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Are children and adolescents living with HIV in Europe and South Africa at higher risk of SARS-CoV-2 and poor COVID-19 outcomes?

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Summary

Children, adolescents and young people living with HIV (CALWHIV), including those in resource-limited settings, may be at increased risk of SARS-CoV-2 infection, poorer COVID-19 outcomes and multisystem inflammatory syndrome (MIS). We conducted a repeat SARS-CoV-2 seroprevalence survey amongst CALWHIV in Europe (n=493) and South Africa (SA, n=307), and HIV negative adolescents in SA (n=100), in 2020-2022. Blood samples were tested for SARS-CoV-2 antibody, questionnaires collected data on SARS-CoV-2 risk factors and vaccination status, and clinical data were extracted from health records. SARS-CoV-2 seroprevalence (95% CI) was 55% (50-59%) in CALWHIV in Europe, 67% (61-72%) in CALWHIV in SA, and 85% (77-92%) among HIV negative participants in SA. Amongst those unvaccinated at time of sampling (n=769, 85%), seroprevalence was 40% (35-45%), 64% (58-70%), and 81% (71-89%), respectively. Few participants (11% overall) had a known history of SARS-CoV-2 positive PCR or self-reported COVID-19. Three CALWHIV were hospitalized, two with COVID-19 (non-severe disease) and one young adult with MIS. Although SARS-CoV-2 seroprevalence was high across all settings, even in unvaccinated participants, it was broadly comparable to general population estimates, and most infections were mild/asymptomatic. Results support policy decisions excluding CALWHIV without severe immunosuppression from high-risk groups for COVID-19.

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Introduction

People living with HIV (PLWHIV) may be at greater risk of severe outcomes following coronavirus disease 2019 (COVID-19, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)) than people who are HIV negative, although the extent of and reasons for any causal relationship remain unclear [1, 2]. The impact of factors such as HIV viral load (VL), CD4 count, antiretroviral therapy (ART) and co-morbidities are incompletely understood [1, 2]. These factors may vary between settings, e.g. depending on country income status, meaning that collection of comparable data from multiple countries is essential.

Data on severity of SARS-CoV-2 infection in children, adolescents and young people living with HIV (CALWHIV) are limited, although two European studies reported only mild disease in this group [3, 4], consistent with data on HIV negative children [5]. A comparison between CALWHIV and HIV negative children in South Africa (SA) found no association between HIV and SARS-CoV-2 mortality, although precision was limited by the reassuringly small number of deaths [6].

While polymerase chain reaction (PCR) tests detect current SARS-CoV-2 infection, serological tests detect antibodies which indicate either previous infection or vaccination. Antibodies against the SARS-CoV-2 nucleoprotein (anti-N antibodies) are an index of natural infection, whereas those against the spike protein (anti-S antibodies) indicate previous infection or vaccination with currently available vaccines. Conversely, absence of antibodies indicates that either an individual has never been infected with or vaccinated against SARS-CoV-2, or that any antibody response to infection or vaccination was below the assay limit of

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detection or has waned over time. SARS-CoV-2 serological tests have high sensitivity and specificity, although sensitivity varies between tests and wanes over time since infection [7].

Seroprevalence data can be compared to clinical data to infer the severity of SARS-CoV-2 infection. Although the extent of protection conferred by infection with previous variants is unclear, these data can inform vaccine policy, e.g. whether CALWHIV should be prioritized for vaccination or messaging to promote vaccine uptake. SARS-CoV-2 seroprevalence data in CALWHIV are limited. A study in Mozambique reported SARS-CoV-2 seroprevalence as 36% amongst 90 unvaccinated adolescents living with HIV compared to 49% amongst 450 HIV negative participants in November 2022 [8], with evidence that seroprevalence was lower amongst adolescents living with HIV on unadjusted, but not adjusted, analysis.

In this study, we estimate the prevalence of SARS-CoV-2 antibody in CALWHIV in Europe and SA, and a comparison group of HIV negative adolescents and young people in SA, and describe how this changed over time, overall and by age group and region.

