SARS-CoV-2 transmission in a highly vulnerable population of Brazil: a household cohort study

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Summary

Background Household transmission studies seek to understand the transmission dynamics of a pathogen by estimating the risk of infection from household contacts and community exposures. We estimated within/extra-household SARS-CoV-2 infection risk and associated factors in a household cohort study in one of the most vulnerable neighbourhoods in Rio de Janeiro city.

Methods Individuals ≥1 years-old with suspected or confirmed COVID-19 in the past 30 days (index cases) and household members aged ≥1 year were enrolled and followed at 14 and 28 days (study period November/2020–December/2021). RT-PCR testing, COVID-19 symptoms, and SARS-CoV-2 serologies were ascertained in all visits. Chain binomial household transmission models were fitted using data from 2024 individuals (593 households).

Findings Extra-household infection risk was 74.2% (95% credible interval [CrI] 70.3–77.8), while within-household infection risk was 11.4% (95% CrI 5.7–17.2). Participants reporting having received two doses of a COVID-19 vaccine had lower extra-household (68.9%, 95% CrI 57.3–77.6) and within-household (4.1%, 95% CrI 0.4–16.6) infection risk. Within-household infection risk was higher among participants aged 10–19 years, from overcrowded households, and with low family income. Contrastingly, extra-household infection risk was higher among participants aged 20–29 years, unemployed, and public transportation users.

Interpretation Our study provides important insights into COVID-19 household/community transmission in a vulnerable population that resided in overcrowded households and who struggled to adhere to lockdown policies and social distancing measures. The high extra-household infection risk highlights the extreme social vulnerability of this population. Prioritising vaccination of the most socially vulnerable could protect these individuals and reduce widespread community transmission.

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Research in context

Evidence before this study

Household transmission studies seek to understand the transmission dynamics of a pathogen by estimating the risk of infection from household contacts and community exposures. Several household transmission studies have been published, however, most of them did not account for the source of infection for secondary cases (within household or extra-household event).

We reviewed the evidence for household SARS-CoV-2 transmission studies in Brazil available as of December 21, 2023, by searching the Medline and the Virtual Health Library (*Biblioteca Virtual em Saúde* of the Pan American Health Organization) databases for articles and preprints, published in English or Portuguese, using the terms ["transmission" OR "secondary attack"] AND "household" AND ["SARS-CoV-2" OR "COVID-19"] AND ["Brazil"]. Few studies described the household transmission of SARS-CoV-2 in urban slums and *favelas* and none of them discriminated between the source of the infection, i.e., if it was a within-household or extra-household transmission event.

Added value of this study

Brazil has been severely affected by COVID-19, and the magnitude of the COVID-19 epidemic in Brazil can be, at least partially, explained by the country's profound socioeconomic inequality. Brazilian poverty is predominantly urban, with 72% of the poor living in urban areas. *Favelas* combine poverty, insecure and inadequate housing conditions, and lack of access to essential services, such as clean water and sanitation. We conducted a household transmission cohort study in one of the poorest neighbourhoods in Rio de Janeiro city (Complexo de Manguinhos), which comprises 16 different slums, to estimate SARS-CoV-2 transmission dynamics. Our main objective was to understand how, compared to other studies, the socioeconomic vulnerability of our population impacted infection risk. Additionally, we discriminated between the source of infection by estimating within-household and extra-household infection probabilities. This study included 2024 individuals from 593 households. RT-PCR testing, COVID-19 symptoms, and SARS-CoV-2 serologies were ascertained for all participants at Days 0, 14 and 28. Extra-household infection risk was 74.2%, while within-household infection risk was 11.4%. Vaccination reduced both within/extra-household infection risks. Within-household infection risk was higher among participants aged 10–19 years, from overcrowded households, and with low family income. Contrastingly, extra-household infection risk was higher among participants aged 20–29 years, unemployed, and public transportation users.

Implications of all the available evidence

Our study provides important insights into COVID-19 household and community transmission in a highly vulnerable population, providing valuable knowledge for informing public health policies and enhancing pandemic response. Compared to prior studies, the much higher extra-household infection risk highlights the extreme social vulnerability of our study population and the need for tailored strategies to mitigate and assist these communities during the emergency of a new transmissible infectious disease. Cash transfer programs can help by providing some level of financial security and, as such, permitting social distancing, whereas prioritizing vaccination of the most socially vulnerable could also protect these individuals and reduce widespread community transmission.

Introduction

Household transmission studies seek to understand the transmission dynamics of a pathogen by estimating the risk of infection from household contacts and community exposures. In the context of SARS-CoV-2, household transmission studies from multiple regions of the globe have shown that households are an important source of infection. Indeed, a meta-analysis found a positive correlation between the incidence rate of COVID-19 and household secondary attack rates (SAR).[1] However, household SAR estimates vary considerably by time and location.[1–3] Early studies conducted during the first few months of the pandemic (January and February of 2020) had estimated a household SAR of 13.4% (pooled estimate with 95% confidence interval [CI] 10.7–16.7), which is much lower than the 31.1% (95% CI 22.6–41.1) pooled estimate found in later studies conducted in mid-2020 to early 2021 (July 2020–March 2021).[2]

Possible explanations for the observed increase in estimated household SAR over time can be attributed to several factors. Advancements in diagnostic tools, such as improved test performance and increased accessibility may have contributed to more accurate case detection and contact tracing.[2,4] The emergence of novel viral variants with increased infectivity and greater ability to evade host immune responses (from both natural infections or immunization) may have intensified transmission dynamics.[3,5] Since 2020, five variants of concern (named alpha, beta, gamma, delta and omicron) have emerged and replaced the previous variants, thus influencing transmission dynamics and SAR.[5] Additionally, differences in study designs (e.g., follow-up duration, testing and monitoring protocols) may have played a role, for instance, longer follow-up periods in recent studies allowed the capture of tertiary transmission within households and/or transmission from non-household

contacts, resulting in higher SAR estimates.[2] Finally, it's paramount to emphasise that considerable heterogeneity exists between studies and caution is necessary when interpreting and comparing their findings.[2,4] Furthermore, disparities in population level COVID-19 vaccine coverage and non-pharmacological public health measures, over time and across different settings have influenced transmission dynamics and consequently estimates of household SAR.[1,6,7]

Additionally, disparities in household SARs by countries may result from differences in the degree to which populations adopted and adhered to non-pharmaceutical interventions. Household SARs estimated in studies from China and Singapore were lower than those estimated in studies from other countries, possibly due to mandated quarantine policies implemented in the former countries.[2,8–10] Finally, most of the studies[2,11,12] did not discriminate between the source of the infection, i.e., if it was a within-household or extra-household transmission event.

Brazil has been severely affected by COVID-19, with over 37 million cases and over 700,000 deaths reported as of December 2023, the second-highest official death toll in the world.[13] The Brazilian Government's omission during the pandemic (presidential term 2019–2022), manifested through a lack of leadership and promotion of disinformation, combined with profound socioeconomic vulnerabilities, contributed to the COVID-19 disaster.[14–16] These factors also impacted regional differences in COVID-19 burden throughout the country.[16] Rio de Janeiro city, for example, which is in the southeast region of Brazil and has over six million inhabitants,[17] 22% of which reside in slums (favelas or *comunidades*) or informal settlements,[18] was severely affected by the pandemic, experiencing one of the highest mortality rates of the country.[19] The political instability experienced in the city during the pandemic (the governor's impeachment and corruption scandals are some examples) contributed to COVID-19's devastating impact.[20]

Slums combine concentrated poverty, insecure and inadequate housing conditions, and lack of access to essential services, such as clean water and sanitation.[21,22] In this household transmission cohort study, we investigated SARS-CoV-2 transmission dynamics in one of the most vulnerable complex of slums (Complexo de Manguinhos) in Rio de Janeiro city and we sought to understand how, compared to other studies, the socioeconomic vulnerability of our population impacted infection risk. Moreover, we assessed which factors increased the likelihood of infection for this specific population. Finally, our main objective was to discriminate between the source of infection by estimating within-household and extra-household infection probabilities in this community.

Methods
Study design, participants, and procedures
Comvida-2 was a household cohort study conducted in the Manguinhos neighbourhood in Rio de Janeiro city, Brazil. Manguinhos is mainly comprised of slums (*Complexo de Manguinhos*) and has the city's 5th worst Human Development Index (HDI).

