The Journal of Infectious Diseases

MAJOR ARTICLE

Seroprofiling of antibodies against endemic human coronaviruses and SARS-CoV-2 in an HIV cohort in Lesotho: correlates of antibody response and seropositivity

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Background: Serological data on endemic human coronaviruses (HCoVs) and SARS-CoV-2 in southern Africa are scarce. Here, we report on i) endemic HCoV seasonality, ii) SARS-CoV-2 seroprevalence, and iii) predictive factors for SARS-CoV-2 seropositivity and strength of SARS-CoV-2 and HCoV serological response during a 17-month period at the start of the COVID-19 pandemic among adults living with HIV.

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DOI: 10.1093/infdis/jiad197

Methods: Plasma samples were collected from February 2020 to July 2021 within an outpatient HIV cohort in Lesotho. We used the ABCORA multiplex immunoassay to measure antibody responses to endemic HCoV (OC43, HKU1, NL63, and 229E) and SARS-CoV-2 antigens.

Results: Results of 3'173 samples from 1'403 adults were included. Serological responses against endemic HCoVs increased over time and peaked in winter/spring. SARS-CoV-2 seropositivity reached >35% among samples collected in early 2021 and was associated with female sex (p=0.004), obesity (p<0.001), working outside the home (p=0.02), and recent tiredness (p=0.005) or fever (p=0.007). Positive correlations were observed between the strength of response to endemic HCoVs and to SARS-CoV-2, and between older age or obesity and the IgG response to SARS-CoV-2.

Conclusions: These results add to our understanding of the impact of biological, clinical, and social/behavioural factors on serological responses to coronaviruses in southern Africa.

Key Words: Serology, COVID-19, coronavirus, HIV, immunoassay, seroepidemiologic studies, southern Africa

INTRODUCTION

Serological analyses are a powerful tool to assess population susceptibility to infectious diseases, disease burden, as well as dynamics and risk factors of infection[1]. Previous serological research has demonstrated that exposure to endemic human coronaviruses (HCoVs) can be protective against SARS-CoV-2 infection and improve the immunological response to SARS-CoV-2 upon infection[2]. However, data on serological cross-protection against SARS-CoV-2 in pre-pandemic samples from sub-Saharan Africa are conflicting[3–6].

In South Africa, SARS-CoV-2 seroprevalence increased from 13% in the third quarter of 2020 to 56% a year later; furthermore, serological analyses demonstrated vast underestimation of SARS-CoV-2 infections using cumulative incidence data of confirmed cases[7]. Comparable data on circulation of endemic HCoVs in southern Africa are scarce, though non-serological studies from specific, largely symptomatic sub-populations provide some indications of seasonality[8,9].

Assessing potential correlates of SARS-CoV-2 seropositivity, a household survey in South Africa observed associations with age, female sex, elevated body mass index (BMI), respiratory symptoms, and lower socioeconomic status, among others[10]. Furthermore, both this and a separate study among pregnant women living with HIV in Mozambique observed lower SARS-CoV-2 seropositivity in people with HIV viraemia[10,11], likely due to weaker immune response in this population[10].

Indeed, previous research has reported poorer immunological responses to SARS-CoV-2 among people living with HIV[12], whereas people living with HIV do not appear to have higher rates of

SARs-CoV-2 infection[10,12–14]. A large study in a South African population with a high burden of comorbidities demonstrated higher COVID-19 mortality among people living with HIV[15], though overall findings on associations of HIV with COVID-19 severity are divergent, with several studies suggesting that poorer COVID-19 outcomes may be linked to ongoing HIV viraemia, low CD4 cell count, comorbidities, or social determinants of health rather than HIV itself[16].

To further elucidate the seroepidemiology of HCoVs in the context of HIV in an understudied population in Lesotho, southern Africa, we use a previously described[2] multifactorial serological assay for seroprofiling of endemic HCoV and SARS-CoV-2 antibody responses in a longitudinal adult HIV cohort.

This study has three objectives. First, we describe the seasonality of endemic HCoVs and correlates of the immunological response to endemic HCoVs in this population. Second, we describe the seroprevalence of SARS-CoV-2 over time. Third, we elucidate factors associated with SARS-CoV-2 seropositivity and serological response, considering endemic HCoV serological, clinical (including HIV-related), demographic, behavioural/social, and symptomatic factors.

METHODS

Participants and human specimens

Plasma samples were collected within the *Dolutegravir in Real Life in Lesotho (DO-REAL)* cohort study[17,18], which was nested within a larger HIV viral load monitoring cohort in Lesotho[19]. The present analyses include DO-REAL participants enrolled at Butha-Buthe Government Hospital for whom one or more blood plasma samples taken between 10 February 2020 (the start of enrolment into DO-REAL) and 13 July 2021 was available. During this period, vaccination against SARS-CoV-2 was generally unavailable in this setting. In brief, all participants were in care for HIV and newly taking dolutegravir-based antiretroviral therapy (ART) after new ART initiation or transitioning from a previous ART regimen. Samples and participant data were collected on the day of starting dolutegravir-based ART, after 16 weeks, and according to routine schedules (annually if virally suppressed) thereafter.

Through most of the study period, COVID-19 screening (temperature screening and questions on symptoms and recent travel) was conducted at the hospital gate, meaning that individuals did not have obvious symptoms at the time of phlebotomy.

Diagnostic procedures

Samples previously stored at -80 °C were heat-inactivated for 30 min at 56 °C and analysed using the ABCORA assay v5.4[2]. In brief, ABCORA is a bead-based multiplex immunoassay measuring 12 SARS-CoV-2-specific antibody parameters, namely four antigens (the spike [S]

glyocoprotein subunits S1 and S2, the angiotensin-converting enzyme 2 receptor-binding domain [RBD] in S1, and the nucleocapsid protein [N]) across three immunoglobulin (Ig) classes (IgG, IgA, IgM). In addition, antibodies against the S1 protein of HCoVs OC43, HKU1, NL63, and 229E are detected.

For each antibody parameter (i.e., for each antibody class against each antigen), the strength of the readout is reported as a continuous logarithmic fold change over the empty bead control score of the median fluorescence intensity (MFI-LFOE; left-censored at 0). ABCORA gives semi-quantitative results and has shown high correlation with other quantitative commercial assays[2]. The ABCORA assay uses data from all 12 SARS-CoV-2-specific antibody parameters to generate a binary diagnosis of seropositivity, i.e. of detectable prior SARS-CoV-2 infection, which we refer to as the ABCORA diagnosis[2].

