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Hepatitis C virus seroprevalence in adults in Africa: a systematic review and meta-analysis

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ABSTRACT. With the introduction of more efficient treatments for hepatitis C virus (HCV), improved epidemiological information is required at the country level to allow evidence-based policymaking for elaboration of national strategies and HCV resources planning. We present a systematic review with meta-analysis of HCV seroprevalence data in adults in African countries. We conducted a systematic review of all HCV seroprevalence estimates reported in African countries from 2000 to 2014 in MEDLINE, AJOL and grey literature. We assessed studies performed in the general population and among blood donors, pregnant women and HIV-positive patients. A meta-regression analysis was used to provide adjusted estimates of HCV seroprevalence in the general adult population in each country, accounting for the heterogeneity in sample age structure and population types in the included studies. We identified 775 national-level estimations, among which 184 were included. Estimates of HCV seroprevalence were produced for 38 countries, in addition to the results from nationwide representative surveys available in Egypt and Libya. Next to Egypt, which clearly stands out, the highest levels of seroprevalence were found in Middle Africa (e.g. Cameroon, Gabon and Angola) and some West African countries (e.g. Burkina Faso, Benin), and the largest absolute numbers of infected adults were found in Nigeria, Ethiopia and Democratic Republic of Congo. This study exposes the diversity of HCV epidemiology among African countries. Egypt and several countries of West and Middle Africa present a HCV burden that will require strong governmental commitment to promote efficient preventive and curative interventions.

Keywords: Africa, epidemiology, hepatitis C, meta-analysis, prevalence.

INTRODUCTION

On the occasion of the 67th World Health Assembly (WHA) in May 2014, a new resolution has been adopted, which, in continuity with the 2010 WHA resolution, recognizes viral hepatitis as a global health challenge. It reaffirmed the need to improve intervention and policymaking with respect to surveillance, prevention and access to screening and treatment at national level supported by a global strategy developed by WHO. This 67th WHA resolution urges member states to take action and as hepatitis C virus (HCV) infection is not preventable by vaccination, also recalls that increased prevention and access to treatments are decisive, especially in the context of the introduction of new regimens which are expected to further improve cure rates [1].

These new treatments are estimated to increase cure rates up to >90%, hence making theoretically possible to cure all HCV-infected patients whose infection stage requires treatment in low- and middle-income countries [2,3]. In addition, the introduction of such new oral direct-acting antivirals (DAA) to treat HCV infection may increase treatment coverage by making indications and initial assessment easier – that is genotyping information may no longer be necessary as several drug regimens will cover all genotypes, by promoting adherence through oral administration and reduced treatment duration and by

Abbreviations: CAR, Central African Republic; DAA, Direct-acting antivirals; DRC, Democratic Republic of the Congo; HCV, Hepatitis C virus; OR, Odds ratio; WHA, World Health Assembly.

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simplifying monitoring in the absence of severe side effects [4].

Yet, improved epidemiological information is required to increase access to anti-HCV treatment by guiding national strategies, planning service provision and negotiating treatment access. In this regard, country-level estimates of HCV seroprevalence are of prime importance. As nationwide surveys have only been completed in Egypt and Libya [5,6], HCV seroprevalence in most countries must be estimated through literature review and meta-analysis. However, those available are either outdated [7,8], aggregated at the regional scale [9], or limited to the few countries where large studies were undertaken [10]. From a practical point of view, providing updated and country-level estimates of HCW seroprevalence for the largest possible number of states calls for synthesizing a broader range of material. We therefore present an expanded systematic review with meta-analysis of HCV seroprevalence in African countries, which makes use of data from the general population but also from blood donors, pregnant women and HIV-positive patients, in peer-reviewed and grey literature.

MATERIALS AND METHODS

The work included four stages: (i) identification of literature on HCV seroprevalence in Africa, (ii) selection of relevant studies, (iii) extraction of data and (iv) modelling of age-specific and general population-specific prevalence of anti-HCV antibodies in each of the African countries. This review was designed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement [11]. All analyses were conducted with *R* 3.0.3, using packages *meta*, *lme4* and *ggplot2* [12–15].

Literature review

Screening was first conducted through an online *MEDLINE* search for English or French-language literature published between January, 2000 and July, 2014. We used appropriate keywords embracing the following items: 'name of the country', 'hepatitis C' or 'HCV', and a third item which could be 'incidence', 'prevalence', 'mortality', 'viremia', 'genotype', 'diagnosis', 'treatment' or 'sustained virological response', following a similar review conducted in Europe [16]. We also searched the *African Journals Online (AJOL)* database. In this case, considering the smaller pool of journals, we extended our research using only the keywords 'hepatitis' and the country name. Some articles were also found through reference list checking. In addition, with the aim of reaching unregistered articles and 'grey literature' on HCV epidemiology, we approached African medical practitioners in the field of hepatology, infectious diseases and family medicine as well as national transfusion institutions and asked for relevant articles, thesis, reports and essays providing data on HCV prevalence using a questionnaire. In two countries, Egypt and Libya, nationwide representative surveys had been performed [5,6]. For these two countries, we only included the results of these surveys.

