World view

By Kanta Subbarao

COVID-19 vaccines: time to talk about the uncertainties

Plan now for decisions on which vaccines should go to whom, when and how often.

I am a physician scientist, and am used to making clinical, scientific and public-health decisions based on data. Part of my job is advising on the composition of each year's influenza vaccine. In this coronavirus pandemic, like everyone else, I have had to adjust to uncertainties. Many uncertainties lie ahead about the roll-out of COVID-19 vaccines.

Vaccines will be licensed only after they have been shown to be safe and effective in a general population. This leaves many unknowns: whether one vaccine is more effective than another, how vaccines will work in people who are at the greatest risk of severe illness (people who are often excluded or under-represented in trials), whether vaccines will prevent transmission or severe disease, how long immunity will last — and which groups might resist or reject immunization because of ideology, mistrust or misinformation.

Despite the uncertainties, public-health officials will need to decide which vaccines to deliver, to whom, when and how often. Individuals will have to decide whether to be vaccinated. And they should understand that an effective vaccine might not stop every immunized person from getting sick or infecting others. The best thing that authorities can do is to be very clear about what is known and not known, to engage the public in discussions, take their input seriously, and build trust through transparency.

Some requirements for success are known. People must be willing to get vaccinated: achieving herd immunity will require rates of vaccine uptake of more than 60%, probably more than 70%. Societal realities must be incorporated into these plans. The shocking inequities exposed by the pandemic, and past injustices, mean that many members of minority ethnic and racial communities will not fully trust their governments. Messages should be tailored to their concerns using social media and other targeted platforms. Also, spreading the news about vaccines must not take away from emphasizing crucial preventive measures: masks, hand washing and physical distancing. Each of these strategies depends on maintaining public trust as knowledge evolves.

Most vaccines — measles, diphtheria, tetanus, polio, pertussis, to name a few — are administered mainly to children, often just once, or with a booster or two. Even annual influenza vaccines are administered to a subset of people. By contrast, COVID-19 vaccines will have to be given as quickly as possible to the vast majority of the world's people. Unprecedented levels of effort and innovation have brought several vaccine candidates into clinical trials already, including those based on nucleic acids, virus vectors, inactivated virus and protein subunits. With luck, some will soon prove safe and effective. Having an array of vaccines will be crucial to ensuring that enough is available to vaccinate more than 7 billion people.

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Most countries have an influenza-pandemic preparedness plan that can serve as a guide for mass vaccination. Health officials should review experience from the 2009 influenza pandemic, and consider every detail of a vaccine roll-out, even before they know which vaccines they will administer. Variations in the number of doses, schedules, storage conditions and supply chains for different vaccines will complicate logistics for public-health authorities.

There will be a lot of tough calls. Each vaccine will be licensed on the basis of comparison with a placebo, not other vaccines. At the start, we will not have the data to compare how well they prevent disease or induce immunity. Health-care workers and first responders are widely considered the highest-priority category because they are at the greatest risk of infection and are essential for keeping society running. The next category are those whose age and underlying health conditions put them at greatest risk of severe illness and death. But early vaccine trials are not likely to show how well the products work in these populations. We know that vaccines often work better in young healthy adults, which is why vaccines for diseases such as influenza and shingles are enhanced for the elderly, with a higher dose or an adjuvant to boost immunity. It is also unclear how well clinical trials will assess effectiveness in those in minority ethnic and racial communities. Most importantly, the trials will not assess whether vaccines will reduce transmission of the virus, so it will be hard to say whether vaccinated young, healthy people can return to work safely without continued precautions.

The public must be engaged in discussions about the risks and benefits of COVID-19 vaccines, including who gets first access to the vaccines and why. Several expert groups have conferred and written on these issues, but the public must have a chance to assess their rationale and weigh in. One way to do so is through 'citizen juries', representative groups of people brought together to consider issues and provide input. Australia did exactly this for pandemic planning based on severe acute respiratory syndrome (SARS) and H5N1 influenza (A. J. Braunack-Mayer *et al. BMC Publ. Health* **10**, 501; 2010).

It is important not to feel overwhelmed because there is good news. Several candidate vaccines have been brought to trials in record time, and data are promising. We will continue to learn how well the vaccines work and how best to use them. As new information is incorporated into our decision making, we will need to make it a priority to be clear and transparent about what we do and don't know.

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