Economic evaluation of combination vaccines

A checklist for assessing their benefits and challenges

While new combination vaccines could be highly valuable to pediatric immunization programs worldwide, vaccine manufacturers have lacked clear guidance for their development and policy bodies have faced challenges in making informed decisions about their introduction and use. In addition, economic evaluations have not assessed the full array of benefits and risks associated with combination vaccines. As part of a broader effort to identify and prioritize high-potential new routine combination vaccines for children, PATH and the World Health Organization (WHO) researched and identified new approaches to measure the full economic value of combination vaccines. The resulting new checklist tool provides analysts with a way to more clearly, consistently, and comprehensively evaluate these vaccines.[1]

Background

Measles-rubella- and diphtheria-tetanus-pertussis-containing vaccines are universally acknowledged as the foundation of pediatric immunization programs. However, even as the number of recommended vaccines has increased, leading to increasingly more crowded immunization schedules, demand for the development of additional, new combination vaccines for children has not been prioritized by policymakers.

New combination vaccines could alleviate some of the challenges facing immunization programs—especially those in low- and middle-income countries—by providing multiple vaccines in fewer shots or immunization visits. They could also help facilitate the adoption of notable new standalone vaccines currently under development. Despite this promise, there are multifaceted barriers to developing combination vaccines, including technical feasibility, programmatic challenges, commercial uncertainties, hurdles in clinical development and regulatory approval, lack of clear policy guidance, and incomplete assessments of their value.[2]

Traditional economic evaluations often fail to capture the comprehensive benefits and challenges of combination vaccines. They may not quantify how fewer injections at an immunization visit affects acceptability and, thus, timely immunization coverage. There is also limited evidence comparing the value of combination vaccines to the delivery of multiple single-antigen vaccines, as most economic evaluations have assessed new vaccines compared to no vaccine. This approach hinders decision-makers from considering the full value of combination vaccines, potentially limiting their development and prioritization in immunization strategies.[3]

Key study findings

- New combination vaccines could ease crowded immunization programs, but existing economic evaluations do not capture the full array of their benefits and risks.
- Through a literature review and extensive consultations with health economics experts and immunization stakeholders, PATH and WHO developed a prioritized checklist of value drivers and metrics to assess combination vaccines.
- The resulting checklist can serve as a tool for analysts to value combination vaccines and help ensure these vaccines are more comprehensively assessed by decision-makers to inform investment decisions or adoption.
- This work also aims to enhance the valuation of new combination vaccines to support manufacturers with prioritizing their development.

PATH
World Health Organization

Methods

PATH and WHO aimed to develop a new tool to more effectively capture the benefits, costs, and risks of combination vaccines. The team began by reviewing the literature on economic evaluations of combination vaccines to more precisely identify and define current gaps in value assessment. Through consultations with numerous immunization stakeholders, they gathered insights regarding the key potential benefits and risks associated with these vaccines, which led to the creation of a list of value drivers and metrics for potential inclusion in future evaluations.

In this context, a "value driver" is an attribute that highlights the advantage or disadvantage of a specific benefit or cost. For example, the benefit of reducing the number of separate injections provided at a single immunization visit can be realized through the value drivers of reduced discomfort and/or improved coverage through reduced hesitancy. In turn, each value driver can be measured by distinct "metrics;" for example, the value driver of reduced discomfort can be measured by the willingness to pay to avoid that discomfort.

The team then engaged with immunization and health economics experts to prioritize and categorize these value drivers and metrics based on specific criteria to develop a checklist. The checklist was further refined at a convening of health economics experts in June 2025, and it was later endorsed by WHO's Immunization and Vaccines-related Implementation Research Advisory Committee.[4]

The team prioritized the value drivers and metrics based on four specific criteria, each organized using a traffic-light classification system (**Table 1**). Value drivers were ranked according to their resonance (perceived alignment with policy priorities) and their magnitude (estimated impact on overall value). Metrics were classified by their quantifiability (can they be measured?) and ease of integration within the existing economic evaluation frameworks (are there existing methodologies or will innovation be required?).

Table 1. Criteria used to prioritize value drivers and associated metrics.