Selection

All identified abstracts were independently reviewed by two co-authors (JR and AB or MAA). They were considered eligible for full-text review if they provided original anti-HCV antibodies prevalence and sample size in one of the 52 included African countries (excluding Egypt and Libya). Articles were excluded if (i) data collection took place before 1995 – an arbitrary threshold meant to omit historical studies; (ii) population consisted of children only; (iii) study sample concerned one of the following populations likely to provide biased estimates of HCV seroprevalence: hepatitis-related conditions (e.g. symptomatic acute hepatitis, hepatocellular carcinoma and lichen planus), having undergone multiple injections (e.g. injecting drug users, multiple blood transfusions for sickle cell disease or haemophilia, end-stage renal disease and haemodialysis, diabetes), and highly exposed populations (e.g. healthcare workers, medical waste handlers, prisoners, relatives of HCV-infected individuals, the military). When abstracts were unavailable or failed to provide enough information, full articles were retrieved to verify eligibility criteria.

We included studies analysing samples from the general population (i.e. subjects from the general population and patients consulting in a hospital for unrelated motives that were recruited in an epidemiological study or as control in a clinical trial). We also considered that, given the scarcity or absence of general population data in some places, studies on blood donors, pregnant women and HIV-infected patients should be included as a possible source of information on HCV prevalence. Obviously, HCV prevalence in these groups may not correspond with that in the general population. Therefore, we designed a statistical adjustment model for HCV seroprevalence in these groups so that the seroprevalence in the general population could be estimated. Regarding blood donors and pregnant women, there may be various reasons why people in these groups would be at lower risk (e.g. perceived good health, higher socio-economic profiles associated with attending to generally urban hospitals and higher rate of contact with health care associated with higher chances of previous HCV testing) or higher risk (e.g. higher rate of contact with health care can also be associated with an increased risk of iatrogenic exposure) of HCV infection. As most studies did not report additional details on the sampled blood donor or pregnant women population, these were analysed as two categories. Regarding HIV infection, the association with HCV infection can be strong among injecting drug users. However, while HIV and HCV both share the percutaneous mode of transmission, the link between these infections is arguably weaker in sub-Saharan Africa where HIV is

mostly transmitted through sexual routes and injecting drug use is relatively infrequent [17]. These hypotheses were confirmed by a recent review of HCV–HIV co-infection in Africa [18]. Following that logic, we included HIV-infected patients of sub-Saharan Africa, but did not include HIV-infected patients of North Africa, as injecting drug use is a significant source of both HCV and HIV infection in this latter region [19].

Data abstraction

Data were independently abstracted by two co-authors (AB or MAA and JR). Eligible articles were abstracted for publication metadata, population sampling approach, anti-HCV assays and testing strategy, sample size, anti-HCV seroprevalence, population median or mean age, and proportion of women on a standardized form. When a study used several separate samples (e.g. from different countries or places, or even case–control studies comparing two kinds of population), it was split and each sample was considered as a unique data point. HCV infection being strongly correlated with age, information on the studied sample age was thoroughly pursued. Emphasis was made on median age, which was directly extracted or estimated through age structure when available. When median age was not provided, we used mean age in replacement. When articles did not provide any information on age, we asked the authors for additional information. We contacted 41 authors and retrieved age data for 16 studies. In the other cases, we considered that seroprevalence could not be properly interpreted without information on sample age and excluded such articles from the analysis. Anti-HCV assays and strategies were evaluated by an expert (SB) and classified in five types: (i) rapid test only, (ii) exclusively one ELISA/EIA test, (iii) rapid test confirmed by ELISA/EIA test, (iv) several ELISA/EIA tests and (v) use of immunoblot test.

Meta-analysis

In synthesizing the results, we tried to account for the measured characteristics of the studies and populations that could have contributed to heterogeneity in the seroprevalence data. First, we considered that age could be linked to HCV prevalence, so that estimates should be adjusted for age differences. Second, as mentioned above, adjusting for the sample type was also necessary. We therefore conducted a meta-regression analysis, modelling the seroprevalence π_{ij} in study j carried out in country i in a logistic mixed model (Equation 1):

$$\text{logit}(\pi_{ij}) = \beta_A \log(a_{ij}) + \beta_{BD} bd_{ij} + \beta_{PW} pw_{ij} + \beta_{HIV} hiv_{ij} + u_i + v_j, \quad (1)$$

where a_{ij} is median or mean age of the sample and β_A the age effect; bd_{ij}, pw_{ij} and hiv_{ij} are indicators of the sample type (blood donors, pregnant women and HIV-positive individuals); β_{BD}, β_{PW} and β_{HIV} are the corresponding effects (relative to the general population); $u_i \sim N\{0, \sigma_U^2\}$ is a country-specific random effect, and $v_j \sim N\{0, \sigma_V^2\}$ is a study-specific random effect.

This is a hierarchical model, with a random intercept for the country and a nested random intercept for each study in a country. This model was fitted at maximum likelihood. Note that this model assumed that the relationship between prevalence and cofactors was the same in all countries, for example that the odds ratio (OR) of 'blood donors' to 'general population' was the same irrespective of the country. We relaxed this assumption in a sensitivity analysis by introducing an interaction term between country and population type in the model and did not find any evidence of heterogeneity of the association across countries (see Appendix S1).