Methods

We carried out a repeat SARS-CoV-2 seroprevalence study amongst CALWHIV enrolled through established cohorts within the European Pregnancy and Paediatric Infections Cohort Collaboration (EPPICC) and the Cape Town Adolescent Antiretroviral Cohort (CTAAC). EPPICC is a network of cohorts of CALWHIV in routine paediatric HIV care in Europe and Thailand [9]; a subset of six cohorts in five countries participated in this study (Belgium, Greece, two cohorts in Spain, Ukraine, UK). Some cohorts include follow-up data after transfer to adult HIV care. CTAAC is a longitudinal cohort study of adolescents living with

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HIV established on ART and a comparison group from the same communities of age-matched HIV negative adolescents in Cape Town, SA [10].

Participants and study procedures

Participants aged <25 years and in follow-up in these cohorts were invited to take part in this study. CALWHIV were eligible if diagnosed with HIV aged <18 years. At the start of the study (October 2020), participation in a SARS-CoV-2 vaccine trial or receipt of a vaccine at baseline were exclusion criteria; the latter criterion was removed in May 2021 as approved vaccines became increasingly available.

Venous blood samples and participant data were collected during routine clinic or study visits at two time points ~6 months apart (allowable range 3-13 months). Participants (or parents/guardians for children) completed questionnaires including information on COVID-19 (physician-diagnosed with or without a positive test, or self-reported) at each visit. Additional details on SARS-CoV-2 vaccination status were added from March 2021.

In some clinics, previous test results from routine SARS-CoV-2 antibody screening or stored samples from routine visits (after 1 March 2020 and ≥4 months before enrolment) were used as the baseline sample. Questionnaires were completed referring to the time of sample collection. All samples were tested for SARS-CoV-2 antibodies using locally available serological assays. Results for anti-S IgG were preferred as these antibodies have the longest half-life [11, 12]; other results (e.g. for IgM and/or anti-N) were also accepted. Results were reported as positive, negative or indeterminate as per manufacturers' instructions.

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At each visit, data were extracted from clinic records, including demographics, HIV (clinical, laboratory and ART data; CD4 counts and HIV VLs measured up to 6 months before to one month after the sample date), co-morbidities at the time of the test, dates of COVID-19 diagnoses (SARS-CoV-2 positive PCR and/or hospitalization with symptoms consistent with COVID-19 according to WHO definition (Supplementary Material)) and multisystem inflammatory syndrome in children (MIS-C, based on the WHO definition [13]), and dates and details of SARS-CoV-2 vaccination. For participants with documented COVID-19 or MIS-C diagnosis, clinicians were asked to provide further details using case report forms based on WHO/ISARIC forms, including reporting of severity as defined by WHO at the time [14] (Supplementary Material), although this was not possible in SA. The MIS-C case definition applies to 0-19 year-olds; we did not systematically collect data on post-SARS-CoV-2 inflammatory syndromes in older participants.

Information on the dominant variant in each setting for each calendar quarter was based on publicly available data from the Global Initiative on Sharing All Influenza Data (GISAID) [15]; a variant was considered dominant from the first month in which it accounted for ≥50% of reports.

Statistical analysis

The original target sample size was 1150 (650 in Europe, 500 in SA). Assuming seroprevalence of 10% [16], this would produce a 95% confidence interval of ±2% in Europe and ±3% in SA. As reduced clinic visits during the pandemic affected enrolment, we revised the target sample size to 950 in November 2021, with minimal impact on precision.

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Participant characteristics at baseline were summarized as frequency/percentage and median [interquartile range]. As our primary outcome, we summarized, we summarized the percentage of participants with at least one SARS-CoV-2 antibody positive blood sample, overall and by sex, age group (<15 vs ≥15 years), presence of any co-morbidity and geographical setting (Europe and SA). Within Europe we further stratified as UK, Ukraine and 'rest of Europe' (Belgium, Greece and Spain) based on sample size. In SA, we stratified by HIV status. Vaccine coverage is presented as the percentage of samples each quarter that were from participants who had received at least one vaccine dose, amongst those with known vaccination status.

