Acceptability and feasibility of a screen-and-treat programme for hepatitis B virus infection in The Gambia: the Prevention of Liver Fibrosis and Cancer in Africa (PROLIFICA) study

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Summary

Background Despite the introduction of immunisation for hepatitis B virus (HBV) in the 1990s, HBV-related morbidity and mortality remain high in sub-Saharan Africa. Identification and treatment of asymptomatic people with chronic HBV infection should reduce the disease burden. We therefore assessed the feasibility of a screen-and-treat programme for HBV infection in The Gambia, west Africa, and estimated the proportion of HBV-infected people who had significant liver disease in need of treatment.

Methods Between Dec 7, 2011, and Jan 24, 2014, individuals living in randomly selected communities in western Gambia were offered hepatitis B surface antigen (HBsAg) screening via a point-of-care test. The test was also offered to potential blood donors attending the central hospital in the capital, Banjul. HBsAg-positive individuals were invited for a comprehensive liver assessment and were offered treatment according to international guidelines. We defined linkage to care as visiting the liver clinic at least once. Eligibility for treatment was judged in accordance with the 2012 European Association for the Study of the Liver guidelines.

Findings HBsAg screening was accepted by 5980 (weighted estimate 68·9%, 95% CI 65·0–72·4) of 8170 adults from 27 rural and 27 urban communities and 5559 (81·4%, 80·4–82·3) of 6832 blood donors. HBsAg was detected in 495 (8·8%, 7·9–9·7) individuals in communities and 721 (13·0%, 12·1–13·9) blood donors. Prevalence was higher in men (239 [10·5%, 8·9–12·1] of 2328 men *vs* 256 [7·6%, 6·5–8·7] of 3652 women; p=0·004) and middle-aged participants. Linkage to care was high in the communities, with 402 (81·3%) of 495 HBsAg-positive individuals attending the clinic. However, only 300 (41·6%) of 721 HBsAg-positive people screened at the blood bank linked into care. Of those who attended the clinic, 18 (4·4%, 2·5–7·7) patients from the communities and 29 (9·7%, 6·8–13·6) from the blood bank were eligible for treatment. Male sex was strongly associated with treatment eligibility (odds ratio 4·35, 1·50–12·58; p=0·007).

Interpretation HBV infection remains highly prevalent in The Gambia. The high coverage of community-based screening, good linkage into care, and the small proportion of HBsAg carriers who need treatment suggest that large-scale screening and treatment programmes are feasible in sub-Saharan Africa.

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Introduction

Hepatitis B virus (HBV) infection is highly prevalent in sub-Saharan Africa, where 80 million people are chronically infected with the virus.[1] Hepatocellular carcinoma remains one of the most common cancers in the region and is mainly attributable to HBV.[2] Hepatitis B vaccine coverage in sub-Saharan Africa is imperfect[3] and many people born before the introduction of the vaccine continue to carry the virus, which confers a risk of cirrhosis and hepatocellular carcinoma.[4]

In 2015, WHO has published its first guidelines on chronic HBV infection, but the recommendations for sub-Saharan Africa are very limited due to insufficient data.[5] In sub-Saharan Africa, screening and treatment for hepatitis B are rarely accessible[6,7] and blood banks are the only places where people are offered free HBV testing. However, these free tests are to ensure the safety of the blood products, and deferred donors are rarely linked to care.[8] Although the prevalence of infection is high in the general population in sub-Saharan Africa,[9] people have very little opportunity to be tested for HBV unless they are infected with HIV or develop advanced liver disease. Screening and treatment interventions that target the general population have never been assessed in sub-Saharan Africa.

Prevention of Liver Fibrosis and Cancer in Africa (PROLIFICA), the first screen-and-treat programme for HBV mono-infected people in sub-Saharan Africa, was started in June, 2011, in The Gambia, west Africa.[10] As part of this programme, we investigated whether mass

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Research in context

Evidence before this study

We searched MEDLINE and Embase for articles written in French or English and published before Sept 1, 2015, with terms incorporating "hepatitis B", "mass screening", and "Africa". We were unable to find any previous studies describing screen-and-treat interventions for hepatitis B virus (HBV) infection that targeted the general population in Africa.

Added value of this study

To our knowledge, PROLIFICA is the first screen-and-treat intervention programme to be implemented in Africa. In addition to showing the feasibility of such an intervention, our results provide new data on screening coverage for HBV testing, the prevalence of hepatitis B surface antigen positivity, linkage of screening to health care, and the proportion of chronically infected people with clinically significant liver disease who need treatment.

