Revaccination outcomes among individuals aged 12+ with suspected hypersensitivity reactions following SARS-CoV-2 vaccination:

A Canadian Special Immunization Clinic (SIC) Network study

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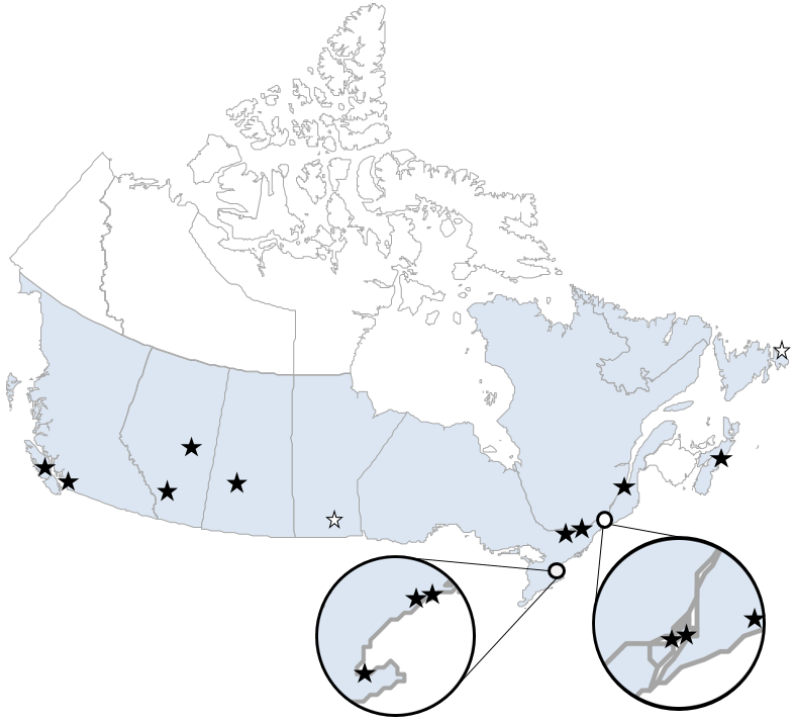
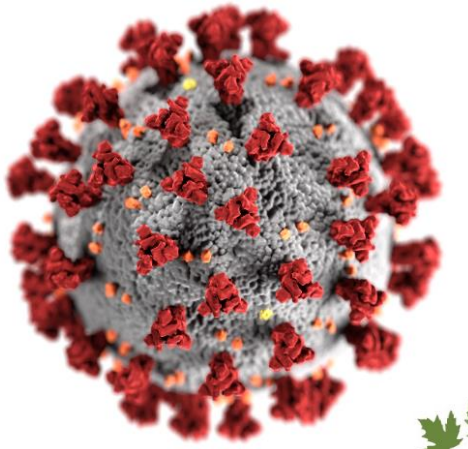
on behalf of the Special Immunization Clinic (SIC) Network investigators

Special Immunization Clinic (SIC) Network



- **Objectives:**
  - Standardize and improve clinical care of patients after an adverse event following immunization (AEFI)
  - Determine the rate of AEFI recurrence

- **SIC Network approach**
  - Patients with AEFIs are referred to one of 15 SICs assessment regarding safety of future vaccinations
  - Standard protocols for evaluation of specific AEFIs of interest
  - Patients are followed up after revaccination to capture AEFI recurrences
  - Data are collected centrally



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Warning after two NHS workers have allergic reaction to Pfizer/BioNTech Covid vaccine

The UK's drug regulator says anyone with a history of "significant" allergic reactions to food, medicine or vaccines should not currently receive the jab

December 9, 2020

https://www.standard.co.uk/news/uk/warning-patients-pfizer-biontech-covid-allergic-reactions-b229762.html

Estimated anaphylaxis reporting rates following COVID-19 vaccines based on VAERS reports and reported doses administered*

Reported vaccine doses administered	Anaphylaxis cases	Reporting rate (analytic period Dec 14-Jan 18)
Pfizer-BioNTech: **9,943,247**	50	5.0 per million doses admin.
Moderna: **7,581,429**	21	2.8 per million doses admin.

- Total COVID-19 vaccine doses administered thru Jan 18 by sex: Female 61%, Male 36%, Unk 3%
- Previously reported rate for Pfizer-BioNTech vaccine: 11.1 per million doses admin (Dec 14-Dec 23)
  https://www.cdc.gov/mmwr/volumes/70/wr/mm7002e1.htm
- Previously reported rate for Moderna vaccine: 2.5 per million doses admin (Dec 21-Jan 10)
  https://www.cdc.gov/mmwr/volumes/70/wr/mm7004e1.htm

* Data through January 18, 2021

https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-01/06-COVID-Shimabukuro.pdf

Research Aim

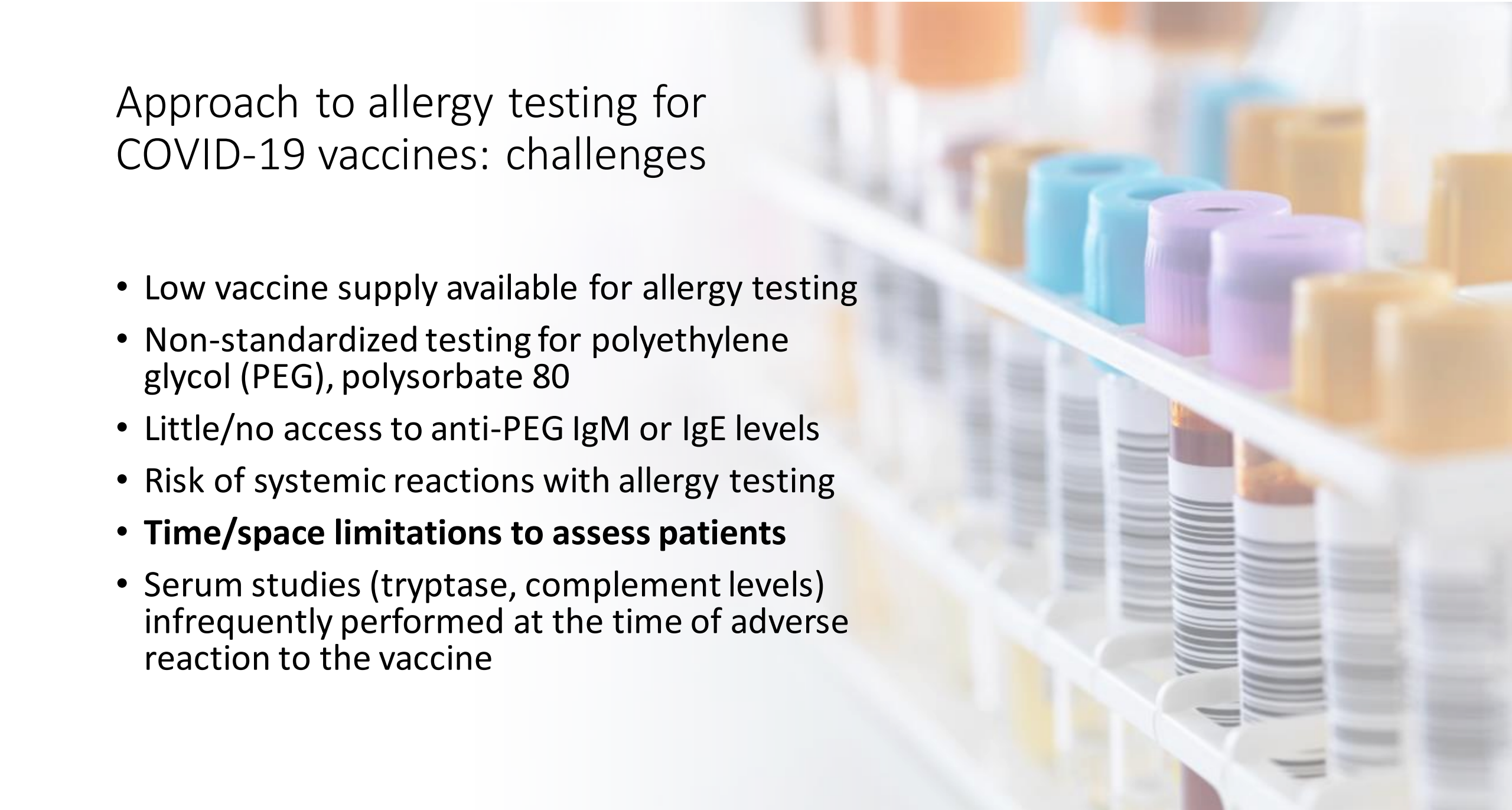
- Describe a national cohort of patients **at-risk of, or referred for, suspected hypersensitivity reactions following COVID-19 vaccination to:**
  - Determine the risk of AEFI recurrence following revaccination
  - Identify risk factors for recurrence, including confirmed allergy to COVID-19 vaccines or their components

