Household Transmission of SARS-CoV-2 from Children and Adolescents

TO THE EDITOR: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in children is often asymptomatic or results in only mild disease.[1] Data on the extent of transmission of SARS-CoV-2 from children and adolescents in the household setting, including transmission to older persons who are at increased risk for severe disease, are limited.[2] After an outbreak of coronavirus disease 2019 (Covid-19) at an overnight camp,[3] we conducted a retrospective cohort study involving camp attendees and their household contacts to assess secondary transmission and factors associated with household transmission (additional details are provided in the Methods section in the Supplementary Appendix, available with the full text of this letter at NEJM.org).

We interviewed 224 index patients who were

Table 1. Unadjusted and Adjusted Odds Ratio for a Secondary Case of SARS-CoV-2 Infection among Household Contacts.*

Variable	Univariable Model	Multivariable Model
	Unadjusted Odds Ratio (95% CI)	Adjusted Odds Ratio (95% CI)
Index patients†		
Age — yr		
7–10	2.3 (0.7–7.0)	0.7 (0.2–2.9)
11–15	1.1 (0.5–2.8)	0.7 (0.3–1.6)
16–19	1.0 (reference)	1.0 (reference)
Covid-19 symptom status		
Symptomatic	5.5 (0.8–40.7)	5.5 (0.8–38.1)
Asymptomatic	1.0 (reference)	1.0 (reference)
Maintained physical distancing		
Yes	0.3 (0.1–0.6)	0.4 (0.1–0.9)
No	1.0 (reference)	1.0 (reference)
Always wore a mask around household contacts		
Yes	0.2 (0.1–0.6)	0.5 (0.2–1.3)
No	1.0 (reference)	1.0 (reference)
Household contacts†		
Contact with index patient‡		
Direct contact	8.2 (2.7–24.7)	5.8 (1.8–18.8)
Close contact	5.4 (1.4–20.9)	5.2 (1.2–22.5)
Minimal to no contact	1.0 (reference)	1.0 (reference)

* A generalized-estimating-equation approach with an exchangeable correlation structure was used to account for intrahousehold correlation. For the multivariable analysis, key characteristics of the index patients (i.e., age, the presence of coronavirus disease 2019 [Covid-19] symptoms, isolation from other persons, and mask use) and the level of contact between the household member and the index patient were selected. The model was fitted after calculation of variance inflation factors to evaluate the resulting design matrix for multicollinearity; all the variance inflation factor values were below 2, which indicated minimal correlation among the model variables. Confidence intervals were not adjusted for multiplicity. Households with more than one index patient were excluded from the univariable and multivariable models. CI denotes confidence interval, and SARS-CoV-2 severe acute respiratory syndrome coronavirus 2.

† An index patient was defined as a camp attendee for whom evidence of SARS-CoV-2 infection on molecular or antigen testing was reported and who had the earliest date of onset of Covid-19 in the household. A household contact was defined as a person who stayed in the household for at least 1 night during the period when the index patient was infectious (i.e., from 2 days before the date of onset of Covid-19 until 10 days after the date of onset of Covid-19).

‡ Direct contact included being a caregiver of the index patient, having face-to-face contact with the index patient, being within 6 ft of the index patient while the patient is coughing or sneezing, or having physical contact with the index patient. Close contact included being within 6 ft of the index patient for at least 15 minutes and sharing a bedroom, meals, or a vehicle.

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7 to 19 years of age and for whom there was evidence of SARS-CoV-2 infection on the basis of molecular or antigen laboratory testing. A total of 198 of these campers (88%) were symptomatic; symptoms developed in 141 of these 198 children or adolescents (71%) after they returned home from camp.

Of 526 household contacts of these index patients, 377 (72%) were tested for SARS-CoV-2, and 46 (12%) of those who were tested had positive results. An additional 2 secondary cases of infection were identified according to clinical and epidemiologic criteria.[4] A total of 38 of the 48 secondary cases (79%) occurred in households where the index patient had become symptomatic after returning home from camp; the median serial interval (i.e., the interval between the onset of symptoms in the index patient and the onset of symptoms in the household contacts infected by that patient) was 5.0 days (95% confidence interval [CI], 4.0 to 6.5). Transmission occurred in 35 of 194 households (18%); in these households, the secondary attack rate was 45% (95% CI, 36 to 54) (48 of 107 household contacts). Among the household contacts who became infected and who were at least 18 years of age, 4 of 41 (10%) were hospitalized (length of hospital stay, 5 to 11 days); none of the 7 persons with a secondary case of infection who were younger than 18 years were hospitalized.

