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COVID-19 Vaccination Burden in Asia

Running Title: COVID-19 Vaccination in Asia

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ABSTRACT: Coronavirus disease 2019 (COVID-19) pandemic had severely impacted the global economies and posed an additional and unwanted burden on their healthcare systems. However, very limited research has been conducted to evaluate the pharmacoeconomic burden of COVID-19 pandemic and COVID-19 vaccination programs in Asian countries. Therefore, we aimed to design a systematic review to evaluate pharmacoeconomic burden of COVID-19 vaccines in Asian countries. For this systematic review, we have followed the "Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)" guidelines to fulfill the study aim and objectives. The databases used for data extraction and collection included PubMed, MEDLINE and EBSCO until November 30, 2025. Only those studies have been extracted that has published from May 2020 to June 2025. The quality of reporting of the included studies was checked using the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) checklist. A total of 170 articles related to pharmacoeconomic burden of COVID-19 vaccination in Asian countries were found, and after following the inclusion criteria, 10 studies were selected for this systematic review. Different economic evaluation parameters i.e., total vaccine cost, total population size, COVID-19 vaccine utility and COVID-19 vaccination efficacy were evaluated. All of the included studies suggested that COVID-19 vaccination was a cost-saving or cost-effective intervention for combating COVID-19 pandemic and to overcome its devastating impact on the healthcare budgets of the countries. Although the COVID-19 outbreak had a significant impact on Asian economies, and contemporary efforts were made to initiate various COVID-19 vaccination programs which were way expensive and were difficult to afford in low- and middle-incomed countries in Asia.

1. INTRODUCTION

The World Health Organization (WHO) proclaimed Coronavirus disease 2019 (COVID-19), a pandemic on March 11, 2020, and it has since emerged as one of the century's deadliest pandemics [1,2]. The COVID-19 had not only affected public but also disturbed the economic infrastructure nearly of all countries across the globe. After the outbreak of the COVID-19 in China, (one of the largest states of 49 Asian nations), this outbreak gained global attention and was declared a devastating pandemic [2-4]. The COVID-19 pandemic had infected more than 200 million individuals and resulted in 4 million deaths worldwide [5,6]. The actions made to stop COVID-19 outspread have had a significant influence on the lives of general populace [6,7]. Every Asian nation except Turkmenistan had at least one confirmed case of the COVID-19 before 25 November 2022 [7,8]. Because of the swift and intense spread of the COVID-19 pandemic, several public healthcare systems went under a hefty pressure worldwide [3-6]. This caused massive financial crises to public funds and affected healthcare budgets of numerous countries by increasing direct and indirect expenditures. The estimation of global pharmacoeconomic burden of the COVID-19 was approx. $3 trillion with numerous years of life lost (YLLs) in the first year of the COVID-19 pandemic [6-8]. Due to unavailability of an efficacious and effective pharmacological management of the COVID-19, different preventive and supportive measures had become a priority among majority of the healthcare systems of different countries [9-11]. These preventive measures include various non-pharmacological interventions like COVID-19 vaccination, social distancing, self-isolation, quarantine, cleaning, sanitizing, face masks, and some supportive vitamin therapies [11,12].

So far numerous COVID-19 vaccines have been developed and administered by several countries. According to WHO, there were around 400 COVID-19 vaccine candidates in development phase, and among them around 50% in clinical trials, and the 50% in pre-clinical stages [11-13]. After passing safety, efficacy and effectiveness evaluations, plentiful COVID-19 vaccines had received permission from concerned regulatory authorities to be used as a preventive measure [6-8]. Several COVID-19 vaccines have been proved safe, effective and efficient in combating COVID-19 widespread in various countries across the globe [10]. Although the WHO had already published comprehensive guidelines for the COVID-19 vaccine prioritization but provision of an adequate supply of the COVID-19 vaccines was entirely dependent on a country's financial resources [12-14].

A study done by Feikin et al., evaluated the duration of effectiveness of COVID-19 vaccines after their administration [15]. They reported that COVID-19 vaccines show immediate and excellent efficacy in preventing and combating severe COVID-19 infections [15]. Maximizing cost-benefit correlations can further aid in addressing the financial issues faced by the healthcare systems across the globe [15-17]. Pharmacoeconomic evolution of the COVID-19 vaccines can be performed by using four different methods: cost-utility analysis, cost-benefit analysis, cost-minimization analysis, and cost-effectiveness analysis. In the current COVID-19 pandemic, undeniably all types of healthcare expenditures have dramatically been increased [16-19]. In this pandemic, families with very low monthly income were totally reliant on the governmental or public healthcare facilities. This necessitated the evaluation of pharmacoeconomic burden of COVID-19 vaccines on the healthcare systems of the countries [18-21].

Global COVID-19 vaccination spending was approx. $51 billion in 2022 and is expected to be $53 billion this year [22]. For the current year and the next year (2024), WHO projected 1.8 COVID-19 vaccination doses per person. International Quality and Value Institute Advisors (IQVIA) estimated up to 1.3 doses per person from 2023 to 2025, when boosters are likely to be used and additional single-shot immunizations are likely to be accessible. It is expected that until end of 2026, around 95% of the world's population would have received COVID-19 vaccination. To effectively use healthcare resources, it has become essential to incorporate cost and benefit analysis into the development and implementation of healthcare innovations and medication therapies [21,23]. This is crucial, especially in developing nations where the expenses of clinical treatments are too high due to poverty and poor living conditions with inadequate government support for healthcare budgets [19-24].

