

Article

Strategies for the Global Alliance for Vaccines and Immunization in International Vaccine Pricing and Procurement

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Highlights

What are the main findings?

- We develop a mathematical model to determine optimal contract prices and quantities for pediatric vaccines, ensuring sufficient manufacturer profit margins and phasing out use of oral polio vaccine products (OPVs).
- Even with increased hexavalent (Hexa) vaccine production, oral polio vaccine products are projected to remain an important driver for the market's ability to provide inoculation against polio.

What are the implications of the main findings?

- If more manufacturers could be incentivized to produce Hexa, Gavi's "IPV2" goal of administering at least two out of the required three doses of polio vaccine with IPV-containing products rather than OPV would become attainable.
- Gavi's incentivization of production of the hexavalent vaccine through contracts and technology rights transfer would play a significant role in achieving UNICEF's Polio Eradication Initiative.

Abstract

Gavi is a multilateral public–private organization that has introduced innovative financial mechanisms to secure funding to help low- and low–middle-income countries procure affordable vaccines through pool procurement in the UNICEF market. UNICEF helps create an affordable vaccine market by organizing tenders in which manufacturers commit to supplying vaccines to meet the expected needs of such countries. The Global Polio Eradication Initiative (GPEI) is designed to eradicate polio. Gavi supports the eradication efforts of GPEI, which calls for the adoption of at least one dose of inactivated polio vaccine (IPV) in conjunction with a novel oral polio vaccine (nOPV). To support this goal, the international community relies on IPV-containing vaccines, including a hexavalent vaccine (Hexa). This study addresses the feasibility of supporting the GPEI's IPV strategy by increasing the supply and adoption of Hexa. We use mathematical programming to examine optimal contract prices and quantities within the global vaccine market captured by a game-theoretic model. We find that new oral polio vaccines will continue to play a critical role in meeting demand for polio vaccines until Hexa production capacity is dramatically increased. We see a feasible avenue for increasing the availability of safer, IPV-containing vaccines in alignment with the GPEI strategy.



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1. Introduction

Poliomyelitis, or polio, is a disease caused by the poliovirus via oral–fecal transmission. The vast majority of infected patients are asymptomatic or show minor symptoms, but a small fraction can develop encephalitis, meningitis, and paralytic poliomyelitis. There is no cure for polio, but the disease can be prevented via vaccination. In 1988, the World Health Organization launched the Global Polio Eradication Initiative (GPEI), which coordinates the efforts of multiple partners in the global health space. As a consequence of the GPEI efforts and the international community, the number of paralytic cases of wild polio dropped from 350,000 cases across 125 countries in 1988 to fewer than 10 cases worldwide in 2021 [1,2]. Moreover, GPEI is working towards the complete eradication of polio by the year 2029 [3].

Instrumental to GPEI's plan to eradicate polio is the introduction of at least one dose of inactivated polio vaccine (IPV) in the immunization schedules, which, although more costly than oral polio vaccines (OPVs), does not carry the risk of circulating vaccine-derived poliovirus (cVDPV). Incorporating IPV into combination vaccines, which cover multiple antigens in a single shot, reduces distribution costs, can improve overall pediatric vaccine coverage in low-income nations, and is a key part of the GPEI strategy to eradicate polio by 2029. Thus, organizations working to eradicate polio and ensure adequate overall pediatric vaccination coverage in low- and lower-middle-income countries continuously assess the feasibility of including at least one dose of IPV in pediatric vaccine schedules, depending on existing market conditions. Moreover, organizations such as Gavi, the Vaccine Alliance, support a two-dose IPV goal. This paper provides a framework for examining whether the eradication plans proposed by the GPEI can be realized through an expansion of the IPV-containing hexavalent vaccine (Hexa), which inoculates against six antigens.

We adapt and apply existing methods to examine global pediatric polio vaccine procurement. Our analysis suggests that dramatically expanding the set of manufacturers producing Hexa (e.g., from two out of twenty manufacturers in our dataset to nine) would enable an increase in Hexa doses from approximately 300 K to nearly 150 M annually. This would allow Gavi to meet the goal of providing at least one dose of IPV to all children at lowest cost. UNICEF has estimated that the annual demand for Hexa would be over 100 million doses by 2030 [4]. The results also indicate that novel oral polio vaccines (nOPV), which carry a reduced risk of cVDPV compared with traditional OPV, will continue to play an important role in meeting demand for polio vaccines.

We start in Section 1.1 by providing background on GPEI, Gavi, and the UNICEF *tenders* used to establish pricing and quantity contracts with pediatric vaccine manufacturers. In Section 1.2, we review the literature relevant to our modeling approach. Then, we outline modeling assumptions and present a generalized model formulation and parameter estimation in Section 2. Then, we discuss results, limitations, and conclusions in Sections 3–5.

1.1. Background on Efforts to Eradicate Polio

1.1.1. The Global Polio Eradication Initiative (GPEI)

From the three strains of wild polio (types 1, 2, and 3), only type 1 remained circulating in two countries in 2025 [2]. The GPEI strategies include improved sanitation, healthcare education, disease monitoring, and vaccination. The GPEI immunization strategy has relied primarily on oral polio vaccines (OPVs), which contain weakened polio viruses, are administered orally, and are inexpensive and easy to distribute. Until 2016, the predominantly used OPV vaccines offered protection to the three polio viral strains (tOPVs) and were replaced systematically at a global level by a bivalent OPV (bOPV), which only offered protection to strain types 1 and 3. This switch was made based on the absence of infections from the type 2 strain of wild polio. However, polio requires sustained high coverage levels (at least 80%) to maintain herd immunity, and an inadequate outbreak response with monovalent type 2 vaccines (mOPV2) resulted in low coverage levels. This caused an increase in circulating vaccine-derived poliovirus type 2 (cVDPV2). Individuals vaccinated with OPV received a weakened form of the polio virus, which is easy to administer orally, is inexpensive, offers robust immunogenicity, and induces intestinal mucosal immunity; this is important to reducing viral shedding during outbreaks [5]. However, the weakened polio virus can be excreted in stool. In areas with poor sanitation and low immunization coverage, this weakened virus propagates from person to person and protects the local population. However, as the virus propagates among unvaccinated and immunocompromised individuals, it can mutate, reactivate, and cause paralysis, similar to that of wild poliovirus [6]. Currently, cVDPV2 is the most prevalent form of polio infection.

To prevent cVDPV2, in 2012, the WHO and the Strategic Advisory Group of Experts on Immunization (SAGE) recommended introducing at least one dose of IPV into all immunization schedules. Inactivated Polio Vaccines (IPVs) do not pose a risk of vaccine-induced infections because they contain inactivated poliovirus that cannot mutate. IPV induces systemic immunity and is excellent at preventing paralytic disease, but it does not induce intestinal mucosal immunity [5]. However, IPV is significantly more expensive than OPV and more challenging to deliver. In 2013, the GPEI launched a strategy to include one IPV dose in immunization schedules (IPV1) [7].

Gavi is a public–private health partnership whose mission is to save lives and protect people’s health by increasing equitable access to immunization in low- and low-middle-income countries (LICs and LMICs). Gavi, as part of the GPEI, has financially supported the implementation of the IPV1 strategy. Gavi-supported countries reached 81% IPV1 coverage by 2019 and moved toward a two-dose IPV goal (IPV2) in 2021 [8].

The GPEI, in its 2022–2026 strategy, calls for countries to adopt a novel OPV vaccine (nOPV), which is safer than previous OPV versions (mOPV) as it is less likely to mutate [5] and also recommends including at least two IPV doses in their immunization schedule. Gavi supports the GPEI initiative and approved financial support to help countries adopt IPV-containing vaccines into their immunization programs, including Hexa, a combination vaccine that offers protection against diphtheria, tetanus, pertussis, hepatitis B, *Haemophilus influenzae* type B, and polio via IPV (DTP-HepB-Hib-IPV) [8,9]. The Gavi market currently uses a pentavalent vaccine (Penta) that inoculates against diphtheria, tetanus, and pertussis (DTwP), hepatitis B (HepB), and *Haemophilus influenzae* type b (Hib). This multivalent vaccine has been successfully integrated into existing contracts.

1.1.2. Vaccine Procurement by Gavi and UNICEF

Between 2000 and 2023, Gavi supported the immunization of more than one billion children and prevented over 18 million deaths from infectious diseases [10]. Gavi’s immu-

nization efforts have increased economic and social stability by improving global health security and nation-building.

Gavi combines the comparative advantages of its partners to increase access to immunization. For example, it relies on the technical expertise of the World Health Organization, financial innovation from private partners and the World Bank, and the humanitarian logistics and procurement expertise of UNICEF [11].

LIC and LMIC countries rely on strategic WHO recommendations to develop their immunization plans. Gavi raises funds through innovative financial mechanisms that allow it to support qualifying countries' funding for their vaccine procurement through the UNICEF vaccine tender system. Gavi and UNICEF aggregate the demand for LIC and LMIC immunization to leverage economies of scale that help them negotiate pricing contracts to secure affordable vaccine supply. UNICEF calls for vaccine tenders, where manufacturers commit supply at accessible pricing conditions. The UNICEF Supply Division purchases vaccines on behalf of Gavi-supported countries, simplifies procurement channels, and coordinates deliveries [11]. LIC and LMIC countries graduate from Gavi support based on their gross national income per capita and the strength of their vaccine procurement systems [12]. UNICEF's work with Gavi promotes approaches to scaling up vaccine coverage and supports efforts to make vaccines more affordable and accessible [13].

1.1.3. UNICEF Tenders

A UNICEF vaccine tender for Hexa, in place for 2021–2027, aims to help Gavi countries introduce hexavalent vaccines in their schedules to meet GPEI's IPV1 strategy and facilitates the adoption of their IPV2 dose. Although countries do not need to use Hexa to integrate IPV into their schedules, the bundled nature of Hexa can decrease immunization and administrative costs in comparison with using simpler vaccines to meet their immunization needs. Using Hexa requires fewer vaccination visits for the same immunity. However, Hexa shares five of its six antigens with Penta (DTP-Hib-HepB), and hence, the adoption of Hexa could affect Penta's demand. Additionally, Penta's supply commitments can prevent manufacturers from converting part of their production capacity into the more attractive Hexa. Delays in entering the Hexa market can affect manufacturers' profitability. Therefore, tenders aimed to ensure the supply for IPV via Hexa should not adversely affect the supply of Penta or other IPV-containing vaccines.

