

Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

eAppendix. Severe Outcomes

A priori, a severe outcome was defined by the occurrence of any of the following complications: cardiac or cardiovascular (cardiac arrest, cardiac ischemia, congestive heart failure, endocarditis, myocarditis, pericarditis, stroke), infectious (disseminated intravascular coagulation, mastoiditis, sepsis with bacteremia, septic shock, toxic shock syndrome), neurologic (encephalitis, meningitis), respiratory (acute respiratory distress syndrome, empyema, necrotizing or cryptogenic organizing pneumonia, pleural effusion or pneumothorax or pneumomediastinum requiring drainage, respiratory failure), and death. In addition, in the absence of one of the above events, performance of any of the following interventions also was deemed to represent a severe outcome: chest drainage, extracorporeal membrane oxygenation, inotropic support, positive pressure ventilation (invasive or noninvasive), and renal replacement therapy. The diagnosis of multi-system inflammatory syndrome in children (MIS-C) and Kawasaki disease were reported as assigned by the clinical care teams and were considered severe if accompanied by one of the above diagnoses or interventions.

eTable 1. Demographic and Clinical Characteristics of SARS-CoV-2-Positive Children by Follow-up Status at 90 Days. All data are n (%) unless otherwise specified.

	Complete follow-up N= 1884	Lost to follow-up N= 289	Follow-up not attempted N= 192
Region			
United States	1204 (63.9)	234 (81.0)	117 (60.9)
Costa Rica	331 (17.6)	21 (7.3)	5 (2.6)
Canada	172 (9.1)	19 (6.6)	38 (19.8)
Spain	133 (7.1)	0	1 (0.5)
Other ^a	44 (2.3)	15 (5.2)	31 (16.1)
Sex, Male	994 (52.8)	149 (51.6)	92 (47.9)
Age			
<1.0 yrs	490 (26.0)	79 (27.3)	57 (29.7)
1.0 - <2.0 yrs	232 (12.3)	32 (11.1)	22 (11.5)
2.0 - <5.0 yrs	295 (15.7)	51 (17.7)	31 (16.2)
5.0 - <10.0 yrs	364 (19.3)	49 (17.0)	34 (17.7)
10.0 - <14.0 yrs	240 (12.7)	41 (14.2)	25 (13.0)
14.0 - <18.0 yrs	263 (14.0)	37 (12.8)	23 (12.0)
Chronic underlying condition, Yes	270 (14.3)	35 (12.1)	17 (8.9)
History of asthma, Yes	260 (13.8)	42 (14.5)	18 (9.4)
Number of symptoms at ED presentation			
None	113 (6.0)	16 (5.5)	12 (6.3)
1-3	754 (40.0)	86 (29.8)	56 (29.2)
4-6	626 (33.2)	100 (34.6)	67 (34.9)
7 or more	391 (20.8)	87 (30.1)	56 (29.2)
Types of symptoms^b			
Any systemic symptom	1478 (78.5)	239 (82.7)	163 (84.9)
Any respiratory symptom	1328 (70.5)	208 (72.0)	137 (71.4)
Any gastrointestinal symptom	749 (39.8)	147 (50.9)	89 (46.4)
Any neurological symptom	538 (28.6)	100 (34.6)	55 (28.7)
Any other symptom	526 (27.9)	136 (47.1)	84 (43.8)

ED, Emergency Department.

^a Includes Argentina (n=13), Italy (n=1), Paraguay (n=28), and Singapore (n=2).

^b Information was missing for a maximum of 3 children for each specific symptom type, unless otherwise noted

eTable 2. Baseline Demographics of Participants and Presence of Self-Reported Persistent, New or Recurring Health Problems 90 Days Following ED Visit for 1884 SARS-CoV-2-Positive Children Enrolled Before January 20, 2021. Data are n/N (%).

