ORIGINAL ARTICLE

A Cost Analysis of COVID-19 Vaccination: A Comparison between mRNA-based and Inactivated Virus Vaccines

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ABSTRACT

Introduction: COVID-19 vaccination is considered a primary preventive measure to combat the COVID-19 pandemic. Several types of COVID-19 vaccines were developed, among them the mRNA-based vaccine and the inactivated virus vaccine. Different COVID-19 vaccines have different purchase price and require different logistics system, which translate into different estimated vaccination costs. Therefore, this study aims to estimate the cost of COVID-19 vaccination using the mRNA-based vaccine compared to the inactivated virus vaccine to assist future decision-making related to COVID-19 vaccination. **Methods:** Direct costs for per-dose vaccination for both vaccines were estimated from the health provider's perspective using the microcosting approach. Vaccination pathways were constructed for both the mRNA-based and the inactivated virus vaccine based on activities involving the acquisition, transportation, storage, and vaccine injection processes. Cost value was obtained from purchase documents, asset records, and market surveys. **Results:** The estimated costs for COVID-19 vaccination were RM 69.71 per dose for the mRNA-based vaccine and RM 91.68 per dose for the inactivated virus vaccine. The difference in estimated vaccination costs was mainly driven by the difference in the vaccine purchase costs which was higher for the inactivated virus vaccine. **Conclusion:** COVID-19 vaccination using the mRNA-based vaccine incur was estimated to incur lower total costs to the health provider compared to the inactivated virus vaccine during the pandemic.
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INTRODUCTION

The global outbreak of the novel coronavirus SARS-CoV-2 (COVID-19) has been ongoing for the past three years, causing significant morbidity and mortality worldwide (1). Hence, COVID-19 vaccination was developed as a primary preventive measure to combat this pandemic (2, 3).

As part of the global community, the Malaysian government has also initiated efforts to provide a nationwide COVID-19 vaccination program. The National COVID-19 Immunization Programme (Program Imunisasi COVID-19 Kebangsaan or PICK) was organized, intending to vaccinate 80 percent of the population (4), provided free of charge for Malaysian citizens and non-citizens (4). Several vaccines were selected for use, including an mRNA-based vaccine and an inactivated virus vaccine (4). The vaccine delivery system constructed for the PICK programme involves the appointment of various COVID-19 Vaccine Storage Centres (Pusat Simpanan Vaksin or PSV) for the storage of mRNA-based vaccines. Additionally, more than 605 COVID-19 Vaccination Centre (Pusat Pemberian Vaksin or PPV) was set up throughout the country to administer COVID-19 vaccine injection to the population (5). These PPVs were set up mainly in government health clinics with some PPVs set in private health clinics, community buildings like stadiums and community halls as well as providing outreach vaccination (4). As of 1 March 2023, around 27 million people (84.3%) had completed at least two doses of COVID-19 vaccination in Malaysia (6). As of 5 October 2022, vaccine coverage for the Malaysian population based on types was mRNA-based vaccine (Pfizer, 61.2%), inactivated virus vaccine (Sinovac, 29.8%), vector vaccine (Astra Zeneca, 7.9%), and another inactivated vaccine (Cansino, 0.3%) (7).

Among different COVID-19 vaccine types, the mRNA-based COVID-19 vaccine is considered a new generation of vaccine (8), being the first commercially used mRNA-based vaccine platform (9) and has demonstrated effectiveness in preventing COVID-19 infections as

well as its related mortality and morbidity (10, 11). The mRNA vaccines have several advantages as compared to other vaccine types. First, compared to traditional vaccines, mRNA vaccines only need virus gene sequences (12) and do not need cell culture or animal matrix (13), enabling shorter-term development (12, 14) and a more scalable production (15). Secondly, because the mRNA-based vaccine does not contain infectious viral elements, the risk of infection is low (15). Despite these advantages, the mRNA-based vaccine structure is relatively unstable (8), therefore requiring a fundamental requirement of storage at ultralow temperature freezers (16), which presents a challenge to ensure effective vaccine delivery to the population. Hence, countries need to invest additional financial costs for the provision of ultra-low cold chain freezers and in addition, construct appropriate ultralow cold-chain logistics arrangements to cater to this need. In contrast, the inactivated virus vaccine is a more conventional vaccine platform (8) which had been used for existing vaccines, namely the typhoid vaccine, Salk polio vaccine, and influenza vaccine (14), The effectiveness of the inactivated virus vaccine against COVID-19 infection and mortality had been well demonstrated (17, 18). The inactivated virus COVID-19 vaccine has several advantages, particularly its safety for use (20, 21). Additionally, the inactivated virus vaccine has a relatively stable protein structure (22), only requiring storage at 2–8 °C (23). Therefore, the inactivated virus COVID-19 vaccine is easier to distribute (24) utilizing the existing vaccine cold-chain system.

