Vaccine Introduction & Uptake Timing Benchmark Project

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Agenda

Part 1: Main study: VPD, Vaccine & Country timelines
  • Project overview & results
  • Questions

Part 2: Country case studies
  • Overview
  • Questions
Project Objectives

• Identify timelines for vaccine introduction and uptake in Gavi-eligible countries for vaccines that address 6 vaccine-preventable disease (VPD) areas:
  - *Haemophilus influenzae* type b (pentavalent vaccines)
  - pneumococcal disease (pneumococcal conjugate vaccines, PCV)
  - rotavirus diarrhea (rotavirus vaccines, RVV),
  - cervical cancer (Human papillomavirus vaccines, HPV)
  - polio (inactivated polio vaccines, IPV) (*country-level analysis only*)
  - meningococcal A (MenA vaccines)

• Describe common bottlenecks in introduction timelines via country case studies
Process & Scope

**Benchmark:** Median of metrics (with ranges) across all vaccine preventable disease (VPD) areas, vaccine products or countries

Analysis of milestone dates, metrics and benchmarks by:

1. **VPD (vaccines):** 6* VPD areas
2. **Vaccine Product:** 42 prequalified vaccine products within 6 VPDs
3. **Country:** 73 Gavi-eligible and graduating Gavi countries

*IPV included in country-level analysis only
Milestone dates (first order) by VPD and across VPDs

- First WHO-recognized NRA licensure
- First WHO PQ approval
- First SAGE recommendation
- First Gavi board approval
- Unicef tender issued
- First Gavi introduction
- 50% target coverage across the Gavi cohort
- 100% target coverage across the Gavi cohort

“universal” or “strong” SAGE recommendation also reviewed
Milestone: Date of a key event

1st WHO-recognized NRA licensure per VPD
1st WHO PQ approval per VPD
1st SAGE recommendation
Gavi Board approval for support
1st actual Gavi country introduction
Universal SAGE recommendation
Universal WHO position paper
UNICEF tender issued
1st Gavi-funded country introduction
Gavi application window opened

1st Order Milestones: critical dates needed to assess benchmark data for vaccine introduction & scale-up

50% of target coverage (e.g. DTP3) reached across the Gavi cohort
100% of target coverage (e.g. DTP3) reached across the Gavi cohort

1st Order Metric: Time between two 1st order milestone dates used to generate timing benchmarks by VPD, vaccine product or country

1st Order Milestone by VPD
2nd Order Milestone by VPD
Chronologic Order of Milestone Can Vary
Milestone dates (first order) by vaccine and country

**Vaccine**
- First WHO-recognized NRA licensure
- First WHO PQ dossier submission
- First WHO PQ approval

**Country**
- Gavi country application submitted
- Gavi country application approved
- Gavi country introduction
- Target coverage achieved in the Gavi country
Output by Vaccine Product & By Country

By Vaccine Product

1st WHO-recognized NRA licensure

WHO PQ dossier submission

WHO PQ approval

Gavi country application submitted (with projected introduction date)

Gavi country application approved

Gavi vaccine introduction grant disbursed to Gavi country

1st shipment to Gavi country

1st actual introduction in Gavi country

Target coverage (e.g., DTP3) reached within Gavi country

By Gavi Country

1 NRA registration date in Gavi countries was not included as a milestone as analysis in selected countries did not show this as a key factor delaying introduction timelines (see Additional Analyses)
**VPD Benchmarks**

*Across 5 VPDs*\(^1\)

- Not all milestones occurred in the expected order, thus resulting in negative metrics

\(^1\)Pentavalent, PCV, Rota, Mena (RI & C), HPV
No common pathway, different bottlenecks

Longest metric(s) by VPD in bold

<table>
<thead>
<tr>
<th>VPD¹</th>
<th>Metric 1</th>
<th>Metric 2</th>
<th>Metric 3</th>
<th>Metric 4</th>
<th>Metric 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>MenA (RI)</td>
<td>SAGE to Gavi</td>
<td>Gavi to Licensure</td>
<td>Licensure to PQ</td>
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<td>HPV</td>
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<td>PQ to Gavi</td>
<td>Gavi to UNICEF</td>
<td>UNICEF to SAGE/Intro</td>
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¹ VPDs listed in order of longest introduction timeline to shortest introduction timeline
Variability in time to introduction
VPDs don’t take the same pathway to introduction

- Bottlenecks most often occurred towards the beginning of the process, with some exceptions

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1. Licensure = 1st WHO-approved NRA licensure per VPD; SAGE = 1st SAGE recommendation; Gavi = Gavi Board approval; PQ = 1st WHO prequalified vaccine by VPD; UNICEF = UNICEF tender issued; Intro = 1st Gavi-funded country introduction; excludes time to target coverage (DTP3) rate reached because only Penta reached 50% target coverage (DTP3) rate milestone:
Vaccine-Specific Benchmarks

Across 39 vaccines, 5¹ VPDs

• For half of the vaccines (n=15), the manufacturers applied for WHO PQ in less than 5 months from time of 1ˢᵗ licensure

• The median time from WHO PQ dossier submission to WHO PQ approval was just over a year (1.1 years) with an overall median of nearly two years from 1ˢᵗ licensure to WHO PQ approval

¹Includes vaccines on the UNICEF Price List for Gavi procurement from 2001-2016 (Pentavalent, PCV, Rotavirus, HPV, MenA)
Half of the countries received Gavi application approval within 0.4 years of their Gavi application submission and introduced a vaccine within 1.5 years from application submission.

The median time to reach target coverage rate was 1.3 years following introduction.

