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Evaluation of vaccine allergy safety track program to assess potential COVID-19 vaccine allergy: a cost-effectiveness analysis

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Abstract

Background: Concerns about new COVID-19 vaccines played a key role in vaccine hesitancy and hampered population uptake. Hong Kong initiated a Vaccine Allergy Safety Track (VAS-Track) program to assess potential COVID-19 vaccine-associated allergies. A 'Hub-and-Spoke' model of predominately non-specialists supported by the allergist hub was established to meet overwhelming demand despite limited specialists.

Objective: To assess the cost-effectiveness of VAS-Track as a pre- and post-vaccination assessment service for individuals potentially at high risk of COVID-19 vaccine-related allergy.

Methods: An individual-level decision-analytical model was constructed using data from VAS-Track participants supplemented by published estimates. Analyses were from a health service provider perspective over 12 months. We calculated the incremental cost-effectiveness ratio (ICER) to estimate the cost per quality-adjusted life years (QALYs) gained. Willingness-to-pay threshold was based on local GDP per capita (US$ 49,590). Sensitivity analyses examined robustness of findings.

Results: Cost-effectiveness varied widely across age groups. VAS-Track was cost-saving for older adults (dominant strategy for age ≥ 50) compared with standard practice across a range of sensitivity analyses. VAS-Track was not cost-effective for younger groups (age 18-49: ICER: US$ 410,914/QALY for pre-vaccination and US$ 213,786/QALY for post-vaccination assessments). Infection rate, cost of treating severe infection, and vaccination rate were most influential on cost-effectiveness estimates.

Conclusions: VAS-Track was cost-effective both as a pre- and post-vaccination assessment service for adults over 50. The 'Hub-and-Spoke' model using non-specialists with limited allergy specialist resources to provide vaccine allergy assessment services would provide high economic value compared with usual care for adults aged 50 and over.

Key words: vaccine, allergy, hesitancy, safety, cost-effectiveness, COVID-19

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Abbreviations:

BT	mRNA Fosun Pharma BioNTech Comirnaty
CHEERS	Consolidated Health Economic Evaluation Reporting Standards
HKIA	The Hong Kong Institute of Allergy
ICER	Incremental cost-effectiveness ratio
GDP	Gross domestic product
QALY	Quality-adjusted life year
SV	Sinovac CoronaVac
VAS	Vaccine Allergy Safety
WHO	World Health Organization
UI	Uncertainty interval
WTP	Willingness-to-pay

Introduction

Vaccines are among the most effective tools developed to control COVID-19 by mitigating serious illness, hospitalization, and even death.[1,2] Given the high transmissibility of SARS-CoV-2 coronavirus, an effective public health intervention requires mass vaccination of the population to achieve herd immunity. Yet despite the well-known protective benefits of vaccines against serious illness and mortality, vaccine hesitancy was widespread and thus a major concern.[3,4] In Hong Kong, 51.5% of the population reported COVID-19 vaccine hesitancy in January 2021;[5] a major driver of vaccine hesitancy and low uptake was anxiety over vaccine safety, possible allergic reactions,[6] and fear of mRNA technology that was exacerbated by daily media reports of adverse side-effects.[7-10] Allergy services can play a key role in increasing individual vaccine uptake but can also provide spillover benefits at the population-level through public education and reassurance against reports of vaccine-related allergic reactions.[11] However, there has been an extreme shortage of allergy specialists and services in Hong Kong like many other countries.[12]

Hong Kong started its free COVID-19 vaccination program in February 2021, providing residents with a choice of inactivated Sinovac CoronaVac (SV) and mRNA Fosun Pharma BioNTech Comirnaty (BT).[13] The Oxford-AstraZeneca ChAdOx1 adenovirus vaccine was withdrawn due to public concerns about safety and vaccine efficacy.[14] Although vaccine-associated allergic reactions and anaphylaxis are extremely rare (only 0.5 per million doses administered),[15] the overall vaccine acceptance rate by the public remained low. Incomplete COVID vaccination, due to fear of vaccine allergy, led to drastically reduced protection as demonstrated by significantly lower COVID-19 antibody levels.[16] By August 2021, the first dose vaccination rate in Hong Kong only reached 55.9% (46.6% for two doses), with particularly low vaccination rates in the elderly despite their vulnerability; first-dose and second-dose rates of 25.0% and 19.4% in over 70s compared to 73.1% and 62.0% in people aged 20-49.[17]

To support the COVID-19 vaccination program, Hong Kong initiated a Vaccine Allergy Safety Track (VAS-Track) Program providing allergy consultation services and allergy tests to assess individuals at higher risk of COVID-19 vaccine-related allergies.[18] However, the demand for assessment and vaccination advice quickly overwhelmed the limited capacity of the VAS clinic leading to waiting time exceeding 8 years.[11,19] To efficiently utilise the limited capacity of publicly available specialist allergy services in a pandemic situation requiring population-wide vaccine rollout, VAS Track employed a novel 'Hub-and-Spoke' model for non-specialists to participate in assessing patients at higher risk of developing COVID-19 vaccine-associated allergies.[20]

In this study, we evaluate the cost-effectiveness of VAS-Track on COVID-19 vaccine uptake, healthcare utilisation, and health outcomes.

Methods

Study setting

The Hong Kong Institute of Allergy (HKIA) published consensus statements to define individuals at higher risk of potential COVID-19 vaccine allergies and guide pre-vaccination and post-vaccination assessment by healthcare workers.[18] Individuals at higher risk of COVID-19 vaccine-associated allergic reactions were advised to seek allergy consultation prior to next dose of COVID-19 vaccination. Individuals deemed at higher risk of COVID-19 vaccine-associated allergic reactions had: (1) suspected allergic reaction(s) to prior COVID-19 vaccination, (2) history of anaphylaxis, or (3) a history of severe, immediate-type allergic reactions to multiple foods or more than one class of drugs.

Under the VAS-Track 'Hub-and-Spoke' model, one allergist-led Hub trained and supervised the seven Spoke clinics established in each geographical cluster in Hong Kong. Patients with excess waiting times were redirected to their respective local Spoke clinic. A total of 2725 pre-vaccination patients and 388 post-vaccination patients were seen under the 'Hub-and-Spoke' model from March to August 2021. Data including age, sex, allergy investigations, and outcome of clinical assessment were retrieved from the Hub and the Hong Kong West Cluster Spoke as they received the largest number of patients in VAS-Track.

Study design

We conducted an economic evaluation to assess the cost-effectiveness of VAS-Track 'Hub-and-Spoke' in Hong Kong compared to standard practice without any pre- and post-vaccination assessment service for individuals with vaccine hesitancy and potentially at high risk of COVID-19 vaccine-related allergies. We constructed a decision-analytic model at the individual patient level to evaluate costs and outcomes over a 12-month time horizon from a health service provider perspective (**Supplementary figure S1**). As VAS-Track received referrals from adults across the entire territory, we construct a hypothetical population of 6 million people are hesitant to receiving the first (2.7 million) or second dose (3.3 million) of COVID-19 vaccine (around 40% and 50% of Hong Kong population with vaccine hesitancy for the first dose and second dose respectively) in the simulation analyses.[15]

Results were aggregated based on the VAS-Track age structure to assess the overall incremental cost-effectiveness ratio (ICER). Analysis was stratified by three age groups (18-49, 50-69, and ≥ 70 years) and two types of assessment (pre-vaccination for higher risk patients before their first dose of COVID-19 vaccine, and post-vaccination for those with a suspected allergic reaction following COVID-19 vaccination). Analysis was reported according to the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) 2022 checklist. This study was approved by the Institutional Review Board of the University of Hong Kong/Hospital Authority Hong Kong West Cluster [UW 21-562].

