INVESTING IN VACCINE SECURITY IN THE ASEAN REGION

DISCUSSION PAPER

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Investing in Vaccine Security in the ASEAN Region

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Abstract: Vaccine security and self-sufficiency have received increased global attention in the wake of the COVID-19 pandemic, as low- and middle-income countries were heavily dependent on high-income countries (HICs) and international organizations for vaccine supply, resulting in global competition for vaccines and huge inequities. Achieving vaccine security and self-sufficiency is of high importance to Southeast Asia. To achieve this goal, the Association of Southeast Asian Nations (ASEAN) established the ASEAN Vaccine Security and Self-Reliance (AVSSR) initiative. Building on the efforts of ASEAN leadership, the World Bank commissioned this study to estimate the public health and economic benefits arising from investments in AVSSR, specifically in vaccine research and development (R&D), manufacturing, and regulation. The study assumes that five ASEAN countries—Indonesia, Malaysia, the Philippines, Thailand, and Vietnam—make public and private investments to strengthen vaccine security. Applying a societal perspective, the study considers four different investments scenarios. Scenario 1 assumes that costs would be shared between these five countries and that these countries alone would benefit from the vaccine security efforts, while Scenario 2 assumes health and economic benefits to the other five ASEAN countries (Brunei, Cambodia, Laos, Myanmar, and Singapore) as well. Scenario 3 assumes that only one country of 100 million people produces and prioritizes vaccines for its population, while Scenario 4 assumes a pandemic of COVID-19 magnitude. The findings of the study clearly show that regional investments in clinical trials, manufacturing and regulatory capacity building would have a substantial public health impact and offer high benefit-cost ratios. Findings from this study align with the AVSSR Strategic and Action Plan 2021–2025, which makes the case for stronger regional vaccine capacity, enhanced vaccine manufacturing capacity, and human resource development to realize the goal of self-reliance.

Keywords: Vaccine security and self-reliance; Vaccine research & development (R&D), manufacture and regulation; ASEAN; COVID-19; Benefit-cost ratio

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Introduction

Vaccine security and self-sufficiency have received increased global attention in the wake of the COVID-19 pandemic. The pandemic has shown that low- and middle-income countries (LMICs) rely heavily on high-income countries (HICs) and international organizations for vaccines, and that such a reliance makes LMICs the most vulnerable to vaccine shortages when there is global competition for doses. As a result, international efforts are now underway to increase vaccine manufacturing capacity in LMICs. The African Union and Africa Centres for Disease Control and Prevention (CDC), for example, have established the Partnership for African Vaccine Manufacturing to make the African continent self-sufficient in vaccine research, development, manufacturing, regulation, and delivery.[1] In addition, the World Health Organization (WHO) and its partners have established an mRNA vaccine technology transfer hub, based in South Africa, that will work with an extensive network of LMIC-based technology recipients to build mRNA vaccine production, quality control, and regulation capacity across LMICs.[2,3] LMICs in Latin America, Europe, and Southeast Asia have also started collaborations with other countries to increase vaccine manufacturing capacity in their respective regions (Zeng et al. 2022).[4]

Establishing vaccine security and self-sufficiency is of particular importance to Southeast Asia. Countries in the region are dependent on imports not only for COVID-19 vaccines, but also to a large extent for national immunization programs. Moreover, Southeast Asia has long been recognized as a hotspot for emerging infectious diseases (Morand et al. 2014). Over the last two decades, the region has experienced outbreaks of avian influenza, severe acute respiratory syndrome, Middle East respiratory syndrome, Nipah virus, Chikungunya fever, dengue fever, Japanese encephalitis, leptospirosis, and extensively drug-resistant tuberculosis, which have collectively resulted in substantial morbidity and mortality (Coker et al. 2011). Increasing vaccine development, manufacturing, and regulation capacity in the region is therefore essential to ensuring that countries can sustain their immunization programs and respond effectively and efficiently to future outbreaks and pandemics. To achieve this goal, the Association of Southeast Asian Nations (ASEAN) established the ASEAN Vaccine Security and Self-Reliance (AVSSR) initiative.

In November 2019, the heads of state and government of ASEAN issued the ASEAN Leaders' Declaration on AVSSR. The declaration highlighted the benefits of collectively attaining AVSSR in order to avoid vaccine shortage, improve the supply of affordable, quality vaccines for normal and emergency situations both at the national and regional levels, and reduce vaccine-preventable disease burden and health care expenditure.[5] In May 2021, following a forum on the economic and health security setbacks from COVID-19 and the need for stronger regional vaccine capacity, enhanced manufacturing capacity, improved regulation capacity, and human resource development, ASEAN health ministers officially adopted the AVSSR Strategic and Action Plan 2021–2025, which has a vision to "Ensure healthy ASEAN through timely, equitable access to affordable and quality-assured vaccines."[6]

Building on the efforts of ASEAN leadership to address gaps in vaccine security, the World Bank commissioned this study to estimate the public health and economic benefits arising from investments in AVSSR, specifically investments in vaccine research and development (R&D), manufacturing, and

regulation. This investment case modeling builds on a previous study on investing in late-stage clinical trials and manufacturing of vaccines and therapeutics, which was published in *Lancet Global Health* in July 2022 (Schäferhoff et al. 2022). This study has two key goals: (1) to model the health and economic benefits that accrue to the ASEAN region for every dollar invested in undertaking vaccine trials, building manufacturing capacity, and augmenting national regulation systems; and (2) to estimate and document the benefits of a regional investment among ASEAN countries compared to a unilateral approach in which ASEAN countries work independently to produce vaccines for their individual domestic markets.