We used the model to obtain empirical best predictions [20] of the HCV seroprevalence at the median age of the adult (15–59) population in each country obtained from the United Nations Population Division website [21]. This method allowed estimating the unbiased HCV seroprevalence in the general population of each country, removing the effect of sample age and population type. Prediction intervals were obtained using bootstrap methods [22,23]. The predictions were used to estimate the absolute number of infected adults using demographic data from the UN Population Division website [21]. More information on the model is available in the Appendix S1.

Sensitivity analyses

We conducted a series of sensitivity analyses to test the impact of several hypotheses underlying the selection criteria and the model specification. We investigated the robustness of the seroprevalence estimates to the following: (i) the inclusion of studies missing information on sample age structure after imputation; (ii) the inclusion of studies measuring HCV seroprevalence in HIV-positive populations of North Africa; (iii) the exclusion of studies using only rapid anti-HCV testing or not providing information on their testing strategy; and (iv) the introduction of an interaction term between the country and the population type, to assess whether the relationship between prevalence and the fixed cofactors is the same in all countries. Further details on the sensitivity analyses are available in the Appendix S1.

RESULTS

We identified 775 unique studies reporting HCV seroprevalence in the 52 included countries, of which 262 (34%) were eligible for full-text review. After application of exclusion criteria, the meta-analysis was based on 206 data points from 184 national-level estimations of anti-HCV prevalence (Fig. 1; a description of all included articles is

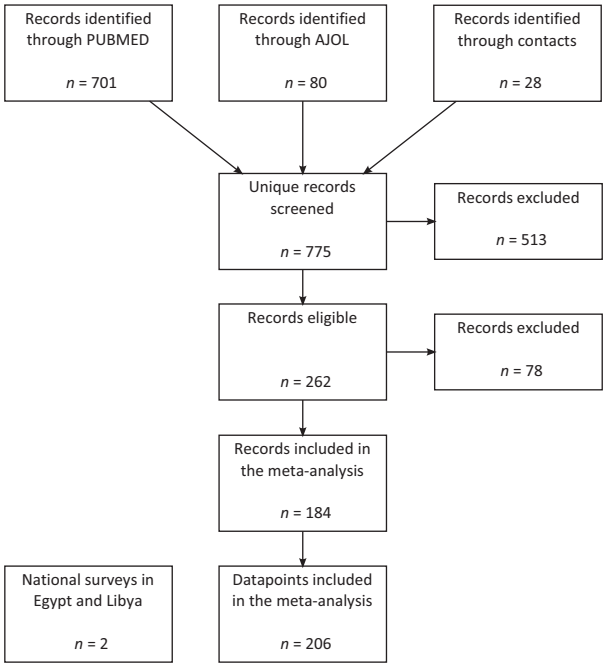

Fig. 1 Flowchart of HCV seroprevalence studies used for the meta-analysis.

available in the Appendix S1). The main exclusion criteria were as follows: missing information on age after having contacted the authors; data collection before 1995; sample issued from a high-risk population; sample already used in another included study; and full-text version unavailable. We did not find any study satisfying inclusion criteria for 14 countries (Cape Verde, Comoros, Chad, Equatorial Guinea, Eritrea, Liberia, Mauritania, Mauritius, Sao Tome Principe, Sierra Leone, South Sudan, Swaziland, Togo and Western Sahara) that represent 4% of the total population of the African continent.

Table 1 provides a description of the included articles by country. The 206 retained seroprevalence estimates were based on a cumulated 854 894 individuals (0.2% of the total adult population of the included countries), of which 21 186 had anti-HCV antibodies. Of these data points, 53 (26%) concerned samples from the general population, 70 (34%) blood donors, 55 (27%) HIV-positive patients and 28 (14%) pregnant women. Reported median or mean sample age ranged from 18 to 70, with a median of 30 and an interquartile range (IQR) of 27–35. Gender was reported in 86% of data points, and women accounted for 30% of the studied individuals. Women were particularly underrepresented in blood donor studies (9%) compared to other groups (35% in the general population and 39% among HIV-positive patients). Among 206 seroprevalence estimates, 166 (81%) reported assays and strategy for anti-HCV status determination with increasing specificity: (i) in 19 cases (11%), the testing strategy consisted of only one rapid test; (ii) in 73 cases (44%), a single ELISA/EIA test was used; (iii) in 14 cases (8%), the strategy included both a rapid test and an ELISA/EIA test; (iv) in 33 cases (20%), several ELISA/EIA tests were used; and (v) in 27 cases (16%), immunoblot tests were included in the strategy.

The reported seroprevalence estimates ranged from 0 to 56%. Table 2 presents the results of the meta-regression model. Compared to the general population, blood donors and pregnant women had slightly lower HCV prevalence, while HIV-infected had higher prevalence. The observed HCV seroprevalence also increased with the median or mean age of the sample [e.g. OR = 1.49 (1.36; 1.64) for an increase of the median age from 25 to 30 years; OR = 1.40 (1.30; 1.52) for an increase from 30 to 35]. Table 3 displays the HCV seroprevalence as predicted by the model for the median age of the adult (15–59 years) population of each country and the estimated total number of infected adults.

