Received: 5 April 2023 | Revised: 19 June 2023 | Accepted: 28 June 2023

DOI: 10.1111/irv.13173

ORIGINAL ARTICLE

WILEY

SARS-CoV-2 seroprevalence and implications for population immunity: Evidence from two Health and Demographic Surveillance System sites in Kenya, February–December 2022

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Abstract

Background: We sought to estimate SARS-CoV-2 antibody seroprevalence within representative samples of the Kenyan population during the third year of the COVID-19 pandemic and the second year of COVID-19 vaccine use.

Methods: We conducted cross-sectional serosurveys among randomly selected, age-stratified samples of Health and Demographic Surveillance System (HDSS) residents in Kilifi and Nairobi. Anti-spike (anti-S) immunoglobulin G (IgG) serostatus was measured using a validated in-house ELISA and antibody concentrations estimated with reference to the WHO International Standard for anti-SARS-CoV-2 immunoglobulin.

Results: HDSS residents were sampled in February–June 2022 (Kilifi HDSS $N = 852$; Nairobi Urban HDSS $N = 851$) and in August–December 2022 ($N = 850$ for both sites). Population-weighted coverage for ≥1 doses of COVID-19 vaccine were 11.1% (9.1–13.2%) among Kilifi HDSS residents by November 2022 and 34.2% (30.7–37.6%) among Nairobi Urban HDSS residents by December 2022.

Population-weighted anti-S IgG seroprevalence among Kilifi HDSS residents increased from 69.1% (65.8–72.3%) by May 2022 to 77.4% (74.4–80.2%) by November 2022. Within the Nairobi Urban HDSS, seroprevalence by June 2022 was 88.5% (86.1–90.6%), comparable with seroprevalence by December 2022 (92.2%;

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Funding information
Bill and Melinda Gates Foundation, Grant/Award Number: INV-039626; Wellcome Trust, Grant/Award Number: 214320

90.2–93.9%). For both surveys, seroprevalence was significantly lower among Kilifi HDSS residents than among Nairobi Urban HDSS residents, as were antibody concentrations ($p < 0.001$).

Conclusion: More than 70% of Kilifi residents and 90% of Nairobi residents were seropositive for anti-S IgG by the end of 2022. There is a potential immunity gap in rural Kenya; implementation of interventions to improve COVID-19 vaccine uptake among sub-groups at increased risk of severe COVID-19 in rural settings is recommended.

KEYWORDS
COVID-19, Health and Demographic Surveillance System, IgG antibody, Kenya, SARS-CoV-2, seroprevalence

1 | INTRODUCTION

Serosurveillance for SARS-CoV-2 antibodies emerged as an important tool for estimating the cumulative incidence of SARS-CoV-2 infection in the early phase of the COVID-19 pandemic. It was particularly important in settings with low COVID-19 testing levels, including many countries in Africa.[1] In these settings, cumulative incidence revealed by SARS-CoV-2 serosurveillance far outstripped the rate of infection inferred from case detection.[2] In the current context, SARS-CoV-2 serosurveillance remains important for assessing temporal changes in seroprevalence, including waning, and identifying potential gaps in population immunity to inform priorities for COVID-19 prevention measures, including vaccination.

By June 2020, roughly 3 months after the first confirmed case of COVID-19 in Kenya, seroprevalence of SARS-CoV-2 anti-spike (anti-S) immunoglobulin G (IgG) was 4% among blood donors.[3] Continued serosurveillance among blood donors in Kenya showed temporal increases in anti-S IgG seroprevalence, reaching 48% by March 2021,[4] 1 year after identification of the first confirmed SARS-CoV-2 infection locally which also coincided with the rollout of the COVID-19 vaccination program by the Government of Kenya. The COVID-19 vaccination program initially targeted frontline workers, older adults aged ≥58 years, and younger adults with comorbidities. It soon opened up to all adults, then to children aged ≥15 years in November 2021, and currently targets individuals aged ≥12 years. To date, the national program has included the following COVID-19 vaccines: Oxford/AstraZeneca (Covishield), Pfizer (BNT162b2), Moderna (mRNA-1273), Johnson & Johnson (Ad26.CoV2.S), and Sinopharm (BBIBP-CorV).

While convenience samples, such as blood transfusion donors, can be leveraged to rapidly generate seroprevalence estimates, serosurveillance among randomly selected residents of Health and Demographic Surveillance System (HDSS) sites avoids the selection biases inherent in convenience sampling and provides a more representative sample of the general population. By May 2021, 2 months after initial rollout of COVID-19 vaccine, serosurveillance among an age-stratified random sample of residents of three HDSS sites found anti-S IgG seroprevalence ranging from 25% to 50%.[5] We undertook a repeat serosurvey at two of these three HDSS sites to assess infection- and vaccination-induced seroprevalence within the general population during the third year of the COVID-19 pandemic and the second year of the COVID-19 vaccination program.

2 | METHODS

2.1 | Study design and participants

Two cross-sectional surveys were conducted at each of two sites, the Kilifi HDSS and the Nairobi Urban HDSS. The characteristics of these HDSS sites have been described in detail previously.[6,7] The Kilifi HDSS is located in a rural area within Kilifi County in south-eastern coastal Kenya, whereas the Nairobi Urban HDSS is located within Nairobi County, the capital city of Kenya (Figure S1). The population of the Kilifi HDSS was 308,581 (April 2022 census) and about 90,000 at the Nairobi Urban HDSS (October 2021 census).

