COVID-19 Vaccine Allergy Safety Track (VAS-Track) pathway: real-world outcomes on vaccination rates and antibody protection

Valerie Chiang,[1] Kelvin Kai Wang To,[2] Ivan Fan Ngai Hung,[3] Chinmoy Saha,[4] Jackie SH Yim,[4] Jane Chi Yan Wong,[4] Elaine YL Au,[1] Tik Suet Chan,[4] Andy Ka Chun Kan,[4] Yuh Dong Hong,[5] Jiaxi Ye,[5] Carmen S Ng,[5] Carmen TK Ho,[4] Chak Sing Lau,[4] Tommy TY Lam,[5] Esther WY Chan,[6] Jianchao Quan,[5] Philip Hei Li[4]

Abstract

Background: Misdiagnosed vaccine-related "allergies" lead to unnecessary vaccine deferrals and incomplete vaccinations, leaving patients unprotected against COVID-19. To overcome limitations and queues for Allergist assessment, the "VAS-Track" pathway was developed to evaluate patients via a multi-disciplinary triage model including nurses, non-specialists, and Allergists.

Objective: We assessed the effectiveness and safety of VAS-Track and evaluate its real-world impact in terms of vaccination rates and COVID-19 protection.

Methods: Patients referred to VAS-Track between September 2021 and March 2022 were recruited. Subgroup analysis was performed with prospective pre- and post-clinic antibody levels.

Results: Nurse-assisted screening identified 10,412 (76%) referrals as inappropriate. 369 patients were assessed by VAS-Track. Overall, 100% of patients were recommended to complete vaccination and 332 (90%) completed their primary series. No patients reported any significant allergic reactions following subsequent vaccination. Vaccination completion rates between patients seen by non-specialists and additional Allergist review were similar (90% vs. 89%, $p = 0.617$). Vaccination rates were higher among patients with prior history of immediate-type reactions (odds ratio: 2.43, $p = 0.025$). Subgroup analysis revealed that only 20% (56/284) of patients had seropositive COVID-19 neutralizing antibody levels ($\geq$ 15 AU/mL) prior to VAS-Track, which increased to 92% after vaccine completion (pre-clinic antibody level 6.0 ± 13.5 AU/mL vs. post-clinic antibody level 778.8 ± 337.4 AU/mL, $p < 0.001$).

Conclusion: A multi-disciplinary allergy team was able to streamline our COVID-19 VAS services, enabling almost all patients to complete their primary series, significantly boosting antibody levels and real-world COVID-19 protection. We propose similar multidisciplinary models to be further utilized, especially in the settings with limited allergy services.

Key words: Allergy, Antibody, COVID-19, Vaccine, Safety

Affiliations:

[1] Division of Clinical Immunology, Department of Pathology, Queen Mary Hospital, Hong Kong
[2] Department of Microbiology, Queen Mary Hospital, The University of Hong Kong, Hong Kong
[3] Division of Infectious Diseases, Department of Medicine, Queen Mary Hospital, The University of Hong Kong, Hong Kong
[4] Division of Rheumatology and Clinical Immunology, Department of Medicine, Queen Mary Hospital, The University of Hong Kong, Hong Kong
[5] School of Public Health, The University of Hong Kong, Hong Kong
[6] Centre for Safe Medication Practice and Research, Department of Pharmacology and Pharmacy, The University of Hong Kong, Hong Kong

Corresponding author:
Philip Hei Li
Division of Rheumatology and Clinical Immunology,
Department of Medicine, The University of Hong Kong,
Queen Mary Hospital,
102 Pokfulam Road, Pokfulam, Hong Kong
E-mail: liphilip@hku.hk

Introduction

The rapidly accumulated experience with Coronavirus disease (COVID-19) vaccines has been an international effort, with many experts recommending varying approaches to vaccine allergy safety (VAS).[1-3] Differences in local policies, available vaccine platforms and medical infrastructure have led to evolving practices of COVID-19 VAS across countries but an international consensus yet to be reached.[4-11] Furthermore, real-world outcomes of such VAS recommendations in terms of vaccination outcomes and COVID-19 antibody titers have seldom been reported.

In Hong Kong, two COVID-19 vaccines have been listed for emergency use: the Fosun Pharma/BioNTech Comirnaty mRNA vaccine BNT162b2 (BNT) and the SinoVac inactivated virus vaccine Coronavac (SV). Both BNT and SV require at least 2 doses (given at an interval of 21- and 28-days, respectively) for completion of their primary series.[12,13] Previous experience and guidance mainly focused on pre-vaccination assessment and risk stratification, without much elaboration on managing patients with post-vaccination reactions.[14,15] This deficit was addressed in September 2021, when the Hong Kong Institute of Allergy (HKIA) published its updated set of Consensus Statements on COVID-19 VAS, which included an algorithm for frontline healthcare providers to assess patients with suspected post-vaccination reactions.[9] This updated consensus recommended that individuals with history of either immediate-type and systemic, or non-immediate and severe, reactions to prior COVID-19 vaccination should not receive further vaccination until Allergist evaluation. Therefore, patients with suspected "allergic" reactions (either suspected or confirmed), could not complete their COVID19 vaccination without Allergist review. However, due to a significant number of referrals, compounded with an extreme shortage of Allergists in Hong Kong, there has been a rapid accumulation of patients waiting for Allergist assessment and subsequent delays in completion of primary series.[16] As of May 2022, the routine waiting time for a new allergy referral to be assessed at Queen Mary Hospital, the only public hospital with a Specialist in Immunology & Allergy in Hong Kong, is over 7 years – obviously an unacceptable delay for vaccination and other Allergy services.

