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The potential effects of introducing microneedle patch vaccines into routine vaccine supply chains

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Abstract

Background: Microneedle patch (MNP) technology is designed to simplify the process of vaccine administration; however, depending on its characteristics, MNP technology may provide additional benefits beyond the point-of-use, particularly for vaccine supply chains.

Methods: Using the HERMES modeling software, we examined replacing four routine vaccines – Measles-containing vaccine (MCV), Tetanus toxoid (TT), Rotavirus (Rota) and Pentavalent (Penta) – with MNP versions in the routine vaccine supply chains of Benin, Bihar (India), and Mozambique.

Results: Replacing MCV with an MNP (5 cm³-per-dose, 2-month thermostability, current single-dose price-per-dose) improved MCV availability by 13%, 1% and 6% in Benin, Bihar and Mozambique, respectively, and total vaccine availability by 1% in Benin and Mozambique, while increasing the total cost per dose administered by \$0.07 in Benin, \$0.56 in Bihar and \$0.11 in Mozambique. Replacing TT with an MNP improved TT and total vaccine availability (3% and <1%) in Mozambique only, when the patch was 5 cm³ and 2-months thermostable but increased total cost per dose administered by \$0.14. Replacing Rota with an MNP (at 5–15 cm³-per-dose, 1–2 month thermostable) improved Rota and total vaccine availability, but only improved Rota vaccine availability in Bihar (at 5 cm³, 1–2 months thermostable), while decreasing total vaccine availability by 1%. Finally, replacing Penta with an MNP (at 5 cm³, 2-months thermostable) improved Penta vaccine availability by 1–8% and total availability by <1–9%.

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Declaration of interests

The authors declared that there is no conflict of interest.

Conclusions: An MNP for MCV, TT, Rota, or Penta would need to have a smaller or equal volume-per-dose than existing vaccine formulations and be able to be stored outside the cold chain for a continuous period of at least two months to provide additional benefits to all three supply chains under modeled conditions.

Keywords

Delivery; Logistics; Microneedle patch; Supply chain

1. Introduction

Microneedle patch (MNP) technology – a patch containing an array of microneedles applied directly to the skin – is currently under development [1-3] to simplify the process of vaccine administration for healthcare workers and mitigate barriers to vaccine uptake, e.g. fear of needles [4] and lack of trained personnel in low- and middle-income countries [5]. In addition to these benefits, the physical and biological properties of MNP technology (e.g. volume-per-dose and thermostability) could offer logistical advantages for vaccine transport and storage throughout the supply chain. The design elements of such new technology could have multiple direct and indirect effects on vaccine supply chains, which are often constrained by cold storage and transport space as well as both human and financial resources [6,7]. By identifying a set of microneedle patch characteristics that could help alleviate constrained vaccine supply chains, researchers and manufacturers developing microneedle patch technology would be better equipped to provide the most value for the end user.

Previous simulation modeling studies using the Highly Extensible Resource for Modeling Supply Chains (HERMES) software have tested the impact of new technologies on vaccine supply chains [8-10]. Using HERMES, our team developed models of country-level routine immunization supply chains of Benin, and Mozambique as well as a state-level model of Bihar, India. We used these models to simulate replacing four routine vaccines in their current formulation – measles (MCV), tetanus toxoid (TT), rotavirus (Rota), and pentavalent (Penta) – with hypothetical microneedle patch versions of each. For each microneedle patch, we ranged the volume-per-dose, temperature stability, and price point to identify the characteristics that will provide the most benefit to each immunization supply chain.

2. Methods

2.1. HERMES model: Benin, Bihar (India), Mozambique

Our team used HERMES simulation models of the routine immunization supply chains of Benin, Bihar (India), and Mozambique. Each supply chain model is a virtual representation of all storage facilities (including refrigerators and freezers), transport routes (including shipping policies, vehicles, drivers, and per diems), personnel, vaccines, administration points (including vial opening policies and population demand), and associated costs for each component.

The HERMES model of the routine vaccine supply chain for the Republic of Benin [11-13] was developed using cold chain and population data from 2012 and is comprised of four levels: 1 national store, 7 department stores, 80 communes, and 763 health posts serving a birth cohort population of 371,022. The vaccine supply chain model for the state of Bihar, India [9] was developed using cold chain and population data from 2013 to 14 and is also comprised of four levels: 1 state store, 7 division stores, 13 of 38 district stores, and 161 of 533 primary health centers serving a birth cohort population of 2,997,442. The vaccine supply chain model for Mozambique was developed using cold chain and population data from 2014. The structure of Mozambique's vaccine supply chain reflects the 2014 redesign [14] and involves delivery from 4 provincial stores directly to health facilities via distribution loops. The remaining 7 provincial stores follow the traditional multi-tiered delivery system. Taken together, this supply chain serves a birth cohort population of 1,085,363 newborns.

