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MAJOR ARTICLE

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Infection and Pregnancy in Sub-Saharan Africa: A 6-Country Retrospective Cohort Analysis

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Received 05 February 2022; editorial decision 7 April 2022

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https://doi.org/10.1093/cid/ciac294

Background. Few data are available on COVID-19 outcomes among pregnant women in sub-Saharan Africa (SSA), where high-risk comorbidities are prevalent. We investigated the impact of pregnancy on SARS-CoV-2 infection and of SARS-CoV-2 infection on pregnancy to generate evidence for health policy and clinical practice.

Methods. We conducted a 6-country retrospective cohort study among hospitalized women of childbearing age between 1 March 2020 and 31 March 2021. Exposures were (1) pregnancy and (2) a positive SARS-CoV-2 RT-PCR test. The primary outcome for both analyses was intensive care unit (ICU) admission. Secondary outcomes included supplemental oxygen requirement, mechanical ventilation, adverse birth outcomes, and in-hospital mortality. We used log-binomial regression to estimate the effect between pregnancy and SARS-CoV-2 infection. Factors associated with mortality were evaluated using competing-risk proportional subdistribution hazards models.

Results. Our analyses included 1315 hospitalized women: 510 pregnant women with SARS-CoV-2, 403 nonpregnant women with SARS-CoV-2, and 402 pregnant women without SARS-CoV-2 infection. Among women with SARS-CoV-2 infection, pregnancy was associated with increased risk for ICU admission (adjusted risk ratio [aRR]: 2.38; 95% CI: 1.42–4.01), oxygen supplementation (aRR: 1.86; 95% CI: 1.44–2.42), and hazard of in-hospital death (adjusted sub-hazard ratio [aSHR]: 2.00; 95% CI: 1.08–3.70). Among pregnant women, SARS-CoV-2 infection increased the risk of ICU admission (aRR: 2.0; 95% CI: 1.20–3.35), oxygen supplementation (aRR: 1.57; 95% CI: 1.17–2.11), and hazard of in-hospital death (aSHR: 5.03; 95% CI: 1.79–14.13).

Conclusions. Among hospitalized women in SSA, both SARS-CoV-2 infection and pregnancy independently increased risks of ICU admission, oxygen supplementation, and death. These data support international recommendations to prioritize COVID-19 vaccination among pregnant women.

Keywords. COVID-19; pregnancy; maternal; neonate; Africa.

Few studies have been published on the impact of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection on pregnancy in sub-Saharan Africa (SSA). Poor maternal and child health outcomes coupled with a high prevalence of communicable and noncommunicable diseases necessitate investigation of the impact of SARS-CoV-2 in these settings [1]. Reports from mostly outside SSA suggest that SARS-CoV-2 infection in pregnant women is associated with increased risk for intensive care unit (ICU) admission, invasive ventilation, and death when compared with similar-age, nonpregnant women with SARS-CoV-2 infection [2–6]. The multinational Multi-National Prospective Cohort Study of the Effects of COVID-19 in Pregnancy and Neonatal Period (INTERCOVID) cohort study determined that SARS-CoV-2 infection in pregnancy was associated with increased maternal and neonatal morbidity and mortality, when pregnant women with (n = 706) and without (n = 1424) SARS-CoV-2 infection were compared [7]. However, it included only 2 (West) African countries (Ghana and Nigeria), representing 5% of the cohort. Consequently, INTERCOVID was not powered to assess outcomes across SSA and did not include a control group of nonpregnant women with SARS-CoV-2 infection.

The African Forum for Research and Education in Health (AFREhealth) COVID-19 Research Collaboration is a multidisciplinary, pan-African consortium addressing maternal and child health issues relevant to SARS-CoV-2 [1, 8, 9]. Routine data collected as part of institutional and national coronavirus disease 2019 (COVID-19) responses are pooled from multiple countries and analyzed to inform health policy and clinical practice in SSA, where comorbidities such as human immunodeficiency virus (HIV), tuberculosis (TB), and malaria are highly prevalent and access to/availability of COVID-19 prevention and treatment is low [1, 10–12]. Here, we aimed to investigate the impact of pregnancy on SARS-CoV-2 infection and of SARS-CoV-2 infection on pregnancy in SSA and to provide evidence for vaccination and other prevention and treatment policy recommendations.

METHODS

Study Design, Participants, and Settings

We conducted a retrospective cohort study comparing clinical outcomes among 3 cohorts: (1) hospitalized pregnant women with Reverse Transcriptase–Polymerase Chain Reaction (RT-PCR)–confirmed SARS-CoV-2 infection, (2) hospitalized nonpregnant women with RT-PCR–confirmed SARS-CoV-2 infection, and (3) hospitalized pregnant women without RT-PCR–confirmed SARS-CoV-2 infection and admitted for other obstetrical or medical reasons. We pooled all available routinely collected COVID-19 data from women of childbearing age hospitalized between 1 March 2020 and 31 March 2021 from 22 sites in 6 SSA countries: the Democratic Republic of Congo, Ghana, Kenya, Nigeria, South Africa, and Uganda. Detailed information on sample size and power, participating sites, regulatory approvals, SARS-CoV-2 RT-PCR testing platforms, and STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) checklist [13] is available in Supplementary Tables 1–5 and Supplementary Figures 3 and 4.

Variables

The World Health Organization (WHO) COVID-19 pregnancy case report form was used to extract demographic and

clinical data from national or institutional COVID-19 datasets and/or hospital charts/registers [14]. Data collected included age and pregnancy status; signs, symptoms, and WHO COVID-19 stage at admission; HIV serostatus; TB (active and past); malaria; noncommunicable disease comorbidities; general clinical outcomes; and pregnancy-specific outcomes, including miscarriage (<28 weeks' gestation), stillbirth (>28 weeks' gestation), prematurity (<37 weeks), low infant birth weight (<2500 g), and mode of delivery (vaginal or cesarean). For missing data on pre-existing comorbidities, we conservatively assumed that the specific comorbidity was absent, to minimize bias.