Methods

- Inclusion criteria: individuals whose final diagnosis was a hypersensitivity reaction following COVID-19 vaccination, and who consented and enrolled at 17 participating SICs prior to April 30, 2022

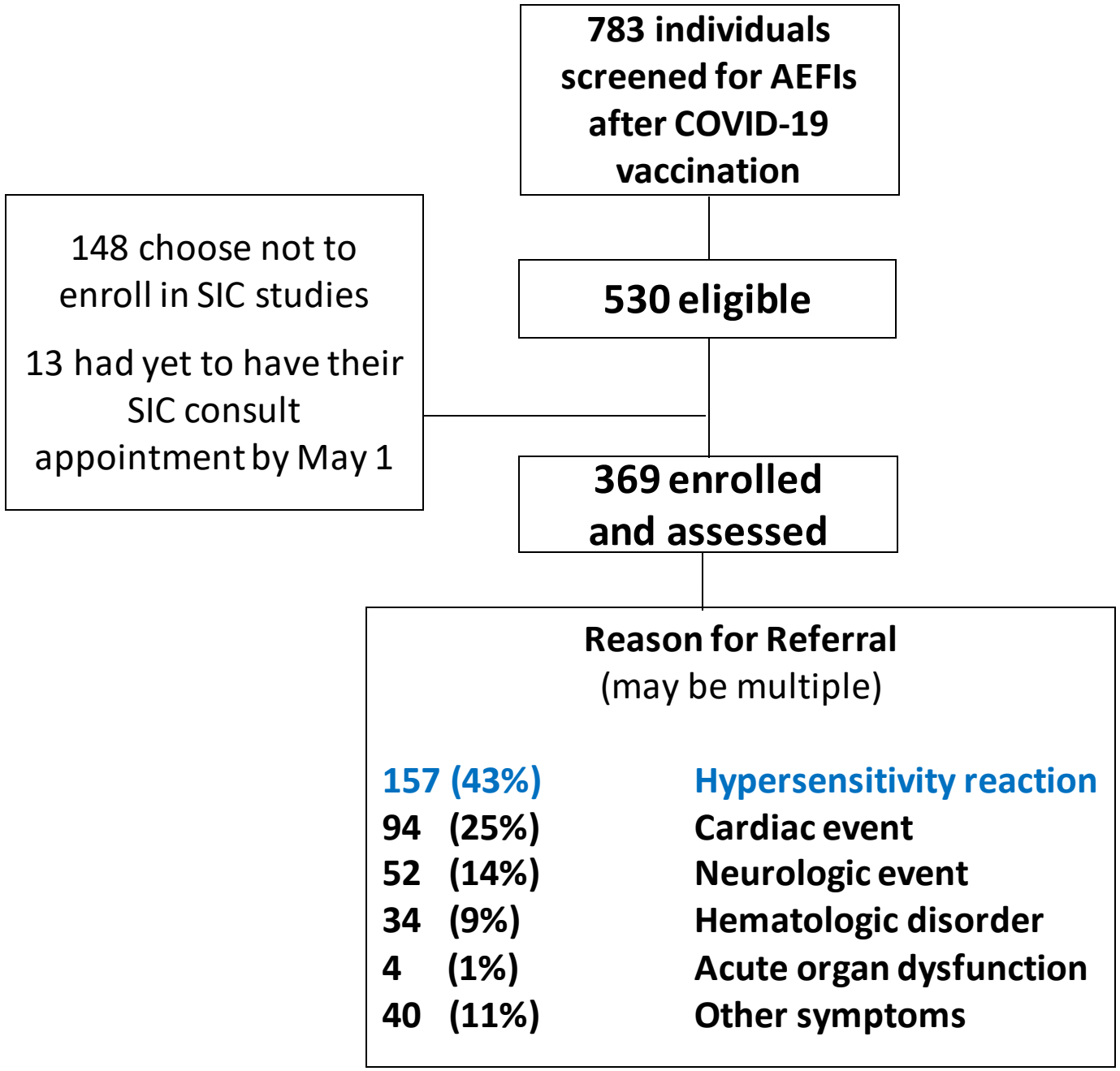
- Clinical assessments and revaccination outcomes were captured in a denomalized database

Approach to allergy testing for COVID-19 vaccines: challenges



- Low vaccine supply available for allergy testing
- Non-standardized testing for polyethylene glycol (PEG), polysorbate 80
- Little/no access to anti-PEG IgM or IgE levels
- Risk of systemic reactions with allergy testing
- **Time/space limitations to assess patients**
- Serum studies (tryptase, complement levels) infrequently performed at the time of adverse reaction to the vaccine

COVID-19 Participants Assessed in SIC Network as of April 30, 2022



3 patient groups of primary interest

1) **Suspected anaphylaxis to a COVID-19 vaccine**
   - Will consider Brighton (primary), NIIAD, WAO case definitions
   - Final diagnosis of a non-hypersensitivity reaction

2) **Confirmed allergy to a COVID-19 vaccine** or any of its components
   - Skin test positive for any COVID-19 vaccine, PS 80, PEG
   - Recurrence of hypersensitivity event upon revaccination

3) **History of immediate hypersensitivity or anaphylaxis to PEG or other vaccine component** prior to receiving a COVID-19 vaccine