Data management and statistical analyses

Participant characteristics:

We describe demographic, clinical, and behavioural/social participant characteristics at the time of the first available sample. CD4 cell nadir was defined as the CD4 cell count recorded at ART initiation (i.e. the last measurement before ART initiation or the first measurement maximally six months after ART initiation). Public transport use refers to the past week; attending public gatherings of more than five people refers to the past two weeks. We report frequencies and percentages for categorical variables, and medians and interquartile ranges (IQRs) for continuous variables.

Throughout analyses, we adjusted for two sets of variables: age, sex, and BMI; or additionally for demographic, clinical, and behavioural/social variables (see **Supplement 1.1**).

Endemic hcov seasonality:

We assessed the seasonality of antibody responses against endemic HCoVs using a periodic mixed-effect TOBIT model accounting for left-censored data and repeated measurements among individuals (see formula in **Supplement 1.2**). The model was run for each Ig subtype and endemic HCoV antigen. For each individual, samples with a positive ABCORA diagnosis and any subsequent samples were excluded due to known interdependencies between antibodies against endemic HCoVs and SARS-CoV-2[2]. Likelihood ratio tests were performed to test for seasonal periodic variation. We reported the calendar timing of peak responsiveness with 95% confidence interval (CI) for each Ig type / HCoV pair.

Correlates of strength of serological response to endemic hcovs:

Correlations between demographic, clinical, and social/behavioural factors with the strength of response to endemic HCoVs were determined within the above-mentioned TOBIT model. We furthermore assessed the effect of the dichotomised strength of response to each endemic HCoV

at the first visit on pre-specified symptoms self-reported at the second visit using a logistic regression, with separate analyses for each symptom / HCoV pair. For this and all subsequent analyses using responses to endemic HCoV antigens as exposure variables, responses were dichotomised as high versus low if above versus below the median across all samples included in the respective analysis.

SARS-cov-2 seroprevalence over time:

We reported the number of tests performed over time by sampling date, including SARS-CoV-2 seropositivity as per ABCORA diagnosis.

Determinants of SARS-cov-2 seropositivity:

We assessed the association of demographic, clinical, and behavioural/social factors with any SARS-CoV-2 seropositivity using a logistic regression model.

In addition, we assessed the correlation of reporting having experienced pre-specified symptoms within the last two weeks at a given visit with seropositivity at the same visit via mixed-effect logistic regression. Samples following the first positive serology were removed from analysis. Analyses were run separately for each symptom.

Among individuals whose first available sample was seronegative for SARS-CoV-2, we assessed the effect of the strength of response to each endemic HCoV (dichotomised as described above) in the first sample with SARS-CoV-2 seropositivity in the next available sample using logistic regression. A sensitivity analysis removing all samples within the top 20% in terms of likelihood for SARS-CoV-2 seropositivity (rather than only those testing seropositive) was conducted to address potential confounding in the case of recent SARS-CoV-2 infection at the time of the first sample, which we hypothesised may cause elevated measurements for endemic HCoV responses through cross-reactivity of the beginning anti-SARS-CoV-2 response while simultaneously yielding a false seronegative result for SARS-CoV-2 if the anti-SARS-CoV-2 response is still below the ABCORA threshold (preventing exclusion from analysis). This could mask potential protective effects of stronger responses to endemic HCoVs against SARS-CoV-2 infection, which have previously been reported[2]. Finally, we plotted the distributions and medians of the strength of endemic HCoV responses in the first samples of each individual among individuals whose subsequent sample was seronegative versus seropositive for SARS-CoV-2.

Correlates of strength of serological response to SARS-cov-2:

We used Bayesian models to assess the correlation of demographic, clinical, and social/behavioural factors with the strength of the antibody response to SARS-CoV-2 considering the first seropositive sample of any individual. We ran both a multivariate model summarising the response of a given Ig subtype against all four SARS-CoV-2 antigens, and a univariate model

assessing each Ig subtype / SARS-CoV-2 antigen pair separately. Further information is provided in **Supplement 1.3**.

Finally, we assessed whether the strength of endemic HCoV responses (dichotomised as described above) measured at the first visit was associated with the strength of SARS-CoV-2 antibody responses at the subsequent visit among participants who were seronegative for SARS-CoV-2 at the first and seropositive at the second visit, using the aforementioned Bayesian models. Upon observing an association of sex and age with HCoV levels, these analyses were repeated with stratification by sex or age.

Statistical tools used:

The cohort dataset was prepared in Stata v16.1. Subsequent analyses were performed with R v4.2.1. The Bayesian analyses were done with Stan using the rstan package in R.

Consenting and ethical considerations

Both the DO-REAL cohort and the viral load monitoring cohort study in which it is nested were approved by the National Health Research Ethics Committee in Lesotho (ID134-2016). DO-REAL was registered with ClinicalTrials.gov on 23 January 2020 (NCT04238767). The study was conducted in accordance with the principles of the Declaration of Helsinki, and participants included in this analysis provided informed consent both for DO-REAL and for the further use of their samples.

RESULTS

Participant characteristics

Results of 3’173 samples from 1’403 individuals were included in this analysis. Participant characteristics are shown in **Table 1**: 821 (58%) were female, median age was 45 years (IQR 37-55), and 1332 (95%) were already taking ART prior to providing the first included sample, with a median of 5.1 years (IQR 2.8-8.3) since ART initiation. The majority of participants, 1’272 (90%), contributed two or more samples to this analysis, and 291 (21%) had at least one sample that was seropositive for SARS-CoV-2.

Seasonality of endemic hcovs

Figure 1 shows the seasonality patterns of antibody responses to endemic HCoVs after adjusting for age, sex, and BMI. For all pairings of the three immunoglobulin classes with the four endemic HCoVs except anti-NL63 IgM, this model indicates statistically significant seasonal variations (anti-NL63 IgM: $p=0.069$; all others: $p<0.001$) with peaks in winter and spring (around August to November; **Figure S1A**). In addition, for all immunoglobulin and HCoV combinations except anti-229E IgG ($p=0.06$), the model indicated a statistically significant ($p<0.001$ for each) increase

over time. These patterns remained robust in sensitivity analyses without or with extended covariate adjustment (**Figures S1-S2**).

Correlates of strength of serological response to endemic hcovs

The association of age, sex, and BMI with the strength of antibody response to endemic HCoVs is shown in **Figure 2**. Female (vs male) sex was mostly associated with a weaker antibody responses to endemic HCoVs. Older age (vs <40 years) was associated with an increased response for some Ig type / HCoV pairs, especially for IgG against HKU1, NL63, and 229E. A corresponding analysis for additional variables is shown in **Figure S3**.