This study aims to determine the conditions under which the introduction of Hexa as an IPV-containing vaccine can effectively support the GPEI's IPV2 initiative without disrupting the supply of Penta.

1.2. Literature Review

To protect vulnerable populations and foster global health, organizations such as Gavi assist lower-income countries in their vaccine procurement process, ensuring affordable pricing. Thus, over the set of available vaccine products and manufacturers, Gavi seeks to negotiate contract prices and quantities that will meet vaccine demand within low-income countries at the lowest total cost. In this paper, we build on previous work that examines similar problems through game theory and optimization frameworks.

The pediatric vaccine pricing problem has been formulated by Behzad and Jacobson using a Bertrand–Edgeworth–Chamberlin price game [14]. This model identifies equilibrium prices and quantities for a single vaccine product when there is competition between asymmetric manufacturers with limited production capacities, linear demand, and differentiated products. They validated the model using a case study in the U.S. pediatric vaccine market.

Cummings et al. [15] embed this pricing game into an optimization framework in which the U.S. Centers for Disease Control and Prevention (CDC) negotiates contract prices and quantities with manufacturers of pediatric vaccines provided through public-sector health programs. Adapting the model of manufacturer competition from Behzad and Jacobson, they conclude that collaboration between the CDC and manufacturers in public-sector price negotiations would improve cost-effective procurement of pediatric vaccines from private manufacturers [15]. Similarly, Martonosi et al. [16] apply this approach to the COVID-19 vaccine market in the U.S. and suggest that it is possible with government mediation to achieve sufficiently low prices and meet demand for vaccines while ensuring sufficient profit for each manufacturer.

Each of the above papers considers the market for a single vaccine product covering a particular set of antigens. Combination vaccines that cover multiple antigens tend to be more expensive than single antigen vaccines. Prior efforts to enhance market access of vaccines via coordination include the work of Proaño et al. that proposes a mixed integer non-linear optimization model for assessing optimal procurement under a hypothetically coordinated global vaccine market [17]. The model aims to maximize the total social surplus from covering countries' antigen demands while ensuring adequate profits for manufacturers under a tiered pricing market. The study illustrates that it is possible to ensure affordability and profit by first determining what vaccines to buy and then the price ranges that ensure maximum affordability and profit for the optimal procurement allocation. The paper shows that vaccine affordability is possible and how "vaccine prices in all market segments become more affordable as the supply of the most complex combination vaccines becomes more available to low-income countries" [17].

Alves-Maciel and Proaño [18] build upon previous research [17] to explore strategies aimed at improving both affordability and profitability within the global vaccine market, which consists of multiple non-cooperative coordinating entities. These entities work to meet the needs of countries grouped into specific market segments at reasonable prices while ensuring that manufacturers can maintain profitability. Their study examines a range of vaccines, antigens, and manufacturers, focusing on how the total social surplus is affected by the number of coordinating entities, the market segments assigned to each entity, the procurement sequence among these entities, and the recovery of fixed costs. Key findings indicate that the order in which coordinating entities negotiate with vaccine producers significantly influences the affordability and profitability of vaccines. Through tiered pricing, low-income countries can achieve greater savings by purchasing vaccines from entities that serve a larger number of market segments. Conversely, upper-middle and high-income countries can enhance affordability by purchasing through coordinating entities that focus on fewer market segments. Implementing a procurement order for coordinating entities based on the descending income levels of their countries provides greater opportunities to improve both affordability and profitability, especially when producers offer volume-based discounts.

Modeling the price competition for the entire set of pediatric vaccines, including combination vaccines that cover multiple antigens, is not trivial. In reality, vaccine products, even those produced by the same manufacturer, can compete. For example, a manufacturer's standalone IPV vaccine competes with all IPV-containing vaccines across all manufacturers. Hexa competes with all vaccine products that contain any of the six antigens it contains. Thus, any demand curve or competition model that relates price and quantity of a given vaccine product must account for the prices and quantities of all vaccine products that contain overlapping antigens.

The primary contribution of this paper is the integration and extension of several existing modeling approaches within a unified optimization framework for vaccine pro-

curement. We combine elements of the aforementioned works to create a new linearized integer optimization model that identifies manufacturer contract prices and quantities to minimize total vaccine procurement costs for all Gavi-supported low-income countries, as well as per-dose distribution costs (incentivizing adoption of combination vaccines) to meet all antigen-level demand. The model extends the linear demand framework from earlier work to capture price competition among all vaccine products with overlapping antigens. In doing so, it incorporates a game-theoretic structure in which manufacturers' pricing decisions are interdependent, allowing the model to characterize the competitive dynamics across substitutable and partially overlapping vaccine markets. The basic game-theoretic structure of the model in our paper adapts the linear demand curve from [14]. Moreover, the model ensures adequate manufacturer profit. We assume that all Gavi countries qualify for support for their IPV-containing vaccines.

2. Materials and Methods

2.1. Model Formulation

Following the GPEI's strategy, we propose a mathematical programming model that incorporates incentives to produce Hexa for the international pediatric vaccine market. For ease of exposition, we use the acronym OPV to refer to all oral polio vaccines, including novel oral polio vaccines (nOPVs). We assume that the tender lengths are the same for all antigens. We define relevant sets for the definition of decision variables and parameters dependent on factors including vaccine type (V), antigens (A), manufacturers (M), and year within the tender length ($1 \dots T$). We then represent the contracting problem as a mixed-integer linear programming problem. For ease of exposition, we describe the objective function and constraints in plain terms here. The complete list of model parameters and notation is shown in Table 1; the full optimization problem is presented in Appendix A.

Table 1. Components of the optimization model in Model A1.

Name	Type	Meaning
V	set	vaccines
A	set	antigens
M	set	manufacturers
T	set	contract years
Γ	set	competing products for each vaccine $v \in V$ (including v)
χ	set	combinations of vaccines with exact coverage of all $a \in A$
p_{it}^v	variable	price for $v \in V, i \in M, t \in T$
q_{it}^v	variable	quantity for $v \in V, i \in M, t \in T$
w_{it}^v	variable	McCormick linearization variable, the product $p_{it}^v q_{it}^v$
x_{it}^v	variable	binary indicator of production of vaccine $v \in V, i \in M, t \in T$
y_i	variable	binary indicator of production of Hexa by $i \in M$
z	variable	bound on absolute price difference
D_{at}	parameter	demand, $a \in A, t \in T$
a^v, b^v, c^v	parameter	demand curve coefficients, $v \in V$
δ^v	parameter	historical upper limit on demand, $v \in V$
ρ^v	parameter	historical upper limit on price, $v \in V$
β_t^v	parameter	upper quantity limit, the minimum of δ^v and the maximum projected demand per antigen for all antigens in v , defined for $v \in V, t \in T$ and used in McCormick linearization
d	parameter	distribution cost
P_i	parameter	minimum profit threshold, $i \in M$
K_i	parameter	total production capacity, $i \in M$

Table 1. Cont.

Name	Type	Meaning
Q	parameter	Hexa production capacity
c_i	parameter	total one-time development cost for Hexa, $i \in M$
γ	parameter	product similarity
μ_1, μ_2, μ_3	parameter	objective function weights
n^v	parameter	number of antigens in vaccine $v \in V$
C_a^v	parameter	binary composition matrix indicating whether vaccine $v \in V$ includes antigen $a \in A$
N	parameter	scaling factor
f^{hex}	parameter	minimum proportion of demand attributed to Hexa
f^{OPV}	parameter	maximum proportion of demand attributed to OPV products
λ	parameter	minimum quantity
ϕ	parameter	minimum price

- **Decision Variables:** We consider a set of manufacturers (M) of pre-qualified vaccine products (V) that have existing contracts to produce vaccines for LIC and LMIC Gavi countries. For each vaccine product v and each year t in the tender horizon $1, \dots, T$, a market coordinator (e.g., Gavi/UNICEF) negotiates quantities, q_{it}^v , and prices, p_{it}^v , with each manufacturer i to achieve its goals.
- **Objective Function:** Gavi seeks contracts that achieve a weighted combination of two goals: low procurement and distribution costs, and high market diversity as reflected by the total number of vaccine products produced across all manufacturers. Additionally, a third term in the model's objective function moves the model towards more realistic solutions in which competing vaccines have similar prices. This does not preclude large price differences from emerging if, for example, doses of a more expensive vaccine are needed to guarantee supply over some years of the tender.
- **Constraints:** Negotiated prices and quantities are restricted by the following constraints.
 - Total demand D_{at} for each antigen a must be met in each year t across all vaccine products that contain antigen a .
 - Each manufacturer has a fixed annual production capacity K_i aggregated over all vaccine products in their portfolio at the start of the tender. We assume that manufacturers can allocate their production capacity across their product portfolio. We further assume that manufacturers will not begin producing new vaccine products other than those already in their portfolio at the start of the tender. This assumption is realistic because a UNICEF tender commits suppliers to particular volumes, quantities, and prices of existing pre-qualified products for a predetermined number of years (2–5 years). A qualification process is complex, expensive, and time-consuming. Hence, it is difficult for new producers to launch a new product in low-income countries during an existing tender. Additionally, manufacturers introduce new product launches first to high-income countries and later to low-income countries through pool procurement tenders that offers them the opportunity to capture high volumes to recover their investment costs. In our model, the only vaccine for which manufacturers can expand their initial production capacity is Hexa, for which there is a fixed cost c_i associated with a given manufacturer i choosing to produce Hexa. We assume that c_i is \$0M USD for those already producing Hexa; it is higher for those that already produce both IPV and Penta; and it is highest for those manufacturers producing neither Hexa, nor both IPV and Penta. This assumption allows us to model the promotion of Hexa production.

