Review

COVID-19 Vaccination How the Assistance to the Patient of Rare Disease Was Delivered

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COVID-19 Vaccination How the Assistance to the Patient of Rare Disease Was Delivered

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Abstract: The anti-COVID-19 vaccination campaign has been fortified on the positive effects that immunization is bringing the nations, since infection rates, hospitalizations, and deaths have been falling according to the data in constant disclosure by official government organs and the channels of communication. In Brazil, the effective and free National Vaccination Program haven't prioritized patients with rare diseases, who have extreme comorbidities, and who had to follow the calendar prepared by the government. The problematic question is why these "rare people" weren´t considered priorities. The understanding of the reasons and the resumption of the debate about the rights of patients with rare diseases justify this study, which sought to be based on regular descriptors issued by official government agencies and by critics of rare disease issues in debates made in scientific articles. We sought to respond to the following objectives: analyze dispensed care of rare disease patients in the vaccination campaign anti-COVID-19; identify the procedures implemented by the National Vaccination Plan for the Brazilian population over 18 years of age; describe the panorama of the pandemic disease since its discovery to the mutations already disseminated; and evaluate the effectiveness of the plan implemented from the perspective of "rare person".

Keywords: rare disease; COVID-19; vaccination; public policy

Introduction

Vaccination has been, for decades, the most efficient method for prevention, mitigation, and even extinction of pathogens that sometimes leave bothersome sequelae and that can still lead to death.

Since the emergence of the new coronavirus, whose severity and lethality date back to the memories of past centuries, the medical and scientific society was united in the creation of vaccines that mitigated the symptomatology, as it is a flu disease inherent in mutations that has led to new studies and new and/or constant processes of immunization.

In the Brazilian National Vaccination Plan, reference worldwide for effectiveness, free of charge, and of universal coverage, rare disease patients, people with extreme comorbidities, did not receive due deference in the vaccination schedule which had started in January 2021, when Covid-19 imposed restrictions and conditioned the health care system to inoperancy in the face of related weaknesses.

The "rare people", assisted by family members and caregivers had to follow the calendar drawn up by organs attached to the Ministry of Health, promoting the questioning of families and support groups and defense of this population and wondering the reason why not having them as an extreme priority. As a matter of fairness and even of intersectional social justice.

The understanding of the reasons and the resumption of the debate about the rights of rare disease carriers that, like the vast majority of Brazilians, are neglected by power holders and discredited by society, justify the realization of this study that sought to substantiate the regular

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descriptors issued by official government bodies and by critics of rare disease issues in debates made in scientific articles available on the web.

In order to develop the critical analysis and relevant considerations, the following objectives were sought:

(a) Analyze the care provided to rare disease patients in the anti-Covid-19 vaccination campaign.
(b) Identify the procedures implemented by the National Vaccination Plan for the Brazilian population over 18 years old.
(c) Describe the panorama of the pandemic disease from its discovery to the mutations already disseminated; and
(d) Assess the effectiveness of the plan implemented from the perspective of the "rare person."

Rare Disorders

There are approximately 7,000 diseases considered rare in the world, however, there is no universal concept for the term"rare disease," being characterized by its reduced appearance in the population.

It is noteworthy that, in most countries, to classify a disease as rare, a cutoff number is used in the prevalence rate. Thus, Clark & Clark (2013, p.70) assert that:

In the European Union (EU), rare diseases are considered potentially fatal or chronically debilitating, with a prevalence lower than 5:10,000, and that require combined efforts between various areas to prevent significant morbidity and mortality or considerable reduction in quality of life or socioeconomic potential of the patient. The number of affected patients in the EU is estimated to be close to 36 million. In the United States, the Orphan Drug Act of 1983 defines rare disease as any disease or condition that affects less than 200,000 people in the country. In Japan, by the definition of the Japanese Medicines Act of 1993, a rare disease cannot affect more than 50,000 people in the country.

With the edition of Ordinance 199, of January 30, 2014, in its 3rd article the Ministry of Health started to define rare disease as one that has an incidence lower than 1.3 per 2,000 inhabitants that afflicts up to 65 people out of 100,000 individuals. In other words, it is that disease that affects less than 5% of a population in a given territory (BRASIL, 2014).