Any vaccination intervention involves costs—both for the vaccine purchase itself, as well as the costs of the vaccine delivery system. The economic burden of COVID-19 vaccination was high, as the Malaysian government had spent an estimated RM 5.5 billion to provide COVID-19 vaccination to the population (25). Knowledge related to both the costs and effectiveness of a specific health intervention is fundamental for decision-making in the selection of a health intervention to ensure that the health provider and society receive the most value from the investment provided in a health intervention programme. As the mRNA-based and inactivated virus of COVID-19 vaccines have different vaccine characteristics and logistics requirements, it is imperative to identify the differences in vaccination costs for both vaccines, information that will be able to assist policy-makers in selecting the most cost-effective COVID-19 vaccine for use in future. Therefore, this study aims to estimate the cost of COVID-19 vaccination utilizing the mRNA-based vaccine and inactivated virus vaccine during the pandemic within the Malaysian setting, focusing on the activities related to vaccine acquisition, transportation, storage, and administration.

MATERIALS AND METHODS

This was a cost-analysis study using the microcosting approach. The direct cost of COVID-19 vaccination was estimated from the perspective of the healthcare provider. Vaccination pathways of COVID-19 vaccination involved activities such as vaccine purchase, vaccine storage, transportation, and vaccine injection were constructed for two types of COVID-19 vaccine; the mRNA-based and inactivated virus vaccine. Both vaccines were selected as they represent two major types of vaccines used in the Malaysian COVID-19 Vaccination Programme (7) and allow comparison between a newer vaccine (the mRNA-based vaccine) and a more conventional vaccine type (the inactivated virus vaccine) with different cold-chain logistics requirement.

Data collection setting

The vaccination pathways assumed that the PPV was housed in a government health clinic located within 50km from a COVID-19 Vaccination Storage Centre (Pusat Simpanan Vaksin or PSV). For the purpose of data collection, two COVID-19 vaccination centres (Pusat Pemberian Vaksin or PPV) located in Negeri Sembilan State were selected as the primary setting for data collection. The selected PPVs were located 50km from the COVID-19 Storage Centre (PSV). Data collection was done between August to December 2022.

Constructing Vaccination Pathway

COVID-19 vaccination costs were estimated by means of constructing a vaccination pathway for either vaccine, referring to the activities related to COVID-19 vaccine purchase, storage, transportation, and providing the vaccine to the population.

To construct the COVID-19 vaccination pathway, the researcher initially conducted a literature search to collect information from the relevant documents related to COVID-19 vaccine storage management (24) and guidelines for vaccine administration (25). The literature search allowed the researcher to obtain the general framework related to vaccine storage, transportation, and administration. To determine the activities and resources used for COVID-19 vaccination, key informants related to vaccine management were interviewed. The key informants were two pharmacists, a medical officer, two health nurses, and an assistant medical officer from the data collection site. As part of the validation for the study, the constructed vaccination pathway was discussed with an expert who had attended national-level training related to COVID-19 vaccine administration, with adjustments done based on the expert's recommendation.

Estimating costs

Based on the vaccination pathway determined, the researcher obtained information related to the resources for COVID-19 vaccination from observation of vaccination activities and interviews of the key informants. A data collection sheet was used to collect all data related to the vaccination activities, the resources

used, and their respective quantities. The direct costs for COVID-19 vaccination in this study include vaccine purchase costs as well as costs for activities involving storage, transportation, and vaccine injection.