Implications of all the available evidence

By providing further evidence for the high prevalence of HBV infection and the good coverage achieved with HBV screening and care, our results show the feasibility of a large-scale screen-and-treat programme for HBV infection in The Gambia. This approach deserves to be assessed in other resource-limited HBV-endemic countries. National health departments in sub-Saharan Africa and WHO should consider integrating such a programme into public health strategies to fight against the epidemic of HBV infection in Africa.

screening for HBV infection is justified by referring to the Wilson and Jungner WHO criteria for disease screening.[11] We previously reported that hepatitis B surface antigen (HBsAg) point-of-care tests perform well in field conditions in the African community setting.[12] We validated inexpensive and simple diagnostic tools for the assessment of liver disease.[13] We also identified risk factors for liver disease progression by following up a population-based cohort in rural Gambia.[14]

In this study, we assessed the acceptability and feasibility of a screen-and-treat HBV intervention programme in west Africa by analysing screening coverage, prevalence of HBsAg, the proportion of HBsAg-positive individuals linked to care, and the proportion of chronically infected people with clinically significant liver disease in need of treatment in community-based and facility (blood bank)-based settings in The Gambia.

Methods

Community screening

We did the community-based screening in the western part of The Gambia (figure 1) where 750 000 people live in 1450 census enumeration areas defined by the Gambia Bureau of Statistics. We used enumeration area as a sampling unit, and one enumeration area can consist of an entire village, part of a large village or town, or a cluster of small hamlets. Because HBV prevalence might differ between urban and rural populations, we first stratified the 1450 enumeration areas into urban (n=1197) and rural (n=253) communities. Then, we selected 27 enumeration areas from each stratum by simple random sampling with a random number generator (Stata). In the selected enumeration areas, all inhabitants aged 30 years or older were eligible for screening. We excluded people younger than 30 years because the national hepatitis B vaccination programme started in 1990 so these people should be covered.[15] We organised a meeting in each enumeration area with the help of the village head. After community approval was obtained, a team of fieldworkers did a census by visiting all households to register the name, age, and sex of all eligible people and to invite them for screening. Pre-test counselling was delivered and written consent obtained. Ethics approval for the study was granted by the Government of The Gambia and MRC Gambia Joint Ethics Committee.

We did finger-prick whole blood test for HBsAg using a point-of-care test (Determine, Alere, Waltham, MA, USA), the performance of which has been validated in the field (sensitivity 88·5%, specificity 100%).[12] We provided the results to the participants on site with post-test counselling, and those who tested positive for HBsAg were referred to the liver clinic at the Medical Research Council (MRC) unit in Fajara (figure 1). People who were invited, but did not attend screening were reminded by the fieldworkers up to three times. Reasons for non-attendance to the screening were captured in a standardised form. Additional questions about knowledge of HBV infection and past experience of HBV testing were administered to all individuals screened between Aug 18 and Nov 1, 2013.

Facility-based screening

Since 2011, in addition to HIV testing, the Edward Francis Small Teaching Hospital (EFSTH), the only tertiary care hospital in Banjul, the capital of The Gambia, started HBV screening at its blood bank by use of a point-of-care test (Onsite Combo Rapid Test, CTK Biotech, San Diego, CA, USA). The manufacturer of the test reports its sensitivity to be 96% and its specificity to be 100%. Blood donors at the EFSTH blood bank must be healthy and aged at least 16 years. Individuals who tested positive for HBsAg were referred to a study nurse posted at EFSTH who provided post-test counselling and advised them to visit the MRC clinic in Fajara. Individuals who were co-infected with HIV and HBV were referred to the national HIV programme.

Linkage to care

In individuals who tested positive for HBsAg in both the community-based and facility-based screening, linkage to care was defined as visiting the outpatient PROLIFICA liver clinic at least once after HBV screening. Those who did not come to the clinic were reminded up to three times via telephone calls from the fieldworkers. We used semi-structured interviews in a subgroup of HBsAg-positive participants (all individuals screened between Aug 1 and Nov 30, 2013) to identify reasons for non-attendance to the clinic.

Assessment of liver disease

Patients who attended the liver clinic underwent a standardised comprehensive liver assessment that included physical examination, abdominal ultrasound (Portable MyLab25Gold, Esaote, Cambridge, UK), fasting liver stiffness measurement with hepatic transient elastography (Fibroscan 402, Echosens, Paris, France),[16] and routine serum haematology and biochemistry tests. Optimum cutoff values for liver stiffness measurements were established previously by use of liver histology as a reference: the cutoff for clinically significant fibrosis was 7·9 kPa (Metavir score ≥F2) and the cutoff for cirrhosis was 9·5 kPa (F4).[13] Liver stiffness measurements were deemed unreliable if they had a ratio of IQR divided by liver stiffness measurement greater than 0·30 when liver stiffness measurement is at least 7·1 kPa.[17] Blood samples were tested for hepatitis B envelope antigen (HBeAg; ELISA-ETI-EBK Plus, Diasorin, Saluggia, Italy) and antibodies to hepatitis C virus (HCV; AxSYM, anti-HCV, Abbott, Chicago, IL, USA) and hepatitis delta virus (HDV; ETI-AB-DELTAK-2, Diasorin). Antibodies to HIV-1 and HIV-2 were detected with an enzyme immunoassay (Genscreen ULTRA HIV Ag-Ab, Bio-Rad, Hercules, CA, USA). HBV DNA levels were measured with an in-house quantitative real-time polymerase chain reaction (qPCR) assay (lower limit of detection of 50 IU/mL), which was validated against commercial HBV qPCR assays (the COBAS TaqMan HBV Version 2.0 test on a COBAS AmpliPrep [Roche, Basel, Switzerland] and the Abbott Real Time HBV assay [Abbott Molecular Diagnostics, Wiesbaden, Germany]; r^2=0·90 for correlation with the commercial assay).[18] All blood samples were tested at the MRC unit in Fajara. Quality control and HBV genotyping were done by a reference laboratory in France (INSERM U1052, Lyon, France).

