The role of children in household transmission of SARS-CoV-2 across four waves of the pandemic

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Abbreviations: Cycle threshold (CT), Household (HH); Interquartile range (IQR); Lower and Middle-Income Countries (LMICs); Variant of Concern (VOC)

Summary: We demonstrate the beneficial effects of COVID-19 vaccination in both protecting the individual from severe illness and preventing onward transmission to close contacts.

Following vaccination and the spread of variants, children remained less infectious than adults in the household setting.

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Abstract

Background

It is important to understand the dynamics of SARS-CoV-2 transmission in close-contact settings such as households. We hypothesized that children would most often acquire SARS-CoV-2 from a symptomatic adult caregiver.

Methods

This prospective cohort study was conducted from April 2020 to July 2022 in a low-resource, urban settlement in Brazil. We recruited families who brought their children to a public clinic. We collected nasopharyngeal and oral swabs from household members and tracked symptoms and vaccination.

Results

In total, 1,256 participants in 298 households were tested for SARS-CoV-2. A total of 4073 RT-PCR tests were run with 893 SARS-CoV-2 positive results (21.9%). SARS-CoV-2 cases were defined as isolated cases (n=158) or well-defined transmission events (n=175). The risk of household transmission was lower if the index case was a child (OR: 0.3 [95% CI: 0.16-0.55], $p<0.001$) or was vaccinated (OR: 0.29 [95%CI: 0.1-0.85], $p=0.024$), and higher if the index was symptomatic (OR: 2.53 [95% CI: 1.51-4.26], $p<0.001$). The secondary attack rate for child index cases to child contacts was 0.29, whereas the secondary attack rate from adult index cases to child contacts was 0.47 ($p=0.08$).

Conclusions

In this community, children were significantly less infectious to their household contacts than adolescents or adults. Most children were infected by a symptomatic adult, usually their mother. There was a double benefit of vaccination as it protected the vaccinee from severe illness and prevented onward transmission to household contacts. Our findings may also be valid for similar populations throughout Latin America.

Keywords: SARS-CoV-2 variants; transmission; COVID-19 vaccines; inactivated vaccines; extended family

Introduction

Since preventing mild illness and SARS-CoV-2 transmission remain difficult, it is important to understand the dynamics of such transmission in close-contact settings such as mass events, schools, and households. In households, if the index case is symptomatic and/or unvaccinated, the risk of infection to other household residents is higher [1, 2]. Another factor that may modify spread within a household is the direction of infection between age groups. A systematic review of studies conducted early in the pandemic concluded that household transmission was less likely if the index case was a child than an adult [3]. However, less is known about whether the role of children in familial clusters has changed with the rollout of vaccination and the emergence of variants of concern (VOC). A study during the VOC Beta wave in Germany found that household transmission from adults was more frequent than from children [4]. Furthermore, as most studies evaluating the direction of transmission took place in high-income countries, little is known about the direction of transmission between age groups in lower resource settings. Behavioral factors influencing COVID-19 exposure may be different in Lower and Middle-Income Countries (LMICs) as there are higher rates of poverty, food insecurity, informal work, lack of access to infrastructure and services such as health care, and high density living situations [5].

In a prior study, we investigated the direction of transmission between adults, adolescents, and children in households in a low-resource, urban community during the first wave of COVID-19 in Brazil [6]. From March to June 2020 the community experienced lock-down. However, by October 2020, the lockdown had been partially relaxed. Schools for children ages 5–15 reopened partially and gradually beginning in August 2021 and fully in November 2021. During the Delta wave, relatively few non-pharmaceutical interventions were implemented but vaccination of working-age adults began. The data suggested that SARS-CoV-2 is primarily transmitted from adolescents and adults to children [6], implying that the opening of schools would not necessarily be harmful at least during the first pandemic wave, when the study was conducted. This leads to the question of whether

immunization and the introduction of new variants has changed these dynamics of transmission. Furthermore, it remains unknown whether the presence of symptoms has any role in household transmission in this type of community. To fill this knowledge gap, this study aimed to define the direction of transmission between age groups in households with SARS-CoV-2 cases across successive variant waves and to evaluate the contribution of symptoms to transmission. We hypothesize that in cases in which children are infected with SARS-CoV-2 by household contacts, the person who transmitted would most often be a symptomatic adult caregiver such as a parent or grandparent. Although we realize the most important contribution of immunization is the prevention of severe COVID-19, we evaluated whether immunization also reduces household transmission.