We used similar methods as previous SARS-CoV-2 serosurveys at the sites.[5] In brief, for each serosurvey a random age-stratified sample of 850 participants was drawn from the respective HDSS site population registers. The sample drawn at each site was independent of that drawn for the surveys conducted in 2020–2021. The simple random sample included 100 children in each 5-year age band <15 years, 50 individuals in each 5-year age band between 15 and 64 years, and 50 adults aged ≥65 years. Individuals were eligible to participate in the study if they were resident in the respective HDSS, had no contraindication for blood sample collection, and provided consent. Individuals were considered not contactable after three unsuccessful attempts to visit them. To compensate for participants who were not found at home, a replacement sample was drawn at random from the HDSS population register.

The study research protocol was aligned to the World Health Organization (WHO) UNITY methods for COVID-19 serosurveillance

studies.[8] Ethical approval was obtained from the Kenya Medical Research Institute Scientific and Ethics Review Unit (KEMRI/SERU/CGMR-C/203/4085), the Oxford Tropical Research Ethics Committee (44–20), and the London School of Hygiene and Tropical Medicine Research Ethics Committee (26950). This activity was also reviewed by CDC and was conducted consistent with applicable federal law and CDC policy as provided for in the Code of Federal Regulations (45 C.F.R part 46 and 21 C.F.R. part 56).

2.2 | Participant consent statement

Written parental/guardian consent was obtained for participants aged <18 years, accompanied by written assent for children aged 13–17 years. Written informed consent was obtained from participants aged ≥18 years.

2.3 | Data and sample collection

Sociodemographic (e.g., age, sex, and location of residence) information and medical history data (e.g., recent COVID-like symptoms, COVID-19 vaccination history, and previous confirmed SARS-CoV-2 infection) were collected from each participant (Supporting Information). COVID-19 vaccination status was ascertained using either official records (i.e., COVID-19 vaccination certificate or text message confirmation from the national COVID-19 vaccine registry) or verbal report. A single 2 mL (children aged <5 years) or 5 mL (individuals aged ≥5 years) venous blood sample was collected in a heparin-coated tube from each participant and labeled with a unique identifier.

2.4 | Laboratory testing

Plasma was extracted from venous blood samples and tested for anti-S IgG to identify either infection- or vaccination-induced antibody response, and for anti-nucleoprotein (anti-N) IgG, to identify infection-induced antibody response.[9] Testing was performed using validated KEMRI-Wellcome Trust Research Programme ELISAs. Sensitivity and specificity for the anti-S IgG ELISAs were, respectively, 93% (95% confidence interval 88–96%) and 99% (98–99%).[3] Sensitivity and specificity for the anti-N IgG ELISA were 83% (76–88%) and 91% (86–95%). Target-specific IgG positivity was defined as a ratio of the sample optical density (OD) over negative control OD > 2. The WHO International Standard (IS) for anti-SARS-CoV-2 immunoglobulin (NIBSC code 20/136) was included in each anti-S IgG ELISA run and used to calculate sample-specific binding antibody concentrations in binding antibody units per milliliter (BAU/mL). A binding antibody concentration of 1000 BAU/mL was assigned to the WHO IS, as recommended by NIBSC.[10] Sample-specific binding antibody concentrations were calculated by dividing each sample-specific OD ratio by the run-specific IS OD ratio after which the quotient was multiplied by 1000.

2.5 | Statistical analysis

The target sample size of 850 participants was sufficient to measure antibody seroprevalence of 50% with an associated 95% confidence interval (CI) of ±3%.

Crude COVID-19 vaccine coverage was calculated as the proportion of individuals reporting vaccination divided by the entire sample. Exact binomial 95% CIs were also calculated. Because the population sample did not represent the age structure of the target population, Bayesian population weighting was performed to generate population-weighted coverage and associated 95% credible intervals (CrI). Coverage with ≥1 doses of COVID-19 vaccine and full vaccination coverage were estimated overall and restricted to participants aged ≥15 years. Full vaccination was defined as receipt of at least one dose of Johnson & Johnson vaccine or receipt of ≥2 doses of other COVID-19 vaccines.

Crude seroprevalence was calculated as the proportion of seropositive samples over all samples, along with exact binomial 95% CIs. Population-weighted anti-S IgG seroprevalence with associated 95% CrIs was also calculated. Anti-S IgG seroprevalence within the entire sample was not adjusted for test performance as validation of the ELISA was performed among unvaccinated individuals; for example, adjustment for test performance using current sensitivity and specificity estimates would overestimate anti-S seroprevalence if in truth assay sensitivity is higher among COVID-vaccinated individuals. To estimate infection-induced seroprevalence, Bayesian population-weighted anti-S IgG seroprevalence was estimated among the subset of participants who were COVID-unvaccinated. Anti-S IgG seroprevalence among COVID-unvaccinated participants was not adjusted for test performance for ease of interpretation given that anti-S IgG seroprevalence within the entire sample was similarly not adjusted for test performance, as described above. To assess the magnitude of inherent assay bias in a sensitivity analysis, Bayesian test-performance adjusted anti-S seroprevalence was also estimated among only COVID-unvaccinated participants.

To assess the contribution of infection to seroprevalence levels, population-weighted and test-adjusted anti-N IgG seroprevalence was calculated separately for COVID-vaccinated and COVID-unvaccinated participants. Although inactivated COVID-19 vaccines can induce anti-N IgG responses,[11] they have had limited use in Kenya; by December 2022, only 31,000 doses of an inactivated virus COVID-19 vaccine (Sinopharm) had been administered out of approximately 23 million doses of vaccine administered nationally.[12] Therefore, it was deemed appropriate to perform adjustment for test performance for the anti-N seroprevalence estimates within the entire sample.