Of the index patients who responded to our question regarding preventive measures, 146 of 217 (67%) reported that they had maintained physical distancing and 73 of 216 (34%) reported that they had always worn masks around contacts during the infectious period after they returned home. In a univariable logistic-regression model, among the index patients who were 18 years of age or younger, the increasing use of physical distancing and masks was associated with the older age of the patient (with age as a continuous variable, odds ratio for physical distancing, 1.4; 95% CI, 1.2 to 1.5; odds ratio for mask use, 1.4; 95% CI, 1.2 to 1.6). In a multivariable regression model, the risk of a secondary case of infection among household contacts was lower among contacts of index patients who had practiced physical distancing than among contacts of index patients who did not (adjusted odds ratio, 0.4; 95% CI, 0.1 to 0.9) (Table 1). Household members who had close or direct contact with the index patient had a higher risk of infection than those who had minimal to no contact (adjusted odds ratio with close contact, 5.2; 95% CI, 1.2 to 22.5; and adjusted odds ratio with direct contact, 5.8; 95% CI, 1.8 to 18.8). We excluded missing data from the regression models, and confidence intervals were not adjusted for multiplicity.

This retrospective study showed that the efficient transmission of SARS-CoV-2 from school-age children and adolescents to household members led to the hospitalization of adults with secondary cases of Covid-19. In households in which transmission occurred, half the household contacts were infected. The secondary attack rates in this study were probably underestimates because test results were reported by the patients themselves and testing was voluntary. In addition, a third of the index patients returned home from camp after the onset of symptoms, when they were presumably not as infectious as they were before and during the onset of symptoms,[5] and two thirds adopted physical distancing because of a known exposure at camp; both of these factors probably reduced the transmission of SARS-CoV-2 in the household. When feasible, children and adolescents with a known exposure to SARS-CoV-2 or a diagnosis of Covid-19 should remain at home and maintain physical distance from household members.

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Adjuvant Nivolumab in Muscle-Invasive Urothelial Carcinoma

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TO THE EDITOR: The benefit of nivolumab maintenance therapy in the study by Bajorin et al. (June 3 issue)[1] appears to have been driven mainly by the 308 patients who received cisplatin as neoadjuvant therapy and reflects cross-sensitivity (hazard ratio, 0.52; 95% confidence interval [CI] 0.38 to 0.71) rather than by the 401 patients who did not (hazard ratio, 0.92; 95% CI, 0.69 to 1.21). This also explains the lack of benefit in the 309 patients with a creatinine clearance of less than 60 ml per minute (hazard ratio, 0.87; 95% CI, 0.64 to 1.18) and by those with primary tumors that did not arise from the bladder (hazard ratios, 1.23 and 1.56 in the renal pelvis and ureter, respectively). In another study,[2] the 269 patients with advanced urothelial cancer who were treated with gemcitabine–carboplatin (hazard ratio, 0.66; 95% CI, 0.47 to 0.91) derived as much benefit from avelumab maintenance as did the 389 patients who were treated with gemcitabine–cisplatin (hazard ratio, 0.69; 95% CI, 0.51 to 0.94), irrespective of creatinine clearance: at 60 ml or more per minute, the hazard ratio was 0.68 (95% CI, 0.50 to 0.92), and at less than 60 ml per minute, the hazard ratio was also 0.68 (95% CI, 0.50 to 0.94).

The lack of benefit in patients of European and Asian ancestry requires clarification and could be related to the use of cisplatin as neoadjuvant therapy, the relative proportion of primary tumors that were not located in the bladder, or the expression of programmed death ligand 1 (PD-L1). Again, the predictive role of PD-L1 expression in the patients who were not eligible to receive cisplatin requires more focus for the purpose of identifying those who derived benefit from adjuvant nivolumab.

TO THE EDITOR: Bajorin et al. recently published the positive results of the phase 3 CheckMate 274 trial, reporting that nivolumab adjuvant therapy is superior to placebo in terms of disease-free survival in patients with radically resected muscle-invasive urothelial carcinoma. These surprising results are discordant with those of the Adjuvant Atezolizumab versus Observation in Muscle-Invasive Urothelial Carcinoma (IMvigor010) trial,[1] which failed to prove the superiority of atezolizumab over observation in the same setting. In comparing the contrasting results of these similar treatments in the adjuvant phase, some questions arise. Why did the placebo group in the CheckMate 274 trial have a relevantly lower rate of disease-free survival than the observation group in the IMvigor010 trial (10.9 vs. 16.6 months)? Why is this difference enhanced in the PD-L1-positive groups, considering that different techniques are used in the evaluation of PD-L1 expression, depending on the immunotherapeutic agent used? Did the different percentages of upper-tract

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