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QUANTIFYING THE IMPACT OF VACCINATING UNDER-IMMUNIZED GROUPS IN POLIO OUTBREAKS: A SIMULATION-BASED STUDY

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ABSTRACT

Polio, an infectious disease that causes paralysis, remains a global health concern, especially with the emergence of circulating vaccine-derived poliovirus (cVDPV) and recurring outbreaks in areas with cohorts of under-immunized individuals. This study assessed how the allocation of vaccines during a polio outbreak response might impact outcomes. Adapting a compartmental simulation model, we projected poliovirus transmission from 2024 to 2026 under different levels of vaccination campaign coverage (i.e., the proportion of the target population reached by vaccination), vaccine allocation schemes (e.g., across different immunity groups), and vaccination campaign delays. Results highlighted that compared to other allocation schemes, priority allocation of vaccines to under-immunized groups (i) significantly reduced the number of paralytic cases, even with lower coverage and longer delay; (ii) achieved die-out of transmission with two rounds of vaccination if the delay was short ($\leq$ 3 weeks) and coverage was high ($\geq$ 70%).

1 INTRODUCTION

There has been tremendous progress towards global polio eradication, with concerted efforts leading to a 99.9% decline in polio cases worldwide since 1988 (Kishore et al. 2024). The widespread administration of inactivated and oral poliovirus vaccines (IPV and OPV, respectively) has been pivotal in diminishing the prevalence of poliovirus. However, challenges in controlling circulating vaccine-derived poliovirus (cVDPV) remain, as cVDPV has contributed to around 98% of global polio (paralytic) cases since 2021 (Global Polio Eradication Initiative 2024a; b).

cVDPV arises from reversion of the live-attenuated virus in the oral poliovirus vaccine (OPV) during prolonged circulation in under-vaccinated populations, which can lead a loss of attenuation to become a highly transmissible and neurovirulent virus that biologically resembles the wild poliovirus (WPV). There are three serotypes of polioviruses, i.e., types 1, 2, and 3. After WPV type 2 was declared eradicated in 2015 (Global Polio Eradication Initiative 2015), the Global Polio Eradication Initiative coordinated a global "switch" from trivalent OPV (tOPV) which contained all three serotypes to bivalent OPV (bOPV) which contained only types 1 and 3 and introduced a single dose of IPV into essential immunization in April 2016 (Bigouette et al. 2023). However, since 2016, cVDPV type 2 (cVDPV2) outbreaks persisted and caused the majority of global cVDPV cases (Bigouette et al. 2023; Kishore et al. 2024). Factors include (i) unsuccessful interruptions of cVDPV2 transmission before the switch; (ii) decreasing population immunity against type 2 poliovirus due to limited immunity provided by the 1-2 IPV doses in essential immunization; and (iii) new cVDPV2 emergences from post-switch monovalent OPV2 (mOPV2) use in poor quality campaigns. A recently developed novel type of OPV2 (nOPV2) contains a more genetically stable live-attenuated virus (compared to mOPV2), but in rare circumstances it can still revert to neurovirulence (Bandyopadhyay et al. 2024). Despite global nOPV2 in (outbreak response) vaccination campaigns since 2021, cVDPV2 outbreaks persist in over 30 countries, some lasting more than 12 months (Global Polio Eradication Initiative 2024a).

Persistent cVDPV2 outbreaks highlight the importance of improving the effectiveness of outbreak response. Standard operation procedures (SOPs) (World Health Organization 2022) recommend initiating outbreak response vaccination campaigns within 28 days of detection, consisting of two rounds with at least 90% coverage and a 4-week interval between rounds. The effectiveness of a vaccination campaign hinges on *coverage*, representing the percentage of the target population vaccinated, and timeliness, or equivalently, the *delay* in time between outbreak detection and vaccination deployment. Moreover, the effectiveness of vaccination campaigns is influenced by the allocation of vaccines across different groups (e.g., determined by geographies, immunity levels, etc.), i.e., the *vaccine allocation scheme*. In this study, we considered vaccine allocation based on immunity groups that are determined by factors such as access to essential immunization, coverage of previous vaccination campaigns, and prior exposures to polioviruses. Children in under-immunized groups who have been repeatedly missed during essential immunization or vaccination campaigns are more likely to contract the disease when in contact with infectious individuals, and, in turn, contribute to the disease spread and the number of paralytic cases; hence, it may be beneficial to preferentially target them for vaccination during an outbreak response. However, under-immunized groups may live in hard-to-reach areas and reaching them might come at a high effort and cost. Hence, during an outbreak response, those who live in easy-to-access areas and already have higher immunity might end up getting vaccinated again and again. Consequently, pockets of under-immunized groups persist, allowing poliovirus to thrive, spread to neighboring communities, and trigger widespread outbreaks despite repeated vaccination efforts.

