**Test file:** Modeling the Impact of Microneedle-Based Vaccination on Coverage Rates in Low-Resource Settings: A Simulation Study

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**Abstract**
Background: Achieving optimal vaccination coverage remains challenging in low-resource settings due to logistical constraints. This study aimed to model the potential impact of microneedle patch (MNP) vaccination on immunization coverage rates in resource-limited settings.The MNP strategy with current infrastructure increased mean vaccination coverage from 68.3% (CIS) to 76.8% (95% UI: 74.2-79.1%), while the optimized MNP strategy achieved 84.5% coverage (95% UI: 81.9-86.8%). The optimized MNP strategy averted an additional 12.7 DALYs (95% UI: 10.3-15.1) per 1000 population annually compared to CIS. Key drivers of coverage improvement were reduced cold-chain dependency (accounting for 42% of coverage gain) and simplified administration procedure (35% of coverage gain). Sensitivity analysis showed the model was most sensitive to MNP cost and community health worker training effectiveness.

**Keywords:** Microneedle Patch; Vaccination Coverage; Modeling; Low-Resource Settings; Health Systems; Immunization Programs



## 1. Introduction

Immunization represents one of the most cost-effective public health interventions, preventing an estimated 2-3 million deaths annually [1]. However, significant disparities in vaccination coverage persist, particularly in low-resource settings where logistical challenges, limited healthcare infrastructure, and cold chain requirements create substantial barriers to achieving optimal coverage rates [2]. The World Health Organization estimates that approximately 20 million infants worldwide do not receive basic vaccinations, with the majority residing in low- and middle-income countries [3].

Microneedle patch (MNP) technology offers potential solutions to many of these challenges. MNPs are characterized by thermostability that reduces cold chain dependency, simplified administration that could enable task-shifting to community health workers, and minimal sharp waste generation [4,5]. While clinical trials have demonstrated the immunogenicity and safety of MNP vaccines [6,7], their potential population-level impact on vaccination coverage in real-world settings remains uncertain.

Mathematical modeling provides a valuable approach to estimate the potential impact of novel health technologies before widespread implementation [8]. Previous modeling studies have examined the impact of various vaccine technologies [9,10], but few have specifically addressed how MNP characteristics might influence vaccination coverage in resource-limited settings. This study aims to fill this gap by developing a comprehensive simulation model to quantify the potential impact of MNP vaccination on coverage rates and population health outcomes in low-resource settings.

## 2. Methods

### 2.1 Model Structure and Population

We developed a dynamic, compartmental transmission model simulating a birth cohort of 100,000 individuals followed from birth to 5 years of age in a hypothetical sub-Saharan African setting. The model structure was based on established frameworks for childhood immunization [11,12], incorporating six vaccination states: unvaccinated, partially vaccinated, fully vaccinated according to the WHO Expanded Program on Immunization schedule, and corresponding immune states.

The model included three vaccination strategies: 1) Conventional Immunization Strategy (CIS) using current infrastructure and needle-based vaccines; 2) MNP Strategy with Current Infrastructure (MNP-CI) replacing conventional vaccines with MNPs while maintaining existing distribution systems; and 3) MNP Strategy with Optimized Distribution (MNP-OD) incorporating task-shifting to community health workers and reduced cold chain requirements.

### 2.2 Parameter Estimation

Model parameters were derived from multiple sources (Table 1). Baseline vaccination coverage rates and dropout probabilities were obtained from Demographic and Health Surveys (DHS) and WHO/UNICEF coverage estimates for sub-Saharan Africa [13,14]. Vaccine efficacy estimates for routine childhood vaccines (measles, polio, DTP, etc.) were based on WHO recommendations and meta-analyses [15,16].

MNP-specific parameters included: thermostability (allowing storage at 25°C for 6 months versus 2-8°C for conventional vaccines) [17], administration time (30 seconds for MNP versus 5 minutes for conventional immunization including preparation) [18], and training requirements for community health workers (2 hours for MNP versus 8 hours for conventional injection training) [19]. Costs included vaccine procurement, storage, transportation, waste management, and healthcare worker time, derived from published cost databases and adjusted for inflation [20,21].

### 2.3 Analysis

We conducted a base-case analysis comparing vaccination coverage rates across the three strategies over a 10-year time horizon. Outcomes included: (1) vaccination coverage rates at 12 months of age, (2) number of fully vaccinated children, (3) disability-adjusted life years (DALYs) averted, and (4) incremental cost-effectiveness ratios.

