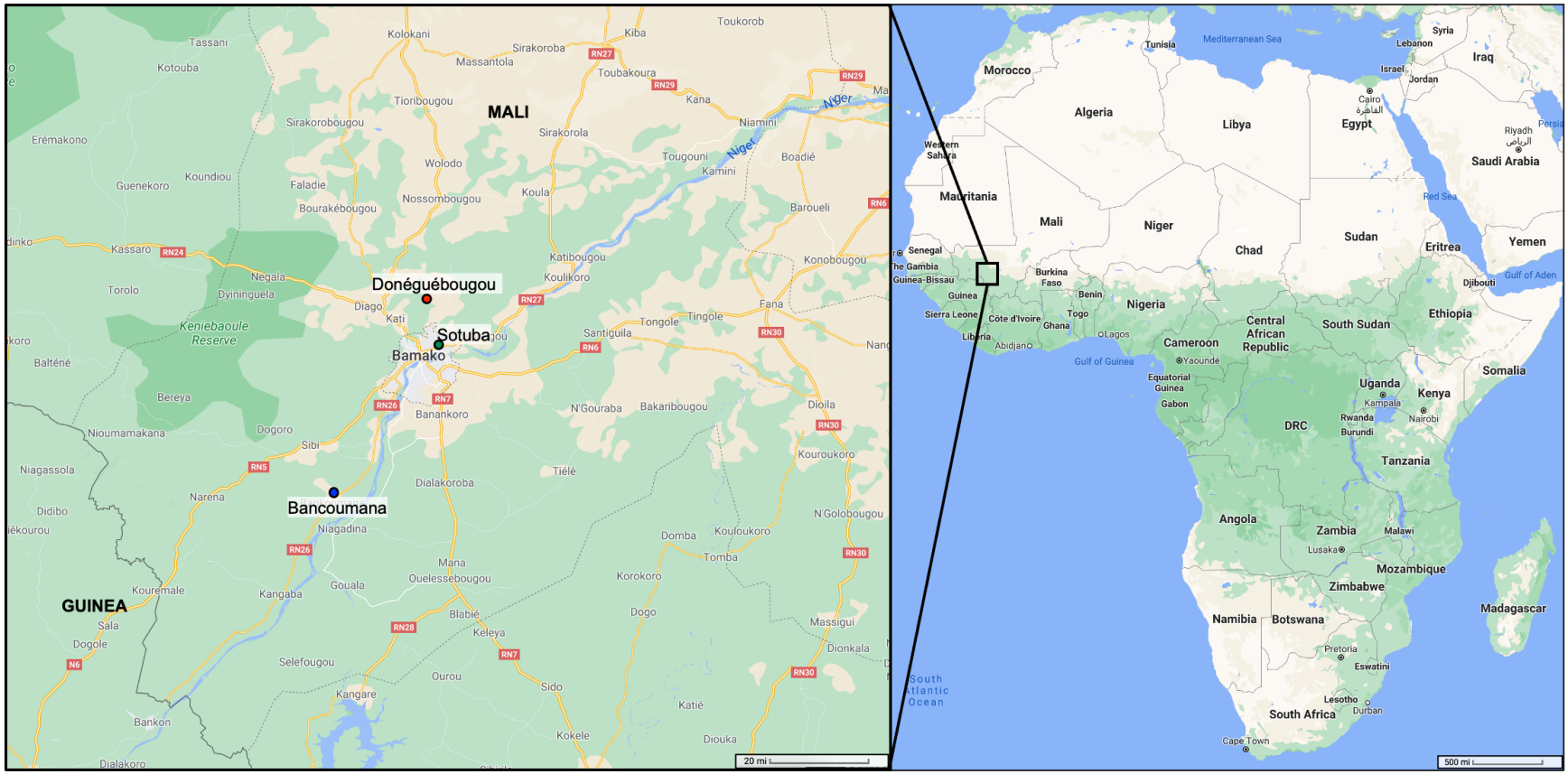


Supplementary Figure 1: Map of study sites
Adapted from Google Maps

Supplementary Text 1: Study sites

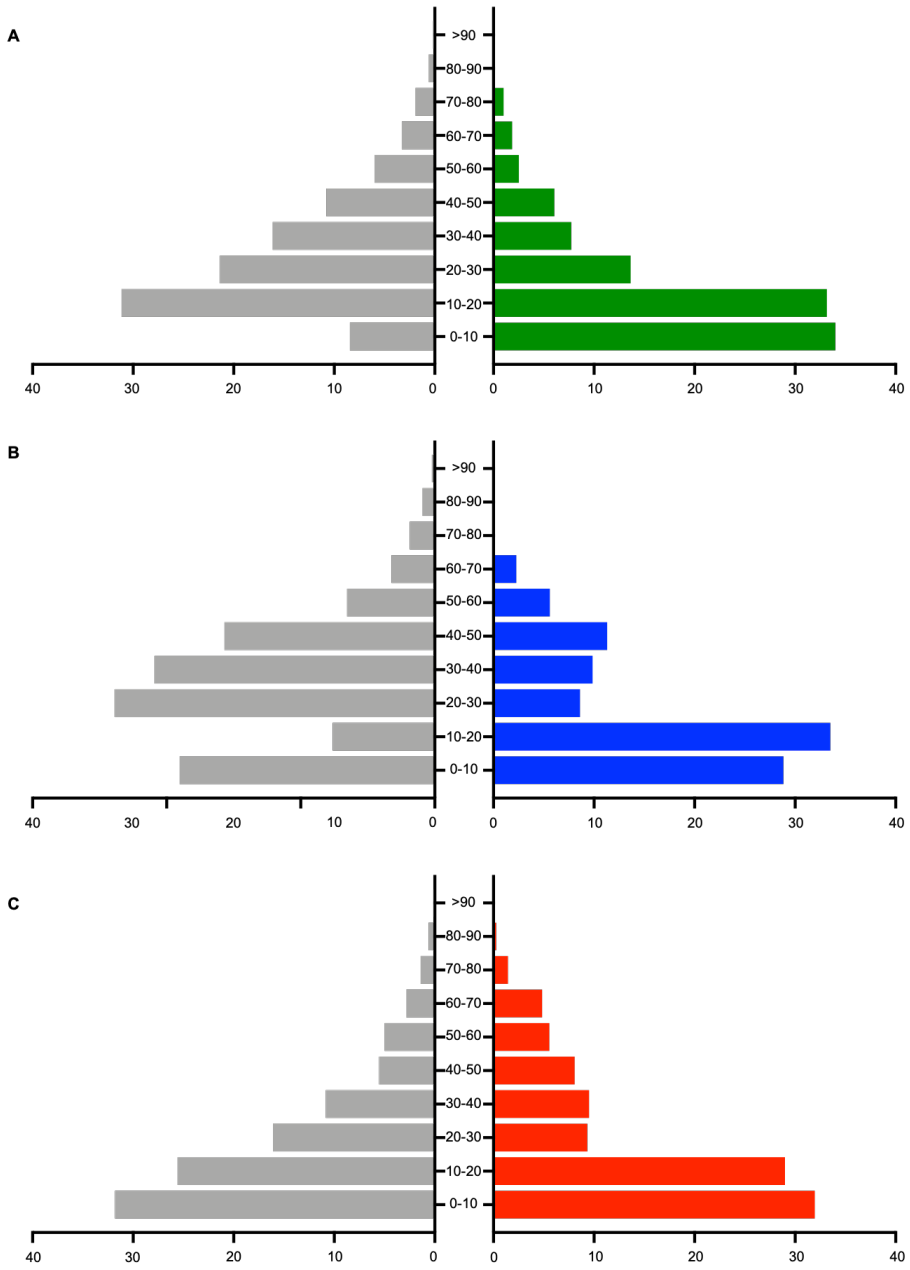
Sotuba is a community population approximately 7,000 located on the bank of the Niger River, in the capital city Bamako (total population ~2.7M). Many clinical trials, as well as epidemiological and entomologic malaria studies, have been conducted in Sotuba. Cumulative malaria exposure in Sotuba is modest compared to highly endemic parts of Mali. The entomologic inoculation rate has been estimated to be low (annual EIR < 15 infective bites per person, per season) [1]. The most recent census data available were collected in 2017.