The resources for cost estimation were obtained from the vaccination pathway. For some cost components which was considered highly dependent on variations between personnel (for example, duration of medical officer consultation and the amount of personnel protective equipment (PPE) used for vaccine injection), assumptions were used based on standard guideline or references. The researcher obtained data related to the costs from several resources; in particular the administrative department and pharmacy department. From these departments, the researcher obtained the costs from several documents, such as purchase records, item procurement invoices, or asset records. Additionally, values related to labor costs were obtained by interviewing the personnel key informants. However, should the relevant costs not be available from these resources, a market survey was conducted to determine the estimated cost for the relevant item, whereby the most conservative price for the respective item was selected as the cost estimate. All data referred to the item costs for the year 2022.

The cost estimate calculation was done for each mRNA-based vaccine and inactivated virus vaccine based on the constructed vaccination pathway. Data resources related to cost (for example, purchase, emolument, and utilities) were obtained based on the costs in the year 2022. All costs were estimated in Ringgit Malaysia (RM) in 2022. No discounting was done. Table I summarizes the overall method of cost estimation.

Some costs were not included, in particular land capital, building capital, personnel training cost, surveillance system for adverse events following immunization (AEFI), provision of COVID-19 vaccine online appointment or vaccine certificate using the mySejahtera application or the use of online Vaccine Management System (VMS). Indirect costs incurred by patients (for example transportation cost to get vaccinated) were not included.

Ethical permission for the study was received from the Medical Research Ethics Committee of the Ministry of Health (reference NMRR-21-1804-61238 (IIR)). Where applicable, the study methods were reported based on the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) reporting guidelines (28).

RESULTS

The constructed vaccination pathway revealed some differences in the vaccine delivery process between the mRNA-based and inactivated virus vaccines. For the mRNA-based vaccine, the vaccine was delivered to the Vaccine Storage Centre (PSV) where the vaccines were stored in the subfreezing temperature for a maximum duration of 6 months after their manufactured date. On a weekly basis, the COVID-19 Vaccination Centre (PPV) personnel collected the mRNA-based vaccines from the respective PSV while maintaining the cold chain during transportation. Interestingly, the transportation of mRNA-based vaccine from PSV to the PPV involved the Royal Malaysian Police (Polis Diraja Malaysia or PDRM), whereby two police officers and a PDRM vehicle escorted the health personnel to transport the vaccines in order to ensure vaccine safety and optimize traffic flow for maintenance of vaccine cold chain. In

Table I: Summary of method for estimation of costs for vaccine purchase and delivery

Activity	Type of cost	Cost	Costing method	Source	Allocation factor
Vaccine purchase	Recurrent	Vaccine purchase	microcosting	Purchase records	-
Vaccine transportation	Capital	Vehicle	microcosting	Asset records	Time
	Recurrent	Labor cost	microcosting	Interview	-
	Recurrent	Vehicle fuel	microcosting	Calculation	-
Vaccine storage	Capital	Purchase of freezer	microcosting	Market Survey	Number of vaccines
	Recurrent	Utility (cost for electricity for freezer)	microcosting	Calculation (26)	-
Vaccine injection	Recurrent	Labor costs	microcosting	Interview	-
		Medical Officer	microcosting	Assumption (27)	
		Nursing	microcosting	Interview	
		Assistant Medical Officer	microcosting	Interview	
	Recurrent	Consumable items	microcosting	Purchase records	-
		PPE	microcosting	Assumption (28)	
		Hand hygiene	microcosting	Assumption (28)	
	Recurrent	Utilities (electricity, water)	Stepdown costing	Administrative records	Floor space
		Building maintenance cost	Stepdown costing	Administrative records	Floor space

the PPV, COVID-19 mRNA-based vaccines can be stored in a vaccine refrigerator at a temperature of 2°C to 8°C for a month (24). These vaccines were then used for the immunization of eligible individuals. Figure 1 summarizes the flow of storage and delivery of mRNA-based vaccines.

For the inactivated virus vaccine, the vaccine suppliers transported the vaccines to the COVID-19 Vaccination Centre (PPV) for storage in the vaccine refrigerator at the temperature of 2°C to 8°C until their expiry date and these vaccines will be used for immunization of eligible population. Figure 2 describes the flow of storage and delivery of the inactivated virus vaccine.