Since December 2019, the emergence of the first COVID-19 case has alarmed the low, middle and high economies due to high rates of hospitalization and mortalities. Similar to other continents, Asian continent had also faced a high number of confirmed cases and causalities [1-5]. Healthcare practitioners and authorities along with local governments had primarily focused on designing and implementing strategies to prevent COVID-19 widespread and to provide optimal care to COVID-19 sufferers [12-14]. Undeniably, policy- and decision makers of a country are primarily responsible for effectual use and optimization of the available financial resources to provide optimum healthcare to the public [7-10]. This aspect becomes more demanding when it comes to low- and middle-income countries like several Asian countries. Few studies have reported that non-pharmacological interventions i.e., COVID-19 vaccines could play a tremendous role in combating COVID-19 pandemic as they are cost-effective and safe choice to avert and control COVID-19 widespread [10-13]. Some other studies regarding COVID-19 vaccination effectiveness and safety have also concluded that the most valuable approach to fight COVID-19 infection is the COVID-19 vaccination because it helps in attaining quicker herd immunity which in return can help in combating COVID-19 wide-reaching effects [22-26].

On the other side, some studies reported that COVID-19 vaccines effectiveness may decrease in future especially after 12-24 months [14-16]. Therefore, further follow-up on COVID-19 vaccines' efficacy and safety is essential for policy- and decision makers. Such information becomes crucial when healthcare and pharmacoeconomic (cost/economic burden) studies are scarce and not much information available for general public as well as for policy- and decision makers [27]. Due to the limited availability of healthcare resources in majority of the Asian countries, cost determination of COVID-19 vaccination is an important aspect in estimation of overall healthcare burden of COVID-19 on these countries. However, studies that comprehensively and thoroughly evaluate pharmacoeconomic burden of the COVID-19 vaccines in Asian countries are currently rare. To fill this literature gap, this systematic review was designed to determine current pharmacoeconomic expenditure of Asian countries for COVID-19 vaccination to their public.

2. MATERIALS AND METHODS

2.1. Study design and study selection

For this systematic review, we have followed "Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)" guidelines to fulfill aim of the study [20]. The data extraction, searching, and screening of the studies have been exhibited through the PRISMA flowchart as shown in figure 1. The databases used for data extraction and collection included PubMed/MEDLINE and EBSCO, until November 30, 2025. The MeSH keywords used for data search were "COVID-19 vaccination burden", "pharmacoeconomic burden of COVID-19 vaccines", "cost of COVID-19 vaccination in Asian countries", "cost of COVID-19 and its vaccines", "cost analysis of vaccines for COVID-19", "economic evaluation", "cost minimization", "cost-effectiveness", "cost utility", "cost-benefit analysis", "willingness-to-pay", "Coronavirus vaccine expenditures", "COVID-19 vaccines" and "healthcare economics of COVID-19 and its vaccine" among all databases. Only those studies were extracted that had published between May 2020 to June 2025. The inclusion and exclusion criteria were followed for screening and selection after data collection, as these are crucial steps for a systematic review.

2.2. Inclusion criteria

The inclusion criteria were as follows:

1) The studies were conducted in Asian countries
2) The studies with study design observational cross-sectional.
3) The studies were on pharmacoeconomic burden of COVID-19 vaccination.
4) The studies published in English language.
5) The studies published in peer-reviewed journals.

2.3. Exclusion criteria

The exclusion criteria were as follows:

1) The studies with general population or healthcare providers.
2) The studies conducted out of Asian countries.
3) The studies with study design other than observational cross-sectional.
4) The studies published in languages other than English.
5) Abstracts, case studies, and systematic reviews or meta-analyses

2.4. Data extraction and analyses

Through electronic databases search, a total of 410 research records were identified, from which 326 studies were screened after removing the duplicate records and renounced records. Among the 326 screened studies, 265 records were excluded that did not match the required keywords or they were reviews and letters etc. A total of 61 research records were shortlisted and among them 4 studies were found as conference proceedings (abstract) only when searched for the full-text articles. After excluding them, a total of 57 studies were left for further evaluation. And among the 57 shortlisted studies, 47 studies were further excluded as they did not meet the inclusion criteria. At the end, 10 studies [28-37] were screened that met the inclusion criteria and were evaluated for the present systematic review. The details are described in the PRISMA flow diagram (Figure 1).

After screening and selection, from each included study, the information related to authors, study year, costing method, location of the study, costing model, sensitivity analysis, cost outcomes (quality-adjusted life years (QALYs), incremental cost-effectiveness ratio (ICER), life years gained (LYG), disability-adjusted life years (DALYs), and other intermediate measures), cost perspective, cost types i.e., direct and indirect, study results/outcome (COVID-19 vaccine effectiveness), and different study perspectives i.e., interventions (if any), time horizon, comparator, costing model, discount rate, willingness to pay and allied sensitivity parameters were extracted. The "Cochrane Bias" tool of LvE for risk assessment was also utilized to rule out the risk of biasness. This biasness assessment was further verified by KT, HdG and LvD. In this systematic review, we analyzed the included studies using descriptive and quantitative analyses. All of the reported costs were converted to USDs using EPPI-Centre Cost Converter similar to other studies reported in literature [38].