Bancoumana town is located 60 kilometers southwest of Bamako on the main road to Guinea-Conakry and has a population of approximately 10,000 people. The site is situated in the south-Sudanian area of Mali. The climate is hot, with daily temperatures ranging from 19°C to 40°C. Many clinical trials, as well as epidemiological and entomologic malaria studies, have been conducted in Bancoumana. Malaria transmission is highly seasonal and intense during the rainy season from July to December. The entomologic inoculation rate has been estimated very high (annual EIR > 100 infective bites per person, per season) [2]. The most recent census data available were collected in 2018.

Donéguébougou is a village located 30 km north of Bamako and has a population of approximately 2,000 people. For the purpose of malaria vaccine trials and epidemiology studies, facilities have been put in place at Donéguébougou within walking distance to the residents' homes. There is a high study participation rate per compound in Donéguébougou, thus this site is well suited for community-wide assessments. Malaria transmission is highly seasonal and intense, with the transmission season taking place from June until December. The entomologic inoculation rate has been estimated very high (annual EIR > 100 infective bites per person, per season) [1]. The most recent census data available were collected in 2019.

Supplementary Text 2: Covariates

Demographic variables included age, sex, and community of residence. Medical comorbidity was defined as the presence of at least one of the following self-reported conditions: obesity, diabetes, human immunodeficiency virus (HIV) or other immunosuppression, hypertension, heart disease, chronic pulmonary disease, chronic liver disease, chronic hematologic disorder, chronic kidney disease, chronic neurological disease, and malignancy. Participants also reported smoking status, history of Bacillus Calmette-Guérin (BCG) vaccination and recent antimalarial use (<4 weeks). In female participants, pregnancy status was recorded. Social history included employment in a healthcare facility, household member employment in a healthcare facility, household member diagnosed with COVID-19, and household size. Symptom history included systemic symptoms: fever, chills, fatigue, myalgia, and headache; respiratory symptoms: sore throat, cough, rhinorrhea, shortness of breath, wheeze, anosmia/loss of taste, and respiratory symptoms not otherwise specified; and gastrointestinal symptoms: nausea/vomiting, abdominal pain, and diarrhea. Symptom severity was estimated based on self-reported school or work absenteeism, presentation for medical attention, and hospitalization. Infants aged 6 to 12 months were co-enrolled with their mother, and a limited history was collected.



Supplementary Figure 2: Age structure of A) Sotuba (urban), B) Bancoumana (rural), and C) Donéguébougou (rural). Age group in years (y-axis) versus percentage of overall population (x-axis).
Grey histograms represent census data for each study site.
Colored histograms represent sample for each study site.

Supplementary Table 1: Seroprevalence of SARS-CoV-2 antibodies at visit 1 and visit 2 at Sotuba (urban), Bancoumana (rural town) and Donéguébougou (rural) sites.

