

1 Durability of SARS-CoV-2 Antibodies from Natural Infection in Children and Adolescents

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33 decision to submit this paper for publication.

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45 **Abbreviations:**

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47 **COVID-19:** coronavirus disease 2019

48 **DSHS:** Department of State Health Services

49 **SARS-CoV-2:** severe acute respiratory syndrome coronavirus 2

50 **Texas CARES:** Texas COVID-19 Antibody Response Survey

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55 **Contributors' Statement Page**

56 Drs. Boerwinkle, Lakey, Pont, Shuford, and Valerio-Shewmaker conceptualized and designed
57 the Texas CARES study.

58 Dr. Messiah drafted the initial manuscript and reviewed and revised the manuscript based on all
59 other authors input.

60 Drs. Shewmaker, Kohl and Kelder and Jessica Ross designed the data collection instruments and
61 collected data. Michael Gonzalez programmed all survey questions in REDCap.

62 Frances Brito carried out the initial analyses and reviewed and revised the manuscript. Drs.
63 DeSantis, Swartz and Yaseen reviewed all analyses.

64 Leqing Wu, Shiming Zhang and Dr. Omega-Njemnobi coordinated and supervised data
65 collection, and critically reviewed the manuscript for important intellectual content.

66 All authors approved the final manuscript as submitted and agree to be accountable for all
67 aspects of the work.

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Abstract

Background. Recent data suggest the SARS-CoV-2 Delta (B.1.617.2) variant is more transmissible among children compared to the Alpha (B.1.1.7) variant. The true incidence and longitudinal presence of antibody response to SARS-CoV-2 infection is not known, however. We provided estimates of antibody response using Texas Coronavirus Antibody REsponse Survey (Texas CARES) data, a prospective population-based seroprevalence project designed to assess antibody status over time among the general population throughout the state.

Methods. In October 2020 Texas CARES began enrolling adults (aged 20-80 years) and children (aged 5-19 years). Participants were offered a series of three SARS-CoV-2 antibody tests over 6-8 months, or every 2-3 months that includes the immunoassay for detection of antibodies to the SARS-CoV-2 nucleocapsid protein (Roche N-test). Descriptive characteristics and COVID-19 infection-related symptom status was determined by questionnaire at the time of enrollment and prior to each successive blood draw. This analysis included participants ages 5-to-19 years old who have completed all three antibody assessments.

Results. From our sample (n=159; mean age 12.5 years, SD 3.6), 96% of those with evidence of nucleocapsid antibodies at baseline assessment continued to have antibodies > six months later (mean 7.0 months, SD 0.97). There was no difference in the presence of antibodies by symptom status (asymptomatic versus symptomatic) or severity (mild-moderate versus severe), sex, age group, or body mass index group (underweight, healthy weight, overweight, obesity) over the three antibody measurement timepoints.

Conclusions. These results suggest that infection-induced antibodies persist and thus may provide some protection against future infection for at least half a year. 57.9% of the sample were negative for infection-induced antibodies at their third measurement point, suggesting a significant proportion of children have still not acquired natural infection.

118 **Introduction**

119 As of November 11, 2021 more than 6.6 million children in the United States have tested
120 positive for COVID-19.¹ In early September, child COVID-19 cases peaked at 252,000 new
121 cases per week and have declined since but remain extremely high. Since the first week of
122 September, there have been almost 1.5 million additional child cases.¹ These recent data suggest
123 the delta (B.1.617.2) variant is more transmissible among children compared to the alpha (B.1.1.7)
124 variant.¹ These data are particularly troubling as they coincide with school openings
125 across the country. Information about the durability of SARS-CoV-2-specific natural immune
126 responses in children is important to inform school-and community-based transmission
127 mitigation and pediatric vaccination strategies. However, the true incidence and longitudinal
128 presence of antibody response to SARS-CoV-2 infection is not known in the pediatric population
129 due to the high proportion of asymptomatic infection² and prioritization of testing for adults and
130 those with severe illness early in the pandemic.

