Inoculation Strategies for Polio: Modeling the Effects of a Growing Population on Public Health Outcomes

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Abstract

The World Health Organization has called for global eradication of Polio by 2018, but the disease remains endemic in three countries. Using an expanded SIR model, the present contribution takes into account the effects of a rapidly growing population on the effectiveness of various vaccination protocols and on the burden of disease in the community. Necessary and sufficient conditions were found for elimination of Polio in such a population in the event of an outbreak.

1 Background

Poliomyelitis, known to most simply as Polio, has afflicted the human race since the late 18th century. It was not until the 1950s that we had any defense against this infectious disease. This was just around the time that Polio was at its peak in the United States, causing paralysis in more than 21,000 Americans in 1952 alone. The first defense against Polio- the injected Polio vaccine (IPV)-was introduced by Jonas Salk in 1955. This was quickly followed by an oral Polio vaccine developed in the early 1960s by Albert Sabin. Each vaccine has its benefits and drawbacks, but these two vaccines continue to be distributed and refined today. Most developed countries have switched to exclusively using IPV because of the vaccine derived infections sometimes caused by OPV, but OPV continues to be used in developing countries because of its cost-effectiveness, reliability for initiating an immune response in the gut, and ease of administration(**?**).

In 1988, the World Health Organization declared the eradication of Polio by 2000 to be a global goal. Complete eradication was not achieved in this time period, but elimination of Wild-Type Polio 2 (WPV2), one of three wild polio strains, was successful. Today, Polio remains present in areas of Africa and Western Asia, mostly in the form of WPV1(**?**), and the WHO has set its sights on 2018 as the new target for eradication. This is a difficult task, since Polio can often remain unnoticed in a population for a long period of time, since the majority of cases are asymptomatic and do not result in the easily detectable Acute Flaccid Paralysis(AFP)(**?**).

Only three countries have never seen eradication of Polio within their borders: Nigeria, Pakistan, and Afghanistan. Each of those countries presents a different public health challenge to the global community, but the greatest worry is that continued infection in those countries will results in Polio reinfecting communities nearby that have already eliminated the disease(**?**). Nigeria in particular is quite close to eradicating Polio, and only four wild Polio cases have been reported this year (though because of Polio's high prevalence of asymptomatic cases, every detected case is considered a full-scale outbreak **?**). One of Nigeria's unique roadblocks is that it has one of the fastest growing populations in the world. In this study, we intend to discover how this non-constant population affects spread of the Polio virus in Nigeria.

The results of this research can be used to examine strategies for preventing the spread of Polio in Nigeria, and can also be easily extrapolated to suggest vaccination methods for other infectious diseases in populations with non-constant growth.

2 Model Development

2.1 Model

Using an SIR modeling approach, we came up with a fundamental model for the spread of Polio in a population, with modifications to include two separate vaccination strategies. Illustrations for those models are included below.
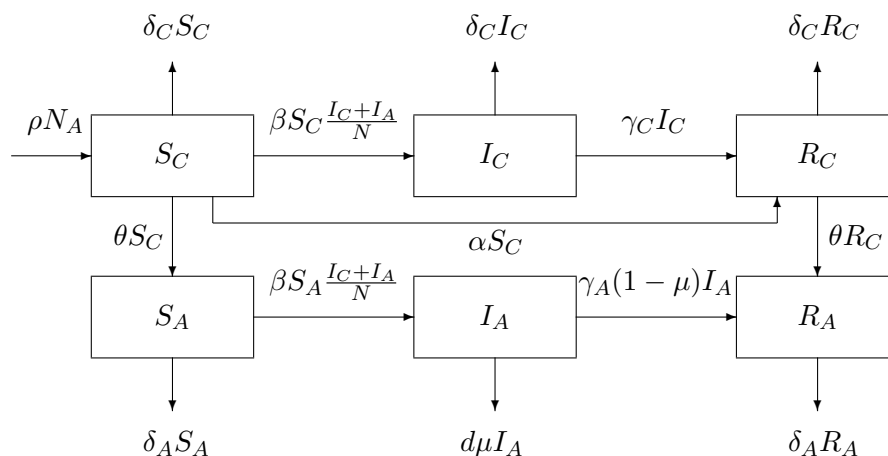