For each set of seroprevalence data, seroprevalence was computed overall, by sex and by seven age strata (<16; 16–24; 25–34; 35–44; 45–54; 55–64; ≥65 years). These age strata were selected to allow comparison with seroprevalence data from the same HDSS sites in 2020–2021.[5]

Reverse cumulative distribution curves (RCDCs) for anti-S IgG concentrations were plotted. Kolmogorov–Smirnov tests were used

to test the equality of the overall distributions across sites, as well as across sex, age group, and COVID-19 vaccination status within each site. The comparison of the distribution of antibodies for COVID-unvaccinated versus COVID-vaccinated individuals was restricted to those aged ≥15 years to minimize confounding by age given that the COVID-19 vaccine rollout has been focused on individuals aged ≥15 years. The proportion of individuals with anti-S IgG ≥ 154 BAU/mL was calculated; ≥154 BAU/mL has been proposed as a threshold of protection against infection with wild-type SARS-CoV-2 following COVID-19 vaccination.[13]

Population weighting and adjustments for test-performance were performed in R with RStan, and all other analyses were performed using Stata.

2.6 | Role of the funding source

The research was funded by the Bill and Melinda Gates Foundation (INV-039626). The funder had no role in study design, data analysis, data collection, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit the paper for publication.

3 | RESULTS

The surveys at the Kilifi HDSS site were conducted between February 15 and May 8, 2022 (Survey 1; median March 23, 2022), and between August 24 and November 27, 2022 (Survey 2; median October 3, 2022). The surveys at the Nairobi Urban HDSS site were conducted within a similar timeframe: March 8–June 22, 2022 (Survey 1; median May 1, 2022) and September 27–December 8, 2022 (Survey 2; median November 2, 2022). At the Kilifi HDSS site, 853 participants were sampled during Survey 1 (representing 73.0% of those approached), and 850 were sampled during Survey 2 (i.e., 75.6% of those approached). One sample collected during Survey 1 at the Kilifi HDSS site, representing 0.1% of the 853 samples collected, was not tested due to a sample labeling issue that had not been resolved by the time antibody testing was conducted. The number of participants sampled during Survey 1 at the Nairobi Urban HDSS site was 851 (87.1% of those approached) and 850 (88.0% of those approached) during Survey 2 (Figure 1). Survey 1 at both sites began after the Omicron BA.1 wave, with the sample collection period at the Nairobi Urban HDSS site continuing up to the first half of the Omicron BA.4/BA.5 wave. Survey 2 at the sites occurred after the Omicron BA.4/BA.5 wave, extending into part of the Omicron BQ.1 wave (Figure S2).

The median age of the participants during the surveys ranged between 26 and 27 years. The proportion of females sampled during Survey 2 at the Nairobi Urban HDSS was significantly lower than during Survey 1 (47.5% vs. 37.1%; $p < 0.001$); this was likely due to differential participant finding, whereby the proportion of females present out of those visited was smaller during Survey 2 than during Survey 1 (Table S1). Among participants in the Kilifi HDSS reporting COVID-19 vaccine receipt, vaccination was ascertained using an official record in 28.7% (27 of 94) during Survey 1 in the Kilifi HDSS and in 50.9% (59 of 116) during Survey 2. In the Nairobi Urban HDSS, COVID-19 vaccine receipt was confirmed using an official record in 27.8% (79 of 284) of participants during Survey 1 and in 73.8% (225 of 303) during Survey 2. COVID-19 vaccine uptake did not change substantially between the surveys and was significantly lower among residents of the Kilifi HDSS than among Nairobi Urban HDSS residents. At Survey 2, population-weighted coverage with ≥1 doses among all enrolled participants was 11.1% (95% CrI 9.1–13.2%) among the Kilifi HDSS participants against 34.2% (30.7–37.6%) among the Nairobi Urban HDSS participants. When restricted to participants aged ≥15 years of age, coverage for ≥1 doses of COVID-19 vaccine was 17.7% (12.3–23.2%) within the Kilifi HDSS and 49.4% (41.7–56.7%) within the Nairobi Urban HDSS at Survey 2. The distribution of COVID-19 vaccine brand doses received is provided in the Supporting Information; only one participant reported receipt of at least one dose of Sinopharm vaccine (Table S2). At both sites, a higher proportion of participants reported ≥1 COVID-like symptoms in the 2 weeks prior to sample collection during Survey 2 compared with during Survey 1. The proportion of participants at the Kilifi HDSS site reporting COVID-like symptoms during Survey 1 was 20.8% (177 of 852) versus 48.2% (410 of 850) during Survey 2 ($p < 0.001$). At the Nairobi Urban HDSS, 48.6% (414 of 851) reported symptoms during Survey 1 versus 60.7% (516 of 850) during Survey 2 ($p < 0.001$). The proportion of participants with symptoms resulting in hospitalization at the Kilifi HDSS was 1.7% (3 of 177) and 2.2% (9 of 410) during Survey 1 and Survey 2, respectively. It was, respectively, 1.4% (6 of 414) and 1.2% (6 of 516) during Surveys 1 and 2 at the Nairobi Urban HDSS (Table S2). The top three symptoms across the surveys were cough (all surveys), headache (all surveys), runny nose (all surveys except Kilifi HDSS Survey 2), and fever (Kilifi HDSS Survey 2). These events were most commonly reported among children aged <16 years (Figures S3 and S4).