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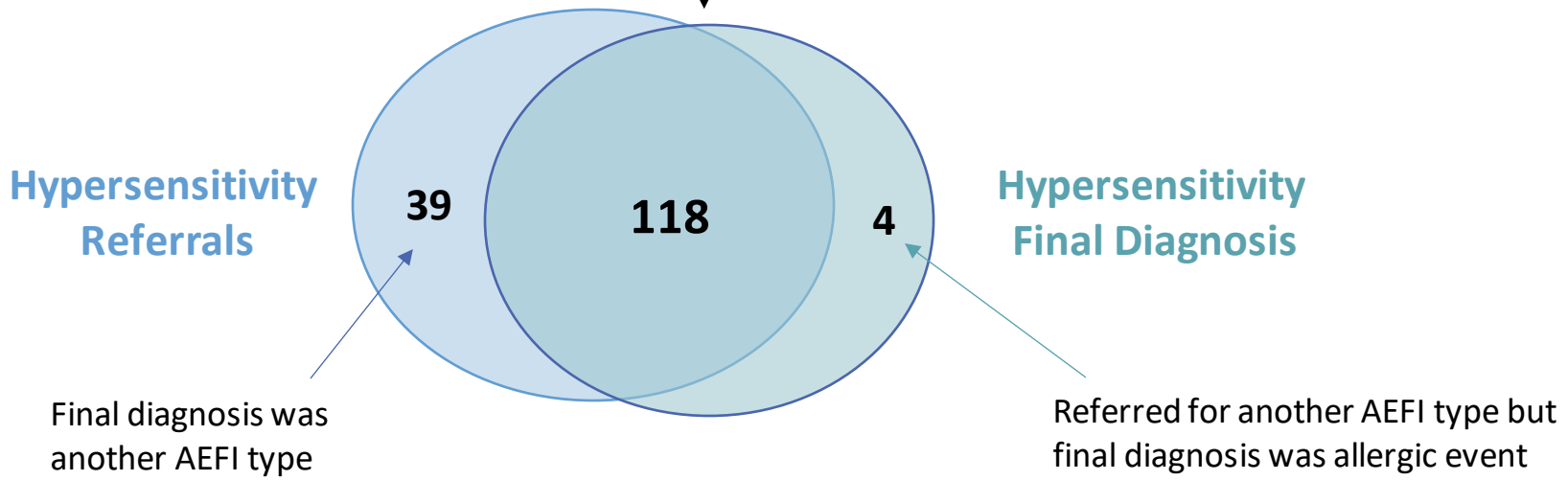
COVID-19 Patients Assessed in SIC Network as of April 30, 2022

Referred for suspected hypersensitivity reaction (N=157)

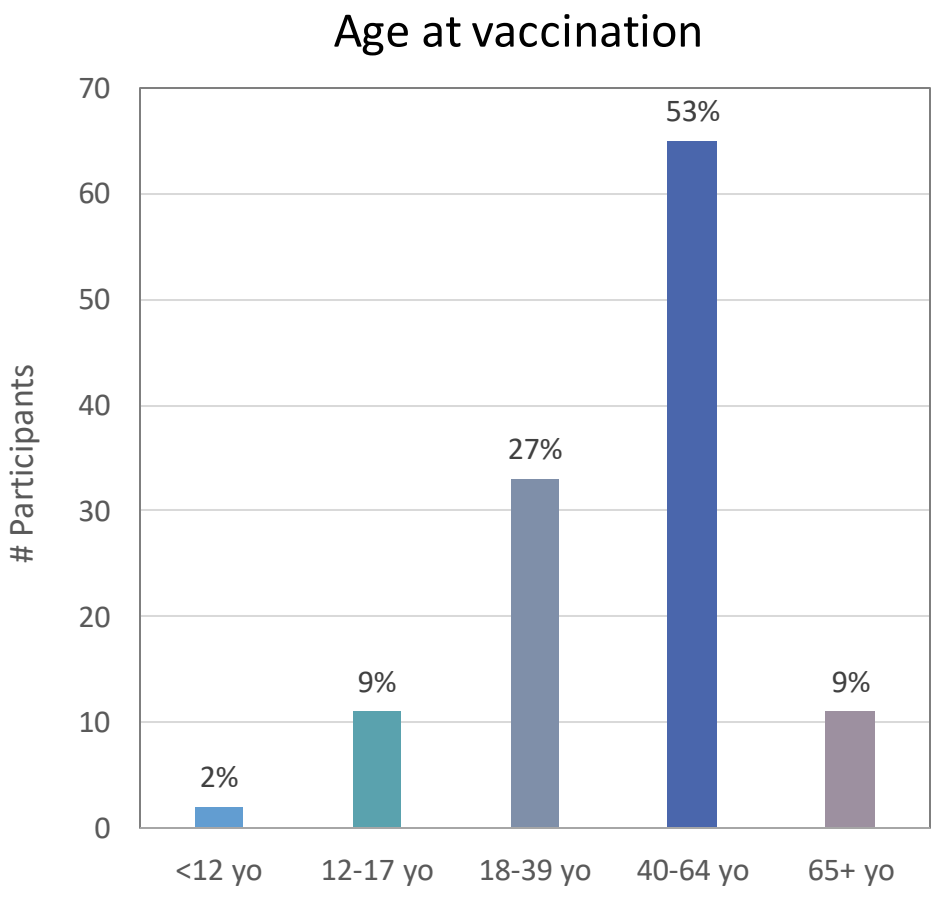
Final Diagnosis of hypersensitivity reaction (N=122)

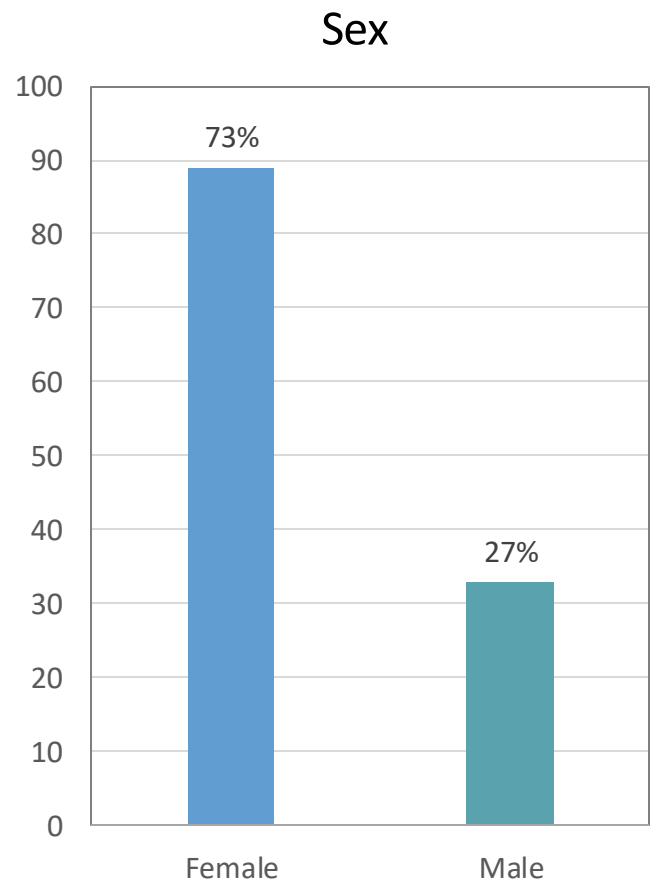
- Non-anaphylaxis immediate hypersensitivity: 54 (44%)
- Suspected anaphylaxis: 35 (29%)
- Delayed onset urticaria/ angioedema: 25 (20%)
- Other events: 8 (7%)

+ Enrolled pre-vaccination with history of allergy to COVID-19 vaccine components (e.g. PEG) **(N=24)**