No robust correlation was observed between the strength of the HCoV response and the symptoms reported for the previous two weeks at the respective visit, though a trend towards fewer symptoms was observed for any symptoms, cough, and fever (**Figure S4**).

SARS-cov-2 seroprevalence over time

SARS-CoV-2 seroprevalence was <10% until October 2020, then increased rapidly to >35% among samples collected in February 2021. **Figure 3** shows the tests conducted, test outcomes, and seroprevalence over the study period.

Determinants of SARS-cov-2 seropositivity

In unadjusted analysis including demographic, clinical, and behavioural/social factors, female sex (vs male; OR 2.4, 95% CI 1.7-3.4, unadjusted p<0.001) and a BMI of 25-30 kg/m^2 (vs 18.5-25; OR 1.8, 95% CI 1.2-2.8, unadjusted p=0.005) or >30 kg/m^2 (vs 18.5-25; OR 3.0, 95% CI 2.0-4.4, unadjusted p<0.001) increased the odds of SARS-CoV-2 seropositivity. In adjusted analysis, female sex (vs male; aOR 1.9, 95% CI 1.2-2.9, p=0.0041), a BMI >30 kg/m^2 (vs 18.5-25; aOR 2.3, 95% CI 1.5-3.6, p<0.001), and working outside the home (vs not working / working from home; aOR 1.5, 95% CI 1.1-2.2, p=0.02) increased the odds of ever having a positive SARS-CoV-2 serology (**Figure 4**; comparable outcomes after exclusion of commonly missing variables shown in **Figure S5**).

In a separate analysis on the correlation between symptoms and seropositivity at a given visit, reporting tiredness (OR 3.4, 95% CI 1.3-8.6, unadjusted p=0.0115; aOR 4.1, 95% CI 1.5-10.7, p=0.0045) and fever (OR 3.8, 95% CI 1.2-12.1, unadjusted p=0.0252; aOR 5.2, 95% CI 1.6-17.1, p=0.0069) during the two weeks preceding the visit were associated with SARS-CoV-2 seropositivity in both unadjusted and adjusted analysis (**Figures 5, S6**).

The strength of the serological response to endemic HCoVs did not appear to modulate the odds of SARS-CoV-2 infection, as among individuals whose first available sample was seronegative for SARS-CoV-2, we did not observe any association between the strength of response to endemic HCoVs in the first sample with SARS-CoV-2 seropositivity of the subsequent sample (**Figure S7**). A sensitivity analysis to address potential masking of HCoV protectiveness against SARS-CoV-2

infection by false negative SARS-CoV-2 diagnoses for the first sample in the case of recent infection did not yield altered results (**Figure S8**). Similarly, plotting the distribution of serological responses to each endemic HCoVs within samples from the first visit did not indicate discernible differences between individuals whose subsequent sample was seronegative versus seropositive for SARS-CoV-2 (**Figure S7**).

Correlates of strength of serological response to SARS-cov-2

Among samples with a positive SARS-CoV-2 serology, a BMI ≥30 kg/m^2 as well as age categories >40 years were associated with higher IgG responses to SARS-CoV-2 antigens in adjusted analysis, and female sex was minimally associated with lower IgM responses (**Figures S9-S11**).

Stronger responses against several endemic HCoVs (specifically, higher response of: IgG, IgA, or IgM to HKU1; IgM to OC43; and IgG or IgA to NL63) were each associated with stronger serological response to SARS-CoV-2 (**Figures 6, S12**). This effect appears to be driven by female participants (**Figures S13-S14**), whereas we did not see any major differences in outcomes when stratifying by age (**Figures S15-S16**).

DISCUSSION

This longitudinal study in people living with HIV in Lesotho investigated antibody responses to endemic HCoVs in conjunction with anti-SARS-CoV-2 antibodies during the first two waves of the pandemic, aiming to determine: i) endemic HCoV seasonality in southern Africa, with peaks observed in winter/spring; ii) SARS-CoV-2 seroprevalence in the first one and a half years of the pandemic, with peaks in seroprevalence in late 2020/early 2021 mirroring major waves reported in southern Africa; iii) factors associated with SARS-CoV-2 seropositivity, notably identifying female sex and elevated BMI; and iv) factors associated with the strength of immunological response, observing a stronger response to SARS-CoV-2 upon prior stronger response to endemic HCoVs.

Prior data on HCoV seasonality in southern Africa is limited. Most previous studies focus on specific, symptomatic populations – notably young children with influenza-like illness[8,9,20,21], and few provide serological data. In the present analysis, antibody responses to endemic HCoVs appear to increase over time and peak in winter and spring. This largely corresponds with reports on endemic HCoV seasonality in temperate climates (such as Lesotho)[22], and matches data from southern Africa for OC43 and HKU1, whereas peaks in warmer months have been reported for NL63 and 229E[8,9]. For SARS-CoV-2, we observed a strong increase in seroprevalence in late 2020 and early 2021, reflecting a major wave in southern Africa and largely aligning with previous reports[7].

We observed associations of SARS-CoV-2 seropositivity with female sex, obesity, and working away from the home, as well as reporting recent tiredness or fever. Numerous studies have shown

male sex[23–26] and obesity[27–29] to be associated with increased disease severity and mortality, whereas links to risk of SARS-CoV-2 infection are less clear. A combination of genetic, epigenetic, hormonal, and immunological sex differences alongside gender-associated social and behavioural factors may account for sex and gender imbalances relating to SARS-CoV-2, and have been reviewed elsewhere[24–26]. However, despite divergent reports[10,30], across Africa and globally there do not appear to be clear sex differences for risk of SARS-CoV-2 infection[7,23]. We thus hypothesise that social and behavioural factors might underlie the higher risk of seroprevalence among female participants, though are unable to further assess potential further confounders. Similarly, multiple factors may link BMI to the risk of seropositivity: despite numerous potential biological factors at play, overall obesity does not appear to be associated with a greater risk of infection or with broadly impaired antibody responses to SARS-CoV-2[31]. Lower antibody persistence in association with obesity after vaccination has been described[32,33], whereas reports on overall seropositivity or serological outcomes after infection are conflicting[10,34–36], possibly due to effects of greater disease severity in obese individuals[27–29] with subsequent more prominent antibody persistence[35]. Finally, underlying confounding factors such as socioeconomic status are likely to be relevant in our study setting. Overall, our findings are supported by a household survey in South Africa conducted during the second wave of the pandemic, in which female sex and elevated BMI were likewise associated with higher seropositivity[10].