1 VPDs include Penta, PCV, Rotavirus, IPV, HPV, Men A (Campaign); 2 Median longer than sum of metrics due to different number of counties included; 3 VPDs include Penta, PCV and Rotavirus; 4 Target coverage in Gavi country defined as 1st year when VPD coverage / DTP3 coverage ≥ 90%
Projected vs. Actual Country Introduction Timelines

- 16% of countries\(^1\) (n=35) introduced on or before their projected introduction dates.
- The majority of countries (84%, n=183) introduced after their projected introduction dates.
  - PCV is the most frequently delayed VPD (96% delayed, n=51) and varies from < 1 month to almost 5 years.
  - HPV had the most on-time or early (42%, n=8) introductions.
  - Even with the global focus on polio eradication, IPV intros were also frequently delayed, but in general, these delays were shorter as compared to PCV.

\(^1\) 218 country data points analyzed across 6 VPDs; Countries with negative introduction or projected introduction timelines excluded.
Summary

• The order of milestones varies by both VPD and country
• Once the first vaccine was licensed, it took as little as 7 months to nearly 7 years for introduction in Gavi countries for each VPD (median of 5.4 years)\(^1\)
  • Only pentavalent vaccine surpassed 50% of target (DTP\(_3\)) coverage across the entire Gavi cohort, taking 13.5 years (21 years from the 1\(^{st}\) Hib-containing vaccine) from 1\(^{st}\) WHO-recognized NRA licensure
• The median time from earliest VPD milestone to Gavi-funded introduction was shortest for pentavalent (5.3 years) and longest for MenA routine (13.6 years)\(^2\)
• PCV and RVV vaccines had longest delays in country introduction, likely due to a variety of reasons such as:
  - Supply constraints/misalignment of demand and desired formulation
  - Cold chain storage limitations
  - Pricing issues
  - Political considerations

\(^1\) IPV included in country-level analysis only \(^2\) Reflects that first Men A (routine) introduction occurred in Sudan July 27, 2016 after conclusion of this study
Stories behind the Data

Case Studies from the Benchmarking Project
Delving deeper: the stories behind the numbers

Case countries & their introduction timelines

The Gambia
- 1997: LTP/Hib
- 2009: DTP-Hib, PCV-7
- 2011: RVV, MenA (C)
- 2013: HPV Demo
- 2014: IPV

Bangladesh
- 2009: Penta
- 2015: PCV-10 & IPV (Dual)

Nigeria
- 2011: MenA (C)
- 2012: Penta
- 2014: PCV-13
- 2015: IPV
Nigeria: new vaccine introductions

- Re-submitted for RVV support in May 2016 (with projected Jan 2018 intro)
- As of 9/15/2016, Phase 3 complete in all but 3 states.
- Jan 1: Expected Graduation

Planned new vaccines: RVV, MenA RI, HPV,
Product trade-offs complicate
The PCV Experience

From Gavi application submission to Gavi Board Approval

- 2 years from submission to approval
- Cold chain constraints helped with 2 dose vial, but readiness requirements due to lack of preservative caused further delays

Submitted Gavi application for PCV-10 support
Re-submitted application (phased) (projected Mar 2012 intro)
“Gavi pause”
Conditional Gavi Board approval
Full Gavi Board approval for Phase 1

May 2009
Sept 2009
2010
2011
Sept 2011
Apr 2012
Many factors delay intro
The PCV Experience

From Gavi Board Approval to Country Introduction

- Strikes, global supply, programmatic constraints, and financing (phase 1)
- VIG disbursed not disbursed until Sept 2013
- Phase 3 start uncertain due to supply. But, Bangladesh’s delays helped free up global supply.
Conclusions

Reviewing Common Themes and Future Learnings
Causes of vaccine intro delay fall under common categories and occur at multiple levels.

Country level:
- Readiness and political will
- Evidence of disease burden
- Public perceptions

Institutional level:
- Global recommendation
- Financing, supply of affordable vx
- Communication with countries

Categories of delay:
- Supply
- Financial considerations
- Programmatic considerations

- Cold chain
- VIG
- Country readiness
- Programmatically suitable products
- Gavi transition
- Self-financing
- Sustainability

Global recommendation:
- Financing, supply of affordable vx
- Communication with countries
What’s needed

1. Programmatically suitable products
2. Awareness around disease & need for vaccine
3. A strong initial SAGE recommendation
4. A strong evidence base & identifying strategies for addressing data which may not be conclusive
5. Parallel processes (e.g. WHO prequalification & licensure)
6. Plan for supply needs
7. Plan for financing
8. Multi-partner collaboration & dialogue with countries
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Carol Marzetta, Applied Strategies
Vaccine Introductions in Bangladesh

a regional leader for vaccine intros

- Overall, among all Gavi countries, a slow vaccine introducer
- However, historically disease burden in Asia has been unclear
- Thus, regionally an early introducer—amongst the first in Asia to introduce penta & PCV
Vaccine Introductions in Bangladesh

About 8.7 years from Gavi window opening (May 2000) to 1st country intro (Jan 2009)

Country’s data helped jumpstart other regional intros

100% target coverage reached in Dec 2009

1st shipment-Dec 2008

Gavi Board approval

VIG disbursed

Baqui et al. case-control study published

Began impact evaluation for penta

Submitted Gavi application (w/ projected Jul 2003 intro)

1st SAGE recommendation

1998

Jan 2000

May 2000

2006

Apr 2007

Jul 2007

Mar 2008

Aug 2008

Jan 2009

About 12.6 years from 1st WHO recognized NRA licensure (July 1996) to 1st country intro (Jan 2009)