

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

Xuechen Xiong,<sup>1</sup> Zhaohua Huo,<sup>2</sup> Valerie Chiang,<sup>3</sup> Jiayi Ye,<sup>1</sup> Yuh Dong Hong,<sup>1</sup> Xingnan Yi,<sup>1</sup>  
Carmen S Ng,<sup>1</sup> Philip H Li,<sup>4\*</sup> Jianchao Quan<sup>1,5\*</sup>

## 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  $\geq 50$ ) 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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<sup>3</sup> Division of Clinical Immunology, Department of Pathology, Queen Mary Hospital, Hong Kong

<sup>4</sup> Division of Rheumatology & Clinical Immunology, Department of Medicine, Queen Mary Hospital, The University of Hong Kong, Hong Kong

<sup>5</sup> HKU Business School, The University of Hong Kong, Hong Kong

\*Equal contribution

### Affiliations:

<sup>1</sup> School of Public Health, LKS Faculty of Medicine, The University of Hong Kong, Hong Kong

<sup>2</sup> Department of Psychiatry, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong

### Corresponding author:

Jianchao Quan  
Patrick Manson Building, 7 Sassoon Road, Pokfulam,  
Hong Kong SAR, China  
E-mail: [jquan@hku.hk](mailto:jquan@hku.hk)

**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.<sup>1,2</sup> 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.<sup>3,4</sup> In Hong Kong, 51.5% of the population reported COVID-19 vaccine hesitancy in January 2021;<sup>5</sup> a major driver of vaccine hesitancy and low uptake was anxiety over vaccine safety, possible allergic reactions,<sup>6</sup> and fear of mRNA technology that was exacerbated by daily media reports of adverse side-effects.<sup>7-10</sup> 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.<sup>11</sup> However, there has been an extreme shortage of allergy specialists and services in Hong Kong like many other countries.<sup>12</sup>

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).<sup>13</sup> The Oxford-AstraZeneca ChAdOx1 adenovirus vaccine was withdrawn due to public concerns about safety and vaccine efficacy.<sup>14</sup> Although vaccine-associated allergic reactions and anaphylaxis are extremely rare (only 0.5 per million doses administered),<sup>15</sup> 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.<sup>16</sup> 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.<sup>17</sup>

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.<sup>18</sup> However, the demand for assessment and vaccination advice quickly overwhelmed

the limited capacity of the VAS clinic leading to waiting time exceeding 8 years.<sup>11,19</sup> 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.<sup>20</sup>

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.<sup>18</sup> 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. 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.<sup>15</sup>

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  $\geq 70$  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.

### **Parameters**

Model inputs were collected from VAS-Track participants and supplemented by published estimates from previous studies. Medical records of 1799 patients between March 2021 to August 2021 were reviewed and followed-up by telephone one month after clinical assessment. 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,<sup>21,22</sup> and prevalence of post-COVID-19 symptoms ('long COVID') were derived from a meta-analysis.<sup>23</sup> The vaccination rate of the standard practice group was based on vaccination rate of the general population (from March 2021 to August 2021),<sup>17</sup> and vaccine hesitancy rate reported by a previous study in Hong Kong (March 2021 to July 2021).<sup>5</sup> The vaccination rate of the standard practice group in our analyses was assumed to be equal to the vaccination rate of vaccine hesitant people.

### **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.<sup>24-26</sup> 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.<sup>27</sup> 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.<sup>28</sup> The health utility loss for long COVID lasting longer than four weeks was estimated as 0.11.<sup>29</sup>

### **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 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**.

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]
<b>Aged 50-69</b>								
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]
<b>Aged ≥ 70</b>								
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).