131 **Methods**

132 The Texas Coronavirus Antibody REsponse Survey (Texas CARES) is an ongoing prospective
133 population-based seroprevalence project designed to assess antibody status over time among a
134 volunteer population throughout the state. The design of Texas CARES has been described
135 previously^{2,3,4} but briefly, includes adults (aged 20-80 years) and children (aged 5-19 years).
136 Texas CARES enrollment commenced in October 2020. Participants ages 5-to-19 years were
137 recruited from large pediatric healthcare systems, Federally Qualified Healthcare Centers, urban
138 and rural pediatric and family medicine practices, health insurance providers, and a social media
139 campaign throughout the state of Texas. Participants were offered a series of three SARS-CoV-2
140 antibody tests over 6-8 months, or every 2-3 months, that includes the immunoassay for

141 detection of antibodies to the SARS-CoV-2 nucleocapsid protein (Roche N-test). The
142 nucleocapsid test uses whole blood and has a sensitivity and specificity exceeding 97%.^{5,6}
143 Descriptive characteristics and COVID-19 infection-related symptom status were determined by
144 questionnaire at the time of enrollment and prior to each successive blood draw. This analysis
145 included participants ages 5-to-19 years old who have completed all three antibody assessments.
146 The presence of SARS-CoV-2 nucleocapsid protein antibodies across the three test timepoints
147 was explored via generalized linear mixed models with a logit link. Random effects for each
148 participant were univariately fit. A likelihood ratio test was performed comparing each model to
149 the intercept-only model to obtain a p-value. All protocols were reviewed and approved by the
150 University of Texas Health Science Center's Committee for the Protection of Human Subjects,
151 but also deemed public health practice by the Texas Department of State Health Services IRB.

152 **Results**

153 From our sample (n=159; mean age 12.5 years, SD 3.6), 96% of those with evidence of
154 nucleocapsid antibodies at baseline assessment continued to have antibodies > six months later
155 (mean 7.0 months, SD 0.97). Two children seroconverted from positive to negative status
156 between their first and second antibody test. Ten children seroconverted from negative to
157 positive between their first and second antibody test, and six between their second and third tests,
158 respectively. There was no difference in the presence of antibodies by symptom status
159 (asymptomatic versus symptomatic) or severity (mild-moderate versus severe), sex, age group, or
160 body mass index group (underweight, healthy weight, overweight, obesity) over the three
161 antibody measurement timepoints. (Table 1)

162 N-test values to detect the presence of IgM, IgG, or IgA antibodies increased from baseline to
163 timepoint two and then decreased by the third immunoassay assessment. The subsequent

164 downward trend was significant between timepoints 1 and 3 ($P=0.007$) and timepoints 2 and 3
165 ($P<0.001$) (Figure1).

166 **Discussion**

167 The data reported here show that the majority of children followed for > six months and
168 who had three successive antibody test results available for analysis retained SARS-CoV-2
169 antibodies over the entire time period regardless of age, sex, COVID-19 symptom status and
170 severity, and body mass index. These results suggest that infection-induced antibodies persist
171 and thus may provide some protection against future infection for at least half a year. We were
172 unable to confirm COVID-19 infection prior to the baseline assessment, thus these data cannot
173 confirm durability beyond six months. It should also be noted that well over half (57.9%) of the
174 sample were negative for infection-induced antibodies at their third measurement point,
175 suggesting a significant proportion of children are still immune-naïve to SARS-CoV-2 due to
176 natural infection. As such, vaccines have an important role to play in providing protection
177 against COVID-19 for children aged 12 years and older, and for those < 12 years as they become
178 eligible.

