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Publish evidence to support changing vaccine strategies

Countries deviating from coronavirus vaccine schedules set out by drug companies must be more transparent — to maintain public trust and to share the benefits of their knowledge.

Coronavirus vaccines have arrived, and many countries have started their vaccination campaigns. The authorities face a race against time as infections and deaths from COVID-19 continue to rise in many parts of the world. It was with this in mind that the United Kingdom's independent vaccine advisers recommended giving as many people as possible the first of the two vaccine doses required (go.nature.com/2mz9i83). That will mean delaying the delivery of each person's second, 'booster' dose from three weeks after the first one to as much as three months later.

The decision, by the Joint Committee on Vaccination and Immunisation (JCVI), was announced on 30 December (see page 182) and endorsed by the chief medical officers of all four UK regions, where, at the time of writing, a new coronavirus variant is contributing to a sharp rise in deaths and COVID-19 infections (see page 177).

The decision so far applies to two of the three vaccines now approved for use in the United Kingdom — those made by Pfizer–BioNTech and the University of Oxford–AstraZeneca. In clinical trials, each was tested using two doses, given at least three weeks apart. The United Kingdom's decision to extend the gap to three months has divided researchers. Pfizer–BioNTech say they do not have evidence of what happens to immunity beyond 21 days after the first dose. The World Health Organization recommends that the second dose of this vaccine be given no later than six weeks after the first, on the basis of available clinical-trial data.

Other countries are studying the United Kingdom's decision closely. There are reports that US president-elect Joe Biden's COVID-19 advisers might recommend that the country provides the first dose of vaccine to as many people as possible, as quickly as possible. This strategy counts on projections that further supplies will arrive in time for boosters to be given on schedule.

Proponents argue that offering a greater number of people some protection will save more lives overall than will giving more protection to fewer people. Others say that an emergency is not the time to alter vaccination protocols that have been established through clinical trials and confirmed by regulators.

The JCVI said in a statement on 6 January: "With most vaccines an extended interval between the prime and booster doses leads to a better immune response to the booster dose." It has provided a summary explanation for its decision, and the minutes of its meetings (go.nature.com/39nuqhy), but has not yet published the data or a more detailed account of its reasoning. It must do so urgently.

> **"Scientific advice must be based on published and easily accessible evidence."**

The JCVI says in its statement that, according to published results, the Pfizer–BioNTech vaccine was 52.4% effective during the three-week period between the two doses. It adds that most vaccine failures recorded during this period occurred shortly after vaccination, and that the short-term protection provided by the first dose seems to be very high from day ten after vaccination. For the AstraZeneca vaccine, it says that vaccine efficacy from 22 days after the first dose was 73%.

The JCVI adds that: "Protective immunity from the first dose likely lasts for a duration of 12 weeks." But it has not published evidence to support this. Moreover, some are concerned that relatively weak immune responses induced by a single dose of vaccine could encourage the emergence of new variants of the virus — and that such variants could be more resistant to immune responses, particularly those generated by vaccines, increasing the risk that these variants could become a global threat. The JCVI has provided no assessment of the risks of such vaccine-resistant variants emerging, nor guidance as to how these strains or fading protection against COVID-19 should be monitored.

But there are reasons to think that there is only a small threat of a vaccine-resistant variant emerging as a result of postponing a second vaccine dose by a few weeks. Natural coronavirus infection already generates a range of immune responses, and the virus, which mutates relatively slowly, would struggle to evade the complex antibody responses generated by vaccines.

Researchers, as well as scientific and medical advisers, should lose no time in monitoring the effects of a change to the dosing schedule so that any benefits or risks can quickly be factored into nations' dosing strategies. This means following the effect on infections, and studying the duration of immunity in those who have received only one dose of a vaccine. Careful surveillance of coronavirus variants will also be required, to keep an eye out for the emergence of any that might weaken vaccine efficacy.

Scientists need to study any unintended consequences of the new strategy — for example, whether, during a lengthy gap between doses, people are more likely to begin resuming pre-pandemic lifestyles, which they should not be doing. It will also be important to study the effect on public trust in vaccination after a sudden change to regulatory guidance. Regulators and scientific advisers need to be ready to be transparent about those consequences with the rest of the world. At the same time, if the strategy works well, then relevant insights should be passed on so that others can benefit.

Ultimately, there should be enough vaccine supplies to go round, so, in the long term, there will be no need to lengthen the gap between doses. But until there are sufficient supplies, scientific advice must be based on published and easily accessible evidence. It's an essential principle of the science–government relationship.