Model structure

The decision-tree model predicted outcomes and costs of patients under the VAS-Track program vs standard practice. For VAS-Track, the first chance node was VAS-Track consultation: recommended vaccine or not. The second chance node modeled patient behavior after recommendation: received vaccine or not. The third chance node after receiving vaccine were having vaccine side effect or not. The four potential outcomes were no infection, infection (mild illness, severe illness, and death). The fifth potential outcomes were having long COVID or not from COVID-19 infection (**Supplementary figure S1**).

Parameters

Model inputs were collected from VAS-Track participants and supplemented by published estimates from previous studies (**Supplementary table S2**). Medical records of 1799 patients between March 2021 to August 2021 were reviewed and followed-up by telephone one month after clinical assessment (characteristics summarized in **Supplementary table S3**). Post-assessment vaccination records were verified against Hong Kong Hospital Authority health records. A 12-month follow-up survey of 100 VAS-Track attendees from September 2021 to August 2022 informed model estimates for medical utilization due to side effects. Severity of COVID-19 infection and vaccine effectiveness against COVID-19 were derived from a previous population-based study in Hong Kong,[21,22] and prevalence of post-COVID-19 symptoms ('long COVID') were derived from a meta-analysis.[23] The vaccination rate of the standard practice group was based on vaccination rate of the general population (from March 2021 to August 2021),[17] and vaccine hesitancy rate reported by a previous study in Hong Kong (March 2021 to July 2021).[5] The vaccination rate of the standard practice group in our analyses was assumed to be equal to the vaccination rate of vaccine hesitant people (**Supplementary table S4**).

Costs

Costs and outcomes were analysed over 12-month time horizon, and thus undiscounted at 2021 prices. Costs were valued from the public healthcare provider perspective and included vaccine costs, medical utilization for vaccine side effects, healthcare utilization (outpatient attendance, inpatient, and intensive care stay) due to COVID-19 infection and 'long COVID'. COVID-19 disease states and costs for vaccination and healthcare utilization due to COVID-19 infection and 'long COVID' were derived from published estimates.[24-26] Unit prices were derived from Hong Kong Hospital Authority charges for non-eligible residents that are set on a cost-recovery basis for public healthcare services.[27] Additional costs of VAS-Track program include physician consultation (non-allergist and specialist allergist), nursing care, and allergy testing.

Outcomes

Outcomes included first dose vaccination coverage, vaccine completion (for the second dose), and quality adjusted life years (QALYs; a measure of life expectancy adjusted for the quality of life) for COVID-19 infection and 'long COVID'. The health utility losses for mild and severe cases were calculated by accounting for the specific health states that a patient experienced over its duration. The health utility loss for 'long COVID' was calculated for patients with symptoms lasted longer than four weeks. Health state utility values were derived from previous studies. The estimated health utility loss for mild and severe COVID-19 cases were 0.43 and 0.60 respectively.[28] The health utility loss for long COVID lasting longer than four weeks was estimated as 0.11.[29]

Incremental cost-effectiveness ratio (ICER)

We calculated the ICER to estimate the additional cost for improved outcomes of VAS-Track. We applied the World Health Organization (WHO) cost-effectiveness threshold (equal to the local GDP per capita of HK$ 386,832 [approximately US$ 49,590] in 2021) as the willingness-to-pay (WTP) threshold, since Hong Kong lacks a formal cost-effectiveness threshold.

Sensitivity analysis

We conducted probabilistic sensitivity analysis drawing variable inputs across their distributions over 1,000 simulations. We conducted one-way deterministic sensitivity analyses to assess how model outcomes vary over plausible range of values for infection rate and vaccination rate. We varied model parameters for COVID-19 infection rate, and vaccination rate of standard care group (**Supplementary table S5**) to test the robustness of the ICER estimates. Analyses were conducted using R statistical software.

Results

Per-person cost and effectiveness of VAS-Track and standard practice in Hong Kong are summarised in **Table 1** (detailed breakdown in **Supplementary table S6**).

Vaccination rates after VAS-Track assessment were similar across age groups though older age groups had higher costs and lower QALYs. After receiving the pre-vaccination assessment, the 50-69 age group had higher vaccination rates (61.5%) than others (age 18-49: 56.2%, ≥ 70: 56.3%). Similar patterns were observed for post-vaccination assessment for the second dose vaccination rates (age 18-49: 61.8%, 50-69: 75.2%, ≥ 70: 66.5%). QALYs ranged from 0.9703-0.9964 after pre-vaccination assessment and 0.9737-0.9967 after post-vaccination assessment. The cost of VAS-Track clinic was constant for age groups (pre-vaccination: US$ 86; post-vaccination: US$ 141) but accounted for a substantial proportion of total costs for younger people (age 18-49: 38% for pre-vaccination service, 51% for post-vaccination service). Total costs over 12 months were US$ 229, US$ 796, and US$ 1,536 per person for age 18-49, 50-69, and ≥ 70 respectively after pre-vaccination assessment, and US$ 276, US$ 596, and US$ 1,414 per person for age 18-49, 50-69, and ≥ 70 respectively after post-vaccination assessment. The downstream costs of medical utilization, particularly treating COVID-19 infection, accounted for an increasing proportion of total costs with age, and was the largest proportion of total costs for those aged 50 and over. For people aged 18-49, 50-69, and ≥ 70, medical utilization to treat COVID-19 infection accounted for 41%, 83%, and 91% of total cost following pre-vaccination assessment and 30%, 66%, and 86% of total cost following post-vaccination assessment.

Table 1. Cost and effectiveness of VAS-Track strategies and standard practice.

	Pre-vaccination				Post-vaccination			
	VAS-Track		Standard practice		VAS-Track		Standard practice	
Aged 18-49	**Mean**	**95%UI**	**Mean**	**95%UI**	**Mean**	**95%UI**	**Mean**	**95%UI**
VAS clinic, USD	86	[84–88]	--	--	141	[123–158]	--	--
Vaccine, USD	41	[37–44]	37	[34–40]	45	[40–49]	35	[28–41]
Medical Utilization, USD	102	[58–146]	111	[63–159]	91	[51–131]	117	[64–170]
Total cost, USD	229	[185–273]	148	[101–196]	276	[233–319]	152	[101–203]
Vaccination rate, %	56.16	[51.71–60.62]	51.49	[47.42–55.57]	61.82	[55.36–68.29]	47.98	[38.98–56.98]
QALYs	0.9964	[0.9951–0.9977]	0.9845	[0.9819–0.9872]	0.9967	[0.9954–0.9979]	0.9961	[0.9947–0.9975]
Aged 50-69								
VAS clinic, USD	86	[84–88]	--	--	141	[124–158]	--	--
Vaccine, USD	45	[42–48]	26	[14–38]	54	[49–59]	25	[16–33]
Medical Utilization, USD	666	[345–986]	894	[443–1345]	401	[194–607]	845	[410–1279]
Total cost, USD	796	[476–1117]	919	[472–1367]	596	[391–802]	870	[438–1301]
Vaccination rate, %	61.53	[57.46–65.59]	35.75	[19–52.49]	75.19	[68.33–82.06]	34.03	[22.51–45.54]
QALYs	0.9866	[0.9839–0.9893]	0.9819	[0.9777–0.9861]	0.9914	[0.9894–0.9934]	0.9827	[0.9791–0.9862]
Aged ≥ 70								
VAS clinic, USD	86	[84–88]	--	--	142	[124–159]	--	--
Vaccine, USD	41	[34–47]	9	[3–15]	48	[35–62]	7	[2–11]
Medical Utilization, USD	1409	[649–2169]	2243	[1075–3410]	1224	[497–1952]	2298	[1096–3500]
Total cost, USD	1536	[1085–3419]	2252	[1085–3419]	1414	[1104–3507]	2305	[1104–3507]
Vaccination rate, %	56.32	[47.33–65.31]	12.46	[4.44–20.49]	66.50	[47.96–85.03]	9.66	[3.45–15.87]
QALYs	0.9703	[0.9621–0.9785]	0.9514	[0.9399–0.9628]	0.9737	[0.9638–0.9836]	0.9500	[0.9386–0.9614]

Notes: Cost of VAS clinic include cost of non-allergist, allergist, nurse care, and allergy test. Cost of vaccine include both the direct cost per dose as well as the operational costs associated with vaccination in Hong Kong. Cost of medical utilization (outpatient attendance, inpatient, and intensive care stay) include treating vaccine side effects, COVID-19 infection, and long COVID.
QALY, quality-adjusted life year; UI, uncertainty interval; VAS, Vaccine Allergy Safety.