After vaccine administration, monitoring of adverse events following immunization (AEFI) was conducted by the National Pharmaceutical Regulatory Agency (NPRA) and PPV using several platforms, namely My Sejahtera application, the NPRA website, and the Pharmacy Information System (PhIS) (25). However, the cost of pharmacovigilance activities was not included in this study.

COVID-19 vaccine administration activities are summarized in Figure 3. The COVID-19 vaccine

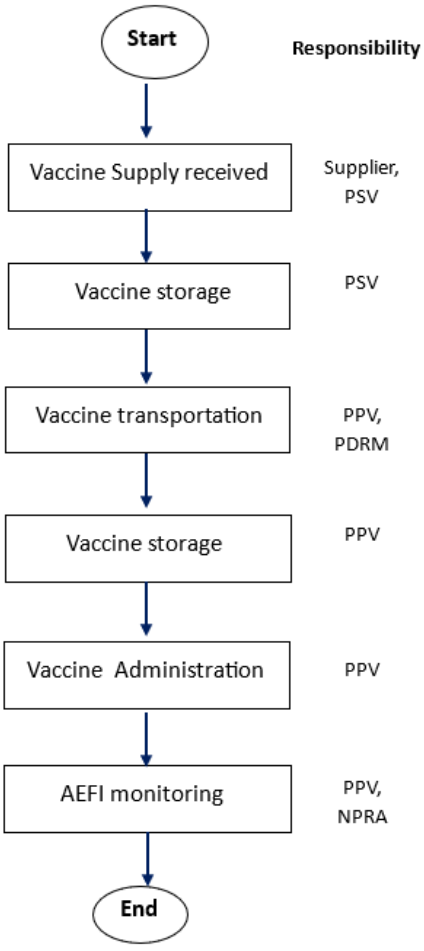

Figure 1: Flow of storage and delivery of mRNA-based vaccine. PSV=COVID-19 Vaccine Storage Center, PPV=-COVID-19 Vaccination Centre

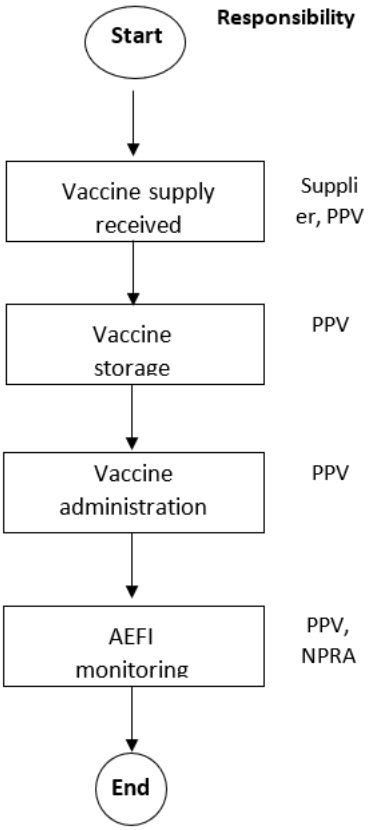

Figure 2: Flow of storage and delivery of inactivated virus COVID-19 vaccine PPV=COVID-19 Vaccination Centre, NPRA= National Pharmaceutical Regulatory Agency

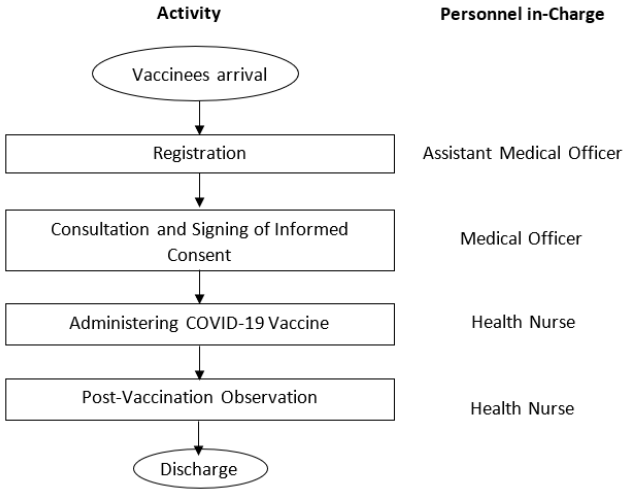

Figure 3: Flow of Activities during Administering the COVID-19 vaccine in the COVID-19 Vaccination Centre

