Comparison of Symptoms Associated With SARS-CoV-2 Variants Among Children in Canada

A Pediatric Emergency Research Canada Study

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Land acknowledgement

The University of Calgary, located in the heart of Southern Alberta, both acknowledges and pays tribute to the traditional territories of the peoples of Treaty 7, which include the Blackfoot Confederacy (comprised of the Siksika, the Piikani, and the Kainai First Nations), the Tsuut'ina First Nation, and the Stoney Nakoda (including Chiniki, Bearspaw, and Goodstoney First Nations). The City of Calgary is also home to the Métis Nation of Alberta Region III.

Disclaimer

Author	Disclaimer
Dr. Brett Burstein	Career grant from Fonds de Recherche Québec Santé
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Dr. Stephen Freedman	Grants from the Public Health Agency of Canada, CIHR, CITF, and Alberta Children's Hospital Foundation

Background

- Emergence of VoCs has influenced course of COVID-19 pandemic
  - Each VoC had unique impacts
  - Reflects transmissibility and clinical characteristics
- WHO has identified five variants of concern
  - Alpha (B.1.1.7)
    - Detected in the United Kingdom in the fall of 2020
  - Delta (B.1.617.2)
    - Designated a VoC in May 2021
    - Became dominant strain worldwide in the summer/fall 2021
    - More likely to lead to severe outcomes
  - Omicron (B.1.1.529)
    - Identified as a VoC in November 2021
    - Led to largest pandemic wave at end of 2021
    - Notable for its high transmissibility

VoC Features

- As SARS-CoV-2 has evolved, so have symptoms and disease severity
- Omicron
  - Propensity to infect upper airways
  - Replicates faster in bronchus than other VoC, slower in lung parenchyma
  - Adults – symptoms differ from Delta variant and mortality is lower
  - Children – associated with croup and upper airway disease
- No reports have compared symptom prevalence from original-type strain to Omicron
- Little is known about disease severity in children

Objectives

To quantify and compare symptoms, emergency department (ED) chest-x-rays, treatments, and disposition across dominant SARS-CoV-2 variants in a prospective ED-based cohort study in Canada.

Study Design

- Prospective observational cohort study
- Recruited children tested for acute SARS-CoV-2 infection
- Presented for care at one of 14 PERC EDs
- August 4, 2020 – February 22, 2022

Eligibility

- Inclusion
  - <18 years old
  - Positive SARS-CoV-2 nucleic acid test
    - Specimen collected from nasopharynx, nares, or throat
    - SARS-CoV-2 testing/laboratory methodologies based on local criteria
  - Provided informed consent/assent as appropriate
- Exclusion
  - Diagnosed with Kawasaki Disease or the MIS-C

Primary Outcome

- Presence of a given symptom/group from illness onset until enrollment

- Symptoms groups
  - Gastrointestinal
  - Lower respiratory
  - Musculoskeletal
  - Neurologic
  - Rash/oral changes
  - Systemic
  - Upper respiratory

Secondary Outcomes

1. Presence of core COVID-19 symptoms
   - ≥1 of ageusia, anosmia, cough, or fever
2. Chest-x-ray and treatments performed/administered
3. Health care resource use
   - Hospitalization
   - ICU admission
   - Revisits within 14 days
     A. ED
     B. Any healthcare provider

VoC Classification

- VoC testing and reporting varied by institution and over time
- When a VoC or mutation linked to a VoC was identified
  - Report used for classification purposes
- When VoC testing was not performed or was inconclusive
  - Classified based on the dominant strain on test date