The incremental cost and effectiveness of VAS-Track pre-vaccination and post-vaccination assessments compared to standard practice are shown in **Table 2**. Vaccination rates, QALYs gained, and costs savings increase with age. After pre-vaccination assessment, first dose vaccination rate increased by 4.7%, 25.8%, 43.9% for people aged 18-49, 50-69, and ≥ 70; and respective QALYs gains of 0.0002, 0.0047, and 0.0193. Pre-vaccination assessments saved US$ 123 per person for people aged 50-69 over 12 months and US$ 716 for age ≥ 70 but cost an additional US$ 124 per person for 18-49 year olds. Cost savings in older adults were mainly driven by reduced medical utilization from COVID-19 infection (per person savings of US$ 228 for age 50-69 and US$ 834 for age ≥ 70). After receiving post-vaccination assessment, second dose vaccination rate increased by 13.8%, 41.2%, 56.8% for people age 18-49, 50-69, and ≥ 70, and respective QALYs gains of 0.0006, 0.0087, and 0.0237. Post-vaccination assessment saved US$ 274 per person for people aged 50-69 over 12 months and US$ 891 for age ≥70 but cost an additional US$ 124 per person for 18-49 year olds. Again, these cost saving were mainly driven by lower medical utilization from COVID-19 infection (per person savings of US$ 444 for age 50-69 and US$ 1,074 for age ≥ 70).

Both pre-vaccination and post-vaccination assessments provided by VAS-Track was cost-effective overall compared with standard practice, but cost-effectiveness varied widely by age group. For the 50-69 and ≥ 70 age groups, VAS-Track was dominant compared to standard practice for both pre- and post-vaccination assessments. The VAS-Track program was not cost-effective in the younger age group (18-49 years) with ICER of US$ 410,914 per QALY gained for pre-vaccination assessments and US$ 213,786 per QALY gained for post-vaccination assessments; both much higher than the local WTP threshold in Hong Kong (US$ 49,590).

Table 2. Incremental cost-effectiveness ratio (ICER) of VAS-Track pre- and post-vaccination strategy versus standard care.

	Pre-vaccination	Post-vaccination
Overall, per person		
Increment vaccination rate	19.11%	26.71%
Increment QALYs	0.0044	0.0051
Increment cost, USD	-104	-87
ICER	Dominant	Dominant
Aged 18-49, per person		
Increment vaccination rate	4.66%	13.84%
Increment QALYs	0.0002	0.0006
Increment cost, USD	81	124
ICER	410,914	213,786
Aged 50-69, per person		
Increment vaccination rate	25.78%	41.16%
Increment QALYs	0.0047	0.0087
Increment cost, USD	-123	-274
ICER	Dominant	Dominant
Aged ≥ 70, per person		
Increment vaccination rate	43.86%	56.84%
Increment QALYs	0.0189	0.0237
Increment cost, USD	-716	-891
ICER	Dominant	Dominant

Notes: All costs in 2021 USD. ICERs shown for pre-vaccination assessment service versus standard practice, and post-vaccination assessment service versus standard practice. "Dominant" indicate VAS-Track was less costly and more effective compared with standard practice.
ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year.

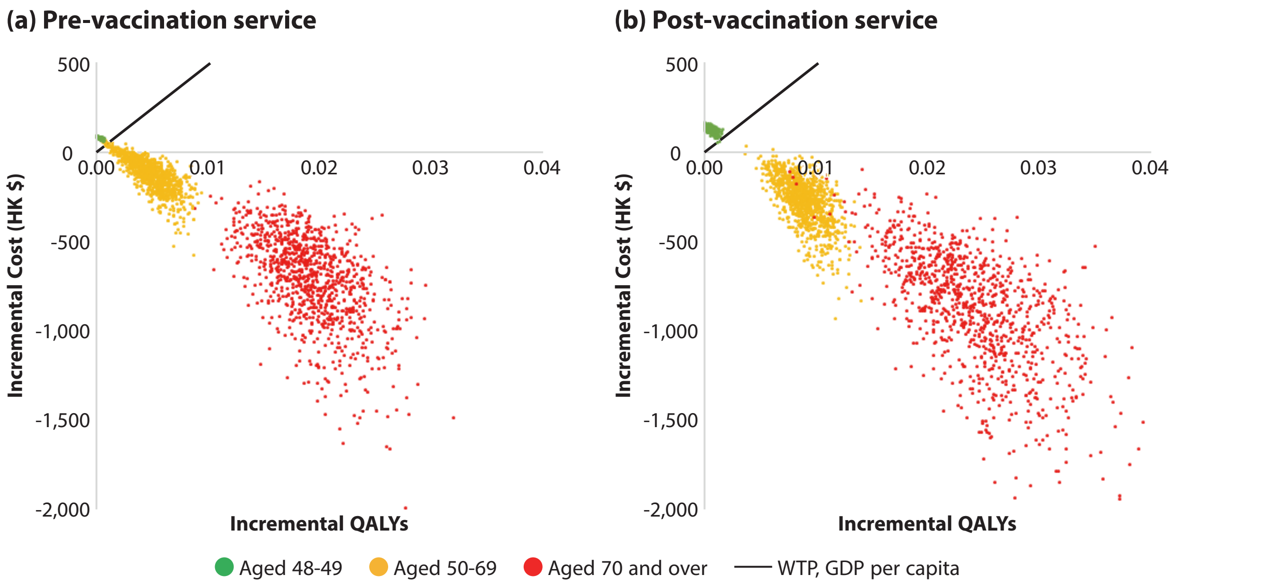

Figure 1. Probabilistic sensitivity analysis of incremental cost-effectiveness ratio (ICER) for VAS-Track versus standard care.

Notes: 1000 simulations are shown. Black solid line represents willingness-to-pay threshold for cost per QALY gained (GDP per capita of Hong Kong; USD 49,590 in 2021).
ICER, incremental cost-effectiveness ratio; GDP, gross domestic product; QALYs, quality-adjusted life years; WTP, willingness-to-pay.

