Post-COVID Conditions Among Children 90 Days after SARS-CoV-2 Testing in Pediatric Emergency Departments: the Multinational PERN-COVID-19 Study

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WHO Webinar on Post-COVID-19 Condition in Children

Disclosures and Funding

Disclosures: Stephen Freedman has **no** financial relationships to disclose or Conflicts of Interest (COIs) to resolve.

Off-label: Stephen Freedman has documented this presentation ***will not*** involve discussion of unapproved or off-label, experimental or investigational use of a drug or device.

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Post-COVID-19 Condition (PCC)

- Definition
  - Persistent, new or returning symptoms or health problems 3 months from onset of COVID-19 with symptoms lasting ≥ 2 months
- Frequency in children is variable and unclear
  - Studies to date have limitation precluding accurate estimate
- Accurate estimate needed to inform:
  - Public health policies
  - Individual decisions (e.g. vaccination, masking)
  - Care of high-risk children

PERN-COVID-19 Prospective Cohort

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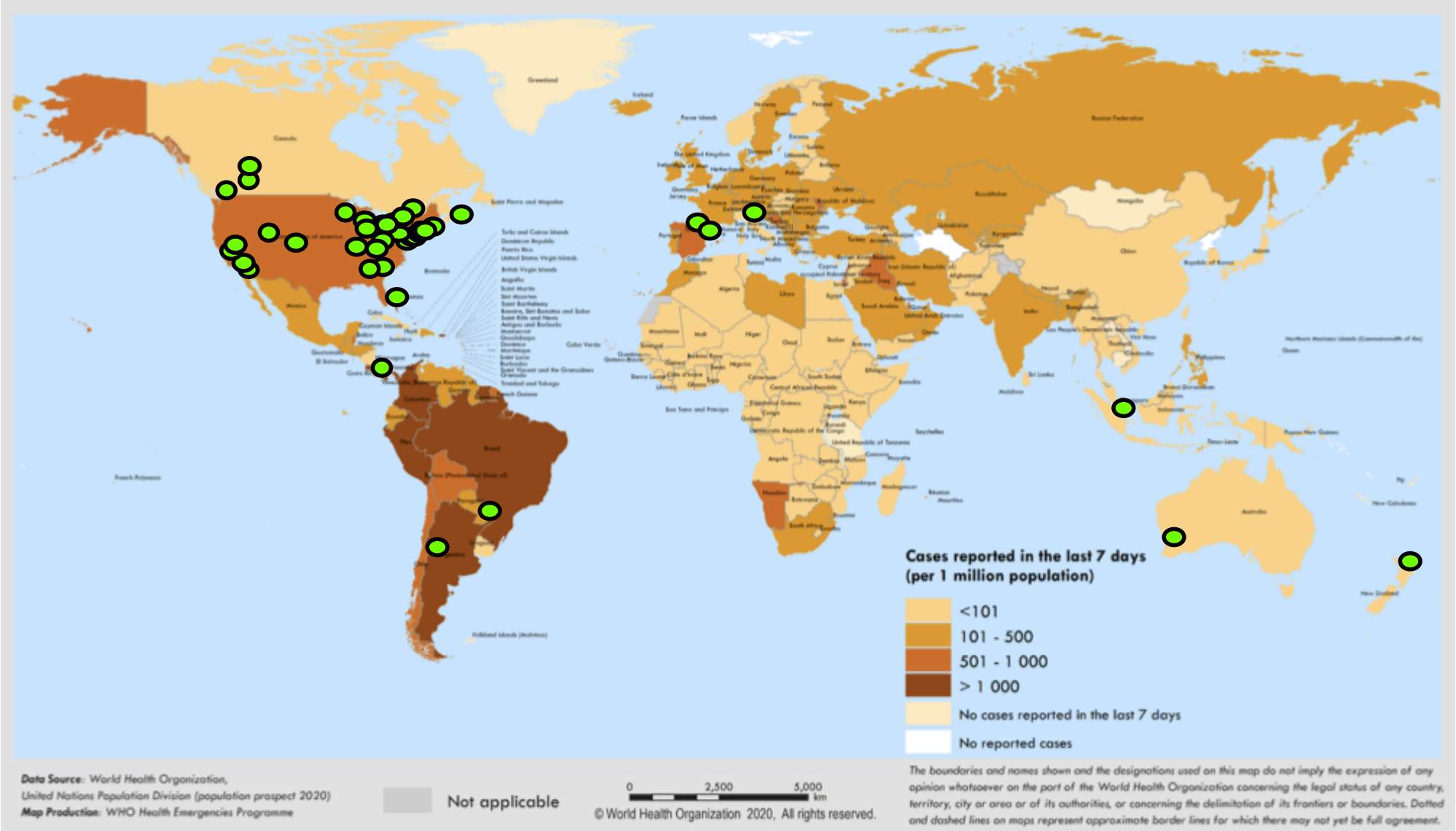
- Pediatric Emergency Research Network
  - Association of 8 pediatric emergency research networks
- PERN-COVID-19 Prospective Cohort Study
  - March 2020 – January 2021
  - 39 emergency departments (ED)
  - 8 countries
  - Follow-up of children tested for SARS-CoV-2 infection
    - Both test-positive & -negative children