	All children	Acute (day 0-14) SARS-CoV-2 outcome		P Value
		Not hospitalized	Hospitalized	
All children	110/1884 (5.8)	66/1437 (4.6)	44/447 (9.8)	<0.001
Region				
United States	79/1204 (6.6)	45/927 (4.9)	34/277 (12.3)	<0.001
Costa Rica	11/331 (3.3)	3/232 (1.3)	8/99 (8.1)	0.004
Canada	17/172 (9.9)	15/158 (9.5)	2/14 (14.3)	0.63
Spain	3/133 (2.3)	3/101 (3.0)	0/32 (0)	>0.99
Other ^a	0/44 (0)	0/19 (0)	0/25 (0)	-
Sex				
Male	53/994 (5.3)	33/748 (4.4)	20/246 (8.1)	0.03
Female	57/890 (6.4)	33/689 (4.8)	24/201 (11.9)	<0.001
Age				
<1.0 yrs	19/490 (3.9)	12/373 (3.2)	7/117 (6.0)	0.18
1.0 - <2.0 yrs	7/232 (3.0)	5/191 (2.6)	2/41 (4.9)	0.61
2.0 - <5.0 yrs	11/295 (3.7)	6/221 (2.7)	5/74 (6.8)	0.75
5.0 - <10.0 yrs	19/364 (5.2)	16/289 (5.5)	3/75 (4.0)	0.78
10.0 - <14.0 yrs	20/240 (8.3)	11/181 (6.1)	16/182 (8.8)	0.42
14.0 - <18.0 yrs	34/263 (12.9)	9/59 (15.3)	18/81 (22.2)	0.39
Chronic condition				
Yes	23/270 (8.5)	12/155 (7.7)	11/115 (9.6)	0.66
No	87/1613 (5.4)	54/1281 (4.2)	33/332 (9.9)	<0.001
Number of symptoms at ED presentation				
None	4/113 (3.5)	1/80 (1.3)	3/33 (9.1)	0.07
1-3	17/754 (2.3)	9/585 (1.5)	8/169 (4.7)	0.03
4-6	34/626 (5.4)	23/478 (4.8)	11/148 (7.4)	0.22
7 or more	55/391 (14.1)	33/294 (11.2)	22/97 (22.7)	0.007
Severe acute illness				
Yes	13/70 (18.6)	-	13/70 (18.6)	-

No	97/1814 (5.4)	66/1437 (4.6)	31/377 (8.2)	0.01
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ED, Emergency Department.

^a Includes Argentina (n=13), Italy (n=1), Paraguay (n=28), and Singapore (n=2).

eTable 3. Characteristics of Self-Reported Persistent, New or Recurring Health Problems 90 Days Following the Index ED Visit for SARS-CoV-2-Positive Participants. All data are n (%) unless otherwise specified.

	All children N=1884	Acute (day 0-14) SARS-CoV-2 Outcome	
		Not hospitalized N=1437	Hospitalized N=447
Persistent, new or recurring health problem, n (%) [95%CI]	110 (5.8) [4.8-7.0]	66/1437 (4.6) [3.6-5.8]	44/447 (9.8) [7.2-13.0]
Number of persistent, new or recurring health problem			
1	65 (3.5)	37 (2.6)	28 (6.3)
2	25 (1.3)	17 (1.2)	8 (1.8)
3+	20 (1.1)	12 (0.8)	8 (1.8)
Types of persistent, new or recurring health problem			
Respiratory, n (%) [95%CI]	38 (2.0) [1.4-2.8]	27 (1.9) [1.2-2.7]	11 (2.5) [1.2-4.4]
Cough	13 (0.7)	9 (0.6)	4 (0.9)
Difficulty breathing, short of breath	13 (0.7)	10 (0.7)	3 (0.7)
Wheeze or asthma exacerbation	8 (0.4)	7 (0.5)	1 (0.2)
Runny nose or congestion	6 (0.3)	4 (0.3)	2 (0.5)
Chest pain	3 (0.2)	3 (0.2)	0
Other respiratory symptoms or diagnoses	12 (0.6)	5 (0.4)	7 (1.6)
Systemic, n (%) [95%CI]	33 (1.8) [1.2-2.5]	24 (1.7) [1.1-2.5]	9 (2.0) [0.9-3.8]
Fatigue or weakness	21 (1.1)	14 (1.0)	7 (1.6)
Fever	9 (0.5)	7 (0.5)	2 (0.5)
Anorexia, loss of appetite	7 (0.4)	7 (0.5)	0
Muscle, joint, or body pain	4 (0.2)	3 (0.2)	1 (0.2)
Mental ‘fuzziness’, loss of focus	4 (0.2)	3 (0.2)	1 (0.2)
Dizziness or lightheaded	2 (0.1)	2 (0.1)	0
Psychological, n (%) [95%CI]	17 (0.9) [0.5-1.4]	9 (0.6) [0.3-1.2]	8 (1.8) [0.8-3.5]
Anxiety	7 (0.4)	3 (0.2)	4 (0.9)
Depression	6 (0.3)	3 (0.2)	3 (0.7)
Other psychological symptoms or diagnoses	7 (0.4)	3 (0.1)	4 (0.9)

