Mathematical modelling of some poliomyelitis vaccination and migration scenarios in Colombia

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Abstract. The Poliomyelitis is an acute infection that has not eradicated worldwide. There are two types of vaccines for prevention: the live attenuated virus (OPV) and the inactivated polio virus (IPV). In Colombia, the poliomyelitis eradication strategy has been implemented, changing the OPV for the IPV, following the recommendations of the World Health Organization (WHO). This paper presents a mathematical model that describes the dynamics of the infection in a population where the two types of vaccines are implemented. The population is divided into two age groups, considering migratory effects between them, the interactions are described using Michaelis-Menten functions. Different vaccination scenarios are simulated and analysed in order to establish the convenience of replacing OPV vaccination with IPV.

1. Introduction
1.1. Disease description
Poliomyelitis is an infectious disease of varying severity that can affect the central nervous system and occasionally cause flaccid paralysis. It also has been called infantile paralysis or Heine-Medin disease [1]. The human is the only natural host of the poliovirus, which can be transmitted via the respiratory route, but its usual infection is via the fecal-oral route, with marked tropism by the intestinal cells. The natural cycle of the virus is usually asymptomatic and corresponds to the multiplication in the intestine [1]. After multiplying in the oropharynx and the small intestine, especially in the lymphatic tissue, the virus spreads through the bloodstream to the Central Nervous System [2]. The distinctive characteristic of poliomyelitis is the selective destruction of motor neurons, which leads to paralysis and, in severe cases, to respiratory arrest and death [3].

The incubation period of polio is from 7 to 21 days, with a range of 4 to 40 days [1]. The poliovirus corresponds to a class of the group of enteroviruses [4], and likewise, enteroviruses are part of the picornavirus family, which also includes rhinoviruses [2]. Specifically, The picornaviruses are small, non-enveloped viruses (20-30nm) formed by an icosahedral nucleocapsid and a single-stranded RNA genome. Picornaviruses multiply in the cytoplasm of cells. They are not inactivated with lipid solvents, such as ether, because they do not have a wrap [2].

An
important fact is that enteroviruses are very resistant to physical and chemical agents, so they persist in the environment, their elimination is done through feces for prolonged periods (about 6 weeks) [3].

1.2. Vaccines and disease control
There are three types of poliovirus antigens (serotypes 1, 2, 3), all polioviruses within a serotype can be neutralized by specific antisera for each type, but a specific treatment against poliomyelitis viruses does not exist [3]. There is an live attenuated oral virus vaccine (OPV) and parenteral inactivated virus vaccine (IPV) that have allowed its eradication and control in most of the planet [4].

Poliomyelitis can be prevented with both the inactivated vaccine and live attenuated vaccine. Both vaccines induce humoral antibodies that neutralize the virus that enters the blood and thus prevents central nervous system infection and polio disease [2]. Those vaccinated with the OPV vaccine excrete the vaccine virus in the feces, which spreads in the environment and can immunize other people who have not received the vaccine (herd immunity). Vaccination with OPV has generated undeniable benefits in the eradication of wild paralytic poliomyelitis [5]. The IPV vaccine also includes the three virus serotypes, it is called an inactivated vaccine and it is given to newborns and immunodeficient individuals by injection. IPV is as effective as OPV in blocking the transmission of the disease, however, by itself, it does not produce the same level of intestinal immunity as OPV, so it does not prevent the wild virus from being excreted in the feces spread in the environment [5]. In 1994, the International Certification Commission for Poliomyelitis Eradication of polio (ICCPE) concluded that the natural circulation of wild poliovirus in the Americas had been interrupted. One of the risks of being faced in the post-eradication stage of polio is the appearance of polio cases due to a vaccine-derived virus [6, 7]. Once a country obtains the certification of polio eradication, the World Health Organization recommends interrupting the use of OPV, passing to applied the IPV [8].

1.3. Research scope
Although such progressive change of vaccines presents risks, due to this disease has not been eradicated worldwide. Thus, the intraregional immigration of people and the differences in conditions of control and surveillance of diseases are factors that increase the potential risk [9]. In this sense, CEPAL in its 2018 report states that the so-called South-South migration, that is between South American countries, represents 37% of the total international migration, surpassing the traditional south-north migration flow in America that represents the 35% [10]. Actually, some epidemiological models introduce parameters or variables representing the people movements to understand: How do peoples’ movements affect the spreading of diseases and its control? [11–13].