Methods and Data

Overview of modeling approach

The study assumes that five ASEAN countries—Indonesia, Malaysia, the Philippines, Thailand, and Vietnam—make public and private investments to strengthen vaccine security.[7] In the study, these countries are referred to as the "focus countries." However, while the focus is on these five countries, the study includes four different investments scenarios, one of which assumes that all ASEAN countries would benefit from investments in vaccine security by focus countries.

The study focuses on five diseases, which were jointly prioritized with an expert panel from the ASEAN region, World Bank team, and the five focus countries: dengue, human papillomavirus (HPV), malaria, pneumonia, and tuberculosis (TB). In addition to these diseases, the study includes a pandemic outbreak scenario, which models the benefits of investing in the local production of COVID-19 vaccines.[8] Appendix G provides an overview of annual cases, disability-adjusted life years (DALYs), and deaths due to each disease in the ASEAN countries.

The study applies a societal perspective with all costs and benefits measured at the societal level. This perspective seeks to answer the question: *How much would society benefit for each US dollar invested in vaccine security?* In the study, the societal perspective assumes that the public sector covers all incurred costs (i.e., the governments of the five focus countries). The societal perspective speaks to the vision outlined in the ASEAN Leaders' Declaration on AVSSR. It is also in line with the World Bank's policy dialogue with the five focus countries. In general, the societal perspective also allows for investments from a larger group of investors—including from the private sector—though it does not make any assumptions about profits. While important, modeling a private investor's perspective would require a different approach.

Scenarios modeled

This study includes four investment case scenarios, as described below:

Scenario 1: In the **"regional"** scenario, the study assumes that costs would be shared between the focus countries and that these countries would benefit from the vaccine security efforts. Specifically, the costs for R&D, tech transfer, regulation, and manufacturing would be shared by the five focus countries and all five countries (Indonesia, Malaysia, the Philippines, Thailand, and Vietnam) would benefit from the health and economic benefits.

Scenario 2: In the **"regional pooled procurement"** scenario, the study shows the health and economic benefits that result when the other five ASEAN countries (Brunei, Cambodia, Laos, Myanmar, and Singapore) purchase vaccines from the focus countries while the focus countries continue to distribute vaccines they produce to their own populations. This scenario assumes that vaccines would be purchased from ASEAN manufacturers as part of the ASEAN Free Trade Area (AFTA) rather than from producers from other regions. In case the global prices of these vaccines are lower, the nonfocus countries should be willing to pay higher prices, or middle- and high-income countries in the region may collectively offer cross-subsidies to LMICs. Again, in this scenario, the costs for R&D, tech transfer, and manufacturing would be covered by the five focus countries. However, the public health and economic benefits would accrue from a wider market (i.e., all 10 ASEAN countries).

Scenario 3: In the **"national"** scenario, the study assumes that one country would only produce vaccines prioritized for its own market. The selected country is one of the five focus countries with a median population (~100 million). This country is referred to as "country X". The national scenario assumes that the costs for R&D, tech transfer, and manufacturing would be covered by one country only. At the same time, the public health and economic benefits would only accrue from one market (i.e., the domestic market of the country).

Scenario 4: In the **"pandemic outbreak"** scenario, the study shows the benefits of investing in vaccine manufacturing in a pandemic outbreak situation. This scenario is equivalent to the regional scenario but now includes a COVID-19 outbreak equal in magnitude to the 2021 COVID-19 pandemic. This scenario assume the 2021 incidence of COVID-19 across the five focus countries would continue for three years (2022 to 2024) before reaching an endemic phase in which the incidence of COVID-19 across the five countries would drop to five million cases per year. A subanalysis of this scenario was also conducted, in which the costs and benefits of investments in COVID-19 vaccines were examined in isolation. More specifically, this subanalysis assumed no R&D or manufacturing investments for the other diseases (i.e., dengue, HPV, malaria, pneumonia, and TB) and therefore no economic or health benefits from these diseases. The subanalysis also assumed no investment in regulation.

In addition to these four scenarios, five sensitivity analyses were conducted to account for uncertainty in parameter estimates and to estimate longer-term economic benefits (Appendices B–F). First, a scenario was added where total manufacturing costs are reduced by 25 percent. This scenario assumes that existing production capacity can be leveraged. Second, while this study assesses the direct financial gains that result from investments in clinical trials and manufacturing (treatment costs averted and vaccine sales), a scenario was included that adds economic productivity gains to capture the longer-term benefits of these investments. Third, Scenarios 1–4 above were modeled using a 5.0 percent discount rate rather than the standard 3.0 percent rate to better reflect the economies of low- and middle-income countries (Haacker, Hallett, and Atun 2020). Fourth, Scenarios 1–4 were modeled using a lower Phase III clinical trial cost to reflect potentially lower costs associated with R&D in the focus countries. Fifth, to account for government-imposed market entry requirements that could delay distribution of vaccines to populations, Scenarios 1–4 were modeled under the assumption that vaccines will only be available to the public two years (rather than one year) after launch from the R&D pipeline.

Model specifications

The analysis assumes a societal perspective, examining the benefits and costs of investments in vaccine R&D, technology transfer, manufacturing, and regulation across the five focus countries. A time horizon of 19 years from 2022 to 2040 is used to capture the long-term health and economic benefits that accrue to countries through the next two decades.

