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.

course during an era in which physicians and health systems around the world are facing a new surge and emergence of new SARS-CoV-2 variants. Establishing whether these identified phenotypes could be helpful in clinical practice and how they could help us promote adequate management strategies in a rapidly changing epidemic will undoubtedly be the next important step.

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Risking further COVID-19 waves despite vaccination

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The sudden outbreak and global spread of COVID-19 took the world by surprise. Policy makers started to work side-by-side with theoreticians, as there were and still are many unknowns, especially regarding properties of virus variants, and the subsequent future development of the pandemic. In times of uncertainty, mathematical models have shed light on the evolution of the pandemic to the best of current scientific knowledge. In *The Lancet Infectious Diseases*, Sam Moore and colleagues[1] present a model to explore the effects of vaccination and the potential danger of lifting restrictions too early in the UK.

With vaccination progressing, we all want restrictions to be lifted as soon as possible. Lifting them only slowly is like being forced to eat a chocolate cake slowly, after not having any for months. So why should one be cautious? It is intuitively clear that if restrictions are lifted too early then another pandemic wave might strike and affect those who have not yet been vaccinated. Furthermore, even some of those individuals recently vaccinated might not yet be immunised by the time of lifting restrictions and thus remain partly susceptible. Risking the health and lives of such individuals would be unethical.

Can Moore and colleagues tell us when precisely we can have the chocolate cake? Unfortunately, no. There are too many unknown factors that might affect the transmission dynamics of SARS-CoV-2 during the vaccination campaign and thereafter. Including such uncertainties is at the heart of designing a good epidemiological model. Moore and colleagues found that the still unknown level of vaccine-induced protection against infection is crucial to the timing and effect of further waves on viral spread. Furthermore, they quantify how low vaccine uptake, together with a lifting of non-pharmaceutical interventions (NPIs), will induce further waves of hospitalisations and deaths, most of which could be prevented. They also show that only in a best-case scenario of high vaccine uptake (85% protection against infection and high efficacy against severe symptoms) could a gradual relaxation of NPIs be allowed without deaths surging over 500 per day.

Moore and colleagues did not explicitly include variants that escape the immune response (either post-infection or induced by vaccines).[1] This approach does not change their general findings and is straightforward to discuss. Escape variants[2] might have a devastating effect; at worst, they could force us to start the vaccination programme from scratch, including the necessity to re-enforce strong restrictions. If escape

variants surge during a new wave of infections, they could hit already overburdened health-care systems, and there will be little capacity to react. Hence, avoiding such a wave is critical to mitigate the impact of potential escape variants.

Is it necessary, then, to have either almost endless restrictions that bring their own detrimental health and economic effects, or accept the surge of another pandemic wave? We would like to propose a midpoint: eating the chocolate cake sufficiently slowly. Lifting restrictions at pace with vaccination allows for increasingly more contact without risking another surge of infections.[3] Alternatively, substantial restrictions would need to be installed at a later point when hospitals are at capacity again. This approach would entail taking the chocolate cake away again after only being allowed one bite. In fact, the progress of releasing restrictions, whether at low or high case numbers, is mainly determined by the pace of vaccination, not on lower or higher levels of infections.[3] The advantage of avoiding another pandemic wave is clear: less so-called long COVID-19, less quarantine, fewer deaths, and reducing the impact of the pandemic on societies and economies.[4] Finally, more infections mean more scope for the spread and evolution of escape variants, which risk a major setback for any vaccination strategy, so avoiding this eventuality will be crucial.

Overall compliance with NPIs has decreased worldwide because of behavioural fatigue.[5] Despite this fatigue, governments and researchers now more than ever should stress the advantages of keeping case numbers low,[5,6] the benefits of high vaccination uptake, and the responsibility that the vaccinated population has to those who are not yet protected, but who are largely expected to keep economies going. As most countries have been much slower at vaccinating their populations than the UK, the country can best support the fight against COVID-19 worldwide by keeping its own national case numbers low. The more progress in vaccination that a country has achieved, the easier it is to maintain low case numbers. This opportunity should be seized.

In every country, we have to decide how to use the protection of vaccines wisely to prevent further waves of SARS-CoV-2. Waves that hit those who have not been offered a vaccine will spread to unprotected people and unprotected countries, which could lead to further evolution of escape variants. Thus, let us enjoy the chocolate cake, responsibly.

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Inactivated COVID-19 vaccines to make a global impact

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Many inactivated vaccines against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) are being tested at various clinical stages. Most of these vaccines are formulated with aluminium hydroxide, and one, VLA-2001, has two adjuvants, CpG oligodeoxynucleotides and aluminium hydroxide.[1,2] Because of the ease of production and scale-up and relatively low cost, inactivated vaccines can capture a sizeable portion of the SARS-CoV-2 vaccine landscape. Inactivated vaccines are well established and can provide advantages in a variety of distinct populations, including those with degrees of immune senescence. Given that the risk of more severe COVID-19 increases with age, the clinical evaluation of the responses of older adults to vaccines is essential.[3]

In *The Lancet Infectious Diseases*, Zhiwei Wu and colleagues[4] report the results of a randomised, double-blind, placebo-controlled phase 1/2 clinical trial evaluating an inactivated COVID-19 vaccine, CoronaVac, in healthy adults aged 60 years and older (72 in