According to the Brazilian Federation of Rare Disease Associations – Febrararas (2020, p.06), people living with rare diseases have, in general, chronic and multisystemic conditions, which place them in a risk group, elderly, with greater physical and psychosocial vulnerability. There are many rare diseases, diverse in their etiologies, signs, symptoms and treatments. But every rare disease has something in common: it affects people. This may seem obvious, but people with rare diseases suffer from little scientific and medical knowledge of their health conditions.

Studies related to rare diseases have gained more and more space in the social context. According to Barbosa (2015, p. 58), one of the possible explanations for this growth is related to the impact of civil associations of rare diseases on society; therefore, through these a breakthrough in genetic research culminated in the discovery of treatments for diseases considered incurable.

Covid-19, a disease responsible for the largest pandemic of the 21st century, has affected people of all ages, whose signs and symptoms can vary according to age and clinical conditions. The age group has great influence on the individual risk of influenza, with a higher incidence in young people and more expressive lethality in the elderly and in individuals who have clinical conditions, or comorbidities, that can put them at risk for influenza complications. These complications include exacerbation of chronic conditions and other serious complications such as bacterial infection, myocarditis, pericarditis, bronchiolitis, and encephalitis (UYEKI, 2014; WHO, 2012).

According to Febrararas (2020, p. 06), for the rare disease carrier, there are few specific reports for coronavirus infection, although there are specific groups of patients who may be more at risk due to a second condition (disease) or a complication of his/ her inherited metabolic disease. These include:

(a) People with chronic lung or heart disease (this may, for example, include some patients with mucopolysaccharidosis, mitochondrial disease, or Pompe disease);
(b) People with muscular dystrophies, as they usually have heart and lung involvement;

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(c) People with diabetes or in a metabolic condition;
(d) Those taking immunosuppressive drugs, for example after a transplant, may have a higher risk of complications if they are affected by coronavirus; metabolic diseases with concomitant neutropenia;
(e) Some people with inherited metabolic disease are at risk of worsening of (decompensation) their metabolic condition to develop a viral infection;
(f) Any patient requiring an emergency regimen, including individuals with defects in the urea cycle, fatty acid oxidation disorders, urine disease in maple syrup, methylmalonic acidemia, glutaric aciduria type 1, or Propylonic acidemia, must have specific supplements or medicines to keep at home for use in case of illness and metabolic decompensation;
(g) Patients with neuromuscular disorders that have impaired ventilation or are using corticosteroids, such as Duchenne Muscular Dystrophy;
(h) Patients with airway malformations.

According to Regina Próspero, in an interview with Portal Kangaroo News (2021), it is estimated that there are about 15 million people with rare diseases in Brazil. Despite the significant number of "rare people", there is still great ignorance about the subject by society and even the medical community, which often results in difficulties in diagnosis, treatment, and monitoring of the condition.

COVID-19

Covid-19 is the largest pandemic in recent human history caused by the new coronavirus (SARS-CoV-2). It is a potentially severe acute respiratory infection with global distribution, which has high transmissibility among people through respiratory droplets or contact with contaminated objects and surfaces.

According to the World Health Organization (WHO), about 80% of people with covid-19 recover from the disease without needing hospital treatment. One in six people infected with SARS-CoV-2 become seriously ill and develop difficulty breathing. The elderly and people with comorbidities, such as high blood pressure, heart and lung problems, diabetes, or cancer, have a higher risk of becoming seriously ill (BRASIL, 2021, p. 13).

Since the initial genomic characterization of the SARS-CoV-2 virus, this virus is divided into different genetic groups or clades and, when specific mutations occur, these can establish a new lineage (or genetic group) of the circulating virus.

It is also common to occur several processes of microevolution and virus selection pressures, and there may be some additional mutations and, as a result, generate differences within that lineage. When this happens, it is characterized as a new variant of that virus and, when mutations cause relevant clinical-epidemiological changes, such as greater severity and greater infectivity potential, this variant is classified as VOC, in English, *variant of concern*, in Portuguese translated into variant of attention and/or concern (BRASIL, 2021, p. 27).

In Brazil, all of the VOCs described by WHO in the world have already been identified and reported, through laboratory and epidemiological monitoring established in the flow of health surveillance services.