Statistical Analysis

The 2 exposures of interest for the analyses (SARS-CoV-2 effect on pregnancy and vice versa) were (1) documented pregnancy and (2) a positive SARS-CoV-2 RT-PCR test. The primary outcome was ICU admission. Secondary outcomes included supplemental oxygen, mechanical ventilation, pregnancy/birth outcomes, and maternal/perinatal in-hospital mortality. All analyses were performed using STATA software version 16.1 (StataCorp, College Station, TX, USA).

Comparison of COVID-19 Outcomes by Pregnancy Status

We summarized baseline demographic and clinical characteristics using frequencies and proportions stratified by pregnancy status (pregnant or nonpregnant). Risk ratios and associated 95% confidence intervals (CIs) estimated by log-binomial regression models were used to measure the strength of association between pregnancy and outcomes. Demographic and comorbidity variables associated with each outcome were explored using bivariable log-binomial regression models, and those with *P* values less than .10 were included in multivariable regression models to identify potential confounders. To further explore the effect of confounding on our estimates of pregnancy effect on each outcome, an inverse probability-of-participation–based weighting (IPPW) regression approach was also used to adjust our analysis for baseline disparities. To estimate the weights, we first fitted a logistic regression model of "pregnant" versus "not pregnant" as a function of baseline characteristics hypothesized as potential confounders, including age, region, diabetes mellitus, HIV status, and history of TB. For each patient, we then estimated the probability of pregnancy from the fitted model based on her characteristics. Finally, we estimated the statistical weight for each patient as the inverse of her estimated probability of being pregnant if the patient was pregnant, or the inverse of the probability of nonpregnancy if the patient was not pregnant.

Time-to-death was evaluated by a competing risk analysis using cumulative incidence function, with patient's hospital transfer as a competing event and hospital discharge as a censoring event. Factors associated with in-hospital mortality were estimated using Fine and Gray's proportional subdistribution hazards model [15]. We used a multivariable proportional subdistribution hazards model to estimate the adjusted subdistribution hazard ratios (aSHRs) and associated 95% CIs. We assessed the proportionality of subhazards assumption by including time interactions on covariates in the model. Significant time × covariate interactions indicate violation of the proportionality assumption. Furthermore, we examined interactions to assess whether a synergistic effect existed between pregnancy and HIV or TB for risk of ICU admission or death among SARS-CoV-2–infected women.

Comparison of Pregnancy Outcomes by SARS-CoV-2 RT-PCR Result Status

We summarized baseline demographic and clinical characteristics using frequencies and proportions stratified by SARS-CoV-2 RT-PCR result status. A complete case analysis approach was used for the primary and secondary outcomes, since the proportion of missing primary outcomes data was low (<4%).

RESULTS

As shown on the patient flow diagrams (Supplementary Figure 1*A*–*C*) and Table 1, we analyzed data from 1315 women in 6 SSA countries, including 510 pregnant women with SARS-CoV-2 infection, 403 nonpregnant women with SARS-CoV-2 infection, and 402 pregnant women without SARS-CoV-2 infection.

Comparison of SARS-CoV-2–Infected Women by Pregnancy Status

Demographics and Clinical Characteristics at Admission

Pregnant women were younger than nonpregnant women, with a median age of 30 years in both pregnant SARS-CoV-2–infected and –uninfected women compared with 33 years in nonpregnant, SARS-CoV-2–infected women (Table 1). The geographic distribution of 913 women with RT-PCR–confirmed SARS-CoV-2 infection was 271 (30%), 67 (7%), 229 (25%), and 346 (38%) from East, West, Central, and Southern Africa regions, respectively. Most pregnant women (46%) with SARS-CoV-2 were from Southern Africa, whereas most nonpregnant women (37.2%) with SARS-CoV-2 were from Central Africa. Most (71.5%) pregnant women with SARS-CoV-2 and known gestational age at admission were in the third trimester (Table 1). At admission, among 913 SARS-CoV-2–infected women, 43.6% had mild, 12.4% moderate, 35.9% severe, and 8.1% had critical COVID-19. Pregnant women were more likely to present with critical or severe disease than nonpregnant women (50% vs 37%, respectively; $P < .001$).

Signs, Symptoms, and Comorbidities

Several symptoms or comorbidities were more common in SARS-CoV-2–infected pregnant (vs nonpregnant) women:

Table 1. Demographic and Clinical Characteristics by Pregnancy and SARS-CoV-2 Infection Status

	Study Groups					
	SARS-CoV-2–Infected Pregnant Women (n = 510)[a]		SARS-CoV-2–Infected Nonpregnant Women (n = 403)		SARS-CoV-2–Uninfected Pregnant Women (n = 402)	
	n	%	n	%	n	%
Region						
East Africa	141	28	130	32	98	2
West Africa	56	11	11	3	18	4
Central Africa	79	16	150	37	101	25
Southern Africa	234	46	112	28	185	46
Age group, y						
11–17	4	1	2	1	5	1
18–24	83	16	46	12	85	21
25–34	278	55	181	45	215	54
35–44	110	27	144	36	95	24
45–49	1	0	20	5	0	0
≥50	0		8	2	0	0
Missing/unknown	2		2		2	
Median (IQR) age, y	30 (26–35)		33 (28–38)		30 (25–34)	
WHO COVID-19 stage at admission						
Mild	168	33	230	57	N/A	N/A
Moderate	89	18	24	6	N/A	N/A
Severe	201	39	127	32	N/A	N/A
Critical	52	10	22	6	N/A	N/A
Gestational age at admission						
0–12 w	29	6	N/A	N/A	18	5
13–27 w	100	21	N/A	N/A	68	17
28–42+ w	336	72	N/A	N/A	308	79
Missing/unknown	5		0		10	
Median (IQR) length of hospital stay,[b] d	8 (5–12)		9 (5–15)		2 (1–7)	

Abbreviations: COVID-19, coronavirus disease 2019; IQR, interquartile range; N/A, not applicable; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; WHO, World Health Organization.