Literature Review: Previous studies investigated the role of under-immunized geographic areas in poliovirus transmission. These studies agreed on the importance of focusing on under-immunized areas in vaccination efforts and highlighted how the failure to do so could largely delay the progress towards stopping the transmission (Thompson and Badizadegan 2024; Thompson and Kalkowska 2020). Some studies systematically evaluated the tradeoff between vaccination campaign coverage and delay. They highlighted the importance of quickly detecting and responding to polio outbreaks and the high risks of waiting for nOPV2 vaccine restocking versus using available mOPV2 vaccine during outbreak response (Thompson and Badizadegan 2024; Thompson and Kalkowska 2020).

Contribution of This Study: In addition to those from under-immunized geographic areas, under-immunized individuals/groups can also be present in other areas with higher population immunity (e.g., poliovirus transmission found in UK and USA in 2022 (Hill et al. 2022)). The potential benefits of vaccinating these groups, regardless of their location, remain an open question. Therefore, adapting a deterministic compartmental model and a previous case study of cVDPV2 transmission in Nigeria (Sun et al. 2024), this study presents the first attempt, to the best of our knowledge, to quantify the advantages of priority allocation of vaccines to under-immunized individuals/groups during outbreak response while considering the complex interplay between coverage and delay.

Assuming that stakeholders can identify and prioritize children who are under-immunized, we evaluated different outbreak response vaccination scenarios varying in coverage, delay, and vaccine allocation schemes. The three vaccine allocation schemes considered for distributing vaccines among immunity groups were (i) priority allocation starting with the lowest immunity group; (ii) proportional allocation based on immunity group size; and (iii) priority allocation starting with the highest immunity group. All scenarios comprised of two nOPV2 vaccination rounds that targeted children aged 0-4 years. These scenarios were compared by two outcome metrics – the outbreak size (i.e., the number of paralytic cases caused by poliovirus infections) and the time until die-out (i.e., the first week if and when the number of new weekly paralytic cases is zero).

2 METHODS

2.1 Live Poliovirus Transmission Model Description and Validation

We adapted a previously calibrated compartmental model to simulate the spread of poliovirus (Sun et al. 2024). Individuals in the modeled population are designated as belonging to one of the following four

compartments: (1) Susceptible (S): can be infected or vaccinated; (2) Exposed (E): infected but cannot infect others; (3) Infectious (I): infected and can infect others; and (4) IPV-injected (H): just received an IPV dose but have not acquired the corresponding immunity, because the immune system is mounting a response to the vaccine.

Table 1 shows how each compartment is further characterized by age groups (a), subpopulations (s), virus strains (j), and immunity groups (i). Age groups are determined based on the studied population's preferential mixing among individuals of similar ages and the age-dependent essential immunization schedule. Subpopulations are characterized by considering geography, historical vaccination coverage (i.e., the estimated percentage of individuals who received poliovirus vaccines), and *accessibility* (i.e., the probability that the poliovirus vaccines can be delivered and administered) in the studied population.

Table 1: Model compartments.

Symbols	Explanations
a	Age groups. The number of age groups depends on the studied population's preferential mixing among individuals of similar ages and the essential immunization schedule.
s	Subpopulations. The number of subpopulations depends on geography, historical vaccination coverage, and accessibility in the studied population.
j	Virus strains: $j = 0$: virus from the novel OPV. $j = 1$: virus from Sabin-strain OPV (i.e., tOPV, bOPV, or mOPV). $j = 2 - 19$: partially and progressively reverted forms of the Sabin-strain virus. $j = 20$: fully reverted form (e.g., cVDPV) of the Sabin-strain virus.
i	Immunity groups: $i = 0$: unimmunized. $i = 1$: IPV-immunized; received most recent IPV doses more than two years ago. $i = 2$: IPV-immunized; received most recent IPV doses within the last two years; 1 IPV dose. $i = 3$: IPV-immunized; received most recent IPV doses within the last two years; 2 IPV doses. $i = 4$: IPV-immunized; received most recent IPV doses within the last two years; ≥ 3 IPV doses. $i = 5$: LPV-immunized; acquired immunity more than two years ago. $i = 6$: LPV-immunized; acquired immunity within the last two years; 1 LPV exposure. $i = 7$: LPV-immunized; acquired immunity within the last two years; ≥ 2 LPV exposures or both LPV exposure and IPV dose.
$S_{i,a,s}$	Susceptible individuals in immunity group i, age group a, and subpopulation s.
$E_{i,j,a,s}$	Exposed individuals infected by virus strain j in immunity group i, age group a, and subpopulation s.
$I_{i,j,a,s}$	Infectious individuals infected by virus strain j in immunity group i, age group a, and subpopulation s.
$H_{i,a,s}$	IPV-injected individuals in immunity group i, age group a, and subpopulation s.

To capture the virus reversion in OPV, the model includes 20 hypothetical virus strains where strain 1 represents the live-attenuated virus in the Sabin-strain OPV (i.e., the Sabin OPV virus), strains 2-19 represent the progressively and partially reverted forms of the Sabin OPV virus, and strain 20 represents the fully reverted form of the Sabin OPV virus – cVDPV. As we assume the virus in the novel type OPV does not revert, the model separately characterizes a hypothetical virus strain to represent the virus in novel type OPV, i.e., strain 0.