North Africa Region

As stated previously, we directly used high-quality nationwide surveys for Egypt and Libya. HCV seroprevalence was outstandingly high in Egyptian adults, with 14.7% [13.9–15.5], corresponding to 6 886 000 infected individuals [5], while low in Libya, with 1.2% [1.1; 1.3] [6]. In the Maghreb region, estimated prevalence of HCV antibodies was relatively low in Algeria [2.0% (0.1; 6.0)], Morocco [1.6% (0.0; 7.5)] and Tunisia [1.8% (0.1; 5.9)].

West Africa Region

HCV seroprevalence in West Africa was particularly patchy. The highest seroprevalence was found in Burkina Faso, with 6.1% [1.3; 14.2] of adults carrying HCV antibodies, with relatively high estimates in Benin [3.8% (0.7; 9.2)], in Ghana [3.2% (0.5; 8.1)] and in Nigeria [3.1% (0.1; 10.0)]. Seroprevalence was lower in other surrounding countries, such as The Gambia [2.4% (0.0; 9.7)], Ivory Coast [2.2% (0.3; 6.1)], Mali [1.9% (0.3; 10.6)], Guinea [1.5% (0.5; 9.5)] and Senegal [1.0% (0.0; 4.6)].

Middle Africa Region

High levels of adult HCV seroprevalence were found in this region, notably in Cameroon with 4.9% [0.9; 11.9], in Gabon with 4.9% [1.0; 11.5] and in Angola with 3.9% [0.6; 10.1]. Intermediate levels of seroprevalence were found in Burundi (3.1% [0.2; 9.1]), the Republic of the Congo [2.9% (0.0; 11.7)] and in Rwanda [3.1% (0.3; 9.0)] and relatively low levels in DRC [2.1 (0.4; 12.0)].

East Africa Region

HCV seroprevalence was intermediate in the Horn of Africa, with 2.7% [0.1; 9.2] in Ethiopia and 2.6% [0.1;

Table 1 Results of the systematic review of adult HCV seroprevalence in Africa and description of included articles

	Systematic review				Reported median or mean age (years, range)	Sample size (*n*, range)	Reported seroprevalence (%, range)
	Screened	Eligible	Included	Data points			
North Africa Region							
Algeria	9	3	3	3	31–58	250–3044	0.6–8.4
Egypt*				0			
Libya*				0			
Mauritania	3	0	0	0			
Morocco	50	12	6	7	27–45	529–169 605	0.2–7.7
Sudan	35	7	5	5	26.1–35	50–423	0.0–4.0
Tunisia	66	9	5	5	24–46.9	100–11 507	0.5–1.3
Western Sahara	7	0	0	0			
West Africa Region							
Benin	25	2	1	1	26	283	7.4
Burkina Faso	20	16	14	17	22–33.2	108–37 647	0.5–10.7
Cape Verde	0	0	0	0			
The Gambia	18	5	4	5	20–35	190–2598	0.5–19.4
Ghana	33	12	10	12	18–37.4	138–51 100	0.2–9.4
Guinea	17	1	1	1	28	10 740	0.3
Guinea-Bissau	3	1	1	1	61.5	1347	5.1
Ivory Coast	7	3	2	4	23–28	206–501	0.8–3.4
Liberia	2	0	0	0			
Mali	11	7	4	5	25.2–62.1	231–25 543	0.2–6.5
Niger	31	2	2	2	24–29.6	2962–3213	1.2–1.4
Nigeria	113	48	29	30	23–47.62	96–33 379	0.4–18.3
Senegal	12	5	4	4	27.7–38	362–3001	0.3–1.6
Sierra Leone	2	0	0	0			
Togo	7	0	0	0			
Middle Africa Region							
Angola	2	2	2	2	24.7–28	40–431	5.0–8.1
Burundi	2	1	1	1	28	5569	8.2
Cameroon	40	23	16	16	25–70	169–5008	0.6–56.0
Car	5	1	1	1	60	905	10.5
Chad	1	0	0	0			
DRC	5	6	2	2	26–28	1015–1079	0.2–3.8
Equatorial Guinea	2	0	0	0			
Gabon	17	8	5	5	24–47	319–25 844	2.1–20.7
Congo Republic	15	2	2	2	30–41.8	480–887	2.0–5.6
Rwanda	4	4	3	3	23–34.6	373–37 000	2.5–5.7
Sao Tome Principe	0	0	0	0			
East Africa Region							
Comoros	2	0	0	0			
Djibouti	1	1	1	1	31	8057	0.3
Eritrea	3	1	0	0			
Ethiopia	23	16	14	17	18–38.9	126–6361	0.2–19.0
Kenya	20	11	6	8	22–39.5	237–518	1.0–11.3
Madagascar	5	2	2	2	29.1–33.3	2169–47 510	0.7–1.6
Malawi	9	8	5	7	25–36.4	100–2041	0.1–7.3
Mauritius	3	0	0	0			
Mozambique	5	2	2	2	27–32.8	679–2887	0.0–1.5
Somalia	9	1	1	1	26	256	2.3
South Sudan	0	0	0	0			
Tanzania	24	11	8	8	26.6–39.9	208–1597	1.0–18.1
Uganda	26	9	7	10	22–38	122–8835	0.7–13.4