VoC Classification

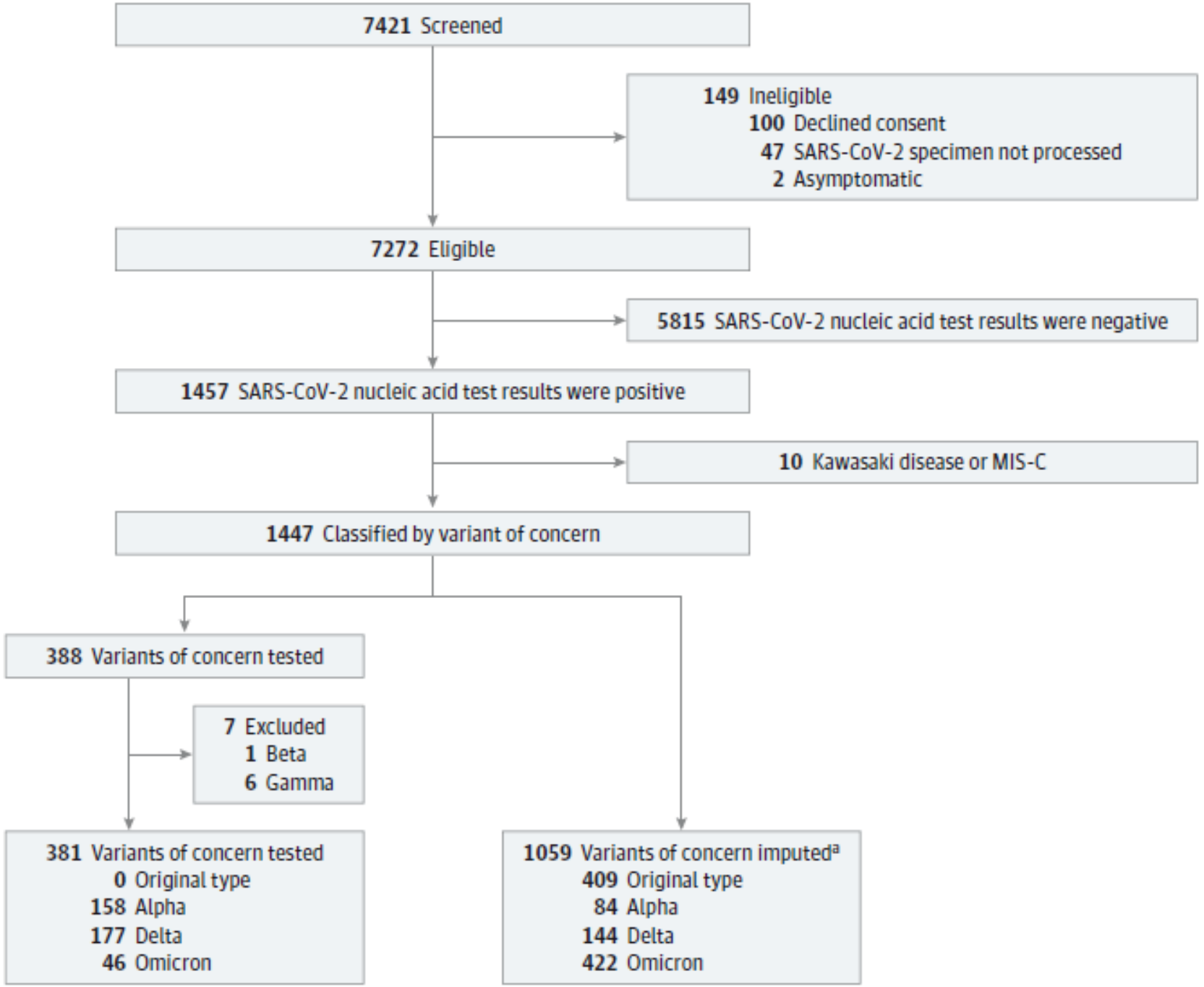
- National data identified variant comprising >50% of reported cases
  - Original-type: prior to April 18, 2021
  - Alpha: April 18, 2021 – June 26, 2021
  - Delta: June 27, 2021 – December 11, 2021
  - Omicron: December 12, 2021 – February 22, 2022