- Each manufacturer i seeks to attain a minimum profit threshold P_i over the duration of the tender across all vaccine products, including the recovery of the fixed investment costs if it chooses to produce Hexa.
- Prices and quantities follow a linear demand curve.
- To reflect the IPV1 goal of administering at least one dose of IPV in the typical three-dose polio vaccine schedule, we restrict the contracted quantity of oral polio vaccines (OPVs) such that it cannot exceed some proportion, f^{OPV} , of projected demand of polio vaccines in any given year. Setting $f^{OPV} = 1$ represents no restriction on OPV consumption. Setting $f^{OPV} = 2/3$ represents requiring at least one dose of the typical three-dose polio vaccine regimen to be IPV rather than OPV (IPV1 goal). Setting $f^{OPV} = 1/3$ represents the IPV2 goal.
- To model Gavi's efforts to promote Hexa production, we require a certain minimum proportion, f^{hex} , of projected demand for each antigen to be met by Hexa. Setting $f^{hex} = 0$ represents no minimum requirement on Hexa production.
- To ensure that the model identifies realistic prices for Hexa that are commensurate with the antigens it contains, the price of Hexa produced by manufacturer i in year t is at least the sum of the prices of any vaccines produced by manufacturer i in year t that collectively contain antigens covering those in Hexa. This assumption is supported by UNICEF pricing data. For example, in 2025, contracted prices for Penta ranged from 0.85 to 1.29 USD/dose and IPV prices ranged from 1.25–2.80 USD/dose. Hexa prices were roughly comparable to the sum of these, ranging from 2.85 to 4.50 USD/dose [19].
- Additional constraints linearize the formulation (as derived in Appendix A.1) and enforce logical relationships between variables.

2.2. Demand Curve Estimation

The linear demand curve is often used in the Bertrand oligopoly model for strategic vaccine price competition [14–16,20]. No examples were found in the literature of estimating demand curve coefficients for products that partially compete with vaccine products, sharing partially overlapping antigens. Thus, one contribution of this work is the linear demand-curve estimation method we develop in this section. The remainder of the parameter estimation can be found in Appendix C.

To estimate the linear demand curve parameters, we used the publicly available World Health Organization's *Market Information for Access to Vaccines (MI4a) Vaccine Purchase Database* [21] and UNICEF's *Vaccines Pricing Data* [22] for the years 2020–2030. We limited our scope to pediatric vaccines against diphtheria, tetanus, pertussis (these three in combination are often abbreviated DTaP or DTwP, depending on whether they contain acellular or whole-cell pertussis antigens), polio (offered as oral polio vaccine in various forms including novel oral polio vaccine, all of which we abbreviate OPV, or as inactive polio vaccine, or IPV), hepatitis B (HepB), and *Haemophilus influenzae* type B (Hib). We made a few simplifying assumptions related to vaccine exclusion, the oral polio vaccine grouping, and DTaP and DTwP antigen grouping, as explained in Appendix B.

Demand D_{at} . We used demand forecast data from UNICEF, provided in 2021 [22]. We filtered data for vaccines with antigens in common with Hexa, forming the set A defined above. Then, for each antigen in each year within the tender length, we summed the demand across all vaccines that contain that antigen. This gave us the total number of doses D_{at} demanded for antigen a in year t .

The original demand forecast data anticipated a phase-out of oral polio vaccine after year three, in reflection of the planned eradication of polio. However, the polio eradication goal has since been extended to 2029, beyond our timeframe of interest. Therefore, the

original data reflect an unrealistic reduction in projected demand for polio antigen. We thus also considered linearly extrapolated demand for polio antigen, reflecting the continued need for vaccination at current rates throughout the tender horizon. We did not consider demand projections beyond achieving a potential polio eradication. After eradication, there would be at least a ten-year period of continued polio immunization, but the type of vaccines to use and the number of doses could differ. These values are given in Table 2.

Table 2. Estimated annual demand per antigen, D_{at} in millions, calculated based on [23].

Antigen	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Year 7
DTP	196.6	200.3	203.8	207.2	210.2	213.2	216.2
HepB	220.7	224.8	228.9	232.8	236.4	239.9	243.2
Hib	190.5	194.2	197.8	201.2	204.2	207.2	210.2
Polio	391.4	401.2	409.0	117.9	120.2	122.4	124.6
Polio (Extrapolated)	391.4	401.2	409.0	416.8	424.6	432.4	440.3

Product similarity, γ . The product similarity parameter ranges from 0 to 1 and reflects the interchangeability of vaccine products covering the same set of antigens, covering brand, packaging, and dosing differences. We used a moderate value of 0.5 based on the work by [16].

Demand curve coefficients, a^v, b^v, c^v . Intercept a^v represents the quantity of vaccine product v that would be sold by manufacturer i in year t if its price and the prices of all competing products were 0. Slope parameter b^v represents the effect a manufacturer's own pricing of vaccine product v has on the quantity v it can sell, while slope parameter c^v represents the effect competing products' pricing has on the quantity of v .

We adapted the original demand curve formulation from [14] to accommodate the vaccine products, manufacturers, and years relevant to the model, as well as competition between nonidentical vaccine products that have overlapping antigens. For each vaccine product v produced by each manufacturer i in year t , the price p_{it}^v and the quantity q_{it}^v must adhere to the curve given in Equation (1).

$$q_{it}^v + b^v \frac{p_{it}^v}{n^v} - c^v \cdot \left(\sum_{j \in M, j \neq i} \frac{p_{jt}^v}{n^v} + \sum_{v' \in \Gamma[v], v' \neq v} \sum_{j \in M} \frac{p_{jt}^{v'}}{n^{v'}} \right) = a^v \quad (1)$$

$$\forall v \in V, i \in M, t \in T$$

We discuss each component of Equation (1) in turn.

- The right-hand-side of the equation is the demand curve intercept a^v , the baseline quantity of vaccine product v that would be sold by manufacturer i in year t if its price and the prices of all competing products were 0.
- On the left-hand-side, the first term of the demand curve, q_{it}^v , is the quantity of vaccine product v that would be sold by manufacturer i in year t .
- The second term on the left-hand-side is the product of demand coefficient b^v with the price per antigen of vaccine v for manufacturer i in year t . This term captures the inverse relationship between price and quantity: as p_{it}^v goes up, q_{it}^v will go down to maintain the linear equality.
- The third term on the left-hand-side, having demand coefficient c^v , captures internal and external price competition between vaccine products that have overlapping antigen coverage with vaccine v . We first represent the per-antigen price of all producers $j \neq i$ of vaccine product v as $\frac{p_{jt}^v}{n^v}$ to capture direct price competition for product v .

Then, we use $\frac{p_{it}^{v'}}{n^{v'}}$ to represent the per-antigen price of all other vaccine products $v' \neq v$ produced by any manufacturer j that share demand for antigen a with v (given by the set $\Gamma[v]$). Scaling to a per-antigen basis is important for two reasons: (1) our demand data are given per-antigen; and (2) a vaccine product containing fewer antigens is inherently less expensive to produce than a product containing more antigens, so we want to model price competition on a per-antigen basis. Because of the negative coefficient on this term, as the price of any of these competing vaccine products goes up, the quantity sold of manufacturer i 's vaccine product v will also go up.

We estimated the demand curve coefficients based on historical data, following the approach of [15]. To estimate a^v , the demand curve intercept, we assumed that when all prices equal zero, demand for an antigen will be distributed evenly over all vaccine products that cover it. This gives us $|A|$ equations of the form

$$D_{at} = \sum_{v \in V} C_a^v m^v \alpha_t^v, \quad (2)$$

where D_{at} is the projected demand for antigen a in year t , C_a^v is a binary composition matrix indicating whether vaccine $v \in V$ includes antigen $a \in A$, m^v is the number of manufacturers producing vaccine v , and α_t^v is the resulting number of doses of vaccine v that will be sold in year t , per manufacturer.

This system is underdetermined and does not address the fact that multivalent vaccines are likely to have higher demand than monovalent vaccines because they cover more antigens, easing their distribution. To capture this, we added equations to system (2) of the form $\frac{\alpha_{t1}^{v_1}}{n^{v_1}} = \frac{\alpha_{t2}^{v_2}}{n^{v_2}}$, where v_1 and v_2 are vaccine products containing overlapping antigens. Rather than capturing all pairs of overlapping vaccine products, we added only six additional constraints, addressing relationships between DTP and Penta, Hexa, DTP-IPV, and DTP-HepB; between HepB and Penta; and between IPV and Hexa.

From the demand intercepts α_t^v , we computed the demand coefficients a_t^v by adapting an equation from [14] to account for overlapping antigens.

$$a_t^v = \alpha_t^v + \frac{10^{\sigma_t^v}}{1 + (\eta_t^v - 1)\gamma} \cdot \kappa_t^v, \quad (3)$$

where η_t^v is the total number of vaccine products that compete with vaccine v , including itself; κ_t^v is the average competing price per antigen for vaccine product v in year t ; and σ_t^v is the approximate order of magnitude difference between α_t^v and κ_t^v (i.e., found through dividing α_t^v by κ_t^v). We computed the average competing price per antigen, κ_t^v , as below.

$$\kappa_t^v = n^v \cdot \frac{\sum_{i \in M} \frac{p_{it}^v}{n^v} + \sum_{i \in M} \sum_{v' \in \Gamma[v]} \frac{p_{it}^{v'}}{n^{v'}}}{\eta_t^v} \quad v' \neq v \quad (4)$$

The first term sums, for all manufacturers, the price per antigen of v . The second term sums across all manufacturers the price per antigen of all competing products $v' \neq v$ contained in $\Gamma[v]$. We scaled the sum of these terms by n^v , the number of antigens in v , and then divided it across all competing products η_t^v .

After calculating the demand coefficients a_t^v , we averaged them over all years to find a^v . Similarly, we determined b_t^v and c_t^v following [14] and then average them to obtain b^v and c^v .

$$b_t^v = \frac{10^{s_t^v} (1 + (\eta_t^v - 2)\gamma)}{((1 + (\eta_t^v - 1)\gamma) \cdot (1 - \gamma))} \quad (5)$$

$$c_t^v = \frac{10^{s_t^v} \gamma}{(1 + (\eta_t^v - 1)\gamma) \cdot (1 - \gamma)}$$

The orders of magnitude s_t^v used in finding b_t^v and c_t^v are computed in a similar manner to σ_t^v , comparing the magnitude of κ_t^v to the magnitude of a_t^v . The resulting demand curve coefficients averaged over historical years are enumerated in the first three rows of Table 3.