2.2. Simulated microneedle patch vaccines

Based on published research and expert consultation, we selected four vaccines from the national routine immunization schedules of Benin, Bihar, and Mozambique for replacement with microneedle patch versions. Microneedle patch testing conducted for the measles vaccine found that the immune response in both rats and non-human primates equaled the conventional subcutaneous injection method [3,15]. A tetanus toxoid MNP produced an effective immune system response in mice [16], while a study of an inactivated rotavirus (IRV) MNP demonstrated an improved immune response compared to using the intramuscular injection [17]. The pentavalent vaccine has not yet been studied as a microneedle patch formulation, but is prioritized as a potential microneedle patch [18]. Table 1 provides the current characteristics of each routine EPI vaccine corresponding to each modeled supply chain and the value ranges for the modeled MNP vaccine characteristics.

2.3. Microneedle patch thermostability and the controlled-temperature chain (CTC)

A potential biological advantage of microneedle patch vaccines is thermostability, i.e. the ability for a vaccine to maintain its efficacy for a certain period of time at ambient temperatures up to 40 °C. As per WHO guidelines, a vaccine with a certain length of thermostability (e.g. 3 days) must be able to be stored at ambient temperatures for that period of time up to the end of its shelf-life. In HERMES, we ranged the thermostability of a vaccine from 3 days to 1 month and 2 months, which fall within the current estimates of how long a thermostable microneedle patch could remain thermostable under ambient temperatures [19].

In each simulation experiment, microneedle patch vaccines were able to be removed from cold storage only at the final storage location where the vaccine would be used (i.e. primary health centers in Bihar, health posts in Benin, and health facilities in Mozambique), and only if the cold storage capacity at a given location was full. Given the range of thermostable lengths and the average time it takes vaccines to move through the supply chain, we did not attempt to simulate the removal of microneedle patch vaccines from locations higher up the supply chain. Once a microneedle patch vaccine was removed from the cold chain, it remained out of cold storage until it was either used or expired.

2.4. Microneedle patch volume-per-dose

Cold chain volume-per-dose is another important characteristic of vaccines that will influence how the presentation affects the vaccine supply chain system. We varied the model input for cold chain volume-per-dose of each microneedle patch vaccine from 5 cm³ to 15 cm³. The World Health Organization's Immunization Practices Advisory Committee (IPAC) working group on delivery technologies identified a maximum size of 26 cm³ and an optimal size of <3 cm³ for its measles-rubella (MR) MNP target product profile [20], though these sizes apply to existing volume-per-dose of MR vaccines rather than likely characteristics of MNP vaccines. As no commercially available microneedle patch vaccine formulations are available, we again based our estimates on expert opinion.

2.5. Microneedle patch price-per-dose

A third variable of microneedle patch technology that can affect the vaccine supply chain is the price-per-dose. We varied the price-per-MNP vaccine to capture a range of potential commercial price points. First, for MR, Rota, and Penta, we identified the price-per-dose of the single-dose presentations and considered this to be the lower bound estimate for their MNP prices. Then, for each of these we added \$1 USD to the price to reflect any potential increases in costs associated with production, packaging, etc. This was considered as the upper bound estimate for MNP prices. For Rota MNP, which will use a different antigen for parenteral administration, no data is available on the potential price of these vaccines, though the price is expected to be lower than the current oral Rota vaccine [21]. For TT, which does not come in a single-dose presentation, we used the current price-per-dose plus \$1 USD as the lower bound, and the current price-per-dose plus \$2 USD as the upper bound. Current literature estimates that the various costs of MNP manufacturing and procurement will be competitive with current vaccine values [22-25]. However, as this technology is not currently manufactured, our price points are meant to capture a wide range of potential prices.

2.6. Experiments

The baseline model simulated the supply chains of Benin, Bihar, and Mozambique, respectively, with all 2018 routine EPI vaccines prior to any MNP introduction (Table 1). Each experimental scenario simulated the effects of replacing one routine vaccine with a microneedle patch formulation (e.g. MCV with MCV_MNP) at one of three volumes (5 cm³, 10 cm³, and 15 cm³) and one of four thermostable profiles (remain in cold chain, thermostable for 3 days, 1 month, or 2 months). Each experiment consisted of running the supply chain simulation for the course of one year. As the simulation proceeded, logistics costs accrued for labor, storage, transport, and buildings.

