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Rapid Assessment of Cost-effectiveness of COVID-19 Vaccine against Severe Illness in Thailand

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Abstract

Though the benefit of COVID-19 vaccine in preventing severe illness is universally accepted, little is known about its benefit relative to its investment in monetary value. This study aimed to assess the cost-effectiveness of the national COVID-19 vaccination campaign compared to a scenario where this had not been introduced. This study used a test-negative matched case-control study design to analyze the occurrence of severe illness. Then, a societal perspective was applied for cost-effectiveness analysis. The cost calculation involved aggregating expenses from both COVID-19 treatment and productivity loss during sickness or premature death. The incremental cost-effectiveness ratio (ICER) was calculated to compare the hypothetical scenario (no vaccination campaign) with the status quo (the vaccination campaign in place). The study found that the three-dose regimen vaccine effectiveness remained over 80% over a year, 0.99 (95% CI 0.96–1.00) in August 2021 to 0.80 (95% CI 0.62–0.89) in June 2022, potentially preventing 71,913 severe illness cases. The ICER analysis showed that preventing one death incurred an extra cost of USD 23,938. Similarly, preventing one intubated case resulted in an additional cost of USD 45,646. Notably, a reduction of vaccine related cost (including administration cost) greatly improved the cost-effectiveness of the campaign. However, a sole reliance on ICER may be insufficient to determine the vaccine campaign's effectiveness. Therefore, this study suggests further analyses, such as research on willingness to pay threshold and budget impact, to gain a more comprehensive understanding for future policy decision-making.

Keywords: COVID-19, vaccination, vaccine effectiveness, incremental cost-effectiveness ratio, ICER, Thailand

Background

The sudden surge in cases and fatalities from severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) posed severe challenges to public healthcare systems in all nations. Challenges included intensive care bed capacity, insufficient medical personnel and resources, and disrupted patient delivery and isolation systems.[1] Many governments responded to the pandemic by implementing measures such as compulsory mask-wearing in public spaces, social distancing, and city lockdowns.[1,2] Additionally, introducing COVID-19 vaccines was considered pivotal when combined with these public health interventions.[3]

From the detection of the first COVID-19 case in January 2020 to June 2022, the number of COVID-19 infections among Thailand's population reached 4,522,915, resulting in a death toll of 30,648.[4,5] To address the pandemic, Thailand's government initiated the national COVID-19 immunization plan in early 2021 with introducing multiple vaccines including CoronaVac, ChAdOx1 nCoV-19, Sinopharm, BNT162b2, and mRNA-1273. The vaccination target groups are in line with the vaccination priorities outlined by the Center for COVID-19 Situation Administration's policy. These groups encompass frontline medical and public health personnel, individuals with underlying conditions such as severe chronic respiratory diseases, heart and coronary artery diseases, chronic kidney diseases, various cancers undergoing treatment, diabetes, and obesity. Additionally, the groups include individuals aged 60 and over, those actively involved in COVID-19 control, pregnant women, public health personnel beyond the frontline, occupational sectors like tourism, international travelers, the population comprising both Thai and foreign nationals, diplomats, industrial and service sector workers, students aged 12–18 years old, and students studying abroad, regardless of registration status. Following the vaccination of those, the government extended vaccine coverage to the entire population, targeting an 80% vaccination rate.[6]

As of June 2022, COVID-19 vaccination rates were at 82% for the first dose, 76% for the second dose, and 43% for the third dose and beyond, among Thailand's population.[7] Prior domestic studies had suggested the clinical effectiveness of various vaccine regimens in Thailand.[8,9] Nevertheless, those studies have not delved into their cost-effectiveness. The cost of vaccines in this study depends on various factors, including the price of the vaccines themselves, the costs associated with their administration, and the cost of treatment. Additionally, the indirect cost of productivity, including the gross domestic product (GDP) loss based on the duration of absenteeism from work should not be ignored.

