Open Forum Infectious Diseases

MAJOR ARTICLE

Hepatitis B Virus Prevalence and Transmission in the Households of Pregnant Women in Kinshasa, Democratic Republic of Congo

Camille E. Morgan,[1] Patrick Ngimbi,[2] Alix J. N. Boisson-Walsh,[3] Sarah Ntambua,[2] Jolie Matondo,[2] Martine Tabala,[4] Melchior Mwandagalirwa Kashamuka,[4] Michael Emch,[1] Jessie K. Edwards,[1] Kimberly A. Powers,[1] Linda James,[3] Nana Mbonze,[4] Samuel Mampunza,[2] Marcel Yotebieng,[5] Peyton Thompson,[6,a] and Jonathan B. Parr[3,7,a]

[1]Department of Epidemiology, Gillings School of Global Public Health, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, USA, [2]Faculté de Médecine, Université Protestante du Congo, Kinshasa, Democratic Republic of the Congo, [3]Institute for Global Health and Infectious Diseases, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, USA, [4]L'École de Santé Publique, Université de Kinshasa, Kinshasa, Democratic Republic of the Congo, [5]Division of General Internal Medicine, Department of Medicine, Albert Einstein College of Medicine, Bronx, New York, USA, [6]Division of Infectious Diseases, Department of Pediatrics, School of Medicine, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, USA, and [7]Division of Infectious Diseases, Department of Medicine, School of Medicine, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, USA

Background. The World Health Organization Africa region has high regional hepatitis B virus (HBV) prevalence, and evidence suggests more frequent horizontal HBV transmission than other regions. Context-specific epidemiological studies are needed to inform additional HBV prevention measures.

Methods. In the cross-sectional Horizontal and Vertical Transmission of Hepatitis B (HOVER-HBV) study, we introduced HBV surface antigen (HBsAg) screening alongside existing HIV screening as part of routine antenatal care in high-volume maternity clinics in Kinshasa, Democratic Republic of Congo. We recruited households of pregnant women ("index mothers") who were HBsAg-positive and HBsAg-negative, defining households as index-positive and index-negative, respectively. Household members underwent HBsAg testing and an epidemiological survey. We evaluated HBsAg prevalence and potential transmission correlates.

Results. We enrolled 1006 participants from 200 households (100 index-positive, 100 index-negative) across Kinshasa. HBsAg-positivity prevalence was more than twice as high in index-positive households (5.0% [95% confidence interval {CI}, 2.8%–7.1%]) as in index-negative households (1.9% [95% CI, .6%–3.2%]). HBsAg-positivity prevalence was 3.3 (95% CI, .9–11.8) times as high among direct offspring in index-positive versus index-negative households. Factors associated with HBsAg positivity included older age, marriage, and having multiple recent partners or any new sexual partners among index mothers; and older age, lower household wealth, sharing nail clippers, and using street salons among offspring in index-positive households.

Conclusions. Vertical and horizontal HBV transmission within households is ongoing in Kinshasa. Factors associated with infection reveal opportunities for HBV prevention efforts, including perinatal prevention, protection during sexual contact, and sanitation of shared personal items.

Keywords. HBV; horizontal transmission; prevention of mother-to-child transmission (PMTCT); vertical transmission; viral hepatitis.

Despite an effective vaccine, hepatitis B virus (HBV) infection remains highly prevalent (~6%) in Asia and Africa, resulting in significant global morbidity and mortality [1, 2]. Without a therapeutic cure, infection prevention remains the primary strategy to reduce HBV morbidity and mortality. However, HBV vaccination alone will not achieve elimination by the 2030 target [3–5]. Modeling studies indicate that test-and-treat interventions can yield marked HBV prevalence reductions in Africa, but studies of prevention options are hindered by the limited epidemiological data from the region [4]. While perinatal transmission is the dominant driver of ongoing endemicity in Asia [6–8], available studies suggest a greater contribution of household and community ("horizontal") transmission in Africa, in both childhood [9, 10] and adulthood [4]. Improved understanding of dominant HBV transmission modes and risk factors is needed to design effective interventions in Africa, especially in HBV-endemic countries like the Democratic Republic of Congo (DRC).

National HBV prevalence in the DRC is estimated to be 3.3% by HBV surface antigen (HBsAg) testing [11], translating to approximately 2.5 million chronic infections in a country where advanced hepatology care is essentially inaccessible [12].

Received 20 December 2023; editorial decision 11 March 2024; published online 9 April 2024

[a]P. T. and J. B. P. contributed equally to this work as joint senior authors.

Correspondence: Camille E. Morgan, PhD, Department of Epidemiology, Gillings School of Global Public Health, University of North Carolina at Chapel Hill (camille_morgan@med.unc.edu).