In this work, we have as the main purpose to study the dynamical behaviour of polio in a scenario in which two types of vaccines are applied to control the disease considering as well immigrants. The model studied corresponds to a system of ordinary differential equations that represents a scenario where the migrations are occurring between subregions that present similar vaccinations coverage and geographic characteristics.

2. The model
There are several mathematical models that allow us to understand the dynamics of polio, for instance, the ones presented by Cvjetanovic et al. 1982 [14], Alvis N. et al. en 2010 [7] and Duarte et al.2013 [8]. The mathematical model studied in this work corresponds to a system
of ordinary differential equations. To obtain such model, we have assumed that the population is compartmentalized, i.e., it is divided in local subpopulations between that the individuals transit or migrate [15]. The territorial division of Colombia does not consider the San Andrés and Providencia departments, the remaining areas are divided into 6 subregions that are chosen by analyzing the geographical characteristics and the data of vaccines coverage registered by the Ministry of Health and Social Protection of Colombia [16]. In the Table 1 the 6 subregions are described.

**Table 1. Description of the 6 subregions.**

| Subregion | Departments                                                                 |
|-----------|-----------------------------------------------------------------------------|
| 1         | Atlántico, Bolívar, Cesar, Córdoba, Magdalena, Guajira, Sucre                |
| 2         | Valle del Cauca, Chocó, Cauca, Nariño, Antioquia, Caldas, Risaralda          |
| 3         | Quindío, Tolima, Huila, Caquetá                                             |
| 4         | Norte Santander, Santander, Boyacá, Cundinamarca, Meta, Arauca, Amazonas,   |
|           | Casanare                                                                    |
| 5         | Guainía, Guaviare, Vichada, Vaupes, Putumayo                                |
| 6         | Bogotá                                                                      |

The model assumptions are: (i) There are migrations between subregions, (ii) The migrations between departments belonging to a subregion are not considered, (iii) The birth and dead rates are equal, (iv) An individual has acquired the infection only if he/she develops flaccid paralysis and it is shown to be caused by poliovirus, (v) After a year, the circulating virus derived from the OPV vaccine can regain virulence, (vi) People who have never been vaccinated and have contact with the vaccine virus (which has mutated between 1% and 15%), can develop an infection, (vii) Some individuals having oral contact with the Sabin virus (which has mutated less than 1%) circulating in the environment develop immunity, (viii) A part of the vaccinated population does not develop antibodies, and (ix) Children are considered vaccinated only if they have received at least 5 doses up to 5 years (complete vaccination schedule). The population is measured in thousands of individuals and it is divided into the following subclasses: (i) Susceptible up to 5 years, (ii) Susceptible over 5 years, (iii) Vaccinated with OPV, (iv) Vaccinated with IPV, and (v) Infected. The meaning of variables in each subregion \( j \) for \( j = 1, 2, ..., 6 \), at time \( t > 0 \) are presented in the Table 2.

**Table 2. Meaning of variables.**

| \( S_j(t) \): | Number of susceptible up to 5 years in the subregion \( j \). |
| \( S_{2j}(t) \): | Number of susceptible over 5 years in the subregion \( j \). |
| \( VO_j(t) \): | Number of Vaccinated with OPV in the subregion \( j \). |
| \( VI_{OPV}(t) \): | Number of Vaccinated with IPV in the subregion \( j \). |
| \( VI_{IPV}(t) \): | Number of Infected in the subregion \( j \). |
| \( ViS_j(t) \): | Population of Sabin virus circulating in the subregion \( j \). |
| \( ViV_j(t) \): | Population of vaccinating virus circulating in the region \( j \). |

The meaning of parameters are given in Table 3.
Table 3. Meaning of parameters.

| Parameter | Definition |
|-----------|------------|
| $\rho_j$  | Covering vaccination rate with OPV in the subregion $j$ |
| $\beta_j$ | Covering vaccination rate with IPV in the subregion $j$ |
| $\mu$    | Birth and dead rate |
| $c$       | Sabin poliovirus rate released to the environment by individual vaccinated with OPV |
| $\alpha$ | Rate at which the circulating Sabin virus recovers virulence |
| $\theta$ | Rate of poliovirus degradation in the environment |
| $\tau$   | Transition rate of susceptible population up to 5 years of age to over 5 years |
| $\omega$ | Rate of infection with the circulating vaccine virus |
| $\delta$ | Herd immunity rate |

