

# Comparison of Symptoms and RNA Levels in Children and Adults With SARS-CoV-2 Infection in the Community Setting

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**IMPORTANCE** The association between COVID-19 symptoms and SARS-CoV-2 viral levels in children living in the community is not well understood.

**OBJECTIVE** To characterize symptoms of pediatric COVID-19 in the community and analyze the association between symptoms and SARS-CoV-2 RNA levels, as approximated by cycle threshold (Ct) values, in children and adults.

**DESIGN, SETTING, AND PARTICIPANTS** This cross-sectional study used a respiratory virus surveillance platform in persons of all ages to detect community COVID-19 cases from March 23 to November 9, 2020. A population-based convenience sample of children younger than 18 years and adults in King County, Washington, who enrolled online for home self-collection of upper respiratory samples for SARS-CoV-2 testing were included.

**EXPOSURES** Detection of SARS-CoV-2 RNA by reverse transcription-polymerase chain reaction (RT-PCR) from participant-collected samples.

**MAIN OUTCOMES AND MEASURES** RT-PCR-confirmed SARS-CoV-2 infection, with Ct values stratified by age and symptoms.

**RESULTS** Among 555 SARS-CoV-2-positive participants (mean [SD] age, 33.7 [20.1] years; 320 were female [57.7%]), 47 of 123 children (38.2%) were asymptomatic compared with 31 of 432 adults (7.2%). When symptomatic, fewer symptoms were reported in children compared with adults (mean [SD], 1.6 [2.0] vs 4.5 [3.1]). Symptomatic individuals had lower Ct values (which corresponded to higher viral RNA levels) than asymptomatic individuals (adjusted estimate for children,  $-3.0$ ; 95% CI,  $-5.5$  to  $-0.6$ ;  $P = .02$ ; adjusted estimate for adults,  $-2.9$ ; 95% CI,  $-5.2$  to  $-0.6$ ;  $P = .01$ ). The difference in mean Ct values was neither statistically significant between symptomatic children and symptomatic adults (adjusted estimate,  $-0.7$ ; 95% CI,  $-2.2$  to  $0.9$ ;  $P = .41$ ) nor between asymptomatic children and asymptomatic adults (adjusted estimate,  $-0.6$ ; 95% CI,  $-4.0$  to  $2.8$ ;  $P = .74$ ).

**CONCLUSIONS AND RELEVANCE** In this community-based cross-sectional study, SARS-CoV-2 RNA levels, as determined by Ct values, were significantly higher in symptomatic individuals than in asymptomatic individuals and no significant age-related differences were found. Further research is needed to understand the role of SARS-CoV-2 RNA levels and viral transmission.

JAMA Pediatr. doi:10.1001/jamapediatrics.2021.2025  
Published online June 11, 2021.

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The COVID-19 pandemic caused by SARS-CoV-2 has resulted in substantial morbidity and mortality worldwide. Early public health interventions, including the closure of schools, were implemented to prevent the spread of SARS-CoV-2. However, the role of children in community SARS-CoV-2 transmission remains poorly understood as most children with SARS-CoV-2 infection are asymptomatic<sup>1</sup> or experience mild disease.<sup>2,3</sup> There have been few community-based studies of pediatric COVID-19 cases, and thus there are limited data on the role of children in the transmission of COVID-19.<sup>4</sup>

One potential driver of SARS-CoV-2 transmissibility is respiratory tract viral load, approximated by quantification of viral RNA levels via reverse transcription-polymerase chain reaction (RT-PCR) cycle threshold (Ct) values. Studies have shown a strong association between lower Ct values (higher RNA levels) and successful isolation of SARS-CoV-2 in culture.<sup>5-7</sup> Early case reports showed that asymptomatic individuals had levels of detectable SARS-CoV-2 RNA comparable with symptomatic individuals,<sup>8-10</sup> and this observation has been supported by a growing body of evidence from larger community-based studies in predominantly adult populations.<sup>11-14</sup> Studies examining SARS-CoV-2 RNA levels in children, which have generally involved small sample sizes and relied on sampling associated with presentation at medical care facilities or community-based contact tracing, have shown conflicting results<sup>15-18</sup> and comparison of community-derived pediatric and adult data has been limited.<sup>19</sup>

In this study, using data from a novel countywide respiratory virus surveillance platform, we described the association between SARS-CoV-2 Ct values and symptoms in SARS-CoV-2-positive children in King County, Washington. We also compared these findings between children and adults with SARS-CoV-2 infection.

## Methods

### Study Platform and Setting

This is a cross-sectional population-based analysis of data collected as part of the Seattle Coronavirus Assessment Network (SCAN). SCAN launched on March 23, 2020, to evaluate the feasibility of testing individuals both with and without COVID-19-like illness via unsupervised home self-collected nasal swabs for detection of SARS-CoV-2 and other respiratory pathogens.<sup>20</sup> The network was originally established in November 2018 as the Seattle Flu Study (SFS),<sup>21</sup> which focused on the community transmission of influenza and other respiratory viruses. SCAN was limited to residents of King County, Washington. We split the county into 16 groupings, defined roughly by the 16 public use microdata areas defined by the US Census Bureau. The proportion of individuals relative to the county population in each grouping dictated the proportion of daily test kits allotted to each public use microdata area. Individuals of all ages, whether they had any COVID-19 symptoms or not, were eligible to enroll on the study website.<sup>20</sup> The website and study materials were translated into 11 non-English languages and translation services were avail-

### Key Points

**Question** How is the presence of symptoms associated with SARS-CoV-2 RNA levels in children vs adults in the community?