Methods

Study Design. This prospective cohort study was conducted from April 1st, 2020, to July 31st, 2022 in Manguinhos, a community with high indices of social and economic deprivation in the municipality of Rio de Janeiro, Brazil. The population of Manguinhos is about 40,000 inhabitants, approximately 26% of whom are children less than 12 years of age. We recruited families who brought their children to a public clinic in the community for routine vaccination or any medical care, independent of whether the child had respiratory symptoms, as previously described [9, 10]. In each household, we collected nasopharyngeal swabs from adults and adolescents and oral swabs from children. We conducted a pilot study in which nasopharyngeal swabs and oral swabs were both collected from children. Nasopharyngeal swab collection was poorly tolerated by the child and the parent/guardian due to the discomfort it caused. For this reason, oropharyngeal swabs were collected in this study. Home visits took place on days 1 (first visit), 14 and 28, and every 3 months during the first year and twice yearly in the second year. When households had symptomatic residents, an additional sample was collected on day 7. Further, the study personnel regularly called the participants to solicit whether anyone in the household was experiencing symptoms. If so, there was an additional visit to collect swabs outside of the regular calendar of study visits. In case of reinfection or immunization the

calendar of study visits for the household was reset to the original schedule of D1, D7, D14, D28, quarterly in year 1, and every six months in year two and the date of reinfection/vaccination was assigned to be D1. to the first intervals, among cases and households contacts.

A case of SARS-CoV-2 infection was defined by SARS-CoV-2 RNA detection using the real-time RT–PCR assays for SARS-CoV-2 Molecular E/RP Kit (Biomanguinhos, Rio de Janeiro, Brazil). Following established protocols [7, 8], the study was divided into four periods, each one defined by the predominant circulating lineage(s) in the community according to genomic surveillance data: pre-VOC (April 1, 2020 to January 25, 2021), Gamma (January 26, 2021-June 17, 2021), Delta (June 18-November 4, 2021), and Omicron (November 5, 2021-July 31, 2022). In particular, wave periods were defined by analyzing the number of cases of SARS-CoV-2 per week in the municipality of Rio de Janeiro from April 2020 to July 2022 and identifying distinct epidemic waves. Each wave period was named for the SARS-CoV-2 lineage that was most abundant in the city during the wave according to genomic surveillance. We assumed that the wave periods in the city of Rio de Janeiro as a whole would also be representative of the Manguinhos district located within the city of Rio de Janeiro. Additionally, we carried out SARS-CoV-2 whole genome sequencing using the COVIDSeq Illumina test (Illumina, Inc., San Diego, California, USA) and the Illumina MiSeq or NextSeq platform of samples eligible for the methodology (cycle threshold, ct < 27 in the RT-PCR test assay for the target E). The lineages and variant responsible for the SARS-CoV-2 infection in each family were determined when possible.

Data Collection. The residents of each household were classified into two age groups: children (0-11 years of age) and older people. The latter included adolescents and adults. In each household with a SARS-CoV-2 case, all other members of the household were tested. The index case or source of transmission was defined as the first SARS-CoV-2 case in the household, and cases occurring subsequently were defined as secondary cases. We classified the households into categories based on

the results of the other household members. If there was no other SARS-CoV-2 positive RT-PCR result 3 weeks before or after a positive RT-PCR result, the household was classified as having an isolated case. If there was one or more positive RT-PCR results among other household members in the same time span, either before or after the index case, the household was considered to have a transmission event. If there were other PCR+ results but they all occurred within a one-week interval of the reference case, they were considered ties in which the index case could not be determined. A household could experience one or more events, if occurring in different SARS-CoV-2 variant periods. The direction of transmission – child to child, child to older person, older person to child, and older person to older person– was evaluated separately within the same time intervals as described earlier.