Antiviral therapy

HBsAg-positive individuals who attended the liver clinic were assessed for eligibility for treatment in accordance with the 2012 European Association for the Study of the Liver (EASL) guidelines[19] (appendix p 3). In the absence of contraindications, tenofovir (tenofovir disoproxil fumarate) was provided free of charge (Viread [Gilead Sciences, Foster City, CA, USA], 300 mg oral dose once per day). Adherence to treatment was assessed with the Morisky adherence scale.[20]

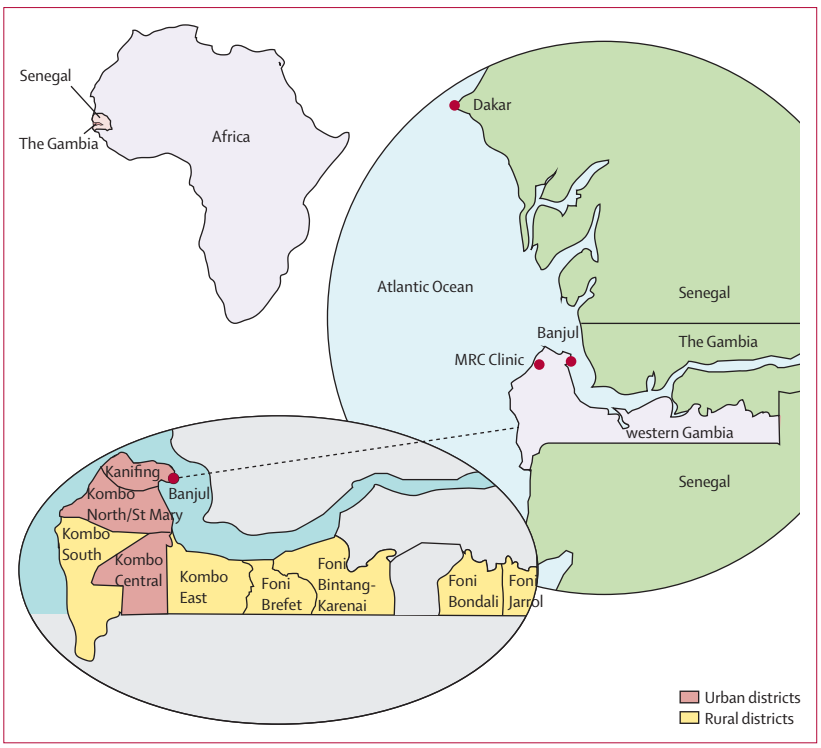

Figure 1: **Locations of the urban and rural community areas selected for screening**

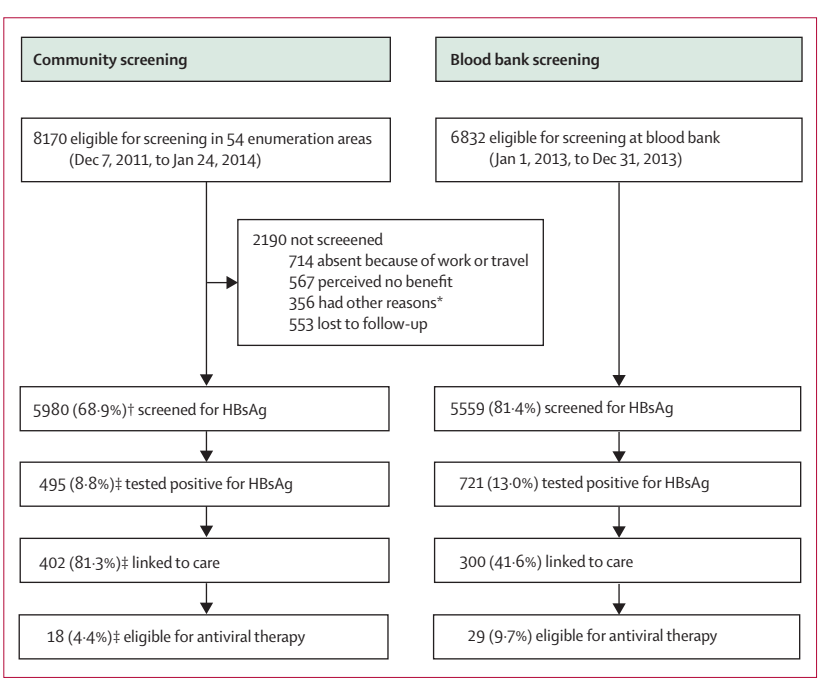

Figure 2: **Flow chart of study participants**

*Other reasons for non-participation were too busy (n=65); feeling ill (n=55); husband refusal (women only; n=43); afraid of bleeding (n=21); no trust in Medical Research Council (n=11); already tested before (n=4); and refusal without revealing any specific reason (n=157). †Estimates accounted for survey design. ‡Estimates accounted for survey design and non-attendance to the programme. HBsAg=hepatitis B surface antigen.

