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Peter K. Quashie, Peter K. Quashie, Joe Kimanthi Mutungi, Francis Dzabeng ...+23 more authors

Institutions: University of Ghana, Francis Crick Institute, University of Paris, Higher College of Technology ...+1 more institutions

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1 Trends of SARS-CoV-2 antibody prevalence in selected regions across Ghana

2 Peter Kojo Quashie^{1,2}, Joe Kimanathi Mutungi¹, Francis Dzabeng¹, Daniel Oduro-Mensah^{1,3},
3 Precious C. Oporum¹, Kesego Tapela^{1,3}, Aniefiok John Udoakang¹, WACCBIP COVID-19
4 Team^{1,3,4}, Ivy Asante⁴, Lily Paemka^{1,3}, Frederick Kumi-Ansah⁵, Osbourne Quaye^{1,3},
5 Emmanuella Amoako⁶, Ralph Armah⁷, Charlyne Kilba⁷, Nana Afia Boateng⁷, Michael Ofori⁸,
6 George B. Kyei^{4,9}, Yaw Bediako^{1,2}, Nicaise Ndam¹⁰, James Abugri¹¹, Patrick Ansah¹²,
7 William K. Ampofo⁴, Francisca Mutapi¹³ and Gordon A. Awandare^{†1,3}

8 *Affiliations:*

- 9 1. West African Centre for Cell Biology of Infectious Pathogens, College of Basic and
10 Applied Sciences, University of Ghana, Legon, Accra, Ghana
- 11 2. The Francis Crick Institute, 1 Midland Rd, London NW1 1AT, United Kingdom
- 12 3. Department of Biochemistry, Cell and Molecular Biology, University of Ghana, Legon,
13 Accra, Ghana
- 14 4. Department of Virology, Noguchi Memorial Institute for Medical Research, University of
15 Ghana, Legon, Accra, Ghana
- 16 5. Department of Microbiology, Cape Coast Teaching Hospital, Cape Coast, Ghana
- 17 6. Department of Pediatrics, Cape Coast Teaching Hospital, Cape Coast, Ghana.
- 18 7. Department of Internal Medicine, Surgery, Pediatrics and Emergency Medicine, Greater
19 Accra Regional Hospital, Accra, Ghana
- 20 8. Immunology Department, Noguchi Memorial Institute for Medical Research, University of
21 Ghana, Legon, Accra, Ghana
- 22 9. Medical and Scientific Research Directorate, University of Ghana Medical Centre, Legon,
23 Accra, Ghana
- 24 10. UMR 216 MERIT-IRD, Université de Paris, France
- 25 11. Department of Applied Chemistry and Biochemistry, C.K. Tedam University of
26 Technology and Applied Sciences, Navrongo, Upper East Region, Ghana
- 27 12. Navrongo Health Research Centre, Navrongo, Upper East Region, Ghana
- 28 13. NIHR Global Health Research Unit Tackling Infections to Benefit Africa (TIBA), and
29 Institute of Immunology and Infection Research, School of Biological Sciences,
30 University of Edinburgh, Ashworth Laboratories, King's Buildings, Charlotte Auerbach
31 Road, Edinburgh, EH9 3FL, UK

32 *Corresponding Author*[‡]: Gordon A. Awandare (gawandare@ug.edu.gh)

33

34

35 **Abstract**

36 To estimate the level of community exposure to SARS-CoV-2 in Ghana, we conducted
37 phased seroprevalence studies of 2729 participants in selected locations across Ghana.
38 Phase I screening (August 2020) covered a total of 1305 individuals screened at major
39 markets/lorry stations, major shopping malls, hospitals and research institutions involved in
40 COVID-19 work. The screening was performed using a strip-in-cassette lateral flow type
41 Rapid Diagnostic Test (RDT) kit that simultaneously and separately detected IgM and IgG
42 antibodies against SARS-CoV-2 nucleocapsid protein. In Phase I, 252/1305 (19%) tested
43 positive for IgM or IgG or both. Exposure rate was significantly higher among individuals
44 tested at markets/lorry stations (26.9%) compared to those at Shopping Malls (9.4%). The
45 41–60-years age group had the highest exposure rate (27.2%). People with only a basic
46 level or no formal education had a higher exposure rate (26.2%) than those with tertiary level
47 education (13.1%); and higher in informally employed workers (24.0%) than those in the
48 formal sector (15.0%). Phases II and III screening activities in October and December 2020,
49 respectively, showed no evidence of increased seroprevalence, indicating either a reduced
50 transmission rate or loss of antibody expression in a subset of the participants. The Upper
51 East region has the lowest exposure rate, with only 4 of 200 participants (2%) seropositivity.
52 Phase IV screening in February 2021 showed that exposure rates in the upper income
53 earners (26.2%) had almost doubled since August 2020, reflective of Ghana's second wave
54 of symptomatic COVID-19 cases, which began in December 2020. The Phase IV results
55 suggest that seroprevalence levels have become so high that the initial socioeconomic
56 stratification of exposure has been lost. Overall, the data indicates a much higher COVID-19
57 seroprevalence in the Greater Accra Region than was officially acknowledged, likely
58 implying a considerably lower case fatality rate than the current national figure of 0.84%.
59 Additionally, the high exposure levels seen in the communities suggest that COVID-19 in
60 Ghana still predominantly presents with none-to-mild symptoms. Our results lay the
61 foundation for more extensive SARS-CoV-2 surveillance in Ghana and the West African

62 sub-region, including deploying rapid antigen test kits in concert to determine the actual

63 infection burden since antibody development lags infection.

64

65 **Background**

66 The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was first reported in
67 Wuhan, China, in late 2019 [1]. By April 20th 2021 there were 141,058,320 COVID-19 SARS-
68 CoV-2 reported infections with 3,015,314 associated deaths (case fatality ratio (CFR): of
69 2.1%) globally. Of these, 4,437,846 COVID-19 cases and 118,133 deaths (CFR: 2.7%),
70 representing 3.07% and 3.85% of all reported global cases and deaths, were from the 55
71 African Union Member States [2]. Ghana, from the first two reported (imported) cases on
72 March 12th 2020, by April 16th 2021 reported a cumulative total of 91,709 confirmed cases
73 with 771 associated deaths (CFR of 0.84%) by this date [3].

74 The current gold standard method for diagnosis of SARS-CoV-2 infection is by real-time
75 reverse transcription polymerase chain reaction (RT-PCR), which detects viral nucleic acid
76 sequences, and thus the virus, present in the upper respiratory tract (nasopharyngeal or
77 oropharyngeal) swab samples [4-6]. Due to limited resources, tests are prioritised on
78 symptomatic, severe, and/or suspected cases, and occasionally on contacts of confirmed
79 cases. Common symptoms of SARS-CoV-2 infection include fever, dry cough, tiredness and
80 other variable ones with onset between 5 to 14 days after infection [7]. Approximately 80%
81 of infected persons show mild or no symptom [8], however, posing a danger of unmitigated
82 transmission and potential rapid rise in disease onset, severity and death [9]. Additionally,
83 RT-PCR sensitivity may be affected by viral load, virus replication rate, RNA isolation
84 method, and the source or timing of swab collection relative to disease stage [10]. This could
85 lead to false negativity of about 20% [11], indicating that actual infections may be higher
86 than reported per test.

