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.
### Demographic and Clinical Characteristics of SARS-CoV-2-Positive Children by Follow-up Status at 90 Days.

All data are n (%) unless otherwise specified.

| Region                  | Complete follow-up N= 1884 | Lost to follow-up N= 289 | Follow-up not attempted N= 192 |
|-------------------------|-----------------------------|---------------------------|--------------------------------|
| 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               |                             |                           |                                |
| Male                    | 994 (52.8)                  | 149 (51.6)                | 92 (47.1)                      |
| 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*               | 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) | -      |

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| No | 97/1814 (5.4) | 66/1437 (4.6) | 31/377 (8.2) | 0.01 |

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^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)                           |
| 2                            | 25 (1.3)            | 17 (1.2)                           |
| 3+                           | 20 (1.1)            | 12 (0.8)                           |
| **Types of persistent, new or recurring health problem** |                     |                                   |
| Respiratory, n (%) [95% CI]  |                     |                                   |
| Cough                        | 13 (0.7)            | 9 (0.6)                            |
| Difficulty breathing, short of breath | 13 (0.7)           | 10 (0.7)                           |
| Wheeze or asthma exacerbation| 8 (0.4)             | 7 (0.5)                            |
| Runny nose or congestion     | 6 (0.3)             | 4 (0.3)                            |
| Chest pain                   | 3 (0.2)             | 3 (0.2)                            |
| 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]                 |
| Fatigue or weakness          | 21 (1.1)            | 14 (1.0)                           |
| Fever                        | 9 (0.5)             | 7 (0.5)                            |
| Anorexia, loss of appetite   | 7 (0.4)             | 7 (0.5)                            |
| Muscle, joint, or body pain  | 4 (0.2)             | 3 (0.2)                            |
| Mental ‘fuzziness’, loss of focus | 4 (0.2)         | 3 (0.2)                            |
| Dizziness or lightheaded     | 2 (0.1)             | 2 (0.1)                            |
| Psychological, n (%) [95% CI]|                      |                                   |
| Anxiety                      | 7 (0.4)             | 3 (0.2)                            |
| Depression                   | 6 (0.3)             | 3 (0.2)                            |
| Other psychological symptoms or diagnoses | 7 (0.4)        | 3 (0.1)                            |

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|                          |                 |                 |                 |
|--------------------------|-----------------|-----------------|-----------------|
| **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] |

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**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 |
|--------------------------|--------------------------|----------------------|
| **Not 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**          |                          |                      |          |                          |                      |          |
| Cough                   | 20 (1.8)                 | 24 (1.5)             | 0.59     | 10 (2.6)                 | 7 (1.8)              | 0.63     |
| Difficulty breathing, short of breath | 8 (0.6) | 11 (0.8) | 0.65 | 4 (1.0) | 2 (0.5) | 0.69 |
| 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**            |                          |                      |          |                          |                      |          |
| Fatigue or weakness     | 21 (1.6) | 6 (0.5) | **0.003** | 8 (2.1) | 5 (1.3) | **0.58** |
| 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**       |                          |                      |          |                          |                      |          |
| Anxiety                 | 9 (0.7) | 2 (0.2) | **0.04** | 8 (2.1) | 5 (1.3) | **0.58** |
| Depression              | 3 (0.2) | 1 (0.1) | 0.37 | 4 (1.0) | 1 (0.3) | 0.37 |
| Other psychological symptoms, diagnoses | 2 (0.2) | 0 | 0.25 | 4 (1.0) | 3 (0.8) | >0.99 |
| **Neurologic**          |                          |                      |          |                          |                      |          |
| Loss of smell or taste  | 9 (0.7) | 5 (0.4) | 0.30 | 6 (1.5) | 4 (1.1) | 0.75 |
| Headache                | 6 (0.5) | 0 | 0.02 | 2 (0.5) | 0 | 0.50 |
| Seizures                | 3 (0.2) | 2 (0.2) | 0.68 | 3 (0.8) | 3 (0.8) | >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 |

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| Condition                        | Count | Rate | p-value | Count | Rate | p-value |
|---------------------------------|-------|------|---------|-------|------|---------|
| 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.*

| Category                                | 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
**Figure 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

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*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*
**Figure 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

- **SARS-CoV-2 positive children, hospitalized**: 474
  - Follow-up not attempted**: 30 (6.3%)
  - Lost to follow-up: 53 (11.2%)
  - Complete 90-day follow-up: 391 (82.5%)

- **SARS-CoV-2 negative children, hospitalized**: 474
  - Follow-up not attempted**: 30 (6.3%)
  - Lost to follow-up: 64 (13.5%)
  - Complete 90-day follow-up: 380 (80.2%)

*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