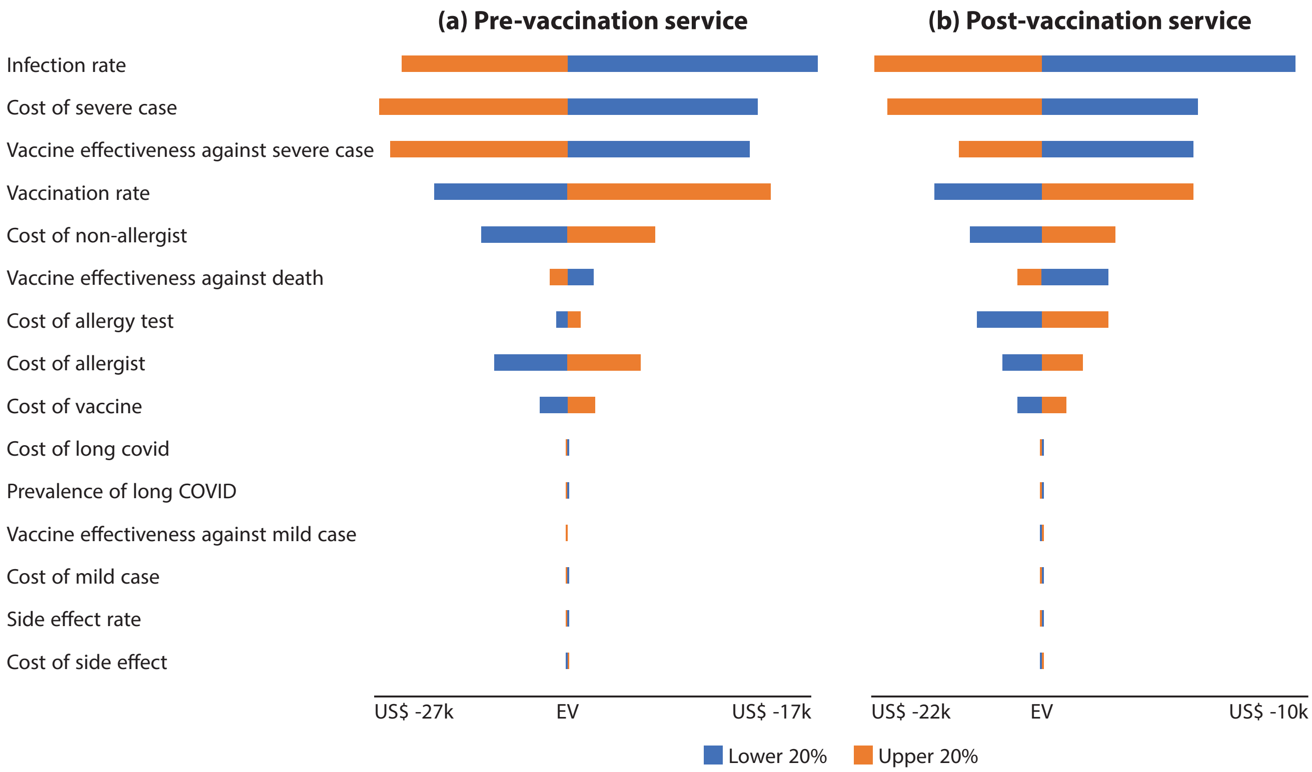

Figure 2. Deterministic one-way sensitivity analysis of incremental cost-effectiveness ratio (ICER) for VAS-Track versus standard care.

Notes: Sensitivity analysis was done on input base value ±20%. Parameters presented in descending order of ICER variation. EV, expected value; ICER, incremental cost-effectiveness ratio.

Sensitivity analysis

Probabilistic sensitivity analysis showed VAS-Track was cost-effective for ≥ 70 year olds in all simulations and for 50-69 year olds in most simulations (98% pre-vaccination simulations, 100% post-vaccination simulations). However, it was not cost-effective for 18-49 age group in any simulation (**Figure 1**). A one-way sensitivity analysis for plausible ranges of parameters values (COVID-19 infection rate, vaccination rate for standard care, vaccine effectiveness against infection, side effect rate, prevalence of 'long COVID', cost of severe case, cost of mild case, cost of 'long COVID', cost of allergist, cost of non-allergist, cost of allergy test, cost of vaccine) varying the input value ±20% found robust results for cost-effectiveness (**Figure 2**). Infection rate, cost of severe case, vaccine effectiveness against severe case, and vaccination rate were most influential variables determining cost-effectiveness.

Specific one-way deterministic sensitivity analyses varied the infected rate (1% to 50%) and vaccination rate in standard care group (0% to general population vaccination rate, **Supplementary table S5**). VAS-Track was more cost-effective at higher infection rates. For 18-49 age group, VAS-Track was cost-effective at infection rate of 50% or higher for pre-vaccination assessments, and 30% or higher for post-vaccination assessments. VAS-Track was cost-effective at infection rates of 1% or higher for ≥ 70 year olds and 3% or higher for 50-69 year olds (**Supplementary table S7**). In the extreme scenario where the standard care comparator led no vaccination in eligible individuals deemed at higher risk of COVID-19 vaccine-related allergies, the VAS-Track program was cost-effective for all age groups. Even when the standard care comparison attained the vaccination rate of the general population, VAS-Track still improved vaccination rates and was cost-effective for people aged 50 and over (**Supplementary table S8**).

Discussion

The VAS-Track program was cost-effective overall but varied widely across age groups. It was cost-saving for people aged 50 or above, and remained cost-saving at low COVID-19 infection rates (5%) and when vaccination rates under standard practice matched the general population. VAS-Track was not cost-effective for people age 18-49 unless COVID-19 infection reached 50% (pre-vaccination) and 30% (post-vaccination). The VAS-Track program was most effective in increasing vaccination rates in those aged 50 and over resulting in reduced treatment costs for COVID-19 infection and overall cost savings compared to standard care. For adults below 50, the VAS-Track program had relatively limited impact on increasing vaccination rate and QALY gains with the costs mainly driven by delivering VAS-Track services.

The variations in cost-effectiveness of the VAS-Track program across age groups was mainly due to differences in vaccine uptake, vaccine hesitancy and vaccine effectiveness. Older adults were more hesitant to take up vaccines due to allergy concerns or poor health status.[30] Several studies have shown allergy or immunology services could help to mitigate COVID-19 vaccine hesitancy;[11,31] we also found older adults were more motivated to get vaccinated after receiving an allergy assessment.[21] Allergy assessments could benefit older adults by addressing their concerns about getting vaccinated,[5,21] underscoring the potential benefit of the allergy assessments for older adults. Our study highlights the importance of considering age-specific factors when designing and implementing the VAS-Track program. Age-specific vaccine promotion strategies have been recommended for COVID-19 vaccines,[32-34] as well as vaccines against influenza, pneumonia, and herpes zoster.[35,36] Previous studies showed that influenza vaccines were cost-saving for adults aged over 64 years in US and Korea compared to the younger age groups.[37-39] Pneumococcal vaccination strategies in older adults were cost-effective in US adults over 64 years and cost-saving in Colombia adults over 50 years.[40,41] Herpes zoster vaccination strategies in older adults were cost-effectiveness in US older adults.[42] Our study specifically focused on the economic impact of providing COVID-19 vaccine allergy services to different age groups. We found that allergy assessment services had a greater economic benefit for older adults age 50 and over, which highlights the importance of prioritizing allergy assessments for older adults.

Implementation of a 'Hub-and-Spoke' model in VAS-Track program of multiple non-specialty Spoke clinics reduced the overall cost of the program, expanded service capacity and increased cost-effectiveness. In Hong Kong, non-allergist doctors from internal medicine, family medicine, and primary healthcare were recruited and trained to participate in their respective Spoke Clinics.[11] Non-allergists provided 76% of pre-vaccine patient assessments for only 50% of total VAS clinic costs, and 75% of post-vaccine patient assessment for 40.7% of total VAS clinic costs. This publicly provided 'Hub-and-Spoke' VAS-Track program to assess vaccine allergy by non-specialists and allergists in Hong Kong reduced vaccine hesitancy and facilitated the rollout of the population-wide vaccination program. The 'Hub-and-Spoke' implementation model in Hong Kong relied on existing health facilities and incurred negligible additional administrative costs. However, it is important to note that implementation, maintenance, and continuity of the 'Hub-and-Spoke' model can be costly and pose potential challenges such as refrigeration storage failures, logistical and transportation errors, and information coordination problems. This optimisation of resources is a fundamental aspect that improve the cost-effectiveness of the VAS-Track program in Hong Kong.

Although reducing VAS-Track program intervention costs naturally help to maximise overall cost-effectiveness, the costs of implementing the 'Hub-and-Spoke' model were not big drivers of the ICER estimates. Even over a relatively short 12-month evaluation period, treatment expenses of COVID-19 infection vastly outweighed the costs of delivering the VAS-Track 'Hub-and-Spoke' model. Sensitivity analyses found the three most influential variables were all outside the VAS-Track program: COVID-19 infection rate, cost of treating severe COVID-19 infection, and the vaccination rate achieved by standard practice. Sensitivity analyses of cost variables related to implementing the VAS-Track program, such as allergist assessment, non-specialist assessment, and allergy tests, all had limited impact on findings.