Funk AL et al. *BMJ Open* 2021. 2021 Jan 1;11(1):e042121

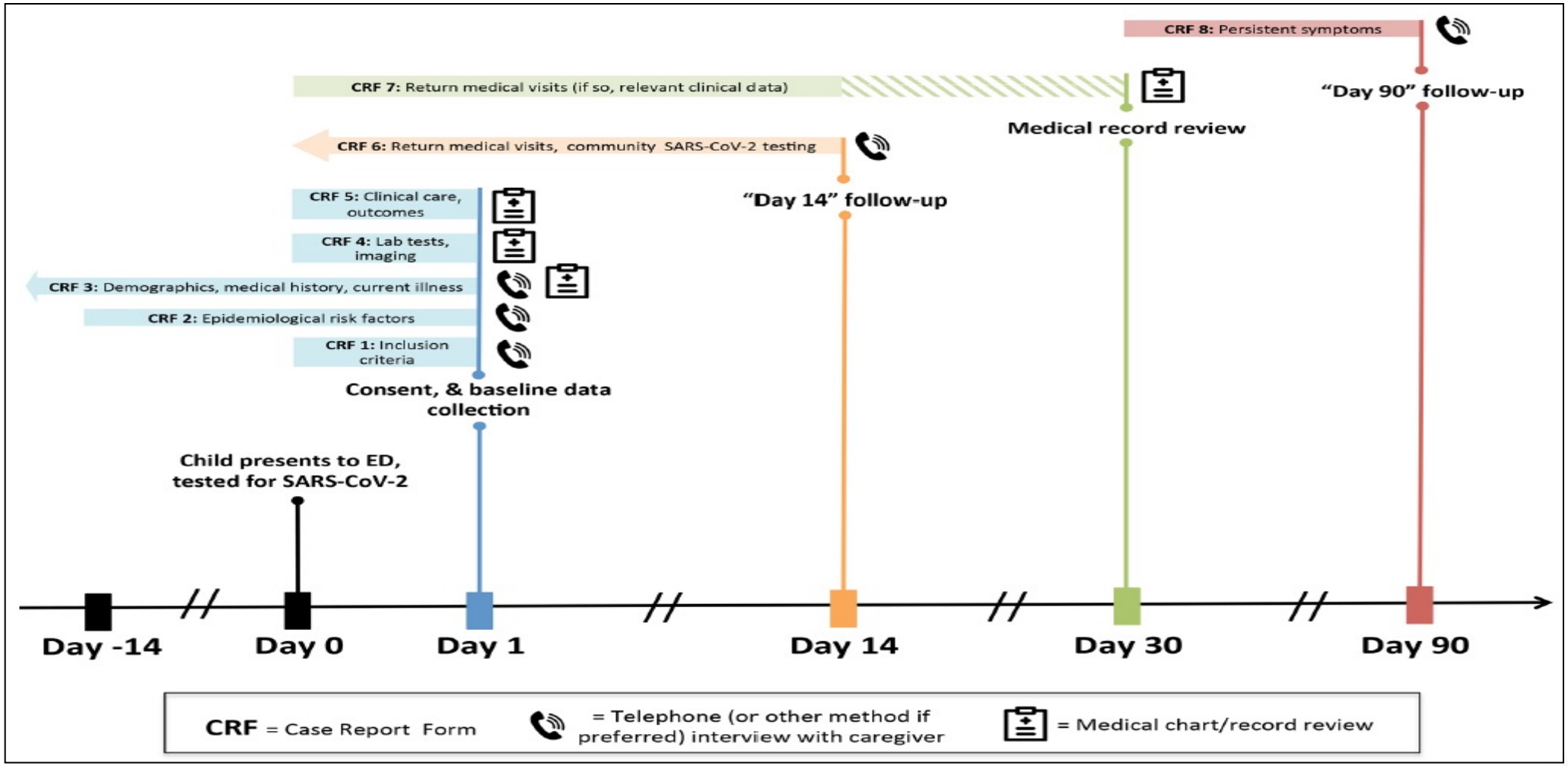
Objectives

- To determine the proportion of children with PCCs 90 days following SARS-CoV-2 testing
- To identify risk factors for PCCs among SARS-CoV-2 positive children
- To compare the prevalence of PCCs between SARS-CoV-2 positive and negative children

Participants

- < 18 years old
- Tested for SARS-CoV-2 in a participating ED
  - Due to symptoms or epidemiological risk factors
- Enrollment
  - Initially was consecutive based on timing of testing
    - Maximum of 5/site/day
    - Led to over-enrollment of test-negative participants
  - Modified in September 2020
    - Enrolled as many test-positive children as possible plus 2 test-negative controls per positive enrolled

Data Collection



Definitions

- SARS-CoV-2 test categorization
  - Based on nucleic acid testing (nares, naso/oropharyngeal)
  - Included index visit and other testing performed in subsequent 14 days
- Acute symptoms
  - Any symptoms between symptom onset and index ED visit
- Hospitalization and illness severity
  - Classified based on events until 14 days post-index ED visit