Neurologic, n (%) [95%CI]	17 (0.9) [0.5-1.4]	10 (0.7) [0.3-1.3]	7 (1.6) [0.6-3.2]
Loss of smell or taste	9 (0.5)	7 (0.5)	2 (0.5)
Headache	7 (0.4)	3 (0.2)	4 (0.9)
Seizures	1 (0.1)	0	1 (0.2)
Gastrointestinal, n (%) [95%CI]	12 (0.6) [0.3-1.1]	4 (0.3) [0.1-0.7]	8 (1.8) [0.8-3.5]
Cardiovascular, n (%) [95%CI]	12 (0.6) [0.3-1.1]	3 (0.2) [0-0.6]	9 (2.0) [0.9-3.8]
Skin condition or rash, n (%) [95%CI]	10 (0.5) [0.3-1.0]	9 (0.6) [0.3-1.2]	1 (0.2) [0-1.2]
Ophthalmologic and/or otolaryngologic, n (%) [95%CI]	4 (0.2) [0.1-0.5]	2 (0.1) [0-0.5]	2 (0.5) [0.1-1.6]
Other symptoms or diagnoses, n (%) [95%CI]	12 (0.6) [0.3-1.1]	6 (0.4) [0.2-0.9]	6 (1.3) [0.5-2.9]

eTable 4. Demographic and Clinical Characteristics (at Time of ED Presentation) of Frequency Matched SARS-CoV-2-Positive and SARS-CoV-2-Negative Children With Complete Follow-up, by Acute Hospitalization Status. Data are n/N (%).

	Not hospitalized within 14 days of testing		Hospitalized within 14 days of testing	
	SARS-CoV-2 positive N=1295	SARS-CoV-2 negative N=1321	SARS-CoV-2 positive N=391	SARS-CoV-2 negative N=380
Sex, Male	667 (51.5)	622 (47.1)	210 (53.7)	197 (51.8)
Age				
<1.0 yrs	338 (26.1)	258 (19.5)	99 (25.3)	84 (22.1)
1.0 - <2.0 yrs	173 (13.4)	265 (20.1)	34 (8.7)	41 (10.8)
2.0 - <5.0 yrs	198 (15.3)	312 (23.6)	60 (15.4)	73 (19.2)
5.0 - <10.0 yrs	260 (20.1)	246 (18.6)	69 (17.7)	70 (18.4)
10.0 - <14.0 yrs	164 (12.7)	133 (10.1)	49 (12.5)	62 (16.3)
14.0 - <18.0 yrs	162 (12.5)	107 (8.1)	80 (20.5)	50 (13.2)
Chronic underlying condition	131 (10.1)	215 (16.3)	104 (26.6)	103 (27.1)
History of asthma	170 (13.1)	193 (14.6)	65 (16.6)	84 (22.1)
Number of symptoms at ED presentation				
None	73 (5.6)	97 (7.3)	24 (6.1)	24 (6.3)
1-3	513 (39.6)	472 (35.7)	149 (38.1)	153 (40.3)
4-6	442 (34.1)	475 (36.0)	128 (32.7)	139 (36.6)
7 or more	267 (20.6)	277 (21.0)	90 (23.0)	64 (16.8)
Types of symptoms				
Any systemic symptom	1027 (79.3)	1004 (76.0)	309 (79.0)	270 (71.1)
Any respiratory symptom	961 (74.2)	813 (61.5)	222 (56.8)	174 (45.8)
Any gastrointestinal symptom	506 (39.1)	583 (44.1)	182 (46.6)	180 (47.4)
Any neurological symptom	372 (28.7)	277 (21.0)	115 (29.4)	88 (23.2)
Any other symptom	483 (37.3)	589 (44.6)	147 (37.6)	158 (41.6)

ED, Emergency Department.

eTable 5. Comparison of Each Reported Type of Persistent, New or Recurring Health Problem Reported Among Frequency Matched SARS-CoV-2-Positive and Negative Participants With Complete 90-Day Follow-up. Data are n/N (%).