During the COVID-19 pandemic VAS-Track program could assure public confidence and increase vaccine uptake. It was cost-effective for people over 50 and could be considered in other countries that need to prioritize their aging populations. Service implementation can be piloted in institutions for the elderly, such as nursing homes, before gradual extension to younger age groups. Although the ICER of VAS-Track program was below local GDP per capita, Hong Kong lacks a formal cost-effective threshold. Other regions will need to consider their own willingness-to-pay and, affordability thresholds for adopting such interventions.

Although the vaccination rate of residents in Hong Kong has already reached high levels (94.6% population with 1st dose, 93.0% population with 2nd dose in October 2023),[17] subsequent COVID-19 booster vaccinations will be required to maintain immunity as protection wanes and new variants emerge.[43] Recently in Hong Kong, roll-out of the new generation XBB mRNA vaccine has been approved.[44] Therefore, demand of vaccine allergy assessment will linger despite high vaccination rates; vaccine allergy services such as VAS-Track may be needed regularly.

Our study had several strengths. To our knowledge, this study is among the first cost-effectiveness analysis of an allergy assessment service for COVID-19 vaccination. Our model incorporated the various health outcomes from vaccine allergy assessments to account for vaccine side effects, COVID-19 infection, and 'long COVID', with their different associated costs and impact on quality of life. We used prospective data collected from patients at higher vaccine allergy risk treated under real-world conditions in a territory-wide 'Hub-and-Spoke' model to parameterise the model. Further studies could assess the cost-effectiveness of 'Hub-and-spoke' allergy care models across diverse settings and balance trade-offs in equity, quality, and efficiency.

Our study had several limitations. First, model inputs including COVID-19 infection rate, vaccination rate, vaccine cost, treatment cost of COVID-19 infection, and cost of 'long COVID' were derived from published studies. However, estimating medical utilization accurately could be challenging due to factors such as the limitation of antigen diagnostic tests to confirm COVID-19, difficulty diagnosing long COVID-19 and the diverse treatment options depending on the type and severity of organ involvement. These limitations could lead to over- or underestimation of medical utilization in our model. Sensitivity analyses to strengthen robustness showed VAS-Track remained cost-effective across various parameter values. Second, the 'Hub-and-Spoke' implementation model in Hong Kong did not incur set-up costs as it utilized existing health facilities. However, analyses in other contexts should consider the potentially high cost of implementation, maintenance, and continuity of the Hub-and-Spoke model and the challenges of implementing this model, especially in low-income countries. Third, the criteria of high-risk individuals for COVID-19 allergic reactions supposed by HKIA were based on self-reported medical histories,[18] which may be subject to recall bias or misinterpretation. In the United Kingdom, primary care providers refer patients to allergy teams for similar COVID-19 allergy consultation services. These referrals were often initiated by patient concerns. Similar to our study, an evaluation of this program demonstrated that vaccination was recommended for 99.9 % of patients.[45] Additionally, analyses were from health system perspective over 12-month horizon and wider social costs and benefits as well as long-term outcomes were not considered. Finally, the unpredictability the COVID-19 pandemic, marked by changing infection rates and emerging variants, posed challenges. In Hong Kong, daily infected cases rose from under 100 to peak at 80,000 in January 2022,[46] reflecting a shift in infection rate from under 1% in 2020-2021 to 30% in 2022. We used a base value of 10% as the COVID-19 infection rate and varied the infection rates from 1% to 50%.

Our finding supports policymaking in other regions considering the "Hub and Spoke" model to offer widespread vaccine allergy assessment services using limited allergy specialist resources. We showed the cost-effectiveness of this model, further supporting its implementation in Hong Kong and other regions. Limited resources occur in both low-income and high-income countries, e.g., allergists per population in United Kingdom, 1:1 million; vs United States, 1:65,000.[47,48] The VAS-Track 'Hub-and-Spoke' model for COVID-19 vaccine allergy assessments could also potentially be extended to other contexts such as anaphylaxis, food allergy, drug allergy, since many countries have a shortage of allergy specialists. Integration of allergy assessment service with care models for other diseases using the already established 'Hub-and-Spoke' model for addressing the shortage of allergists could be even more cost-effective strategy.

Conclusion

The VAS-Track 'Hub-and-Spoke' model provide assessment and vaccination advice for individuals at high risk of COVID-19 vaccine-related allergies using non-specialists with limited allergy specialist resources. The VAS-Track program improved vaccine uptake and health outcomes and was cost-saving for people aged 50 and over. It remained cost-saving for older adults even at low COVID-19 infection rates. However, VAS-Track was not cost-effective for adults under 50, either as pre-vaccination or post-vaccination service.

Author Contributions

- Concept and design: Quan, Li
- Acquisition of data: Chiang, Ye, Hong, Yi, Ng
- Analysis and interpretation of data: Xiong, Huo, Quan
- Drafting of the manuscript: Xiong, Quan
- Critical revision of the paper for important intellectual content: Xiong, Quan
- Obtaining funding: Li, Quan,
- Supervision: Quan

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Role of the funder/sponsor

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Ethics approval and consent to participate

This study was approved by the Institutional Review Board of the University of Hong Kong/Hospital Authority Hong Kong West Cluster [UW 21-562].

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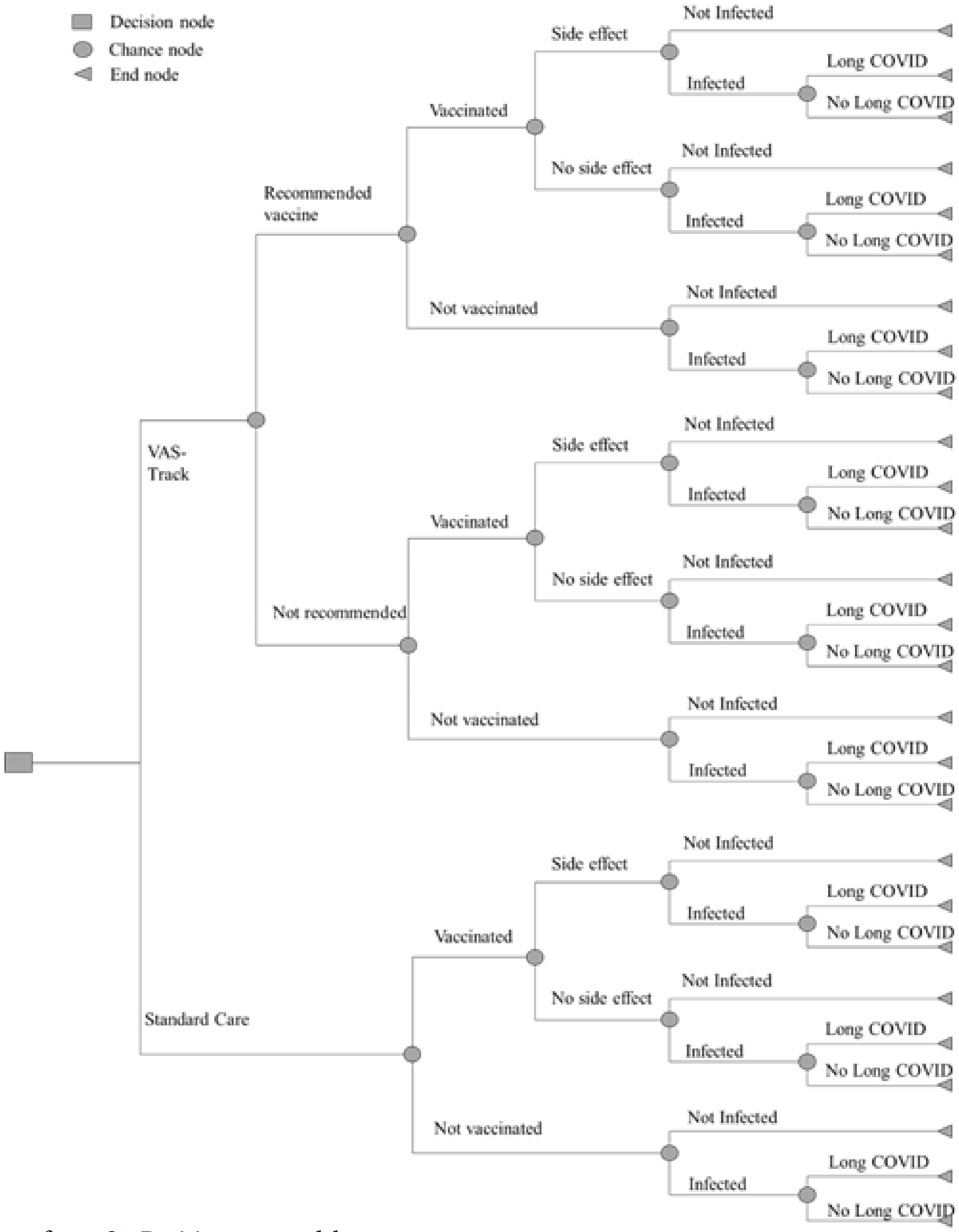
Supplementary material