We also present the percentage of tests that were positive, with exact 95% CIs, by calendar quarter in Europe (overall and for UK, Ukraine and rest of Europe) and SA (by HIV status), where the denominator was ≥10.

To assess seroprevalence due to infection (rather than vaccination), we carried out two separate analyses restricted to 1) samples from participants reported as unvaccinated at the time of blood sampling, and 2) tests for N-antibodies.

To assess antibody status amongst vaccinated participants, we estimated the percentage with a positive S-antibody result on their first test after vaccination. Finally, amongst all participants who were seropositive on their first test, we estimated the percentage who reverted to seronegative on their second.

Results

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Between October 2020 and April 2022, 906 participants were enrolled across six countries, providing 1679 serology test results. Eighteen results for 16 participants were indeterminate; three of these participants had no valid results and were excluded, whereas 13 had one remaining valid result. Therefore 1661 tests for 903 participants were included in analyses (for types of tests see Supplementary Table S1). Samples were taken between May 2020 and July 2022 (Supplementary Figure S1). Amongst 758 participants with two test results, the median time between samples was 192 days [IQR 176-259]. The time between samples was <90 days for eight participants and >395 days for 28; although outside the recommended range, these were retained in analyses. 898/903 (99%) participants completed at least one questionnaire and 657/758 (87%) of those with two tests completed two questionnaires.

Participant characteristics at baseline

Most participants were enrolled in SA (410/903, 45%), UK (202/903, 22%) or Ukraine (160/903, 18%). 800/903 (89%) were CALWHIV; 103 (11%) were HIV negative participants in SA (Table 1). Median age at enrolment was 15 years [IQR 12-18] in Europe, 19 [IQR 17-20] amongst CALWHIV in SA, and 17 [IQR 16-19] amongst HIV negative participants in SA. Approximately half of participants were female. Details of co-morbidities are given in Supplementary Table S2. Two participants reported enrolment in a vaccine trial during the study (one each in UK and SA).

Almost all participating CALWHIV had initiated ART before enrolment. In Europe, 5% of CALWHIV had a CD4 count <350 cells/μL versus 22% in SA (2% and 9% were severely immunocompromised with CD4 <200 cells/μL). 85% of CALWHIV in Europe and 62% in SA were virologically suppressed <50 copies/mL (with 95% and 76% suppressed <1000 copies/mL).

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COVID-19 disease and vaccination at baseline and follow-up

At time of enrolment, among those with data, 15 participants (all were CALWHIV in Europe) had a previous SARS-CoV-2 positive PCR in their clinic records (3% of CALWHIV in Europe, 2% of participants overall) (Table 2). By the end of follow-up, 5% (44/866) of all participants had a positive PCR recorded. This percentage was highest amongst CALWHIV in Europe (Table 2). By end of follow-up, a further 55 (all in Europe) had self-reported COVID-19 but without a recorded positive PCR in their clinic records.

At enrolment, 47/463 (10%) participants in Europe with known SARS-CoV-2 vaccine status had been vaccinated, and none in SA. This increased during follow-up, to 202/870 (23%) of all participants (Table 2). Of those vaccinated, 73/202 (36%) had received one dose (including 13 single-dose schedule Janssen vaccines), 114/202 two doses (56%), and 15/202 (7%) >2 doses. Manufacturer was reported for 259 doses, with the most common being Pfizer/BioNTech (193/259, 75%). Vaccine coverage (≥1 dose) varied by setting and increased over time: amongst participants providing samples in the final quarter of the study, vaccine coverage reached 50% (95% CI 35-65%) in Europe, 33% (95% CI 20-48%) in CALWHIV in SA, and 30% (95% CI 17-47%) in HIV negative participants (Supplementary Figure S1). Within Europe, vaccine coverage was markedly lower in Ukraine (6/160, 4%) than in the UK (86/196, 44%) and the remaining European cohorts (54/127, 43%).