Study enrolment started on November 11th, 2020 and ended on November 30th, 2021 with the last study visit on December 8th, 2021. Individuals aged one year or older, with a suspected or confirmed diagnosis of COVID-19, who reported the start of COVID-19 symptoms in the past 30 days were eligible for the study as index cases. The 30-day symptom-initiation threshold was defined based on our operational ability to, given the receipt of the information from primary health clinics or community members of potential eligible index cases, to locate them, their household and to conduct enrolment visits of all household members. Index cases were mainly identified in the two primary health care clinics (*Clínica da Família Victor Valla* and *Centro de Saúde Escola Germano Sinval Faria*) that provide public primary health care to Manguinhos' population within the Brazilian Public Health System (*Sistema Único de Saúde*, SUS). Index cases could also be identified within the community through referral to the study team from neighbours or other residents in the area. All household members (individuals who dwell under the same roof [e.g., house or apartment unit]) of the index cases aged one year or older were eligible for the study.

A study team that included two interviewers and one laboratory technician visited the index cases' addresses and invited all eligible household members to participate in the study. After written informed consent, participants (index case and household members) were interviewed, underwent venipuncture for blood collection for SARS-CoV-2 serologies, and had nasal swabs collected for SARS-CoV-2 RNA rt-PCR test. Follow-up household visits were scheduled at 14 (±3 days) and 28 days (±3 days) after enrolment and included interview, venipuncture for blood collection for SARS-CoV-2 serologies, and nasal swabs for SARS-CoV-2 PCR test. To improve retention, as needed, households were visited more than once (at least two attempts, including one during the weekend) to conduct the study procedures with all household members.

In all study visits, interviews were conducted using structured questionnaires programmed using REDCap software forms on cell phones. The questionnaire had multiple sections that prompted participants' answers regarding clinical information (including COVID-19 symptoms in the past 2 weeks), demographics, socioeconomic information, behaviour (i.e., adherence to social distancing), household composition and household characteristics. Participants' sociodemographic information (gender, age, education level, race/skin colour

[White, Black, Pardo (Mixed-Black), Asian, Indigenous] and household details (household size, number of rooms (excluding bathrooms) and number of bedrooms) were collected. Household crowding was calculated as a person per bedroom (PPB, the number of dwellings in each household divided by the number of bedrooms).[23] PPB was categorised as: ≤1; 1.1–1.5; 1.6–2.0, 2.1–3.0; 3.1–4.0 and > 4.0. The cut-offs used for PPB were based on the American Crowding Index which defines "household crowding" as PPB greater than 1 and severe crowding" as PPB greater than 1.5; and on the UN-Habitat definition of overcrowding as PPB greater than 3.0[23]. Participants were questioned about their employment status (i.e., not working, working in person, working remotely). Family income was measured by the number of minimum wages (monthly minimum wage was 1045 Brazilian Reais [BRL] in 2020, which corresponds to 199 United States Dollars [USD]). Participants were asked if any household member was a beneficiary of the *Bolsa Familia* or *Auxílio Financeiro Emergencial* cash transfer programs. *Bolsa Familia* is a nationwide conditional cash transfer program for families in extreme poverty conditions that was instituted in 2004. *Auxílio Financeiro Emergencial* was an emergency financial assistance program implemented during the COVID-19 pandemic (April 2020 through October 2021) targeting low-income informal workers, the self-employed, and those already registered in *Bolsa Familia* who were eligible to receive this transfer in place of their regular *Bolsa Familia* benefits.[24] Participants were questioned about their level of adherence to social distancing measures (response options "very little", "little", "more or less", which were categorized as "poor", and "quite a lot", "practically isolated from everyone else", which were categorized as "good") and how frequently they left the house (response option "stayed at home all the time" was categorized as "never", response options "left the house for essential things" and "left the house a few times" were categorised as "a few times", and response options "left the house regularly for work or another regular activity" and "left the house every day" were categorised as "regularly"), both questions used a recall-time period of the prior two weeks. Participants also reported their main means of transportation used during the COVID-19 pandemic (categorised as: "walk or bike", "drive own car or motorcycle", "cab/ridesharing apps/mototaxi", or "public transport [bus, subway, train]"). Lastly, participants were asked if they had been vaccinated for COVID-19 and, if yes, with which vaccine (response options: CoronaVac, AstraZeneca, Pfizer, Janssen, Moderna, Sputnik and unknown), and how many doses they had received and respective dates.

The target sample size for our study was not based on statistical criteria but rather on the operational capacity of the study team to execute the protocol. The aim was to enrol 500 households comprising an estimated total of 2000 participants (index and contacts, based on an average household size of 4 persons) and 6000 longitudinal visits (3 visits per participant).

All participants gave written informed consent before participating in the study. For individuals younger than 18 years, parents or a legal representative provided consent. Local ethics committees approved the study (Instituto Nacional de Infectologia Evandro Chagas (INI)/Fiocruz, Escola Nacional de Saúde Pública (ENSP)/Fiocruz, and Instituto Oswaldo Cruz (IOC)/Fiocruz, CAAE # 3555558920.6.0000.5262).

Laboratory analysis

Nasal swabs and blood samples were collected in all study visits, according to the study protocol. Samples were transported in refrigerated containers to INI/Fiocruz clinical research laboratory. Samples' temperature was monitored to follow the assay manufacturer's instructions (2–8° Celsius). Nasal swabs and blood samples were processed on the same day. In addition, nasal swabs and serum aliquots were stored at –80 °C for future use or repetition, as needed.

SARS-CoV-2 RNA was detected in nasal swabs by reverse transcription followed by PCR (RT-PCR) with real-time detection, according to the "Berlin-Charitè" protocol from January 2017, in the Laboratory of Respiratory Viruses and Measles, reference laboratory of the World Health Organization (WHO) for COVID-19 at Fiocruz.[25]

Serum samples were processed and analysed for the presence of anti-SARS-CoV-2 IgG antibodies using two assays: (i) SARS-CoV-2 IgG II Quant assay on ARCHITECT analyser (Abbott Ireland, Sligo, Ireland; reference 6S60-22), a chemiluminescent microparticle immunoassay (CMIA) that quantifies IgG antibodies against the spike protein receptor-binding domain of SARS-CoV-2 (anti-S) with a 50AU/ml as a positive cut-off and upper limit of quantification of 40,000 AU/mL (80,000 AU/mL at 1:2 dilution). According to the manufacturer, the sensitivity and specificity of the test are 99.37% and 99.55%, respectively[26]; (ii) SARS-CoV-2 IgG (Abbott Ireland, Sligo, Ireland; reference 6R86-22 & 6R86-32; on ARCHITECT analyser), a CMIA designed to detect IgG antibodies to the nucleocapsid protein of SARS-CoV-2 (anti-N) with a cut-off of 1.40 Index (S/C). According to the manufacturer, the test sensitivity and specificity are 100% and 99.63%, respectively.[27]

Outcome definition

For our primary analyses, we defined SARS-CoV-2 infection (yes/no binary variable) based on the presence of at least one of the available proxies/biomarkers of infection, following the hierarchical order: i) SARS-CoV-2 rt-PCR positivity in nasal swabs; ii) presence of COVID-19 symptoms (fever, cough, dyspnoea, anosmia or ageusia) in the past two weeks; iii) reactive anti-N IgG antibodies; and iv) reactive anti-S IgG antibodies. If more

than one proxy/biomarker of infection was observed, then the date of infection was defined by the hierarchical order described; additional details are in the Statistical Analysis section. For participants who reported having received a COVID-19 vaccine (either with 1 or 2 doses), isolated reactive anti-S IgG antibodies, meaning that all other proxies of infection were negative (negative PCR, no symptoms, non-reactive anti-N IgG antibodies) was not considered as a biomarker for SARS-CoV-2 infection (n = 122 participants), since the anti-S reactivity could be due to seroconversion after vaccination.

Socioeconomic context and epidemiological situation in Rio de Janeiro during the study period

The municipality of Rio de Janeiro is organised in 162 neighbourhoods and had an estimated total population of 6,320,446 inhabitants in the 2010 population census.[18] Manguinhos neighbourhood is located in the north zone of the city, and is mainly comprised of slums (16 *favelas/comunidades*) with an estimated population of 36,160 inhabitants in 2010 (last population census with available data by neighbourhood).[28,29] Manguinhos' population is served by two primary health clinics (*Clínica da Família Victor Valla* and *Centro de Saúde Escola Germano Sinval Faria*) that provide public health care through the Family Health Program (Programa de Saúde da Família), within the Brazilian Public Health System (*Sistema Único de Saúde*, SUS).[30]

In order to provide socioeconomic context for the study area, we obtained HDI and population density (inhabitants per square kilometre) by neighbourhood from Rio de Janeiro city.[31] Maps were created with QGIS version 3.22.