	Not acutely hospitalized			Acutely hospitalized		
	SARS-CoV-2 Positive N=1295	SARS-CoV-2 Negative N=1321	P Value	SARS-CoV-2 Positive N=391	SARS-CoV-2 Negative N=380	P Value
Respiratory	20 (1.8)	24 (1.5)	0.59	10 (2.6)	7 (1.8)	0.63
Cough	8 (0.6)	11 (0.8)	0.65	4 (1.0)	2 (0.5)	0.69
Difficulty breathing, short of breath	8 (0.6)	4 (0.3)	0.26	3 (0.8)	0	0.25
Wheeze or asthma exacerbation	4 (0.3)	7 (0.5)	0.55	1 (0.3)	1 (0.3)	>0.99
Runny nose or congestion	3 (0.2)	6 (0.5)	0.51	2 (0.5)	1 (0.3)	>0.99
Chest pain	3 (0.2)	1 (0.1)	0.37	0	1 (0.3)	0.49
Sneezing	0	1 (0.1)	>0.99	0	0	-
Sore throat	0	1 (0.1)	>0.99	0	0	-
Other respiratory symptoms & diagnoses	4 (0.3)	3 (0.2)	0.72	6 (1.5)	3 (0.8)	0.51
Systemic	21 (1.6)	6 (0.5)	0.003	8 (2.1)	5 (1.3)	0.58
Fatigue or weakness	12 (0.9)	0	<0.001	6 (1.5)	1 (0.3)	0.12
Fever	6 (0.5)	5 (0.4)	0.77	2 (0.5)	0	0.50
Anorexia, loss of appetite	7 (0.5)	1 (0.1)	0.04	0	0	-
Muscle, joint, or body pain	3 (0.2)	0	0.12	1 (0.3)	2 (0.5)	0.62
Mental ‘fuzziness’, loss of focus	3 (0.2)	0	0.12	1 (0.3)	0	>0.99
Dizziness or lightheaded	2 (0.2)	1 (0.1)	0.62	0	2 (0.5)	0.24
Psychological	9 (0.7)	2 (0.2)	0.04	8 (2.1)	5 (1.3)	0.58
Anxiety	3 (0.2)	1 (0.1)	0.37	4 (1.0)	1 (0.3)	0.37
Depression	3 (0.2)	0	0.12	3 (0.8)	2 (0.5)	>0.99
Other psychological symptoms, diagnoses	2 (0.2)	0	0.25	4 (1.0)	3 (0.8)	>0.99
Neurologic	9 (0.7)	5 (0.4)	0.30	6 (1.5)	4 (1.1)	0.75
Loss of smell or taste	6 (0.5)	0	0.02	2 (0.5)	0	0.50
Headache	3 (0.2)	2 (0.2)	0.68	3 (0.8)	3 (0.8)	>0.99
Seizures	0	3 (0.2)	0.25	1 (0.3)	1 (0.3)	>0.99
Gastrointestinal	4 (0.3)	4 (0.3)	>0.99	8 (2.0)	5 (1.3)	0.58
Cardiovascular	3 (0.2)	0	0.12	6 (1.5)	0	0.03