As reported in the Epidemiological Bulletin nº 73 (BRAZIL, 2021b, p. 56), the SARS-CoV-2 virus, as well as other viruses, undergo expected mutations and to evaluate the genomic characterization, in the network of laboratory surveillance of respiratory viruses of the MS there is a flow of sending to reference laboratories (Oswaldo Cruz Foundation - Fiocruz/ RJ, Evandro Chagas Institute - IEC/ PA and Adolfo Lutz Institute - IAL/ SP), of a number of samples confirmed for Covid-19, by RTqPCR, which are sent for genomic sequencing and other complementary analyzes, if it is considered necessary.

And in the period between January 3 and July 10, 2021, when the epidemiological week (SE) ended 27, 7,545 records of Covid-19 cases were observed for variants of care and/or concern (VOC), in the 27 FU of Brazil, being: 3 cases of VOC Beta (B.1.351) - identified in two municipalities of São Paulo; 27 cases of VOC Delta (B.1.617.2) - identified in 7 federated units; 182 of VOC Alpha (B.1.1.7)

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identified in 14 federated units; and 7,333 of VOC Gamma (P.1) - in all federated units, with VOC circulating predominantly in the country (BRAZIL, 2021, p. 28).

By the end of the Epidemiological Week (SE) 29 of 2021, on July 24, 2021, 193,730,907 cases of Covid-19 were confirmed worldwide. The United States was the country with the highest number of cumulative cases (34,428,050), followed by India (31,371,901), Brazil (19,670,534), France (6,041,146) and Russia (6,025,698) (Figure 1A). Regarding deaths, 4,152,497 were confirmed worldwide until July 24, 2021. The United States was the country with the highest cumulative number of deaths (610,835), followed by Brazil (549,448), India (420,551), Mexico (238,316) and Peru (195,243) (BRAZIL, 2021b, p. 02).

By the end of SE 29, according to Epidemiological Bulletin 73, 80.4% (128,107,515/159,302,857) of people infected with Covid-19 in the world recovered, and data from the United States were ignored. India was the country with the highest number of recoveries (30,543,138 or 23.8%), followed by Brazil (18,340,760 or 14.3%), Turkey (5,415,937 or 4.2%), Russia (5,405,818 or 4.2%), and Argentina (4,480 or 4,333 or 2022%) (BRAZIL, 2021b, p. 02).

Also, according to the Bulletin, in relation to deaths, in SE 29 of 2021, Indonesia recorded the highest number of new deaths worldwide, reaching 9,524 deaths. Brazil was the second country with the highest number of new deaths, reaching 8,182 deaths. India presented a total of 6,942 new deaths, while Russia recorded 5,361 new deaths, and South Africa 2,812, occupying the following positions in the world ranking of new deaths in SE 29.

Vaccination

The National Immunization Program (PNI), created on September 18, 1973, is responsible for the national immunization policy and its mission is to reduce morbidity and mortality due to preventable diseases, strengthening integrated health surveillance actions for health protection and prevention of the Brazilian population. It is one of the largest vaccination programs in the world, being recognized nationally and internationally. The PNI serves the entire Brazilian population, currently estimated at 211.8 million people, being a moral patrimony of the Brazilian state, maintained by the commitment and dedication of health professionals, managers, and the entire population (BRAZIL, 2021, p. 10).

In order to collaborate in the preparation of this plan, the Ministry of Health established the Technical Advisory Chamber on Immunization and Communicable Diseases through the GAB/SVS Ordinance n. 28 of September 3, 2020, with the Coordination of the Secretariat of Health Surveillance, composed of representatives of this ministry and other governmental and non-governmental bodies, as well as Scientific Societies, Class Councils, specialists with expertise in the field, Pan American Health Organization (PAHO), National Council of Health Secretaries (CONASS) and National Council of Municipal Health Secretariats (CONASEMS).

In the current scenario of great global health complexity, an effective and safe vaccine is recognized as a potential solution for the control of the pandemic, combined with the maintenance of prevention measures already established.

Until March 12, 2021, WHO reported 182 COVID-19 vaccines candidates in pre-clinical phase of research and 81 vaccine candidates in clinical research phase. Of the vaccine candidates in clinical studies, 21 were in phase III of clinical trials for efficacy and safety evaluation, the last stage before approval by regulatory agencies and subsequent immunization of the population (BRAZIL, 2021, p. 18).