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188 Ashraf Yaseen, PhD; Luis León-Novelo, PhD; Eric Boerwinkle, PhD; Jessica Ross, BS; Frances
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203 **Data Sharing Statement**

204 Texas CARES investigators are committed to data sharing. Granular results and user-specified
205 data summaries are currently publicly available on the Texas CARES portal
206 (<https://sph.uth.edu/projects/texascares/dashboard>). When baseline recruitment is complete, a
207 deidentified individual level dataset will be available for download from the same portal.

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254 **Table 1. Sars-CoV-2 antibody status over 3 timepoints (each separated by 2-3 months) by**
 255 **symptom status and severity and descriptive characteristics.**
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	Timepoint 1 (N=159)		Timepoint 2 (N=159)		Timepoint 3 (N=159)		p-value ^a
	Positive	Negative	Positive	Negative	Positive	Negative	
	53 (33.3%)	106 (66.6%)	61 (38.4%)	98 (61.6%)	67 (42.1%)	92 (57.9%)	
<i>Symptom Status</i>							0.498
Symptomatic	25 (50.0%)	30 (29.4%)	26 (44.8%)	29 (30.9%)	26 (40.6%)	29 (33.0%)	
Asymptomatic	25 (50.0%)	72 (70.6%)	32 (55.2%)	65 (69.1%)	38 (59.4%)	59 (67.0%)	
Missing	3	4	3	4	3	4	
<i>Symptom Severity^b</i>							0.872
Mild-Moderate	21 (87.5%)	24 (80.0%)	21 (84.0%)	24 (82.8%)	21 (84.0%)	24 (82.8%)	
Severe	3 (12.5%)	6 (20.0%)	4 (16.0%)	5 (17.2%)	4 (16.0%)	5 (17.2%)	
<i>Sex</i>							0.942
Males	22 (42.3%)	43 (40.6%)	25 (41.7%)	40 (40.8%)	28 (42.4%)	37 (40.2%)	
Females	30 (57.7%)	63 (59.4%)	35 (58.3%)	58 (59.2%)	38 (57.6%)	55 (59.8%)	
<i>Age Group</i>							0.977
5-9 years	15 (28.3%)	23 (21.7%)	16 (26.2%)	22 (22.4%)	17 (25.4%)	21 (22.8%)	
10-14 years	20 (37.7%)	48 (45.3%)	25 (41.0%)	43 (43.9%)	30 (44.8%)	38 (41.3%)	
15-19 years	18 (34.0%)	35 (33.0%)	20 (32.8%)	33 (33.7%)	20 (29.9%)	33 (35.9%)	
<i>Body Mass Index Group^c</i>							0.117
Underweight	1 (2.1%)	4 (4.0%)	1 (1.8%)	4 (4.3%)	2 (3.3%)	3 (3.4%)	
Healthy	31 (64.6%)	66 (65.3%)	37 (66.1%)	60 (64.5%)	40 (65.6%)	57 (64.8%)	
Overweight	8 (16.7%)	21 (20.8%)	10 (17.9%)	19 (20.4%)	11 (18.0%)	18 (20.5%)	
Obesity	8 (16.7%)	10 (9.9%)	8 (14.3%)	10 (10.8%)	8 (13.1%)	10 (11.4%)	
Missing	5	5	5	5	6	4	

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258 ^ap value calculated from likelihood ratio test

259 ^bPercent of symptomatic children total

260 ^cBased on standardized body mass index percentiles adjusted for age and sex

261 (<https://www.cdc.gov/nccdphp/dnpao/growthcharts/resources/sas.htm>)