The rate of infection with circulating virus denoted by $\omega$ and the herd immunity rate denoted by $\delta$ are depending of the population of virus circulating, which are defined by:

$$
\omega = \frac{aV_iV}{1 + aV_iV}, \quad \delta = \frac{bV_iS}{1 + bV_iS}.
$$

(1)

Such functions are adaptations of the Michaelis-Menten functions used in enzymatic reactions, and properly describe the contagion, because it considers incidence rates that include saturation effects, which are used in epidemiological models [17,18], i.e. if $ViV \to +\infty$ then $\omega \to 1$, and if $ViS \to \infty$ then $\delta \to 1$. Thus, $\omega$ and $\delta$ grow asymptotically with the amounts of poliovirus, vacunal and Sabin, respectively, present in the environment. Meanwhile, parameter $a$ represents the infectivity rate of the vaccine virus and $b$ the immunization rate of the Sabin virus [8] and the migration rates values are given in Table 4. Information obtained from DANE [19]. Additionally, let us denote by $X_j$ the different population subclasses, where $X$ can be replaced by some of the notations $S_1, S_2, VO, VI, I$, for each subregion $j$ with $j = 1, 2, ..., 6$. Thus, for each $X_j$ is defined,

$$
propX_j = \frac{X_{j0}}{\sum_{j=1}^{6} X_{j0}},
$$

(2)

where $propX_j$ corresponds to the fraction that $X_j$ to calculate on initial data $X_{j0}$. Additionally, we introduce in Table 4 some notations for representing the number of individuals that leave and enter the region daily.

Table 4. Migration rate between regions.

| Region | 1    | 2    | 3    | 4    | 5    | 6    |
|--------|------|------|------|------|------|------|
| 1      | 0    | 0.005| 0.029| 0.029| 0.002| 0.033|
| 2      | 0.004| 0    | 0.046| 0.009| 0.002| 0.018|
| 3      | 0.020| 0.044| 0    | 0.041| 0.004| 0.062|
| 4      | 0.015| 0.007| 0.025| 0    | 0.012| 0.085|
| 5      | 0.001| 0.008| 0.006| 0.018| 0    | 0.007|
| 6      | 0.011| 0.013| 0.038| 0.124| 0.005| 0    |

The evolution of the different subclasses is represented for the system of Equations (3) and Table 5,
\begin{align*}
\frac{dS_1}{dt} &= \mu(S_2 + V_0 + V_I + I_j) - (\rho + \beta + \omega + \delta + \mu + \tau)S_1 + (in_j - em_j)propS_1 \\
\frac{dS_2}{dt} &= \tau S_1(t) - (\omega + \delta + \mu)S_2(t) + (in_j - em_j)propS_2 \\
\frac{dV_0}{dt} &= (\rho + \delta)S_1 + \delta S_2 - \mu V_0 + (in_j - em_j)propV_0 \\
\frac{dV_I}{dt} &= \beta S_1 - \mu V_I + (in_j - em_j)propV_I \\
\frac{dI}{dt} &= \omega(S_1 + S_2) - \mu I_j(t) + (in_j - em_j)propI \\
\frac{dV_S}{dt} &= \epsilon V_0 - (\theta + \alpha)V_S \\
\frac{dV_V}{dt} &= \alpha V_S - \theta V_V
\end{align*}

(3)

Table 5. Flux of migrations.

| $in_j$: Number of individuals entering to the subregion j | Corresponds to adding the column j in the matrix of migrations Table 5 |
| $em_j$: Number of individuals leaving the region j | Corresponds to adding the row j in the matrix of migrations Table 5 |

for each subregion $j$, with $j = 1, 2, \ldots, 6$. The initial data is denoted by $S_{1j0}, S_{2j0}, V_{0j0}, V_{Ij0}, I_{j0}, V_{iSj0}$, and $V_{iVj0}$, which are given in Table 6 that were estimated from the information obtained by the census of 2005 in Colombia applied by DANE [19].

