Household transmission of SARS-CoV-2 in the United States: living density, viral load, and disproportionate impact on communities of color

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Summary: Households are hotspots for SARS-CoV-2 transmission. In the US, the COVID-19 pandemic has had a disproportionate impact on communities of color. Household crowding in the context of high-inoculum infections may amplify the spread of COVID-19, potentially contributing to disproportionate impact on communities of color.
ABSTRACT

Background Households are hotspots for SARS-CoV-2 transmission. In the US, the COVID-19 pandemic has had a disproportionate impact on communities of color.

Methods Between April-October 2020, the CO-HOST prospective cohort study enrolled 100 COVID-19 cases and 208 of their household members in North Carolina, including 44% who identified as Hispanic or non-white. Households were enrolled a median of 6 days from symptom onset in the index case. Incident secondary cases within the household were detected by quantitative PCR of weekly nasal swabs (days 7, 14, 21) or by seroconversion at day 28.

Results Excluding 73 household contacts who were PCR-positive at baseline, the secondary attack rate among household contacts was 32% (33/103, 95% CI 22%-44%). The majority of cases occurred by day 7, with later cases confirmed as household-acquired by viral sequencing. Infected persons in the same household had similar nasopharyngeal viral loads (ICC=0.45, 95% CI 0.23-0.62). Households with secondary transmission had index cases with a median viral load that was 1.4 log₁₀ higher than households without transmission (p=0.03) as well as higher living density (>3 persons occupying <6 rooms) (OR 3.3, 95% CI 1.02-10.9). Minority households were more likely to experience high living density and had a higher risk of incident infection than did white households (SAR 51% vs. 19%, p=0.01).

Conclusions Household crowding in the context of high-inoculum infections may amplify the spread of COVID-19, potentially contributing to disproportionate impact on communities of color.
INTRODUCTION

Households are hotspots for SARS-CoV2 transmission [1]. Person-to-person transmission is difficult to control in shared living spaces. For those isolating at home with young children in small living spaces, following guidelines to physically distance and use separate sleeping, eating, and lavatory facilities is difficult [2]. Because the period of peak infectiousness starts prior to the onset of symptoms, spread can occur before these measures are taken [3–5].

Meta-analyses of secondary household attack rates (SAR) in the first six months of the pandemic range from 15-20% [6,7], but these analyses incorporated both retrospective and prospective analyses [6,7]. Prospective testing of household contacts regardless of symptom status is required to capture all secondary cases. Previously identified risk factors associated with increased transmission include the presence of symptoms [6–8] and high viral load in the index case [9]. Among household contacts, spouses and those over age 18 (i.e. adults compared to children) are more likely to acquire infection [6,7,10]. Measuring secondary household attack rates in vulnerable communities and identifying risk factors for transmission in these communities is critical.

The UNC CO-HOST (COVID-19 Household Transmission Study) is the largest, single-site observational household cohort in the US to date and the most ethnically and racially diverse. Weekly sampling for quantitative viral loads combined with SARS-CoV-2 antibody testing at baseline and at one month provided an extended period to evaluate transmission. The objective of this study was to measure the incident SAR in a setting where infected individuals were asked to quarantine at home and given standard guidance. Household and individual demographics as well as daily symptoms and weekly viral loads were collected to identify risk factors and timing of household transmission.

METHODS

Study design and enrollment

The CO-HOST Study evaluated SARS-CoV-2 acquisition among persons undergoing quarantine in their home after a care-seeking household member (the index case) tested positive for SARS-CoV-2. The study was approved by the Institutional Review Board at the University of North Carolina. Recruitment occurred between April-October 2020, prior to the introduction of SARS-CoV-2 vaccines in the US. Inclusion criteria for the index cases were >18 years with a positive qualitative nasopharyngeal (NP) swab for SARS-CoV-2 RNA using PCR performed at the UNC Hospitals clinical laboratory, willingness to self-isolate at home for a 14-day period, living with at least one household contact who was also willing to participate, and living within driving distance (<1 hour) from study site. Inclusion criteria for household contacts of index patients included age > 1 year, and currently living in the same home as the index case without plans to live elsewhere during the 28-day study. All participants (or their parents/guardians) gave written, informed consent. Minors over the age of 7 provided assent.
As shown in Figure S1, all households were visited on Day 1 by a study team. NP and nasal mid-turbinate (NMT) swabs were collected for SARS-CoV-2 PCR and blood samples were collected for serology. All study participants received instruction on self-collection of NMT swabs and completed baseline questionnaires that included basic demographic and household information, abbreviated medical history, symptoms, recent travel history, and exposure to confirmed cases of COVID-19.

