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Dual-chamber injection device for measles-rubella vaccine: The potential impact of introducing varying sizes of the devices in 3 countries

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ABSTRACT

Introduction: By pairing diluent with vaccines, dual-chamber vaccine injection devices simplify the process of reconstituting vaccines before administration and thus decrease associated open vial wastage and adverse events. However, since these devices are larger than current vaccine vials for lyophilized vaccines, manufacturers need guidance as to how the size of these devices may affect vaccine distribution and delivery.

Methods: Using HERMES-generated immunization supply chain models of Benin, Bihar (India), and Mozambique, we replace the routine 10-dose measles-rubella (MR) lyophilized vaccine with single-dose MR dual-chamber injection devices, ranging the volume-per-dose (5.2–26 cm^3) and price-per-dose ($0.70, $1.40).

Results: At a volume-per-dose of 5.2 cm^3, a dual-chamber injection device results in similar vaccine availability, decreased open vial wastage (OVW), and similar total cost per dose administered as compared to baseline in moderately constrained supply chains. Between volumes of 7.5 cm^3 and 26 cm^3, these devices lead to a reduction in vaccine availability between 1% and 14% due to increases in cold chain storage utilization between 1% and 7% and increases in average peak transport utilization between 2% and 44%. At the highest volume-per-dose, 26 cm^3, vaccine availability decreases between 9% and 14%. The total costs per dose administered varied between each scenario, as decreases in vaccine procurement costs were coupled with decreases in doses administered. However, introduction of a dual-chamber injection device only resulted in improved total cost per dose administered for Benin and Mozambique (at 5.2 cm^3 and $0.70-per-dose) when the total number of doses administered changed <1% from baseline.

Conclusion: In 3 different country supply chains, a single-dose MR dual-chamber injection device would need to be no larger than 5.2 cm^3 to not significantly impair the flow of other vaccines.

1. Introduction

By pairing diluent with vaccines, dual-chamber vaccine injection devices [1–3] simplify the process of reconstituting vaccines before administration and thus decrease associated open vial wastage [4–6] and adverse events [7–9]. However, since these devices are larger than current vaccine vials for lyophilized vaccines, manufacturers need guidance as to how the size of these devices may affect vaccine distribution and delivery. Many routine supply chains are constrained [10,11], and increasing the volume of vaccines in these systems can have multiple negative effects [12,13]. At larger sizes, dual-chamber devices may offset the benefits of reduced wastage and fewer adverse events by increasing cold storage utilization and limiting the availability of other vaccines. In addition, this decrease in available storage space could impede the potential for new vaccine introductions. The earlier vaccine manufacturers can identify the device size above which a

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supply chain becomes more constrained and incorporate this into their technology, the more time and resources can be saved in creating a successful product [14,15].

To identify the ideal size of dual-chamber injection devices for use in routine immunization programs, this study uses vaccine supply chain models of the Republic of Benin, Bihar (India), and the Republic of Mozambique, developed using the HERMES supply chain modeling software, to simulate the effects of replacing 10-dose lyophilized measles-rubella (MR) vaccines with single-dose dual-chamber injection devices of varying sizes and prices. The optimal volume-per-dose was identified as either improving or causing no change in vaccine availability, vaccine wastage, and supply chain costs compared to the existing program.

2. Methods

2.1. HERMES vaccine supply chain models: Benin, Bihar, Mozambique

Our team used three previously developed stochastic, discrete-event vaccine supply chain simulation models of Benin [16–18], Bihar [19] and Mozambique [20]. These models were developed using the Highly Extensible Resource for Modeling Supply Chains (HERMES) software and virtually represent all of the storage facilities, refrigerators and freezers, shipping routes, vehicles, personnel, and vaccines in each supply chain.

For all fixed parameters, including cold storage and transport storage capacity, travel times on each route, personnel at each facility, and associated unit costs for each of these, data was provided from country partners for each model. To better simulate the reality of each supply chain, certain parameters that are not static, like the number of vaccination sessions per day at a given clinic, are stochastically drawn from distributions (e.g. a Poisson distribution of the average number of vaccinations per session).