See Online for appendix

Statistical analysis

We estimated screening coverage for the enumeration areas included in the study by dividing the number of individuals screened by the population according to the census. We estimated the effects of individual-level variables (sex and age) and community-level variables (urban or rural, screening season, screening during weekend, and assistance of village health workers) on the coverage of community screening with logistic regression adjusted for age and sex. We estimated linkage to care by dividing the number of individuals who visited the liver clinic by the number of HBsAg-positive individuals identified at screening. We calculated the proportion eligible for treatment by dividing the number of individuals who fulfilled the treatment criteria by the number of HBsAg-positive participants assessed at the clinic. We used logistic regression to estimate odds ratios (OR) for the factors associated with linkage to care and treatment eligibility. For the community screening, all of these estimates accounted for survey design (correlation within enumeration areas and stratification by urban or rural area) by use of the svy command in Stata 11.0. We did not apply finite population correction because the sample size was small relative to the population size. The HBsAg prevalence, the proportion of HBsAg-positive individuals linked to care, and the proportion eligible for treatment among community screening participants were weighted for non-attendance to screening; the weighting was a reciprocal of the probability of screening coverage derived from a logistic regression with predictors (sex, age, and communities).

	Total eligible (n=8170)	Attended	p value	Adjusted for age and sex	
				Odds ratio (95% CI)	p value
Individual-level factors					
Sex					
Male	3523 (43%)	2328 (60%)	<0·0001	1·0	<0·0001
Female	4646 (57%)	3652 (76%)	..	1·8 (1·5–2·1)	..
Age (years)					
30–39	3259 (40%)	2397 (72%)	<0·0001*	1·0	<0·0001*
40–49	1822 (22%)	1456 (77%)	..	1·3 (1·1–1·5)	..
50–59	1211 (15%)	988 (78%)	..	1·5 (1·2–1·8)	..
≥60	1347 (16%)	1127 (81%)	..	1·9 (1·6–2·2)	..
Community-level factors					
Area					
Urban	3785 (46%)	2511 (66%)	0·0001	1·0	0·006
Rural	4385 (54%)	3469 (79%)	..	1·6 (1·2–2·2)	..
Season					
Dry	6095 (75%)	4372 (68%)	0·5	1·0	0·7
Rainy	2075 (25%)	1608 (72%)	..	1·1 (0·7–1·8)	..
Timing of screening					
Weekdays only	5779 (71%)	4155 (67%)	0·02	1·0	0·02
Weekend	2391 (29%)	1825 (74%)	..	1·4 (1·1–2·0)	..
Village health worker					
Absent	5856 (72%)	4155 (68%)	0·005	1·0	0·05
Present	2314 (28%)	1825 (79%)	..	1·6 (1·0–2·4)	..

Data are n (%) unless stated otherwise. Estimates accounted for survey design. *Test for trend.

Table 1: **Factors associated with screening coverage in the community**

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

Between Dec 7, 2011, and Jan 24, 2014, all selected enumeration areas agreed to participate in the study and 5980 (68·9%, 95% CI 65·0–72·4) of 8170 eligible people participated in the community screening (figure 2). Median duration of screening per enumeration area was three days (IQR 3–5; range 2–8). The median age of participants was 43 years (IQR 35–55) and 2328 (38·9%) were men. Screening coverage varied between enumeration areas, from 48·9% to 95·1%, and was higher in women than in men (p<0·0001) and in older people than in younger people (p<0·0001; table 1). Of the community-level factors, after adjusting for age and sex, rural area (p=0·006), screening during the weekend (p=0·02), and assistance from village health workers (p=0·05) were associated with increased coverage (table 1). The two most common causes of non-attendance were absence due to work or travel (440 [36·8%] men and 274 [27·6%] women) and perceived lack of benefit (284 [23·8%] men and 283 [28·5%] women; figure 2).

Of the 5980 people screened in the communities, 495 (8·8%, 95% CI 7·9–9·7) were identified as being HBsAg-positive. Prevalence of HBsAg varied between enumeration areas from 1·9% to 18·2%. Prevalence was higher in men (239 [10·5%, 8·9–12·1] of 2328 men) than in women (256 [7·6%] 6·5–8·7] of 3652 women; p=0·004), and in both sexes, prevalence decreased with age (p<0·0001 for men and p=0·004 for women; figure 3) and was higher in urban (218 [8·9%] of 2511 individuals) than in rural areas (277 [8·2%] of 346 individuals), although the difference was not significant after adjustment for age and sex.

