SARS-CoV-2 incidence and risk factors in a national, community-based prospective cohort of U.S. adults

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ABSTRACT

Background: Prospective cohort studies of SARS-CoV-2 incidence complement case-based surveillance and cross-sectional seroprevalence surveys.

Methods: We estimated the incidence of SARS-CoV-2 infection in a national cohort of 6,738 U.S. adults, enrolled March-August 2020. Using Poisson models, we examined the association of social distancing and a composite epidemiologic risk score with seroconversion. The risk score was created using LASSO regression to identify factors predictive of seroconversion. The selected factors were household crowding, confirmed case in household, indoor dining, gathering with groups ≥ 10, and no masking in gyms/salons.

Results: Among 4,510 individuals with ≥1 serologic test, 323 (7.3%, 95% confidence interval [CI] 6.5%-8.1%) seroconverted by January 2021. Among 3,422 participants seronegative in May-September 2020 and retested during November 2020-January 2021, 161 seroconverted over 1,646 person-years of follow-up (9.8 per 100 person-years [95%CI 8.3-11.5]). Seroincidence rate was lower among females compared to males (IRR: 0.69, 95% CI 0.50-0.94) and higher among Hispanic (IRR: 2.09, 95% CI 1.41-3.05) participants compared to White non-Hispanic. In adjusted models, participants who reported social distancing with people they did not know ($IRR_{always\ vs.\ never}$: 0.42, 95% CI 0.20-1.0) and with people they knew ($IRR_{always\ vs.\ never}$ 0.64, 95%CI 0.39-1.06; $IRR_{sometimes\ vs.\ never}$ 0.60, 95% CI 0.38-0.96) had lower seroconversion risk. Seroconversion risk increased with epidemiologic risk score ($IRR_{medium\ vs.\ low}$ 1.68, 95% CI 1.03-2.81; $IRR_{high\ vs.\ low}$ 3.49, 95% CI 2.26-5.58). Only 29% of those who seroconverted reported isolating and 19% were asked about contacts.

Conclusion: Modifiable risk factors and poor reach of public health strategies drove SARS-CoV-2 transmission across the U.S.

KEYWORDS: COVID-19; serology, seroconversion, asymptomatic infection, physical distancing; natural history study, epidemiologic study, essential workers, public health interventions, community transmission

INTRODUCTION

A major challenge of controlling community transmission of SARS-CoV-2 is the asymptomatic and pre-symptomatic spread of infection [1,2], including by fully-vaccinated individuals [3]. One national study in the United States (U.S.) prior to the vaccine era estimated five undiagnosed infections for every diagnosed case [2]. While SARS-CoV-2 is transmitted from person-to-person via airborne and droplet spread, to date, the incidence of SARS-CoV-2 infection and its risk factors have not been adequately characterized by routine case-based surveillance or by cross-sectional seroprevalence studies [4–6]. It is critical for prospective studies to investigate COVID-19's evolving epidemiology, risk factors for SARS-CoV-2 incidence in communities, uptake and impact of non-pharmaceutical interventions (NPIs) [7], and the reach of public health strategies aimed at controlling community transmission, including testing, quarantine, isolation, contact tracing, and vaccination. Globally, few community-based prospective epidemiologic studies of SARS-CoV-2 incidence and risk factors have been undertaken. One systematic review found 18 prospective observational studies of SARS-CoV-2 that employed serologic or polymerase chain reaction (PCR) testing [8]. Most studies focused on healthcare workers or other occupational groups and individuals in congregate settings [8]. While national community-based prospective cohort studies have been conducted in the United Kingdom [9–11], such studies have been scarce in the U.S. Community-based studies with longitudinally collected biomarkers data can help inform implementation of public health responses and policies, both for the current pandemic and future ones.

In March 2020, we launched the prospective Communities, Households and SARS-CoV-2 Epidemiology (CHASING) COVID Cohort [12]. We describe the incidence of SARS-CoV-2 infection and risk factors for SARS-CoV-2 seroconversion during May 2020-January 2021, and the reach and uptake of public health strategies aimed at controlling community spread among those who seroconverted.

METHODS

Recruitment

We used internet-based strategies [13,14] to recruit a geographically and socio-demographically diverse cohort of adults into longitudinal follow-up with at-home specimen collection. Informed consent was obtained from all participants prior to enrollment. To be eligible for inclusion in the cohort, individuals had to: 1) reside in the U.S. or a U.S. territory; 2) be ≥18 years old; 3) provide a valid email address; and 4) demonstrate early engagement in study activities (provide baseline specimen or complete of >1 recruitment/enrollment visit). Details of the study design and recruitment procedures are described elsewhere [15]. The full cohort includes participants from all 50 U.S. states, the District of Columbia, Puerto Rico, and Guam (Supplemental Materials 1, Figure S2). Of the 6,738 participants in the full cohort, 4,510 (67%) had at least one serologic test and comprised the study population for this analysis (Supplemental Materials 1, Table S1).

