# COVID-19 vaccination: a systematic review of vaccination strategies based on economic evaluation studies

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**ABSTRACT**

**Introduction: Countries must employ the most efficient way to vaccinate their population with the COVID-19 vaccines, given the vaccines' low availability compared to its demand. This review aims to identify and compare the different COVID-19 vaccine delivery strategies employed internationally in the recent year based on the economic evaluation findings and subsequently to recommend the most cost-effective strategy among them.**

**Material and Methods: A systematic review was conducted by examining online databases (Scopus, MEDLINE and Science Direct) to identify health economic evaluation studies of COVID-19 vaccines. Critical appraisal of studies was conducted using the Consolidated Health Economic Evaluation Reporting Standards (CHEERS).**

**Results: A total of nine studies were selected for analysis. Results show two strategies that were cost-effective compared to its comparators: mass vaccination program compared to no vaccination and universal vaccination approach compared to a risk-stratified vaccination approach. Several other strategies were found to increase the cost-consequences in the COVID-19 vaccination program: higher vaccine effectiveness, higher vaccination pace, increased vaccination coverage, and vaccine prioritisation for an at-risk population. The study findings were restricted to analysis based on the current available data.**

**Conclusion: COVID-19 vaccination policies should aim for increased vaccine production as well as a rapid and extensive vaccine delivery system to ensure the maximal value of vaccination strategies. These results can aid policymakers in opting for the most efficient approach to vaccinating the population during this COVID-19 pandemic and future pandemic.**

**KEYWORDS:**
*Economic evaluation; cost-effectiveness; COVID-19; vaccine*

## INTRODUCTION

The coronavirus disease 2019 (COVID-19) pandemic had significantly affected the global community, infecting over 635 million people with over 6.6 million deaths as of 6 January 2023.[1] To curb the spread of infections during early stages of the pandemic, countries adopted non-pharmacological approaches such as lockdowns and social distancing policies. Unfortunately, these resulted in severe economic repercussions. In essence, lockdowns and social distancing policies resulted in reduced demand and supply of goods[2], increased unemployment as well as crisis in foreign investment[3], manufacturing, media and tourism industries.[4] It was estimated that the global unemployment in 2020 was 114 million jobs[5] with the loss of global working hours at around 8.8%, which was approximately four times greater than during the global financial crisis in 2009.[5] The global merchandise trade volume was expected to fall by 9.2% in the year 2020.[6] Additionally, the world tourism lose up to USD 1.2 trillion from the pandemic.[7] The projected loss of revenue for the global sports industry in 2020 was estimated around 57% from 2019 revenue, equivalent to USD 73.7 billion.[8] Consequently, the global gross domestic product (GDP) in the year 2020 was estimated to contract by 5.2%.[9] Worse still, the economic impact of COVID-19 was not uniform across countries and population groups.[2] The estimated GDP contraction from the pandemic varied between countries as follows: for low-income countries GDP contracted as by 5.2%, middle-income countries (8.7%) and high-income countries (6.4%).[9] Across population groups, women 10, people with low education[5], low-skilled workers[5] and the low-income population were severely impacted by COVID-19.[11,12] Small-and medium-sized businesses were severely affected.[13]

The COVID-19 pandemic and the non-pharmacological approaches to controlling its spread also have serious impact on health and wellbeing. The World Health Organization (WHO) estimated that the total excess deaths from COVID-19 were 3 million people.[14] The COVID-19 pandemic was expected to contribute towards undernourishment of up to 132 million people around the world in 2020.[15] Globally, around 100 million people were expected to fall into extreme poverty.[16] The prevalence of depression during COVID-19 was expected to be 25%, higher than the global estimate at 3.44%.[17] School closures had forced 1.2 billion students to be out of school.[18] Hence, the best way out of this calamity is to vaccinate the world population.

### COVID-19 Vaccines

COVID-19 vaccines are imperative to prevent serious illness[19], reduce hospitalisation, thus saving lives and costs.[20] COVID-19 vaccination is expected to ease social restriction measures[21], therefore people can resume near-normal daily activities and revive the economy.[22] Hence, vaccination is critical for global economic recovery.[23] Revival of the

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economy is an important aim for the world population as better economy is associated with higher life span, healthier children, fewer disabilities and mortalities.[24] Thus, COVID-19 vaccination is expected to be of high value to society. For instance, it was estimated that installed capacity for 3 billion annual vaccine courses for COVID-19 is associated with a global benefit of USD 17.4 trillion, equivalent to USD 5800 per course.[25]