The Bihar model is based on data from 2013 to 2014 and consists of four levels, including one state store, seven division-level stores, 38 district stores, and 425 primary health centers (PHCs) [21]. The birth cohort population modeled is 2,997,442. The model for Benin is based on data from 2012 and consists of one national store, six departmental stores and one regional store, 80 commune stores, and 763 service delivery points [16–18]. The birth cohort population modeled is 371,022. The Mozambique model is based on data from 2014 and consists of one national store (which doubles as a provincial store), 10 strictly provincial stores, 104 district stores, 1428 health facilities and 254 mobile brigades. The birth cohort population modeled is 1,085,363 [20].

2.2. Comparing 10-dose MR vials to single-dose MR dual-chamber injection devices

In order to simulate the effects of replacing the current 10-dose MR vials with single-dose MR dual chamber injection devices, we included 10-dose MR vials in the standard EPI (Expanded Programme on Immunization) schedules of Benin, Bihar, and Mozambique, replacing the measles (M) vaccine. We maintained all other vaccines that were included in the routine immunization schedules in the years for which data was provided to create the models (see Section 2.1). Table 1 includes the EPI vaccines modeled in each supply chain. The 10-dose lyophilized MR presentation has a vaccine volume-per-dose of 2.1 cm^3 and a diluent volume-per-dose of 3.1 cm^3 for a total volume of 5.2 cm^3. Diluent provided with the MR vaccine can be stored at room temperature through the majority of the supply chain, being placed into refrigeration only prior to reconstitution at the service delivery level. By contrast, dual-chamber injection devices are designed to include both the vaccine and the diluent in the same unit, therefore requiring the diluent to be stored alongside the vaccine throughout the entire cold chain. We varied the volume-per-dose of the single-dose MR dual-chamber injection device from 5.2 cm^3, representing the current total volume of 10-dose lyophilized MR vaccine plus diluent, to 26 cm^3, which is the current total volume-per-dose of single-dose lyophilized MR and diluent.

Table 1
Vaccine characteristics.

Supply chain model	Vaccine	Doses per vial	Packed vol (cm^3)/dose of vaccine (*combined vaccine & diluent for MR DCID*)	Packed vol (cm^3)/dose of diluent	Price per vial
Benin	BCG	20	1.2	0.7	$ 2.16
	Measles-Rubella/MR DCID[a]	10/1	2.1/5.2–26	3.1/diluent incl. in vol-per-dose of vaccine	$ 6.30/$ 0.70, $1.40
	OPV	20	1	0	$ 2.40
	PCV13	1	12	0	$ 3.30
	Pentavalent	2	11	0	$ 3.88
	Tetanus Toxoid	10	3	0	$ 6.10
	Yellow Fever	10	2.5	6	$ 1.10
Bihar	BCG	20	1.2	0.7	$ 2.16
	DTP	10	3	0	$ 1.78
	Hepatitis B	10	3.8	0	$ 2.10
	Japanese Encephalitis	5	3	2.9	$ 2.10
	Measles-Rubella/MR DCID	10/1	2.1/5.2–26	3.1/diluent incl. in vol-per-dose of vaccine	$ 4.90/$ 0.70, $1.40
	OPV	20	1	0	$ 2.40
	Tetanus Toxoid	10	3	0	$ 6.10
Mozambique	BCG	20	1.2	0.7	$ 2.16
	IPV	1	14.3	0	$ 2.80
	Measles-Rubella/MR DCID	10/1	2.1/5.2–26	3.1/diluent incl. in vol-per-dose of vaccine	$ 6.30/$ 0.70, $1.40
	OPV	10	2	0	$ 1.25
	PCV10	2	4.8	0	$ 6.10
	Pentavalent	10	2.6	0	$ 6.90
	Rotavirus	1	17.1	0	$ 2.27
	Tetanus Toxoid	10	2.61	0	$ 1.29

[a] MR DCID: Measles-rubella dual-chamber injection device.