It is also noteworthy that in the scope of people with comorbidities and people with permanent disabilities are included people with rare diseases that imply a greater risk for the unfavorable outcomes of covid-19. For example, immunosuppressive diseases such as Cushing's syndrome, systemic lupus erythematosus, Crohn's disease, primary immunodeficiency with a predominance of antibody defects, diseases that cause chronic lung impairment such as cystic fibrosis are cited; diseases that cause intellectual and/or motor and cognitive disabilities such as Cornelia de Lange syndrome, Huntington's disease; and other rare diseases such as sickle cell anemia and thalassemia major (BRAZIL, 2021, p. 32).

According to Technical Note 467/2021, the definition of priority groups for vaccination was carried out based on epidemiological analyses, evidence-based, and discussions with experts with expertise in immunization and the main scientific societies, within the Technical Advisory Chamber

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on Immunization and Communicable Diseases, also based on the recommendations of SAGE - Strategic Advisor Group of Experts on Immunizing (Immunizing), of the World Health Organization; in partnership with Tripartite, with the National Councils of Health Secretaries and Municipal Health Secretariats (Conass and Conasems) (BRAZIL, 2021a, p. 04).

Also, according to NT 467, given the still limited quantity in the availability of vaccines to offer to the target population of the National Vaccination Campaign against Covid-19 2021, PNI ratifies the importance of those made available to those predetermined groups, which, initially, already have a higher risk of exposure, complication, and death from covid-19, according to priorities listed in the National Plan for the Operationalization of Vaccination against Covid-19 (PNO).

According to Alexandre Padilha, member of the Committee on the Rights of Persons with Disabilities of the Chamber of Deputies of Brazil, those who suffer from a rare disease in Brazil have vulnerabilities that go beyond their clinical or epidemiological situations. The criterion of vaccination priority in the country cannot be a "cut and glue" of the reality of other countries, where social inequality is lower (PADILHA, 2021).

According to him, the definition of a priority group for any vaccination campaign takes into account two evidences: clinical or epidemiological vulnerability. These indicators show that a person may have a more severe risk of an illness or other vulnerabilities.

According to Pagno (2021), people with rare diseases and who have more risk for coronavirus are included in the group of comorbidities and permanent disabilities. Among the diseases are those that cause immunosuppression, such as Cushing syndrome, systemic lupus erythematosus, primary immunodeficiency with predominance of antibody defects, diseases that cause chronic pulmonary impairment, such as cystic fibrosis, sickle cell anemia, thalassemia major and syndromes that cause intellectual disability, such as Cornelia de Lange.

The analysis of vaccination coverage by age groups in the population aged 18 and by federative unit (FU) and based on complete vaccination schedule data (D2 for Sinovac/Butantan and Covishield/AstraZeneca/Fiocruz and Pfizer) and DU for the Janssen vaccine, showed different scenarios in different groups and FU (BRAZIL, 2021b, p. 102).

According to the Epidemiological Bulletin nº 73, the vaccination coverage (CV) national average in each group was below 15% with variations between just over 2% in the group of 18 and 19 years of age and 14% in the groups of 40 to 44 and 45 to 49 years of age.

Vaccines

(a) Also, according to the Ministry of Health (BRAZIL, 2021, p. 19), the COVID-19 vaccines distributed for use so far in the National Campaign are:

(b) Butantan Institute (IB): vaccine adsorbed covid-19 (Inactivated). Producer: Sinovac Life Sciences Co., Ltd. Partnership: Sinovac/Butantan;

(c) Oswaldo Cruz Foundation - Institute of Technology in Immunobiologicals - BioManguinhos (Fiocruz/BioManguinhos): covid-19 vaccine (recombinant) Manufacturer: Serum Institute of India Pvt. Ltd. Partnership: AstraZeneca/Fiocruz;

(d) AstraZeneca: vaccine against Covid-19 (ChAdOx1-S (recombinant). Vaccine from the Covax Facility consortium;

(e) Pfizer/Wyeth: covid-19 vaccine (mRNA) (Comirnaty) - Pfizer/Wyeth;

(f) Janssen: covid-19 vaccine (recombinant). Vaccine from the Covax Facility consortium.

=Up to the 30th Technical Report of 26/7/2021, 32 vaccine distribution guidelines have been carried out, which have already made it possible to deliver approximately 168 million doses, with approximately 84.2 million doses of AstraZeneca/ Fiocruz vaccine; 59,1 million doses of Sinovac/Butantan vaccine; 19.9 million of the Pfizer/Comirnaty vaccine and 4.5 million doses of the Janssen vaccine (Johnson & Johnson), reaching approximately 92.7 million people vaccinated (BRAZIL, 2021b, p. 93).