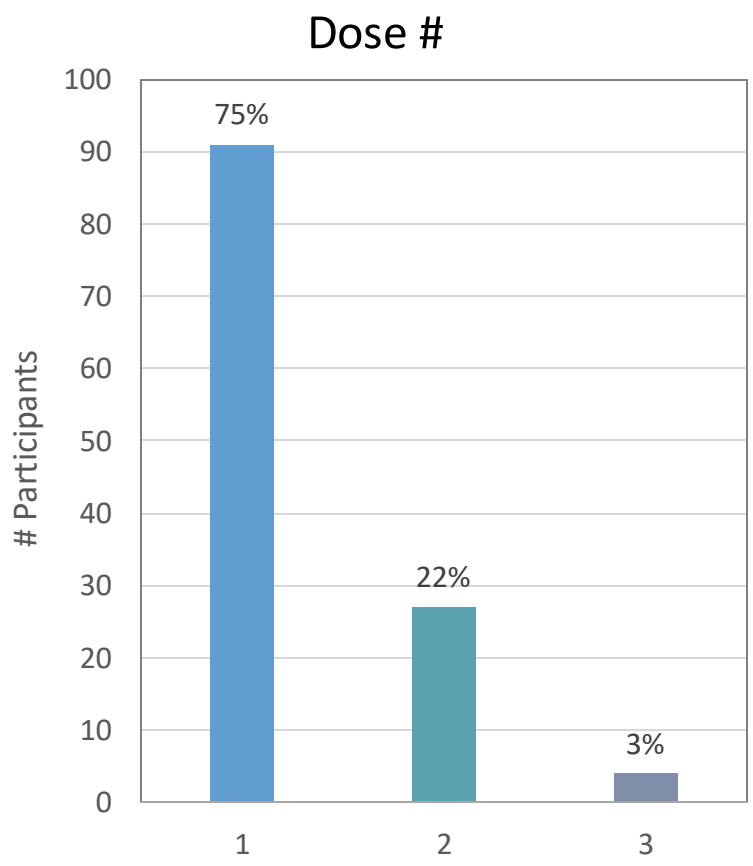


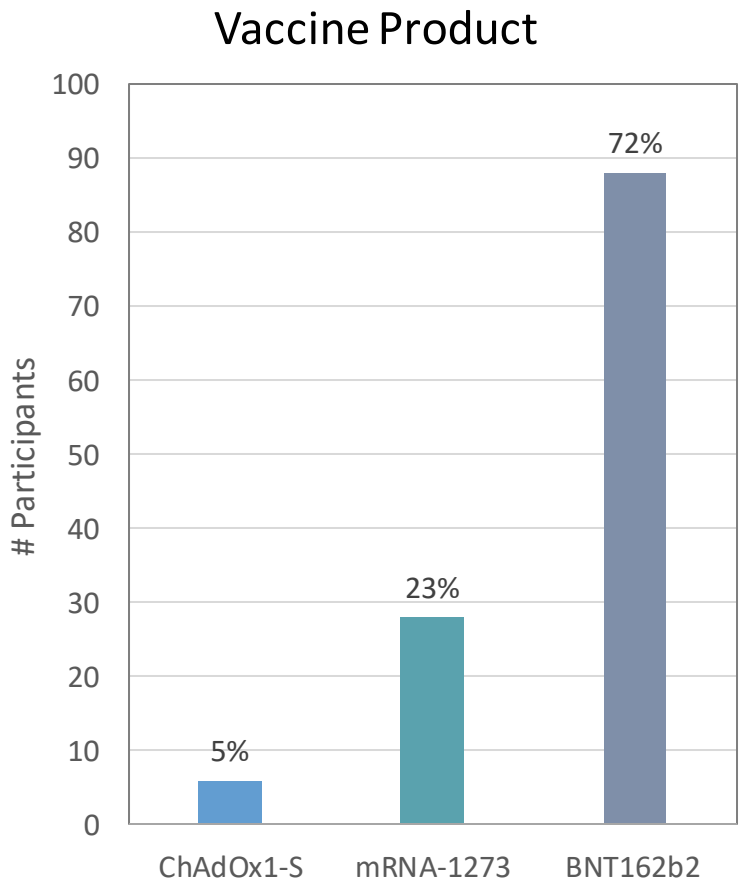
Socio-demographic characteristics of participants with a diagnosis of an allergic event following COVID-19 vaccination



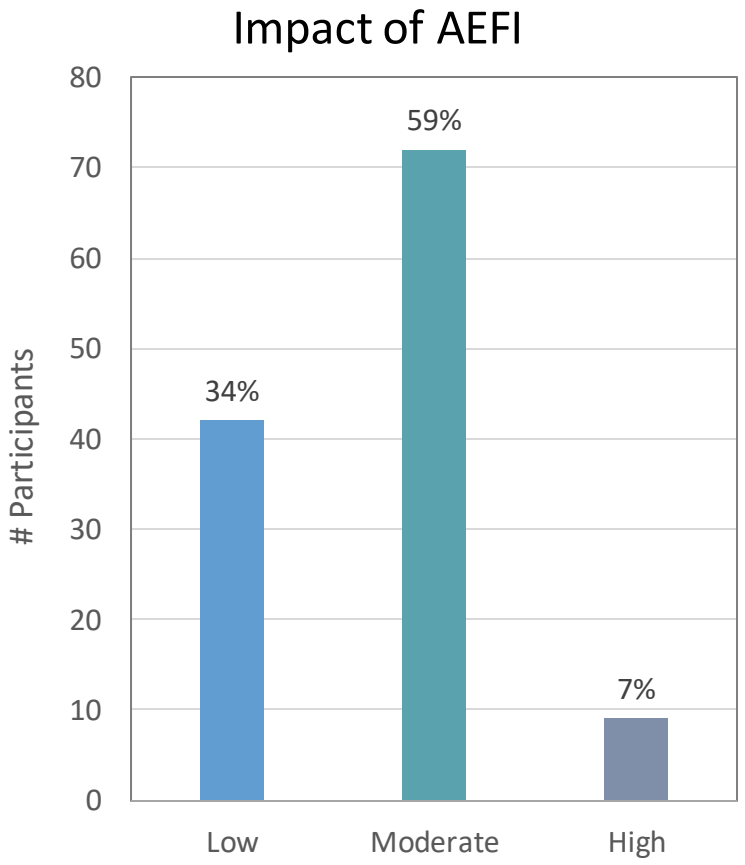


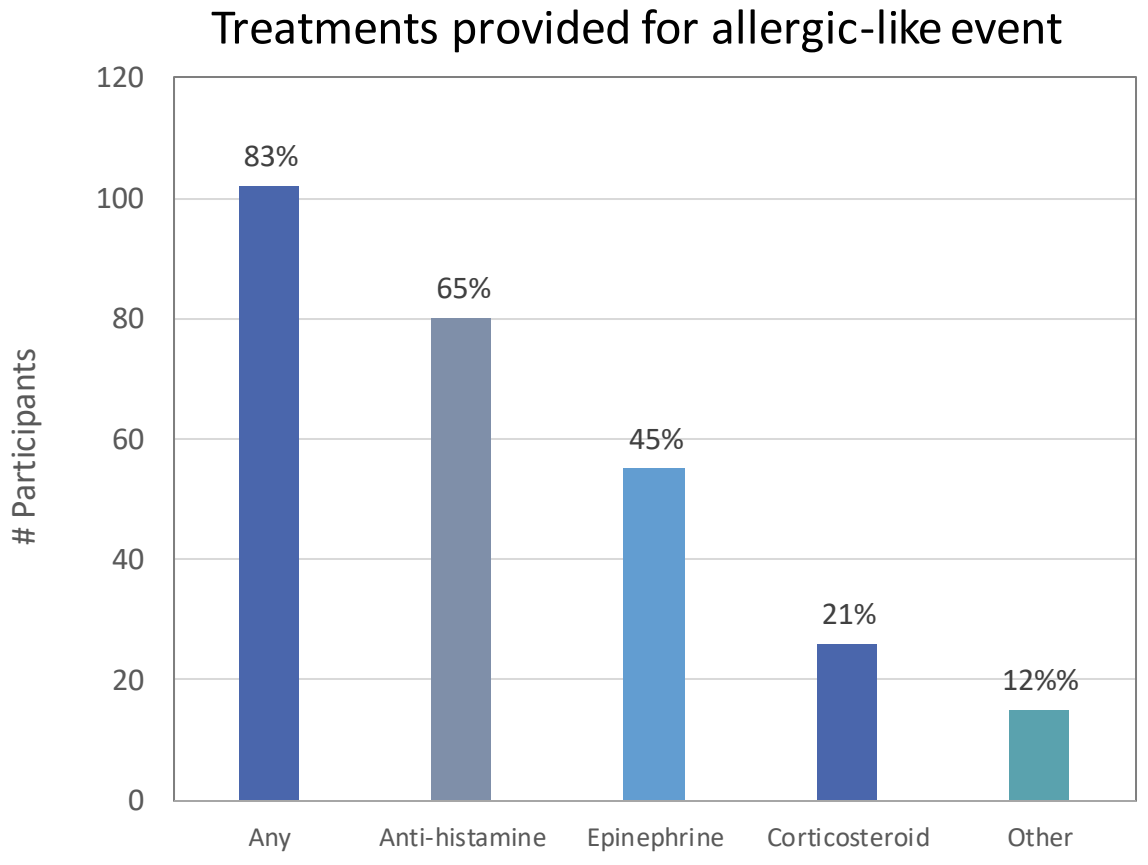
Vaccination characteristics





Impact and treatment for referral AEFI





Median onset time: 15 mins (range: 1 min to 15 days; IQR: 6.5-45mins),
10 mins for anaphylaxis (range 1 min to 2 hrs; IQR: 5-15mins)