With respect to R&D costs, the analysis assumes early and late-stage R&D (Phase I, II, and III clinical trials) is needed for those diseases that do not currently have a vaccine, or that have a vaccine with low effectiveness (TB). For those diseases with vaccines already in later stages of the R&D pipeline (dengue and forthcoming malaria vaccines), the analysis assumes the need for one additional Phase III clinical trial.[9] For those vaccines that have been on the market for a long time and have proved safe for use (HPV and pneumonia), the analysis assumes there is no need for Phase III trials but rather a need for one smaller study ("vaccination pilot project") per disease. The five focus countries therefore incur the cost of Phase I, II, and III clinical trials as well as clinical trial site operating costs and vaccination pilot projects where relevant. The number of Phase I, II, and III clinical trials required to launch one new vaccine for each disease as well as the costs and duration of each phase is based on data from the portfolio-to-impact (P2I) tool (Young et al. 2020; Bandara et al. 2020).[10,] The analysis also assumes one clinical trial site is needed per product candidate, and that each site incurs an operating cost during the time in which clinical trials are running. The annual operating cost is based on information shared by the countries. The cost of a vaccine pilot project is assumed to be one-fourth the cost of a Phase III clinical trial.

In terms of manufacturing costs, the analysis assumes the five focus countries together will build four new fully integrated manufacturing sites (each with a capacity of 30 million doses per year) and two new fill and finish sites (each with a capacity of 30 million doses per year). This assumption was changed for the national scenario (Scenario 3): Under this scenario, the manufacturing requirement is limited only to one fully integrated and one fill and finish site based on the minimum capacity needed to address the disease burden in the selected country. This assumption was also changed for the pandemic outbreak scenario (Scenario 4): Under this scenario the analysis assumed the need for one mRNA vaccine production facility in addition to the four fully integrated and two fill and finish sites. For the pandemic outbreak scenario subanalysis, the analysis assumed the five focus countries would only build one mRNA vaccine manufacturing site instead of four fully integrated and two fill and finish sites. Overall, the focus countries therefore incur construction and annual operating costs associated with each new site. One-time construction costs and annual operating costs are based on data shared by the International Finance Corporation (IFC) as well as the countries themselves. The model currently assumes new manufacturing sites are operational one year after investments are made. The model also assumes that a one-time technology transfer cost will be incurred by the five focus countries to manufacture vaccines for those diseases that already have an effective/WHO-endorsed vaccine available (malaria, dengue, HPV, pneumonia, and COVID-19).

In terms of regulation costs, the analysis assumes three of the five focus countries make annual investments in their national regulatory authorities (NRAs) amounting to US$8.86 million per country per year. These investments were drawn from resource need identified by respective institutional

development plans (IDPs) to strengthen national regulatory capacity. The pandemic outbreak scenario subanalysis assumes no investment in regulation.

Regarding the health benefits, the analysis assumes vaccines will be available to the public one year after launch from the R&D pipeline. The analysis also assumes that vaccination coverage increases by 10 percentage points per year with a maximum attainment of 80 percent coverage for each vaccine. Reductions in incidence are therefore the product of disease incidence, vaccination coverage, and vaccine efficacy. Using these assumptions, the cases, deaths, and DALYs averted by the introduction of vaccines into the population are modeled. Annual incidence data are based on information from the Institute for Health Metrics and Evaluation (IHME). Case fatality rates, years lived with disability (YLD) per case of disease, and years of life lost (YLL) per case of disease that result in death are based on data collected through literature reviews. The pandemic outbreak scenario (and subanalysis) assumes that vaccination coverage increases by 20 percent in the first year (rather than 10 percent) to account for rapid national responses as seen during the 2020 COVID-19 pandemic.

Regarding the economic benefits, the analysis models treatment costs averted as the product of cases averted, treatment coverage, and treatment cost per case. Unless specific data from the five focus countries were received or relevant data through literature reviews were found, treatment coverage levels of 50 percent were assumed for all diseases and across all countries. Treatment costs per case of each disease are based on averages obtained by the five focus countries. These averages reflect the average costs incurred by health systems to treat one case of each disease, and are based on the actual number of patients diagnosed and treated at health facilties that submit such data. For Scenario 2, the regional pooled procurement scenario, vaccine purchases are included as an additional economic benefit (resulting from vaccines sold beyond the five focus countries).[11] For Scenario 4, the pandemic outbreak scenario, COVID-19 treatment costs averted are based on the proportion of cases that require outpatient care vs. inpatient care. In addition, inpatients are further stratified by those with mild symptoms, those who require oxygen, those who require ventilation, and those who require extracorporeal membrane oxygenation. As highlighted above, Appendix C includes a sensitivity analysis for each scenario that captures the longer-term benefits resulting from increased economic productivity. An annual discount rate of 3.0 percent was used for all monetary costs and benefits. For each scenario a threshold analysis is also conducted, where the year in which cumulative economic benefits exceed the total costs of investment is calculated. Table 1 below summarizes the main model parameters. All model equations are detailed in Appendix A.

Table 1. Summary of Key Model Specifications

Countries	Indonesia, Malaysia, Philippines, Thailand, and Vietnam
Diseases	Dengue, HPV, malaria, pneumonia, TB, and COVID-19.
Time horizon	2022 to 2040 (19 years)
R&D costs	• Phase I, II, and III clinical trials are needed for TB. • Only phase III clinical trials are needed for dengue, HPV, malaria, pneumonia, and COVID-19.

