

On the Effect of Age on the Transmission of SARS-CoV-2 in Households, Schools, and the Community

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Background. There is limited information on the effect of age on the transmission of SARS-CoV-2 infection in different settings.

Methods. We reviewed published studies/data on detection of SARS-CoV-2 infection in contacts of COVID-19 cases, serological studies, and studies of infections in schools.

Results. Compared to younger/middle-aged adults, susceptibility to infection for children younger than 10 years is estimated to be significantly lower, while estimated susceptibility to infection in adults older than 60 years is higher. Serological studies suggest that younger adults (particularly those younger than 35 years) often have high cumulative incidence of SARS-CoV-2 infection in the community. There is some evidence that given limited control measures, SARS-CoV-2 may spread robustly in secondary/high schools, and to a lesser degree in primary schools, with class size possibly affecting that spread. There is also evidence of more limited spread in schools when some mitigation measures are implemented. Several potential biases that may affect these studies are discussed.

Conclusions. Mitigation measures should be implemented when opening schools, particularly secondary/high schools. Efforts should be undertaken to diminish mixing in younger adults, particularly individuals aged 18–35 years, to mitigate the spread of the epidemic in the community.

Keywords. SARS-CoV-2; susceptibility; seroprevalence; age; children; young adults; primary schools; secondary schools; high schools.

Among those infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), elderly patients have had the most severe outcomes, including the highest death rates, whereas infected younger persons, particularly children aged 1–18 years, if symptomatic at all, are far more often mildly ill [1]. While this age-dependent pattern of illness severity has become well established, the roles of different age groups in transmission has not been as clear. Recently, evidence has accumulated that susceptibility to infection generally increases with age (eg, [2, 3]). This, however, does not suggest that the oldest individuals necessarily have the highest SARS-CoV-2 incidence—in fact, serological studies suggest that younger adults, particularly those younger than 35 years, often experience the highest cumulative rates of infection [4–8], possibly due to age-related differences in mixing. Additionally, there is uncertainty as to how susceptibility to infection varies with age in children, and how it compares to susceptibility to infection in different age groups of adults. The effect of the ongoing and future openings

of primary, secondary, and high schools and higher-educational institutions on the spread of infection requires a better characterization of transmission dynamics in different age groups. Here, we review the relevant evidence based on household, school, and community studies, and draw some conclusions regarding the relevant public health policies.

AGE VARIATION IN SUSCEPTIBILITY TO INFECTION GIVEN CONTACT

We undertook a literature review using the Living Evidence on COVID-19, a database collecting coronavirus disease 2019 (COVID-19) related published articles from PubMed and EMBASE and preprints from medRxiv and bioRxiv [9], with articles containing the words ([children] OR [age] OR [aged] OR [years old] OR [secondary]) AND ([household] OR [households] OR [contacts]) in the title/abstract, published before 5 October 2020 examined for relevance. Studies were eligible for inclusion if they reported the estimates of either secondary attack rate, susceptibility to, or odds ratio (OR) for infection in different age groups, and where the setting for the contact (eg, household or other), either was the same for all contacts, or was adjusted for (as a covariate in a model) in those estimates (to reduce the effects of heterogeneity in exposure on those estimates).

We used published, deidentified data, with no informed consent from the participants sought.

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Relative Susceptibility to Infection in Children Versus Adults

In this section we present the 14 included studies that assess relative susceptibility for different age groups, describe some potential biases in those studies, and present evidence for lower susceptibility to infection in children younger than 10 years, and higher susceptibility to infection in adults older than 60 years compared to young/middle-aged adults.