Table 1 *(continued)*

	Systematic review				Reported median or mean age (years, range)	Sample size (*n*, range)	Reported seroprevalence (%, range)
	Screened	Eligible	Included	Data points			
South Africa Region							
Botswana	5	2	2	2	35.8–37	50–250	0.0–0.8
Lesotho	1	1	1	1	40	205	0.5
Namibia	1	1	1	1	31.6	24 761	0.6
South Africa	65	11	6	6	29–40	100–1937	0.0–6.4
Swaziland	0	0	0	0			
Zambia	3	2	2	2	37–37	323–352	1.2–1.5
Zimbabwe	6	3	3	4	24–52	124–1591	0.0–9.1

CAR, Central African Republic, DRC, Democratic Republic of the Congo. *Nationwide surveys in Egypt and Libya.

Table 2 Association between seroprevalence and population type (from the meta-regression model)

	Multivariable mixed model* odds ratio (95% CI)
Population type	
General population	Reference
Blood donors	0.65 (0.56; 0.76)
HIV-positive patients	1.41 (1.18; 1.69)
Pregnant women	0.80 (0.56; 1.15)

*Logistic mixed model of HCV seroprevalence that includes a random intercept of the country and a nested random intercept for each study, with adjustment on age (after logarithmic transformation).

8.5] in Somalia. Similar patterns were found in Kenya [2.8% (0.4; 7.3)], Tanzania [2.7% (0.2; 7.8)] and Uganda [2.7% (0.4; 7.0)]. Seroprevalence tended to be lower in the southern part of the region, in Madagascar [1.7% (0.0; 7.7)], Malawi [2.0% (0.0; 7.0)] and Mozambique [1.3% (0.1; 6.9)].

South Africa Region

HCV seroprevalence was low in most countries of the South Africa Region, with 1.6% [0.0; 7.3] in Namibia, 1.1% [0.1; 5.8] in South Africa, 1.1% [0.0; 3.7] in Zambia and 1.6% [0.0; 5.9] in Zimbabwe.

DISCUSSION

This study is the first update on HCV seroprevalence in the general population focusing on African countries since Madhava's 2002 paper [7]. Starting from a large range of raw HCV seroprevalence estimates (from 0 to 56%) captured in heterogeneous samples, our final results showed that adult HCV seroprevalence is in the range 1.0% to 14.7% depending on the country, and identified Middle Africa, some West African countries and Egypt as being the regions with the largest HCV seroprevalence in Africa, consistently with previous reviews (Table 3). Next to Egypt, the highest estimates were found in Burkina Faso, Gabon, Cameroon, Angola and Benin (Table 3 and Fig. 2). In some countries, our approach led to lower estimates than previously reported, especially for Cameroon (4.9% instead of 11.6–13.8%) and Gabon (4.7% instead of 9.2–11.2%) [7,8,10]. The rather large prediction intervals for the estimates illustrated the scarceness of data in some countries. It is noteworthy that countries with the largest populations such as Ethiopia and Nigeria ended up with the largest absolute number of infections next to Egypt, exceeding one and two million infected individuals, respectively, even if the estimated adult HCV seroprevalence was not among the largest (2.7% and 3.1%, respectively). The global burden of infection for the continent was estimated to 19 million infected, which is also lower compared to previous estimates – 18 million for sub-Saharan Africa only [7]; 28 million for Africa [8]; 18 million for sub-Saharan Africa and 33 million for Africa and Middle East [9]; and 28.5 million for sub-Saharan Africa only and 43 million for Africa and Middle East [10].

This study also highlights the extremely heterogeneous HCV seroprevalence among countries in the same region, so that estimates calculated at the regional level may not provide reliable information at the country level. This heterogeneity may reflect differential historical exposure to iatrogenic transmission. For instance, the uncommonly high prevalence of HCV observed in Egypt has been linked to parenteral antischistosomal therapy mass treatment campaigns with lax sterilization practices in the 1960s and the 1970s [24]. Earlier, during the 1930–1950s, the propagation of HCV genotype 4 has been associated with mass treatment campaigns against yaws, malaria and syphilis decided by colonial authorities in Cameroon, Gabon, the Central African Republic and the Democratic Republic of the Congo

Table 3 Estimation of adult HCV seroprevalence in Africa at the country level and comparison with other reviews

