

Taxonomy of the Full Value of mRNA Influenza and COVID-19 Combination Vaccines for Adults

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INTRODUCTION

Vaccines confer benefits not only on population health and health systems but also on the broader economy and society.^{1,2}

Recommendation and reimbursement decisions should reflect vaccines' full value. Full value taxonomies (FVTs), which specify the elements of this full value, support improved coverage decisions by facilitating the consideration and quantification of all the value elements. Multiple mRNA seasonal influenza and COVID-19 combination vaccines ("mRNA combination vaccines") are under clinical investigation and may soon be the subject of recommendation and reimbursement decisions. No FVT exists for these vaccines, and existing taxonomies may inadequately represent the full value of these mRNA combination vaccines.

OBJECTIVE

Develop a full value taxonomy (FVT) for mRNA seasonal influenza and COVID-19 combination vaccines based on the results of a targeted literature review (TLR).

METHODS

We (1) defined six relevant literatures (denoted L1-L6), (2) selected six reference studies²⁻⁷ representing recent, high-quality, and prominent value taxonomies (spanning L1-L3), (3) used forward snowballing to find L1-L3 studies published after the reference studies, (4) used targeted PubMed searches within L4-L6 to identify value elements excluded from existing value taxonomies, (5) conducted title and abstract reviews of 1671 studies and full text reviews of 79 studies, and (6) used our expert judgment to synthesize the results of 33 studies into a FVT of adult mRNA combination vaccines (**Table 1**).

METHODS (continued)

Literatures Reviewed

- L1: General (i.e. vaccine-agnostic) taxonomies of the full value of health technologies and vaccines.
- L2: Taxonomies of COVID-19's full burden or of COVID-19 vaccination's full value.
- L3: Taxonomies of seasonal influenza's full burden or of seasonal influenza vaccination's full value.
- L4: Individual studies of aspects of the full burden of COVID-19 or seasonal influenza, or aspects of the full value of COVID-19 vaccination or seasonal influenza vaccination, that are not captured in L1-L3.
- L5: Any studies that describe distinctive value of combination vaccines in general, and combination COVID-19 and influenza vaccination in particular.
- L6: Any studies that describe distinctive value of mRNA vaccines in general, and COVID-19 or influenza mRNA vaccines in particular.

RESULTS

Table 1. Full Value Taxonomy of mRNA Influenza and COVID-19 Combination Vaccines for Adults

	Narrow health-related values	Broad societal values
Traditional values	<p>1.1. Health outcomes related to disease manifestations of the vaccine-targeted pathogen and to the vaccine</p> <p>1.1.1. Direct health effects (mortality, morbidity, vaccine adverse effects)</p> <p>1.1.2. Indirect health effects (e.g., herd effects)</p> <p>1.2. Health system costs</p> <p>1.2.1. Direct costs borne by health system payers</p> <p>1.2.2. Vaccination program costs</p>	<p>2.1. Financial costs of seeking and receiving healthcare borne by patients, unpaid caregivers, households, and other non-health system payers</p> <p>2.2. Productivity costs faced by patients, unpaid caregivers, households, and firms</p> <p>2.3. Other time costs of seeking and receiving care faced by patients, unpaid caregivers, and households</p> <p>2.4. Costs of social services and social care</p>
Novel values	<p>3.1. Individual-related values</p> <p>3.1.1. Process utility (e.g., convenience and reduced fear of needles due to combined dose)</p> <p>3.1.2. Adherence-improving values given the simplified schedule</p> <p>3.1.3. Immune interactions (e.g., complementarity or interference)</p> <p>3.1.4. – 3.1.9. Non-specific/off-target effects; Interactions with comorbidities; Caregiver and family health; Patient preferences; Health risk protection; Peace of mind</p> <p>3.2. Public health-related values</p> <p>3.2.1. – 3.2.6. Other transmission values; Control of disease; Antimicrobial resistance; Health security; Variant control; Public health costs</p> <p>3.3. Societal preferences regarding health</p> <p>3.3.1. Health equity-, disparity-, and priority-related values</p> <p>3.3.2. – 3.3.5. Burden of disease; Autonomy; Fair innings; Inclusivity and access</p> <p>3.4. Health system-related values</p> <p>3.4.1. Health care worker-related benefits (reduced injuries, provider preferences)</p> <p>3.4.2. – 3.4.10. Health system strengthening, resilience, and security; Reduced nosocomial infections; Foregone care (demand- and supply-side); Financial sustainability; Health-related R&D; Litigation costs; Future unrelated health system costs; Public trust in the health system; Externalized health system costs</p>	<p>4.1. Economic values</p> <p>4.1.1. Individual-level economic values: consumption, leisure, financial risk protection, education, net income and wealth, caregiver and family impacts (e.g., well-being, adaptation of the home to the patient's needs, babysitting needs, care and support utility)</p> <p>4.1.2. Macro-level economic values (e.g., GDP, economic growth, fiscal effects)</p> <p>4.2. Non-economic values</p> <p>4.2.1. Broader aspects of individual well-being (e.g., happiness, social well-being, meaning and purpose)</p> <p>4.2.2. Macro-level non-economic values</p> <p>4.2.2.1. Social preferences (equity, fairness)</p> <p>4.2.2.2. Government (e.g., international commitments)</p> <p>4.2.2.3. Environment</p>

DISCUSSION

Many key mRNA combination vaccine values are traditional narrow values:

1. **Faster development times for mRNA vaccines** allow for improved strain matching and increased vaccine effectiveness, which improve health outcomes (1.1) and reduce direct costs (1.2.1).
2. **Simplified vaccine schedules** increase patient uptake, acceptability, and timely compliance with vaccine schedules; and reduce doses. This also improves health outcomes (1.1) and reduces direct costs (1.2.1).
3. **Targeting multiple pathogens with common clinical syndromes** improves health outcomes (1.1).
4. **Reduced doses** reduce vaccine program costs, including from reduced materials costs and streamlined ordering and delivery (1.2), and adverse effects (1.1.1); Reduced doses also implicate novel narrow values, e.g., process utilities (patient convenience; reduced anxiety and trauma from fear of needles, 3.1.1), adherence (3.1.2), equity in coverage and health outcomes (3.3.1), health worker benefits (provider satisfaction, acceptability, and convenience; fewer needle-stick injuries, 3.4.1).
5. **mRNA technology** may have increased cold storage requirements and adverse events risk, and faster waning, affecting vaccination program costs (1.2.2), health outcomes (1.1), and direct costs (1.2.1).

Many important value attributes can be accommodated into existing economic evaluations without having to adopt a broad perspective or innovate beyond standard cost-utility analysis. Quantifying some novel narrow and broad values may require advances in modeling, empirical research, and economic evaluation methods.

CONCLUSIONS

- **mRNA combination vaccines can provide health, economic, and other benefits to individuals, health care systems, and society in general.**
- **A full value taxonomy can inform the development of policies and implementation strategies related to mRNA combination vaccines.**

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