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Challenges for implementation of the COVID-19 vaccination campaign in Brazil

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Due to the rapid spread of COVID-19 on all continents of the world, on January 30, 2020, the World Health Organization (WHO) declared the outbreak of the novel coronavirus (SARS-CoV-2) a public health emergency of international concern, the highest level of alarm. WHO recommendations included the fast-track development of vaccines, therapies, and diagnostics [1].

In this context, a race was launched for the development of a vaccine. Some 200 vaccine development projects have been registered with the WHO, 13 of which are in phase 3, for the evaluation of efficacy, the last phase before a vaccine's approval by the regulatory agencies, followed by the population's immunization [2]. The existence of so many projects already reaching the final test phase since confirmation of the first cases of COVID-19 is only possible due to gigantic investment by governments of developed countries and pharmaceutical companies, including partnerships, as well as nongovernmental institutions, in the search for safe and effective vaccines.

Besides the usually known platforms, such as inactivated virus, attenuated virus, protein subunits, recombinant vaccines, and viral vectors, new nucleic acid technologies (DNA and mRNA) are being used [2].

Another unprecedented measure was the creation of the COVAX Facility, led by the WHO, which aims to accelerate the development and production of COVID-19 vaccines in order to guarantee fair and equitable access for all countries of the world, and more than 170 countries have already joined this strategy, including Brazil. Through the COVAX Facility initiative, the Brazilian Ministry of Health will have the right to reserve 40 million doses [3].

In the endeavor to guarantee more doses for the Brazilian population, three technology transfer agreements have been signed in Brazil: one between the Immunological Technology Institute of Oswaldo Cruz Foundation (Bio-Manguinhos/Fiocruz)/ Brazilian Ministry of Health with AstraZeneca [4], in partnership with the University of Oxford (United Kingdom), which determined the initial supply of 100 million doses; another between Butantan Institute of the State of São Paulo, with the Chinese company Sinovac (Coronavac) [5], guaranteeing the supply of 46 million doses; and the third between the Paraná State Institute of Technology (TECPAR) in the State of Paraná, Brazil with the Gamaleya Institute of Russia

(Sputnik V) [6], thus far with no information on the number of doses to be supplied. However, as of early December 2020, no contract had been signed to supply vaccines through the latter two laboratories to the Brazilian Ministry of Health, which announced in the mass media that it was meeting with pharmaceutical companies Pfizer, Janssen, Moderna, and Bharat Biotech and the Russian Direct Investment Fund (RDIF) and was awaiting further information on progress with the results of trials and their release by the regulatory agencies for a decision on new vaccine acquisitions [7].

The Fiocruz partnership was the only one financed by the Brazilian Ministry of Health, suggesting that only the doses delivered to Fiocruz, besides those reserved through COVAX, will be part of the vaccination strategy of the National Immunization Program (PNI). This will be the first challenge for vaccination activities: if the Brazilian Ministry of Health only acquires the Oxford vaccine plus the reserved vaccines through COVAX, the states of Brazil may purchase vaccines themselves and establish separate vaccination strategies from those set of the Ministry of Health.

In this context, the expectation is that in the first semester of 2021, after approval of the vaccines' use by the regulatory authorities (in Brazil, the Brazilian Health Regulatory Agency – ANVISA), the country will begin to receive the first doses for use in the country. This will be the first major challenge, since despite all the fast-track development thus far, there are still many gaps in knowledge, creating an enormous difficulty for organizing the vaccination plan.

The companies Pfizer and Moderna, and the Gamaleya Institute announced preliminary results of the phase 3 studies, in which their vaccines' efficacy presented results greater than 90%, with no serious adverse effects, also demonstrating the safety of these immunobiological products. The results of AstraZeneca's provisional primary analysis pointed to efficacy of 62.1% for participants that received two standard doses and 90% for those who received first a half dose and a full dose a month later. These results are promising, since due to the current urgency, the WHO has determined that a vaccine with protection greater than 50% will be acceptable [8,9].

It is still not possible to know whether the vaccines will induce lasting immune memory, which will determine whether nor not revaccination of the target population is necessary. Most of the trials have been done in populations over 18 years of age, so the vaccines cannot be used in children, adolescents, or pregnant and breastfeeding women. It is thus essential for the Brazilian Ministry of Health to plan complementary studies both to assess the vaccine's effectiveness after its use in the target population defined by the PNI and the persistence of immune memory from the different vaccines that may be used in the country, besides the vaccine's efficacy in other groups not included in the phase 3 trials, aimed at the expansion of vaccination in the Brazilian population.