Data collection

Cohort recruitment and multiple rounds of interviews occurred between March 28-August 21, 2020. Demographic and COVID-19 related risk factors were collected at baseline. From three follow-up interviews between August-November 2020, we obtained repeated measurements of COVID-19 symptoms, laboratory testing (PCR or serologic), hospitalizations, use of NPIs such as mask use and social distancing, and public health strategies such as quarantine, isolation, and contact tracing.

During May-September 2020 (Period 1) and November 2020-January 2021 (Period 2), participants were invited to complete serologic testing using an at-home dried blood spot (DBS) specimen self-collection kit. DBS cards were returned to the study laboratory (Molecular Testing Laboratories [MTL], Vancouver, Washington) via the U.S. Postal Service using a self-addressed, stamped envelope containing a biohazard bag™. All DBS specimens were tested by the study laboratory for total antibodies (Total Ab) using the Bio-Rad Platelia test for IgA, IgM, and IgG which targets the SARS-CoV-2 nucleocapsid protein (manufacturer sensitivity 98.0%, specificity 99.3%) [16]. Other studies have independently

validated this assay and found average sensitivity and specificity of 91.7% and 98.8%, respectively [17–19]. This assay was also validated for use with DBS by the study laboratory, which found 100% sensitivity and 100% specificity (Supplemental Materials 2).

Outcomes

Cumulative incidence of SARS-CoV-2 infection. Among participants who underwent serologic testing, we estimated the serology-based cumulative incidence of SARS-CoV-2 as the number of individuals with a positive Total Ab test in either of the two time periods divided by the total number of persons with one or more Total Ab tests. We adjusted cumulative incidence estimates for laboratory test error, assuming a sensitivity of 91.7% and a specificity of 98.8% [17–19] using the following formula [20]:

$$Adjusted\ cumulative\ incidence = \frac{Crude\ cumulative\ incidence + Specificity - 1}{Sensitivity + Specificity - 1}$$

Observed SARS-CoV-2 seroconversion. Among individuals with two Total Ab tests, an observed seroconversion was defined as a negative Total Ab test in Period 1 followed by a positive Total Ab test in Period 2. We estimated person-years of follow-up using the specimen collection dates in Periods 1 and 2. We used the date the laboratory received the sample for missing collection dates. The seroconversion date was assigned as the midpoint between the first and second specimen collection dates for person-time calculations. To address the possibility of misclassifying some individuals with recent infections who had not yet seroconverted by the time of the second antibody test, we conducted a sensitivity analysis including reports of recent positive SARS-CoV-2 PCR or rapid test in the incidence estimate.

Exposures

Individual-level COVID-19 risk factors. Individually and as part of a composite score, we considered epidemiologic risk factors for SARS-CoV-2 reported by participants prior to specimen collection, including: Household factors (household crowding defined as ≥4 people living in a multi-family dwelling, having a child in the household, and having a confirmed COVID-19 case in a household member prior to participant testing positive); spending time

in public places (attending mass gatherings, indoor dining in a restaurant/bar, outdoor dining at a restaurant/bar, visiting places of worship, or visiting public parks/pools); mask use indoors (for grocery shopping, visiting non-household members, at work, and in salons/gyms); mask use outdoors; gathering in groups with 10 people; travel during the pandemic (air travel and public transit use); and individual-level factors that may increase the risk of severe COVID-19 (substance use, binge drinking, and comorbidities).

Global social distancing assessment. While social distancing in specific scenarios is addressed in some of the above individual risk factors, we were interested in the association between social distancing in general and incident SARS-CoV-2 infection. We asked two global questions on social distancing: "In the past month, how often have you practiced social distancing with: a) *people you know* and b) *people you do not know*," with possible response options of *Always, Sometimes, or Never*. These assessments were not included in the calculation of the composite risk score.

Composite score of COVID-19 risk factors. We computed a composite COVID-19 risk score as many of the above COVID-19 risk factors may be highly correlated. We applied Least Absolute Shrinkage Selection Operator (LASSO) regression to select the set of risk factors which best predicted seroconversion [21]. The LASSO model selected household crowding, having a confirmed COVID-19 case in a household member, indoor dining in a bar/restaurant, gathering with groups of ≥10, and no mask use indoors in salons/gyms as the most predictive of seroconversion in our cohort. Scores were assigned to each participant based on their engagement in the risk factors selected by the LASSO model and were normalized between 0 and 100. High scores indicate engagement in high-risk activities (Details in Supplemental Materials 1, Statistical Appendix). The composite score was divided into tertiles for analysis.