**Findings** In this cross-sectional study of 555 children and adults with SARS-CoV-2 confirmed by reverse transcription-polymerase chain reaction, symptomatic individuals had higher SARS-CoV-2 RNA levels (as indicated by lower mean cycle threshold values) compared with asymptomatic individuals. No significant differences in RNA levels were found between asymptomatic children and asymptomatic adults or between symptomatic children and symptomatic adults.

**Meaning** Regardless of age, in this community-based study, SARS-CoV-2 RNA levels were higher in symptomatic individuals.

able. This study was approved by the University of Washington Institutional Review Board. This study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline.<sup>29</sup> All patients who enrolled online provided written informed consent.

### Data and Sample Collection

After signing an electronic consent form, all participants, or parents or guardians for participants younger than 18 years, completed an electronic questionnaire to collect data on sociodemographic and clinical characteristics, exposures, and health-related behaviors. Race and ethnicity were self-classified by participants using provided standard race and ethnic categories.<sup>22</sup> Race and ethnicity data were collected to examine disparities between racial/ethnic groups in study participation as well as in outcomes, such as SARS-CoV-2 positivity. Study data were collected and managed using REDCap Electronic Data Capture version 10.9.2 (Vanderbilt University) hosted at the University of Washington.<sup>23,24</sup> Within 24 hours of enrollment, sample collection kits were delivered using a private courier for contactless receipt at the participants' homes. Samples were self-collected by participants 13 years and older via unsupervised middle turbinate (MTB) or anterior nares (AN) swabs.<sup>25</sup> Parents or guardians performed swab collection for children younger than 13 years. Swab collection instructions were included with the swab kit (eFigure 1 in the Supplement) and were available on the study website.<sup>26,27</sup> Swab samples were returned to the laboratory within 48 hours via private courier.

This study included participants who enrolled in SCAN from March 23 to November 9, 2020, and who collected at home a nasal swab that tested positive for SARS-CoV-2 by RT-PCR. Repeated samples from individuals were excluded from analysis. Children were defined as participants younger than 18 years. For privacy, all adults older than 85 years were classified as aged 85 years. Symptomatic participants reported at least 1 symptom (ie, runny or stuffy nose, fever, headache, cough, fatigue, sore throat, muscle or body aches, chills, sweats, loss of smell or taste, diarrhea, eye pain, nausea or vomiting, trouble breathing, ear pain or discharge, or rash) within 7 days prior to study enrollment. Asymptomatic participants were

those who reported no symptoms in this time frame. Per guidelines from the US Centers for Disease Control and Prevention at the time of the study, close contact was defined as an encounter in the past 2 weeks in which the individual spent at least 10 minutes within 6 feet of a person who tested positive for SARS-CoV-2.

### Laboratory Analyses

From March 23 to July 23, 2020, MTB swabs (Copan) were returned in 3-mL tubes of BD universal viral transport media (Becton, Dickinson and Company) or viral transport media (Brainbits) at room temperature, and aliquoted and stored at 4° C prior to testing. After July 23, 2020, AN swabs (US Cotton #3) were used by participants and returned in empty transport tubes. AN swabs were rehydrated and eluted in 1 mL of either phosphate-buffered saline or Tris-EDTA buffer. All samples were processed, including rehydration, within 48 hours of collection. Stability studies have shown consistent SARS-CoV-2 Ct values at 4° C and 40° C for both AN and MTB swabs up to 3 days<sup>28</sup> and 9 days,<sup>21</sup> respectively. Laboratory testing was performed at the Brotman Baty Institute for Precision Medicine, Seattle, Washington, and the Northwest Genomics Center, Seattle, Washington. Total nucleic acids were extracted (before October 18, 2020, MagNA Pure 96, Roche; on or after October 18, 2020, KingFisher, Thermo Fisher) and tested for the presence of SARS-CoV-2 and the human marker ribonuclease P (RNase P) using a Clinical Laboratory Improvement Amendments-compliant laboratory developed test. RNase P Ct values were used as an extraction and sample collection control. The laboratory developed test consisted of 2 unique multiplexed assays run in duplicate for a total of 4 RT-PCR reactions; each multiplex reaction included a target for SARS-CoV-2 and RNase P. One assay targeted Orflb with FAM fluor (Life Technologies 4332079 assay #APGZJKF) and was multiplexed with an RNase P probe set with VIC or HEX fluor (Life Technologies A30064 or Integrated DNA Technologies) on a QuantStudio 6 (Applied Biosystems), and the other targeted the S gene (Life Technologies 4332079 assay #APXGVC4) and was also multiplexed with RNase P-VIC or RNase P-HEX assay. Standard curves demonstrated a linear association with mean Ct values and logarithm of SARS-CoV-2 RNA copy numbers for each primer set and from each collection method (MTB vs AN) (eFigure 2 in the Supplement). At least 3 replicates for RNase P had to be detected for a valid test result. For a positive result, 3 or more SARS-CoV-2 targets must have had a Ct value of less than 40. Most samples were also tested for the presence of 24 respiratory pathogens by TaqMan RT-PCR on the OpenArray platform (Thermo Fisher).