Table 6. Initial conditions of the populations

| Region | 1       | 2      | 3      | 4      | 5      | 6      |
|--------|---------|--------|--------|--------|--------|--------|
| S1     | 41.72   | 132.34 | 69.85  | 106.51 | 28.43  | 115.24 |
| S2     | 450.53  | 1242.57| 716.18 | 1013.82| 260.99 | 1087.17|
| V0     | 8264.31 | 5675.15| 9638.74| 6082.14| 560.54 | 5508.50|
| VI     | 88.45   | 71.21  | 105.30 | 72.75  | 8.59   | 67.77  |
| I      | 0       | 0      | 0      | 0      | 0      | 0      |
| ViS    | 0       | 0      | 0      | 0      | 0      | 0      |
| ViV    | 0       | 0      | 0      | 0      | 0      | 0      |

3. Simulations

To approximate the solutions of (3), it has been applied the method Runge-Kutta of order 4 for systems [20], implemented in Matlab® [21].

Computational tests were done to simulate the behaviour of human populations (Susceptible, Vaccinated and Infected) and of the virus (Sabin virus and vaccine virus), some representative ones are presented here. Initially there are neither vaccines with IPV, nor infected individuals (see Figure 1 and Figure 2).

The parameters values are: (i) $\epsilon = 1.1/365$, estimated from the direct proportion of the amount of virus contained in Plaque Forming Units (PFU) and the amount of Sabin virus thrown into the environment by one vaccinated per day for 15 days [22,23]; (ii) $\alpha = 1/365$ considering that from one year the vaccine...
virus begins to recover virulence; (iii) It is considered that a 5% of the virus decays daily, so that \( \theta = 0.05 \); and (iv) \( a = 0.1, \ b = 0.1 \), which is equivalent to assuming that the infective of the vaccine virus and the immunization of the Sabin virus are 10% effective.

For the purposes of the simulations, initial populations are considered (in thousands) given in the Table 6 and calculated from information provided by DANE [19], the migrations are presented in the Table 5 [19] and the OPV vaccination coverage given in the Table 7 [16] (see Figure 1 and Figure 2).

### Table 7. Vaccination coverage in each region.

| Region | 1     | 2     | 3     | 4     | 5     | 6     |
|--------|-------|-------|-------|-------|-------|-------|
| OPV    | 0.942833 | 0.804167 | 0.923667 | 0.8436  | 0.658813 | 0.82  |

#### Figure 1.
(a): This figure corresponds to a scenario with migrations, there are vaccination coverings with OPV, there are no vaccination with IPV and initially there is no presence of virus of any type. (b): This figure corresponds to a scenario with migrations, there are vaccination coverings with OPV, initially there is presence of viruses.

#### Figure 2.
(a): The figure corresponds to a scenario with migrations, there are vaccination coverage for OPV decreased by 80% compared to the initial coverage, there is no coverage with IPV, there is presence in regions 2 and 6 of 1 ViS virus and there is 1 ViV virus. After 6 months, coverage by IPV is implemented by 40%. (b): The figure corresponds to a scenario with migrations, there are no OPV vaccination coverage, there is no coverage with IPV, there is presence in regions 3 and 5 of 1 ViS virus and there is 1 ViV virus. After 6 months it is implemented IPV coverage by 50%.
4. Conclusion and future perspectives

Through the simulations, we conclude that the evolution of the different populations subclasses involved in the dynamics, mainly, depends on the initial number of circulating virus in the environment and the number of susceptible up to 5 years, while it is independent of Vaccination coverage when it is assumed that poliovirus is present in the environment. Therefore, a greater vaccination coverage with OPV in the susceptible population up to 5 years, implies a greater risk of future infections, in case of suspension or replacement of the OPV vaccine. This is because after 1 year the circulating Sabin virus provided by the OPV vaccine regains virulence, which increases the probability that a susceptible person will be infected. Such conclusion suggests that it must be completely sure that there is no presence of virus in the environment to initiate the vaccine change, that is, a total eradication of the disease. Otherwise, migration contributes to the redistribution of the disease in those populations where there is only vaccination with IPV.

In addition, due to its geographic condition, Colombia becomes an attractive country for the passage of migrants from other neighbouring countries, and even continents. These migrants, who may come from countries where polio has not been eradicated or whose vaccination coverage has been insufficient for their eradication, put the population at risk because they can expel viruses, either in their wild form or in virulence during their transit or stay in Colombia. Thus, the results of this work leads us to corroborate that the substitution of OPV vaccination for IPV in Colombia is not recommended. The projection of this work is the inclusion of internal migration rates and the study of the behaviour of polio applying other mathematical techniques as the theory of complex networks.

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