

Economic Evaluation of Covid-19 Vaccines: A Literature Review

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Abstract. The Covid-19 epidemic and virus variants affect public health security worldwide continuously. Conducting Covid-19 vaccination economic evaluation by measuring the cost and outcomes helps governments or healthcare departments choose a better policy or adjust the vaccination policy periodically. We systematically reviewed the health economic evaluation studies on different immunization policies of vaccines in Covid-19. It is found that the existing studies still need to be improved. For model design, studies lack compelling predictions of dynamic transmission between epidemiological regions; for parameters, researchers reduce the selection of related indexes in cost calculation to simplify the model; for data collection, some research needs real-world data support. Therefore, comparative research should be conducted more dynamically and sustainably by improving the evaluation's quality and promoting standards and conclusions to strengthen the guiding role of vaccination economic evaluation in policy selection.

Keywords: Covid-19 Vaccine; Vaccination Strategy; Economic Evaluation; Systematic Review.

1. Introduction

The novel coronavirus outbreak at the end of 2019 has seriously endangered global health and triggered significant public health emergencies worldwide. In February 2022, the World Health Organization (WHO) named the pandemic Corona Virus Disease 2019 (Covid-19). The pathogen infection of SARS-CoV-2 has been proven to be the leading cause of it (Chen et al. 2020; Emrani et al. 2021; Wang et al. 2020). Because SARS-CoV-2 is a forward single-stranded RNA virus, the mutation rate turns relatively high (Fan et al. 2022). From May 2020 to the present, SARS-CoV-2 variants have been found in South Africa, the United Kingdom, Brazil, India, Peru, and other places. Virus variation has brought more uncertainty for epidemic prevention and control. According to WHO statistics, as of November 2022, there had been more than 630 million confirmed cases and more than 6.58 million deaths worldwide. (WHO. WHO Coronavirus (Covid-19) Dashboard [EB/OL]. (2022-11-10) [2022-11-14]. <https://Covid19.who.int/>).

Vaccination is one of the more effective ways to prevent and control the epidemic (De Salazar et al. 2021). Vaccines based on multiple technology platforms are being developed, approved for emergency use, or marketed, for instance, DNA, RNA, inactivated, recombinant protein subunit, viral vector, and virus-like particle vaccines. Up to November 2022, more than 12.885 billion doses of vaccine had been administered worldwide, and 63.85% of the population had received at least one dose of the Covid-19 vaccine (World Health Organization. Tracking SARS - CoV - 2 variants [EB/OL]. (2022-11-10) [2021-12-14]. <http://www.who.int/en/activities/tracking-SARS-CoV-2-variants/>).

However, the global availability of licensed vaccines is insufficient to control Covid-19 (Wang et al. 2022). The continued mutation of the virus has caused reduced vaccine efficacy (Fan et al. 2022) and caused problems such as vaccine-induced immune escape (Cox et al. 2022). Therefore, when governments carry out vaccination campaigns, especially with limited vaccine resources, it is essential to prioritize vaccination by measuring different vaccination policies (Hagens et al. 2021).

The economic evaluation of vaccination in Covid-19 is one policy tool for dealing with the above requirements. Studies have been conducted in some countries or regions to execute the economic evaluation of the Covid-19 vaccination campaign. This study aims to systematically review these research progresses, provide information for further promotion of the economic evaluation of vaccines in Covid-19, and formulate economic, appropriate, feasible, and good prevention and control effects of health intervention policies.

2. Theoretical Perspectives

Economic evaluation is the comparative analysis of alternative courses of action in terms of costs and consequences. With increasing healthcare expenditures and limited resources, it is crucial to consider the economic impact of their interventions (Rudmik and Drummond 2013). The main types of economic evaluation are cost-effectiveness analysis(CEA), cost-utility analysis (CUA), and cost-benefit analysis(CBA)(Rai and Goyal 2018). Their costs are measured in monetary terms, meaning the outcome is evaluated differently(Higgins and Harris 2012).