### Statistical Analyses

Mean SARS-CoV-2 Ct values were obtained using the 2 Ct values for the Orflb gene primer. Results were not affected by the primer used (eFigure 3 in the Supplement) but we excluded analysis by S gene because of better Orflb sensitivity and reproducibility. Analysis by RNase P Ct values did not show evidence of confounding by age or symptom status (eFigure 4 in the Supplement). We generated descriptive statistics for all variables. Proportions of missing data were reported. Data analy-

ses were performed using R version 4.0.5 (The R Foundation). Statistical comparisons between groups were determined using  $\chi^2$  tests, Welch *t* test, and multiple linear regression. Two-tailed tests were used for all comparisons and statistical significance was defined as  $P < .05$ . AN swabs were used in the later portion of the study when rates of positivity in children, many of whom were asymptomatic, increased. Therefore, because swab type is a confounder of the association between age and SARS-CoV-2 RNA levels, we used multiple linear regression to adjust individual Ct values to the average swab type in the study. This ensured that our figures would show an unconfounded comparison of ages and symptom status, while preserving the mean Ct value across the sample. Although 2 different nucleic acid extraction platforms were used, multiple linear regression analysis showed that the extraction platform used did not have statistically significant or clinically meaningful associations with our results.

## Results

From March 23 to November 9, 2020, 37 067 samples were tested for SARS-CoV-2 via SCAN. Overall, 673 samples (1.8%) had positive results (493 of 31 664 [1.6%] of adult samples and 180 of 5356 [3.4%] of child samples; 47 positive samples did not have age data). Of these positive samples, 180 samples (26.7%) were from children younger than 18 years and 493 (73.3%) were from adults. We excluded 118 samples: 42 that represented repeated positive testing in SCAN and 76 that were missing clinical information.

Of the 555 participants with SARS-CoV-2-positive results, 123 (22.2%) were children and 432 (77.8%) were adults (Table 1), ranging in age from 73 days to 85 years. The mean (SD) age was 33.7 (20.1) years: 7.5 (5.3) years for children and 41.2 (16.0) years for adults. Among 123 SARS-CoV-2-positive children in this study, 50 (40.7%) were younger than 5 years, 45 (36.6%) were aged 5 to 11 years, and 28 (22.8%) were aged 12 to 17 years. Of the total positive sample, 320 (57.7%) were female. Of 123 SARS-CoV-2-positive children, 64 (52.0%) were female, 55 (44.7%) were White, and 30 (24.4%) were Hispanic or Latino. The most common underlying conditions among SARS-CoV-2-positive children included seasonal allergies (9 [7.3%]) and asthma (5 [4.1%]), but most children reported no previous underlying medical conditions (106 [86.2%]). Compared with the mean King County household size of 2.4 people,<sup>30</sup> people of all ages with SARS-CoV-2-positive results reported larger mean (SD) household sizes (3.8 [1.6]). Most children (91 [74.0%]) resided in households of 4 or more people. Most children (98 [79.7%]) had at least 1 known SARS-CoV-2-positive contact, and most contacts (84 [68.3%]) were in the same household. In contrast, only 179 of 432 SARS-CoV-2-positive adults (41.4%) reported any known positive contact.

Fewer children were symptomatic compared with adults (76 of 123 children [61.8%] vs 401 of 432 adults [92.8%];  $P < .001$ ) (Table 2). When symptomatic, fewer symptoms were reported in children compared with adults (mean [SD], 1.6 [2.0] vs 4.5 [3.1]) (Figure 1). Symptomatic children reported a mean

**Table 1. Demographic Characteristics of SARS-CoV-2-Positive Children and Adults in Seattle Coronavirus Assessment Network (SCAN) From March 23 to November 9, 2020**