87 Rapid immunodiagnostic tests (RDTs) can be used to detect either SARS-CoV-2-expressed
88 proteins (antigens) in respiratory tract samples (e.g., sputum, throat swab) or human anti-
89 SARS-CoV-2 specific antibodies in blood or serum within minutes. Rapid antigen tests have
90 utility for rapid detection of transmissible infections but have lower sensitivity than PCR-
91 based methods [12] and have become common for routine SARS-CoV-2 screening at ports

92 of entry. Some RDTs also detect the presence of antibodies against SARS-CoV-2 in bodily
93 fluids. These are useful for performing population level surveillance of viral exposure. Unlike
94 antigen RDT's which pick up active and often transmissible infection, antibody RDTs tend to
95 pick up the evidence of previous or recent infection and cannot be used to detect active
96 infection [12]. There are more than 280 Conformité Européenne-*in vitro* diagnostics (CE-
97 IVD)-marked COVID-19 antibody detection RDT kits listed with the Foundation for Innovative
98 Diagnostics (FIND) [13]. Currently, lateral flow immunoassays (LFIAs), chemiluminescence
99 immunoassays (CLIAs), or enzyme-linked immunosorbent assays (ELISAs) are commonly
100 used for detection of SARS-CoV-2 IgM and IgG antibodies [14, 15]. Similar to other
101 infections, SARS-CoV-2 elicits an immune response [16], and the presence of the virus-
102 specific antibodies in blood indicates previous or current infection regardless of the presence
103 or absence of symptoms [17, 18]. Generally, IgM or IgG are produced early and later in
104 infection, respectively [19]. It is currently unknown how long SARS-CoV-2 IgM and IgG
105 antibodies persist, however, seroconversion of IgM appears to peak simultaneously with IgG
106 within 2 to 3 weeks after symptoms onset [10, 17, 20-24]

107 In addition to retrospectively evaluating infection dynamics and the population disease
108 burden, serology tests are useful for vaccine trials, therapeutic antibodies results analyses,
109 and tests for individual and herd immunity. Antibody presence can also help identify COVID-
110 19-recovered individuals and potential donors of convalescent plasma for immunotherapy of
111 critically sick COVID-19 patients [25]. Some seroprevalence studies have used cross-
112 sectional snapshots to evaluate community level exposure of SARS-CoV-2 [26] but to our
113 knowledge, no single study has attempted to track the spatial-temporal dynamics of SARS-
114 CoV-2 exposure in Africa. Ghana reported its first two (imported) cases on March 12th, 2020
115 [3]. By April 4th, positive cases who had neither travel history nor known contact with
116 confirmed cases, were detected, implying local transmission. To estimate COVID-19
117 community spread in Ghana, over a 7-month period, we randomly screened for IgM and IgG
118 antibodies against SARS-CoV-2 in people at various public places in Accra (National capital,

119 where >50% of reported cases occur), Kasoa (a densely-populated town in the Central
120 Region, and a COVID-19 transmission hotspot [27] and which shares a border with Accra),
121 Cape Coast (Central Regional capital), Akropong (a small town in the Eastern Region, a 15-
122 minute drive away from Accra), Navrongo (a small town in the Upper East Region, which
123 hosts a public university and a government Health Research Centre) and Bolgatanga (the
124 Upper East Regional capital) (Figure 1). A questionnaire administered during the study
125 collected demographic data as well and evaluated the COVID-19 knowledge, attitudes and
126 perceptions (KAP) of study participants.

127

128

129 **Methods**

130 *Study design*

131 This study was a multi-site repeated observational cross-sectional study carried out over a
132 period of 7 months from July 27, 2020 to February 26, 2021. Phase I was performed
133 between 27 July and September 14, 2020 (designated August 2020), followed by additional
134 phases in October 2020, December 2020 and February 2021 to identify changes from the
135 initial rates observed at public places (Figure S1). For ease of reference in the text, and for
136 site anonymity, the sites were assigned codes based on site type and risk factors: markets
137 and lorry stations (ML), malls (M), research centres (R), hospitals (H) and generalised
138 community screening (C). Generalised community screening included attendees at a concert
139 since that reflected individuals who would be otherwise dispersed through the community. A
140 research centre involved in mass COVID-19 testing and a COVID-19 treatment centre were
141 given the respective codes, RC and HC. Phase I participants were invited to volunteer for
142 the study at two shopping malls, three major markets/lorry stations (ML1-3), two research
143 institutes involved in COVID-19 work (R1) and COVID-19 testing (RC), and three major
144 hospitals, one of which was a COVID-19 treatment centre (H1, H2, and HC). Informed
145 consent was obtained from all study participants. Exposure to COVID-19 was detected using
146 a strip-in-cassette lateral flow rapid diagnostic test kit which simultaneously detects IgM and
147 IgG antibodies against SARS-CoV-2 antigens. Phase II screened participants at one market
148 (ML4), one research centre (R1) and two hospitals (H1, H4) while Phase III screened
149 participants at ML1 and across two towns in the Upper East Region (C1). During Phase IV,
150 the exposure levels of upper-income earners were evaluated by screening at 2 malls (M1
151 and M3) and a repeat screening at H2. In addition, the exposure level in a small town (C3) in
152 the Eastern Region, near Accra, was estimated. Screening at hospitals and research
153 facilities included only staff members and their close contacts; patients at the hospitals were
154 excluded from this study. All tests were performed on-site and participants were
155 subsequently informed of their exposure status and counselled to adhere to COVID-19

156 mitigation protocols. When IgM was detected, participants were referred for a COVID-19
157 PCR test.

158

159 *Testing kit*

160 The 'UNSCIENCE COVID-19 IgG/IgM antibody Rapid Test Kit' (Catalogue# UNCOV-40, Lot
161 Number 20200326) was registered with the Ghana FDA, and the kit validation report was
162 submitted to the Ghana Food and Drug Authority (FDA). For the validation exercise, sera
163 from RT-PCR confirmed COVID-19 cases were used to evaluate several kits' performance
164 since there were no established SARS-CoV-2 antibody detection standards for use at the
165 commencement of this study. This kit had a manufacturer-declared IgG sensitivity and
166 specificity of over 98% (<https://covid-19-diagnostics.jrc.ec.europa.eu/devices/detail/634>).
167 Using the Ghana Food and Drugs Authority (FDA) validation protocol³⁶, the UNSCIENCE kit
168 demonstrated a sensitivity of 66% when tested using 100 Ghanaian convalescent COVID-19
169 patient sera (2-4 weeks after a PCR-positive result). We checked the existence of pre-
170 existing cross-reactive antibodies using sera from 100 PCR-verified COVID-19 negative
171 samples and obtained a specificity of 94%. In the validation exercises, when a test result
172 was not obvious, at least 3 researchers validated the reading. In the rare case of an invalid
173 test (no control line, or wrong location of bands), the test was repeated. A representative set
174 of randomly chosen positive and negative test results are shown in Figure S2. The kit was
175 also adjudged to have a concordance of 72% with the WHO-recommended Wantai ELISA kit
176 (<https://www.fda.gov/media/140929/download>).

177

178 *Data management and analysis*

179 A short questionnaire was administered to capture participant demographic data, knowledge
180 of COVID-19 and COVID-19 testing history. The data, including the antibody test results
181 were entered and managed using Research Electronic Data Capture suite (REDCap) [28].
182 The data were cleaned by checking for completeness, duplication and consistency. Cleaned
183 data were analyzed with Stata 16 (StataCorp, College Station, Texas, USA) and R/RStudio

184 [29, 30]. GraphPad Prism version 8.0.0 [31] was used for some additional analysis and
185 generation of figures. Descriptive analyses were performed and univariate and multivariate
186 logistic regression models were used to assess the association between seroprevalence and
187 risk factors. Multivariable logistic models for seropositivity were obtained by using a
188 backward stepwise procedure. Demographic variables that were associated with
189 seropositivity at the $P < 0.25$ level were included. The overall goodness of fit was assessed
190 using the Wald statistic. Unadjusted and adjusted odds ratios with 95% confidence intervals
191 were computed and presented as parallel dot plots with error bars. Statistical significance
192 was inferred for p -values below 0.05.

193

194 **Results**

195 ***Study sites and participant characteristics***

196 A total of 2729 participants were screened for this study (Figure S1), including 1305 in
197 Phase I (10 sites: August, 2020), 395 in Phase II (4 sites: October, 2020), 393 in Phase III (2
198 sites: December, 2020) and 636 in Phase IV (4 sites: February 2021) . Altogether, four
199 markets/lorry stations (ML-1 was visited twice), three malls (M1, twice), two research
200 institutes (R, twice), two sets of small towns locations (C1 and C3) and four hospitals (H1
201 and H2, twice) were screened across all Phases. During Phase III, 200 individuals were also
202 screened from Navrongo and Bolgatanga in the Upper East Region (C1), which had the
203 lowest reported COVID-19 cases in Ghana at the time the study began. Attendees (81) at a
204 free Afrochella concert in Accra were also screened during Phase III (C2), potentially
205 representing a general cross-section of the GAR population.

