

IFMSA Policy Proposal Vaccination

Proposed by Liaison Officer to Student Organizations
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Policy Commission

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Policy Statement

Introduction:

Vaccination is an effective method of preventing infectious diseases from spreading and is therefore closely linked to the Sustainable Development Goals (SDG) Agenda, especially SDG 3 (health and wellbeing), and is necessary to achieve other SDGs i.e. SDG 5 (gender equality), SDG 8 (work and economic growth), SDG 10 (reduced inequalities), SDG 12 (responsible production and consumption) and SDG 13 (climate action). Vaccine inequity, vaccine hesitancy movements, lack of access and other factors often result in disease outbreaks and deaths from vaccine-preventable diseases in different regions. These factors threaten to unravel years of progress in this field, and are becoming emerging global health threats.

IFMSA position:

The International Federation of Medical Students Associations (IFMSA), as a representative of medical students, believes that our duty is not only towards the future of our individual patients, but also towards communities at all levels. IFMSA acknowledges that holistic, transversal and interprofessional approaches are mandatory requirements to address this global health problem and stresses upon the importance of strengthening vaccination coverage worldwide, by increasing and improving the research, production, fair distribution as well as education and awareness on vaccines.

Call to Action:

Therefore, the IFMSA calls on:

Governments and Ministries of Health to:

- Ensure access, availability, equity to quality, and proper population adherence for the established National Immunization Programs (NIPs), also providing coverage to vulnerable populations and remote or less privileged areas;
- Establish a NIP and a national vaccine regulation interdisciplinary entity, built on functional, end-to-end supply chain to ensure the quality of the products and the correct administration of the resources;
- Regularly update their national immunization programs (NIPs) based on recent studies;
- Invest resources and funds in Research and Development (R&D) strategies in order to reach effective outcomes;
- Invest in mass education and awareness strategies in order to improve the population adherence (e.g. parents toward NIPs for children) the vaccination plan and to address vaccine hesitancy (e.g. through Social Media);
- Implement vaccine production and price data transparency policies to establish a stricter control on Good Manufacturing Practices (GMP) regulations compliance, allowing countries to conduct reasonably priced licitations;
- Implement effective health surveillance to appropriately weigh the national burden of communicable diseases and adequately adjust the administrative response.

The WHO and other relevant international organizations to:

- Ensure the access to immunization programs for everyone, with a focus on disadvantaged groups within countries and refugees as well as Low and Middle Income Countries (LMICs);
- Work on regulating the distribution and sale of new vaccines so that no significant difference exist between different areas or countries and to decrease the regional or international burden of spreading communicable diseases;
- Actively encourage and support the innovation and research of new and improved vaccines that are more efficient and affordable;

- Insist on the transparency of vaccines' prices from governments and other intergovernmental entities, especially the ones who are actively involved in vaccine price negotiations;
- Encourage the multinational organizations and the leading countries in vaccination to democratize the access to the intellectual property regarding the vaccines' production and distribution;
- Consult countries and agencies, such as EMA, on the development of need-based immunization strategies;
- Continue making annual progress reports, reviewing existing programmatic policies and implementing new ones according to potential changes in world politics, population migration, scientific advancement, etc.;
- Continue collaborating with various Non-State Actors and wider civil society to improve the vaccination coverage.

Universities and other educational/professional bodies to:

- Provide holistic education and training on vaccination, with a focus on enhancing the communication skills of health workers so they can better address public concerns and needs accordingly;
- Incorporate 'vaccine education' in the university health curriculum led by experts where students from all disciplines learn about vaccines, the legislature of their country and international laws; as well as learn about their personal vaccination records and schedules;
- Provide free access to data and resources and support funding to encourage vaccine research and development;
- Facilitate means of networking, communication, and collaboration among international educational institutes and research facilities;
- Allocate funding and resources to sustainable research of new vaccines or the improvement of existing vaccines;
- Ensure and advocate for evidence-based vaccine education and research through the One Health approach.

Healthcare NGOs and professional associations to:

- Initiate and develop vaccination programs to boost the vaccination coverage among the general population;
- Advocate for the universal vaccination coverage and vaccine price transparency, especially for LMICs, as well as for vulnerable populations;
- Collaborate with governmental organizations in developing immunization related policies;
- Support and advocate research that reflects the global burden of infectious diseases;
- Promote active provision of objective knowledge about vaccination to the public, through the launch of grassroots vaccination campaigns.