Supplementary figure S1. Decision-tree model.

Notes: The decision-tree model predicted outcomes and costs of patients under the VAS-Track program vs standard practice. For VAS-Track, the first chance node was VAS-Track consultation: recommended vaccine or not. The second chance node modeled patient behavior after recommendation: received vaccine or not. The third chance node after receiving vaccine were having vaccine side effect or not. The four potential outcomes were no infection, infection (mild illness, severe illness, and death). The fifth potential outcomes were having long COVID or not from COVID-19 infection.

Supplementary table S2. Key model parameters.

Parameters		N	Value	Distribution	Source
Vaccination rate of standard practice group, 2021.03–08					
First dose	age 18–49	3,028,000	51.5% [47.5–55.5]	Beta[#]	[1] [2] Estimated
	age 50–69	2,317,000	35.6% [18.9–52.3]	Beta[#]	
	age ≥ 70	987,000	12.5% [4.3–20.6]	Beta[#]	
Second dose	age 18–49	3,028,000	48.0% [39.0–56.9]	Beta[#]	
	age 50–69	2,317,000	33.9% [22.3–45.4]	Beta[#]	
	age ≥ 70	987,000	9.7% [3.1–16.0]	Beta[#]	
Infection rate of COVID-19	age 18–49	3,028,000	13.0% [11.8–14.2]	Beta[#]	[3]
	age 50–69	2,317,000	8.5% [7.4–9.7]	Beta[#]	
	age ≥ 70	987,000	7.3% [5.7–8.9]	Beta[#]	
Infection severity of COVID-19					
Probability of mild cases among infected patients	age 18–49	3198	95.0% [94.2–95.7]	Beta	[4]
	age 50–69	1620	57.2% [55.3–59.0]	Beta	
	age ≥ 70	748	9.1% [8.5–9.7]	Beta	
Probability of severe cases among infected patients	age 18–49	170	5.0% [4.3–5.8]	Beta	
	age 50–69	1214	42.8% [41.0–44.7]	Beta	
	age ≥ 70	7491	90.9% [90.3–91.5]	Beta	
Probability of death among severe infected patients	age 18–49	81	47.6% [40.2–55.1]	Beta	
	age 50–69	764	62.9% [60.2–65.6]	Beta	
	age ≥ 70	6021	80.4% [79.5–81.3]	Beta	
Long COVID prevalence					
among non-hospitalized patients		735,006	34.5% [21.9–49.7]	Beta	[5]
among hospitalized patients			52.6% [43.5–61.6]	Beta	
Vaccine effectiveness against COVID-19 infection					
Protection against mild/moderate disease from one dose	age 18–49	384	39·9% [24.8–52.3]	Beta	[4]
	age 50–69		0	Constant	
	age ≥ 70		0	Constant	
Protection against severe disease from one dose	age 18–49	1269	95·4% [90·7–98·1]	Beta	
	age 50–69		70·0% [51·8–82·0]	Beta	
	age ≥ 70		72·2% [56·7–82·6]	Beta	
Protection against mild/moderate disease from two dose	age 18–49	3443	38.4% (30.0, 45.7)	Beta	
	age 50–69		0	Constant	
	age ≥ 70		0	Constant	
Protection against severe disease from two doses	age 18–49	1112	96.1% [94.4, 97.3]	Beta	
	age 50–69		88.5% [85.6, 90.8]	Beta	
	age ≥ 70		74.5% [69.4, 78.8]	Beta	
Protection against long COVID			53.9% [29.5–98.7]	Beta	[6]

Supplementary table S2. (Continued)

Parameters		N	Value	Distribution	Source
Procedure of pre-vaccination assessment service					
Hub: recommended 1st dose	age 18–49	250	98.8% [97.5–100]	Beta	VAS-Track participants
	age 50–69	324	99.1% [98.0–100]	Beta	
	age ≥ 70	80	98.8% [96.3–100]	Beta	
Hub: received 1st dose after recommendation	age 18–49	247	62.8% [56.7–68.8]	Beta	
	age 50–69	321	78.5% [74.0–83.0]	Beta	
	age ≥ 70	79	73.4% [63.7–83.1]	Beta	
Spoke: recommended 1st dose	age 18–49	319	88.4% [84.9–91.9]	Beta	
	age 50–69	360	88.3% [85.0–91.6]	Beta	
	age ≥ 70	78	88.5% [81.4–95.5]	Beta	
Spoke: received 1st dose after recommendation	age 18–49	282	61.3% [55.7–67.0]	Beta	
	age 50–69	318	63.8% [58.6–69.1]	Beta	
	age ≥ 70	69	58.0% [46.4–69.5]	Beta	
Procedure of post-vaccination assessment service					
Recommended 2nd dose	age 18–49	219	98.6% [97.1–100]	Beta	
	age 50–69	145	99.3% [98.0–100]	Beta	
	age ≥ 70	24	100.0%	Beta	
Received 2nd dose after recommendation	age 18–49	216	62.5% [56.1–68.9]	Beta	
	age 50–69	144	75.7% [68.7–82.7]	Beta	
	age ≥ 70	24	30.8% [18.3–43.2]	Beta	
Side effect rate					
Side effect rate of patients after received the first dose	age 18–49	523	8.1% [5.8–10.3]	Beta	VAS-Track participants
	age 50–69	642	6.1% [4.3–7.9]	Beta	
	age ≥ 70	156	1.3% [0–3.0]	Beta	
Side effect rate of patients after received the second dose	age 18–49	205	6.4% [3.2–9.6]	Beta	
	age 50–69	141	2.8% [0.1–5.4]	Beta	
	age ≥ 70	21	12.5% [0–25.5]	Beta	
Medical utilization for side effect					
Age 18–49, number of primary care attendances		62	1.3 [0–2.8]	Gamma	VAS-Track participants
Age 50–69, number of primary care attendances		27	0.8 [0–1.8]	Gamma	
Age ≥ 70, number of primary care attendances		9	1.7 [0.7–2.7]	Gamma	
Medical utilization for infected case					
For mild disease: number of primary care attendances		-	1	Constant	Assumed
For severe disease: number of primary care attendances		-	1	Constant	Assumed
Severe disease: number of specialist care attendances		-	1	Constant	Assumed
Mild disease: Duration, days		331	9.8 [4.4, 10.6]	Gamma	[7]
Severe disease: Stay in hospital, days		1084	26.0 [18.0–41.0]	Gamma	[8, 9]
For fatal disease: Stay in ICU, days		373	8.0 [4.1–14.0]	Gamma	[9]