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According to the Epidemiological Bulletin nº 73 (BRAZIL, 2021b, p. 102), at least three of the four Covid-19 vaccines available in the country should be administered in two doses to ensure greater effectiveness.

It continues:

In collaboration with experts from its network of institutions and research worldwide, the World Health Organization (WHO) routinely evaluates variants of the SARS-CoV-2 virus. These analyses mainly observe whether the behavior of the new variants results in changes in transmissibility, in the disease clinic, and also in severity; some changes may suggest decision-making and implementation of new measures for prevention and control of the disease. An established and timely genomic surveillance contributes to the strengthening of such guidelines, and with the current pandemic scenario, this is a guiding tool for managers' decision-making (BRASIL, 2021b, p. 57).

By that, a third dose is already planned for the priority groups, as provided in the initial plan already signed, with speed before the experience already acquired in the first seven months of the vaccination campaign.

Analysis

The coronavirus surprised the world with its speed and lethality, a fact that caused concern, despair, and union of the scientific and political community around the world because people were dying.

The investigative process about the disease has led scientists from all over the world to work intensively in research and testing, and to discuss health in all its aspects, especially structural, whose weaknesses were evidenced before the health emergency in several countries.

In this sense, according to the World Health Organization, the detection and spread of an emerging respiratory pathogen are accompanied by uncertainty about the epidemiological, clinical, and viral characteristics of the new pathogen and particularly its ability to spread in the human population and its virulence (case - severity) (BRAZIL, 2021, p. 16).

And it continues, by stating that "in view of this, the pandemic resulting from human infection by the new coronavirus has caused impacts with global losses of social and economic order, becoming the greatest public health challenge".

The issues of the Covid-19 pandemic showed the underprivileged by health systems, among which are those with rare diseases that, according to the material identified in the research, were not evidenced in the vaccination process, since they were included in the comorbidities group.

Marina Pagno, in an official website, reported that the Ministry of Health "defined a strategy for vaccination against Covid-19 for people with permanent disabilities, pregnant women, postpartum women up to 45 days postpartum, and people with comorbidities, including some rare diseases".

Based on this plan, according to Pagno (2020), vaccination would occur in two stages that, although encompassing people with general comorbidities, did not favor "rare people". He has quoted:

In phase 1, the following shall be vaccinated:

- people with Down syndrome, regardless of age.
- people with chronic kidney disease on renal replacement therapy (dialysis), regardless of age.
- pregnant women and postpartum women with comorbidities, regardless of age.
- people with comorbidities aged 55 to 59.
- people with permanent disabilities registered in the Continuing Benefit Program (BPC) aged 55 to 59 years.
- Phase 2, on the other hand, should consider older for younger (50 to 54 years, 45 to 49 years, 40 to 44 years, 30 to 39 years, and 18 to 29 years):
- people with comorbidities.
- people with permanent disabilities registered with the BPC.
- pregnant and puerperal women, regardless of pre-existing conditions.

It is known that rare disease patients need special care and many of them require constant care, specific, expensive medicines and orphans, part of the routine of families that have "rare people" in their care.

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In this sense, families raised a question about the inconsistency of the National Vaccination Plan implemented, including those with rare diseases in the category "comorbidities" and family members, usually their caregivers, in the general category, when the respective age groups were contemplated.

Thus, in a Public Hearing promoted by the Commission for the Defense of the Rights of Persons with Disabilities - CPD, on June 8, 2021, Mrs. Andréa Medrado Monteiro raised the following question:

A) Why in some states, such as Rio de Janeiro, is vaccination of caregivers of people with rare diseases happening, and in the other states it is not? Why not expand to all of Brazil as a priority group? After all, if there are more than 13 million people with rare diseases in the country, imagine how many parents are there?

From the Vaccine Already PCD and Rare Diseases Movement came the question and observation:

A) People with rare diseases are dying and this segment does not have time for your evaluation and possible full PNI contemplation. We ordered Vaccine Now! Most are children and their caregivers, usually parents who go to work and expose themselves to the virus. When will these caregivers/parents be in the PNI?

b) Communication is everything! State-of-the-art health workers are not vaccinating the few that are contemplated, are not vaccinating the few that are contemplated, for example, neurological diseases. They refuse to vaccinate cases of rare patients due to ignorance of the disease.