Following the emergence of the ancestral COVID-19 strain in early 2020, Thailand subsequently witnessed various mutations, notably the Alpha (B.1.1.7), Beta (B.1.351), Gamma (P.1), Delta (B.1.617.2), and Omicron (B.1.1.529, BA.2, BA.2.75, BA.4/BA.5, BA.4, and BQ.1) variants.[10,11] This study, conducted in Thailand from 1 Jul 2021 to 30 Jun 2022, revealed that during the latter half of 2021, the Delta variant (B.1.617.2) from India held primary dominance, whereas throughout 2022, the Omicron variant (B.1.1.529) from South Africa prevailed.[9,11]

In comparison to the ancestral variant, both the Delta and Omicron variants exhibited higher transmission rates, likely attributed to their increased transmissibility and enhanced capacity to evade the immune response and recognition by T-lymphocytes, as evidenced by a higher reproductive number when compared to earlier variants. During the scenario of the specific variants predominating in Thailand, the Delta variant (with a basic reproductive number: R_0=1.22 and 95% confidence interval (CI) 1.22–1.22) and the Omicron variant (R_0=1.91 and 95% CI 1.87–1.95) were approximately 1.13 and 1.77 times more transmissible than the Alpha variant (R_0=1.08 and 95% CI 1.08–1.08) from England, which was prevalent at the beginning of 2021.[12-14]

Disease severities varied among variants. Alpha, Gamma, and Delta showed comparable profiles, while Omicron infections were less severe. However, breakthrough infections were more common with Omicron. Delta posed a higher mortality risk than the Alpha variant, while Omicron, despite high transmissibility, was less deadly.[15]

Vaccine distribution challenges prompted this research on the cost-effectiveness of COVID-19 vaccines in Thailand. The study aimed to guide policymakers by evaluating costs and outcomes related to the vaccine campaign from July 2021 to June 2022. Assessing economic feasibility in preventing severe illness, the study provided insights for prioritizing strategies to reduce morbidity, mortality, and direct costs from a payer's perspective. Therefore, the objective was to evaluate the cost-effectiveness of the national COVID-19 vaccination campaign compared to a scenario where the vaccination policy was absent.

Materials and Methods

Study Design

This study conducted a test-negative matched case-control study to examine the occurrence of severe illness from 1 Jul 2021 to 30 Jun 2022 by utilizing nationwide data of individuals who were tested for SARS-CoV-2. For each case in this study, two controls were selected who closely matched in terms of age, testing date, and the location where their samples were collected. Then, cost calculation involved aggregating expenses from a societal perspective and the incremental cost-effectiveness ratio (ICER) by comparing the status quo (vaccination campaign in place) with a hypothetical (no vaccination campaign) were calculated.

Data Collection

Data were collected from the Co-Lab, Co-Ward, COVID-19 death, and Ministry of Public Health Immunization Centre (MOPH-IC) databases. These databases are managed by the Department of Medical Sciences, Department of Medical Services, Department of Disease Control, and Bureau of Digital Health under the Ministry of Public Health, respectively. The Co-Lab database serves as the national laboratory recording system, encompassing health service records of individuals undergoing the polymerase chain reaction test or the professional-use antigen-detecting rapid diagnostic test for SARS-CoV-2 across both public and private health facilities. The Co-Ward database nationally monitors hospital bed capacity and clinical severity. The COVID-19 death contains all death records associated with COVID-19 infection. The study received a nationwide immunization history from MOPH-IC.

Case-control Study

In this study, severe illness was characterized by either severe pneumonia requiring intubation support or resulting in a fatal outcome. A case was identified as a Thai national testing positive for SARS-CoV-2, either through the polymerase chain reaction testing or professional-use antigen-detecting rapid diagnostic testing, and experienced severe illness between 1 Jul 2021 and 30 Jun 2022. Each occurrence of severe pneumonia requiring intubation and subsequent death was counted as a single case. Conversely, a control was an individual testing either negative for SARS-CoV-2 or positive without experiencing severe illness throughout the study period.