SIC Suggested Approach to Allergy Investigation

	Controls			PEG3350		Polysorbate 80	Vaccine
	Saline (negative control)	Histamine (positive control)	Methylprednisolone succinate (solu-medrol) – use as additional control if needed	Methylprednisolone acetate (Depo-medrol) – contains PEG	PEG3350 (Miralax**)	Polysorbate 80 (Refresh sterile eye drops)	Vaccine
Epicutaneous	yes	yes	40 mg/mL	40 mg/mL	1:1* (1.7 mg/mL)	1:1	1:1*
Intradermal	Yes	No	0.4 mg/mL	0.4 mg/Ml		1:10	1:100
Intradermal	Yes		4 mg/mL	4 mg/mL			1:10

Table adapted from Banerji, A., Wickner, P.G., Saff, R., et al., mRNA Vaccines to Prevent COVID-19 Disease and Reported Allergic Reactions: Current Evidence and Suggested Approach. J Allergy Clin Immunol Pract, 2021 Apr;9(4):1423-1437. doi: 10.1016/j.jaip.2020.12.047.

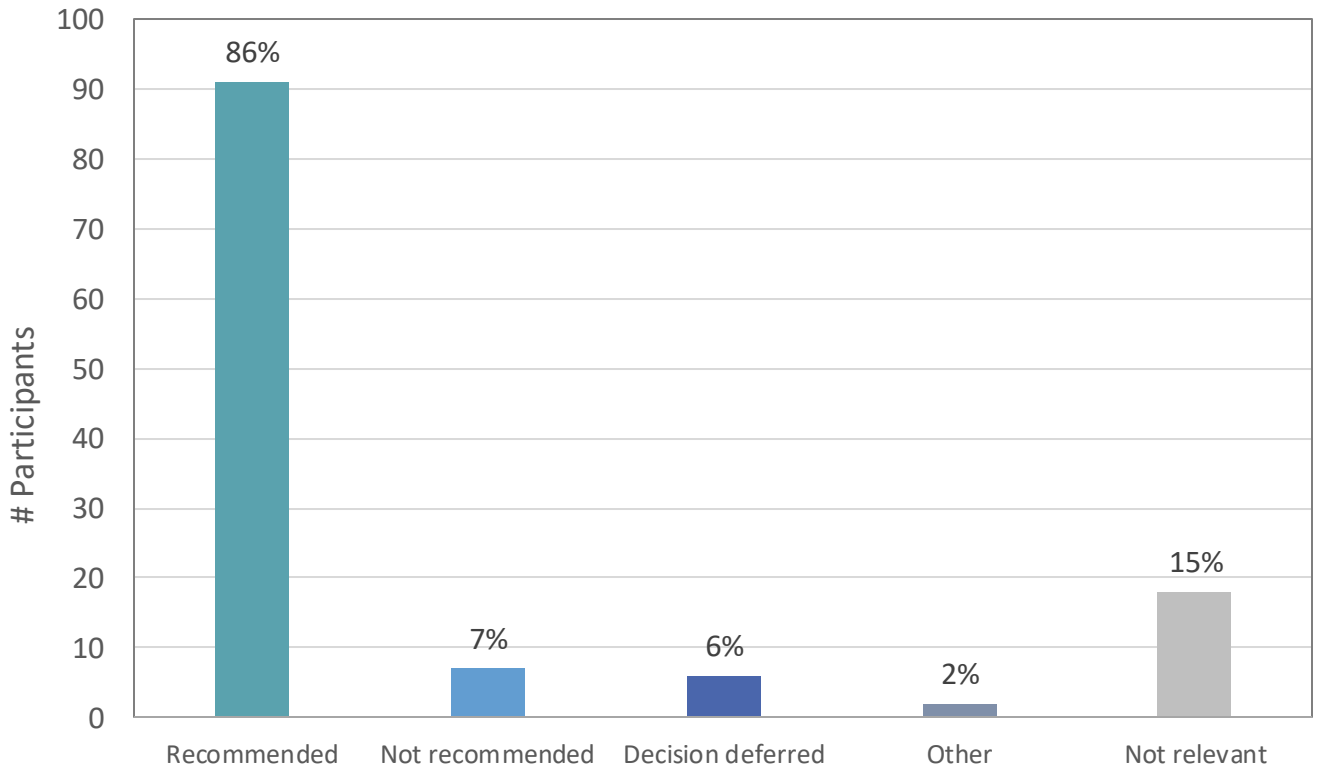
Summary: Allergy skin testing outcomes

7/42 (17%) tested participants were positive for ≥1 allergens

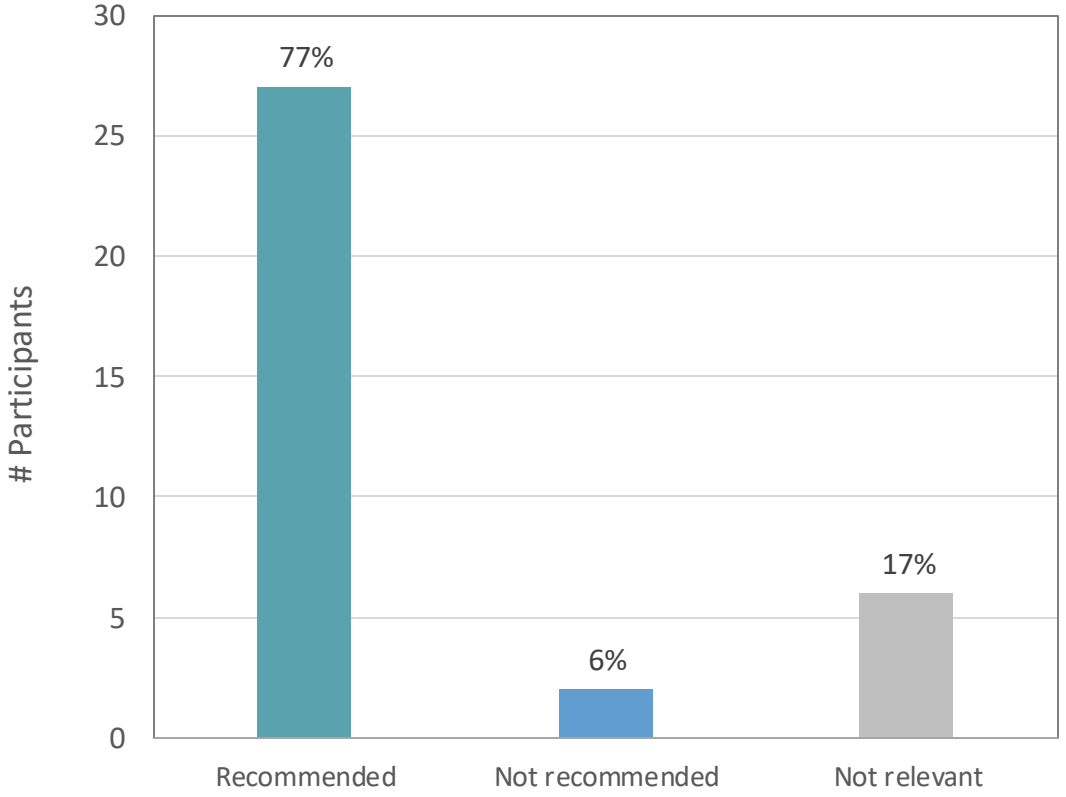
- 2 BNT162b2 vaccine only
- 1 mRNA-1273 vaccine only
- 1 PS 80 only
- 1 PEG3350 only
- 1 tree nuts only
- 1 Methylprednisolone acetate, PEG 3350, and BNT162b2