By the end of 2020, there were already COVID-19 vaccines manufactured to be distributed to the world population. However, the global demand for vaccine exceeded the supply.[26] For some countries, despite vaccine availability in global market, governments were facing issues with vaccine costs27 and securing finances for vaccine purchase.[26] As a result, these issues warranted countries to find the most efficient way to achieve allocation efficiency. In general, immunisation strategies selection depends on the goal of vaccination; for example, routine vaccination given to a specific population cohort aimed for elimination or containment of certain disease[28], mass vaccination strategies targeted a large number of population, aimed for rapid containment of a disease during an emerging or ongoing epidemic, or specific immunisation campaign targeted for any disease not included in routine immunisation or for specific additional population groups.[28]

Within the context of existing knowledge, several factors influence the overall outcome of COVID-19 vaccination. The fundamental factor is the vaccine efficacy. The recommended efficacy of a COVID-19 vaccine was set at a minimum of 50% in order to be licenced for use[29], 70% efficacy for epidemic prevention, and 80% to end an epidemic without any other public health measures.[20] In addition, the benefits of any COVID-19 vaccine will also depend on vaccination coverage[20,30], and the pace of vaccination.[20] Within the constraints in vaccine supply, obtaining an optimal reduction in mortality and morbidity can be achieved by prioritising vaccination for people at higher risk for severe COVID-19 disease, in particular, the elderly.[30,31] The environmental condition also affects the outcome of COVID-19 vaccination, in particular, introducing the vaccine at the time of low COVID-19 community transmission rate will produce more desirable outcome in disease and mortality reduction.[32]

Vaccination strategies permit countries to provide effective vaccination policies to produce the optimal output in terms of reduction of disease and deaths from COVID-19.[25] The selection of vaccination strategies to achieve allocative efficiency requires careful planning and evidence-based decision-making.[28] Hence, evidence from economic assessment is fundamental to make these informed decisions.[28]

**Health Economic Evaluation**

An economic evaluation is a systematic approach to compare the cost and consequences of two or more alternative interventions to foster accountability and transparency in decision-making.[33] Several types of economic evaluation studies include cost-minimization analysis (CMA), cost-effectiveness analysis (CEA), cost-utility analysis (CUA), and cost-benefit analysis (CBA).[33] In economic evaluation, the main focus is on which alternative intervention provides the best value for the resources spent? Conducting economic evaluation studies in the COVID-19 vaccination program allows policymakers to determine the value of different vaccination strategies for appropriate program planning.

In economic evaluation, a perspective is the point of view adopted when deciding the types of costs and health benefits to be included.[34] For instance, the payer perspective usually includes the cost of medical treatment and relevant social and clinical services[34] while the societal perspective encompasses all direct and indirect costs borne by the provider, payer, and patients.[34]

The cost-consequences of an economic evaluation are described in several ways. The results of a CEA are commonly expressed as incremental cost-effectiveness ratio (ICER) using the formula.

ICER= (Cost for intervention A - Cost for intervention B) / (Effectiveness for Intervention A - Effectiveness for intervention B)

In essence, the ICER describes the additional costs that an intervention imposes over another compared to the additional benefits it delivers.[35] If a new intervention (intervention A) is less costly and more effective than the comparator (intervention B), intervention A is described as cost-saving or dominant.[35] However, if intervention A is more costly yet more effective than B, then the ICER value can objectively determine how much more costly intervention A is from B compared to the extra benefits that intervention A can give.[36] Ultimately, the decision to select the new intervention will depend on how much value the provider, patient, or society is willing to pay for additional effectiveness obtained from a new intervention.[37] A similar concept is also applied to the incremental cost-utility ratio (ICUR), except that the measure of consequences in ICUR is the utilities – either quality-adjusted life years (QALY) or disability-adjusted life years (DALY).[35]

A CBA describes both cost and consequences of an intervention in the form of monetary value.37 The results can be described as a benefit-cost ratio (BCR) which is calculated from this formula

Benefit-cost ratio (BCR) = (Total benefit) / (Total costs)

The BCR described the value of benefits obtained for every unit of monetary value spent for the intervention costs.[33] A BCR of more than one generally indicates that the total benefit value of an intervention is more than its costs.[33]

Another measure of cost-consequences is the net monetary benefit (NMB), calculated using the following formula

$$\text{Net Monetary Benefit (NMB)} = \Delta E\ \lambda - \Delta C$$

where E refers to effectiveness measure, $\lambda$ refers to willingness-to-pay and C refers to cost.[33] The NMB result of greater than zero indicates that the respective intervention is cost-effective.[37]

As countries develop their COVID-19 immunisation programs to alleviate the pandemic, there is a need to identify the strategies that provide maximum value by means of the overall cost-consequences. Hence, this review's aims are two-fold: to identify the different strategies of COVID-19 vaccination and compare them based on the economic evaluation findings and to recommend the most cost-effective strategies of COVID-19 vaccination available to date. This review addresses the question, "What are the strategies that facilitate the achievement of the optimal value from COVID-19 vaccination programs?"