[a]Includes 12 women from the Democratic Republic of the Congo cohort in the Nachega et al [16] study and 100 women from the South Africa cohort in de Waard et al [6] study.

[b]Median length of hospital stay between pregnant and nonpregnant women with SARS-CoV-2 infection was not significant; however, there was a statistically significant difference between hospital stay for SARS-CoV-2–infected vs –uninfected pregnant women ($P < .001$).

cough (318/489 [65%] vs 229/396 [58%]; $P = .028$), history of previous TB (21/510 [4%] vs 6/403 [2%]; $P = .02$), HIV infection (107/510 [21%] vs 30/403 [7%]; $P < .001$), and acute malaria (15/510 [3%] vs 2/403 [1%]; $P = .017$). Nonpregnant women were more likely to have fever (145/391 [37%] vs 144/478 [30%]; $P = .03$), chest pain (70/239 [29%] vs 66/407 [16%]; $P < .001$), diarrhea (23/248 [9%] vs 21/470 [4%]; $P = .011$), and a history of diabetes mellitus (39/403 [10%] vs 24/510 [5%]; $P = .003$). Regional comorbidity distribution is shown in Supplementary Table 6.

Clinical Outcomes

Among 913 hospitalized women with SARS-CoV-2 infection, 1.3% had undocumented outcomes. Among 901 women with documented outcomes, 85.8% were discharged, 8.0% died, 3.6% were transferred to another facility, and 2.7% remained hospitalized at the end of data collection. Patient flow diagrams (Supplementary Figure 1*A*–*C*) show the proportion of women who were admitted to an ICU, received supplemental oxygen or mechanical ventilation, or died, by pregnancy and SARS-CoV-2 infection status. Figure 1 highlights key unadjusted findings: pregnant women with SARS-CoV-2 infection were significantly more likely than nonpregnant women with SARS-CoV-2 infection to be admitted to an ICU, require supplemental oxygen, and die in-hospital. The ICU admission rates among women with SARS-CoV-2 infection varied by region: 22% in West Africa, 14% in Southern Africa, 11% in East Africa, and in 10% Central Africa. Regional differences in supplemental oxygen requirement, invasive ventilation, and mortality were also noted (Supplementary Figure 2).

Supplementary Table 7 shows the association between potential confounders and pregnancy before and after adjusting with IPPW. Figure 2 shows the unadjusted (*A*) and IPPW-adjusted (*B*) comparison of outcomes between hospitalized pregnant and nonpregnant women with SARS-CoV-2 infection. Adjusting for differences in age, HIV status, diabetes,

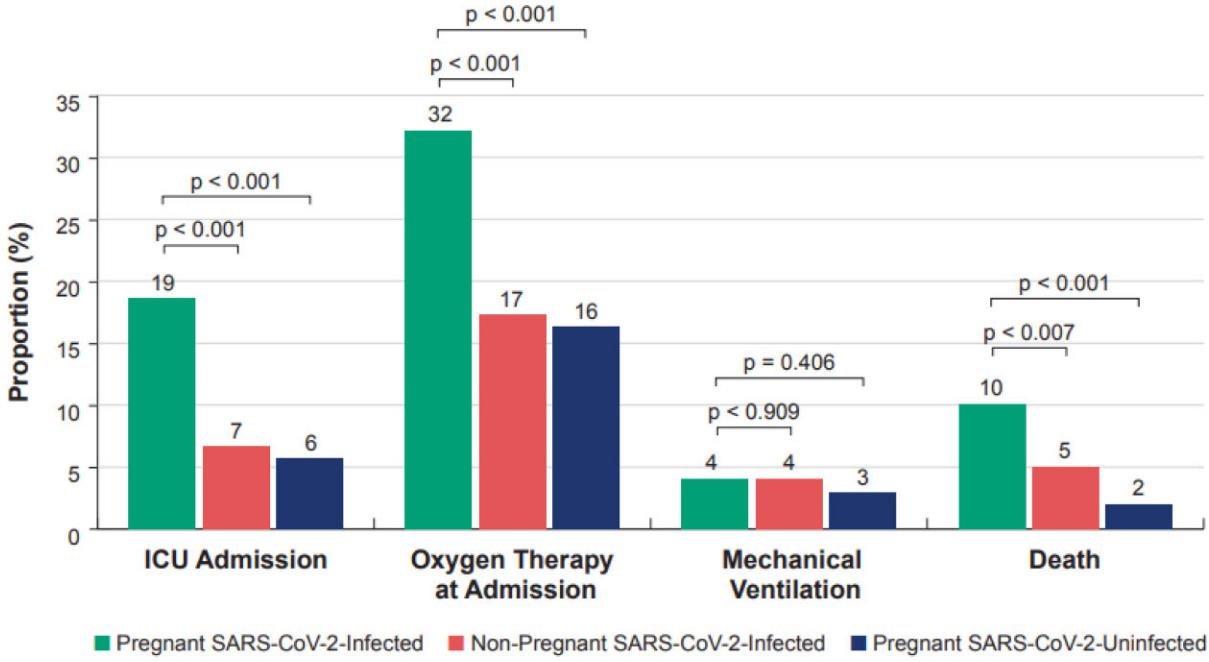

Figure 1. Clinical outcomes among pregnant SARS-CoV-2–infected compared with nonpregnant SARS-CoV-2–infected and pregnant SARS-CoV-2–uninfected women (total N = 1315). Abbreviations: ICU, intensive care unit; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

region, and history of previous TB, being pregnant was associated with a significantly higher risk of ICU admission (adjusted RR [aRR] = 2.38; 95% CI: 1.42–4.01). More pregnant than nonpregnant women received supplemental oxygen, adjusting for baseline differences (aRR = 1.81; 95% CI: 1.30–2.50). Among SARS-CoV-2–infected women, 51 (10%) pregnant women died, compared with 21 (5%) nonpregnant women. In unadjusted analyses, pregnancy increased the risk of death by more than 90% (RR = 1.94; 95% CI: 1.19–3.17). In IPPW-adjusted analyses, pregnancy remained marginally associated with a higher risk of mortality (aRR = 1.66; 95% CI: .95–2.88).