Figure 1: SIR Model For 1-5 Year-Old Vaccination Strategy

The models used are split population models, where S_C, I_C, and R_C denote the susceptible, infectious, and recovered compartments for children, and S_A, I_A, and R_A denote the susceptible, infectious, and recovered compartments for adults. For the purposes of these models, children are considered to be persons in the 1-4 year age range, and adults
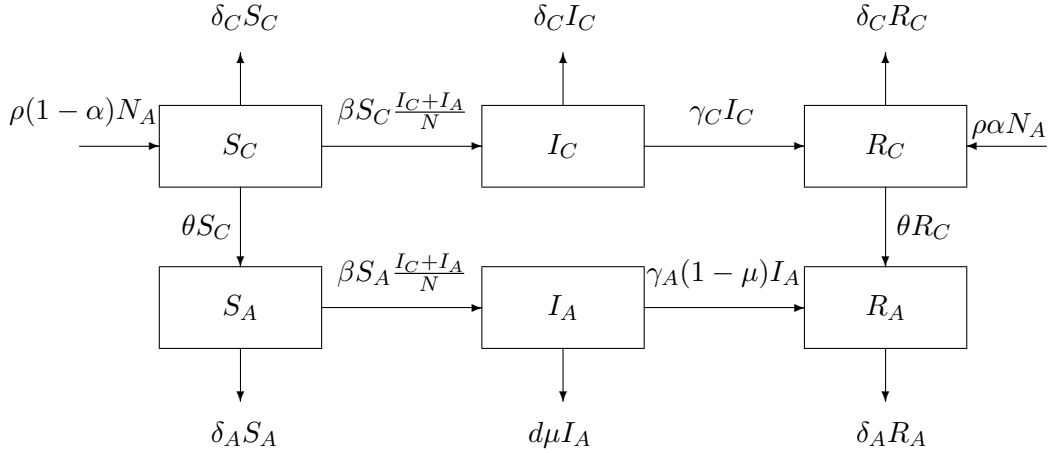
$$\delta_C S_C \qquad\qquad \delta_C I_C \qquad\qquad \delta_C R_C$$

$$\rho(1-\alpha)N_A \quad \boxed{S_C} \quad \beta S_C \frac{I_C+I_A}{N} \quad \boxed{I_C} \quad \gamma_C I_C \quad \boxed{R_C} \quad \rho\alpha N_A$$

$$\theta S_C \qquad\qquad\qquad\qquad \theta R_C$$

$$\boxed{S_A} \quad \beta S_A \frac{I_C+I_A}{N} \quad \boxed{I_A} \quad \gamma_A(1-\mu)I_A \quad \boxed{R_A}$$

$$\delta_A S_A \qquad\qquad d\mu I_A \qquad\qquad \delta_A R_A$$

Figure 2: SIR Model For Newborn Vaccination Strategy

to be any person age 5 or above. The child class age range was chosen to reflect the standard ages at which children are vaccinated. In Nigeria, vaccinations for this age class in particular are conducted during nation-wide Supplemental Immunization Activities(SIAs) every several months. Nigeria also has a highly imbalanced population distribution, with a median age of 18 and more than 40% of the population under the age of 14, which has an important impact on the public health burden of an outbreak in a Nigerian community. This public health burden is exacerbated by the fact that 25-30% of adults infected with Polio ultimately die from the disease, and those adults who survive take much longer to recover than children. Conversely, children tend to die at a much faster rate from all other causes. To simulate maturation of individuals from the child to adult classes, we introduce a maturation rate for the susceptible and recovered classes, but disregard maturation in the infectious class because the infectious period is fairly short.

Another critical aspect of this model is the non-constant population and non-constant death rates. As mentioned above, Nigeria's child mortality rate is much higher than its crude death rate, both of which we assume to be independent from death from the disease. We make the assumption that no children die from the disease (since research suggests that only 1% of child Polio cases result in death). However, we cannot make this assumption for infectious adults, whose mortality rate is about one quarter. Instead, we assume that infectious adults will not die from other causes, since the infectious period is so short. It is also important to note that the birth rate is dependent only on the adult population, since those in the child classes cannot reproduce.