Immunity groups (IGs) are characterized by the source of immunity, the timing of the most recently acquired immunity, and the number of exposures to live polio virus (LPV) or the number of IPV doses. The model includes 7 IGs which are ordered by increasing immunity levels: IG 0 represents individuals with no immunity. IGs 1-4 represent individuals with humoral immunity induced by IPV and who received the most recent IPV doses: IG 1 – more than two years ago; IG 2 – within the last two years and had one IPV dose in life; IG 3 – within the last two years and had two IPV doses in life; IG 4 – within the last two years and had at least three IPV doses in life (IG 4). IGs 5-7 represent individuals with intestinal mucosal immunity induced by LPV and who acquired immunity: IG 5 – more than two years ago; IG 6 – within the last two years but had only one LPV exposure in life; IG 7 – within the last two years and had both LPV exposures and IPV doses in life or had at least two LPV exposures in life.

The model tracks the transitions of individuals between compartments due to infection, vaccination, virus reversion, waning immunity, aging, birth, and death. Figure 1 provides a simplified illustration of the transitions between compartments due to exposure to LPV strain j, vaccination by IPV, and virus reversion. More details of the model including feasible combinations of IG i and IG i' and mathematical definitions can be found in Sun et al. 2024.

Model parameters of this study were based on a previous case study of cVDPV2 outbreaks in Northwest and Northeast Nigeria (Sun et al. 2024). This case study estimated most parameter values based on existing polio modeling studies and epidemiology and demography data (e.g., historic vaccination coverage and vaccine effectiveness), but also estimated the values for some uncertain parameters (e.g., the die-out threshold and the populations mixing between subpopulations) by an iterative calibration process (Hyndman and Athanasopoulos 2018). There are 11 age groups (i.e., ages 0-2 and 3-11 months; and ages 1, 2, 3, 4, 5-9, 10-14, 15-24, 25-39, and ≥ 40 years) and 7 subpopulations (SPs) that included 2 general SPs, 3 under-vaccinated SPs, and 2 isolated SPs (see Figure 2). More details of model parameters, calibration, and validation can be found in Sun et al. 2024. Appendix A describes the initial conditions used to seed the simulations in this study.

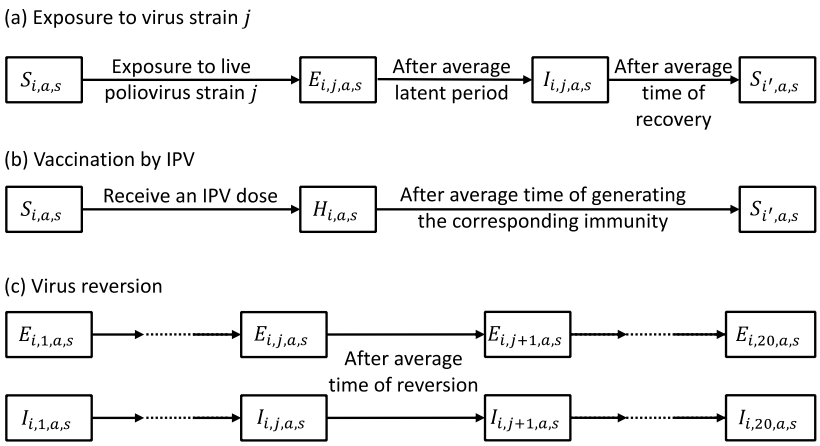

Figure 1: Simplified illustration of transitions between the compartments in the model due to (a) exposure to virus strain j; (b) vaccination by IPV; and (c) virus reversion.

2.2 Simulation of cVDPV2 Outbreak Response Scenarios

2.2.1 Outbreak Response Scenarios

We tested the impact of various outbreak response supplemental immunization activity (oSIA) scenarios over a three-year study period (i.e., 2024-2026). All oSIA scenarios used nOPV2, had 2 rounds of vaccinations (of 4 days) with a 4-week interval in between, and targeted children aged 0-4 years. Tested

oSIA scenarios varied in three factors: vaccine allocation scheme (V), vaccination campaign coverage (c), and vaccination campaign delay (d) (see Table 2).

Three vaccine allocation schemes were considered to specify how oSIAs can allocate vaccines to different immunity groups: (i) V^L – *Priority allocation starting with the lowest immunity group* where vaccination campaigns try to reach susceptible individuals in lower IGs (even though this might require more cost/effort); (ii) V^P – *Proportional allocation* which proportionally allocates vaccines among the susceptible individuals of all IGs based on the IG size (i.e., the number of susceptible individuals each IG); and (iii) V^H – *Priority allocation starting with the highest immunity group* where vaccination campaigns reach susceptible individuals in higher IGs (this might partly align with what currently happens in practice, i.e., individuals who are easier to reach may get vaccinated many times).