Statistical analysis

Cumulative incidence estimates were stratified by baseline characteristics and epidemiologic risk factors. Crude and adjusted Incidence Rate Ratios (IRRs) of seroincidence and associated 95% confidence intervals (CIs) were estimated using Poisson regression. We

examined crude seroconversion rates by sociodemographic characteristics and each risk factor. Finally, we separately modeled three exposure variables: 1) social distancing with "people you know" (always/sometimes/never); 2) social distancing with "people you don't know" (always/sometimes/never); and 3) the composite COVID-19 risk score (high/medium/low). Two multivariable models were constructed for each exposure variable, adjusting for age, gender, race/ethnicity and comorbidities (Model 1); and further controlling for changes in community-level COVID-19 transmission (Model 2). All data were cleaned and analyzed in R (version 4.0.3) and SAS (V9.4).

Ethical Approval

The study protocol was approved by the Institutional Review Board at the City University of New York (CUNY) and all methods were performed in accordance with relevant guidelines and regulations.

RESULTS

Sample characteristics

Of the 4,510 participants who tested at least once, 3,605 (80%) tested at both time points (Table 1). A total of 4,232 persons underwent serologic testing in Period 1, and 3,883 in Period 2 (Supplemental Materials 1, Table S1). Differences between participants testing in Period 1 and Period 2 were negligible (Supplemental Materials 1, Table S1). The median time between specimen collection dates for participants providing specimens for both serologic tests was 190 days (IQR 152-201) (Supplemental Materials 1, Figure S1).

Cumulative incidence of SARS-CoV-2 as of January 31, 2021

We observed 323 unique seropositives among the 4,510 participants who tested at least once during follow-up, for overall crude and adjusted serology-based cumulative incidence estimates of 7.3% (95% CI 6.5%-8.1%) and 6.7% (95% CI 5.9%-7.6%), respectively (Supplemental Materials 1, Table S2).

SARS-CoV-2 seroincidence, May 2020-January 2021

There were 3,422 seronegative participants in Period 1 with a subsequent serologic test in Period 2. There were 161 observed seroconversions over 1,646 person years of follow-up,

for an overall incidence rate of 9.8 per 100 person-years (95% CI 8.3-11.5) (Table 2). The rate of incident SARS-CoV-2 infection was lower for females compared to males (IRR=0.69, 95% CI 0.50-0.94), and higher for Hispanic (IRR=2.09, 95% CI 1.41-3.05) and Black non-Hispanic (IRR=1.69, 95% CI 0.96-2.82) compared with White non-Hispanic participants. Essential workers had higher incidence than non-essential workers (IRR=1.65, 95% CI 1.10-2.26). Incidence rates were higher among participants from the South (IRR=1.67, 95% CI 1.08-2.59) compared to the Northeast U.S.

Table 3 shows the seroincidence and crude incidence rate ratios by epidemiologic risk factors that were measured prior to serologic tests. Compared to those in single-family dwellings with <4 household members, incidence was higher among those living in multifamily dwellings with ≥4 household members (IRR=2.1, 95% CI 1.1-3.7) and those living in congregate settings (IRR=2.5, 95% CI 1.2-4.8). A confirmed case in a household member was associated with a 15-fold higher incidence (IRR=16.3, 95% CI 9.6-27.8). Incidence was higher among participants who dined indoors at restaurants or bars (IRR=1.93, 95% CI 1.39-2.70); visited a place of worship (IRR=1.92, 95% CI 1.26-2.84); gathered in groups ≥10 outdoors only (IRR=1.59, 95% CI 1.07-2.34) as well as both indoors and outdoors (IRR=2.40 95% CI 1.41-3.09); visited indoors with non-household members sometimes wearing a mask (IRR=1.79; 95% CI 1.11-2.96) or never wearing a mask (IRR=2.42; 95% CI 1.41-4.21); worked indoors at a place of employment while never wearing a mask (IRR=2.45, 95% CI 0.96-5.34); wore masks only sometimes while attending a salon/gym (IRR=3.16, 95% CI 1.86-5.18); and reported travelling by air during August-November 2020 (IRR=1.50, 95% CI 1.04-2.14).

Poisson models of SARS-CoV-2 seroconversion, May 2020-January 2021

In crude analyses, participants who reported that they *always or sometimes* engaged in social distancing with people they know (versus never) had a statistically significantly lower seroincidence ($IRR_{always\ vs\ never}$=0.54, 95% CI 0.34-0.90; $IRR_{sometimes\ vs\ never}$=0.53, 95% CI 0.34-0.85). In multivariable analyses adjusted for sociodemographics and comorbidities (Model 1, $aIRR_{always\ vs\ never}$=0.60, 95% CI 0.37-0.99), and additionally for community-level transmission

(Model 2, $aIRR_{always\ vs\ never}$=0.64, 95% CI 0.39-1.06), participants who reported *always* social distancing with those they know (versus never) had lower seroincidence, although the 95% confidence intervals were wider. Participants who reported social distancing *always* or *sometimes (vs. never)* with people they did not know also had lower seroincidence rates in both crude and adjusted models, but results were marginally significant. The composite risk score for SARS-CoV-2 incidence was associated with seroconversion in dose-response fashion ($IRR_{medium\ vs\ low}$=1.68, 95% CI 1.03-2.81; $IRR_{high\ vs\ low}$=3.49, 95% CI 2.26-5.58) (Table 4).