Revaccination recommendation

Any hypersensitivity event

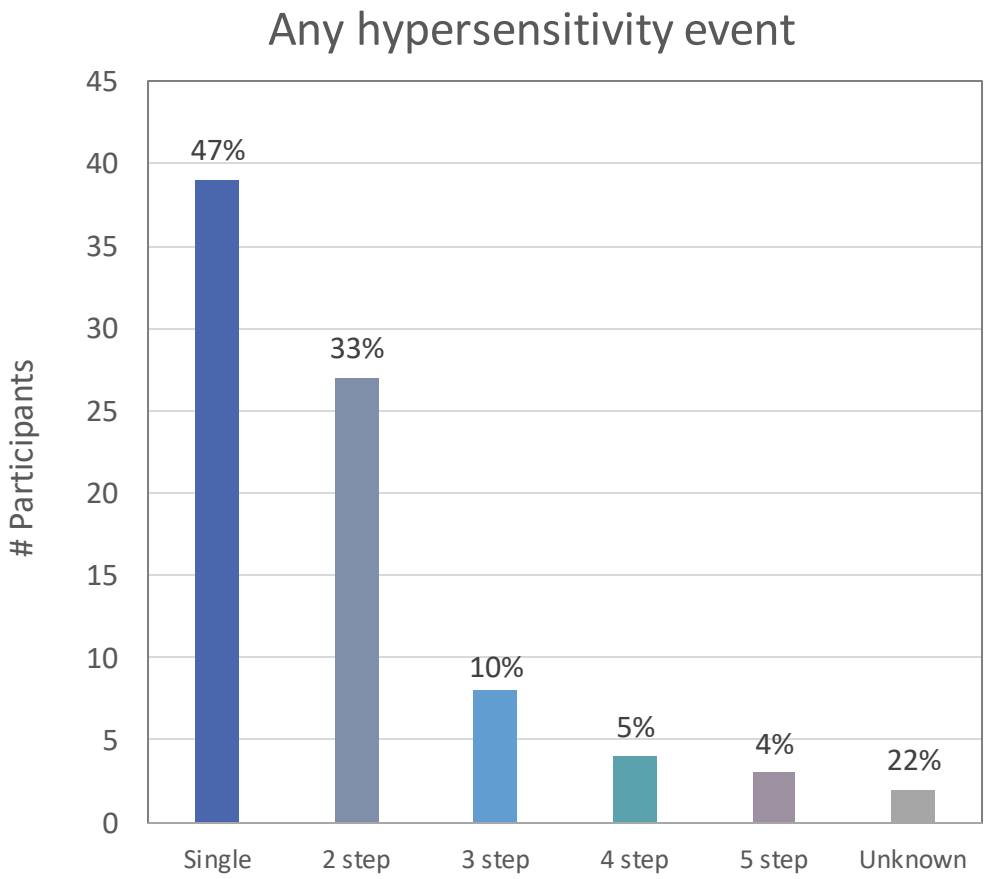


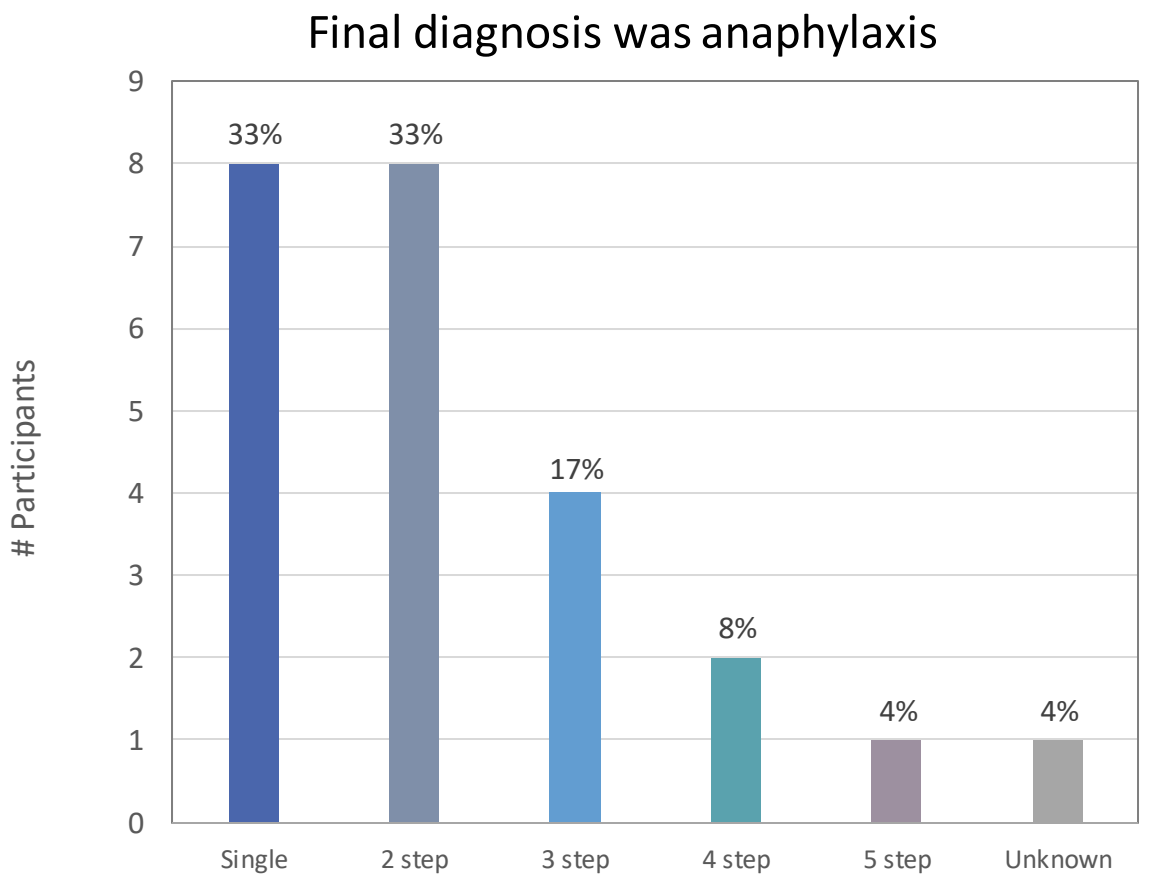
Diagnosed with anaphylaxis



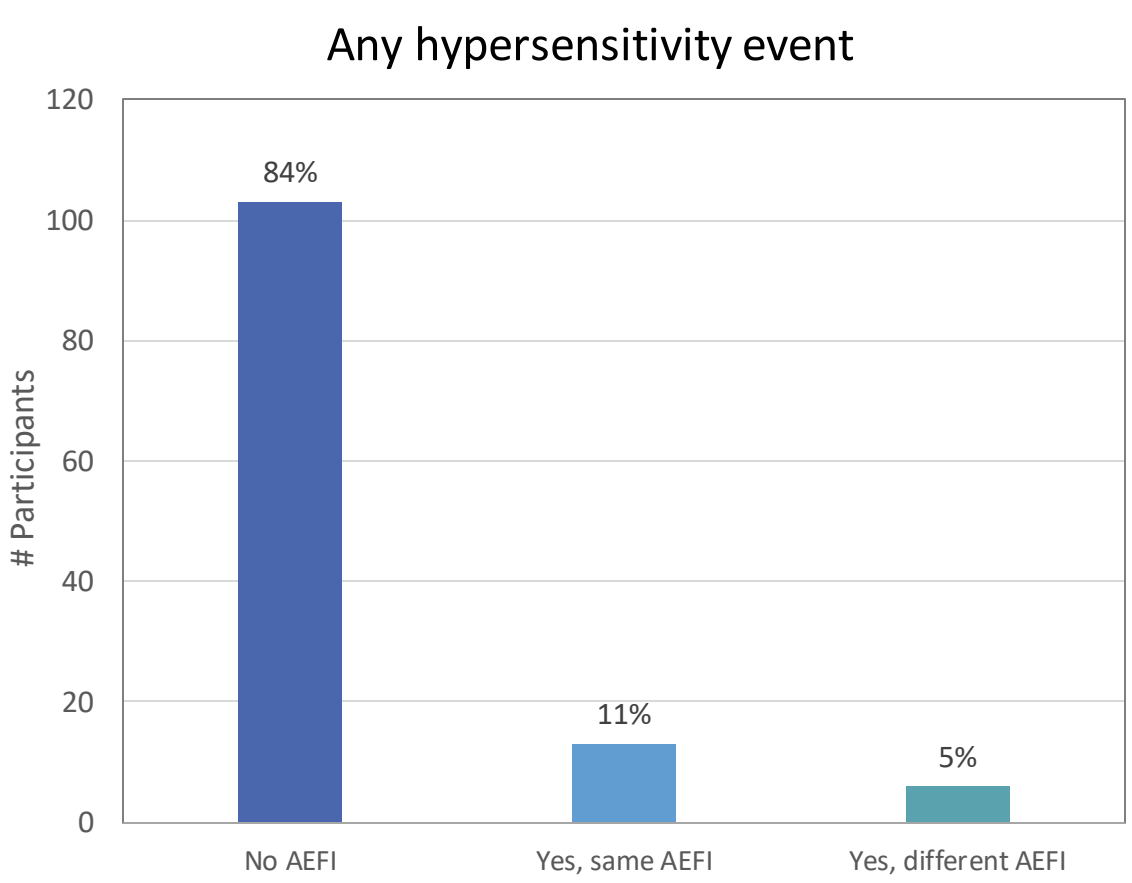
83/101 (82%) due for an additional primary series dose were revaccinated