Characteristic	No. (%)		
	Total sample	Children	Adults
Total, No.	555	123	432
Sex			
Female	320 (57.7)	64 (52.0)	256 (59.3)
Male	235 (42.2)	59 (48.0)	176 (40.7)
Race/ethnicity <sup>a</sup>			
American Indian or Alaskan Native	1 (0.2)	0	1 (0.2)
Asian	75 (13.5)	13 (10.6)	62 (14.4)
Black or African American	35 (6.3)	10 (8.1)	25 (5.8)
Native Hawaiian or other Pacific Islander	11 (2.0)	2 (1.6)	9 (2.1)
White	283 (51.0)	55 (44.7)	228 (52.8)
Other <sup>b</sup>	76 (13.7)	17 (13.8)	59 (13.7)
Multiple races	42 (7.6)	19 (15.4)	23 (5.3)
Not reported	32 (5.8)	7 (5.7)	25 (5.8)
Hispanic or Latino ethnicity			
Yes	118 (21.3)	30 (24.4)	88 (20.4)
No	414 (74.6)	89 (72.4)	325 (75.2)
Not reported	23 (4.1)	4 (3.3)	19 (4.4)
Age, y			
0-4	50 (9.0)	50 (40.7)	NA
5-11	45 (8.1)	45 (36.6)	NA
12-17	28 (5.0)	28 (22.8)	NA
18-49	305 (55.0)	NA	305 (70.6)
50-64	93 (16.7)	NA	93 (21.5)
65-85 <sup>c</sup>	34 (6.1)	NA	34 (7.9)
Mean (SD)	33.7 (20.1)	7.5 (5.3)	41.2 (16)
Comorbidity			
None	394 (71.0)	106 (86.2)	288 (66.7)
Allergy	77 (13.8)	9 (7.3)	68 (15.7)
Asthma	41 (7.4)	5 (4.1)	36 (8.3)
Cardiovascular disease	9 (1.6)	0	9 (2.1)
Cancer	2 (0.4)	0	2 (0.5)
Chronic lung disease, not asthma	3 (0.5)	0	3 (0.7)
Diabetes	24 (4.3)	0	24 (5.6)
Hypertension	42 (7.5)	1 (0.8)	41 (9.5)
Unknown/not reported	16 (2.9)	2 (1.6)	14 (3.2)
Household size (including participant)			
1	36 (6.5)	0	33 (7.6)
2	116 (20.9)	21 (17.1)	95 (22.0)
3	83 (15.0)	11 (8.9)	72 (16.7)
4	123 (22.0)	38 (30.9)	88 (20.4)
5	95 (17.1)	30 (24.4)	65 (15.0)
≥6 <sup>d</sup>	102 (18.4)	23 (18.7)	79 (18.3)
Mean (SD)	3.8 (1.6)	4.1 (1.4)	3.7 (1.6)
SARS-CoV-2-positive close contacts <sup>e</sup>			
None	69 (12.4)	10 (8.1)	59 (13.7)
Any positive contact	277 (49.9)	98 (79.7)	179 (41.4)
Household	225 (40.5)	84 (68.3)	141 (32.6)
Friend	45 (8.1)	14 (11.4)	31 (7.2)
Coworker	16 (2.9)	0	16 (3.7)
Unsure/not reported	209 (37.7)	15 (12.2)	194 (44.9)

Abbreviation: NA, not applicable.

<sup>a</sup> Race/ethnicity categories were treated as mutually exclusive groups; multiple races was defined as 2 or more of the above groups.<sup>b</sup> This included unlisted races not specified by participant.<sup>c</sup> For privacy, all adults older than 85 years were classified as aged 85 years.<sup>d</sup> For the purpose of analysis, we assumed a household size of 6 for individuals who reported 6 or more household members.<sup>e</sup> Close contact was defined as an encounter in the past 2 weeks in which the individual spent at least 10 minutes within 6 feet of a person who tested positive for SARS-CoV-2.

Table 2. Reported Signs and Symptoms and Duration in SARS-CoV-2-Positive Children and Adults at Enrollment

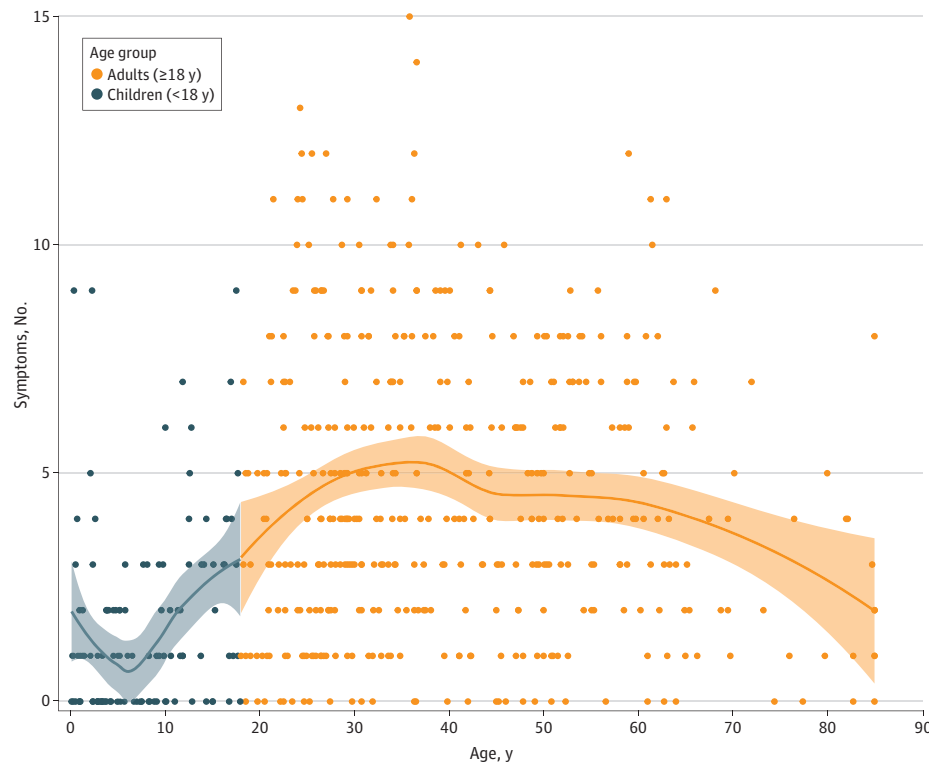
Sign or symptom <sup>a</sup>	No (%)			P value	
	Children Aged ≤4 y (n = 50)	Children Aged 5-17 y (n = 73)	Adults (n = 432)	Children aged ≤4 y vs children aged 5-17 y	All children vs adults
No symptoms	23 (46.0)	24 (32.9)	31 (7.2)		
Any symptom	27 (54.0)	49 (67.1)	401 (92.8)	.20	<.001
Runny or stuffy nose	14 (28.0)	22 (30.1)	192 (47.9)	.97	.004
Fever	11 (22.0)	15 (20.5)	161 (40.1)	>.99	.001
Headache	5 (10.0)	19 (26.0)	247 (57.2)	.05	<.001
Cough	12 (24.0)	12 (16.4)	235 (58.6)	.42	<.001
Fatigue	5 (10.0)	14 (19.2)	213 (53.1)	.26	<.001
Sore throat	4 (8.0)	14 (19.2)	169 (42.1)	.14	<.001
Muscle or body aches	3 (6.0)	10 (13.7)	197 (49.1)	.29	<.001
Chills	2 (4.0)	8 (11.0)	130 (32.4)	.29	<.001
Sweats	2 (4.0)	4 (5.5)	96 (23.9)	>.99	<.001
Loss of smell or taste	0	6 (8.2)	81 (20.2)	.10	<.001
Diarrhea	4 (8.0)	2 (2.7)	70 (17.5)	.37	.002
Eye pain	2 (4.0)	3 (4.1)	46 (11.5)	>.99	.04
Nausea or vomiting	0	4 (5.5)	49 (12.2)	.24	.01
Trouble breathing	1 (2.0)	0	47 (11.7)	.85	<.001
Ear pain or discharge	0	1 (1.4)	23 (5.7)	>.99	.06
Rash	0	0	3 (7.5)	NA	.80
No. of symptoms, mean (SD)	1.3 (2.0)	1.8 (2.0)	4.5 (3.1)	.15	<.001
Symptom duration, mean (SD), d <sup>b</sup>	4.1 (5.3)	3.6 (2.6)	4.9 (4.1)	.28	.03