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The United Kingdom's strategy has been widely reported worldwide, and other countries are considering whether it is both safe and efficacious to recommend this approach as more vaccines are rolled out. Transparency is essential for safety and efficacy – and for public confidence, particularly given that relatively large numbers of people are hesitant about receiving vaccines.

The world's vaccine plan must succeed

An initiative to secure vaccines for the most vulnerable populations must be better supported so that it can get back on track.

In a significant moment for the fight against the coronavirus, international funders came together in early June and pooled funding towards an ambitious undertaking: to buy enough COVID vaccines to immunize the 20% of people most vulnerable to the virus worldwide, such as health-care workers and the elderly. High- and middle-income countries would pay into the fund and receive a share of the vaccines procured, and poorer countries would receive vaccines free of charge. But the project, a pioneering effort called COVAX, is struggling to meet expectations.

High-income countries have been buying up large tranches of the current and future vaccine doses directly from vaccine suppliers. Middle-income countries are also negotiating their own supplies. This has left relatively few vaccines for COVAX, which needs to deliver 2 billion doses by the end of this year to reach its goal. COVAX has confirmed purchases for 1.07 billion doses and options reserved on at least 900 million more, according to researchers.

But, as the director-general of the World Health Organization (WHO), Tedros Adhanom Ghebreyesus, said in an impassioned plea last week, COVAX is competing for these supplies. Some people in the lowest-income countries might need to wait until at least 2022 to get their vaccines.

Last August, Sweden's prime minister, Stefan Löfven, declared: "This cannot be a race with a few winners." But nations are not only competing, they are in the most unequal of races. It must now be a priority for governments everywhere to get the COVAX project back on track – both to help the world's most vulnerable people and as a means to control the pandemic.

Governments no doubt think they are acting in the best interests of their people by negotiating directly with suppliers. But, by competing in this way, they are sowing panic and undermining the principle of mutuality that underpins COVAX, which they initially agreed to back, and which researchers argue could help to bring a faster end to the pandemic.

> **"Until the virus is controlled everywhere, every nation is at risk of further outbreaks."**

COVAX was conceived to prevent what happened with vaccines for pandemic influenza A (H1N1) in 2009, when richer countries monopolized vaccine supplies by doing one-on-one deals with suppliers. At the start of the coronavirus pandemic, COVAX's founders were convinced that a better system could be found to ensure more-equitable access to vaccines, especially for the world's most vulnerable populations.

At one level, COVAX has had a strong start. It has 190 member countries. It has so far raised just over US$4 billion of its $6.8-billion funding target for 2021. COVAX says it has enough vaccines in the pipeline to achieve its target of providing low-income countries with access to 1.3 billion doses, free of charge, by the end of this year. Nothing like this has been attempted before, says Seth Berkley, the chief executive of Gavi, an organization that funds vaccine provision for low-income countries and which helped to create COVAX, together with the WHO and the Coalition for Epidemic Preparedness Innovations, a consortium of funders, companies, governments and researchers involved in vaccine development.

But one reason why COVAX might not be able to reach the target set out in its timetable is its funding mechanism, called the COVAX Facility. This allows countries to make their own purchases – as many have been doing – at the same time as putting money into COVAX. Pressure groups are also concerned about a lack of transparency on pricing. Nations buying their vaccines through COVAX are placing orders without knowing precisely how much they will need to pay.

At present, says Andrea Taylor, a researcher at Duke University in North Carolina who is studying COVID vaccine manufacturing capacity around the world, it looks likely that in 2021 COVAX will deliver around 570 million doses, which is between one-quarter and one-third of its total target for the year. COVAX disagrees, and says it has many more deals with suppliers in the pipeline.

However, in an effort to help steady the ship, COVAX launched a scheme in mid-December by which countries can donate surplus vaccine doses. COVAX says some of these donations could be imminent, but, with vaccination programmes just starting, it is not clear at what point countries will be willing to let go of excess supplies. The WHO is urging nations to release any surplus stock immediately.

In the middle of a pandemic, perhaps it was too much to expect countries to prioritize a collective scheme over securing their own supplies. Even the European Union's collective vaccine-procurement scheme is struggling to prevent individual member states from seeking to do separate deals to obtain vaccines.

COVAX has to succeed. It is essential for the lowest-income countries, which lack the purchasing power that comes with economies of scale. A pandemic must be managed at a global scale. Until the virus is controlled everywhere, every nation is at risk of further outbreaks. And until COVAX gets the support it deserves, there is little hope of vaccinating the most vulnerable one-fifth of humanity. Not only would this have an obvious human cost, but, without it, it will take longer for the pandemic to end.