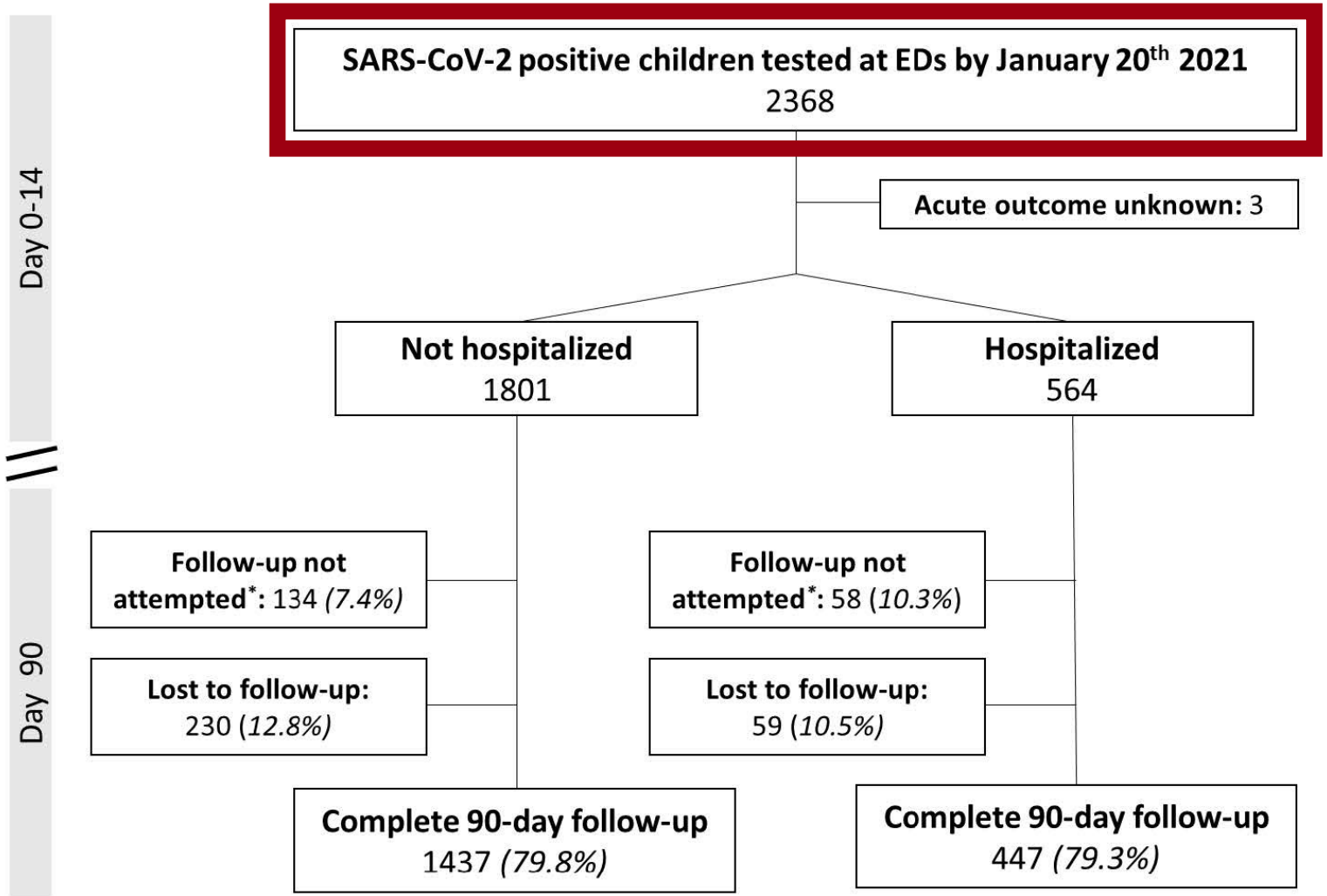
Definitions

- Post-COVID-19 Condition **Present**
  - If caregiver indicated ‘yes’ to questions about any persistent, new or returning symptoms or health problems at the 90-day interview
- Post-COVID-19 Condition **Absent**
  - Symptoms were not persistent (i.e. completely recovered)
  - Symptoms were not novel (i.e. underlying condition without exacerbation)
- Could respond via checkbox or free text
  - Free text was analyzed and grouped blinded to SARS-CoV-2 test result

Statistical Analysis

- Primary Outcome (PCC)
  - Stratified by hospitalization status
  - Combined countries with few positives
  - Multiple logistic regression to identify associated factors
    - Covariates: country, sex, age, chronic conditions, # of acute symptoms, hospitalization, calendar month
- Secondary Outcomes
  - Frequency-matched positive and negative participants
    - Based on country and calendar month
  - Multiple logistic regression as per above with inclusion of SARS-CoV-2 test result in model

Results



ED=Emergency Department *In a few sites, consistent 90-day follow-up was not feasible amid human resource constraints during the COVID-19 pandemic