PCR-Based Studies of SARS-CoV-2 Infection in Close Contacts

Several studies found much lower secondary attack rates (measured by polymerase chain reaction [PCR]-positive cases among contacts) in children as contacts—using different age cutoffs of children up to age 20 years—compared to adults. In a hospital-based study near Wuhan, China [10], the OR for infection in contacts aged <18 years relative to adults was 0.18 (95% confidence interval [CI], .06–.54). In a Guangzhou, China study [2], the multivariable OR for infection in contacts younger than 20 years versus contacts older than 60 years was 0.23 (95% CI, .11–.46), while for contacts aged 20–59 years versus contacts older than 60 years it was 0.64 (95% CI, .43–.97). For household contacts of confirmed cases in Zhuhai, China [11], the OR for infection in children aged 4–18 years relative to persons aged 19–60 years was 0.09 (95% CI, .01–.73). In a Chinese study of close contacts [3], the multivariable OR for infection in children aged <15 years compared to adults aged 15–64 years was 0.34 (95% CI, .24–.49). In a Hunan, China study [12] the multivariable OR for infection in contacts younger than 15 years versus contacts aged 15–64 years was 0.58 (95% CI, .34–.98). A study modeling transmission within households in Israel [13] found that susceptibility in children younger than 20 years was 0.45 (95% CI, .40–.55) that of adults. For a study of household contacts in New York State [14], the OR for infection in children aged <18 years relative to adults aged 18–29 years was 0.41 (95% CI, .17–.99).

A few studies showed similar secondary attack rate (SAR) in children or adults. For a study of household contacts in Wisconsin and Utah [15], the OR for infection in children aged <18 years relative to adults aged 18–49 years was 0.88 (95% CI, .37–2.02). For the study in Shenzhen, China [16], infection rates in close contacts were similar across age groups. However, 298/391 of index cases in this study were travelers, with joint travel being associated with an OR of 7.1 (95% CI, 1.4–34.9) for infection in close contacts, suggesting the possibility of acquisition of infection at the source of travel and making the interpretation of the estimates in [16] difficult. For a multivariable analysis involving contacts of COVID-19 cases in Guangzhou, China [17], the OR for infection in contacts aged <18 years relative to contacts aged 18–44 years was 0.78 (95% CI, .41–1.50). For household contacts of COVID-19 cases in 2 Indian states [18], OR for infection in children aged <18 years relative to

adults aged 18–34 years was 0.96 (95% CI, .71–1.29). For a study of family members of SARS-CoV-2 cases in Greece [19], OR for infection in pediatric contacts versus adult contacts was 1.69 (95% CI, .7–4.2).

Serological Studies of SARS-CoV-2 Infection in Close Contacts

For a study of household contacts of hospitalized cases in Italy [20], the OR for infection in children aged <18 years relative to adults was 0.77 (95% CI, .27–2.17). For a study of household contacts in Utah and Wisconsin [21] (not retrieved from [9]), the OR for infection in children aged <18 years relative to adults was 1.39 (95% CI, .55–3.53).

Potential Biases for the Estimates of Susceptibility in Children Versus Adults

Estimates of relative susceptibility in children versus adults based on household attack rates may be influenced (generally downward biased) due to contact patterns because certain adult-adult contacts may be more sustained than adult-child contacts: that is, higher secondary attack rates in adults versus children may reflect greater exposure in addition to differences in susceptibility given the same exposure. A serological study of a SARS-CoV-2 outbreak on a US Navy ship [22] found that cumulative incidence of infection was higher among persons who reported sharing the same sleeping berth with a crew member who had positive test results compared with those who did not (OR = 3.3; 95% CI, 1.8–6.1). This suggests that among contacts of an index case in a household, the spouse might face an additional risk for infection due to shared bed or room. In fact, for adult contacts in the Wuhan study [10], the SAR among spouses of index cases was 27.8% (25/90), whereas the SAR among other adults in the household was 17.3% (35/202), with the relative risk (RR) for infection for a spouse of the index case versus a nonspouse adult household contact being 1.60 (95% CI, 1.02–2.51). In the Zhuhai study [11], 12/23 spouses of index cases were infected, compared to 31/89 of other adult contacts of index cases, with the RR for infection being 1.50 (95% CI, .92–2.43).