## METHODOLOGY

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline was used to conduct and report this systematic review.[38] Published articles were collected from three databases: Scopus, Ebscohost/Medline and Science Direct with data search dated up to 23 June 2021. A key term search strategy was employed using the combination of the following keywords:

(cost-effectiveness OR cost-utility OR cost-benefit OR 'economic evaluation') AND (COVID-19 OR SARS-CoV-2 OR coronavirus) AND (vaccine OR vaccination OR immunisation)

Articles were selected using the following inclusion criteria: (i) conduct any economic evaluation study in the form of cost-effectiveness, cost-utility, or CBA, and (ii) available in the English language. We excluded CMA studies as CMA studies emphasise only on costs while assuming similar outcome for interventions under comparison. A reviewer (K.S) conducted the screening and selection process. All the articles in selected databases were screened, duplicates were removed and titles and abstracts were scanned for relevancy of the research questions and objectives. Articles not meeting the inclusion criteria were removed, and reasons for exclusion were noted. In the event of uncertainty, the reviewer (K.S) discussed with another reviewer (A.M) to reach a consensus related to the article selection. Study qualities were appraised using The Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement.[39]

The systematic review was based on the PICO themes – Population, Intervention (vaccination strategy), comparator and outcome (consequences)[40] when data were extracted from the studies.

Key information was collected from the selected articles using a data extraction table. The studies were then categorised into groups of strategies with similar characteristics (themes), namely i) comparing vaccination vs no vaccination, ii) vaccine efficacy/effectiveness, iii) comparison of different population strategies, iv) strategy based on anaphylaxis reaction, v) vaccine coverage and vi) pace of vaccination. In each of these themes, the studies were evaluated based on their outcome measures to determine if they are efficient or otherwise. The cost-consequences measure selected for this review can be presented as any of the following: cost-effectiveness (measured in cost-effectiveness ratio (CER), incremental cost-effectiveness ratio (ICER) or net monetary benefit (NMB), or benefit-cost ratio (BCR) and were measured at any time horizon of interest depending on the specific study. These measures were obtained from texts, tables or appendices within the selected articles.

## RESULTS

A total of nine studies met the selection criteria and requirements for our review. Figure 1 shows the search strategy process. Six studies were conducted in high-income countries.[41-46] while three were conducted within the context of middle and low-income countries.[47-49] For the cost-consequences analysis, four studies adopted provider perspective[41,42,44,48], two studies used societal perspective[43,45] and two studies applied both.[46,47] Additionally, one study specifically adopted donor perspective to demonstrate the cost-consequences of vaccination strategies in low- and middle-income countries.[49]

All studies utilised various modelling methods for the estimation of cost-consequences, in particular decision tree model[45], Markov model[42,43,46], microsimulation model[48,49], continuous-time model[41] or transmission model.[44,47] All studies analysed estimated direct costs, referring to the costs of vaccine purchase and delivery system as well as the costs from managing COVID-19 infections (including hospitalisations and critical care). On the other hand, some studies also include indirect costs, referring to productivity loss from loss of work days from attending vaccination and experiencing vaccine side effects[46] or COVID-19 infections[43,46,47] and productivity loss from premature deaths.[47] The time horizon of selected studies ranges from 180 days or 6 months[41,46], 1 year[42,43,45,47-49] and 10 years.[44]

The studies included in this review have modelled different strategies to gain the optimal value from COVID-19 vaccination programs. These strategies include having a vaccination program versus no vaccination[41,42,43], comparing different vaccine efficacy[44,46,47,48], strategies linked to prioritisation of population at-risk for COVID-19[41,42], having a universal program versus risk-stratified program (based on anaphylaxis reaction) [45], as well as comparing different pace[48] and coverage[48,49] of a vaccination programme.