Knowledge of HBV infection was extremely low in the communities; only two men (0·4%, 95% CI 0·0–6·1) out of 489 participants interviewed in 2013 had heard about HBV infection and had been tested for HBV in the past. None of the 54 HBsAg-positive individuals among these 489 participants had been previously tested and knew their status.

Between Jan 1, and Dec 31, 2013, of the 6832 individuals who came for blood donation at the EFSTH (figure 2), 5559 (81·4%) were screened , of whom 5523 (99·3%) were men. Of these potential male donors, 159 were aged

16–19 years, 2480 were aged 20–29 years, 1932 were aged 30–39 years, 766 were aged 40–49 years, 175 were aged 50–59 years, and 11 were aged 60 years or older. 1273 (18·6%) individuals were not tested because of a shortage of HBsAg test kits.

721 (13·0%, 95% CI 12·1–13·9) of 5559 potential blood donors were HBsAg positive. Among men, prevalence was lowest in those aged 16–19 years (3·1%, 1·0–7·1) and highest in those aged 30–39 years (15·6%, 14·0–17·3; figure 3). Age-specific HBsAg prevalence in men screened at the blood bank did not differ compared with men from community-based screening. In women, there was no clear association between HBsAg prevalence and age, probably because the sample size was small (n=36). In a subset of potential donors (n=694) with available information, most (570 [82·1%]) were first-time donors and HBsAg positivity did not differ significantly between first-time and repeat donors after adjustment for age (data not shown).

Of the 495 HBsAg-positive individuals identified in community screening, 402 (81·3%, 95% CI 76·6–85·2) attended the liver clinic (figure 2), and more of these people were from rural than from urban areas, although there was no association with age and sex (appendix p 1). Absence of symptoms and poor understanding of the disease were the main reasons for non-attendance among a subgroup of 25 HBV-infected individuals who did not attend the liver clinic and were able to be interviewed. Linkage to health care was poorer (300 [41·6%, 38·0–45·3] of 721 HBsAg-positive individuals), in people screened at the blood bank than in those screened in the community (p<0·0001), possibly because of the unavailability of the coordinating nurse, especially during Ramadan and the last month of the year.

Most (617 [87·9%, 95% CI 85·3–90·1] of 702 individuals) of the HBsAg-positive individuals who attended the clinic after screening in both settings were classified as being inactive chronic carriers (table 2). HBeAg positivity was detected in 13 [3·3%] of 395 individuals from the community and 23 [7·9%] of 291 individuals from the blood bank for whom data were available.

Of the HBsAg-positive individuals screened in the community with available data, 48 (12·2%) of 394 had alanine aminotransferase (ALT) levels over the upper limit of normal (40 IU/mL) and 41 (10·7%) of 382 had HBV DNA levels of 2000 IU/mL or more. After excluding 11 participants without valid liver stiffness measurements, ten (2·6%) of 384 individuals had extensive fibrosis (F3) and 11 (2·9%) had cirrhosis (F4). Co-infection with HIV, HCV, or HDV was detected in 3·3%, 1·0%, and 2·0% of participants, respectively. Among the HBV-infected individuals screened at the blood bank who had data available, 55 (18·8%) of 292 had ALT levels over the upper limit of normal (40 IU/mL), 38 (14·4%) of 264 had HBV DNA levels of 2000 IU/mL or more, and 50 (17·5%) of 286 had extensive fibrosis or cirrhosis (≥F3).

47 (6·7%, 95% CI 5·1–8·8) of 702 HBV-infected individuals were eligible for treatment according to the EASL criteria (table 2; appendix p 3).[19] More people screened at the blood bank (29 [9·7%, 6·8–13·6] of 300 individuals) were eligible than were those screened in the community (18 [4·4%, 2·5–7·7] of 402 individuals; p=0·007). Use of the American Association for the Study of Liver Diseases criteria (appendix p 3)[21] did not substantially change the number of people eligible for treatment (table 2). The difference in treatment eligibility between the community and blood bank disappeared after we restricted the analysis to male participants (appendix p 2). Multivariable analysis showed that male sex (p=0·007) was associated with treatment eligibility (table 3). Age younger than 30 years also seemed to be associated with treatment eligibility, but the association was not significant (p=0·07). None of the eligible patients refused antiviral therapy. 12 months after the start of tenofovir therapy, 38 (80·9%) of 47 patients had high adherence scores, seven (14·9%) had medium adherence scores, and two (4·3%) had low adherence scores. After 12 months of treatment, 43 (91·5%) of 47 patients achieved a virological response defined as an undetectable HBV viral load, 38 (79·7%) had normal aminotransferase levels (<40 IU/mL), and nine (19%) had ALT levels over the upper limit of normal (40 IU/mL; median 46 IU/mL, IQR 43–62), with a baseline median ALT level of 49 IU/mL (IQR 34–104). No clinical or biological adverse events were observed after 12 months of treatment.