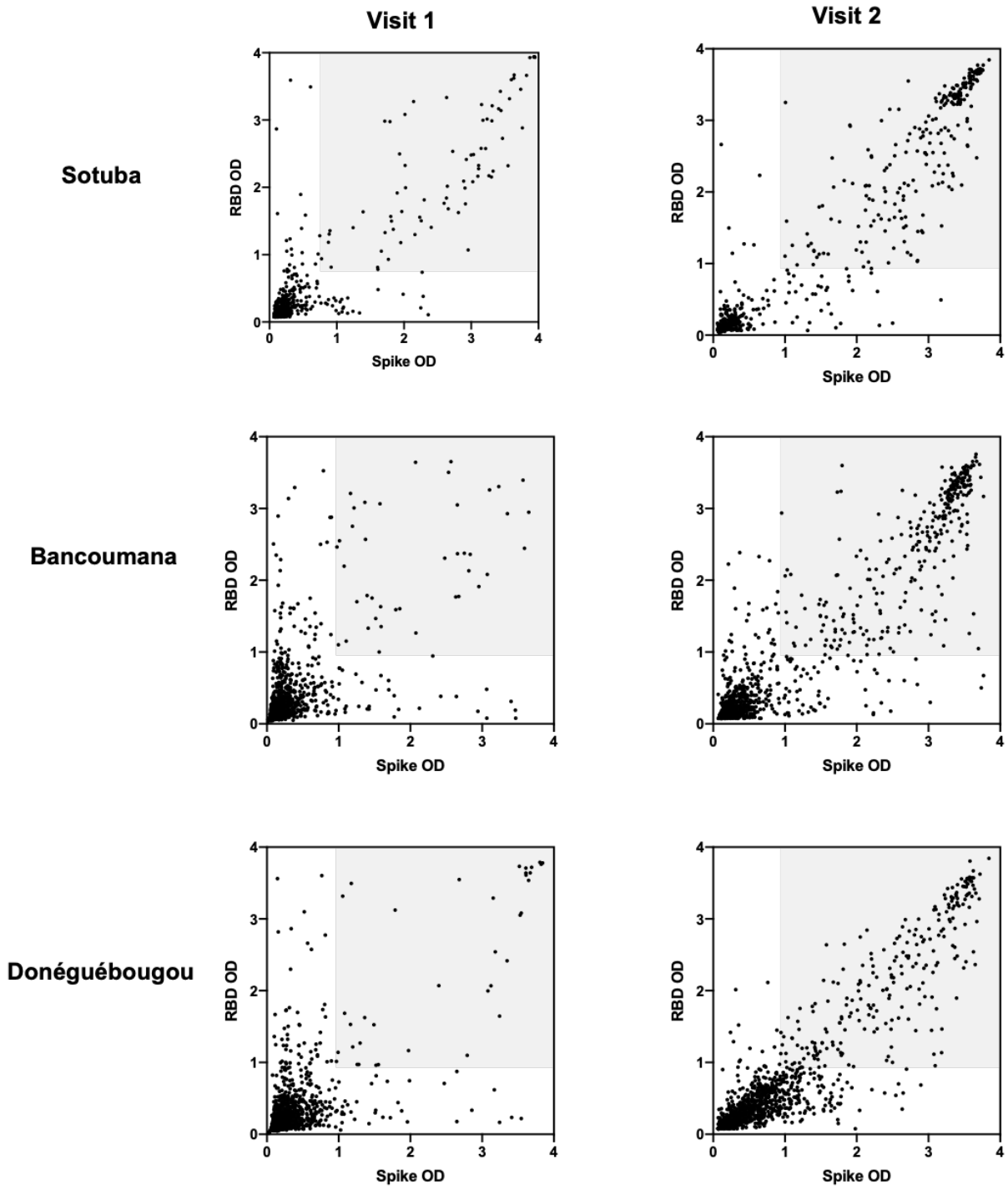
Site	Dates of sample collection	Crude seropositivity rate (95% CI)	Adjusted seropositivity rate (95% CI)[1]
Sotuba (visit 1) N=587	29 July to 16 October 2020	13.1% (10.4-15.9)	19.0% (14.2-23.8)
Sotuba (visit 2) N=528	21 December 2020 to 26 January 2021	44.9% (40.7-49.1)	70.4% (56.8-84.1)
Bancoumana (visit 1) N=963	29 July to 24 September 2020	5.3% (3.9-6.7)	6.5% (4.1-9.0)
Bancoumana (visit 2) N=904	28 December 2020 to 29 January 2021	35.5% (32.4-38.6)	52.1% (41.9-62.3)
Donéguébougou (visit 1) N=1109	28 July to 27 August 2020	4.1% (2.9-5.2)	5.0% (2.8-7.1)
Donéguébougou (visit 2) N=1088	14 December 2020 to 15 January 2021	25.8% (23.2-28.4)	35.0% (27.9-42.1)

[1]Adjusted for population age distribution and assay sensitivity and specificity [3].

Supplementary Table 2: Age-stratified seroprevalence of SARS-CoV-2 antibodies at visit 1 and visit 2 at Sotuba (urban), Bancoumana (rural town) and Donéguébougou (rural) sites.

Site	Dates of sample collection	Crude seropositivity rate (95% CI)			Adjusted seropositivity rate (95% CI)[1]		
		<10 years	10-17 years	≥18 years	<10 years	10-17 years	≥18 years
Sotuba (visit 1) N=587	29 July to 16 October 2020	10.7% (6.3-15.1)	11.7% (6.6-16.7)	16.2% (11.4-21.0)	13.8% (8.4-19.2)	15.1% (9.0-21.1)	21.3% (14.8-27.8)
Sotuba (visit 2) N=528	21 December 2020 to 26 January 2021	29.1% (22.4-35.7)	47.3% (39.4-55.2)	57.2% (50.4-64.0)	38.8% (28.9-48.7)	63.7% (49.5-77.9)	77.2% (61.5-92.9)
Bancoumana (visit 1) N=963	29 July to 24 September 2020	4.0% (1.5-6.4)	6.0% (3.1-8.8)	5.7% (3.4-8.1)	4.6% (1.6-7.6)	7.3% (3.8-10.9)	7.0% (3.9-10.1)
Bancoumana (visit 2) N=904	28 December 2020 to 29 January 2021	24.2% (19.1-29.4)	36.6% (30.8-42.4)	42.6% (37.6-47.6)	32.3% (24.2-40.3)	49.2% (38.3-60.0)	57.3% (45.6-69.0)
Donéguébougou (visit 1) N=1109	28 July to 27 August 2020	3.1% (1.2-5.1)	1.7% (0.0-3.5%)	6.2% (4.0-8.5)	3.4% (0.9-6.0%)	1.5% (0-3.9)	7.7% (4.6-10.8)
Donéguébougou (visit 2) N=1088	14 December 2020 to 15 January 2021	12.2% (8.8-15.7)	28.5% (23.2-33.7)	34.7% (30.4-39.1)	15.8% (11.0-20.7)	41.0% (31.5-50.5)	46.6% (36.8-56.3)

[1]Adjusted for assay sensitivity and specificity [3].

