Evaluating the potential cost-effectiveness of microarray patches for expanding hepatitis B birth dose vaccination in low-and middle-income countries: A modelling study

Supplemental Materials

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Appendix 1: Regional aggregation of low and middle-income countries within the model

Analysis focused on low-and middle-income countries (LMICs) providing hepatitis B birth dose vaccination for all newborns in the WHO/UNICEF estimates of National Immunization Coverage (WUENIC) [1]. Coverage estimates for LMICs could be from either 2019 or 2020, with the most recent in each LMIC used for modelling. From these countries, we modelled the six WHO regions, plus a composite “All LMICs” region encompassing all 77 LMICs. Population-weighted parameter averages (using 2020 births) [2] from relevant country subsets were used for regional analysis, excluding those with missing data.

Each modelled LMIC also needed to be aggregated into a Global Burden of Disease (GBD) world region for estimation of HBeAg prevalence among 15-49y females (reproductive age) [3], GBD Super Regions for estimates of costs associated with vaccination outreach [4], and World Bank income classification for estimation of human resource costs [5]. Missing data for modelled LMICs was imputed using the relevant WHO regional average (Table 2, Main Text).

Table A: Regional classification and basic epidemiological profile of modelled LMICs

| LMIC      | WHO Region [6] | GBD World Region [7] | GBD Super Region [7] | World Bank Income Classification# [8] | Hepatitis B birth dose coverage (WUENIC) [1] |
|-----------|----------------|-----------------------|----------------------|----------------------------------------|---------------------------------------------|
| Afghanistan | EMR            | North Africa and Middle East | North Africa and Middle East | Low Income                           | 38%                                         |
| Albania    | EUR            | Central Europe         | Central Europe, Eastern Europe and Central Asia | Upper Middle Income                  | 99%                                         |
| Algeria    | AFR            | North Africa and Middle East | North Africa and Middle East | Upper Middle Income                  | 99%                                         |
| Argentina  | AMR            | Southern Latin America | Latin America and Caribbean | Upper Middle Income                  | 72%                                         |
| Armenia    | EUR            | Central Asia           | Central Europe, Eastern Europe and Central Asia | Upper Middle Income                  | 97%                                         |
| Country                   | Region | Income Group       | Income Group Region | Income Group Percentage |
|---------------------------|--------|--------------------|---------------------|-------------------------|
| Azerbaijan                | EUR    | Central Asia       | Central Europe,    | 98%                     |
|                           |        |                    | Eastern Europe and Central Asia |                |
| Belarus                   | EUR    | Eastern Europe     | Central Europe,    | 97%                     |
|                           |        |                    | Eastern Europe and Central Asia |                |
| Belize                    | AMR    | Caribbean          | Latin America and Caribbean | 67%       |
| Benin                     | AFR    | Western Sub-Saharan Africa | Sub-Saharan Africa | 21%       |
| Bhutan                    | SEAR   | South Asia         | South Asia          | 85%                     |
| Brazil                    | AMR    | Tropical Latin America | Latin America and Caribbean | 63%       |
| Bulgaria                  | EUR    | Central Europe     | Central Europe,    | 98%                     |
|                           |        |                    | Eastern Europe and Central Asia |                |
| Cabo Verde                | AFR    | Western Sub-Saharan Africa | Sub-Saharan Africa | 96%       |
| Cambodia                  | WPR    | Southeast Asia     | Southeast Asia, East Asia and Oceania | 94%       |
| China                     | WPR    | East Asia          | Southeast Asia, East Asia and Oceania | 95%       |
| Colombia                  | AMR    | Central Latin America | Latin America and Caribbean | 88%       |
| Costa Rica                | AMR    | Central Latin America | Latin America and Caribbean | 87%       |
| Côte d’Ivoire             | AFR    | Western Sub-Saharan Africa | Sub-Saharan Africa | 62%       |
| Cuba                      | AMR    | Caribbean          | Latin America and Caribbean | 99%       |
| Dominican Republic (the)  | AMR    | Caribbean          | Latin America and Caribbean | 99%       |
| Ecuador                   | AMR    | Andean Latin America | Latin America and Caribbean | 66%       |
| Egypt                     | EMR    | North Africa and Middle East | North Africa and Middle East | 92%       |
| El Salvador               | AMR    | Central Latin America | Latin America and Caribbean | 75%       |
| Fiji                      | WPR    | Oceania            | Southeast Asia, East Asia and Oceania | 99%       |
| Georgia                   | EUR    | Central Asia       | Central Europe,    | 97%                     |
|                           |        |                    | Eastern Europe and Central Asia |                |
| Grenada                   | AMR    | Caribbean          | Latin America and Caribbean | 92%       |
| Guatemala                 | AMR    | Central Latin America | Latin America and Caribbean | 48%       |
| Guyana                    | AMR    | Caribbean          | Latin America and Caribbean | 70%       |
| Honduras                  | AMR    | Central Latin America | Latin America and Caribbean | 71%       |
| India                     | SEAR   | South Asia         | South Asia          | 54%                     |
| Indonesia                 | SEAR   | Southeast Asia     | Southeast Asia, East Asia and Oceania | 73%       |
| Iran (Islamic Republic of)| EMR    | North Africa and Middle East | North Africa and Middle East | 95%       |
| Iraq                      | EMR    | North Africa and Middle East | North Africa and Middle East | 47%       |
| Country                                      | Region | Primary Region | Secondary Region          | Income Level   | Income % |
|----------------------------------------------|--------|----------------|---------------------------|----------------|----------|
| Kazakhstan                                  | EUR    | Central Asia   | Central Europe, Eastern Europe and Central Asia | Upper Middle Income | 93%      |
| Kiribati                                    | WPR    | Oceania        | Southeast Asia, East Asia and Oceania | Lower Middle Income | 95%      |
