

O Globo newspaper - Questions for Peter Piot:

Pace of vaccination in Europe:

Procurement of various Covid vaccines have shown the value added of the European Union, as this has guaranteed enough vaccines for every citizen in Europe. The first shipment of the Pfizer/BioNTech vaccine happened to all member states on 23 December. The Moderna vaccine received provisional approval today. EMA is expecting any day the formal submission of the AstraZeneca/Oxford request for provisional market authorisation .

The actual vaccination deployment is very unequal by country, with some starting very early, such as Germany and Denmark, and others having a slow start, such as in France, which has a high overall level of vaccine hesitancy. In some countries more vaccines have been delivered by Pfizer than being used, in others the company has delivered fewer vaccines than originally agreed. Let us not forget we are all in early days, and it will take a while to reach cruise speed for vaccine deployment.

A main lesson is that you need to prepare both logistics and public opinion for vaccine deployment, even before you have the actual vaccine.

1. In your opinion, which are the best ways to deal with the anti-vaccination movements and the negationist governments?
 - Anti-vaccination sentiment as well as vaccine hesitancy have both been around for as long as vaccines themselves. With safe and effective vaccine(s) for Covid being the only viable option to navigate ourselves out of the pandemic, both issues need to be addressed.
 - First, we need to distinguish between vaccine hesitancy and the anti-vaccination movements. The former often stems from often legitimate queries or anxieties about the safety and efficacy of vaccines by concerned individuals and parents/carers of children and loved ones. We need to treat people's legitimate concerns with respect in order to engage with them effectively.
 - Vaccine hesitancy needs to be addressed up front and be an integral part of vaccination programmes. Many approaches to increasing vaccine uptake do not take into account the social, historical and political realities of the public for whom information alone is not the antidote to vaccine hesitancy. Instead of older demand-creation models, a new model and language of engaging with the public is needed, starting with better listening and prompt responding to concerns as well as building on local capacities. Inclusion of non-traditional partners, new modes of digital communication, social scientists, and religious and traditional leaders have been invaluable in addressing hesitancy around polio vaccination, and the engagement of teenage girls in co-designing social media outreach to address HPV vaccination concerns had positive effects on vaccine uptake in Denmark, for examples. With safety anxieties being reported as one of the top reasons for vaccine hesitancy, aligning vaccine safety research with dominant safety concerns will also be important for confidence building.
 - Anti-vaccination movements are often associated with distrust in government, institution, big pharma, and the scientific community and feed on people's anxiety about being control and losing their personal freedom and choice. National populism fuelled by some prominent public figures in recent years have severely degraded trust in institutions across the world. The triumph of science in 2020 in delivering multiple safe and effective Covid vaccines in record speed with some using new technologies also fuelled unfounded rumours of short-cuts being made in their development.

- The pandemic presents an incredible opportunity to address some of these issues by rebuilding trust with people. It is really important to get people to understand the gravity of Covid, not only as a disease that kills but also a serious and long-lasting debilitating illness for those who survive. The vaccine should be positioned as an opportunity for people, not a mandate, to protect themselves as well as others in their communities and paves way for us to return to our normal way of life sooner.
 - Key for public trust is transparency of decision making and reasons for decision, consistency of decisions (in contrast to ever changing and last minute changes, such as in the UK), support by trusted public figures, constant communication.
2. From a public health perspective, how important are the reported efficacy differences in preventing symptomatic disease between the various vaccines?
- The US Food and Drug Administration had said it would consider granting emergency approval for vaccines that showed just 50 percent efficacy.
 - Of the 6 vaccines (Pfizer/BioNTech, Moderna, AstraZeneca/Oxford, Sputnik, Sinovac, and Sinopharm) that have received either emergency use authorization or full approval in different countries, they have all reached at least 60% or above vaccine efficacy that is way above the US FDA requirement of 50% efficacy to be considered for granting emergency approval. Having said this, the two mRNA vaccines seem to offer the best protection at the moment.
 - However, a safe and effective vaccine itself does not save lives but vaccination of such vaccines does. It is now critical to get these vaccines to as many people in at-risk groups in the world as quickly as possible in order to change the course of the pandemic.
 - Ultimately, it will be issues such as longevity of protection, adverse effects, single or double injection, logistic issues, price, and manufacturing capacity, which will determine which vaccine to use by a country.
3. Although the numbers are small, according to the data made public so far, all vaccines appear to be equally effective in protecting against severe Covid-19. In your opinion, what is the importance, if any, of this observation for the evaluation of both the vaccine efficacy and to stimulate their uptake by the general population?
- The high level of vaccine efficacies reported of the few approved Covid vaccines are impressive and arguably above the expectations of many experts.
 - It is important for governments, civil societies, communities as well as individuals to recognize that without an equally high level of uptake among the general population these impressive performances achieved under the ideal and controlled circumstances in clinical trials will not be translated into reality to save lives and make a real impact on the trajectory of pandemic
 - The first, and very important impact of vaccination will be a major decline in deaths and severe disease.
 - What is unclear is how much impact vaccination on the spread of SARS-Cov-2, though it is likely that there will at least be a reduction.
 - A top priority for all countries now is to accelerate deployment of vaccination to reach asap herd immunity.
4. How satisfied are you that these vaccines are as safe as other vaccines that are part of the normal/routine vaccination calendar, particularly in reference to severe allergic reactions?