The contact infection and recovery rates reflect the typical rates used in SIR models, though they are specific to Polio and Nigeria. This model takes into account different recovery rates for children and adults, but assumes that the contact infection rates will be the same, since there is no clear data that indicates otherwise.

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Figure 1 demonstrates our first vaccination strategy: vaccinating those in the susceptible children class. In this model, children ages 1-4 flow from the susceptible class to the recovered class at a vaccination rate α. This is reflective of the SIA campaigns where public health officials try to vaccinate some percentage (α) of susceptible children in this age range.

The second vaccination model that is considered (Figure 2) portrays the scenario in which immunized children finish their polio vaccine series before the age of 1, so they enter the population in the recovered class. In this case, the vaccination rate α represents the percentage of newborns that are vaccinated in their first year of life. We assume for both models that the administered vaccine series provides lifelong immunity.

We can express the model in which 1-5 year-olds are vaccinated as the following system of differential equations:

$$S'_C(t) = \rho N_A(t) - \beta S_C(t)\frac{I_C(t)+I_A(t)}{N(t)} - (\theta + \delta_C + \alpha)S_C(t)$$

$$I'_C(t) = \beta S_C(t)\frac{I_C(t)+I_A(t)}{N(t)} - (\gamma_C + \delta_C)I_C(t)$$

$$R'_C(t) = \gamma_C I_C(t) - (\delta_C + \theta)R_C(t) + \alpha S_C(t)$$

$$S'_A(t) = \theta S_C(t) - \beta S_A(t)\frac{I_C(t)+I_A(t)}{N(t)} - \delta_A S_A(t)$$

$$I'_A(t) = \beta S_A(t)\frac{I_C(t)+I_A(t)}{N(t)} - (\gamma_A(1 - \mu) + d\mu)I_A(t)$$

$$R'_A(t) = \theta R_C(t) + \gamma_A(1 - \mu)I_A(t) - \delta_A R_A(t)$$

$$S_A(t) + I_A(t) + R_A(t) = N_A(t)$$

$$S_C(t) + I_C(t) + R_C(t) = N_C(t)$$

$$N_C(t) + N_A(t) = N(t).$$

The differential equations for our second model considering vaccination of newborns are similar, but the following two equations replace the original equations for $S'_C(t)$ and $R'_C(t)$:

$$S'_C(t) = (1 - \alpha)\rho N_A(t) - \beta S_C(t)\frac{I_C(t)+I_A(t)}{N(t)} - (\theta + \delta_C)S_C(t)$$

$$R'_C(t) = \gamma_C I_C(t) - (\delta_C + \theta)R_C(t) + \alpha \rho N_A(t).$$

2.2 Disease Free State

In order to evaluate the efficacy of our vaccination models, we must first determine their behavior at the disease free state. We can model the child and adult classes at a disease free state (note that with a growing population this is not an equilibrium) by the following system of equations:

$$N'_C(t) = \rho N_A(t) - (\delta_C + \theta)N_C(t)$$

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$$N'_A(t) = \theta N_C(t) - \delta_A N_A.$$

We can use these results to compare an ideal population model (no disease) to the outcomes of introducing Polio into a population, which will increase net death due to adult mortality from the disease.

We find that for our newborn vaccination scenario, the following equilibria are reached for the non-dimensionalized compartments:

$$\frac{S}{N}(t) = (1 - \alpha), \qquad \frac{I}{N}(t) = 0, \qquad \text{and} \qquad \frac{R}{N}(t) = \alpha.$$

Specifically, we have

$$\frac{S_C}{N}(t) = (1 - \alpha)\frac{N_C}{N} \qquad \text{and} \qquad \frac{S_A}{N}(t) = \alpha\frac{N_A}{N}.$$

2.3 Perturbation of the Disease Free State

Due to our split population model, we do not have a single infectious class to monitor when the disease free state is perturbed, so we must introduce a new standard to consider what it means for Polio to be epidemic. The following method outlines this approach, where we perturb the disease free state by a small amount $(\vec{\epsilon}(t))$ and then observe whether $\vec{\epsilon}$ subsides to $\vec{0}$ or takes off exponentially. This observation indicates whether or not the disease free state is stable (when $\vec{\epsilon}'(0)$ is negative) or unstable(when $\vec{\epsilon}'(0) \geq 0$).