3. Results

Baseline results are provided in Table 2 and results for each experimental scenario are provided in Table 3. Results for each scenario were averaged over 23 runs to calculate an average result that is statistically close to the actual value; the results have a standard deviation of <1%.

3.1. Current system with existing vaccine formulations

Total vaccine availability (i.e. successful immunizations administered to patients as % of all immunizations needed) in the baseline scenarios was 80% for Benin (4,733,087 doses administered), 60% for Bihar (14,068,342 doses administered) and 66% for Mozambique (14,012,268 doses administered) and total open vial wastage (OVW) (i.e. unused doses discarded after opening a new vial as a % of total doses) was 13%, 20%, and 23%, respectively. The lyophilized vaccines (MCV, BCG, YF, and JE) accounted for a significant portion of open vial wastage across the three supply chains, while rotavirus vaccine also showed high OVW in Bihar.

Peak average storage capacity utilization (i.e. the maximum percentage of available storage capacity occupied by products at any time, averaged across all storage devices at a given level of a supply chain) was 99% at the top level of each supply chain, and 9%, 18% and 27% at the lowest level of Benin, Bihar, and Mozambique's supply chain, respectively. As such, bottlenecks were more likely to occur at the top level of each supply chain, where storage capacity utilization was high, compared to the lower levels, where locations had more cold chain space available.

Total logistics costs and total vaccine procurement costs were \$1,183,284 and \$6,166,689 in Benin, \$715,859 and \$12,372,454 in Bihar, and \$4,692,485 and \$25,843,340 in Mozambique. This resulted in a logistics cost per dose administered and total cost per dose administered of \$0.25 and \$1.55 in Benin, \$0.05 and \$01.30 in Bihar, and \$0.33 and \$2.18 in Mozambique.

3.2. Effects of replacing the routine measles-containing vaccine with a microneedle patch measles-containing vaccine

Replacing the routine measles-containing vaccine (MCV) with a microneedle patch version positively affected the modeled supply chains, but only at a volume-per-dose of 5 cm³ while remaining in the cold chain or if the thermostability of the vaccine was long enough such that the vaccines did not expire once removed from the cold chain. Additionally, the benefits of using the MNP vaccine did not result in an overall positive increase in vaccine availability in Bihar, where top-level storage constraints and transport constraints were exacerbated by the larger volume of the MNP.

In their current state, the modeled supply chains have an MCV OVW between 47% and 49%, meaning that nearly half of the doses that were opened were discarded. Replacing the routine 10-dose MCV with a single-dose MNP demonstrated a universal benefit by reducing MCV OVW to zero. Since the measles vaccine was no longer wasted when switching to a single-dose MNP, nearly half as many doses of the measles vaccine needed to be procured. However, the reduction in OVW did not necessarily translate into an increase in either measles vaccine or total vaccine availability.

Each modeled supply chain had high existing cold storage constraints at the top level. As the volume-per-dose of the MNPs were 5 cm³ or greater, an increase of at least 2.9 cm³-per-dose compared to the routine 10-dose MCV, the total volume of measles vaccine procured increased in each MNP scenario, compared to baseline. In Bihar, cold storage and transport

storage were most constrained; therefore, a MNP between 5 cm³ and 15 cm³ always resulted in a decrease in the flow of other vaccines, regardless of how long the vaccine could be stored outside of the cold chain. In Benin and Mozambique, however, the cold chain availability was sufficient when using an MNP of 5 cm³ reducing all MCV OVW and resulting in an increase in both measles and total vaccine availability, even with the MNP remaining in cold storage.

In addition to reducing all OVW, using MNPs with a thermostability of at least 2 months in Benin and Mozambique helped to alleviate cold storage constraints compared to storing the MNPs in the cold chain. The effects of removing MNPs from the cold chain, which only occurs at fully utilized facilities in the last level of the supply chain, were more pronounced in Mozambique, where average storage capacity utilization was 27% at the lowest level, compared to 9% in Benin. Because most locations replenish vaccines monthly and vaccinate in regular intervals between each shipment, an MNP with only 3 days of thermostability will have little time to be used before expiration. In Bihar, vaccines were used quickly enough so that 1-month thermostability was sufficient for preventing vaccine expiration, but in Benin and Mozambique, a vaccine needed to have be thermostable for at least 2 months to prevent any vaccines from expiring once removed from the cold chain.

At 5 cm³ and 2 months thermostability, removing the measles MNP from the cold chain improved Benin's measles and total vaccine availability by <1% compared to keeping the MNPs in cold storage, but in Mozambique, where storage capacity utilization was higher at the lower levels, measles vaccine availability improved by 3% while total vaccine availability improved by 1%.