Most of the vaccines that have reached phase 3 will have a two-dose vaccination regimen, with the second dose applied 14 to 29 days after the first dose [2]. This will require enormous effort and organization by health services to guarantee adherence by a high population contingent to be vaccinated in a short time frame, for both doses. This will also require the vaccinated person's identification at the vaccination posts, with the need to create a simplified nominal system capable of recording the data quickly to monitor the vaccination's evolution. Meanwhile, it will be necessary to implement timely and active surveillance of adverse events following immunization, aimed at guaranteeing the vaccination's safety throughout the process. Additional important monitoring after the start of

vaccination will focus on pregnant women that have been vaccinated inadvertently, that is, at the moment of vaccination they did not know they were pregnant, and they need to be monitored to assess the safety of vaccination during gestation. This measure is essential, because if this monitoring proves that vaccination is safe during pregnancy, the vaccine can then be released for application in pregnant women, who are an important risk group for COVID-19.

Since there are no studies indicating whether it will be possible to administer COVID-19 vaccines simultaneously with other vaccines, in case the vaccination is conducted during the same period as the national influenza vaccination campaign, the logistic organization of these two campaigns will pose another enormous challenge, ranging from the storage of huge amounts of doses (the influenza campaign has a target population of 75 million persons) to sufficient numbers of teams to conduct two campaigns at the same time with distinct target populations (children, pregnant women and postpartum, for example, will not be included initially in the COVID-19 vaccination campaign), not to mention the need for teams to maintain the routine administration of the vaccines on the National Vaccination Calendar.

Vaccines are thermolabile products, that is, they can be transformed when exposed to variations in temperature, so it is indispensable to maintain them in conditions capable of preserving their characteristics, from production until the moment of administration in the target population, in order to guarantee the recommended protection. It is thus essential to have a structured cold network from the manufacturing laboratory to the vaccination room with well-defined responsibilities for receiving, storing, and distributing these vaccines. The cold network of the PNI is organized to receive products at temperatures of 2ºC to 8ºC. The DNA and mRNA vaccines require storage between -20ºC and -70ºC [9], and in case the PNI includes these vaccines in the list of products to be supplied in the vaccination rooms, it will be necessary to restructure this network, since it currently lacks the capacity for storage and transportation of these products.

Another challenge will be the prices of these new vaccines and the impact on the budget of the PNI for purchasing these products. While the Oxford/AstraZeneca vaccine will cost USD 3.00 to USD 4.00 per dose; the other vaccines will cost around USD 10.00 to USD 37.00 [9]. This price difference may be an obstacle to the incorporation of these vaccines in the PNI in low and middle-income countries. Since AstraZeneca will not have the capacity to meet the global demand, in case countries intend to launch a more ostensive campaign, they will need to turn to these high-cost vaccines.

It will be necessary to define the prioritization of groups to be vaccinated, ranked according to the risk of acquiring COVID-19, suffering complications, and dying: individuals with chronic diseases such as cancer, diabetes, cardiovascular diseases, renal disease, respiratory disease, hematological disorders, obesity, and persons over 60 years of age. Since healthcare workers are on the front line of care for COVID-19 patients, they may be the first group to be vaccinated. Other groups should include the vaccination strategy when the vaccines are available, such as indigenous people, quilombolas, the riverside population, and deprived of liberty, teachers, among other workers considered essential.

In this sense, it is extremely relevant to determine an efficient communication strategy to explain to the population why certain groups will be vaccinated and others will not, or even within the prioritized groups, because the vaccination will take place in stages, which should be followed in order to avoid the population's race to the vaccination posts (which

could generate crowding and possible shortages). Since the vaccination will take place by stages, to the extent that the vaccines are delivered, it will be essential to link the various sectors of society to mobilize the population, especially in the states that acquire vaccines on their own. Meanwhile, such communication should seek strategies to confront the anti-vaccine groups and the fake news already circulating on the social networks, thus avoiding the population's hesitancy to vaccinate and guaranteeing adherence to vaccination.

Finally, Brazil's PNI has longstanding experience in organizing mass vaccination campaigns, reaching high vaccination coverage and the program's objective, which is to protect the health of the target population of these strategies. By reaching high vaccination coverage rates, besides reducing cases of the disease in the target population for the vaccination, it contributes to decreasing the circulation of infectious agents in communities, positively impacting the health of those who will not be vaccinated, but who will be protected indirectly (herd immunity) [8,10]. Thus, the importance of vaccination is not only individual protection; it avoids the mass spread of diseases that can lead to death or severe sequelae, jeopardizing the health and quality of life of the population as a whole.

The COVID-19 pandemic has global repercussions and impacts that are not only biomedical and epidemiological, but also social, economic, political, cultural, and historical, without precedent in the recent history of epidemics. It is thus extremely important to have a national vaccination plan to organize the campaign's logistics, in order to achieve success, regardless of which instruments or sources of funds are used to purchase all the types of vaccines that will be available in the country.

Additional information

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