administration was provided using an appointment basis. On a daily basis, the medical officer of the COVID-19 Vaccination Centre (PPV) accessed the MySejahtera system to review the details of individuals who were registered for vaccination. Based on the number of vaccinees daily, the nurse on duty collected a sufficient amount of vaccines for use from the pharmacy. As scheduled vaccinees arrived for vaccination, they underwent registration whereby the assistant medical officer reviewed the respective vaccinee details, record

keeping in the MySejahtera System for the vaccinee and record keeping in the Vaccine Administration System (MyVAS) system for information related to the administered vaccine. Subsequently, a medical officer conducted the consultation session to provide an explanation related to the vaccine, ensure that the vaccinees were eligible for vaccination, address their concerns, and advise on the actions to be taken for adverse events following immunization. The vaccination consent form was obtained. Once the consultation session was completed, the vaccinees proceeded to the injection room to receive the COVID-19 vaccine injections. Vaccine preparation for mRNA-based vaccines and inactivated vaccines were slightly different. For the mRNA-based vaccine, one vial of vaccine contained 6 doses of vaccine and needed to be diluted to the required concentration to obtain 0.3ml of vaccine per dose (25). Meanwhile, for inactivated virus vaccines, one vial contained 2 doses of vaccine and did not need any dilution (25). The vaccinees were given the injection intramuscularly, with the injection site covered with cotton wool and surgical tape. Afterwards, the vaccinees waited for 15 minutes in the observation area to observe symptoms of anaphylaxis (25). If they did not develop anaphylaxis symptoms (for example, giddiness, headache, or rash), they were discharged.

The pathways for COVID-19 vaccine storage, delivery, and vaccine administration were used to estimate vaccination costs.

Estimated Per Unit Cost of COVID-19 Vaccination

From this study, it was estimated that the cost for COVID-19 vaccination was RM 69.41 per dose (for mRNA-based vaccine) and RM 91.68 per dose (for inactivated virus vaccine). Table II summarizes the estimated total cost per dose of COVID-19 vaccination for different vaccines and their components. Vaccine purchase costs were estimated to consist of between 69 to 78 percent of the overall estimated vaccination costs. The vaccine storage, transportation, and administration (injection) cost of the mRNA-based vaccine was estimated to be RM 17.30 per dose while the inactivated virus vaccine was RM 12.30 per dose.

Table II: Unit Cost for COVID-19 Vaccination using the mRNA-based and Inactivated Virus Vaccine

Activity	Type of Cost	Cost Estimate (RM)	
		mRNA-based vaccine	inactivated virus vaccine
Overhead cost		0.67	0.67
Vaccine purchase	Recurrent	48.38	71.27
Vaccine storage	Capital	0.67	0.28
	Recurrent	0.00	0.00
Vaccine Transportation	Capital	0.29	
	Recurrent	1.7	
Vaccine injection	Capital	0.08	0.08
	Recurrent	11.61	11.04
Vaccine wastage		6.01	8.34
	Total	**69.41**	**91.68**

*Estimated recurrent costs for vaccine storage (fuel) at less than RM0.001 per unit cost and rounded to RM 0.00
*Vaccine wastage assumed at 10 percent