IFMSA members and NMOs to:

- Provide healthcare students with the necessary information and education on vaccines and immunization, as well as efficient advocacy tools to approach the different stakeholders and policy makers in the field;
- Advocate, promote, and participate in local and national campaigns to raise awareness among healthcare students as well as the general population;
- Collaborate with governments and other organizations to promote the importance of immunization in a proper legal framework;
- Collaborate with academic institutions in promoting a multidisciplinary approach to vaccine education;
- Promote an intersectional approach of vaccination whether being research exchanges in R&D, vaccine equity, vaccination in the academic curriculum, and so on.

One Health partners to:

- Support veterinarians to establish a vaccination program that caters to the needs of the animals being treated within their region, and educate pet owners on the importance of vaccination and the risk of disease transmission;

- Support vaccine manufacturers to develop new management methods of the vaccines' disposals' waste, in order to minimize its burden on nature and animals;
- Develop safety protocols related to development of vaccines, specifically those obtained from animals and wildlife;
- Establish new or fortify existing regulations for the rational use of vaccines on livestock following rigorous research;
- Constantly monitor and develop regulations on the use of animals for research purposes in the development and trial phases of vaccines.

Position Paper

Background information:

A vaccine is a biological preparation that simulates a specific disease in order to stimulate the body's immune system to produce antibodies. They contain a microorganism or virus in a weakened, live or killed state, or proteins or toxins from the organism which the human body identifies, destroys and memorizes. As a result, they increase the human body's defense to work against the possible infection when exposed to the same microbe as before and thus, they help prevent sickness from infectious diseases. [1]

Vaccination is the most effective method of preventing infectious diseases. According to the Centers for Disease Control and Prevention (CDC), vaccines are needed because "it is always better to prevent a disease than to treat it after it occurs." [2]

The first successful vaccine was the smallpox vaccine created in 1796 by Edward Jenner, who inoculated a young patient with vaccinia virus, cowpox, in order to create immunity to smallpox. Smallpox was one of the deadliest diseases and it was the only human disease that was eradicated because of this breakthrough. [3]

Following this breakthrough, various scientists began developing vaccines for diseases such as Cholera in 1897, the plague in the late 19th century and Diphtheria in 1923. Later, between 1950-1985, the polio vaccine emerged, first in the inactivated followed then by the live attenuated virus, and has been very successful in its endeavors [4]. Now, there are vaccines against more than 20 deadly diseases, and prevent 2-3 million deaths yearly from diseases like diphtheria, tetanus, pertussis, influenza and measles.

There are several types of vaccines, including the following: live attenuated, inactivated, subunit, and toxoid. Live-attenuated vaccines utilize a weakened form of the specific agent, which in turn creates a long lasting immune response and requires either one or two doses, i.e. tuberculosis, oral polio vaccine, etc. Inactivated vaccines utilize the killed version of the agent and in turn the immunity aspect requires several booster shots over a period of time, i.e. whole-cell pertussis, inactivated poliovirus, hepatitis A, etc. Subunit vaccines also known as recombinant, polysaccharide, and conjugate vaccines utilize a specific part of the agent and like the inactivated vaccines they too require booster shots, ie pneumococcal, hepatitis B, haemophilus influenzae, ect. Toxoid vaccines are based on toxins produced by certain bacteria, but are rendered harmless. These toxoids cannot cause disease and elicit a strong immune response that is reinforced with booster shots over time, i.e. tetanus and diphtheria [1].

To be vaccinated is an indispensable part of primary healthcare and falls under the umbrella of the human right to health. Following the development of these vaccines, countries have introduced vaccination programs to reach the goal of eradication of vaccine-preventable diseases worldwide. With the implementation of such programs, countries around the world have been able to reduce the prevalence of various diseases and in some circumstances achieve total elimination in various countries. The Global Polio Eradication Initiative is an example of a global collaborative effort to eradicate polio worldwide. Since its launch in 1988, there has been a 99% fall in newly reported cases of polio worldwide. The WHO Region of the Americas, Western Pacific Region, European

Region, and South-East Asia Region have all been certified polio-free meaning that 80% of the world population is living within a polio free region [5].