Open Forum Infectious Diseases®

https://doi.org/10.1093/ofid/ofae150

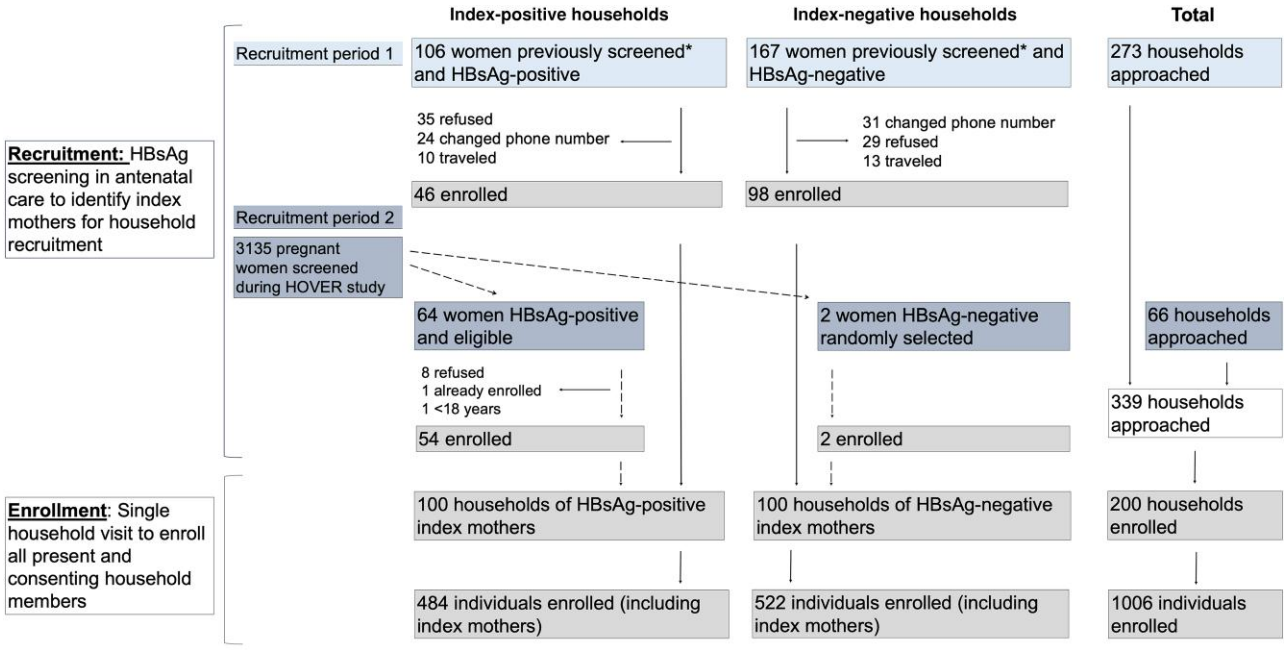

Figure 1. Recruitment and enrollment of households of hepatitis B surface antigen (HBsAg)–positive and HBsAg-negative index mothers. *Previous screening occurred before the Horizontal and Vertical Transmission of Hepatitis B (HOVER-HBV) study; total number of women screened not available.

Estimated prevalence is higher among blood donors [13], women with human immunodeficiency virus (HIV) presenting to urban antenatal care (ANC) settings [14], pregnant women in rural areas [15, 16], healthcare workers [17], and survivors of sexual violence [18]. Blood donor screening and the 3-dose infant pentavalent vaccine series are the only HBV prevention measures implemented nationally in DRC, but complete infant HBV vaccination coverage is <70% [19]. For prevention of mother-to-child transmission, the World Health Organization recommends ANC HBsAg screening, maternal antiviral prophylaxis, and infant birth-dose vaccination to prevent perinatal transmission [20]. These activities are feasible in the DRC but not yet implemented [21, 22].

To investigate HBV correlates and inform expanded interventions in the DRC, we conducted the Horizontal and Vertical Transmission of Hepatitis B (HOVER-HBV) study. We built upon the established prevention of mother-to-child HIV transmission (PMTCT) program infrastructure to introduce ANC HBsAg screening, characterize HBV prevalence in ANC patients' households across urban Kinshasa, and identify attributes and practices associated with HBsAg positivity.

PATIENTS AND METHODS

Study Design and Participant Recruitment

To recruit households, we introduced DETERMINE 2 [23] (Abbott, Abbott Park, Illinois) point-of-care (POC) HBsAg testing alongside existing ANC HIV testing in high-volume maternity centers in Kinshasa (Figure 1). During 2 recruitment periods, pregnant women screened for HBsAg were offered enrollment of their households in the study. In this matriarchal design, recruited women served as "index mothers" for enrolled households, with a prespecified target of 100 households of HBsAg-positive mothers and 100 households of HBsAg-negative mothers (Supplementary Materials). Women presenting for ANC in the recruitment period were born prior to infant HBV vaccine introduction and thus were assumed to be unvaccinated.

Study Procedures

Data collection at the single household visit included POC HBsAg testing (including repeat testing of the index mothers), collection of dried blood spot (DBS) specimens, and administration of household and individual questionnaires (Supplementary Appendix 1) covering demographics and potential sources of horizontal HBV transmission within household and community settings. HIV infection and antiretroviral therapy (ART) use, particularly tenofovir-lamivudine based regimens given anti-HBV activity, were determined by self-report. As HBV can remain infectious on surfaces for at least 7 days [24], we collected information about household and community practices that could result in HBV transmission, based on past findings from other countries in the region [16, 25–27]. We offered the 3-dose Euvax-B HBV (LG Life Sciences, Republic of Korea) vaccination to all HBsAg-negative individuals living with someone who was HBsAg-positive, and recorded all resulting vaccinations

occurring at the 2 centers where we offered them up to 6 months after the last enrollment.

Analytical Approach

We defined index-positive and index-negative households as households of index mothers who were HBsAg-positive and HBsAg-negative during ANC recruitment, respectively. Incident infections among index mothers were defined as index mothers who were HBsAg-negative at ANC recruitment and HBsAg-positive at household enrollment; we defined cleared infections among index mothers as ones who were HBsAg-positive at recruitment and HBsAg-negative at enrollment. In sensitivity analyses, we alternately defined "index-positive" and "index-negative" households based on the index mother being ever versus never HBsAg-positive, HBsAg-positive at both timepoints versus once or never, and HBsAg-positive at enrollment versus not (Supplementary Materials). We conducted descriptive analyses of household composition, HBsAg positivity patterns within households, and household/participant demographics, including composite indices of modern housing (materials of walls, floors, roofs, and windows reflecting permanent construction) and wealth (utilities and goods) to approximate standard of living across households (Supplementary Materials; Supplementary Figures 1 and 2). We considered participant age both continuously and categorically, defining categories based on age relative to the introduction of the 3-dose HBV vaccination in the national infant immunization program (Supplementary Materials) [28, 29].

In our primary analysis, we compared HBsAg prevalence between members of index-positive and index-negative households and between household member types (offspring vs other). We estimated prevalence ratios (PRs) for each comparison, first unadjusted and then adjusted for household clustering using a random intercept for household. To examine potential correlates of HBV infection, we also estimated measures of association between HBsAg positivity and attributes and practices reflecting potential HBV transmission, collected from individual and household questionnaires. Variable coding is detailed in the Supplementary Materials. In brief, individual attributes included age and marital status; household variables included household wealth, sharing personal objects within the household, and premasticating food for another household member; sources of potential community transmission included receiving blood transfusions, manicures/pedicures, tattoos, traditional scarification, and a variety of sexual behaviors. Given the case-control design of index mother recruitment, we used logistic regression to estimate odds ratios (ORs) for these factors' associations with maternal HBsAg positivity. For the analysis among household members, we conducted stratified analyses by household member type (offspring vs other household member), estimating a PR for each attribute/practice from multilevel log-binomial regression with a random intercept to account for household clustering. Where log-binomial models failed to converge, we used the OR from the logistic regression model to approximate the PR, which is minimally biased for rare outcomes (<10% prevalence) such as HBsAg positivity [30]. We calculated 95% confidence intervals (CIs) to assess precision of each estimate. In subgroups with <10 HBsAg infections, we calculated Fisher exact *P* values. We also calculated ORs for all variables to facilitate comparison of HBsAg positivity correlates between subgroups.