| Korea (the Democratic People's Republic of) | SEAR   | East Asia      | Southeast Asia, East Asia and Oceania | Low Income     | 99%      |
| Kyrgyzstan                                  | EUR    | Central Asia   | Central Europe, Eastern Europe and Central Asia | Lower Middle Income | 95%      |
| Lao People's Democratic Republic (the)       | WPR    | Southeast Asia | Southeast Asia, East Asia and Oceania | Lower Middle Income | 58%      |
| Lebanon                                     | EMR    | North Africa and Middle East | North Africa and Middle East | Upper Middle Income | 77%      |
| Malaysia                                    | WPR    | Southeast Asia | Southeast Asia, East Asia and Oceania | Upper Middle Income | 99%      |
| Maldives                                    | SEAR   | Southeast Asia | Southeast Asia, East Asia and Oceania | Upper Middle Income | 99%      |
| Marshall Islands (the)                      | WPR    | Oceania        | Southeast Asia, East Asia and Oceania | Upper Middle Income | 98%      |
| Mexico                                      | AMR    | Central Latin America | Latin America and Caribbean | Upper Middle Income | 52%      |
| Micronesia (Federated States of)            | WPR    | Oceania        | Southeast Asia, East Asia and Oceania | Lower Middle Income | 64%      |
| Moldova (the Republic of)                   | EUR    | Eastern Europe | Central Europe, Eastern Europe and Central Asia | Lower Middle Income | 95%      |
| Mongolia                                    | WPR    | Central Asia   | Central Europe, Eastern Europe and Central Asia | Lower Middle Income | 98%      |
| Morocco                                     | EMR    | North Africa and Middle East | North Africa and Middle East | Lower Middle Income | 41%      |
| Myanmar                                     | SEAR   | Southeast Asia | Southeast Asia, East Asia and Oceania | Lower Middle Income | 21%      |
| Namibia                                     | AFR    | Sub-Saharan Africa | Sub-Saharan Africa | Upper Middle Income | 81%      |
| Nauru                                       | WPR    | Oceania        | Southeast Asia, East Asia and Oceania | Upper Middle Income | 99%      |
| North Macedonia                             | EUR    | Central Europe | Central Europe, Eastern Europe and Central Asia | Upper Middle Income | 97%      |
| Palestine, State of                         | EMR    | North Africa and Middle East | North Africa and Middle East | Lower Middle Income | 99%      |
| Papua New Guinea                            | WPR    | Oceania        | Southeast Asia, East Asia and Oceania | Lower Middle Income | 24%      |
| Peru                                        | AMR    | Andean Latin America | Latin America and Caribbean | Upper Middle Income | 75%      |
| Philippines (the)                           | WPR    | Southeast Asia | Southeast Asia, East Asia and Oceania | Lower Middle Income | 53%      |
| Romania                                     | EUR    | Central Europe | Central Europe, Eastern Europe and Central Asia | Upper Middle Income | 97%      |
| Saint Lucia                                 | AMR    | Caribbean      | Latin America and Caribbean | Upper Middle Income | 86%      |
| Saint Vincent and the Grenadines            | AMR    | Caribbean      | Latin America and Caribbean | Upper Middle Income | 96%      |
| Samoa                                       | WPR    | Oceania        | Southeast Asia, East Asia and Oceania | Upper Middle Income | 79%      |
| Country                  | Region        | Sub-Region                               | Region                      | Income Level  | Percentage |
|--------------------------|---------------|------------------------------------------|-----------------------------|---------------|------------|
| São Tomé and Principe    | AFR           | Western Sub-Saharan Africa               | Sub-Saharan Africa          | Lower Middle Income | 95%        |
| Senegal                  | AFR           | Western Sub-Saharan Africa               | Sub-Saharan Africa          | Lower Middle Income | 86%        |
| Serbia                   | EUR           | Central Europe                           | Central Europe,             | Upper Middle Income | 99%        |
| Solomons Islands         | WPR           | Oceania                                  | Southeast Asia, East        | Lower Middle Income | 70%        |
| Suriname                 | AMR           | Caribbean                                | Latin America and           | Upper Middle Income | 79%        |
| Tajikistan               | EUR           | Central Asia                             | Central Europe,             | Low Income     | 99%        |
| Thailand                 | SEAR          | Southeast Asia                           | Southeast Asia, East        | Upper Middle Income | 99%        |
| Timor-Leste              | SEAR          | Southeast Asia                           | Southeast Asia, East        | Lower Middle Income | 72%        |
| Tonga                    | WPR           | Oceania                                  | Southeast Asia, East        | Upper Middle Income | 99%        |
| Tunisia                  | EMR           | North Africa and Middle East             | North Africa and Middle East | Lower Middle Income | 74%        |
| Turkey                   | EUR           | North Africa and Middle East             | North Africa and Middle East | Upper Middle Income | 99%        |
| Turkmenistan             | EUR           | Central Asia                             | Central Europe,             | Upper Middle Income | 99%        |
| Tuvalu                   | WPR           | Oceania                                  | Southeast Asia, East        | Upper Middle Income | 99%        |
| Ukraine                  | EUR           | Eastern Europe                           | Central Europe,             | Lower Middle Income | 69%        |
| Uzbekistan               | EUR           | Central Asia                             | Central Europe,             | Lower Middle Income | 97%        |
| Vanuatu                  | WPR           | Oceania                                  | Southeast Asia, East        | Lower Middle Income | 59%        |
| Venezuela (Bolivarian     | AMR           | Central Latin America                    | Latin America and           | Upper Middle Income | 50%        |
| Republic of)             |               |                                          | Caribbean                   |               |            |
| Viet Nam                 | WPR           | Southeast Asia                           | Southeast Asia, East        | Lower Middle Income | 82%        |
| Zambia                   | AFR           | Eastern Sub-Saharan Africa               | Sub-Saharan Africa          | Lower Middle Income | 94%        |