	Estimated adult seroprevalence (%, 95% PI)	Estimated number of adult carriers (thousands, 95% PI)	Evidentiary support	Other published estimations of seroprevalence (%)				
				Lavanchy [8]	Madhava, *et al.* [7]	Ezzikouri, *et al.* [32]	Mohd Hanafiah, *et al.* [9]	Gower, *et al.* [10]
North Africa Region								
Algeria	2.0 [0.1; 6.0]	478 [26; 1475]	Moderate	0.2		1.4	3.6 [3.2; 4.1][‡]	1.4 [0.2; 2.5]
Egypt[*]	14.7[*] [13.9; 15.5][*]	6886 [6511; 7261][*]		14				14.7 [10.3; 18.0]
Libya[*]	1.2[*] [1.1; 1.3][*]	46 [43; 50][*]		1.6		1.5		1.2 [1.2; 2.3]
Mauritania				1.1	1.1	1.9		1.9 [1.1; 10.7]
Morocco	1.6 [0.0; 7.5]	335 [9; 1534]	Moderate	1.9		1.3		1.6 [0.6; 1.9]
Sudan	1.7 [0.1; 5.4]	318 [12; 1019]	Moderate	2.8	2.8			
Tunisia	1.8 [0.1; 5.9]	126 [4; 416]	Moderate	1.2		1.2		1.3 [0.3; 2.5]
Western Sahara				3				
West Africa Region							2.8 [2.4; 3.3]	
Benin	3.8 [0.7; 9.2]	190 [36; 456]	Limited	1.6	1.6			3.6 [3.6; 12.8]
Burkina Faso	6.1 [1.3; 14.2]	475 [98; 1107]	Extensive	5.2	4.9			
Cape Verde				3				
The Gambia	2.4 [0.0; 9.7]	20 [0; 82]	Moderate					
Ghana	3.2 [0.5; 8.1]	426 [64; 1092]	Extensive	1.7	1.7			
Guinea	1.5 [0.5; 9.5]	83 [29; 540]	Limited	5.5	5.5			
Guinea-Bissau	1.8 [0.0; 8.0]	15 [0; 68]	Limited	4.7				
Ivory Coast	2.2 [0.3; 6.1]	224 [26; 612]	Moderate	3.3	3.3			3.3 [0.8; 12.8]
Liberia				3				
Mali	1.9 [0.3; 10.6]	131 [19; 720]	Moderate	3.3				
Niger	2.4 [0.1; 7.9]	177 [6; 573]	Limited	3.2	1.8			
Nigeria	3.1 [0.1; 10.0]	2575 [95; 8222]	Extensive	2.1	2.1			8.4 [3.9; 12.8]
Senegal	1.0 [0.0; 4.6]	70 [1; 309]	Moderate	3	2.2			
Sierra Leone				2				
Togo				3.3	3.9			
Middle Africa Region							2.3 [1.6; 3.1]	
Angola	3.9 [0.6; 10.1]	370 [52; 958]	Limited	5				
Burundi	3.1 [0.2; 9.1]	150 [11; 439]	Limited	11.3	11.3			
Cameroon	4.9 [0.9; 11.9]	525 [98; 1263]	Extensive	13.8	13.8			11.6 [4.3; 29.7]
Car	2.3 [0.1; 11.2]	54 [3; 260]	Limited					
Chad				5	4.8			
DRC	2.1 [0.4; 12.0]	647 [130; 3743]	Limited					
Equatorial Guinea				1.7	1.7			
Gabon	4.9 [1.0; 11.5]	41 [8; 96]	Moderate	9.2	9.2			11.2 [2.1; 20.7]
Congo Republic	2.9 [0.0; 11.7]		Limited					

Table 3 *(continued)*

	Estimated adult seroprevalence (%, 95% PI)	Estimated number of adult carriers (thousands, 95% PI)	Evidentiary support	Other published estimations of seroprevalence (%)				
				Lavanchy [8]	Madhava, *et al.* [7]	Ezzikouri, *et al.* [32]	Mohd Hanafiah, *et al.* [9]	Gower, *et al.* [10]
Rwanda	3.1 [0.3; 9.0]	175 [15; 502]	Moderate	4.9	4.1			
Sao Tome Principe				1				
East Africa Region							2.0 [1.6; 2.4]	
Comoros								
Djibouti	1.3 [0.0; 5.7]	6 [0; 28]	Limited	0.3				
Eritrea				1.9	1.9			
Ethiopia	2.7 [0.1; 9.2]	1206 [28; 4025]	Extensive	1.9	1.9			1.3 [0.7; 5.8]
Kenya	2.8 [0.4; 7.3]	601 [80; 1587]	Extensive	0.9	0.9			
Madagascar	1.7 [0.0; 7.7]	183 [5; 844]	Limited	1.7	2.1			1.2 [0.8; 1.7]
Malawi	2.0 [0.0; 7.0]	145 [1; 516]	Moderate	6.8	0.7			
Mauritius				2.1				
Mozambique	1.3 [0.1; 6.9]	158 [15; 826]	Limited	3.2	2.8			
Somalia	2.6 [0.1; 8.5]	119 [3; 393]	Limited	1	1.5			
South Sudan								
Tanzania	2.7 [0.2; 7.8]	604 [44; 1776]	Extensive	3.2	3.2			
Uganda	2.7 [0.4; 7.0]	439 [67; 1123]	Extensive	6.6	6.6			
South Africa Region							2.1 [1.7; 2.5]	
Botswana	1.1 [0.3; 6.7]	13 [3; 80]	Limited	1.6				
Lesotho	1.1 [0.3; 6.7]	13 [3; 76]	Limited	1				
Namibia	1.6 [0.0; 7.3]	20 [0; 91]	Limited	0.9				
South Africa	1.1 [0.1; 5.8]	341 [40; 1841]	Moderate	1.7	0.1			1.7 [1.0; 2.5]
Swaziland				1.5				
Zambia	1.1 [0.0; 3.7]	72 [2; 243]	Limited	1.5	0.2			
Zimbabwe	1.6 [0.0; 5.9]	113 [1; 411]	Moderate	2	2			1.6 [1.0; 9.1]
Total		18 631		28 000	18 000†		18 000†–33 000‡	28 500†–43 000‡