A second source of bias in the estimated relative susceptibility of children versus adults is the possibility of index misclassification, as for example in the following scenario: a child is infected first in a household and transmits to an adult, but because the child has no or mild symptoms, the child is not tested initially, and the adult is considered the household index. For example, in studies [10–12], conducted early in the pandemic, hospitalized individuals/persons with pneumonia were identified as index cases, and given the underrepresentation of children among severe cases compared to all SARS-CoV-2 infections, pediatric index cases could have been missed in those studies. For studies based on PCR detection of contacts, this error would bias the SAR estimates in children

downward if the true index child is classified as an uninfected pediatric contact, and upwards if the true index child is subsequently detected and misclassified as a secondary case. For serological studies of household contacts, this would bias the SAR estimate in children upward (because the index child is classified as an infected pediatric contact in the estimates of SAR). A further limitation related to serological studies is that they cannot assess whether nonindex cases were infected in the household (eg, delay between infection in the index case and serological testing in [20]).

We note that the last 2 sources of bias may help explain why in studies based on PCR testing of contacts, the estimated susceptibility to infection in children is generally lower than in adults, while in the serological studies of household contacts [20, 21] (where these biases are expected to be upwards for children), the differences in the estimated susceptibility to infection in children and adults are smaller.

Lower Relative Susceptibility to SARS-CoV-2 Infection for Children Younger Than 10 Years Versus Adults

An approach that minimizes these potential biases is to compare infection in different age subgroups of children among household contacts. For one study we reviewed [13], the data are available to compare secondary attack rates in children aged 0–4 years and 5–9 years to those of older children; SAR in these younger groups are less than half those in children aged 15–19 years (Table 5 in [13]). Given that there is no evidence that 15–19 year olds are more susceptible than adults, this within-childhood comparison can support the inference that children younger than 10 years are at most half as susceptible as adults.

Elevated Susceptibility to Infection for Adults Older Than 60 Years Compared to Younger/Middle-aged Adults

The study reported in [2] estimates that for household contacts among persons aged 20–59 years, the OR for infection is 0.64 (95% CI, .43–.97) compared to household contacts older than 60 years. The study reported in [3] estimates that for close contacts among persons older than 65 years, the OR for infection is 1.67 (95% CI, 1.12–1.92) compared to household contacts aged 15–64 years. The study reported in [12] estimates that for close contacts among persons older than 65 years, the OR for infection is 1.64 (95% CI, 1.02–2.63) compared to household contacts aged 15–64 years. For the multivariable analysis involving contacts of COVID-19 cases in Guangzhou, China [17], the OR for infection in contacts older than 60 years relative to contacts aged 18–44 years was 2.34 (95% CI, 1.39–3.97), whereas the OR for infection in contacts aged 45–59 years relative to contacts aged 18–44 years was 1.16 (95% CI, .70–1.92). No significant differences in susceptibility for older versus younger adults were found in the studies reported in [11, 14, 18].

Table 1 summarizes the above estimates for the relative susceptibilities/OR for infection in different age groups.

AGE VARIATION IN INFECTIVITY

There is limited evidence in the literature regarding age-related differences in infectivity, although point estimates in several studies suggest that infectivity may increase somewhat with age. For the household contacts examined in 2 Indian states [18], the OR for infection in contacts of a person aged <18 years versus 40–64 years was 0.63 (95% CI, .32–1.15) and OR was 0.58 (95% CI, .45–.74) for infection in contacts of a person aged 18–39 years versus 40–64 years. The Bnei Brak,

Table 1. Odds Ratios (or Relative Susceptibility) for Infection in Close Contacts of an Infected Person by Age Group Relative to the Reference Age Group in 14 Studies [2, 3, 10–21]