Abbreviation: NA, not applicable.

<sup>a</sup> Signs and symptoms reported at enrollment.

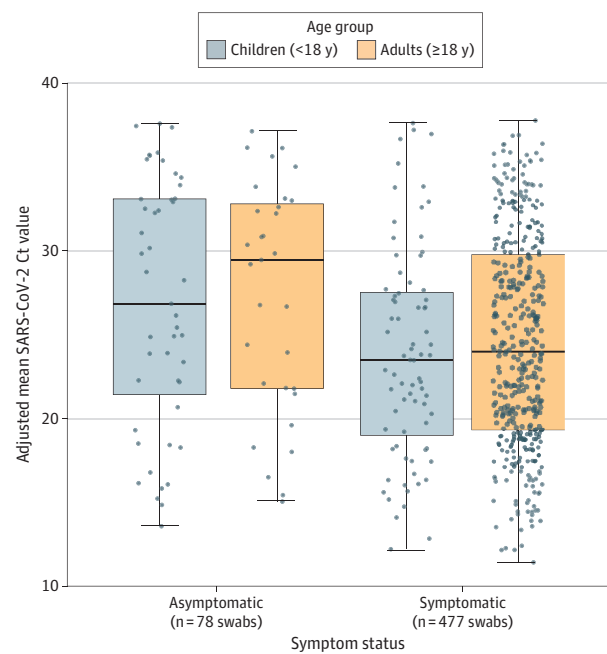
<sup>b</sup> Number of days between participant-reported date of symptom onset and swab collection date. Symptom duration was limited to 10 or fewer days. Date of symptom onset was not reported by 392 participants (327 adults and 65 children).

Figure 1. Number of COVID-19 Signs and Symptoms Reported by Participants at Enrollment by Age



The total number of signs and symptoms at enrollment are shown by age group with individual locally estimated scatterplot smoothing regression lines plotted for each age group. Data points represent SARS-CoV-2-positive individuals. Shaded areas represent 95% CIs.

**Figure 2. Adjusted Mean SARS-CoV-2 Orf1b Cycle Threshold (Ct) Values by Age Group, Grouped by Symptom Status**



Boxes range from the first to third quartiles. Midlines represent median values. Error bars represent the minimum and maximum values. Individual points represent SARS-CoV-2-positive individuals. There were 47 asymptomatic children, 31 asymptomatic adults, 76 symptomatic children, and 401 symptomatic adults. Ct values are adjusted for swab type.

(SD) of 3.8 (3.8) days of symptoms compared with 4.9 (4.1) days in symptomatic adults. The most common signs or symptoms reported in children were runny or stuffy nose, fever, headache, and cough, while adults most frequently reported headache, cough, and fatigue (eFigure 5 in the Supplement).