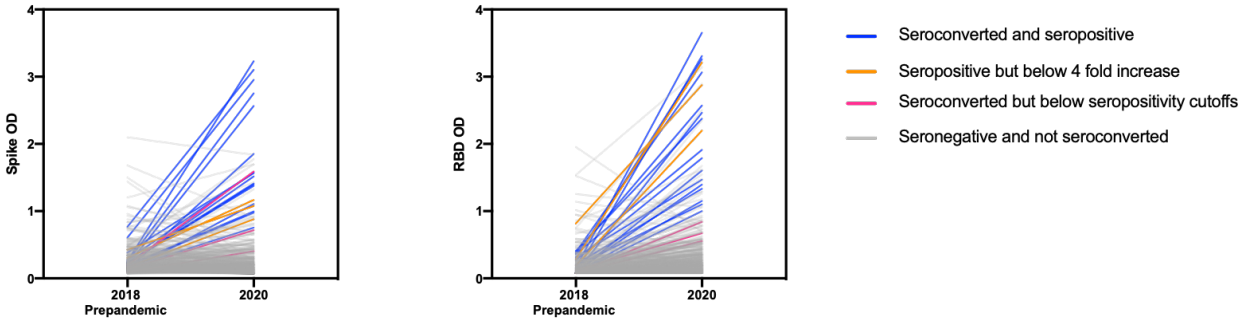


Supplementary Figure 3: SARS-CoV-2 antibody reactivity to spike protein and RBD over time at study sites: Sotuba (top row), Bancoumana (middle row) and Donéguébougou (bottom row).
RBD: receptor binding domain, OD: optical density
Visit 1: 28 July to 16 October 2020
Visit 2: 14 December 2020 to 29 January 2021
Shaded region represents ELISA measurements that exceed cutoffs to define seropositive cases

Supplementary Text 3: SARS-CoV-2 seroconversion from pre-pandemic to Visit 1 (July to August 2020)

To assess assay performance, seroconversion episodes were assessed in participants with pre-pandemic blood samples available. Seroconversion was defined as a fourfold increase in absorbance value for SARS-CoV-2 spike protein and RBD. Very low absorbance values were replaced with the assay limit of blank to improve the accuracy of seroconversion estimates [4]. To confirm the performance of the assay cutoffs, concordance between crude seropositivity and seroconversion episodes was assessed by Cohen's kappa.

Pre-pandemic samples were available for 402 participants from Bancoumana to evaluate seroconversion episodes (Supplementary Figure 4). In the group with pre-pandemic blood samples available, 19/402 demonstrated dual SARS-CoV-2 spike and RBD antigen seroconversion, and 19/402 were seropositive. There was a strong concordance between seroconversion and seropositivity, confirming the utility of the assay cutoffs. A total of 16/402 demonstrated both dual antigen seroconversion and seropositivity (Cohen's kappa 0.83 (95% CI: 0.70 to 0.96)).



Supplementary Figure 4: Seroconversion and seropositivity of SARS-CoV-2 antibodies to spike protein and RBD in 402 participants with pre-pandemic blood samples from Bancoumana
RBD: receptor binding domain, OD: optical density
Seroconversion: fourfold increase in spike protein and RBD OD value from pre-pandemic sample
Seropositive: spike protein and RBD OD value above cutoff

Supplementary Table 3: Univariate comparison of seronegative and seropositive subpopulations at visit 1 (n=2659, July/October 2020)

	Seronegative	Seropositive	p-value
Sample size	2486	173	
Co-enrolled infants	13	0	
Demographics			
Sex, male (%, n/N)	50.9% (1266/2486)	41.6% (72/173)	**0.018**
Age, years (median, IQR)	14 (8-31)	18 (10-36)	**0.0066**
Age group (%, n/N)			
<10 years	31.5% (783/2486)	24.9% (43/173)	
10-17 years	28.0% (696/2486)	23.7% (41/173)	
>/=18 years	40.5% (1007/2486)	51.4% (89/173)	
Medical factors (% (n/N)			
Any comorbidity	1.5% (37/2473)	2.9% (5/173)	0.19
Pregnancy (any stage)	0.8% (21/2473)	1.2% (2/173)	0.66
Smoking	2.8% (66/2343)	2.5% (4/157)	>0.99
Antimalarial use	2.1% (52/2473)	3.5% (6/173)	0.27
BCG administration	80.5% (1992/2473	79.8% (138/173)	0.77
Social factors			
Works at healthcare facility	2.8% (69/2473)	5.8% (10/173)	**0.035**
Household member works at healthcare facility	12.8% (317/2473)	19.7% (34/173)	**0.015**
Household size (mean, SD)	7.6 (4.2)	8.6 (5.4)	**0.0043**
Symptoms (%, n/N)			
No symptoms since onset pandemic	91.2% (2242/2486)	79.2% (137/173)	
Symptoms since March 2020 (any)	9.8% (244/2486)	20.8% (36/173)	**<0.0001**
Systemic symptoms (any)	6.4% (159/2473)	14.5% (25/173)	**0.0003**
Fever	4.0% (100/2473)	8.7% (15/173)	**0.010**
Chills	0.4% (9/2473)	1.7% (3/173)	**0.039**
Fatigue	0.7% (17/2473)	1.2% (2/173)	0.36
Myalgia	0.7% (18/2473)	3.5% (6/173)	**0.0036**
Headache	3.7% (91/2473)	11.0% (19/173)	**<0.0001**
Respiratory symptoms (any)	4.5% (112/2473)	8.1% (14/173)	**0.041**
Sore throat	0.4% (9/2473)	1.2% (2/173)	0.16
Cough	2.4% (59/2473)	4.1% (7/173)	0.20
Rhinorrhea	3.6% (89/2473)	5.2% (9/173)	0.29
Dyspnea	0% (0/2473)	0% (0/173)	>0.99
Wheezing	0% (0/2473)	0% (0/173)	>0.99
Loss of smell/taste	0.2% (4/2473)	0.6% (1/173)	0.29
Other respiratory symptoms	<0.1% (1/2473)	0% (0/173)	>0.99
Gastrointestinal symptoms (any)	2.7% (67/2473)	5.8% (10/173)	**0.031**
Nausea/vomiting	1.5% (37/2473)	2.9% (5/173)	0.19
Abdominal pain	1.3% (31/2473)	2.9% (5/173)	0.082
Diarrhea	0.6% (16/2473)	0.6% (1/173)	>0.99
Symptom severity (%, n/N)[1]			
Missed work or school	39.2% (93/237)	36.1% (13/36)	0.85
Sought medical attention	49.4% (117/237)	33.3% (12/36)	0.077
Hospitalized[2]	0.4% (1/237)	0% (0/36)	>0.99
Duration of symptoms (any) (mean, SD)	6.4 (8.2)	3.6 (3.0)	0.11
Symptomatic at visit 1	21.1% (50/237)	36.1% (13/36)	0.056

[1]Indices of symptom severity collected in participants reporting any symptoms. Details were not collected from infants aged 6-12 months.

[2]Reported hospitalization: seronegative case: 8 year old female with fever, and nausea and vomiting.