Cost Evaluation

This study conducted a comprehensive cost evaluation, considering both direct and indirect costs from a societal perspective. Provider-related costs, specifically treatment expenses, were sourced from the National Health Security Office, providing average direct medical costs for severe illness cases.[16] The market cost of each vaccine type at the end of 2021 was utilized, and GDP per capita data for the Thai population in 2021 from the World Bank informed the calculation of indirect costs.[17,18] The contribution of GDP per capita by age groups was assumed to follow the income distribution by age groups, as recommended by the Office of the National Economic and Development Council.[19-21] No cost discounting was applied in this study.

Direct cost

From the healthcare provider's viewpoint, encompassing entities or individuals responsible for healthcare service payments, costs considered included vaccine prices, administration costs, and treatment expenses for intubated patients, along with admission costs in the intensive care unit. A rough assumption was made for fatalities, equating their intensive care unit stay duration to that of intubated patients.

Indirect cost

Indirect costs were evaluated from broader social and economic perspectives, examining the societal implications of financial decisions. The focus was on quantifying the economic impact, specifically GDP loss, due to the daily absence of the workforce among admitted patients and instances of fatalities. This calculation considered two age categories: individuals under aged 60 and those aged 60 and beyond.

Data Analytic

A conditional logistic regression, implemented with the sklearn package and linear model module in Python 3.12, estimated the odds of intubation or fatality among vaccinees compared to the unvaccinated group. Results were expressed in odds ratios (OR) with a 95% CI. Vaccine effectiveness (VE) was calculated as VE = 1 – OR. Expected numbers of severe illness cases were determined by dividing actual cases by OR. This study then subtracted the actual number of severe illness cases from the expected number to obtain the number of cases averted by the vaccine campaign.

ICER Calculation

For cost calculation, two scenarios were considered: the status quo (the vaccination campaign in place), and a hypothetical scenario (no vaccination campaign). A 14-day productivity loss for severe illness patients was assumed.[22] Regarding mortality, the time remaining until life expectancy was calculated by subtracting the median ages of deaths from the overall life expectancy of the Thai population. This result was multiplied by age-specific GDP contribution.[23] The incremental cost-effectiveness ratio (ICER) was calculated by dividing the difference in the total costs between two scenarios by the difference in health outcomes (number of intubated cases and fatalities averted).

The status quo (the vaccination campaign in place)

The total costs included medical costs, vaccine costs, vaccine administration costs, and GDP loss. The total vaccine expenses were calculated by adding up the result of multiplying the cost of each vaccine brand (based on market cost) with its corresponding share of vaccine uptake among the Thai population, as sourced from the MOPH-IC databases.

Hypothetical scenario (no vaccination campaign)

The total expenses were computed using a method similar to the status quo, excluding vaccination costs. The expected severe illness numbers were deduced from OR.

Moreover, to gain a broader understanding of the cost-effectiveness of the COVID-19 vaccination campaign, this study performed a sensitivity analysis by adjusting the cost related to vaccine administration (vaccine vial expense and logistic cost) by reducing these costs from 100% to 80% and 50% respectively. This approach allowed us to explore potential impact of cost reductions on the overall effectiveness and feasibility of implementing the vaccination policy in the future given the change in the market price of vaccines.

Results

Descriptive Study

Receiving a higher number of vaccine doses resulted in greater effectiveness against severe illness (Table 1). Despite showing a declining trend, the three-dose and four-dose regimens maintained over 80% effectiveness throughout a one-year duration. The one-dose regimen lost its protective effect after a one-year period.