- Sensitivity analysis
  - No significant differences between imputed and tested

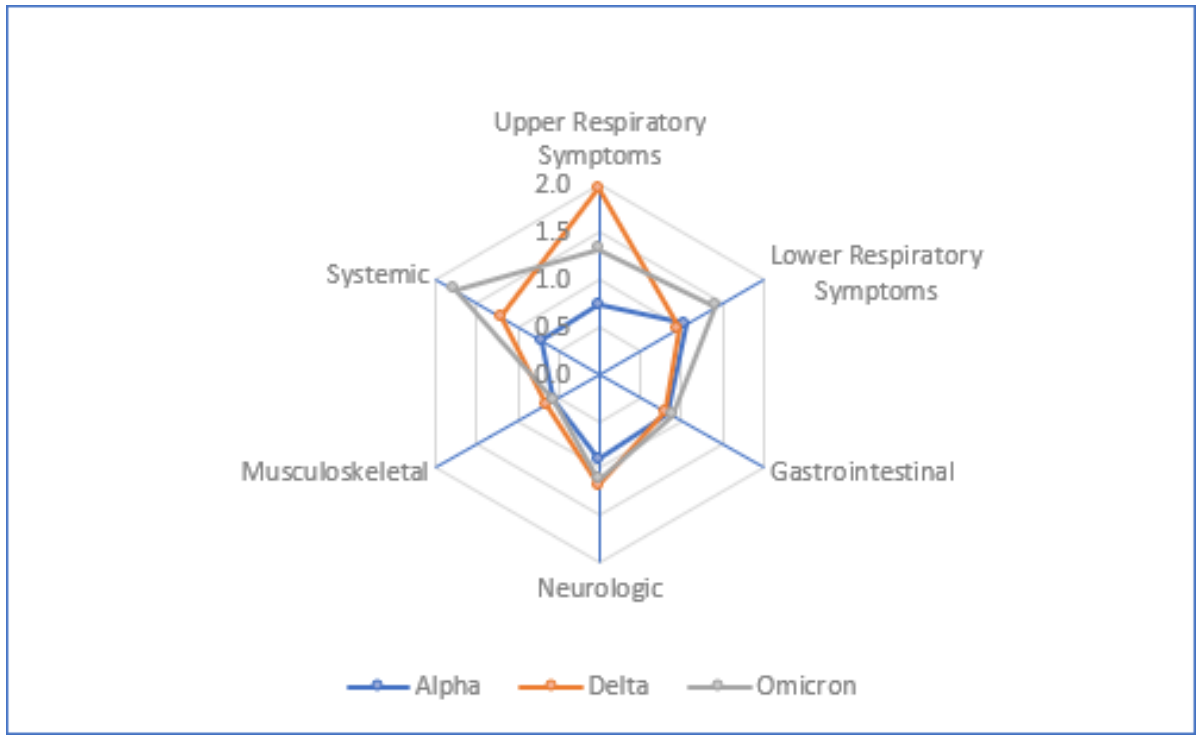
VoC Classification

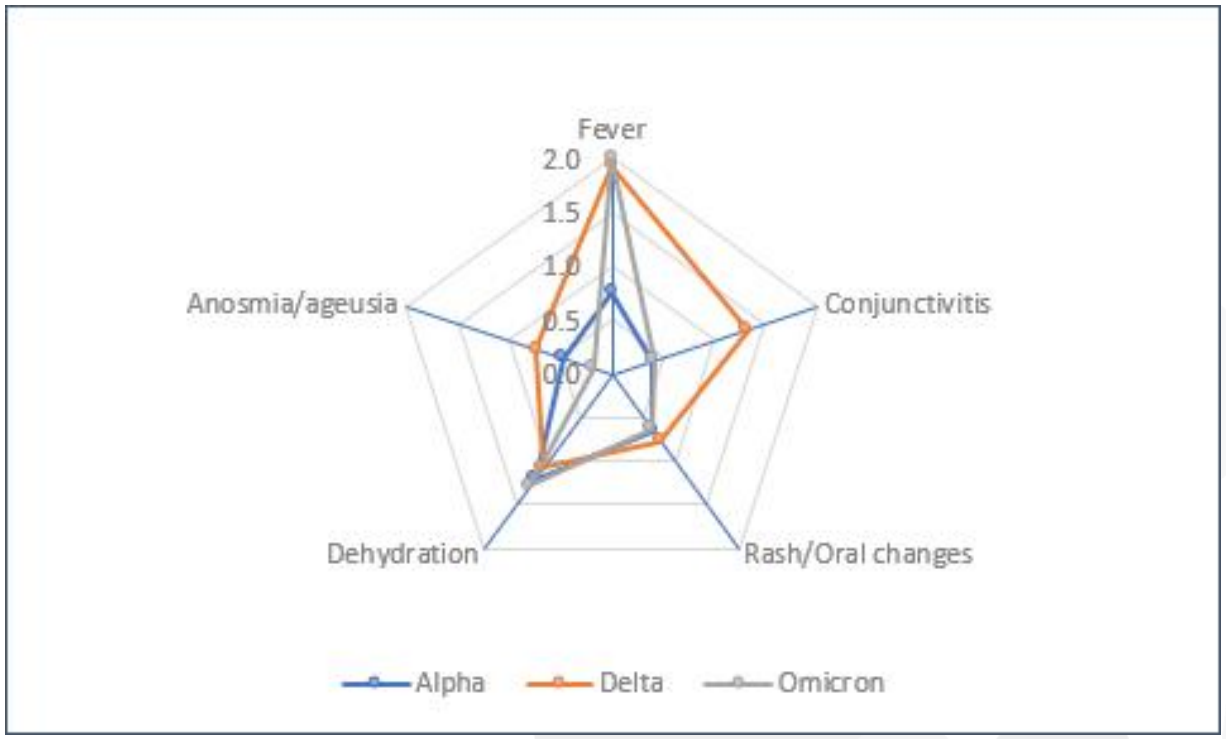
- Between June 13 and 26, 2021
  - No variant exceeded 50% of cases
  - Alpha was most prevalent during this period (43% of cases)
  - Missing variant data were classified as Alpha
- Beta, Eta and Gamma
  - Never assumed dominance
  - Peak proportions were
    - Beta: 2.6% (week of April 4, 2021)
    - Eta: 4.8% (week of March 28, 2021)
    - Gamma: 26.3% (week of April 4, 2021)
  - Small number of participants (N=7) with these variants in our cohort
    - Excluded from our analysis