To tackle this overwhelming demand, we developed the "VAS-Track" pathway to streamline the assessment of patients with suspected post-vaccination reactions via a multi-disciplinary triage model. The VAS-Track involved an integrated approach with a team of trained nurses, non-specialists, and Allergists. Nurses were trained to facilitate screening of referral letters and ensure adequate information was available from referring doctors.

Patients were then assessed by a non-specialist doctor at a Triage Clinic, and triaged as either low- or high-risk. Low-risk patients were recommended to proceed with COVID-19 vaccination, while high-risk patients were referred for further Allergist evaluation.

This study aims to assess the impact and real-world outcomes of a multi-disciplinary triage model (VAS-Track) on patients with suspected post-COVID-19 vaccination allergic reactions. We investigate the effectiveness, safety, vaccination rates and prospective COVID-19 antibody levels in patients evaluated by the VAS-Track pathway.

Methods

The Hospital Authority is the sole publicly funded health care provider in Hong Kong. VAS-Track was established at the Hong Kong West Cluster, Department of Medicine of Queen Mary Hospital/The University of Hong Kong. The center is led by a Specialist in Immunology & Allergy and remains the only publicly provided referral center with accredited immunology or allergy services in Hong Kong. Nurses and non-specialist doctors from the Department of Internal Medicine participated in the Triage Clinic of VAS-Track. All nurses and doctors attended dedicated training seminars on post-COVID-19 vaccination assessment and performed simulation training sessions on mock scenarios with an Allergist. Referrals were deemed inappropriate by nurses if they contained insufficient information or did not meet criteria for Allergist referral according to updated HKIA guidance.[9] For such referrals, the referring physicians and patients were contacted in attempt to retrieve supplementary information. If additional information could still not be retrieved despite the nurses' best efforts, or there was still insufficient clinical evidence to meet criteria for referral, these residual referrals were then deemed inappropriate. All referrals were double-checked and reviewed by an Allergist. Non-specialist doctors were provided with protocol-driven algorithms in accordance with updated HKIA recommendations (**Supplementary Figure 1**). All participating non-specialists were educated on common post-vaccine complaints, including reactogenic symptoms such as injection-site reactions, myalgia, headache, fever, fatigue, and mild urticaria.[17-20] They were also trained to recognize common allergic conditions that are falsely labelled as vaccine-related allergies, including asthma, atopic dermatitis, and chronic spontaneous urticaria.[15] All consultations were reviewed and signed off with an Allergist as per the consulting physician's discretion.

Patients who received one prior dose of COVID-19 vaccination were invited and consented to join the study. Blood was drawn once at baseline (i.e., pre-clinic), and again 4 weeks after completion of 2nd dose COVID-19 vaccination (i.e., post-clinic). All patients were followed-up and reviewed at least one month after VAS-Track assessment. Vaccination statuses were also confirmed via electronic health records on Hospital Authority's Clinical Management System.

The neutralization antibody levels were determined using a surrogate virus neutralization test (iFlash-2019-nCoV neutralization antibody assay, Shenzhen YHLO Biotech Co. Ltd., Shenzhen, China) according to manufacturer's instructions as we described previously.[21] A value of ≥ 15 AU/mL was defined as seropositive, and 800 AU/mL was the maximum measurable result.

Clinical data was extracted from medical records of patients attending VAS-Track between September 2021 and March 2022. Only complete patient records were included for analysis and all data was anonymized after data extraction. Extracted clinic data included age, sex, COVID-19 vaccine platform(s) received, indicators for referral, comorbidities, index reactions (including symptom onset time [<1 and ≥1 hour for immediate- and non-immediate-type, respectively]) and outcome of evaluation. Subgroup analysis was performed only on patients who agreed to return for both pre- and post-clinic blood taking.

Categorical variables were expressed as number (percentage) and continuous variables as median (range) where appropriate. Paired t-tests were used to analyze within-patient longitudinal antibody data. Chi-squared association analysis was performed to compare vaccination rates from two types of assessments (non-specialist only vs. with additional Allergist assessment). Logistic regression was used to calculate the odds ratios of vaccination rates associated with variables and comorbidities. A p-value of less than 0.05 was considered statistically significant. STATA version 16 (StataCorp LLC, TX) were used for all statistical analyses.

Patients gave written informed consent, and the study was approved by the institutional review board of the University of Hong Kong and Hospital Authority Hong Kong West Cluster.