Asymptomatic children were younger than symptomatic children (mean [SD] age, 6.2 [4.5] years compared with 8.3 [5.7] years;  $P < .001$ ). Although there were differences in percentage symptomatic and symptoms reported between children younger than 5 years and children aged 5 to 17 years, these differences were not statistically significant. No comorbidities were reported for asymptomatic children. A higher proportion of asymptomatic children than symptomatic children reported any SARS-CoV-2-positive contact (41 of 47 [87.2%] vs 57 of 76 [75.0%]), most of whom were household contacts (36 of 47 [76.6%] vs 48 of 76 [63.2%]).

Of the 555 SARS-CoV-2-positive swabs, 487 were tested for 24 respiratory pathogens by RT-PCR. Only 3 of 108 children (2.8%) tested for other respiratory pathogens had another virus detected by RT-PCR. Rhinovirus was detected in 2 children and adenovirus in 1 child. Ten of 379 adults (2.6%) tested by respiratory pathogen RT-PCR had another virus identified, with rhinovirus predominantly detected (7 of 10); adenovirus (1 of 10), enterovirus (1 of 10), and influenza virus (1 of 10) were also detected.

MTB swabs were used by 176 participants (18 children and 158 adults) and AN swabs were used by 379 participants (105

children and 274 adults). Multiple linear regression of mean SARS-CoV-2 Ct value by age group and swab type showed that MTB swabs were associated with a 4.0-point higher mean Ct value compared with AN swabs ( $P < .001$ ) (eFigure 6 in the Supplement).

Mean SARS-CoV-2 Ct values between children and adults were not significantly different (adjusted estimate for difference in mean Ct values, 0.3; 95% CI, -1.1 to 1.6;  $P = .67$ ) after adjusting for swab type (Figure 2). Subgroup analyses showed that symptomatic individuals had consistently lower Ct values than asymptomatic individuals, regardless of age, after adjusting for swab type (adjusted estimate for children, -3.0; 95% CI, -5.5 to -0.6;  $P = .02$ ; adjusted estimate for adults, -2.9; 95% CI, -5.2 to -0.6;  $P = .01$ ) (eTable in the Supplement). The difference in mean Ct value between symptomatic children and adults was not significant (adjusted estimate, -0.7; 95% CI, -2.2 to 0.9;  $P = .41$ ). Among 399 symptomatic individuals who reported a symptom onset date, the difference in mean Ct values between symptomatic children and symptomatic adults remained not significant after adjusting for swab type and for the number of days between symptom onset and swab collection (adjusted estimate, 0.5; 95% CI, -1.0 to 2.0;  $P = .50$ ). The difference in mean Ct value between asymptomatic children and adults was also not significant (adjusted estimate, -0.6; 95% CI, -4.0 to 2.8;  $P = .74$ ). No evidence of interaction by age and symptom status was found. Mean SARS-CoV-2 Ct values (as a continuous variable) did not vary significantly across age, even when adjusted for swab type (Figure 3).

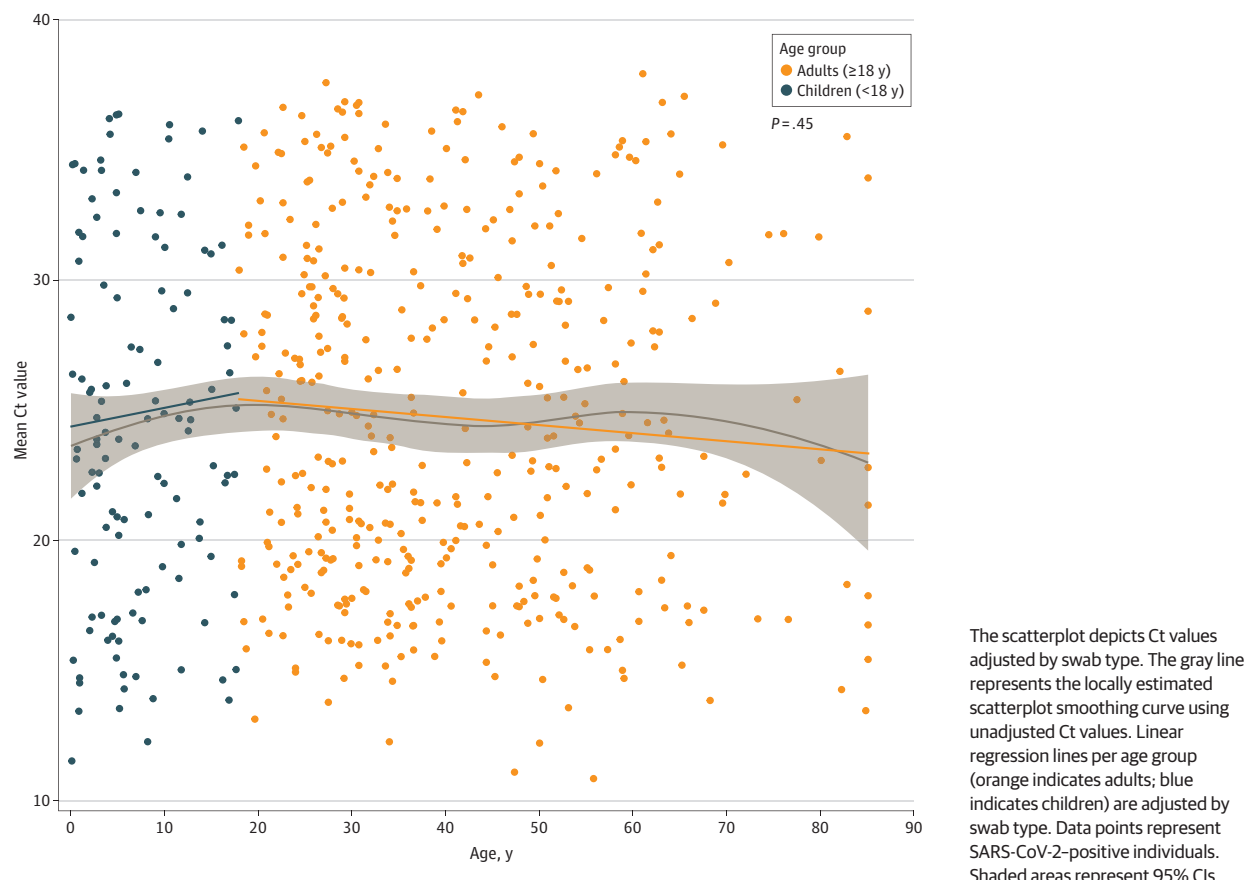
There was a nonsignificant association of lower mean Ct values with an increase in the number of symptoms reported (eFigure 7 in the Supplement). Longer time since symptom onset to date of swab collection was associated with higher Ct values. There was not a significant difference between children and adults in this association (eFigure 8 in the Supplement).