All participants received a daily symptom questionnaire via email until no symptoms were reported for two consecutive days. Household contacts who remained asymptomatic received the questionnaire for 21 days to monitor for new symptoms. On Days 7, 14 and 21, a study staff member conducted home visits to collect self-collected NMT swabs. At the final study visit (Day 28), participants were asked about COVID-related care-seeking and underwent serologic testing.

**Laboratory analyses**

Details for all laboratory methods are found in the Supplementary Material. Quantitative PCR testing for SARS-CoV-2 was performed using a Centers for Disease Control (CDC) RT-qPCR protocol authorized by the Food and Drug Administration (FDA) for emergency use, as previously described [11]. Serology was performed using an enzyme linked immunoassay assay (ELISA) that detects antibodies to the receptor binding domain (RBD) of the spike protein with high sensitivity and specificity [17, 18]. When ELISA results were not available (i.e. in kids who did not undergo venipuncture), results from a BioMedomics COVID-19 IgM/IgG Rapid Test [12–14] were used.

To evaluate the prevalence of the 614G variant, which predominated in North Carolina at the time of the study, in our study samples, we developed a real-time PCR assay targeting a 107 bp region encompassing the D614G mutation in the S1 segment of the SARS-CoV-2 spike protein.

Finally, to help determine whether secondary cases were acquired outside the household rather than due to household transmission, we performed high density amplicon sequencing on NP/NMT swab samples from households with late secondary cases to assign SARS-CoV-2 clades and determine the genetic relatedness of viral isolates within and between households.

**Statistical analysis**

We summarized baseline demographic characteristics and underlying conditions of index cases and household contacts, as well as their household demographics. We evaluated if baseline NP SARS-CoV-2 viral loads were correlated within households by the intraclass correlation coefficient (ICC), which compares within versus between household variation.
We evaluated the secondary household attack rate among household members of persons who tested positive for SARS-CoV-2. For each household, if multiple participants were positive at enrollment, the index case was defined as the person with the earliest onset of infection based on reported onset of symptoms and known date(s) of PCR test positivity. If this was ambiguous, then baseline antibody positivity was used as evidence of less recent infection. We calculated the SAR as the risk of incident infection among household contacts, defined as the proportion of contacts who were PCR-negative at baseline, but then developed SARS-CoV-2 infection during the 28-day study follow-up, confirmed by either PCR or antibody seroconversion. Those with evidence of prior infection (antibody-positive and PCR-negative) or household contacts who reported the same COVID exposure outside the household as the index case were excluded from the analysis. To avoid misclassification of asymptomatic infection, household contacts who tested PCR-negative at weekly nasal swabs (D7, D14, D21) but without D28 antibody results were also excluded. A 95% CI for the SAR was calculated using a robust variance estimation for the intercept term in a logistic regression model to account for outcome dependence within a household.

Potential risk factors for secondary transmission within the household, including characteristics of index cases, households, and household contacts were examined. These risk factors and details of symptom severity evaluation are described in the Supplementary Material. Statistical significance was tested by either Fisher’s exact or chi-square test for categorical variables and Mann-Whitney test for continuous variables. To explore if the association between index race-ethnicity and SAR was related to housing density or viral load (which were correlated with race/ethnicity and/or transmission in unadjusted analyses), we calculated the odds ratio of the race-ethnicity specific SAR, with 95% CI estimated using the same robust variance estimation described above, then added the other risk factors as covariates in the logistic regression model to calculate adjusted odds ratios.