In total, amongst those with data, 199/475 (42%) CALWHIV in Europe, 35/280 (13%) CALWHIV in SA and 24/97 (25%) HIV negative participants in SA had any of the following by the end of follow-up: a SARS-CoV-2 positive PCR, self-reported COVID-19 or vaccination (Table 2).

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Two participants in Europe were hospitalized with COVID-19 (both PCR positive), neither of whom were classified as having severe disease. No cases of MIS-C were reported although one 22-year-old participant living with HIV in Europe was diagnosed with Multisystem Inflammatory Syndrome in Adults (MIS-A). They were hospitalized and subsequently discharged. One participant died. This participant was a CALWHIV enrolled in SA, and their death was not related to either COVID-19 or HIV.

SARS-CoV-2 antibody status

In analyses including all participants, irrespective of vaccination status, 55% (95% CI 50-59%) of CALWHIV in Europe, 67% (95% CI 61-72%) of CALWHIV in SA and 85% (95% CI 77-92%) of HIV negative participants were SARS-CoV-2 seropositive on at least one sample (Figure 1, blue bars). When analysis was restricted to samples taken from unvaccinated participants (n=769), these figures were 40% (95% CI 35-45%), 64% (95% CI 58-70%) and 81% (95% CI 71-89%), respectively (Figure 1, yellow bars).

Trends in seroprevalence over time and by participant characteristics

The percentage of tests that were positive increased over time in all groups (Figure 2). Overall seroprevalence reached 78% (95% CI 63-88%), 84% (95% CI 71-93%) and 95% (95% CI 83-99%) in CALWHIV in Europe, CALWHIV in SA, and HIV negative participants in SA, respectively. The corresponding figures among unvaccinated participants were 65% (95% CI 43-84%), 76% (95% CI 58-89%) and 93% (95% CI 76-99%). In Europe, seroprevalence in Ukraine varied little over time compared to other countries (Supplementary Figure S3). In all settings, seroprevalence increased following the emergence of new SARS-CoV-2 variants of concern, particularly Omicron.

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In CALWHIV, seroprevalence was higher in those aged ≥15 years (65%, 95% CI 61-69%) than in younger participants (45%, 95% CI 39-52%) while in HIV negative participants, seroprevalence was higher in <15 year-olds (100% versus 84% in ≥15 year-olds), although with wide CIs. Amongst CALWHIV, seroprevalence was higher amongst participants with baseline CD4 counts ≥350 cells/μL (59% (95% CI 55-63%)) versus <350 cells/μL (46% (95% CI 35-57%)), while it did not appear to differ by baseline virological status. Similar patterns were observed when analysis was restricted to samples taken from unvaccinated participants (Figure 1, yellow bars).

Antibody status among vaccine recipients, seroreversion, and N-antibody results

Amongst participants known to be vaccinated before blood sampling, 108/119 (91%) were seropositive for S-antibodies on the first test result following vaccination (median 105 days [IQR 35-179] after vaccination). Details of the 11 seronegative participants are shown in Supplementary Table S3.

Amongst 283 participants (both vaccinated and unvaccinated) who were seropositive on their first test and had two tests, 45 were subsequently seronegative (Supplementary Table S4).

A total of 199 participants had at least one N-antibody result: 160 in Ukraine, 28 in the UK and 11 in the rest of Europe. Of these, 83/199 (42%) were positive for N-antibodies on ≥1 test, indicating definite infection rather than vaccination.