Complete vaccination was defined as completion of at least two vaccine doses, with the last dose at least two weeks before the household transmission event. The secondary attack rate was defined as the number of confirmed cases among household contacts of the index case divided by the total number of household contacts who participated in the study. Participants were defined as symptomatic (COVID-19) if they presented any of the following findings: cough, sore throat or runny nose, anosmia, ageusia, diarrhea, abdominal pain, fever, chills, myalgia, fatigue, and/or headache. The study was approved by the Institutional Review Board at the London School of Hygiene and Tropical Medicine and the Brazilian National Ethics Committee.

Statistical analysis. We constructed a multiple logistic regression model using Stata 17 in which the dependent variable was the occurrence or non-occurrence of onward transmission within each household. The independent variables were whether the index case was a child or older person, presence of symptoms, whether the index case had completed the primary vaccine series, and the SARS-CoV-2 variant. Odds ratios are depicted with confidence intervals in Figure 2. We calculated the SAR attack rate in each household with a transmission event, then divided the households into two

groups: pediatric index cases and adolescent/adult index cases. A t-test was used to compare the mean SARs in the two groups.

Results

In total, 1,256 participants living in 298 households were tested for SARS-CoV-2 by a RT-PCR assay at least once during the study (**Figure S2**). In total, 4,073 RT-PCR tests were run with 893 SARS-CoV-2 positive results (21.9%). With respect to the variant periods, both the positivity rate and the attack rate were highest during Gamma (23.7% and 32.3%, respectively) and lowest during Delta (14.4% and 15.1%) (**Table S2, Figure S3**). Isolated cases occurred in 158 SARS-CoV-2 cases. There were 175 well-defined transmission events. Of these, one transmission chain was detected in 158 households, two events in different periods were detected in seven households and three in one household. The median number of members of each household that were enrolled was 4 (interquartile range [IQR]: 3-5). Of 298 households, 33% had residents who declined participation. The median number of refusals was one individual per household (IQR: 1-2). Households with refusals had significantly more residents than those without refusals (median of 5.5 and 4.3, respectively, $p<0.001$, **Table S4**). However, there was no difference between households with and without refusals in terms of the number of rooms, the average age of the residents, or the proportion of residents who were female.

Fully 124(41.6%) of 298 households had additional samples collected on day 7 due to symptomatic residents. The mean duration of follow-up for the index cases was 11 months (IQR: 5-19). At the end of the period of analysis of this manuscript in July 2022, 13.4% of the index cases had two years of follow-up. The median duration of follow-up for the index cases was 11 months (IQR: 5-19). Fully

26.2% of the index cases remained in follow-up at the end of the analysis period, with the possibility of additional assessment points (Figure S3).

The median participant age was 24 years (IQR: 9-39) (**Table 1**). In total, 32.1% (N=403) of the study population was aged 11 years or under. Most participants, 59.5% (N=747), were female. Among adult participants, 43.0% (N=431) had not graduated from high school and 42.1% (N=324) either graduated high school or attended college but without graduating. Nearly 2/3 of adult participants, 64.8% (N=499), were non-white based on self-defined race/ethnicity.

Among children, vaccination rates were < 20% from May 2020 to January 2022 (**Figure S1**). Coverage subsequently increased and by July 2022 64% of the children had received two doses. Half of the children received two doses of the BNT162b2 vaccine and half CoronaVac. Among adolescents and adults, rates were < 20% through July 2021 and increased continuously thereafter reaching 87% by July 2022 consisting of 29% ChAdOx1, 20% CoronaVac, and 38% BNT162b2.

The unit of analyses was the household and the analysis included all 298 households. In total, 19.8% of index cases were children, 90.5% of index cases were symptomatic, 15.9% of index cases were symptomatic children, and 10.3% of index cases had completed the primary vaccine series (for symptom frequencies see Table S3). There were significant differences in the household transmission events among periods (p=0.029, **Table 1**). The highest rate of household transmission occurred during the Gamma wave. The Gamma and Delta waves were tied for the lowest number of isolated cases (**Table 1**).

In this study, 40.1% (132/329) of index cases and 15% (24/158) of the isolated cases were confirmed by sequencing (**Table S1**). Of the 156 sequences representing household transmission, only one-third were from children (N=53, 34%). Sequencing verified that the viruses circulating during each period (pre-VOC, Gamma, Delta, and Omicron) were mainly the dominant strain. In particular, the dominant strain constituted 94% of the genomes Pre-VOC, 89% during Gamma, 97% during Delta, and 100% during Omicron.