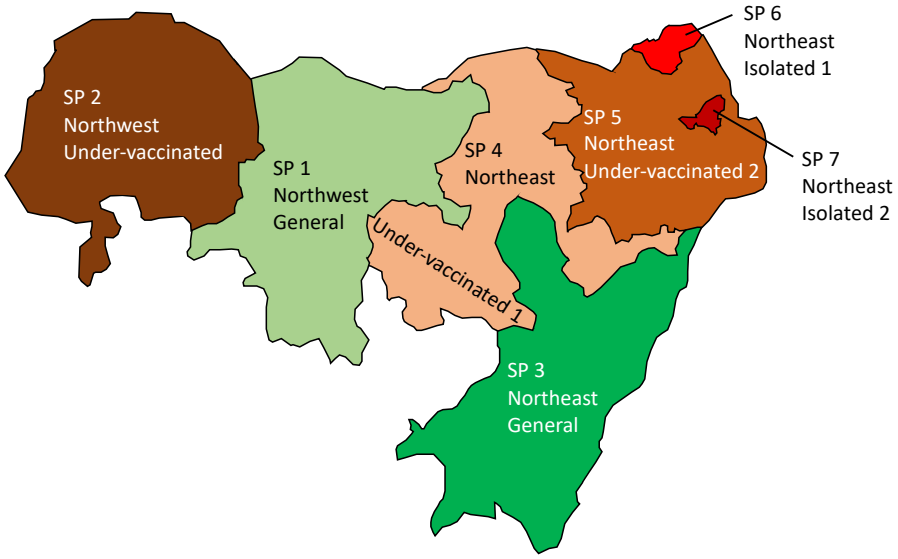

Figure 2: Subpopulations of Northwest and Northeast Nigeria.

Table 3 provides a detailed explanation of how vaccine allocation is captured in the model. Suppose in age groups 0-4 years of a subpopulation, we have 10 susceptible individuals in each IG and a vaccination campaign of 20% coverage (i.e., in total, 16 vaccine doses to be used or 16 susceptible individuals to be vaccinated). With V^L, since the lowest immunity groups have the priority allocation, 10 vaccine doses will be used on the 10 susceptible individuals of IG 0, 6 remaining doses will be used on 6 out of 10 susceptible individuals of IG 1, and no doses will be used on susceptible individuals of IGs 2-7. Similarly, as V^H has priority allocation to the highest immunity groups, 10 doses will be used in IG 7, with the 6 remaining doses in IG 6 and no doses in other IGs. As in V^P, due to the proportional allocation, i.e., the number of doses used in a SP is proportional to the number of susceptible individuals in that SP, each SP will have two susceptible individuals vaccinated.

Given that current oSIAs try to reach and vaccinate target individuals regardless of their vaccination history, the real-life vaccine allocation/distribution can fall between the proportional allocation and the priority allocation starting with the highest immunity group, as the higher immunity levels of these individuals can be attributed to their higher accessibility to vaccinations. We treat priority allocation starting with the lowest immunity group as a theoretical but ideal situation where individuals of under-immunized immunity groups can be identified and prioritized in vaccination campaigns. It can represent the efforts to reach and vaccinate repeatedly missed children.

Table 2: Outbreak response supplementary immunization activity scenarios.

Scenario parameters	Definition	Values
Vaccine allocation scheme (V)	Allocation of vaccines to individuals of different immunity groups in outbreak response	V^L– Priority allocation starting with the lowest immunity group (IG) (vaccination order is from IG 0 to IG 7) V^P – Proportional allocation V^H – Priority allocation starting with the highest immunity group (vaccination order is from IG 7 to IG 0)
Vaccination campaign coverage (c)	Percentage of children aged 0-4 years that are targeted to receive vaccines	10%-90% in 10% increments
Vaccination campaign delay (d)	Number of weeks between the outbreak detection and the start of the outbreak response vaccination campaigns	1 week-9 weeks in 1-week increments

Table 3: An example of how vaccine allocation scheme works.

Vaccine allocation schemes[1]	Number of vaccine doses allocated to each immunity group[2] (IG)								
	IG 0	IG 1	IG 2	IG 3	IG 4	IG 5	IG 6	IG 7	SUM
V^L	10	6	0	0	0	0	0	0	16
V^P	2	2	2	2	2	2	2	2	16
V^H	0	0	0	0	0	0	6	10	16

[1]Assumed 16 vaccine doses in total to be used

[2]Assumed each immunity group has 10 susceptible individuals

Vaccination campaign coverage is defined as the percentage of children aged 0-4 years that are targeted to be vaccinated in an oSIA round. Coverage is different than *effective* coverage which measures the percentage of children who actually receive a vaccine dose and generate the corresponding immunity after the oSIA round. Effective coverage depends on coverage, vaccine effectiveness, accessibility, etc. For example, an oSIA round with 30% coverage using the nOPV2 in SP 4 means that 30% of children aged 0-4 years (regardless of immunity groups) in SP 1 are targeted to receive one dose of nOPV2 in this round. However, given effectiveness of 70% and accessibility of 90%, only 18.9% (i.e., the effective coverage) of children aged 0-4 years in SP 4 receive one nOPV2 dose and generate corresponding immunity in the end.