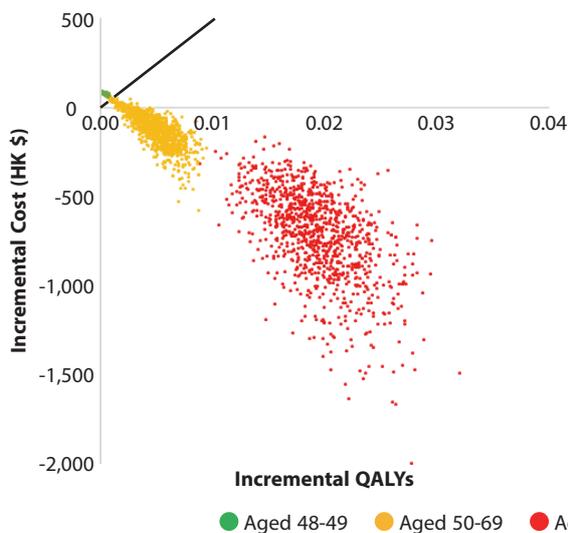
Both pre-vaccination and post-vaccination assessments provided by VAS-Track was cost-effective overall compared with standard practice, but cost-effectiveness varied widely by age group. For the 50-69 and ≥ 70 age groups, VAS-Track was dominant compared to standard practice for both pre- and post-vaccination 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.**

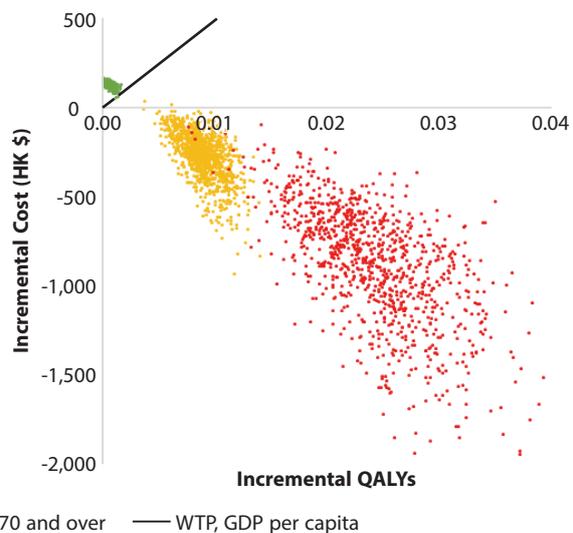
	Pre-vaccination	Post-vaccination
<b>Overall, per person</b>		
Increment vaccination rate	19.11%	26.71%
Increment QALYs	0.0044	0.0051
Increment cost, USD	-104	-87
ICER	Dominant	Dominant
<b>Aged 18-49, per person</b>		
Increment vaccination rate	4.66%	13.84%
Increment QALYs	0.0002	0.0006
Increment cost,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