Define $\vec{x}(t) = \begin{pmatrix} S(t) \\ I(t) \\ R(t) \end{pmatrix}$ and $\vec{x}'(t) = \Im(\vec{x}(t))$. Let $\vec{\epsilon}(t) > \vec{0}$ for all $t > 0$ and suppose that $\vec{x} = \vec{x}_{DFS}(t) + \vec{\epsilon}(t)$. Then $\vec{x}'(t) = \Im(\vec{x}) = \Im(\vec{x}_{DFS}(t) + \vec{\epsilon}(t))$. Using a Taylor expansion around $\vec{x}_{DFS}(t)$, we can approximate $\Im(\vec{x}) = \Im(\vec{x}_{DFS}(t) + D_x\Im(\vec{x}_{DFS}(t))\vec{\epsilon}(t)$. Thus, we find that $\vec{\epsilon}'(t) = D_x\Im(\vec{x}_{DFS}(t))\vec{\epsilon}(t)$. We can then find $J = D_x\Im(\vec{x}_{DFS}(t))$, the Jacobian of our system of differential equations evaluated at the disease free state. For our model considering vaccination of 1-5 year-olds, we find that

$$J_1 = \begin{pmatrix} -\delta_C - \theta - \alpha & -\beta\frac{S_C}{N} & 0 & \rho & \rho - \beta\frac{S_C}{N} & \rho \\ 0 & \beta\frac{S_C}{N} - \gamma_C - \delta_C & 0 & 0 & \beta\frac{S_C}{N} & 0 \\ \alpha & \gamma_C & -\delta_C - \theta & 0 & 0 & 0 \\ \theta & -\beta\frac{S_A}{N} & 0 & -\delta_A & -\beta\frac{S_A}{N} & 0 \\ 0 & \beta\frac{S_A}{N} & 0 & 0 & \beta\frac{S_A}{N} - d\mu - \gamma_A(1-\mu) & 0 \\ 0 & 0 & \theta & 0 & \gamma_A(1-\mu) & -\delta_A \end{pmatrix}.$$

In order for the disease free state to be stable, all six eigenvalues of the Jacobian must be negative. Using Routh-Hurwitz criteria, we find that satisfaction of the following inequalities are necessary and sufficient conditions for this stability:

$$(\delta_C + \theta)\delta_A > \rho\theta \tag{1}$$

$$\frac{\beta\frac{S_C}{N}}{\delta_C + \gamma_C} + \frac{\beta\frac{S_A}{N}}{d\mu + \gamma_A(1-\mu)} < 1. \tag{2}$$

Likewise, we find the following Jacobian for our vaccinating newborns model:

$$J_2 = \begin{pmatrix} -\delta_C - \theta & -\beta\frac{S_C(t)}{N(t)} & 0 & \rho(1-\alpha) & \rho(1-\alpha) - \beta\frac{S_C(t)}{N(t)} & \rho(1-\alpha) \\ 0 & \beta\frac{S_C(t)}{N(t)} - \gamma_C - \delta_C & 0 & 0 & \beta\frac{S_C(t)}{N(t)} & 0 \\ 0 & \gamma_C & -\delta_C - \theta & \rho\alpha & \rho\alpha & \rho\alpha \\ \theta & -\beta\frac{S_A(t)}{N(t)} & 0 & -\delta_A & -\beta\frac{S_A(t)}{N(t)} & 0 \\ 0 & \beta\frac{S_A(t)}{N(t)} & 0 & 0 & \beta\frac{S_A(t)}{N(t)} - d\mu - \gamma_A(1-\mu) & 0 \\ 0 & 0 & \theta & 0 & \gamma_A(1-\mu) & -\delta_A \end{pmatrix}$$

and the following Routh-Hurwitz inequalities:

$$1 - \frac{(\delta_C + \theta)\delta_A}{\rho\theta} < 2\alpha \tag{3}$$

$$\frac{\beta\frac{S_C}{N}}{\delta_C + \gamma_C} + \frac{\beta\frac{S_A}{N}}{d\mu + \gamma_A(1-\mu)} < 1.$$