AFR: African WHO Region, AMR: American WHO Region, EMR: Eastern Mediterranean WHO Region, EUR: European WHO Region, SEAR: Southeast Asian WHO Region, WPR: Western Pacific WHO Region.

# World Bank Income Classification is for the 2020 calendar year
Appendix 2: Additional disease and vaccination model detail

**Fig A:** Perinatal hepatitis B transmission and progression model. **Note:** Horizontal (non-MTCT) transmission is explicitly excluded from the model.

HBsAg = hepatitis B surface antigen, HBeAg = hepatitis B envelope antigen, MTCT=mother-to-child transmission risk, VE(t) = Vaccine effectiveness at each modelled postpartum time-strata (day 1, day 2, days 3-7, days 8-41 and unvaccinated).
Baseline distribution of hepatitis B birth dose coverage: facilities vs community

To account for reported coverage inequities amongst births occurring outside of health facilities (i.e., in the community) within the model [9, 10], baseline estimates of hepatitis B birth dose vaccination coverage were weighted according to the below formula. This was required as national estimates of hepatitis B birth dose coverage are reflective of coverage across an entire annual birth cohort, and hence do not capture any heterogeneity across birth locations.

A weighting factor (w.f.) of 2 was used within the model, consistent with observational data indicating odds of vaccination of births at home are approximately half that of those occurring within health facilities [11, 12].

\[
\text{Facility:} \\
\text{Facility Coverage}(BD) = \begin{cases} 
BD + BD \left( \frac{w_f-1}{w_f+1} (2 \times \text{Community}) \right) & \text{if } BD \leq 50\% \\
BD + (1 - BD) \left( \frac{w_f-1}{w_f+1} (2 \times \text{Community}) \right) & \text{if } BD > 50\%
\end{cases}
\]

\[
\text{Community:} \\
\text{Community Coverage}(BD) = \begin{cases} 
BD - BD \left( \frac{w_f-1}{w_f+1} (2 \times \text{Facility}) \right) & \text{if } BD \leq 50\% \\
BD - (1 - BD) \left( \frac{w_f-1}{w_f+1} (2 \times \text{Facility}) \right) & \text{if } BD > 50\%
\end{cases}
\]

\(BD\): Baseline hepatitis B birth dose vaccine coverage, \(w_f\): Weighting Factor; odds of facilitated vaccination against community, Facility/Community: Proportion of facility/community births

Baseline distribution of hepatitis B birth dose coverage: timing of delivery

It was assumed that birth dose vaccination timing would be prompter for facility births, as compared to those in the community, given vaccine availability and vaccine access considerations. At baseline, we assumed that 80% vaccinations given in a health facility would be timely (<24 hours); a midpoint average between observed values of 64% and 90% [13, 14]. Remaining doses were
uniformly distributed among the non-timely vaccination strata (i.e., 6.7% on each of day 2, days 3-7 and days 8-41).