Table 3. Estimated demand curve parameter values indexed by vaccine product. a^v is the demand curve intercept. Slope parameter b^v is the rate of effect a manufacturer's own pricing of vaccine product v has on the quantity v it can sell. Slope parameter c^v is the rate of effect competing products' pricing has on the quantity of v . n^v is the number of antigens covered by vaccine product v , and m^v is the number of manufacturers currently producing v .

Name	DTP	HepB	IPV	OPV	Penta	Hexa	DTP-IPV	DTP-HepB
a^v (MIL)	4.280	4.326	4.403	81.726	16.206	17.204	6.820	2.998
b^v (MIL/USD)	1.586	1.317	0.185	4.638	1.615	0.193	0.192	0.730
c^v (MIL/USD)	0.114	0.083	0.015	0.362	0.085	0.006	0.008	0.037
n^v (antigens)	1	1	1	1	3	4	2	2
m^v (mfrs.)	4	7	5	11	10	2	1	2

2.3. Computational Framework

We used a variety of optimization solvers on the online NEOS server [24] for initial testing. The results reported here were computed on a high-performance computing server and solved using the AMPL modeling language and Gurobi optimization software. The specification ranges per task include a 15 h limit on runtime, 8 to 12 CPUs per task, and 8 to 15 GB per CPU. An optimality gap of 5% was used. All code is available in the GitHub repository [25].

3. Results

3.1. Scenarios

We wish to understand the market implications of adopting Hexa to introduce at least one dose of IPV in the immunization schedule (IPV1 goal). We examine the following scenarios in combination.

- **Hexa Manufacturing Capability:** We consider different sets of manufacturers capable of producing Hexa, from most restricted to least restricted.
 - *Original Hexa:* Only those manufacturers who are known to have historically manufactured Hexa are allowed by the model to produce Hexa; this reflects the scenario with no further expansion of Hexa production. (This corresponds to two out of twenty manufacturers in our dataset.)
 - *Penta and IPV:* We additionally enable any manufacturer currently producing both Penta and IPV to produce Hexa by incurring a Hexa development cost c_i . (This adds two manufacturers to the Hexa-capable set, for a total of four eligible to produce Hexa.)
 - *All:* All manufacturers are able to produce Hexa by incurring a Hexa development cost c_i .

- **Polio Demand:** We vary the projected demand for polio vaccine, considering two scenarios.
 - *Phase-out:* Demand for polio is taken from the initial dataset, which anticipates a sharp decline in demand for oral polio vaccine forms, attributed to the original GPEI eradication strategy [22].
 - *Extrapolated:* Demand for polio vaccine is extrapolated for 2027 onward using the approximate growth rate for the previous projections, representing demand growth under the GPEI eradication extension strategy and reflecting the ongoing need for IPV and novel oral polio vaccines even post-eradication [3].
- **Scale of Upper Price Limit:** We constrain the upper limit on the contracted prices for each vaccine.
 - *Scale of Upper Price Limit = 1:* Prices are limited to their estimated upper bound, ρ^v , from the historical price data.
 - *Scale of Upper Price Limit = 10:* Prices are limited by ten times the estimated bound, thus expanding the set of possible feasible solutions.

For each of these scenarios, the remaining parameters are as given in Table 4. Specifically, we examine the case where OPV forms can meet no more than two-thirds of the demand for polio inoculation ($f^{OPV} = 0.67$). This aligns with the IPV1 goal that at least one dose of a three-dose polio sequence be IPV. To model the introduction of Hexa, we require it to meet at least 5% of demand for each antigen ($f^{hex} = 0.05$). Without loss of generality, we assume that the development cost of Hexa, c_i , for existing manufacturers of Hexa would be \$0M USD; \$50M USD for manufacturers that already produce both Penta and IPV; and \$100M USD for new manufacturers that produce neither Hexa nor both IPV and Penta. We assume that each manufacturer's profit constraint threshold per vaccine product, P_i , is 50% of the median historical market share per vaccine product. For justification of these values, we refer the reader to Appendix C.

Table 4. Baseline parameter values for scenario testing. f^{OPV} is the maximum fraction of polio demand that can be met by OPV. f^{hex} is the minimum fraction of antigen demand that must be met by Hexa. c_i is the Hexa development cost for manufacturer i , categorized by initial Hexa manufacturing capability.

Parameter	Baseline Value	Note
f^{OPV}	0.67	IPV1 goal
f^{hex}	0.05	Hexa introduction
c_i	\$0 USD \$50M USD \$100M USD	Existing mfrs. Penta + IPV mfrs. New mfrs.
P_i	50%	% market share

3.2. Analysis

Table 5 reports the range of model-output contracted Hexa price and quantity over all manufacturers and years obtained in each scenario.

First, if no new manufacturers begin to produce Hexa beyond the original two producers, then there are no feasible solutions that allow oral forms of polio vaccine to be phased out in favor of IPV-containing products while satisfying profit targets and price competition constraints. Even in the case where Penta and IPV-producing manufacturers are allowed to develop Hexa and the upper historical price limit is allowed to increase to ten times its historical values, there are still no feasible solutions. We believe the infeasibility is driven by the constraints enforcing price competition: the target profit constraint tries

to maximize the value of $p_{it}^v q_{it}^v$, implying that manufacturers will need both contracted prices and quantities to be sufficiently high to meet target profits and justify production. The requirement that the Hexa price must meet or exceed the prices of constituent vaccines pushes Hexa prices to be higher than those of other vaccines; however, price competition in the demand curve limits contracted prices when quantities are high, as would be the case when there are only a few manufacturers available to produce Hexa.

Table 5. Model output for ranges of Hexa contracted price and quantity across all years and manufacturers, for each scenario. All other parameters are at their baseline values given in Table 4: proportion OPV is limited to two-thirds ($f^{OPV} = 0.67$); at least 5% of antigen demand must be met by Hexa ($f^{hex} = 0.05$); Hexa development cost is \$100M USD for manufacturers that produce neither Hexa nor IPV and Penta, and \$50M USD for manufacturers that produce both IPV and Penta; and the profit constraint threshold for each manufacturer is 50% of the median historical market share per-vaccine-product.

Hexa Mfg. Capability	Polio Demand	Scale of Upper Price Limit	
		1	10
Original Hexa	Phase-out	Infeasible	Infeasible
	Extrapolated	Infeasible	Infeasible
Penta. and IPV	Phase-out	Infeasible	Infeasible
	Extrapolated	Infeasible	Infeasible
All	Phase-out	\$19.99–\$77.14 (USD) 14.54–16.50 M	\$52.55–\$125.26 (USD) 11.82–15.87 M
	Extrapolated	\$23.22–\$73.84 (USD) 14.77–16.42 M	\$34.47–\$57.93 (USD) 15.63–16.65 M

Only when all manufacturers can produce Hexa do we find a feasible result that meets the minimum required Hexa production, the IPV1 target, and the target profits. In this solution, nine manufacturers are ultimately selected to produce Hexa to achieve this result. Moreover, the quantity of Hexa production is also two orders of magnitude higher than initial production in our source data, increasing from approximately 300 K doses per year [23] to nearly 150 M doses per year in the model output. (This required volume exceeds the UNICEF vaccine demand estimate for Hexa of 100 M doses by 2030 by 50 M doses.) This may not be a unique optimal solution; there might exist other cost-minimizing solutions meeting target profits and other constraints that require less Hexa procurement. Nonetheless, this optimal solution signals that dramatic increases to Hexa production capacity would facilitate a cost-effective distribution of multivalent vaccines to Gavi-supported countries. Increasing the set of Hexa-capable manufacturers is necessary for achieving the IPV1 goal within the target profit and competitive pricing constraints of the model.

To examine feasible results more closely, we selected 2026 ($t = 3$) to be a representative year as it is far enough into the 7-year tender for manufacturers to have started developing Hexa but also captures some of the price fluctuations. We consider the extrapolated polio demand scenario and let the upper price limit be its historical value. Reported nonzero prices and quantities for this scenario are tabulated in Table 6; manufacturers and vaccine products not listed have model-output contracted quantities equal to zero.

First, we see that the portfolio of contracted vaccine products is far simpler than the current market: only four vaccine products are needed to meet all demand at the lowest cost. The sparsity of this solution is likely a natural result of the algorithmic tendencies of linear programming solvers to return sparse optimal solutions among the set of possible

optimal solutions. Nonetheless, the existence of such an optimal solution indicates that a simpler market structure is feasible, particularly if Hexa is widely produced.

Observe that all nine manufacturers the model selects to contract with in 2026 include Hexa in their production portfolios. Further, with the exception of OPV products, all vaccine products are multivalent, even when monovalent vaccines (such as IPV, HepB, or DTP) were an option. The model identifies a contract with 137.7 M doses of Hexa, 264 M doses of OPV, and 7.2 M doses of DTP-IPV for polio coverage. Meanwhile, Penta production remains robust at 97.4 M doses. However, some market risk is present in this proposed contract: with only a single manufacturer producing the DTP-IPV combination vaccine, only two manufacturers producing OPV, and only two manufacturers producing Penta, the market would be sensitive to production disruptions and shortages affecting any of these products.

Table 6. Model output contracted prices per dose (USD) and nonzero quantities by vaccine product and manufacturer in year 2026 for the scenario in which polio demand is extrapolated, the upper price limit is its historical value, and all manufacturers are permitted to develop Hexa. All other parameters are at their baseline values given in Table 4: proportion OPV is limited to two-thirds ($f^{OPV} = 0.67$), reflecting the IPV1 goal; at least 5% of antigen demand must be met by Hexa ($f^{hex} = 0.05$); Hexa development cost is \$100 M USD for manufacturers that produce neither Hexa nor IPV and Penta (Manufacturers 1–15 and 20); \$50 M USD for manufacturers that produce both IPV and Penta (Manufacturers 16 and 19); \$0 M USD for manufacturers already producing Hexa (Manufacturers 17 and 18); and the profit constraint threshold for each manufacturer is 50% of the median historical market share per-vaccine-product. Vaccine products and manufacturers not listed have model-output contracted quantities of zero.