95% PI: 95% prediction interval, CAR: Central African Republic, DRC: Democratic Republic of the Congo. Evidentiary support: Extensive: ≥8 data points, Moderate: 3–7 data points, Limited: 1–2 data points. *From nationwide surveys in Egypt and Libya. †Sub-Saharan Africa only. ‡Includes Middle East.

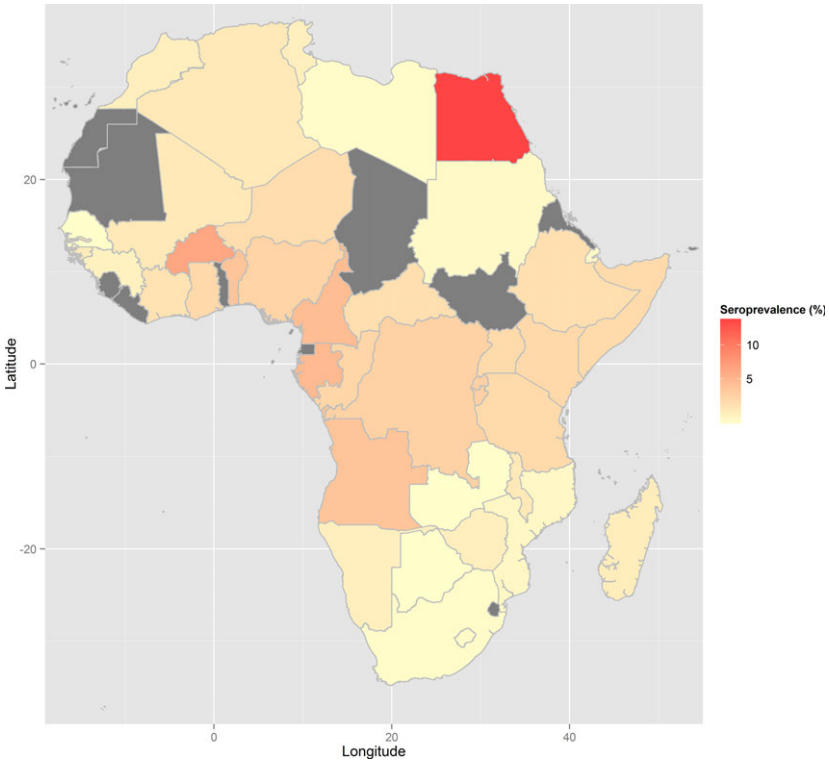

Fig. 2 Estimated adult HCV seroprevalence in Africa.

[25–28]. The local and disparate nature of such interventions could explain the heterogeneity of the HCV epidemiology in Africa, highlighted in this study.

Several reasons may explain the lower estimates found in this analysis. Historical changes in HCV prevalence related to the extinction of older, highly exposed age groups and the use of more specific serological tests after the year 2000 may explain the differences found with older reviews that included studies conducted in the 1990s [7]. Concerning more recent reviews, disparities may stem from methodological differences. Similarly to this study, the review by Mohd Hanafiah *et al.* [9] included studies conducted in the general population, pregnant women and blood donors (but not HIV-positive patients) and used an age-averaging analysis method. HCV seroprevalence estimates were then produced by GBD region, based on the assumption that they were 'epidemiologically homogeneous as possible so that information from detailed studies in one country can plausibly be extrapolated to other countries in the region'. While we do not question the utility of GBD studies for many health conditions, we believe that the assumption of 'epidemiological homogeneity' is not adapted to the highly heterogeneous seroprevalence of HCV in Africa and led to nonmeaningful estimates for seroprevalence in certain regions (e.g. a prevalence estimate of 3.6% [3.2; 4.1] across North Africa and Middle East that combined as different situations as Egypt and Libya, where reliable nationwide surveys reported estimates of 14.7% [13.9; 15.5] and 1.2% [1.1; 1.3], respectively) [5,6].