- They are as safe as other vaccines, but need to monitor long term safety.
 - Vaccines are designed to be given to often healthy individuals as a preventative measure against a potential infection. When it is given to millions or even billions of people, even rare but serious side effects would have enormous negative impact on many people. Therefore, the bar for a vaccine to be approved by medicines regulator such as FDA is set very high, even higher than other medicines, and generally only mild and moderate side effects would be acceptable.
 - There is some evidence from clinical trials to suggest slightly higher levels of mild to moderate side effects of Covid vaccines than other routinely used vaccines which may prevent people from going about their daily activities. However, the most common side effects such as pain, headache, and fatigue, and fever, were transient and severe reactions were very rare. These are no surprise to vaccine researchers as side effects can be symptoms of the body's immune response by the vaccination. Authorities should prepare their vaccinees for these known side effects in order to maintain public confidence and trusts in the vaccines.
 - Transparency will be key to trust and uptake of the vaccines once the vaccines are rolled out in scale across the world.
5. According to data recently published in the NEJM about the Pfizer vaccine, protection starts less than two weeks after the first dose. The same seems to occur with the other vaccines. Thus, in your opinion, which would be the best strategy: to postpone the second dose for a few weeks (in the case of vaccines where this has not been tested) and thus rapidly vaccinate more people or to keep to the schedules that have been tested?
- I understand the urgent needs of the public health emergency in many countries.
 - The Pfizer/BioNTech vaccine was authorized by the EMA and the FDA based on a two-dose regimen given 21 days apart. Any divergence from this dosing schedule would be considered 'off label' use and would require separate authorization. WHO also just recommends against diverting from proven vaccination schedules.
 - While its phase 3 trial results reported in the NEJM suggest protection by the vaccine started as early as 12 days after the first dose (with reported vaccine efficacy at 52% between the first dose and second dose), there is a lack of evidence of how long the protection that the first dose confers might last. Trial participants received a second shot at the end of the recommended interval of 21 days.
 - In addition, levels of neutralizing antibodies were quite low after the first injection with the Pfizer mRNA vaccine, whereas they became very significant after the second dose. .
 - Delaying the second dose may increase the risk of vaccine-resistant mutations. The virus may be transmitted between large number of partially protected individuals in the community before they received their second injection. Delaying the second dose extends the time interval within which the mutations may take place. Furthermore, the longer the gap is the more people may forget to receive their second dose.
 - However, given the urgency that many countries, including the UK, are facing with the rapid spread of the highly transmissible new variant and overstretched health systems, there may be an argument to consider whether the potential benefit of rapidly vaccinating twice as many people with a delayed second injection outweighs the potential risks. The jury is still out on that question.

- The situation may be quite different for adenovector-based vaccines such as the AstraZeneca/Oxford vaccine, for which a longer interval between injections may actually improve immunogenicity and long term protection.
 - I am eagerly waiting for the results of the Janssen/JnJ vaccine trial, which is assessing the efficacy of a single injection. If it works as well as the currently licensed vaccines, the Janssen vaccine will be very appealing for mass vaccination campaigns.
6. Given that it is unlikely that data will be available in the foreseeable future, how do you see the possibility of “mixing vaccines”, i.e., a first dose of one, a second of another? Could this be a safe and efficacious way to guarantee that more people are vaccinated faster or is it an unnecessary risk?
- I would not recommend this, as there are absolutely no data. And we cannot substitute for much needed rigorous trials, rather than experimenting with people in uncontrolled circumstances.
 - Given the constraints of vaccine supply and different logistical challenges in vaccine roll-out in different countries, the idea of using one vaccine for the first dose and another available vaccine for the second dose may be worth investigating. A trial of this nature is under way investigating the safety and immunogenicity of the Oxford/AZ vaccine in combination with the Russian Sputnik vaccine.¹ Results of this trial will help answer any question regarding safety and efficacy of such an approach.
 - In situations where the same vaccine may be unavailable or if a patient failed to recall the vaccine s/he received at their first injection, having a second injection with a different vaccine may provide more benefit to the patient than not having a second injection at all.