The median number of participants was higher ($p < 0.001$) in households in which SARS-CoV-2 transmission occurred. The proportion of transmission events in which a child was the source was very small (**Figure 1**). During the VOC Omicron season, transmission from children to older people increased, but remained lower than transmission from older people to children. **Figure 2** shows household transmission events by age, vaccination status and presence of symptoms during the pre-VOC period and with subsequent variants. Overall, across all variants, a child household contact was significantly less likely to be infected by a child index case than by an adult/adolescent index (OR: 0.3 [95% CI: 0.16-0.55], **Table 2**). Symptomatic index cases were significantly more likely to transmit to household contacts (OR: 2.53 [95%CI: 1.51-4.26]). The most frequent symptoms among index cases were . The odds of household transmission were significantly lower when the index case had completed the primary vaccine series (OR 0.29 [95% CI: 0.1-0.85]). None of the children who lived in a household in which there was a household transmission event had been vaccinated before the event.

The secondary attack rates for child index cases to child contacts was 0.29, whereas the secondary attack rate from adult index cases to child contacts was 0.47 (p=0.08). The adult household contact who most frequently infected children was their mother (12/38), followed by their father (5/38). The household contact to whom children most frequently transmitted SARS-CoV-2 was also their mother (38/74). Two adult study participants were hospitalized due to oxygen desaturation, received

supplemental oxygen (but not invasive mechanical ventilation), and were discharged within five days. No children were hospitalized.

Discussion

Based on our household transmission study prior to the emergence of VOCs [6], we hypothesized that children are less likely to transmit SARS-CoV-2 to household contacts than adults or adolescents. In this community, the data supported the hypothesis insofar as children were less infectious, including after the re-opening of schools.. This finding aligns with systematic reviews of studies published early in the pandemic, which concluded that it was more common for adults to be the index cases responsible for onward transmission than children [9, 10]. Lower infectiousness of children could be due to inherently lower susceptibility in this population, less exposure to SARS-CoV-2 among children in the initial months of the pandemic, lower viral load. In this population, perhaps due to lower viral loads, fewer children could be sequenced than adults. On the other hand, a study from India published early in the pandemic concluded that transmission from adults to children was less common than transmission from children to children [11]. This discrepancy may be attributable to differences in case ascertainment. The study in India focused on symptomatic individuals whereas our study also included asymptomatic index cases, which would have resulted in the detection of a higher number of cases overall.

In this community, the risk of onward transmission from the index case was higher if there were more participants in the household, underscoring that crowding within the home plays a role in transmission events. Furthermore, with the emergence of VOCs, the data continued to support the finding that children were less infectious than adolescents/adults, although the difference in infectiousness between age groups was less pronounced. This finding aligns with those reported in systematic reviews of household transmission events [3, 12] and subsequent cohort studies in the US [13], which found no significant differences in infectiousness between pediatric and adult index cases following

the emergence of VOCs. We hypothesize that the odds of household transmission could also vary by variant. *In vitro* studies suggest that while the wildtype lineage SARS-CoV-2 was less effective at replicating in pediatric nasal epithelia than that of adults, the VOC Omicron replicates equally well in epithelial cells from both age groups [14]. The aforementioned studies analyzed the Alpha, Delta, and Omicron variants. A novel contribution of the present analysis is that we provide evidence of a similar pattern of transmission during the Gamma wave. The Gamma variant was associated with major morbidity and mortality in Brazil but did not become as prevalent in other countries [15]. In this community, the highest number of cases of household transmission occurred during Gamma with a trend towards statistical significance.

In our population, the emergence of VOCs coincided with the relaxation of social distancing policies and the rollout of COVID-19 vaccination. We found that the odds of household transmission were higher in households in which the index case was unvaccinated compared to households in which the index case was vaccinated. This aligns with findings of a household transmission study in Thailand, which similarly to Brazil primarily used adenovirus and inactivated vaccines at the beginning of the COVID-19 immunization campaigns [16]. Our findings about vaccination in households also align with those from other close-contact settings such as prisons in which COVID-19 vaccination reduces infectiousness [17]. Taken together, these results underscore the beneficial effects of COVID-19 vaccination in both protecting the individual from severe illness and preventing onward transmission to close contacts.