Within the community (births outside of health facilities), barriers currently inhibiting timely vaccination coverage include suboptimal qualified health worker attendance and/or travel distance from a health facility where birth dose vaccines are kept [15-17]. To capture these potential latencies, we assumed that 30% of baseline coverage in the community was timely (<24 hours), 40% delivered on day 2, and 15% on each of the days 3-7 and days 8-41-time strata.

Appendix 3: Additional details on vaccination costing

Vaccine Supply Chain Costs

A supply chain cost component was used to account for the costs associated with transporting vaccines from a national store to a health facility, and storage of vaccines in a cold chain. Economic costs were taken from a review by Portnoy and colleagues, which estimated the non-commodity costs of introducing a new vaccine into a routine immunization program [18]. Costs were available for 78 (98%) modelled LMICs and assumed constant for both vial and MAP presentation of vaccine.

Source costs were presented in 2018 US$ and modelled in 2020 US$ (CPI adjusted). Impacts of alternate assumptions for MAPs were quantified in a one-way sensitivity analysis (Main Text, Fig 3).

Table E: Modelled per dose supply chain costs for each WHO region (2020 US$; population-weighted averages)
Vaccine Commodity Costs

Within the model, per dose commodity costs considered three individual components: vaccines, needle and syringe, disposal boxes; plus, an allowance for wastage where required. Across all modelled LMICs, commodity costs were assumed equal.

- **Vaccines**: Baseline birth dose coverage assumed a combination of 10-dose (MDV) and single-dose (SDV) vials were being used for vaccinations. Modelled costs were the average, and uncertainty the range, of available UNICEF-Supply and Demand (UNICEF-SD) price points for pediatric presentations in 2020 [19]. A procurement ratio of 3 MDV: 1 SDV was used in analysis, guided by UNICEF purchasing data [20]. For MAP presentations, vaccine costs of US$1.65, US$3.30 and US$5.00 were investigated as part of analysis.

- **Vaccine Wastage**: Vaccine wastage rates were estimated using the WHO Vaccine Wastage Calculator tool [21]. A wastage rate of 17.5% (range: 10%, 25%) was applied for MDV vaccines and 4% (range: 3%, 5%) for SDVs. Cost-effectiveness outcomes for MAP vaccines included a 4% wastage allowance, consistent with other single dose presentations.

- **Needle and Syringe**: 0.5mL auto-disable needle and syringes are needed for vial presentations and included in the cost estimates. Modelled costs were the average, and uncertainty the range, of UNICEF-SD price points for devices in 2020 [22]. We assumed a 10% wastage rate for needles and syringes, consistent with UNICEF and WHO assumptions for procurement. A needle and syringe component were not needed for MAP presentations.

- **Disposal Box**: 5L disposal boxes were included in the per dose cost for vial vaccines. Modelled costs were the average, and uncertainty the range, of UNICEF-SD price points for devices in 2020 [22]. Per dose costs were calculated assuming each disposal box could hold
100 0.5mL auto-disable needle and syringe devices and included allowance for needle and syringe wastage. A disposal box component was assumed as not required for disposal of MAPs.

**Table F:** Modelled per dose vaccine commodity costs (2020 USD); assumed fixed for each modelled setting.

| Vaccine Type | Per Dose Vaccine Cost (range) | Vaccine Wastage*, % (range) | Per dose 0.5mL auto disable needle and syringe cost (range) | 0.5mL auto disable needle and syringe wastage*, % (range) | Per dose disposal box cost (range) | Per dose total commodity cost (range) |
|--------------|-------------------------------|-------------------------------|----------------------------------------------------------|----------------------------------------------------------|-----------------------------------|---------------------------------------|
| Multi Dose Vial (MDV) | $0.25 (0.24, 0.25) | 17.5 (10, 25) | $0.041 (0.031, 0.066) | 10% | $0.0062 (0.0045, 0.0093) | $0.34 (0.31, 0.41) |
| Single Dose Vial (SDV) | $0.55 (0.49, 0.60) | 4 (3, 5) | $0.041 (0.031, 0.066) | 10% | $0.0062 (0.0045, 0.0093) | $0.62 (0.54, 0.71) |
| 3 MDV: 1 SDV (baseline) weighted estimate | --- | --- | --- | --- | --- | $0.41 (0.36, 0.48) |
| Microarray Patch (MAP) | $1.65/$3.30/$5.00 | 4 | --- | --- | --- | $1.72/$3.44/$5.21 |