Table 2 summarizes factors associated with ICU admission for all women with SARS-CoV-2 infection, after adjusting for pregnancy status and region. Living with HIV, history of previous TB, diabetes, and sickle cell disease were independently associated with higher risk of ICU admission. Adjusting for pregnancy status and region, women with multiple (>1) comorbidities had a significantly higher risk of ICU admission compared with women without comorbidities. No synergistic interaction was observed between pregnancy and HIV or TB for risk of ICU admission or death among SARS-CoV-2–infected women.

Supplementary Table 8 shows associations between demographic and clinical factors and the hazard of in-hospital mortality in all women with SARS-CoV-2 infection, using Fine and Gray's model. In this competing risk analysis, being pregnant was significantly associated with an increased hazard of in-hospital death (Figure 3*A*). Furthermore, adjusting for pregnancy status and region, chronic kidney disease, asthma, and diabetes were independently associated with risk of death. Women with multiple comorbidities were at increased risk of death compared with those without comorbidities (Figure 3*B*). Residing in Southern or West Africa was associated with higher risk of mortality compared with East African residence (Figure 3*C*).

Comparison of Pregnant Women by SARS-CoV-2 Infection Status

Demographics, Clinical Characteristics, and Mortality

We compared 510 SARS-CoV-2–infected pregnant women (Supplementary Figure 1*A*) with 402 SARS-CoV-2–uninfected pregnant women (Supplementary Figure 1*C*). There were no significant differences in demographic and clinical characteristics between SARS-CoV-2–infected and –uninfected pregnant women, except for regional residence, as shown in Table 1. Figure 2 shows the unadjusted (*C*) and IPPW-adjusted (*D*) comparisons of ICU admission, need for supplemental oxygen, mechanical ventilation, and death between pregnant SARS-CoV-2–infected and –uninfected women. SARS-CoV-2 infection increased the risk of ICU admission, receiving oxygen supplementation, and maternal death. In a competing risk analysis, SARS-CoV-2–infected (vs uninfected) pregnant women had a 5-times greater hazard of in-hospital death (Figure 3*D*).

Pregnancy and Perinatal Outcomes

Among 510 SARS-CoV-2–infected pregnant women, 32% had not delivered at the time of data collection and 19% had missing