3.1 | Anti-S IgG seroprevalence and concentrations among all participants

Population-weighted anti-S IgG seroprevalence was 69.1% (95% CrI 65.8–72.3%) among all participants at the Kilifi HDSS site during Survey 1, increasing to 78.1% (75.1–80.9%) by Survey 2. Between Surveys 1 and 2, seroprevalence increased among children aged <16 years and adults aged 25–34 years (Figure 2, Table S3). Overall seroprevalence at the Nairobi Urban HDSS site during Survey 1 was 88.5% (86.1–90.6%) and was 92.0% (89.9–93.8%) by Survey 2. During both surveys, children <16 years of age within the Nairobi Urban HDSS tended to have lower seroprevalence than some adult age groups (Figure 2, Table S3). Seroprevalence at the Kilifi HDSS site was significantly lower than at the Nairobi Urban HDSS site at both Surveys 1 and 2 as illustrated by non-overlapping 95% CrIs. During

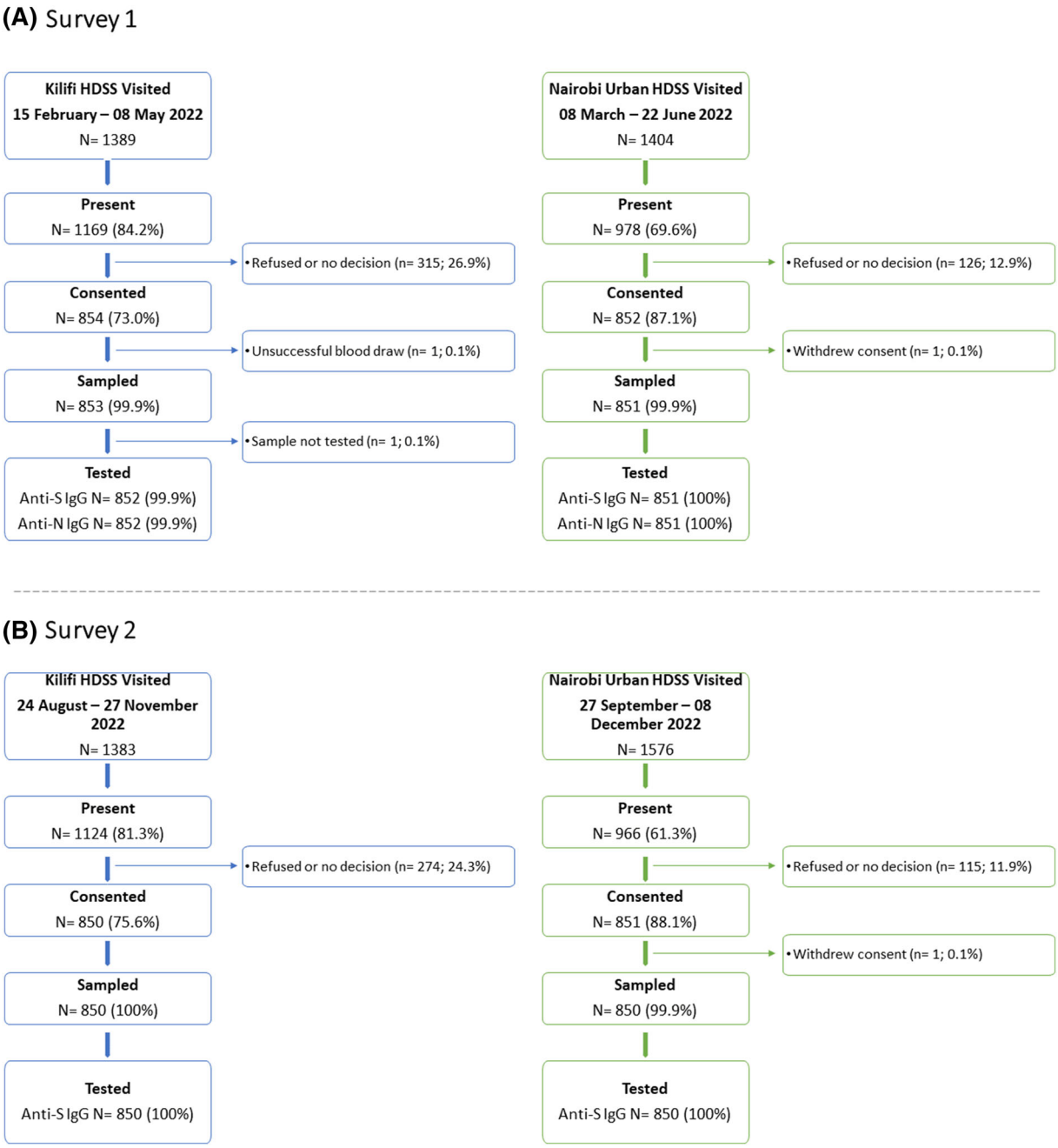

FIGURE 1 Study participant flow.

Survey 1, seroprevalence was lower across all age and sex strata among Kilifi HDSS residents compared with Nairobi Urban HDSS residents. In Survey 2, seroprevalence was lower among all age and sex strata within the Kilifi HDSS than within the Nairobi Urban HDSS except for individuals aged 16–24 years and adults aged 25–34 years (Figure 2, Table S3).

The geometric mean anti-S IgG concentration was 272 BAU/mL (95% CI 247–299 BAU/mL) and 230 BAU/mL (213–248 BAU/mL) among Kilifi HDSS residents during Surveys 1 and 2, respectively. It was 555 BAU/mL (515–597 BAU/mL) and 439 BAU/mL (411–470 BAU/mL) during Surveys 1 and 2, respectively, within the Nairobi Urban HDSS (Table S4). The proportion of individuals with anti-spike IgG ≥ 154 BAU/mL was 62.7% and 65.5% during Surveys 1 and 2, respectively, within the Kilifi HDSS and 85.9% and 85.5% during Surveys 1 and 2, respectively, at the Nairobi Urban HDSS (Figure 3 and Table S5). Overall anti-S IgG concentrations were significantly lower within the Kilifi HDSS than within the Nairobi Urban HDSS for both surveys ($p < 0.001$). Within the Nairobi Urban HDSS, the antibody concentrations were significantly lower at Survey 2 than at Survey 1.