Supplementary Table 4: Univariate comparison of seronegative and new seropositive subpopulations at visit 2 (n=2353, July/October 2020 to December 2020/January 2021)

	Seronegative[1]	Seropositive[2]	p-value
Sample size	1629	724	
Co-enrolled infants	10	0	
Demographics			
Sex, male (%, n/N)	51.7% (843/1629)	49.6% (359/724)	0.35
Age, years (median, IQR)	12 (7-28)	18 (11-27)	**<0.0001**
Age group (%, n/N)			
<10 years	37.7% (614/1629)	18.5% (134/724)	
10-17 years	26.5% (432/1629)	30.7% (222/724)	
>/=18 years	35.8% (583/1629)	50.8% (368/724)	
Days between enrollment and follow up (mean, SD)	128.1 (13.1)	129.1 (19.8)	0.17
Medical factors (% (n/N)			
Any comorbidity	1.1% (17/1619)	2.2% (16/724)	**0.036**
Pregnancy (any stage)	0.6% (10/1629)	1.2% (9/724)	0.14
Smoking	3.2% (51/1619)	2.1% (15/724)	0.18
Antimalarial use	2.0% (32/1619)	1.9% (14/724)	>0.99
BCG administration	81.5% (1320/1619)	77.2% (559/724)	**0.016**
Social factors			
Works at healthcare facility	3.2% (52/1619)	2.2% (16/724)	0.23
Household member works at healthcare facility	11.2% (181/1619)	16.0% (116/724)	**0.0015**
Household size (mean, SD)	7.6 (4.2)	7.5 (4.3)	0.82
Symptoms (%, n/N)			
No symptoms since visit 1	50.7% (826/1629)	51.4% (372/724)	
Symptoms since visit 1 (any)	49.3% (803/1629)	48.6% (352/724)	0.79
Systemic symptoms (any)	22.7% (368/1619)	27.8% (201/724)	**0.0092**
Fever	8.3% (134/1619)	9.9% (72/724)	0.21
Chills	2.1% (34/1619)	3.7% (27/724)	**0.025**
Fatigue	2.5% (41/1619)	4.3% (31/724)	**0.028**
Myalgia	2.4% (39/1619)	2.9% (21/724)	0.48
Headache	19.1% (309/1619)	22.7% (164/724)	0.051
Respiratory symptoms (any)	36.9% (598/1619)	32.3% (234/724)	**0.032**
Sore throat	3.0% (48/1619)	2.8% (20/724)	0.89
Cough	21.6% (349/1619)	19.1% (138/724)	0.19
Rhinorrhea	29.7% (481/1619)	26.1% (189/724)	0.075
Dyspnea	0.2% (4/1619)	0.3% (2/724)	>0.99
Wheezing	0% (0/1619)	0% (0/724)	>0.99
Loss of smell/taste	1.3% (21/1619)	2.2% (16/724)	0.11
Other respiratory symptoms	0.4% (6/1619)	0.1% (1/724)	0.45
Gastrointestinal symptoms (any)	5.6% (90/1619)	7.0% (51/724)	0.19
Nausea/vomiting	2.3% (38/1619)	3.7% (27/724)	0.076
Abdominal pain	3.5% (56/1619)	5.0% (36/724)	0.085
Diarrhea	1.1% (17/1619)	0.7% (5/724)	0.49
Symptom severity (%, n/N)[3]			
Missed work or school	12.5% (100/797)	15.6% (55/352)	0.16
Sought medical attention	45.9% (366/797)	63.4% (223/352)	**<0.0001**
Hospitalized[4]	0.3% (2/797)	0.9% (3/352)	0.17
Duration of symptoms (any) (mean, SD)	4.5 (6.2)	4.4 (3.1)	0.19
Symptomatic at visit 2	38.3% (305/797)	32.1% (113/352)	**0.046**

[1]Seronegative refers to seronegative individuals at visit 1 and visit 2

[2]Seropositive refers to new seropositive individuals at visit 2 (seronegative at visit 1)

[3]Indices of symptom severity collected in participants reporting any symptoms. Details were not collected from infants aged 6-12 months.

[4]Reported hospitalizations: seronegative cases: 22 year old female with fever, headache, nausea and vomiting, and abdominal pain, 14 year old male with cough. Seropositive cases: 2 year old male with fever, cough and rhinorrhea, 12 year old male with headache, and 30 year old male with fever, headache and rhinorrhea.

Supplementary Text 4: SARS-CoV-2 antibody dynamics between Visit 1 and Visit 2

In a longitudinal assessment of participants that were seropositive at visit 1 (July to October 2020), almost three-quarters remained seropositive at visit 2 (December 2020 to January 2021) (73.2%, 115/157) (Supplementary Table 5). The mean time between sample collections was 131.6±14.5 days. Among the 26.8% (42/157) of subjects that seroreverted, 21/42 reverted below the threshold for both spike protein and RBD, while 19/42 seroreverted RBD only, and 2/42 seroreverted spike protein only (Figure 2). In all participants seropositive at visit 1, RBD assay absorbance values waned faster than spike protein assay absorbance values at each study site (-0.47 OD units/100 days (95% CI: -0.60 to -0.34) versus -0.10 OD units/100 days (95% CI: -0.23 to +0.03). In an exploratory univariate comparison of serostable and seroreverting individuals, seroreversion was associated with male sex and smaller household size (Supplementary Table 6).

Supplementary Table 5: Longitudinal assessment of participants seropositive at visit 1 (n=157, July/October 2020 to December 2021/January 2021)

	Sotuba	Bancoumana	Donéguébougou	Overall
Sample size	66	46	45	157
Serostable (%, n/N) (Seropositive/Seropositive)	83.3% (55/66)	67.4% (31/46)	64.4% (29/45)	73.2% (115/157)
Seroreverted (%, n/N) (Seropositive/Seronegative)	16.7% (11/66)	32.6% (15/46)	35.6% (16/45)	26.8% (42/157)
Spike OD at enrollment (mean, SD)	2.73 (0.87)	1.92 (0.90)	2.23 (1.17)	2.35 (1.03)
RBD OD at enrollment (mean, SD)	2.35 (0.91)	2.29 (0.82)	2.30 (1.11)	2.32 (0.94)
Days between enrollment and follow up (mean, SD)	139.4 (14.2)	123.4 (11.5)	128.6 (11.8)	131.6 (14.5)
Rate of change Spike OD (OD/100 days) (mean, 95% CI)	-0.11 (-0.32 to 0.10)	-0.03 (-0.32 to 0.26)	-0.15 (-0.34 to 0.04)	-0.10 (-0.23 to 0.03)
Rate of change RBD OD (OD/100 days) (mean, 95% CI)	-0.26 (-0.48 to -0.04)	-0.66 (-0.87 to -0.45)	-0.60 (-0.82 to -0.38)	-0.47 (-0.60 to -0.34)

