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Intense SARS-CoV-2 transmission among affluent Manaus residents preceded the second wave of the epidemic in Brazil

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The city of Manaus, located in the Brazilian Amazon, had an explosive epidemic of SARS-CoV-2 infections, with deaths and hospitalisations due to COVID-19 peaking in early May, 2020. Based on blood donor antibody surveillance, the cumulative proportion of the population infected was estimated to be more than 70%,[1] similar to other regions in the Amazon Basin.[2] COVID-19-related deaths fell and remained low for 7 months between May and December, 2020, despite the relaxation of non-pharmaceutical control measures.[3] A second large epidemic wave then occurred at the beginning of 2021, which coincided with the emergence of the P.1 (gamma) variant of concern, first identified in Manaus.[4] These relatively unique transmission dynamics in Manaus warrant further study and explanation.[3]

In *The Lancet Global Health*, Pritesh Lalwani and colleagues[5] publish results from the DETECTCoV-19 cohort of adult Manaus residents tested for anti-SARS-CoV-2 nucleocapsid IgG antibodies using an in-house serology assay. Participants who provided a blood sample at the first study visit, between Aug 19 and Oct 2, 2020, were recalled for a second blood draw between Oct 19 and Nov 27, 2020. Of the 2496 participants who provided two blood samples, crude seropositivity was 27·72% (95% CI 25·98–29·53) at the first visit and increased to 34·33% (32·47–36·24) at the second visit. The estimated incidence of seroconversion among initially seronegative participants was 13·06% (95% CI 11·52–14·79) over a median follow-up period of 57 days (IQR 54–61). Notably, around half of the seroconversions were asymptomatic. Incidence was higher in those who reported relaxing physical distancing, not wearing a mask, having a SARS-CoV-2-positive household contact, or non-remote working.

The sampling frame of the DETECTCoV-19 cohort is important to understand these results in the wider context of Manaus. Participants were recruited by advertisement on social media and on a university website. This led to an oversampling of people living in the centre-south area of the city, close to the Federal University of Amazonas. Comparing sociodemographic characteristics of the cohort against census data for Manaus showed that 60% of the cohort were employed in higher professional level jobs, in contrast to only 12% of the wider population; the proportion of study participants with a family income in the highest bracket was twice that of the Manaus population, and 62% had private health insurance—3 times the city's average. Participants also tended to be older, self-identify as White, and were more likely to live in an apartment.

This sampling frame requires cautious interpretation. As acknowledged in the Article, the results should not be generalised to the wider population of Manaus, but instead generalised to the affluent, professionally employed subpopulation represented by the DETECTCoV-19 cohort. It is interesting that a high level of transmission persisted among this group, at a time (August to November, 2020) when population-level hospitalisations and deaths were low, presumably partly due to wide-spread population immunity,[1,4] which seemingly might not have extended to this more affluent group. These results also accord with observations in the media of a relative uptick in private hospitalisations due to COVID-19 during this period.[6] Although somewhat speculative, these conclusions highlight the importance of heterogeneity in SARS-CoV-2 transmission dynamics, especially in the context of socioeconomic inequality.[7]

Another important caveat to these results relates to the in-house serology test used in the study. The quoted sensitivity of 94% was based on sera from SARS-CoV-2 RT-PCR-positive patients, the majority of whom required hospitalisation. Given that roughly half the seroconversions in the cohort were asymptomatic, and presumably few participants required hospitalisation, the panel of samples used to determine sensitivity reflects greater disease severity than that seen in the DETECTCoV-19 cohort. The true sensitivity for the authors' use case is likely to be lower. This is spectrum bias and is widely recognised as a problem in test validation.[8] Furthermore, because of antibody waning, the sensitivity is likely to be highest at around 14 days after symptom onset (when it was estimated), then to fall over time during convalescence. This pattern is universal in nucleocapsid IgG assays that do not use an

antigen sandwich technique.[9] Indeed, backing up this observation is the fact that 142 (20%) of the 712 positive cases at visit 1 had become negative by visit 2.[5] As most cases in the first wave in Manaus occurred in March and April, 2020, 4 months had elapsed before visit 1 in August. This allowed for significant positive–negative transition to have occurred before this blood draw. In the face of antibody waning, multiple timepoints are required to correctly interpret seroprevalence data.

Despite these caveats, Lalwani and colleagues' study provides useful insights into the SARS-CoV-2 epidemic in Manaus. The results highlight heterogeneities in transmission and hint at a possible asynchronous COVID-19 peak among more affluent Manaus residents who were better able to isolate during the first wave.[7]

We declare no competing interests.

Lewis F Buss, Ester C Sabino
lewisbuss@usp.br

Departamento de Molestias Infecciosas e Parasitarias and Instituto de Medicina Tropical da Faculdade de Medicina, Universidade de São Paulo, São Paulo, Brazil (LFB, ECS)

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