*Per dose wastage cost for vaccines and 0.5mL auto disable needle and syringes calculated as: unit cost*(1/1-wastage (%))*

**Human Resource (Vaccine Administration Time) Costs**

Human resource costs captured the health worker time required to deliver a hepatitis B birth dose vaccine. We limited time to the administration of a birth dose vaccination from a given vaccine presentation (SDV, MDV, MAP) and excluded time-cost associated with provision of other post-birth services and other vaccine program activities. A PATH time-in-motion analysis was used to estimate vaccination delivery times, weighted proportional to MDV and SDV usage where relevant [23]. Delivery times for a CPAD within the PATH analysis were used as a proxy for MAPs, consistent with application times in a childhood MAP vaccination study [24]. However, target product profiles for MAPs indicate this time could be much longer and remain acceptable for use [25], hence the impact was evaluated in one-way sensitivity analysis (Main Text, Fig 3).
Valuation of time was linked to per capita GDP, using multipliers from an econometric analysis by Serje and colleagues according to World Bank Income Classification status [5]. Health workers were assumed to work 37.5-hour weeks for 48 weeks per year and that doctors, nurses and midwives would vaccinate births with an equal probability; however, costs were weighted proportionally to the number of each cadre within a LMIC [26, 27]. Valuation of trained lay-health workers to administer MAPs to births in the community used the “other health workers” multiplier as a proxy.

Regional analysis used population weighted (2020 births) averages across relevant subsets of LMICs.

**Table G:** Vaccine administration time for each modelled modality. Values approximated from a PATH time and motion analysis [23]

| Vaccine Delivery Modality         | Administration Time (seconds) | Range      |
|----------------------------------|-------------------------------|------------|
| 10-Dose Vial (MDV)               | 15.2                          | 8-35       |
| Single Dose Vial (SDV)           | 19.3                          | 10-40      |
| MAP (using CPAD as proxy)        | 7.6                           | 5-20       |

**Table H:** Modelled per dose human resource costs (2020 USD) for each WHO region; uncertainty represents lower and upper bound vaccine administration time estimates.

|                        | AFRO     | AMRO     | EMRO     | EURO     | SEARO    | WPRO     | All LMICs |
|------------------------|----------|----------|----------|----------|----------|----------|-----------|
| Cold Chain, QHW        | $0.02 (0.01-0.05) | $0.05 (0.02-0.10) | $0.03 (0.02-0.07) | $0.04 (0.02-0.09) | $0.03 (0.01-0.06) | $0.06 (0.03-0.13) | $0.04 (0.02-0.08) |
| MAPs, QHW              | $0.01 (0.007-0.03) | $0.02 (0.01-0.06) | $0.01 (0.009-0.04) | $0.02 (0.01-0.05) | $0.01 (0.008-0.03) | $0.03 (0.02-0.07) | $0.02 (0.01-0.05) |
| MAPs, LHW              | $0.006 (0.004-0.02) | $0.01 (0.008-0.03) | $0.007 (0.005-0.02) | $0.01 (0.007-0.03) | $0.006 (0.004-0.02) | $0.01 (0.009-0.04) | $0.01 (0.006-0.03) |

QHW: Qualified Health Worker, LHW: Trained Lay-Health Worker, CTC: Controlled Temperature Chain, MAP: Microarray Patch

**Outreach Costs**

Outreach aimed to capture costs associated with providing a birth dose vaccination in the community, including transport costs and travel time. Costs were taken from an analysis by Nayagam and colleagues [4]; however, costs in the South Asia GBD Super Region were deemed unrealistic.
($32 per dose, 2020 USD). For LMICs within this region, a population weighted (2020 births) average of outreach costs elsewhere was used *in lieu*.

As the study only provided point estimate costs, uncertainty was modelled as a uniform ±5% from point estimates.

**Table I**: Modelled per dose outreach costs to reach a birth within the community (2020 USD) for each WHO region.

|                | AFRO | AMRO | EMRO | EURO | SEARO | WPRO | All LMICs |
|----------------|------|------|------|------|-------|------|-----------|
| Outreach Cost  | $3.59| $0.02| $0.49| $2.94| $1.55 | $0.64| $1.18     |
Appendix 4: Additional figures and tables

![Figure B: Cost-effectiveness of MAPs against willingness-to-pay (WTP) thresholds, using median ICERs across three investigated MAP price points for 80 LMICs.](image)

Note: Published estimates of WTP per DALY averted were only available for 51/80 (64%) of modelled LMICs [28].
Appendix 5: Supplemental Analyses

Sensitivity analysis: larger coverage gains due to MAPs

Incremental gains in additional coverage only (scenario 1) were associated with greater health benefits (Table L); however, did not impact cost-effectiveness of MAPs (i.e., ICERs did not change).