We note that inequality (2) is present for both models, and that it bears remarkable similarity to typical R_0 values for simple constant population models. In the case of our newborn vaccination models, we can use the above calculation for the disease free state to find inequality (2) in terms of the vaccination rate as follows:

$$\frac{\beta(1-\alpha)\frac{N_C}{N}}{\delta_C + \gamma_C} + \frac{\beta(1-\alpha)\frac{N_A}{N}}{d\mu + \gamma_A(1-\mu)} < 1.$$

This derivation is significant in that both inequalities for the newborn model are dependent on the vaccination rate, which is much easier to manipulate than birth or death rates. We observe that if the vaccination rate is 1 (which would correspond to 100% vaccination of newborns), both inequalities would automatically be satisfied. We can use inequalities (2) and (3) to find the minimum vaccination rate necessary to prevent an epidemic when Polio is introduced to a previously disease free population.

2.4 Finding Equilibria

In addition to examining the necessary conditions for prevention of an epidemic in the case of an outbreak, we are interested in the long term effects of the disease on the population. It is critical to the eradication endgame to determine whether or not the disease will reach an endemic equilibrium. However, this is much more difficult to discern given a growing population.
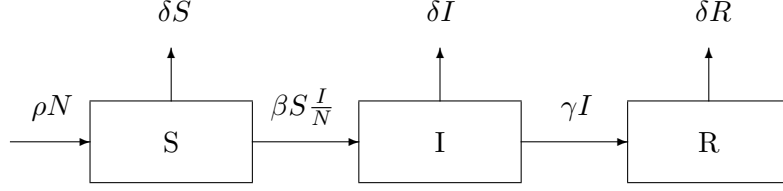
Figure 3: Basic SIR Model with Non-Constant Population

Before diving in with our split population model, we examine the effects of a non-constant population on the simple SIR model pictured above in Figure 3.

For the above system, we assume that $\rho > \delta$, which gives us a growing population. Note that in this special case, birth and death from the population are uniform and proportional to the total population.

We can express this model as a system composed of the following ordinary differential equations:

$$S'(t) = \rho N(t) - \delta S(t) - \beta S(t)\frac{I(t)}{N(t)}$$

$$I'(t) = -\delta I(t) - \gamma I(t) + \beta S(t)\frac{I(t)}{N(t)}$$

$$R'(t) = \gamma I(t) - \mu R(t)$$

where

$$N(t) = S(t) + I(t) + R(t).$$

Then $N'(t) = (\rho - \delta)N(t)$. So $N(t) = N_0 e^{(\rho-\delta)t}$. Let $n(t) = \frac{N(t)}{N_0}, s(t) = \frac{S(t)}{N_0}, i(t) = \frac{I(t)}{N_0}, r(t) = \frac{R(t)}{N_0}$. Then $s'(t) = \rho n(t) - \delta s(t) - \beta s(t)\frac{i(t)}{n(t)}$. We rearrange this equation to find that $s'(t) - (\rho - \delta)s(t) = \beta s(t)\frac{i(t)}{n(t)} + \rho(i(t) + r(t))$. Thus $\frac{d}{dt}(s(t)e^{-(\rho-\delta)}) = (-\beta s\frac{i(t)}{n(t)} + \rho(i(t)+r(t)))e^{-(\rho-\delta)t}$. Since we know that $n(t) = e^{(\rho-\delta)t}$, we rewrite the previous equation as $\frac{d}{dt}\left(\frac{s(t)}{n(t)}\right) = -\beta\frac{s(t)}{n(t)}\frac{i(t)}{n(t)} + \rho(\frac{i(t)}{n(t)} + \frac{r(t)}{n(t)})$. Similarly, we find that $\frac{d}{dt}\left(\frac{i(t)}{n(t)}\right) = \beta\frac{s(t)}{n(t)}\frac{i(t)}{n(t)} - (\rho + \gamma)\frac{i(t)}{n(t)}$ and $\frac{d}{dt}\left(\frac{r(t)}{n(t)}\right) = \gamma\frac{i(t)}{n(t)} - \rho\frac{r(t)}{n(t)}$.