Recruitment



Results – Symptom Profile

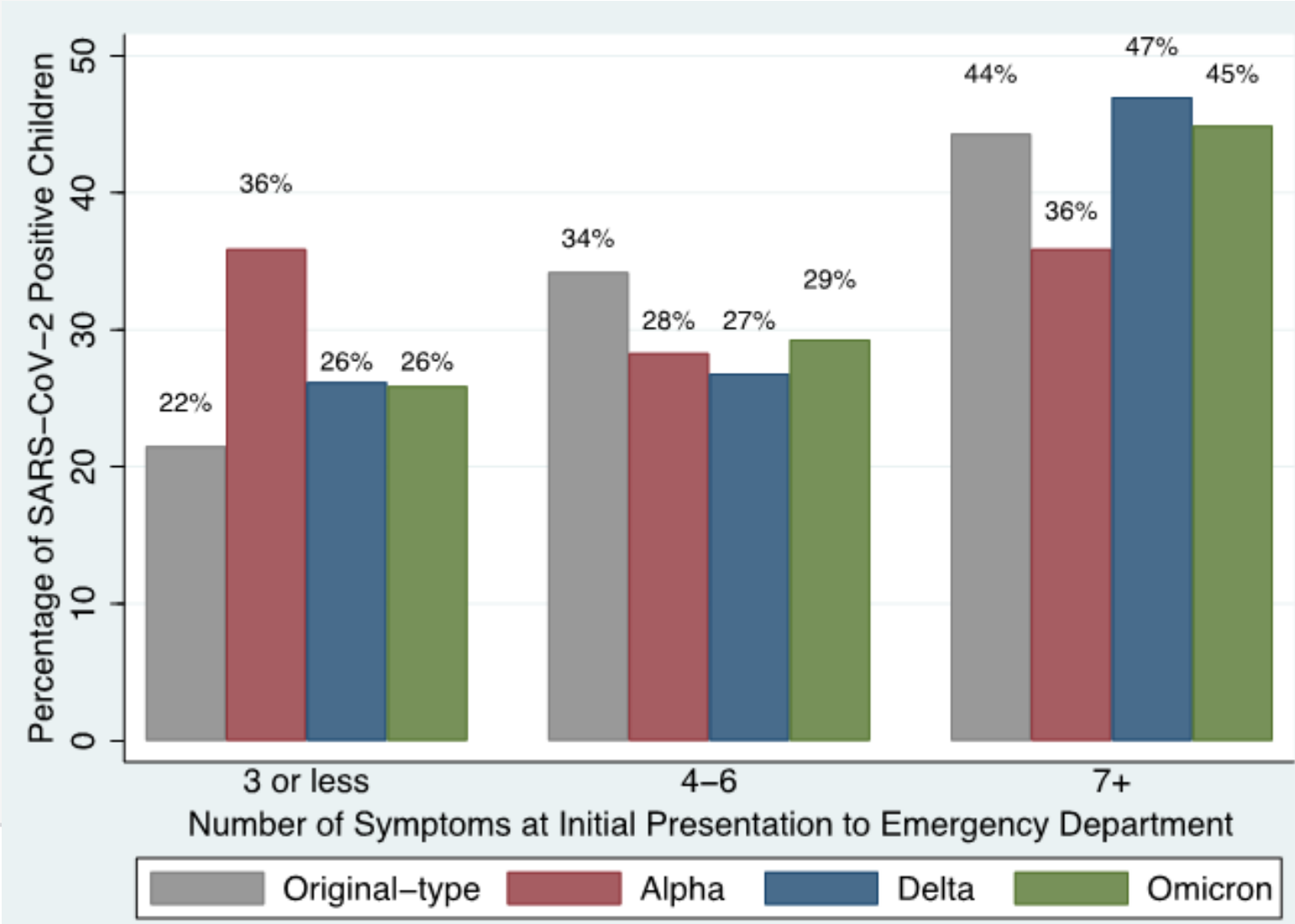




of Presenting Symptoms

Significant differences:

- <3 category
  - Alpha vs. Omicron (adjusted P=0.05)