Cost-effectiveness analysis (CEA) is used increasingly in medicine to determine whether the health benefit of an intervention is worth the economic cost(Díez et al. 2021). It is used to achieve defined plan objectives, such as non-monetary health outcome measures (e.g., saved lives and prevented cases), at the lowest cost. CUA is a development of CEA, evaluated as a unit of disability-adjusted life years (DALYs). The method is used to express preferences or choices for different health outcomes to reflect the importance of this health outcome(Hunter et al. 2015). CBA is an analytical technique that quantifies the relationship between a health intervention's net cost and net benefit, and both are expressed in monetary units(Weaver, Bischoff-Ferrari, and Shanahan 2019).

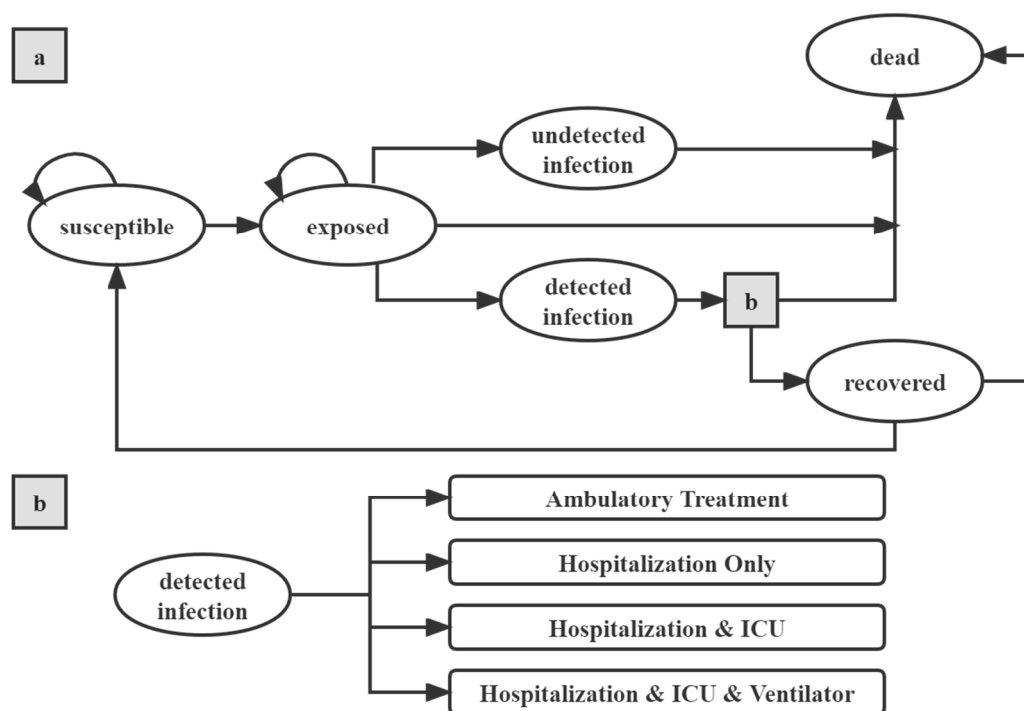
Nevertheless, because it is challenging to convert clinical results of quality of life into monetary units and the operation is complex, the application of CBA in results research of medical intervention measures is limited(Higgins and Harris 2012). The incremental method is usually adopted for health economic evaluation. The difference in cost and result between two or more interventions is expressed as the incremental cost-effectiveness ratio (ICER)(Wu et al. 2021). The above evaluation methods of health economics are all reference tools for policymakers before health resource allocation, but they do not constitute the only criteria for health resource allocation.

3. Methods of Empirical Analysis

The CEA, CUA, and CBA methods have been applied in the economic evaluation of vaccination in Covid-19. Among them, more articles are published by scholars in the United States, China, and the United Kingdom and more in Europe, Southeast Asia, and South America. The related studies on the economic evaluation of vaccination in Covid-19 are characterized by cross-regional cooperation.

The research contains diverse perspectives, such as social perspective(Fu et al. 2022a, 2022b; Jiang, Cai, and Shi 2022; Orangi et al. 2022; Wang et al. 2022), sanitation-system perspective(Fernandes et al. 2022; Li et al. 2022b; Morales-Zamora et al. 2022; Padula et al. 2021), as well as the mixed one(Lopez et al. 2021).