Table 1. Odds ratio and vaccine effectiveness of developing severe infection in different vaccine regimens over time

Month (year)	Doses received	Odds ratio (95% CI)	Vaccine effectiveness (95% CI)
July 2021	1	0.33† (0.29–0.37)	0.67† (0.63–0.71)
	2	0.07† (0.06–0.09)	0.93† (0.91–0.94)
	3	NA	NA
August 2021	1	0.34† (0.30–0.38)	0.66† (0.62–0.70)
	2	0.10† (0.08–0.13)	0.90† (0.87–0.92)
	3	0.01† (0.00–0.04)	0.99† (0.96–1.00)
September 2021	1	0.40† (0.35-0.45)	0.60† (0.55–0.65)
	2	0.13† (0.11-0.16)	0.87† (0.84–0.89)
	3	0.02† (0.01-0.05)	0.98† (0.95–0.99)
October 2021	1	0.53† (0.44–0.63)	0.47† (0.37–0.56)
	2	0.13† (0.11–0.16)	0.87† (0.84–0.89)
	3	0.02† (0.01–0.03)	0.98† (0.97–0.99)
November 2021	1	0.54† (0.42–0.70)	0.46† (0.30–0.58)
	2	0.15† (0.12–0.18)	0.85† (0.82–0.88)
	3	0.01† (0.00–0.22)	0.99† (0.98–1.00)
December 2021	1	0.77 (0.55–1.07)	0.23 (-0.07–0.45)
	2	0.24† (0.19–0.30)	0.76† (0.70–0.81)
	3	0.04† (0.02–0.08)	0.96† (0.92–0.98)
January 2022	1	0.88 (0.48–1.61)	0.12 (-0.61–0.52)
	2	0.37† (0.27-0.53)	0.63† (0.48–0.73)
	3	0.07† (0.03–0.16)	0.93† (0.84–0.97)
	4	NA	NA
February 2022	1	0.77 (0.47–1.26)	0.23 (-0.26–0.53)
	2	0.46† (0.34–0.61)	0.54† (0.39–0.66)
	3	0.15† (0.10–0.23)	0.85† (0.77–0.90)
	4	0.04† (0.01–0.13)	0.96† (0.87–0.99)
March 2022	1	0.60* (0.42–0.85)	0.40* (0.15–0.58)
	2	0.27† (0.22–0.34)	0.73† (0.66–0.78)
	3	0.08† (0.06–0.11)	0.92† (0.89–0.94)
	4	0.00† (0.00–0.02)	1.00† (0.98–1.00)
April 2022	1	0.59* (0.41–0.85)	0.41* (0.15–0.59)
	2	0.42† (0.34–0.52)	0.58† (0.48–0.66)
	3	0.13† (0.09–0.17)	0.87† (0.83–0.91)
	4	0.04† (0.01–0.10)	0.96† (0.90–-0.99)
May 2022	1	0.66 (0.34–1.30)	0.34 (-0.30–0.66)
	2	0.35† (0.24–0.50)	0.65† (0.50–0.76)
	3	0.16† (0.10–0.26)	0.84† (0.74–0.90)
	4	NA	NA
June 2022	1	1.66 (0.77–3.60)	NA
	2	0.44† (0.27–0.70)	0.56† (0.30–0.73)
	3	0.20† (0.11–0.38)	0.80† (0.62–0.89)
	4	0.13† (0.03–0.61)	0.87† (0.39–0.97)

*Before January 2022, as the number of those receiving four doses was extremely small, thus we focused on one to three doses only. *p-value < 0.01. †p-value < 0.001. NA: denotes not applicable as the number of the vaccinees in particular vaccine category was too small to perform valid calculation (such as causing negative vaccine effectiveness).*

The actual recorded severe illness cases amounted to 65,165 (Table 2). Had the vaccine campaign not been established, the number of severe illness cases would have reached 137,078 (95% CI 111,618–191,922). As a result, 71,913 (95% CI 46,453–126,757) cases of severe illness, including 33,822 fatalities, were effectively averted. The volume of prevented cases was prominent among individuals aged 60 years or older.