Analyses were performed using R 4.0.2 (R Core Team, Vienna, Austria). All hypothesis tests were two-sided at a significance level of 0.05 with no adjustments for multiple comparisons.

RESULTS

Study enrollment

Between April-October 2020, the UNC CO-HOST study enrolled 102 households across the central Piedmont Region of North Carolina, US (Figure S2). After excluding participants who did not complete follow-up, had evidence of prior infection, or those who were possibly infected at the same time as the index case based on a common exposure, 91 households were included in the baseline analysis (Figure 1). Households were enrolled a median of 6 (IQR 4-7) days after symptom onset of the designated index case, which was reassigned in 11 households. Baseline characteristics of the 91 index cases and 176 household contacts (HCs) are shown in Table 1. The median index case age was 37 years (IQR 23-49 years), while HCs ranged from 2 to 77 years of age with 34% under 18
years. Overall, 44% of participants identified as other than White, non-Hispanic race-ethnicity and 33% of adults were obese (BMI >30 kg/m²) (Table 1, other comorbidities in Table S1).

**Household characteristics**

The median size of households was 4 persons (Table S2), though in 38% of households, at least one household member chose not to participate. Households with a non-white index case were more likely to live in a home <2,000 square feet (71% versus 43%, p=0.01). This led to a higher “living density” for non-white households: 43% had >3 household members living in a home with fewer than 6 rooms, compared to 8% of white households (p<0.001).

SARS-CoV-2 viral burden was correlated within households (Figure 2). When comparing the baseline nasopharyngeal viral load within versus between households, viral burden showed significant clustering within households (ICC=0.45, 95% CI 0.23-0.62, p<0.001). Differences in viral load are not attributable to D614G mutation in the viral spike protein that has been associated with increased viral load and infectivity [15], as 90/92 (98%) of genotyped SARS-CoV-2 isolates contained the 614G mutant, while only 2/92 were wild-type at this locus.

**Secondary attack rate among household contacts**

The incident SAR among household contacts was 32% (33/103, 95% CI 22%-44%). Among 91 households, 73/176 (41%) household contacts tested PCR positive at baseline and were excluded from the primary SAR analysis (Figure 1, Table S3 for demographics of baseline infected cases). Among the remaining 103 household contacts of 51 index cases, 33 incident SARS-CoV-2 infections were observed during the 28-day study follow-up (SAR=32% (33/103)). Of these 33 secondary cases, 22 were identified by both PCR and seroconversion from Day 1 to Day 28, 4 were identified by PCR only, and 7 were identified on seroconversion alone. The majority of secondary cases in the household experienced symptoms (27/33), while 18% (n=6) remained asymptomatic.

Secondary household transmission occurred early, within the first week following enrollment for the majority of cases (n=21/26 for those identified by PCR) (Figure 1). Five cases were detected by PCR after the first week of enrollment, at Day 14 or 21. Four of these late secondary cases occurred in households of 5 or more (including two from the same household), which suggests the possibility of sequential transmission within the household. High density amplicon sequencing of viral isolates from these late secondary cases and others in their household confirmed that 4/5 were indeed due to household transmission (1 isolate failed sequencing), and not community-acquired (Figure 3).
Risk factors for household transmission

At the household level, 44% of households (40/91) had at least one infected household member at enrollment besides the index case, rising to 69% (63/91) of households one month later. Sixty households contained susceptible HCs at enrollment and were thus included in the risk factor analysis.

Secondary transmission in the household was associated with a higher nasopharyngeal viral load in index cases at enrollment. The median NP viral load among index cases was $1.4 \log_{10}$ higher in households with secondary cases detected during the study versus those with no incident cases in the household ($p=0.03$) (Table 2). This difference persisted when the analysis was restricted to index cases who were still antibody-negative, and thus more recently infected [14,16] (Figure 4). Symptom severity was not associated with household transmission, though secondary transmission did occur in households of the 4 index cases that were hospitalized (Table 2).