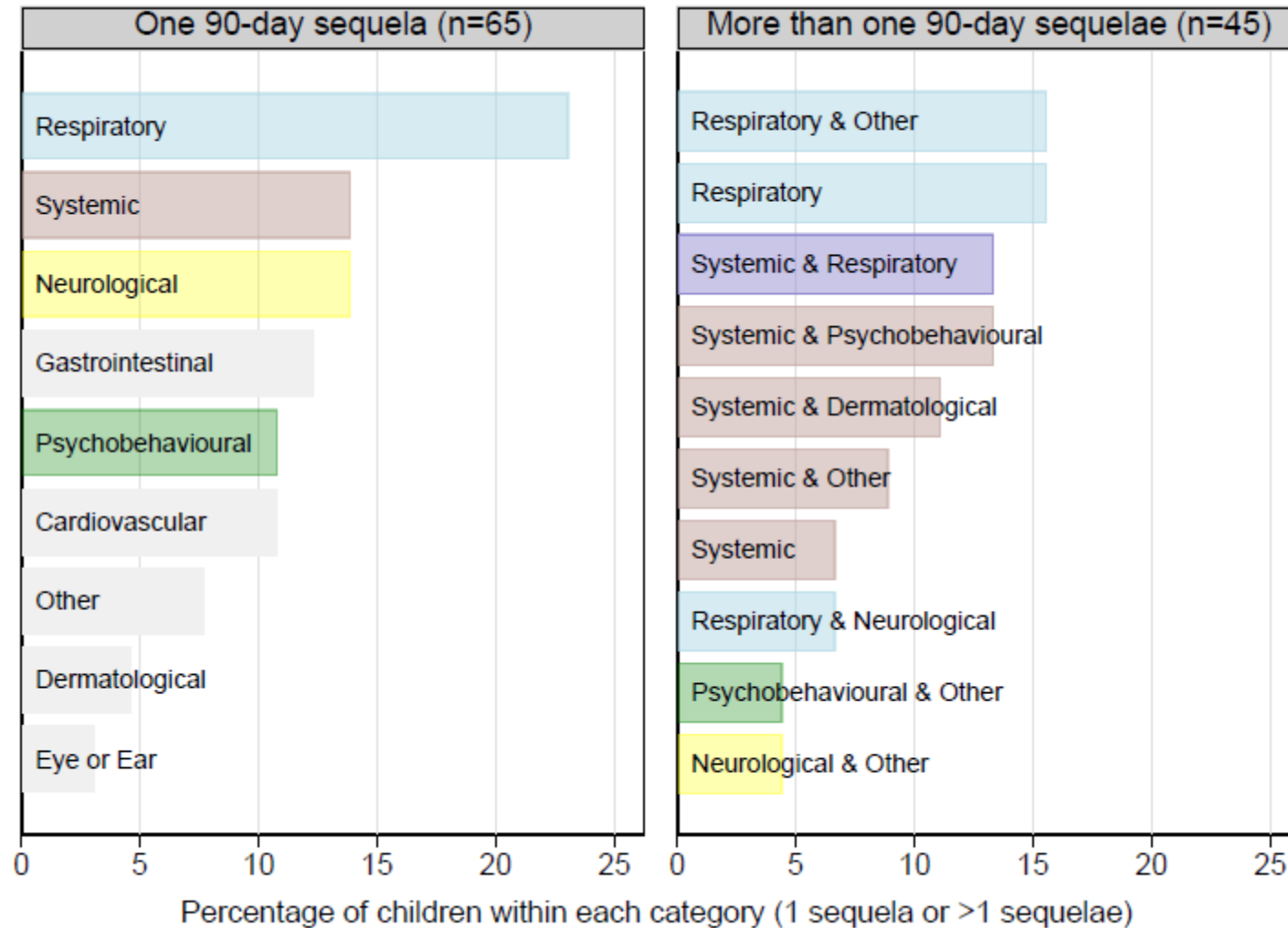
Skin condition or rash	5 (0.4)	1 (0.1)	0.12	1 (0.3)	0	>0.99
Ophthalmologic and/or otolaryngologic	2 (0.2)	0	0.25	2 (0.5)	0	0.50
Other symptoms or diagnoses	5 (0.4)	4 (0.3)	0.75	5 (1.3)	2 (0.5)	0.45

eTable 6. Results of Multiple Logistic Regression Models Examining the Association of SARS-CoV-2 Positivity With Categories of Reported 90-Day Persistent, New or Recurring Health Problems.*