Quality assessment of the included studies was done using Consolidated Health Economic Evaluation Reporting Standards (CHEERS) checklist [39]. The CHEERS checklist is comprised of 24 items, which mainly include title, abstract, introduction, study setting and location, study perspective, methods, population size, results, cost estimation/analyses, model assumptions, funding sources, and conflict of interest etc. A percentage score was calculated with an assumption that all criteria were weighted equally. Points were assigned to each study based on their reporting items' completion, i.e., 1 point for complete reporting of the items, 0.5 for partial reporting, and 0 for not reporting. Studies were also categorized into 3 different categories based on the overall quality of the study. Studies quality criteria were assigned/assumed based on a previous published study [40]. High quality was assumed if a study met >75% or above of these criteria. Moderate quality was assumed if a study met 50%-75% of the criteria and low quality was assumed if a study met < 50% of the criteria.

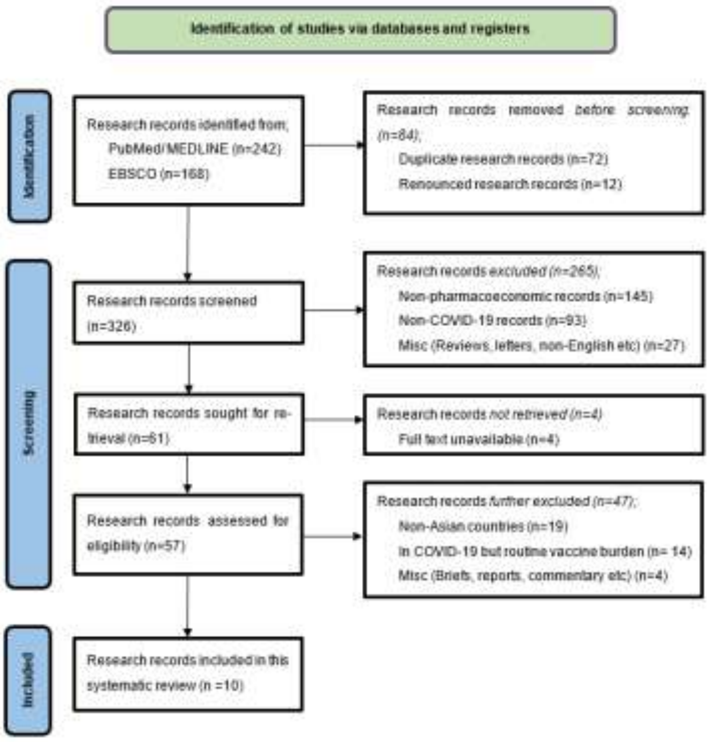

Figure 1. PRISMA flowchart of the included studies

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According to the CHEERS checklist criteria, 5 studies [28,29,31,33,35] were classified as high-quality studies, 4 studies [30,32,36,37] were classified as moderate-quality. Only 1 [34] study was categorized as low-quality study. The abstract, introduction and results were reported in majority of the included studies. The majority of the studies reported their currencies but their conversion and the years of costing (YoC) were missing in some of the studies. Among most of the included studies, funding sources were mentioned but their roles were not reported. The results of the CHEERS checklist are presented in table 1.

Table 1: Quality assessment of included studies using CHEERS checklist

CHEERS checklist	Study 1 [28]	Study 2 [29]	Study 3 [30]	Study 4 [31]	Study 5 [32]	Study 6 [33]	Study 7 [34]	Study 8 [35]	Study 9 [36]	Study 10 [37]
Title identified as economic evaluation	Y	Y	Y	Y	N	Y	N	Y	N	Y
Structured abstract	Y	Y	N	Y	Y	N	Y	N	Y	Y
Intro provide the context and research question	Y	N	N	Y	N	Y	Y	Y	Y	N
Population	Y	Y	N	N	Y	N	N	Y	N	Y
Settings and location	N	Y	Y	N	Y	Y	N	Y	N	N
Study perspective	N	Y	N	Y	N	Y	Y	N	Y	N
Comparators	Y	Y	N	N	Y	Y	N	Y	N	Y
Time horizon	Y	N	Y	Y	N	Y	N	Y	N	Y
Discount rate	Y	N	Y	Y	Y	N	N	Y	Y	Y
Outcomes and relevance	N	Y	N	Y	Y	N	Y	N	Y	N
Preference based outcomes	Y	Y	N	N	Y	N	N	Y	N	Y
Measurement of effectiveness	Y	N	Y	Y	N	Y	N	Y	N	Y
Resources and cost estimation	N	Y	Y	Y	Y	Y	Y	Y	N	N
Currency date and conversion	Y	N	Y	Y	N	Y	N	Y	Y	Y
Model justifications	Y	N	Y	Y	N	Y	N	Y	N	Y
Model assumption	Y	Y	N	Y	Y	N	Y	N	Y	Y
Parameters of value	N	N	N	Y	N	Y	Y	Y	Y	Y