The sensitivity analysis that also included individuals who were seronegative at time 2, but who reported a positive PCR or rapid test (n=187) did not materially alter the findings (Supplemental Table S3).

Clinical and public health outcomes among persons with SARS-CoV-2 seroconversion during May 2020-January 2021

Among the 161 individuals who seroconverted during May 2020-January 2021, 97 (60.3%) reported ever testing for SARS-CoV-2 outside the study, but only half (26.7% of total) reported ever having a positive SARS-CoV-2 test. (Table 5). About 28% reported no symptoms of COVID-like illness. Only 29.2% reported having ever isolated themselves from people outside their household because of their infection, and, among those who did not live alone, even fewer (17.4% overall) reported having ever isolated themselves from others within their household. Less than one-fifth (19.3%) of all seroconverters were asked about contacts following diagnosis and only 11.8% had been informed by a contact tracer about contact with a confirmed SARS-CoV-2 case. Only 5.0% of all seroconverters were told by a contact tracer to isolate because they had COVID-19.

DISCUSSION

We report findings from a large community-based prospective epidemiologic study of SARS-CoV-2 incidence and risk factors in the U.S. during May 2020-January 2021. Using serologic tests, we longitudinally characterized the incidence of SARS-CoV-2 infection in relation to a range of risk factors. We found that social distancing and a low epidemiologic risk score

composed of modifiable risk factors was protective against infection, even after controlling for other measured confounders. Finally, public health strategies such as quarantining, testing, isolation, and contact tracing had low coverage and adoption among seroconverters, limiting their effectiveness at reducing community transmission. Taken together, our study findings document some of the principal reasons why the U.S. has continued to experience sustained community transmission, hospitalizations, and deaths from COVID-19 in many areas.

Social distancing was protective against seroincidence even after controlling for other risk factors. This suggests a need for more effective and consistent messaging around social distancing. We observed substantially increased risk for several other key epidemiologic risk factors reflected in a composite risk score. Among participants in the top tertile of the risk score seroincidence risk was 3-fold higher, accounting for 55% of the observed seroconversions. Reducing multiple risk factors (e.g., through policies on masking, mass gatherings, indoor dining/bars, social distancing, air travel) would likely substantially reduce community transmission even in the vaccine era.

Our findings suggest that elevated risk among essential workers, observed early in the U.S. pandemic, persisted into the second phase of the pandemic. Essential workers risk exposure to SARS-CoV-2 not only in their workplaces, but also in their communities and as part of their work commute if they use public transportation. Household members of essential workers share their high infection risk [28]. Workplace safety measures, such mask/vaccine mandates, have the added benefit of protecting household members and other close contacts of essential workers.

We identified gaps in the reach of public health interventions aimed at reducing SARS-CoV-2 spread. Most who seroconverted did not report a prior positive PCR test, and a substantial proportion were asymptomatic. Moreover, few people who seroconverted in our study reported being reached by contact tracers. These results highlight the barriers to successful implementation of isolation, contact tracing, and quarantine. Now that rapid home tests are

easily available, frequent proactive testing at home can be a more effective way to capture asymptomatic and pre-symptomatic cases early and prevent onward transmission.

Our study highlights that the drivers of racial/ethnic disparities in SARS-CoV-2 risk need to be targeted by governments, health departments and researchers [29]. Structural factors, such as household crowding, the need to work in-person to avoid income loss, and inequitable access to SARS-CoV-2 testing [30], create and perpetuate a disparate burden of SARS-CoV-2 exposure and incidence [31]. To date, no targeted strategies or policies have been deployed that aim to protect those who cannot afford missing work, including essential workers. Public health leaders and policy makers should proactively design pandemic response strategies that counteract the prevailing structural forces, including structural racism, that create, maintain, or exacerbate inequities in safety and health during a public health crisis [32–35].

Our study has several limitations. The observed cumulative incidence may be lower than the true cumulative incidence in our cohort because of waning of SARS-CoV-2 antibodies [36]. Recent studies suggest waning of antibodies to both nucleocapsid and spike proteins [5]. Combined with the timing of specimen collection relative to infection for many participants in our cohort (median 190 days) [12], this could mean that we underestimated the true cumulative incidence. The frequency of observed seroconversion in our cohort was 5% over 6 months (9.8 per 100 person-years), a level that is associated with slightly reduced positive predictive value in single use assays, and may have resulted in misclassification of some individuals as having seroconverted when they did not. This would bias estimated risk factor associations toward the null. Next, estimated associations between SARS-CoV-2 risk factors and incidence are subject to confounding. The crude associations we presented may vary by setting, with interpretation for some associations further hampered by small sample sizes. The LASSO model is a predictive model, and the selected risk factors used in the composite risk score may not be causally associated with seroconversion. Some risk behaviors may have been underreported, due to social desirability, which would bias observed associations toward the null. Finally, our study period for the current analysis pre-dated the vaccine era