  - Alpha vs. Original-type (adjusted P=0.001)
- ≥ 7 category.
  - Alpha vs. Delta (P=0.05)



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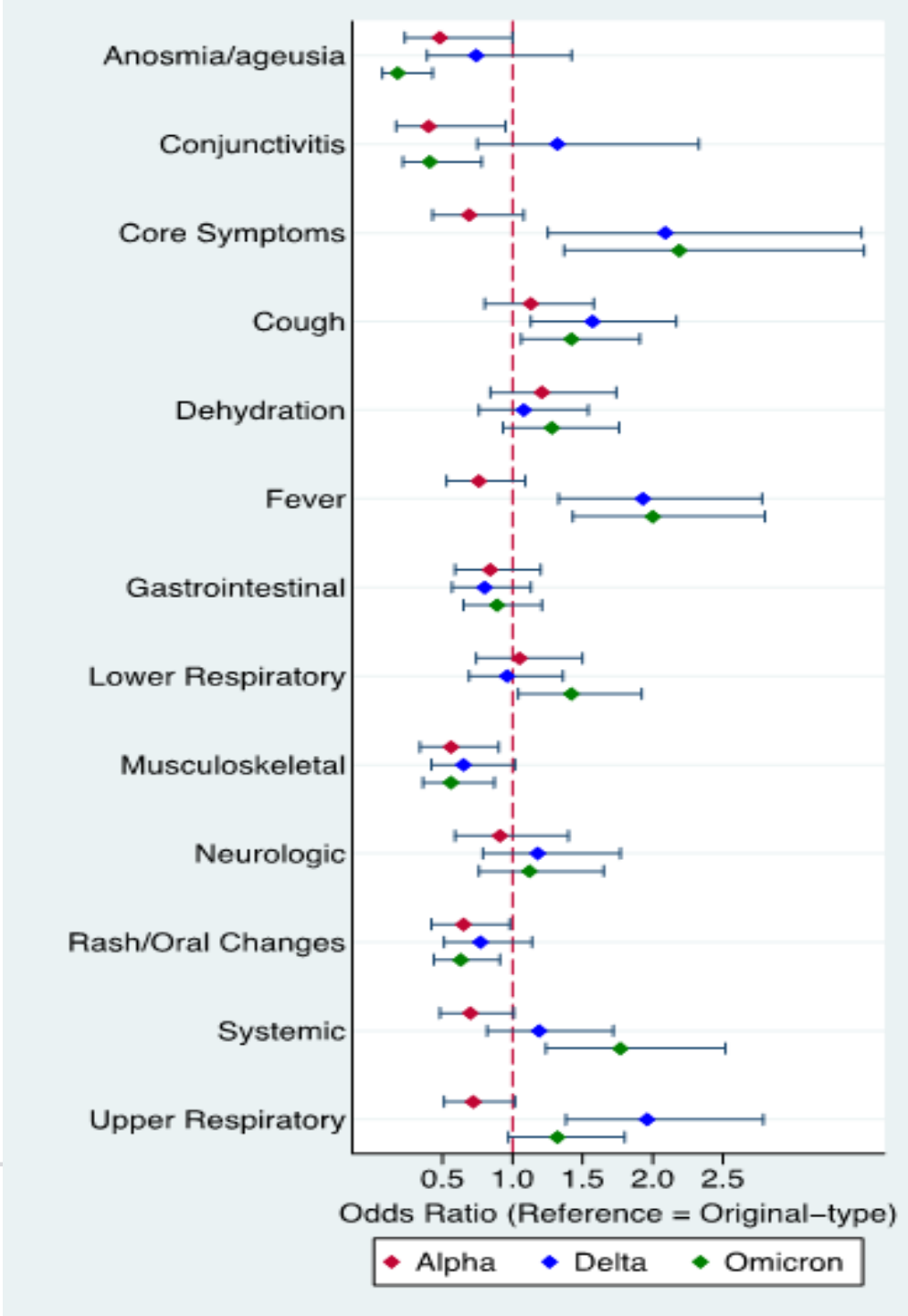
OR of Experiencing Symptom/Symptom Group