The research model involves two components, as figure 1 shows: (a) An epidemiological model is developed to estimate age-stratified incidence and deaths of Covid-10 infection under different vaccine characteristics and vaccination strategies scenarios, as *Part A* illustrates. The transmission model is developed based on SEIR(susceptibility-exposure-infection-rehabilitation model) (Debrabant, Gronbaek, and Kronborg 2021; Orlewska, Wierzba, and Sliwczynski 2022; Padula et al. 2021; Wang et al. 2022; Xiong et al. 2022), SIRD(susceptibility-infection-rehabilitation-death model) (Hagens et al. 2021; Kohli et al. 2021; Morales-Zamora et al. 2022), dynamic differential equation model for clinical and economic analysis of intervention (Debrabant et al. 2021). (b) Use the Decision Tree-Markov Model or its modified one to stratify the *Defected Infection* compartment, as *Part B* shows. The Defected Infection is divided into four genres, ambulatory treatment, hospitalization only, intensive care unit, and intensive care unit with a ventilator(Fu et al. 2022b; Jiang et al. 2022; Li et al. 2022a). Specific epidemiology, clinical, and vaccination parameters are used in these models. The outputs from the epidemiological model are fed into the economic model to evaluate the economic consequences of different vaccination strategies.



(a) Patients progressed through a combination of the “SEIR” process and “SIRD” progress. The model was used to conduct the economic evaluation and the budget impact model.
(b) Probability tree linking transitions from the “detected Infection” state in the Markov Model. Arrows represent the movements between the health states.

Figure 1. Markov Model Diagram of disease progression with Covid-19

The detailed indicators are shown in table 1, including direct medical, non-medical, and indirect costs (Wang et al. 2022). The level of protection of the vaccine is distinguished according to the single dose and double dose, wherein the hypothetical threshold for the effectiveness of a single dose of vaccine is 50%-70%, and the hypothetical threshold for the effectiveness of a double dose of vaccine is 90%-95% (Hagens et al. 2021; Li et al. 2022b; Wang et al. 2022). Scenario analysis distinguishes the basic situation of no vaccination, no priority vaccination, or priority vaccination. (Morales-Zamora et al. 2022). The final assessment results are described in terms of QALYs(Fernandes et al. 2022), DALYs, and ICERs(Wang et al. 2022). In addition, the period of the data panel is selected as one year(Fernandes et al. 2022; Wang et al. 2022).

Robustness check involves single-variable sensitivity analysis (such as Data Structure Analysis, DSA, and Probabilistic Safety Assessment) (Fu et al. 2022a; Wang et al. 2022) and multivariate sensitivity analysis(Morales-Zamora et al. 2022). Meanwhile, the control variables (such as vaccination coverage and social distance contact rate) should be added. Tornado charts display the sensitivity analysis results. The analysis shows that the cost-benefit result of the model was the most sensitive to the efficacy parameters of the vaccine(Morales-Zamora et al. 2022; Wang et al. 2022; Xiong et al. 2022), and vaccine supply and management costs have no significant impact on model results. However, if the loss of productivity is included in the costing, this parameter has a significant impact on the cost-effectiveness of the Covid-19 vaccine (Debrabant et al. 2021).

Table 1. Indicators for Covid-19 vaccination economic evaluation

Cost variables			Outcome variables
direct medical costs	direct non-medical costs	indirect costs	/
(a) the treatment cost	(a) cost of quarantine at	(a) the impact of social	(a) QALYs,

<ul style="list-style-type: none"> (b) the cost of real-time reverse (c) transcription polymerase chain reaction (RT-PCR) (d) personal protective equipment (PPE) for technicians (e) costs of tracing derived from literature (f) costs for transmission prevention, including face masks, disinfection agents, hygiene, and sanitizing per person per year (g) costs for the vaccination program, including vaccine price (for two doses), supply chain and logistics and (h) hospital-based administration (i) costs of treating thromboembolic events (a serious adverse event, AE) 	<p>designated facilities (including accommodation and meals for certain days)</p>	<p>distancing on the economy</p> <ul style="list-style-type: none"> (b) other control variables to control for local and global Covid-19 cases, global economic status, and other government policies (c) loss of productivity from premature death (d) sick leave 	<p>ICERs</p> <ul style="list-style-type: none"> (b) DALYs, ICERs
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Notes: (a) Direct medical costs for Covid-19 infection treatment can be retrieved from the hospital or national health e-claim databases. (b) Direct non-medical costs might be obtained from the disease control department. (c) Indirect costs referring to the impact of social distancing on the economy could be estimated using gross domestic product or the stock market index. (d) Outcome estimates can be measured in QALYs, DALYs, and ICERs according to the WHO life table records (World Health Organization. Mortality and global health estimates: Life tables by country [EB/OL]. (2022-12-06) [2020-12-06]. [https:// apps. who.int/gho/data/node. main. LIFECOUNTRY? lang=en](https://apps.who.int/gho/data/node.main.LIFECOUNTRY?lang=en)) (Fernandes et al. 2022; Wang et al. 2022).