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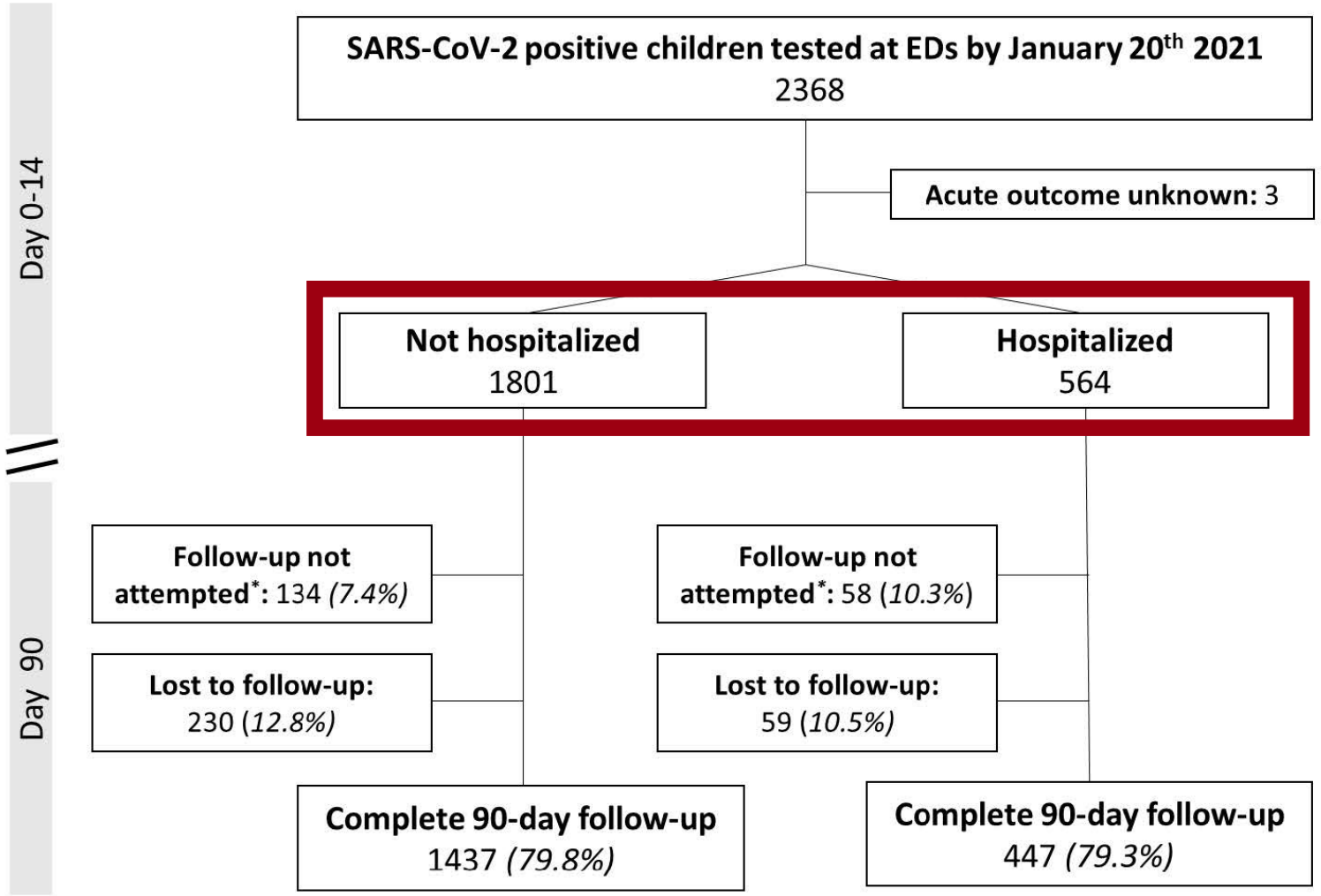