However, while vaccine availability improved, switching to a single-dose price for MCV resulted in an increase in vaccine procurement costs and an increase in the total cost per dose administered in Benin, Bihar, and Mozambique (Table 3).

3.3. Effects of replacing the routine tetanus toxoid vaccine with a microneedle patch tetanus toxoid vaccine

Replacing the routine tetanus toxoid vaccine (3.1 cm³ volume-per-dose) with an MNP generally had negative effects on both TT and total vaccine availability and costs. Only in Mozambique, where low level storage constraints were the highest, did an MNP of 5 cm³-per-dose and 2-months thermostability lead to an improvement in both TT and total vaccine availability.

Unlike the lyophilized measles vaccine, which must be discarded on the same day it is opened, the tetanus toxoid vaccine can be stored in refrigeration for up to 28 days after being opened. Without any open vial wastage, switching from a multi-dose vial with a smaller volume-per-dose to a larger single-dose MNP only increased the volume of vaccines flowing into the system. In turn, the primary logistical benefit of replacing the routine TT vaccine with an MNP version is to take advantage of storing the vaccine outside the cold chain.

In Benin, where cold storage utilization at the lowest level is 9%, even a TT MNP stabilized for 2 months did not free up enough space to improve TT or total vaccine availability

compared to baseline. In Bihar, where cold storage utilization is 18%, a TT MNP with thermostability of 1 month or 2 months improved TT and total vaccine availability compared to storing the microneedle patch in the cold chain; however, thermostability did not improve vaccine availability compared to baseline, as the constraints on the system from the larger MNP vaccine were too great. In Mozambique, however, where constraints at the lowest level were highest (27%) at baseline, using a 5 cm³ TT MNP with a thermostability of 2 months resulted in a slight increase in both TT vaccine availability (+4%) and total vaccine availability (<1%) compared to baseline.

However, the increase in doses administered in Mozambique did not improve the total cost per dose administered at either of the price points. The total cost per dose administered increased by \$0.16 at the modeled price-per-dose of \$1.10 for a single-dose TT MNP vaccine.

3.4. Effects of replacing the routine rotavirus vaccine with a microneedle patch rotavirus vaccine

Replacing the routine rotavirus vaccine with a rotavirus MNP vaccine had positive effects on both Benin and Mozambique's supply chain (where single-dose rotavirus vaccines are used) and mixed effects on Bihar's supply chain (where multi-dose rotavirus vaccines are used).

In Benin and Mozambique, switching from the routine rotavirus vaccine at 17.1 cm³-per-dose to a rotavirus MNP of 5–15 cm³-per-dose had net benefits for both rotavirus and total vaccine availability when the vaccines either (1) remained in the cold chain or (2) had a thermostability of 2 months. In Benin, rotavirus and total vaccine availability also improved when the vaccine had a thermostability of 1 month, though this did not occur in Mozambique, as too many vaccines expired before being used. Similarly, at a thermostability of 3 days, too many vaccines expired before being used, resulting in a sharp decrease in the availability of rotavirus vaccine.

In Bihar, however, the benefits of switching to a rotavirus MNP vaccine were mixed. As a multi-dose vial, the rotavirus vaccine used in India had an OVW at baseline of approximately 35%, but the initial volume-per-dose of the rotavirus vaccine was 3.2 cm³. As such, while using a single-dose MNP reduced OVW to zero, it also increased the volume-per-dose of vaccine by at least 1.8 cm³. In Bihar, this resulted in a 2% improvement in rotavirus vaccine availability when the MNP remained in the cold chain and a 3% improvement when the MNP had a thermostability of 1 or 2 months. However, with increased constraints on the system, the flow of other vaccines decreased slightly, leading to a decrease in total vaccine availability in all scenarios.

In addition to improving rotavirus and total vaccine availability in Benin, using a rotavirus MNP resulted in an improved total cost-per-dose administered at the current single-dose price point for Rota vaccine compared to baseline when the vaccine remained in the cold chain or was thermostable for 1–2 months. In Bihar, however, where a multidose vial of Rota was being used, switching to a single-dose vial and price point sharply increases vaccine procurement costs, while in Mozambique, the improvement in vaccine availability resulted in the same total cost per dose administered (\$2.18) as the current system.

3.5. Effects of replacing the routine pentavalent vaccine with a microneedle patch pentavalent vaccine

Replacing the routine pentavalent vaccine with a pentavalent MNP vaccine had positive effects on all modeled supply chain systems. Although the volume-per-dose of the pentavalent vaccines differed between each supply chain (11 cm³ in Benin, 5.3 cm³ in Bihar, and 2.6 cm³ in Mozambique), switching to a single-dose microneedle patch version of size 5 cm³ and a thermostability of 2 months resulted in an improvement in pentavalent vaccine availability (9%, 1%, and 4%, respectively) and total vaccine availability (9%, 1%, and <1%, respectively) compared to baseline.