Households with non-white index cases were more likely to experience incident transmission in the household (Table 2), despite there being no difference in index case viral loads by race/ethnicity (median NP viral load for white vs. non-white: 8.3 vs. 8.3 $\log_{10}$ copies/mL). This corresponds to a SAR of 51% (95% CI 33%-69%) in households with a non-white or Hispanic index case compared to 19% (95% CI 10%-35%) in white, non-Hispanic households ($p=0.008$). Higher living density, defined as greater than 3 household members living in a home with fewer than 6 rooms, was associated with a greater odds of transmission (OR 3.3, 95% CI 1.02-10.9, $p=0.047$) (Table 3), and a greater proportion of non-white/Hispanic households met this definition of high living density (42%, 11/26) compared to white, non-Hispanic households (12%, 4/34) ($p=0.01$). However, after adjusting for viral load and living density, Hispanic/non-white race-ethnicity remained associated with secondary household transmission (Table 4).

Among susceptible household contacts, those sharing a bathroom with the index case were at higher risk of acquiring infection (Table S4). Obesity and being female were also associated with a higher risk of incident infection, though these associations were not statistically significant. Though a slightly greater percentage of participants in households without secondary transmission reported wearing a mask at home in the week prior to enrollment (22% vs 13% for index cases and 30% vs 20% in household contacts), these differences were not statistically significant.

DISCUSSION

Household transmission is one of the main drivers of the SARS-CoV-2 pandemic. By incorporating timely recruitment of index cases, prospective sampling to 21 days regardless of symptom status, and confirmatory viral sequencing in a subset of households, we show that household transmission occurs in a substantial proportion of COVID-positive households, with racial-ethnic disparities in
secondary attack rates and higher risk of infection in more crowded households. Our data also suggest that those infected with a high viral load are not only more likely to transmit virus to other household members, but that they may seed other high-viral load infections, putting the entire household at higher risk for more severe illness.

The incident SAR in this study was 32%, rising to 51% in minority households. While a meta-analysis of household transmission studies conducted in the first six months of the pandemic (prior to circulation of new variants) found a much lower overall household SAR of 17% (95% CI 14%-19%), it noted significant heterogeneity between studies (ranging 4-45%) and combined both retrospective studies based on contact tracing data and prospective analyses [6]. As expected, prospective studies with increased frequency of testing regardless of symptom status generally show higher infection rates [7]. In the US, a retrospective study in New York that included household testing offered regardless of symptom status reported a SAR of 38% [17], while two prospective studies following households in Utah and Wisconsin (58 households, SAR 29%)[18], and Tennessee and Wisconsin (101 households, SAR 53%) [10] also reported higher SARs. Altogether, these studies document high secondary household attack rates within US households.

To our knowledge, this is the first study to show increased transmission in non-white US households. Though they experience similar case fatality rates, African American/Black and Hispanic populations in the US experience disproportionately higher rates of SARS-CoV-2 infection [19–21]. These racial disparities are likely due to differences in health care access and exposure risk that are driven by systemic societal inequities rather than individual biological or behavioral characteristics [22–25]. Our limited findings are consistent with this explanation. While the sample size precluded full investigation of drivers of increased transmission in minority households, we found that high living density/household crowding was more common in non-white households, while viral load and reported masking in the home did not differ by race-ethnicity.

We also found that SARS-CoV-2 viral burden was correlated within households. Increased viral load increases infectivity in vivo [26], and a study of 282 clusters in Spain showed an increased risk of transmission with shorter time to onset of symptoms among contacts as viral load of the index cases increased [9]. Since greater viral burden (high viral load or lower Ct values by PCR) is associated with disease severity [27–30], our findings imply that when a person is hospitalized, others in the same household may be at a higher risk for a similar outcome than would be predicted based on their individual risk factors alone. An inoculum effect may underlie this finding [31] and also explain why secondary cases in households appear to be overdispersed, with either most or all members infected, or none at all [6,32,33].