Table 2. Number of severe illness cases in actual situation and in the scenario with an absence of vaccine campaign

Scenario	Illness level	Age groups—10^3 persons (95% CI)		
		All age groups	<60 years	≥60 years
Actual situation	Intubated cases	34.52	9.67	24.85
	Fatalities	30.65	8.58	22.07
	Total severe illness cases	65.17	18.25	46.92
No vaccination campaign	Intubated cases	72.61 (59.12–101.66)	20.33 (16.55–28.46)	52.28 (42.57–73.19)
	Fatalities	64.47 (52.50–90.26)	18.05 (14.70–25.27)	46.42 (37.80–64.99)
	Total severe illness cases	137.08 (111.62–191.92)	38.38 (31.25–53.74)	98.70 (80.37–138.18)
Prevented cases	Intubated cases	38.09 (24.61–67.14)	10.67 (6.89–10.67)	27.43 (17.72–48.34)
	Fatalities	33.82 (21.85–59.62)	9.47 (6.12–16.69)	24.35 (15.73–42.92)
	Total severe illness cases	71.91 (46.45–126.76)	20.14 (13.01–35.49)	51.78 (33.45–91.27)

CI: confidence interval.

During the study period, the total cost of the vaccine campaign amounted to US dollar (USD) 1,846 million and the total treatment cost for all severe illness cases under the status quo consequently reached USD 176 million. Considering these altogether with the GDP loss (USD 861 million), a total cost incurred for the status quo was USD 2,882 million (Tables 3, 4).

In the hypothetical scenario (no vaccination campaign), the estimated total treatment cost was USD 369 million (95% CI USD 300–517 million). When stratified by age group, the treatment cost for individuals under 60 years was USD 103 million (95% CI USD 84–145 million), accounting for 28% of the treatment cost. The remaining 72% of the total treatment cost, equivalent to USD 266 million (95% CI USD 217–372 million), was attributed to individuals aged 60 years and above.[24] The expected overall GDP loss for all age groups combined was USD 1,812 million (95% CI USD 1,475–2,536 million), leading to the grand cost for the hypothetical scenario of USD 2,181 million (95% CI USD 1,776–3,051 million).

Table 3. Treatment cost (in million USD) due to severe infection in actual situation and in the scenario with an absence of vaccine campaign

Scenario	Illness level	Age groups—million, USD* (95% CI)		
		All age groups	<60 years	≥60 years
Actual situation	Intubated cases	93.04	2,602	6,682
	Fatalities	82.61	231.19	59.49
	Total severe illness cases	175.65	49.06	126.31
No vaccination campaign	Intubated cases	195.38 (159.29–273.76)	54.98 (44.55–76.69)	140.69 (114.75–197.36)
	Fatalities	173.67 (141.25–243.03)	48.49 (39.47–67.95)	125.18 (101.78–175.08)
	Total severe illness cases	369.05 (300.83–516.79)	103.47 (84.30–144.63)	265.87 (216.53–372.16)
Prevented cases	Intubated cases	102.62 (66.26–180.72)	28.76 (18.61–45.11)	73.87 (47.65–130.25)
	Fatalities	91.07 (58.92–160.70)	25.37 (16.35–45.11)	65.69 (42.29–115.59)
	Total severe illness cases	193.69 (125.18–341.42)	54.13 (34.96–95.58)	139.56 (90.22–245.85)

**Based on 1 US dollar (USD) was equivalent to 35.47 Thai Baht (THB). CI: confidence interval.*

Table 4. GDP loss (in million USD) due to severe infection in actual situation and in the scenario with an absence of vaccine campaign

Scenario	Illness level	Age groups—million, USD* (95% CI)		
		All age groups	<60 years	≥60 years
Actual situation	Intubated cases	4.51	3.38	1.13
	Fatalities	856.81	856.81	-
	Total severe illness cases	861.32	860.19	1.13
No vaccination campaign	Intubated cases	9.59 (7.61–12.97)	7.33 (5.92–10.15)	2.26 (1.69–3.10)
	Fatalities	1,802.14 (1,467.48–2,523.33)	1,802.14 (1,467.48–2,523.33)	-
	Total severe illness cases	1,811.73 (1,475.09–2,536.30)	1,809.47 (1,473.40–1,473.40)	2.26 (1.69–3.10)
Prevented cases	Intubated cases	4.80 (3.10–8.74)	3.67 (2.54–6.77)	1.13 (0.85–1.97)
	Fatalities	945.61 (610.67–1,666.53)	945.61 (610.67–1,666.53)	-
	Total severe illness cases	950.41 (614.06–1,675.27)	949.28 (613.21- 1,673.29)	1.13 (0.85–1.97)