Cost-effectiveness of replacement coverage (scenario 2) was enhanced with higher levels of additional coverage, but remained less cost-effective (i.e., higher ICERs) compared to additional coverage only (scenario 1).

**Fig C**: Outcomes of assumptions on incremental coverage gains from MAPs within the model. Shaded region represents Interquartile Range (IQR) of 1000 model simulations.
Table L: Outcomes of sensitivity analysis where MAPs provide larger coverage gains.

| MAPs Administered | DALYs Averted (vs baseline) | Disease Management Costs ('000 USD) | Vaccination Costs (excluding MAP commodity costs; '000 USD) | ICER, USD per DALY averted (MAP Procurement Price = US$1.65 per dose) | ICER, USD per DALY averted (MAP Procurement Price = US$3.30 per dose) | ICER, USD per DALY averted (MAP Procurement Price = US$5.00 per dose) |
|-------------------|-----------------------------|-----------------------------------|------------------------------------------------|------------------------------------------------|------------------------------------------------|------------------------------------------------|
| All LMICs (80 countries, 80.1 million births) | | | | | | |
| Baseline (MDV+SDV) | -- | 1,538,536 | 399,541 | 163,807 | -- | -- |
| 1% Additional Coverage | | | | | | |
| +1% additional coverage with MAPs | 49,162 | 2,468 | 398,795 | 163,955 | -154.44 | -119.64 |
| 1% additional coverage with replacement coverage with MAPs | 194,369 | 3,476 | 398,507 | 163,966 | -132.86 | -41.04 |
| +1% additional coverage with MAPs | 773,426 | 7,552 | 397,357 | 163,647 | -101.92 | -64.17 |
| +1% additional coverage with replacement coverage with MAPs | 1,498,144 | 12,640 | 395,919 | 163,427 | -92.77 | -296.78 |
| 5% Additional Coverage | | | | | | |
| +5% additional coverage with MAPs | 245,808 | 12,431 | 395,811 | 164,644 | -154.44 | -119.64 |
| +5% additional coverage with replacement coverage with MAPs | 391,625 | 13,332 | 395,525 | 164,591 | -148.97 | -101.56 |
| +5% additional coverage with replacement coverage with MAPs | 971,847 | 17,381 | 394,373 | 164,423 | -132.86 | -40.04 |
| +5% additional coverage with replacement coverage with MAPs | 1,694,224 | 22,517 | 392,935 | 164,197 | -92.77 | -296.78 |
| 10% Additional Coverage | | | | | | |
| +10% additional coverage with MAPs | 491,616 | 24,681 | 392,105 | 165,446 | -154.44 | -119.64 |
| +10% additional coverage with replacement coverage with MAPs | 637,162 | 25,681 | 391,794 | 165,363 | -150.76 | -110.59 |

Note: The table shows the outcomes of sensitivity analysis where MAPs provide larger coverage gains. The table includes columns for each coverage scenario, showing the number of MAPs administered, DALYs averted, disease management costs, vaccination costs, and ICERs for different MAP procurement prices.
+10% additional and 5% replacement coverage with MAPs

| Costs (2020 USD) | Mean | Upper Quartile | Lower Quartile | ICER | Upper 95% CI | Lower 95% CI |
|------------------|------|----------------|----------------|------|--------------|--------------|
| 1,218,070        | 29,680 | (23,774; 37,520) | (282,288; 530,614) | 165,367 | (-225.45; -69.69) | (-157.11, 0.02) |
| 390,644          | 348,096 | (281,568; 529,147) | (138,364; 203,668) | 165,011 | (-222.07; -59.75) | (-126.66; 40.51) |
| 165,367          | -140.87 | (-225.45; -69.69) | (-157.11, 0.02) | -73.39 | (-88.93; 77.60) | (-73.39; 77.60) |
| 348,096          | 390,644 | (281,568; 529,147) | (138,364; 203,668) | 165,011 | (-222.07; -59.75) | (-126.66; 40.51) |
| 165,367          | -140.87 | (-225.45; -69.69) | (-157.11, 0.02) | -73.39 | (-88.93; 77.60) | (-73.39; 77.60) |

+10% additional and 10% replacement coverage with MAPs

| Costs (2020 USD) | Mean | Upper Quartile | Lower Quartile | ICER | Upper 95% CI | Lower 95% CI |
|------------------|------|----------------|----------------|------|--------------|--------------|
| 1,943,693        | 37,763 | (27,847; 43,981) | (281,568; 529,147) | 165,011 | (-222.07; -59.75) | (-126.66; 40.51) |
| 389,206          | 390,644 | (281,568; 529,147) | (138,364; 203,668) | 165,011 | (-222.07; -59.75) | (-126.66; 40.51) |
| 165,011          | -132.86 | (-222.07; -59.75) | (-126.66; 40.51) | -41.04 | (-34.88; 152.73) | (-126.66; 40.51) |
| 389,206          | 1,943,693 | (27,847; 43,981) | (281,568; 529,147) | 165,011 | (-222.07; -59.75) | (-126.66; 40.51) |
| 165,011          | -132.86 | (-222.07; -59.75) | (-126.66; 40.51) | -41.04 | (-34.88; 152.73) | (-126.66; 40.51) |