These studies have demonstrated several key findings: (i) having a vaccination policy is cost-saving or cost-effective as compared to having no vaccination programme, (ii) vaccination strategy by utilising a higher vaccine efficacy is more cost-effective, (iii) prioritising vaccination for at-risk population is cost-effective, (iv) a mass vaccination strategy is cost-effective even with the risk of anaphylaxis reaction, (v) the pace of vaccination roll-out affects cost-effectiveness and (vi) providing higher vaccination coverage is more cost-effective. The summary of studies characteristics and results are included in Table I.

### Vaccine is Cost-Saving or Cost-Effective as Compared to No-Vaccination Strategy

Several studies have documented that adopting a vaccination policy was cost-saving as compared to the absence of any vaccination strategy. In the USA, a vaccination programme was estimated to be able to reduce health costs by 90% and reduce disease burden by 50%.[43] Additionally, from societal perspective, the COVID-19 vaccination program in the USA was estimated to reduce

**Table I: Descriptive studies**

| Country | Author (Year) | Perspective | Model | Time Horizon | Cost | Cost-Consequences Measure | Results |
|---|---|---|---|---|---|---|---|
| Denmark | Debrabant et al., (2021) [41] | Provider | Continuous Time Model Based on SEIR | 6 months | Direct | ICER per life years | **Comparing different vaccination strategies vs no vaccination**<br>• Vaccination of 1.5 million persons ≥ 60 years old was cost-effective (ICER = USD 11,150/LYS)<br>• Vaccination of 1.5 million persons < 60 years old was cost-effective (ICER = USD 11, 359/ LYS)<br>• Vaccination of 900,000 persons < 60 years old & 1.5 million person ≥ 60 years old was cost-effective (ICER = USD 25, 208/ LYS) |
| USA | Padula et al., (2020) [43] | Societal | Markov Model With SEIR | 1 year | Direct Indirect | ICER per QALY | • Vaccination programme dominates the no-intervention approach (ICER = USD - 8,854/QALY) |
| USA | Kohli et al, (2020) [42] | Provider | Markov Model | 1 year | Direct | ICER per QALY | **Different vaccine strategies vs no vaccine**<br>• Vaccination using age-based prioritization scheme dominates no vaccination<br>• Vaccination using risk-based prioritization scheme dominates no vaccination<br>• Vaccination based on occupational-based prioritization was cost-effective (ICER =USD 20,000 / QALY saved) |
| USA, UK & Canada | Shaker et al., (2021) [45] | Societal | Decision-tree model | 1 year | Direct | ICER per death prevented | • Universal vaccination (vaccinating everyone irrespective of history of anaphylaxis) dominates risk-stratification vaccine strategy (people with a history of anaphylaxis reaction excluded from vaccination) (ICER = - USD 66,201/death prevented)<br>• Compared to no vaccination, a vaccination programme yield an incremental NMB ranging from £12·0 billion - £334·7 billion |
| UK | Sandman etal., (2021) [44] | Provider | Dynamic transmission model | 10 years | Direct | NMB | **Vaccination effectiveness scenario vs no vaccination**<br>• In the worst-case scenario (having vaccine efficacy of 50% and 45-week immunity duration), the NMB range between –£1·1 billion and £56·9 billion<br>• In the best-case scenario (having vaccine efficacy 95% with 3 years immunity duration), the NMB range from £12·0 billion to £334·7 billion across different physical distancing scenarios |
| Turkey | Hagens et al., (2021) [47] | Provider & Societal | Dynamic Transmission Compartmental Model | 1 year | Direct Indirect | ICER per QALY | **Comparison of vaccine effectiveness (VE) vs No vaccine**<br>• From provider perspective, having a more effective vaccine (VE on transmission (90%) & VE on disease (90%)) was cost-effective (ICER = USD 511/ QALY)<br>• From provider perspective, having a less effective vaccine (VE on transmission (45%) & VE on disease (90%)) was still cost-effective (ICER = USD 1045/ QALY)<br>• From societal perspective, utilization of both vaccines with different effectiveness were cost-saving as compared to no vaccination |

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**Table I: Descriptive studies**