In our analysis, the odds of transmission were significantly higher from an adult/adolescent index case than from a child index case. On the other hand, a household transmission study in Singapore during the Delta wave concluded that children 0-11 were significantly more infectious than young adults aged 18-29, even after adjusting for the effect of vaccination [18]. This could be due to differences in exposure to COVID-19 among young adults. In our setting, young adults in this low-resource

community had low rates of adherence to social distancing during the Delta wave probably due to factors such as the financial need to return to work outside the home and the use of public transport. We speculate that greater exposure to COVID-19 among young adults in our setting made it more likely for them to transmit SARS-CoV-2 to children than vice versa. In this community, schools began to reopen for in person learning in August 2021 and fully reopened in November 2021 for younger children >= 5 years of age. This coincided with the end of the Delta wave and the beginning of the Omicron wave. We did not detect an increase in the proportion of pediatric index cases during the Omicron wave, which tends not to suggest a strong correlation between returning to school and SARS-CoV-2 household transmission by children in this cohort.

In this cohort, the family member most likely to transmit SARS-CoV-2 or contract the virus from a child under 12 was the mother. This likely reflects the mother's proximity to the child as the main caregiver in the community. Older adult household members such as grandparents were far less likely to contract SARS-CoV-2 from children. Perhaps these findings could help inform the development of guidelines about measures that can be taken to prevent onward transmission when a member of the family is suspected to have SARS-CoV-2.

We found that adults and adolescents who transmitted SARS-CoV-2 to their household contacts were significantly more likely to have COVID-19 symptoms than children who were index cases. This aligns with the fact that children are generally less symptomatic when infected with SARS-CoV-2. Possible mechanisms that may explain differences observed in the clinical evolution of COVID-19 by age include higher levels of expression of interferon genes in the respiratory epithelium of children and a more diverse repertoire of T cells in the pediatric population [19]. Furthermore, we were able to sequence a higher proportion of samples from cases of household transmission than isolated cases. Perhaps this could be attributable to higher viral load in index cases responsible for onward transmission in the household. This is consistent with a household transmission study in the US in

which levels of viral culture positivity in index cases were correlated with the risk of infection of in other household members [20].

One of the strengths of the study was the longitudinal follow-up of participants throughout four epidemic waves, which allowed us to monitor infection systematically and estimate positivity rates with higher accuracy than other settings using passive surveillance. To date, SARS-CoV-2 household transmission investigations have been conducted in dozens of countries following WHO protocols. The secondary attack rates observed in these studies have varied widely from 20-90%; surprisingly, this variation does not appear to be attributable to differences in income status, geographic region, method of case ascertainment, or predominant variant [21]. Our analysis suggests that an important parameter which could explain the wide variation in household attack rates may be the chronological age of the index case. With respect to generalizability of study results, one additional strength of our study is that our findings are highly pertinent to similar populations in low resource urban settings, particularly in Latin America. Although communities with such high levels of poverty and violence are common in lower income countries, the direction of household transmission of SARS-CoV-2 in this type of setting has seldom been studied due to the challenges of conducting fieldwork in this context.

This study had some limitations. We defined cases based on PCR results only rather than serology. Had we identified cases based on antibodies indicative of past exposure, we may have arrived at different conclusions about who in the household was the index case vs. a secondary case. However, the use of serology to define infection is problematic due to the difficulty of distinguishing infection from vaccination, particularly when inactivated viral vaccines are used with antibodies developed to other epitopes besides the spike protein. Another shortcoming is that we did not perform sequencing to confirm intrahousehold transmission. Furthermore, the samples we collected from children for PCR testing were oropharyngeal swabs. There is scant pediatric data on the sensitivity of oropharyngeal

swabs. Another limitation is that it is possible that children had more previous COVID-19 infections than adults in the early part of the pandemic with resultant immunity making them less likely to subsequently develop symptomatic infection and spread COVID-19. Finally, selection bias may have been introduced by recruiting families who brought their children to clinics for vaccinations or other medical care rather than from the general community. Despite the fact that Brazilians have wide access to free neighborhood clinics, it is possible that those accessing them and vaccinating their children for other diseases responded differently to the COVID-19 pandemic than others.