	• One clinical trial site needed per product candidate; each site incurs an operating cost during the time in which clinical trials are running.
Manufacturing costs	• 4 new fully integrated manufacturing sites (each with a capacity of 30 million doses per year), and 2 new fill and finish sites (each with a capacity of 30 million doses per year). • Under the national scenario, 1 fully integrated site and 1 fill and finish site. • Under the pandemic outbreak scenario, 4 fully integreated sites, 2 fill and finish sites, and 1 mRNA production site. • One-time construction costs and annual operating costs based on data shared by the IFC as well as the countries. Manufacturing sites are operational one year after investments are made. • One-time technology transfer cost will be incurred to manufacture vaccines for those diseases that have an effective/WHO-endorsed vaccine available (HPV, pneumonia, malaria, dengue, COVID-19).
Health benefits	• Vaccination coverage increases by 10 percentage points per year up to a maximum of 80 percent coverage. • Annual reductions in incidence are the product of disease incidence, vaccination coverage, and vaccine efficacy. • The cases, deaths, and disability-adjusted life years averted by the introduction of vaccines into the population were estimated.
Economic benefits	• Treatment costs averted are the product of cases averted, treatment coverage, and treatment cost per case. • Treatment coverage data were collected from WHO and other sources or shared by countries. If data were unavailable, treatment coverage levels of 50 percent were assumed. • Treatment costs per case of each disease are based on averages shared by the five focus countries.
Discount rate	• A discount rate of 3.0% was used for all monetary costs and benefits.

Note: HPV = Human papillomavirus; TB =Tuberculosis; R&D = Research and development; IFC = International Finance Corporation; WHO = World Health Organization.

Data sources

Data sources used for model parameters included peer-reviewed literature as well as consultations with the World Bank, IFC, and focus country partners. Table 2 summarizes the inputs of the model, parameter values, and data sources.

Table 2: Current Model Inputs

(All Costs in 2022 US$)

Input	Value	Source
Phase I trial cost	$2,360,000.00	Portfolio-2-Impact Tool (P2I)
Phase II trial cost	$13,550,000.00	P2I
Phase III trial cost	$122,210,000.00	P2I

Input	Value	Source
Phase I trial duration	1.57	P2I
Phase II trial duration	2.23	P2I
Phase III trial duration	2.33	P2I
Phase I trial transition probability	0.684	P2I
Phase I trial transition probability	0.459	P2I
Phase I trial transition probability	0.708	P2I
Clinical trial site annual operational cost	$105,000.00	Data shared by countries
Vaccination pilot project cost	$30,000,000.00	Assumption
Construction cost for full integrated manufacturing site	$225,000,000.00	IFC
Construction cost for fully integrated manufacturing site (mRNA technology)	$275,000,000.00	IFC
Annual operational cost of fully integrated manufacturing site	$9,342,701.02	Data shared by countries
Construction cost for fill and finish manufacturing site	$72,000,000.00	IFC
Annual operational cost of fill and finish manufacturing site	$2,708,319.54	Data shared by countries
Technology transfer costs	$20,000,000.00	IFC
Treatment cost per case (COVID-19, outpatient)	$42.51	Data shared by countries
Treatment cost per case (COVID-19, inpatient with mild symptoms)	$865.05	Data shared by countries
Treatment cost per case (COVID-19, inpatient requiring oxygen)	$6,670.38	Data shared by countries
Treatment cost per case (COVID-19, inpatient requiring ventilation)	$9,493.36	Data shared by countries
Treatment cost per case (COVID-19, inpatient requiring extracorporeal membrane oxygenation)	$57,385.76	Data shared by countries
Treatment cost per case (dengue)	$290.48	Data shared by countries
Treatment cost per case (HPV)	$725.00	Data shared by countries
Treatment cost per case (malaria)	$116.06	Data shared by countries
Treatment cost per case (pneumonia)	$728.78	Data shared by countries
Treatment cost per case (TB)	$360.74	Data shared by countries
Incidence – COVID-19	123,480,000	Literature reviews
Case fatality rate (without treatment) – COVID-19	0.0163	Literature reviews
Case fatality rate (with treatment) – COVID-19	0.0102	Literature reviews
YLD per case (without treatment) – COVID-19	0.0104	Literature reviews
YLD per case (with treatment) – COVID-19	0.0040	Literature reviews
YLL per death – COVID-19	39.4784	Literature reviews
Incidence – dengue	6,684,211	IHME
Case fatality rate (without treatment) – dengue	0.0001	Literature reviews
Case fatality rate (with treatment) – dengue	0.0054	Literature reviews
YLD per case (without treatment) – dengue	0.0027	Literature reviews

Input	Value	Source
YLD per case (with treatment) – dengue	47.7133	Literature reviews
YLL per death – dengue	0.0018	Literature reviews
Incidence – HPV	44,734	IHME
Case fatality rate (without treatment) – HPV	0.4827	Literature reviews
Case fatality rate (with treatment) – HPV	0.0483	Literature reviews
YLD per case (without treatment) – HPV	0.3700	Literature reviews
YLD per case (with treatment) – HPV	0.1850	Literature reviews
YLL per death – HPV	21.3630	Literature reviews
Incidence – malaria	802,229	IHME
Case fatality rate (without treatment) – malaria	0.0012	Literature reviews
Case fatality rate (with treatment) – malaria	0.0007	Literature reviews
YLD per case (without treatment) – malaria	0.0025	Literature reviews
YLD per case (with treatment) – malaria	0.0013	Literature reviews
YLL per death – malaria	36.9395	Literature reviews
Incidence – pneumonia	35,997,397	IHME
Case fatality rate (without treatment) – pneumonia	0.0033	Literature reviews
Case fatality rate (with treatment) – pneumonia	0.0037	Literature reviews
YLD per case (without treatment) – pneumonia	0.0009	Literature reviews
YLD per case (with treatment) – pneumonia	21.5887	Literature reviews
YLL per death – pneumonia	0.0052	Literature reviews
Incidence – TB	943,459	IHME
Case fatality rate (without treatment) – TB	0.1423	Literature reviews
Case fatality rate (with treatment) – TB	0.0100	Literature reviews
YLD per case (without treatment) – TB	0.9990	Literature reviews
YLD per case (with treatment) – TB	0.0167	Literature reviews
YLL per death – TB	21.2379	Literature reviews
Vaccine efficacy (COVID-19)	62.4%[a]	Literature reviews
Vaccine efficacy (dengue)	61.0%[b]	Literature reviews
Vaccine efficacy (HPV)	95.4%[c]	Literature reviews
Vaccine efficacy (malaria)	65.0%[d *]	Literature reviews
Vaccine efficacy (pneumonia)	65.0%[e]	Literature reviews
Vaccine efficacy (TB)	65.0%	Assumption
Vaccine purchase price per dose	$10.00	Assumption
Treatment coverage (COVID-19, percent of nonhospitalized cases that receive care)	10.0%	Assumption
Treatment coverage (COVID-19, percent of all cases that require hospitalization)	5.6%[f]	Literature reviews
Treatment coverage (COVID-19, percent of hospitalized cases with mild symptoms)	77.0%	Data shared by countries
Treatment coverage (COVID-19, percent of hospitalized cases requiring oxygen)	20.0%	Data shared by countries