Analysis method	Y	Y	N	N	N	Y	N	Y	N	Y
Incremental cost	N	Y	Y	N	Y	Y	N	Y	N	N
Heterogeneity explanation	N	Y	N	Y	Y	Y	Y	N	Y	N
Model sensitivity analysis	Y	Y	N	N	Y	Y	N	Y	N	Y
Conflict of interests	Y	Y	Y	Y	N	Y	N	Y	N	Y
Funding sources	Y	Y	Y	Y	Y	Y	N	Y	Y	Y
Total	N	Y	N	Y	Y	N	Y	Y	Y	N

Y: Yes; N: No

3. RESULTS

3.1. Characteristics of included studies

In this systematic review, a total of 10 original research papers which assessed pharmacoeconomic impact of COVID-19 vaccination burden in Asian countries were included for final analyses. Out of the 10 included studies, 8 studies were single-country studies, and 2 studies were conducted in multiple countries. Single-country studies were performed in Turkey, Pakistan, Iran, Thailand, Taiwan, and Hong Kong. And multiple countries studies were performed in Hong Kong, Indonesia China, Philippines, Singapore, Thailand, Bangladesh, Congo, Egypt, Ethiopia, Indonesia, Kenya, Myanmar, Nigeria, Pakistan, Philippines, Tanzania and Vietnam. Six studies were performed in 2021 while four studies were conducted in 2022. All of the included studies aimed to estimate economic impact of different vaccination strategies. Only one study which was conducted in Thailand, compared the intradermal COVID-19 vaccine with the intramuscular COVID-19 vaccine. Most of the Asian countries, being low- and middle-incomed countries (LMIC), tried to invest in COVID-19 vaccination programs in collaboration with WHO and National Health Services. General characteristics of the included studies are presented in table 2.**Table 2.** Characteristics of the included studies

Authors	Study year	Costing method	Study location	Costing model	SA	Costing outcome
Hagens et al [28]	2021	Cost utility analysis	Turkey	Age-structured compartmental model	One-way	QALYs
Pearson et al [29]	2021	Cost utility analysis	Pakistan	Compartmental transmission model	One-way	DALYs
Vaezi & Meysamie [30]	2021	Cost utility analysis	Iran	Epidemiological model	-	DALYs
Suphanchaimat et al [31]	2021	Cost utility analysis	Thailand	Compartmental model	One-way	DA
Wang et al [32]	2021	Mix	Taiwan	Markov model	One-way	QALDs and BCR

Jiang et al [33]	2021	Cost utility analysis	Hong Kong, Indonesia China, Philippines, Singapore and Thailand	Decision tree	One-way and PSA	QALYs
Mungmunpuntipantip and Wiwanitkit [34]	2022	Mix	Thailand	-	-	CPU
Siedner et al. [35]	2022	Cost-effectiveness analysis	Bangladesh, Congo, Egypt, Ethiopia, Indonesia, Kenya, Myanmar, Nigeria, Pakistan, Philippines, Tanzania, Vietnam	CEACOV model	One-way	YLS
Wang et al [36]	2022	Cost utility analysis	Thailand	Age-structured dynamic model	One-way and PSA	QALYs
Xiong et al [37]	2022	Cost utility analysis	Hong Kong	Markov model	One-way and PSA	QALYs

SA = Sensitivity analysis, DA = Death averted, BCR = Benefit-cost ratio, CPU = Cost per utility

3.2. Key results

Overall, all of the included studies reported that COVID-19 vaccination was a cost-effective strategy to combat the COVID-19 pandemic. Most of the studies used their own specific willingness-to-pay thresholds and their calculations were different from each other. Two single-country studies which were conducted in Taiwan [32] and Hong Kong [37] used self-willingness-to-pay thresholds. And one multiple countries study [35] which was conducted in Bangladesh, Congo, Egypt, Ethiopia, Indonesia, Kenya, Myanmar, Nigeria, Pakistan, Philippines, Tanzania and Vietnam used self-willingness-to-pay threshold. Two single-country studies in Turkey [28] and Iran [30] used one to three times of the GDP per capita as the threshold value for willingness-to-pay threshold. One multiple-county study [33] also used one to three times of the GDP per capita as the threshold value for willingness-to-pay threshold. Studies conducted in Pakistan [29], Thailand [31], and Thailand [34] did not define their willingness-to-pay thresholds. Every study included in this systematic review used a different evaluation method to evaluate cost-effectiveness of the COVID-19 vaccines. Most prominent methods used were total procurement of the COVID-19 vaccines, total coverage of the COVID-19 vaccines, COVID-19 vaccination priority for special need populations, and efficacy and availability of the COVID-19 vaccines.

3.3. Costing models' characteristics

3.3.1. Sensitivity analysis (SA)

Salient sensitivity parameters which were discussed in the sensitivity analyses of the included studies were the COVID-19 vaccination price, total program cost, vaccine efficacy, target population, infection rate, hospitalization cost, total mortality and discount rate (if offered). Some of the included studies [30,35] did not conduct SA to determine the uncertainty of the analyses. Among the studies that performed SA, studies from Turkey [28], Pakistan [29], Thailand [31], and Taiwan [32], used deterministic SA i.e., one-way SA. None of the included study performed probabilistic SA. Studies done by Jiang et al., 2021 [33], Wang et al., 2022 [36] and Xiong et al., 2022 [37] used both types of SA methods i.e., one- way and probabilistic.