Results
Nurse-assisted screening identified that over 75% of referrals were inappropriate

A detailed breakdown of patient pathways and outcomes of VAS-Track is shown in **Figure 1**. A total of 13,779 COVID-19 vaccine-related referrals received, of which 10,412 (76%) were deemed inappropriate (incomplete information or did not meet criteria) after nurse-assisted screening. All patients deemed as inappropriate referrals were advised to proceed with COVID-19 vaccination if no further information was provided.
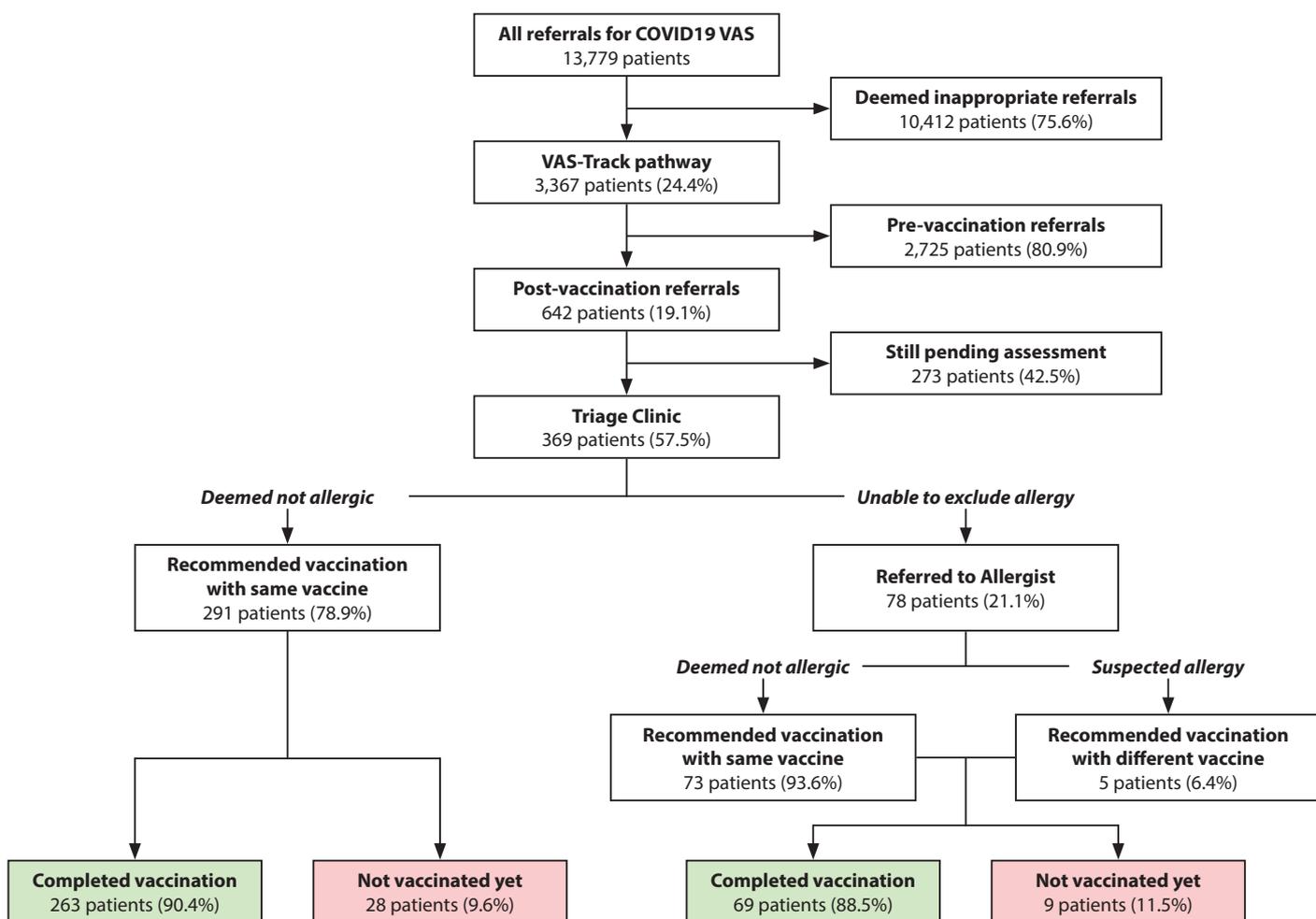

All referrals for COVID19 VAS
13,779 patients

Deemed inappropriate referrals
10,412 patients (75.6%)

VAS-Track pathway
3,367 patients (24.4%)

Pre-vaccination referrals
2,725 patients (80.9%)

Post-vaccination referrals
642 patients (19.1%)

Still pending assessment
273 patients (42.5%)

Triage Clinic
369 patients (57.5%)

Deemed not allergic

Unable to exclude allergy

Recommended vaccination with same vaccine
291 patients (78.9%)

Referred to Allergist
78 patients (21.1%)

Deemed not allergic

Suspected allergy

Recommended vaccination with same vaccine
73 patients (93.6%)

Recommended vaccination with different vaccine
5 patients (6.4%)

Completed vaccination
263 patients (90.4%)

Not vaccinated yet
28 patients (9.6%)

Completed vaccination
69 patients (88.5%)

Not vaccinated yet
9 patients (11.5%)

Figure 1. Patient pathway and outcomes of VAS-Track.

Of the 3,367 remaining referrals, 642 (19%) were referrals for suspected post-vaccination "allergy". As of March 2022, 369 (58%) of patients have been assessed by VAS-Track. The median age was 46 (19-86) and the female-to-male ratio was 3.2:1. Around 62% (230) had received BNT, and 38% (139) SV for their first dose of COVID-19 vaccine. No patients had received their second dose vaccinations before VAS-Track attendance. Detailed breakdown of demographics, comorbidities, and outcomes are shown in **Table 1**. There was no significant difference between demographics and comorbidities between patients having received BNT and SV.

All patients (100%) were recommended to proceed with COVID-19 vaccination

A total of 291 (79%) patients seen were triaged as low-risk and directly recommended for further vaccination without requiring Allergist input. The remaining 78 patients were triaged as high-risk and assessed at the Allergist-led clinic, of which 73 (94%) were advised to complete their primary series with the same vaccine, and 5 (6%) were advised to switch platforms. All 369 (100%) patients were recommended to complete COVID-19 vaccinations after assessment.