- Mixed-effect binary logistic regression
- Original-type as referent group
- Adjusted for age, sex, number of days of illness at emergency department presentation, and hospitalization status



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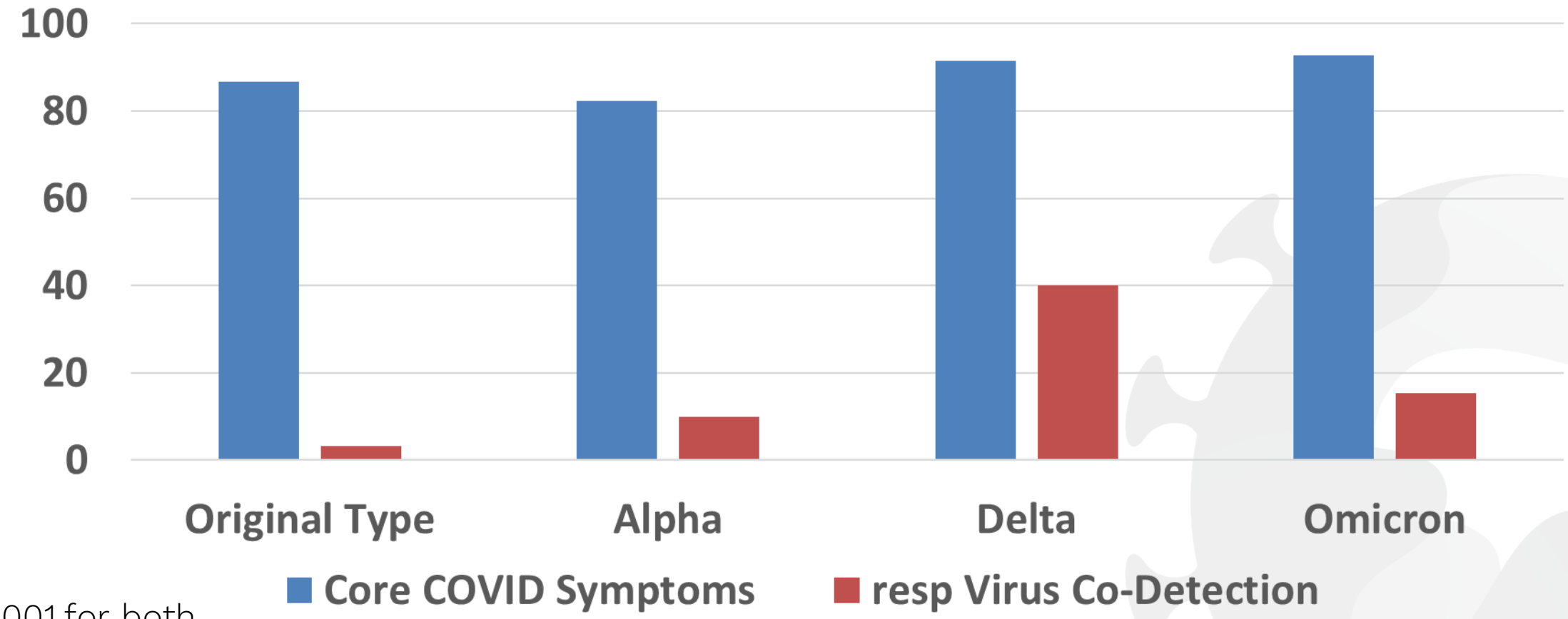
Core COVID-19 Symptoms & Co-Detections