All data were imported into R (v4.2.2) [31] using the *REDCapR* package (v1.1.0). We analyzed data using the *tidyverse* (v2.0.0), *tableone* (v0.13.2), and *lme4* (v1.1.32) packages. R code is publicly available at https://github.com/IDEELResearch/hbv_hover. This study was approved by the Institutional Review Board at the University of North Carolina (19–1875) and the Ethics Committee at Université Protestante au Congo (CE/UPC/0062).

RESULTS

Study Population

From February 2021 to September 2022, we offered enrollment to 339 households, and enrolled 200 households and 1006 individuals (Figure 1). Overall, 190 index mothers were recruited from 2 maternity centers, and 10 women from 9 other maternity centers. Participating households were located in neighborhoods across metropolitan Kinshasa (Figure 2*A*). Few households (20.5%) lived in modern housing structures, and most participants were transient (median of 2 years [interquartile range {IQR}, 1–5 years] in the home) (Table 1, Supplementary Table 1). We enrolled a median of 5 (IQR, 3–6) members per index-positive and index-negative household (Figure 2*B*). Most recruited index mothers were multiparous: In 176 (88%) households, we enrolled at least 1 direct offspring, with a median of 3 children (IQR, 1–4) enrolled in both index-positive and index-negative households (Table 1). In 86 households (43%), we enrolled the index mother's sexual partner, with partners enrolling in a considerably higher proportion of index-positive (52%) than index-negative (34%) households. Index mothers had a median age of 32 years (IQR, 27–37 years), with a higher median age among mothers in index-positive (33 years) versus index-negative households (30 years). We enrolled 467 direct offspring of index mothers (228 index-positive, 239 index-negative), with similar age distributions in index-positive and index-negative households. Most offspring (82% index-positive, 84% index-negative) were 13 years of age or younger in 2022, and thus born after 3-dose infant HBV vaccination was introduced in DRC. We enrolled 331 other household members, with the most common relationships to index mothers being nieces/nephews (n = 93), siblings (n = 90), and partners (n = 86).

HBsAg-positivity Prevalence

HBsAg-positivity prevalence among index mothers' household members was 5.0% (95% CI, 2.8%–7.1%) and 1.9% (95% CI,

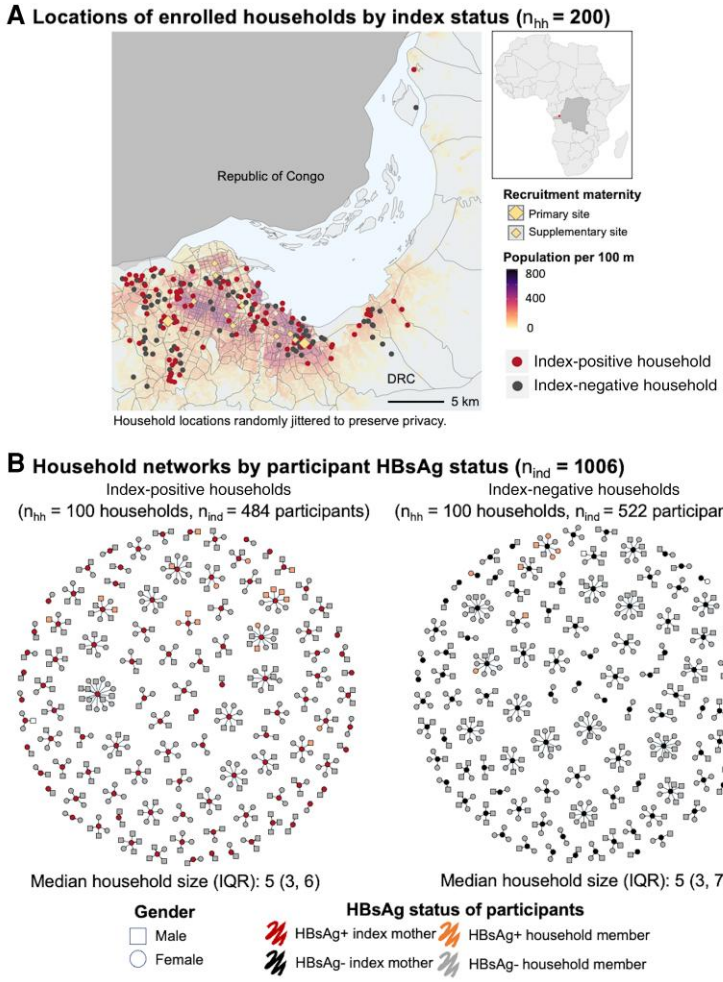

Figure 2. Enrolled households by geography and household structure. *A*, Locations of enrolled households in Kinshasa, Democratic Republic of Congo, by household index status (n_{hh} = 200). *B*, Household networks by participant hepatitis B surface antigen (HBsAg) status (n_{ind} = 1006). *C*, Categorization of households by patterns of HBsAg positivity among enrolled individuals. *Categories are mutually exclusive. †In 4 index-positive households, index mothers recovered from infection between antenatal recruitment and household enrollment (HBsAg-positive to HBsAg-negative). ‡The index mother had an incident infection between antenatal recruitment and household enrollment (HBsAg-negative to HBsAg-positive). Abbreviations: DRC, Democratic Republic of Congo; HBsAg, hepatitis B surface antigen; IQR, interquartile range.

Table 1. Characteristics of Study Households and Participants Enrolled in the Horizontal and Vertical Transmission of Hepatitis B Study

Household Characteristics	Index-Positive Households (HBsAg-Positive Index Mother)[a]	Index-Negative Households (HBsAg-Negative Index Mother)[a]	Overall
No.	100	100	200
Household members enrolled, median (IQR)	5 (3–6)	5 (3–7)	5 (3–6)
Enrolled direct offspring of index mothers per household, median (IQR)	3 (1–4)	3 (1–4)	3 (1–4)
Household structures			
Vertical: Index mother/direct offspring	87 (87)	89 (89)	176 (88)
Sexual: Index mother and male partner enrolled	52 (52)	34 (34)	86 (43)
Modern housing[b]	21 (21)	20 (20)	41 (20.5)
Wealth quartile[c]			
Lowest	28 (28)	22 (22)	50 (25)
Lower middle	20 (20)	30 (30)	50 (25)
Upper middle	24 (24)	26 (26)	50 (25)
Highest wealth	28 (28)	22 (22)	50 (25)