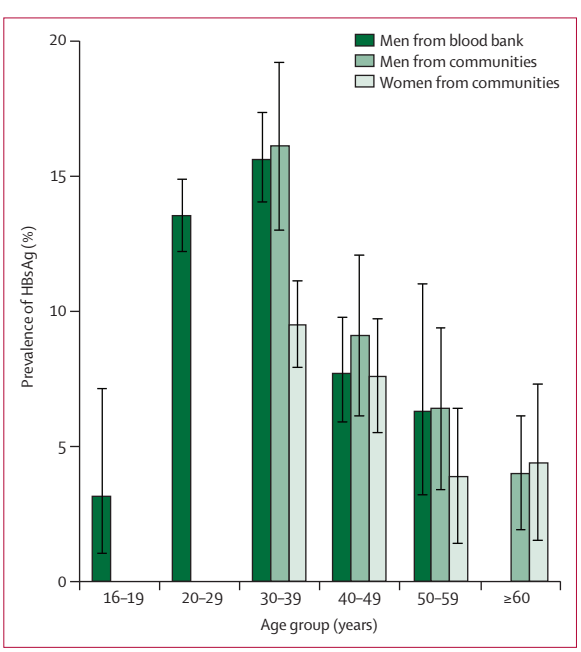

Figure 3: **Prevalence of HBsAg positivity by age and sex in blood bank and community screening**
Error bars represent 95% CIs. For blood bank screening, the analysis was restricted to males because of the small number of female blood donors (n=36). Error bars omitted for male donors aged 60 years or older because of small population (n=11). HBsAg=hepatitis B surface antigen.

	Community screening (n=402)	Blood bank screening (n=300)	p value
Age (years)	38 (33–47)	31 (27–35)	<0·001
Male sex	193 (48·0%)	291 (97·0%)	<0·001
Attended primary school	179/386 (46·4%)	185/223 (83·0%)	<0·001
Body-mass index (kg/m²)	22·5 (20·0– 26·5)	22·4 (20·4–25·2)	0·9
Ever drank alcohol	28/397 (7·1%)	25/297 (8·4%)	0·5
Ever smoked cigarettes	125/387 (32·3%)	104/225 (46·2%)	0·001
Family history of hepatocellular carcinoma	16 (4·0%)	7 (2·3%)	0·2
Liver stiffness (kPa)*	4·7 (3·9–5·7)	5·9 (4·9–7·5)	<0·001
METAVIR score*			
F0–1	357 (93·0%)	229 (80·1%)	<0·001
F2	6 (1·5%)	7 (2·5%)	
F3	10 (2·6%)	29 (10·1%)	
F4	11 (2·9%)	21 (7·3%)	
Alanine aminotransferase (IU/L)	23 (18–30)	27 (21–36)	<0·001
Alanine aminotransferase ≥40 IU/mL	48/394 (12·2%)	55/292 (18·8%)	0·02
Aspartate aminotransferase (IU/L)	29 (24–34)	32 (27–39)	<0·001
γ-glutamyl transferase (IU/L)	25 (19–34)	28 (22–39)	<0·001
Alkaline phosphatase (IU/L)	90 (76–112)	81 (68–97)	<0·001
Platelets (10^9 cells per L)	203 (159–253)	170 (142–205)	<0·001
HBeAg positive	13/395 (3·3%)	23/291 (7·9%)	0·007
Undetectable HBV DNA	188/382 (49·2%)	107/264 (40·5%)	0·03
HBV DNA (IU/L)†	297 (134–1577)	350 (118–1884)	0·8
HBV DNA ≥2000 IU/mL	41/382 (10·7%)	38/264 (14·4%)	0·2
HBV genotype			0·6
A	28/167 (16·8%)	15/104 (14·4%)	
E	139/167 (83·2%)	89/104 (85·6%)	
HIV positive	13/398 (3·3%)	NA§	NA
HDV positive	8/394 (2·0%)	1/292 (0·3%)	0·06
HCV positive	4/394 (1·0%)	5/280 (1·8%)	0·4
Inactive chronic carrier	364 (90·5%)	253 (84·3%)	0·01
Eligible for EASL criteria	18 (4·4%)‡	29 (9·7%)	0·007
Eligible for AASLD criteria	14 (4·1%)‡	21 (7·0%)	0·03

Data are n (%), n/N (%), or median (IQR). Some characteristics have different denominators because of missing data. NA=not applicable. HBeAg=hepatitis B envelope antigen. HBV=hepatitis B virus. HCV=hepatitis C virus. HDV=hepatitis delta virus. EASL=European Association for the Study of the Liver. AASLD=American Association for the Study of Liver Diseases. *Excludes 18 participants without measurement, seven with transient elastography measurement failure, and seven with unreliable measurements. †Excludes 295 participants with undetectable HBV DNA. ‡Percentages were calculated with weights for stratification and non-attendance to the screening and liver clinic. §The individuals who tested positive for HIV were not referred to our liver clinic, but were instead referred to the HIV clinic.