and the emergence of the highly transmissible and possibly more virulent Delta and Omicron variants. We could not, therefore, examine risk factors for infection among vaccinated persons. Lower vaccine effectiveness has been observed against the Delta and Omicron variants for infection [37-41], and high viral loads have been documented among fully vaccinated persons [3,42]. Thus, our findings related to transmission risk factors also likely apply to vaccinated persons, as they remain at risk for breakthrough infection and onward transmission of SARS-CoV-2 when engaging in some of the same risk factors.

Conclusion

Modifiable risk factors and poor reach of public health strategies continue to drive transmission of SARS-CoV-2 across the U.S. While continuing to increase vaccine coverage, it remains critical for public health agencies to simultaneously reduce risk factors and address structural factors that contribute to high incidence and persistent inequities. Future research will include monitoring SARS-CoV-2 outcomes in the vaccine, and Delta and Omicron variant eras.

NOTES

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AUTHOR CONTRIBUTIONS

DN, MSR, SGK, MMR, conceptualized the study. MSR, MC and DN performed statistical analyses. DN and MSR wrote the first draft of the paper. DN, MSR, MC, SGK, and AP contributed to interpreting the data, DN, RZ, MSR, MC, SGK, WY, AB, CM, SK, AM, MMR, DAW, AP, LW, and CG contributed to the writing and revising of the manuscript. SGK, WY,

AB, CM, SK, and DN contributed to data collection, cleaning and management. DN, SGK, MMR and CG contributed to obtaining funding for the research.

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1 **TABLES**

Table 1. Baseline characteristics of CHASING COVID Cohort Study participants who provided a dried blood spot sample for antibody testing

	Participants with one or more serologic tests	
	N	%
Total	4,510	100.00
Two serologic tests	3,605	79.93
Age		
Median (IQR)	41 (31, 55)	
18-29	876	19.42
30-39	1,253	27.78
40-49	858	19.02
50-59	658	14.59
≥ 60	865	19.18
Gender		
Male	2,018	44.75
Female	2,360	52.33
Non-Binary/Transgender	132	2.93
Race/Ethnicity		

White non-Hispanic	2,966	65.76
Hispanic	679	15.06
Black non-Hispanic	378	8.38
Asian/Pacific Islander	304	6.74
Other	168	3.73
Missing	15	0.33
Education		
Less than high school	54	1.20
High school graduate	403	8.94
Some college	1,151	25.52
College graduate	2,902	64.35
Employment		
Employed	2,774	61.51
Out of work	544	12.06
Homemaker	242	5.37
Student	367	8.14
Retired	583	12.93
Household income		
<$35,000	1,186	26.30

$35,000-49,999	496	11.00
$50,000-69,999	643	14.26
$70,000-99,999	741	16.43
≥$100,000	1,329	29.47
Don't know	112	2.48
Missing	3	0.07
Setting		
Urban	1,911	42.37
Suburban	1,186	26.30
Rural	1,412	31.31
Missing	1	0.02
Geographic region		
Northeast	1,320	29.27
Midwest	805	17.85
South	1,269	28.14
West	1,111	24.63
US Territories	5	0.11
Healthcare worker		
No	4,048	89.76

Yes	425	9.42
Don't know	37	0.82
Essential worker *		
No	3,170	70.29
Yes	1,340	29.71
Higher risk for severe COVID **		
No	2,097	46.50
Yes	2,413	53.50

* Combined from three follow-up interviews between August and November 2020

** >60 years old, or reported co-morbidity, or current smoker. Comorbidity was defined as having history of heart attack, depression, angina, immunosuppression, type 2 diabetes, high blood pressure, cancer, asthma, COPD, chronic kidney disease, and/or HIV/AIDS

Table 2: Crude associations of COVID-19 sociodemographic factors with seroincidence, May 2020-January 2021

	No. of seronegative participants in Period 1 *	No. of incident infections in Period 2 **	Total person-years of follow up	Seroincidence per 100 person-years	Rate Ratio (95% CI)
Total	3,422	161	1,646.04	9.8 (8.3, 11.5)	
Age group					
18-29	617	37	300.00	12.33 (8.9, 16.7)	(ref)
30-39	934	46	449.00	10.24 (7.6, 13.5)	0.83 (0.53, 1.28)
40-49	654	33	310.00	10.65 (7.5, 14.7)	0.86 (0.53, 1.38)
50-59	514	23	249.00	9.24 (6.1, 13.7)	0.74 (0.43, 1.25)
≥ 60	703	22	339.00	6.49 (4.2, 9.8)	0.52 (0.30, 0.88)
Gender					
Male	1,516	88	748.00	11.76 (9.6, 14.3)	(ref)
Female	1,810	69	850.00	8.12 (6.4, 10.2)	0.69 (0.50, 0.94)