To situate our study in the epidemiological COVID-19 situation in Rio de Janeiro, we obtained data on the prevalence of SARS-CoV-2 variants from the Corona-ômica-RJ Network,[32] number of confirmed COVID-19 cases in Rio de Janeiro city from the Rio de Janeiro state Health Secretary[33] and COVID-19 vaccine coverage (two doses) from Rio de Janeiro city Health Secretary[34] for the study period.

Statistical analyses

The original longitudinal structure of the study dataset (i.e., three visits per participant, each visit contained information on results and dates of nasal swabs, COVID-19 symptoms, anti-N and anti-S IgG antibodies) was transformed into a transversal structure with one row per participant, a unique outcome variable and an outcome date. This was performed by applying the previously mentioned hierarchical definition for the outcome. Within the same participant, we selected the row where the highest hierarchical proxy/biomarker of infection was first detected.

For the descriptive statistics, participants' characteristics were described according to the participant's household PPB measure. Absolute and relative frequencies for categorical variables and median and IQR for quantitative variables were calculated.

Chain binomial transmission models[35,36] were fit to estimate: i) the average probabilities of infection by a single infected household contact (within-household transmission) and ii) the average probabilities of infection from extra-household exposures (community exposures). We assumed that infected individuals could not get reinfected (a plausible assumption given the interval from first to last visit, ~4 weeks), and that all individuals were susceptible at the start of the study. The statistical analysis proposed by Bi et al., 2021,[35] and used by us, reconstructs all possible sequences of SARS-CoV-2 infection introductions to each household and subsequent transmission events within the household, each chain being equally likely. For example, in a household with two infected individuals, both could have been infected outside of the household, or one could have been infected outside and then infected one other person within the household. We fitted complete case models to estimate the within-household and extra-household transmission probabilities according to the characteristics of the potential infectees (including age, gender, socioeconomic variables, extra-household exposure risk variables [i.e., work status, main means of transportation, social distancing measures] and vaccination against SARS-CoV-2) and, for within-household risk, those of the potential infectors (COVID-19 symptoms past two weeks, age). Our primary objective was to estimate the proportion of infections that can be attributed to exposures occurring outside the household as well as those within the household. Tables S3, S4 and S5 show models performance (see Supplementary Material).

We implemented the models in the Stan probabilistic programming language and used the rstan package (version 2.21.0) to sample from the posterior distribution and analyses outputs.[37] We used weakly informative priors on all parameters to be normally distributed on the logit scale with a mean of 0 and a standard error of 1.5. We ran four chains of 2000 iterations, each with 500 warm-up iterations, and assessed convergence visually and using the monitor() function from rstan, which generates the statistics Bulk_ESS, Tail_ESS, and Gelman-Rubin Convergence Statistic (R-hat)[38] for each parameter. ESS well above 100 was observed for each chain. R-hat remained less than 1.05 in all simulations. We slightly modified the code published by Bi et al., 2021[35] in order to accommodate the new variables collected in our work (see Supplementary Material). All estimates are medians of the posterior distribution, with this distribution's 2.5th and 97.5th percentiles reported as the 95% credible interval.

Role of the funding source

The funders had no role in study design, data collection, data analysis, data interpretation, or writing of the

report. All authors had full access to the data in the study and had final responsibility for the decision to submit it for publication.

Results

Fig. 1 shows maps of Rio de Janeiro municipality with the spatial distribution of HDI and population density across its neighbourhoods. In 2010, Rio de Janeiro municipality's HDI was 0.842, ranging from 0.970 to 0.700, and Manguinhos' HDI was 0.726 (5th worst HDI). Furthermore, Manguinhos was 2.6-fold more densely populated than Rio de Janeiro municipality (13,810 versus 5265 inhabitants per square kilometre).

Between November 11th, 2020, and November 30th, 2021, 2024 individuals from 593 households were successfully enrolled in the Comvida 2 study (Figure S1, Supplementary Material). Most of the households (344/593, 58.0%) were completely enrolled (meaning that all individuals dwelling in that household were included in the study). From the remaining 249 households, 292 individuals were not included in the study and were deemed as inclusion failures (292/2316, 12.6%). We did not collect information on the reason for the inclusion failure, and thus we were unable to discriminate those who refused to participate from those who were absent during the household visits. Moreover, inclusion failures of index cases and their corresponding households were also not recorded.

Fig. 2 shows number of households recruited per day during the study period. In order to provide the local epidemiological background for our study, Fig. 2 also presents the daily number of confirmed COVID-19 cases, the relative frequency of SARS-CoV-2 variants, and the COVID-19 vaccine coverage for the primary series (2 doses) in Rio de Janeiro city.

The median number of persons per household (household size) was 4 (interquartile range [IQR] = 3.5), and the median number of persons per bedroom (PPB) was 2 (IQR = 1.5, 3.0). Median age of participants was 32 years (IQR = 17, 49). Children and adolescents were more likely to reside in overcrowded households: 98.1% (253/258) of children aged 1–9 years and 96.6% (343/355) of children and adolescents aged 10–19 years resided in households with >1 PPB, whereas 10.2% (35/344) of adults aged 50–64 years and 17.7% aged 65 or older (28/158) resided in households with ≤1 PPB (Table 1). 60% of the participants were female, and households with 2.1–3.0 PPB had the highest proportion of females (62.5%) (Table 1).

Family income was highest for individuals residing in households with ≤1 PPB, 10.9% (15/138) reported a family income >3 minimum wages per month compared to none (0/(217 + 128)) residing in households with >3 PPB. Households with >4 PPB were more likely to have recipients of *Bolsa Familia* (66.4%, 85/128), whereas households with 3.1–4.0 PBB were more likely to have recipients of *Auxílio Financeiro Emergencial* (78.3%, 170/217). *Bolsa Familia* and *Auxílio Financeiro Emergencial* were least frequent in households with ≤1 PPB: 14.5% (20/138) and 37.7% (52/138), respectively. Remote work during the study period was scarce, reported by only 4.0% (81/2024) of the participants, while 28.2% (571/2024) reported in-person work, and 66.3% (1282/2024) were unemployed during the study period. Unemployment was highest (71.9%, 92/128) in households with >4 PBB, and lowest in households with ≤1 PPB (60.1%, 83/138) (Table 1).

The most common means of transportation was public transportation (bus, train, subway), reported by 44.6% (903/2024) of participants. Good adherence to social distancing measures in the past 2 weeks was reported by 37.9% (768/2024) of participants, with the highest percentages among those residing in households with ≤1 PPB (50%, 69/138) and the lowest among those residing in households with >4 PPB (18.8%, 24/128). Adherence to social distancing measures was highly correlated across individuals living in the same household (chi-squared test p-value <0.001).
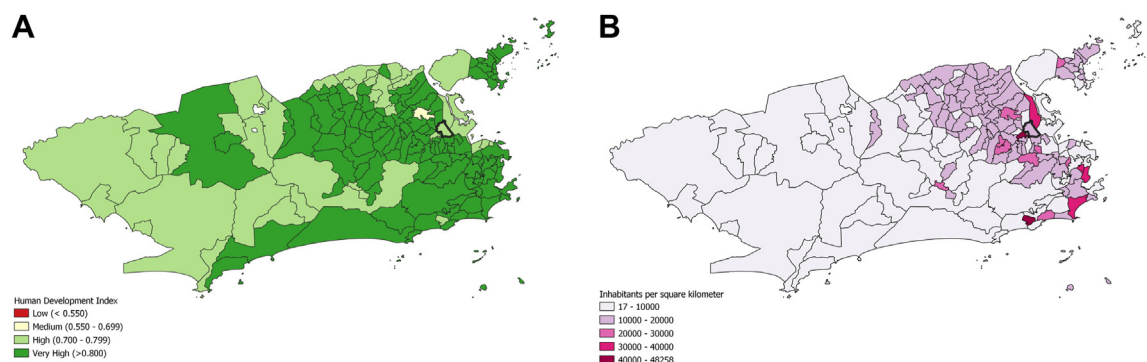