Vaccination is closely related to sustainable development. In 2015, the United Nations adopted the Sustainable Development Goals to end poverty, protect the planet, and ensure that by 2030 all people enjoy peace and prosperity. The SDG directly involved with vaccination is SDG 3, defined as Good health and well-being. Its targets are, by 2030, to end the epidemics of AIDS, tuberculosis, malaria and neglected tropical diseases and combat hepatitis, water-borne diseases and other communicable diseases. Moreover, it aims to achieve universal health coverage, including financial risk protection, access to quality essential health-care services and access to safe, effective, quality and affordable essential medicines and vaccines for all. The SDG 3 aims to support the research and development of vaccines and medicines for the communicable and noncommunicable diseases that primarily affect developing countries, and to provide access to affordable essential medicines and vaccines, in accordance with the Doha Declaration on the TRIPS Agreement and Public Health. This declaration affirms the right of developing countries to use the full provisions in the Agreement on Trade Related Aspects of Intellectual Property Rights regarding flexibilities to protect public health, and, in particular, provide access to medicines for all. Nevertheless, there are other SDGs that contribute to the outcomes mentioned above, such as SDG 1, 2, 4, 5, 6, 8, 9, 10, 11, 16 and 17. [6] [7]

Discussion:

Research in the field of vaccination

Research and open access to publications have a crucial role in raising knowledge of the microorganisms' cycle and their progression. The understanding of infectious agents and their interaction with the host immune system are aspects of the biological development that support the vaccines' enhancement. This knowledge leads to a more efficient and faster identification and, consequently, to a proper evaluation of the innovative measures that we ought to use and perform in order to ensure an acceptable coverage regarding vaccines and immunization [8].

To develop a new vaccine, different tests and screenings must be done before its use on humans. The process first starts with the preclinical phase, where the vaccines are tested on cell cultures and later on animals and in this way, safety can be assessed and the immune response can be measured. The preclinical stages often last 1-2 years.

If they pass each of these stages of testing they are then approved by the public health safety authority (FDA in the United States) to start a three-phase series of human testing:

- In Phase I, the vaccine is given to a small number of young and healthy adults (20-80). The goals of Phase I testing are to assess the safety of the candidate vaccine and to determine the type and extent of immune response that the vaccine provokes.
- In Phase II the vaccines are given to hundreds of volunteers. A group of volunteers that did not receive the vaccine is included (placebo group) in order to compare whether the changes in the vaccinated group are attributed to the vaccine or another factor. During this phase the safety but also the effectiveness and the ideal dose of the vaccine are evaluated.
- In the third and last phase, the vaccine is given to thousands of volunteers. The trials are randomized and double blind and involve the experimental vaccine being tested against a placebo. Vaccine safety and vaccine efficacy are tested. Usually this phase is conducted in several countries and sites in order to evaluate its performance on different populations. This phase usually requires several years to complete.

After a successful Phase III trial, the vaccine developer will submit a Biologics License Application to the FDA. Then the FDA will review the results of the clinical trials, safety tests, purity tests, and manufacturing methods and will inspect the factory where the vaccine will be made and approve the labeling of the vaccine. After FDA approval, the FDA continues to monitor the manufacturing protocols, batch purity, and the manufacturing

facility itself. Additionally, most vaccines also undergo phase IV trials, which monitor the safety and efficacy of vaccines in tens of thousands of people, or more, across many years. [9]

Currently, R&D resources are focused on those vaccine-preventable diseases that reflect a significant global burden, including TB, HIV/AIDS, Chikungunya, Plague, Yellow fever, Dengue, Ebola and other. In 2021, a malaria vaccine was approved by the World Health Organization, the RTS,S/AS01 and has shown effectiveness against the disease. [10]