Non-Binary/Transgender	96	4	48.71	8.21 (2.6, 20.6)	0.69 (0.21, 1.73)
Race/Ethnicity					
White non-Hispanic	2,307	92	1,141.00	8.06 (6.5, 9.8)	(ref)
Hispanic	500	37	219.00	16.89 (12.3, 22.6)	2.09 (1.41, 3.05)
Black non-Hispanic	261	16	117.00	13.68 (8.2, 21.5)	1.69 (0.96, 2.82)
Asian/PI	222	7	106.78	6.56 (2.9, 13.5)	0.81 (0.34, 1.66)
Other	132	9	63.02	14.28 (7.1, 25.9)	1.77 (0.84, 2.77)
Education					
Less than high school	37	2	16.10	12.42 (2.1, 39.4)	(ref)
High school graduate	278	14	121.00	11.57 (6.7, 18.9)	0.93 (0.24, 6.05)
Some college	815	44	377.00	11.67 (8.7, 15.4)	0.93 (0.27, 5.76)
College graduate	2,292	101	1,132.00	8.92 (7.3, 10.8)	0.71 (0.21, 4.33)
Employment					

Employed	2,102	109	1,020.00	10.69 (8.8, 12.8)	(ref)
Out of work	402	18	188.90	9.53 (5.9, 14.9)	0.89 (0.52, 1.44)
Homemaker	179	7	78.70	8.89 (3.9, 18)	0.86 (0.35, 1.68)
Student	253	12	126.00	9.52 (5.2, 16.4)	0.89 (0.46, 1.57)
Retired	486	15	233.00	6.44 (3.7, 10.6)	0.60 (0.33, 1.01)
Household income					
<$35,000	880	43	405.00	10.62 (7.8, 14.1)	(ref)
$35,000-49,999	383	23	182.00	12.64 (8.3, 18.5)	1.19 (0.70, 1.96)
$50,000-69,999	505	18	241.00	7.47 (4.6, 11.7)	0.70 (0.39, 1.20)
$70,000-99,999	592	34	286.00	11.89 (8.4, 16.3)	1.12 (0.70, 1.75)
≥$100,000	993	38	495.00	7.68 (5.5, 10.5)	0.72 (0.46, 1.12)
Don't know	77	5	37.00	13.5 (5.1, 29.5)	1.27 (0.44, 3.01)
Missing	2	--	--		

Setting					
Urban	1,442	62	707.00	8.7 (6.8, 11.1)	(ref)
Suburban	904	42	438.00	9.58 (7.1, 12.8)	1.11 (0.74, 1.65)
Rural	1,076	57	501.00	11.37 (8.8, 14.6)	1.29 (0.89, 1.29)
Geographic region					
Northeast	977	34	477.00	7.13 (5, 9.9)	(ref)
Midwest	629	34	300.00	11.33 (8.1, 15.6)	1.59 (0.98, 2.56)
South	953	53	445.00	11.91 (9.1, 15.3)	1.67 (1.08, 2.59)
West	859	39	413.00	9.44 (6.9, 12.8)	1.32 (0.83, 2.11)
U.S. Territories	4	--	--	--	--
Healthcare worker					
No	3,074	140	1,481.00	9.45 (8, 11.1)	(ref)
Yes	315	19	150.00	12.67 (7.9, 19.3)	1.34 (0.80, 2.12)
Don't know	33	2	14.00	14.3 (2.5, 43.8)	1.51 (0.25, 5.07)
Essential worker					
***					

No	2,407	95	1,160.00	8.1 (6.7, 9.9)	(ref)
Yes	1,015	66	486.00	13.6 (10.7, 17.0)	1.65 (1.10, 2.26)
High Risk group ****					
No	1,574	83	761.00	10.91 (8.8, 13.4)	(ref)
Yes	1,848	78	885.00	8.81 (7.1, 10.9)	0.80 (0.59, 1.10)

* May - September 2020

** November 2020 - January 2021

*** Combined from three follow-up interviews between August and November 2020

**** >60 years old, or reported co-morbidity, or current smoker. Comorbidity was defined as having history of heart attack, depression, angina, immunosuppression, type 2 diabetes, high blood pressure, cancer, asthma, COPD, chronic kidney disease, and/or HIV/AIDS

Table 3: Crude associations of COVID-19 risk factors with seroincidence, May 2020-January 2021