We furthermore observed stronger antibody responses to endemic HCoVs in males and to a certain degree in older participants, and higher SARS-CoV-2 antibody responses at least for some Ig type / antigen pairs with increased age, increased BMI, and male sex. Similar to our findings, stronger antibody responses to SARS-CoV-2 have previously been reported for males and older individuals, as well as for people with severe COVID-19 requiring hospitalisation[37].

We observed no association HIV-related clinical factors (including CD4 nadir, known past viraemia, WHO stage at ART initiation, or time since HIV diagnosis or ART initiation) with SARS-CoV-2 seropositivity. Previous studies have, perhaps surprisingly, reported similar[13] or even lower[10,12,14] SARS-CoV-2 incidence, assessed either by test positivity[13,14] or seroprevalence[10–12], among people living with HIV and/or people with unsuppressed HIV. Observations of lower incidence may be related to behavioural factors including greater cautiousness[12,14] or, in the case of seropositivity, to weaker serological response upon SARS-CoV-2 infection and subsequent negative serological testing despite prior infection among people living with HIV or people with unsuppressed HIV[10–12]. A study in the United States did not observe any association between CD4 counts below 200 cells/μL or an unsuppressed viral loads and SARS-CoV-2 seropositivity[12], whereas low CD4 counts have been associated with adverse COVID-19 outcomes[12,15,38]. While behavioural considerations differ between infection and vaccine studies, the latter also provide relevant information on serological responses to SARS-CoV-2 among people living with HIV. Several studies have shown adequate response to

vaccination for people living with HIV[39–44], however, there is evidence for poorer outcomes with HIV especially in conjunction with low CD4 cell count or viraemia[40,45–48].

As reported previously[2], we found that stronger serological response to endemic HCoVs correlated with stronger serological response to SARS-CoV-2. However, we did not observe a protective effect of stronger serological response to endemic HCoVs against SARS-CoV-2 infection as previously observed in a Swiss population-based study[2]. This discrepancy may be due to differences in the regional endemic HCoV waves, as the type and timing of endemic HCoV exposure close to SARS-CoV-2 encounter may shape protective effects. Notably, the protection conferred by cross-reacting endemic HCoV immunity is modest and may result in asymptomatic disease courses[2]. It is therefore important to note that the present study relied on retrospective serological testing for SARS-CoV-2 positivity. PCR testing as performed in the Swiss study[2] has a higher chance of detecting asymptomatic infections which often induces less pronounced antibody responses that wane more rapidly[49,50]. Detection of SARS-CoV-2 infection in the present study may thus have been biased towards detecting more severe disease linked with more profound and sustained antibody responses.

This study has several limitations. No PCR or antigen testing was available to complement serological data. This means that factors decreasing the serological response might lead to false negative inferences on infection, as it was not possible within this study to differentiate between the absence of prior infection and prior infection with a negative ABCORA diagnosis. Furthermore, the timing of past infection was not known and could thus not be included in models, and endemic HCoV responses were not measured at the time point of SARS-CoV-2 exposure or infection. True pre-pandemic samples were not available, though sample collection began before the first case of COVID-19 was recorded in Lesotho or neighbouring South Africa. As with any observational research, potential unmeasured confounding factors cannot be fully accounted for. Finally, all participants were living with HIV, meaning that we could not assess the impact of HIV infection on serological outcomes.

In summary, sex, age, and BMI correlated with several serological outcomes relating to endemic HCoVs and SARS-CoV-2 among adults living with HIV in Lesotho, with positive associations between responses to endemic HCoVs and SARS-CoV-2. These findings add to our understanding of the role of biological, clinical, and social/behavioural factors on the epidemiology of and serological responses to coronaviruses in southern Africa.

Author contributions: NDL conceptualised the DO-REAL cohort, and NDL and JAB were centrally involved in its design. BLN managed the cohort onsite and oversaw onsite procedures including consenting, enrolment, data collection, and sample collection. JAB led the cohort offsite, managed cohort data, and prepared the dataset for this study. HFG initiated this collaborative project between DO-REAL and the University of Zurich. IAA led the development of the previously published ABCORA assay with key support from AT and SE. SE and TM conducted the assays for this study under the guidance of IAA. CP developed the bioinformatic analyses of

ABCORA. AH performed all analyses, with input from CP and RDK. HFG, AT, IAA, JAB, NDL, RDK, AH and CP regularly reviewed and interpreted ongoing data analyses. JAB wrote the first draft of the manuscript. All authors contributed to and reviewed the manuscript.

Acknowledgements: We thank all contributors to the DO-REAL study as well as the staff at Butha-Buthe Government Hospital and SolidarMed Lesotho. We gratefully acknowledge the study participants.

This work was supported by the Swiss National Science Foundation (grant number PCEFP3_181355, awarded to NDL; grant number 196906, awarded to HFG, RDK and AT), a grant of the Pandemiefonds of the University of Zurich Foundation (awarded to AT), and the Gilead COVID-19 RFP Research Program COMMIT (grant number IN-SW-983-6078, awarded to HFG, AT, and RK). JAB receives her salary from grants from the University of Basel Research Fund for Junior Researchers (grant number 3ZW1422; awarded to JAB) and Fondation Botnar (REG-19-008, awarded to NDL). IAA is supported by a research grant of the Promedica Foundation.

HFG reports having received honoraria from Gilead Sciences, Merck, ViiV, GSK, Janssen, Johnson and Johnson, and Novartis for serving on DSMB and/or advisory boards, and has received a travel grant from Gilead Sciences. In addition, he has received grants from the Swiss National Science Foundation (SNSF), the Swiss HIV Cohort Study, the Yvonne Jacob Foundation, the NIH and unrestricted research grants from Gilead Sciences, all paid to the institution. NDL reports having received travel grants to attend scientific conferences from Gilead Sciences. He has received grants from SNSF, Fondation Botnar, Botnar Center for Child Health, the Swiss Agency for Development and Cooperation, and Moritz Straus Stiftung. AT has received honoraria from Roche Diagnostics for consultant activity, and grants from the SNSF, the Swiss HIV Cohort Study, the Pandemiefonds of the UZH foundation and unrestricted research grants from Gilead Sciences. IA has received honoraria from MSD and Sanofi, a travel grant from Gilead Sciences, and a grant from Promedica foundation. RDK has received grants from SNSF, the National Institutes of Health, and Gilead Sciences. JAB has received funds from the University of Basel Research Fund. All other authors declare that they have no competing interests.