The largest benefits occurred in Benin, where switching to a microneedle patch size of 5 or 10 cm³ reduced pentavalent OVW from 3% to 0% and improved pentavalent and total vaccine availability between 0% and 9%, so long as the vaccine remained in cold storage or had a thermostability of 1–2 months. In Bihar, the pentavalent vaccine was the only MNP to result in an improvement in both the pentavalent and total vaccine availability. At 5 cm³, the pentavalent MNP maintained the same vaccine availability when remaining in the cold chain and improved both pentavalent and total vaccine availability by 1% when stored outside of the cold chain for 1–2 months. In Mozambique, despite an increased volume-per-dose, a pentavalent MNP at 5 cm³-per-dose and 4 months thermostability increased pentavalent vaccine availability by 4% and total vaccine availability by <1%.

Additionally, at the current price-per-dose of a single-dose Penta vaccine, switching to a 5 cm³, 2-month thermostable vaccine led to a decrease in the total cost-per-dose administered in Benin, though not in Bihar or Mozambique, where vaccine procurement costs increased.

4. Discussion

Replacing routine needle-and-syringe vaccines with microneedle patches can provide benefits to constrained vaccine supply chains that include reducing open vial wastage and relieving storage constraints by allowing vaccines to be stored outside of the cold chain. The extent of these benefits will vary, however, depending on the characteristics of the microneedle patch and the vaccine being replaced, the location of constraints within a supply chain, and the length of MNP thermostability.

Replacing the 10-dose lyophilized measles-containing vaccine (or any lyophilized multidose vaccine with a 6-h open vial expiratory period) with a single-dose MNP will reduce open vial wastage. As the MCV results indicate, however, reducing open vial wastage will not always provide a significant benefit to the supply chain system, particularly when there is an increase in the volume-per-dose between the standard and MNP formulation of a vaccine that offsets the decrease in open vial wastage. In Benin, Bihar, and Mozambique, the top levels of the supply chain were highly constrained; therefore, increasing the total volume of vaccine flowing into the supply chain led to a reduction in storage capacity for other vaccines. Conversely, if an MNP has a smaller volume-per-dose than the routine vaccine it is replacing (e.g. rotavirus microneedle patch in Benin and Mozambique), the effects on the supply chain will be positive.

Improving a vaccine's thermostability is a second benefit of MNPs, but only if the time interval for thermostability is long enough to allow the MNP to be used before expiring. In Bihar, vaccines with 1 month of thermostability were used before expiry, while in Benin and Mozambique, the vaccines needed a longer time interval (2 months) to be used before expiring. At 3 days of thermostability, most of the vaccines that were removed from the cold chain expired before they could be used. Across each modeled supply chain, an MNP would need to have approximately 2 months of thermostability remaining once removed from refrigeration to be used before expiring.

In addition to how long an MNP can remain outside the cold chain, the supply chain level at which microneedle patches are removed can affect the extent of the benefit. Since this study modeled thermostability at time intervals of 3 days to 2 months, the MNPs could only be removed at the lowest level of each supply chain. If removed higher up the supply chain, the vaccines would mostly expire before being used. However, in each of the supply chains, the primary storage constraints existed at higher levels, while the lower levels were relatively unconstrained. In Benin, where average storage capacity utilization was 9% at the lowest level of the supply chain, removing MNPs from constrained cold storage locations had little effect on the availability of other vaccines. In Mozambique, however, where health facility storage capacity utilization was highest among the three supply chains (27%), being able to remove microneedle patches from the cold chain created space for other vaccines and led to an improvement in the total vaccine availability.

Microneedle patch design can have both positive and negative effects on vaccine supply chains. Although a single-dose microneedle patch will reduce open vial wastage, an increase in volume-per-dose may exacerbate existing constraints, offsetting the benefits of reduced OVW. Further, a microneedle patch that is thermostable for a short time interval may result in high numbers of vaccine expiration, as vaccines may not be used quickly enough in routine settings. Therefore, developing a single-dose microneedle patch that maintains or reduces the current volume-per-dose of routine vaccines, and can maintain room temperature storage for a period of at least 2 months, will provide benefits to routine supply chains and immunization programs in addition to the expected benefits for vaccine administration.