Uncertainty parenthesized as the Interquartile Range (IQR) of 1000 model iterations. Costs presented in 2020 USD. Negative ICERs indicative of cost-savings (i.e., health benefits achieved at a lower overall cost compared to baseline expenditure).

Abbreviations: MAP: Microarray Patch, MDV: Multiple Dose Vial, SDV: Single Dose Vial.
Sensitivity analysis: MAPs do not create new coverage, but are used to replace existing needle and syringe coverage (and hence improve timing of delivery only)

Cost-effectiveness of using MAPs to replace existing coverage only (Supplemental Figure 3, right panel) was equal across all analyzed increments (1%, 5% and 10%). While less cost-effective than additional coverage from MAPs (i.e., higher ICERs for a given MAP price), this sensitivity analysis indicates use of MAPs to only achieve gains in birth dose timeliness may present some value.

**Fig D:** Comparative outcomes of MAPs when replacement coverage is paired with additional coverage (left) and when modelled in isolation (right). Shaded region represents Interquartile Range (IQR) of 1000 model simulations.
Sensitivity analysis: When MAPs replace existing coverage it always results in day 1 coverage, rather than a left shift in the timing of delivery

Instead of a left shift in timing distribution of vaccines delivered by qualified health workers, this sensitivity analysis explored a best-case scenario: MAPs enable all delayed vaccinations to occur on the day of birth (i.e., timely).

Subsequent gains in vaccine effectiveness mean that cost-effectiveness of MAPs is enhanced, relative to baseline assumptions.

**Fig E:** Comparative outcomes of MAPs when timing gains from maps are left shifted one time-strata (left) or if all replacement coverage is shifted to the day of birth (right) within the model. Shaded region represents Interquartile Range (IQR) of 1000 model simulations.
Sensitivity analysis: MAPs also provide additional, new coverage in facilities (rather than just additional coverage in the community).

For this supplemental analysis, we assumed that additional coverage from MAPs in facilities was half of that in the community (i.e. 0.5% additional coverage). However, as the majority of births remain in health facilities and vaccination does not incur an outreach cost, even constrained use in this setting improves cost-effectiveness.

**Fig F:** Comparative outcomes of MAPs when additional coverage is limited to community births only (left) or if additional coverage can also occur for facility births (right) within the model. Shaded region represents Interquartile Range (IQR) of 1000 model simulations.
Appendix 6: Sensitivity Analysis – cost-effectiveness of MAPs if implemented with a baseline CTC approach

The hepatitis B birth dose is deemed a CTC priority vaccine by the WHO CTC Working Group [29]. In this sensitivity analysis, we investigated how a theoretical baseline scenario where the CTC approach was already being used would impact the cost-effectiveness of MAPs to deliver the birth dose.

We assumed that all vial vaccines used under a CTC approach would be single-dose, and that each vial would be fitted with a combined vaccine vial monitor (VVM) and threshold temperature indicator (TTI). As vaccines were in vials, administration remained a task for qualified health workers only (i.e., required a needle and syringe). Consistent with previous CTC hepatitis B birth dose modelling studies [30, 31], at baseline, CTC provided an additional 5% timely (day 1) coverage of births in facilities and 10% timely coverage of births in the community. Additionally, CTC improves timeliness of 5% of facility and 10% of community vaccinations by replacing existing cold chain coverage, modelled as a left shift (i.e., days 8-41 to days 3-7, days 3-7 to day 2, and day 2 to day 1) in vaccine timing.

Results from this analysis suggest introduction of MAPs under a baseline scenario with a CTC approach would have negligible impact on their cost-effectiveness, as compared to a baseline scenario entirely reliant upon the cold chain.
Table M: Per dose component costs of vial vaccines delivered under a CTC approach, presented in $US 2020.

| Component                                      | All LMICs         |
|------------------------------------------------|-------------------|
| Supply Chain Cost [18]                         | $1.96             |
|                                                | ($0.58, $5.03)    |
| Vaccine Cost (inc. needle and syringe, disposal and wastage) [19, 22] | $0.65             |
|                                                | ($0.57, $0.75)    |
| Temperature Threshold Indicator (TTI) [32]     | $0.035            |
|                                                | ($0.03, $0.04)    |
| Delivery Cost [5, 23, 26, 27]                  | $0.04             |
|                                                | ($0.02, $0.09)    |
| Outreach Cost (community births) [4]           | $1.18             |