Mfr.	Vaccine Product			
	OPV (Price, Quantity)	Pent. (Price, Quantity)	Hex. (Price, Quantity)	DTP-IPV (Price, Quantity)
3	(0, 0)	(0, 0)	(\$57.81, 15.3 M)	(0, 0)
6	(0, 0)	(0, 0)	(\$57.79, 15.3 M)	(0, 0)
10	(0, 0)	(0, 0)	(\$57.79, 15.3 M)	(0, 0)
12	(0, 0)	(\$2.65, 48.7 M)	(\$57.79, 15.3 M)	(0, 0)
15	(0, 0)	(0, 0)	(\$57.81, 15.3 M)	(0, 0)
16 (Penta + IPV)	(0, 0)	(0, 0)	(\$57.81, 15.3 M)	(0, 0)
17 (Hexa)	(0, 0)	(0, 0)	(\$57.81, 15.3 M)	(\$17.64, 7.2 M)
18 (Hexa)	(\$0.01, 132 M)	(\$2.62, 48.7 M)	(\$57.81, 15.3 M)	(0, 0)
19 (Penta + IPV)	(\$0.01, 132 M)	(0, 0)	(\$57.79, 15.3 M)	(0, 0)

The model-generated prices for Penta and DTP-IPV are in realistic ranges. The model-generated price for Hexa is \$57.79 USD for all manufacturers, which is consistent with private-sector pricing for Hexa, which ranges from \$20.20 to \$44.54 USD per dose and uses acellular pertussis antigens rather than whole-cell antigens [26]. However, this model-generated price is an order of magnitude higher than Hexa prices observed in the current UNICEF contract, which range from \$2.85 to \$4.90 USD per dose [27]. This highlights the need for additional financial incentives for manufacturers to produce Hexa to ensure a competitive and profitable market. We also note that the model-generated prices for OPV products approach the minimum price $\phi = 0.01$ USD, while reported Gavi prices for bOPV in 2025 are listed as ranging from \$0.11 to \$0.23 USD [26]. These low prices may be driven by the linear demand curve relationship as in our model's solution, manufacturers 18 and 19 jointly produce over 250 million doses of OPV products, while only around 150 million doses of IPV-containing vaccines are produced. Thus, in the price, demand, and capacity trade-off, we see a small number of manufacturers continuing to produce OPV products, with low prices driving large quantities needed for revenue targets to be attained.

OPV products account for approximately 62% of total polio demand across all seven years, which approaches our limit of no more than two-thirds of total polio demand for OPV products. We conclude that even with nine manufacturers investing in Hexa production, oral polio vaccine products will continue to play a major role in protecting against polio.

3.3. Sensitivity Analysis

We assessed the sensitivity of the solutions to certain parameter values by considering four scenarios based on profit threshold and OPV production limits and then examining ranges of contracted prices and quantities obtained as two additional parameters, Hexa requirement and Hexa development cost, are varied.

Scenarios

- We assessed the impact of the manufacturer profit threshold parameter value, P_i , on our results. The proportion of the profit threshold to be met may be 50% (no change from the previous value) or 45% (a 10% decrease from the previous value) of the median historical market share per vaccine product. The 10% decrease from the previous value relaxes the profit requirement, thereby improving feasibility.
- Similarly, we analyzed the impact of limiting OPV production on feasibility by allowing the maximum proportion of polio demand met by OPV, f^{OPV} , to be $2/3$ (as in previous results) or $1/3$ (heavily restricting OPV use, reflecting Gavi's IPV2 goal of at least two doses of IPV in the three-dose polio vaccine sequence).

Parameter variations

- To examine the extent to which development cost may hinder the production of Hexa, we scale the projected cost by either 1.0 (no change from previous results) or by 0.9 (reduced development cost). Thus, for manufacturers that have historically produced neither Hexa nor IPV, the development costs would be \$100 M or \$90 M USD. For manufacturers that have historically produced IPV and Penta, the development costs would be \$50 M or \$45 M USD. For manufacturers already producing Hexa, the development cost would be \$0 M USD in either case. These costs should be considered relative to the assumed development costs discussed in this paper.
- The minimum proportion of demand to be met by Hexa, f^{hex} , may be 5% (no change from previous results) or 1% (relaxing the requirement on Hexa production).

When we allow only the two historical manufacturers of Hexa to continue producing it, all combinations remain infeasible unless OPV production is fully unrestricted ($f^{OPV} = 1$). This shows that without intervention to expand production capabilities, Gavi's IPV1 goal is unattainable. The same is true when the two manufacturers of Penta and IPV are also allowed to produce Hexa. These results provide compelling evidence that OPV distribution cannot be limited while ensuring market profitability without extensive expansion of Hexa production. This echoes the recommendations included in the GPEI.

To avoid infeasible results, we focus on the case where all manufacturers are allowed to invest in Hexa production, and we scale the upper price limit by 10 to allow sufficient pricing flexibility. We focus on the extrapolated polio demand scenario as it should more closely reflect the natural growth of polio demand without any policy interventions. Results of the sensitivity analysis are summarized in Table 7. In general, they concur with the results in Section 3.2.

When all twenty manufacturers are allowed to produce Hexa (instead of just the two producing Hexa in the original data or the additional two producing Penta and IPV), and the upper price limit is increased, we find that even the case where $f^{OPV} = 1/3$ (corresponding to IPV2) is feasible. This suggests that, all else unchanged, dramatically increasing the number of Hexa-capable manufacturers improves the ability to satisfy constraints specified

in the model by meeting demand for polio-containing vaccines. Thus, incentivization of Hexa production is a pathway to achieving Gavi's two-dose IPV2 goal.

Moreover, further investigation of the results reported in Table 7 reveals that the OPV proportion constraint, which limits the proportion of polio doses that can be delivered orally, is tight and, therefore, a driver of infeasibility in the model. Indeed, additional testing when $f^{OPV} = 1$ (no restriction on oral polio vaccine product production) yields feasible results for all manufacturing scenarios.

Table 7. Sensitivity analysis results. Hexa and OPV price (USD) and quantity range outputs by the sensitivity analysis by vaccine product across all years, manufacturers, and all other parameter values, for the scenario in which all manufacturers may produce Hexa, polio demand is extrapolated after 2027, and the price limit is ten times its historical value.

Profit Scale	OPV Limit			
	$f^{OPV} = 1/3$		$f^{OPV} = 2/3$	
	Hex.	OPV	Hex.	OPV
45%	\$0.01–\$65.79 14.5–18.8 M	\$0.01–\$20.60 1.0–112.6 M	\$25.73–\$67.13 15.2–17.0 M	\$0.01–\$9.18 89.4–146.7 M
50%	\$0.01–\$67.28 14.9–18.7 M	\$0.01–\$20.60 1.0–110.3 M	\$32.83–\$71.41 15.1–16.6 M	\$0.01–\$16.93 46.7–146.7 M

In general, our sensitivity analysis indicates that oral polio vaccine products play a critical role in meeting polio demand. This, in turn, suggests a trade-off between reducing reliance on oral polio vaccine products and the number of Hexa manufacturers and their supply. Such a trade-off demonstrates the viability of Hexa as a potential solution to meeting IPV1 and IPV2 goals, provided that enough manufacturers have the capacity to produce Hexa. Coupling this with the goal of polio eradication means that it may indeed be feasible to limit the use of oral polio vaccine products to outbreak management, according to the GPEI strategy extension. Clearly, the challenge for enhancing the Hexa supply is to determine the necessary financial and logistic incentives to attract new manufacturers without disrupting the agreements and Penta's supply. A means of achieving such a balance may require having Penta, Hexa, and IPV-containing synchronized tenders and offering longer tender durations for manufacturers to participate. However, the impact of such mechanisms needs further analysis, which is not considered in this study.

4. Limitations and Future Work

This study explores the feasibility of implementing the Polio Eradication recommendations by incorporating additional doses of Inactivated Poliovirus Vaccine (IPV) into national immunization schedules through IPV-containing vaccines while also enhancing access to the Hexavalent vaccine. We evaluate these recommendations within a framework that assumes low-income countries (LICs) primarily obtain World Health Organization (WHO) pre-qualified products via UNICEF's pooled procurement mechanisms.

We intentionally set aside potential impacts on product availability, which may arise from variations in national procurement regulations, uncertainties in national immunization budgets, supply chain disruptions, and manufacturing challenges, as these factors can all influence product supply. Moreover, we do not factor in geopolitical influences or vaccine hesitancy, both of which can affect product demand. Although these aspects could significantly alter the polio market by introducing uncertainties, our framework isolates their effects to provide an analysis that clarifies the feasibility of the IPV GPEI recommendations via Hexa expansion. Our study assumes a scenario with steady-state supply conditions. In reality, over the last fifty years, product changes resulting from

the introduction of alternative polio vaccines have generated significant temporary shortages [28].

Technology transfer issues are not considered in this study because large multinational manufacturers do not produce Hexa vaccines for LICs. The hexavalent vaccines accessible to high-income markets rely on acellular pertussis antigens and, until 2026, were produced by three major multinational pharmaceutical companies. In contrast, the hexavalent vaccine available for LIC is made exclusively with whole-cell pertussis antigens. The available nOPV2 vaccine for low-income countries was developed to ensure accessibility in LICs. By 2026, two manufacturers will supply nOPV2 for LICs.

Finally, our study does not consider post-eradication plans, which require maintaining immunization for a decade and may involve the exclusive use of IPV-containing vaccines [29].

This work offers several promising directions for future exploration as follows. This work attempts to capture the goal of administering at least one dose of IPV by limiting OPV production to at most two-thirds of polio demand. However, our model assumes that the OPV production constraint is applied uniformly over the tender duration. An extension of our model could explore a temporal roll-out of Hexa that would ensure the OPV production constraint is met by the end of the tender. This would allow exploration of the timeline for achieving the IPV1 or IPV2 goals and the rate at which Hexa production increases over the tender.

Though we assume linear demand as a function of price per dose, vaccine demand may not always follow a linear curve, especially in light of the pandemic aftermath and existing outbreaks. Future work could expand upon the model by incorporating alternative demand models to account for these factors. The linear demand curve is a common framework for our analyses, and assessing sensitivity to this modeling assumption would fundamentally change the structure of the optimization model. Consequently, the inability to evaluate the sensitivity of the model to the linear demand assumption constitutes a limitation of this study.