206 During Phase I, 946 individuals were sampled in public spaces, including 616 at
207 markets/lorry stations and 330 at malls, while 359 were sampled in healthcare (254) and
208 research (105) facilities (Table 1). There was a slightly higher number of female participants
209 than males. The modal age range was 21–40 years, and over 40% of the participants had a
210 tertiary education. Tertiary education was defined as having a post-secondary qualification
211 such as a diploma, degree or above. Most respondents worked in the informal sector, with
212 low or mid-level socioeconomic status. Over 90% of participants had good knowledge of
213 COVID-19 symptoms, transmission routes and preventative measures (Figure S3). Such
214 knowledge did not, however, correlate with participants' seropositivity status or mask-
215 wearing prior to recruitment. Only 7% of participants had previously received a COVID-19
216 PCR test (Figure S4). Similar participant characteristics were observed in Phases II, III and
217 IV with smaller numbers of participants.

218 **Table 1: Socio-demographic characteristics of participants (N=2729)**

Characteristics	Phase 1 (n=1305)		Phase 2 (n=395)		Phase 3 (n=393)		Phase 4 (n=636)	
	number	Percentage	number	Percentage	number	Percentage	number	Percentage
Exposure risk groups								
Shopping malls (M)	330	25.3					356	56.0
Markets/Lorry stations (ML)	616	47.2	152	38.5	115	36.5		
COVID testing/treatment centres (RC/HC)	105	8.0						
Other Health Research centres/Hospital R/H	254	19.5	243	61.5			81	12.7
Navrongo/Bolgatanga (C1)					200	63.5		
Afrochella Concert (C2)					78	19.8		
Akropong (C3)							199	31.3
Gender								
Male	591	45.3	124	31.4	177	45.0	295	46.4
Female	714	54.7	271	68.6	216	55.0	341	53.6
Age group (in years)								
<21	63	4.8	13	3.3	63	16.0	44	6.9
21-40	769	58.9	216	54.7	251	63.9	362	56.9
41-60	365	28.0	119	30.1	57	14.5	167	26.3
60+	89	6.8	13	3.3	7	1.8	62	9.7

Characteristics	Phase 1 (n=1305)		Phase 2 (n=395)		Phase 3 (n=393)		Phase 4 (n=636)	
	number	Percentage	number	Percentage	number	Percentage	number	Percentage
Missing	19	1.5	34	8.6	15	3.8	1	0.2
Educational level								
None/Basic	402	30.8	128	32.4	117	29.8	202	31.8
Secondary	245	18.8	54	13.7	148	37.7	139	21.9
Tertiary	616	47.2	133	33.7	106	27.0	279	43.9
Missing	42	3.2	80	20.3	22	5.6	16	2.5
Employment type								
Formal	520	39.8	171	43.3	72	18.3	257	40.4
Informal	655	50.2	175	44.3	190	48.3	261	41.0
Student	59	4.5	21	5.3	114	29.0	48	7.5
Unemployed	44	3.4	19	4.8	11	2.8	70	11.0
Missing	27	2.1	9	2.3	6	1.5	0	0.0
Socio-economic status								
Lowest	524	40.2	170	43.0	158	40.2	249	39.2
Middle	259	19.8	122	30.9	78	19.8	124	19.5
Higher	522	40.0	103	26.1	157	39.9	263	41.4

219 ***Anti-SARS-CoV-2 seropositivity in Phase I***

220 In Phase I, SARS-CoV-2 IgG, IgM or both antibodies were detected in 19% of all participants
221 (Figure 2A), with the highest rate amongst participants sampled in markets/lorry stations
222 (27%). Among health workers, those at COVID-19 treatment/testing sites had higher
223 exposure rates compared to their colleagues who were not directly handling COVID-19
224 patients or samples. There was no significant difference in seropositivity across genders
225 (Figure 2B). When stratified by age categories, the highest level of seroprevalence (27.1%)
226 was observed in the 41–60 years age group (Figure 2C). Participants with higher
227 educational backgrounds (Figure 2D), those employed in the formal sector (Figure 2E) and
228 those with higher economic standing (Figure 2F) had lower exposure levels than participants
229 with lower educational background, informal sector workers and poor economic background.
230 Only 20.9% of seropositive participants reported having had COVID-19-like symptoms
231 (Figure 3).

232 Logistic regression analysis was performed on data from Phase I to identify factors that
233 correlated with increased risk of SARS-CoV-2 exposure (Figure 4). Univariate modelling
234 showed that socio-demographic factors were significantly associated with increased or
235 decreased exposure. These were: being sampled at either markets and lorry stations (Odds
236 ratio, OR:3.6, 95% confidence interval, CI: 2.4-5.4) or a COVID-19 treatment/testing centre
237 (OR: 2.4, 95% CI:1.3-4.4.), being employed in the informal sector (OR: 1.8, 95% CI:1.3-2.4)
238 having a high education (OR: 0.4, 95% CI:0.3-0.6) or having a high income (OR:0.6, 95%
239 CI:0.5-0.9). In a multivariate model, sampling location, participant educational level and
240 income/socioeconomic status remained significantly associated with COVID-19 exposure
241 status; participants were significantly more likely to have COVID-19 antibodies if they were
242 sampled in markets/lorry stations (adjusted odds ratio, aOR: 2.5, 95% CI: 1.5-4.2), and
243 COVID-19 testing/treatment centre (aOR:3.6, 95%CI:1.7-7.5). Participants who had basic or
244 no formal education (aOR: 0.8, 95% CI: 0.5-1.3) had a higher risk of COVID-19
245 seropositivity. Unemployed individuals (aOR: 0.7, 95% CI: 0.2-2.1) (Table 2, Figure 4), those

246 with high educational level (aOR: 0.8, 95%CI: 0.5-1.3) and high socioeconomic status (aOR:
247 0.8, 95%CI: 0.6-1.2) had reduced risk of COVID-19 seropositivity, but these associations
248 were not statistically significant (Table 2, Figure 4).

Table 2: Summary of participant seropositivity status (N=2729)

	August 2020 (n=1305)		Oct 2020 (n=395)		Dec - 2020 (n=393)		Jan- Feb 2021 (n=636)	
	Number	Antibody Positivity	Number	Antibody Positivity	Number	Antibody Positivity	Number	Antibody Positivity
	Sampled	%	Sampled	%	Sampled	%	Sampled	%
Sampling location (Code)								
Shopping malls (M)	330	9.4					356	25.3
Markets/Lorry stations (ML)	616	26.9	152	19.7	115	23.5		
COVID testing/treatment Centres (RC/HC)	105	20.0						
Health Research Centres/Hospital (R/H)	254	13.4	243	14.0			81	22.2
Navrongo/Bolgatanga (C1)					200	2.0		
Afrochella Concert (C2)					78.0	15.4		
Akropong (C3)							199	18.6
Gender								
Male	591	18.1	124	14.5	131	1.7	10.7	22.7
Female	714	20.3	271	17.0	184	2.8	11.1	22.9
Age group (in years)								
4-21	63	17.5	13	0.0	63	11.1	44	9.1
21-40	769	16.1	216	11.1	251	11.6	362	24.9
41-60	365	27.1	119	21.8	57	10.5	167	22.8
60+	89	18.0	13	38.5	7.0	14.3	62	21.0
Missing	19	10.5	34	26.5	15	0.0	1	0.0