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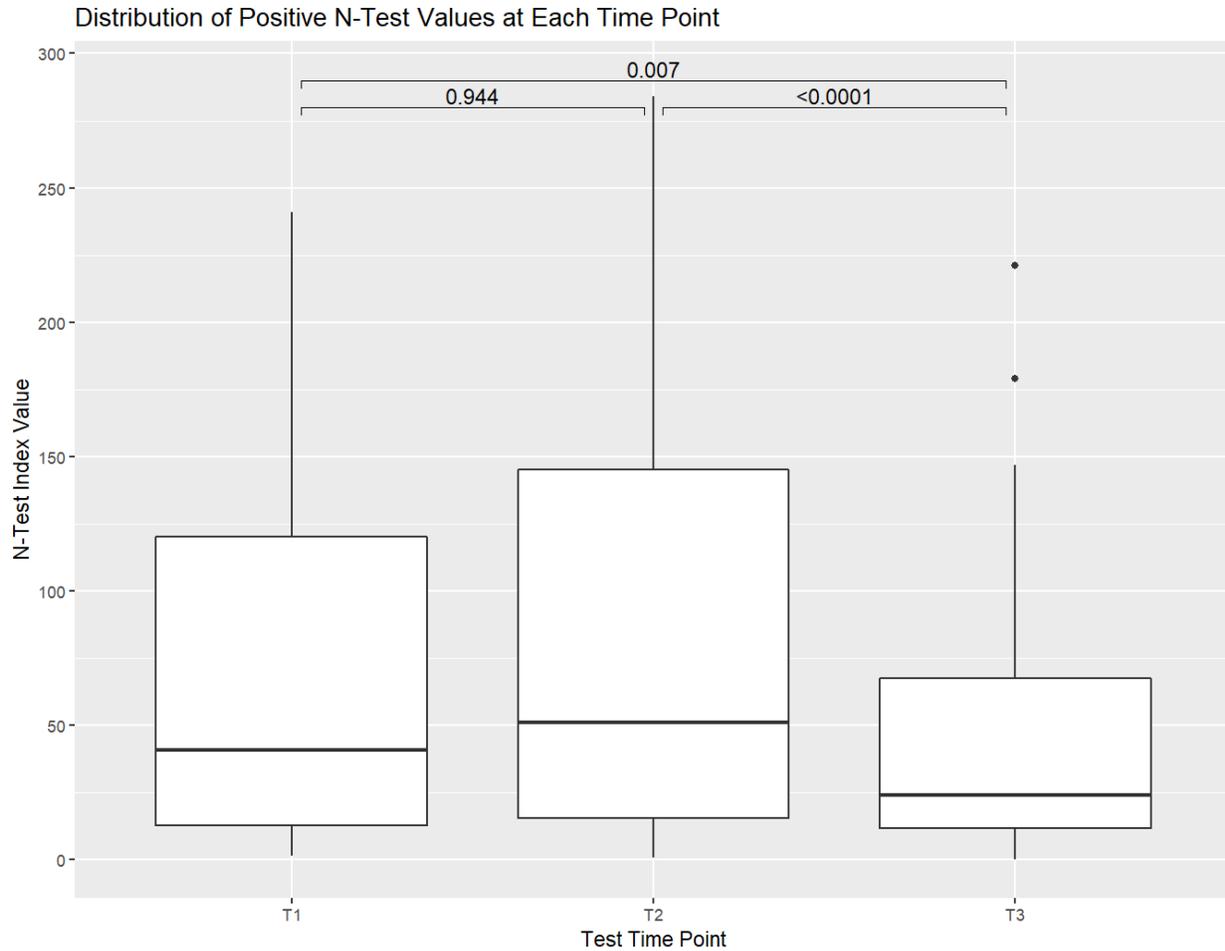
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271 **Figure 1.** Boxplots of N-test values at each time point.

272 Boxplot for the N-test values across the three timepoints for the sample that were positive at the first timepoint
273 (N=53). The N-test value denotes prior COVID-19 infection. Each box represents data falling between the 25th and
274 the 75th percentiles. The horizontal bar within the box represents the median, and the whiskers extend 1.5 times the
275 interquartile range below the 25th and above the 75th percentiles, and the points that lie beyond the whiskers can
276 be considered extreme values.

277 P values calculated by Wilcoxon Signed Rank test. Note that this is not a test for the difference in medians, but
278 rather a non-parametric test for differences in sets of pairs.

279 *significant at the p=0.05 level

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