Discussion

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This is, to our knowledge, the first study to assess SARS-CoV-2 antibody status in a large, geographically diverse sample of CALWHIV. We found a high seroprevalence (78-84%) of SARS-CoV-2 antibodies by mid-2022 amongst CALWHIV in Europe and South Africa, and 65-76% amongst participants with no history of SARS-CoV-2 vaccination at the time of the test. Three CALWHIV in Europe were hospitalized: two with COVID-19 (both with non-severe disease) and one young adult with MIS-A (although we did not systematically collect data on MIS-A). Nonetheless, the lower prevalence of documented or self-reported SARS-CoV-2 infection or COVID-19 disease compared to seroprevalence implies that many infections were asymptomatic or mild, consistent with other analyses of CALWHIV enrolled in EPPICC [3] and elsewhere [4, 8]. The apparent increases in seroprevalence following the emergence of novel variants, particularly Omicron, are consistent with the increased transmissibility and immune evasion of these variants [17].

Comparisons of seroprevalence between settings and groups are complicated by the extended period over which samples were taken, and so we did not undertake formal comparisons. However, seroprevalence appeared to vary between settings, being lowest in Europe and highest in HIV negative participants in SA and, within Europe, highest in the UK. This may reflect several factors, including age (the UK cohort was older than the other European cohorts, and studies have shown seroprevalence increases with age [18-20]), the timing of testing in relation to SARS-CoV-2 circulation in different settings, and variation in mitigation strategies between settings. Seroprevalence was higher amongst CALWHIV with CD4 counts ≥350 cells/μL than those with lower CD4 counts, consistent with other studies [21]. This could reflect an impaired serological response in those with lower CD4 count (lack of detectable response, lower peak antibody levels or faster waning) or greater avoidance of social contact in those with lower CD4 counts. For example, early in the pandemic, the

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British HIV Association advised adult PLWHIV with a CD4 count <200 cells/μL, detectable VL or not on ART to strictly follow social distancing advice [22]. We did not see a difference in seroprevalence by viral suppression status (<50 copies/mL), although previous studies have reported higher seroprevalence amongst PLWHIV who were virologically suppressed [11, 23].

It is difficult to compare our results for CALWHIV with those of general population studies due to differences in key characteristics (e.g. age groups and sources of samples) and calendar period, as well as variation in SARS-CoV-2 dynamics in different settings and populations. Household serosurveys in SA reported seroprevalence ranging from 56% to ~80% in children and adolescents in October-December 2021 [19, 24]. This is broadly consistent with our results for the same time frame in SA: 72% amongst CALWHIV overall and 68% amongst unvaccinated CALWHIV, and 77% amongst all HIV negative participants versus 74% in unvaccinated HIV negative participants. In the UK, population-based studies reported a seroprevalence of 20% by April-June 2021 amongst 0-18 year-olds in England [25], again somewhat lower than our estimates for the corresponding quarter of 34% overall and 28% in unvaccinated participants, respectively (likely reflecting the older age of our study participants).

Vaccine coverage was relatively low amongst study participants (≤50% in each of the three cohort groups by the end of the study period), but increased over time corresponding to vaccine availability. For example, in the UK, PLWHIV aged ≥16 years were eligible for vaccination from February 2021; younger PLWHIV became eligible with the rest of their age group (September 2021 for 12-15 year-olds, February 2022 for 5-11 year-olds) [26]. In SA, people aged 18-34 years were eligible for vaccination from September 2021 [27], and 12-17

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year-olds from October 2021 [28], with PLWHIV being prioritized. Therefore the lower vaccine coverage in SA compared to Europe in our study probably reflects later access in SA.

In SA, vaccine coverage was similar amongst CALWHIV and HIV negative participants. Published population data show 26.2% of 12-17 year olds and 36.6% of 18-34 year-olds having received at least one dose by March 2022 [29], similar to our findings. Vaccine coverage (≥1 dose) amongst CALWHIV in Europe in our study (50%) was similar to coverage amongst 12-15 year-olds in the general population in England (53.5%) by August 2022 [30]. As in adults [31], coverage varied by factors such as ethnicity and deprivation [30], analysis of which is beyond the scope of this paper. It will be important to monitor uptake of vaccines amongst CALWHIV and better understand the causes including delayed access in high HIV burden settings and/or vaccine hesitancy, all of which are critical in informing future pandemic preparedness.