	August 2020 (n=1305)		Oct 2020 (n=395)		Dec - 2020 (n=393)		Jan- Feb 2021 (n=636)	
	Number	Antibody Positivity	Number	Antibody Positivity	Number	Antibody Positivity	Number	Antibody Positivity
	Sampled	%	Sampled	%	Sampled	%	Sampled	%
Educational level								
None/Basic	402	26.6	128	22.7	117	12.0	202	17.8
Secondary	245	24.5	54	14.8	148	11.5	139	25.9
Tertiary	616	13.5	133	15.0	106	10.4	279	24.7
Missing	42	4.8	80	8.8	22	4.5	16	25.0
Employment type								
Formal	520	15.0	171	11.7	72	6.9	257	23.7
Informal	655	24.0	175	20.6	190	13.7	261	24.9
Student	59	16.9	21	4.8	114	9.6	48	12.5
Unemployed	44	9.1	19	21.1	11	0	70	18.6
Missing	27	11.1	9	33.3	6	16.7		
Socio-economic status								
Low	524	23.1	170	17.1	158	15.8	249	18.1
Middle	259	19.7	122	15.6	78	10.3	124	25.0
High	522	15.3	103	15.5	157	6.4	263	26.2
		IgG		IgG		IgG		IgG
		13.0		15.2		9.7		22.8
		IgM		IgM		IgM		IgM
		1.6		1.3		2.3		2.2

251 ***Phases II and III: Targeted follow-up seroprevalence surveys***

252 As follow-ups to Phase I, the trend of population seroprevalence was again investigated in
253 Phase II and III. Two months after the initial public places screening (October, 2020), 144
254 individuals were screened at a lorry station in Accra and 212 participants at two hospitals in
255 Accra and Cape Coast. Overall, seroprevalence at the lorry station was 19.7%, and 13% at
256 the two hospitals. The H4 facility staff had higher (18.5%) seroprevalence level than those at
257 H1, previously sampled in Phase I. A Phase III screening exercise was conducted at M1,
258 which was originally sampled in Phase I, and that showed an estimated seroprevalence of
259 23.5%. Additionally, 200 individuals were screened in the Upper East Region (C1), an area
260 with low population density and very few reported COVID-19 cases at the time. Here, 4 out
261 of 200 individuals (2%) tested positive for SARS-CoV-2 antibodies (Table 1). Individuals
262 screened at the Afrochella concert (C2) showed an estimated seroprevalence of 16%, which
263 was similar to the Phase I data, with the HC site excluded.

264 ***Phase IV: Impact of the second wave***

265 Beginning in late December 2020, large numbers of symptomatic COVID-19 cases started to
266 be detected at hospitals and treatment centres in Accra and other major cities. The patients
267 were mostly of high socio-economic standing [32]. We therefore performed repeat screening
268 at M1 and H2 (both sampled in Phase I) and sampled again at M3 and a small town in the
269 Eastern Region (C3). The average seroprevalence at the two malls (M1 and M3) was at
270 27%, whilst H1 and C3 recorded 25% and 17% respectively.

271 **Discussion**

272 This study was necessitated by a dearth of epidemiological data on COVID-19 prevalence in
273 Ghana. In the first few months of the pandemic when prevalence was low, Ghana ranked
274 high among African countries, and even globally, for administering high numbers of tests per
275 million people [33]. To meet the high demand for testing, Ghana's main testing centre,
276 Noguchi Memorial Institute for Medical Research, employed "sample pooling" methods [34-

277 37]. However, since then, Ghana has declined significantly to number 22 in tests per million
278 of population in Africa [38]. Data from the Ghana Health Service's COVID-19 archives [3]
279 indicates that testing has significantly reduced after peaking in June, correlating with a drop
280 in daily reported cases. Among other factors, the reduced testing could be due to the fact
281 that at the current positivity rate of 8.3% of tested cases, sample pooling is no longer a
282 viable cost-cutting and test-rate enhancing measure. The seroprevalence rate average of
283 19.3% obtained from our public screening exercises is probably a better reflection of SARS-
284 CoV-2 infections in Ghana, especially in the large and densely populated urban areas.
285 Additionally, currently, most RT-PCR tests in the country are administered to travellers,
286 representing a higher economic tier of society. The relatively low (9.3%) seroprevalence
287 initially observed in malls, assumed to be frequented by the higher tiers of society, may
288 correlate well with the official 10% RT-PCR test positivity rate reported in September 2020
289 [3].

290 Participants across all sites demonstrated good knowledge of COVID-19 risks, symptoms
291 and preventive measures. This did not however translate into observation of protocols in the
292 markets and lorry stations, where, by visual estimation, 10–50% of the study participants
293 arrived mask-less and had to be requested to wear a mask donated by the study. This
294 attitude corresponds with two surveys on mask-wearing, carried out by the Ghana Health
295 Service which showed public mask wearing of ~40% and 10% in July and September,
296 respectively [39, 40]. Our previous genomic study showed evidence of undetected
297 community spread likely caused by asymptomatic individuals [27]. Of note, nearly 80% of
298 people who were seropositive did not report significant COVID-19 symptoms (Figure 3),
299 confirming that SARS-CoV-2 infections in Ghana are predominantly asymptomatic,
300 consistent with reported global trends [8]. With the 19.3% seroprevalence in the Greater
301 Accra Region (GAR), we inferred that nearly 1 million out of the estimated 5 million GAR
302 residents may have already been exposed to SARS-CoV-2. This staggering number
303 suggests that the actual fatality rate of COVID-19 in Ghana may be much lower than the

304 reported CFR of 0.7%, since that would have translated to approximately 7000 deaths in a
305 large metropolis like Accra, which would have been rather very obvious . Additionally, there
306 was no evidence of a stressed or panicked healthcare system nor visible or anecdotal
307 evidence of excess deaths during the Phase I hospital screening.

308 Given the higher-than-expected seroprevalence observed in the Greater Accra Region,
309 follow-up surveys were conducted at some of the Phase I locations as well as other parts of
310 the country to confirm the findings and obtain vital information about infection dynamics over
311 time. Repeated screening of markets and lorry stations in October and December yielded
312 seroprevalence rates of 19.7% and 23.5%, respectively. The seeming plateau in
313 seroprevalence in lower socioeconomic status individuals may be indicative of, either a
314 peaking of infections -coincident with the onset of Phase I seroprevalence [3], or loss of
315 antibody expression in some section of the population over time. Phase II surveys at the
316 health and research facilities which were not directly handling patients or testing samples, in
317 October, also showed a similar overall seroprevalence (13%), as observed in August.
318 Participants in Navrongo and Bolgatanga in the Upper East region (C1), with some of the
319 lowest reported cases, showed very low (2%) seroprevalence, confirming the reliability of
320 this study. Consistent with global reports, participants in the 40-60 and 60+ year age groups
321 exhibited the highest seroprevalence levels across all 3 phases (Figure 4, S4, S5). The
322 results of Phase IV reflected the high levels of new COVID-19 cases and hospitalisations in
323 Ghana, mainly in the middle socioeconomic class [32]. As such, it was not surprising that the
324 socioeconomic divide in prevalence observed in Phase I had mostly disappeared and even
325 appeared reversed by Phase IV.

326 Our observed seropositivity rates are in line with previous reports from other African
327 countries[41, 42]. A study in Kenya estimated 20% SARS-CoV-2 seropositivity in adults
328 (~1.6 million people) at a time when the total reported infections were 2093 (with
329 approximately 90% asymptomatic cases) and 71 deaths of all ages [43]. The initial trend
330 relating income disparity and COVID-19 seropositivity is not surprising. Even in countries

331 where lower seroprevalence was reported, such as China (1.63%), lower income status
332 correlated with the highest seroprevalence (5.62%) [44], and this trend was initially reflected
333 in this current study. The shift to high prevalence even in high socioeconomic brackets is
334 likely due to poor adherence to COVID-19 protocols during the period of this study, likely
335 due to election activities [45] and the 2020 Christmas/2021 New Year holiday festivities.