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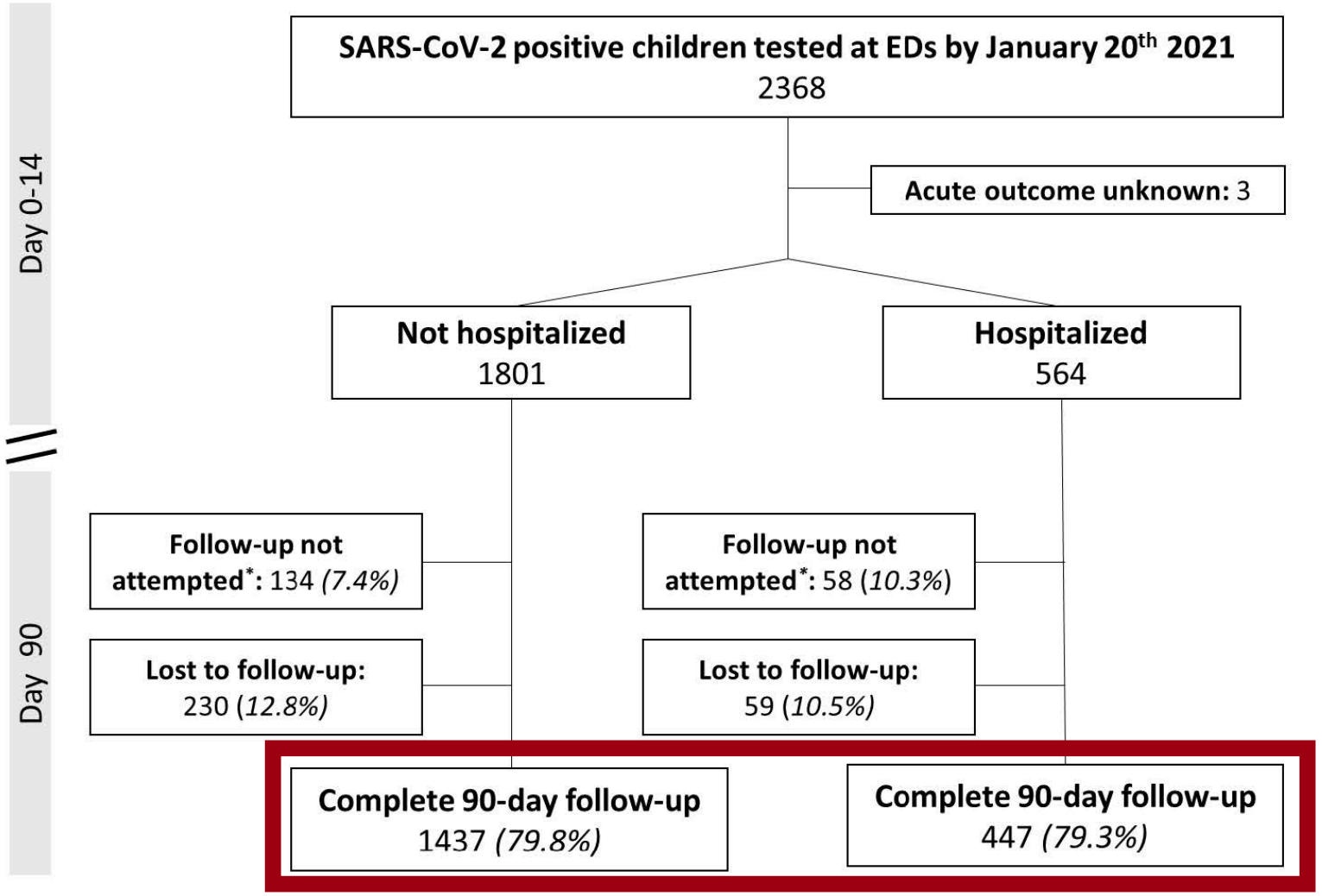

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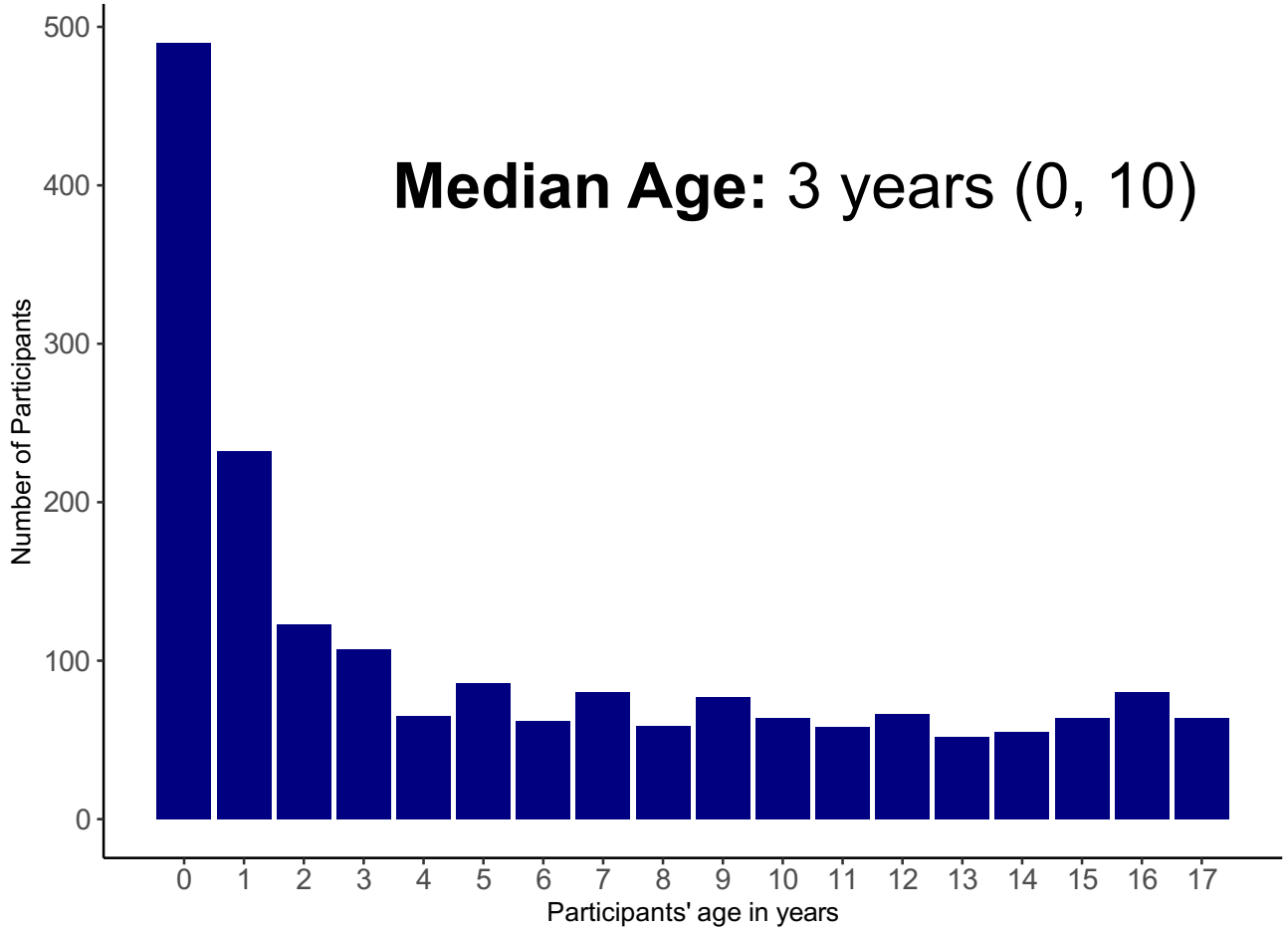
Participant Characteristics