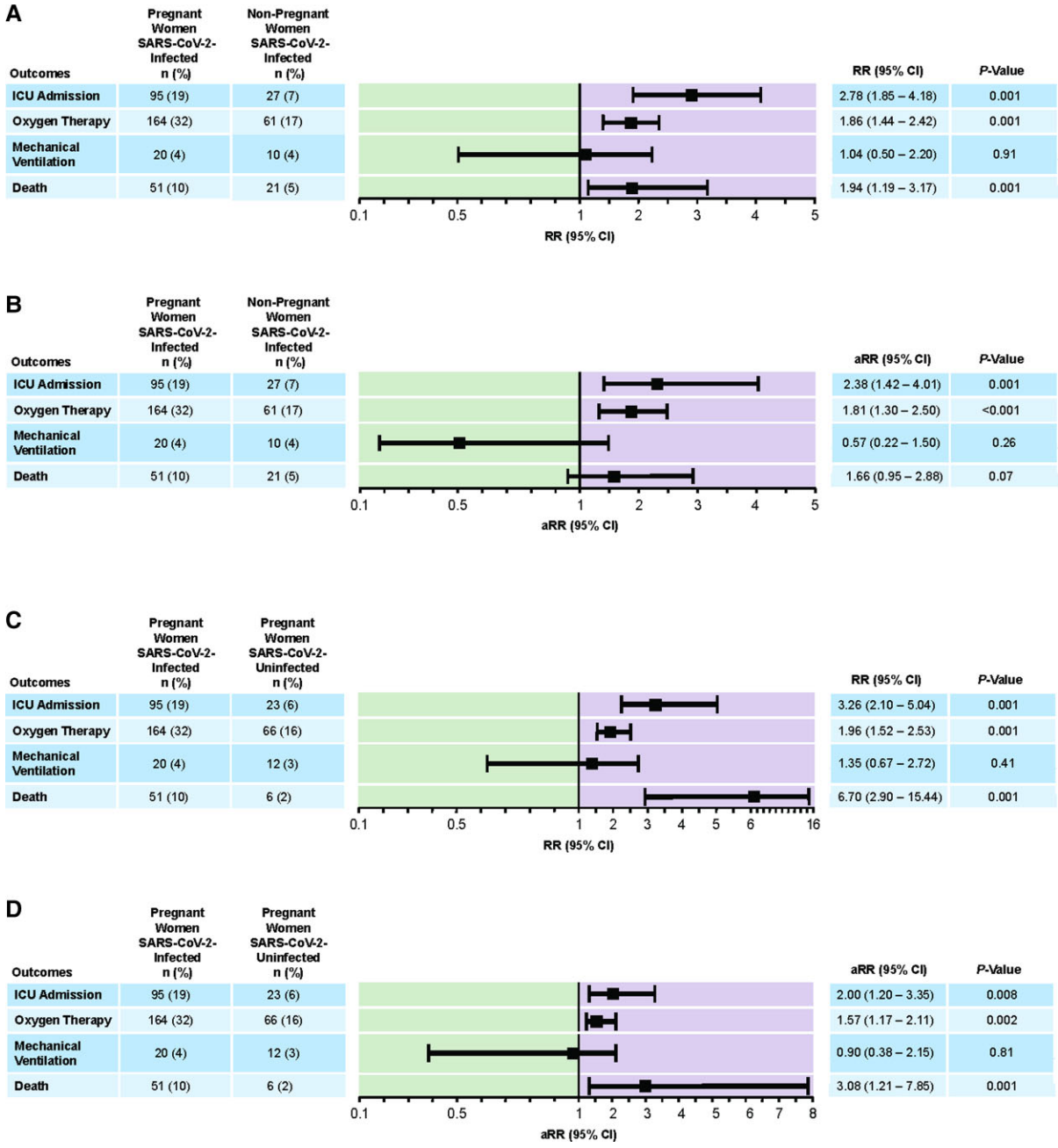

Figure 2. Unadjusted (*A*) and adjusted (*B*) comparisons of outcomes between pregnant (n = 510) and nonpregnant (n = 403) women with SARS-CoV-2 infection. Unadjusted (*C*) and adjusted (*D*) comparisons of outcomes between SARS-CoV-2–infected pregnant women (n = 510) and SARS-CoV-2–uninfected pregnant women (n = 402). Note: The analysis supporting panels *B* and *D* used IPPW to adjust confounding. Abbreviations: aRR, adjusted risk ratio; CI, confidence interval; ICU, intensive care unit; IPPW, inverse probability of participation-based weighting; RR, risk ratio; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

information; among 402 SARS-CoV-2–uninfected pregnant women, 5% had not delivered at the time of data collection and 9% had missing information. Among 250 SARS-CoV-2–infected pregnant women with documented pregnancy outcomes, 213 (85%) had live births and 37 (15%) experienced fetal loss (14 miscarriages, 2 induced abortions, and 21 stillbirths) (Supplementary Table 9). Among 345 SARS-CoV-2–uninfected pregnant women with documented pregnancy outcomes, 302 (88%) had live births and 43 (12%) experienced fetal loss (24 miscarriages, 2 induced abortions, and 17 stillbirths). Cesarean delivery was more frequent among SARS-CoV-2–infected than –uninfected women (RR = 1.56; 95% CI: 1.29–1.89), and the proportions of preterm (69/213 [32%] vs 94/302 [31%], respectively; $P = .87$) and low-birth-weight infants

Table 2. Factors Associated With Intensive Care Unit Admission Among Pregnant and Nonpregnant Women With SARS-CoV-2 Infection

Variable	n	Admitted to ICU, n (%)	Unadjusted RR (95% CI)	*P*	Adjusted RR[a] (95% CI)	*P*
Pregnancy status						
Nonpregnant	403	27 (7)	1		1	
Pregnant	510	95 (19)	2.78 (1.85–4.18)	<.001	2.73 (1.74–4.28)	<.001
Region						
East Africa	271	31 (11)	1		1	
West Africa	67	15 (22)	1.96 (1.12–3.41)	.018	1.13 (.56–2.26)	.73
Central Africa	176	17 (10)	0.99 (.61–1.62)	.98	1.17 (.68–2.01)	.56
Southern Africa	346	50 (14)	1.26 (.83–1.92)	.27	0.76 (.44–1.30)	.32
Age group, y						
11–17	11	1 (9)	1		…	
18–24	204	20 (10)	.55 (.08–3.62)	.54	…	
25–34	622	59 (10)	0.74 (.12–4.49)	.74	…	
35–44	349	36 (10)	0.73 (.12–4.52)	.74	…	
45–49	21	2 (10)	0.57 (.06–5.27)	.62	…	
50+	8	3 (8)	2.25 (.30–16.63)	.43	…	
WHO disease stage						
Mild/moderate	511	16 (3)	1		…	
Severe/critical	402	106 (26)	8.42 (5.06–14.01)	<.001	…	
HIV-positive status						
No	776	90 (12)	1		1	
Yes	137	32 (23)	2.01 (1.40–2.89)	<.001	1.94 (1.18–3.18)	.009
HIV-1 RNA Viral Load						
Undetectable	47	12 (26)	1		…	
Detectable	13	4 (31)	1.21 (.47–3.12)	.70	…	
CD4 count, cells/mm^3						
≥200	75	16 (21)	1		…	
<200	25	7 (28)	1.31 (0.9–2.82)	.49	…	
History of TB						
No	886	112 (13)	1		1	
Yes	27	10 (37)	2.93 (1.74–4.93)	<.001	2.32 (1.17–4.58)	.015
Hypertension						
No	783	96 (12)	1		1	
Yes	130	26 (20)	1.63 (1.10–2.41)	.014	1.37 (.82–2.31)	.23
Diabetes mellitus						
No	850	107 (13)	1		1	
Yes	63	15 (24)	1.89 (1.18–3.04)	.009	2.01 (1.04–3.86)	.036
Chronic neurological disorder						
No	911	121 (13)	1		1	
Yes	2	1 (50)	3.76 (.93–15.20)	.06	1.02 (.12–8.49)	.99
Chronic cardiac disease						
No	897	117 (13)	1		1	
Yes	16	5 (31)	2.40 (1.14–5.05)	.043	1.76 (.66–4.70)	.26
Chronic pulmonary disease						
No	909	119 (13)	1		1	
Yes	4	3 (75)	5.73 (3.17–10.34)	<.001	1.90 (.53–6.82)	.32
Acute malaria						
No	898	119 (13)	1		…	
Yes	15	3 (20)	1.51 (.54–4.21)	.43	…	
Asplenia due to sickle cell disease						
No	909	119 (13)	1		1	
Yes	4	3 (75)	5.73 (3.18–10.34)	<.001	6.23 (1.67–23.29)	.007
Cancer						
No	910	121 (13)	1		…	
Yes	3	1 (33)	2.51 (.50–12.53)	.26	…	

Abbreviations: CI, confidence interval; COVID-19, coronavirus disease 2019; HIV, human immunodeficiency virus; ICU, intensive care unit; RR, risk ratio; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; TB, tuberculosis; WHO, World Health Organization.

[a]Log-binominal regression model adjusted for pregnancy status, age, region, noncommunicable disease (chronic cardiac disease, hypertension, diabetes mellitus, chronic pulmonary diseases, chronic neurologic diseases, asplenia), and communicable disease (HIV status and history of tuberculosis) comorbidities. WHO COVID-19 staging is not included in multivariable analyses because its components are in the causal pathway of the primary ordinal outcome.