<table>
<tr><th>Country</th><th>Author (Year)</th><th>Perspective</th><th>Model</th><th>Time Horizon</th><th>Cost</th><th>Cost-Consequences Measure</th><th>Results</th></tr>
<tr><td>LMIC</td><td>Siedner et al., (2021) [49]</td><td>Donor</td><td>Discrete Microsimulation Model</td><td>1 year</td><td>Direct</td><td>ICER per infection prevented and life years saved</td><td>Comparing different vaccine coverage<br>• Achievement of 20% vaccine coverage was cost-effective compared to no vaccination<br>• Compared to 20% vaccine coverage, increment of vaccine coverage to 50% was cost-effective with increasing ICER<br><table><tr><th>Vaccine coverage</th><th>ICER/Infection prevented</th><th>ICER/YLS</th></tr><tr><td>20%</td><td>USD 20</td><td>USD 250</td></tr><tr><td>30%</td><td>USD 40</td><td>USD 870</td></tr><tr><td>40%</td><td>USD 80</td><td>USD 2,820</td></tr><tr><td>50%</td><td>USD 150</td><td>USD7,240</td></tr><tr><td>70%</td><td>USD 760</td><td>USD 41,900</td></tr></table>• Vaccination coverage of 67% of the population was cost-saving as compared to no vaccination</td></tr>
<tr><td>South Africa</td><td>Reddy et al., (2021) [48]</td><td>Provider</td><td>Dynamic state-transition Monte-Carlo Microsimulation Model</td><td>1 year</td><td>Direct</td><td>ICER per life years saved</td><td>Comparison of different vaccination coverage vs 40% coverage<br>• Vaccine coverage 67% was cost-effective compared to 40% vaccination coverage (ICER = $9,960/YLS)<br>• Vaccination coverage 80% showed an estimated ICER of $4,270/YLS compared to 40% vaccination coverage</td></tr>
<tr><td>Israel</td><td>Wang et al., (2021) [46]</td><td>Provider and Societal</td><td>Markov model with SIR approach</td><td>180 days</td><td>Direct<br>Indirect</td><td>BCR (with effectiveness measure in QALD)</td><td>Comparison of different vaccine pace scenario vs no vaccination<br>• Vaccination pace of 150,000 vaccination/day dominated the no vaccination strategy<br>• 200,000 vaccination/day was dominated lower vaccination pace<br>• 300,000 vaccination/day dominates lower vaccination pace<br>• Vaccination utilizing any vaccine with a coverage rate of 70% was dominant against no vaccination<br><br>Benefit–cost ratio of different vaccines<br>BCR1: Saving on medical cost divided by the direct cost of vaccine (provider perspective)<br>BCR2: Saving on the (direct medical cost + indirect cost) divided by direct cost of vaccine (societal perspective).<br>BCR: Cost saving on (direct medical cost + indirect cost + economic impacts of productivity + education loss) divided by investment on vaccine.<br>BCR4: Benefit from life saved from vaccination divided by investment on vaccine.<br><table><tr><th></th><th colspan="3">Vaccine</th></tr><tr><th></th><th>Moderna</th><th>Pfizer</th><th>Astra Zeneca</th></tr><tr><td>BCR1</td><td>2.79</td><td>4.77</td><td>7.21</td></tr><tr><td>BCR2</td><td>6.05</td><td>10.39</td><td>14.46</td></tr><tr><td>BCR3</td><td>13.54</td><td>23.32</td><td>28.85</td></tr><tr><td>BCR 4</td><td>175.84</td><td>23.32</td><td>28.85</td></tr></table></td></tr>
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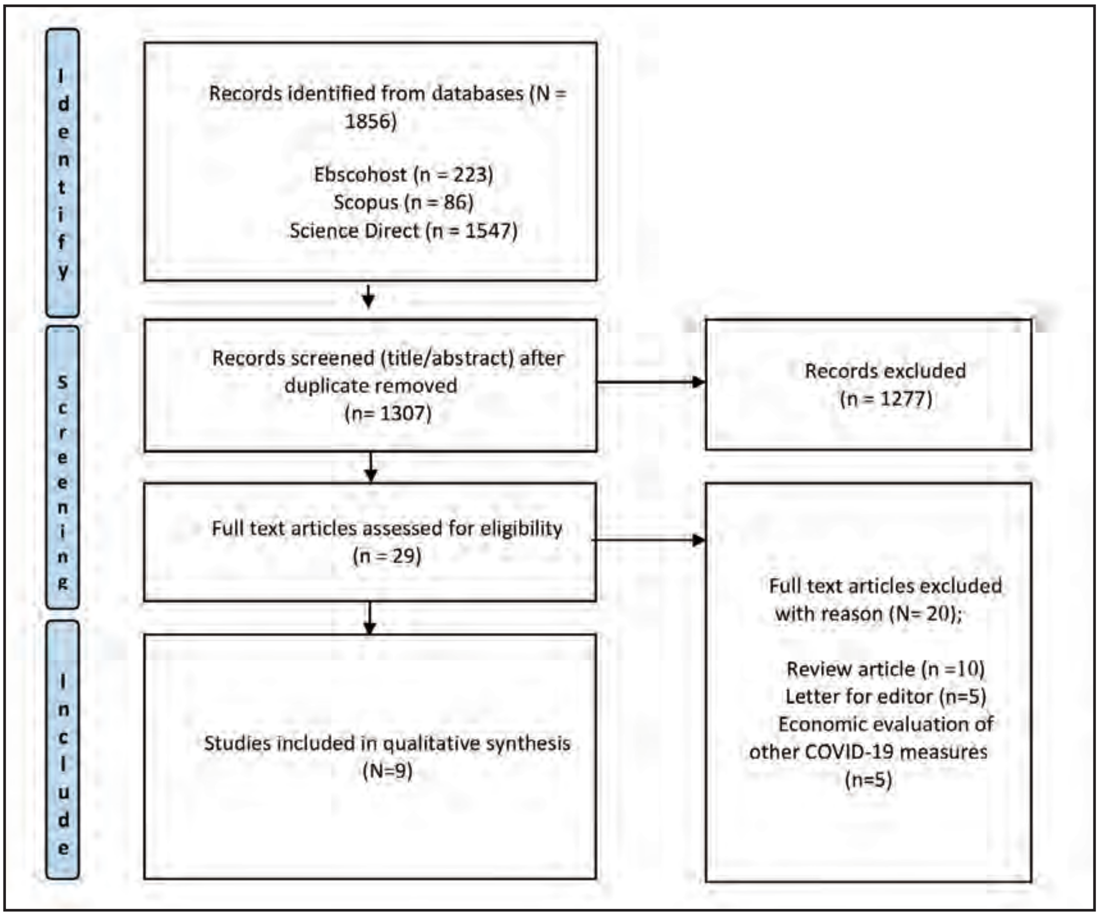