This study has several limitations. First, although we enrolled most households within 24-48 hours of a positive SARS-CoV-2 test result, delays in testing meant that it was common for others in the household to be PCR-positive at enrollment. While 33 household contacts met our endpoint as
incident SARS-CoV-2 cases, 73 household contacts were infected at study baseline and hence could not be categorized definitively as due to household transmission and were excluded from the analysis. Thus, we likely underestimated the true SAR, and the resultant small sample size was not sufficient to investigate all drivers of household transmission. We were similarly limited in our ability to do adjusted analyses beyond a simplistic exploration of whether living density might account for the observed racial disparity in SAR. In the households with multiple infected household members at baseline, we cannot be certain that the designated index case was the source of infection for all infected household members. This may have affected our evaluation of index case risk factors associated with transmission.

Additionally, we were unable to adequately assess the effects of age, mask-wearing, and the presence of symptoms on transmission. We recruited adult index cases, and in 38% of households, at least one household member (most often young children) declined to participate. While mask use was queried, mask use prior to any COVID diagnosis in the household was not specifically elicited. All index cases except one were tested because they were symptomatic.

In conclusion, SARS-CoV-2 transmits early and often among household members. While masking, physical distancing, and quarantining the whole household may reduce or prevent transmission beyond the household, these strategies are less effective within the household, especially in the setting of high viral load infections and crowded living spaces. Frequent point-of-care testing and post-exposure prophylaxis in those at-risk for severe illness [34], and ultimately widespread and equitable distribution of vaccines [35], are needed to lessen the impact of COVID-19 within households and vulnerable communities.
NOTES

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CONFLICT OF INTEREST

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Table 1. Demographics of study participants

| INDIVIDUALS          | Index cases (n) | Index cases (%) | Household contacts (n) | Household contacts (%) |
|----------------------|-----------------|-----------------|------------------------|------------------------|
|                      | 91              | %               | 176                    | %                      |
| Male                 | 43              | 47              | 87                     | 49                     |
| Female               | 48              | 53              | 89                     | 51                     |

**Race/Ethnicity**

|                       | 52              | 57              | 96                     | 55                     |
| White, non-Hispanic   | 39              | 43              | 77                     | 44                     |
| Non-White             | 10              | 11              | 17                     | 9.7                    |
| Black or African American | 26          | 29              | 58                     | 33                     |
| Hispanic/Latinx       | 3               | 3.3             | 2                      | 1.1                    |
| Other, non-Hispanic   | 0               | 0.0             | 3                      | 1.7                    |
| Unknown               | 0               | 0.0             | 3                      | 1.7                    |

**Language**

|                  | 13              | 14              | 28                     | 16                     |
| Spanish speaking (yes) | 78          | 86              | 148                    | 84                     |

**Age**

|                   | 2               | 2.2             | 38                     | 22                     |
| 0-12y              | 6               | 6.6             | 22                     | 13                     |
| Age Group  | Education (excluding <18y) | Occupation (excluding <18y) | Co-Morbidities (excluding <18y) |
|----------|---------------------------|-----------------------------|---------------------------------|
|          | Total Responses for Adults >18y | % | % | % | % |
| 18-24y   | 20 | 22 | 23 | 13 | |
| 25-49y   | 41 | 45 | 56 | 32 | |
| 50-64y   | 18 | 20 | 27 | 15 | |
| >65y     | 4  | 4.4| 10 | 5.7| |
|          | Education               | High school or lower        | College degree                  | Graduate degree |
|          | Total Responses for Adults >18y | % | % | % | % | |
|          | 80 | % | 113 | % | |
|          | 36 | 45 | 54 | 48 | |
|          | 23 | 29 | 34 | 30 | |
|          | 21 | 26 | 25 | 22 | |
|          | Occupation               | Healthcare worker           | Retail/hospitality/other frontline worker | Student |
|          | Total Responses for Adults >18y | % | % | % | % | |
|          | 83 | % | 116 | % | |
|          | 3  | 3.6 | 6 | 5.2 | |
|          | 11 | 13 | 9 | 7.8 | |
|          | 19 | 23 | 22 | 19 | |
|          | 7  | 8.4 | 12 | 10 | |
|          | 23 | 28 | 34 | 29 | |
|          | 6  | 7.2 | 6 | 5.2 | |
|          | 14 | 17 | 27 | 23 | |
| Diabetes | 4  | 4.8 | 9 | 7.8 | |
| High blood pressure | 12 | 15 | 24 | 21 | |
| BMI >30  | 28 | 34 | 38 | 33 | |
| BMI 25-29.9 | 24 | 29 | 31 | 27 |
| BMI >30 and one or more co-morbidity | 16 | 19 | 22 | 19 |
| Adults >18y (n = 83 index, 116 HC) | 7 | 32 | 12 | 32 |
| Adults >50y (n = 22 index, 37 HC) |
Table 2. Potential risk factors for SARS-CoV-2 transmission from index cases