**(a) Pre-vaccination service**



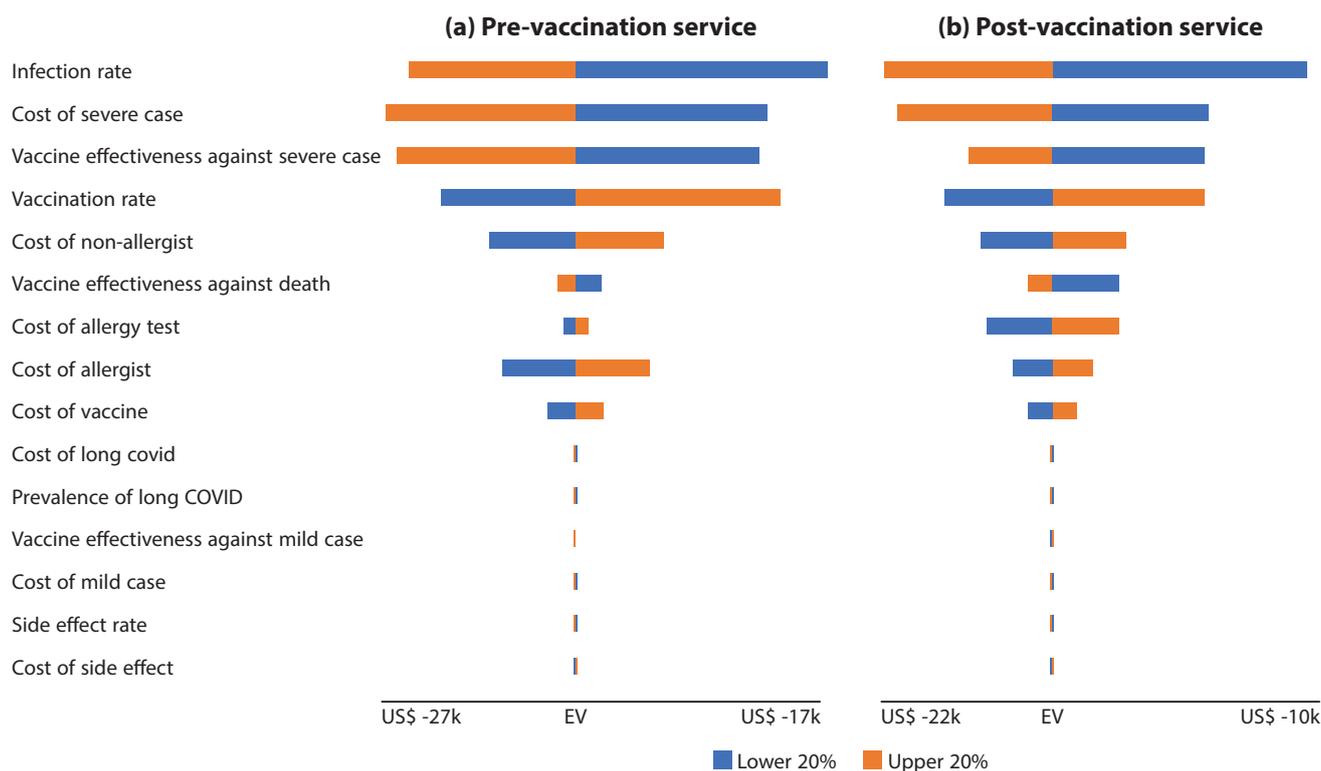
**(b) Post-vaccination service**



**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  $\pm 20\%$ . 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  $\geq 70$  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  $\pm 20\%$  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). 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  $\geq 70$  year olds and 3% or higher for 50-69 year olds.

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.

### 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.<sup>30</sup> Several studies have shown allergy or immunology services could help to mitigate COVID-19 vaccine hesitancy;<sup>11,31</sup> we also found older adults were more motivated to get vaccinated after receiving an allergy assessment.<sup>21</sup> Allergy assessments could benefit older adults by addressing their concerns about getting vaccinated,<sup>5,21</sup> 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,<sup>32-34</sup> as well as vaccines against influenza, pneumonia, and herpes zoster.<sup>35,36</sup> 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.<sup>37-39</sup> Pneumococcal vaccination strategies in older adults were cost-effective in US adults over 64 years and cost-saving in Colombia adults over 50 years.<sup>40,41</sup> Herpes zoster vaccination strategies in older adults were cost-effective in US older adults.<sup>42</sup> 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.<sup>11</sup> 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 1<sup>st</sup> dose, 93.0% population with 2<sup>nd</sup> dose in October 2023),<sup>17</sup> subsequent COVID-19 booster vaccinations will be required to maintain immunity as protection wanes and new variants emerge.<sup>43</sup> Recently in Hong Kong, roll-out of the new generation XBB mRNA vaccine has been approved.<sup>44</sup> 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,<sup>18</sup> 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.<sup>45</sup> 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,<sup>46</sup> 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.<sup>47,48</sup> 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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## 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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## References