Within the Kilifi HDSS, antibody concentrations were significantly lower among children <16 years than among all other age groups

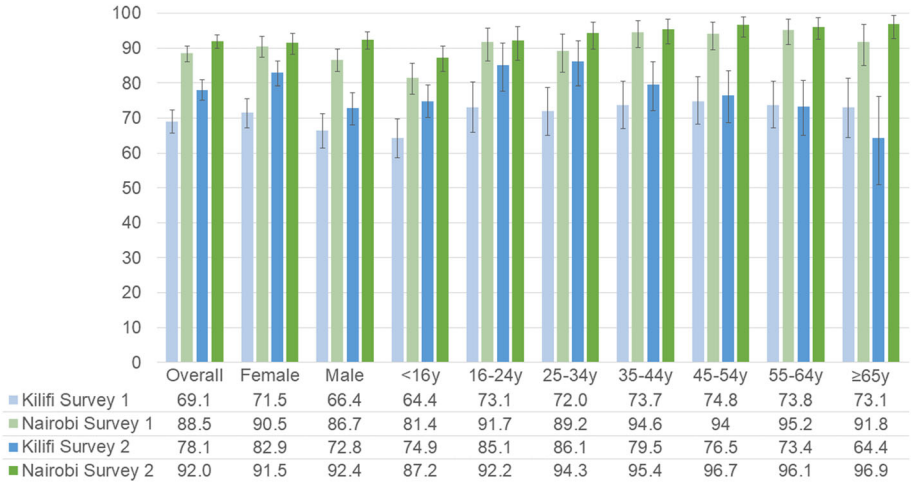

FIGURE 2 Population-weighted anti-spike IgG seroprevalence among all study participants by site, sex, and age category.

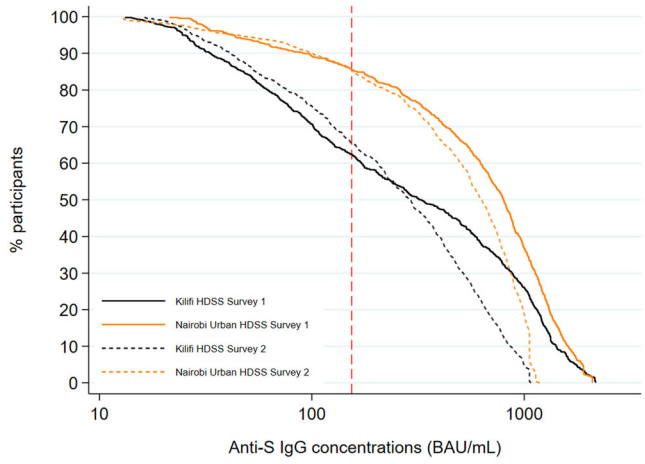

FIGURE 3 Reverse cumulative distribution curves of anti-S IgG concentrations within the Kilifi Health and Demographic Surveillance System (HDSS) and Nairobi Urban HDSS. The red vertical line represents an antibody concentration of 154 binding antibody units per milliliter.

($p \leq 0.007$) other than adults aged ≥65 years during both surveys. Antibody concentrations for children aged <16 years within the Nairobi Urban HDSS were significantly lower than among all other age groups ($p < 0.001$) during both surveys. During all surveys, antibody concentrations were significantly lower among COVID-unvaccinated participants aged ≥15 years than among COVID-vaccinated participants ($p < 0.001$; Figure S5; Tables S3 and S4).

3.2 | Anti-S IgG seroprevalence among COVID-unvaccinated participants

COVID-unvaccinated participants represented 89.0% (758 of 852) and 86.3% (734 of 850) participants at the Kilifi HDSS site during Surveys 1 and 2, respectively. At the Nairobi Urban HDSS site, they represented, respectively, 66.6% (567 of 851) and 64.0% (544 of 850) of participants during Surveys 1 and 2.

Population-weighted anti-S IgG seroprevalence among COVID-unvaccinated participants at the Kilifi HDSS rose from 66.7% (63.3–70.0%) during Survey 1 to 76.1% (72.9–79.2%) during Survey 2. Within the Nairobi Urban HDSS, it was comparable across the two surveys; 85.3% (82.1–88.2%) during Survey 1 and 90.0% (87.1–92.5%) during Survey 2. During Survey 1, seroprevalence was significantly lower among COVID-unvaccinated Kilifi HDSS residents than among COVID-unvaccinated Nairobi Urban HDSS residents overall as well as by sex and age (i.e., non-overlapping CrIs). During Survey 2, it was again significantly lower in the Kilifi HDSS than in the Nairobi Urban HDSS overall, by age and by sex, except for individuals aged 16–24 and 25–34 years (Table 1). Seroprevalence estimates among COVID-unvaccinated participants were slightly higher after adjustment for test performance, but the difference was not significant (Table S6).

3.3 | Anti-N IgG seroprevalence

Population-weighted, test-adjusted anti-N IgG seroprevalence during Survey 1 was 53.5% (95% CrI 46.5–61.1%) at the Kilifi HDSS site, lower than the 85.6% (95% CrI 80.0–90.3%) seroprevalence at the Nairobi Urban HDSS site. Anti-N IgG seroprevalence was comparable among COVID-unvaccinated and COVID-vaccinated participants, except for children aged <16 years at the Nairobi Urban HDSS site (Figure 4, Table S7).

