

teachers and 20 schoolteachers in Sweden received intensive care for Covid-19 up until June 30, 2020 (20 per 103,596 schoolteachers, which is equal to 19 per 100,000). As compared with other occupations (excluding health care workers), this corresponded to sex- and age-adjusted relative risks of 1.10 (95% confidence interval [CI], 0.49 to 2.49) among preschool teachers and 0.43 (95% CI, 0.28 to 0.68) among schoolteachers (see the Supplementary Appendix).

The present study had some limitations. We lacked data on household transmission of Covid-19 from schoolchildren, and the 95% confidence intervals for our results are wide.

Despite Sweden's having kept schools and preschools open, we found a low incidence of severe Covid-19 among schoolchildren and children of preschool age during the SARS-CoV-2 pandemic. Among the 1.95 million children who were 1 to 16 years of age, 15 children had Covid-19, MIS-C, or both conditions and were admitted to an ICU, which is equal to 1 child in 130,000.

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## Duration of Culturable SARS-CoV-2 in Hospitalized Patients with Covid-19

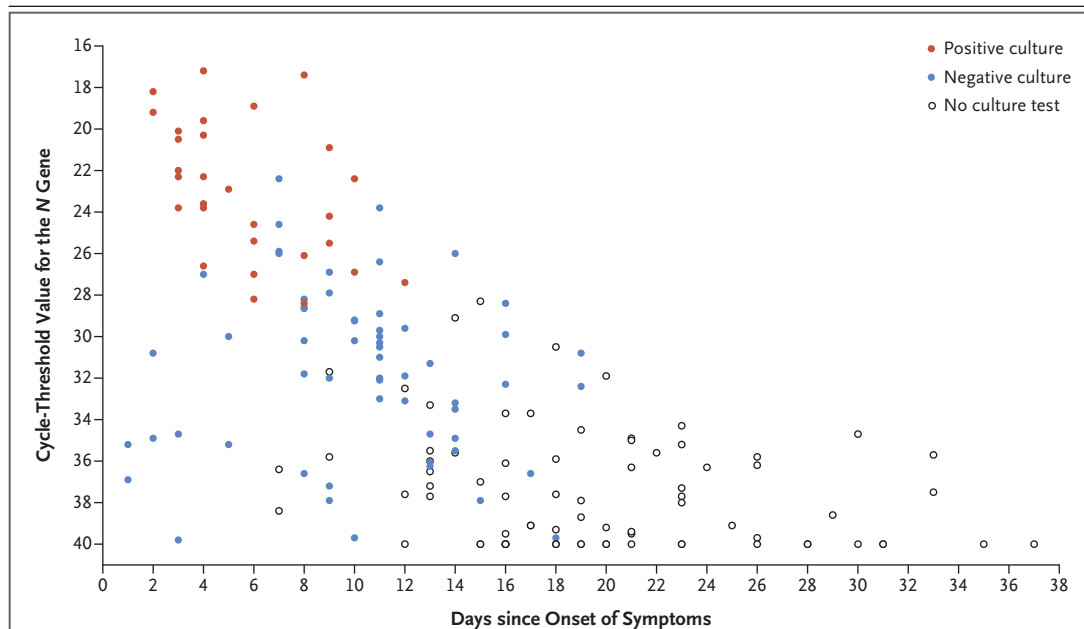
**TO THE EDITOR:** The duration of transmissibility of coronavirus disease 2019 (Covid-19) and the associated level of contagion have been uncertain. We cultured severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in serial respiratory samples obtained from hospitalized patients with Covid-19 to assess the duration of shedding of viable virus.

The data reported here represent all the patients with Covid-19, as confirmed by positive real-time reverse transcriptase–polymerase chain reaction (RT-PCR) testing, who were hospitalized at Chung-Ang University Hospital in Seoul, South Korea, between February and June 2020. The Allplex 2019-nCoV Assay (Seegene) for nasopharyngeal and oropharyngeal samples was used for real-time RT-PCR testing.<sup>1</sup> Patients were isolated until two consecutive negative or inconclusive results on real-time RT-PCR were document-

ed, at least 24 hours apart.<sup>2,3</sup> We endeavored to obtain samples at approximately 2-day intervals, but this was not always possible. Viral RNA was quantitated with the use of the cycle-threshold value for the N gene of SARS-CoV-2.<sup>4</sup> Viral cultures were conducted by means of a plaque assay until at least two consecutive cultures showed no growth.

We compared the time from the onset of illness to viral clearance in culture with the time to clearance in real-time RT-PCR tests.<sup>5</sup> Detailed methods and sensitivities of the culture and real-time RT-PCR assay and the definition and estimation of the time to viral clearance are described in the Supplementary Appendix, available with the full text of this letter at NEJM.org.