Value drivers: Assessing resonance and magnitude of impact **Resonance:** Level of alignment with decision-makers' priorities, policy goals, and perceived needs. **Magnitude:** Expected level of influence on the value of the combination vaccine.				
Resonance classification	**Interpretation**		**Magnitude classification**	**Interpretation**
🟢	Strong alignment with decision-maker priorities		🟢	Substantial impact on value of product
🟡	Moderate alignment with decision-maker priorities		🟡	Moderate impact on value of product
🔴	Low alignment with decision-maker priorities		🔴	Minimal impact on value of product
⚫	Unclear/hard to generalize, i.e., it is product/country/context dependent		⚫	Unclear/hard to generalize, i.e., it is product/country/context dependent (requiring contextual analysis)
Metrics: assessing quantifiability and fit within existing economic evaluation frameworks **Quantifiability:** Feasibility to measure using the currently available data or methods, with a preference for primary data over modeled estimates. **Fit within existing economic evaluation frameworks:** Possibility to integrate the metric in existing evaluation methods, for example, cost-effectiveness analysis.				
Quantifiability classification	**Interpretation**		**Framework fit classification**	**Interpretation**
🟢	Data available and methods feasible		🟢	Clearly integrates with existing economic evaluation framework
🟡	Data may be available and/or methods may require innovation		🟡	May integrate with existing framework
🔴	Data not available or methods not presently feasible		🔴	Unlikely to integrate with existing framework

The combination vaccine checklist

The consolidated checklist (**Table 2**) reflects the highly valuable inputs received during the expert convening and validated by health economics experts.[1] It is meant to complement other analyses and provide a helpful tool for determining the relevant value drivers and metrics when conducting a specific combination vaccine evaluation. While some of the value drivers and metrics correspond to those used in evaluations of single-antigen vaccines, others are unique to combination vaccines. The inclusion of additional and potentially lower magnitude value drivers and metrics may change the findings of some economic evaluations of single-antigen vaccines, resulting in markedly different outcomes.

Table 2. Checklist of prioritized value drivers and metrics sorted by themes.

Value driver	Resonance	Magnitude	Associated metric	Quantifiability	Framework fit
Coverage, timeliness, and health impact					
Coverage	🟢	🟢	Coverage of focal vaccine	🟢	🟢
			Coverage of other vaccine/intervention	🟡	🟡
Timeliness	🟡	🟡	Coverage by age	🟡	🟢
Effectiveness, impact on disease burden and health	🟢	🟢	Changes in cases, hospitalizations, deaths, DALY*, QALY**, etc. attributable to focal vaccine	🟢	🟢
			Changes in cases, hospitalizations, deaths, DALY*, QALY**, etc. attributable to broader health system impacts or another vaccine introduction	🔴	🟡
Financial costs					
Overall vaccine program costs	🟢	🟢	Commodity costs	🟢	🟢
			Cold chain costs	🟡	🟢
			Supply chain costs	🟡	🟢
			Waste disposal costs	🟡	🟢
			Other vaccine delivery costs	🔴	🟢
Environmental costs	🟡	🔴	Carbon emissions	🔴	🟢
AEFI*** costs	🔴	⚫	AEFI*** costs	🟡	🟢
Cost of illness (health system perspective)	🟢	🟢	Health system direct medical costs	🟡	🟢
Cost of illness (household perspective)	🟡	🟡	Household direct medical costs	🟡	🟢
Household travel costs	🟡	🟡	Household travel costs – illness	🟡	🟢
			Household travel costs – immunization	🟡	🟢

