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The Need for Novel Approaches in Assessing the Value of COVID-19 Vaccines

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Numerous coronavirus disease 2019 (COVID-19) vaccine development programs are under way, and several vaccines with potentially differing clinical and manufacturing profiles are expected to reach the market.¹ We argue for the need to adopt new approaches for assessing the value of COVID-19 vaccines, calling for clinical, manufacturing, and cost aspects to be complemented by societal value considerations to inform the vaccines' further development, reimbursement, and pricing decisions.

DISEASE, MANUFACTURING, AND CLINICAL VALUE ASPECTS

The World Health Organization² (WHO) has published Target Product Profiles for minimally acceptable and preferred COVID-19 vaccine profiles to guide their clinical development for high-risk populations and outbreaks. Aspects of value considered in WHO Target Product Profiles relate to target population,

posology, formulation, production, efficacy, and safety, as illustrated in the top branches of Figure 1, together with examples of relevant indicators for assessing product performance.

Clinical end points for COVID-19 range from infection protection to modification of viral replication and disease; the most commonly used are protection from infection as defined by seroconversion and prevention of clinical symptomatic disease, including decrease in need for high-intensity medical care and hospitalization.³ In terms of safety, vaccine-induced infection severity is a critical concern for all vaccines; together with antibody-dependent enhancement of viral replication and vaccine-associated enhanced respiratory disease, they have been suggested to be potential risks associated with COVID-19 vaccine development. Durability of clinical effects, product stability, and storage characteristics, including distribution and cold-chain requirements, are also crucial to consider.³ Supply chain, logistics, and service

delivery infrastructure account for the largest cost share of existing immunization programs in low- and middle-income countries, with human resources and cold-chain equipment and overhead constituting the largest portion of such non-vaccine-related cost at the health system level.

ECONOMIC AND SOCIETAL VALUE ASPECTS

The WHO Target Product Profile focuses on vaccines' effects, together with product quality and manufacturing and disease population aspects. Once a new vaccine is authorized or approved by regulatory agencies, direct costs form a key consideration in reimbursement and pricing decisions by payers and insurance bodies (Figure 1). Traditionally, pricing and reimbursement decisions for new health interventions are informed with economic evaluations that focus on cost per health outcome metrics per patient, failing to account for vaccines' full societal benefits contributed to the community.⁴

A societal perspective considers socioeconomic implications beyond clinical outcomes and costs, to capture additional benefits and contextual considerations.⁵ These relate to burden of disease (e.g., disease severity and unmet need), equity (distribution of health benefits in the population, e.g., in terms of age, sex, gender, health status, and welfare), innovation (e.g., mechanism of action, spillover effects enabling further product development), indirect costs (e.g., absenteeism, presenteeism, early retirement), public health benefits, financial risk benefits, and fear of contagion benefits; the latter three value aspects are specific to prophylactic interventions such as COVID-19 vaccines, capturing broader societal benefits for the entire population at risk.

FIGURE 1— Disease, Manufacturing, Clinical, Economic, and Societal Value Aspects for Coronavirus Disease 2019 (COVID-19) Vaccines With Examples of Performance Indicators for Their Assessment

Note. TPP = Target Product Profile; WHO = World Health Organization.

Public health benefits relate to reducing the risk of developing and transmitting a disease among healthy individuals (including the population not receiving the intervention), effectively reflecting a societal value dimension for physical risk reduction and prevention and also accounting for any herd immunity effects.⁵ For

example, the effect of a new COVID-19 health intervention against such a value aspect may range from no risk reduction (e.g., for a symptomatic pharmacological treatment), to reduction of prevalence risk factors, to reduction in transmission, to prevention and prophylaxis from the disease (e.g., for an effective vaccine).

Protection against financial implications is complementary to the physical risk reduction and prevention aspects of public health benefits for the population at risk (i.e., healthy individuals).⁶ For example, the relevant financial implications for the population at risk may range from health care expenses resulting after becoming infected and

needing medical attention to productivity losses resulting from physical and social distancing measures such as travel bans and public quarantines, which became nearly universal in COVID-19. Once new COVID-19 vaccines become available, their protective effect on this value aspect could be measured by the amount of financial expenditures avoided or gains accumulated as a percentage of income—for instance, by determining the difference with earlier waves of the disease. Together, these two aspects of physical risk reduction and financial protection have been referred to as “insurance value.”⁶

Fear of contagion benefits relating to emotional risk reduction and prevention is another relevant societal value component.⁶ Fear of contagion corresponds to the emotional state of stress or anxiety because of the risk of future exposure to and spread of a disease. This includes the fear of a disease's non-health-related consequences, such as fear of staying in quarantine for an extended time or the actual stress or anxiety once quarantine has been imposed. Given that COVID-19 poses a universal health risk and that the non-health-related consequences are relevant for everyone, such an emotional state affects the entire society (including healthy populations), and evidence already suggests that psychological effects and mental health burden from COVID-19 are widespread. Therefore, vaccine benefits include reduction of emotional risk as a result of decreased anxiety and worry because of less uncertainty in future outcomes.⁴

MEASUREMENT OF COVID-19 VACCINES' VALUE

Multiple criteria decision analysis (MCDA) allows appraisal of COVID-19

vaccines on disease, manufacturing, clinical, economic, and societal aspects by quantifying their values, trade-offs, and uncertainties.⁷ MCDA has been advanced for drug benefit-risk assessment by the European Medicines Agency⁸ and has been recommended as a methodology for consistent decision-making across the life cycle of new drugs by the US National Academies of Sciences, Engineering, and Medicine.⁹ The US Institute of Medicine has successfully applied MCDA in vaccine development to inform funding decisions by public health payers,¹⁰ and it has been recommended by the WHO and European experts for transparently presenting and integrating vaccines' health economic evidence to support decision-making.¹¹

MCDA can incorporate societal values to inform resource allocation decisions in two main ways. First, a cost per health outcome threshold could be extrapolated proportionally to how much of the MCDA model's weight corresponds to non-health-related outcome value components, to create an extended value threshold. In practice, the establishment of a standardized and comprehensive value function accounting for all technologies could be required, mapping out a conversion of an economic evaluation threshold to an MCDA value threshold. For this, the value of a COVID-19 vaccine would need to be estimated against other health interventions, which can be informed through large-scale surveys of public preferences with established methodologies such as discrete choice experiments. Second, vaccines' purchasing costs could be used to derive cost-value ratios to inform resource allocation decisions within a fixed budget, similar to a portfolio optimization approach. The latter approach could also

accommodate a reduction in the “acceptable” cost of the vaccines if this were deemed ethically or practically necessary—for example, as recommended in buying their patent rights and dropping their price to convert them into global public goods.¹²

CONCLUSIONS

Novel approaches are needed to measure the value of COVID-19 vaccines for development, reimbursement, and pricing decisions. Resource allocation in vaccine development should be conducted with WHO Target Product Profiles as guidelines while considering the potential trade-offs among candidates when ideal Target Product Profile levels cannot be reached. For reimbursement and pricing, the value of any COVID-19 vaccine extends beyond health outcomes and costs, encompassing wider societal benefits that ideally need to be evaluated with public preferences to inform access policies and maximum vaccine prices. Only in this way can the evaluation processes capture, rigorously and transparently, what matters most to the relevant experts and societies as a whole. *AJPH*

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CONTRIBUTORS

A. Angelis wrote the original draft of the editorial. All authors contributed to the conceptualization, review, and editing of the editorial.

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CONFLICTS OF INTEREST

A. Angelis is cofounder of a software company developing tools for better decision-making in health care evaluation. T. Tervonen is employed by Evidera Ltd.

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