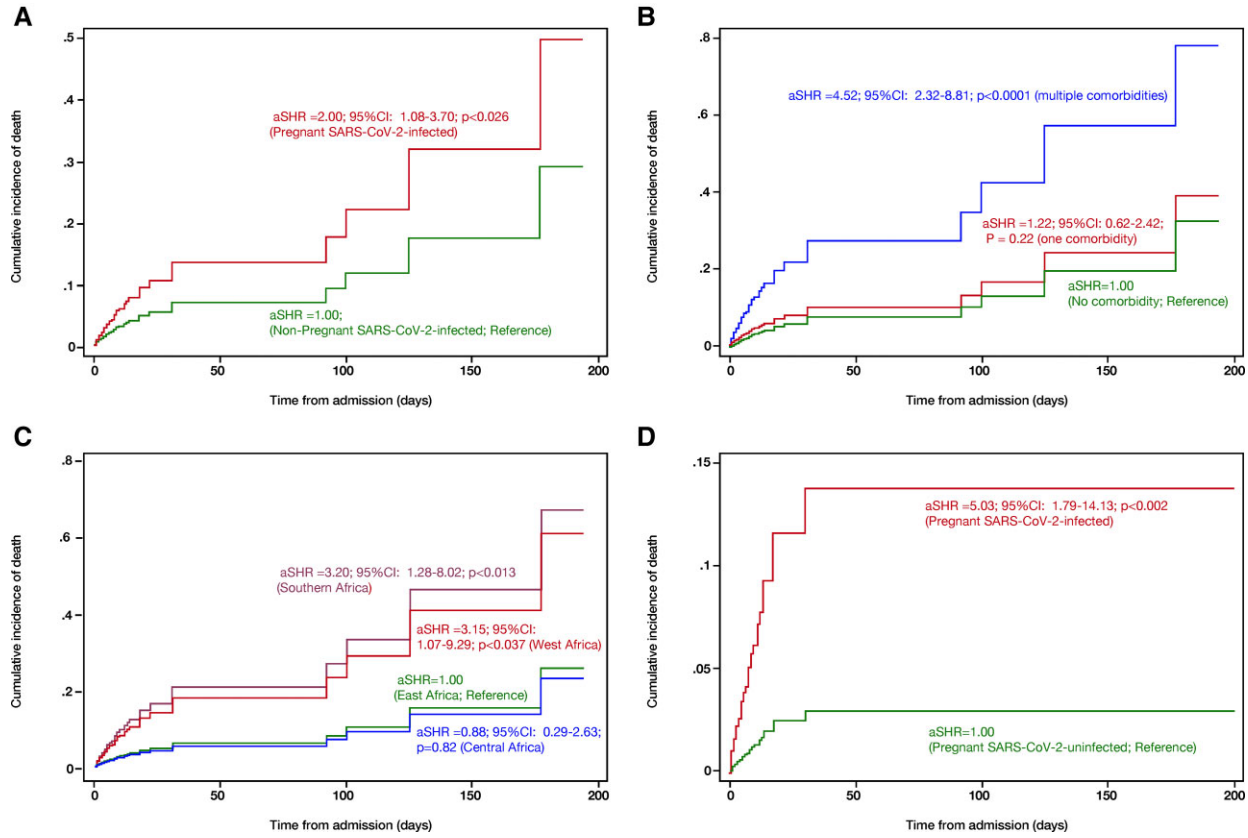

Figure 3. Cumulative incidence functions for in-hospital mortality in SARS-CoV-2–infected women according to pregnancy status (*A*), number of comorbidities (*B*), region (*C*), and by SARS-CoV-2 infection status in pregnant women (*D*). Abbreviations: aSHR, adjusted sub-distribution hazard ratio; CI, confidence interval; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

(72/213 [34%] vs 97/314 [31%]; $P = .71$) were similar. Early neonatal in-hospital death occurred among 4% and 3% infants of SARS-CoV-2–infected and –uninfected mothers, respectively (RR = 1.46; 95% CI: .56–3.84).

DISCUSSION

In this large multicountry cohort analysis in SSA, we found that, among women with SARS-CoV-2 infection, pregnancy independently increased the risk of in-hospital morbidity (ICU admission or supplemental oxygen requirement) and, in competing risk analyses, increased hazard of in-hospital death. Among pregnant women, SARS-CoV-2 infection independently increased the risk of ICU admission, oxygen supplementation, and death. Furthermore, among all (pregnant and nonpregnant) women with SARS-CoV-2 infection, HIV infection, prior TB, sickle cell anemia, and nongestational diabetes increased the risk of ICU admission.

Similar to our findings, the 18-country INTERCOVID study (including Ghana and Nigeria) reported higher risks of ICU admission and mortality among pregnant women with (n = 706) compared with without (n = 1424) SARS-CoV-2 infection [7]. However, unlike our study, INTERCOVID included nonhospitalized asymptomatic women and did not include nonpregnant women with SARS-CoV-2 infection. Analysis of 2 smaller cohorts of SARS-CoV-2–positive pregnant women from the Democratic Republic of Congo (N = 12) and Ethiopia (N = 27) did not find associations between pregnancy and adverse outcomes, likely due to small numbers and/or lack of control groups [16, 18], and an initial US retrospective cohort study found pregnancy associated with higher morbidity but not mortality [19]. In contrast, in a US Centers for Disease Control and Prevention report on a larger cohort of women (23 434 pregnant and 386 028 nonpregnant) with SARS-CoV-2 infection, pregnancy was associated with a 1.7 times (95% CI: 1.2–2.4) increased risk of mortality in adjusted analyses [2]. Similarly, a Mexican study including more than 260 000 SARS-CoV-2–infected women found that pregnancy increased the risk of death among women aged 15 to 44 years by 61% [17]. These large studies corroborate our findings: in an adjusted competing-risk analysis, pregnancy increased the hazard of maternal death 2-fold among SARS-CoV-2–infected women.