High vaccine completion rate, with no difference between non-specialists or Allergist review

Out of all 369 patients recommended to proceed with further vaccination, 332 (90%) proceeded and completed their primary series of COVID-19 vaccinations. No patients reported any significant allergic reactions following second dose vaccination.

There was no difference between the vaccination rates between patients who attended Triage Clinic only (i.e., non-specialist) and those who had additional Allergist review (90.4% vs. 88.5%, $p = 0.617$). Vaccination rates were significantly higher among patients with prior history of immediate- than non-immediate-type reactions (odds ratio: 2.43 [95% confidence interval: 1.12-5.27], $p = 0.025$). There were no associations between vaccination rate and other studied parameters (**Supplementary Table 1**).

Majority (80%) of referred patients still seronegative prior to VAS-Track evaluation

Baseline (pre-clinic) blood samples were available for 284 (77%) patients and their neutralization antibody levels are shown in **Figure 2**. Of these, 228 (80%) (117 [71%] following BNT, and 111 [93%] following SV) had COVID-19 neutralizing antibody levels < 15 AU/mL (i.e., seronegative).

Table 1. Characteristics and outcomes of all patients with breakdown by type of vaccine.

	All patients (n = 369)	First dose BNT (n = 230)	First dose SV (n = 139)
Age (range)	46 (19-86)	43 (19-81)	50 (21-86)
Female	281 (76.1%)	179 (77.8%)	102 (73.4%)
Smoking status	25 (6.8%)	15 (6.5%)	10 (7.2%)
Onset time of suspected reaction			
Immediate (< 1 hour)	170 (46.1%)	104 (45.2%)	66 (47.5%)
Non-immediate (≥ 1 hour)	199 (53.9%)	126 (54.8%)	73 (52.5%)
Comorbidities			
Hypertension	37 (10.0%)	17 (7.4%)	20 (14.4%)
Diabetes Mellitus	10 (2.7%)	5 (2.2%)	5 (3.6%)
Asthma/COPD	15 (4.1%)	13 (5.7%)	2 (1.4%)
CSU	127 (34.4%)	80 (34.8%)	47 (33.8%)
Outcomes			
Recommended for 2nd dose vaccination	369 (100%)	230 (100%)	139 (100%)
Completed 2nd dose vaccination	332* (90.0%)	204 (88.7%)	128 (92.1%)