Input	Value	Source
Treatment coverage (COVID-19, percent of hospitalized cases requiring ventilation)	2.9%	Data shared by countries
Treatment coverage (COVID-19, percent of hospitalized cases requiring extracorporeal membrane oxygenation)	0.1%	Data shared by countries
Treatment coverage (dengue)	18.4%	Data shared by countries
Treatment coverage (HPV)	50.0%	Assumption
Treatment coverage (malaria)	32.1%[g]	Literature reviews
Treatment coverage (pneumonia)	68.5%[h]	Literature reviews
Treatment coverage (TB)	57.9%[i]	Literature reviews

Sources: a. Risk et al. 2022; b. "Dengue Vaccine Arrives as Global Warming Boosts Infection Risk." https://www.bloomberg.com/news/newsletters/2022-11-07/dengue-vaccine-arrives-as-global-warming-boosts-infection-risk; c. Basu et al. 2021; d. Wilby et al. 2012; e. Tereziu and Minter 2022; f. COVID Data Tracker, https://covid.cdc.gov/covid-data-tracker/#new-hospital-admissions; g. Global Health Observatory, https://www.who.int/data/gho/data/indicators/indicator-details/GHO/number-of-malaria-cases-treated-with-any-first-line-tx-courses-including-artemisinin-based-combination-therapies-acts; h. UNICEF Data: Pneumonia, https://data.unicef.org/topic/child-health/pneumonia/; i. https://www.who.int/data/gho/data/indicators/indicator-details/GHO/tuberculosis-treatment-coverage.

Notes: IFC = International Finance Corporation; HPV = Human papillomavirus; YLD = Years lived with disability; YLL = Years of life lost; IHME = Institute for Health Metrics and Evaluation; TB = Tuberculosis.

* Recent data suggest a malaria vaccine developed at the University of Oxford may have an efficacy up to 80 percent (https://pharmaphorum.com/news/high-hopes-as-new-malaria-vaccine-shows-unprecedented-efficacy/). However, for this study we use a more conservative estimate of 65 percent as indicated by clinical trial data for the Mosquirix vaccine (https://pubmed.ncbi.nlm.nih.gov/22408046/).

Results

Scenario 1: Regional scenario

Under the regional scenario, the development and manufacturing of vaccines would cost a total of US$2.7 billion, while the net benefits would amount to US$82.3 billion. As such, the benefit-cost ratio (BCR) amounts to 30.88 (Table 3). Under this scenario, cumulative benefits exceed cumulative costs beginning in Year 5 (2026) of the time horizon. See Table 4 for more details on the costs.

Table 3. Regional Scenario—Total Costs, Benefits, and Benefit-Cost Ratio

Total costs (2022 US$ millions)*	$2,664.86
Net benefits (2022 US$ millions)**	$82,285.18
BCR***	30.88
Threshold****	Year 5

Source: Authors' calculations.
Notes: BCR = Benefit-cost ratio.
*Regulation, clinical trials, tech transfer, and manufacturing costs.
**Treatment costs averted.
***Net benefits/total costs.
****Year in which cumulative economic benefits exceed total costs.

Table 4. Regional Scenario—Clinical Trial, Manufacturing, and Regulation Costs

Clinical trial costs (2022 US$ millions)	
Phase I trial costs	$4.58
Phase II trial costs	$39.47
Phase III trial costs*	$532.85
Clinical trial site operational costs	$3.16
Manufacturing costs (2022 US$ millions)	
Site construction costs	$1,013.59
Site operational costs	$612.88
Tech transfer costs	$77.67
Regulation costs (2022 US$ millions)	
IDP investments	$380.66

Source: Authors' calculations.
Notes: IDP = Institutional development plan.
*Includes pilot project costs.

Through the tools developed and produced in the region, a total of 194.71 million cases, 0.93 million deaths, and 22.80 million DALYs would be prevented under the regional scenario (Table 5).

Table 5. Regional Scenario—Health Benefits

Cases averted (millions)	194.71
Deaths averted (millions)	0.93
DALYs averted (millions)	22.80
DALYs averted as a percent of baseline DALYs	21.3%

Source: Authors' calculations.
Notes: DALYs = Disability-adjusted life years.

Scenario 2: Regional pooled procurement scenario

Under the regional pooled procurement scenario, the BCR is 35.09. This BCR is higher compared to Scenario 1 for two reasons: first, the vaccines are sold by the five focus countries, which generates an additional benefit; and second, the treatment costs averted across all ASEAN countries are larger than in Scenario 1. See Tables 6 and 7 for details on the costs and economic benefits. Under this scenario cumulative benefits exceed cumulative costs beginning in Year 5 (2026) of the time horizon.