DISCUSSION

This study estimated the per dose unit cost for the mRNA-based COVID-19 vaccine (RM 69.41 per dose), which was lower than the estimated cost for the inactivated virus vaccine (RM 91.68 per dose). At the point of time that this report was written, there was still a paucity of knowledge related to COVID-19 vaccination costs, especially for studies done under the microcosting approach. Available data from the African region estimated that the cost for mRNA-based vaccination was comparable to the estimated cost from this study, with their results ranging from USD 11.8 (RM 51.89) to USD 24.63 (RM 108.30) depending on vaccine price and speed of vaccine roll-out programme (30) while a Thailand study used the value of 488 Baht (RM 62.90) per dose of mRNA-based vaccine (31). In contrast, a microcosting study from Kenya had estimated that the vaccination cost for two-doses vaccine per person ranged from USD 24.8 (RM 108.12) to USD 29.7 (RM 130.55) for a COVID-19 vaccination programme (32), a much lower estimate from the results of this study. Unfortunately, there were no available data related to the estimated cost for the inactivated virus vaccine. Nevertheless, estimated vaccination costs depend on a multitude of factors including the cost of vaccine purchase, cost of labor, capital costs, and consumables. Understandably, as vaccine and resource market prices differ between countries, compounded with different costing approaches and cost components used in different studies, wide variations in the estimated COVID-19 vaccination costs are expected.

The vaccine delivery costs (referring to the cost of storage, transportation, and injection) of the mRNA-based vaccine were estimated to be higher than the inactivated virus vaccine, owing to the fact that the mRNA-based vaccine requires additional storage on ultralow temperature cold chain and transportation system. The vaccine delivery cost estimate from this study was higher than the estimate by the World Health Organization (WHO) at USD 1.41 (RM 6.29) per dose, which is expected considering the WHO estimate excluded labor costs from their estimation (28). The vaccine delivery cost value estimated from this study was also relatively close to the delivery cost for the COVID-19 vaccine paid by the Malaysian government to the private healthcare practitioner who joined the COVID-19 vaccination programme, which was RM 14 per dose administered (33).

Our study has provided evidence that the estimated cost

of COVID-19 vaccination using the mRNA-based vaccine in Malaysia during the pandemic was lower compared to the inactivated virus vaccine. Clearly, the major drive of the lower estimated vaccination cost for the mRNA-based vaccine was the lower vaccine purchase cost for the mRNA-based vaccine. The lower purchase price for the mRNA-based vaccine used in Malaysia (BNT162b2) was made possible by the three-tier pricing strategy policy adopted by its manufacturer, the Pfizer company (34). In this three-tier pricing strategy, in order to support vaccine equity, countries were offered vaccine purchase costs based on their income (34). Therefore, the low-income countries were offered vaccines at a low price while the high-income countries purchased vaccines at a higher price (35) with the vaccine costs ranging from RM 31 to RM 75 per dose (35). Therefore, Malaysia, as an upper-middle-income country was offered to purchase the mRNA-based vaccine according to its income level, which was lower than the purchase costs for inactivated virus vaccine offered by its manufacturer. However, for high-income countries, the estimated purchase cost for the mRNA-based vaccine (RM 89.56) was higher than the inactivated virus vaccine (RM 61.63) (35). In these circumstances, the estimated cost for COVID-19 vaccination is expected to be higher for the mRNA-based vaccine compared to the inactivated virus vaccine. Although reports have not suggested other explanations of the potential lower cost for mRNA-based vaccines compared to the inactivated virus vaccine, studies have always suggested that mRNA-based vaccine is simpler to produce as it only involves synthetic production (13, 36), with shorter production cycle and is easier to scale up (15, 36), hence offering possible easier industrialization process (36). These factors may also contribute to the ability to produce the mRNA-based vaccines at a lower cost compared to the inactivated virus vaccine.

The COVID-19 vaccine purchase prices during the years 2020 to 2022 were considered low prices under the term called 'pandemic price' (37). During this period, vaccine manufacturers emphasized that the vaccine prices offered were lower prices in order to assist countries in alleviating the COVID-19 pandemic, especially as the demand for vaccines was high (37). As the year 2023 approached with weaker COVID-19 vaccine demand (38), the vaccine manufacturer declared the increased price of COVID-19 vaccines, for example, the Pfizer company announced a marked price increase of its mRNA-based vaccine, ranging from USD 110 (RM 487) to USD 130 (RM 557) per dose (39). Meanwhile, the manufacturers of the inactivated virus vaccine had not made such an announcement, albeit a similar situation was expected for any COVID-19 vaccines as market conditions like demand, competition prices, and efficacy determine the COVID-19 vaccine prices (39). In essence, the overall vaccination cost estimates obtained from this study were based on the context of vaccination costs during the period of the COVID-19 pandemic.