	Index-positive households			Index-negative households			
Participant Characteristics	Index Mothers	Direct Offspring	Other Household Members	Index Mothers	Direct Offspring	Other Household Members	Overall
No.	100	228	156	100	239	183	1006
HBsAg testing, No.	100	227	156	100	237	183	1003
HBsAg-positive at enrollment	96 (96.0)	12 (5.3)	7 (4.5)	2 (2.0)	3 (1.3)	5 (2.9)	125
Age, y, median (IQR)	33 (29–37)	6 (2.6–11)	26 (13–40)	30 (25–37)	6 (2–11)	22 (13.2–38)	15 (5–30)
Age group[d]							
>13 y	100 (100.0)	41 (18.0)	121 (77.6)	100 (100.0)	38 (15.9)	145 (79.2)	545 (54.2)
≤13 y	0 (0.0)	187 (82.0)	35 (22.4)	0 (0.0)	201 (84.1)	38 (20.8)	461 (45.8)
Female sex	100 (100.0)	119 (52.5)	76 (48.1)	100 (100.0)	142 (59.5)	95 (55.2)	637 (63.3)
Relationship to index mother							
Index mother	100 (100.0)	0 (0.0)	0 (0.0)	100 (100.0)	0 (0.0)	0 (0.0)	200 (19.9)
Son/daughter	0 (0.0)	228 (100.0)	0 (0.0)	0 (0.0)	239 (100.0)	0 (0.0)	475 (46.4)
Current male partner	0 (0.0)	0 (0.0)	52 (33.1)	0 (0.0)	0 (0.0)	34 (18.6)	86 (8.5)
Brother/sister	0 (0.0)	0 (0.0)	39 (24.8)	0 (0.0)	0 (0.0)	60 (32.8)	90 (9.9)
Nephew/niece	0 (0.0)	0 (0.0)	41 (26.1)	0 (0.0)	0 (0.0)	53 (29.0)	93 (9.3)
Other	0 (0.0)	0 (0.0)	25 (15.9)	0 (0.0)	0 (0.0)	36 (19.7)	61 (6.0)
Marital status[e]							
Married or living with someone	85 (85.0)	0 (0.0)	56 (50.0)	75 (75.0)	2 (7.4)	49 (37.4)	267 (52.8)
Never married	7 (7.0)	36 (100.0)	45 (40.2)	16 (16.0)	25 (92.6)	66 (50.4)	195 (38.5)
Divorced/widowed	8 (8.0)	0 (0.0)	11 (9.8)	9 (9.0)	0 (0.0)	16 (12.2)	44 (8.7)
Household is primary residence	98 (98.0)	225 (98.7)	135 (86.5)	98 (98.0)	234 (98.3)	163 (89.1)	954 (94.8)
Slept in household last night	100 (100.0)	225 (99.1)	144 (92.9)	99 (99.0)	238 (99.6)	178 (97.2)	984 (98.0)
≥1 past positive HBV test	90 (90.0)	0 (0.0)	3 (1.9)	0 (0.0)	1 (0.4)	1 (0.5)	95 (9.4)
Past positive HIV test	16 (16.0)	3 (1.3)	1 (0.6)	1 (1.0)	0 (0.0)	1 (0.5)	22 (2.2)
Current ART regimen							
Tenofovir, lamivudine, dolutegravir	15 (93.8)	1 (33.3)	1 (100.0)	1 (100.0)	0 (0.0)	1 (100.0)	19 (86.4)
Dolutegravir, abacavir	0 (0.0)	2 (66.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (9.1)
Not taking	1 (6.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (4.5)
Pregnant at household enrollment	56 (56.6)	0 (0.0)	0 (0.0)	13 (13.0)	0 (0.0)	3 (4.4)	72 (20.2)

Data are presented as No. (%) unless otherwise indicated.

Abbreviations: ART, antiretroviral therapy; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; HIV, human immunodeficiency virus; IQR, interquartile range.

[a]Index status of households based on index mother's antenatal recruitment point-of-care HBsAg screening.

[b]Modern housing is a composite variable of materials used in the roofing, walls, flooring, and windows, using previously published categorizations further described in the Supplementary Materials.

[c]Wealth index is calculated by a principal components analysis accounting for household attributes further described in the Supplementary Materials.

[d]Age in 2022 dichotomized using 13 years to approximate whether participant was born before or after infant pentavalent vaccination introduction in 2009, further described in the Supplementary Materials.

[e]Survey question asked to participants aged ≥15 years.

.6%–3.2%) in index-positive and index-negative households, respectively, corresponding to an unadjusted PR of 2.61 (95% CI, 1.20–6.25), and PR adjusted for household clustering of 2.52 (95% CI, .88–7.23) (Table 2, Supplementary Figure 3). Overall, we observed 27 household members who were HBsAg-positive (19 index-positive, 8 index-negative) from 17 distinct households (Figure 2*B* and 2*C*). We observed 15 HBsAg infections among direct offspring; HBsAg-positivity prevalence among direct offspring was 5.3% (95% CI, 2.4%–8.2%) in index-positive households and 1.3% (95% CI, .0%–2.7%) in index-negative households, corresponding to an unadjusted PR of 4.18 (95% CI, 1.35–18.16) and adjusted PR of 3.33 (95% CI, .94–11.84). Among these 15 direct offspring who were HBsAg-positive, 12 had mothers who were HBsAg-positive at both timepoints; the remaining 3 came from 2 households in which index mothers had possible incident infections. We observed 12 HBsAg infections among other household members; HBsAg-positivity prevalence was 4.5% (95% CI, 1.2%7.7%) and 2.7% (95% CI, .4%–5.1%) among other household members in index-positive and index-negative households, respectively, corresponding to an unadjusted PR of 1.64 (95% CI, .53–5.45) and adjusted PR of 1.01 (95% CI, .24–4.25). We observed 1 HBsAg infection among male partners in index-positive households and 1 among male partners in index-negative households, for a PR of 0.65 (95% CI, .04–10.10) comparing those in index-positive to index-negative households.

In sensitivity analyses using alternate definitions of index grouping of households, household prevalence estimates of HBsAg positivity were largely consistent with those obtained under the primary definition (Supplementary Figure 3), except for the analysis of direct offspring (all direct offspring infected lived with a mother who was HBsAg-positive at least once). Of the 100 index mothers who were HBsAg-positive at recruitment, 96 were HBsAg-positive and 4 were HBsAg-negative at enrollment (Figure 2*C*). Two women who were HBsAg-negative at recruitment were HBsAg-positive at enrollment, representing possible incident cases of horizontal transmission, and 98 index mothers were HBsAg-negative at both points.