| INDEX CASES                              | All Indexes (n, %) | Household transmission (n, %) | No transmission (n, %) | p-value |
|------------------------------------------|-------------------|------------------------------|-----------------------|---------|
|                                          | 60 (100%)         | 32 (53%)                     | 28 (47%)              | -       |
| Age                                      |                   |                              |                       |         |
| <18y                                     | 7 (12%)           | 4 (13%)                      | 3 (11%)               |         |
| 18-50y                                   | 45 (75%)          | 25 (78%)                     | 20 (71%)              | NS      |
| >50y                                     | 8 (13%)           | 3 (9%)                       | 5 (18%)               |         |
| Sex                                      |                   |                              |                       |         |
| Female                                   | 33 (55%)          | 15 (47%)                     | 18 (64%)              | NS      |
| Male                                     | 27 (45%)          | 17 (53%)                     | 10 (36%)              |         |
| Mask wearing prior to enrollment (missing n = 3) | | | | |
| Mask wearing at home                     | 10 (18%)          | 4 (13%)                      | 6 (22%)               | NS      |
| Race/Ethnicity                           |                   |                              |                       |         |
| White, non-Hispanic                      | 34 (57%)          | 13 (41%)                     | 21 (75%)              | 0.01*   |
| Black or African American                | 7 (12%)           | 5 (16%)                      | 2 (7%)                |         |
| Other, non-Hispanic                      | 4 (7%)            | 4 (12%)                      | 0 (0%)                |         |
| Hispanic/Latinx                          | 15 (25%)          | 10 (31%)                     | 5 (18%)               |         |
| Symptom severity                         |                   |                              |                       |         |
| Mild                                     | 12 (21%)          | 4 (14%)                      | 8 (29%)               | 0.07    |
|                | White (n = 42) | Black (n = 30) | Hispanic (n = 18) |
|----------------|---------------|----------------|------------------|
| Moderate/Severe| 41 (72%)      | 21 (72%)       | 20 (71%)         |
| Hospitalized   | 4 (7%)        | 4 (14%)        | 0 (0%)           |

**Duration of symptoms at enrollment**

|                     | Median days (IQR) |
|---------------------|-------------------|
| White (n = 42)      | 5 (4-7)           |
| Black (n = 30)      | 5 (4-7)           |
| Hispanic (n = 18)   | 6 (4-7)           |
| NS                  |                   |

**Nasopharyngeal viral load (log10 copies/mL) at enrollment (missing n = 6)**

|                     | Median (IQR)     |
|---------------------|------------------|
| White (n = 42)      | 8.3 (5.9-9.5)    |
| Black (n = 30)      | 8.8 (7.3-10.1)   |
| Hispanic (n = 18)   | 7.4 (5.3-8.7)    |
| p = 0.03            |                   |

**Co-Morbidities for adults >18y (missing n = 1 for diabetes, n = 3 for obesity)**

|                  | White (n = 42) | Black (n = 30) | Hispanic (n = 18) |
|------------------|---------------|----------------|------------------|
| Diabetes         | 0 (0%)        | 0 (0%)         | 0 (0%)           |
| Obesity, BMI >30 | 21 (42%)      | 13 (50%)       | 8 (33%)          |
|                  | NS            | NS             | NS               |