Supplementary Table 6: Univariate comparison of serostatus at visit 2 in participants seropositive at visit 1 (n=157, July/October 2020 to December 2021/January 2021)

	Seropositive[1]	Seronegative[2]	p-value
Sample size	115	42	
Co-enrolled infants	0	0	
Demographics			
Sex, male (%, n/N)	36.5% (42/115)	54.8% (19/42)	**0.046**
Age, years (median, IQR)	20 (10-39.5)	11.5 (8-28)	0.069
Age group (%, n/N)			
<10 years	21.7% (25/115)	33.3% (14/42)	
10-17 years	20.9% (24/115)	30.9% (13/42)	
>/=18 years	57.4% (66/115)	35.7% (15/42)	
Days between enrollment and follow up (mean, SD)	132.4 (14.9)	129.3 (13.2)	0.23
Medical factors (% (n/N)			
Any comorbidity	2.6% (3/115)	0% (0/42)	0.56
Pregnancy (any stage)	1.7% (2/115)	0% (0/42)	>0.99
Smoking	1.7% (2/115)	4.8% (2/42)	0.29
Antimalarial use	3.5% (4/115)	2.4% (1/42)	>0.99
BCG administration	80.9% (93/115)	81.0% (34/42)	>0.99
Social factors			
Works in healthcare	5.2% (6/115)	7.1% (3/42)	0.70
Household member works in healthcare	19.1% (22/115)	19.0% (8/42)	>0.99
Household size (mean, SD)	9.1 (6.1)	7.1 (3.3)	**0.050**
Symptoms (%, n/N)			
No symptoms since visit 1	49.1% (68/115)	54.8% (23/42)	
Symptoms since visit 1	40.9% (47/115)	45.2% (19/42)	0.72
Systemic symptoms	23.5% (27/115)	28.6% (12/42)	0.54
Fever	11.3% (13/115)	9.5% (4/42)	>0.99
Chills	4.3% (5/115)	2.4% (1/42)	>0.99
Fatigue	7.0% (8/115)	9.5% (4/42)	0.73
Myalgia	7.0% (8/115)	2.4% (1/42)	0.45
Headache	20.9% (24/115)	21.4% (9/42)	>0.99
Respiratory symptoms	31.3% (36/79)	26.2% (11/42)	0.69
Sore throat	5.2% (6/115)	2.4% (1/42)	0.68
Cough	18.3% (21/115)	14.3% (6/42)	0.64
Rhinorrhea	23.5% (27/115)	21.4% (9/42)	0.83
Dyspnea	0% (0/115)	2.4% (1/42)	0.27
Wheezing	0% (0/115)	0% (0/42)	>0.99
Loss of smell/taste	3.5% (4/115)	4.8% (2/42)	0.57
Other respiratory symptoms	0% (0/115)	0% (0/42)	>0.99
Gastrointestinal symptoms	9.6% (11/115)	7.1% (3/42)	0.76
Nausea/vomiting	5.2% (6/115)	2.4% (1/42)	0.68
Abdominal pain	5.2% (6/115)	7.1% (3/42)	0.70
Diarrhea	0.9% (1/115)	0% (0/42)	>0.99
Symptom severity			
Missed work or school	23.4% (11/47)	15.8% (3/19)	0.74
Sought medical attention	57.4% (27/47)	63.2% (12/19)	0.78
Hospitalized	0% (0/47)	0% (0/19)	>0.99
Duration of symptoms (any) (mean, SD)	4.9 (5.4)	2.8 (1.9)	0.19
Symptomatic at Visit 2	29.8% (14/47)	36.8% (7/19)	0.57

[1]Seropositive refers to participants seropositive at visit 1 and serostable at visit 2

[2]Seronegative refers to participants seropositive at visit 1 and seronegative at visit 2.

Supplementary Text 5: Clinical presentation in SARS-CoV-2 seroconverters participating in clinical trials

In a subset of participants co-enrolled in clinical trials at the Bancoumana site [5], and the Donéguébougou site [6], clinical trial MedDRA coded adverse events occurring between visit 1 and 7 days before visit 2 were assessed to better understand the clinical presentation of COVID-19. Adverse event rates were compared based on serostatus at visit 2 in all participants seronegative at visit 1 using Fisher's Exact Test. Adverse events were graded using the modified FDA Toxicity Grading Scale for healthy adult and adolescent subjects enrolled in Preventive Vaccine Clinical Trials.

In a subset of 146 healthy adult participants co-enrolled in a Phase 2 clinical trial at the Bancoumana site during this SARS-CoV-2 seroprevalence study,[2] clinical trial adverse events occurring between visit 1 and 7 days before visit 2 were assessed to better understand the clinical presentation of COVID-19. There was a low frequency of most clinical and laboratory adverse events irrespective of serostatus (Supplementary Table 7). Pain (non-specific) was more common in the newly seropositive group compared to the seronegative group (8.2% (5/61) vs 0% (0/85), p=0.014). There was no statistically significant difference in the frequency of potentially COVID-19 related adverse events including bronchitis (1.6% (1/61) vs 3.5% (3/85), p=0.64), cough (3.3% (2/61) vs 1.2% (1/85), p=0.57), pyrexia (1.6% (1/61) vs 0% (0/85), p=0.43), chills (1.6% (1/61) vs 0% (0/85), p=0.42), headache (11.5% (7/61) vs 15.3% (13/85), p=0.63), rhinitis (34.4% (21/61) vs 23.5% (20/85), p=0.26), sinobronchitis (3.3% (2/61) vs 3.5% (3/85), p>0.99), leukopenia (9.8% (6/61) vs 4.7% (4/85), p=0.20), or thrombocytopenia (3.3% (2/61) vs 0% (0/85), p=0.17). There was no difference in the grading of the most commonly reported adverse events between the seropositive group and the seronegative group (Supplementary Table 8).