4 | DISCUSSION

We estimate anti-S IgG seroprevalence of 78% by November 2022 in Kilifi and 92% by December 2022 in Nairobi. As we did not adjust anti-S IgG seroprevalence for test performance, these likely represent conservative estimates. Yet, only about 1 in 10 of study participants in Kilifi and about 3 in 10 in Nairobi had received any doses of COVID-19 vaccine, indicating the substantial contribution of natural infection to anti-S IgG seroprevalence. Indeed, anti-S IgG

TABLE 1 Population-weighted anti-spike IgG seroprevalence among COVID-unvaccinated individuals by site, sex, and age category.

	Survey 1				Survey 2			
Kilifi HDSS	**Sample size**	**Seropositive**	**Crude seroprevalence (95% CI)**	**Population-weighted seroprevalence(95% CrI)**	**Sample size**	**Seropositive**	**Crude seroprevalence (95% CI)**	**Population-weighted seroprevalence (95% CrI)**
Overall	758	508	67.0 (63.5–70.4)	66.7 (63.3–70.0)	734	548	74.7 (71.3–77.8)	76.1 (72.9–79.2)
Sex								
Female	422	293	69.4 (64.8–73.8)	69.3 (64.7–73.7)	401	318	79.3 (75.0–83.2)	81.1 (77.1–84.8)
Male	336	215	64.0 (58.6–69.1)	63.8 (58.6–68.7)	333	230	69.1 (63.8–74.0)	70.5 (65.5–75.3)
Age category								
<16 years	312	194	62.2 (56.5–67.6)	64.4 (59.1–69.0)	309	232	75.1 (69.9–79.8)	74.8 (70.0–79.4)
16–24 years	74	53	71.6 (59.9–81.5)	68.8 (62.5–76.0)	76	65	85.5 (75.6–92.5)	83.2 (75.0–90.2)
25–34 years	86	59	68.6 (57.7–78.2)	68.1 (61.6–75.0)	76	65	85.5 (75.6–92.5)	82.0 (73.7–89.4)
35–44 years	88	63	71.6 (61.0–80.7)	69.2 (63.1–76.1)	80	61	76.3 (65.4–85.1)	75.9 (67.4–83.7)
45–54 years	81	58	71.6 (60.5–81.1)	69.1 (62.8–76.3)	78	56	71.8 (60.5–81.4)	72.2 (62.8–80.6)
55–64 years	75	51	68.0 (56.2–78.3)	68.0 (61.1–74.6)	71	45	63.4 (51.1–74.5)	65.8 (55.1–75.4)
≥65 years	42	30	71.4 (55.4–84.3)	68.9 (61.7–77.0)	44	24	54.5 (38.8–69.6)	59.5 (45.2–72.6)
	Survey 1				**Survey 2**			
Nairobi Urban HDSS	**Sample size**	**Seropositive**	**Crude seroprevalence (95% CI)**	**Population-weighted seroprevalence (95% CrI)**	**Sample size**	**Seropositive**	**Crude seroprevalence (95% CI)**	**Population-weighted seroprevalence (95% CrI)**
Overall	567	479	84.5 (81.2–87.4)	85.3 (82.1–88.2)	544	485	89.2 (86.2–91.6)	90.0 (87.1–92.5)
Sex								
Female	283	248	87.6 (83.2–91.2)	88.5 (84.5–92.0)	226	199	88.1 (83.1–92.0)	89.7 (85.2–93.4)
Male	284	231	81.3 (76.3–85.7)	82.5 (77.8–86.7)	318	286	89.9 (86.1–93.0)	90.4 (86.9–93.3)
Age category								
<16 years	300	242	80.7 (75.7–85.0)	81.4 (76.8–85.5)	303	260	85.8 (81.4–89.5)	87.0 (82.9–90.4)
16–24 years	60	52	86.7 (75.4–94.1)	86.8 (79.7–92.7)	49	43	87.8 (75.2–95.4)	89.7 (82.4–94.9)
25–34 years	65	55	84.6 (73.5–92.4)	85.8 (78.7–91.8)	64	60	93.8 (84.8–98.3)	92.3 (86.9–96.8)
35–44 years	48	45	93.8 (82.8–98.7)	89.7 (82.5–95.9)	42	39	92.9 (80.5–98.5)	91.8 (85.6–96.7)
45–54 years	40	35	87.5 (73.2–95.8)	86.3 (77.7–93.3)	38	36	94.7 (82.3–99.4)	92.4 (86.4–97.4)
55–64 years	39	38	97.4 (86.5–99.9)	90.5 (82.8–97.1)	34	33	97.1 (84.7–99.9)	93.0 (87.0–98.0)
≥65 years	15	12	80.0 (51.9–95.7)	84.7 (72.0–93.2)	14	14	100.0 (76.8–100.0)	92.7 (85.6–98.4)

Abbreviation: HDSS, Health and Demographic Surveillance System.