	No. of seronegative participants in Period 1 *	No. of incident infections in Period 2 **	Total person-years of follow up	Incidence rate per 100 person-years (95% CI)	Rate Ratio (95% CI)
Total	3,422	161	1,646.04	9.8 (8.3, 11.5)	
Household factors					
Multi-family with ≥4 household members	171	14	78.00	17.9 (10.5, 28.6)	2.1 (1.1, 3.7)
Multi-family with <4 household members	1,160	54	577.00	9.4 (7.2, 12.1)	1.1 (0.7, 1.6)
Single-family with ≥4 household members	625	27	289.00	9.3 (6.3, 13.4)	1.1 (0.7, 1.7)
Single-family with <4 household members	1,374	57	660.00	8.6 (6.7, 11.1)	ref
Dorm, Group home, Other	92	9	42.04	21.4 (10.8, 37.2)	2.5 (1.2, 4.8)
Child in household	965	45	440.00	10.2 (7.6, 13.5)	1.1 (0.7, 1.5)
No child in household	2,457	116	1,206.00	9.6, 8.0, 11.5)	ref
Confirmed case in household member	28	15	123.6	12.1 (7.2, 19.6)	16.3 (9.6, 27.8)
No confirmed case in household member	3,394	146	19,630.80	0.7 (0.6, 0.9)	ref

Social distancing					
Social distancing with people you do not know					
Always	2,616	113	1,258.00	8.9 (7.4, 10.7)	0.29 (0.14, 0.69)
Sometimes	660	34	319.00	10.6 (7.6, 14.7)	0.35 (0.16, 0.86)
Never	53	7	23.30	30.0 (13.8, 52.4)	ref
Not Applicable	53	4	24.50	16.3 (5.3, 37.5)	0.53 (0.13, 1.83)
Social distancing with people you know					
Always	1,137	51	543.00	9.4 (7.1, 12.2)	0.54 (0.33, 0.89)
Sometimes	1,787	79	868.00	9.1 (7.3, 11.3)	0.52 (0.33, 0.84)
Never	300	24	139.00	17.3 (11.5, 24.8)	ref
Not Applicable	158	4	74.50	5.4 (1.7, 13.9)	0.31 (0.09, 0.83)
Spent time in public places					
Attended mass gathering(s)	350	18	174.89	10.3 (6.4, 16.5)	1.05 (0.63, 1.69)
Did not attend mass gathering(s)	3,072	143	1,471.15	9.7 (8.2, 11.5)	ref
Indoor dining/bar	1,755	108	843.86	12.8 (10.5, 15.5)	1.93 (1.39, 2.70)
No indoor dining/bar	1,667	53	802.18	6.6 (5.0, 8.7)	ref
Outdoor dining/bar	1,869	109	924.35	11.8 (9.8, 14.1)	1.1 (0.8, 1.4)

No outdoor dining/bar	1,553	78	721.70	10.8 (8.7, 13.3)	ref
Visited place of worship	359	29	168.87	17.2 (11.7, 25.1)	1.92 (1.26, 2.84)
Did not visit place of worship	3,063	132	1,477.17	8.9 (7.5, 10.6)	ref
Visited public park/public pool	2,334	100	1,147.00	8.7 (7.2, 10.5)	0.71 (0.52, 0.98)
Did not visit public park/pool	1,088	61	499.00	12.2 (9.5, 15.5)	ref
Gathered in groups ≥ 10					
No	1,961	70	939.00	7.4 (5.9, 9.4)	ref
Indoors only	230	11	109.00	10.1 (5.4, 7.7)	1.35 (0.68, 2.48)
Outdoors only	686	40	337.00	11.8 (8.7, 15.9)	1.59 (1.07, 2.34)
Indoors and outdoors	522	39	249.00	15.6 (11.4, 20.9)	2.40 (1.41, 3.09)
Do Not Know	23	1	11.70	8.5 (0.4, 41.0)	1.14 (0.05, 5.80)
Mask Use					
Mask while grocery shopping					
Did not go grocery shopping	173	9	84.60	10.6 (5.3, 19.7)	ref
Always	3,084	140	1,489.12	9.4 (7.9, 11.1)	0.88 (0.46, 1.84)
Sometimes	132	12	57.22	21.0 (11.6, 38.0)	1.97 (0.82, 4.86)
Never	33	0	15.11	0	0 (0, 2.21)

Mask while indoors visiting non-household members					
Did no visit non-household members indoors	710	22	342.00	6.4 (4.1, 9.7)	ref
Always	1,118	43	546.26	7.9 (5.8, 10.7)	1.22 (0.73, 2.07)
Sometimes	1,131	63	546.44	11.5 (8.9, 14.9)	1.79 (1.11, 2.96)
Never	463	33	211.58	15.6 (10.9, 22.22)	2.42 (1.41, 4.21)
Mask while indoors at work					
Did not attend indoor workplace	1,683	66	811.00	8.1 (6.4, 10.3)	ref
Always	1,372	71	660.60	10.7 (8.5, 13.6)	1.32 (0.94, 1.85)
Sometimes	299	18	144.08	12.5 (7.8, 20.1)	1.53 (0.88, 2.54)
Never	68	6	30.05	20.0 (8.6, 46.2)	2.45 (0.96, 5.34)
Mask while at salon/gym					
Did not attend salon/gym	1,607	59	771.00	7.6 (5.9, 9.8)	ref
Always	1,527	75	743.45	10.1 (8.0, 12.7)	1.31 (0.94, 1.86)
Sometimes	180	20	82.69	24.2 (15.2, 38.5)	3.16 (1.86, 5.18)
Never	108	7	48.94	14.3 (6.6, 30.8)	1.86 (0.78, 3.90)
Outdoor mask use					
Mask use outdoors	1,562	67	753.27	8.9 (7.0, 11.4)	0.84 (0.67, 1.15)