Although we evaluated the infectiousness of children within the household setting, we can only conjecture as to whether transmission patterns observed in households are generalized to other close contact settings such as schools. Systematic reviews have reported that the reopening of schools does not increase community transmission of SARS-CoV-2 [12, 22]. Perhaps this is because, similarly to household settings, infectiousness or susceptibility to SARS CoV-2 vary with age.

Conclusions

In this community, children were significantly less infectious to their household contacts than adolescents or adults. Among grandparents in this cohort, the risk of becoming infected with SARS-CoV-2 through contact with their grandchildren appears to have been minimal. Most children were infected by a symptomatic adult, usually their mother. There was a double benefit of vaccination as it protected the vaccinee from severe illness and prevented onward transmission to household contacts. Our results support the benefits of offering COVID-19 vaccination to all children 6 months of age and older as recommended by the Brazilian Ministry of Health. Our findings may also be valid for similar populations throughout Latin America.

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References

1. Madewell ZJ, Yang Y, Longini IM, Jr, Halloran ME, Dean NE. Factors Associated With Household Transmission of SARS-CoV-2: An Updated Systematic Review and Meta-analysis. JAMA Network Open. **2021**;4(8):e2122240-e.

2. Passaretti CL, Priem JS, Agner TG, McCurdy L. Reducing the rates of household transmission: The impact of COVID-19 vaccination in healthcare workers with a known household exposure. Vaccine. **2022**;40(9):1213-4. PubMed PMID: WOS:000760201300005.

3. Chen FF, Tian Y, Zhang LX, Shi Y. The role of children in household transmission of COVID-19: a systematic review and meta-analysis. International Journal of Infectious Diseases. **2022**;122:266-75. PubMed PMID: WOS:000836319700007.

4. Schumm L, Blankenburg J, Kahre E, et al. Lower SARS-CoV-2 household transmission in children and adolescents compared to adults. Scientific Reports. **2022**;12(1):22453.

5. Prabhakaran D, Singh K, Kondal D, et al. Cardiovascular Risk Factors and Clinical Outcomes among Patients Hospitalized with COVID-19: Findings from the World Heart Federation COVID-19 Study. Global heart. **2022**;17(1):40. PubMed PMID: 35837356. Pubmed Central PMCID: PMC9205371. Epub 2022/07/16. eng.

6. Lugon P, Fuller T, Damasceno L, et al. SARS-CoV-2 Infection Dynamics in Children and Household Contacts in a Slum in Rio de Janeiro. Pediatrics. **2021**;148(1). PubMed PMID: WOS:000677676000049.

7. Brasil P, Damasceno L, Fuller T, et al. Cohort-profile: Household transmission of SARS-CoV-2 in a low-resource community in Rio de Janeiro, Brazil. BMJ Open. **2022**;12(12):e067212.

8. Carvalho MS, Bastos LS, Fuller T, et al. Incidence of SARS-CoV-2 over four epidemic waves in a low-resource community in Rio de Janeiro, Brazil: A prospective cohort study. The Lancet Regional Health – Americas. **2022**;12.

9. Ludvigsson JF. Systematic review of COVID-19 in children shows milder cases and a better prognosis than adults. Acta paediatrica (Oslo, Norway : 1992). **2020**;109(6):1088-95. PubMed PMID: 32202343. Pubmed Central PMCID: PMC7228328. Epub 2020/03/24. eng.

10. Zhu YS, Bloxham CJ, Hulme KD, et al. A Meta-analysis on the Role of Children in Severe Acute Respiratory Syndrome Coronavirus 2 in Household Transmission Clusters. Clinical Infectious Diseases. **2021**;72(12):E1146-E53. PubMed PMID: WOS:000670819400031.

11. Laxminarayan R, Wahl B, Dudala SR, et al. Epidemiology and transmission dynamics of COVID-19 in two Indian states. Science. **2020**;370(6517):691-+. PubMed PMID: WOS:000586868600039.