Conflicts of interest: HFG reports having received honoraria from Gilead Sciences, Merck, ViiV, GSK, Janssen, Johnson and Johnson, and Novartis for serving on DSMB and/or advisory boards, and has received a travel grant from Gilead Sciences. In addition, he has received grants from the Swiss National Science Foundation (SNSF), the Swiss HIV Cohort Study, the Yvonne Jacob Foundation, the NIH and unrestricted research grants from Gilead Sciences, all paid to the institution. NDL reports having received travel grants to attend scientific conferences from Gilead Sciences. He has received grants from SNSF, Fondation Botnar, Botnar Center for Child Health, the Swiss Agency for Development and Cooperation, and Moritz Straus Stiftung. AT has received honoraria from Roche Diagnostics for consultant activity, and grants from the SNSF, the Swiss HIV Cohort Study, the Pandemiefonds of the UZH foundation and unrestricted research grants

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Previous presentations of the data: These findings were presented at the International Workshop on HIV and Hepatitis Observational Databases (IWHOD) 2023, held from 23 to 25 March 2023 without publication.

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Table 1: Participant characteristics at time of first sample.

	N=1403
Sex, n (%)	
Female	821 (59%)
Male	582 (41%)
Age by category, n (%)[1,2]	
<40	420 (31%)
40–60	732 (54%)
>60	193 (14%)
Age, median (IQR) [1,2]	46 (37.5-55)
BMI in kg/m^2, n (%)[1,3]	
<18.5	79 (6%)
18.5–25	618 (44%)
25–30	335 (24%)
>30	367 (26%)
WHO stage at ART initiation, n (%)[4]	
1	598 (45%)
2	410 (31%)
3	294 (22%)
4	18 (1%)

CD4 nadir in cells/µL, n (%)[5]	
<200	422 (41%)
200–500	458 (45%)
>500	147 (14%)
Years since HIV diagnosis, median (IQR)[1,6]	6.7 (3.5-10.0)
Years since ART initiation, median (IQR)[1]	5.6 (3.3-8.8)
Any previous VL >50 copies/mL, n (%)[1,7]	407 (31%)
VL >50 at VL closest to first visit[8]	106 (8%)
Work (at least partially) away from home, n (%)[9]	523 (39%)
Use public transport, n (%)[9]	422 (31%)
Attended a gathering of >5 people, n (%)[9]	486 (36%)
Household size, n (%)[10]	
1	270 (20%)
2–3	500 (37%)
>3	586 (43%)
Number of samples analysed, n (%)	
1	131 (9%)
2	782 (56%)
3	482 (34%)
4	8 (1%)
Any positive ABCORA diagnosis for SARS-CoV-2, n (%)	291 (21%)

[1] At time of first sample of the respective participant included in this analysis
[2] Missing for 58 participants
[3] Missing for 4 participants
[4] Missing for 83 participants
[5] Missing for 376 participants
[6] Missing for 86 participants
[7] Missing for 85 participants
[8] Missing for 14 participants
[9] Missing for 61 participants
[10] Missing for 47 participants

Figure 1: Seasonality of endemic human coronavirus (HCoV) seroprevalence (2364 samples from 1062 individuals). Antibody reactivity to HCoV antigen is depicted as logarithmic fold change over the empty bead control (LFOE). Results are adjusted for age, sex, and BMI. Dark red lines along the x axis indicate the estimated seasonality with red ribbons indicating 95% confidence intervals for each immunoglobulin type/HCoV pairing. Vertical red lines show the estimatedpeaks. P-values refer to likelihood ratio tests assessing the statistical significance of adding a seasonality parameter, i.e. of assuming periodic variation of LFOE. IgA: immunoglobulin A; IgG: immunoglobulin G; IgM: immunoglobulin M.

Figure 1

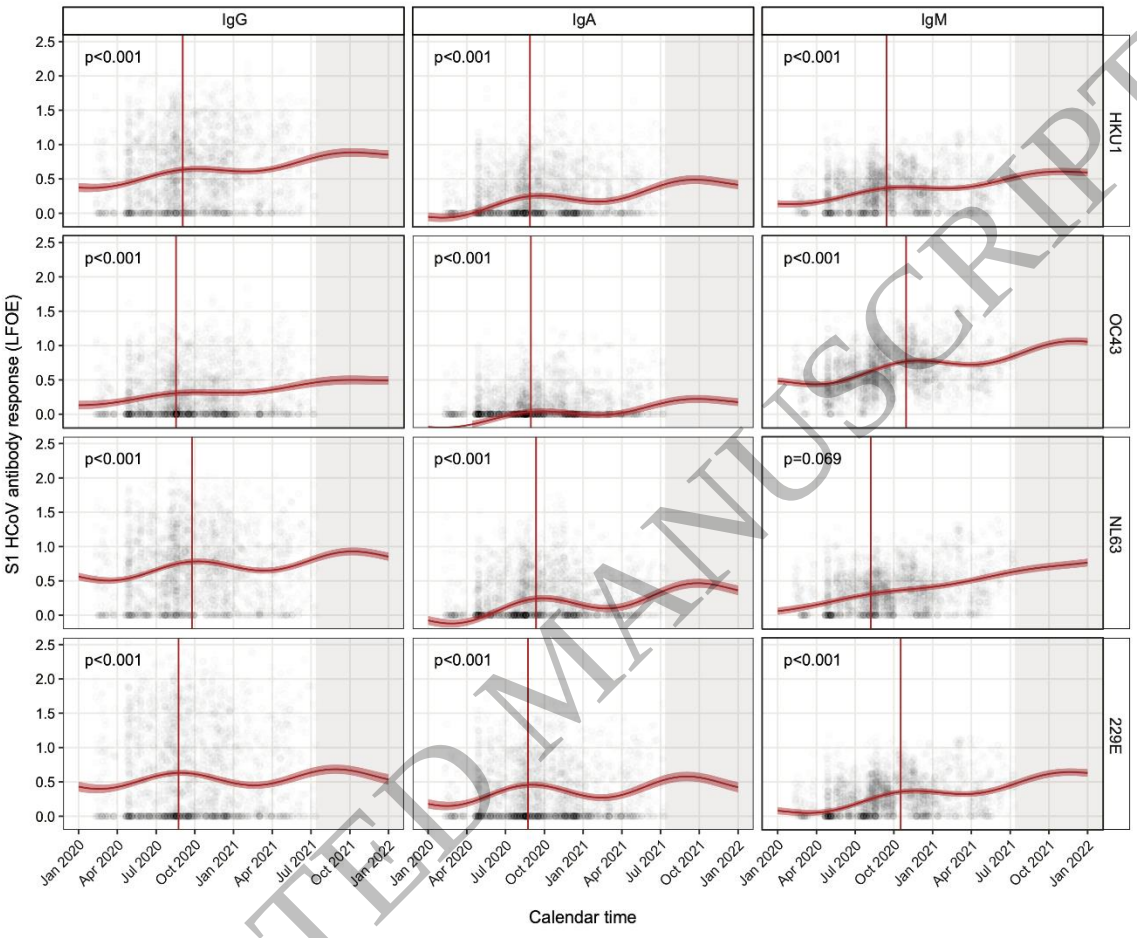


Figure 2: Correlation of sex, age, and BMI with serological response to endemic HCoVs (2364 samples from 1062 individuals). Effect sizes with 95% confidence intervals are indicated. Correlations are assessed for sex (reference: male), age category (reference: <40 years), and BMI category (reference: 18.5–25 kg/m^2). Adjusted results consider age, sex, and BMI. BMI: body mass index; IgA: immunoglobulin A; IgG: immunoglobulin G; IgM: immunoglobulin M; LFOE: logarithmic fold change over the empty bead control.