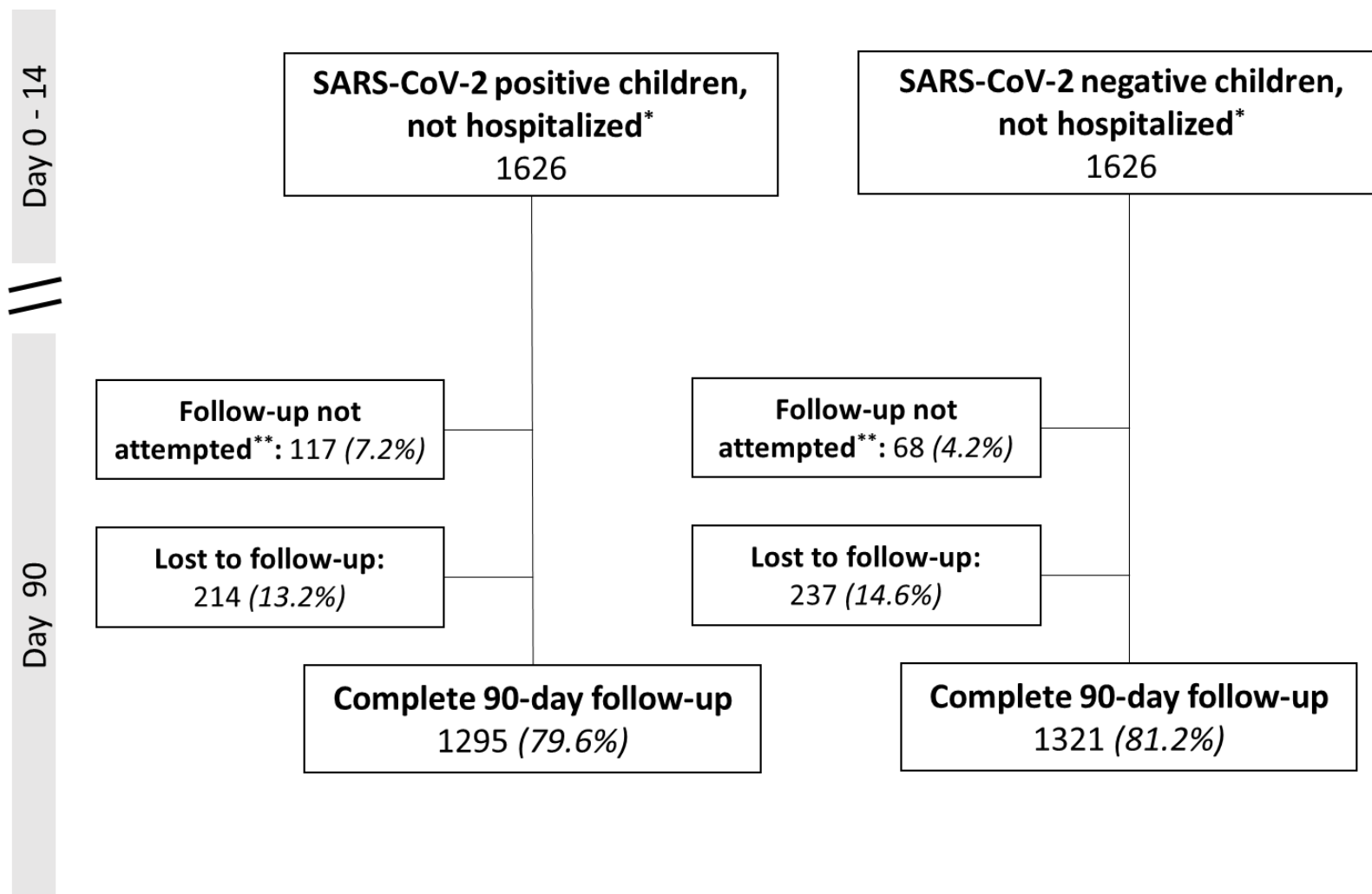
	Number of events	Adjusted odds ratio (SARS-CoV-2) (95% confidence interval)	p-value	Covariates included in Final Models in Addition to SARS-CoV-2 Test Result
Any reported persistent, new or recurring health problem	147	1.63 (1.14, 2.35)	0.008	Country of enrolment, sex, age category, having a chronic condition other than asthma acute hospitalization, # acute symptoms, season of infection
Respiratory	61	0.88 (0.52, 1.48)	0.62	Country of enrolment, age category, # acute symptoms
Systemic	40	2.44 (1.19, 5.00)	0.02	Having a chronic condition other than asthma, sex, age category, acute hospitalization, # acute symptoms
Neurologic	24	1.29 (0.56, 2.99)	0.55	Age category
Psychological	22	1.96 (0.74, 5.18)	0.17	Sex, age category, acute hospitalization, # acute symptoms
Gastrointestinal	21	1.35 (0.57, 3.21)	0.50	None

* Only persistent, new or recurring health problem categories for which there were at least 20 events were examined in a multiple logistic regression model. Acute hospitalization was included as a three-category variable: not hospitalized, hospitalized < 48 hours, hospitalized for ≥ 48 hours.

eFigure 1. Types of 90-Day Persistent, New or Recurring Health Problem According to Number of Health Problems Reported Among the 110 SARS-CoV-2-Positive Children Reporting Any Persistent New or Recurring Health Problem