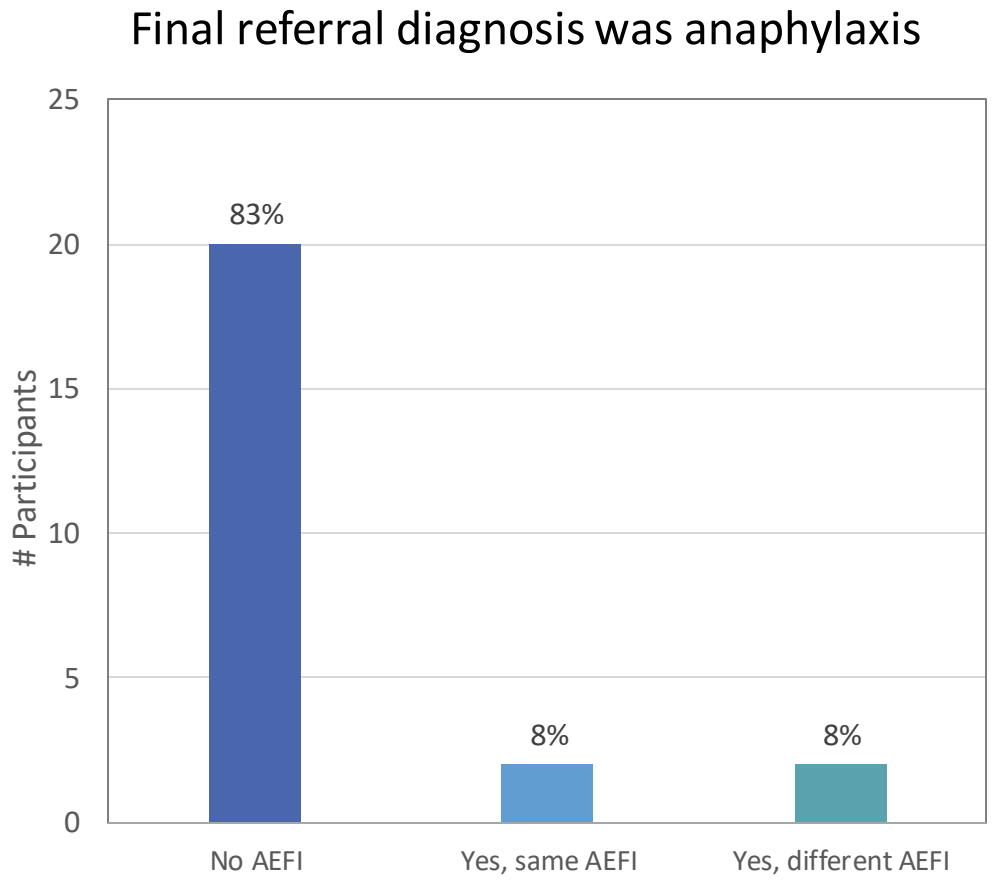
Administration of graded doses



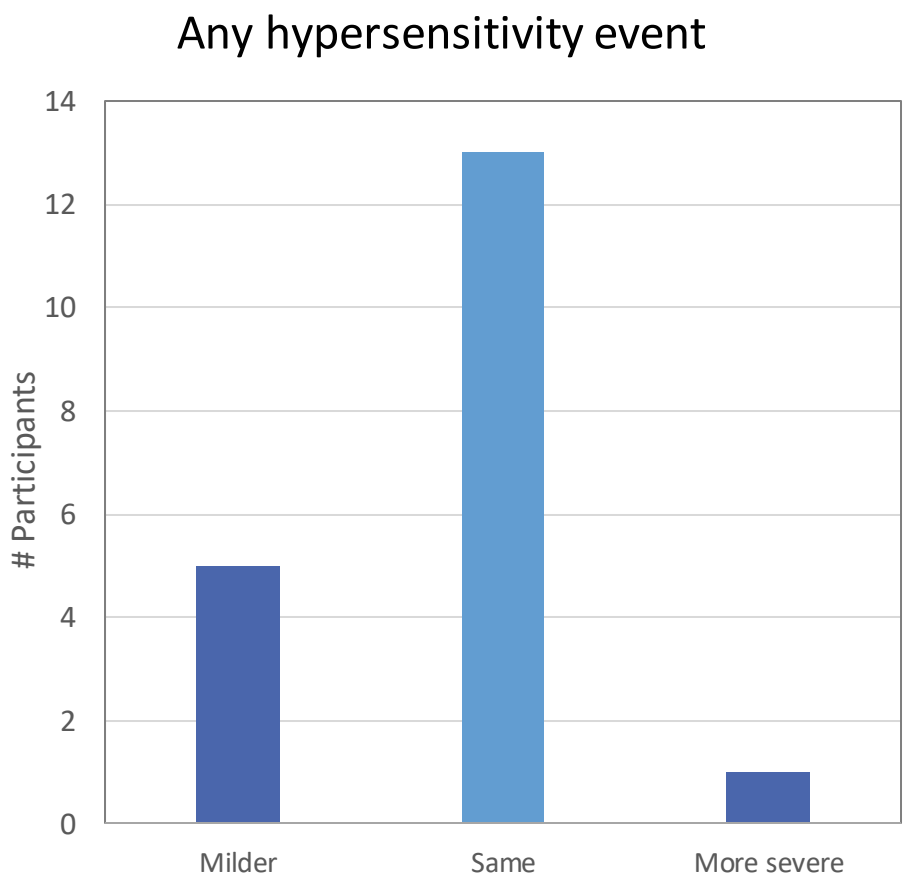


84% of patients had NO AEFI upon revaccination





Relative severity of revaccination AEFI compared to referral AEFI



Both recurrences among individuals with anaphylaxis were milder

Vaccination outcomes among people with positive allergy tests

- Revaccination was recommended for 5/6 (83%) due for additional doses
  - 5 (100%) were revaccinated
  - 5 (100%) received 5-step graded dosing (induction of drug tolerance)

- Making a recommendation was deferred for 1 participant, as reassessment was needed

- AEFIs recurred in 4/5 (80%) revaccinated participants
  - 2 experienced the same AEFI
    - 1 was more severe than referral AEFI (both were moderate impact)
    - 1 less severe (low impact)

Allergy testing and recommendations among participants with a prior history of allergy or anaphylaxis to other vaccines (N=24)

Testing

- 20/24 (83%) received allergy testing
  - 3 (15%) were positive for a COVID-19 vaccine component
    - 1 PEG, 2 Pfizer

Vaccination: All 24 received at least 1 dose of a COVID-19 vaccine

Dosing for first COVID-19 vaccine dose

- 7/24 (29%) received graded dosing (2 step)

AEFI occurrences post dose 1

- None experienced symptoms of type I hypersensitivity post-vaccination

Conclusions

- Most patients seen for allergy-like AEFIs were safely revaccinated after allergist assessment
- Patients referred for prior history of allergic reaction to vaccine component did not experience type I hypersensitivity to COVID-19 vaccines
- Few referrals received among adolescents and children 5-11 years to date