Figure 2

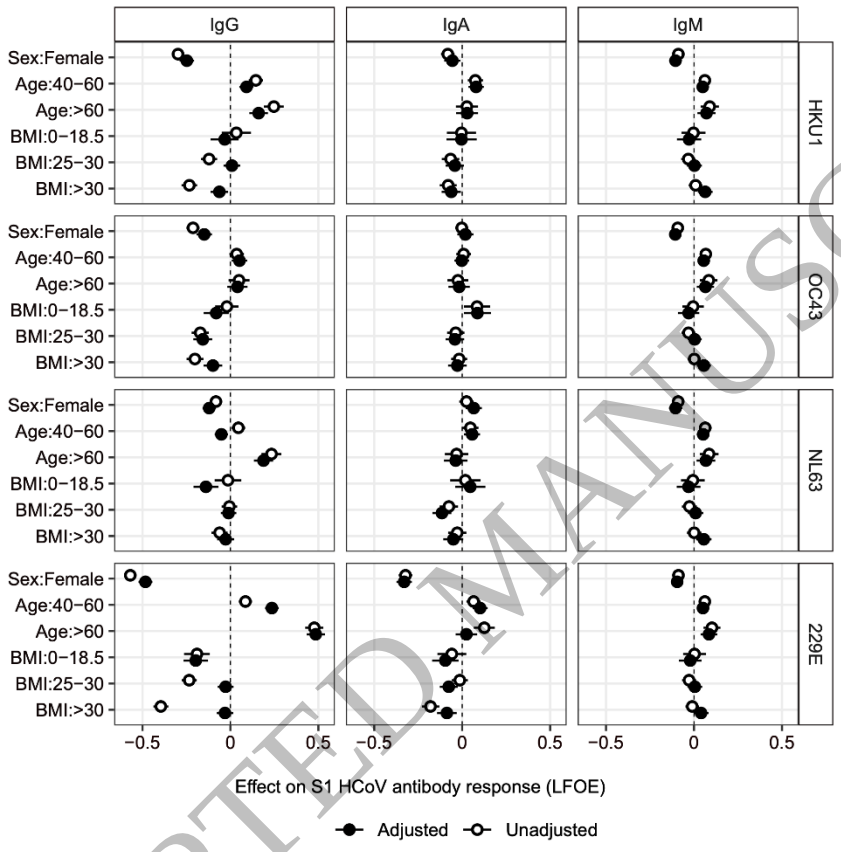


Figure 3: SARS-CoV-2 seroprevalence from February 2020 through July 2021 (3173 samples from 1403 individuals). A: Number of samples tested for SARS-CoV-2 seropositivity and ABCORA test outcome over time. B: SARS-CoV-2 seroprevalence among tested samples over time. The light grey area indicates the 95% confidence interval.