Fig. 1: Spatial distribution of the human development index (HDI, panel A) and population density (inhabitants per square kilometre, panel B) across Rio de Janeiro's neighbourhoods with Manguinhos highlighted in black, according to the 2010 census.
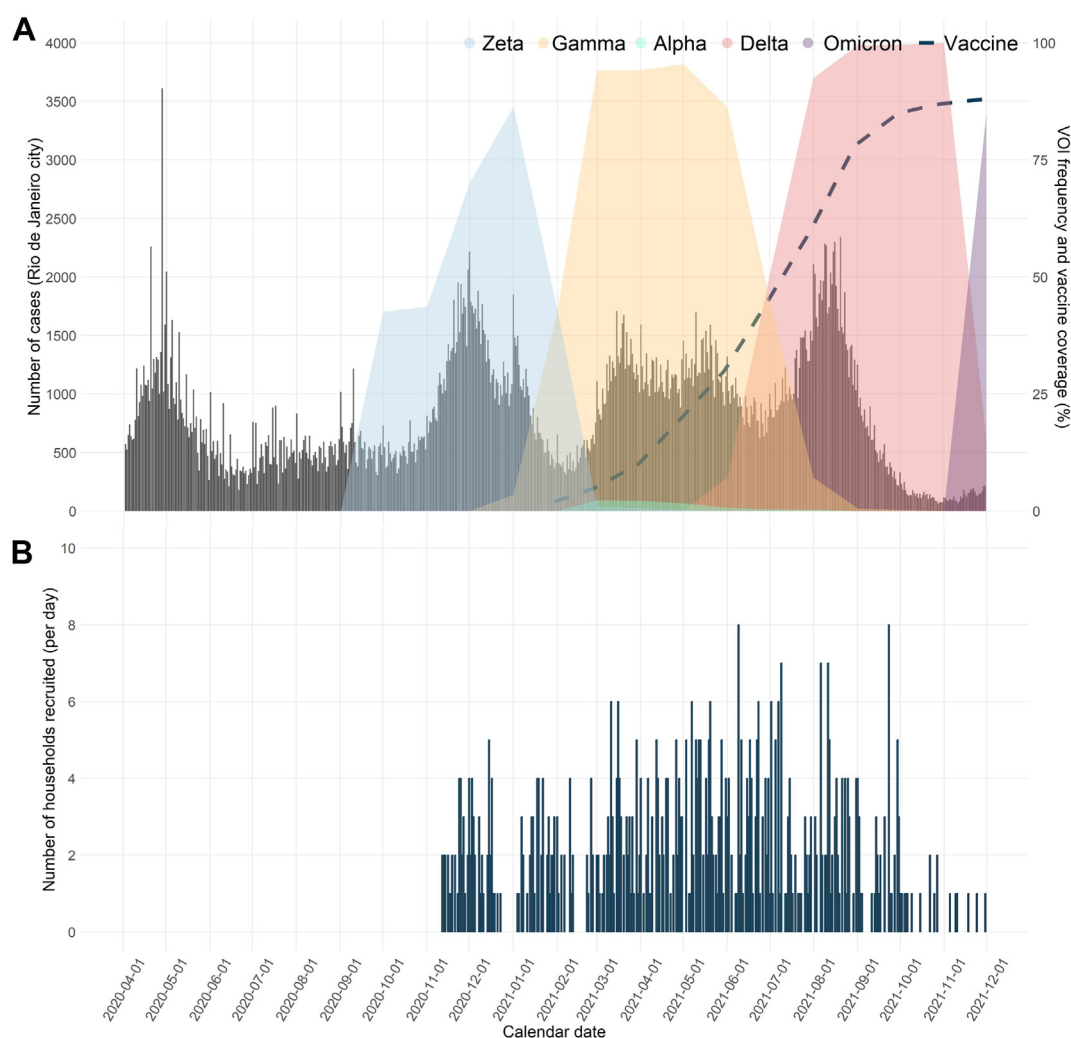
Fig. 2: Panel A: Number of confirmed COVID-19 cases per day, relative frequency of SARS-CoV-2 variants of interest (VOI) and COVID-19 vaccine coverage (2 doses) in Rio de Janeiro city over time. Panel B: Number of households enrolled per day in the Comvida-2 study over time.

Given the timing of the study and of the roll-out of COVID-19 vaccines in Rio de Janeiro city, 70.9% of the individuals (1436/2024) were not vaccinated against SARS-CoV-2: 17.7% had received one dose (359/2024), and only 6.6% had received two doses (133/2024) (Table 1). Among those 492 participants who received either one or two doses of vaccine, the most frequently reported was AstraZeneca (32.1%, n = 158 individuals), followed by CoronaVac (18.3%, n = 90), Pfizer (18.3%, n = 90), and lastly by Janssen (2.4%, n = 12); 142 (28.9%) participants did not report vaccine's manufacturer. Vaccination was more frequent in individuals aged 65 or older (28.5% and 24.7% had received one and two doses, respectively), followed by those aged 50–64 (31.4% and 9.9% had received one and two doses, respectively). The proportion of vaccinated individuals was much lower in younger age groups, as expected, given the age-targeted

vaccination roll-out implemented in Rio de Janeiro city (Table S1, Supplementary Material).

By the end of follow-up, 78.9% (1617/2024) of participants were deemed to have had SARS-CoV-2 infection, defined by a hierarchical definition that considered, in order: i) SARS-CoV-2 rt-PCR positivity in nasal swabs (n = 299); ii) presence of COVID-19 symptoms (fever, cough, dyspnoea, anosmia or ageusia) in the past two weeks (n = 966); iii) anti-N IgG antibodies reactivity (n = 571); and iv) anti-S IgG antibodies reactivity (n = 1225). Isolated anti-S IgG antibodies reactivity, meaning that all other proxies of infection were negative, was not considered as a biomarker for SARS-CoV-2 infection among participants who had received at least one dose of SARS-CoV-2 vaccine (n = 122) (Table S2, Supplementary Material).