**Fig. 1:** The PRISMA flowchart for the selection of EBSCOhost

societal costs to only USD 9.9 billion, a 98% cost reduction compared with no intervention.[43] Within the societal perspective, immunisation not only reduces the cost of treating COVID-19 but allows people to be healthy and able to work to provide for society in general. Therefore, as the societal perspective considered the costs related to the loss of productivity from COVID-19 infections, a vaccination strategy provides significant benefits to society.[46] Within the context of South Africa, an immunisation program targeted to cover 67% of the population was also determined as cost-saving as compared to no vaccination.[48] In the United Kingdom, an effective vaccination was expected to minimise community transmission without the need for long-term physical distancing policies, therefore, estimated to yield incremental net monetary values ranging from £12 billion to £334·7 billion for 10 years.[44]

Meanwhile other studies demonstrated that a vaccination policy was cost-effective compared to no vaccination.[47,49] For example, a vaccination program for low- and middle-income countries (LMIC) with donor investment of USD 6.4 billion to achieve 20% coverage would be highly cost-effective resulting in an incremental cost-effectiveness ratio (ICER) of USD 20 for every infection prevented and USD 250 per year of life saved (YLS) compared with no vaccination.[49] Hence, highlighting the need for the global community to support LMIC with the necessary resources to vaccinate large proportions of their populations and ensure equity in vaccine distribution.[49]

**Vaccination Strategy by Utilising a Higher Vaccine Efficacy is More Cost-Effective**

As COVID-19 vaccines prevent COVID-19 infections and reduce the severity of COVID-19 disease, studies had demonstrated consistent findings, whereby a higher vaccine efficacy resulted in better cost-effectiveness. A Turkish study demonstrated that for vaccines with 45% effectiveness in disease transmission and 90% effectiveness in disease reduction, the incremental cost-effectiveness ratio (ICER) was USD 1045 per QALY saved, which was considered cost-effective.[47] However, if the vaccine had higher effectiveness in disease transmission (90%) with similar effectiveness in disease reduction (90%), the ICER reduced to an even better value of USD 511 per QALY [47], which demonstrates that the selection of a vaccine with higher effectiveness gives more value for a vaccination programme. Similarly, the model from the UK demonstrated that with higher vaccine effectiveness and a long duration of induced immunity, the net monetary benefit of a vaccination program will increase.[44]