Future work could also revise the model to relax some modeling assumptions. For example, we assume that manufacturer capacity is aggregated over all vaccine products in their portfolio. In reality, only vaccine products that require the same production technology can share manufacturing capacity. Another concern not addressed by our formulation is the potential for over-vaccination. When combination vaccines are used to meet the demand for certain antigens, their coverage may exceed the required doses for other antigens included in the combination vaccine. Especially in the case where we exceed demand, it is possible that there would be overlap in vaccines that inoculate against the same antigen(s). An extension to our work would be to formulate a mechanism such that demand is met within a small threshold.

5. Conclusions

Our computational results suggest that if no new manufacturers begin producing Hexa, and demand for the polio vaccine grows annually at its current rate, even when Penta and IPV manufacturers enter the market, continued procurement of oral polio vaccine products remains critical to meeting polio vaccine demand. Conversely, when all manufacturers have the ability to produce Hexa, we may even meet at least two-thirds of polio vaccine demand with IPV-containing products rather than OPV. These results, combined with the knowledge that OPV-limiting constraints are tight, highlight oral polio vaccine production and Hexa incentivization as a central component in satisfying demand for polio vaccine.

The results regarding the role of oral polio vaccines suggest that Gavi's incentivization of Hexa production through contracts and technology transfers would play a significant

role in polio eradication. In this way, we see a feasible avenue for increasing the availability of safer, IPV-containing vaccines in alignment with the GPEI strategy.

In summary, this study integrates several established approaches into a unified framework to examine global pediatric polio vaccine procurement. The analysis suggests that novel oral polio vaccine products will continue to play a significant role in satisfying international demand for pediatric polio vaccines, especially in cases where the manufacturer's supply capacities to produce Hexa remain largely unchanged. However, as more manufacturers begin producing Hexa, the feasibility of meeting polio demand with IPV-containing products improves greatly. This suggests the need for significant Gavi-incentives for Hexa production to provide a pathway to introducing IPV. Our analysis validates that Gavi's efforts to introduce Hexa in the global vaccine market may significantly contribute to the Global Polio Eradication Initiative. However, to maintain efforts to support the incremental production Hexa, a stable and attractive price per dose must be maintained.

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Abbreviations

The following abbreviations are used in this manuscript:

bOPV	Bivalent oral polio vaccine
CDC	U.S. Centers for Disease Control and Prevention
cVDPV	Circulating vaccine-derived poliovirus
cVDPV2	Circulating vaccine-derived poliovirus, type 2
DTP	Diphtheria, tetanus and pertussis vaccine
DTaP	Diphtheria, tetanus and acellular pertussis vaccine
DTwP	Diphtheria, tetanus and whole-cell pertussis vaccine
GPEI	Global Polio Eradication Initiative
Hexa	Hexavalent vaccine
HepB	Hepatitis B vaccine
Hib	Haemophilus influenza type B vaccine
IPV	Inactivated polio vaccine
IPV1	Single-dose IPV vaccination goal
IPV2	Two-dose IPV vaccination goal
LIC	Low-income country
LMIC	Low-middle-income country
MI4a	Market Information for Access to Vaccines
mOPV	Monovalent oral polio vaccine
OPV	Oral polio vaccine
nOPV	Novel oral polio vaccine
Penta	Pentavalent vaccine

SAGE	Strategic Advisory Group of Experts on Immunization
tOPV	Trivalent oral polio vaccine
UNICEF	United Nations International Children's Emergency Fund
USD	United States dollar
WHO	World Health Organization

Appendix A. Model

The sets, variables and parameters used in the optimization model can be found in Table 1. The full model formulation can be found in Model A1.

$$\text{minimize} \quad \sum_{i \in M} \sum_{t \in T} (\mu_1 \cdot \sum_{v \in V} (w_{it}^v + d \cdot q_{it}^v) - \mu_2 \cdot \sum_{v \in V} (x_{it}^v)) + \mu_3 \cdot z \quad (\text{A1})$$

$$\text{subject to} \quad z \geq p_{it}^v - p_{jt}^v - \rho^v \cdot (1 - x_{it}^v) - \rho^v \cdot (1 - x_{jt}^v) \quad i \neq j \quad \forall v \in V, i \in M, t \in T \quad (\text{A2})$$

$$q_{it}^{hex} \leq Q \cdot y_i \quad \forall i \in M, t \in T \quad (\text{A3})$$

$$p_{it}^{hex} \leq Q \cdot y_i \quad \forall i \in M, t \in T \quad (\text{A4})$$

$$\sum_{i \in M} q_{it}^{hex} \geq f^{hex} \cdot D_{at} \quad \forall a \in A, t \in T \quad (\text{A5})$$

$$p_{it}^{hex} \geq -N \cdot (1 - x_{it}^{hex}) + \sum_{v \in \ell} p_{it}^v \quad \forall \ell \neq hex \in \chi, i \in M, t \in T \quad (\text{A6})$$

$$\sum_{i \in M} \sum_{v \in V} q_{i,t}^v \cdot C_a^v \geq D_{at} \quad \forall a \in A, t \in T \quad (\text{A7})$$

$$\sum_{v \in V} q_{it}^v \leq K_i \quad v \neq hex, i \in M, t \in T \quad (\text{A8})$$

$$\sum_{t \in T} \sum_{v \in V} w_{it}^v \geq P_i \cdot \sum_{t \in T} \sum_{v \in V} x_{it}^v + c_i \cdot y_i \quad i \in M \quad (\text{A9})$$

$$q_{it}^v + \frac{b^v p_{it}^v}{n^v} - c^v \cdot \left(\sum_{j \in M, j \neq i} \frac{p_{jt}^v}{n^v} + \sum_{v' \in \Gamma[v], v' \neq v} \sum_{j \in M} \frac{p_{jt}^{v'}}{n^{v'}} \right) \geq a^v - \delta^v \cdot (1 - x_t^v), \quad \forall v \in V, i \in M, t \in T \quad (\text{A10})$$

$$q_{it}^v + \frac{b^v p_{it}^v}{n^v} - c^v \cdot \left(\sum_{j \in M, j \neq i} \frac{p_{jt}^v}{n^v} + \sum_{v' \in \Gamma[v], v' \neq v} \sum_{j \in M} \frac{p_{jt}^{v'}}{n^{v'}} \right) \leq a^v + \delta^v \cdot (1 - x_t^v), \quad \forall v \in V, i \in M, t \in T \quad (\text{A11})$$

$$\sum_{i \in M} q_{it}^{OPV} \leq f^{OPV} \cdot D_{polio} \quad t \in T \quad (\text{A12})$$

$$q_{it}^v \geq \lambda \cdot x_{it}^v \quad \forall v \in V, i \in M, t \in T \quad (\text{A13})$$

$$\delta^v \cdot x_{it}^v \geq q_{it}^v \quad \forall v \in V, i \in M, t \in T \quad (\text{A14})$$

$$p_{it}^v \geq \phi \cdot x_{it}^v \quad \forall v \in V, i \in M, t \in T \quad (\text{A15})$$

$$\rho^v \cdot x_{it}^v \geq p_{it}^v \quad \forall v \in V, i \in M, t \in T \quad (\text{A16})$$

$$w_{it}^v \geq \beta_t^v p_{it}^v + \rho^v q_{it}^v - \beta_t^v \rho^v \quad \forall v \in V, i \in M, t \in T \quad (\text{A17})$$

$$w_{it}^v \leq \beta_t^v p_{it}^v \quad \forall v \in V, i \in M, t \in T \quad (\text{A18})$$

$$w_{it}^v \leq \rho^v q_{it}^v \quad \forall v \in V, i \in M, t \in T \quad (\text{A19})$$

Model A1. Model to optimize pediatric vaccine pricing. Sets, parameters, and variables are defined in Table 1.

We consider a set of manufacturers ($i \in M$) of competing vaccine products. These manufacturers all have existing contracts with Gavi to produce vaccines for low-income Gavi countries. For each vaccine product $v \in V$ and each year $t \in T$, through the tenders, Gavi/UNICEF negotiates quantities, q_{it}^v and prices, p_{it}^v with each manufacturer to minimize the total cost of vaccine administration, which includes procurement and distribution costs. To improve market diversity and reduce sparsity in the solution, we prioritize solutions that increase the total number of vaccine products across all manufacturers. Finally, as in Cummings et al. [15], we denote z to be the maximum absolute difference between the Gavi-negotiated prices of any vaccine product $v \in V$ produced by manufacturers $i, j \in M$ in year $t \in T$ to induce the model towards optimal solutions in which competing vaccines have similar prices. This, in combination with constraint (A2), yields the weighted objective function in Equation (A1).

Minimal absolute price difference. Constraint (A2) defines the maximum value, z , for the absolute price difference between any vaccine v produced in year t by two different manufacturers, i and j . We include terms with the binary indicator variable for each of the vaccine products so that the difference is considered only if manufacturers i and j actually produce vaccine v in year t .

Hexa constraints. Constraints (A3) and (A4) ensure that only those manufacturers that have invested in the fixed development cost to produce Hexa can have nonzero contracted quantities and prices for Hexa. Constraint (A5) models Gavi's efforts to promote Hexa production by requiring a proportion, f^{hex} , of projected demand for each antigen to be met by Hexa. (Using $f^{hex} = 0$ represents no minimum requirement on Hexa production.) Constraint (A6) ensures realistic prices for Hexa that are commensurate with the antigens it contains. Specifically, the price of Hexa produced by manufacturer i in year t (p_{it}^{hex} , when $x_{it}^{hex} = 1$) must be at least the sum of the prices of any vaccines produced by manufacturer i in year t that collectively contain antigens covering those in Hexa. As an example, χ is a set of sets of vaccine products that cover all six antigens of Hexa, so $\ell = \{\text{penta, IPV}\}$ is an element of χ . Constraint (A6) requires the price of Hexa produced by any manufacturer in any year to be at least the sum of that manufacturer's prices for Penta and IPV.