Of 1884 children:

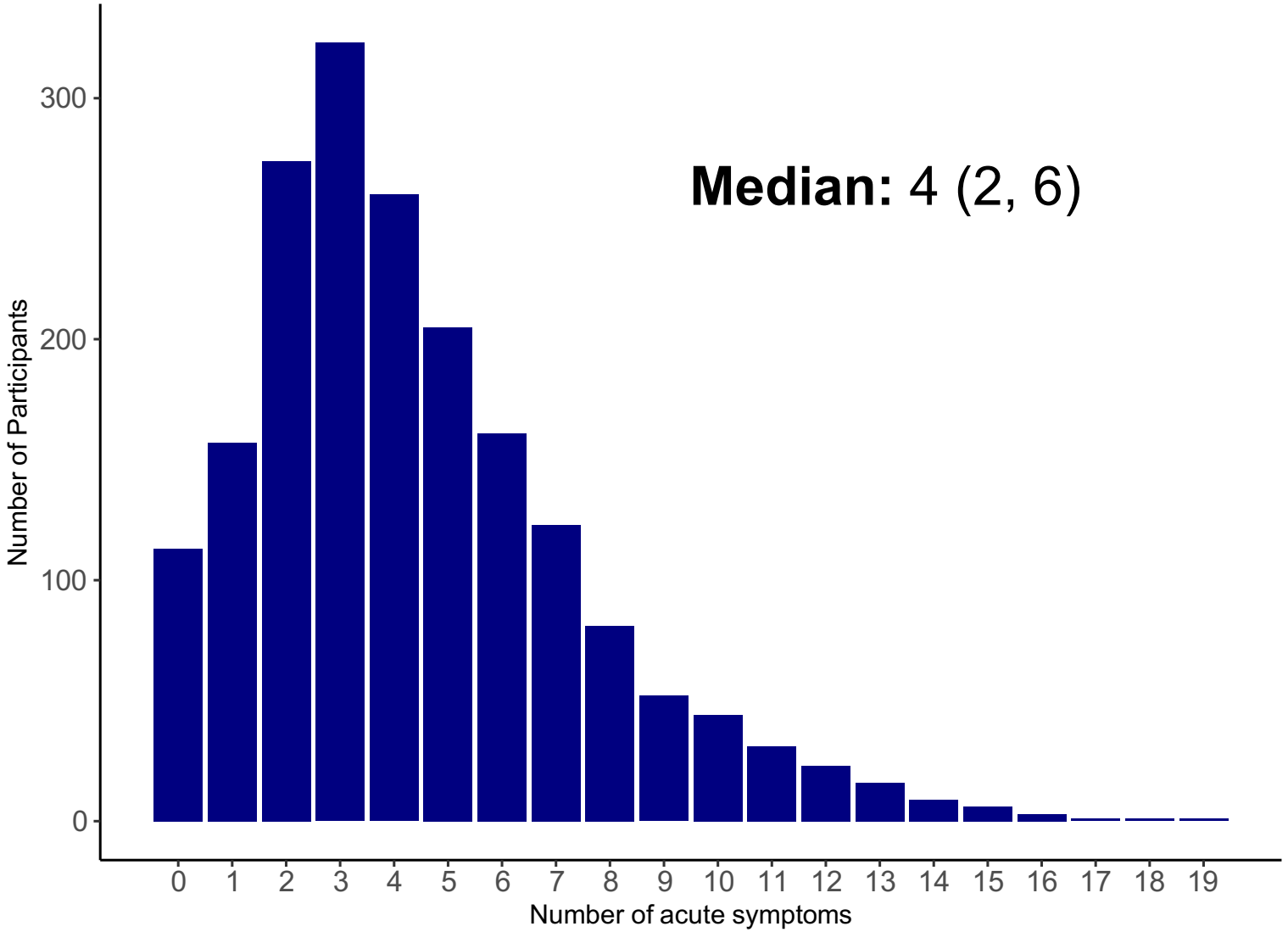
- 1771 (**94%**) symptomatic
- 994 (**53%**) male
- 270 (**14%**) chronic illness

Country / region of enrolment:

- 1204 (**64%**) United States
- 331 (**18%**) Costa Rica
- 172 (**9%**) Canada
- 177 (**9%**) Other



Results: Index ED Visit Symptoms



Median: 4 (2, 6)

SARS-CoV-2 Positive Participants

90-Day PCCs

Overall: 5.8% (95%CI: 4.8, 7.0)

Hospitalized: 9.8%

Discharged: 4.6%

Difference: 5.3% (95%CI: 2.5, 8.5)

Hospitalized – severe outcome: 18.6%

Hospitalized – no severe outcome: 8.2%

Difference: 10.4% (95%CI: 2.3, 21.3)

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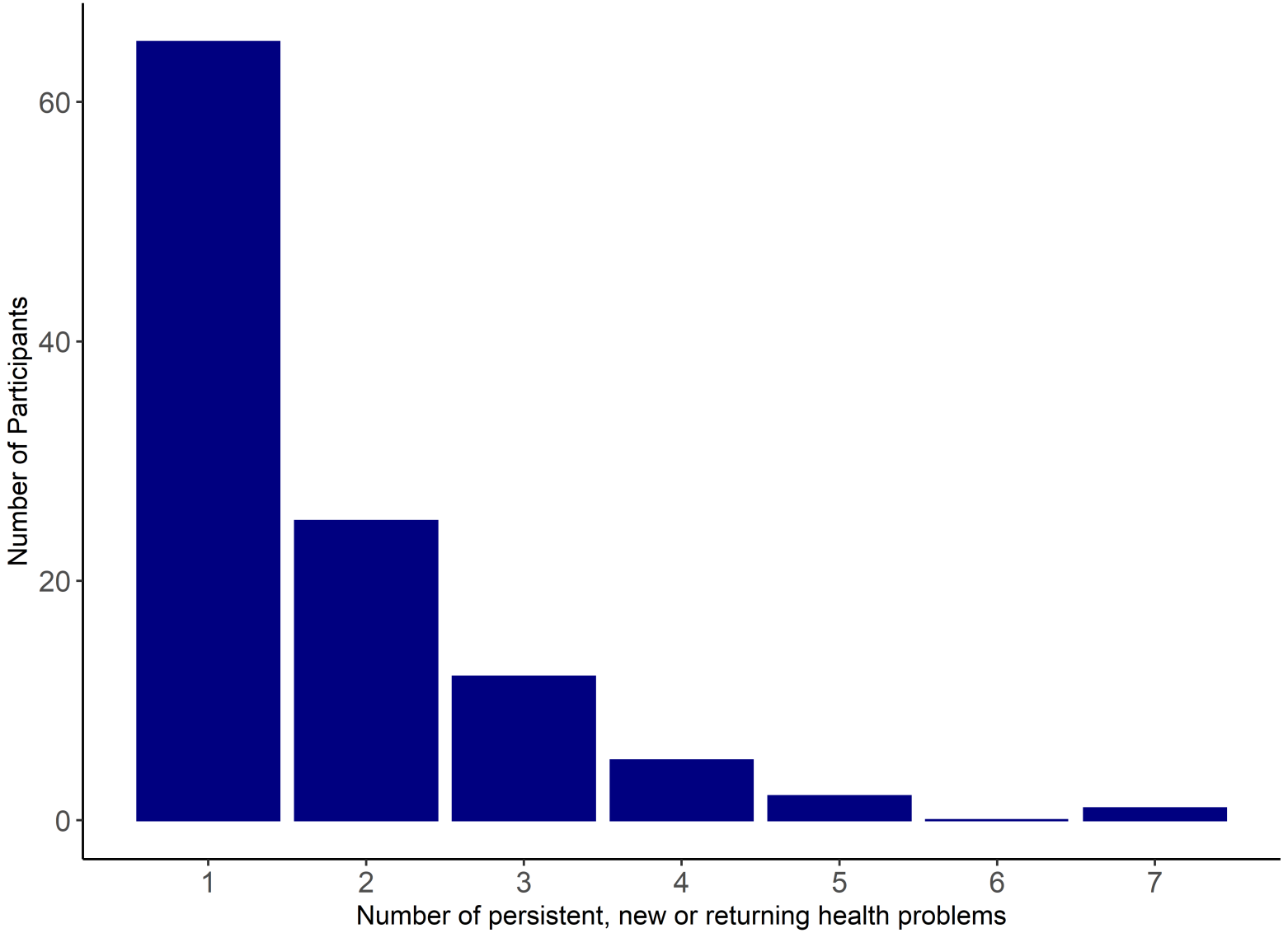
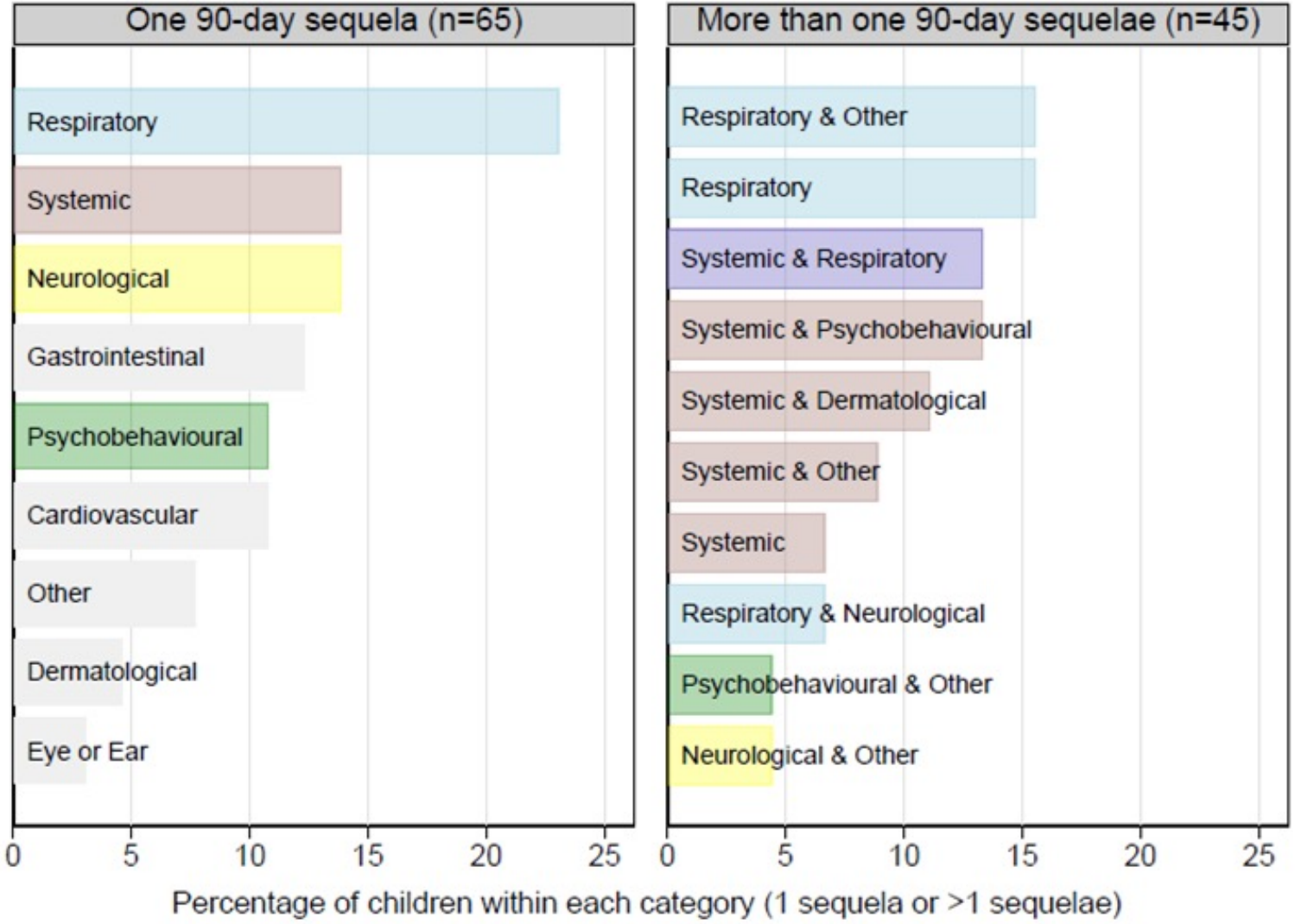
Results: # of PCC Symptoms