DOI: 10.1093/infdis/jiad197

Figure 3

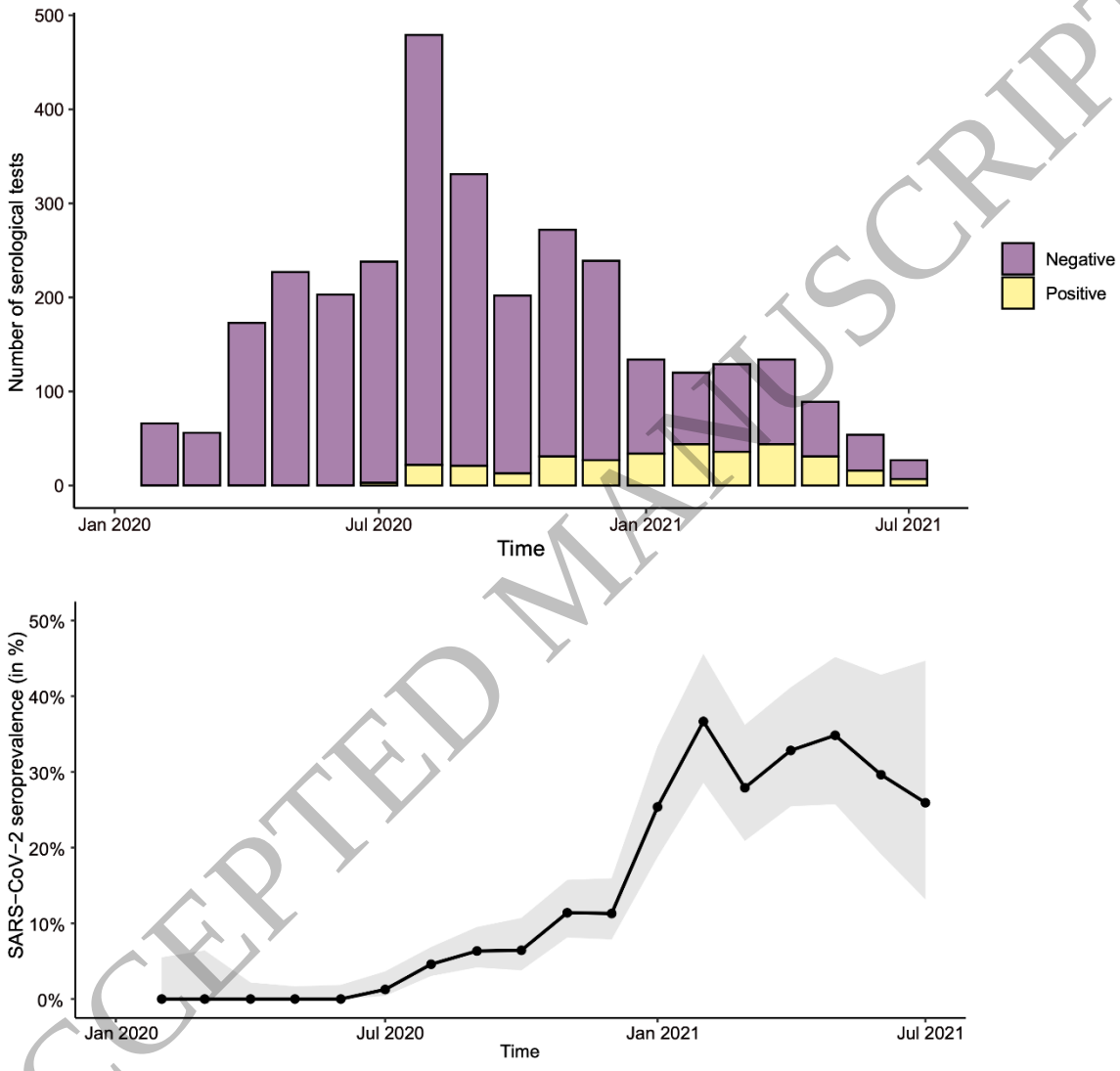


Figure 4: Association of demographic, clinical, and behavioural/social factors with SARS-CoV-2 seropositivity (885 samples from 885 individuals). The association of demographic, clinical, and behavioural/social factors (assessed at the time of the first sample) with SARS-CoV-2 seropositivity across all included samples of the respective individual was assessed by logistic regression. Adjusted results are shown using all included variables as covariates. P-values refer to the adjusted analyses. ART: antiretroviral therapy; BMI: body mass index; VL: viral load; WHO: World Health Organization.

Figure 4

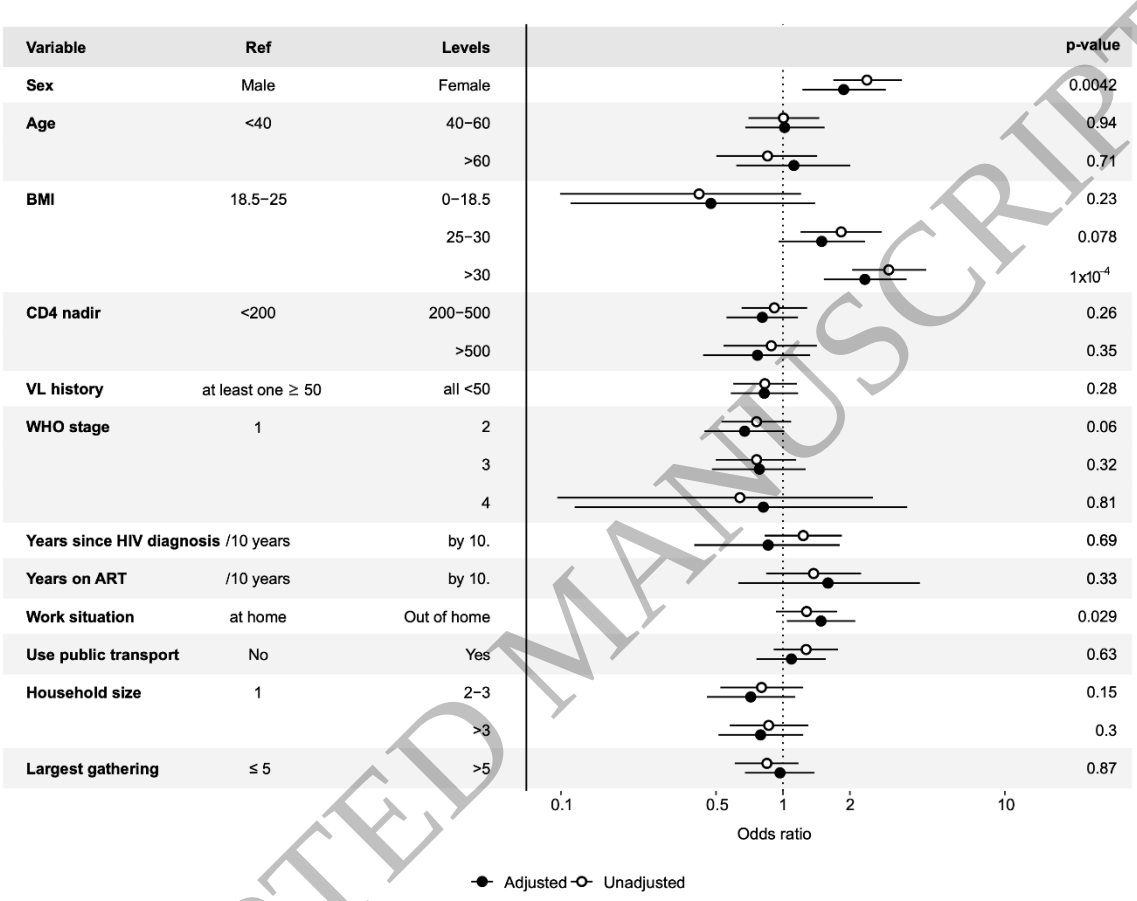


Figure 5: Association of self-reported recent symptoms with SARS-CoV-2 seropositivity (3037 samples from 1345 individuals). The association of symptoms reported for the past two weeks at a given visit with SARS-CoV-2 seropositivity at the respective visit (removing samples taken after a positive ABCORA diagnosis) was assessed using a mixed-effect logistic regression. Separate analyses were conducted for each symptom, using all symptom responses as well as sex, age category, and BMI category as covariates for the adjusted odds ratio. P-values refer to the adjusted analyses.