A total of 21 patients with Covid-19 were enrolled. Their clinical characteristics are shown in Table S1 in the Supplementary Appendix. The



**Figure 1. Timing of Presence or Absence of Viable SARS-CoV-2 on Viral Culture and Cycle-Threshold Values for 165 Serial Samples Obtained from 21 Consecutive Patients Hospitalized with Covid-19.**

Viral loads were determined with the cycle-threshold value for the *N* gene of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).<sup>4</sup> Sampling intervals ranged from 1 to 5 days (median, 2). Each circle represents a sample obtained on the specified day. Viral culture was positive only in samples with a cycle-threshold value of 28.4 or less and in those that were obtained as long as 12 days after symptom onset. Covid-19 denotes coronavirus disease 2019.

median age of the patients was 62 years, and 76% of the patients were men. A total of 71% of the patients had pneumonia, and 38% were receiving supplemental oxygen therapy. The median Sequential Organ Failure Assessment (SOFA) score was 0 (scores range from 0 to 24, with higher scores indicating more severe organ dysfunction and a higher risk of death), and the median Acute Physiology and Chronic Health Evaluation (APACHE) II score was 5 (scores range from 0 to 71, with higher scores indicating more severe disease and a higher risk of death); these scores indicated mild-to-moderate illness. A total of 165 samples were tested by means of real-time RT-PCR at intervals of 1 to 5 days (median, 2). Of these 165 samples, 89 were cultured for SARS-CoV-2. The timing of the tests, the kinetics of the viral loads, and the clinical course in each patient are shown in Table S2.

SARS-CoV-2 was cultured in 29 of the 89 samples (33%) (Fig. 1). The median time from symptom onset to viral clearance in culture was 7 days (95% confidence interval [CI], 5 to 10), and the

median time from symptom onset to viral clearance on real-time RT-PCR was 34 days (lower boundary of the 95% CI, 24 days) (Fig. S1 and Table S4). The latest positive viral culture was 12 days after symptom onset (in Patient 6). Viable virus was identified until 3 days after the resolution in fever (in Patient 14). Viral culture was positive only in samples with a cycle-threshold value of 28.4 or less. The incidence of culture positivity decreased with an increasing time from symptom onset and with an increasing cycle-threshold value (Table S3).

Our findings may be useful in guiding isolation periods for patients with Covid-19 and in estimating the risk of secondary transmission among close contacts in contact tracing. Given the small sample size, inconsistent timing of sampling, and relatively mild illness of the enrolled patients, our results should be verified in larger and more diverse groups of patients.

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## Five-Year Outcomes for Refractory B-Cell Lymphomas with CAR T-Cell Therapy

**TO THE EDITOR:** CD19-directed chimeric antigen receptor (CAR)-modified T cells are now widely used to treat some relapsed or refractory aggressive B-cell lymphomas.<sup>1-5</sup> However, data on outcomes beyond 2 years after CAR T-cell infusion are limited. We previously reported 28-month outcomes in patients with relapsed or refractory diffuse large B-cell lymphoma and follicular lymphoma who were treated with CD19-directed, 4-1BB costimulated CAR T cells (tisagenlecleucel [CTL019]).<sup>5</sup> We now report the results of the 5-year outcomes of that trial.

Patients were followed for a median of 60.7 months. Assignment to trial groups and the characteristics of the patients and lymphomas are described in Figure S1 and Tables S1 and S2 in the Supplementary Appendix, available with the full text of this letter at NEJM.org. Complete or partial responses were observed in 14 of 24 patients with diffuse large B-cell lymphoma (best overall response [i.e., the percentage of patients with a complete or partial response], 58%), with 11 of 24 patients (46%) having a complete response; at 5 years, progression-free survival was

31% (95% confidence interval [CI], 14 to 51) (Fig. 1A). The median duration of response was 61.4 months (95% CI, 3.2 to could not be estimated), with 60% of patients (95% CI, 27 to 82) having a sustained response at 5 years (Fig. S2A). Of the patients with follicular lymphoma, complete or partial responses were observed in 11 of 14 patients (best overall response, 79%), with 10 of 14 (71%) having a complete response. At 5 years, 43% of patients (95% CI, 18 to 66) were progression-free (Fig. 1B). The median duration of response has not been reached (95% CI, 9.5 months to could not be estimated), and 60% (95% CI, 25 to 83) had a sustained response at 5 years (Fig. S2B). Lymphodepletion regimens varied but did not affect clinical outcomes (Table S3).

We assessed the long-term persistence of CTL019 cells. In the patients who had complete remissions beyond 1 year, the CAR19 transgene was continuously detectable throughout the follow-up period in 6 of 12 patients (50%) by quantitative polymerase-chain-reaction assay (median duration, 39.4 months; range, 22.5 to 57.3); transgene could not be detected in 4 patients