What makes the COVID-19 pandemic remarkable is that the whole research and development pipeline, from the first SARS-CoV-2 viral sequencing to interim analyses of vaccine efficacy trials, was accomplished in just under 300 days, a procedure that usually takes between 5 and 10 years. Despite the particular pace at which the steps of anti-COVID 19 vaccine's production were executed, the efficacy, quality and security of this vaccine were not altered. From vaccine development during public health emergencies arose the Coalition for Epidemic Preparedness Innovations (CEPI), a not-for-profit organization dedicated to timely vaccine development capabilities in anticipation of epidemics. CEPI initially focused on diseases chosen from a list of WHO priority pathogens. The goal of CEPI was to advance candidate vaccines through phase 2 and to prepare stockpiles of vaccine against eventual use/testing under epidemic circumstances. CEPI had also prepared for 'disease X' by investing in innovative rapid response platforms that could move from sequence to clinical trials in weeks rather than months or years, such as mRNA and DNA technology, platforms that were useful when COVID-19 was declared a global health emergency in January 2020. [11]

Quality of vaccine production and handling process

While having access to vaccines themselves is important, this access is rendered futile unless the product inoculated has the adequate quality for the physiological response to arise as expected, and thus providing the desirable immunity. In order for a vaccine to be approved, an assessment process that ensures quality, safety and efficacy takes place, through a procedure called prequalification (PQ).

Emergency Use Listing Procedure (EUL) is a risk-based procedure for assessing and listing unlicensed vaccines, therapeutics and in vitro diagnostics with the ultimate aim of expediting the availability of these products to people affected by a public health emergency. The procedure is a key tool for companies wishing to submit their products for use during health emergencies, like a pandemic.

Once the vaccine is authorized, manufacturing begins to scale up. Then it is made in bulk quantities, it is bottled in glass vials and carefully packaged for safe cold storage and transport. Vaccine packaging must be able to withstand extreme temperatures, as well as the risks involved in being transported globally. Therefore, vaccine vials are most commonly made from glass, as it is durable and able to maintain its integrity in extreme temperatures.

When a vaccine is too hot or too cold, it becomes less effective or even inactive. If stored at the incorrect temperature, vaccines can be ruined or unsafe for use. Most vaccines require refrigerated storage at between 2 and 8 °C. Some vaccines require temperatures as cold as -20°C. Some of the newer vaccines need to be kept ultra cold at -70°C. For frozen vaccines some of them can be safely stored for a limited time between 2 and 8°C.

Regular refrigerators cannot maintain an even temperature consistently, which could be a major problem especially in peripheral countries. Consequently, specialized medical refrigerators are required for these precious products [12]

Once vaccines start being administered, national authorities and WHO constantly monitor for – and establish the severity of – any possible adverse side effects and responses from people who have received the vaccine. The safety of the vaccine is paramount, with regular assessments and post-approval clinical studies to report on its safety and effectiveness.

Global and Regional Vaccination Coverage

The definition of Vaccination Coverage is the proportion of people who receive recommended vaccines [13]. It reflects the vaccination program's performance and the access to healthcare [14].

One of the most common vaccines used to analyze the global coverage panorama is DTP (diphtheria-tetanus-pertussis). The coverage of the DTP1 vaccine is an indicator of vaccination acceptance and access to primary health care [14]. The dropout between the administration of DTP1 and DTP3 may be suggestive of barriers to the health system, flaws in educating parents to bring their children back for subsequent doses, insufficient registration tracking of children at the healthcare or underspending of accessible vaccination services [14,15]. The DTP3's scope by the age of 12 months represents the situation and development of the immunization program. From 2019 to 2020, the DTP1 global coverage decreased from 90% to 87% and for DTP3 from 86% to 83%, which represents 3.7 million children not receiving DTP3. [15] Moreover, the countries with the most unvaccinated children for DTP3 are Nigeria, the Democratic Republic of the Congo, Ethiopia, and Angola [16].

Based on WHO's data of 2020, the vaccination coverage is unequal [15]:

- In the African region, 79% of the population received the first dose of DTP, but only 72% received the three doses;
- In the Americas region, 88% of the population received the first dose of DTP, but only 82% received the three doses;
- In the Eastern Mediterranean region, 87% of the population received the first dose of DTP, but only 81% received the three doses;
- In the European region, 97% of the population received the first dose of DTP, but only 94% received the three doses;
- In the South-East Asia region, 88% of the population received the first dose of DTP, but only 85% received the three doses;
- In the Western-Pacific region, 96% of the population received the first dose of DTP, but only 95% received the three doses

According to the WHO [16], the Global Vaccination Coverage's panorama in 2020 was:

- *Haemophilus influenzae type b* (Hib) Vaccine was introduced in 192 Member States, and its full series global coverage is estimated to be 70%;
- *Hepatitis B* (HepB) Vaccine was introduced in 190 Member States, and the global coverage with completed series is estimated at 83%;
- *Human papillomavirus* (HPV) Vaccine had been introduced in 111 Member States, and the final doses' global coverage is estimated at 13% ;
- Measles Vaccine (2 doses) was received by 70% of children and its program had been included in 179 Member States;
- Mumps Vaccine was introduced in 123 Member States;
- Pneumococcal Vaccine had a global third dose coverage's estimation in 49%, and had been introduced in 151 Member States;
- Polio Vaccine: its three doses were received by 83% of infants. Only Afghanistan and Pakistan haven't eradicated Polio;
- *Rotaviruses* Vaccine's global coverage was estimated to be 46%, and it was introduced in 114 countries;
- *Rubella* Vaccine (RCV) had been introduced in 173 Member States and its global coverage's estimation is 70%;

The Global Vaccination Coverage decreased for most vaccines in 2020 compared with 2019, i.e. DTP, Hib, HepB, HPV and RCV's vaccines. [15,16]. Moreover, in 2020, approximately 23 million children worldwide missed out on vaccination, being the highest number since 2009. Nonetheless, in 2020, 19 vaccine introductions were reported, less than 50% of any year in the last 20 years [17]. This alarming scenario is related to COVID-19 pandemic, as a consequence of the health system's overwhelming, social distancing measures, reduction of

transportation, concerns about exposure by health workers and caregivers, and the disruption of supply chain [15,17].

The Immunization Agenda (IA2030), endorsed by The World Health Assembly, draws global strategies and plans for vaccination in the decade 2021-2030. It supports immunization as essential for the right to health and also seeks to increase equality in this matter. In order to achieve the vision for the decade “A world where everyone, everywhere, at every age, fully benefits from vaccines for good health and well-being”. Some of its goals and targets are:

- Polio eradication by 2023;
- Neonatal tetanus elimination;
- Measles and rubella elimination in at least five WHO regions by 2020;
- Cholera control: reducing its related deaths by 90% by 2030 ;
- Elimination of viral hepatitis as a major public health threat: reducing new cases of chronic viral hepatitis B infections by 95% by 2030;
- Control of vector-borne diseases: reducing its related mortality by at least 75% by 2030;
- Elimination of yellow fever epidemics: reducing its outbreaks to zero by 2026;
- Elimination of meningitis epidemics by 2030 and reduction of cases and deaths by 2030;
- Reduction of seasonal influenza burden;
- Zero deaths from dog-mediated rabies by 2030 [18].

Distribution and access to vaccines

Health is an essential human right that should be a step towards conquering other human rights. Therefore, the right to health also encompasses the provision of immunization in an equitable process (OHCHR). The access to vaccines is related to the geopolitical scenarios, sustainability of the health systems, and providing support to oppressed populations.

- *Dismantlement of Health Systems and its threatenings*

Public Health Systems are fundamental to guarantee the right to health. Inside its structure, Primary Health Care is the closest level of attention to the community that mainly guarantees access to vulnerable populations, and also relates directly to vaccination campaigns. However, Public Health Systems worldwide are suffering from mercantilization, underfunding, and segmentation, especially the dismantlement and disruption of Primary Healthcare. On the other hand, the private sector and the high out-of-pocket expenses contribute to structural inequality in access to healthcare. This critical scenario directly impacts the assurance of equitable access to vaccination and the vulnerability of some populations [19].

- *Global Vaccine Distribution Inequality*

There is an inequity among the worldwide distribution of vaccination. According to data at the end of March 2021, nearly 3 months after the beginning of the anti-COVID 19 vaccination campaigns around the world, 20% of the population had around 95% of the COVID-19 Vaccines [20]. Moreover, as stated by WHO in a press release in April 2021 [21], in rich countries, 1:4 people were vaccinated, but in poorer countries only 1:500 were. In addition, in some marginalized countries, the vaccination coverage against COVID-19 will only be a reality after 2023. Therefore, while the central countries population can be vaccinated, the peripheral ones are facing a major risk of death [22].