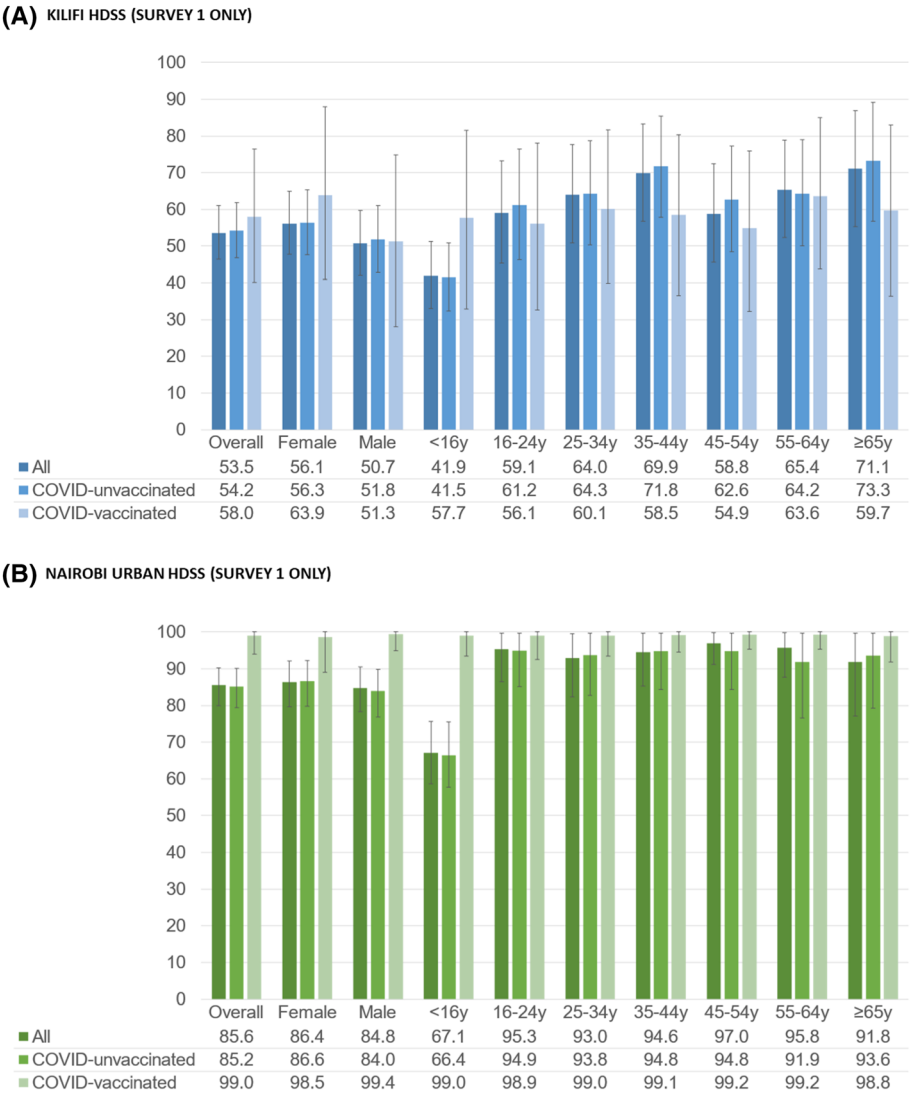

FIGURE 4 Population-weighted and test-adjusted anti-nucleoprotein IgG seroprevalence among study participants overall and by COVID-19 vaccination status, sex, and age category within the (A) Kilifi Health and Demographic Surveillance System (HDSS) and the (B) Nairobi Urban HDSS.

seroprevalence among COVID-unvaccinated participants—who made up the majority of the study sample—was 76% by November 2022 in Kilifi and 90% by December 2022 in Nairobi, indicative of infection-induced immune responses. Furthermore, 54% of COVID-unvaccinated participants in Kilifi and 85% in Nairobi were positive for anti-N IgG, supporting the inference of infection-driven anti-S IgG seroprevalence in this group. Anti-S IgG seroprevalence among COVID-vaccinated individuals appeared to be driven by both infection and vaccination as anti-N IgG seroprevalence in that group was 58% in Kilifi and 99% in Nairobi. However, the low number of COVID-vaccinated individuals suggests a marginal role of hybrid immunity[14] at the population level.

Our findings also indicate temporal increases in SARS-CoV-2 seroprevalence within the general population in Kenya. Anti-S IgG seroprevalence by the end of 2022 had increased more than threefold within the Kilifi HDSS site and more than twofold within the Nairobi Urban HDSS site since May 2021, when it was 20% and 40%, respectively.[5] This temporal increase was driven by COVID-19 vaccination rollout beginning in March 2021, as well as by the four COVID-19 waves occurring since May 2021, that is, the Delta variant, Omicron BA.1,[15] Omicron BA.4/5, and Omicron BQ.1 waves. Between May 2022 and November 2022, increases in seroprevalence in Kilifi were observed among children aged <16 years—likely due to infection given low COVID-19 vaccine uptake in that age group—and among adults aged 25–34 years. Seroprevalence did not change appreciably between June and December 2022 within the Nairobi Urban HDSS; given the high seroprevalence estimates in Nairobi despite non-adjustment for test performance, this suggests near-ubiquitous presence of anti-SARS-CoV-2 antibodies.

The findings from Kenya contrast with evidence from settings like the United Kingdom where high anti-S IgG seroprevalence was achieved primarily through COVID-19 vaccination rather than through natural infection. By December 2020, just before phased rollout of COVID-19 vaccine in the United Kingdom, anti-S IgG seroprevalence among UK blood donors was 7%.[16] By December 2021, coverage with ≥1 doses of COVID-19 vaccine in the United Kingdom was 69%, and anti-S IgG seroprevalence was 98%, whereas anti-N IgG seroprevalence was 23%.[17] Thus, natural infection played a small role in the large increase in SARS-CoV-2 antibody prevalence observed in the United Kingdom between December 2020 and December 2021.

By September 2021, the pooled SARS-CoV-2 antibody seroprevalence among general population samples within the African continent was 65%.[2] More recent published seroprevalence estimates are available from South Africa, a setting with comparable COVID-19 vaccine uptake to Kenya. Seroprevalence in Gauteng, a predominantly urban province in South Africa, was 73% by December 2021 and 91% by June 2022.[18,19] It was 95% nationally by March 2022 as estimated using nationally representative samples from South African blood banks.[20] Despite slightly lower seroprevalence in Kilifi and Nairobi compared with the data from South Africa, collectively, these data point to high seroprevalence of anti-SARS-CoV-2 IgG in similar settings by the end of 2022.