	Households grouped according to person per bedroom (PPB)							Total
	≤1	1.1–1.5	1.6–2.0	2.1–3.0	3.1–4.0	>4	missing	
Number of participants (%)	138 (6.8)	356 (17.6)	547 (27.0)	560 (27.8)	217 (10.7)	128 (6.3)	78 (3.9)	2024 (100)
SARS-CoV-2 infection (n, %)								
No	35 (25.4)	74 (20.8)	107 (19.6)	103 (18.4)	45 (20.7)	26 (20.3)	17 (21.8)	407 (20.1)
Yes	103 (74.6)	282 (79.2)	440 (80.4)	457 (81.6)	172 (79.3)	102 (79.7)	61 (78.2)	1617 (79.9)
Age, median (IQR)	46.5 (28, 62)	38 (20, 53)	35 (20, 51)	26 (13, 44)	26 (11, 44)	21.5 (10,36)	33 (21, 49)	32 (17, 49)
Age, categorical (n, %)								
1–9	5 (3.6)	25 (7)	44 (8)	103 (18.4)	44 (20.3)	29 (22.7)	8 (10.3)	258 (12.7)
10–19	12 (8.7)	62 (17.4)	88 (16.1)	113 (20.2)	43 (19.8)	30 (23.4)	7 (9)	355 (17.5)
20–49	58 (42)	161 (45.2)	268 (49)	235 (42)	90 (41.5)	53 (41.4)	44 (56.4)	909 (44.9)
50–64	35 (25.4)	77 (21.6)	101 (18.5)	78 (13.9)	29 (13.4)	9 (7)	15 (19.2)	344 (17)
65+	28 (20.3)	31 (8.7)	46 (8.4)	31 (5.5)	11 (5.1)	7 (5.5)	4 (5.1)	158 (7.8)
Gender (n, %)								
Female	81 (58.7)	205 (57.6)	328 (60)	350 (62.5)	129 (59.4)	72 (56.2)	50 (64.1)	1215 (60)
Male	57 (41.3)	151 (42.4)	219 (40)	210 (37.5)	88 (40.6)	56 (43.8)	28 (35.9)	809 (40)
Family income (monthly minimum wages) (n, %)								
No income	18 (13)	38 (10.7)	60 (11)	112 (20)	35 (16.1)	35 (27.3)	0 (0)	298 (14.7)
≤1	48 (34.8)	116 (32.6)	222 (40.6)	213 (38)	87 (40.1)	71 (55.5)	0 (0)	757 (37.4)
>1 & ≤2	29 (21)	120 (33.7)	145 (26.5)	125 (22.3)	61 (28.1)	10 (7.8)	0 (0)	490 (24.2)
>2 & ≤3	28 (20.3)	54 (15.2)	74 (13.5)	43 (7.7)	34 (15.7)	12 (9.4)	0 (0)	245 (12.1)
>3	15 (10.9)	21 (5.9)	42 (7.7)	59 (10.5)	0 (0)	0 (0)	0 (0)	137 (6.8)
Missing	0 (0)	7 (2)	4 (0.7)	8 (1.4)	0 (0)	0 (0)	78 (100)	97 (4.8)
Bolsa Família (n, %)								
No	118 (85.5)	290 (81.5)	402 (73.5)	343 (61.3)	113 (52.1)	43 (33.6)	0 (0)	1309 (64.7)
Yes	20 (14.5)	62 (17.4)	139 (25.4)	212 (37.9)	104 (47.9)	85 (66.4)	0 (0)	622 (30.7)
Missing	0 (0)	4 (1.1)	6 (1.1)	5 (0.9)	0 (0)	0 (0)	78 (100)	93 (4.6)
Auxílio Financeiro Emergencial (n, %)								
No	86 (62.3)	160 (44.9)	247 (45.2)	209 (37.3)	47 (21.7)	57 (44.5)	0 (0)	806 (39.8)
Yes	52 (37.7)	196 (55.1)	300 (54.8)	351 (62.7)	170 (78.3)	71 (55.5)	0 (0)	1140 (56.3)
Missing	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	78 (100)	78 (3.9)
Employment status (n, %)								
Not working	83 (60.1)	220 (61.8)	346 (63.3)	372 (66.4)	146 (67.3)	92 (71.9)	23 (29.5)	1282 (63.3)
Remote work	7 (5.1)	18 (5.1)	25 (4.6)	17 (3)	9 (4.1)	2 (1.6)	3 (3.8)	81 (4)
In-person work	45 (32.6)	109 (30.6)	158 (28.9)	157 (28)	56 (25.8)	32 (25)	14 (17.9)	571 (28.2)
Missing	3 (2.2)	9 (2.5)	18 (3.3)	14 (2.5)	6 (2.8)	2 (1.6)	38 (48.7)	90 (4.4)
Main means of transportation (n, %)								
Walk/bike	12 (8.7)	54 (15.2)	96 (17.6)	81 (14.5)	33 (15.2)	44 (34.4)	9 (11.5)	329 (16.3)
Own car/motorcycle	36 (26.1)	78 (21.9)	109 (19.9)	112 (20)	18 (8.3)	5 (3.9)	9 (11.5)	367 (18.1)
Cab/ridesharing apps/mototaxi	31 (22.5)	64 (18)	80 (14.6)	93 (16.6)	45 (20.7)	18 (14.1)	3 (3.8)	334 (16.5)
Public transport (bus, subway, train)	56 (40.6)	150 (42.1)	243 (44.4)	260 (46.4)	116 (53.5)	59 (46.1)	19 (24.4)	903 (44.6)
Missing	3 (2.2)	10 (2.8)	19 (3.5)	14 (2.5)	5 (2.3)	2 (1.6)	38 (48.7)	91 (4.5)
Left the house (past 2 weeks) (n, %)								
Never	36 (26.1)	76 (21.3)	106 (19.4)	167 (29.8)	56 (25.8)	25 (19.5)	6 (7.7)	472 (23.3)
Few times	42 (30.4)	120 (33.7)	195 (35.6)	147 (26.2)	58 (26.7)	50 (39.1)	14 (17.9)	626 (30.9)
Regularly	46 (33.3)	124 (34.8)	171 (31.3)	174 (31.1)	64 (29.5)	32 (25)	14 (17.9)	625 (30.9)
Missing	14 (10.1)	36 (10.1)	75 (13.7)	72 (12.9)	39 (18)	21 (16.4)	44 (56.4)	301 (14.9)
Self-reported adherence to social distancing (past 2 weeks) (n, %)								
Poor	55 (39.9)	167 (46.9)	273 (49.9)	267 (47.7)	87 (40.1)	83 (64.8)	24 (30.8)	956 (47.2)
Good	69 (50)	153 (43)	200 (36.6)	221 (39.5)	91 (41.9)	24 (18.8)	10 (12.8)	768 (37.9)
Missing	14 (10.1)	36 (10.1)	74 (13.5)	72 (12.9)	39 (18)	21 (16.4)	44 (56.4)	300 (14.8)

(Table 1 continues on next page)

	Households grouped according to person per bedroom (PPB)							Total
	≤1	1.1–1.5	1.6–2.0	2.1–3.0	3.1–4.0	>4	missing	
(Continued from previous page)								
SARS-CoV-2 vaccination status (n, %)								
None	84 (60.9)	248 (69.7)	376 (68.7)	435 (77.7)	172 (79.3)	92 (71.9)	29 (37.2)	1436 (70.9)
1 dose	39 (28.3)	74 (20.8)	105 (19.2)	83 (14.8)	31 (14.3)	21 (16.4)	6 (7.7)	359 (17.7)
2 doses	12 (8.7)	26 (7.3)	50 (9.1)	26 (4.6)	7 (3.2)	10 (7.8)	2 (2.6)	133 (6.6)
Missing	3 (2.2)	8 (2.2)	16 (2.9)	16 (2.9)	7 (3.2)	5 (3.9)	41 (52.6)	96 (4.7)

Table 1: SARS-CoV-2 infection (outcome) and participants characteristics by the household density (number of persons per bedroom).

Results from the fitted household transmission models showed that the cumulative risk of infection from extra-household exposures was 74.2% (95% credible interval [CrI] 70.3–77.8) whereas the risk of infection by a single infected household member was 11.4% (95% CrI 5.7–17.2) (Fig. 3A). Young adults aged 20–49 years had the highest risk of infection from extra-household exposures, while children and adolescents aged 10–19 years had the highest risk of infection by a single infected household member. In all age groups, females were more likely to be infected from extra-household exposures, and males were more likely to be infected from a single infected household member (Fig. 3A).

The risk of infection from a single infected household member was highest in overcrowded households, particularly in those with >4 PPB, and lowest in households with <2 PPB, though the 95% CrI included zero in all categories (Fig. 3B). In contrast, residing in overcrowded households was not associated with the risk of infection from extra-household exposures (Fig. 3B).

The risk of infection from extra-household exposures was highest in individuals who were currently unemployed. Contrastingly, the risk of infection from a single infected household member was highest among those who reported remote work status (note the broad 95% CrI due to the scarcity of remote work in the study population) (Fig. 4A). Low family income was associated with within-household infection probability in all age groups. For extra-household transmission, the lowest income category (<1 minimum wage monthly) and the highest income category (>3 minimum wages monthly) were associated with higher probabilities of infection (Fig. 4B). *Bolsa Familia* benefit was associated with lower infection risk from extra-household members but not with within-household infection risk (Fig. 4C). *Auxilio Financeiro Emergencial* was not associated with extra-household nor within-household transmission (Fig. 4D).

Probabilities of infection from extra-household exposures were highest for individuals reporting the use of public transportation (bus, trains, subways) as their main means of transportation. In contrast, the probability of
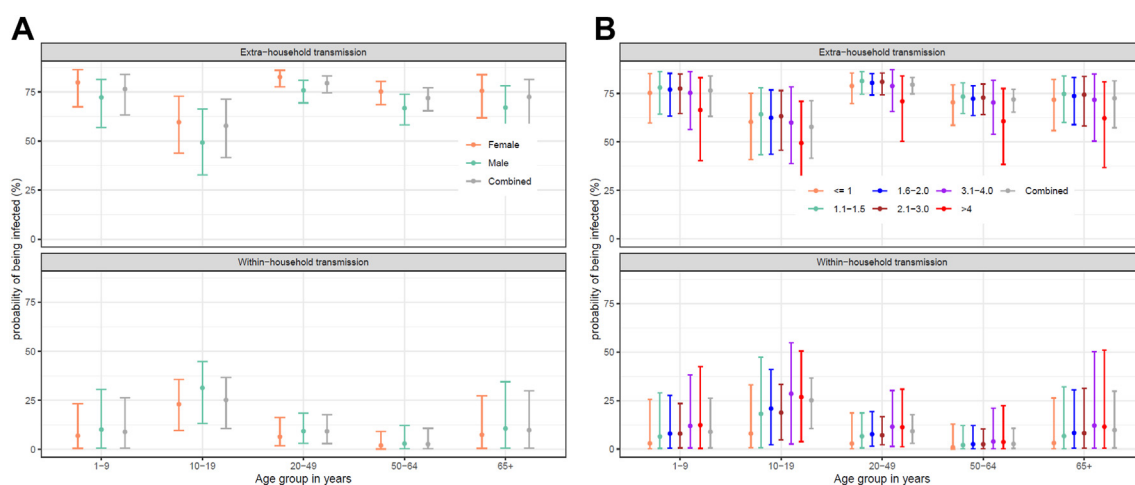