P<0.001 for both

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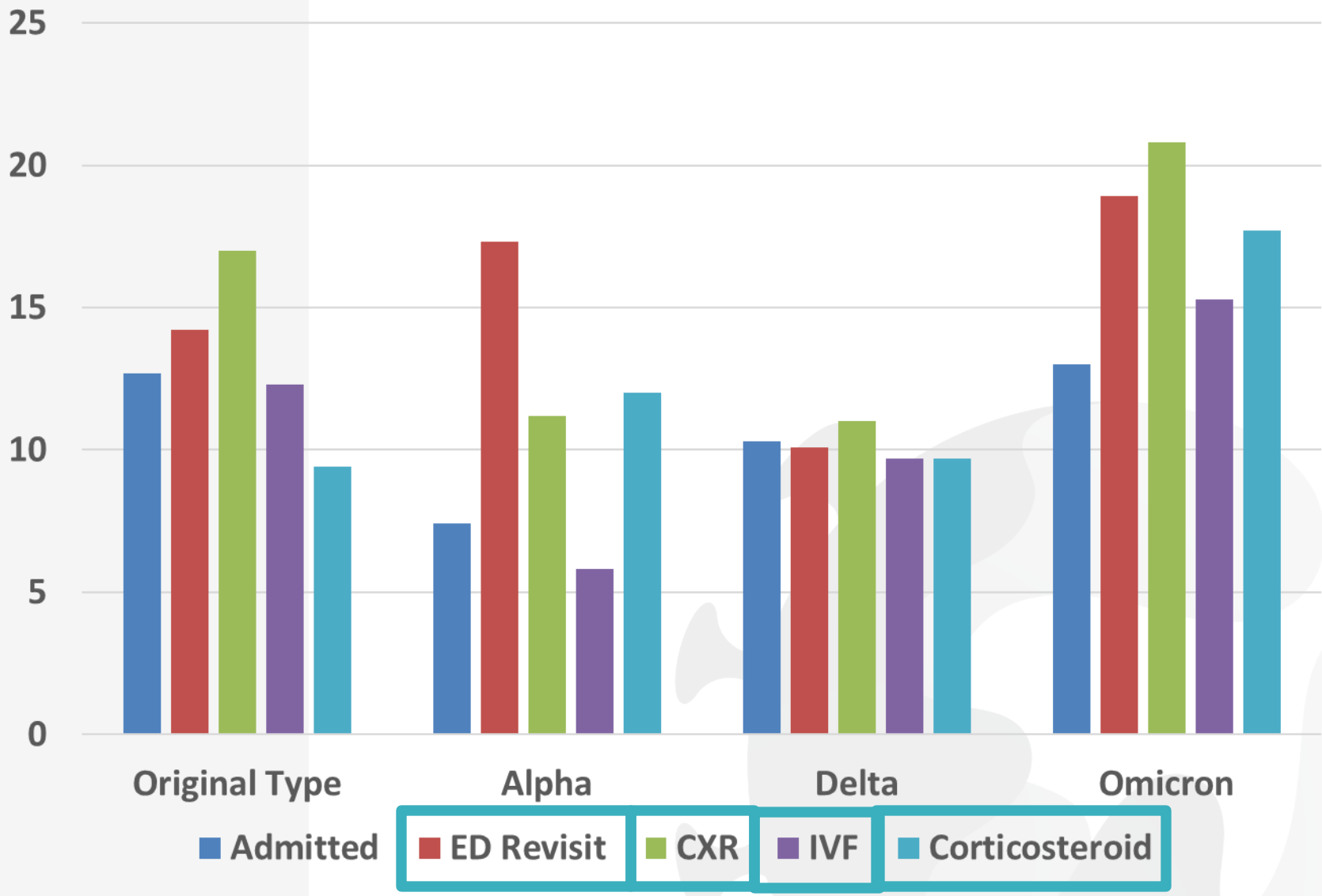
Clinical Course