336 ***Strengths and Limitations of this study***

337 By surveying participants at different sites and times, representing categories of different
338 perceived risk factors, this study obtained credible estimates for population-level prevalence
339 across these sites and how that changed over the sampling period. This will allow future
340 screening at these sites to determine the seroprevalence trends. However, most
341 seroprevalence studies only reflect past disease burden. Using Markets and Lorry Stations
342 enabled sampling of a broad cross-section of the Ghanaian populace.

343 Phase I of the study was conducted in the region with the greatest burden of reported
344 infections and it was expected that a country-wide survey would yield less seroprevalence.
345 Site H3, situated in the town of Cape Coast, a tourist hub and Central regional capital,
346 exhibited a very high prevalence at 18.5% during Phase II, but this was not surprising given
347 that M4, located in Kasoa, also in the Central Region, exhibited an exposure rate of 28%
348 during Phase I. The low seroprevalence observed at C1 (2%) during Phase III hinted that
349 community size/density may play a role in COVID-19 transmission. Given the geographical
350 remoteness of C1 to the major hotspots of Accra and Kumasi, another small community (C3)
351 in the country's Southern belt with higher population density was screened, yielding an
352 observed prevalence rate of 17%, and showing that SARS-CoV-2 exposure is not just a
353 metropolitan burden, but one that needs to be tracked across the country. This, however,
354 does not rule out that towns with lower population densities and who are far from
355 metropolitan areas may exhibit lower seroprevalence levels.

356 During validation, this kit showed a sensitivity of 66%, when compared to PCR positivity.
357 This is despite the manufacturer reporting sensitivity and specificity values above 98%. The
358 apparent lower than expected sensitivity observed in local validation could at least partly be
359 due to weak or delayed antibody responses in some of the infected persons. The import of
360 this is that the seroprevalence levels reported in this study are likely underestimates of true
361 disease prevalence.

362 One oft-repeated concern with SARS-CoV-2 seroprevalence studies in Africa is cross-
363 reactivity due to pre-existing antibodies to other viruses and vaccines [46]. Some studies
364 have reported extensive cross-reactivity against SARS-CoV-2 in Africa [47]). However, most
365 of these studies had limitations, and as such their conclusions are unreliable. These flaws
366 include extremely small study sizes (below 500 and even sometimes below 100) [48], tend
367 to be based at single institutions and/or cities [47] and use samples collected at widely
368 divergent time periods for their 'Western' and 'African' pre-COVID-19 samples [48]. The
369 UNSCIENCE COVID-19 IgG/IgM antibody Rapid Test Kit used in our study exhibited 94%
370 specificity during validation (with plasma from 100 COVID-19 PCR-negative individuals).
371 Antibody RDTs are contraindicated in cases of active fever, based on manufacturer's
372 information leaflets, unpublished analyses and other studies [47]. We confirmed that none of
373 the study respondents had temperature above 38, thereby reducing the likelihood of fever
374 affecting the results.

375 Antibody cross-reactivity with other pathogens is often manifested in IgM detection [49, 50].
376 During validation, and in the field, detection of IgM was uncommon, and when detected, IgM
377 was often accompanied by IgG. This reduced the likelihood that those IgM detections were
378 as a result of cross-reactivity. That said, a cross-reactivity rate of 6% with IgM was detected
379 during validation. However, the test kit performed even better in the field; Navrongo and
380 Bolgatanga in the Upper-East region of Ghana are towns with populations highly vaccinated
381 against other pathogens, yet only 2% of 200 individuals (4 individuals) showed seropositivity
382 in this study. This low seropositivity correlated well with the low level of reported COVID-19 in

383 those towns at the time and hinted that the rates observed in Accra and environs were due
384 to the SARS-CoV-2 exposure rate, but not from cross-reactivity. Taken together, there is a
385 low likelihood that cross-reactive antibodies played a significant role in this study.

386 **Conclusions and Recommendations**

387 This study highlights a relatively high level of SARS-CoV-2 infections in the Greater Accra,
388 Central and Eastern Regions, but not in the Upper East region. Most of these infections
389 were unreported and likely asymptomatic.

390 As one of the first studies with such depth and nuance, we provide some of the first
391 evidence of low levels of symptomatic COVID-19 infection, previously only anecdotally
392 reported. These findings imply that there is a need for increased enforcement of COVID-19
393 mitigation protocols and more effective public education.

394 Large scale cross-sectional studies of seroprevalence across Ghana and West Africa may
395 be a practical approach for disease tracking even as vaccines are being deployed^{55,56}. The
396 dynamism observed in demographic exposure risk over time highlights the need for
397 continuous risk and prevalence assessments to track highly transmissible disease agents
398 like SARS-CoV-2.

399 Finally, resources should be mobilised to research the molecular and immunological
400 mechanisms underlying the apparent high tolerance to COVID-19 observed in Ghana, the
401 West African sub-region, and Africa as a whole.

402

403

404 **Ethical Approval**

405 Procedures in this study conform with the Ghanaian Public Health Act, 2012 (Act 851) and
406 the Data Protection Act, 2012 (Act 843). Ethical approval was received from the Ethics
407 Board of the College of Basic and Applied Sciences, University of Ghana (ECBAS 063/19-
408 20), and the Ethical Review Committee of the Ghana Health Service (GHS-ERC 011/03/20).

409

410 **Consent**

411 In line with the ethical protocol above, written informed consent was obtained for all study
412 participants. Upon consent, each participant was assigned a unique identification number
413 (ID). This ID was used for testing and data recording, thereby delinking participant
414 identification with the test results and questionnaire answers. All consent forms are kept in a
415 locked cabinet accessible to only the study PI and the WACCBIP Data Manager.

416 **Other WACCBIP COVID-19 Team members**

417 Kyerewaa Boateng¹, Jerry Quaye^{1,3}, Aaron Adom Manu¹, Eugene Boateng^{1,3}, Daniel
418 Lorlorson Okpatah^{1,3}, Louisa Baaba Obbeng¹, Oforiwaa Ofori^{1,3}, Peggy Afua Agypomaah
419 Birikorang^{1,3}, Simon Donkoh¹, Sylvester Languon^{1,3}, Stephen Kotei Kotey^{1,3}, Alexandra
420 Lindsey Zune Djomkam^{1,3}, Adelaide Fierti^{1,3}, Claudia Adzo Anyigba^{1,3}, Nancy Nyakoe^{1,3},
421 Felix Ansah^{1,3}, Darius Quansah^{1,3,4}, Sylvia Tawiah-Eshun¹, Barikisu Anna Ibrahim¹, Elizabeth
422 Fosua¹, Raymond Adjei¹

423 **Author contributions**

424 GAA and FM conceived the study. GAA and PKQ designed the study, wrote the SOP for the
425 fieldwork and supervised all aspects. YB, JKM, PCO, PKQ, WKA, AJU and some members
426 of WCT performed validation of the kit. PKQ, JKM, PCO, DO-M, AJU, WCT, FK, EA, IA, LP,
427 RA, CK, NAB, YB, JA, PA and GAA participated in seroprevalence screening activities. KB
428 planned the site visits and partook in screening activities. PKQ, FD and PCO analysed the
429 data. PKQ, JKM and GAA wrote the manuscript with additional editing by DO-M, YB, OQ and
430 NN. All authors read and approved the final version of the manuscript before submission.