Results: Types of PCC Symptoms



Results: Risk Factors for PCCs

		Odds Ratio	95% CI	P-value
Female		1.39	0.92 – 2.09	0.11
Age category	< 1 year	ref		
	1– <2 years	0.88	0.36 – 2.14	0.74
	2 – <5years	0.89	0.39 – 2.02	0.78
	5 – <10 years	1.45	0.74 – 2.83	0.28
	10 – <14 years	**1.98**	**1.01 – 3.87**	**0.05**
	14 – <18 years	**2.77**	**1.50 – 5.14**	**0.001**
# of symptoms at index ED Visit	0	1.34	0.43 – 4.12	0.62
	1 – 3	ref		
	4 – 6	**2.34**	**1.27 – 4.29**	**0.006**
	≥7	**4.85**	**2.66 – 8.83**	**<0.001**
Hospitalized	No	ref		
	Yes, < 48 Hours	1.99	0.97 – 4.08	0.06
	Yes, ≥ 48 Hours	2.55	1.58 – 4.13	<0.001

Notes on multiple logistic regression model:

Also adjusted for:

Country / region of enrolment

Initial model also included:

Chronic conditions, calendar month.

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SARS-CoV-2 Pos (N=474) vs Neg (N=1626)

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- Discharged SARS-CoV-2 positive vs. negative
  - 4.2% (95%CI: 3.2, 5.5) vs. 2.7% (95%CI: 1.9, 3.7)
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- Logistic regression model predicting PCC
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Limitations

- Unmeasured/residual confounding is possible
- Knowledge of test status
- Control group contamination
- Emerging variants of concern

Conclusions

- PCCs at 90 days
  - ~10% of children hospitalized
  - ~5% of those discharged

- Risk factors for reporting PCCs
  - Number of acute symptoms
  - Hospitalization
  - Older age

- SARS-CoV-2 test positivity was associated with PCCs

Thank you!

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