From the societal perspective, despite variability in the effectiveness of available vaccines, having a vaccination strategy was cost-saving as compared to no vaccination.[46] A study from Israel concluded that despite variable vaccine effectiveness, the benefit-cost ratio (BCR) of mass vaccination against COVID-19 with three current available vaccines was cost-saving for gaining more lives and less costs incurred.[46] In addition, when the global economy and education losses were taken into consideration, the benefit-cost ratio for the three vaccines was inflated.[46]

**Prioritising Vaccination for At-Risk Population is Cost-Effective**

Studies had found that a vaccination strategy by prioritising vaccine provision is cost-effective. For example, in Denmark, the inclusion of the elderly population 60 years of age or older was more cost-effective than a vaccination strategy targeting only those younger than 60 years old.[41] A study from the USA demonstrated that in the event of vaccine supply constraint, prioritising vaccination of persons over age 65 appears to be cost-saving because of the high cost from higher incidence of intensive care and ventilation.[42] For similar reason, a prioritisation scheme to high-risk groups defined by a residency in nursing homes (without consideration of age) was also found to be cost-saving as compared to no vaccination strategy.[42] Finally, prioritising vaccination based on occupation, whereby those considered to have a priority occupation i.e., healthcare personnel and emergency care workers are given vaccination priority was estimated to be cost-effective compared to no vaccination, as demonstrated by the value of ICER of USD 20,000 for every quality-adjusted life year (QALY) saved.[42]

**Even with Risk of Anaphylaxis Reaction: A Mass Vaccination Strategy is Cost-Effective**

The occurrence of anaphylaxis cases after COVID-19 vaccination had prompted health authorities in some countries to issue a precaution for vaccination in those with a history of a severe drug or vaccine reaction or severe food allergy.[45] As a result, a model was constructed to compare between a universal vaccination policy (no restriction of vaccination) and a risk-stratified approach (person with a history of anaphylaxis contraindicated from vaccination).[45] From a healthcare perspective, a universal vaccination strategy dominates risk-stratification. However, when the risk of vaccine-associated anaphylaxis exceeded 0.8%, the risk-stratified approach was the most cost-effective strategy.[45] The findings of this study suggested that a universal vaccination strategy gives more value to healthcare providers and overall society. However, if the risk of vaccine anaphylaxis is more than 0.8%, a risk-stratified approach should be considered.[45]

**The Pace of Vaccination Affects Cost-Effectiveness**

Studies have documented that having a faster vaccination pace produces maximal benefits in reducing the number of populations affected by COVID-19. In the case of South Africa, it was demonstrated that an immunisation programme with the highest vaccination pace (300,000 vaccinations daily) dominates the lower vaccination pace (200,000 and 150,000 vaccinations per day).[48] In other words, a higher pace of vaccine roll-out resulted in the most favourable clinical outcomes and lowest total costs incurred to the healthcare provider.

**Providing Higher Vaccine Coverage is More Cost-Effective**

Studies showed that increasing the vaccination coverage does not only have a significant reduction in morbidity and mortality but was more cost-effective.[48,49] Within the context of South Africa, a 67% population vaccination coverage resulted in ICER of USD 9,960 per life years as compared to 40% of vaccine coverage which was considered cost-effective. However, increasing the vaccination coverage to 80% will reduce the ICER value (USD 4,270 per life years), meaning that higher vaccination coverage is more cost-effective.48 Interestingly, within the context of the LMIC, with vaccination coverage increasing from 20% to 50%, the ICER value persistently increased, albeit the results were still cost-effective.[49] However, beyond 50% vaccination coverage, the ICER continued to increase, suggesting that the reductions in infections and deaths continued, despite its diminishing efficiency.[49] In essence, having better vaccination coverage of provides value much value to the health provider as well as the society.

## DISCUSSION

Within the context of this review, economic evaluation studies had consistently provided compelling evidence that nationwide vaccination policies for COVID-19 provide massive value for the healthcare providers and overall society. Given the severity of the pandemic and the number of lives lost due to COVID-19, the resource investment for a vaccination strategy was expected to be lower than the costs for treating COVID-19 diseases. Even with the high cost of vaccination programme, it is still considered as cost-effective to provide COVID-19 vaccination to the population.