Fig. 3: Panel A: Estimated median of the posterior distribution of the extra-household and within-household infection probability (dot) and 95% credible interval (bar) by age and gender. Panel B: Estimated median of the posterior distribution of the extra-household and within-household infection probability (dot) and 95% credible interval (bar) by age and household density (persons per bedroom).
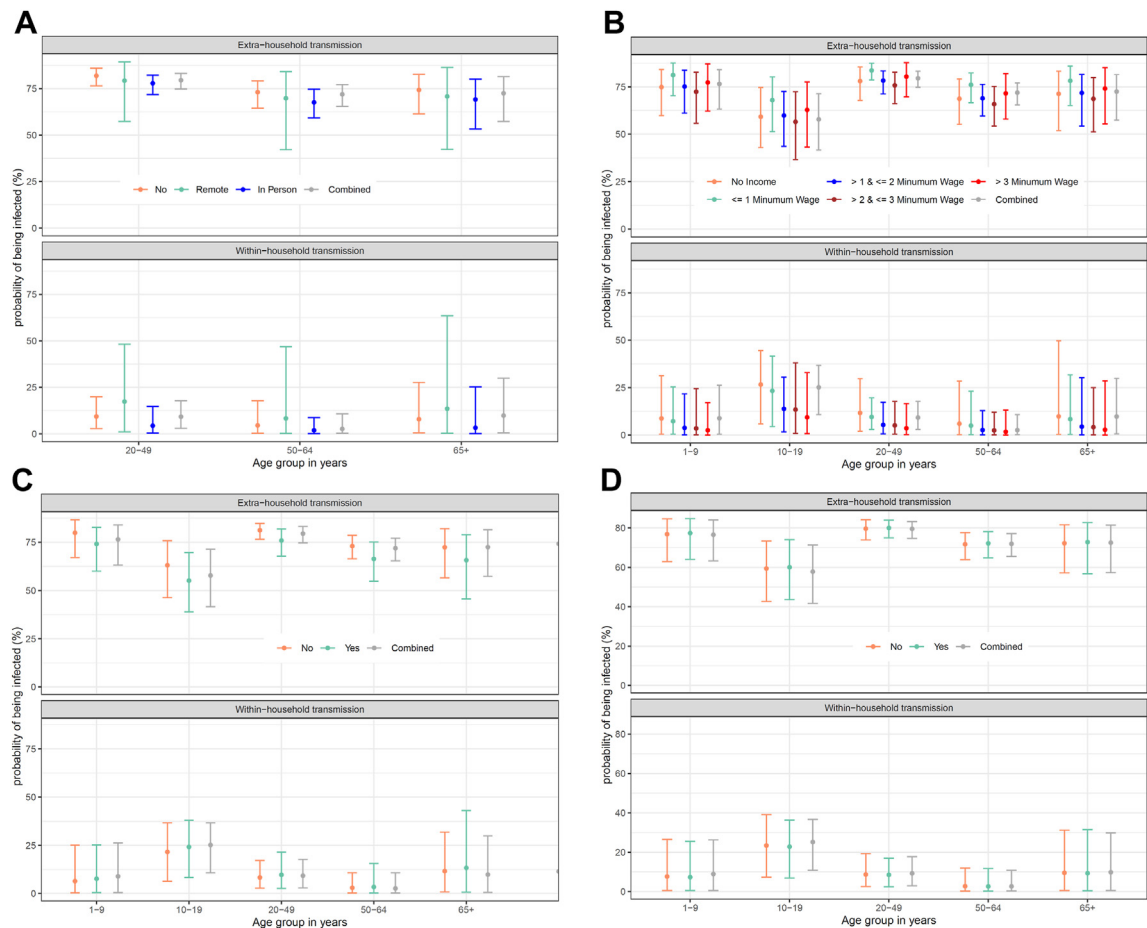
Fig. 4: Panel A: Estimated median of the posterior distribution of the extra-household and within-household infection probability (dot) and 95% credible interval (bar) by age and employment status. Panel B: Estimated median of the posterior distribution of the extra-household and within-household infection probability (dot) and 95% credible interval (bar) by age and monthly family income categorized according to the number minimum wages. Panel C: Estimated median of the posterior distribution of the extra-household and within-household infection probability (dot) and 95% credible interval (bar) by age and receipt of the cash transfer program *Bolsa Familia*. Panel D: Estimated median of the posterior distribution of the extra-household and within-household infection probability (dot) and 95% credible interval (bar) by age and receipt of the cash transfer program *Auxílio Financeiro Emergencial*.

infection from a single infected household member was highest among those who reported mainly using their own vehicles (car/motorbike) for transportation (Fig. 5A). Self-reported adherence to social distancing measures was not associated with extra-household nor within-household infection probabilities (Fig. 5B and C).

Although overall COVID-19 vaccine coverage was low during the study period, receiving at least one dose of the vaccine was associated with a lower probability of infection from a single infected household member and extra-household exposures relative to participants with no vaccine (Fig. 6). Probabilities of within- and extra-household infection among individuals who reported two doses of vaccines were 4.1% (95% CrI 0.4, 16.6) and 68.9% (95% CrI 57.3, 77.6), respectively (Table S5, model M1vaccine).

Discussion

In the present study, we estimated the risk of COVID-19 transmission from extra-household exposures and a single infected household member in a highly vulnerable setting, a complex of slums (*Complexo de Manguinhos*) in Rio de Janeiro city. Our analyses incorporated a complex and intertwining set of demographics, economic, behavioural, and structural factors, as well as COVID-19 vaccine receipt to investigate factors associated with COVID-19 transmission risk. We found that the risk of infection from extra-household exposures, estimated at 74.2%, was considerably higher than the risk of infection from a household member, estimated at 11.4%. We also found that receiving at least one dose of COVID-19 vaccine reduced the risk of infection from within-household and extra-
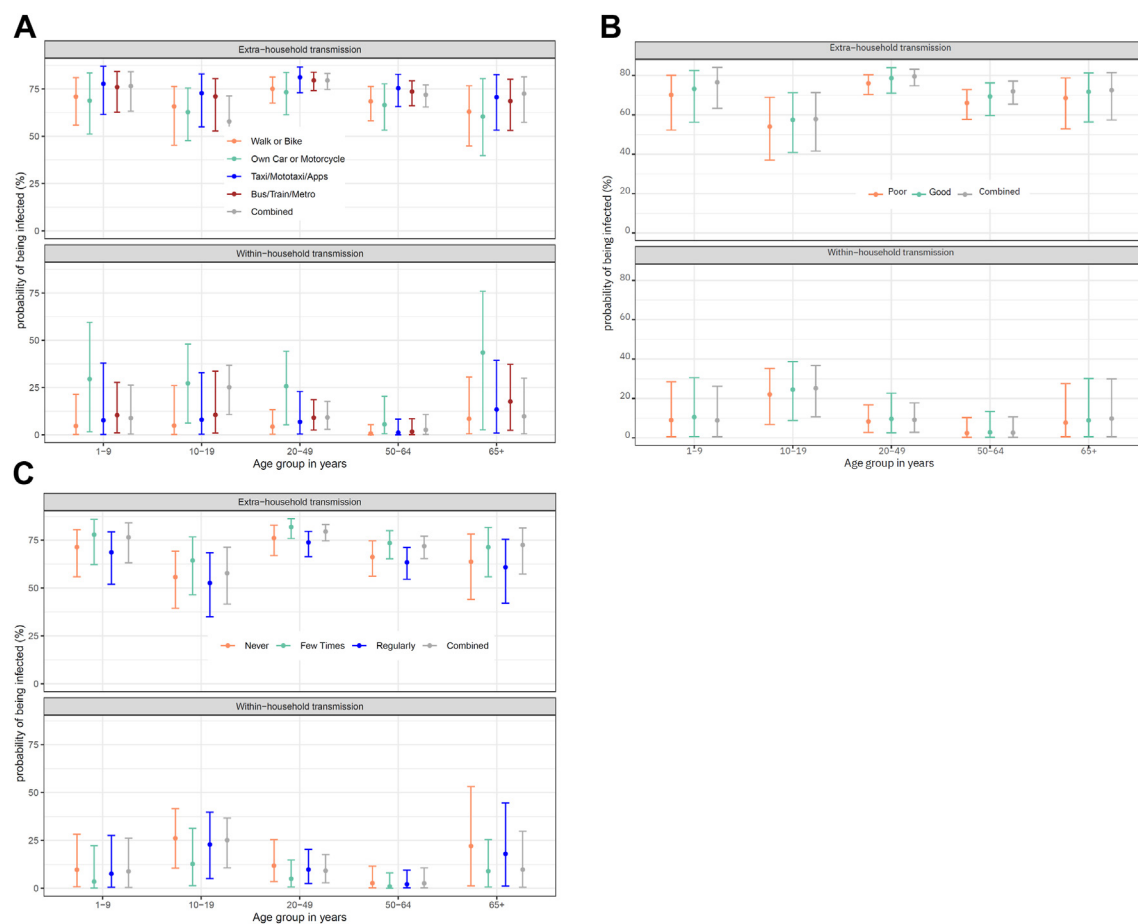
Fig. 5: Panel A: Estimated median of the posterior distribution of the extra-household and within-household infection probability (dot) and 95% credible interval (bar) by age and reported means of transportation. Panel B: Estimated median of the posterior distribution of the extra-household and within-household infection probability (dot) and 95% credible interval (bar) by age and reported adherence to social distancing measures. Panel C: Estimated median of the posterior distribution of the extra-household and within-household infection probability (dot) and 95% credible interval (bar) by age and reported frequency of leaving one's house.