The higher seroprevalence amongst the HIV negative participants compared to CALWHIV in SA, albeit with wide CIs, is consistent with previous results from SA [11], Mozambique [8] and the USA [32]. We also found that seroprevalence was lower in CALWHIV with CD4 counts ≥350 cells/μL than amongst HIV negative participants. The authors of the US study proposed that PLWHIV may have been more careful to avoid infection [32], and presented evidence of a diminished IgG response to SARS-CoV-2 infection, both of which might apply in our study. Diminished antibody responses to childhood vaccines amongst CALWHIV, compared to HIV-exposed uninfected children, have also been reported [33].

This study has some important limitations. Our pragmatic approach to data collection meant that a variety of tests were used; the predominance of S-antibody tests means that, among the

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one-quarter of participants who were ever vaccinated, we cannot distinguish between infection- versus vaccine-induced antibodies. However, we also present estimates for unvaccinated participants and, where available, N-antibodies; 42% of those with N-antibody results were seropositive, indicating definite infection. Variations in antibody test sensitivity and specificity, and potentially antibody waning, mean that our seroprevalence estimates amongst the unvaccinated may be minimum estimates of the prevalence of previous SARS-CoV-2 infection (for example, some participants who were seronegative at enrolment may have been previously seropositive). We combined data from Belgium, Greece and Spain due to small numbers, potentially masking differences between countries. Although our data suggest that some CALWHIV revert from seropositive to seronegative, we cannot estimate the duration of antibody persistence; furthermore, cell-mediated immunity may provide protection and persist even in the absence of detectable antibody [34]. Finally, in this cohort of CALWHIV, largely comprising older adolescents with perinatally acquired HIV, almost all were on ART, most had undetectable VL and few were immunosuppressed, therefore our findings may not be generalisable to settings with younger cohorts and less well-controlled HIV.

We report a high seroprevalence of SARS-CoV-2 antibody amongst CALWHIV in Europe and South Africa, frequently in the absence of vaccination or reported prior infection/disease. We therefore infer that a high proportion of SARS-CoV-2 infections were mild or asymptomatic in this population. Further data on the extent and duration of protection conferred by infection- and vaccination-induced antibodies, and the relative importance of cell-mediated immunity, in this population are needed to better define their future susceptibility to (re-)infection and severe disease, and to optimize vaccination strategies.

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List of abbreviations

ART	Antiretroviral therapy
CALWHIV	Children and adolescents living with HIV
CI	Confidence interval
CTAAC	Cape Town Adolescent Antiretroviral Cohort
EPPICC	European Pregnancy and Paediatric Infections Cohort Collaboration
HIV	Human immunodeficiency virus
IQR	Interquartile range
ISARIC	International Severe Acute Respiratory and emerging Infection Consortium
MIS-C	Multisystem inflammatory syndrome in children
PCR	Polymerase chain reaction
SA	South Africa
UK	United Kingdom
VL	Viral load
WHO	World Health Organization

Ethics approval and consent to participate

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. Informed consent was obtained from participants aged ≥16 years (or the local legal adult age). For younger participants, parent/carer consent was obtained, with participant assent where appropriate. The study was approved by the UCL Research Ethics Committee (Ref 17493/002) and local ethics committees.

The study is registered on clinicaltrials.gov (NCT04726137).

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Availability of data and materials

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to their sensitive nature and privacy and ethical considerations.

Conflicts of interest

We declare no conflicts of interest.

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Authors' contributions

IJC, AJ, CJ and SC designed the study, with substantial input from all authors in the project team. AB, ABS, TG, AN-J, MLP, VS, KS, AV and HJZ coordinated data collection in their respective cohorts. SMJ led development of the study participant questionnaire. CJ led the data analysis with input from SC, and drafted the manuscript. KCG provided immunological expertise. All authors critically reviewed and edited the manuscript, and all have read and approved the final manuscript.

