control from non-pharmaceutical interventions to vaccines and naturally acquired protection. This shift is expressed by the symmetric role played by p_c , the relative reduction in transmission rates due to non-pharmaceutical interventions, and p_i , the proportion of non-transmitting immune individuals, in the formula $R=(1-p_c)\times(1-p_i)\times R_0$, in which R is the effective reproductive number and R_0 is the reproduction number in the absence of control measures in a fully susceptible population.¹⁴ In England, 92% of adults had SARS-CoV-2 antibodies during the July, 2021, survey conducted by the Office for National Statistics,¹⁵ showing that the target is in reach, provided vaccines are safe enough for children to benefit from them.

However, although vaccines are very effective against severe forms of COVID-19, the accumulating evidence of waning vaccine effectiveness against infection has changed the expectations towards the elimination of severe COVID-19, rather than elimination of SARS-CoV-2 infection. A bumpy road to elimination is expected due to the combination of waning immunity, re-vaccination or re-infection, new variant emergence, and vaccine improvement. Non-pharmaceutical interventions will gradually become less strict, and provided that past immunity continues to protect against severe forms of disease the overall impact of epidemic surges on the health system will gradually decrease. At a global level, monitoring of variants and distributing vaccines equitably around the world will be required to both protect the global community and prevent the emergence of new variants.¹⁶

The benefits of increasing vaccination capacity far outweigh the costs

Guntram B Wolff (Economist, Director of Bruegel [Brussels European and Global Economic Laboratory], Belgium)

Vaccination is an effective way to reduce the number of cases, helping to control the pandemic and substantially reducing human suffering. However, the reality is that only a small proportion of the world's population is highly vaccinated.

A key question for global public health is, therefore, whether vaccination can be accelerated globally, and access be broadened to susceptible populations within countries and across the world. Access to vaccines is unequal both within countries and across countries. In advanced economies, vaccination rates correlate positively with income levels and education, calling for additional campaigns to increase the take-up of vaccine offers.¹⁷ With regard to LMICs, providing adequate financing is a crucial part of the answer, as we argued in a report to the G20 finance ministers.¹⁸ The return on a global vaccine roll-out would be high: the International Monetary Fund estimates that US\$50 billion would be sufficient to vaccinate 70% of global population by mid-2022, and the benefit to the global economy could be US\$9 trillion.¹⁹ Increasing and regionally diversifying production capacities for medical counter-measures will be equally important.

However, COVID-19 could become endemic at a high level of virus circulation and morbidity.²⁰ Further, levels of infectiousness of vaccinated individuals might be too high for even a fully vaccinated population to eliminate the virus through herd immunity.²¹ Thus, contention measures such as non-pharmaceutical interventions will continue to play an important role in managing the pandemic, including regular and representative testing strategies combined with preventive measures and even targeted lockdowns.

Without equitable vaccination, the cost of elimination outweighs its benefits

Agnes Binagwaho (Paediatrician, Vice Chancellor of the University of Global Health Equity, Rwanda)

Given that the ultimate goal of public health measures is to improve health outcomes and wellbeing, strategies adopted against any health threat need to maximise the likelihood of achieving this aim. As we hope to reduce suffering and deaths from COVID-19, the most obvious choice would be elimination. However, regardless of the public health measures enforced within a country, lack of coordination at the global level will introduce new cases into a country, as has been evidenced multiple times; the spike in cases in June, 2021, in Australia was one such consequence.²² Moreover, elimination requires equitable global vaccination. However, as of August, 2021, only 1.1% of the population in low-income countries had been vaccinated, and many countries cannot receive all vaccines ordered and paid for due to huge global needs and insufficient production capacities.²³ Furthermore, prolonged lockdowns endanger the livelihoods of the most vulnerable individuals—those who lack savings and work hand to mouth especially within the informal sector. Poverty is expected to rise for the first time in 20 years,²⁴ reducing the living standard of vulnerable people, threatening access to health care, and thereby worsening health outcomes. Thus, since elimination is not feasible now, we need to do our best to mitigate the virus's adverse effects. Strategies to control the spread of the virus and minimise strain on health systems include contact tracing, surveillance, and clear and consistent communication, as well as prevention and control measures such as physical distancing, mask wearing, and separate COVID-19 treatment wards. These strategies were adopted by Rwanda to control the spread of the virus and mitigate its impact, leading Rwanda to be ranked seventh in the world for its ability to manage the pandemic by the Lowy Institute.²⁵

Vaccines shift the balance and elimination is no longer preferable

Gregory J Dore (Infectious Diseases Physician, Head of the Viral Hepatitis Clinical Research Program, Kirby Institute, UNSW Sydney, Australia)

With the prospect of high-level immunity from severe COVID-19 disease, vaccination has shifted the balance in

the equation of whether pursuing elimination delivers enhanced benefits compared with other approaches. First, the recent resurgence of SARS-CoV-2 cases in many elimination strongholds, particularly in the Asia-Pacific region, demonstrates the difficulty in maintaining elimination as more infectious variants emerge. Second, more infectious variants such as the delta variant make complete herd immunity unlikely in any setting. Third, longer-term economic benefits will rely upon international mobility, with the benefits Australia gains from international students a prime example. Finally, the burden on human rights necessary to maintain elimination—justifiable on the basis of public health benefits—will become greater the longer this strategy is pursued.