Vaccination campaign delay is defined as the number of weeks between the detection of an outbreak and the start of the oSIAs. In the simulations, an outbreak in an SP was detected when the number of new weekly paralytic cases in that SP surpassed the fixed detection threshold of 1 case/week.

In simulated scenarios, coverage ranged from 10% to 90% at increments of 10%, and delay ranged from 1 week to 9 weeks, at increments of 1 week. Each scenario is represented by a triplet (V, c, d) . For example, $(V^P, 70\%, 5)$ represents the oSIA scenario where vaccines are proportionally allocated across IGs with coverage of 70% and delay of 5 weeks.

2.2.2 Outcome Metrics

We compared oSIA scenarios using two outcome metrics: the 1-year outbreak size and the time until die-out. We reported the outcome metrics by the overall population and/or the subpopulations.

The 1-year outbreak size was defined to be the total number of cVDPV2 paralytic cases within 1 year since the start day of the study period (i.e., January 1, 2024 in this study). We opted for a one-year time frame instead of three years (i.e., the duration of the study period) to analyze the impact of two oSIA rounds in containing outbreaks. In situations where die-out does not happen but transmission remains very low and hard to be detected by surveillance, there could be breakthrough polio cases that emerge months after the conclusion of the two rounds. The breakthrough cases will signal the continuation of the transmission and then elicit new oSIA rounds, which therefore falls out of scope of the previous two oSIA rounds. Also, SOPs suggest that when there is no sufficient evidence of sensitive surveillance, 13 months free of poliovirus detections are needed to announce the closure (i.e., die-out) of an outbreak (World Health Organization 2022).

The time until die-out was defined for each SP and for the overall population. For an SP, the time until die-out is the first week when the number of new weekly paralytic cases within that week becomes 0 in that SP. For the overall population, the time until die-out is the first week when the number of new weekly paralytic cases within that week becomes 0 in all SPs. More details of the die-out mechanism can be found in Sun et al. 2024.

3 RESULTS

Figure 3 shows contour plots of the 1-year outbreak size in the overall population as vaccine allocation scheme (V), vaccination campaign coverage (c), and vaccination campaign delay (d) vary.

At the same vaccination campaign coverage and delay, oSIA scenarios with priority allocation starting with the lowest immunity group (V^L) consistently resulted in smaller 1-year outbreak sizes compared to oSIA scenarios that proportionally allocated vaccines (V^P) or with priority allocation starting with the highest immunity group (V^H). For example, when $c = 70\%$ and $d = 5$ weeks, the 1-year outbreak size is 36% lower under V^L and 280% higher under V^H, compared to V^P.

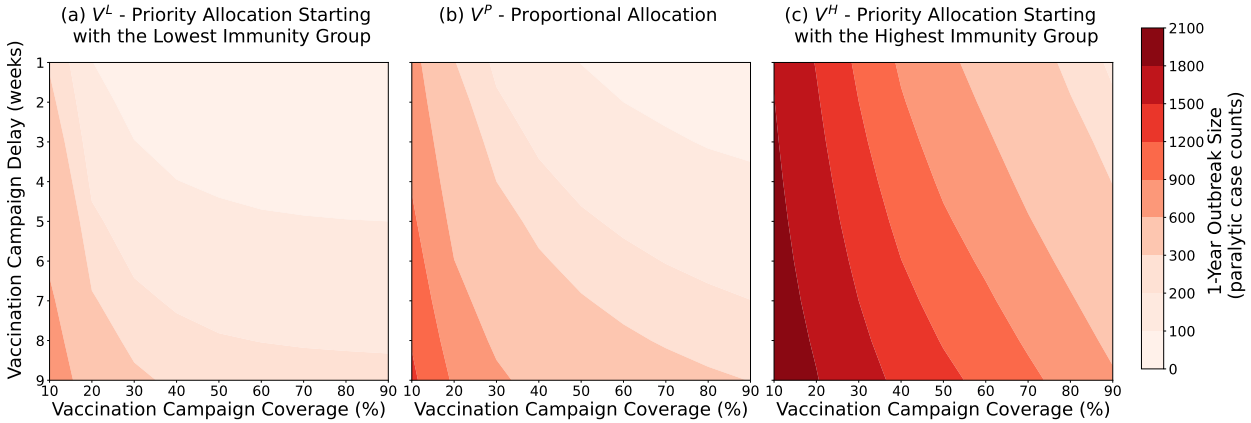

Figure 3: Contour plots of 1-year outbreak sizes in the overall population with varying vaccination campaign coverage and delay for different vaccine allocation schemes: (a) V^L – Priority allocation starting with the lowest immunity group; (b) V^P – Proportional allocation; and (c) V^H – Priority allocation starting with the highest immunity group.