## Discussion

This countywide community-based study of SARS-CoV-2 infection in King County, Washington, showed that symptomatic individuals had lower Ct values than those who were asymptomatic. Ct values did not differ significantly between asymptomatic children vs asymptomatic adults or in symptomatic children vs symptomatic adults. This study was unique in that participant-driven community-wide surveillance was instituted in a large metropolitan area using methods without direct participant contact and directed at persons who were not actively seeking medical care or follow-up.

Overall, children with documented SARS-CoV-2 infection in our study were younger, with 40% younger than 5 years, than in other community-based studies.<sup>17-19</sup> A variety of signs and symptoms were reported by SARS-CoV-2-positive children or their caregivers, with runny nose documented in nearly half of the children, followed by fever, headache, and cough. The predominance of rhinorrhea contrasts with other studies, which have shown fever and cough to be more common symptoms.<sup>17,31,32</sup> The variation in symptoms and lack of predictive value of specific symptoms have been suggested as rea-

Figure 3. Mean SARS-CoV-2 Orf1b Cycle Threshold (Ct) Values by Age



sons for failure of symptom-based testing when screening children for COVID-19.<sup>33</sup>

This study was not designed to measure the prevalence of asymptomatic SARS-CoV-2 infection. The high proportion of asymptomatic infection we observed in children is within the upper limit of the asymptomatic ranges of 40% to 45% estimated in other studies.<sup>34,35</sup> The high proportion of asymptomatic infection we observed in children might be attributed to household enrollment of children following interest in study participation from adults with symptoms. The true frequency of asymptomatic SARS-CoV-2 infection might be closer to 16% to 22%, as suggested by other pediatric studies.<sup>16,32,35,36</sup>

Because we only assessed symptoms at one point before specimen collection, it is possible that we misclassified some participants who were presymptomatic (who would be expected to have low Ct values) as asymptomatic. Regardless, we were able to show a significant difference in Ct values between symptomatic and asymptomatic groups. Our findings of higher SARS-CoV-2 Ct values in asymptomatic children corroborate results from a small study of asymptomatic and mildly symptomatic SARS-CoV-2-positive children in South Korea<sup>16</sup> and a large study of asymptomatic and symptomatic SARS-CoV-2-positive children from 9 US pediatric hospital testing programs.<sup>15</sup> Two large community-based studies found similar SARS-CoV-2 Ct values in symptomatic and asymptomatic children.<sup>17,18</sup> In these studies, children were tested as part of contact tracing, and both asymptomatic and sympto-

matic children might have had similarly low Ct values because of recent exposures to infected individuals. In contrast to early studies, which suggested that symptomatic children might have lower Ct values than symptomatic adults,<sup>37,38</sup> we did not find a significant difference in SARS-CoV-2 Ct values between symptomatic children and symptomatic adults. As these prior studies included participants who sought medical attention, they likely involved more acutely ill children who might have had higher SARS-CoV-2 RNA levels corresponding to lower Ct values. For both symptomatic and asymptomatic individuals, SARS-CoV-2 Ct values did not vary by age when compared as a continuous or categorical variable (ie, children and adults), corroborating studies that examined viral loads and age.<sup>1,19,39,40</sup> However, the comparison of SARS-CoV-2 Ct values between children and adults depends on the proportion of symptomatic vs asymptomatic individuals in each group and might differ in other settings.