Table 6. Regional Pooled Procurement Scenario—Total Costs, Benefits, and Benefit-Cost Ratio

Total costs (2022 US$ millions)*	$2,664.86
Net benefits (2022 US$ millions)**	$93,510.27
BCR***	35.09
Threshold****	Year 5

Source: Authors' calculations.
Notes: BCR = Benefit-cost ratio.
*Regulation, clinical trials, tech transfer, and manufacturing costs.
**Treatment costs averted and vaccines sold.
***Net benefits/total costs.
****Year in which cumulative economic benefits exceed total costs.

Table 7. Regional Pooled Procurement Scenario—Clinical Trial, Manufacturing, and Regulation Costs

Clinical trial costs (2022 US$ millions)	
Phase I trial costs	$4.58
Phase II trial costs	$39.47
Phase III trial costs*	$532.85
Clinical trial site operational costs	$3.16
Manufacturing costs (2022 US$ millions)	
Site construction costs	$1,013.59
Site operational costs	$612.88
Tech transfer costs	$77.67
Regulation costs (2022 US$ millions)	
IDP investments	$380.66

Source: Authors' calculations.
Notes: IDP = Institutional development plan.
*Includes pilot project costs.

A total of 219.98 million cases, 1.06 million deaths, and 25.96 million DALYs would be averted in the ASEAN region under this scenario (Table 8).

Table 8. Regional Pooled Procurement Scenario—Health Benefits

Cases averted (millions)	219.98
Deaths averted (millions)	1.06
DALYs averted (millions)	25.96
DALYs averted as a percent of baseline DALYs	21.2%

Source: Authors' calculations.
Note: DALYs = Disability-adjusted life years.

Scenario 3: National scenario

Under the national scenario, the BCR is 9.51, a significantly smaller economic return compared with the regional scenarios above (Scenarios 1 and 2). In this scenario, cumulative benefits do not exceed cumulative costs until Year 7 (2028) of the time horizon. Tables 9 and 10 provide details on the costs and economic benefits.

Table 9. National Scenario—Total Costs, Benefits, and Benefit-Cost Ratio

Total costs (2022 US$ millions)*	$1,245.58
Net benefits (2022 US$ millions)**	$11,841.53
BCR***	9.51
Threshold****	Year 7

Source: Authors' calculations.
Notes: BCR = Benefit-cost ratio.
*Regulation, clinical trials, tech transfer, and manufacturing costs.
**Treatment costs averted.
***Net benefits/total costs.
****Year in which cumulative economic benefits exceed total costs.

Table 10. National Scenario—Clinical Trials and Manufacturing Costs

Clinical trial costs (2022 US$ millions)	
Phase I trial costs	$4.58
Phase II trial costs	$39.47
Phase III trial costs*	$532.85
Clinical trial site operational costs	$3.16
Manufacturing costs (2022 US$ millions)	
Site construction costs	$288.35
Site operational costs	$172.62
Tech transfer costs	$77.67
Regulation costs (2022 US$ millions)	
IDP investments	$126.89

Source: Authors' calculations.
Notes: IDP = Institutional development plan.
*Includes pilot project costs.

The number of averted deaths amounts to 0.14 million and DALYs to 3.58 million. A total of 26.78 million cases would be averted (Table 11).

Table 11. National Scenario—Health Benefits

Cases averted (millions)	26.78
Deaths averted (millions)	0.14
DALYs averted (millions)	3.58
DALYs averted as a percent of baseline DALYs	20.8%

Source: Authors' calculations.
Note: DALYs = Disability-adjusted life years.

Scenario 4: Pandemic outbreak scenario

Under the pandemic outbreak scenario (a modification of the regional scenario that includes COVID-19), the development and manufacturing of vaccines would cost a total of US$3.2 billion, while the net benefits would amount to US$90.6 billion. As such, the benefit-cost ratio amounts to 28.27. Under this scenario, cumulative benefits exceed cumulative costs beginning in Year 3 (2024) of the time horizon (Table 12). See Table 13 for a breakdown of costs.

Table 12. Pandemic Outbreak Scenario—Total Costs, Benefits, and Benefit-Cost Ratio

Total costs (2022 US$ millions)*	$3,205.50
Net benefits (2022 US$ millions)**	$90,605.14
BCR***	28.27
Threshold****	Year 3

Source: Authors' calculations.
Notes: BCR = Benefit-cost ratio.
*Regulation, clinical trials, tech transfer, and manufacturing costs.
**Treatment costs averted.
***Net benefits/total costs.
****Year in which cumulative economic benefits exceed total costs.

Table 13. Pandemic Outbreak Scenario—Clinical Trials and Manufacturing Costs

Clinical trial costs (2022 US$ millions)	
Phase I trial costs	$4.58
Phase II trial costs	$39.47
Phase III trial costs*	$651.50
Clinical trial site operational costs	$3.47
Manufacturing costs (2022 US$ millions)	
Site construction costs	$1,282.04
Site operational costs	$746.70
Tech transfer costs	$97.09
Regulation costs (2022 US$ millions)	
IDP investments	$380.66

Source: Authors' calculations.
Notes: IDP = Institutional development plan.
*Includes pilot project costs.

Under the outbreak scenario, 256.39 million cases, 1.90 million deaths, and 61.54 million DALYs would be prevented (Table 14).

Table 14. Pandemic Outbreak Scenario—Health Benefits

Cases averted (millions)	256.39
Deaths averted (millions)	1.90
DALYs averted (millions)	61.54
DALYs averted as a percent of baseline DALYs	15.8%

Source: Authors' calculations.
Note: DALYs = Disability-adjusted life years.