1. Moreira ED, Kitchin N, Xu X, Dychter SS, Lockhart S, Gurtman A, et al. Safety and Efficacy of a Third Dose of BNT162b2 Covid-19 Vaccine. *N Engl J Med.* 2022;386:1910-21.
2. Sadoff J, Gray G, Vandebosch A, Cardenas V, Shukarev G, Grinsztejn B, et al. Safety and Efficacy of Single-Dose Ad26.COV2.S Vaccine against Covid-19. *N Engl J Med.* 2021;384:2187-201.
3. Robertson E, Reeve KS, Niedzwiedz CL, Moore J, Blake M, Green M, et al. Predictors of COVID-19 vaccine hesitancy in the UK household longitudinal study. *Brain Behav Immun.* 2021;94:41-50.
4. Yasmin F, Najeeb H, Moed A, Naem U, Asghar MS, Chughtai NU, et al. COVID-19 Vaccine Hesitancy in the United States: A Systematic Review. *Front Public Health.* 2021;9:770985.
5. Xiao J, Cheung JK, Wu P, Ni MY, Cowling BJ, Liao Q. Temporal changes in factors associated with COVID-19 vaccine hesitancy and uptake among adults in Hong Kong: Serial cross-sectional surveys. *Lancet Reg Health West Pac.* 2022;23:100441.