Supplementary table S2. (Continued)

Parameters	N	Value	Distribution	Source
Unit Cost (USD)				
Cost of allergist, per visit	-	153	Constant#	[10]
Cost of non-allergist, per visit	-	57	Constant#	
Cost of nurse, per visit	-	17	Constant#	Assumed
Cost of allergy tests, per visit	-	256	Constant#	Assumed
Cost of vaccine, per dose	-	72	Constant#	[11]
Cost of primary care, per visit	-	57	Constant	[10]
Cost of specialist care, per visit	-	153	Constant	
Cost of hospital of stay, per visit	-	654	Constant	
Cost of stay in intensive care, per visit	-	3128	Constant	
Cost of care for long COVID, per person	-	256	Constant#	Assumed
Utility Loss of (QALYs)				
Health utility loss of mild case	432	0.43 [0.40, 0.46]	Gamma	[12]
Health utility loss of severe case	80	0.60 [0.40, 0.80]	Gamma	
Health utility loss of long COVID	349	0.11 [0.09–0.13]	Gamma	[13]

Notes: #Deterministic sensitivity analysis conducted. ICU: Intensive Care Unit; QALYs, quality-adjusted life years; VAS-Track, Vaccine Allergy Safety Track.

Supplementary table S3. Characteristics of VAS-Track participants, n = 1799.

Variables		n	%
Total		1799	100%
Age	18-49	788	43.8%
	50-69	829	46.1%
	over 70	182	10.1%
Sex	Male	479	26.6%
	Female	1320	73.4%
Service	Pre-vaccination	1411	78.4%
	Post-vaccination	388	21.6%

Notes: Participants from March to August 2021were retrieved from the VAS-Track Hub and the Hong Kong West Cluster Spoke as this Spoke clinic received the largest number of patients.

Supplementary table S4. Assumption of vaccination rates by age for standard practice group.

Receive 1st dose	Vaccination rate of VAS-Track	Vaccination rate of general population	Hesitancy rate in 2021					Minimum of vaccination rate of hesitant people					Minimum	Maximum	Mean (μ)
			March	April	May	June	July	March	April	May	June	July			
Age 18-49	58%	73%	64%	58%	53%	34%	25%	58%	53%	49%	21%	--	45%	58%	52%
Age 50-69	67%	61%	43%	42%	44%	31%	20%	10%	9%	12%	--	--	10%	61%	36%
Age over 70	62%	25%	55%	54%	51%	46%	39%	--	--	--	--	--	0%	25%	12%
Receive 2nd dose															
Age 18-49	62%	62%	74%	68%	63%	44%	35%	41%	34%	28%	--	--	34%	62%	48%
Age 50-69	75%	52%	53%	52%	54%	41%	30%	24%	16%	9%	--	--	16%	52%	34%
Age over 70	67%	19%	65%	64%	61%	56%	49%	--	--	--	--	--	0%	19%	10%

Notes: Vaccination rate for the standard practice group was based on vaccination rate of the general population (from March 2021 to August 2021) [1] and vaccine hesitancy rate reported by a previous study in Hong Kong (March 2021 to July 2021) [2].

(1) We assumed that vaccines uptake was divided into two groups (non-hesitant and vaccine hesitant people).
(2) We calculated the minimum vaccination rate among the vaccine hesitant group by assuming a 100% vaccination uptake in non-hesitant people. We averaged the monthly vaccination rate of vaccine hesitant people to get the minimum value.
(3) Maximum vaccination rate in the vaccine hesitancy group was assumed to be equal to the general population or VAS-Track participants.
(4) Midpoint vaccination rate in vaccine hesitancy group used as the base value in analyses.
(5) Vaccination rate of vaccine hesitant group was modelled using a normal distribution with mean (μ) and variance (s) equal to one-sixth of the range.
(6) Vaccination rate of the standard practice group was assumed to be equal to the vaccine hesitant group.
(7) In model simulation, vaccination rate was converted from a Gaussian to beta distribution according to the following formula [14]:
$\alpha + \beta = [\mu(1 - \mu)/s^2]-1, \alpha = \mu (\alpha + \beta), \beta = (\alpha + \beta) - \alpha$.

Supplementary table S5. Range of vaccination rates for patients in standard care group for sensitivity analyses.

Receive 1st dose	No vaccination	Vaccination rate of the general population
Aged 18-49	0%	73%
Aged 50-69	0%	61%
Aged over 70	0%	25%
Receive 2nd dose		
Aged 18-49	0%	62%
Aged 50-69	0%	52%
Aged over 70	0%	19%

Notes: In baseline scenario, age-specific vaccination rates in standard care group were based on vaccination rates of the general population in August 2021 and vaccine hesitancy rate reported by a previous study in Hong Kong. In sensitivity analyses, we varied model parameters for vaccination rate of standard care group from 0% to the general population vaccination rate for each age group to assess the robustness of findings.

Supplementary table S6. Detailed cost and effectiveness of VAS-Track strategies and standard practice.

	Pre-vaccination				Post-vaccination			
	VAS-Track		No VAS-Track		VAS-Track		No VAS-Track	
Aged 18-49	Mean	95%UI	Mean	95%UI	Mean	95%UI	Mean	95%UI
VAS clinic, USD	86	[84–88]	--	--	141	[123–158]	--	--
Spoke (Non-Allergist)	43	[42–44]	--	--	57	[57–57]	--	--
Hub (Allergist)	43	[40–46]	--	--	83	[66–101]	--	--
Vaccine, USD	41	[37–44]	37	[34–40]	45	[40–49]	35	[28–41]
Medical Utilization, USD	102	[58–146]	111	[63–159]	91	[51–131]	117	[64–170]
Side effect	0	[0–1]	0	[0–0]	0	[0–1]	0	[0–0]
COVID	93	[50–136]	102	[54–149]	82	[42–121]	108	[55–160]
Long COVID	9	[5–13]	9	[5–13]	9	[5–13]	9	[5–14]
Total cost, USD	229	[185–273]	148	[101–196]	276	[233–319]	152	[101–203]
Vaccination rate, %	56.16	[51.71–60.62]	51.49	[47.42–55.57]	61.82	[55.36–68.29]	47.98	[38.98–56.98]
QALYs	0.9954	[0.9939–0.9968]	0.9952	[0.9937–0.9966]	0.9956	[0.9942–0.997]	0.9950	[0.9934–0.9965]
Aged 50-69								
VAS clinic, USD	86	[84–88]	--	--	141	[124–158]	--	--
Spoke (Non-Allergist)	43	[42–44]	--	--	57	[57–57]	--	--
Hub (Allergist)	43	[40–46]	--	--	84	[67–101]	--	--
Vaccine, USD	45	[42–48]	26	[14–38]	54	[49–59]	25	[16–33]
Medical Utilization, USD	667	[338–996]	893	[440–1346]	401	[194–607]	845	[410–1279]
Side effect	0	[0–0]	0	[0–0]	0	[0–0]	0	[0–0]
COVID	659	[331–988]	885	[433–1338]	395	[189–601]	837	[403–1271]
Long COVID	7	[5–9]	8	[6–10]	6	[4–8]	8	[5–10]
Total cost, USD	797	[469–1126]	919	[470–1369]	596	[391–802]	870	[438–1301]
Vaccination rate, %	61.53	[57.47–65.58]	35.73	[18.89–52.58]	75.19	[68.33–82.06]	34.03	[22.51–45.54]
QALYs	0.9857	[0.9829–0.9885]	0.9810	[0.9764–0.9855]	0.9907	[0.9886–0.9928]	0.9818	[0.978–0.9855]
Aged ≥ 70								
VAS clinic, USD	86	[84–88]	--	--	142	[124–159]	--	--
Spoke (Non-Allergist)	43	[42–44]	--	--	57	[57–57]	--	--
Hub (Allergist)	43	[40–46]	--	--	85	[67–102]	--	--
Vaccine, USD	41	[34–47]	9	[3–15]	48	[35–62]	7	[2–11]
Medical Utilization, USD	1409	[646–2173]	2242	[1075–3410]	1224	[497–1952]	2298	[1096–3500]
Side effect	0	[0–0]	0	[0–0]	0	[0–1]	0	[0–0]
COVID	1404	[640–2167]	2234	[1067–3400]	1219	[492–1945]	2289	[1088–3491]
Long COVID	6	[4–8]	9	[6–11]	5	[3–7]	9	[6–11]
Total cost, USD	1536	[1085–3418]	2251	[1085–3418]	1414	[1104–3507]	2305	[1104–3507]
Vaccination rate, %	56.34	[47.37–65.31]	12.48	[4.5–20.46]	66.50	[47.96–85.03]	9.66	[3.45–15.87]
QALYs	0.9696	[0.961–0.9782]	0.9503	[0.939–0.9617]	0.9731	[0.9629–0.9832]	0.9489	[0.9373–0.9606]