5. Limitations

All factors that may affect the impact of MNP vaccines on a supply chain cannot be represented by a model alone. For example, the cold chain data modeled for this study reflects previous years and may not capture the latest supply chain capacity. Further, these models do not capture all aspects of the vaccine supply chain that may affect vaccine availability, such as potential stockouts due to vehicle breakdown and refrigerator outages, or poor quantification of vaccine demand. Our experiments assumed that microneedle patch vaccines would have the same vaccine efficacy and require the same level of training and experience as conventional formulations. Since MNPs have not yet come to market for vaccine delivery, no definitive commercial costing data exist. Potential product price points were estimated based on information from the production process which has been shown to be comparable to conventional vaccine formulation costs if scaled [1].

As MNPs remain in development for potential use in vaccine delivery [1,2], the physical characteristics of MNPs were generalized to three categories of volume based on expert opinion. Our model examined the introduction of just one MNP vaccine into the supply chain independent of any other changes. The benefits of replacing multiple or all EPI vaccines with MNP versions was not examined in this study but may lead to greater improvements in vaccine availability, cost reduction and vaccine wastage. Additionally, this study only examined vaccine delivery through routine immunization. Other methods such as outreach sessions and mobile vaccination campaigns were not examined.

6. Conclusion

A microneedle patch vaccine for any of four routine vaccines (MCV, TT, Rota, Penta) would need to have a smaller or equal volume-per-dose than its routine vaccine counterpart and be able to be stored outside the cold chain for a continuous period of at least two months to provide additional benefits to all three modeled vaccine supply chains. MNP versions of MCV and TT could provide benefits to certain systems at a larger volume-per-dose (5 cm³) by reducing open vial wastage (in the case of MCV) or alleviating existing cold storage constraints (in the case of TT in Mozambique), while MNP versions of Rota would benefit certain systems simply by reducing the volume-per-dose from 17.1 cm³. However, these benefits are not consistent across each supply chain – due to varying cold storage capacity and constraints and the average vaccine time-through-system – or vaccine – due to varying volumes-per-dose and rates of open vial wastage.

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Table 1

Vaccine characteristics.

Supply chain model	Vaccine	Doses per person	Doses per vial	Cold chain volume-per-dose (cm ³)	Price-per-dose (2018 \$)
Benin	BCG	1	20	1.2	\$ 0.11
	IPV	1	10	2.46	\$ 0.88
	Measles-Rubella	1	10	2.1	\$ 0.63
	OPV	4	20	1	\$ 0.13
	PCV13	3	1	12	\$ 3.30
	Pentavalent	3	2	11	\$ 1.94
	Rotavirus	1	1	17.1	\$ 2.21
	Tetanus Toxoid	2	10	3	\$ 0.11
	Yellow Fever	1	10	2.5	\$ 0.11
	BCG	1	10	1.2	\$ 0.21
Bihar	Hepatitis B	1	10	3.8	\$ 0.18
	Japanese Encephalitis	2	5	3	\$ 0.41
	Measles	2	10	2.1	\$ 0.31
	OPV	5	20	1	\$ 0.13
	Pentavalent	3	10	5.3	\$ 0.69
	Tetanus Toxoid	4	10	3	\$ 0.11
	Rotavirus	3	10	3.2	\$ 0.92
	BCG	1	20	1.2	\$ 0.11
	IPV	1	1	14.3	\$ 2.80
	Measles-Rubella	2	10	2.1	\$ 0.63
Mozambique	OPV	4	10	2	\$ 0.18
	PCV10	3	2	4.8	\$ 3.05
	Pentavalent	3	10	2.6	\$ 0.69
	Rotavirus	2	1	17.1	\$ 2.19
	Tetanus Toxoid	2	10	2.61	\$ 0.11
	Measles-containing vaccine (MCV) microneedle patch	Same number of doses as antigen in routine immunization program	1	5, 10, 15	\$2.25 (\$3.25)
	Tetanus toxoid (TT) microneedle patch				\$1.10 (\$2.20)
	Rotavirus (Rota) microneedle patch				\$2.21 (\$3.21)
	Pentavalent (Penta) microneedle patch				\$1.10 (\$2.20)
All Models					

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* Price-per-dose for MNP vaccines includes the single-dose price-per-dose and \$1 USD additional (in parentheses), for TT, which there is no single-dose price-per-dose, the price is \$1 and \$2 plus the current 10-dose price-per-dose.

Table 2

Baseline results for Benin, Bihar, and Mozambique’s routine vaccine supply chains.

Supply chain model	Vaccine availability				Total open vial wastage	Total cost per dose administered (in 2018 \$)
	M	TT	Rota	Penta		
Benin	70%	82%	83%	81%	80%	\$1.55
Bihar	56%	58%	54%	58%	60%	\$1.30
Mozambique	64%	65%	67%	65%	66%	\$2.18

Table 3

Summary of microneedle patch results by supply chain, volume, thermostability, and price.

