Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

6 Dowling DJ. Recent advances in the discovery and delivery of TLR7/8 agonists as vaccine adjuvants. *Immunohorizons* 2018; **2:** 185–97.
7 Xia S, Duan K, Zhang Y, et al. Effect of an inactivated vaccine against SARS-CoV-2 on safety and immunogenicity outcomes: interim analysis of 2 randomized clinical trials. *JAMA* 2020; **324:** 951–60.
8 Zhang Y, Zeng G, Pan H, et al. Safety, tolerability, and immunogenicity of an inactivated SARS-CoV-2 vaccine in healthy adults aged 18–59 years: a randomised, double-blind, placebo-controlled, phase 1/2 clinical trial. *Lancet Infect Dis* 2020; **21:** 181–92.

Navigating post-vaccine COVID-19 futures in the health and economic context

Published **Online** March 18, 2021 https://doi.org/10.1016/S1473-3099(21)00126-2

See **Articles** page 962

The economic costs of the pandemic have been high, and vaccines offer an exit strategy. In *The Lancet Infectious Diseases*, Frank Sandmann and colleagues model a range of future scenarios in the UK depending on vaccine efficacy, duration of protection, and use of physical distancing, and the respective health and economic impacts of these scenarios.[1] This study is the first full economic evaluation of different vaccination scenarios compared with an unmitigated epidemic, with varying degrees of physical distancing. It shows that lockdowns and physical distancing reduce economic losses, which refutes the false perceived dichotomy of protecting the economy at the expense of pandemic control. The authors also show the health and economic benefits of mass vaccination of adults in the UK.

In the best-case vaccination scenario, with 95% vaccine efficacy and 3-year protection against infection, requirements for increased physical distancing (ie, reducing contacts by 90% outside of the home) are minimal. In the worst-case scenario, with 50% vaccine efficacy and 45-week protection against disease, but not infection, recurrent epidemics will occur with ongoing need for increased physical distancing.[1] Although the study considers hypothetical scenarios of higher and lower vaccine efficacy, there is already wide variation in efficacy of available vaccines. Phase 3 trials show 63–95% efficacy against symptomatic infection, with the highest efficacy shown for mRNA vaccines.[2–4] The ChAdOx1 nCoV-19 vaccine trial is the only one to date presenting data on prevention of asymptomatic infection, and efficacy is much lower for this endpoint.[2]

Economic losses are substantially less when high-efficacy vaccines are used, whereas lower-efficacy vaccines with short duration of protection will provide marginal benefits compared with no vaccination.[1] The best-case vaccination scenario will result in substantial economic gains compared with no vaccination, but the worst-case scenario might not, depending on vaccine costs and the wider societal cost of ongoing lockdowns. Duration of vaccine-induced immunity is also an important factor that affects the economic value of vaccination, but vaccine-induced protection could be extended by boosters. Therefore, the most influential factor is the efficacy of the vaccines being used, and thus vaccine choices matter enormously for economic recovery. Governments should grasp the importance of procuring the highest-efficacy vaccines as the route to achieving a best-case economic scenario. In countries that rely on lower-efficacy vaccines, be it by choice or lack thereof, the long-term health and economic burden might be similar to if no vaccine were used, if a very high threshold (eg, 100 cases per 100 000 population) were used to trigger physical distancing measures.

The study shows that if natural immunity is long lasting, the economic value of immunisation decreases.[1] However, the mRNA vaccines result in higher neutralising antibody titres than in convalescent sera.[5] Furthermore, in Manaus, Brazil, where 76% of the population had been infected by October, 2020—higher than the hypothesised herd immunity threshold—a large second wave has since occurred.[6] In addition, variants of concern show evidence of vaccine escape.[7] The South African Government paused the planned rollout of the ChAdOx1 nCoV-19 vaccine because the efficacy against the B1.351 variant was found to be 10·4%.[8] All vaccines can be matched to emergent variants, but we are likely to face a situation of regular revision of vaccine antigens, which will add to future cost.

The variants of concern also pose a challenge because they are more contagious. If they become dominant, this will require higher vaccine coverage and higher-efficacy vaccines, making a compelling case for use of the highest-efficacy vaccines at the outset to avoid

an intermediate or worst-case scenario and to reduce selective pressure for emergence of more variants.

Sandmann and colleagues' study assumes high vaccine uptake in all scenarios, but in many countries, vaccine supply might be limited, so targeted vaccine use could be needed initially. Vaccine hesitancy and inequity in distribution and access might also contribute to a patchy uptake. The most common approach for use of limited supply is age-based or risk-based targeting, but ring vaccination should also be considered. Many vaccines are effective as post-exposure prophylaxis (PEP), including those for measles, hepatitis A, and smallpox, and the long incubation period of SARS-CoV-2 means vaccines might work as PEP.[9] Sandmann and colleagues show that if the start of the vaccination programme is delayed, outcomes are worse. A slow trickle in uptake will also lead to worse health and economic outcomes than rapid uptake.[9] Israel achieved rapid, early mass vaccination in less than 2 months with an mRNA vaccine, and showed a measurable impact of vaccination on pandemic dynamics.[10]

The health and economic burden of living with COVID-19 in the intermediate and worst-case scenarios creates a double disadvantage of high disease burden and high economic cost of ongoing physical distancing measures. While we do not yet know if herd immunity is possible, only the use of high-efficacy vaccines (at least 80–90% against all infection) can possibly achieve it, especially if children can also be vaccinated.[9] Sandmann and colleagues' research provides a rational pathway to aiming for a best-case health and economic scenario.