The other recent review by Gower *et al.* only included studies conducted in representative adult populations (i.e. general population, blood donors, pregnant women, hospital patients, soldiers and healthcare workers) with a minimum sample size of 1000 published since 2000 [10]. These strict inclusion criteria led to the retaining of only 33 data points in 15 countries in addition to Egypt and Libya, including 12 studies in Nigeria only while seroprevalence in the other countries was estimated using 1–3 data points. Unless based on a nationally representative sample (e.g. DHS), any approach restricted to few locations takes the risk of missing the vast geographical heterogeneity of HCV seroprevalence within a single country and leads to biased estimates, particularly if the motivation for performing a study in a given area was a suspicion of high HCV prevalence, or the reason for reporting was high HCV prevalence. For example in Cameroon, the seroprevalence estimate of 11.6% [4.3; 29.7] was based on only one study [29]. Our estimate of 4.9% [0.9; 11.9] was based on 16 studies (including the same one) that reported prevalences ranging from 1.8% to 56% in samples with median age varying from 25 to 70. Of note, we detected minor factual errors in Gower *et al.*, the estimate for Benin [3.6% (3.6; 12.8)] being based on two studies conducted in Nigeria [30,31], and the estimates for Algeria [1.4% (0.2; 2.5)] and Mauritania [1.9% (1.1; 10.7)] being based on a previous review from Ezzikouri *et al.* [32] that included studies published before 2000, hence in contradiction with the inclusion criteria in Gower *et al.*

Finally, in a recent review, Bhargavi Rao *et al.* [18] reported a pooled HCV seroprevalence across low-risk cohorts varying from 6.9% [6.0; 7.8] in the central Africa region to 4.3% [4.0; 4.7] in west Africa and 0.9% [0.8; 1.0] in south-east Africa. These results are coherent with our general conclusions concerning the regions with the highest HCV burden, although this study did not attempt to produce any adjusted estimates in the general population at the national level.

This study is based on a specific methodology that highly influences the results. The statistical adjustment method was simple and based on the available data (Table 2). These adjustment factors were consistent with previous studies conducted in Egypt (a country where general population seroprevalence has been extensively studied): a smaller prevalence in blood donor groups and to a lesser extent in pregnant women groups [33]. Similar effect sizes were reported in an independent review of HCV seroprevalence in sub-Saharan Africa by Bhargavi Rao *et al.* [18] that reported pooled HCV seroprevalence of 2.7% [2.5; 2.8] across low-risk cohorts *vs* 3.0% [2.2; 3.8] in antenatal clinic groups, 2.0% [1.9; 2.1] in blood donors and 5.7% [4.9; 6.6] in HIV-positive samples. We also found indication for a large increase in seroprevalence with age, as is common for infectious diseases and has been reported for HCV seroprevalence in many settings in Africa [5,27,34,35]. In sensitivity analyses, we showed that our estimates were robust to major assumptions (see Appendix S1).

It was not possible to obtain seroprevalence estimates for the following countries: Chad, Equatorial Guinea, Eritrea, Liberia, Mauritania, Sierra Leone, South Sudan, Togo and Western Sahara, as no data were available at all. In other countries, Angola, Burundi, Botswana, Benin, the Central African Republic, the Republic of Congo, Djibouti, Guinea, Guinea-Bissau, Lesotho, Madagascar, Mozambique, Namibia, Niger, Somalia or Zambia, estimates were obtained from few studies or limited sample sizes. Publication bias may also alter results if studies reporting high HCV seroprevalence levels are more likely to be published. Nationwide representative surveys as performed in Egypt, and currently under analysis in Cameroon and Burkina Faso, remain the choice approach to obtain valid estimations of HCV prevalence at national level.

From a clinical standpoint, it is worth recalling that HCV antibody carriage is not evidence of chronic infection. Indeed, it has been found that the proportion of viremic individuals among those having HCV antibodies range between 54% and 86% [36]. We therefore suggest to consider that approximately two-thirds of antibody carriers are chronically infected in countries where treatment is not routinely available, similar to the 67.7% observed during the Egyptian DHS [5]. More relevant than the proportion of viremic would be the distribution of infected individuals by fibrosis stage, to know what proportion of individuals urgently needs treatment (F3 and compensated F4 on the METAVIR scale). Unfortunately, this information is hardly available and would request adding simple staging procedures (FIB-4 or elastometry) to representative samples of infected individuals [37,38]. Finally, one of our main concerns was the possibility of false positive results due to poor specificity of serological tests as mentioned in several studies in sub-Saharan Africa [39,40]. For interested readers, we provide, in the Appendix S1, the serological testing strategies performed in the studies analysed in this review and a sensitivity analysis aimed to quantify this possible effect, but cannot exclude that some studies were suffering from this bias.

These results have great relevance at the time countries are elaborating their national strategies against viral hepatitis and new treatments are becoming available. Better estimates of the number of people to treat will be important for resources planning, and more accurate seroprevalence estimates will allow more accurate monitoring of the impact of future preventive and curative interventions. Innovative drug pricing models will be required to allow access to treatment in low- and middle-income countries. These evidence-based estimates will contribute to the ongoing negotiations taking place among governments, international organizations, nongovernmental organizations and pharmaceutical companies regarding drug pricing. In this regard, the recent signing of an agreement between the Egyptian government and the Gilead company for the provision of 12 weeks of sofosbuvir at US$900 is a step in right direction [41]. However, treatment subsidization, as available for AIDS, malaria and tuberculosis through the international donors (Global Fund, PEPFAR) will be the next necessary step to allow treatment access, as costs of US$500 to US$1000 per treatment will still be out of reach for most governments and patients in African countries.

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DISCLOSURES

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SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

Appendix S1: Supplementary material