Factors Associated With HBsAg Positivity

Among index mothers, several individual attributes and potential sources of community HBV exposure were associated with HBsAg positivity. Increasing age was associated with higher odds of HBsAg positivity, with an OR of 1.06 (95% CI, 1.01–1.11) per 1-year increase in age (Figure 3, Supplementary Figure 4, Supplementary Table 2). Never having been married was associated with 0.39 (95% CI, .14–.96) times the odds of HBsAg positivity compared with being married. Declining to answer age of sexual debut was associated with 4.53 (95% CI, 1.81–12.79) times the odds of HBsAg positivity compared with reporting sexual debut at 18 years or older. All variables assessing recent multiple and new sexual partners were

Table 2. Hepatitis B Surface Antigen Prevalence Among Household Members in Index-Positive and Index-Negative Households

Stratification	Comparison	HBsAg-Positive	HBsAg-Negative	Total	Prevalence, %	(95% CI)[a]	Unadjusted PR	(95% CI)	Adjusted PR[b]	(95% CI)[c]
Overall	Index positive[d]	19	364	383	5.0	(1.9–8.0)	2.61	(1.20–6.25)	2.52	(.88–7.23)
	Index negative	8	412	420	1.9	(.0–3.9)	Ref	…	Ref	…
Direct offspring	Index positive	12	215	227	5.3	(1.6–9.0)	4.18	(1.35–18.16)	3.33	(.94–11.84)
	Index negative	3	234	237	1.3	(.0–3.2)	Ref	…	Ref	…
Other	Index positive	7	149	156	4.5	(.0–9.9)	1.64	(.53–5.45)	1.01	(.24–4.25)
	Index negative	5	178	183	2.7	(.0–5.5)	Ref	…	Ref	…
Male partner[e]	Index positive	1	51	52	1.9	(.0–5.8)	0.65	(.04–10.10)	0.65	(.04–10.10)
	Index negative	1	33	34	2.9	(.0–8.9)	Ref	…	Ref	…
Index positive	Direct offspring	12	215	227	5.3	(1.6–9.0)	1.17	(.49–3.10)	1.25	(.48–3.24)
	Other	7	149	156	4.5	(.0–9.9)	Ref	…	Ref	…
Index negative	Direct offspring	3	234	237	1.3	(.2–5.0)	0.46	(.10–1.86)	0.91	(.26–3.17)
	Other	5	178	183	2.7	(1.0–7.4)	Ref	…	Ref	…

Abbreviations: CI, confidence interval; HBsAg, hepatitis B surface antigen; PR, prevalence ratio.

[a]Prevalence CIs calculated using Wald-type interval on the probability scale, accounting for household clustering in the study design, using *svydesign()* and *svyciprop()* (unweighted) from the *survey* package (v4.1.1) in R v4.2.2.

[b]Adjusted for household clustering using a random intercept term for household in *glmer()* from *lme4* package in R4.2.2.

[c]Wald CIs from multilevel model, which accounts for household clustering.

[d]Index status defined by index mother's HBsAg status at antenatal recruitment. See the Supplementary Materials for sensitivity analyses for alternate definitions of index groupings by HBsAg positivity of index mothers across recruitment and enrollment timepoints.

[e]Male partners are included in the "other" category elsewhere in the analysis, but are separated here for the purpose of examining sexual relationships.