Pregnant and nonpregnant women with SARS-CoV-2 infection who were living with HIV or had a prior history of TB had

a nearly 2-fold increased risk of ICU admission compared with those without these chronic infections. Published data on the impact of HIV on SARS-CoV-2 infection outcomes have been conflicting [6, 20, 21]. However, a recent data analysis by the WHO found that HIV in hospitalized adults was independently associated with a 1.29 times higher risk of death from SARS-CoV-2 infection after adjusting for age, sex, and underlying conditions [22]. Our finding of an association between prior TB and COVID-19 severity may reflect decreased pulmonary reserve due to post-TB sequelae, as described by Tadolini et al [23]. The finding of higher rates of acute malaria in pregnant compared with nonpregnant women with SARS-CoV-2 infection was expected, as pregnant women are more susceptible to malaria due to hormonal and immunological changes [24]. We also found higher rates of diabetes mellitus among nonpregnant compared with pregnant women with SARS-CoV-2 infection, but a lack of detailed data limits interpretation. Furthermore, the association between sickle cell anemia and ICU admission calls for further investigation on the impact of asplenia and hemoglobinopathy on COVID-19. Finally, we found a higher risk of ICU admission and/or supplemental oxygen use and mortality in Southern and West Africa compared withEastern Africa, which may reflect regional differences in health system capacities (Southern Africa has the strongest health infrastructure and higher capacity for ICU admissions) and/or severity of SARS-CoV-2 infection related to variant virulence, regional prevalence of HIV infection (highest in Southern Africa), or other unmeasured confounding factors.

With regard to pregnancy-specific outcomes, we found a high rate of cesarean delivery among SARS-CoV-2–uninfected pregnant women. This is likely attributable to our study sites, which comprise referral hospitals where cesarean rates are typically higher than in local hospitals and clinics. SARS-CoV-2–uninfected women were tested secondary to suspected COVID-19 symptoms in our study and may represent a group at higher risk for pregnancy complications compared with pregnant women in general due to other unmeasured factors. Data on whether SARS-CoV-2 infection is a risk factor for stillbirth are inconsistent [4, 25–27]. Among pregnant women with known pregnancy outcomes in our cohort, the rates of stillbirth, miscarriage, preterm birth, and low birth weight did not differ based on SARS-CoV-2 infection status. However, our analyses are likely underpowered and are in contrast to INTERCOVID results, which documented that pregnant women with SARS-CoV-2 infection had higher rates of preterm birth and stillbirth [7].

Our study had some limitations. First, the retrospective cohort design limited collection of some variables of interest (eg, body mass index) and relied on pooling of available pregnancy data at the time of retrieval from heterogeneous sites in SSA. The establishment of a pregnancy COVID-19 registry has proved challenging in SSA. However, the WHO has set up a global COVID-19 pregnancy prospective cohort study from multiple countries (including in Africa) that will minimize recorder bias [28]. Second, given that comparison groups were not evenly distributed geographically, some identified differences might be explained by regional variations (eg, HIV prevalence and health infrastructure). Third, we studied only symptomatic women whose symptoms prompted SARS-CoV-2 RT-PCR testing and hospitalization, which included heterogenous control groups with a range of illnesses that could also be associated with adverse pregnancy outcomes, potentially leading to a dilution of differences. Finally, our findings are not necessarily generalizable to asymptomatic pregnant women with SARS-CoV-2 infection who were not hospitalized.

Our findings have important clinical and public health implications. First, given the increased morbidity and mortality in both pregnant and nonpregnant women with SARS-CoV-2 infection and in pregnant women with and without SARS-CoV-2 infection [4, 29–31], pregnant women (among other at-risk groups) should be prioritized for COVID-19 vaccination in African countries, where vaccine supply is limited but steadily increasing [32, 33]. Although pregnancy was an exclusion criterion in early COVID-19 vaccine and SARS-CoV-2 treatment trials, more trials are enrolling pregnant women [34], preliminary reports do not demonstrate safety issues for pregnant women receiving mRNA vaccines [35, 36], and several systematic reviews find that COVID-19 vaccination in pregnant and lactating individuals is immunogenic, safe with respect to vaccine-related adverse events and obstetrical and neonatal outcomes, and effective [37–40]. Finally, further research is needed to better understand the pathogenesis and optimal management of SARS-CoV-2 infection in pregnancy.

Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

Author Contributions. J. B. N., N. A. S.-A., R. N. M., and L. M., designed and wrote the study protocol as well as drafted the initial manuscript. R. N. M. led the data management and statistical analysis. All authors provided (1) additional contributions to the conception or design of this work or the acquisition, analysis, or interpretation of data for the work; (2) drafting of the manuscript or revising it critically for important intellectual content; and (3) approval of the final version submitted. J. B. N. and R. N. M. had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Acknowledgments. The authors thank John L. Johnson, MD, Professor of Medicine, Case Western Reserve University, Cleveland, Ohio, USA; Siobán D. Harlow, PhD, Professor of Epidemiology and Global Public Health, Professor of Obstetrics and Gynecology, and Director, Center for Midlife Science, University of Michigan, Michigan, USA; Peter H. Kilmarx, MD, Deputy Director, US National Institutes of Health/Fogarty International Center, Bethesda, Maryland, USA; and Ethan Borre, BA, Duke University School of Medicine, Durham, North Carolina, USA, for critical review and helpful advice. They also thank all members of the AFREhealth Research Collaboration on COVID-19, and appreciate the continued support of the AFREhealth Executive Secretariat in Kumasi, Ghana (Ireneous N. Dasoberi, Clara Sam-Woode, and Georgina Yeboah). AFREhealth is a pan-African organization that seeks to work with Ministries of Health, training institutions, and other stakeholders to improve the quality of healthcare in Africa through research, education, and capacity-building (www.afrehealth.org). Also, the authors remember and recognize the foundational statistical input of our colleague, Birhanu Ayele, PhD, Associate Professor of Biostatistics at Stellenbosch University, South Africa, who died from COVID-19 complications in February 2021. This work is dedicated to him, his family, and people across Africa who have been affected by COVID-19. Finally, this work was presentated at the virtual 2022 Conference on Retroviruses and Opportunistic Infections (CROI), which occurred 12–16 February 2022 (Abstract No. 671; https://www.croiconference.org/croi-2022/).