- SIC consult may support patient confidence and comfort in being (re)vaccinated against COVID-19

Lessons learned

Collaboration

- Specialists + MOHs worked to streamline referrals
- SIC investigators worked with other networks (Canada-Australia SIC, International Network of Special Immunization Services) as AEFIs occurred

Expanded research networks

- Community-based Allergy Immunology specialists
- Systematic study of individuals presenting with adverse reactions to COVID19 vaccines;
- Near doubling of participant sites to include specialists that treat adults with AEFIs

Vaccine promotion

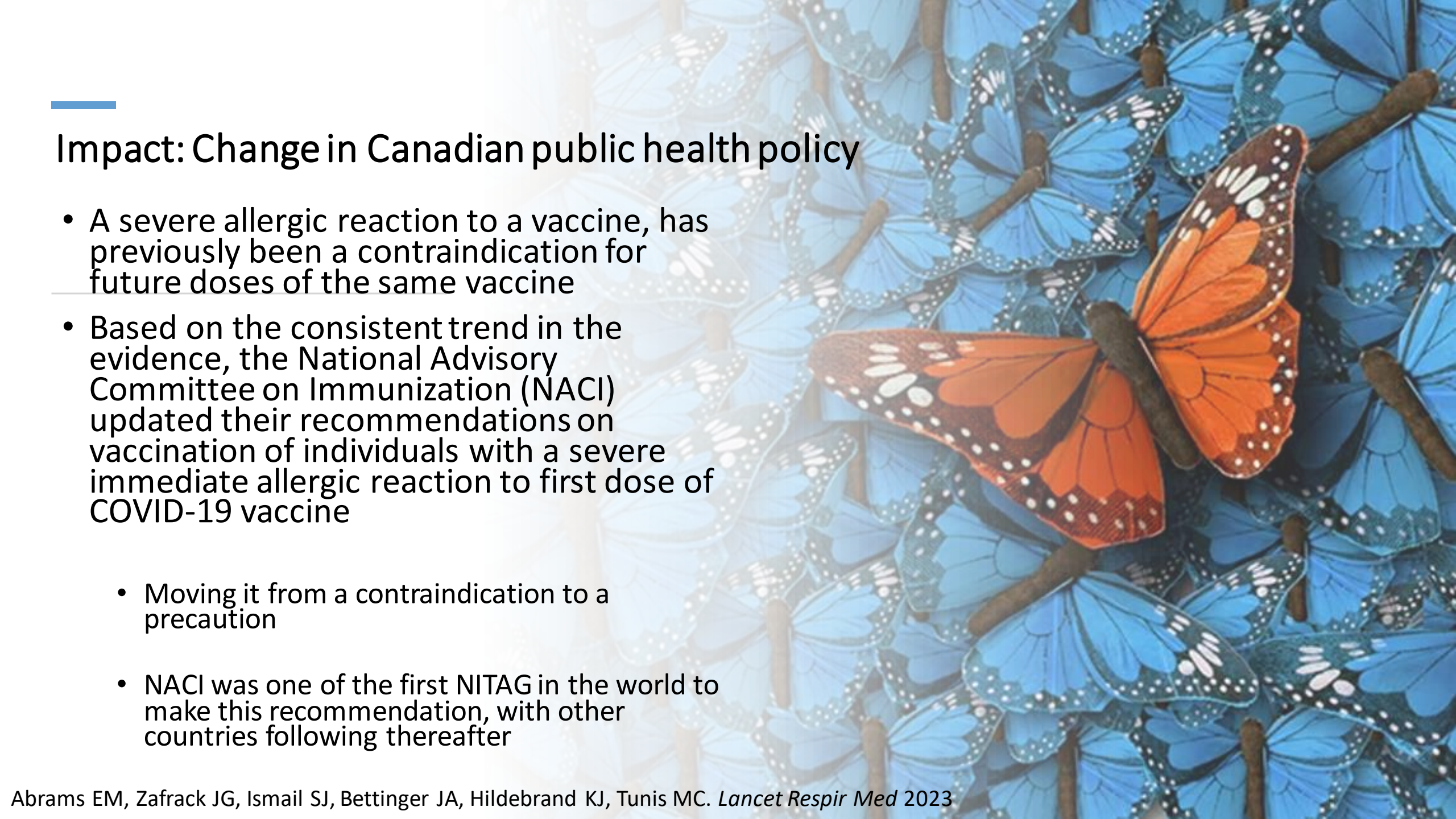
- Increase uptake of the COVID19 vaccines by offering allergy assessments +/- graded dosing of vaccine

Advocacy

- For patients with inborn errors of immunity to receive COVID19 vaccines

Impact: Change in Canadian public health policy

- A severe allergic reaction to a vaccine, has previously been a contraindication for future doses of the same vaccine
- Based on the consistent trend in the evidence, the National Advisory Committee on Immunization (NACI) updated their recommendations on vaccination of individuals with a severe immediate allergic reaction to first dose of COVID-19 vaccine
    - Moving it from a contraindication to a precaution
    - NACI was one of the first NITAG in the world to make this recommendation, with other countries following thereafter



Abrams EM, Zafrack JG, Ismail SJ, Bettinger JA, Hildebrand KJ, Tunis MC. *Lancet Respir Med* 2023

Acknowledgements

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SIC Site investigators

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