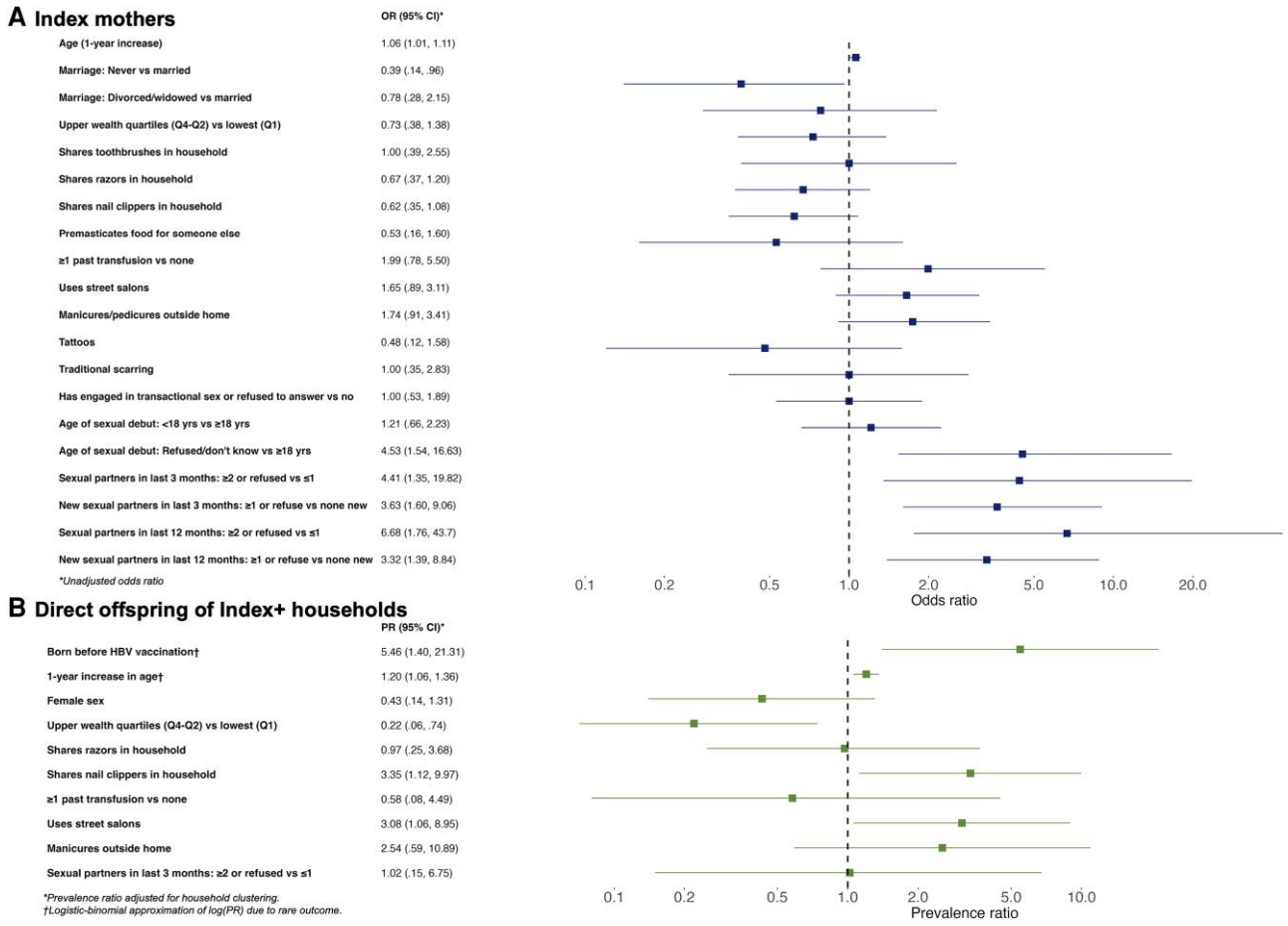

Figure 3. Attributes and practices associated with hepatitis B surface antigen (HBsAg) positivity among index mothers (*A*) and direct offspring of index-positive households (*B*). Index mothers' HBsAg result from recruitment screening used for index mothers and index-positive household grouping of direct offspring. The Supplementary Materials show sensitivity analyses using other definitions of index grouping of households. Unadjusted odds ratio shown as measure of association for index mothers due to case-control recruitment of mothers. Prevalence ratio adjusted for household clustering shown for direct offspring. Abbreviations: CI, confidence interval; HBV, hepatitis B virus; OR, odds ratio; PR, prevalence ratio.

associated with higher odds of HBsAg positivity compared with the referent; for example, having at least 1 new sexual partner in the last 3 months or declining to answer was associated with 3.63 (95% CI, 1.60–9.06) times the odds of HBsAg positivity compared with having no new sexual partners in the last 3 months. All associations held across sensitivity analyses in which definitions of index-positive and index-negative households were varied (Supplementary Figure 4). We did not observe evidence that engaging in transactional sex was associated with higher odds of HBsAg positivity (OR, 1.00 [95% CI, .53–1.89]).

Among direct offspring in index-positive households, a 1-year increase in age was associated with higher HBsAg-positivity prevalence (adjusted PR, 1.42 [95% CI, 1.07–1.89]). Offspring older than 13 years in 2022 (born before pentavalent vaccine introduction in DRC) had 13.24 (95% CI, 1.61–108.63) times the HBsAg-positivity prevalence of those ≤13 years (Figure 3, Supplementary Figure 5, Supplementary Table 3). Offspring from wealthier index-positive households had 0.22 (95% CI, 95% CI, .06–.74]) times the HBsAg-positivity prevalence of those from index-positive households in the lowest wealth quartile. Sharing nail clippers in the household (adjusted PR, 3.35 [95% CI, 1.12–9.97]) and using street salons (adjusted PR, 3.08 [95% CI 1.06–10.89]) in the community were both associated with higher HBsAg-positivity prevalence among direct offspring in index-positive households. No attributes or practices were associated with HBsAg positivity among direct offspring in index-negative households, but this analysis was limited by few (n = 3) offspring who were HBsAg-positive (Supplementary Table 4).

Other household members in index-positive and index-negative households had too few infections (n = 7 and n = 5, respectively) to estimate PRs within these subgroups, but in index-positive households, history of traditional scarring was associated with HBsAg positivity ($P = .002$; Supplementary Table 5). Among other household members in index-negative households, no attributes or practices were significantly associated with HBsAg positivity (Supplementary Table 6).

HBV Vaccination

A total of 330 HBsAg-negative household members were living with someone who was HBsAg-positive. At 6 months following enrollment completion, 162 (49%) had initiated the vaccine series and 149 (45%) had completed the series (92% completion rate); 51 (15%) had refused vaccination outright; the remainder had accepted but did not present for vaccination. When we followed up with vaccine-eligible participants, the most cited reasons for nonvaccination were vaccine hesitancy and distance to the maternities where we offered vaccination.

DISCUSSION

In this large household HBV investigation in the DRC, we identified evidence of ongoing HBV transmission and opportunities for a range of HBV prevention efforts. Prevalence of HBsAg positivity was higher in the households of HBsAg-positive mothers overall and within the direct offspring and other household member subgroups. Adjusting for living in the same household resulted in a shift in the PR toward the null in each comparison, suggesting intrahousehold clustering of HBV in this context. These findings indicate that the existing HIV PMTCT infrastructure in countries like the DRC could be used to identify households for targeted prevention. Factors associated with HBsAg positivity among index mothers included increasing age, current marriage, and recent sexual behavior (having at least 2 recent partners, having at least 1 new recent partner, or declining to answer recent partner questions). Among direct offspring in index-positive households, HBsAg positivity was associated with increasing age, fewer household resources, and use of shared nail clippers or street salons. We also observed evidence that traditional scarring could be associated with HBsAg positivity among other household members. These potential sources of HBV infection corroborate findings from past studies in other African settings [25, 32] and suggest priority behaviors or subgroups for intervention in urban Kinshasa that may be relevant to other megacities in Africa.

Rollout of infant HBV vaccination within the pentavalent series starting at 6 weeks of age is one possible explanation for the HBV prevalence among children in index-positive households, which was >13 times as high for those who were aged >13 years compared to those who were aged ≤13 years in 2022. Our findings are consistent with results of a study conducted in Burkina Faso, which also reported lower HBsAg positivity among children born to 215 HBsAg-positive mothers after HBV vaccine rollout but before birth dose [33]. We observed relatively few HBsAg-positive offspring of HBsAg-positive mothers, suggestive of infrequent perinatal transmission given that PMTCT measures have not been implemented in DRC. Our observation of possible incident and cleared infections among mothers further suggests recent HBV exposures and that horizontal transmission is occurring. Accumulation of HBV exposures in households and communities over time is a plausible explanation for the observed increasing HBsAg positivity risk with age.

The strong observed association with sexual behaviors provides further evidence of horizontal HBV transmission. The strongest association with HBsAg positivity was observed for index mothers who reported multiple recent or any new sexual partners or who declined to discuss. This finding is in line with a past study of DRC healthcare workers that found an association between multiple sexual partners and HBsAg positivity [17]. We did not observe evidence that engagement in transactional sex was associated with HBsAg positivity. Interestingly, we observed lower prevalence of HBsAg-positivity among male partners of HBsAg-positive mothers compared with HBsAg-negative mothers. While precision was limited, one explanation for this finding is that sexual partners have been previously exposed and recovered from infection, which could be clarified by serological analysis that was not feasible with DBS samples. Together, our findings indicate that development of HBV prevention efforts for the broader population of women of childbearing age are needed in the DRC.