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735 ***Tables***

736 Table 1: Participant characteristics at enrolment to the study.

Characteristic		**Median [IQR] or n (%)**		
		Europe (N = 493)	**SA, HIV+ (N = 307)**	**SA, HIV- (N = 103)**
Cohort	South Africa	---	307 (100)	103 (100)
	United Kingdom	202 (41)	---	---
	Ukraine	160 (32)	---	---
	Spain	91 (18)	---	---
	Greece	21 (4)	---	---
	Belgium	19 (4)	---	---
Sex, female		263 (53)	161 (52)	52 (50)
Age, years (n = 492, 307, 103)		15 [12-18]	19 [17-20]	17 [16-19]
Any co-morbidity		53 (11)	6 (2)	1 (1)
Perinatally acquired HIV (n = 469, 307)†		462 (99)	307 (100)	---
Age at HIV diagnosis, years (n = 467, 307)		1.2 [0.3-3.7]	0 [0-0]	---
Initiated ART before enrolment (n = 455, 307)		451 (99)	307 (100)	---
Age at ART start, years (n = 453, 307)		2.1 [0.4-5.9]	4.0 [1.9-7.0]	---
CD4 count, cells/μL (n = 424, 296)‡		739 [553-960]	533 [374-690]	---
CD4 count <350 cells/μL (n = 424, 296)‡		22 (5)	66 (22)	---
Undetectable viral load* (n = 465, 297)		396 (85)	184 (62)	---
Undetectable viral load** (n = 465, 297)		441 (95)	226 (76)	---

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† Reported as vertical acquisition or with unknown mode of acquisition diagnosed before age 10 years.

‡ 88% of baseline CD4 measurements were taken on the day of the baseline serology test.

*<50 copies/mL or below lower limit of detection. 94% of baseline VL measurements were taken on the day of the baseline serology test.

**<1000 copies/mL or below lower limit of detection.

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746 Table 2: SARS-CoV-2 / COVID-19 infection and vaccination status at baseline and follow-up.

	n/N (%)							
	Baseline				**Follow-up**			
	Europe	**SA, HIV+**	**SA, HIV-**	**Total**	**Europe**	**SA, HIV+**	**SA, HIV-**	**Total**
SARS-CoV-2 PCR+	15/482 (3)	0/281 (0)	0/97 (0)	15/860 (2)	40/485 (8)	2/282 (1)	2/99 (2)	44/866 (5)
Self-reported COVID-19, no PCR+*					55/440 (13)	0/290 (0)	0/99 (0)	55/829 (7)
Ever received SARS-CoV-2 vaccine	47/463 (10)	0/263 (0)	0/90 (0)	47/816 (6)	146/483 (30)	34/287 (12)	22/100 (22)	202/870 (23)
Any of the above					199/475 (42)	35/280 (13)	24/97 (25)	258/534 (48)

747 * Self-reported COVID-19 prior to test date not collected at baseline

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Figure legends

Figure 1. Percentage of A) CALWHIV and B) HIV negative participants with at least one positive serology test result, overall and by key characteristics. Results are shown based on all tests (blue bars) and on tests from samples taken from unvaccinated participants (yellow bars). Error bars show exact 95% confidence intervals.