household exposures. The risk of infection from a household member was higher among children and adolescents (10–19 years old), individuals residing in overcrowded households, with low family income, and employed individuals who reported remote work status. In contrast, young adults (20–29 years old), unemployed individuals, and those reporting the use of public transportation as their main means of transportation had a higher risk of infection from extra-household exposures. Interestingly, a higher income increased the risk of infection from extra-household exposures, whereas *Bolsa Familia* reduced the risk of infection from extra-household transmission.

To fully understand our findings, it is essential to situate our study in space (*Complexo de Manguinhos*) and time (from November 2020 to December 2021) and be mindful of the epidemiological context in which the study occurred. First, our study was undertaken in a deeply vulnerable neighbourhood in Rio de Janeiro city comprised of 16 slums. This area holds the 5th worst HDI of the city and is characterised by concentrated poverty, high rates of violence, inadequate housing conditions, and lack of access to essential services, such as clean water and sanitation. Prior work from our group conducted in this geographical location revealed a high prevalence of anti-SARS-CoV-2 antibodies (59%) from September 2020 to February 2021.[30] Second, three consecutive SARS-CoV-2 variants (zeta, gamma and delta) emerged during the study period and became the dominant variant in Rio de Janeiro and Brazil. From early 2020 through the end of 2021, the COVID-19 epidemic in the country was characterised by two large epidemic waves.[39] The first wave (March through September 2020) resulted from multiple introduction events and was characterised by the circulation of several SARS-CoV-2 lineages (including B.1.1.28 and
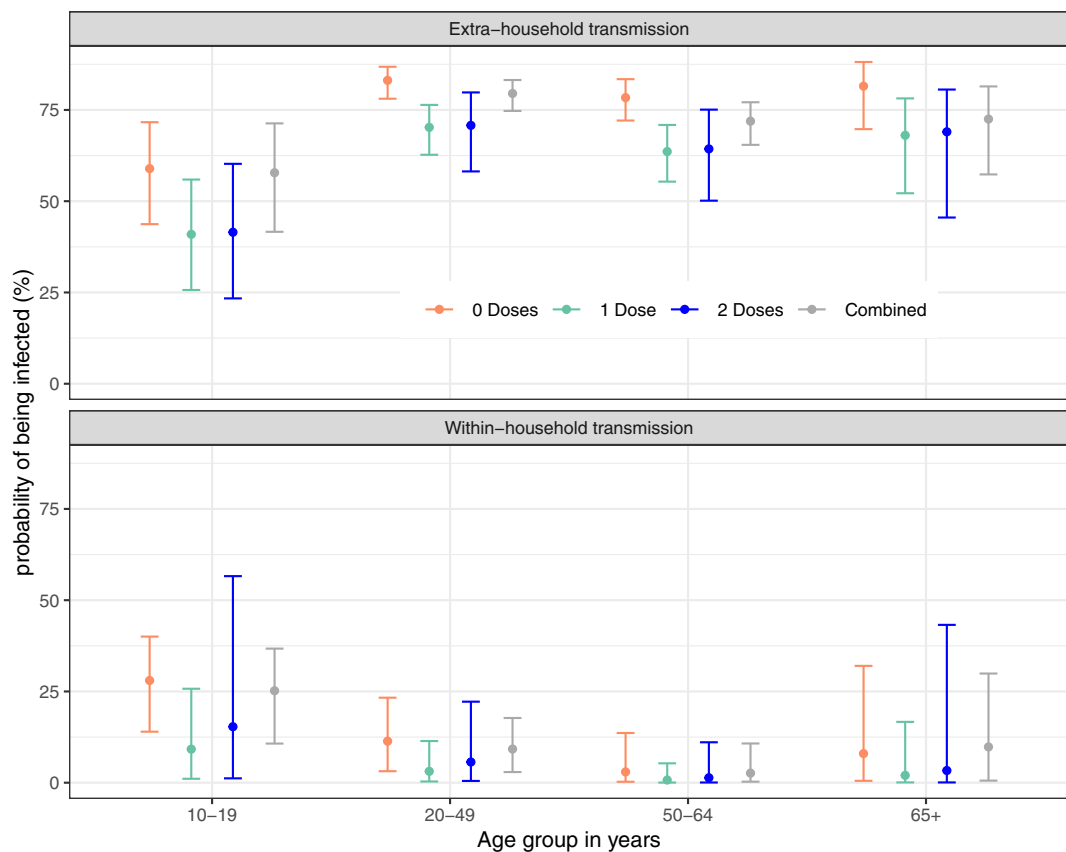
Fig. 6: Estimated median of the posterior distribution of the extra-household and within-household infection probability (dot) and 95% credible interval (bar) by age and reported receipt of COVID-19 vaccine doses.

B.1.1.33). The onset of the second wave occurred in October 2020 and resulted from the emergence and circulation of novel consecutive variants such as zeta and gamma. The gamma variant remained dominant from January 2021 until July 2021, when delta replaced it. During gamma dominance, reported COVID-19 deaths and cases increased to a historical maximum, likely due to a large susceptible population and low vaccination coverage. Following gamma, the emergence of delta was not associated with an increase in the number of cases or deaths, and that likely resulted from a reduced pool of susceptible individuals in the community, either due to natural immunity (induced by prior gamma infection) or to the increasing vaccination coverage.[39] Of particular relevance, our study period coincides largely with the second wave, specifically with the gamma dominance period, and may describe transmission dynamics resulting from dominant variants transitions. Third, approximately halfway through our study period, COVID-19 vaccines became available and were distributed using an age-targeted strategy that initially included elders and progressively included younger individuals. By the end of our study period,

vaccine coverage (two doses) reached almost 90% of the Rio de Janeiro city population aged 12 years old or older.[34]