Fig G: Comparative outcomes of MAPs when comparing a cold chain baseline (left) with a hypothetical future controlled temperature chain (CTC; right) baseline within the model. Shaded region represents IQR of 1000 model simulations.
**Table N**: Sensitivity analysis of MAP cost-effectiveness for delivering the hepatitis B birth dose in 77 LMICs under cold chain and cold chain plus CTC baseline assumptions. Costs in US$ 2020, uncertainty in parenthesis represents IQR of 1000 model iterations.

| Cold Chain Only (80 countries, 80.1 million births) | MAPs Administered | DALYs Averted (for MAPs additional DALYs averted vs baseline) | Disease Management Costs ('000 USD) | Vaccination Costs (excluding MAP commodity costs; '000 USD) | ICER, USD per DALY averted (MAP Procurement Price = US$1.65 per dose) | ICER, USD per DALY averted (MAP Procurement Price = US$3.30 per dose) | ICER, USD per DALY averted (MAP Procurement Price = US$5.00 per dose) |
|---|---|---|---|---|---|---|---|
| Baseline (MDV+SDV) | --- | 1,538,536 | 399,541 | 163,807 | --- | --- | --- |
| +1% additional coverage with MAPs | 49,162 (43,425; 55,272) | 2,468 (1,396; 3,116) | 398,795 (287,021; 540,606) | 163,955 (136,714; 203,425) | -154.44 (-242.33; -86.88) | (-204.17; -52.48) | (-171.22; -15.44) |
| +1% additional and 1% replacement coverage with MAPs | 194,369 (184,273; 204,183) | 3,476 (2,785; 4,398) | 398,507 (286,803; 540,317) | 163,966 (136,808; 203,421) | -132.86 (-222.07; -59.75) | (-126.66; 40.51) | (-34.88; 152.73) |
| +1% additional and 5% replacement coverage with MAPs | 773,426 (746,364; 799,418) | 7,552 (5,952; 9,643) | 397,357 (286,139; 539,162) | 163,647 (136,855; 202,958) | -101.92 (-205.27; -9.78) | (-41.07; 179.19) | (115.71; 386.49) |
| +1% additional and 10% replacement coverage with MAPs | 1,498,144 (1,446,550; 1,546,363) | 12,640 (9,818; 16,240) | 395,919 (285,373; 537,718) | 163,427 (136,590; 202,456) | -92.77 (-205.03; 11.27) | (-16.26; 233.87) | (161.09; 478.89) |

| Cold Chain plus CTC | MAPs Administered | DALYs Averted (for MAPs additional DALYs averted vs baseline) | Disease Management Costs ('000 USD) | Vaccination Costs (excluding MAP commodity costs; '000 USD) | ICER, USD per DALY averted (MAP Procurement Price = US$1.65 per dose) | ICER, USD per DALY averted (MAP Procurement Price = US$3.30 per dose) | ICER, USD per DALY averted (MAP Procurement Price = US$5.00 per dose) |
|---|---|---|---|---|---|---|---|
| Baseline (MDV+SDV) | --- | 1,459,002 | 378,708 | 168,350 | --- | --- | --- |
| +1% additional coverage with MAPs | 44,245 (39,083; 49,745) | 2,221 (1,742; 2,805) | 378,056 (272,587; 513,343) | 168,462 (141,792; 207,369) | -154.44 (-242.33; -86.88) | (-204.17; -52.48) | (-171.22; -15.44) |
| +1% additional and 1% replacement coverage with MAPs | 180,029 (171,063; 188,786) | 3,164 (2,540; 4,005) | 377,718 (272,406; 513,086) | 168,457 (141,846; 207,318) | -132.82 (-222.16; -59.04) | (-123.12; 44.46) | (-30.94; 156.98) |
| +1% additional and 5% replacement coverage with MAPs | 721,394 (697,457; 744,803) | 6,990 (5,508; 8,932) | 376,507 (271,866; 521,058) | 168,572 (141,896; 206,988) | -101.61 (-205.22; -9.07) | (-39.44; 182.88) | (118.49; 392.54) |
| +1% additional and 10% replacement coverage with MAPs | 1,399,969 (1,352,838; 1,443,121) | 11,760 (9,110; 15,140) | 375,160 (271,085; 510,746) | 168,455 (141,806; 206,588) | -92.42 (-204.51; 13.67) | (-15.92; 236.72) | (161.02; 484.54) |

Negative ICER (Incremental Cost Effectiveness Ratio) reflective of dominance (cost-savings over the cohort lifetime). CTC = Controlled Temperature Chain, MDV = 10-dose vial, SDV = Single Dose Vial, MAP = Microarray Patch
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