3.3.2. Cost parameters (CPs)

Among the included studies, cost utility analysis (CUA) was performed in studies from Turkey [28], Pakistan [29], Iran [30], Thailand [36], Hong Kong [37] and in a study performed by Jiang et al., 2021 [36] (multi-country study). Among these CUA based studies, four studies [28,33,36,37] used quality-adjusted life years (QALYs) as an outcome while two studies [29,30] used disability-adjusted life years (DALYs). None of the included study performed cost-benefit analysis (CBA) i.e., no study determined net monetary value or cost-benefit ratio (CBR) as its outcome measure. One multi-country study [35] used cost-effectiveness analysis (CEA) technique, and measured years of life saved (YLS) as an outcome. One of the included studies, done by Suphanchaimat et al., 2021 in Thailand [31] used averted cases and deaths as an outcome. Another study from Thailand by Mungmunpuntipantip and Wiwanitkit, 2022 [34] also used CEA method and measured COVID-19 anti-RBD antibody response as an outcome. A study conducted by Wang et al., 2021 in Taiwan [32] used two concurrent cost assessment methods, i.e., CBA with CBRs and CEA with quality-adjusted life days (QALDs) as outcomes.

3.3.3. Costing models (CM)

Dynamic transmission model to evaluate costs was used by five included studies [28,29,31,35,36]. Two studies from Taiwan [32] and Hong Kong [37] also used the Markov model for cost estimation. And Vaezi & Meysamie, 2021 [30] utilized epidemiological model as the cost evaluation method. A multi-country study by Jiang et al., 2021 [33] used a decision tree for cost estimation whereas study by Mungmunpuntipantip and Wiwanitkit, 2022 [34] did not provide details about the used model for cost evaluation. Regarding the time horizon, short-time horizon was utilized in 2 studies [30,32], longer time horizon was used in one study [29] and one study did not report any particular time horizon [34]. As a matter of fact, for longer time horizons (> 1 year), a discount rate must be determined and reported [41]. Half of the included studies did not report the discount rates.

3.3.4. Cost perspective (CP)

Among the 10 included studies, one study used a payer perspective [35], one study used a policymaker perspective [30], two studies used a societal perspective [33,36], four studies used a healthcare perspective [31,33,37,39], and two studies used healthcare plus societal perspective [28,29]. Regarding the COVID-19 vaccination coverage, five studies reported a coverage of >50% [28,32,33,36,37]. However, three studies did not report any particular coverage of COVID-19 vaccination in their population [29,30,34].

3.3.5. Cost estimation (CE)

Evaluation of different types of cost elements is one of the most crucial factors in assessing burden of COVID-19 vaccination. All of the included studies reported vaccine costs in order to know the effectiveness of COVID-19 vaccination programs in their respective population. Moreover, the majority of the included studies also reported COVID-19 vaccine administration cost which was varied from $0.50 to $20.16 [31,32,33]. Total medical, non-medical, direct and indirect costs were also reported in most of the studies. Most of the included studies had considered COVID-19 vaccination costs, hospitalization costs and COVID-19 infection treatment costs as direct medical costs [28-30,32,33,35]. Four of the included studies considered COVID-19 vaccine wastage, vaccine transportation, social awareness campaigns about benefits of COVID-19 vaccination, and COVID-19 related quarantines as direct non-medical costs [29,32,35,36]. Three of the included studies considered productivity loss due to COVID-19 pandemic as indirect non-medical costs [28,33,37]. Table 3 presented information about cost elements of the included studies.

Table 3: Pharmacoeconomic burden of COVID-19 vaccination

Research record	Cost perspective	Direct cost	Indirect cost	COVID-19 vaccine effectiveness	SA details	WTP
Study 1 [28]	Healthcare and societal	Healthcare (hospitalization and home), COVID-19 vaccination	Productivity loss (sickness or death)	COVID-19 vaccination was cost-effective and prevented 50% COVID-19 transmission (ICER $1045 per QALYs).	COVID-19 vaccine price and total susceptible cases	Yes (GDP/capita)

Study 2 [29]	Healthcare and societal	COVID-19 vaccine procurement and administration	-	COVID-19 vaccination was cost-effective and prevented 70% COVID-19 transmission (ICER $27.9 per DALYs).	COVID-19 vaccine price	-
Study 3 [30]	Policy maker	Healthcare (hospitalization) and- COVID-19 vaccination	-	COVID-19 vaccination was cost-effective (except CoronaVac and Janssen) and prevented COVID-19 transmission (ICER $6.2-$121.2 per DALYs).	-	Yes (GDP/capita)
Study 4 [31]	Healthcare and provider	Healthcare (treatment), COVID-19 vaccination and its administration	-	COVID-19 vaccination was cost-effective and prevented COVID-19 transmission (ICER $2282 per life).	COVID-19 vaccine price	-