In some scenarios, V^L compensated for lower coverage or longer delay, resulting in smaller 1-year outbreak sizes compared to V^P and V^H under higher coverage or shorter delay. For example, (i) the 1-

year outbreak sizes under (V^L, c, d) when $c \geq 30\%$ were smaller than that under $(V^P, 70\%, d)$; (ii) the 1-year outbreak sizes under (V^L, c, d) were smaller than that under $(V^H, c, 3)$ for all tested values of d.

In V^L scenarios, the relative sensitivity of the 1-year outbreak size to the coverage compared to the delay changed when the coverage reached 30%:

- When $c < 30\%$, the 1-year outbreak size was more sensitive to the coverage. For example, compared to $(V^L, 20\%, 2)$: (i) decreasing the coverage by 10%, i.e., $(V^L, 10\%, 2)$, increased the 1-year outbreak size by 1.7 times; (ii) increasing the delay by 1 week, i.e., $(V^L, 20\%, 3)$, increased the 1-year outbreak size by 0.2 times.
- When $c \geq 30\%$, the 1-year outbreak size was more sensitive to the delay: (i) when d went up from 1 to 9, the increase in the 1-year outbreak size ranged from 3.9 times ($c = 30\%$) to 4.5 times ($c = 90\%$); (ii) when c went down from 90% to 30% , the increase in the 1-year outbreak size ranged from 0.4 times ($d = 9$ weeks) to 0.6 times ($d = 1$ week).

In V^P and V^H scenarios, the 1-year outbreak size was more sensitive to the coverage but less sensitive to the delay, compared to V^L scenarios. For example, under (V^H, c, d): (i) when d went up from 1 week to 9 weeks, the increase in the 1-year outbreak size ranged from 0.1 times ($c = 10\%$) to 2.5 times ($c = 90\%$); (ii) when c went down from 90% to 10%, the increase in the 1-year outbreak size ranged from 2.1 times ($d = 9$ weeks) to 8.8 times ($d = 1$ week).

Figure 4 shows the time until die out in SPs 1-5 under V^L as coverage and delay vary. Die-out was not achieved in any of SPs 1-5 under V^P and V^H. There was no transmission in isolated SPs 6 and 7 in tested oSIA scenarios.