Our personal experience conducting this study was that integration of antenatal HBsAg testing alongside existing HIV testing is acceptable to maternity center staff and patients, consistent with prior research on feasibility and acceptability of implementing HBV prevention measures in maternity centers [21, 22]. While rapid HBsAg tests are available for just over 1 US dollar per test, scaling this effort is often hindered by a siloed approach to healthcare in which HIV funders do not cover HBsAg or syphilis screening, both of which are recommended for triple elimination [34]. Women who are HBsAg-positive could be offered HBV antiviral prophylaxis and HBV birth-dose vaccine for their newborns and given the opportunity to have household members screened and vaccinated. ANC visits also provide opportunities for health education. While these measures are not currently offered in the DRC, increasing evidence indicates that they would be effective and feasible in the DRC [21].

Our study has several limitations. First, our cross-sectional study design does not allow for analysis of the timing of infection, preventing definitive determination of vertical versus horizontal transmission. The described incident cases among index mothers may reflect varying levels of antigenemia and/or reversion to a positive test. Serological analysis and HBV sequencing could improve our characterization of these transmission patterns, but HBV serology is largely inaccessible in-country, and serological assays for DBS samples collected in this study and often used in resource-limited settings like DRC continue to perform poorly for HBV [35]. Second, enrollment of households several months to over a year after recruitment during antenatal screening meant that we inherently selected

a population based in Kinshasa. Individuals with frequent time out of Kinshasa might have a different prevalence of HBV infection and associated behaviors not captured in this study. Third, household members absent during our enrollment visit could not be included, potentially resulting in biased prevalence estimates. However, our estimates remain useful for clinicians assessing household infection risk as part of routine ANC and for development of targeted prevention programs.

In the largest and most detailed household investigation of HBV in DRC conducted to date, we found that HBV screening as part of existing HIV PMTCT programs can be used to identify infected mothers and household members as well as households where vaccination may be particularly beneficial. In addition to World Health Organization–recommended efforts to prevent mother-to-infant HBV transmission, prevention of horizontal transmission within households and communities should be prioritized. Possible interventions include education to reduce blood exposure through household item sharing and to use barrier protection (such as condoms) during sexual intercourse, as well as targeted vaccination programs in adults. While additional research is needed to determine precise HBV transmission mechanisms in settings like the DRC, our findings provide a foundation for developing new HBV transmission prevention strategies.

Supplementary Data

Supplementary materials are available at *Open Forum 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. P., P. T., M. Y., and S. M. conceptualized the study. P. N., S. N., J. M., M. T., N. M., and M. M. K. collected data. C. E. M., A. J. N. B., P. N., S. N., J. M., N. M., M. M. K., L. J., J. B. P., P. T., M. E., J. K. E., and K. A. P. analyzed and interpreted results. C. E. M., A. J. N. B., J. B. P., P. T., M. E., J. K. E., and K. A. P. drafted the manuscript. All authors have reviewed and approved the manuscript.

Acknowledgments. We would like to thank all participants who offered their time and participation in this study. We would also like to thank the staff at Binza and Kingasani maternities for their collaboration in conducting antenatal HBsAg screening and administering Euvax HBV vaccination. We would also like to thank Dr Alpha Oumar Diallo for his contributions establishing the REDCap study database. Last, we thank the late Dr Steve Meshnick for his mentorship and contributions to the conceptualization of this study. De-identified data have been made publicly available through the Carolina Digital Repository: https://cdr.lib.unc.edu/concern/data_sets/hh63t625t.

Patient consent. This study was approved by the Institutional Review Board at the University of North Carolina (19–1875) and the Ethics Committee at Université Protestante au Congo (CE/UPC/0062). All participants provided written informed consent if 18 years and older, or assent and parental permission if under 18 years.

Financial support. This investigator-sponsored research study was funded by Gilead Sciences, Inc. It was partially supported by the National Institutes of Health (grant numbers F30AI169752 and D43TW009340 supporting C. E. M.; K08AI148607 to P. T.; R01HD087993 to M. Y.; U01AI096299 and R01HD105526 supporting M. T., N. M., and M. Y., and UL1TR002489 to University of North Carolina [UNC] NCTracs for REDCap data collection). C. E. M. is also supported by the UNC Royster Graduate Fellowship.

Potential conflicts of interest. J. B. P. and P. T. report nonfinancial support from Abbott Laboratories (donation of hepatitis B laboratory testing and reagents for other studies), and J. B. P. reports consulting for Zymeron Corporation, all outside the submitted work. All other authors report no potential conflicts.