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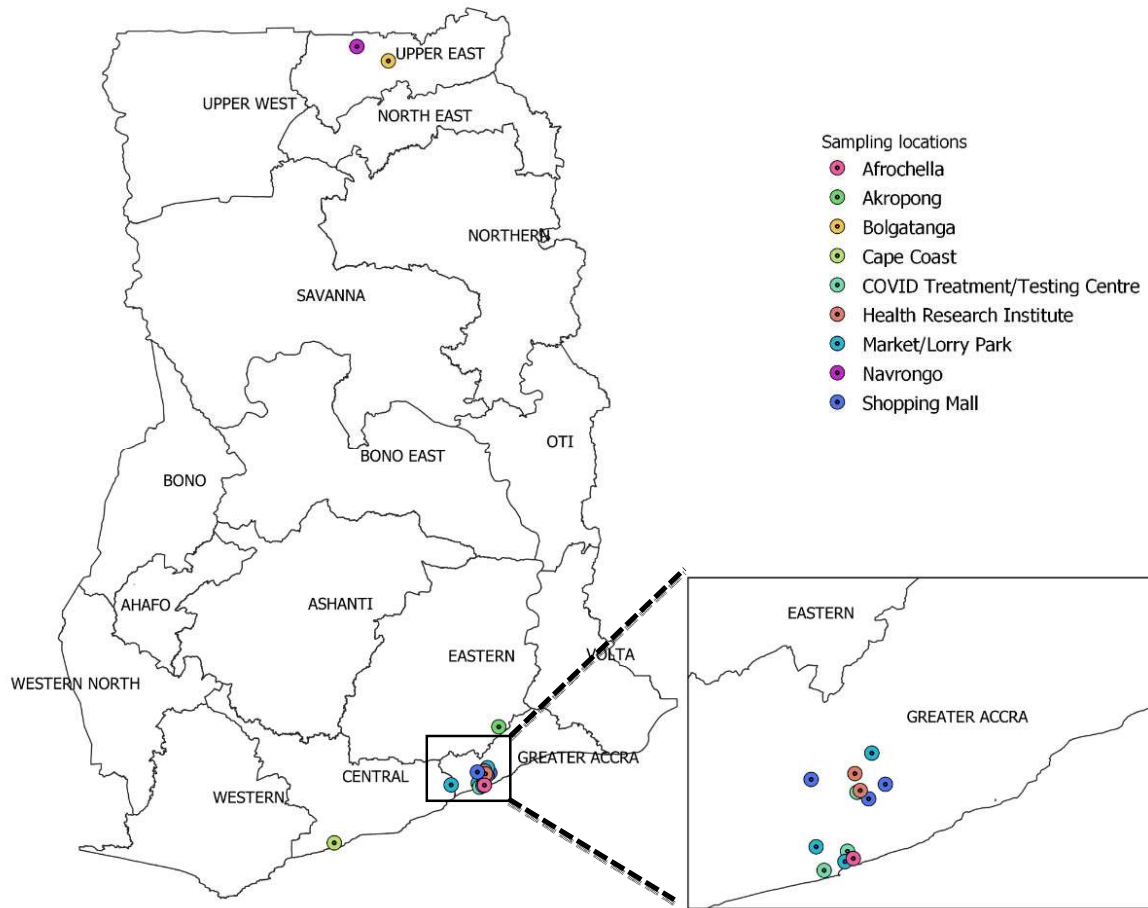
446 **Conflicts of Interest**

447 None to declare

448

449

450 **Figures**



452 **Figure 1: Map of Ghana showing study sites.** Figure was generated using QGIS (QGIS
453 Development Team, 2009. QGIS Geographic Information System. Open Source Geospatial
454 Foundation. URL <http://qgis.org>)

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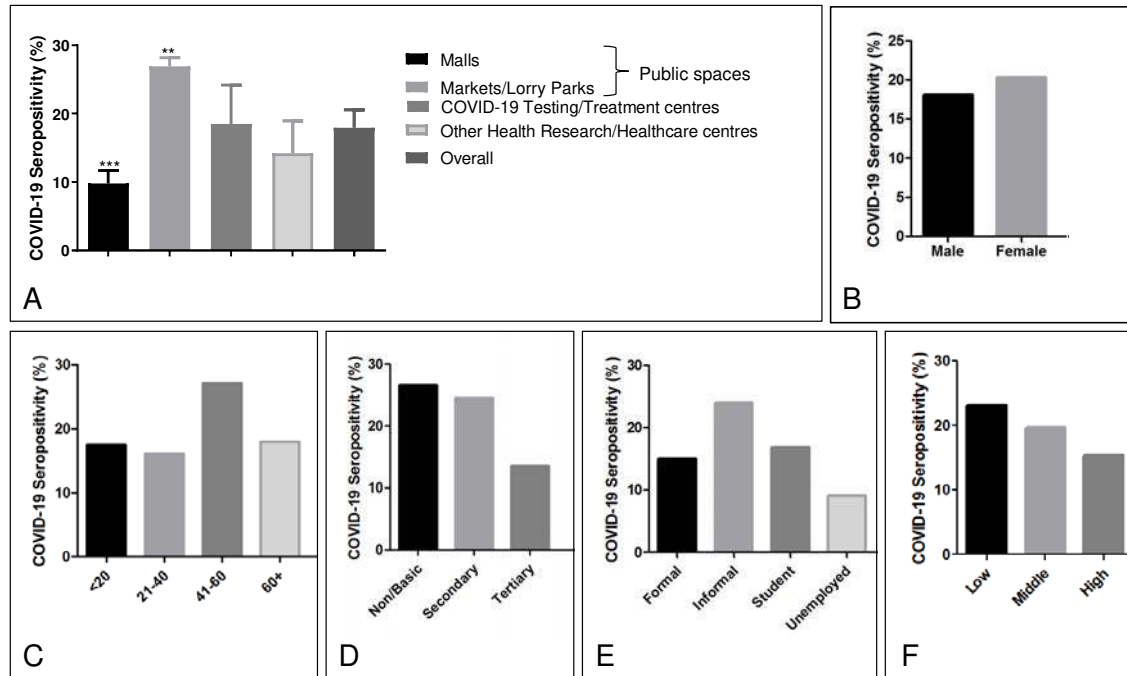
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463 **Figure 2: SARS-CoV-2 seropositivity reported by (A) Sampling sites, (B) gender, (C)**

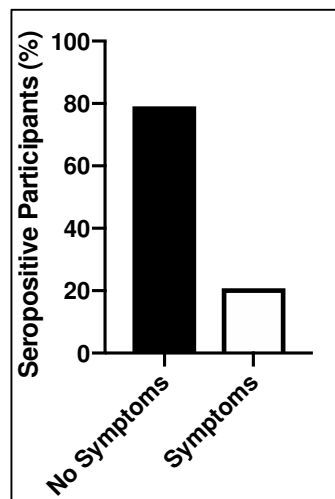
464 **Age, (D) Highest education level, (E) Employment status and (F) Socioeconomic**

465 **status.** Error bars reflect the standard error of measurement. Where relevant, p-values are

466 indicated as follows $p < 0.05$; *, $p < 0.01$; **, $p < 0.001$; ***. Error bars, where relevant, represent

467 standard deviation across sites.