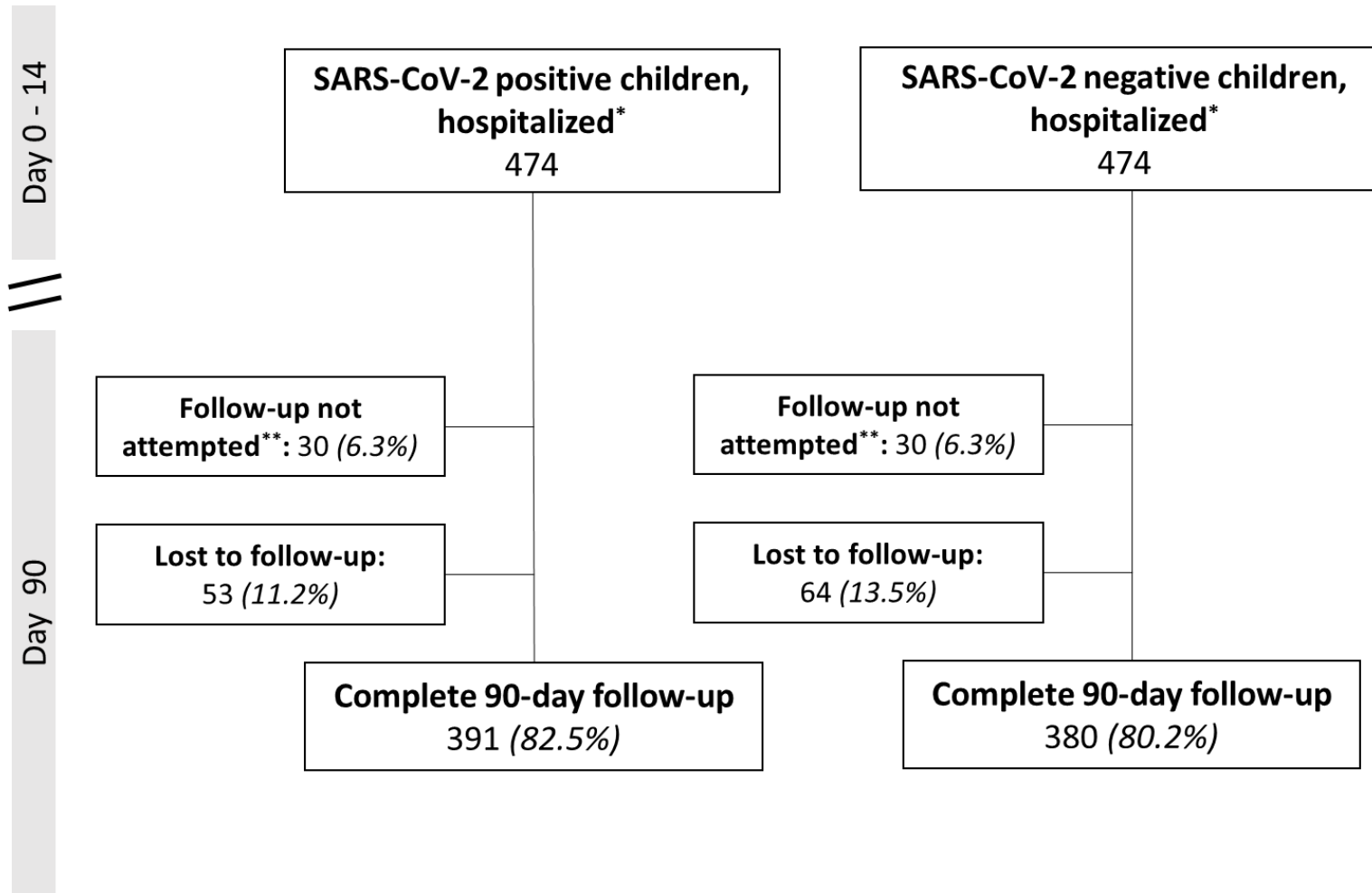


eFigure 2. Follow-up of Frequency Matched SARS-CoV-2-Positive and Negative Children Who Were Not Hospitalized During the Acute Phase (Day 0-14) of Illness



* Within 14 days of testing ** In a few sites, consistent 90-day follow-up was not feasible amid human resource constraints during the COVID-19 pandemic

eFigure 3. Follow-up of Frequency Matched SARS-CoV-2-Positive and Negative Children Who Were Hospitalized During the Acute Phase (Day 0-14) of Illness



* Within 14 days of testing **In a few sites, consistent 90-day follow-up was not feasible amid human resource constraints during the COVID-19 pandemic