| Study [Reference] | Age Group 1 | | Age Group 2 | | Age Group 3 | | Age Group 4 | | Age Group 5 | |
|-------------------|---|-------------------------|-------------|-------------------|-------------|------------------|-------------|------------------|-------------|----------------|
| | Age, y | OR (95% CI) | Age, y | OR (95% CI) | Age, y | OR (95% CI) | Age, y | OR (95% CI) | Age, y | OR (95% CI) |
| PCR, H+C [3] | <15 | 0.34 (.24–.49) | 15–64 | 1 (ref.) | > 65 | 1.67 (1.12–1.92) | ... | ... | ... | ... |
| PCR, H+C [2] | <20 | 0.23 (.11–.46) | 20–59 | 0.64 (.43–.97) | > 60 | 1 (ref.) | ... | ... | ... | ... |
| PCR, H+C [12] | 0–14 | 0.58 (0.34, 0.98) | 15–64 | 1 (ref.) | > 65 | 1.64 (1.02–2.63) | ... | ... | ... | ... |
| PCR, H [11] | 0–3 | 1.13 (.29–4.48) | 4–18 | 0.09 (.01–.73) | 19–60 | 1 (ref.) | > 60 | 1.23 (.51–2.98) | ... | ... |
| PCR, H [14] | <18 | 0.41 (.17–.99) | 18–29 | 1 (ref.) | 30–49 | 1.74 (.70–4.32) | 50–64 | 2.23 (.87–5.75) | > 65 | 1.99 (.67–6.0) |
| PCR, H [10] | <18 | 0.18 (.06–.54) | > 18 | 1 (ref.) | ... | ... | ... | ... | ... | ... |
| PCR, H [13] | <20 | Suscept. 0.45 (.40–.55) | > 20 | Suscept. 1 (ref.) | ... | ... | ... | ... | ... | ... |
| PCR, H+C [17] | 0–17 | 0.78 (.41–1.50) | 18–44 | 1 (ref.) | 45–59 | 1.16 (.70–1.92) | > 60 | 2.34 (1.39–3.97) | ... | ... |
| PCR, H [18] | 0–17 | 0.96 (.71–1.29) | 18–39 | 1 (ref.) | 40–64 | 0.89 (.67–1.19) | > 65 | 1.31 (.75–2.19) | ... | ... |
| PCR, H [15] | 0–18 | 0.88 (.37–2.02) | 18–49 | 1 (ref.) | > 50 | 1.86 (.73–4.65) | ... | ... | ... | ... |
| PCR, H+C [16] | No age-related differences in susceptibility were found | | | | | | | | | |
| PCR, H [19] | <18 | 1.69 (.7–4.2) | > 18 | 1 (ref.) | ... | ... | ... | ... | ... | ... |
| Serology, H [20] | <18 | 0.77 (.27–2.17) | > 18 | 1 (ref.) | ... | ... | ... | ... | ... | ... |
| Serology, H [21] | <18 | 1.39 (.55–3.53) | > 18 | 1 (ref.) | ... | ... | ... | ... | ... | ... |

See the caveats in the “Potential biases for the estimates of susceptibility in children versus adults” section.

Abbreviations: CI, confidence interval; H, household contacts; H+C, household plus community contacts (multivariable analysis adjusting for contact setting, etc.); OR, odds ratio; PCR, study based on polymerase chain reaction testing of close contacts; ref., reference; serology, study based on serological testing of close contacts; suscept, susceptibility.

Israel study [13] estimated the relative infectivity for children younger than 20 years compared to adults as 0.85 (95% CI, .65–1.1). For the multivariable analysis in Hunan, China [12], the OR for infection in contacts of persons aged 0–14 years versus contacts of persons aged 15–64 years was 0.28 (95% CI, .04–2.04), whereas the OR for infection in contacts of persons older than 65 years versus contacts of persons aged 15–64 years was 0.56 (95% CI, .22–1.43). Data from 54 households in the Netherlands [23] yielded lower point estimates for transmissibility of infection to close contacts from children younger than 19 years, and higher point estimates for adults older than 70 years compared to persons aged 19–69 years. For the South Korean study [24], while the household SAR increased with the age of the index for adult index cases, for index cases aged 10–19 years, the household SAR was significantly higher than for index cases aged 20–49 years. However, a related study from South Korea [25] adjusting for potential index misclassification in [24] finds a significantly lower SAR for pediatric indices compared to that for adult indices.

Potential Biases in Infectivity Studies

As in studies of age-specific susceptibility, there may be errors in ascertaining index cases, as well as conflation of differences in infectivity with differences in susceptibility and intensity of contacts.

AGE VARIATION IN SEROPREVALENCE

We reviewed all seroprevalence studies in the Living Evidence on COVID-19 database [9] with words (seroprevalence) OR ((antibody) OR (serological)) AND [survey]) in the abstract/title.