Abbreviations: COPD, Chronic obstructive pulmonary disease; CSU, Chronic spontaneous urticaria;
*Total of 332/369 = 263/291 (90.4%) completed vaccination after Triage Clinic + 69/78 (88.5%) completed vaccination after Allergist Review.
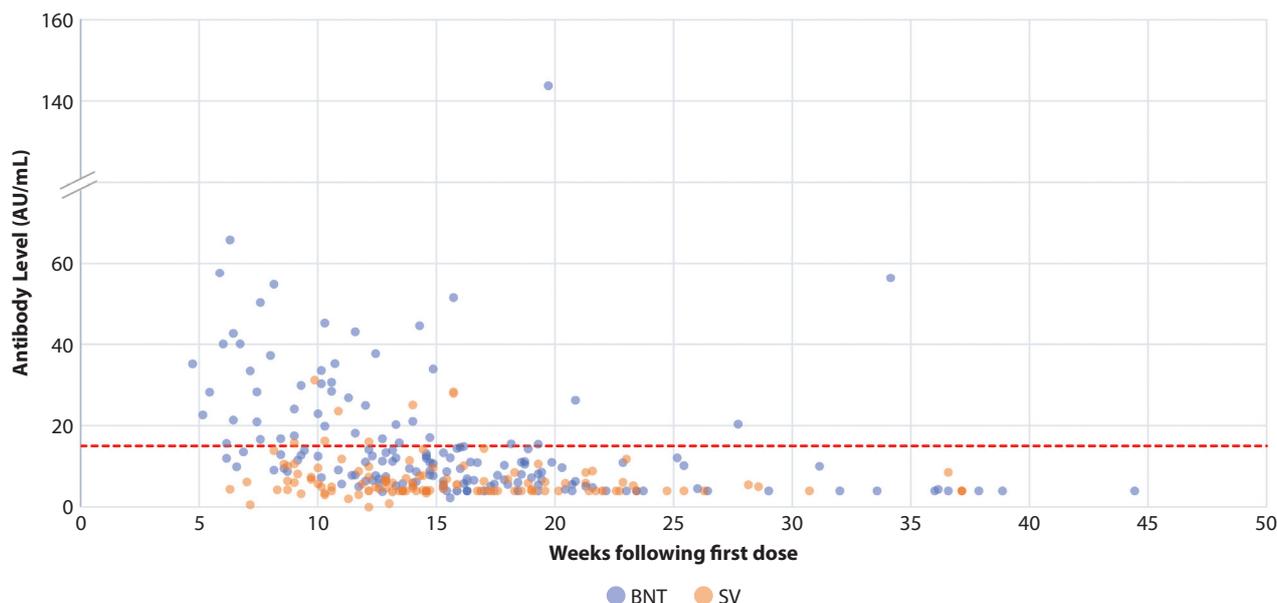
Figure 2. Baseline COVID-19 neutralisation antibody levels prior to VAS-Track attendance.
BNT, Fosun Pharma/BioNTech Comirnaty vaccine; SV, Sinovac CoronaVac vaccine. Red line denotes the manufacturer's cut-off level of neutralisation antibody.
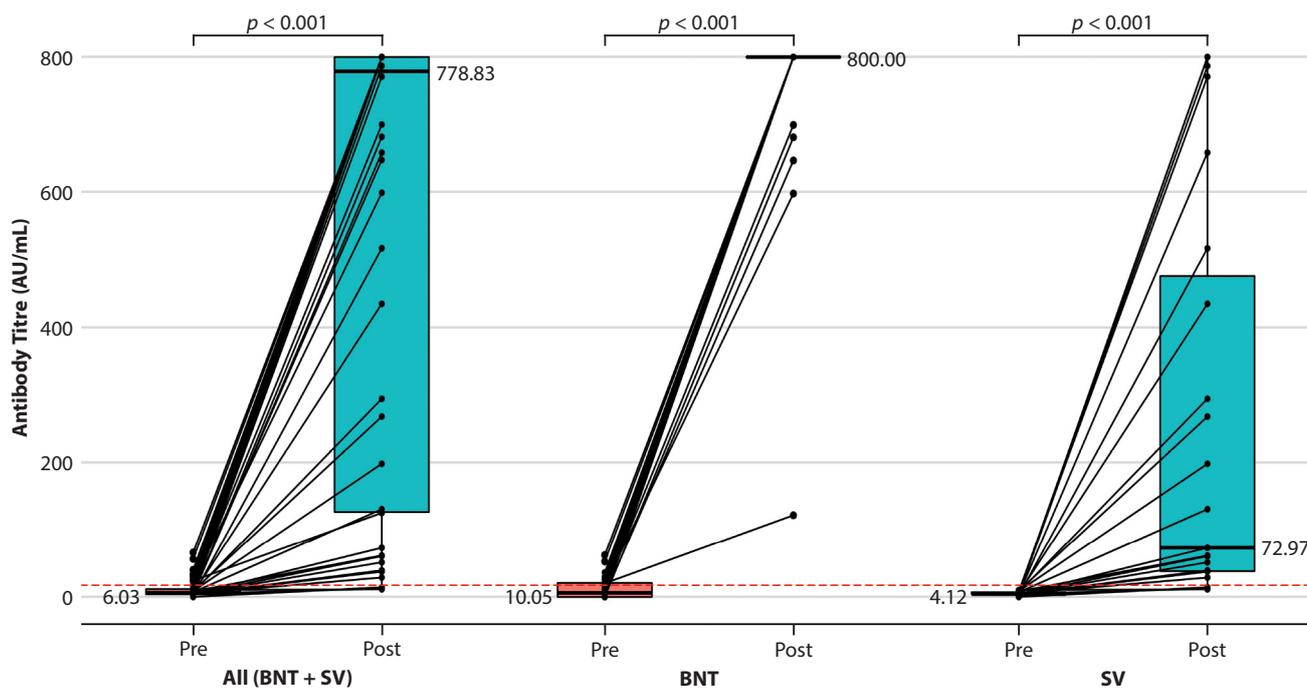

Figure 3. Box-and-whisker plots showing longitudinal neutralisation antibody levels.
Fosun Pharma/BioNTech Comirnaty vaccine; SV, Sinovac CoronaVac vaccine; Pre, Pre-clinic neutralisation antibody levels, Post, Post-clinic neutralisation antibody levels. Number denotes median antibody levels (AU/mL). Red line denotes the manufacturer's cut-off level of neutralisation antibody.

After VAS-Track, 92% of vaccinated achieved seropositive antibody levels

Further subgroup analysis was performed for 51 vaccinated patients with serial blood samples (i.e., both pre- and post-clinic) available. Longitudinal changes in COVID-19 neutralization antibody levels are shown in **Figure 3**. Regardless of vaccine platform, there was significant increase in over all antibody levels (6.0 ± 13.5 AU/mL vs. 778.8 ± 337.4 AU/mL, $p < 0.001$), with 47 (92%) patients achieving seropositive levels. 100% of BNT recipients (10.05 AU/mL vs. 800 AU/mL, $p < 0.001$) and 83% of SV recipients (4.12 AU/mL vs. 72.97 AU/mL, $p < 0.001$) reached adequate levels of antibodies after VAS-Track.

Discussion

Prior studies had not investigated the longitudinal clinical or immunological impact of COVID-19 protection following allergist intervention. We report the first study on the real-world impact and outcomes of a COVID-19 vaccine allergy service, highlighting the significant role of the Allergy Clinic in enhancing COVID-19 protection during the pandemic. We demonstrate that a multidisciplinary allergy team (via the VAS-Track model) was able to streamline our COVID-19 VAS services with nurse-assisted referral screening, and non-specialists to risk-stratify patients before Allergist review. More importantly, we found that fewer than 15% of patients had seropositive antibody levels against COVID-19 prior to assessment, which was boosted up to 92% after vaccination following VAS-Track review.

Reactions following COVID-19 vaccines are common, with most being mild and transient.[2,17] Unfortunately, many reactogenic symptoms are often misdiagnosed as "allergy". Despite HKIA's Updated VAS Consensus Statements, risk stratification remains challenging, and many patients were recommended to defer further vaccinations until Allergist evaluation. A build-up of inappropriate referrals leads to unnecessary patient anxiety and further drops in vaccine confidence, similar to our previous experience in pre-vaccination workup.[15,22] Taking advantage of a multi-disciplinary allergy team with nurses and non-specialists, the VAS-Track model was able to minimize unnecessary delays in completing COVID-19 vaccinations.