6. Freeman D, Lambe S, Yu LM, Freeman J, Chadwick A, Vaccari C, et al. Injection fears and COVID-19 vaccine hesitancy. *Psychol Med*. 2023;53:1185-95.
7. Leong C, Jin L, Kim D, Kim J, Teo YY, Ho TH. Assessing the impact of novelty and conformity on hesitancy towards COVID-19 vaccines using mRNA technology. *Commun Med (Lond)*. 2022;2:61.
8. Kharbanda EO, Vazquez-Benitez G. COVID-19 mRNA Vaccines During Pregnancy: New Evidence to Help Address Vaccine Hesitancy. *JAMA*. 2022;327:1451-3.
9. Freeman D, Loe BS, Chadwick A, Vaccari C, Waite F, Rosebrock L, et al. COVID-19 vaccine hesitancy in the UK: the Oxford coronavirus explanations, attitudes, and narratives survey (Oceans) II. *Psychol Med*. 2022;52:3127-41.
10. Robertson E, Reeve KS, Niedzwiedz CL, Moore J, Blake M, Green M, et al. Predictors of COVID-19 vaccine hesitancy in the UK household longitudinal study. *Brain Behav Immun*. 2021;94:41-50.
11. Chiang V, Saha C, Yim J, Au EYL, Kan AKC, Hui KSH, et al. The Role of the Allergist in Coronavirus Disease 2019 Vaccine Allergy Safety: A Pilot Study on a "Hub-and-Spoke" Model for Population-Wide Allergy Service. *Ann Allergy Asthma Immunol*. 2022;129:308-12.e1.
12. Lee TH, Leung TF, Wong G, Ho M, Duque JR, Li PH, et al. The unmet provision of allergy services in Hong Kong impairs capability for allergy prevention-implications for the Asia Pacific region. *Asian Pac J Allergy Immunol*. 2019;37:1-8.
13. Vaccine Pass [Internet]. The Government of the Hong Kong Special Administrative Region; c2023 [cited 2023 Aug 8]; Available from: <https://www.coronavirus.gov.hk/eng/vaccine-pass.html>.
14. Press Releases [Internet]. The Government of Hong Kong Special Administrative Region; c2021 [cited 2023 Sep 4]; Available from: <https://www.info.gov.hk/gia/general/202110/12/P2021101200714.htm?fontSize=1>.
15. Chiang V, Leung ASY, Au EYL, Ho MHK, Lee TH, Wu AYY, et al. Updated consensus statements on COVID-19 Vaccine Allergy Safety in Hong Kong. *Asia Pac Allergy*. 2022;12:e8.
16. Chiang V, To KKW, Hung IFN, Saha C, Yim JS, Wong JCY, et al. COVID-19 Vaccine Allergy Safety Track (VAS-Track) pathway: real-world outcomes on vaccination rates and antibody protection. *Asian Pac J Allergy Immunol*. 2023;
17. Daily count of vaccination by age groups [Internet]. DATA.GOV.HK; c2021- [cited 2023 Sep 4]; Available from: <https://data.gov.hk/en-data/dataset/hk-hhb-hhbcovid19-vaccination-rates-over-time-by-age>.
18. Chiang V, Leung ASY, Au EYL, Ho MHK, Lee TH, Wu AYY, et al. Consensus Statements on the Approach to COVID-19 Vaccine Allergy Safety in Hong Kong. *Front Allergy*. 2021;2:
19. Chiang V, Mok SWS, Chan JKC, Leung WY, Ho CTK, Au EYL, et al. Experience of the first 1127 COVID-19 Vaccine Allergy Safety patients in Hong Kong – Clinical outcomes, barriers to vaccination, and urgency for reform. *World Allergy Organ J*. 2022;15:100622.
20. Chan YT, Ho HK, Lai CK, Lau CS, Lau YL, Lee TH, et al. Allergy in Hong Kong: an unmet need in service provision and training. *Hong Kong Med J*. 2015;21:52-60.
21. McMenamin ME, Nealon J, Lin Y, Wong JY, Cheung JK, Lau EHY, et al. Vaccine effectiveness of one, two, and three doses of BNT162b2 and CoronaVac against COVID-19 in Hong Kong: a population-based observational study. *Lancet Infect Dis*. 2022;22:1435-43.
22. Ceban F, Kulzhabayeva D, Rodrigues NB, Di Vincenzo JD, Gill H, Subramaniapillai M, et al. COVID-19 vaccination for the prevention and treatment of long COVID: A systematic review and meta-analysis. *Brain Behav Immun*. 2023;111:211-29.
23. O'Mahoney LL, Routen A, Gillies C, Ekezie W, Welford A, Zhang A, et al. The prevalence and long-term health effects of Long Covid among hospitalised and non-hospitalised populations: A systematic review and meta-analysis. *EclinicalMedicine*. 2023;55:101762.
24. Xia L, Chen J, Friedemann T, Yang Z, Ling Y, Liu X, et al. The Course of Mild and Moderate COVID-19 Infections-The Unexpected Long-Lasting Challenge. *Open Forum Infect Dis*. 2020;7:ofaa286.
25. Chu RBH, Zhao S, Zhang JZ, Chan KCK, Ng PY, Chan C, et al. Comparison of COVID-19 with influenza A in the ICU: a territory-wide, retrospective, propensity matched cohort on mortality and length of stay. *BMJ Open*. 2023;13:e067101.
26. Lam HY, Lam TS, Wong CH, Lam WH, Leung CME, Au KWA, et al. The epidemiology of COVID-19 cases and the successful containment strategy in Hong Kong-January to May 2020. *Int J Infect Dis*. 2020;98:51-8.