No mask use outdoors	1,860	94	892.78	10.5 (8.6, 13.0)	ref
Movement during the pandemic					
Avoided public transit	2,692	124	1293	9.6 (8.1, 11.3)	ref
Used public transit	730	37	353	10.5 (7.6, 14.3)	1.09 (0.74, 1.56)
Recent Air travel (Aug-Nov)					
Yes	582	39	287.91	13.5 (9.9, 18.2)	1.50 (1.04, 2.14)
No	2,840	122	1,358.00	8.9 (7.5, 10.6)	ref
Other potential risk factors					
Alcohol use ***	694	40	334.00	11.9 (8.8, 16.1)	1.50 (1.01, 2.22)
Substance use ****	914	45	443.40	10.1 (7.5, 13.7)	1.05 (0.73, 1.47)
Any comorbidities ^^	1,490	69	714.52	9.7 (7.6, 12.3)	0.97 (0.71, 1.33)
Changes in county-level community transmission					
High (0.327-3.30)	1,139	76	536.00	14.2 (11.4, 17.5)	ref
Medium (0.211-0.327)	1,140	37	557.00	6.6 (4.8, 9.1)	0.46 (0.31, 0.69)
Low (0-0.211)	1,139	48	550.00	8.7 (6.5, 11.4)	0.61 (0.42, 0.88)

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Table 4: Crude and adjusted incidence rate ratios (IRRs) for seroincidence in the CHASING COVID Cohort Study, May 2020-January 2021

	Crude		Adjusted (Model 1 *)		Adjusted (Model 2 **)	
	IRR	**95% CI**	**IRR**	**95% CI**	**IRR**	**95% CI**
Social distancing with people you do not know (ref:Never)						
Always	0.30	0.15, 0.72	0.37	0.18, 0.89	0.42	0.20, 1.00
Sometimes	0.35	0.16, 0.86	0.42	0.19, 1.05	0.47	0.22, 1.19
Not applicable (as per participant)	0.54	0.14, 1.80	0.70	0.18, 2.36	0.71	0.18, 2.38
Social distancing with people you do know (ref:Never)						
Always	0.54	0.34, 0.90	0.60	0.37, 0.99	0.64	0.39, 1.06
Sometimes	0.53	0.34, 0.85	0.57	0.36, 0.91	0.60	0.38, 0.96
Not applicable (as per participant)	0.31	0.09, 0.80	0.34	0.10, 0.90	0.37	0.10, 0.97
Composite measure of risk factors (ref:Low)						
Medium	1.59	0.98, 2.62	1.69	1.03, 2.81	1.68	1.03, 2.81
High	3.62	2.38, 5.71	3.53	2.29, 5.64	3.49	2.26, 5.58

* Model 1: Adjusted for age, gender, race/ethnicity, and comorbidities

** Model 2: Adjusted additionally for county-level changes in community level transmission

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Table 5. Clinical and public health outcomes among persons with seroincident SARS-CoV-2, May 2020-January 2021

	N	%
Total	161	100%
Symptoms and clinical outcomes		
PCR confirmed diagnosis	43	26.7
Asymptomatic *	45	28
Mild (symptomatic, but didn't seek care)	99	61.5
Ever had COVID like illness*	114	70.8
Nasal discharge, congestion or sneezing	100	62.1
Cough/Cough up phlegm	75	46.6
Cough up blood	0	0
Sore throat	65	40.4
Itchy eye or eye pain	53	32.9
Shortness of breath or chest pain	32	19.9
Stomachache, diarrhea, nausea or vomiting	67	41.6
Rash	12	7.5
Loss of smell	31	19.3
Headache	89	55.3

Fever, chills or repeated chills	44	27.3
Myalgia	58	36
Ever hospitalized	4	2.5
Public health outcomes and testing history		
Ever tested for COVID	97	60.3
Positive SARS-CoV-2 PCR test	43	26.7
Isolated from people outside household	47	29.2
Isolated from people within household **	28	17.4
Quarantined after contact with COVID	31	19.3
Asked about contacts after COVID diagnosis	31	19.3
Told about contacts with COVID case	19	11.8
Encouraged to get tested because of exposure to case	10	6.2
Told to stay home for a period of time	8	5

* Based on Council of State and Territorial Epidemiologists case definition

** Among those with others in the household