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Study 5 [32]	Healthcare and societal	Healthcare (diagnosis, treatment, hospitalization), COVID-19 vaccination and its administration	Adverse and unwanted effects	COVID-19 vaccination was cost-effective and prevented COVID-19 transmission. CUAs $321.14/QALD (Moderna) $356.75/QALD (Pfizer) $341.44/QALD (AstraZeneca) CBAs $13 (Moderna) $23 (Pfizer) $28 (AstraZeneca)	Hospitalization fee, COVID-19 vaccine price and % of asymptomatic patients	Yes & ICER <$50 000
Study 6 [33]	Healthcare and societal	Healthcare (treatment) and- COVID-19 vaccination	Productivity loss	COVID-19 vaccination was cost-effective and prevented COVID-19 transmission Hong Kong ($105.18), Indonesia ($98.15), China ($99.70), Philippines ($60.48), Singapore ($112.00), Thailand ($103.47)	COVID-19 vaccine efficacy, price and infection severity	Yes (GDP/capita)

Study 7 [34]	Healthcare	COVID-19 vaccination and its administration	-	Cost per utility and cost per safety for intradermal COVID-19 vaccination were lower than cost per utility and cost per safety of intramuscular vaccination	-	-
Study 8 [35]	Donor	COVID-19 vaccination program and its administration	-	COVID-19 vaccination coverage to 15% would prevent 11 million new infections and 120 000 deaths with an ICER of $670/YLS. And COVID-19 vaccination coverage to 60% would additionally prevent up to 68 million infections and 160 000 deaths with ICER of $7820/YLS.	COVID-19 vaccination program costs	Varied COVID-19 vaccination coverage with varied ICER ($670/YLS to $7820/YLS)
Study 9 [36]	Societal perspectives	Healthcare (diagnosis, treatment, hospitalization, COVID-19 screening, adverse effects, masks, sanitizers, social distancing, quarantine), COVID-19 vaccination and its administration	-	COVID-19 vaccination was cost-effective and prevented COVID-19 transmission.	COVID-19 vaccine efficacy	<$17499
Study 10 [37]	Healthcare	Healthcare (diagnosis, ICU treatment, hospitalization), and COVID-19 vaccination	Productivity loss	ICER before Omicron was $5383060/QALYs and the ICER during Omicron was $74721	COVID-19 vaccine efficacy and rate	<$240963

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WTP = Willingness to pay, – = Not reported, GDP = Gross domestic product, DALYs = Disability-adjusted life years, QALYs = Quality-adjusted life years, ICER = Incremental cost-effectiveness ratio, YLS = Years of life saved, ICU = Intensive care unit**4.**

4. DISCUSSION

In this systematic review, a total of 10 studies were identified regarding the pharmacoeconomic burden evaluation of the COVID-19 vaccination in Asian countries. The obtained results showed that the COVID-19 vaccination programs were cost-effective and even cost-saving. Besides, COVID-19 vaccine effectiveness, costs (direct and indirect), and coverage were the paramount influential factors to determine the cost-effectiveness of the COVID-19 vaccination in Asian countries. Undeniably, the COVID-19 vaccination is considered safe, cost-effective, and appropriate approach to handle the COVID-19 pandemic worldwide. The COVID-19 vaccination is considered to be more cost-effective and efficacious in a shorter (lesser) time period than other precautions, preventions and therapeutic interventions like sanitizing, social distancing or treatment [42]. In literature, the majority of the pharmacoeconomic evaluation studies of COVID-19 vaccination are from high income countries and few are from middle income countries, while fewer is reported from low income and poor countries. This systematic review has been conducted to evaluate pharmacoeconomic burden of the COVID-19 vaccination in different Asian economies.

Asian countries with the maximum number of reported COVID-19 cases were South Korea, India, Turkey, Vietnam, and Iran. Although being the first region of the world to be affected by the pandemic, many Asian states particularly Taiwan, Vietnam, and Bhutan fared quite well with their quick widespread responses [11]. China received criticism for downplaying the seriousness of the outbreak at first, but since March 2020, the disease had been largely controlled due to its extensive response. Iran, Indonesia, India, and Turkey were the countries that reported with highest mortality rate till July 2021 and each with more than 1 million total deaths [10]. In the last couple of years, with the advancement health informatics, the healthcare community has done several interventions regarding earlier disease detection and precise management worldwide. Healthcare budgets are being revised and expanded to provide optimum healthcare to the general public. This recent COVID-19 outbreak was a huge burden on low- and middle-incomed countries across the globe especially in Asian region. Indeed, the local governments worked well along with their healthcare authorities to cope up with this devastating pandemic and to provide optimal healthcare facilities to their public. However, economic efficiency must be implemented in order to make the best use of medical resources, and this may be done by using precise pharmacoeconomic evaluations, advanced healthcare policies and their appropriate implementation [12].

Among all of the included/studied research records, it was observed that cost calculation methods were varied in terms of target population, discount rates, analysis models, cost perspectives, cost analysis model selection components as well as COVID-19 vaccination coverage in each country. The majority of the studies included in this systematic review used a decision analytic modeling method to calculate the cost-effectiveness of the COVID-19 vaccination in Asian countries. The cost (direct and indirect) estimation models regarding COVID-19 vaccine efficacy, their assumptions and determination parameters were varied in most of the included studies. Some of the included studies used dynamic models to calculate the cost of the COVID-19 vaccination in Asia. These models assessed herd immunity probabilities by considering dynamic shift in age distribution and predicted infectious disease transmission rate in the studied countries. In the included studies, different cost-evaluation perspectives (healthcare, societal, governmental, patients etc) were used in determination of the COVID-19 vaccination-related costs.