For the pandemic outbreak scenario, the analysis only modeled COVID-19-specific costs and benefits and assumed no R&D or manufacturing investments for the other diseases (i.e., dengue, HPV, malaria, pneumonia, and TB) and therefore no economic or health benefits from these diseases. This subanalysis assumes investments for one Phase III trial of a COVID-19 vaccine, one mRNA vaccine manufacturing facility, and technology transfer. Investments in regulation are not included in this scenario. With these modifications, the development and manufacturing of vaccines would cost US$540.64 million, the net benefits would amount to US$31.9 billion, the BCR would be 58.96, and cumulative economic benefits would exceed total costs by the end of Year 1 (Tables 15–17).

Table 15. Pandemic Outbreak Scenario (Subanalysis)—COVID-19-Specific Costs, Benefits, and Benefit-Cost Ratio

Total costs (2022 US$ millions)*	$540.64
Net benefits (2022 US$ millions)**	$31,873.93
BCR***	58.96
Threshold****	2022 (Year 1)

Source: Authors' calculations.
Notes: BCR = Benefit-cost ratio.
*Clinical trials, tech transfer, and manufacturing costs.
**Treatment costs averted.
***Net benefits/total costs.
****Year in which cumulative economic benefits exceed total costs.

Table 16. Pandemic Outbreak Scenario (Subanalysis)—COVID-19-Specific Clinical Trial and Manufacturing Costs

Clinical trial costs (2022 US$ millions)	
Phase I trial costs	$0.00
Phase II trial costs	$0.00
Phase III trial costs	$118.65
Clinical trial site operational costs	$0.31

Manufacturing costs (2022 US$ millions)	
Site construction costs	$268.45
Site operational costs	$133.82
Tech transfer costs	$19.42
Regulation costs (2022 US$ millions)	
IDP investments	$0.00

Source: Authors' calculations.
Note: IDP = Institutional development plan.

Table 17. Pandemic Outbreak Scenario (Subanalysis)—COVID-19-Specific Health Benefits

Cases averted (millions)	60.71
Deaths averted (millions)	0.97
DALYs averted (millions)	38.74
DALYs averted as a percent of baseline DALYs	13.69%

Source: Authors' calculations.
Note: DALYs = Disability-adjusted life years.

Limitations

There are important limitations to consider when interpreting the results of this analysis. First, the study models investments in manufacturing and regulation capacity, but only estimates the benefits that accrue from a limited set of vaccines for dengue, HPV, malaria, pneumonia, tuberculosis, and COVID-19. Investments in manufacturing and regulation capacity could potentially improve vaccine access for a wider range of infectious diseases, thereby further increasing economic and health returns beyond what is modeled in this study. Second, the study assumes that Phase III clinical trials require at least two years to complete and that vaccines enter the market and become available to the public one year after completion of Phase III trials. The COVID-19 pandemic has shown that adaptive clinical trial designs and regulatory efficiencies can substantially reduce the time from initiation of Phase III clinical trials to market approval to under one year. Results from this study may therefore overestimate the time needed for new vaccines to enter the market, and thus underestimate economic and health benefits accrued to the population. Third, the study only estimates the economic and health benefits of increased vaccination coverage within ASEAN. However, with increased vaccine production and regulation capacity, ASEAN countries may sell their vaccines to other regions, provided their prices are competitive in international markets or they are able to produce vaccines for neglected tropical diseases in which major international manufacturers are not much interested, thereby further increasing the economic and health benefits of the investments modeled in this study. Fourth, except for the costs to strengthen national regulatory capacity, this study does not include costs needed before entering the clinical stage (i.e., costs for basic research and related scientific infrastructure, such as laboratories). These costs are difficult to determine. Fifth, it is important to note that while this study focuses on investments in vaccine R&D, manufacturing, and regulation, robust health systems with adequate infrastructure, personnel, policies, supply chains, and data capture mechanisms are required to

efficiently deliver vaccines to populations. Consequently, the investments modeled in this study should be considered alongside other investments that support health system strengthening across the priority countries. Lastly, developing regional vaccine manufacturing capabilities is certaintly an important step toward achieving vaccine security and self-reliance. However, vaccine security may also be achieved through sustainable procurement. Other studies should therefore explore the value of investments to optimize vaccine procurement mechanisms in ASEAN.

Discussion

This study provides new evidence on the health benefits and the economic returns of investing in vaccine security in ASEAN countries. It shows that investments in trials and manufacturing would have a substantial public health impact. The study suggests that under the regional scenario, product development and manufacturing in the five focus countries could avert a total of 194.71 million cases and 0.93 million deaths over a 19-year time frame. In addition, 22.80 million or 21.3 percent of all DALYs from dengue, HPV, malaria, pneumonia, and TB would be prevented through the tools developed and produced in the region. Under the regional pooled procurement scenario, the public health gains would be even higher, while the health gains would be more limited under the national scenario that only covers the population of one country.

Results from this study also show that investing in clinical trials and local production pays off from an economic perspective. Economic returns would be especially high if new vaccines were produced for multiple markets rather than for domestic markets only: under the regional scenario, returns outweigh investments by a factor of 31, and by a factor of 35 under the regional pooled procurement scenario. These returns are substantial, even though we only include the direct economic benefits and limit the regional pooled procurement scenario to the ASEAN countries. If the ASEAN manufacturers are able to offer competitive prices, their vaccines could be sold beyond AFTA, and the returns would be even higher. In addition, the study modeled the longer-term indirect benefits (see Appendix C on productivity gains). The BCRs of the regional scenario and the regional pooled procurement scenario increase to 40 and 46, respectively. These results correspond with findings from the larger health economics literature, which shows that vaccinations are among the most cost-effective public health interventions (Bloom 2011; Zeng et al. 2019; Jeulannd et al. 2009; Lusvan et al. 2019), with a high return on investment (Sarker et al. 2018; Pindyck, Tate, and Parashar 2018; Rodrigues and Plotkin 2020) and broad economic benefits (Quilici, Smith, and Signorelli 2015; Nandi and Shet 2020; Rémy et al. 2015).