Given this changing dynamic in the era of vaccination, what should key goals be at country and global levels? All countries should pursue high vaccination coverage. The incredible effectiveness of available vaccines against severe disease and hospitalisation, even in the setting of emergent variants of concern, makes this goal feasible. High vaccine coverage will also provide herd immunity effects, reducing the spread of SARS-CoV-2 in the community despite the false promise of complete herd immunity. In parallel with this country-level goal—being rapidly pursued in high-income countries—efforts for global vaccine access must be enhanced. It would be immoral and compromise global health, due to the risk of new variants, if already privileged countries pursue elimination through frequent vaccine boosters to reach infection immunity at the expense of an initial vaccination roll-out in LMICs to confer protection from severe disease. SARS-CoV-2 can be rendered an endemic low-burden infection, but only through concerted global efforts.

The final stages of the pandemic

Progressive elimination is feasible but might not be optimal without improved vaccines

Michael G Baker (Professor of Public Health, Director of the Health Environment Infection Research Unit, University of Otago, New Zealand)

During the first year of the COVID-19 pandemic, elimination approaches protected more than 20% of the world's populations across multiple jurisdictions including China, Hong Kong, Taiwan, Singapore, Australia, and New Zealand. Although these countries had setbacks in the form of outbreaks, they were mostly able to return to elimination status—ie, absence of community transmission—within a few months. But although elimination appears to be the best initial response for emerging pandemics, whether it is optimal in the longer term once populations are highly vaccinated with effective vaccines is not clear.¹² At that stage there is a choice between progressive elimination—ie, progressively increasing the number of regions that reach an elimination status—as used with polio and measles, or mitigation as used with endemic diseases such as seasonal influenza for which vaccines have relatively low effectiveness.

There is insufficient evidence to make a definitive decision on an optimal long-term strategy for COVID-19. Such a decision will depend on the feasibility and desirability of progressive elimination across the globe. We know this approach is feasible as it has been successfully used in the Asia-Pacific region. It will also become more sustainable with increasing vaccine coverage and improvements in the effectiveness of vaccines, and potentially antivirals, at interrupting virus transmission.

However, the desirability of progressive elimination depends on balancing the benefits against the costs. Major benefits include prevention of acute illness, death, and long-term disability from long COVID. Rapidly reducing global infections also seems the best way to limit emergence of more dangerous virus variants.¹⁶ This effort will need global mobilisation of resources as envisioned in the review of the COVID-19 pandemic response by the Independent Panel for Pandemic Preparedness and Response.²⁶ Otherwise the opportunity cost of eliminating COVID-19 might be too high for LMICs.

On balance, there is a case for progressive elimination of COVID-19 across the globe, particularly if vaccine and antiviral effectiveness can be improved. Even if success is not guaranteed, the health infrastructure to support this programme would provide much-needed capacity building to help prevent the next pandemic.²⁶

Elimination versus mitigation is a false dichotomy

Gavin Yamey (Professor of Global Health and Public Policy, Director of the Center for Policy Impact in Global Health, Duke University, NC, USA)

The USA is still in the grip of a fourth wave of COVID-19, driven by the highly transmissible delta variant. As of Oct 3, 2021, there are still about 100 000 new cases daily.²⁷ Many areas with low vaccination coverage are seeing high rates of hospitalisations and deaths, and only 55% of the population is fully vaccinated.²⁷ This situation shows just how challenging it would be to reach elimination within the USA. Even if achieved, this state would need to be maintained through aggressive detection of every single case and managed isolation of all imported cases. Clearly, it would be a very long road for the USA to get there—indeed, I do not believe elimination would be feasible.

But as argued before, “none of this should be cause for fatalism”.²⁸ Cases can be driven down by pushing up vaccination coverage, including in adolescents and young people, and through a range of other interventions such as community-wide mask wearing and workplace and school safety measures (including improved ventilation).²⁹ Vaccination dramatically reduces the chances of severe illness or death and reduces the transmission of SARS-CoV-2 to others. With a concerted nationwide effort, involving comprehensive and integrated public health measures, the USA should be able to achieve very low levels of infection and illness (ie, low endemicity).