Production constraints. Constraint (A7) enforces that total demand D_{at} for each antigen a will be met in each year t across all vaccine products that contain antigen a . Whether or not a manufacturer has invested in Hexa development, each manufacturer i has a fixed production capacity K_i aggregated over all vaccine products, excluding Hexa, as reflected in constraint (A8). (Hexa production capacity is constrained by Q once a manufacturer has invested in its production.)

Profit constraint. Constraint (A9) ensures that each manufacturer achieves a sufficient target profit level in aggregate over the duration of the tender. Specifically, the total revenue earned by manufacturer i in year t for vaccine product v is captured by the variable w_{it}^v , which comes from the McCormick linearization of the product $p_{it}^v \cdot q_{it}^v$. Summing over all years in the tender horizon and all vaccine products gives the total revenue on the left-hand-side of constraint (A9). P_i represents an average per-vaccine-product target profit for each manufacturer. The number of vaccine products that manufacturer i produces is given by $\sum_{t \in T} \sum_{v \in V} x_{it}^v$; thus manufacturer i must achieve a minimum total revenue of $P_i \cdot \sum_{t \in T} \sum_{v \in V} x_{it}^v$, plus recuperation of the fixed Hexa development cost, c_i , if the manufacturer has invested in Hexa, as indicated by variable y_i .

Linear demand curve. As used in the optimization models of [15,16], we assume that demand follows a linear curve and we adapt their demand curves to the context of multiple vaccine products with overlapping antigens. Constraints (A10) and (A11) ensure that prices and quantities follow a linear demand curve. For a given vaccine product v , produced by manufacturer i in year t , the first term, q_{it}^v , is the quantity produced. The second term is the

product of demand coefficient, b^v , with the per-antigen contracted product price, p_{it}^v/n^v . This scaling is important for two reasons: (1) our demand data is given on a per-antigen basis; and (2) a vaccine product containing fewer antigens is inherently less expensive to produce than a product containing more antigens, so we want to model price competition on a per-antigen basis. The third term captures per-antigen price competition between vaccine products that contain overlapping antigens. This reflects the fact that manufacturer i is competing not only against other manufacturers producing vaccine product v but also against all manufacturers (including i itself) that produce any vaccine product containing overlapping antigens with v . For example, if manufacturer i produces both DTP and DTP-IPV, then the demand for their DTP product is impacted not only by the prices of DTP of competing manufacturers but also by the price of manufacturer i 's own competing DTP-IPV product because the antigens overlap. Constraints (A10) and (A11) set the previous terms equal to the demand intercept a^v in the case where manufacturer i produces vaccine v in year t ($x_t^v = 1$), and relax the linear demand equality otherwise.

OPV phase-out. To represent a market less dominated by the presence of oral polio vaccine products, constraint (A12) constrains the contracted quantity of OPV products not to exceed a proportion, f^{OPV} , of projected demand for polio vaccines in any given year. Setting $f^{OPV} = 1$ represents no restriction on OPV production.

Binary variable linkage. Constraints (A13)–(A16) link the value of the binary variable x_{it}^v , which indicates whether or not manufacturer i produces vaccine product v in period t , to nonzero prices and quantities. Specifically, when $x_{it}^v = 0$, p_{it}^v and q_{it}^v are forced to be zero. When $x_{it}^v = 1$, the contracted quantity q_{it}^v is forced to the interval $[\lambda, \delta^v]$, and the contracted price p_{it}^v is forced to the interval $[\phi, \rho^v]$, thus ensuring reasonable minimum and maximum contracted quantities and prices.

McCormick linearization. Constraints (A17)–(A19) ensure that the quantity w_{it}^v appearing in the objective function and in profit constraint (A9) is a close approximation to the nonlinear contract cost $p_{it}^v q_{it}^v$. The McCormick linearization is derived below.

Appendix A.1. McCormick Linearization

The total cost in the objective function and the manufacturers' profit constraints are dependent on the product $p_{it} q_{it}$, which is nonlinear in the decision variables and causes unnecessary computational complexity. We linearize this term in the objective function and profit constraints shown in Model A1 using McCormick linearization. We start by defining the upper and lower bounds of price and quantity:

$$0 \leq p_{it}^v \leq \rho^v$$

$$0 \leq q_{it}^v \leq \beta_t^v$$

The following describes how to constrain w_{it}^v using linear constraints so that it captures the existing limitations on price and quantity.

Consider the following relationships.

$$\text{Let } A = \rho^v - p_{it}^v. \text{ We see that } A \geq 0.$$

$$\text{Let } B = \beta_t^v - q_{it}^v. \text{ Likewise, } B \geq 0.$$

$$\text{Thus their product } AB = -\beta_t^v p_{it}^v - \rho^v q_{it}^v + \beta_t^v \rho^v + p_{it}^v q_{it}^v \geq 0.$$

Replacing $p_{it}^v q_{it}^v$ by w_{it}^v gives us constraint (A17):

$$w_{it}^v \geq \beta_t^v p_{it}^v + \rho^v q_{it}^v - \beta_t^v \rho^v. \quad (\text{A20})$$

Now we derive constraint (A18).

Let $A = p_{it}^v - 0$. We see that $A \geq 0$.

Let $B = \beta_t^v - q_{it}^v$. Likewise, $B \geq 0$.

Thus their product $AB = (p_{it}^v - 0)(\beta_t^v - q_{it}^v) \geq 0$.

$$AB = \beta_t^v p_{it}^v - p_{it}^v q_{it}^v \geq 0.$$

Replacing $p_{it}^v q_{it}^v$ by w_{it}^v gives us the second constraint on w_{it}^v :

$$w_{it}^v \leq \beta_t^v p_{it}^v. \quad (\text{A21})$$

Lastly, we derive constraint (A19).

Let $A = \rho^v - p_{it}^v$. We see that $A \geq 0$.

Let $B = q_{it}^v - 0$. Likewise, $B \geq 0$.

Thus their product $AB = (\rho^v - p_{it}^v)(q_{it}^v - 0) \geq 0$.

$$AB = \rho^v q_{it}^v - p_{it}^v q_{it}^v \geq 0.$$

Replacing $p_{it}^v q_{it}^v$ by w_{it}^v gives us the third constraint on w_{it}^v :

$$w_{it}^v \leq \rho^v q_{it}^v. \quad (\text{A22})$$

Now we find the final constraint.

Let $A = p_{it}^v - 0$. We see that $A \geq 0$.

Let $B = q_{it}^v - 0$. Likewise, $B \geq 0$.

Thus their product $AB = p_{it}^v q_{it}^v \geq 0$.

Because our lower bounds are zero, this constraint on w_{it}^v by McCormick linearization is the non-negativity constraint, declared in the variable definition:

$$w_{it}^v \geq 0.$$

We acknowledge that McCormick relaxations are exact only when one variable is binary. In our formulation, although both variables are continuous, the relaxation provides valid convex envelopes. The solver ensures feasibility with respect to the relaxed constraints, and the obtained solution is subsequently verified against the original bilinear formulation to confirm feasibility.

Appendix B. Assumptions

- **Vaccine exclusion.** We exclude vaccines that have either ceased contracting or are missing historical data, even if they contain relevant antigens: (1) We exclude the DTaP-Hib-IPV vaccine as it was only funded in 2016 and has no projected demand from Gavi countries. (2) We exclude the DTwP-Hib vaccine as there is no historical demand from Gavi countries. (3) We exclude the DTwP-HepB vaccine as there is no projected demand from Gavi countries. (4) We exclude the monovalent Hib vaccine as it was contracted by only one manufacturer from 2016 to 2019 and is primarily manufactured for high income non-Gavi countries. However, because of its prior

significance we include it in historical demand calculations [21]. We assume that the remaining vaccine products considered by the model cover existing demand for these antigens.

- **Oral polio vaccine grouping.** The oral polio vaccine products contracted by Gavi include bOPV, mOPV1, mOPV2, nOPV2, and tOPV. This continues to evolve as traditional OPV forms, such as bOPV and tOPV, are decommissioned in favor of novel OPV forms, such as nOPV2. Due to the relative price uniformity, we make a simplifying assumption that all forms of oral polio vaccine may be considered as the same product [21] for the purposes of examining the role of IPV and Hexa in the market. In the model, we let the historical price of the OPV vaccine product be the average historical price of all oral polio vaccine product forms, and we let the demand for the OPV vaccine product be the sum of the demand for all oral polio vaccine product forms.
- **DTaP and DTwP antigen grouping.** Although the combination vaccines DTaP and DTwP contain three separate antigens (diphtheria, tetanus, and pertussis), these are traditionally offered to children in combination and not as separate vaccines. Therefore, for numerical simplicity, we treat it as a monovalent vaccine, as in [14,15]. Moreover, DTP-containing vaccines may contain acellular pertussis (DTaP) or whole-cell pertussis (DTwP). However, the majority of demand attributed to DTP-containing products comes from DTwP products [21]. Because these products are highly similar, we make a simplifying assumption that DTaP and DTwP need not be distinct and instead consider them both to satisfy DTP demand. We approach historical price and demand estimation in the same manner as for the OPV grouping.
- **Uniform offerings by vaccine type.** In some cases, manufacturers offer multiple versions of the same type of vaccine, e.g., 1-dose and 5-dose vials. We assume uniformity across vaccine types and generalize this assumption across manufacturers.
- **Production of new vaccine products.** We assume that manufacturers maintain their historical portfolio of vaccine production, with the exception of allowing manufacturers to invest in the capabilities to begin new production of Hexa.
- **Fixed distribution cost.** We attribute to each vaccine a fixed per-dose distribution cost, as used in [16], such that the cost of administering a single dose is the same across all types of vaccine. This captures the efficiency of multivalent vaccines as receiving a single dose of a multivalent vaccine incurs a lower distribution cost than receiving the necessary individual doses of monovalent vaccines to cover the same set of antigens. Although this assumption does not capture variations by country nor other factors influencing distribution cost, it is useful for studying the average cost per administration at the international level as relevant to Gavi.
- **Global market share.** We reference existing data for the pentavalent (DTaP-HepB-Hib) and IPV vaccine products to determine the global market share as together, they cover all antigens relevant to the model. We assume that the shares in this data represent the shares for the overall vaccine market (excluding other vaccines).