Similarly, in a subset of 1037 participants of all ages co-enrolled in a community Phase 2 clinical trial at the Donéguébougou,[3] there was a low frequency of most clinical and laboratory adverse events irrespective of serostatus (Supplementary Table 9). Headache (18.3% (46/252) vs 9.4% (74/785), p=0.0003) and rhinitis (33.3% (84/252) vs 25.1% (197/785), p=0.012) were more common in the newly seropositive group compared to the seronegative group. There was no statistically significant difference in the frequency of other potentially COVID-19 related adverse events. Dental caries (3.2% (8/252) vs 1.1% (9/785), p=0.042) and gastritis (1.2% (3/252) vs 0.1% (1/785), p=0.047) were also observed more frequently in the seroconverting group. There was no difference in the grading of the most commonly reported adverse events between the seropositive group and the seronegative group, including headache and rhinitis (Supplementary Table 10).

Supplementary Table 7: Adverse events according to serostatus between visit 1 (July/August 2020) and visit 2 (December 2020/January 2021) in individuals co-enrolled in a clinical trial at the Bancoumana site (n=146)

	Seronegative[1]	Seropositive[2]	p-value
Sample size	85	61	
Adverse event (%, n/N)			
Clinical, possibly COVID-19 related			
Abdominal pain	1.2% (1/85)	1.6% (1/61)	>0.99
Bronchitis	3.5% (3/85)	1.6% (1/61)	0.64
Cough	1.2% (1/85)	3.3% (2/61)	0.57
Chills	0% (0/85)	1.6% (1/61)	0.42
Decreased appetite	0% (0/85)	1.6% (1/61)	0.42
Enteritis	0% (0/85)	1.6% (1/61)	0.42
Gastroenteritis	2.4% (2/85)	0% (0/61)	0.51
Headache	15.3% (13/85)	11.5% (7/61)	0.63
Influenza (clinical)	2.4% (2/85)	3.3% (2/61)	>0.99
Nausea	1.2% (1/85)	0% (0/61)	>0.99
Paronychia	1.2% (1/85)	0% (0/61)	>0.99
Pyrexia	0% (0/85)	1.6% (1/61)	0.43
Rhinitis	23.5% (20/85)	34.4% (21/61)	0.26
Sinobronchitis	3.5% (3/85)	3.3% (2/61)	>0.99
Clinical, other			
Back pain	0% (0/85)	1.6% (1/61)	0.42
Conjunctivitis	9.4% (8/81)	3.3% (2/61)	0.19
Dental caries	9.4% (8/85)	0% (0/61)	0.021
Dermatosis	1.2% (1/85)	0% (0/61)	>0.99
Dizziness	1.2% (1/85)	0% (0/61)	>0.99
Ear infection	0% (0/85)	1.6% (1/61)	0.42
Ecchymosis	0% (0/85)	1.6% (1/61)	0.42
Eye burns	1.2% (1/85)	0% (0/61)	>0.99
Food poisoning	1.2% (1/85)	1.6% (1/61)	>0.99
Gastritis	2.4% (2/85)	6.6% (4/61)	0.24
Genitourinary tract infection	2.4% (2/85)	3.3% (2/61)	>0.99
Hemorrhoids	1.2% (1/85)	0% (0/61)	>0.99
Hypertension	1.2% (1/85)	0% (0/61)	>0.99
Malaria	29.4% (25/85)	32.8% (20/61)	0.72
Oropharyngeal pain	1.2% (1/85)	0% (0/61)	>0.99
Pain	0% (0/85)	8.2% (5/61)	**0.014**
Strangulated umbilical hernia	1.2% (1/85)	0% (0/61)	>0.99
Tonsillitis	0% (0/85)	1.6% (1/61)	0.42
Typhoid fever	2.4% (2/81)	3.3% (2/61)	>0.99
Urticaria	1.2% (1/85)	0% (0/61)	>0.99
Wound	4.7% (8/84)	8.2% (5/61)	0.49
Laboratory			
Alanine aminotransferase increased	1.2% (1/85)	0% (0/61)	>0.99
Blood creatinine increased	4.7% (4/85)	1.6% (1/61)	0.084
Hemoglobin decreased	0% (0/85)	0% (0/61)	>0.99
Leukopenia	4.7% (4/85)	9.8% (6/61)	0.20
Neutropenia	5.9% (5/85)	11.5% (7/61)	0.24
Thrombocytopenia	0% (0/85)	3.3% (2/61)	0.17
White blood cell count increased	1.2% (1/85)	0% (0/61)	>0.99

[1]Seronegative refers to seronegative individuals at visit 1 and visit 2

[2]Seropositive refers to new seropositive individuals at visit 2 (seronegative at visit 1)

Supplementary Table 8: Grading of commonly reported adverse events in individuals co-enrolled in a clinical trial at the Bancoumana site (n=146)

	Seronegative[1]	Seropositive[2]
Sample size	85	61
Adverse event (%, n/N)		
Headache	15.3% (13/85)	11.5% (7/61)
Grade 1	15.4% (2/13)	14.3% (1/7)
Grade 2	84.6% (11/13)	85.7% (6/7)
Grade 3	0% (0/13)	0% (0/7)
Rhinitis	23.5% (20/85)	34.4% (21/61)
Grade 1	5.0% (1/20)	0% (0/21)
Grade 2	95.0% (19/20)	100% (21/21)
Grade 3	0% (0/20)	0% (0/21)
Malaria	29.4% (25/85)	32.8% (20/61)
Grade 1	0% (0/25)	0% (0/20)
Grade 2	96.0% (24/25	100% (20/20)
Grade 3	4.0% (1/25)	0% (0/20)

[1]Seronegative refers to seronegative individuals at visit 1 and visit 2
[2]Seropositive refers to new seropositive individuals at visit 2 (seronegative at visit 1)

Supplementary Table 9: Adverse events according to serostatus between visit 1 (July/August 2020) and visit 2 (December 2020/January 2021) in individuals co-enrolled in a clinical trial at the Donéguébougou site (n=1037)