References

1. World Health Organization. Global progress report on HIV, viral hepatitis and sexually transmitted infections, 2021: accountability for the global health sector strategies 2016–2021. Actions for impact: web annex 1: key data at a glance. 2021. Available at: https://apps.who.int/iris/handle/10665/342808. Accessed 12 October 2021.
2. Razavi-Shearer D, Gamkrelidze I, Nguyen MH, et al. Global prevalence, treatment, and prevention of hepatitis B virus infection in 2016: a modelling study. Lancet Gastroenterol Hepatol **2018**; 3:383–403.
3. Nayagam S, Thursz M, Sicuri E, et al. Requirements for global elimination of hepatitis B: a modelling study. Lancet Infect Dis **2016**; 16:1399–408.
4. McNaughton AL, Lourenço J, Bester PA, et al. Hepatitis B virus seroepidemiology data for Africa: modelling intervention strategies based on a systematic review and meta-analysis. PLoS Med **2020**; 17:e1003068.
5. World Health Organization. WHO releases first-ever global guidance for country validation of viral hepatitis B and C elimination. 2021. Available at: https://www.who.int/news/item/25-06-2021-who-releases-first-ever-global-guidance-for-country-validation-of-viral-hepatitis-b-and-c-elimination. Accessed 14 July 2021.
6. Cui Y, Jia J. Update on epidemiology of hepatitis B and C in China. J Gastroenterol Hepatol **2013**; 28(Suppl 1):7–10.
7. Edmunds WJ, Medley GF, Nokes DJ, O'Callaghan CJ, Whittle HC, Hall AJ. Epidemiological patterns of hepatitis B virus (HBV) in highly endemic areas. Epidemol Infect **1996**; 117:313–25.
8. Shan S, Cui F, Jia J. How to control highly endemic hepatitis B in Asia. Liver Int **2018**; 38(Suppl 1):122–5.
9. Dumpis U, Holmes EC, Mendy M, et al. Transmission of hepatitis B virus infection in Gambian families revealed by phylogenetic analysis. J Hepatol **2001**; 35: 99–104.
10. Kiire CF. The epidemiology and prophylaxis of hepatitis B in sub-Saharan Africa: a view from tropical and subtropical Africa. Gut **1996**; 38(Suppl 2):S5–12.
11. Thompson P, Parr JB, Holzmayer V, et al. Seroepidemiology of hepatitis B in the Democratic Republic of the Congo. Am J Trop Med Hyg **2019**; 101:226–9.
12. Naughton B, Abramson R, Wang A, Kwan-Gett T. DRC survey: an overview of demographics, health, and financial services in the Democratic Republic of the Congo. Seattle: University of Washington Strategic Analysis, Research and Training (START) Center, **2017**.
13. Shindano TA, Kabinda JM, Mitashi P, Horsmans Y. Hepatitis B virus infection in the Democratic Republic of Congo: a systematic review of prevalence studies (2000–2016). J Public Health (Berl) **2018**; 26:595–603.
14. Mpody C, Thompson P, Tabala M, et al. Hepatitis B infection among pregnant and post-partum women living with HIV and on antiretroviral therapy in Kinshasa, DR Congo: a cross-sectional study. PLoS One **2019**; 14:e0216293.
15. Mudji J, Madinga B, Horsmans Y. Seroprevalence of viral hepatitis B and C and knowledge of the hepatitis B virus among pregnant women attending prenatal care in the Democratic Republic of Congo. Am J Trop Med Hyg **2021**; 104:1096–100.
16. Kabinda JM, Akilimali TS, Miyanga AS, Donnen P, Michèle DW. Hepatitis B, hepatitis C and HIV in pregnant women in the community in the Democratic Republic of Congo. World J AIDS **2015**; 5:124–30.
17. Lungosi MB, Muzembo BA, Mbendi NC, et al. Assessing the prevalence of hepatitis B virus infection among health care workers in a referral hospital in Kisantu, Congo DR: a pilot study. Ind Health **2019**; 57:621–6.
18. Bisimwa PB, Masemo DB, Byabene AK, et al. High prevalence of hepatitis B and HIV among women survivors of sexual violence in South Kivu Province, eastern Democratic Republic of Congo. medRxiv [Preprint]. Posted online 25 September **2023**. doi:10.1101/2023.09.22.23295978
19. United Nations Children's Fund. UNICEF data warehouse, V1.15. WHO/UNICEF estimates of national immunization coverage, 2021 revision: Democratic Republic of Congo, time period: 2020. 2021. Available at: https://data.unicef.org/resources/data_explorer/unicef_f/. Accessed 19 June 2023.
20. World Health Organization (WHO). Prevention of mother-to-child transmission of hepatitis B virus: guidelines on antiviral prophylaxis in pregnancy. Geneva, Switzerland: WHO, **2020**. Available at: https://apps.who.int/iris/handle/10665/333391. Accessed 20 November 2022.
21. Thompson P, Morgan CE, Ngimbi P, et al. Arresting vertical transmission of hepatitis B virus (AVERT-HBV) in pregnant women and their neonates in the

Democratic Republic of the Congo: a feasibility study. Lancet Global Health **2021**; 9:e1600–9.
22. Boisson A, Morgan CE, Fried B, et al. Barriers and facilitators to timely birth-dose vaccines in Kinshasa province, the DRC: a qualitative study. J Global Health Rep **2022**; 6:e2022028.
23. Alere Medical Co., Ltd. Fact sheet: DETERMINETM HBsAg 2. Available at: https://www.globalpointofcare.abbott/ww/en/product-details/determine-hbsag-2.html. Accessed 8 December 2023.
24. Centers for Disease Control and Prevention. Hepatitis B FAQs. 2020. Available at: https://www.cdc.gov/hepatitis/hbv/bfaq.htm. Accessed 14 June 2021.
25. Martinson FEA, Weigle KA, Royce RA, Weber DJ, Suchindran CM, Lemon SM. Risk factors for horizontal transmission of hepatitis B virus in a rural district in Ghana. Am J Epidemiol **1998**; 147:478–87.
26. Eroglu C, Zivalioglu M, Esen S, Sunbul M, Leblebicioglu H. Detection of hepatitis B virus in used razor blades by PCR. Hepat Mon **2010**; 10:22–5.
27. Awili HO, Gitao GC, Muchemi GM. Seroprevalence and risk factors for hepatitis B virus infection in adolescent blood donors within selected counties of western Kenya. Biomed Res Int **2020**; 2020:8578172.
28. Government of the Democratic Republic of Congo. Annual progress report 2007. **2008**. Available at: https://www.gavi.org/sites/default/files/document/annual-progress-report-congo%2C-democratic-republic-of-the-2007pdf.pdf. Accessed 8 December 2023.
29. Le gouvernement de Republique Democratique du Congo. Rapport annuel de situation 2008. **2009**. Available at: https://www.gavi.org/sites/default/files/document/annual-progress-report-congo%2C-democratic-republic-of-the-2008–francais-pdf.pdf. Accessed 8 December 2023.
30. Cummings P. The relative merits of risk ratios and odds ratios. Arch Pediatr Adolesc Med **2009**; 163:438–45.
31. R Core Team. R: A Language and Environment for Statistical Computing. Vienna, Austria: R Foundation for Statistical Computing, **2024**. https://www.R-project.org/.
32. Tazinkeng NN, Teuwafeu DG, Asombang AW, et al. Factors associated with hepatitis B and C among adults in Buea, Cameroon: a community-based cross-sectional study. Liver Int **2022**; 42:2396–402.
33. Guingané AN, Kaboré R, Shimakawa Y, et al. Screening for hepatitis B in partners and children of women positive for surface antigen, Burkina Faso. Bull World Health Organ **2022**; 100:256–67.
34. Zhang L, Tao Y, Woodring J, et al. Integrated approach for triple elimination of mother-to-child transmission of HIV, hepatitis B and syphilis is highly effective and cost-effective: an economic evaluation. Int J Epidemiol **2019**; 48: 1327–39.
35. Amini F, Auma E, Hsia Y, et al. Reliability of dried blood spot (DBS) cards in antibody measurement: a systematic review. PLoS One **2021**; 16: e0248218.