The mechanisms of how SARS-CoV-2 RNA levels might influence transmission have yet to be fully delineated. One large retrospective cohort study suggested that children and adolescents were more likely to transmit SARS-CoV-2 in households.<sup>41</sup> In contrast, multiple studies of household infections have suggested that children are not the key drivers of SARS-CoV-2 transmission.<sup>18,42-44</sup> It could be that lack of symptoms is associated with decreased viral transmission; studies have found lower relative risks of SARS-CoV-2 transmission from asymptomatic infected household members<sup>35,41,45</sup> and close contacts.<sup>46</sup>

Another explanation is that asymptomatic infected individuals have lower levels of transmissible SARS-CoV-2 owing to their ability to rapidly clear the virus.<sup>47,48</sup> In regards to disease acquisition, most transmission studies suggest that children might be less susceptible to SARS-CoV-2 infection.<sup>41,44,45,49</sup> In contrast, a household seroprevalence study suggests that children are at equal risk as adults for SARS-CoV-2 infection.<sup>50,51</sup> Current epidemiologic tracing methods might not be detecting asymptomatic infections or infections associated with brief windows of viral detection. Transmission studies have focused on household transmission and even those studies might have been confounded by school and daycare closures, which precluded evaluation of transmission within school or daycare settings. In the King County, Washington, region, public schools were closed for in-person learning during the study period. This may have decreased the number of SARS-CoV-2-positive children and our data may be reflective of secondary SARS-CoV-2 infections transmitted primarily from adult household members. As a result, studies completed thus far might not have fully identified the potential transmission risks by children. To confirm whether there are age-dependent factors associated with SARS-CoV-2 transmissibility, more epidemiological studies are needed.

### Limitations

Our study had limitations. First, enrollment in the study relied on individuals to self-request home-collection kits. Individuals needed to be familiar with the study and to have had access to a device with internet capabilities. Therefore, while our study aimed to sample from across various demographic categories (eg, age, race/ethnicity, residence, and household income), our study findings might not be representative of the county population as a whole or completely generalize to other US counties. Second,

demographic and illness-related information were self-reported and therefore subject to response bias. Although the study accepted both asymptomatic and symptomatic individuals, individual self-reporting of symptoms might have been biased by participant-perceived eligibility criteria. Third, the exact duration of symptoms prior to obtaining a swab were self-reported and not independently verified. Fourth, the number of children enrolled increased in the later part of the study when we switched to using AN swabs because of supply chain disruptions. Because AN swabs had higher yield of viral RNA compared with MTB swabs, likely because of increased comfort and ease of swabbing, we adjusted for the different types of swabs in our analysis. Fifth, this study relied on Ct values from semiquantitative RT-PCRs as proxies for viral RNA levels; more studies using quantitative RT-PCRs to generate direct viral RNA levels are needed. Sixth, the cross-sectional design of this study in addition to brief delays between symptom reporting and swab collection might have led to misclassification of asymptomatic and presymptomatic individuals at the time of sample collection. Characteristics, including Ct values, might differ between these 2 groups.

### Conclusions

In this community-based cross-sectional study, SARS-CoV-2 RNA levels, as determined by RT-PCR Cts, were significantly higher in symptomatic individuals than in asymptomatic individuals. There were no significant differences in RNA levels in asymptomatic children vs asymptomatic adults or in symptomatic children vs symptomatic adults. Further research is needed to understand the role of SARS-CoV-2 RNA levels in transmission among children and adults.

#### ARTICLE INFORMATION

**Accepted for Publication:** May 10, 2021.

**Published Online:** June 11, 2021.

doi:10.1001/jamapediatrics.2021.2025

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**Conflict of Interest Disclosures:** Drs Adler and Lockwood and Ms Lacombe report grants from the Bill and Melinda Gates Foundation during the conduct of the study. Dr Shendure is a consultant with Guardant Health, Maze Therapeutics, Camp4 Therapeutics, Nanostring, Phase Genomics, Adaptive Biotechnologies, and Stratos Genomics; and has a research collaboration with Illumina. Dr Boeckh is a consultant for Moderna, VirBio, and Merck; has received research support from Regeneron, Ridgeback, Merck, and VirBio outside the submitted work; and has received research support from the Bill and Melinda Gates Foundation during the conduct of the study. Dr Hughes reports grants from the Bill and Melinda Gates Foundation during the conduct of the study and National Institutes of Health outside the submitted work. Dr Bedford reports grants from the Bill and Melinda Gates Foundation, The Pew Charitable Trusts, and the National Institute of General Medical Sciences during the conduct of the study. Dr England receives research support paid to her institution from AstraZeneca, the Bill and Melinda Gates Foundation, Chimerix, GlaxoSmithKline, Novavax, Merck, and Pfizer; and is a consultant for Sanofi Pasteur and Meissa Vaccines. Dr Chu has served as a consultant with Ellume, Pfizer, the Bill and Melinda Gates Foundation, GlaxoSmithKline, and



Merck; and has received research funding from Sanofi Pasteur and support and reagents from Ellume and Cepheid outside of the submitted work. No other disclosures were reported.

**Funding/Support:** This work was funded by the Bill and Melinda Gates Foundation. This work was supported in part by the National Institutes of Health (grant T32HD007233 to Dr Chung). Dr Bedford is a Pew Biomedical Scholar and is supported by National Institutes of Health grant R35 GM119774-01.

**Role of the Funder/Sponsor:** The funders had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

**Disclaimer:** The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention or the funder.

**Additional Contributions:** We thank the study participants for their contribution of samples.

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