Anti-S IgG seroprevalence and concentrations were significantly lower in Kilifi, a rural setting, than in Nairobi. These findings suggest a population immunity gap in Kilifi, though this is probably indicative of rural Kenya in general. Rural–urban heterogeneity in SARS-CoV-2 antibody prevalence has been observed in other African settings.[2] Of note, about 30% of COVID-unvaccinated adults aged ≥65 years in Kilifi were seronegative for anti-S IgG, and there was no significant change in anti-S IgG seroprevalence within the same age group between May 2022 and November 2022. COVID-19 vaccine uptake was substantially lower among adults aged ≥65 years in Kilifi than among their counterparts in Nairobi; this may in part explain the lower anti-S IgG seroprevalence and concentration among the Kilifi elderly. Recent evidence demonstrates a disproportionate excess mortality burden among adults aged ≥65 years in Kilifi during the COVID-19 era,[21] underscoring vulnerability to severe SARS-CoV-2 infection within that sub-group.

Anti-S IgG seroprevalence and concentrations were also significantly lower among children aged <16 years than among older age groups (except for adults ≥65 years in Kilifi). In addition, we found that recent COVID-like symptoms were more likely to be reported among children aged <16 years than in other age groups. Although the burden of severe COVID-19 appears to be lower in children than among adults, as children age into adulthood, there may accumulate a significant population immunity gap. Furthermore, a sizeable proportion of potentially susceptible children (unvaccinated and with no evidence of an infection-induced SARS-CoV-2 immune response) may substantially contribute to continued transmission within the community.

The relevance of our findings for public health planning was strengthened by use of the WHO IS for anti-SARS-CoV-2 immunoglobulin, which provided an opportunity to estimate anti-S IgG concentrations. We demonstrated that 63% of study participants within the Kilifi HDSS and 86% within the Nairobi Urban HDSS had anti-S IgG concentrations associated with 80% protection against wildtype SARS-CoV-2 among individuals vaccinated using 1–2 doses of mRNA or vectored COVID-19 vaccines. Although correlates of protection for SARS-CoV-2 are variant-specific and are intended to inform vaccine development/licensure, existing and future thresholds may inform inferences about population immunity in settings that are characterized by high seroprevalence but low COVID-19 vaccination uptake, such as Kenya. We also found that anti-S IgG concentrations were higher among COVID-vaccinated individuals compared with COVID-unvaccinated individuals (possibly driven by hybrid immunity), underscoring the utility of vaccination for boosting antibody levels. Furthermore, the distribution of anti-S IgG concentrations trended towards lower values during Survey 2 compared with Survey 1, suggesting waning antibody levels.

The findings may be subject to some limitations. First, despite reasonable attempts to reach all initially randomly sampled individuals, about 20–30% were not contactable and were therefore replaced. This may underestimate seroprevalence if individuals typically not found at home were more likely to have been infected with SARS-CoV-2 or to have been vaccinated. Second, full COVID-19 vaccination coverage was lower in the study sample compared with the respective county-specific estimates from the national COVID-19 vaccination program; therefore, the study sample may not be representative of the general population within the respective counties. If COVID-unvaccinated individuals were more likely to have been previously infected, we may have overestimated cumulative incidence. However, we found that anti-N IgG seroprevalence was comparable among COVID-vaccinated and COVID-unvaccinated individuals. Third, the majority of the COVID-19 vaccination data were collected using verbal report. However, as mentioned previously, COVID-vaccinated individuals made up a minority of the study sample, and, in an ongoing exercise, a majority of verbal COVID-19 vaccination reports have been verified against documented vaccination. Finally, anti-S seroprevalence levels may have been underestimated in the primary analyses as they were not adjusted for test-performance.

5 | CONCLUSION

At the end of 2022, more than 70% of Kilifi residents and 90% of Nairobi residents were seropositive for anti-S IgG. On the basis of our findings, we have two key recommendations for policymakers. First, we recommend support for ongoing SARS-CoV-2 serosurveillance to ensure availability of up-to-date seroprevalence data for public health planning. Incorporation of the WHO IS for anti-SARS-CoV-2 immunoglobulin in serosurveillance will be important for informing population-level protection. Second, given a potential population immunity gap in rural Kenya, we recommend a focus on efforts to ensure that COVID-19 vaccines reach rural dwellers at high risk of severe disease, such as the elderly and immunocompromised.

DISCLAIMER

The findings and conclusions in this study are those of the authors and do not necessarily represent the official position of the US Centers for Disease Control and Prevention.

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ACKNOWLEDGMENTS

We thank residents of the Kilifi HDSS and the Nairobi Urban HDSS, field staff teams, administrative staff, laboratory staff, and community engagement teams who worked on the study. We thank the members of the Kilifi County Health Management Team (CHMT), members of the Nairobi CHMT, participating health facilities, and members of the Kenya Multisite Integrated Serosurveillance Steering Committee. The study was funded by the Bill and Melinda Gates Foundation (INV-039626). JAGS is supported by a Wellcome Trust Research Fellowship (214320). This paper is published with the permission of the Director, Kenya Medical Research Institute.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

PEER REVIEW

The peer review history for this article is available at https://www.webofscience.com/api/gateway/wos/peer-review/10.1111/irv.13173.

DATA AVAILABILITY STATEMENT

The data underlying this manuscript can be accessed at https://doi.org/10.7910/DVN/L4AUEG.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Kagucia EW, Ziraba AK, Nyagwange J, et al. SARS-CoV-2 seroprevalence and implications for population immunity: Evidence from two Health and Demographic Surveillance System sites in Kenya, February–December 2022. *Influenza Other Respi Viruses*. 2023;17(9): e13173. doi:10.1111/irv.13173