Table 2: **Clinical and biological characteristics of the HBV-infected participants from the community and the blood bank screening**

Discussion

Although able to prevent chronic infection,[22] vaccination against HBV has been introduced only in the past 20 years or so in sub-Saharan Africa. Coverage is less than ideal in many African countries, and even vaccination of neonates born to HBsAg-positive mothers has barely been implemented.[5] Therefore, there is still a large legacy of chronically infected adults who will remain undiagnosed until they develop severe complications. The prevalence of HBsAg remains high in Gambian adults born after 1990, the year when The Gambia integrated the HBV vaccine into the national vaccination programme; in our study 3·1% of people screened at the blood bank aged 16–19 years were HBsAg positive, a higher proportion than that previously reported in a community-based study of the same age group (1·8%).[23] Despite the implementation of HBV vaccination in The Gambia, the burden of HBV-related liver disease will probably remain high during the coming decades. It is therefore crucial to identify infected individuals through HBV screening and to manage them adequately to prevent liver complications. In The Gambia, HBV screening in the community by use of a rapid point-of-care test was well accepted, with coverage of almost 70%. This coverage is similar to that reported in other sub-Saharan African countries for community-based HIV (63% in rural Ugandan communities[24] and 86% in semi-rural areas in Mozambique[25]) or malaria (64% in Zanzibar[26]) screening. Large-scale HBV screening might be challenging in sub-Saharan Africa because the disease is usually asymptomatic and awareness of HBV infection is poor in the general population and among health workers. Almost no participants enrolled in our study had previously been tested for HBV infection and were aware of their status. In fact, there is not even a term to define cirrhosis in Mandinka, the main local language in The Gambia.

In our study, a large proportion of HBsAg-positive individuals identified through community screening attended the liver clinic as advised and adherence to treatment was high; 81% of patients had good adherence 1 year after the initiation of antiviral therapy, similar to that (77%) reported for antiretroviral HIV therapy elsewhere in Africa.[27] Additionally, 91·5% achieved a virological response at 1 year, which is in line with data from a European HBV cohort.[28]

By contrast with hospital-based studies, which are likely to overestimate the proportion of HBV carriers with advanced liver disease, 90·5% of chronically infected individuals from the community screening had inactive chronic hepatitis and only 4·4% needed antiviral therapy, supporting the feasibility of a community-based screen-and-treat intervention programme for HBV mono-infection in sub-Saharan Africa. Blood donors represent a different population to the community, being both younger and mostly male, with a higher proportion of individuals having detectable HBV viral loads. However, although the proportion of people eligible for treatment was higher at the blood bank than in the community, this difference was not significant after adjustment for age and sex. This finding is supported by a previous Ghanaian study of blood donors, which reported a similarly low proportion of individuals needing antiviral therapy based on ALT levels alone.[8] By applying our findings to sub-Saharan Africa, we estimate that only 4 million people chronically infected with HBV (roughly 5% of the 80 million infected people) will require treatment: less than half the number of

HIV-infected patients in need of antiretroviral therapy in sub-Saharan Africa.

Screening coverage in the community was lower in young men than in women or older individuals, which is consistent with observations from community screening for HIV in sub-Saharan Africa. Low coverage in young men is problematic because they are more likely to be infected with HBV and in need of treatment. About a third (36·8%) of men who did not attend our community screening were absent because of work or travel during the screening session, which suggests that screening during weekends might increase coverage in this group. By contrast, many young men came to donate their blood and accepted screening for HBV. However, less than half of those individuals identified as being HBsAg positive attended the liver clinic. In sub-Saharan Africa, care and treatment of deferred donors with HBV infection need to be improved, because blood banks offer an opportunity to reach this high-risk and difficult-to-manage group. Nevertheless, only a small proportion of young men donate blood, meaning that the overall population covered would remain small.

Notably, we found that 18·6% of people attending the blood bank were not tested for HBV because of a shortage of diagnostic kits. This concurs with the findings of the 2012 WHO report on blood safety,[29] which showed that 24% of blood banks do not systematically screen for transfusion-transmissible infections in resource-limited countries, with irregular supply of test kits cited as being the main barrier.[29]

Our study has some limitations. First, although the study implementation was adapted to real-life local conditions, it had the support of well-trained fieldworkers from a well-known research institution (the MRC Unit, The Gambia). Consequently, screening coverage and linkage to care could have been overestimated with respect to real-life implementation. Second, we might have underestimated the prevalence of HBsAg by using a rapid immunochromatography test, which has a sensitivity of 89–96% with ELISA as a reference. False-negative results in such tests are reported to be associated with low HBsAg levels and inactive disease state,[12,30] suggesting that the clinical impact of their moderate sensitivity is negligible since the people not identified would not need treatment. We noted a significant decrease in HBsAg prevalence as age increased, and this might be explained by false-negative results in older people with chronic infection who tend to have low HBsAg levels. Nevertheless, this trend has been consistently reported in population-based serosurveys in sub-Saharan Africa[22,31,32] and is often attributed to spontaneous seroclearance of HBsAg and higher mortality in people with chronic HBV infection than in people without HBV infection. Third, to quantify HBV DNA, we used an in-house qPCR assay that had a limit of detection slightly higher than that of commercial assays (50 IU/L *vs* <20 IU/L), which might have overestimated the proportion of participants with undetectable HBV DNA. Fourth, in accordance with the recommendations of the scientific committee, we targeted our screening in the community at individuals aged 30 years or older, because younger age groups would have benefited from the high coverage of HBV infant vaccination in The Gambia (estimated at >90%).[3] Nevertheless, the results of our screening in young people at the blood bank show that HBV screening remains important in Gambians younger than 30 years, with a high proportion of people in this age group needing antiviral therapy. Fifth, we might have underestimated