However, the BCR is substantially different if only domestic markets are targeted. In the national scenario, the BCR is 9.51, a significantly smaller economic return compared with the regional scenario and the regional pooled procurement scenario. In addition, cumulative benefits do not exceed cumulative costs in this scenario until Year 7 of the time horizon. In the regional scenario and the regional pooled procurement scenario, it would only take five years before the benefits outweigh the costs. This study therefore supports regional action for clinical trials and product manufacturing compared to narrow national efforts. Developing and producing vaccines for a larger group of countries is favorable compared to narrowly targeting domestic markets.

Findings from this study are fully in line with the AVSSR Strategic and Action Plan 2021–2025,[12] which discusses the economic and heath security setbacks from COVID-19 and the need for stronger regional vaccine capacity, enhanced vaccine manufacturing capacity, and human resource development to realize the goal of self-reliance. In addition, the results are also coherent with a previous study on clinical trials and manufacturing capacity in India, Kenya, and South Africa from 2021 to 2036 for five diseases—human immunodeficiency virus (HIV), tuberculosis, malaria, pneumonia, and diarrheal diseases (Schäferhoff et al. 2022). This previous study found that these investments have substantial public health impacts and economic returns, especially if products are produced for regional markets rather than for domestic markets only. However, as has been highlighted in previous work, ASEAN member state governments should commit for long-term purchase contracts (advanced market commitments [AMCs]) for vaccine development and manufacture in the region. This upfront commitment is critical to attract investments—both public and private—to ensure that vaccines are developed and produced in a reliable and sustainable way.

The pandemic outbreak scenario also shows the health and economic benefits of investing in regional vaccine manufacturing capacity. Under the pandemic outbreak scenario, 256.39 million cases, 1.90 million deaths, and 61.54 million DALYs would be prevented with a BCR of 28.27. Investments in local manufacturing will contribute to pandemic preparedness and strengthening the response to future outbreaks. The COVID-19 pandemic has shown that many low- and middle-income countries fully or to some extent relied on external support. Limited vaccine manufacturing capacity was one of the main factors driving COVID-19 vaccine inequity, and is one of the most pressing issues for future pandemic preparedness and response. A key lesson from the COVID-19 pandemic is to increase and geographically diversify vaccine manufacturing. Through investments in trial sites and manufacturing capacity for both traditional vaccine technologies and new mRNA vaccine technologies, ASEAN countries would be enabled to leverage their own research, product development, and manufacturing capacity in times of health crisis rather than relying on external support. Such initiative also helps to reduce the burden of priority neglected tropical diseases in the region. Investing in building capacity for trials and manufacturing will enable middle income countries (MICs) to react faster and more effectively to outbreaks.

The pandemic outbreak scenario also highlights the health and economic gains that could arise from investments to curtail future pandemics from other infectious diseases. For example, given that avian flu has a higher case-fatality rate than COVID-19 (Poovorawan et al. 2013), investments in vaccine manufacturing capacity for this disease could result in higher health and economic savings than what is seen in the pandemic outbreak scenario assuming an avian flu pandemic similar in magnitude to the COVID-19 pandemic.

Investments in vaccine security have many other benefits: Investments in trial sites and manufacturing will be useful for a much broader range of infectious and noncommunicable diseases, as well as for the development and production of other medical countermeasures such as therapeutics and diagnostics. Investments in local manufacturing will also produce new jobs, thereby generating additional economic growth. Improved regulatory capacity will have an impact on the quality of locally produced medicines.

Locally produced medicines might also have lower prices in comparison to imported medicines. Lower prices can help mitigate health inequalities within and across countries. In addition, vaccinations have multiple other socioeconomic benefits, and they also have benefits throughout health systems (see Appendix J).

Vaccine security is also an affordable investment, with small fiscal implications. The total costs for vaccine security only represent a very small percentage of domestic general government health expenditure (GGHE-D) of ASEAN countries (Appendix J). Over 19 years, the focus countries would have to invest 0.3 percent of their combined health expenditures. In addition, the threshold analysis shows that it will take five years before the economic gains exceed total costs. This is a short time horizon.

Going forward, countries should jointly invest in vaccine security or closely coordinate to invest on the vaccine value chain from research and development to last-mile logistics as an important regional public good. Governments should create an enabling environment for private sector investment through long-term purchase contracts. Initially, it may also require a commitment by those ASEAN countries that purchase the vaccines to pay a higher price compared to established producers from other regions. This will help to establish a strong regional ecosystem for vaccine security, with substantial medium-term health, economic, and societal benefits. At the 2023 World Economic Forum, Larry Summers, former US treasury secretary and former chief economist of the World Bank, emphasized that another "COVID-scale problem" within the next 15 years is a top economic risk and that the world continues to be utterly unprepared for that eventuality.[13] ASEAN countries should prepare themselves through investments in vaccine security. In addition to financial investments in R&D and manufacturing, they should take targeted policy action, for example through stronger regional regulatory harmonization.

In our discussion, it is worth mentioning that current vaccine investments in the study countries are driven mostly by public sector companies and research institutes. However, the region is actively collaborating and engaging with the private sector. Our study provides evidence to inform coordinated action to strengthen investments in vaccine security by both public and private sector actors.