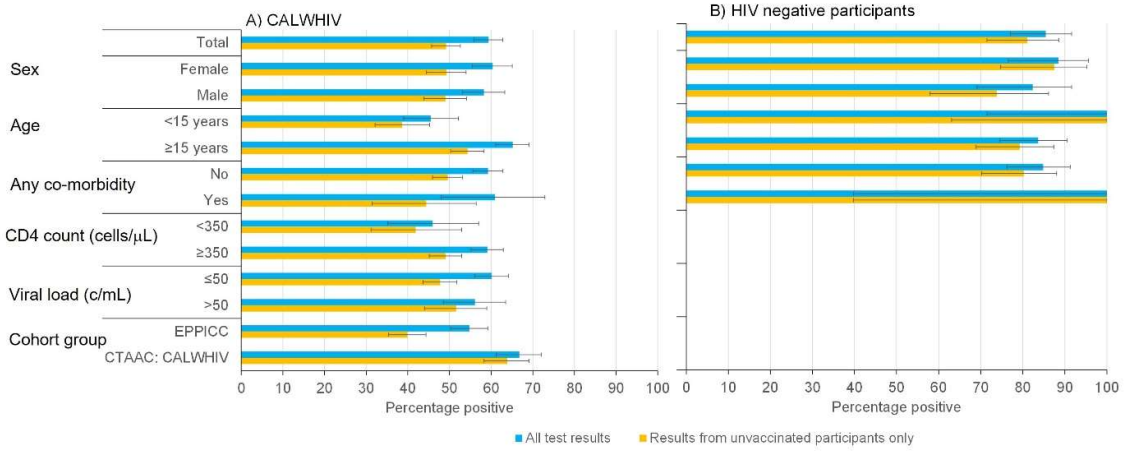

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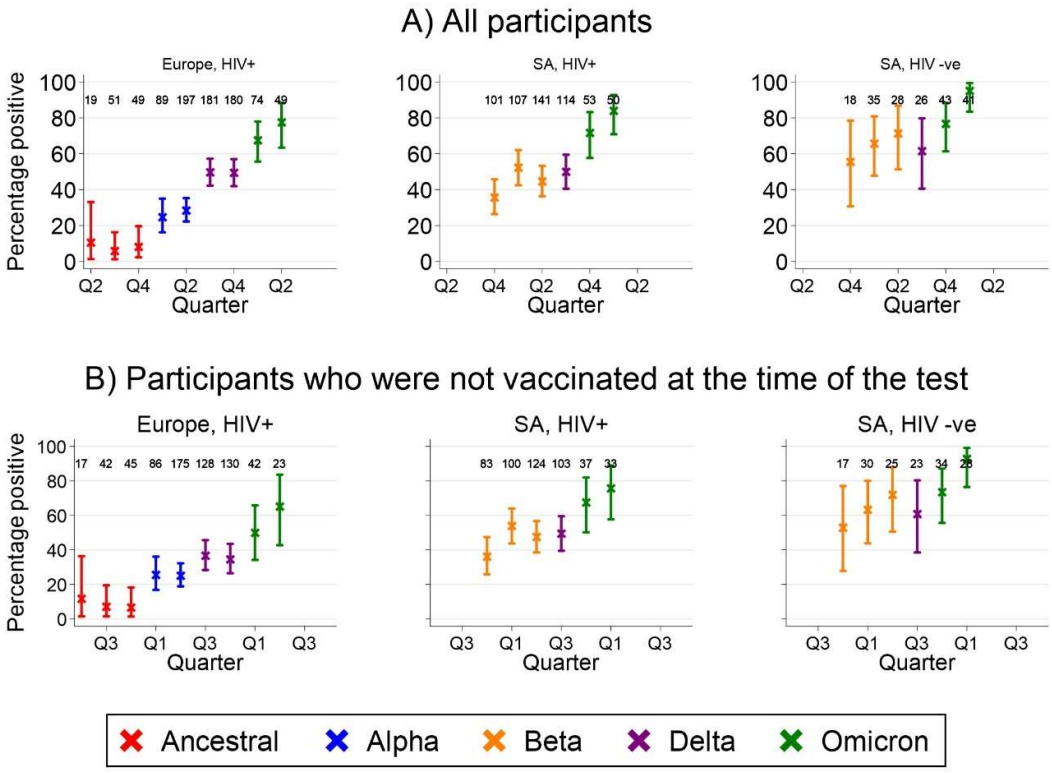
Figure 2. Percentage of serology tests that were positive by cohort group and calendar quarter, overall (top) and amongst participants who were unvaccinated at the time of the test (bottom). Numbers show the denominator for each estimate.



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