27. Fees and Charges [Internet]. Hospital Authority; c2023 [cited 2023 Sep 7]; Available from: [https://www.ha.org.hk/visitor/ha\\_visitor\\_index.asp?Content\\_ID=10045&Lang=ENG](https://www.ha.org.hk/visitor/ha_visitor_index.asp?Content_ID=10045&Lang=ENG).
28. Basu A, Gandhay VJ. Quality-Adjusted Life-Year Losses Averted With Every COVID-19 Infection Prevented in the United States. *Value Health*. 2021;24:632-40.
29. Tsuzuki S, Miyazato Y, Terada M, Morioka S, Ohmagari N, Beutels P. Impact of long-COVID on health-related quality of life in Japanese COVID-19 patients. *Health Qual Life Outcomes*. 2022;20:125.
30. Xiao J, Cheung JK, Wu P, Ni MY, Cowling BJ, Liao Q. Temporal changes in factors associated with COVID-19 vaccine hesitancy and uptake among adults in Hong Kong: Serial cross-sectional surveys. *Lancet Reg Health West Pac*. 2022;23:100441.
31. Turner PJ, Larson H, Dubé É, Fisher A. Vaccine Hesitancy: Drivers and How the Allergy Community Can Help. *J Allergy Clin Immunol Pract*. 2021;9:3568-74.
32. Hogan AB, Wu SL, Toor J, Mesa DO, Doohan P, Watson OJ, et al. Long-term vaccination strategies to mitigate the impact of SARS-CoV-2 transmission: A modelling study. *PLoS Med*. 2023;20:
33. Jentsch PC, Anand M, Bauch CT. Prioritising COVID-19 vaccination in changing social and epidemiological landscapes: a mathematical modelling study. *Lancet Infect Dis*. 2021;21:1097-106.
34. Ferreira LS, de Almeida GB, Borges ME, Simon LM, Poloni S, Bagattini AM, et al. Modelling optimal vaccination strategies against COVID-19 in a context of Gamma variant predominance in Brazil. *Vaccine*. 2022;40:6616-24.
35. Triglav TK, Poljak M. Vaccination indications and limits in the elderly. *Acta Dermatovenerol Alp Pannonica Adriat*. 2013;22:65-70.
36. Weinberger B. Vaccines for the elderly: current use and future challenges. *Immun Ageing*. 2018;15:
37. Deans GD, Stiver HG, McElhaney JE. Influenza vaccines provide diminished protection but are cost-saving in older adults. *J Intern Med*. 2010;267:220-7.
38. Nichol KL, Margolis KL, Wuorenma J, Von Sternberg T. The efficacy and cost effectiveness of vaccination against influenza among elderly persons living in the community. *N Engl J Med*. 1994;331:778-84.
39. Kim YK, Song JY, Jang H, Kim TH, Koo H, Varghese L, et al. Cost Effectiveness of Quadrivalent Influenza Vaccines Compared with Trivalent Influenza Vaccines in Young Children and Older Adults in Korea. *Pharmacoeconomics*. 2018;36:1475-90.
40. Smith KJ, Wateska AR, Nowalk MP, Raymund M, Lee BY, Zimmerman RK. Modeling of Cost Effectiveness of Pneumococcal Conjugate Vaccination Strategies in US Older Adults. *Am J Prev Med*. 2013;44:373-81.
41. Ordóñez JE, Orozco JJ. Cost-effectiveness analysis of pneumococcal conjugate vaccine 13-valent in older adults in Colombia. *BMC Infect Dis*. 2014;14:
42. Hornberger J, Robertus K. Cost-Effectiveness of a Vaccine To Prevent Herpes Zoster and Postherpetic Neuralgia in Older Adults. *Ann Intern Med*. 2006;145:317-25.
43. Feikin DR, Higdon MM, Abu-Raddad LJ, Andrews N, Araos R, Goldberg Y, et al. Duration of effectiveness of vaccines against SARS-CoV-2 infection and COVID-19 disease: results of a systematic review and meta-regression. *Lancet*. 2022;399:924-44.
44. Press Release [Internet]. The Government of the Hong Kong Special Administrative Region; c2023 [cited 2023 October 20]; Available from: <https://www.info.gov.hk/gia/general/202310/11/P2023101100582.htm?fontSize=1>.
45. Moghaddas F, Tsioungkos N, Grammatikos A, Bright PD, Johnston S, Gompels M. COVID-19 vaccine allergy advice and guidance: The experience of a UK tertiary referral centre. *World Allergy Organ J*. 2023;16:100740.
46. Coronavirus Pandemic (COVID-19) [Internet]. Our World in Data; c2020 [cited 2023 Sep 02]; Available from: <https://ourworldindata.org/coronavirus>.
47. Warner JO, Kaliner MA, Crisci CD, Del Giacco S, Frew AJ, Liu GH, et al. Allergy practice worldwide: a report by the World Allergy Organization Specialty and Training Council. *Int Arch Allergy Immunol*. 2006;139:166-74.
48. Chong AC, Diwakar L, Kaplan CM, Fox AT, Abrams EM, Greenhawt M, et al. Provision of Food Allergy Care in the United Kingdom and United States: Current Issues and Future Directions. *J Allergy Clin Immunol Pract*. 2023;11:2054-66.