Results from this study imply that despite the need to purchase the ultralow temperature freezer and construct an additional logistics system to provide the mRNA-based COVID-19 vaccine in Malaysia, the COVID-19 vaccination using the mRNA-based vaccine had lower estimated costs compared to the inactivated virus vaccine. Hence, in terms of economic costs, the selection of the mRNA-based vaccine as the major vaccine for use in nationwide COVID-19 vaccination provides good benefits in terms of its lower costs to the health provider. Because of the potential future use of COVID-19 vaccines for booster doses or seasonal vaccination, this information may assist policy decisions for the healthcare provider. Hence, the utilization of the mRNA-based vaccine will benefit the healthcare provider for future COVID-19 vaccination policy. Regardless, a cost-effectiveness analysis will provide a better indication of the value of different COVID-19 vaccines by considering the value of vaccine effectiveness.

The cost estimation in this study should be appreciated within its limitations and assumptions. First, the World Health Organization (WHO) listed some costs relevant to planning and implementation of a nationwide vaccination, for example, planning and managing the programme, training healthcare workers, costs for vaccine outreach, and pharmacovigilance activities to monitor vaccine side effects (28). In Malaysia, these activities include the utilization of the online MySejahtera application for managing vaccine registration, appointments, and certification (39), the use of a Vaccine Management System (VMS) for the management and distribution of COVID-19 vaccines (24) and personnel training incur costs, which were not included in this study. Secondly, in this study, vaccine delivery was assumed to be done in existing health facilities with the exclusion of building and land capital costs. In reality, for the Malaysian COVID-19 Vaccination Programme (PICK), the government outsources some vaccine delivery services by collaborating with private healthcare practitioners with additional costs involving providing vaccine services in rented facilities and organizing outreach programmes (40). Additionally, the estimated costs for the mRNA-based vaccine for this study were based on the assumption of a 50-kilometre distance between the COVID-19 Vaccination Storage (PSV) and the COVID-19 Vaccination Centre (PPV). In reality, there were a total of 54 PSV and 605 PPV in Malaysia during the peak COVID-19 Vaccination Programme (5), with various differences of distance between PSV and PPV, as well as different methods of mRNA-based vaccine transportation between them. Therefore, the lower distance between the PSV and PPV in the urban areas may result in lower estimated mRNA-based COVID-19 vaccination costs and vice versa for the COVID-19 vaccination logistics in rural or remote areas. Hence, the vaccination costs estimated from this study are likely to be a conservative value.

Third, estimated values for some items (for example, the capital cost of vehicles for vaccine transportation) were obtained from market surveys, where in the event of several values available, the most conservative estimate will be used. This results in potential underestimation of the costs. Fourth, any data used for a cost analysis will have some uncertainties related to it. Therefore, the estimated costs from this study depend on the method used, data resources, and the time when the data was collected.

In short, the estimated values for COVID-19 vaccination from this study in no way represent the actual financial and economic cost for the implementation of the COVID-19 vaccination programme (Program Imunisasi COVID-19 Kebangsaan or PICK) in Malaysia during the COVID-19 pandemic. However, the estimates from this study have successfully disproved the impression that using the mRNA-based COVID-19 vaccine incurs a higher cost to the government compared to the inactivated virus vaccine. Subsequently, considering that the mRNA-based COVID-19 vaccination incurs lower costs to the government, compounded with its estimated higher effectiveness against COVID-19 complications (10, 11), the mRNA-based vaccine is expected to provide great value and benefit to the Malaysian population during the pandemic.

CONCLUSION

COVID-19 vaccination using the mRNA-based vaccine was estimated to incur lower total costs to the health provider compared to the inactivated virus vaccine during the pandemic. Hence, the mRNA-based vaccine is expected to provide great value to the Malaysian population during the COVID-19 pandemic. The findings from this study highlighted that future estimation of COVID-19 vaccination costs should be done within the context of post-pandemic vaccine purchase costs. Additionally, a comprehensive economic evaluation should be done to estimate the cost-effectiveness of different COVID-19 vaccines followed by a budget impact analysis in Malaysia to assist in policy-making in future decisions related to COVID-19 vaccination.

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