Outcome	P Value
Admit	0.23
ED Revisit	0.04
CXR	0.004
IVF	0.01
Steroids	<0.001



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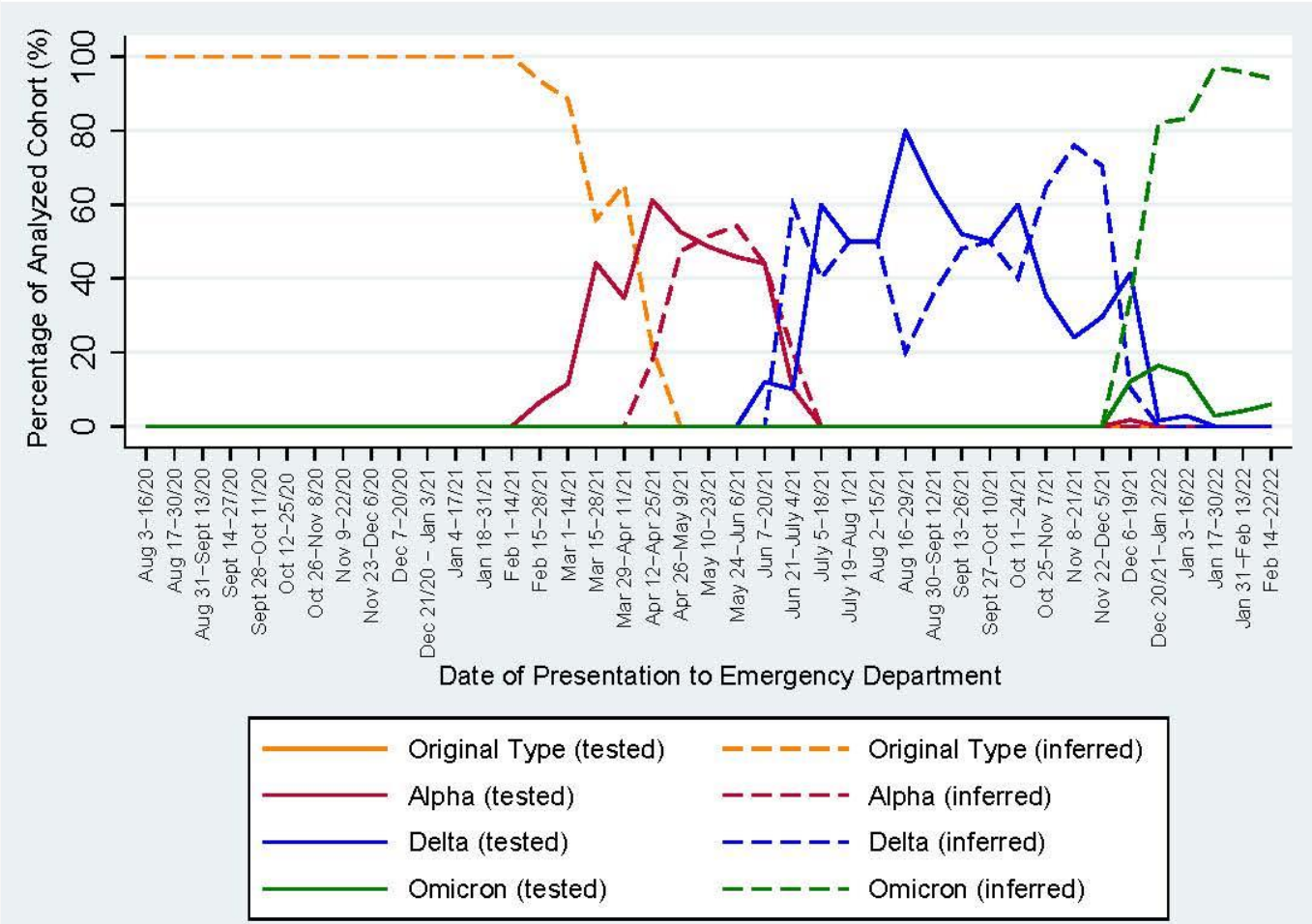
Limitations

- Only 1/3rd had VoC testing Performed
- Proportion imputed varied between strains



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Limitations

- Selection bias – kids with classic symptoms more likely tested
- Symptoms were self-reported
- Viral co-infection could influence symptoms reported
- Variants not circulating simultaneously
  - Cannot account for variation in natural and vaccine-induced immunity

Conclusions

- Omicron-infected children
  - More likely to present with fever, lower respiratory symptoms, and systemic manifestations
- Need to remain vigilant to evolving clinical presentations
  - Testing patients when clinically indicated
- Although presenting symptoms have changed as virus has evolved, unlike in adults, proportions of children experiencing undesirable outcomes has remained stable

Thank you to our amazing study team!

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- Co-Principal Investigator: Madeleine Sumner
- Site Investigators & Coordinators
- Participants and their families

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