MNP	Supply chain	Volume-per-dose	Antigen Vaccine Availability (Total Vaccine Availability)				Total cost per dose administered in 2018 \$ (Results in parentheses based on higher price-per-MNP)			
			CC		3 days TS		1 month TS		2 months TS	
			CC	3 days TS	1 month TS	2 months TS	CC	3 days TS	1 month TS	2 months TS
M	Benin	5 cm3	0.83 (0.81)*	0.17 (0.77)	0.79 (0.80)*	0.83 (0.81)**	1.62 (1.68)	1.71 (1.78)	1.63 (1.69)	1.62 (1.68)
		10 cm3	0.81* (0.79)	0.17 (0.75)	0.78* (0.78)	0.81* (0.79)	1.63 (1.68)	1.72 (1.78)	1.63 (1.69)	1.63 (1.68)
	Bihar	15 cm3	0.81* (0.78)	0.17 (0.74)	0.77* (0.78)	0.81* (0.78)	1.65 (1.71)	1.74 (1.81)	1.66 (1.72)	1.65 (1.71)
		5 cm3	0.56 (0.58)	0.27 (0.56)	0.57* (0.58)	0.57* (0.58)	1.86 (2.17)	1.95 (2.27)	1.86 (2.16)	1.86 (2.16)
		10 cm3	0.52 (0.55)	0.25 (0.53)	0.53 (0.55)	0.53 (0.55)	1.84 (2.13)	1.89 (2.2)	1.82 (2.12)	1.85 (2.14)
TT	Mozambique	15 cm3	0.47 (0.51)	0.24 (0.50)	0.49 (0.51)	0.49 (0.51)	1.85 (2.15)	1.89 (2.2)	1.83 (2.13)	1.83 (2.13)
		5 cm3	0.67 (0.66)*	0.26 (0.62)	0.62 (0.66)	0.70 (0.67)**	2.31 (2.43)	2.49 (2.64)	2.33 (2.46)	2.29 (2.42)
		10 cm3	0.65* (0.64)	0.24 (0.60)	0.61 (0.64)	0.68* (0.65)	2.29 (2.42)	2.48 (2.63)	2.31 (2.44)	2.28 (2.4)
	Benin	15 cm3	0.63 (0.62)	0.23 (0.59)	0.60 (0.63)	0.67* (0.63)	2.3 (2.42)	2.47 (2.61)	2.3 (2.42)	2.26 (2.39)
		5 cm3	0.80 (0.79)	0.16 (0.72)	0.77 (0.79)	0.80 (0.79)	1.67 (1.8)	1.85 (1.99)	1.68 (1.81)	1.68 (1.8)
Rota	Bihar	10 cm3	0.79 (0.78)	0.18 (0.71)	0.77 (0.78)	0.79 (0.78)	1.7 (1.82)	1.87 (2.02)	1.7 (1.83)	1.7 (1.82)
		15 cm3	0.78 (0.77)	0.19 (0.71)	0.76 (0.77)	0.78 (0.77)	1.68 (1.8)	1.84 (1.98)	1.68 (1.81)	1.68 (1.8)
		5 cm3	0.51 (0.55)	0.26 (0.51)	0.53 (0.55)	0.53 (0.55)	1.95 (2.62)	2.11 (2.84)	1.93 (2.6)	1.93 (2.6)
	Mozambique	10 cm3	0.47 (0.51)	0.24 (0.48)	0.48 (0.52)	0.48 (0.52)	1.85 (2.48)	1.98 (2.67)	1.83 (2.46)	1.83 (2.46)
		15 cm3	0.43 (0.47)	0.22 (0.43)	0.44 (0.48)	0.44 (0.48)	1.81 (2.42)	1.94 (2.6)	1.98 (2.66)	1.78 (2.39)
Bihar	Benin	5 cm3	0.65 (0.65)	0.29 (0.61)	0.60 (0.64)	0.69 (0.66)**	2.34 (2.52)	2.55 (2.76)	2.36 (2.55)	2.32 (2.5)
		10 cm3	0.63 (0.62)	0.24 (0.59)	0.60 (0.63)	0.67* (0.64)	2.33 (2.5)	2.55 (2.75)	2.34 (2.52)	2.3 (2.47)
		15 cm3	0.60 (0.60)	0.21 (0.57)	0.58 (0.61)	0.65 (0.62)	2.33 (2.5)	2.34 (2.52)	2.32 (2.5)	2.29 (2.47)
	Mozambique	5 cm3	0.89 (0.86)*	0.17 (0.82)	0.85 (0.86)*	0.89 (0.86)**	1.53* (1.68)	1.66 (1.83)	1.54* (1.69)	1.53* (1.68)
		10 cm3	0.86 (0.84)*	0.17 (0.79)	0.83 (0.83)*	0.86 (0.84)*	1.55 (1.7)	1.65 (1.82)	1.56 (1.71)	1.55 (1.7)
Bihar	Benin	15 cm3	0.84 (0.81)*	0.17 (0.77)	0.81 (0.81)*	0.84 (0.81)*	1.55 (1.7)	1.65 (1.82)	1.56 (1.71)	1.55 (1.7)
		5 cm3	0.56* (0.59)	0.27 (0.55)	0.57* (0.59)	0.57* (0.59)	1.79 (2.77)	1.92 (2.98)	1.79 (2.76)	1.78 (2.76)
		10 cm3	0.49 (0.53)	0.25 (0.51)	0.51 (0.54)	0.51 (0.54)	1.77 (2.74)	1.87 (2.88)	1.76 (2.71)	1.76 (2.71)
	Mozambique	15 cm3	0.46 (0.51)	0.24 (0.48)	0.47 (0.51)	0.48 (0.51)	1.73 (2.67)	1.82 (2.81)	1.71 (2.64)	1.72 (2.65)