Mrs. Raquel Carvalho Pinheiro, seeing herself at risk, raised the following question:

a) Hello! I am a caregiver of a child with rare syndrome and we need to be vaccinated. Who will take care of our children if we get sick? Moreover, they are from risk group if contaminated. Vaccinating people with rare diseases and syndromes and their caregivers is an act of humanity. And I'm talking about the vaccine for domestic caregivers. The reality of families is not having professional caregivers. Look at this reality, please.

The reality of families is delicate because there is no guarantee of cure and not a hundred percent immunity to the disease with the application of available vaccines, especially with the spread of variants from other continents, with the prevalence of the Delta Variant, with greater power of contagion and lethality.

This reality is consistent with what the PNI says:

In collaboration with experts from its network of institutions and research worldwide, the World Health Organization (WHO) routinely evaluates SARS-CoV-2 virus variants. With this genomic sequencing analysis, it is mainly observed whether the behavior of the new variants has resulted in changes in transmissibility, in the clinic of the disease, in severity, and also in the vaccine response; some changes may suggest the decision-making of national authorities to implement new measures for prevention and control of the disease. An established and timely genomic surveillance collaborates in strengthening such guidelines, and with the current pandemic scenario, this is a guiding tool for managers' decision-making (BRAZIL, 2021, p. 27).

The worsening of the Covid-19 pandemic due to the variants, which is common in flu syndromes, not only threatens "rare patients", with greater fragility but all those who are already participating in the vaccination program, because immunizers act, according to experts, relief of symptoms and aggravations caused by SARS-CoV-2.

When discussing public health, in the current scenario, it goes back to management that undoubtedly has the power over the planning, procurement, operation, and control of processes, registration, validation, and dissemination of results.

The "rare person", stigmatized, is not seen and does not receive the attention of the society where is inserted, which extends to their families.

These have recently been seen and served by governmental actions and non-governmental organizations, celebrating some achievements and yet fighting for their rights with the judiciary more often than desired.

As Padilha emphasizes (2021),

Even in the face of this frightening scenario, we cannot lose the fighting horizon. No one can think that we will be protected by ensuring individual vaccination. We will be safe only with

collective vaccination. And even if we have a vaccination for everyone, it is important that vaccination is still a priority. These two groups and their caregivers should be in the priority population.

To this end, the immunization program must be continuous, but with the desire that these unprivileged and their close ones are actually considered as priority members in this process of life preservation.

Final Remarks

The new coronavirus highlighted the strength, importance, and power of science that managed to map the genome of the virus in record time, identify drugs intended for palliative treatment, and the development of various immunizations that have been meeting the expectations of states and nations.

Given the mutations that the virus has been suffering, the effectiveness of vaccines has been investigated, considering the application of a booster dose for the priority groups determined by the National Vaccination Plan, in which rare disease patients and family members are still deprecated when inserted, the former in the group of general comorbidities and the others conditioned to the order determined by age group.

It is worth mentioning, in this analysis, that the most recent data date back to July 2021, when groups composed of age groups from 18 to 45 years had not yet been contemplated with the first doses of the vaccine, not even the single dose, of the pharmaceutical Johnson & Johnson.

As the Ministry of Health recalls about vaccination:

Its main objective was defined as priority, the preservation of the functioning of health services; the protection of individuals at greater risk of developing severe forms of the disease; the protection of other vulnerable individuals to the greatest impacts of the pandemic; followed by the preservation of the functioning of essential services (BRAZIL, 2021, p. 31).

So, with the SARS-CoV-2 variants owning the territories of all continents, it is necessary to expand the immunization campaign, with the application of reinforcement; acquisition, upon approval by a corresponding body (in the case of ANVISA), of new immunizers; the expansion to groups aged under 18; and reconsidering, as soon as possible, the "rare people" with exceptional priority, since their weaknesses are evident more quickly.

Efforts must still be made to disseminate information safely and effectively so that the objectives of the PNI are achieved, at least in their minimum coverage expectations, believing that there will be awareness of the population in accepting immunizations and compliance with the current safety protocols.

As for rare disease patients, managers need to pay greater attention to the group that exists and resists in the family, with glances aimed at this public neglected even by health agents.

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