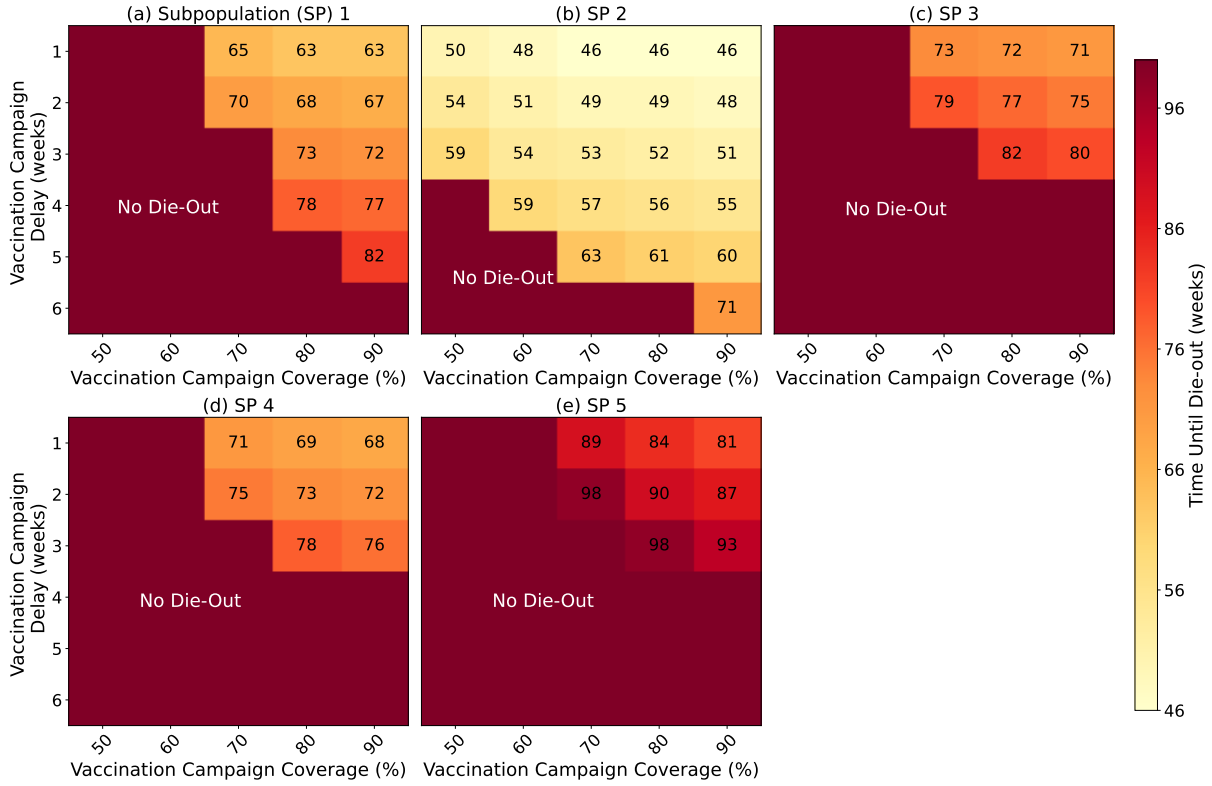

Figure 4: Time until die-out in scenarios with priority allocation starting with the lowest immunity group (V^L) as vaccination campaign coverage and delay vary in (a) Subpopulation (SP) 1; (b) SP 2; (c) SP 3; (d) SP 4; (e) SP 5.

In V^L scenarios, complete die-out (i.e., die-out in all subpopulations) was achieved when: (i) $c = 70\%$ and $d \leq 2$ weeks; (ii) $c \geq 80\%$ and $d \leq 3$ weeks. No die-out was achieved in any SPs when $c \leq 50\%$ or $d \geq 6$ weeks.

Among V^L scenarios where complete die-out happened, the time until complete die-out (i.e., the time until die-out in SP 5 in this case study) was more sensitive to delay than coverage: (i) when c was fixed, decreasing delay by 1 week reduced the time until complete die out by 6-9 weeks; (ii) when d was fixed, increasing coverage by 10% reduced the time until complete die out by 3-8 weeks.

Appendix B includes the detection time of the outbreak in each SP.

4 DISCUSSION

Despite progress in the development of a novel OPV which reduces the risk of reversion, challenges persist in controlling cVDPV2 outbreaks, partially driven by the inability to effectively reach and vaccinate under-immunized groups. While over 1 billion doses of nOPV2 were used globally since 2021 (Bandyopadhyay et al. 2024), over 1,500 cVDPV2 paralytic cases were observed in 2021-2023 (Global Polio Eradication Initiative 2024a). During August 2021 – July 2023, 61 cVDPV2 paralytic cases linked to nOPV2 use were detected in six African countries including Burundi and Democratic Republic of the Congo (Davlantes et al. 2023).

The results of this study highlighted the importance of robustly seeking out under-immunized individuals in outbreak response vaccinations. In our simulations, despite the potential need for extra efforts/costs and consequent long delay and low coverage, outbreak response vaccinations with priority allocation starting with the lowest immunity group (i.e., those most under-immunized) yielded similar or even smaller case burden compared to scenarios (with shorter delay and higher coverage) that allocated vaccines proportionally across immunity groups or with priority allocation starting with the highest immunity group (i.e., those most well-immunized).

We also highlighted the drawbacks of large and generalized vaccination campaigns that repeatedly reach already immunized groups but miss under-immunized children, a scenario that may occur in real life due to the ease of access to those well-immunized groups and the limitations preventing vaccine delivery to under-immunized children (e.g., insecurity, hesitancy, etc. (Mshelia et al. 2020)). Our results revealed that if individuals of well-immunized immunity groups were primarily vaccinated in outbreak response, very few or no individuals of under-immunized immunity groups would be vaccinated, particularly when coverage was low. This approach led to a significant susceptible population, repeatedly being missed by the vaccination campaigns and remaining vulnerable to infection, subsequently increasing the case burden.

In vaccination scenarios with priority allocation starting with the lowest immunity group, it became more efficient to decrease the case burden by reducing the delay than increasing the coverage once the coverage was at least 30%. This threshold was crucial because, at 30% coverage, nearly all unimmunized individuals (at the vaccination time point) in our case study would receive vaccines. Further increasing coverage vaccinated more immunized individuals, which had minimal impact on paralytic cases, as we assumed only unimmunized individuals might develop paralysis after infection (Sun et al. 2024). Reducing delay ensured prompt vaccination of more unimmunized individuals before possible poliovirus infections.

However, in vaccination scenarios without priority allocation starting with the lowest immunity group, increasing the coverage became more significant than reducing the delay to decrease the case burden. In these scenarios, increasing the coverage across the overall population became imperative to attain equivalent coverage among under-immunized immunity groups as observed when they received vaccines first before others. Only reducing the delay did not result in increased vaccination uptake among under-immunized immunity groups.

In our case study, priority allocation starting with the lowest immunity group was the only vaccine allocation scheme that achieved die-out of cVDPV2 transmission throughout the entire population. High

coverage (e.g., $\geq 70\%$) and short delay (e.g., ≤ 3 weeks) remain crucial in completely stopping cVDPV2 transmission.