We define $\sigma(t) = \frac{s(t)}{n(t)}, \eta(t) = \frac{i(t)}{n(t)}, \xi(t) = \frac{r(t)}{n(t)}$. Thus,

$$\sigma'(t) = -\beta\sigma(t)\eta(t) + \rho(\eta(t) + \xi(t)),$$

$$\eta'(t) = \beta\sigma(t)\eta(t) - (\rho + \gamma)\eta(t),$$

$$\xi'(t) = \gamma\eta(t) - \rho\xi(t).$$

We observe that $\sigma(t) + \eta(t) + \xi(t) \equiv 1$. This enables us to consider only $\sigma(t)$ and $\eta(t)$, since we can gather the behavior of $\xi(t)$ from our observations of these other two functions. We now write $\sigma'(t) = -\beta\sigma(t)\eta(t) + \rho(1 - \sigma(t))$.

To find the endemic state of the non-dimensionalized populations, we consider

$$\frac{\sigma'(t)}{\eta'(t)} = \frac{-\beta\sigma(t)\eta(t) + \rho(1 - \sigma(t))}{\beta\sigma(t)\eta(t) - (\rho + \gamma)\eta(t)} = -1 + \frac{\rho(1 - \sigma(t) - \eta(t)) - \gamma\eta(t)}{\beta\sigma(t)\eta(t) - (\rho + \gamma)\eta(t)}.$$

If $\frac{\sigma'(t)}{\eta'(t)} > 0$, then we will be left with with an endemic state.

The above result is significant because it suggests that non-dimensionalized non-constant populations behave similarly to constant populations in the way they reach equilibrium. It remains an open conjecture whether or not this results holds true for models including death from the disease, but initial numerical analysis suggests this is reasonable.

3 Results

Since we are particularly interested in minimizing the impact of Polio when it is reintroduced into a disease free population, we want to evaluate whether the vaccination strategies outlined above could be effective in the case of an outbreak, and, if so, to determine what the minimum vaccination rate must be to avoid an epidemic.

For our first model that considers vaccination of children in the 1-5 age class, we find that the growing population is an obstacle to satisfaction of inequality (1), and that using the current birth and death rates in Nigeria, it is impossible to satisfy. Due to the feedback into the population from births, it will be impossible empty the susceptible children class fast enough to prevent an increasing rate of new infections once the disease is introduced.

Our second approach that models vaccination of newborns yields more promising results. We find that inequality (3) is satisfied if the newborn vaccination rate exceeds 0.244. We then find that satisfaction of inequality (2) requires a vaccination rate of 0.784, which would also satisfy inequality (3). We then used Mathematica to simulate what infection of a disease free population with this minimum vaccination rate would look like.

We can also observe the effects of a higher or lower vaccination rate on the population in the case of an outbreak. Note that although the infectious population tends to zero in each case, that result is achieved much more quickly in the cases where the vaccination rate is below or above the minimum non-epidemic value. However, we observe that the maximum
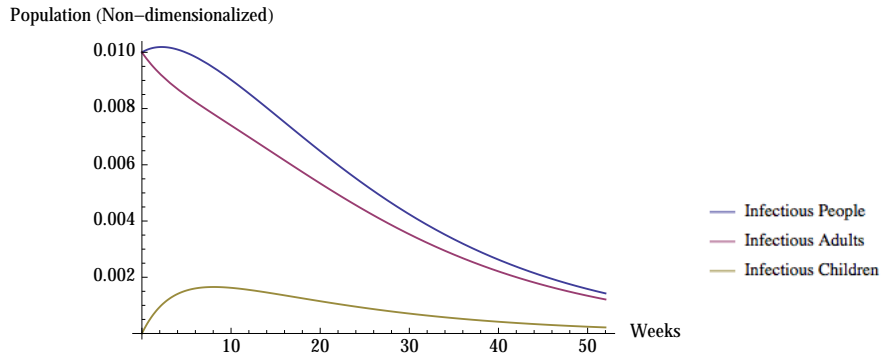
Figure 4: Graph Demonstrating Progress of an Outbreak in Population with 0.78 Vaccination Rate