This exacerbated inequality is explained by the richest countries' concentration of manufacturers to produce vaccines, which have been funded by public resources. Also, another explanation is that the vaccine industry charges differently to different countries. For example, some Latin American countries pay 50% more per dose for the same vaccine than the United States; and some African countries pay more than twice the price for

European countries [19,23]. Moreover, although the low-income countries helped develop vaccines by participating in clinical trials, they only had access to a very small percentage of vaccines [23].

The COVAX programme was promoted by WHO as a global collaboration to “accelerate the development, production, and equitable access to COVID-19 tests, treatments, and vaccines” [24]. Despite all the efforts to provide vaccine equity, it is still a small amount of vaccines delivered to poorer countries, in comparison to the richest countries' realities. For example, by 18th August 2021, the COVAX could only fully immunize 2,1% of Africa, 25% of South America and 8,3% of India, in contrast with 70% of the UK and 59% of the USA. On top of that, it does not solve the main issue of knowledge and structure gap for development of technology or intellectual property sharing [23, 25].

- *Patent Breaking*

According to the TRIPS (Trade-Related Aspects of Intellectual Property Rights) Agreement, pharmaceutical companies have at least 20 years (starting from the officialization of a patent) to profit over the creation of the product.

Regarding COVID-19 vaccines, the public sector worldwide had spent 86.6 billion euros on vaccines that would not exist without this support. Despite that, it was commercialized and the five major pharmaceutical companies were expected to make 38.5 billion dollars from sales of COVID-19 in 2021.

At the same time, the poorer countries could not acquire vaccines without being into more debt. The World Bank lent 500 million dollars for vaccines for mainly 42 poorer nations of the world. It reflects a historical neocolonial past of international division of work that the debt increases the inequities between the richest and poorest countries.

The patent breaking would not restrict the production of vaccines and would increase the equitable access to it. A decolonised approach to vaccination as a human right will be able to provide access to vaccines and ensure that every country will have resources to conquer the right to health [26,27]

- *Vulnerable population and its access to vaccination*

Society oppressed groups are more vulnerable, due to the loopholes in the health system and their Governments' neglect to provide equitable access to health care. These minorities' situation during the COVID-19 pandemic confirmed the reality of their marginalization and reinforced it.

Gender minorities: The lack of consideration of gender data in several parts of the world negatively impacts the analysis of the pandemic's consequences and the vaccination's statistics in the concerned population. Nonetheless, it is remarkable that structural society oppression results in disadvantageous women's position as risk-labor responsibilities (as frontline healthcare workers) and informal work. Hence, due to the economically vulnerable situation, this gender minority has been less able to adhere to social distancing measures. Consequently, women have an increased risk of infection, low access to prevention and treatment of pandemics, as COVID-19 [19, 28, 29].

Indigenous population: Indigenous communities suffer from socioeconomic ostracization and marginalization, resulting in a high risk of extreme poverty, low access to healthcare, and more consequences in health emergencies. (PAHO). This minority social group has an increased risk of severe cases and death by COVID-19 and other infections [30, 31].

Black population: The low access to vaccination by this minority reinforces the neglect and marginalization of the Black population by health systems. The existing disparity between the Black and the White populations, when it comes to vaccination coverage, is exemplified in some national data: In Brazil, according to data from March 2021, black people are vaccinated almost two times less than white people [32]. In the United States, however, the race-related gap regarding vaccination rates tightened over time. Between March 1st 2021 and

January 10th 2022, 54% of individuals among the Black population received at least one dose of the anti-COVID 19 vaccine, parallel to 60% in the White population. [33] Nevertheless, further strategies are to be developed to ensure total racial equity in vaccination.

Refugees and migrants: Refugees and migrants suffer from social, political, and economic exclusion, resulting in more exposure to infections and increased vulnerability. They are exposed to infection risk factors in daily life as overcrowded dormitories and unofficial/essential works. This vulnerable group also faces barriers to vaccination and access to healthcare such as lack of official documentation (leading to fear of violence and deportation), financial resources or information, language barriers, loss of confidence in authorities, and vaccine safety. Consequently, refugees and migrants have a higher risk of COVID-19 severe infection, hospitalization, and death [34].

Nevertheless, vaccination data must promote further analysis of social minorities, as the previously mentioned examples only represent a brief overview of the inequalities occurring during the current COVID-19 crisis. Hence, an approach to the process of vaccination management that prioritizes social minorities and recognizes the responsibility of equitable access is needed.