I report grants from Sanofi and other support from Seqirus, AstraZeneca Australia, and Janssen, outside of the submitted work.

C Raina MacIntyre
r.macintyre@unsw.edu.au

The Biosecurity Program, The Kirby Institute, The University of New South Wales, Sydney, NSW 2052, Australia

1 Sandmann F, Davies NG, Vassall A, Edmunds WJ, Jit M. The potential health and economic value of SARS-CoV-2 vaccination alongside physical distancing in the UK: a transmission model-based future scenario analysis and economic evaluation. *Lancet Infect Dis* 2021; published online March 18. https://doi.org/10.1016/S1473-3099(21)00079-7.

2 Voysey M, Clemens SAC, Madhi SA, et al. Single-dose administration and the influence of the timing of the booster dose on immunogenicity and efficacy of ChAdOx1 nCoV-19 (AZD1222) vaccine: a pooled analysis of four randomised trials. *Lancet* 2021; **397:** 881–91.

3 Polack FP, Thomas SJ, Kitchin N, et al. Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine. *N Engl J Med* 2020; **383:** 2603–15.

4 Baden LR, El Sahly HM, Essink B, et al. Efficacy and safety of the mRNA-1273 SARS-CoV-2 vaccine. *N Engl J Med* 2020; **384:** 403–16.

5 Walsh EE, Frenck RW Jr, Falsey AR, et al. Safety and immunogenicity of two RNA-based Covid-19 vaccine candidates. *N Engl J Med* 2020; **383:** 2439–50.

6 Sabino C, Buss LF, Carvalho MPS, et al. Resurgence of COVID-19 in Manaus, Brazil, despite high seroprevalence. *Lancet* 2021; **397:** 452–55.

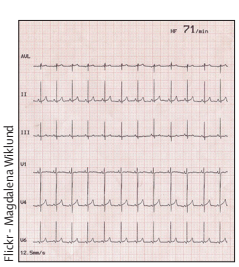
7 Xie X, Liu Y, Liu J, et al. Neutralization of SARS-CoV-2 spike 69/70 deletion, E484K and N501Y variants by BNT162b2 vaccine-elicited sera. *Nature* 2021; published online Feb 8. https://doi.org/10.1038/s41591-021-01270-4.

8 Madhi SA, Baillie VL, Cutland CL, et al. Safety and efficacy of the ChAdOx1 nCoV-19 (AZD1222) Covid-19 vaccine against the B.1.351 variant in South Africa. *medRxiv* 2021; published online Feb 12. https://doi.org/10.1101/2021.02.10.21251247 (preprint).

9 MacIntyre CR, Costantino V, Trent MJ. Modelling of COVID-19 vaccination strategies and herd immunity, in scenarios of limited and full vaccine supply in NSW, Australia. *medRxiv* 2020; published online Dec 19. https://doi.org/10.1101/2020.12.15.20248278 (preprint).

10 Rossman H, Shilo S, Meir T, Gorfine M, Shalit U, Segal E. Patterns of COVID-19 pandemic dynamics following deployment of a broad national immunization program. *medRxiv* 2021; published online Feb 9. https://doi.org/10.1101/2021.02.08.21251325 (preprint).

Cardiac safety of multidrug-resistant tuberculosis treatment: moving towards individualised monitoring



Flickr - Magdalena Wiklund

Published **Online** February 12, 2021 https://doi.org/10.1016/S1473-3099(20)30836-7

See **Articles** page 975

We are not alone in welcoming the study by Kelly E Dooley and colleagues[1] that sheds light on the QT prolonging effects of the combination of bedaquiline and delamanid, two key drugs for the treatment of multidrug-resistant or rifampicin-resistant tuberculosis. Clinicians treating multidrug-resistant or rifampicin-resistant tuberculosis worldwide only recently started losing sleep over the fear of QT interval prolongation, a well-known adverse event of many drugs. A heart rate-corrected QT interval (QTc) of 500 ms or more increases the risk of potentially fatal ventricular arrhythmias, including torsade de pointes.[2] Despite the frequent, long-term use of QT interval-prolonging drugs, including moxifloxacin, which is used as a positive control in thorough QT studies,[3] ECG monitoring became routine during multidrug or rifampicin-resistant tuberculosis treatment only after the first phase 2 trials showed QT prolongation during treatment with bedaquiline and delamanid. These concerns initially led WHO to formulate conservative recommendations regarding their use in combination.[4] Many of these fears have since been dispelled by increasing evidence.[5–7] In particular, WHO guidelines, based on a review of data done in 2019 including the results of the study by