Our nurse-assisted screening was able to filter out more than 10,000 unnecessary referrals within the study period alone – all of whom would not have been able to complete COVID-19 vaccination, and otherwise add to the already-overwhelmed clinic waiting times. Thereafter, an adequately trained non-specialist was able to independently assess more than 78% of cases without the need for direct Allergist-input. Among even the minority which warranted Allergist review, only six patients were recommended to switch vaccine platforms due to suspected vaccine-associated allergies. Ultimately, 100% of patients were recommended to proceed with second dose vaccination with no reports of any subsequent allergic reactions following vaccination. This reinforces that COVID-19 vaccines are extremely safe, and almost all patients can complete their primary series without need for Allergist input. Furthermore, basic allergy training enabled non-specialists to exercise safe and effective clinical judgement on COVID-19 VAS.

Although all patients were recommended to proceed with vaccination, our follow-up data found that 10% still did not complete vaccination in spite our advice. Interestingly, patients who only attended the Triage Clinic (i.e., non-specialist) were just as likely to complete vaccination as those who were reviewed by an Allergist. Even though vaccine-associated allergy is often perceived as highly specialized advice, patients were likely just as receptive to recommendations given by non-specialists. This illustrates that non-specialists with appropriate training are also capable of empowering and reassuring patients.

Compounded with the extreme shortage of Allergists in Hong Kong, this corroborates the potential opportunities of further multidisciplinary initiatives.[16]

Our study found that patients with a history of prior immediate-type reactions were significantly more likely to complete vaccinations than patients with non-immediate-type reactions. This phenomenon could be attributed to a few reasons: firstly, lack of allergy investigations for non-immediate-type reactions may have weakened patient confidence. Vaccine skin tests and *in-vitro* allergy tests have shown to be unreliable in diagnosing non-immediate-type reactions.[23,24] The lack of available investigations made it more difficult to convince patients regarding tolerance of subsequent vaccinations, especially for those whose symptoms had persisted for a long time. Secondly, patients are routinely monitored for up to 30 minutes (or longer) following vaccinations at all vaccination centers. This reassured patients that even in the event of any immediate-type reaction, medical personnel are available on site to provide urgent care where necessary. In contrast, patients are not routinely followed-up for non-immediate reactions outside of research settings, and therefore, these patients may be less receptive to subsequent vaccinations, not only fearing that symptoms may recur, but also without guarantee of easy access to Allergist assessment. In light of this, we plan to instigate additional mechanisms, such as nurse-led follow-up clinics, to further encourage patients with history of non-immediate-type reactions to get vaccinated. Future studies dedicated to investigating the specific reasons behind persistent vaccination delays will be important to further optimize vaccination uptake and COVID-19 protection.

Most strikingly, we identified that the vast majority of patients pending consultation had poor protection against COVID-19, as demonstrated by suboptimal neutralizing antibody levels. Were it not for the establishment of VAS-Track, these patients deemed "allergic" to prior COVID-19 vaccination would have been ineligible for further vaccination. With only one dose of COVID-19 vaccine, they would have psersistently low or absent antibodies against COVID-19. Patients who completed primary series vaccinations after VAS-Track had significant improvement in antibody levels, reinforcing the significant role of allergy teams in boosting population-wide COVID-19 protection.

There were several limitations in this study. Firstly, not all patients agreed to participate in serial blood taking and there were only a relatively small number of patients with longitudinal antibody levels available. This limited our ability to perform further subgroup analysis. Secondly, due to the extremely limited manpower, validation studies on the VAS-Track model could not be conducted and there is a possibility of inter-observer variability. Thirdly, although follow-up reviews were conducted for all patients at least one month following VAS-Track, it is possible that some patients completed their vaccinations after review

(therefore underestimating our reported 90% vaccination rate). Furthermore, we could not exclude the possibility of temporal confounders, especially as external factors (such as local incidence of COVID-19, and perceived risk of COVID-19 infection) may have also influenced vaccination rates. Fortunately, the COVID-19 pandemic did not significantly affect Hong Kong until the fifth wave, which peaked in March 2022 and already being towards the end of the study period. Lastly, this study was conducted in a single center among Hong Kong Chinese patients, which may limit the external validity of our findings. These limitations can be addressed by multi-center and longitudinal studies in the future.

Conclusion

In conclusion, there are still an abundant number of misdiagnosed vaccine-related "allergies" leading to unnecessary vaccine deferrals. Most of these patients remain unprotected against COVID-19, with suboptimal antibody levels due to incomplete vaccinations. Our study demonstrated that a multidisciplinary allergy team was able to streamline COVID-19 VAS services which enabled almost all patients to complete their primary series and achieve COVID-19 seroconversion without the obligatory need for Allergist review. We propose that the VAS-Track model can be expanded and initiated in other centers to expand the capacity of VAS services.

Acknowledgements

Conflict of interest

The authors have no conflict of interest in relation to this work.