Data availability. The dataset used for this study, including individual deidentified participant data and a data dictionary defining each field in the set, will be made available at publication on request to Professor Jean Nachega (jbn16@pitt.edu).

Disclaimer. The funder of this study (National Institutes of Health/Fogarty International Center) had no role in the study design, data collection, data analysis, data interpretation, or writing of the manuscript.

Financial support. This work was supported by the US National Institutes of Health (NIH)/Fogarty International Center (FIC) (grant number 1R25TW011217-01) to the African Forum for Research and Education in Health (AFREhealth) (Principal Investigators: Prisca Adejumo, Jean B. Nachega, Nelson K. Sewankambo, Fatima Suleman), and payment to the University of Ibadan, Ibadan, Nigeria (P.A.); Makerere University, Kampala, Uganda (N.K.S.); University of Kwazulu Natal, Durban, South Africa (F.S.); Stellenbosch University Faculty of Medicine and Health Sciences, Cape Town, South Africa (J.B.N.); to C. N.'s institution; to E. K. A.'s institution; and M. Y. Y.'s institution; and to the following authors: N. A. S.-A., R. N. M., S. S., N. M., O. W. G., J. K., S. B., P. S., E. A., A. B. O., A. M. A., A. U. M., D. K. I., M. T. P., C. B.-P. N., L. N. S., P. M., and L. W. U.

Potential conflicts of interest. J. B. N. is an infectious disease internist and epidemiologist and Principal Investigator (PI) of NIH/FIC grant numbers 1R25TW011217-01, 1R21TW011706-01, and 1D43TW010937-01A1; and payment to University of Pittsburgh. N. A. S.-A. is a clinician-scientist in Pediatric Infectious Diseases and implementation research; she is supported by the NIH National Institute of Child Health and Human Development (NICHD) grant number R01HD089866; by an NIH/FIC award through the Adolescent HIV Prevention and Treatment Implementation Science Alliance (AHISA) for the Central and West Africa Implementation Science Alliance (CAWISA) (payment to institution); and by NIH/FIC grant number 1D43TW012280-01. F. S., N. K. S., and A. P. are supported as PIs by NIH/FIC grant number 1R25TW011217-01. A. Z. is PIs of the Pan-African Network on Emerging and Re-Emerging Infections (PANDORA-ID-NET; https://www.pandora-id.net) funded by the European Developing Countries Clinical Trial Partnership (EDCTP) and the European Union Horizon 2020 Framework Program for Research and Innovation, paid to institution (University College London, London, UK). R. N. M. reports grants or contracts unrelated to this work, and payment to their institution: NIH/FIC1D43TW010547-01—The African Center for Biostatistical Excellence (ACBE). P. J. R. reports the following grants or contracts unrelated to this work and paid to their institution: 5R01AI075045-12, 5R01AI139179-04, and 5R01AI117001-07. E. R. S. reports a Bill and Melinda Gates Foundation grant for a prospective meta-analysis of COVID-19 in pregnancy, unrelated to this work, and payment to George Washington University. A. B. reports grants or contracts unrelated to this work—NIH: IMPAACT Vice-chair Funding for P1106; and UNITAID: Benefit KIDS funding for PETITE Study. P. A. reports grants or contracts unrelated to this work and paid to the University of Ibadan, Nigeria: NIH/FIC R25 grant number 1R25TW011217-01 to AFREhealth. J. W. N. reports grants paid to the University of Pittsburgh from the NIH to the Pitt-Ohio State Clinical Trials Unit (UM1 AI068636), the University of Pittsburgh Virology Support Laboratory (UM1 AI106701), the I4C Martin Delaney Collaboratory for an HIV Cure (UM1 AI126603), the REACH Martin Delaney Collaboratory for HIV Cure (UM1 AI164565), and from the National Cancer Institute through Leidos contract numbers HHSN261200800001E and 75N91019D00024 USAID; Gilead Sciences, Inc; and Janssen Pharmaceuticals. J. W. N. also reports consulting fees from Gilead Sciences, Inc (Scientific Advisory Board), Accelevir Diagnostics (Consulting Agreement), and Merck (Consulting Agreement); shares from Abound Bio, Inc, share options from Co-Crystal Pharma, Inc, and share options from Infectious Diseases Connect; a consulting agreement with Xi'an Yufan

Biotechnologies; and employment with the University of Pittsburgh. M. S. reports grants or contracts unrelated to this work and paid to their institution (MGH-Boston, MA, USA): NIH/NIA R01AG059504-03 and NIH/NHLBI R01 HL141053-04. A.-P. K. reports research support unrelate to this work paid to their institution (South African Medical Research Council): NIH/FIC 1R21TW011706-01-Dolutegravir, Weight Gain and Metabolic Outcomes in South Africa. L. M. reports consulting fees from the World Health Organization on COVID in pregnancy and mother to child SARS-CoV-2 transmission (this contract is now completed); and payment from Virology Education for a talk on SARS-CoV-2 in pregnancy and possibility of mother-to-child SARS-CoV-2 transmission for continuing education sponsored by Virology Education. M. Y. is PI of the NIH/National Institute of Allergy and Infectious Diseases (NIH/NIAID) grant number 5U01AI096299-13 of the Central Africa-International epidemiology to Evaluate AIDS (CA-IeDEA). M. Y. also reports grants or contracts unrelated to this work and paid to their institution: NIH grant numbers 5U01AI096299 (NIAID), R01HD087993 (NICHD), U54CA254568 (National Cancer Institute), and R01HD105526 (NICHD). All other authors report no potential conflicts.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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