**Education for adults >18y (missing n = 3)**

|                   | White (n = 42) | Black (n = 30) | Hispanic (n = 18) |
|-------------------|---------------|----------------|------------------|
| High school or lower | 21 (42%)   | 13 (52%)       | 8 (32%)          |
| College degree     | 17 (34%)     | 9 (36%)        | 8 (32%)          |
| Graduate degree    | 12 (24%)     | 3 (12%)        | 9 (36%)          |
| p = 0.05           |               | NS             |                  |

P-values only reported if ≤ 0.10, otherwise noted as not significant (NS)

*compares white, non-Hispanic versus all other categories*
Table 3. Potential household-level risk factors for SARS-CoV-2 transmission

| HOUSEHOLDS       | All Households (n, %) | Infected (n, %) | Uninfected (n, %) | p-value |
|------------------|-----------------------|-----------------|-------------------|---------|
|                  | 60 (100%)             | 32 (53%)        | 28 (47%)          | -       |

**Household size**

|                  | Mean                  | 3.8             | 4.2               | 3.4     | 0.03   |

**Living space (missing n = 3)**

|                  | <2000 sq ft           |                  |                   |         |        |
|------------------|-----------------------|-----------------|-------------------|---------|
|                  | 29 (51%)              | 18 (60%)        | 11 (41%)          | NS      |
|                  | >2000 sq ft           | 28 (49%)        | 12 (40%)          | 16 (59%)| NS     |

**Number of rooms***

|                  | 2 or fewer rooms      |                  |                   |         |        |
|------------------|-----------------------|-----------------|-------------------|---------|
|                  | 5 (8%)                | 2 (6%)          | 3 (10%)           |         |
|                  | 3-5 rooms             | 27 (45%)        | 19 (59%)          | 8 (29%) | 0.06   |
|                  | 6 or more rooms       | 28 (47%)        | 11 (34%)          | 17 (61%)|        |

**Living density**

|                  | >3 people and <6 rooms|                  |                   |         |        |
|------------------|-----------------------|-----------------|-------------------|---------|
|                  | 15 (25%)              | 13 (41%)        | 2 (7%)            | 0.003   |

**Home ownership (missing n = 1)**

|                  | Renting apartment     |                  |                   |         |        |
|------------------|-----------------------|-----------------|-------------------|---------|
|                  | 4 (7%)                | 2 (7%)          | 2 (7%)            | NS      |
|                  | Renting home          | 17 (29%)        | 11 (36%)          | 6 (21%) | NS     |
|                  | Own home              | 38 (64%)        | 18 (58%)          | 20 (71%)| NS     |

*Number of rooms includes bedrooms, kitchen, and common rooms, but not bathrooms or garage

p-values only reported if ≤ 0.10, otherwise noted as not significant (NS)
Table 4. Risk factors for SARS-CoV-2 transmission in the household

| Index or household risk factors                     | Susceptible HCs | Incident secondary cases | SAR (95% CI) | OR (95% CI) | aOR (95% CI) |
|-----------------------------------------------------|-----------------|--------------------------|--------------|-------------|--------------|
| All                                                 | 103             | 33                       | 32% (22-44%) |             |              |
| Non-white                                           | 41              | 21                       | 51% (33-69%) | 4.4 (1.5-13.0) | 4.8 (1.5-15.4) |
| White, non-Hispanic                                 | 62              | 12                       | 19% (10-35%) | -           |              |
| Higher index NP viral load*                         | -               | -                        | -            | 3.5 (1.5-8.1) | 3.6 (1.5-8.5) |
| High living density**                               | 29              | 15                       | 52% (27%-75%) | 3.3 (1.02-10.9) | 1.4 (0.4-4.6) |
| Not high living density                             | 74              | 18                       | 24% (15%-37%) | -           |              |

*OR for 3 log10 increase in index viral load. For example, the odds of transmission in a household where index VL is 1x10^9 copies/mL is 3.5 times greater than in a household where index VL is 1x10^6 copies/mL.