Author contributions

- V.C. researched the data and wrote the manuscript.
- K.K.W.T., I.F.N.H., J.S.H.Y., J.C.Y.W., E.Y.L.A., T.S.C., A.K.C.K., Y.D.H., J.Y. and C.S.N. researched the data.
- C.S. researched the data and performed statistical analyses.
- C.T.K.H., C.S.L., T.T.Y.L., E.W.Y.C., J.Q. and P.H.L. supervised the project and critically reviewed and edited the manuscript.
- All authors contributed to the final version of the manuscript.

References

1. Krantz MS, Kwah JH, Stone CA Jr, Phillips EJ, Ortega G, Banerji A, et al. Safety Evaluation of the Second Dose of Messenger RNA COVID-19 Vaccines in Patients With Immediate Reactions to the First Dose. JAMA Intern Med. 2021;181:1530-3.
2. Chapin-Bardales J, Gee J, Myers T. Reactogenicity Following Receipt of mRNA-Based COVID-19 Vaccines. JAMA. 2021;325:2201-2.
3. Krantz MS, Bruusgaard-Mouritsen MA, Koo G, Phillips EJ, Stone CA Jr, Garvey LH. Anaphylaxis to the first dose of mRNA SARS-CoV-2 vaccines: Don't give up on the second dose! Allergy. 2021;76:2916-20.
4. Rutkowski K, Mirakian R, Till S, Rutkowski R, Wagner A. Adverse reactions to COVID-19 vaccines: A practical approach. Clin Exp Allergy. 2021;51:770-7.
5. Banerji A, Wickner PG, Saff R, Stone CA Jr, Robinson LB, Long AA, et al. mRNA Vaccines to Prevent COVID-19 Disease and Reported Allergic Reactions: Current Evidence and Suggested Approach. J Allergy Clin Immunol Pract. 2021;9:1423-37.
6. Sokolowska M, Eiwegger T, Ollert M, Torres MJ, Barber D, Del Giacco S, et al. EAACI statement on the diagnosis, management and prevention of severe allergic reactions to COVID-19 vaccines. Allergy. 2021;76:1629-39.
7. Greenhawt M, Abrams EM, Shaker M, Chu DK, Khan D, Akin C, et al. The Risk of Allergic Reaction to SARS-CoV-2 Vaccines and Recommended Evaluation and Management: A Systematic Review, Meta-Analysis, GRADE Assessment, and International Consensus Approach. J Allergy Clin Immunol Pract. 2021;9:3546-67.
8. Banerji A, Wolfson AR, Wickner PG, Cogan AS, McMahon AE, Saff R, et al. COVID-19 Vaccination in Patients with Reported Allergic Reactions: Updated Evidence and Suggested Approach. J Allergy Clin Immunol Pract. 2021;9:2135-8.
9. 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:
10. Asia Pacific Association of Allergy Asthma and Clinical Immunology [Internet]. Dubai (United Arab Emirates): Asia Pacific Association of Allergy Asthma and Clinical Immunology; c2021 [cited 2022 May 4]. ADVERSE REACTIONS TO COVID-19 VACCINES; [about 8 p.]. Available from: https://067bfc60-b466-4428-926d-1db6acd6462e.usrfiles.com/ugd/067bfc_75caa2fc919b45bfa9d8e0ad0aa32eb2.pdf
11. Australasian Society of Clinical Immunology and Allergy [Internet]. Brookvale (Australia): Australasian Society of Clinical Immunology and Allergy; c2021 [cited 2022 May 4]. Allergy, Immunodeficiency, Autoimmunity and COVID-19 Vaccination Position Statement; [about 5 p.]. Available from: https://www.allergy.org.au/images/stories/pospapers/ASCIA_HP_Position_Statement_COVID-19_Vaccination_2021-09-20.pdf
12. World Health Organization. Interim recommendations for use of the inactivated COVID-19 vaccine, CoronaVac, developed by Sinovac: interim guidance, 24 May 2021. Geneva: World Health Organization; 2021. Report No.: WHO/2019-nCoV/vaccines/SAGE_recommendation/Sinovac-CoronaVac/2021.1.
13. World Health Organization. Interim recommendations for use of the Pfizer–BioNTech COVID-19 vaccine, BNT162b2, under emergency use listing: interim guidance, first issued 8 January 2021, updated 15 June 2021, updated 19 November 2021, updated 21 January 2022. Geneva: World Health Organization; 2022. Report No.: WHO/2019-nCoV/vaccines/SAGE_recommendation/BNT162b2/2022.1.
14. 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;2:690837.
15. 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.
16. 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.
17. Lai FTT, Leung MTY, Chan EWW, Huang L, Lau LKW, Peng K, et al. Self-reported reactogenicity of CoronaVac (Sinovac) compared with Comirnaty (Pfizer-BioNTech): A prospective cohort study with intensive monitoring. Vaccine. 2022;40:1390-6.
18. Centers for Disease Control and Prevention [Internet]. Atlanta (United States): U.S. Department of Health and Human Services; c2021 [cited 2022 Apr 5]. Pfizer-BioNTech COVID-19 Vaccine Reactions & Adverse Events; [about 10 screens]. Available from: https://www.cdc.gov/vaccines/covid-19/info-by-product/pfizer/reactogenicity.html
19. Pitlick MM, Joshi AY, Gonzalez-Estrada A, Chiarella SE. Delayed systemic urticarial reactions following mRNA COVID-19 vaccination. Allergy Asthma Proc. 2022;43:40-3.
20. Blumenthal KG, Freeman EE, Saff RR, Robinson LB, Wolfson AR, Foreman RK, et al. Delayed Large Local Reactions to mRNA-1273 Vaccine against SARS-CoV-2. N Engl J Med. 2021;384:1273-7.