Vaccine hesitancy movement

WHO defines vaccine hesitancy as a “delay in acceptance or refusal of vaccines despite availability of vaccination services”, and it depends on factors that are influenced by time, place, and the type of vaccine. Until 2019, vaccine hesitancy has been outlined in more than 90% of the countries [35, 36].

According to research predominantly in rich countries, there are five determinants of vaccine hesitancy, also known as 5C: confidence, complacency, convenience (or constraints), risk calculation, and collective responsibility. The first one is the trust in the safety and effectiveness of vaccines, the system that manages vaccination and the motivation to be vaccinated. Complacency is when the perceived risk of the vaccine to prevent diseases is low, and it is not considered necessary. Constraints are related to barriers, such as structural or psychological, that influence the intention to be vaccinated becoming the uptake itself. Risk calculation is an individual comparison that perceives higher risks of being vaccinated than getting infected. Collective responsibility is the commitment to protect others by being vaccinated through population immunity. This framework can't be generalized to all continents, because of the limited scope of the research [37].

Although vaccine hesitancy is not restricted to the COVID-19 vaccination, it has been a risk for all the world population, through the unnecessary perpetuation of the pandemic [37]. According to surveys in 2021, only 50-60% of the interviewed group worldwide was willing to be vaccinated against COVID-19, and WHO recognized vaccine hesitancy as one of the 10 global health threats in 2019 [36].

The Director-General of WHO, during the COVID-19 pandemic, in 2020, said that “We're not just fighting an epidemic; we're fighting an infodemic” [38]. Apart from social media, misinformation was also shared and significantly spread by political figures through official media, which has the greatest impact on the population [38, 39, 40].

Vaccine hesitancy can be traced all the way back to the first discovery of vaccination. Motives for opposing vaccination were most often religious [41] in nature or rooted in distrust in physicians and medicine. Identical reasons can also be seen today. Reasons for vaccine hesitancy vary greatly and depend on time, region and type of vaccine. Some of these reasons include beliefs, knowledge or awareness level, past experiences with vaccination or lack of trust in the health system. That is exactly why there is no single intervention that addresses all instances of vaccine hesitancy.

To tackle this matter, it's important to understand the vaccine hesitancy contextualized in each country, especially in the ones where the scope of this research is still limited, as in African countries, since it will provide information

to design interventions more specifically to the social needs [37]. In addition, the Governments must provide information based on scientific evidence, and be transparent about the programs and availability of the vaccines.

Nevertheless, the media should be responsible and transparent to promote true and safe information. People using the internet and social media must avoid spreading fake news or language that could lead to misinterpretation and result in vaccine hesitancy [42]. It has also been suggested that modern ways of communication such as reminders via smartphones or tablets could be used to inform people of their waning immunity. Future vaccination strategies should therefore include regular and well-documented booster shots, e.g. against tetanus and diphtheria, throughout adulthood [43].

Education was proven to be an effective intervention since “health workers remain the most trusted advisor and influencer of vaccination decisions” [44]. This is a great responsibility that healthcare workers need to be conscious of. That is why special thought needs to be put into training them to communicate their message efficiently. Medical and epidemiological education should be evidence based, with a special focus on the delivery of the information as proper communication techniques are crucial for a physician to maintain their patients' trust [45].

Compulsory and Consigned vaccination

The COVID-19 vaccine and its opponents have led to many discussions regarding mandates and compulsory vaccination. A decreased coverage becomes a major problem, when the herd immunity threshold cannot be reached and vulnerable populations are left unprotected. Enforcing mandatory vaccinations has a precedent in history and is one of the strategies that some countries have adopted and others are considering in order to face this issue. Depending on local legislations, legal consequences for those who do not accept the uptake can be very different, ranging from pecuniary penalties to hurdles to attend public schools. In some cases, parents may even incur penal consequences. [46]

On the one hand, mandatory vaccination seems to be an easy option to increase vaccine coverage short-term in order to protect vulnerable populations, who cannot get vaccinated themselves and are relying on herd immunity. With regard to the concept of vaccine hesitancy, mandatory is a strong measure to break complacency. [47] A study published in the Lancet states that by the mid-19th century in Europe, regions with mandatory vaccination proved to have substantially fewer deaths from smallpox than those that relied on voluntary vaccination [48].