Several serological studies estimate that younger adults, particularly those younger than 35 years, have the highest seroprevalence of all or nearly all age groups. Serological studies in US blood donors, in England, Rio de Janeiro, Brazil, Tokyo, Japan, as well as Heinsberg, Germany, estimate that SARS-CoV-2 seroprevalence is highest in adults younger than 35 years [4–7, 26]. In Geneva, Switzerland, persons aged 20–49 years had the highest estimated seroprevalence, followed by those aged 10–19 years [8].

A serological study in a slum community in Buenos Aires, Argentina found no difference in seroprevalence according to age among those older than 14 years in multivariable analysis, although the highest seroprevalence was found in male adolescents aged 14–19 years [27]. A study of Kenyan blood donors found the highest seroprevalence in persons aged 35–44 years, followed by persons aged 15–34 years [28]. Studies in Corsica [29] and 3 regions in France [30] found that seroprevalence in persons younger than 50 years was significantly higher than in persons older than 50 years. In a serological study in Brazil [31], the highest seroprevalence estimates belong to persons aged 20–59 years. Serosurveillance of adults outside grocery stores in

New York State found that rates of infection in individuals older than 55 years were significantly lower than in persons aged 18–54 years [32]; the highest infection rates in New York State were in persons aged 45–54 years. Serological studies in Los Angeles County and Karachi, Pakistan found similar seroprevalence estimates in different age groups of adults in each study [33, 34]. A serological study in Mumbai, India in which infection rates were found to be high in slum populations, infection rates generally decreased with age in nonslum populations and increased with age in the slum populations [35]. A serological study in Iceland has the highest estimate for the cumulative incidence of infection in persons aged 40–50 years (Figure 2E in [36]), although a sizeable proportion of individuals with serologically confirmed infection were travelers, and rates of seropositivity in different age groups in this study were low. A study of seroprevalence in 10 US locations [37] found that the age group with the highest seroprevalence estimate varied by location, with highest rates observed in adults aged 19–49 years in 3 locations, adults aged 50–64 years in 3 locations, adults aged 65 years and older in 2 locations, and those aged 0–18 years in 2 locations.

For the serological study in Spain [38], the highest seroprevalence for the point-of-care test was in persons older than 50 years, while for the immunoassay, the highest estimates belonged to younger adults. Additionally, serological studies in Hungary [39], Liguria and Lombardia, Italy [40], and Wuhan, China [41] had the highest seroprevalence estimates in persons older than 60 years.

Potential Biases in Seroprevalence Studies

Participants in seroprevalence surveys are almost never fully representative of the source population, as convenience samples might be more likely to reach generally healthy people (eg, blood donors [4, 5, 26, 28, 41]), people who are not sheltering in place (grocery store shoppers [32]), or other groups with unrepresentative risks of exposure. Additionally, estimates of sensitivity and specificity for antibody tests are derived from groups of individuals that might be different from the general population in the serological studies. Overestimation of test sensitivity due to calibration on more severe cases and differences in test sensitivity by age [42] may also complicate interpretation of the estimates and produce downward biases. It is also worth remembering that age-seroprevalence data may reflect the unusual social dynamics of epidemic and/or lockdown periods, and contact patterns may change, leading to different age-specific attack rates, over time.

TRANSMISSION OF SARS-COV-2 IN SCHOOLS

We reviewed all studies related to school outbreaks in the Living Evidence on COVID-19 database [9].

There is some evidence, particularly from spring 2020 [43–45], that given no or limited mitigation measures (eg, limited

testing and quarantine of infected individuals and their contacts in schools, no reduction in class sizes, and limited mask use), robust spread of SARS-CoV-2 can occur in secondary/high schools. A cluster investigation linked to a high school in a town in northern France found high rates of seroprevalence for anti-SARS-CoV-2 antibodies among high school students. While even higher seroprevalence among the school staff was found following an outbreak in that school, much lower seroprevalence was identified among parents and siblings of pupils, suggesting that the school was likely the source of transmission [43]. An outbreak investigation in a regional public school in Jerusalem, Israel found high rates of PCR-detected SARS-CoV-2 infection in both the staff and students in grades 7–9, but not grades 10–12, suggesting that in-school, rather than just community transmission, contributed to the rates of infection in students in grades 7–9 [44]. A serological study in Santiago, Chile [45] following an outbreak that led to a school closure found high rates of anti-SARS-CoV-2 antibody seroprevalence among preschool through secondary school students, with even higher seroprevalence rates among the staff.