Among the different cost evaluation perspectives, societal perspective always provides in-depth, comprehensive and ample data in decision-making process of cost evaluations as it covers both direct and indirect costs. In most of the included studies, healthcare perspective was used despite the fact that it only evaluates direct cost not the indirect cost. The reason could be because the data were very limited and seldom available during the COVID-19 pandemic worldwide. In most of the included studies, 1 year time frame or 6 months are used to estimate the cost which could be due to the COVID-19 infection nature and the expected effects (harmful or beneficial) of the COVID-19 vaccination. Discount rate may not be used in shorter duration studies while performing sensitivity analysis. Among the included studies, a study that used a shorter time horizon i.e., ≤1 year, reported narrow effects of COVID-19 vaccination [43]. Conversely, another study that performed on a longer time horizon i.e., >1 year, reported longer effects of the COVID-19 vaccination [29]. A study by Pearson et al., concluded that COVID-19 vaccination immunity could last for approximately 10 years [29]. Hence, discounting the vaccine costs and their effects became optimum in such scenarios [43].

These days, several types of COVID-19 vaccines are available which are manufactured in different countries and are all different in terms of efficacy, safety and affordability (cost). These different types of the COVID-19 vaccines also differ in their types (manufacture), the number of jabs required, doses to be administered and potential side effects. Unquestionably, the COVID-19 vaccination could prevent COVID-19 transmission, but unfortunately not every country across the globe can afford the same type of COVID-19 vaccine. Therefore, the pharmacoeconomic evaluation of the COVID-19 vaccination burden becomes imperative for the healthcare providers, healthcare manager, and policymakers to decide on the implementation strategies for their countries. The majority of the included studies reported COVID-19 vaccine efficacy was around 70% (60-90%). These results further advocate the fact that COVID-19 vaccination could decrease mortality, disease severity, treatment cost, and hospitalization rate among the COVID-19 sufferers and healthy individuals [9,44]. Another study also reported that COVID-19 vaccination can curtail several adverse disease outcomes among chronic disease patients which suffer from COVID-19 infection [44].

Our review results indicate that COVID-19 vaccination could be considered a cost-effective, and safe intervention in combating COVID-19 pandemic. Combined with other precautionary measures like lockdown, social distancing, and sanitization, the COVID-19 vaccination is appraised to have decreased over 150 million cases and 3 million deaths worldwide [45]. In addition, COVID-19 vaccination can decrease COVID-19 infection and its transmission without adopting any physical precautionary measures [45]. Our study analyses also summarized that massive COVID-19 vaccination campaigns were cost-effective and cost-saving in terms of total lives saved [46]. From pharmacoeconomic perspective, COVID-19 vaccination coverage campaigns have high returns in terms of benefits like increased COVID-19 vaccination rate, decreased COVID-19 cases, less COVID-19 infection severity and decreased COVID-19 related deaths [46,47]. According to the obtained results, several aspects can influence the COVID-19 vaccination prioritizing criteria like COVID-19 vaccine safety, effectiveness, availability, affordability and executed strategies [48]. For instance, in Thailand, prioritizing the population/individuals which were at a higher risk of acquiring COVID-19 infections showed additional cost-effective effect of COVID-19 vaccination than the general public [49]. Similarly, in the US, prioritizing COVID-19 vaccines for older people (≥ 60-years-old) was more cost-effective than the healthy individuals, provided productivity loss was not considered in sensitivity analysis [50]. Conversely, a study from Denmark reported that prioritization of the COVID-19 vaccination for people < 60 years was also cost-effective even if the productivity loss is considered in sensitivity analysis [51].

Financial decision-makers should choose apposite willingness-to-pay thresholds in pharmacoeconomic assessments. Usually, economic burden (cost) is determined to evaluate financial resource dearth that may happen when a resource is consumed for one purpose and is not available for other purpose. Making accurate and effective estimates in willingness-to-pay thresholds could better assist policymakers in constructing abreast and accurate financial decisions for the healthcare budgets of their populations [52]. The willingness-to-pay estimation is normally based on the notion that societal choices are pondered in making choices on how to distribute financial resources in a healthcare system of a country [53]. And, if a specific willingness-to-pay threshold is not accessible, a threshold of < 3 times of a country's annual gross domestic product per capita is suggested by the WHO Choosing Interventions that are Cost-Effective (CHOICE) project. This project recommends that if any financial intervention costs < 1 time of a country's annual gross domestic product per capita, it could be considered cost-saving and cost-effective [54].

In literature, various studies reported that effectiveness of a vaccine (COVID-19 or routine), the priority of its administration (to a particular population/group), and its overall coverage are the 3 leading aspects to declare a vaccine's cost-effectiveness and cost-saving. Earlier studies also concluded that COVID-19 vaccination was way more cost-effective than no vaccination at all. COVID-19 vaccination programs have proved to be the most cost-effective approach to combat the COVID-19 pandemic and its devastating effects in any situation and under all circumstances. On the other side, herd immunity which can also lower mortality rate among COVID-19 patients, is greatly influenced by COVID-19 vaccine effectiveness and vaccination coverage. Additionally, population/group priorities also play an important role in a vaccine effectiveness because a vaccine could be useless and impractical if not administered to the right populace [28-33].