Appendix C. Parameter Estimation

Here, we describe the data used, as listed in Table A1 of the paper. Except where otherwise noted, all data are from the World Health Organization's *Market Information for Access to Vaccines (MI4a) Vaccine Purchase Database* [21] and UNICEF's *Vaccine Pricing Data* [22].

Appendix C.1. Sets

Parameters, variables, and constraints in our model are indexed over sets of antigens, vaccines, manufacturers, and years, which we define here.

Antigens and Vaccines: We limit our scope to pediatric vaccines protecting against diphtheria, tetanus, pertussis (these three in combination are often abbreviated DTaP or DTwP, depending on the vaccine form, and we abbreviate this as DTP), polio (offered as one of several oral polio vaccine forms, or OPV, or as inactive polio vaccine, or IPV), hepatitis B (HepB), and Haemophilus influenzae type B (Hib). Thus our set of antigens is given by

$$A = \{\text{DTP, HepB, Hib, Polio}\}.$$

The specific vaccine products considered form the set

$$V = \{\text{DTP, HepB, IPV, OPV, Penta, Hexa, DPT-IPV, DTP-HepB}\}.$$

Manufacturers: Twenty manufacturers are listed in the data as producing any of the above vaccines in the regions of interest.

Years: We use data and projections for the years 2024–2030, reflecting a 7-year tender.

Appendix C.2. Demand Curve Parameters

Demand curve parameters are estimated in Section 2.2.

Appendix C.3. McCormick Bound Parameters

Table A1. Estimated McCormick bound parameter values indexed by vaccine product. δ^v is the historical upper limit on demand, and ρ^v is the historical upper limit on price of vaccine product v .

Name	DTP	HepB	IPV	OPV	Penta	Hexa	DTP-IPV	DTP-HepB
δ^v (MIL)	279.1	291.0	1831.0	938.0	291.0	1831.0	1831.0	291.0
ρ^v (USD)	4.5	18.1	47.3	20.6	26.5	207	177	23

Historical upper limit on demand, δ^v . We took the maximum historical demand in any year for each antigen contained in v , as given in [21], and attributed the greatest antigen demand to δ^v . Values are given in Table A1.

Historical upper limit on price, ρ^v . We tabulated the maximum historical price for each vaccine product v using data from [21]. We scaled this parameter in our sensitivity analysis. Values are given in Table A1.

Upper quantity limit, β_t^v . We defined the upper limit on quantity to be the minimum of δ^v and the maximum of projected demand per antigen in year t for all antigens in vaccine product v [22], for the purpose of defining the McCormick linearization variable. Values are given in Table A2 for the cases of extrapolated polio demand and OPV phase-out demand.

Table A2. β_t^v : The McCormick linearization upper limit on quantity for vaccine v in year t first with extrapolated polio demand and then with phase-out (MIL).

Extrapolated Polio demand								
Year	DTP	HepB	IPV	OPV	Penta	Hexa	DTP-IPV	DTP-HepB
1	196.6	220.7	391.4	391.4	220.7	391.4	391.4	220.7
2	200.3	224.8	401.2	401.2	224.8	401.2	401.2	224.8
3	203.8	228.9	409.0	409.0	228.9	409.0	409.0	228.9
4	207.2	232.8	416.8	416.8	232.8	416.8	416.8	232.8
5	210.2	236.4	424.6	424.6	236.4	424.6	424.6	236.4
6	213.2	239.9	432.4	432.4	239.9	432.4	432.4	239.9
7	216.2	243.2	440.3	440.3	243.2	440.3	440.3	243.2

Table A2. Cont.

Year	Polio demand with phase-out							
	DTP	HepB	IPV	OPV	Penta	Hexa	DTP-IPV	DTP-HepB
1	196.6	220.7	391.4	391.4	220.7	391.4	391.4	220.7
2	200.3	224.8	401.2	401.2	224.8	401.2	401.2	224.8
3	203.8	228.9	408.0	408.0	228.9	408.0	408.0	228.9
4	207.2	232.8	117.9	117.9	232.8	117.9	117.9	232.8
5	210.2	236.4	120.2	120.2	236.4	120.2	120.2	236.4
6	213.2	239.9	122.4	122.4	239.9	122.4	122.4	239.9
7	216.2	243.2	124.6	124.6	243.2	124.6	124.6	243.2

Appendix C.4. Production Parameters

Rate of linear distribution cost, d . Distribution costs vary significantly among countries, and even within countries, depending on the cold chain needs for each vaccine product. We simplified this estimate as outlined in our assumptions and followed the existing modeling framework from [16], using WHO estimates from per-dose investment costs for the flu vaccine. We scaled down the distribution cost to 1 USD to not over-constrain the solution space.

Minimum manufacturer profit threshold, P_i . We used estimates of global vaccine market shares to determine the percentage of the market each manufacturer represents. We scaled the annual profit of 322 M USD for the Serum Institute of India according to each manufacturer's market share [30]. From Gavi market share data accessed via [23], we isolated IPV or Penta suppliers and cross reference WHO data to assign manufacturers to listed suppliers [21]. Given that the Serum Institute of India holds approximately 25.77% of the market share and has an estimated annual profit of \$322 M USD, we estimated the baseline profit (i.e., 100%) to be \$1.25B USD. We focused on Penta manufacturers because their market share distribution is better represented by our supplier data. Since there are limited manufacturer data available, we extrapolated the WHO data to the rest of the market, assigning the median value of the market shares, \$252 M USD, as the profit target for all other manufacturers. To reduce constraints on the model, we scaled this target profit by 50% in the baseline scenario. Values are given in Table A3.

Total production capacity, K . We estimated production capacity from [23] demand projections, where capacity is the sum of demand for all antigens in the first year of the tender. To prevent overconstraining the model, we ensured that any manufacturer could meet the demand of any antigen by scaling this estimate by 2 and using the same capacity value for all manufacturers. In this way, we estimated the production capacity to be 1998.5 million doses.

Production capacity for Hexa, Q . The predominant competitors of Hexa are DTP, HepB, IPV, OPV, and Penta products. We assumed that the proportion of historical demand allotted to the DTP-IPV and DTP-HepB was small enough in comparison to the other five competitors for us to exclude them. Because of this, we approximated the production capacity for Hexa to be 1/5 of the total demand in the first year of the tender, using [23] projections. We scaled this value by 2 to avoid imposing an artificial constraint. This gives a value of 799.4 million doses. We also assumed that the capacity for Hexa did not vary by manufacturer.

Table A3. Minimum profit threshold, P_i (MIL USD), and Hexa development cost c_i (MIL USD), by manufacturer.

Mfr	P_i	c_i	Vaccines Produced
1	252	100	IPV
2	252	100	OPV
3	252	100	OPV, Penta
4	252	100	IPV
5	252	100	OPV
6	330	100	DPT, HepB, Penta
7	252	100	OPV
8	252	100	OPV
9	252	100	OPV, Penta
10	252	100	DPT, HepB, Penta
11	252	100	DTP
12	116	100	HepB, Penta
13	229	100	Penta
14	252	100	OPV
15	252	100	HepB, OPV, Penta
16	252	50	IPV, Penta
17	252	0	IPV, OPV, Hexa, DTP-IPV
18	322	0	DTP, HepB, OPV, Penta, Hexa, DTP-HepB
19	252	50	HepB, IPV, OPV, Penta, DTP-HepB
20	252	100	HepB

Total one-time Hexa development cost, c_i . We estimated the new fixed cost for a manufacturer to enter the Hexa market based on a manufacturer's production portfolio. For manufacturers that already produce Hexa, the additional fixed cost for producing Hexa is 0. The simplest pathway to introducing a new hexavalent vaccine is assumed to be for manufacturers that already produce both Penta and IPV. For these manufacturers, the Hexa development cost is assumed to be \$50 M USD. For all other manufacturers, the Hexa development cost is assumed to be \$100 M USD. As this fixed cost must be recuperated by manufacturing revenues in constraint (A9) of the model, under- or overestimating this parameter affects the feasibility of a manufacturer entering the market. These values for each manufacturer are given in Table A3. (It is worth noting that these estimates have an appropriate order of magnitude for developing Hexa out of existing component vaccines. For reference, ref. [31] report the cost of developing the COVID-19 vaccine from nearly ground zero to be on the order of \$1B USD.)

Appendix C.5. Other Parameters

Objective function weights, μ_1, μ_2, μ_3 . The objective function balances three competing criteria: minimizing the total cost of vaccine procurement and distribution (weighted by μ_1), maximizing market diversity (weighted by μ_2), and minimizing price differences between products. The total cost of vaccine distribution is in units of million USD and has an order of magnitude of one thousand, so we chose $\mu_1 = 1$. Market diversity counts the total number of vaccine products produced across all manufacturers and years and is on the order of hundreds, so we chose $\mu_2 = 10$, allowing it to carry equal priority with the cost objective. The absolute price difference between pairs of vaccine products is in units of USD and is on the order of tens, so we chose $\mu_3 = 1$ so that it carried less weight than the previous two terms.

Intrinsic vaccine parameters. n^v is the number of antigens contained in vaccine v and is given in Table 2. We note that *DTP* is counted as a single antigen because there are no vaccine products in the dataset that cover strict subsets of these three. m^v is the number of

manufacturers which historically produce vaccine v , taken from [21] and given in Table 2. C_a^v is a binary matrix relating vaccines v to the antigens a which they contain. N scales the constant term in constraint (A6) of the model by 100 because prices are at most on the order of tens.

Policy parameters. To examine the impact of policies such as requiring Hexa production, or phasing out OPV usage, we defined parameters f^{hex} and f^{OPV} . f^{hex} is the minimum proportion of polio demand that must be met by Hexa. We used $f^{hex} = 0.05$ in the baseline scenario. f^{OPV} is the maximum proportion of demand that is allowed to be met by the oral polio vaccine. Because many countries require three total doses of polio vaccine, and there is a push to ensure at least one of the three doses is met by IPV rather than OPV, we let $f^{OPV} = 2/3$.

Finally, to avoid unreasonably small quantities and prices, we enforced that if a manufacturer produces v in year t , they must produce at least $\lambda = 1$ million doses with a price of at least $\phi = 0.01$ USD.

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