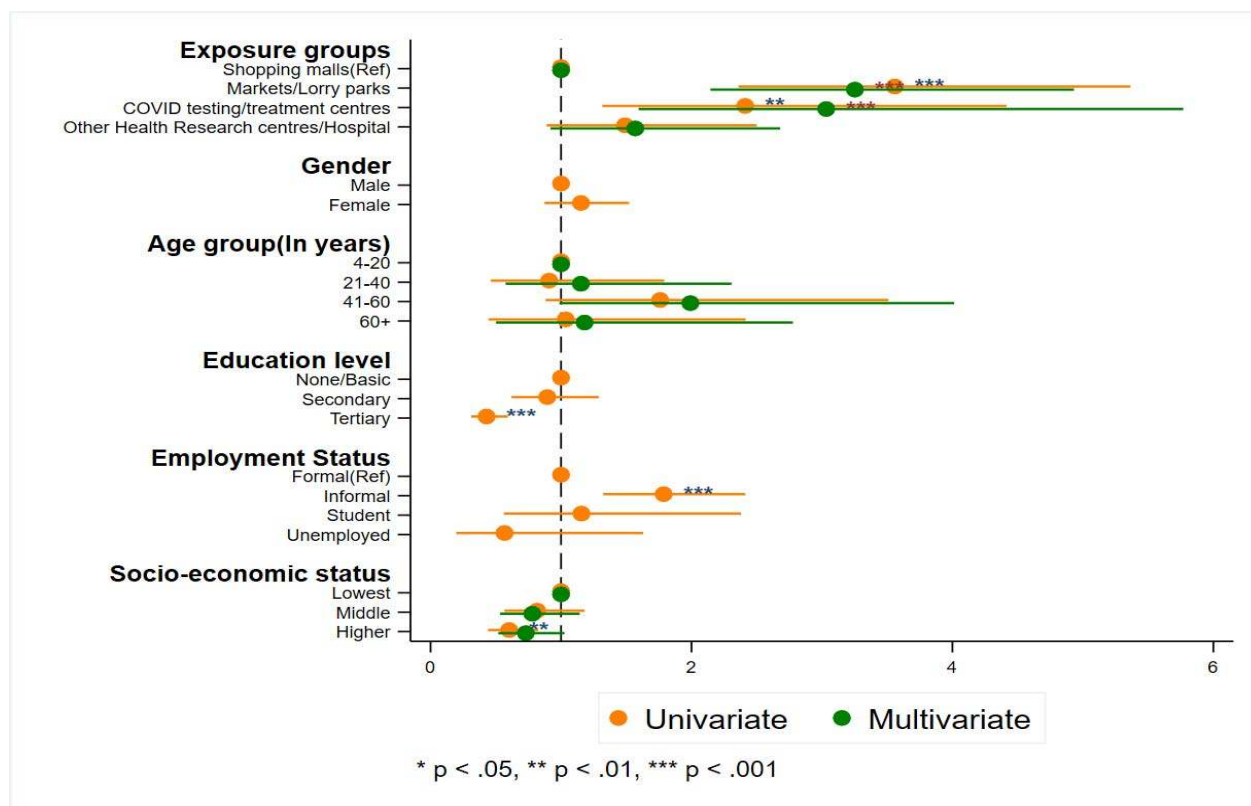
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469

470 **Figure 3 Presence of two or more self-reported COVID-19 symptoms in seropositive**

471 **individuals in the month preceding the study.**



472

473 **Figure 4: Modelling of COVID-19 exposure risk across Phase I study participant**

474

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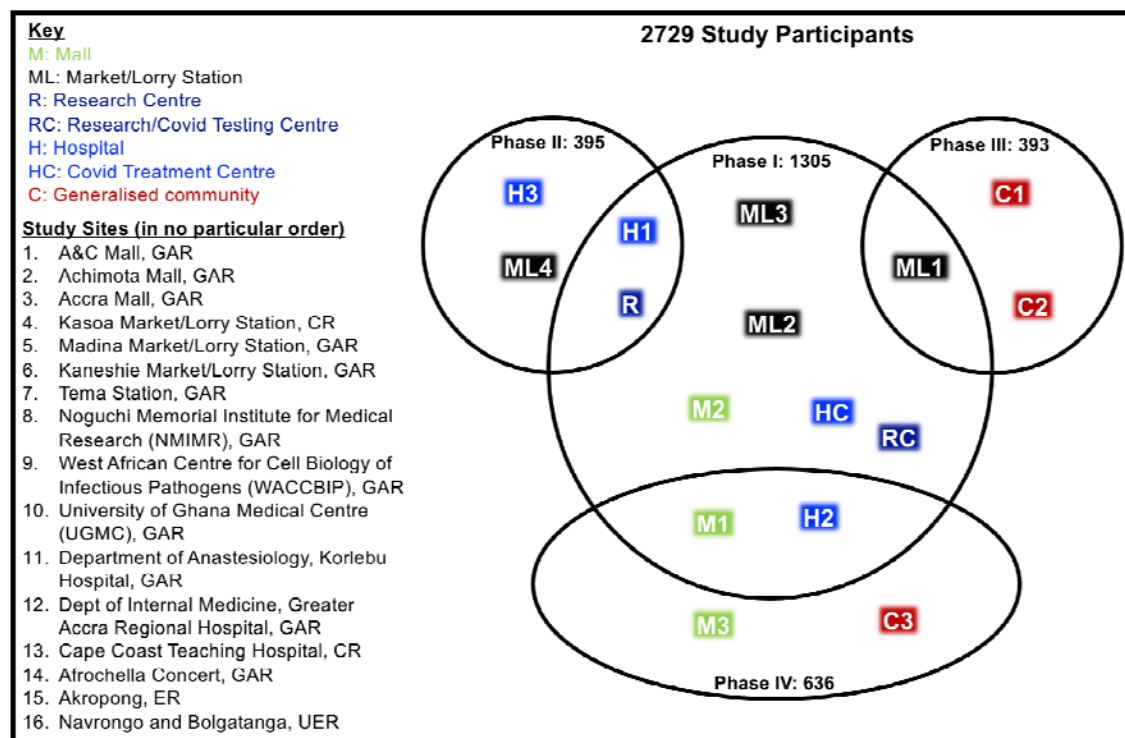
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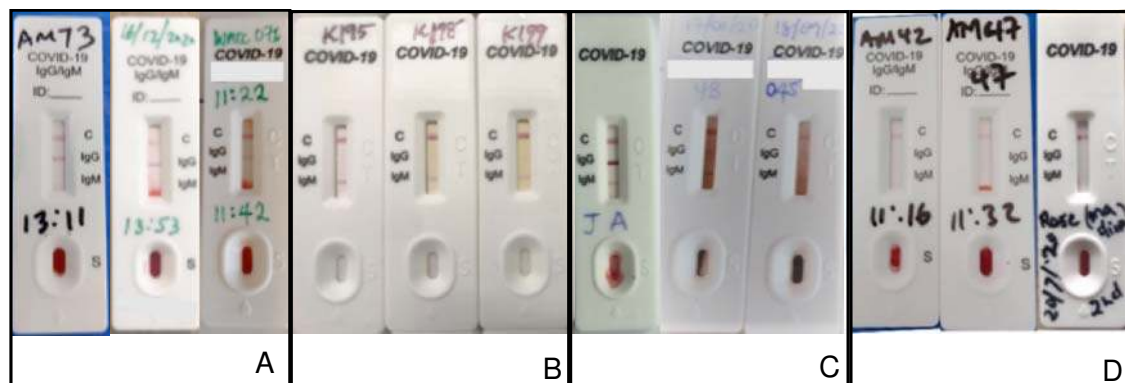
613 **Supplemental Files**



614

615 **Figure S1. Venn Diagram showing distribution of participants and sites across the**
 616 **different Phases of the study.** GAR refers to the Greater Accra Region, CR refers to the
 617 Central Region and UER refers to the Upper East Region.

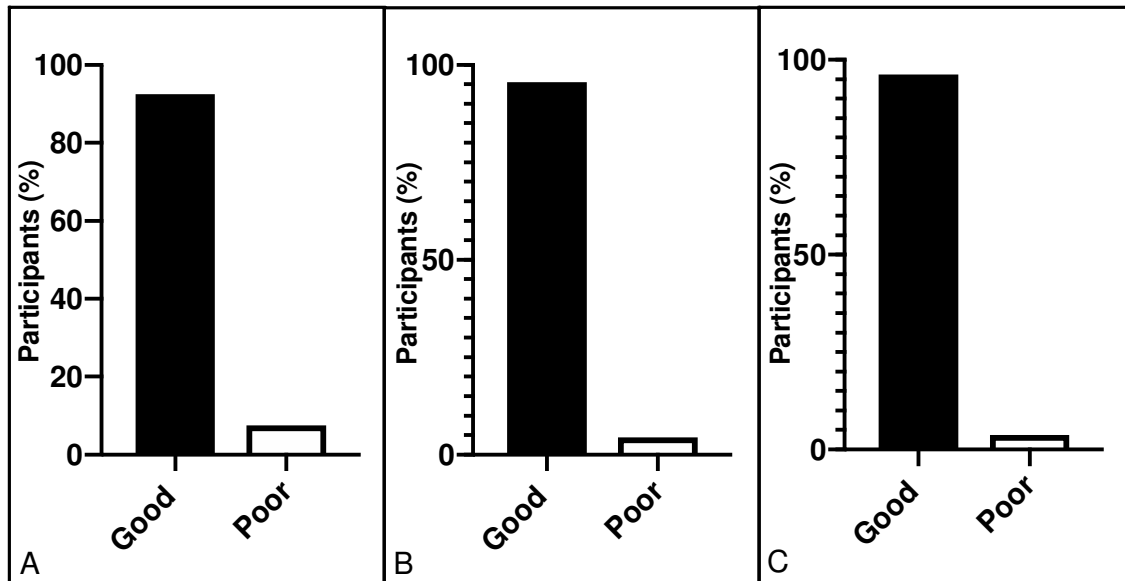
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620 **Figure S2: Representative pictures of study cassettes showing (A) Positive IgG, (B)**
 621 **Positive IgM*, (C) Combined positive IgM/IgG and (D) antibody negative test results.**