4. Literature Results

Research shows that, firstly, if the vaccine can prevent infection, compared to not being vaccinated, the vaccine saves costs for the population. But the older the population, the lower the incremental cost-utility ratio. Secondly, if the vaccine only reduces the severity, vaccination of adults with Covid-19 could prevent more infections, vaccinate the elderly and save a DALY at a lower cost (Fu et al. 2022a; Orlewska et al. 2022; Wang et al. 2022). Giving priority to the elderly and vaccinating high-risk groups with other illnesses at the same time is the most cost-effective (Morales-Zamora et al. 2022; Orlewska et al. 2022). Thirdly, the age group analysis results can help establish vaccination priority plans (Fernandes et al. 2022). According to the priority of implementing vaccination programs for different groups, universal intensive vaccination (Li et al. 2022a) will provide maximum epidemiological and economic benefit (Morales-Zamora et al. 2022). However, the cost-effectiveness of vaccination strategies depends on the vaccine type (Orangi et al. 2022; Wang et al. 2022) and the booster policy (Mungmunpantipantip and Wiwanitkit 2022). Given the vaccine's reduced potency and the virus strain variation (Nurchis et al. 2022), the economic evaluation of the Covid-19 vaccine needs further analysis for a longer time (Fu et al. 2022a).

It is recommended that according to the changes in the epidemiological situation, the emergency vaccination plan should be formulated, and the vaccination strategies should be adjusted in time, which should also consider the type of vaccine efficiency, the level of efficacy, and the duration of protection.

5. Discussion

In the decision-making and optimization of the epidemic vaccination plan for COVID-19, economic evaluation research is conducted to promote the rational allocation of health resources and stage adjustment, thereby facilitating the effective development of epidemic prevention and control and maximizing the benefit of vaccination. However, the application of health economic evaluation in the policy process of vaccination in Covid-19 is relatively limited, and there are still some research problems that need to be paid attention to in the application of methodology:

(a) For model design, methods need to be improved, and dynamic monitoring needs to be added. The existing economic evaluation models cannot accurately predict the dynamic transmission between regions. In order to simplify the model, most studies assume no flow between regions (Morales-Zamora et al. 2022; Pearson et al. 2021). Hence, a significant gap exists between reality and study, which reduced the guidance value of economic evaluation for the Covid-19 vaccination policy.

(b) For parameters, the existing models focus on age as the primary risk group standard and take less into account the occupational differences of the population, such as healthcare workers and teachers (Orangi et al. 2022), whose occupational characteristics increase their exposure to the epidemic. Thus, the decision on vaccination priorities in Covid-19 needs to be further optimized.

(c) For data collection, due to the lack of real-world data, the existing economic evaluation research can only partially calculate the economic burden of Covid-19 disease from the perspective of the whole society. It is necessary to quantify further the cost savings achieved after vaccination, such as the indirect effects on social stability and economic recovery and development. The insufficient collection of indicator parameter data has affected the quality of decision-making references to a certain extent. It also indicates that due to the spread of the Covid-19 epidemic and the continuation of virus variation, the economic evaluation of vaccination needs to be more refined and long-term application.

Policy intervention in epidemic prevention and control of COVID-19 needs to explore further the most cost-effective vaccination strategy in the actual scene. At the same time, governments and healthcare departments must introduce diversified measures, such as promoting the R&D of oral COVID-19 vaccines and reducing unnecessary lockdowns (Fu et al. 2022a; Patenaude and Ballreich 2022). Better in this way can promote economic development and sustainable health system operation and more effectively safeguard social health.

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