infectious population is much higher in the 60% case, and occurs at around 17 weeks from the introduction of the disease. Above the minimum non-epidemic vaccination rate, the infectious class only shrinks in size, and the peak is at t = 0 weeks. It is also clear that fewer total people are infected in the above-minimum case compared to the minimum value case. Therefore there is clear benefit to over-vaccinating rather than under-vaccinating or vaccinating at the minimum value for epidemic prevention.
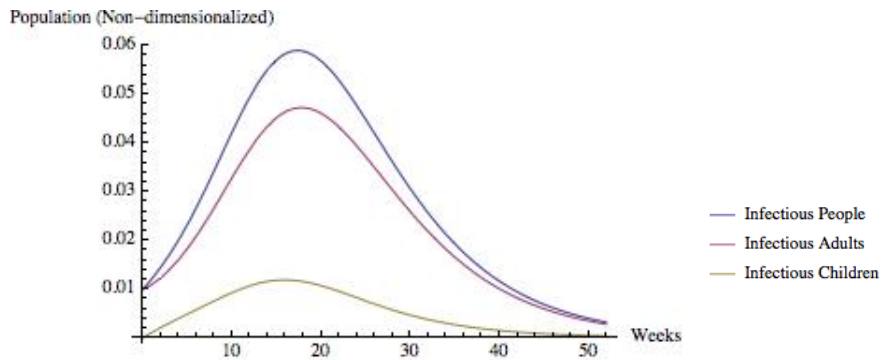

Figure 5: Graph Demonstrating Progress of an Outbreak in Population with 0.6 Vaccination Rate

4   Suggestions for Future Work

Moving forward, there are opportunities to refine the model at hand and use it to test further vaccination strategies. Considering the imbalanced population distribution in Nigeria,
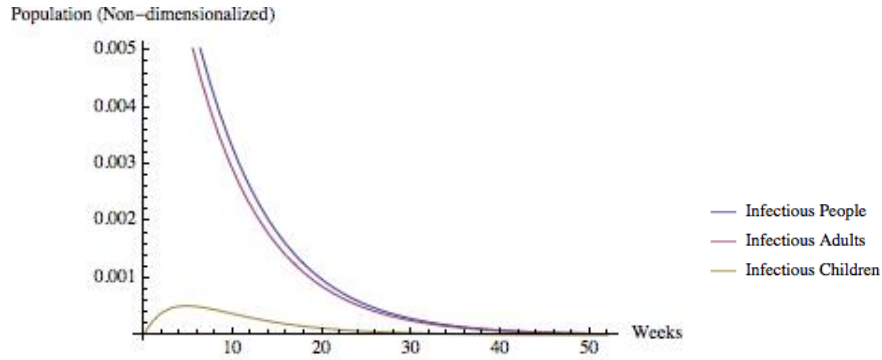
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Figure 6: Graph Demonstrating Progress of an Outbreak in Population with 0.9 Vaccination Rate

it would be illuminating to adjust or increase the age classes and observe whether this has any effect on the disease spread and minimum vaccination rate predictions. One could also use the present model to test a combination intervention strategy, where vaccination is provided to both children in the 1-5 age category as well as newborns, since this is closer to the strategy currently implemented in Nigeria.

It is our intent to continue research into the effects of varying birth and death rates on disease spread by extending our proof of the non-dimensionalized equilibrium of the infectious class to account for death from the disease and multiple age classes.

5 Acknowledgements

A
Table of Values Used

Variable	Rate	Value
β	contact infection rate	1
γ_C	child recovery rate	0.33
γ_A	adult recovery rate	0.17
ρ	birth rate	$7.3 * 10^4$
δ_C	child death rate	$2.4 * 10^3$
δ_A	adult death rate	$2.5 * 10^4$
d	disease death rate	0.25
μ	disease death percentage	0.25
θ	maturation rate	$4.8 * 10^3$

Values are obtained from **?**, **?**, and **?**.