**Defined as >3 people occupying <6 rooms

aOR adjusts for viral load as a continuous variable and racial-ethnicity and living density as dichotomous variables
FIGURE LEGENDS

Figure 1. CO-HOST enrollment and secondary household attack rate (SAR). Among 100 households that completed the 28-day follow-up, household contacts were excluded if they had evidence of prior infection (negative PCR and positive antibody test at enrollment), were possibly infected at the same time as the index case based on a common exposure event, or negative PCR testing could not be confirmed with a negative antibody test at Day 28. Of the remaining 176 household contacts of 91 index cases, 41% (73) were already PCR-positive at baseline and thus excluded from the primary SAR analysis. During study follow-up, 33 incident SARS-CoV-2 cases were identified, yielding a SAR of 32% (33/103). Among the 33 secondary cases, 22 were identified by both PCR and seroconversion from Day 1 to Day 28, 4 were identified by PCR only, and 7 were identified based on seroconversion.

Figure 2. SARS-CoV-2 viral burden is correlated within families. The viral load obtained at enrollment from nasopharyngeal swabs in households with multiple COVID-positive household members are shown (n=42 households). Each vertical row in red depicts an individual household, with circles delineating the log viral load of each member within the household. Circles shaded in gray represent values derived from a nasal mid-turbinate swab if NP sampling was not performed. This was based on a linear regression equation generated from >100 study participants with positive viral load from both NP and NMT swabs [11]. Households are depicted across the x-axis in order of decreasing viral load. Data drawn from 148 participants. The intraclass correlation coefficient ICC = 0.45, 95% CI (0.23, 0.62), p-value < 0.001.

Figure 3. Bayesian phylogeny showing high relatedness within household infections, indicating household transmission. High density amplicon sequencing was performed on all available viral isolates from ten households with secondary infections to assess relatedness between infections. Whole genome sequences were assembled according to the Wuhan reference genome, assigned to major clades, and then used for Bayesian phylogeny reconstruction. Index cases within each numbered household are written in bold. Households contacts are numbered sequentially starting with the index case number, i.e. X-1, X-2, etc. Minors are indicated with a c prior to the case number. Each asterisk indicates one study week preceding a positive qPCR test, i.e. * indicating a D7 positive test, ** indicating a D14 positive test, and *** indicating a D21 positive test. Household contacts without asterisks were PCR-positive at baseline.

Figure 4. Association of index nasopharyngeal viral load and transmission in the household. Households with secondary cases were more likely to have index cases with high nasopharyngeal viral load compared to households without secondary transmission (median NP viral load log 8.8 vs 7.4 copies/mL, respectively p=0.03). Index cases that were not yet antibody-positive at enrollment, as a marker of more recent infection, are depicted to the right in gray.
Figure 1

Households enrolled
n=102

Excluded: n=2
Dropout

Households completed follow-up
n=100

Index cases
n=100

Excluded: n=91
All household contacts infected with common exposure (n=88) or with existence of prior infection (n=3)

Index cases
n=91

Household contacts
n=176

Excluded: n=73
PCR-positive at baseline

SAR Analysis

Index cases
n=60

Transmission in household
n=32

No transmission
n=28

Secondary cases
n=33
PCR+ at D7 (n=21)
PCR+ at D14 (n=3)
PCR+ at D21 (n=2)
Seroconversion Ab+ at D28 (n=3)

Uninfected
n=70

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Figure 2

Nasopharyngeal viral load (copies/mL)

Households with multiple COVID+ individuals
Figure 3

Major SARS-CoV-2 Clades
- 20B
- 20A
- 20C
- 20G
Figure 4

Index NP viral load at baseline (copies/mL) among households with or without transmission.

- Including Ab+
- Excluding Ab+

Households

Transmission vs. No transmission