12. Viner R, Waddington C, Mytton O, et al. Transmission of SARS-CoV-2 by children and young people in households and schools: A meta-analysis of population-based and contact-tracing studies. Journal of Infection. **2022**;84(3):361-82. PubMed PMID: WOS:000781133400013.

13. Sumner KM, Karron RA, Stockwell MS, et al. Impact of Age and Symptom Development on SARS-CoV-2 Transmission in Households With Children—Maryland, New York, and Utah, August 2020–October 2021. Open Forum Infectious Diseases. **2022**;9(8).

14. Zhu Y, Chew KY, Wu M, et al. Ancestral SARS-CoV-2, but not Omicron, replicates less efficiently in primary pediatric nasal epithelial cells. PLOS Biology. **2022**;20(8):e3001728.

15. Ranzani OT, Hitchings MDT, Dorion M, et al. Effectiveness of the CoronaVac vaccine in older adults during a gamma variant associated epidemic of covid-19 in Brazil: test negative case-control study. BMJ (Clinical research ed). **2021**;374:n2015. PubMed PMID: 34417194. Pubmed Central PMCID: PMC8377801 at www.icmje.org/coi_disclosure.pdf and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work. Epub 2021/08/22. eng.

16. Muadchimkaew M, Siripongboonsitti T, Wongpatcharawarakul S, et al. Effect of Inactivated SARS-CoV-2 Vaccines and ChAdOx1 nCoV-19 Vaccination to Prevent COVID-19 in Thai Households (VacPrevent trial). International Journal of Infectious Diseases. **2022**;124:190-8.

17. Chin ET, Leidner D, Zhang Y, et al. Effectiveness of Coronavirus Disease 2019 (COVID-19) Vaccines Among Incarcerated People in California State Prisons: Retrospective Cohort Study. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. **2022**;75(1):e838-e45. PubMed PMID: 35083482. Pubmed Central PMCID: PMC8807311. Epub 2022/01/28. eng.

18. Ng OT, Koh V, Chiew CJ, et al. Impact of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Vaccination and Pediatric Age on Delta Variant Household Transmission. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. **2022**;75(1):e35-e43. PubMed PMID: 35323887. Pubmed Central PMCID: PMC9129132. Epub 2022/03/25. eng.

19. Yoshida M, Worlock KB, Huang N, et al. Local and systemic responses to SARS-CoV-2 infection in children and adults. Nature. **2022**;602(7896):321-7.

20. Deyoe JE, Kelly JD, Grijalva CG, et al. Association of Culturable-Virus Detection and Household Transmission of SARS-CoV-2, California and Tennessee, 2020–2022. The Journal of Infectious Diseases. **2023**.

21. Lewis HC, Marcato AJ, Meagher N, et al. Transmission of SARS-CoV-2 in standardised first few X cases and household transmission investigations: A systematic review and meta-analysis. Influenza and Other Respiratory Viruses. **2022**;16(5):803-19. PubMed PMID: WOS:000811435700001.

22. Walsh S, Chowdhury A, Braithwaite V, et al. Do school closures and school reopenings affect community transmission of COVID-19? A systematic review of observational studies. BMJ Open. **2021**;11(8):e053371. PubMed PMID: 34404718. Pubmed Central PMCID: PMC8375447. Epub 2021/08/19. eng.

Figure Legends

Figure 1. Number of household transmission events by the age of the index case and the secondary cases, stratified by the predominant SARS-CoV-2 lineage during the event.

Figure 2. The effect of age, symptoms, vaccination, and variant on household transmission. The graph shows the marginal odds across variants, when the dependent variable is held fixed to one, representing households with transmission events. Vaccination is shown for Omicron because index cases were only completely vaccinated with two doses by the time of this wave.

Table 1. Demographic characteristics and educational attainment of study participants (N=1,256) and household level characteristics. The *p*-value for lineage indicates that there were significant differences in the household transmission rates among lineages.