	All HBsAg-positive individuals (n=702)	Eligible for therapy (%)	p value	Adjusted for age and sex	
				Odds ratio (95% CI)	p value
Sex					
Female	218	4 (1·8%)	0·001	1·00	0·007
Male	484	43 (8·9%)		4·35 (1·50–12·58)	
Age (years)					
17–29	130	16 (12·3%)	0·01*	1·00	0·07*
30–39	350	22 (6·3%)		0·65 (0·33–1·30)	
≥40	220	9 (4·1%)		0·45 (0·19–1·07)	
Primary school					
Never	245	10 (4·1%)	0·01	1·00	0·4
Ever	364	34 (9·3%)		1·36 (0·62–3·02)	
BMI (kg/m^2)					
<30	638	47 (7·4%)	0·05	1·00	NA
≥30	51	0		NA	
Alcohol					
Never	641	43 (6·7%)	0·8	1·00	0·9
Ever	53	4 (7·6%)		0·93 (0·32–2·74)	
Cigarettes					
Never	383	24 (6·3%)	0·2	1·00	0·9
Ever	229	21 (9·2%)		0·98 (0·51–1·88)	
Family history of hepatocellular carcinoma					
Absent	679	44 (6·5%)	0·2	1·00	0·1
Present	23	3 (13·0%)		2·74 (0·75–9·95)	
HIV					
Negative	682	46 (6·7%)	0·9	1·00	0·6
Positive	16	1 (6·3%)		1·73 (0·21–14·24)	
HDV					
Negative	677	47 (6·9%)	0·4	1·00	NA
Positive	9	0		NA	
HCV					
Negative	665	44 (6·6%)	0·6	1·00	0·6
Positive	9	1 (11·1%)		1·88 (0·22–15·98)	
Genotype					
E	228	26 (11·4%)	0·6	1·00	0·6
A	43	6 (14·0%)		1·27 (0·48–3·37)	
Screening settings					
Community	402	18 (4·5%)	0·007	1·00	1·0
Blood bank	300	29 (9·7%)		1·02 (0·47–2·22)	

HBsAg=hepatitis B surface antigen. HCV=hepatitis C virus. HDV=hepatitis D virus. BMI=body-mass index. NA=not applicable. *Test for trend.

Table 3: **Factors associated with eligibility for antiviral treatment**

HBsAg prevalence at the blood bank because we were unable to exclude repeat donors from the analysis. However, the effect should be minimal because HBsAg screening was only started at blood banks in 2011 and frequent shortages of testing kits have occurred. In a subset of participants with available information about previous blood donation, HBsAg prevalence was similar between first-time and repeat donors. Finally, we assessed treatment eligibility at a single timepoint, but the longitudinal follow-up of our cohort is likely to identify additional eligible patients. We will address this question in the future.

In high-income countries, community-based screening for viral hepatitis has rarely been done without assessment of the proportion of infected individuals in need of treatment.[33,34] Consequently, our study provides original and important data about need for treatment, particularly in the general population, which will be useful for clinicians as well as policy makers.

According to the Wilson and Jungner WHO screening criteria,[11] our results confirmed that HBV mass screening is justified in The Gambia (appendix p 4) and our screening strategy in the community is cost-effective, as reported in a companion paper in this journal.[35] Whether such an intervention should be incorporated within other national screening programmes (eg, for HIV or non-communicable diseases) should be investigated in the future.

In conclusion, HBV screen-and-treat programme targeting the general population is a feasible and realistic public health intervention in The Gambia. Such an intervention deserves to be assessed on a larger scale in sub-Saharan Africa and in other resource-limited countries, with eventual integration into international and national guidelines to fight against the burden of HBV infection in endemic areas.

Contributors

MRT is the chief investigator of the PROLIFICA programme and designed the study with ML, YS, RN, HW, SDT-R, and MM. ML and RN were responsible for the clinical assessment with the support of GN, ST, LS, AK, and SN; YS, AJa, and WS contributed to the fieldwork; LM contributed to the qualitative data collection; IC, SG, HFN, AJe, AS, CT-K, PS, JH, and MM did the laboratory assays; and ML, YS, and MRT did the data analyses. SM, MT, ON, TC, HW, and UD'A supported the conduct of the study. ML, YS, and MRT drafted the manuscript, and all the authors reviewed and approved it.

Declaration of interests

MRT has received fees for advisory boards and lectures from Abbvie, BMS, Gilead, Janssen, and Merck. The other authors declare no competing interests related to this study.

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