622 *Pictures of IgM are from patients, not from field due to low incidence of IgM only observed
 623 in the field and faintness of igM bands in the field

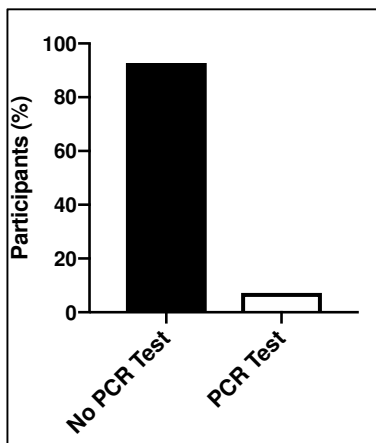


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625 **Figure S3: Summary of Phase I participants' knowledge of (A) COVID-19 symptoms,**

626 **(B) mode of transmission and (C) prevention**

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629 **Figure S4: Participants who had previously taken a PCR test that detects SARS-CoV-2**

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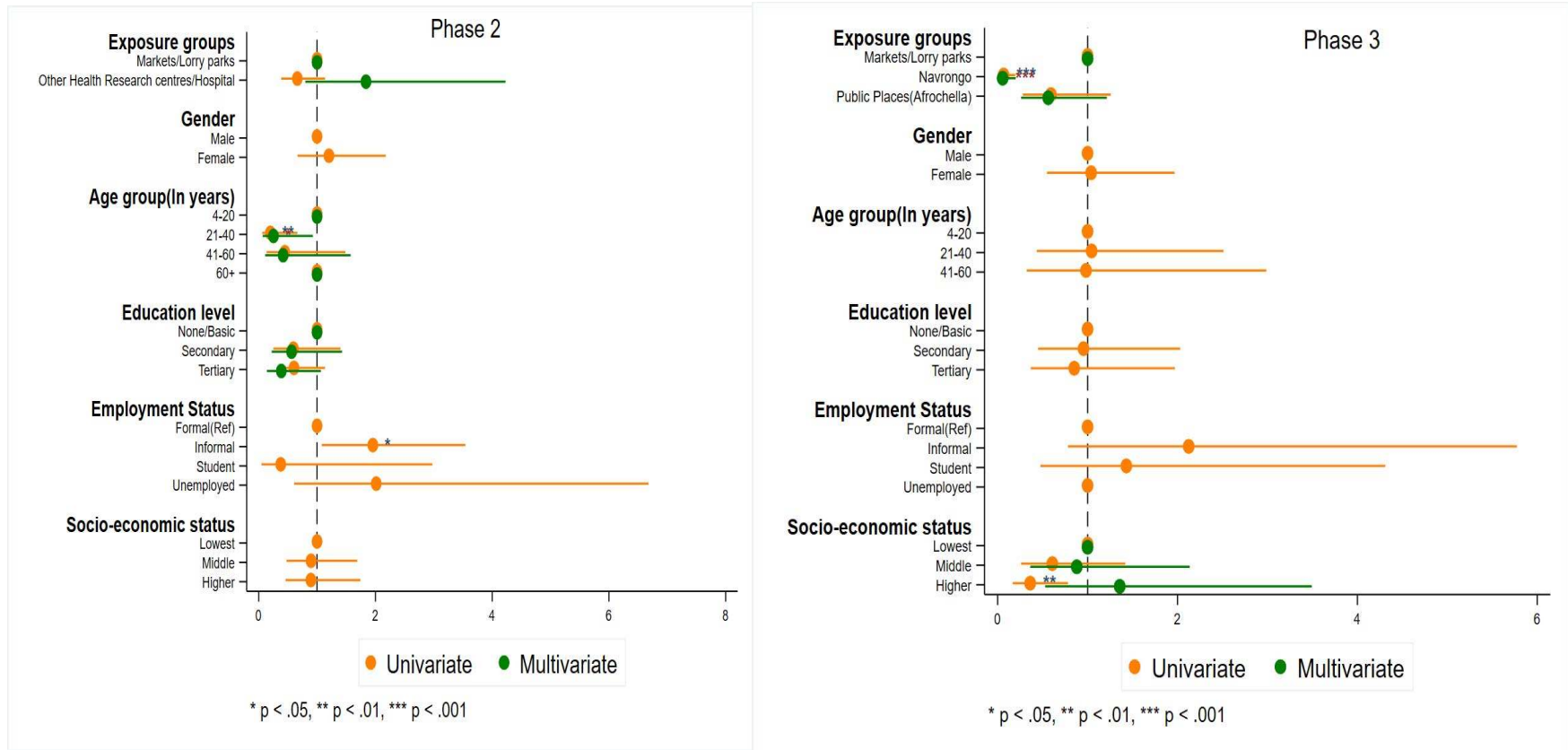
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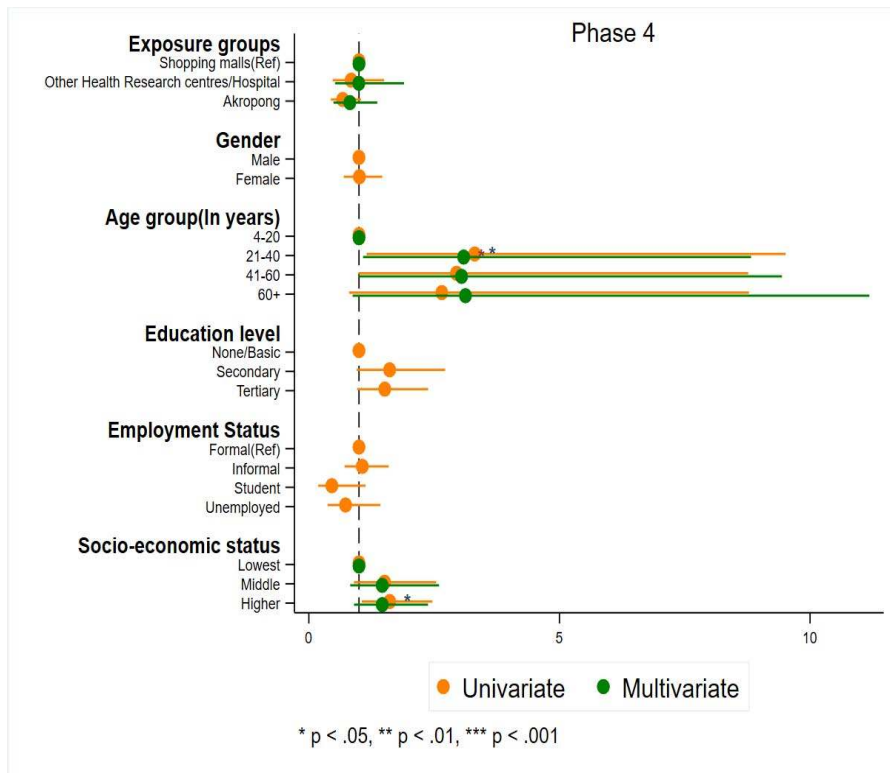
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637 **Figure S4: Regressional analysis of Phase II and III exposure rates**

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640 **Figure S5: Regressional analysis of results of Phase IV exposure rates**

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