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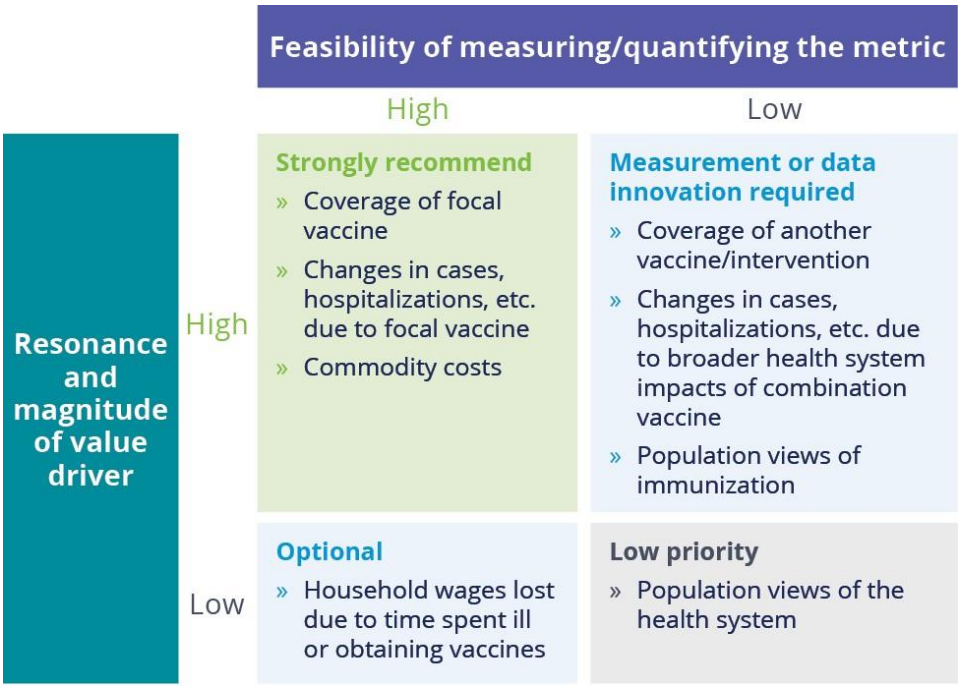
Value driver	Resonance	Magnitude	Associated metric	Quantifiability	Framework fit
Opportunity costs					
Health worker time associated with treating disease	🟢	🟡	Wages	🟢	🟢
			Health impact of next most valuable use of health worker time	🔴	🟡
Health worker time associated with immunization delivery	🟢	🟡	Wages	🟢	🟢
			Health impact of next most valuable use of health worker time	🔴	🟡
Household time associated with illness	🟡	🔴	Income	🟡	🟢
			Minimum wage	🟢	🟢
			Value of time spent outside of work (e.g., leisure time)	🔴	🟢
Household time associated with immunization	🟡	🔴	Income	🟡	🟢
			Minimum wage	🟢	🟢
			Value of time spent outside of work (e.g., leisure time)	🔴	🟢
Country autonomy over schedule	🟢	🟡	Country willingness to pay to maintain schedule autonomy	🟡	🟢
Beneficiary experience					
Pain, comfort, and anxiety	🟡	🟡	Willingness to pay to avoid an injection	🟡	🟢
Perception of vaccination	🟢	🟢	Population share with positive views of immunization	🟡	🟡
Perception of the health system	🟡	🟡	Population share with positive views of the health system	🟡	🔴
Safety					
Errors	🟡	🔴	Coverage	🔴	🟢
			Costs of errors	🟡	🟢
			Health impact of next most valuable use of lost health worker time	🔴	🟢
AEFI***	🟡	🟡	Number and severity of reported AEFI***	🟡	🟡
Equity					
Equity	🟢	🟡	Coverage by group (e.g., high-risk populations, sociodemographic breakdown based on gender or income)	🟡	🟡
			Coverage in geographically isolated areas	🟡	🟡
			Averted catastrophic health expenditure/improved financial protection	🟡	🟡

**DALY: Disability-adjusted life year or the loss of the equivalent of one year of full health; **QALY: Quality-adjusted life year or the equivalent of one year in perfect health, accounting for quality of life; ***AEFI: Adverse event following immunization.*

Limited resources for analyses of specific combination vaccines may necessitate prioritizing the most critical value drivers and metrics and their underlying data for decision-makers. The checklist is intended to facilitate that process by indicating which value drivers decision-makers might find most informative and which metrics are most feasible for inclusion in an evaluation.

Figure 1. Illustrative example of a prioritization matrix.



The value drivers and metrics classified as green across all four dimensions indicate a high priority for inclusion in combination vaccine evaluations. If a value driver is green for resonance and magnitude, but orange or red for quantifiability and framework fit, it signifies strong interest from decision-makers but uncertain feasibility for inclusion and a potential research gap. Conversely, value drivers rated as orange or red for resonance and magnitude, combined with a green for quantifiability and framework fit, indicate low to moderate interest but higher feasibility of inclusion in analyses. **Figure 1** shows an illustrative example of a matrix showing value drivers and metrics alongside their score based on the various prioritization dimensions.

Conclusion

Due to global economic and geopolitical factors, pediatric routine immunization programs face increasing pressure to achieve more with limited resources. One effective strategy to support the ongoing and expanded use of vaccines, especially as additional new vaccines are developed and recommended for use, is the development and adoption of new combination vaccines. Despite their potential, the current literature does not capture the full value of these combination vaccines. This checklist of prioritized value drivers and metrics provides a new tool for developers, stakeholders, and decision-makers to consider the comprehensive economic value of combination vaccines and help inform investment decisions or adoption. While new combination vaccines will also require broader assessments of their potential feasibility and acceptability, this approach to providing improved economic evaluations may be helpful for increasing demand for their development.

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