Notes: QALYs, quality-adjusted life years; UI, uncertainty interval; VAS-Track, Vaccine Allergy Safety.

Supplementary table S7. Scenarios analysis of incremental cost-effectiveness ratio (ICER) varying COVID-19 infection rate from 1% to 50%.

Infection rate	Pre-vaccination			Post-vaccination		
Age 18-49	**Incremental Cost, USD**	**Incremental QALYs**	**ICER**	**Incremental Cost, USD**	**Incremental QALYs**	**ICER**
1%	89 [85–93]	0.000 [0.000-0.000]	4,494,708	148 [130–166]	0.000 [0.000-0.000]	2,550,399
3%	87 [84–90]	0.000 [0.000-0.000]	1,469,241	143 [125–160]	0.000 [0.000-0.000]	819,966
5%	85 [82–89]	0.000 [0.000-0.000]	864,147	137 [119–156]	0.000 [0.000-0.001]	473,879
10%	81 [72–90]	0.000 [0.000-0.000]	410,327	124 [99–150]	0.001 [0.000-0.001]	214,314
20%	72 [52–93]	0.000 [0.000-0.001]	183,417	98 [51–145]	0.001 [0.000-0.002]	84,532
30%	64 [31–96]	0.001 [0.000-0.001]	107,781	72 [1–143]	0.002 [0.000-0.003]	41,271
50%	47 [-10–104]	0.001 [0.000-0.002]	47,271	19 [-101–140]	0.003 [0.000-0.005]	6,663
Age 50-69						
1%	82 [69–95]	0.000 [0.000-0.001]	175,927	126 [98–155]	0.001 [0.001-0.001]	144,448
3%	36 [-13–86]	0.001 [0.000-0.002]	26,066	38 [-40–115]	0.003 [0.002-0.004]	14,335
5%	-9 [-97–79]	0.002 [0.001-0.004]	Dominant	-51 [-181–79]	0.004 [0.003-0.006]	Dominant
10%	-123 [-308–62]	0.005 [0.001-0.008]	Dominant	-273 [-536–10]	0.009 [0.006-0.012]	Dominant
20%	-351 [-730–29]	0.009 [0.003-0.016]	Dominant	-717 [-1248–187]	0.018 [0.011-0.024]	Dominant
30%	-578 [-1152–5]	0.014 [0.004-0.024]	Dominant	-1162 [-1960–363]	0.026 [0.017-0.036]	Dominant
50%	-1034 [-1997–71]	0.023 [0.007-0.039]	Dominant	-2050 [-3384–715]	0.044 [0.028-0.060]	Dominant
Age ≥ 70						
1%	35 [-12–81]	0.002 [0.001-0.003]	18,209	75 [11–139]	0.002 [0.001-0.003]	31,850
3%	-132 [-277–13]	0.006 [0.004-0.008]	Dominant	-139 [-338–59]	0.007 [0.004-0.010]	Dominant
5%	-299 [-542–55]	0.009 [0.006-0.013]	Dominant	-354 [-689–20]	0.012 [0.007-0.017]	Dominant
10%	-715 [-1206–225]	0.019 [0.012-0.026]	Dominant	-891 [-1567–215]	0.024 [0.014-0.033]	Dominant
20%	-1549 [-2534–564]	0.038 [0.024-0.052]	Dominant	-1965 [-3324–606]	0.047 [0.028-0.067]	Dominant
30%	-2382 [-3861–903]	0.057 [0.036-0.078]	Dominant	-3039 [-5081–997]	0.071 [0.042-0.100]	Dominant
50%	-4049 [-6517–1581]	0.095 [0.060-0.130]	Dominant	-5187 [-8596–1778]	0.118 [0.069-0.167]	Dominant

Note: "Dominant" indicated pre- or post-vaccination assessment of VAS-Track was less costly and more effective compared with standard practice. "Dominated" indicated pre- or post-vaccination assessment of VAS-Track was more costly but was less effective than standard practice.
ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year.

Supplementary table S8. Scenarios analysis of incremental cost-effectiveness ratio (ICER) varying vaccination rate of standard care group.

Pre-vaccination				Post-vaccination			
Vaccination rate	Incremental Cost, USD	Incremental QALYs	ICER	Vaccination rate	Incremental Cost, USD	Incremental QALYs	ICER
Age 18-49							
0%	128 [117–139]	0.514 [0.474–0.555]	249	0%	168 [138–197]	0.480 [0.390–0.569]	350
13%	81 [72–90]	0.000 [0.000–0.000]	410,327	10%	124 [99–150]	0.001 [0.000–0.001]	214,314
25%	61 [50–73]	-0.214 [-0.255–0.174]	Dominated	19%	112 [82–142]	-0.139 [-0.229–0.050]	Dominated
Age 50–69							
0%	19 [-208–247]	0.360 [0.196–0.523]	53	0%	-203 [-463–57]	0.348 [0.236–0.460]	Dominant
35%	-123 [-308–62]	0.005 [0.001–0.008]	Dominant	34%	-273 [-536–10]	0.009 [0.006–0.012]	Dominant
61%	-223 [-481–34]	-0.246 [-0.410–0.083]	908	52%	-310 [-595–26]	-0.170 [-0.283–0.058]	1,821
Age 70+							
0%	-634 [-1116–152]	0.142 [0.066–0.219]	Dominant	0%	-827 [-1490–164]	0.119 [0.060–0.178]	Dominant
52%	-715 [-1206–225]	0.019 [0.012–0.026]	Dominant	48%	-891 [-1567–215]	0.024 [0.014–0.033]	Dominant
73%	-797 [-1331–263]	-0.105 [-0.181–0.029]	7,588	62%	-953 [-1662–244]	-0.069 [-0.128–0.009]	13,902

Notes: “Dominant” indicated pre- or post-vaccination assessment of VAS-Track was less costly and more effective compared with standard practice. “Dominated” indicated pre- or post-vaccination assessment of VAS-Track was more costly but was less effective than standard practice.
ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year.

In these cases, the positive numerical value of the ICERs with negative costs and negative health comes indicates that money is being saved, but at the expense of reduced health outcomes. This tradeoff occurs when vaccination coverage is highest. The reason for these slightly unusual results is that when vaccination coverage is already high, the incremental benefits of further increasing the coverage become smaller. As a result, the incremental cost of vaccinating additional individuals may outweigh the incremental health benefits gained. In these cases, the ICERs can become positive numerically, indicating cost savings, but it is important to recognize that this comes at the expense of reduced health outcomes.

It is essential to consider these tradeoffs and analyze the broader context when interpreting the results. Vaccination programs aim to achieve a balance between cost-effectiveness and maximizing health outcomes. These results highlight the importance of carefully assessing the cost-effectiveness of vaccination strategies, particularly when coverage rates are already high.

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