MNP	Supply chain	Volume-per-dose	Antigen Vaccine Availability (Total Vaccine Availability)				Total cost per dose administered in 2018 \$ (Results in parentheses based on higher price-per-MNP)			
			3 days TS		1 month TS		3 days TS		1 month TS	
			CC	TS	CC	TS	CC	TS	CC	TS
Mozambique		5 cm3	0.72 (0.71) *	0.23 (0.66)	0.63 (0.71)	0.74 (0.72) **	2.18 (2.45)	2.4 (2.71)	2.22 (2.5)	2.18 (2.45)
		10 cm3	0.70 (0.69) *	0.25 (0.65)	0.62 (0.69)	0.72 (0.70) *	2.18 (2.44)	2.37 (2.67)	2.2 (2.48)	2.16 * (2.43)
		15 cm3	0.68 (0.67) *	0.25 (0.63)	0.62 (0.68)	0.71 (0.69) *	2.19 (2.45)	2.36 (2.66)	2.19 (2.45)	2.15 * (2.42)
Penta	Benin	5 cm3	0.89 (0.89) *	0.17 (0.76)	0.86 (0.88) *	0.89 (0.89) **	1.37 * (1.58)	1.63 (1.9)	1.38 * (1.6)	1.37 * (1.58)
		10 cm3	0.83 (0.82) *	0.17 (0.70)	0.80 (0.81)	0.83 (0.82) *	1.38 * (1.59)	1.64 (1.9)	1.4 * (1.61)	1.38 * (1.59)
		15 cm3	0.78 (0.78)	0.18 (0.67)	0.76 (0.77)	0.78 (0.78)	1.42 * (1.63)	1.67 (1.93)	1.43 * (1.64)	1.42 * (1.63)
Bihar		5 cm3	0.58 (0.60) *	0.29 (0.56)	0.59 (0.61) *	0.59 (0.61) **	1.47 (1.96)	1.58 (2.11)	1.46 (1.95)	1.47 (1.95)
		10 cm3	0.51 (0.54)	0.26 (0.51)	0.52 (0.55)	0.52 (0.55)	1.49 (1.97)	1.56 (2.08)	1.47 (1.95)	1.47 (1.95)
		15 cm3	0.47 (0.51)	0.24 (0.48)	0.48 (0.51)	0.48 (0.51)	1.46 (1.94)	1.53 (2.03)	1.44 (1.91)	1.44 (1.91)
Mozambique		5 cm3	0.65 (0.65)	0.29 (0.61)	0.61 (0.65)	0.69 (0.66) **	2.25 (2.46)	2.49 (2.74)	2.28 (2.5)	2.23 (2.44)
		10 cm3	0.61 (0.62)	0.35 (0.59)	0.59 (0.62)	0.66 (0.63)	2.25 (2.46)	2.43 (2.66)	2.25 (2.46)	2.21 (2.42)
		15 cm3	0.59 (0.59)	0.30 (0.56)	0.58 (0.60)	0.64 (0.61)	2.24 (2.45)	2.44 (2.67)	2.23 (2.44)	2.19 (2.4)

CC = cold chain (i.e. remains in the cold chain for its entirety).

* Boxes with asterisk represent an improvement in one or both metrics compared to baseline.

** Boxes with double asterisk represent the optimal design characteristics (including multidose N&S vaccines) for each supply chain.