**Based on 1 US dollar (USD) was equivalent to 35.47 Thai Baht (THB). CI: confidence interval.*

When total cost was accounted, this study separately calculated ICERs for averting one additional intubated case and one additional death. It was important to note that intubated cases and fatal cases were analyzed mutually exclusively. The ICER for an intubated case averted was USD 45,646 (95% CI USD 24,675–72,210) and for a death averted was USD 23,938 (95% CI USD 320–53,856) respectively. The ICER for preventing an intubated case would decline to USD 35,952 (95% CI USD 19,176–57,204) and USD 21,412 (95% CI USD 10,926–34,694) in presumptive scenarios where total vaccination cost diminished to 80% and 50% of the total original cost respectively. The same pattern was also observed in the ICER sensitivity analysis for preventing a fatal case, and was even more apparent if all vaccine-related costs reduced by half since the result became negative—denoting that the program became cost saving (Tables 5, 6).

Table 5. Incremental cost-effectiveness ratio for preventing an intubated case

Scenario	Number of cases	Grand cost in million USD*	ICER— USD*/case (95% CI)		
			Main analysis	Sensitivity analysis[a]	Sensitivity analysis[b]
Actual situation	34,517	1,944	45,646 (24,675–72,210)	35,952 (19,176–57,204)	21,412 (10,926–34,694)
No vaccination campaign	72,608 (59,122–101,658)	205 (167–287)			

Figures in brackets denote 95% confidence limit. Presumptive scenarios where total vaccination cost diminished to 80% (a) and to 50% (b).
**Based on 1 US dollar (USD) was equivalent to 35.47 Thai Baht (THB). ICER: incremental cost-effectiveness ratio. CI: confidence interval.*

Table 6. Incremental cost-effectiveness ratio for death aversion

Scenario	Number of cases	Grand cost in million USD*	ICER— USD*/case (95% CI)		
			Main analysis	Sensitivity analysis[a]	Sensitivity analysis[b]
Actual situation	30,648	2,786	23,938 (320–53,856)	15,901 (-4,240–41,414)	-475 (-13,530–16,062)
No vaccination campaign	64,470 (52,495–90,263)	1,976 (1,609–2,766)			

Figures in brackets denote 95% confidence limit. Presumptive scenarios where total vaccination cost diminished to 80% (a) and to 50% (b).
**Based on 1 US dollar (USD) was equivalent to 35.47 Thai Baht (THB). ICER: incremental cost-effectiveness ratio. CI: confidence interval.*

Discussion

As this study did not incorporate time-to-event data from the point of vaccination to the study period, the VE derived from this study might not precisely represent the exact amount of declination in VE over time. Nevertheless, the findings were consistent with a domestic study, demonstrating that the three-dose regimen exhibited superior effectiveness compared to the two-dose regimen.[9] Similarly, the two-dose regimen demonstrated higher effectiveness than the one-dose vaccination, albeit the two-dose effectiveness in this study was notably lower than the meta-analysis conducted by Zheng et al., which might be attributed to variations in vaccine regimens and the prevailing viral strains during the study period.[25] Consistent with other studies abroad, this study's findings indicate that a national vaccination campaign significantly helped reduce the number of severe illnesses by more than half.[26–28]

The reduction in severe illnesses also came along with savings in treatment costs and potential economic losses that would have occurred in the absence of vaccination.[22] When examining the breakdown of costs in the hypothetical scenario, this study found that approximately 80% of the total cost was attributed to productivity loss, while the remaining 20% was attributed to treatment expenses. Further analysis revealed that almost three quarters of the treatment cost was associated with elderly infections, whereas the GDP loss was largely influenced by those aged less than 60 years.[23]