Effective SARS-CoV-2 transmission is influenced by pathogen features (i.e., variant transmissibility and resistance to neutralizing antibodies), host susceptibility and behaviour, household features and other structural factors, as well as community factors such as the population-level burden of infection, population density, and vaccination coverage (direct and indirect effects).[40,41] As mentioned briefly in the Introduction, several studies have estimated SARS-CoV-2 household infection risk and SARs in different countries, however, most did not discriminate the source of infection for the secondary cases (i.e., within-household transmission versus extra-household transmission).[2,5,11,12] In a study conducted in Guangzhou, China (January–February, 2020), the risk of infection was estimated at 17.2% within the household and 2.6% from extra-household contacts.[42] In another study conducted in Geneva, Switzerland (April–June, 2020), the risk of infection within the household was three times greater than the risk of infection from extra-household exposures (17.3% versus 5.1%).[35] Contrasting

with these two studies, we found that the risk of infection was 6.5 times greater from extra-household exposures than from a single infected household member (74.2% and 11.4%, respectively). Adherence to social distancing measures and other non-pharmaceutical interventions was poor in Brazil, particularly among the most vulnerable populations.[43] Fear of unemployment and income insecurity have been associated with poor adherence to social distancing. In vulnerable communities, such as the Manguinhos neighbourhood, large proportions of the inhabitants are informal or low-paid workers, often working in the service sector (e.g. food, delivery, cleaning) and who did not or were unable to stop working.[30,44] The role of Federal leadership (presidential term 2019–2022) in antagonizing the protective benefits of lockdown and non-pharmacological interventions had deleterious effects on individuals' behavior.[45,46] Additionally, even among mask users, the use of cloth masks was highly prevalent (relative to surgical or N95 masks), and the protective effect of such masks remains unknown and may vary according to the material and layers used.[47,48] Altogether, we speculate that even during the peak of the SARS-CoV-2 transmission, including the second wave and gamma variant dominance period, adherence to lockdown and non-pharmaceutical preventive measures was poor and extra-household transmission exposures were frequent. The use of public transportation (bus, train, subway), where the limited number of passengers or minimal distancing requirements were not observed, potentially increased extra-household exposure events. Indeed, our results showed that the risk of infection from extra-household exposures was higher among those who reported using public transportation.

Our findings on the risk of infection according to proxies of socioeconomic status, namely employment, family income and receipt of *Bolsa Família* benefit, highlight the challenges of adhering to social distancing among vulnerable populations. First, our results indicated that the risk of infection from extra-household exposures was higher among those who reported unemployment and low income. To adequately meet survival needs, individuals who were unemployed or with low-paid jobs likely increased their exposure to infection by seeking informal or temporary jobs. In line with this reasoning, we found that receipt of *Bolsa Família* reduced the risk of infection from extra-household exposures probably because it provided minimum financial security, allowing individuals to adhere to social distancing measures. A study conducted during the COVID-19 pandemic in two slums in São Paulo found that families who received the *Bolsa Familia* benefit had fewer experiences of severe or moderate food insecurity.[49] Contrastingly, the risk of infection from extra-household exposures was also higher among individuals in the highest income category, and this finding may indicate that those individuals with formal

"well"-paid jobs, particularly those working in the service sector, did not, or, more realistically, could not adhere to social distancing measures.

As for the socioeconomic factors related to increased risk of infection from household exposure, we found that higher household density (measured as persons per bedroom) and low income were associated with increased risk. Similar findings had been reported previously, mainly in vulnerable settings and minority communities, and may result from precarious housing conditions (i.e., poor ventilation, small household size, and lack of adequate sanitation and clean water) coupled with the impossibility of isolating an infected household member.[40,50] Finally, though the prevalence of remote work was very low in our study population, we nonetheless found that individuals who reported working remotely had a higher risk of infection from a single household contact, which may result from intense cohabiting.

Lastly, our results showed that the COVID-19 vaccine was associated with a lower risk of infection from both within-household and extra-household exposures. This finding corroborates those from clinical trials and observational studies showing the efficacy and effectiveness of multiple COVID-19 vaccines.[7,51] Nonetheless, vaccine coverage was low in the study population, and the proportion of vaccinated individuals was higher in older age groups, as expected given the age-targeted roll-out of vaccination. Vaccination in Rio de Janeiro city began on January 20th, 2021, and up to May 2021, vaccination was restricted to priority groups and elders. In June 2021, vaccination was extended to the general population aged 12 or older, and 90% of the city population had received two doses by December 2021.[34] COVID-19 vaccines were extended to children below 12 years old in January 2022, when this study's data collection had already ended.

Our study has several limitations. First, our study was conducted on an extremely vulnerable neighbourhood in Rio de Janeiro, Brazil, and findings may not be generalizable to other settings, with different structural, socioeconomic, or behavioural characteristics. Nevertheless, our findings may well reflect similar marginalized urban populations of Brazil and other low/middle income countries of Latin America. Second, our study relied on primary health clinics and community referrals for index cases identification and may not be generalisable to the entire Manguinhos's population. Third, given that our selection of study participants preferably targeted symptomatic individuals, it may have overrepresented severe cases and thus overestimated transmission risk. Fourth, our study period largely coincided with gamma variant dominance, and findings may not be generalisable to other time periods. For instance, the omicron variant surge and dominance occurred soon after the conclusion of our study (late December, 2021).[52] Omicron has shown increased

transmissibility and ability to evade host immunity induced by one or two doses of COVID-19 vaccines, which resulted in high transmission rates observed in settings with high vaccine coverages or natural immunity.[52,53] Fifth, our study could have been prone to unmeasured individual and structural confounding factors, such as those associated with public health measures to curb COVID-19 transmission, including population vaccine coverage, population mobility and adherence to non-pharmacological measures. Sixth, our cohort study was subject to some selection bias in the form of non-random losses-to-follow-up: females and older participants were more likely to be retained in the study. Seventh, study participants were asked to report on adherence to social distancing and how frequently they left the house in the past 2 weeks; those responses may be prone to recall and reporting bias. In fact, we found a lack of protective association between adherence to social distancing measures and risk of extra-household transmission that may have resulted from reporting bias given the face-to-face format of our interviews, with individuals likely overestimating their adherence.[54] Eighth, we have used a combination of available proxies/biomarkers of COVID-19 infection to define the outcome of interest, following a hierarchical order as described in the methods. Therefore, we were not able to precisely define the timing of infection or the duration of infectiousness. Moreover, our COVID-19 outcome definition is also limited by rt-PCR performance and timing of the swab collection during infection, by the low positive predictive value of COVID-19 symptoms, and by the high IgG antibodies prevalence rates. Nineth, though we gathered our data through a cohort study design and there are statistical models designed to handle longitudinal data structures,[55] it has proven challenging to accurately reconstruct each participant's incubation and infectious periods. This information is crucial for informing an appropriate chain binomial model. In our analytical approach, we had to simplify the data by collapsing it over time, essentially mimicking a cross-sectional design. We utilized cumulative time-related information as the input for our model. Regrettably, this simplification leads to less precise estimates compared to what could be achieved with a more detailed longitudinal analysis.[42] Furthermore, while we haven't explicitly adjusted for calendar time effects, it's noteworthy that time-dependent transmission rates may tend to cancel out when comparing groups. This rationale aligns with the approach used to estimate vaccine efficacy in randomized controlled trials conducted during infectious disease outbreaks.[56,57] Moreover, chain binomial modelling assumes single infection events. It is accepted that immunity to SARS-CoV-2 is incomplete and reinfections can occur. The relatively low likelihood of reinfection events during the study follow-up period (4 weeks) supports our methodological choice. Finally, our analytical framework

assumes homogeneous mixing within households. While relaxing this assumption to account for heterogeneous mixing patterns would be ideal, it is currently not a straightforward modification within the standard chain binomial modelling framework. We acknowledge that this assumption limits the model's ability to capture the full complexity of transmission dynamics within households. However, it is important to note that our estimates provide valuable insights into the average transmission pattern within the studied population. Future research avenues could involve incorporating data on contact patterns within households if available. This would allow for the development of models that account for heterogeneous mixing and potentially reveal distinct qualitative outcomes, such as the role of superspreaders in transmission dynamics.

Strengths of our study include a study design that ensured that all participants underwent the same procedures in all study visits, regardless of symptoms, comorbidities and other factors that could influence testing and contact tracing. The methodological approach employed in the analysis allowed the estimation of the relative contribution of within-household and extra-household exposures in COVID-19 transmission. In addition, we combined the results of consecutive molecular and immunological tests (regardless of symptoms) and major clinical symptoms to ensure high sensitivity and specificity in detecting the outcome.

In conclusion, our study provides important insights into COVID-19 household and community transmission in a highly vulnerable population residing in precarious and overcrowded households in a community that struggled to adhere to lockdown policies and social distancing measures. Compared to prior studies, the much higher extra-household infection risk highlights the extreme social vulnerability of these populations and the need for tailored strategies to mitigate and assist these communities during the emergency of a new transmissible infectious disease. Cash transfer programs can help by providing some level of financial security and, as such, permitting social distancing, whereas prioritizing vaccination of the most socially vulnerable could also protect these individuals and reduce widespread community transmission.

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