Characteristics of individual participants	
Median age in years (IQR)	24 (9-39)
Age (years)	
0-11, N(%)	403 (32.1%)
12-20, N(%)	172 (13.7%)
21-30, N(%)	172 (13.7%)
31-40, N(%)	236 (18.8%)
41-50, N(%)	122 (9.7%)
51-60, N(%)	69 (5.5%)
Over 60 years of age, N (%)	82 (6.5%)
Female sex, N(%)	747 (59.5%)
Education	
Illiterate or did not graduate from primary school,	150 (19.5%)

N (%)	
Graduated from primary school but did not graduate from secondary school, N(%)	181 (23.5%)
Graduated from secondary school but did not graduate from college, N(%)	324 (42.1%)
Graduated from college, N (%)	75 (9.7%)
Education missing, N (%)	40 (5.2%)
Race/ethnicity	
Asian	4 (0.5%)
Black	153 (19.9%)
Multiracial	341 (44.3%)
Brazilian indigenous	1 (0.1%)
White	245 (31.8%)
Ethnicity/race missing	26 (3.4%)
People living with HIV	6 (0.5%)

Median number of swabs per participant (IQR)	3 (2-5)			
Characteristics of SARS-CoV-2 cases				
Characteristic	**Overall n = 333**	Onward transmission events n = 175	Isolated case in the household n = 158	*p*-value
Median participants per household (IQR)	4.15 (3.9-4.3)	4.5 (4.2-4.7)	3.8 (3.5-4.0)	0.0002
Predominant lineage	N (%)	N (%)	N (%)	0.029
Pre-VOC, N(%)	108 (32%)	54 (31%)	54 (34%)	
Gamma, N(%)	97 (29%)	63 (36%)	34 (22%)	
Delta, N(%)	61 (18%)	27 (15%)	34 (22%)	
Omicron, N(%)	67 (20%)	31 (18%)	36 (23%)	

IQR, interquartile range; VOC, Variant of Concern.

Table 2. Effect of the child vs. adolescent/adult index, presence of symptoms, completed vaccine primary series of the index case, and variant on household transmission of SARS-CoV-2. Of 175 transmission events, the direction of transmission could be established based on the date of the positive PCR test for 126 events. The sample size for the logistic regression was 284 because the 126 households with onward transmission were compared to the 158 with isolated cases. There was no missing data in the covariates.

	OR (95% CI)	**P**
Index case child 0-11 years old vs. adolescent/adult index case	0.3 (0.16-0.55)	<0.001
Presence of symptoms	2.53 (1.51-4.26)	<0.001
Index case completed primary vaccination series	0.29 (0.1-0.85)	0.024
Variant		
Variant Gamma vs. Pre-VOC	1.76 (0.93-3.32)	0.08
Variant Delta vs. Pre-VOC	0.75 (0.35-1.63)	0.47
Variant Omicron vs. Pre-VOC	2.08 (0.76-5.66)	0.15

Figure 1

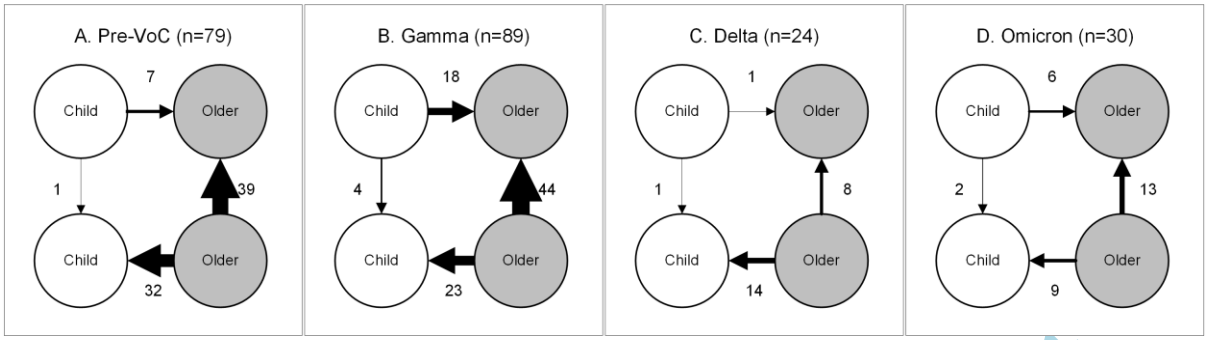

Figure 2