These results suggest that if policymakers aim to reduce morbidity and mortality rates and focus on minimizing direct costs from the payer's perspective, the focus should be on the elderly population. However, from a macroeconomic standpoint, vaccinating individuals in the working age groups is more cost-effective.[28]

Compared with a scenario with no vaccination, the ICER analysis demonstrates that the Thai government invested approximately USD 45,646 to prevent one additional intubated case and USD 23,938 to prevent one additional death. Additionally, this study found that reducing the cost of vaccines and other related administration cost significantly improved the cost-effectiveness of the national vaccination campaign. Thus, policymakers should find ways to lower the vaccine related cost, either by enhancing bargaining power with the vaccine suppliers or by gradual shift from vaccine importation to investment on vaccine domestic supply.[29,30]

It should be noted that the ICER is not the only tool to determine cost-effectiveness and feasibility of implementing the vaccination campaign. It is advisable to consider integrating additional information, such as incorporating a willingness to pay threshold and budget impact analysis, to complement the ICER. These points also warrant further studies and offer a more comprehensive perspective for policy decision-making on budget allocation.[26]

The methodology of this study is marked by significant strengths, particularly in the utilization of routine nationwide service data. This approach stands out as a key advantage, allowing the findings to authentically mirror the real-world effectiveness of vaccines within the regular functioning of the health system.

Limitations

Several limitations should be acknowledged in interpreting the study findings. Firstly, the reliance on secondary data from diverse sources introduced inconsistencies in information collection, leading to excluded data on underlying diseases, occupation, and individual risk factors. To mitigate residual confounding, matching based on age, province, and specimen collection time was implemented, though potential confounding effects persist.

Secondly, the ICER analysis assumed fixed parameters without considering potential variations, such as viral mutations that may affect VE or changes in treatment costs due to shifts in national healthcare guidelines. Consequently, the estimated number of cases averted may not fully capture real-world epidemic dynamics.

Thirdly, while the study aimed to encompass a broad range of costs, certain items were not assessed, including the cost of GDP loss for adverse events following immunization, expenses for continuing care given long-term complications, and treatment costs for long COVID symptoms. These costs, along with those related to non-severe illness care, were beyond the study's scope.

Finally, the data, collected through a test-negative case-control design, might not perfectly align with a population-based case-control study due to underreporting of COVID-19 cases. This limitation is particularly relevant for asymptomatic or mildly symptomatic infection. Despite this, the study deemed the test-negative design a practical and valid choice, offering advantages in controlling biases related to initial symptom presentation and diagnostic suspicion.

Finally, the 95% CI yielded from the VE (and the ICER thereafter) was quite wide in value, this might be due to the small number of severe illness cases in different vaccine strata in each month. Thus, the interpretation of the results should be made with caution since the wide 95% CI meant non-negligible uncertainty of the estimates.

Conclusion

The COVID-19 vaccination campaign was effective in reducing the number of severe illness cases and fatalities. It also resulted in remarkable reduction in both treatment cost and GDP loss compared to a hypothetical scenario where vaccination campaign had not been in place. Besides, the vaccination policy can be even more cost-effective should the total vaccination cost be reduced. Further studies on willingness to pay threshold and budget impact analysis are of huge value for a more comprehensive policy decision making.

Recommendations

According to the vaccine effectiveness in this study, the booster dose policy still offers favorable merits in preventing severe illness. Therefore, it remains crucial to continually promote COVID-19 booster shot, especially among the elderly. Another important policy implication is that although the current vaccination policy can save money relative to no vaccination in place, it could be even more cost-effective in preventing severe illness cases if all related vaccination costs were reduced. Thus, cost bargaining, through bilateral or multilateral negotiations with the vaccine suppliers, and enhancing investment in domestic vaccine production, should be explored.

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Author Contributions

Conceptualization: RS and NN; Methodology RS, NN, and PP; Formal analysis: RS and PP; Writing-original draft: PP; Writing, review, and editing: PP and RS; Supervision: RS.

Declaration of Conflict of Interest

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