21. Lu L, Chen LL, Zhang RR, Tsang OT, Chan JM, Tam AR, et al. Boosting of serum neutralizing activity against the Omicron variant among recovered COVID-19 patients by BNT162b2 and CoronaVac vaccines. EBioMedicine. 2022;79:103986.
22. Kwok KO, Li KK, Tang A, Tsoi MTF, Chan EYY, Tang JWT, et al. Psychobehavioral Responses and Likelihood of Receiving COVID-19 Vaccines during the Pandemic, Hong Kong. Emerg Infect Dis. 2021; 27:1802-10.
23. Wolfson AR, Robinson LB, Li L, McMahon AE, Cogan AS, Fu X, et al. First-Dose mRNA COVID-19 Vaccine Allergic Reactions: Limited Role for Excipient Skin Testing. J Allergy Clin Immunol Pract. 2021;9: 3308-20.e3.
24. Bianchi L, Biondi F, Hansel K, Murgia N, Tramontana M, Stingeni L. Skin tests in urticaria/angioedema and flushing to Pfizer-BioNTech SARS-CoV-2 vaccine: Limits of intradermal testing. Allergy. 2021;76: 2605-7.

Supplemental material

Supplementary Table 1. Association analysis on factors associated with vaccination rate.

	Odds Ratio	95% Confidence Interval	p-value
Non-specialist only vs additional Allergist review	0.73	0.32–1.71	0.473
Age	1.27	0.95–1.71	0.109
Female	0.96	0.42–2.22	0.926
Smoking	0.49	0.14–1.66	0.251
Immediate vs non-immediate onset	**2.43**	**1.12–5.27**	**0.025**
BNT vs SV	1.13	0.51–2.48	0.768
Hypertension	1.53	0.31–7.57	0.599
Diabetes mellitus	0.77	0.08–7.32	0.820
Asthma/COPD	0.57	0.14–2.25	0.422
CSU	1.58	0.70–3.56	0.274

Bold denotes statistical significance ($p < 0.05$).
BNT, Fosun Pharma/BioNTech Comirnaty vaccine; SV, Sinovac CoronaVac vaccine; COPD, Chronic obstructive pulmonary disease; CSU, Chronic spontaneous urticaria.
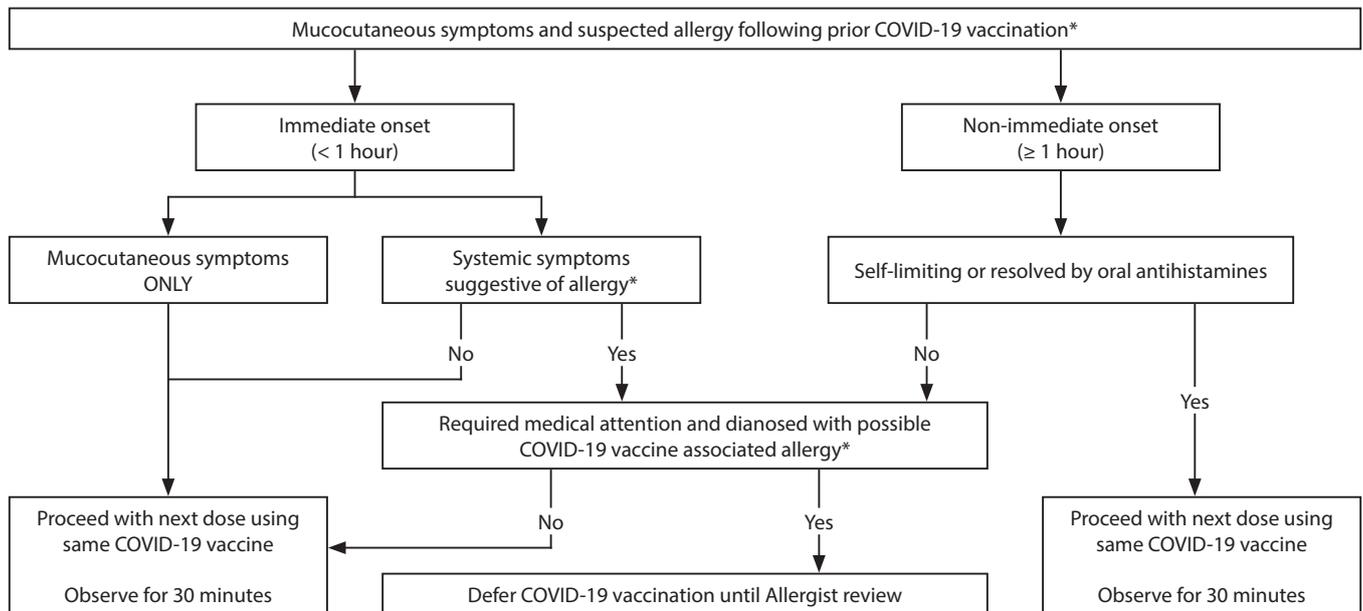
*Allergy = clinician diagnosed **inappropriate** immune-mediated response following vaccination
(i.e. NOT reactogenic symptoms such as injection-site pain, localised rash/swelling, fever, myalgia, headache

Supplementary Figure 1. Protocol-driven algorithms for management by non-specialists.
Adapted from HKIA Updated Consensus Statements on COVID-19 VAS.[9]