For some countries with rigid mandates like Australia and State of California, penalties of financial kind have been set for vaccine exempted individuals [47]. Others have a relatively less rigid mandate with room to opt out of vaccination on conscientious grounds of ethical or philosophical nature, without any penalties. Whereas in some other countries only a proof of participation in an education program regarding immunization is required for exemption from vaccination programs, without any penalties or social restrictions.

On the other hand, although implemented in several countries, mandatory vaccination is discussed controversially in public health as the impact on vaccine coverage is not clear yet, as it provides no guarantees of achieving high uptake rates long term. In a European study no relationship between vaccination coverage and national policies on compulsory vaccinations in the EU/EEA countries could be found. [46] Furthermore, mandates do not improve vaccine confidence, but they make opposition to vaccines even stronger. [47] The resulting anger can even lead to lower vaccine coverage rates. [49] This indicates that while being effective in decreasing complacency, mandates are not the right measure to increase trust in vaccination, as broader determinants of vaccine hesitancy are not addressed.

Many countries have systems where only some, but not all vaccines are compulsory. This bears the risk of a decrease in the vaccination coverage of the non-compulsory vaccine. Reasons are a reactance to the mandate [50] and the perception that non-compulsory vaccines might be less important.

Finally, mandatory vaccinations are a very restrictive public health measure from a human rights perspective, limiting freedom of choice and autonomy. A clear and strong indication should be present, when such measures are taken. Considering all these perspectives, it becomes apparent that there is no universal solution.[51] Any decision about a proposal for vaccines strategies, whether recommendations or mandates, should be elaborated

in agreement with local contextual habits, the size of the problem, the urgency of the situation and ethical considerations. A transparent decision making process should be encouraged to ensure that the right measures for the situation are taken.

Likewise, the discussions on a compulsory COVID-19 vaccine have been controversial. As of December 2021, COVID vaccinations are already a requirement for public life in many parts of the world and many countries consider introducing mandatory vaccinations for all. In Austria, a special lockdown for the unvaccinated was introduced on Nov. 15, leaving them unable to enter nonessential businesses, entertainment and sports venues. Greece will mandate vaccination for people 60 and older in January 2022, and Czech Republic's government as of March 1.

A study found that restrictions that targeted only the unvaccinated increased people's willingness to take the shot compared with restrictions targeting everyone regardless of their immunity status. The survey by the Munich-based Ifo economic research institute examined vaccination rates in districts along the border between Austria and Germany and found that vaccination increased in Austria under a lockdown targeting only the unvaccinated, from a 61.1% vaccination rate on Oct. 4 to 68% by Dec. 4, after Austria had imposed a lockdown on the unvaccinated. [52]

Interprofessional collaboration

In order to eliminate vaccine-preventable diseases, the focus should not be placed only on human vaccination. In fact, diseases with animal-reservoirs may require a more inclusive "One Health" approach. Rabies, for example, is a disease responsible for about 59,000 human deaths per year and over 3.7 millions Disability-Adjusted Life Years (DALY) [53]. Up to 99% of human cases are transmitted by dogs. Therefore mass vaccination campaigns targeting dogs are, nowadays, the main strategy of rabies control [54]. However, it is not sufficient on its own and human vaccination is still required. This shows the huge need for collaboration between medical and veterinary sectors in order to prevent the unnecessary burden of rabies, as well as other infectious diseases transmitted by animals.

Apart from the veterinary sector, interprofessional collaboration is needed for vaccine distribution and increase of vaccine uptake, through tackling vaccine hesitancy and complacency. Vaccine distribution strategies require regional and local public health officials in coordination with their partners in health systems and government, in order for vaccines to be disseminated and accessible to the broader community. [55]

Offering pharmacists the option to deliver adult vaccination has shown an increase in vaccine uptake in several countries [56]. The effect is notable through reaching under-vaccinated populations [57], as well as a greater engagement with public health messaging and immunization advocacy [56]. Increased collaboration with pharmacists and pharmaceutical students, including adequate training, may help to increase vaccination coverage and public trust.

Finally, to maximize the success of vaccination programmes, a joint effort between different disciplines including clinicians, public health doctors, epidemiologists and policy makers is necessary.

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