In pharmacoeconomic evaluations, sensitivity analysis and its influencing factors are crucial to explore as they help a lot in interpreting the obtained results. Identifying and understanding the most influential parameter in sensitivity analysis also helps to determine the ICER values. Accuracy and preciseness of the cost-determination models can be further confirmed once sensitivity analysis results are in line to the base-case analysis' results. This confirmation further confirms the accuracy and cost-effectiveness of the model use [55]. In late 2026, it is expected that the COVID-19 vaccine category would generate $19.97 billion in revenue. Income is anticipated to grow at a compound annual growth rate (CAGR) of 27.82% from 2022 to 2027, with a market size of $3.52 billion by that year [56]. The successful operation of the healthcare system, availability of high-quality pharmaceuticals, the efficiency of the pharmaceutical industry, and government funding for healthcare facilities and political stability are only a few of the many variables that affect the practical execution of the healthcare budgets of Asian countries [57].

Since most of the Asian region is comprised of low- and middle-income countries (Pakistan, India, Sri Lanka, Bangladesh, Afghanistan. Iran, Myanmar, and Nepal,) and high-income countries (China, Japan, South Korea, and others) which could provide effective pharmacoeconomic evaluation of COVID-19 and its vaccine. But only few studies were evident in the literature from Asia to evaluate pharmacoeconomic burden of COVID-19 and its vaccination in Asian countries. The studies included from different Asian countries narrated that the proportion of investment was directly promotional to the population residing in these countries. Due to heavy losses by the COVID-19 pandemic, the local governments implemented the COVID-19 vaccination emergency programs to evaluate their cost-effectiveness in overcoming the COVID-19 pandemic. In some of the included studies, the cost of COVID-19 diagnosis, its treatment and COVID-19 vaccination are also included in their total cost of pharmacoeconomic burden evaluation. However, the number of published economic evaluation studies identified in this review might not truly reflect the research efforts in the region. And the actual number of economic evaluation studies on public health interventions might be higher as studies are more likely to be written in local languages for submission to local authorities in this region.

A study from the United States reported that the COVID-19 vaccination programs in the US were found to be 60% efficacious and prevented around 31% of the expected COVID-19 deaths in the United States [58]. At the start of the COVID-19 vaccination campaigns, three major vaccines BNT162b2 mRNA (Pfizer-BioNTech), mRNA-1273 (Moderna), and Ad26.COV2.S (Johnson & Johnson) had been given approval to be used in Asian countries [59]. Later on, other vaccines from other parts of the world had also received approvals to be used in Asian countries [50]. No doubt, the investment costs for the COVID-19 vaccination programs were high for the low and middle-incomed countries of Asia and they were considered as an extra burden on their economies [60,61]. The COVID-19 vaccine per dose cost was around $10-$30 in several Asian countries, whereby these expenses multiplied in two doses and with one or two booster doses as well [61-63]. These COVID-19 vaccination costs caused a massive burden on the healthcare systems of low- and middle-incomed countries of Asia. Additionally, it can be attributed to the fact that several Asian countries did not have enough healthcare resources like developed or rich countries and it could be considered a major barrier in provision of optimum healthcare facilities to the public especially in such devastating situation like COVID-19 pandemic.

Strength and Limitations

The current systematic review, which is based on studies conducted in different Asian countries, presents an enormous perspective of pharmacoeconomic burden evaluation of the COVID-19 vaccines. Although the included studies had varied sample sizes, yet policymakers from different Asian countries could use our study findings about pharmacoeconomic burden evaluations of the COVID-19 vaccination and accelerate ongoing COVID-19 vaccination programs. The studies excluded from this review were in languages other than English or were conference proceedings as abstracts that were not available as full-length papers. Excluding such studies from the systematic review may represent a small hindrance in understanding the current pharmacoeconomic burden of COVID-19 vaccines in Asian countries.

There are a few limitations of the recent systematic review which can be addressed through further research. The first limitation of the study was the geographical gap, as we discussed and analyzed the data only from Asian countries, not the entire globe, and did not compare it with other continents such as Australia, the USA, Russia and the Europe. The second limitation of the study was the unavailability of extensive data about the COVID-19 vaccine expenditures in the studied Asian countries. The third research gap was the selection and evaluation of limited number (available) of economic evaluations which lack the heterogeneity in case of results summarization.

5. CONCLUSIONS

The findings of this review revealed that in most of the Asian countries, the COVID-19 vaccination was considered cost-effective and a safe intervention to combat COVID-19 pandemic. The majority of the included studies reported that the COVID-19 vaccination efficacy was more than 60% which is similar to most of the studies reported in the other parts of the world. As the COVID-19 vaccine expenditure was an additional burden on the local healthcare budgets of the Asian countries, COVID-19 vaccination prioritization approach was adopted and it worked well in preventing COVID-19 devastating impact on their population. Our review results could also be used as a baseline information by the policymakers and healthcare managers to design and implement policies to combat a possible future pandemic where vaccination is needed.

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