Some nations have tried to pursue elimination. Like many countries, the US Government has not explicitly

stated its so-called end game. But in some ways it is a false dichotomy to argue that we must choose either elimination or mitigation. The tools used by nations that have tried to achieve local elimination—test and trace, case isolation, quarantining of exposed people, border management, aggressive outbreak control, and now vaccination—are the same tools that a nation can use to prevent transmission and reach low endemicity. In discussions of elimination and endemicity, “thinking that we need to choose one or the other is a mistake that can impede public understanding of how to manage the pandemic”.²⁸

Protecting children from COVID-19 needs to be considered

Ayman El-Mohandes (Paediatrician and Public Health Academic, Dean of the City University of New York Graduate School of Public Health and Health Policy, NY, USA)

Among the relief of social re-opening in the USA associated with vaccination roll-out, we must not ignore the fact that COVID-19 and its variants were raging among children during the summer of 2021. Children made up 19% of new COVID-19 cases in the USA, yet, as of September, 2021, only 34% of American parents with children aged 5–11 years said they will get them vaccinated when able, 24% say they will not vaccinate their children, 32% are waiting for more information, and 7% will get them vaccinated if required by the children’s school.¹⁷

With the goal to eliminate the virus as the only real hope to avoid another resurgence and economic downturn, are children going to be a new threat to reaching such a goal? An estimated 16–23% of adults in the USA have expressed resistance to the COVID-19 vaccine, but it seems that resistance will be much higher among parents of children.¹⁷ The original misconception of children being protected from serious COVID-19 illness is being refuted by recent outbreaks, and the role they could play, even if asymptomatic, in propagating the virus and acting as a vehicle for new mutations, should be considered very seriously. Vaccinating children and educating their parents of its necessity is an essential step towards eliminating the virus in the USA and globally.

COVID-19: the outlook

Miquel Oliu-Barton, Bary S R Pradelski, Jeffrey V Lazarus
The availability of effective vaccines provides an additional, potent tool to exit the pandemic, allowing the progressive reduction of non-pharmaceutical interventions while maintaining low incidence. This change in the state of play has led to varying positions regarding the desirability and feasibility of elimination among the authors. First, strict public health interventions such as school closures, curfews, or lockdowns might no longer be justified as the risk attached to contracting COVID-19 has been starkly reduced by vaccines. Second, countries’ persistent efforts to control the virus have led to an increasing fatigue among the population.³⁰ Thus, it is increasingly difficult to

gain the necessary public support to implement ambitious objectives, notably in countries where trust in scientific institutions and government is low or has deteriorated throughout the pandemic. In addition, the lack of coordination between countries might render an effective elimination strategy infeasible due to the excessive cost of maintaining low incidence when surrounded by countries that do not follow the same approach. Some contributors even argue that the shortcoming of international solidarity—particular with regards to inequitable vaccine distribution—creates a prohibitively high burden for LMICs to pursue an elimination strategy.

With the experience thus far, and building on the expert deliberation, we believe that it is unlikely that a common global or even regional strategy will be agreed upon soon. Thanks to vaccines, immunity from infection, non-pharmaceutical interventions, and possibly treatment, countries might reach acceptable levels of endemicity in the future, potentially sustained by booster doses for the most clinically vulnerable individuals. Reminiscent of measles, some countries might at times reach an elimination status. Nevertheless, without wide-reaching coordination, we might face years of increased morbidity and mortality due to not only SARS-CoV-2 itself, but also the resulting economic instability and increased inequalities. At a minimum, the international community should ensure faster global vaccine distribution and agree on non-discriminatory conditions for travel, including a harmonised recognition of vaccines and tests.

Contributors

MO-B, BSRP, and JVL wrote the first draft of the summary, and the introduction and outlook sections. YA, VP, AP, AF, GBW, AB, GJD, MGB, GY, and AE-M all wrote individual sections on coordination, vaccination, or the final stages of the pandemic. All authors contributed to the refinement of the final version and agreed to the decision to submit for publication.

Declaration of interests

MGB is a member of the New Zealand Ministry of Health’s COVID-19 technical advisory group and took a leading role in formulating New Zealand’s elimination strategy. AF is a member of the French COVID-19 Scientific Council, and a member of the French COVID-19 Vaccine Strategy Committee. GBW is a member of the G20 High Level Independent Panel on Financing the Global Commons for Pandemic Preparedness and Response. JVL is a member of the *Lancet* COVID-19 Commission Public Health Taskforce. All other authors declare no competing interests.

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