DOI: 10.1093/infdis/jiad197

Figure 5

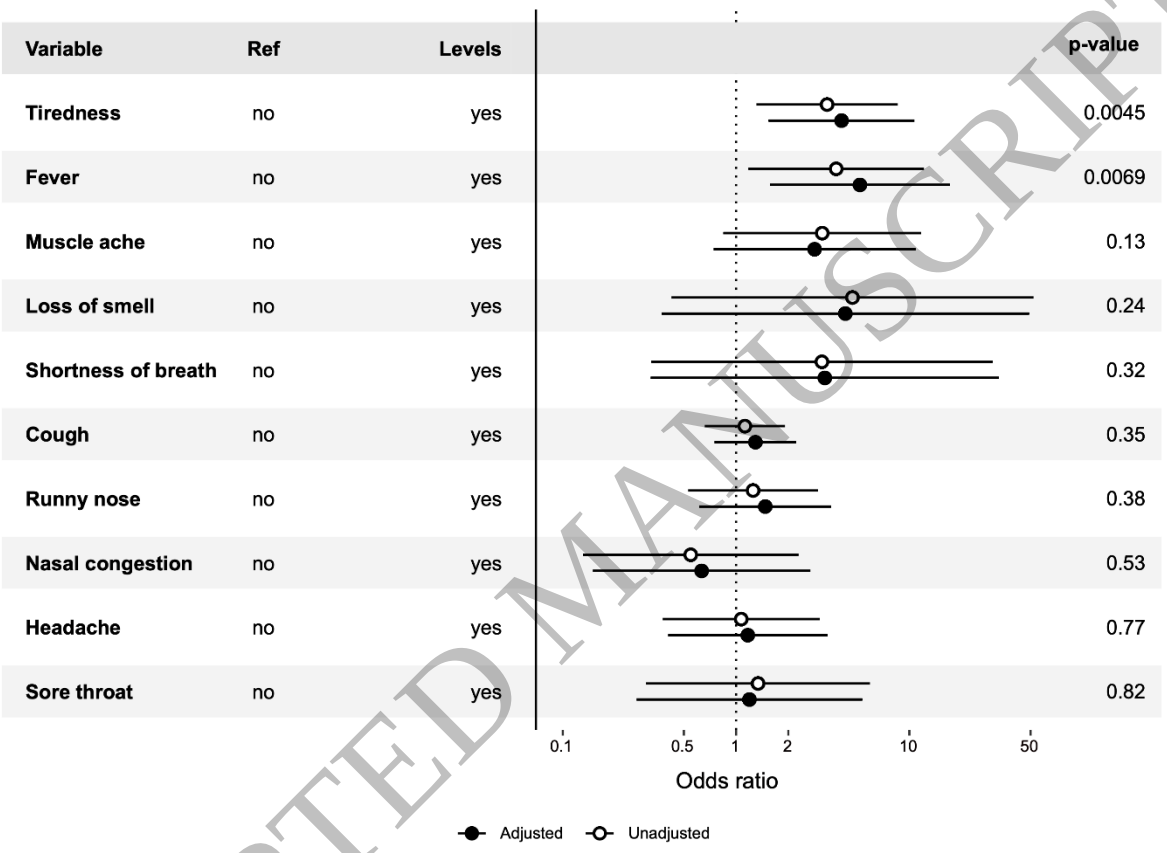
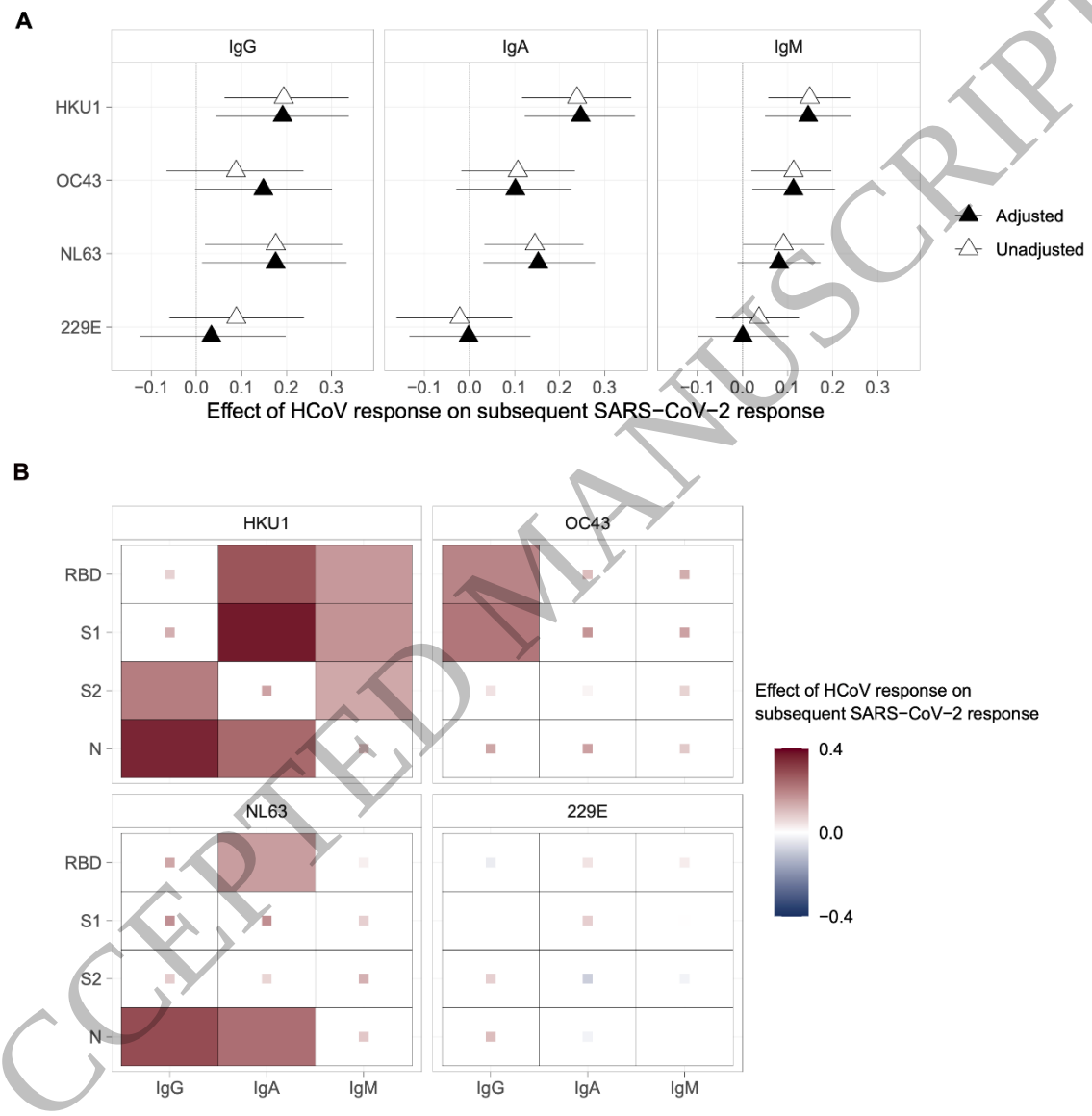


Figure 6: Association of strength of response to endemic HCoVs at one visit with strength of SARS-CoV-2 response at the subsequent visit (120 samples from 120 individuals). Sample pairs were included if they tested negative for SARS-CoV-2 at the first and positive at the subsequent visit. Adjusted for age, sex, and BMI. A: Multivariate Bayesian model. B: Univariate analysis with colouring indicating the effect on the antibody response to SARS-CoV-2 and full coloured blocks when the 95% credibility interval does not cross 0.

DOI: 10.1093/infdis/jiad197

Figure 6



DOI: 10.1093/infdis/jiad197