Our study has some limitations. First, in model calibration, we identified a set of parameter values that aligned well with the cVDPV2 transmission dynamics in the case study. Given the large space of feasible parameter values, future work will more systematically explore this space to identify other parameter sets which might provide a good fit and evaluate their impact on the outcomes by comparing oSIA scenarios. Our preliminary sensitivity analyses around key parameters, such as the die-out threshold, showed that our conclusions drawn from the oSIA scenarios tested in this study remained robust despite variations in these parameter values (e.g., given an oSIA scenario, changes in the outbreak size were within 1% when the die-out threshold decreased or increased by 3 times compared to its base value, i.e., 5×10^{-6}). Second, we utilized a deterministic compartmental model to generate average simulation outcomes, without stochastic elements involved in real life (e.g., infectious contacts). However, our study demonstrated the advantages of priority allocation of vaccines to under-immunized individuals in reducing the case burden and achieving disease eradication. Evaluating average outcomes allowed clear distinctions among vaccine allocation schemes with less complexity than stochastic models. Third, we assumed a "perfect" nOPV2 strain that has no reversion, but reversion of the virus in nOPV2 seeded new emergence of cVDPV2, especially in situations where vaccination campaigns had low coverage and repeatedly vaccinated already immune individuals. As reversion properties largely impact the effectiveness of vaccination campaigns, future studies will consider sensitivity analysis of the nOPV2 reversion assumption. Fourth, in our case study of Nigeria, we decided subpopulations by grouping multiple geopolitical states. This is a simplification of real-life heterogeneities that happen in community-wise poliovirus transmission, which could impact die-out of transmission. Also, with the changes in local insecurity, road banditry, and settlement occupation, the population mixing within one subpopulation changes, which necessitates considering subpopulations with greater granularity in our future case studies. Fifth, we limited our simulations to two vaccination rounds with four weeks apart, in line with the current SOPs (World Health Organization 2022). However, if the initial two rounds fail to stop outbreaks, SOPs recommend additional vaccination rounds. Aside from the delay from detection to vaccination deployment, the delay from one round to the next round also remains as an issue. Our future studies will explore the impact of additional rounds and delay between two consecutive rounds until die-out is achieved. Sixth, we assumed outbreak response scenarios that allocated vaccines to different immunity groups, of which the implementation would require careful thoughts. Often, immunity, as a combined result of previous infections and vaccinations, is hard to tell, either for individuals or the overall population. Allocating vaccines based on individuals' vaccination records could be more practical, which will be tested in our future studies. Further, delivering vaccines to some under-immunized individuals is challenging because they may live in hard-to-reach areas. Exploring the benefit of reaching these individuals via innovative approaches (Higgins et al. 2019), such as using vaccine tracking, satellite imagery analysis, and community informants, could be an avenue for future research.

5 CONCLUSIONS

In this study, we quantified the benefits of priority allocation of vaccines to under-immunized immunity groups in polio outbreak response using a deterministic compartmental model, while accounting for the complex interplay between vaccination campaign coverage and delay. Our findings emphasized that (i) priority allocation of vaccines to under-immunized immunity groups largely decreased the case burden and achieved die-out in the entire population, even with lower coverage and longer delay, compared to scenarios with no priority allocation to the under-immunized; (ii) with priority allocation to the under-immunized, reducing the delay would more substantially decrease the case burden and the time needed to achieve die-out, compared to increasing the coverage.

Currently, it may not be practical to test immunity levels quickly to identify and primarily vaccinate under-immunized individuals during an outbreak response. However, with advances in technology and medicine, such practices might become easier over time, and hence, this modeling study demonstrates the

benefits of vaccination campaigns that deliberately reach those who need vaccines the most (e.g., being under-immunized and repeatedly missed by vaccination campaigns), compared to current SIAs that vaccinate children regardless of their immunity levels. We also highlight to stakeholders that in regions with persistent polio outbreaks, achieving die-out after only two vaccination rounds could be hard as it might need coverage over 70% and delay less than 3 weeks, even when all novel OPV (with no reversion) doses were primarily used among the under-immunized individuals. Our future research will investigate the potential benefits of more practical vaccine allocation schemes, such as (i) prioritizing under-vaccinated individuals based on their vaccination records and (ii) prioritizing regions known to have a high percentage of under-immunized individuals.

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A INITIAL CONDITION

The initial condition specifies the number of individuals in all model compartments at the start of simulation runs to seed the simulations. The initial condition used in this study was estimated in a previous case study of Northwest and Northeast Nigeria, following a scenario where two rounds of nOPV2 oSIAs were assumed to be implemented in SPs 1-5 in 2022 and 2023 (see "Scenario 1" in Sun et al. 2024).

B DETECTION TIME OF POLIOVIRUS TRANSMISSION

Table B1 specifies the detection time (in weeks) of poliovirus transmission in each subpopulation. No transmission was predicted in isolated SPs 6 and 7. Note that the detection week is indicated by the Monday of the week. For example, if the detection happens in the week from January 1 to January 7 in 2024, the detection week is denoted as January 1, 2024 (i.e., Monday).

Table B1: Detection weeks of polio transmission in subpopulations.

Subpopulations (SPs)	Detection Weeks (in 2024)
SP 1	July 22
SP 2	February 5
SP 3	July 15
SP 4	July 22
SP 5	June 17

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