There is evidence of a more limited spread of SARS-CoV-2 in primary schools compared to high schools ([43] versus [46]), which agrees with the evidence about lower susceptibility to infection in children younger than 10 years compared to older children or adolescents [13]. Nonetheless, outbreaks have been reported in certain primary schools [45].

Classroom crowding and other factors related to social distancing in classrooms/schools may play a role in the spread of SARS-CoV-2 in schools. The Jerusalem school with an outbreak [44] reported crowded classes with 35–38 students per class. The school serological study in Santiago, Chile [45] concerned a large private school with 14 grades (from preschool to high school) and large class sizes (25–27 students in preschool, 36–38 students in the rest of the school). Some of the infections recorded in this study [45] could have taken place after the school was closed on 13 March 2020. However, following the introduction of infection into a preschool by adults (parent/teacher), seroprevalence in preschool and primary school students was higher than in high school students, suggesting infections in younger students before the school closure.

As suggested above, in-school transmission has likely contributed to the large outbreaks [43–45]. We note the importance of denominator when interpreting school outbreaks as larger outbreaks may be more readily detected, whereas smaller outbreaks where mitigation measures have helped prevent larger outbreaks are less likely to be reported.

There are several examples demonstrating that mitigation measures prevent large outbreaks. During the spring wave of the SARS-CoV-2 epidemic in New South Wales, Australia, a small number of secondary infections were recorded in a small number of schools where cases were found [47], with widespread testing in schools and schools being closed for 24–48

hours following case detection with contacts of detected cases subsequently quarantined. In Baden-Württemberg, Germany, where halving of group sizes and other mitigation efforts (although not mask use) were implemented [48], of 137 detected cases of infection in schoolchildren, only 6 were found to have caused further infections in the school setting despite extensive contact tracing (infecting a total of 11 of 1155 close contacts). A national study of COVID-19 outbreaks in schools in Germany found that those outbreaks were small, with about half the cases being the school staff [49]. A variety of mitigation measures including staggering timetables and restricting class sizes were applied throughout Germany [49]. In the Salt Lake County, Utah school study, where masks in schools were mandated, the vast majority of reported outbreaks in schools were small (under 15 cases, p. 10 in [50]), with a fewer, larger outbreaks mostly taking place in high schools.

CONCLUSIONS

We found evidence that compared to younger/middle-aged adults, children younger than 10 years have significantly lower estimated susceptibility to SARS-CoV-2 infection, while adults older than 60 years have elevated susceptibility to infection, and they merit extra efforts for protection against infection (such as allocating certain time slots for grocery shopping among the elderly only, etc.). Some uncertainty remains about the magnitude of the difference in susceptibility of children versus adults due to presence of biases in several published studies. On the other hand, comparisons between younger and older children are arguably more robust and—in the one study that reports them [13]—reach the same conclusion. Future studies using both virological and serological testing of contacts, and stool specimens in addition to upper respiratory samples to decrease the likelihood of missed infections, may help mitigate the biases we describe.

When there is a combination of limited mitigation of SARS-CoV-2 spread in schools and relatively high community transmission, there is evidence of robust SARS-CoV-2 spread in secondary/high schools, and more limited spread in primary schools, with factors such as classroom size possibly affecting that spread. Therefore community transmission levels and combination of mitigation efforts such as social distancing, avoiding crowding/reduction in class size, widespread/timely testing, quarantine for detected cases and their contacts, and mask wearing (especially by teachers) according to the WHO guidelines as well as measures to prevent staff to staff transmission (preventing crowding in teacher rooms, mask wearing) should be considered when opening schools, particularly secondary/high schools.

Notes

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