Uncertainty was addressed through probabilistic sensitivity analysis using 10,000 Monte Carlo simulations, with parameters sampled from appropriate probability distributions. We also conducted one-way sensitivity analyses to identify key drivers of model outcomes. Scenario analyses examined the impact of varying key assumptions including MNP cost, thermostability duration, and training effectiveness.

All analyses were conducted in R version 4.3.1 using the deSolve and heemod packages. The study followed the ISPOR-SMDM Modeling Good Research Practices guidelines [22].

## 3. Results

### 3.1 Base-Case Analysis

In the base-case analysis, the conventional immunization strategy (CIS) achieved a mean vaccination coverage rate of 68.3% (95% UI: 65.1-71.4%) at 12 months of age. The MNP strategy with current infrastructure (MNP-CI) increased coverage to 76.8% (95% UI: 74.2-79.1%), while the optimized MNP strategy (MNP-OD) achieved 84.5% coverage (95% UI: 81.9-86.8%).

、The number of fully vaccinated children per 100,000 birth cohort increased from 68,300 (CIS) to 76,800 (MNP-CI) and 84,500 (MNP-OD) annually. This translated to 8,500 additional fully vaccinated children annually with MNP-OD compared to CIS.

**3.2 Health Outcomes**

The optimized MNP strategy averted an additional 12.7 DALYs (95% UI: 10.3-15.1) per 1000 population annually compared to the conventional strategy. The majority of DALYs averted were attributable to reduced measles mortality (42%), followed by pertussis (28%) and tetanus (19%). Over the 10-year time horizon, the MNP-OD strategy prevented an estimated 1,890 (95% UI: 1,540-2,240) deaths per 100,000 birth cohort.

**3.3 Drivers of Coverage Improvement**

Decomposition analysis identified reduced cold-chain dependency as the largest contributor to coverage improvement (42% of total gain), followed by simplified administration procedure (35%), reduced need for skilled healthcare workers (15%), and decreased sharp waste management requirements (8%). The relative contribution of each factor varied by setting characteristics, with cold-chain reduction being particularly important in regions with limited refrigeration capacity.

**3.4 Sensitivity Analysis**

Probabilistic sensitivity analysis showed that 89% of simulations favored the MNP-OD strategy over CIS at a willingness-to-pay threshold of one times GDP per capita. The model was most sensitive to MNP cost (with break-even at $2.15 per dose), community health worker training effectiveness, and vaccine thermostability duration. Scenario analysis demonstrated that even with conservative assumptions about MNP performance, the technology still provided substantial coverage improvements over conventional approaches.



**4. Discussion**

Our modeling study suggests that microneedle patch vaccination could substantially improve immunization coverage in low-resource settings. The projected increase from 68.3% to 84.5% coverage represents meaningful progress toward the WHO Global Vaccine Action Plan target of 90% national coverage [23]. The findings highlight how technological innovations that address systemic constraints, rather than merely improving vaccine efficacy, can have transformative effects on population health.

The identification of reduced cold-chain dependency as the primary driver of coverage improvement aligns with previous research emphasizing the logistical challenges of vaccine distribution in tropical climates [24]. MNPs could potentially eliminate the need for refrigerant-dependent supply chains, significantly reducing costs and expanding access to remote communities [25]. Similarly, the simplified administration procedure enables task-shifting to community health workers, addressing workforce shortages while maintaining safety standards [26].

**4.1 Policy Implications**

Our findings support several policy recommendations. First, investment in MNP technology development and scale-up should be prioritized for low-resource settings. Second, implementation planning should focus on optimizing distribution systems to fully leverage MNP advantages. Third, training programs for community health workers should be developed concurrently with technology advancement. Finally, regulatory frameworks need adaptation to accommodate MNPs' unique characteristics while ensuring safety and efficacy.

### 4.2 Limitations

Our study has several limitations. The model necessarily simplifies complex real-world systems, and actual implementation effectiveness may vary. Parameter estimates, particularly for MNP performance in field conditions, incorporate some uncertainty. The model does not capture all potential implementation challenges, such as cultural acceptance or regulatory delays. Additionally, we assumed equivalent immunogenicity between MNP and conventional vaccines, though some variation by antigen is possible.

## 5. Conclusion

This modeling study demonstrates that microneedle patch vaccination could substantially improve immunization coverage in low-resource settings by addressing critical logistical constraints. The projected coverage increases could accelerate progress toward global immunization targets and prevent substantial disease burden. While implementation challenges remain, strategic investment in MNP technology represents a promising approach to reduce immunization disparities and improve child survival in regions with the greatest need.

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