The limited supply of COVID-19 vaccines during the early phase of the pandemic had forced countries to select different strategies of vaccine distribution and roll-out. Hence, not only is it valuable to have a vaccination policy in a country during the pandemic, it is also vital to ensure that the vaccination policies are designed to ensure optimal outcomes in terms of prevention of mortality and morbidity as well as improving quality of life of the population. Therefore, different vaccination strategies should be planned for different population context. In the scenario of a limited vaccine supply, a strategy concentrated on prioritised vaccination of the pockets of the population which were at the most risk of hospitalisation and death is crucial and gives the most benefit. Therefore, countries are recommended to prioritise vaccination for people at risk and subsequently extend vaccine roll-out to populations at lower risk. For countries and international bodies, this review also highlights the importance of concentrating efforts to accelerate vaccine roll-out to improve the pace and coverage of COVID-19 vaccination. This is possible by establishing effective vaccine distribution and administration systems to ensure prompt vaccine delivery to the community to gain the most benefit from COVID-19 vaccination. As concerns of vaccine hesitancy hamper the efforts to introduce new vaccines and achieve adequate population coverage [50], the value of COVID-19 vaccination not only rely on the ability to provide sufficient vaccine access [49], but also depends on countries' ability to address vaccine hesitancy in the community. Higher vaccine hesitancy is expected to decrease demand for vaccine[50], subsequently reducing the value of COVID-19 vaccination strategies, which necessitates strategic measures to investigate and address COVID-19 vaccine hesitancy within the context of respective countries.

Within the global community, strategies to improve global vaccine production, addressing the bottlenecks of vaccine production as well as ensuring equity in vaccine distribution is fundamental to ensure that the global population will benefit from the COVID-19 vaccines. Hence, the collaboration of various stakeholders is necessary to achieve vaccine equity.

## LIMITATIONS

There are several limitations to this review. First, the cost-effectiveness or cost-consequences value was bounded by the various parameters and assumptions included in the economic evaluation studies. At this point, as much information is still unknown related to vaccine effectiveness, namely the duration of induced immunity and effectiveness against different COVID-19 variants, interpretation of the findings should be taken within the context of current, available data. Secondly, most studies conducted simulations for a brief time horizon of one year or less and based on the current pandemic situation. Hence, these studies did not provide information related to the value of COVID-19 vaccination in the long run. With the introduction of booster doses and the possibility of COVID-19 vaccination activities become seasonal or regular in the future, cost-effectiveness measures should be investigated depending on the future available data and context. Third, the outcomes selected for these studies (for example, QALY, life years, or death prevented) were mainly based on the direct impact of COVID-19 infections, hence the cost-effectiveness value is expected to be a conservative estimation. Although some studies included societal perspective and took into consideration the productivity loss from COVID-19 and economic gain from vaccination, there is still a multitude of health and social impact of prevention of COVID-19 morbidity and mortality (such as the resumption of health services towards pre-pandemic level, improved physical and mental health as community return to work and school) as well as the return of international travel norm. Therefore, taking these factors into consideration, the value of COVID-19 vaccination is expected to be higher. Fourth, studies often did not consider issues related to COVID-19 vaccination hesitancy that may impair COVID-19 vaccination effectiveness in the population. Finally, as COVID-19 vaccination is a relatively new intervention with potential rapid publications of more economic evaluations, there is a need to revisit this review in future.

## CONCLUSION

In summary, the vaccination programme is a valuable tool to combat the COVID-19 pandemic across the world. Various strategies affect the cost consequences of COVID-19 vaccination programme, namely the prioritisation of high-risk population, vaccine effectiveness as well as the pace and coverage of vaccination. Hence, it is recommended that the international and national actors involved in the global vaccination effort to take these factors into consideration for future COVID-19 vaccination policies.

The COVID-19 pandemic has demonstrated a unique case of providing global vaccination to achieve the most benefit within a short duration of time. Within this context, it is recommended that all countries should strive for a rapid and effective vaccine distribution by providing an effective delivery system and addressing vaccine hesitancy among the population. The future directions recommended include having more economic evaluations done at various levels of population-based vaccination programs to help policymakers in efficiently allocating scarce resources especially for COVID-19 and other vaccine-preventable diseases. Economic evaluation for vaccination programs should be done early on such as at the start of a pandemic, and this can be done using disease or mathematical modelling approaches so that the findings of these evaluations can be used in a timely manner when policies are drafted for the implementation of the vaccination programs.

For countries with issues related to COVID-19 vaccine supply and distribution, the focus is on providing early vaccine distribution to at-risk population while strengthening effort to achieve access to vaccine supply and improving the healthcare system to provide efficient vaccine delivery. Additionally, collaborative international efforts should be employed to assist countries with severe COVID-19 vaccine supply problems. This can be done by offering either financial assistance, technology advancements or the technical expertise to ensure that these countries are able to receive adequate vaccine supply as well as designing their effective vaccine delivery and distribution system.

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