	Seronegative[1]	Seropositive[2]	p-value
Sample size	785	252	
Adverse event (%, n/N)			
Clinical, potentially COVID-19 related			
Abdominal pain	3.1% (24/785)	3.6% (9/252)	0.68
Arthralgia	0.5% (4/785)	0% (0/252)	0.58
Bronchitis	2.3% (18/785)	3.2% (8/252)	0.49
Chills	0.4% (3/785)	0.4% (1/252)	>0.99
Cough	0.4% (3/785)	0.8% (2/252)	0.60
Decreased appetite	0.8% (6/785)	1.2% (3/252)	0.46
Diarrhoea	0.1% (1/785)	0% (0/252)	>0.99
Gastroenteritis	1.4% (11/785)	2.4% (6/252)	0.27
Headache	9.4% (74/785)	18.3% (46/252)	**0.0003**
Myalgia	0.6% (5/785)	0% (0/252)	0.34
Nasopharyngitis	1.5% (12/785)	2.4% (6/252)	0.41
Nausea	0% (0/785)	0.4% (1/252)	0.24
Oropharyngeal pain	0.4% (3/785)	0% (0/252)	>0.99
Pharyngitis	10.7% (84/785)	7.1% (18/252)	0.11
Pneumonia	0.3% (2/785)	0% (0/252)	>0.99
Pyrexia	1.9% (15/785)	3.6% (9/252)	0.15
Rhinitis	25.1% (197/785)	33.3% (84/252)	**0.012**
Rhinorrhoea	0.1% (1/785)	0% (0/252)	>0.99
Sinobronchitis	1.5% (12/785)	0.4% (1/252)	0.21
Vomiting	0.6% (5/785)	0% (0/252)	0.34
Clinical, other			
Abscess	0.1% (1/785)	0% (0/252)	>0.99
Abscess limb	0.1% (1/785)	0% (0/252)	>0.99
Arthropod sting	0.1% (1/785)	0.4% (1/252)	0.43
Asthenia	0.6% (5/785)	0.8% (2/252)	0.68
Back pain	0.1% (1/785)	0% (0/252)	>0.99
Chest pain	0.1% (1/785)	0% (0/252)	>0.99
Conjunctivitis	0.3% (2/785)	0.4% (1/252)	0.57
Dental caries	1.1% (9/785)	3.2% (8/252)	**0.042**
Dermatosis	0.1% (1/785)	0% (0/252)	>0.99
Dizziness	0.8% (6/785)	1.6% (4/252)	0.27
Dysentery	0.4% (3/785)	0.8% (2/252)	0.60
Dysmenorrhoea	0% (0/785)	0.4% (1/252)	0.24

Ear infection	0.1% (1/785)	0% (0/252)	>0.99
Epistaxis	0.1% (1/785)	0% (0/252)	>0.99
Food poisoning	0.1% (1/785)	0% (0/252)	>0.99
Fungal skin infection	0.1% (1/785)	0% (0/252)	>0.99
Furuncle	0.1% (1/785)	0.4% (1/252)	0.43
Gastritis	0.1% (1/785)	1.2% (3/252)	**0.047**
Genital infection	0.1% (1/785)	0% (0/252)	>0.99
Gingivitis	0.1% (1/785)	0% (0/252)	>0.99
Hordeolum	0.1% (1/785)	0% (0/252)	>0.99
Hypertension	0.1% (1/785)	0% (0/252)	>0.99
Infection parasitic	0.1% (1/785)	0% (0/252)	>0.99
Injection site pain	3.8% (30/785)	4.8% (12/252)	0.58
Ligament sprain	0.1% (1/785)	0% (0/252)	>0.99
Limb injury	0.4% (3/785)	0.4% (1/252)	>0.99
Malaria	41.1% (323/785)	41.7% (105/252)	0.88
Mastitis	0.1% (1/785)	0.4% (1/252)	0.43
Otitis externa	0.3% (2/785)	0.4% (1/252)	0.57
Otitis media	0.3% (2/785)	0.4% (1/252)	0.57
Pain	0.3% (2/785)	0% (0/252)	>0.99
Pruritus	0% (0/785)	0.4% (1/252)	0.24
Sciatica	0.3% (2/785)	0% (0/252)	>0.99
Snake bite	0.1% (1/785)	0% (0/252)	>0.99
Tachycardia	0.3% (2/785)	0% (0/252)	>0.99
Thermal burn	0.1% (1/785)	0% (0/252)	>0.99
Tonsillitis	0.3% (2/785)	0.4% (1/252)	0.57
Urinary tract infection	0.5% (4/785)	0.8% (2/252)	0.64
Urticaria	0.3% (2/785)	0.8% (2/252)	0.25
Wound	1.3% (10/785)	1.2% (3/252)	>0.99
Wound infection	0.4% (3/785)	0.8% (2/252)	0.60
Laboratory			
Alanine aminotransferase increased	0.8% (6/785)	1.6% (4/252)	>0.99
Blood creatinine increased	0.8% (6/785)	1.2% (3/252)	0.46
Hemoglobin decreased	0.3% (2/785)	1.2% (3/252)	0.096
Leukocytosis	0.5% (4/785)	0.8% (2/252)	0.64
Leukopenia	5.6% (44/785)	7.1% (18/252)	0.36
Neutropenia	6.8% (53/785)	7.9% (20/252)	0.57
Thrombocytopenia	0.6% (5/785)	1.6% (4/252)	0.23

[1]Seronegative refers to seronegative individuals at visit 1 and visit 2

[2]Seropositive refers to new seropositive individuals at visit 2 (seronegative at visit 1)

Supplementary Table 10: Grading of commonly reported adverse events in individuals co-enrolled in a clinical trial at the Donéguébougou site (n=1037)

	Seronegative[1]	Seropositive[2]
Sample size	85	61
Adverse event (%, n/N)		
Headache	9.4% (74/785)	18.3% (46/252)
Grade 1	98.6% (73/74)	97.8% (45/46)
Grade 2	1.4% (1/74)	2.2% (1/46)
Grade 3	0% (0/74)	0% (0/46)
Rhinitis	25.1% (197/785)	33.3% (84/252)
Grade 1	91.4% (180/197)	90.5% (76/84)
Grade 2	7.1% (14/197)	9.5% (8/84)
Grade 3	1.5% (3/197)	0% (0/84)
Malaria	41.1% (323/785)	41.7% (105/252)
Grade 1	77.1% (249/323)	78.1% (82/105)
Grade 2	17.6% (57/323)	17.1% (18/105)
Grade 3	5.3% (17/323)	4.8% (5/105)

[1]Seronegative refers to seronegative individuals at visit 1 and visit 2

[2]Seropositive refers to new seropositive individuals at visit 2 (seronegative at visit 1)

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