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The Disease and Economic Burden of HBV and HCV in Ethiopia

Alexis S. Voeller¹ | Asgeir Johannessen^{2,3}  | Zebideru Zewdie Abebe⁴ | Wegene Adugna⁴ | Ivane Gamkrelidze¹  | Eleni Seyoum⁵ | Lia Tadesse Gebremedhin⁴ | Mirtie Getachew Meselu⁴ | Seblewongel Abate Nigussie⁶ | Asmamaw Silesh⁷ | Homie Razavi¹ | Devin Razavi-Shearer¹ | Ghion Tirsite⁶ | Hailemichael Desalegn⁸ 

¹Center for Disease Analysis Foundation, Lafayette, Colorado, USA | ²Department of Infectious Diseases, Vestfold Hospital Trust, Tønsberg, Norway | ³Sustainable Health Unit (SUSTAINIT), Faculty of Medicine, University of Oslo, Oslo, Norway | ⁴Ethiopia Ministry of Health, Addis Ababa, Ethiopia | ⁵Joint United Nations Program on HIV/AIDS (UNAIDS) Ethiopia, Addis Ababa, Ethiopia | ⁶World Health Organization Ethiopia, Addis Ababa, Ethiopia | ⁷Clinton Health Access Initiative Ethiopia, Addis Ababa, Ethiopia | ⁸Department of Internal Medicine, St. Paul's Hospital Millennium Medical College, Addis Ababa, Ethiopia

Correspondence: Alexis S. Voeller (avoeller@cdafound.org)

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ABSTRACT

As the second most populated country in Africa, Ethiopia needs public health measures to control diseases that impact its population. The goal of this study is to analyse disease burdens of HBV and HCV, while also highlighting their estimated associated costs for the country. A literature review and a Delphi process reflecting input of Ethiopian experts and the National Viral Hepatitis Technical Working Group were used to complement mathematical modelling to estimate HBV and HCV disease and economic burdens. Two scenarios were created for HCV: 2023 base and WHO elimination. For HBV, three scenarios were created: 2023 base, WHO elimination and universal birth dose. Using current country costs, each scenario was also examined through an economic lens. There were an estimated 7.6 million HBV infections in 2023. To impact transmission, a universal birth dose and pregnant women screening program would allow Ethiopia to vaccinate approximately 3.9 million infants annually, with a budget of \$4.68 million USD, meeting the WHO prevalence elimination target ($\leq 0.1\%$ in ≤ 5 -year-olds) by 2043. Ethiopia had an estimated 690,000 HCV infections in 2023. To achieve HCV elimination, the country would need to expand screening and treatment to 74,000 individuals annually with a peak budget of \$12 million USD per year until 2032, decreasing to less than \$2 million USD in 2035. Ethiopia can begin making steps towards elimination of HBV through expansion of birth dose vaccination. However, larger investments will be needed to scale-up treatment and diagnosis interventions for both diseases.

Abbreviations: AIDS, acquired immune deficiency syndrome; ALT, alanine aminotransferase; APRI, aspartate aminotransferase to platelet ratio index; DAA, direct acting antiviral; DPT, diphtheria, tetanus and pertussis; HBeAg, hepatitis B e-antigen; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; HepB3, hepatitis B 3 dose vaccine; HepB-BD, hepatitis B birth dose; Hib, *Haemophilus influenzae* type b; HIV, human immunodeficiency virus; PrEP, pre-exposure prophylaxis; PSA, probabilistic sensitivity analysis; SVR, sustained virologic response; UI, uncertainty intervals; UN WPP, United Nations World Population Prospects; USD, United States dollar; WHO, World Health Organization; YLL, years life lost.

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1 | Introduction

Africa as a continent, has the second highest burden of viral hepatitis after Asia, and it is an important region for the focus of public health efforts and resources. The lack of complete epidemiological data throughout the region, makes it difficult to fully understand how different diseases spread, complicating the creation of evidence-based policy solutions.

Africa currently has the highest prevalence of hepatitis B virus (HBV) infections in the world. In 2022, the overall adjusted prevalence of HBsAg in Africa was found to be 5.4% corresponding to 64.8 million infections [1]. Only 4% of these infected patients were diagnosed and 1% of those eligible were treated. In the same year, 3 out of the 10 countries with the highest number of HBV infections were in Africa, with Ethiopia having the 5th most HBV infections behind Nigeria [1]. Mother-to-child transmission is one of the most significant routes of HBV transmission on the continent. Among children aged five and under, HBV infections in African children are estimated to be two-thirds of the global childhood infections [2]. In 2022, the global HBV prevalence in children under five was 0.7%, whereas the prevalence in the African region was 1.7% or 3,600,000 infections [1]. Despite recommendations for universal hepatitis B birth dose (HepB-BD) vaccination programs, only 14 countries in the WHO African region have implemented birth dose prophylaxis programs as of 2021 [3]. Consequently, only about 17% of newborns in Africa receive HepB-BD, the lowest regional coverage worldwide [4]. While birth dose coverage is low, hepatitis B (HepB3) immunisation coverage among 1-year-olds is improved at 74%, still the lowest regional coverage worldwide, but all 47 countries within Africa provide this vaccination [3, 4].

Furthermore, the African region has the third highest prevalence of hepatitis C virus in the world. In 2020, the prevalence of anti-HCV was 0.6% corresponding to 7.8 million infections. Ten percent of patients were diagnosed and only 0.4% of those were treated [5]. In the same year, 3 out of the top 18 countries with the highest prevalence were in Africa with Ethiopia ranking 13th in the list [5].

Ethiopia, being the second most populous country in Africa, had an estimated population of 126.5 million in 2023 (UN WPP 2023) and a per-capita gross national income of \$1020 USD, falling into the World Bank low-income category [6]. In terms of mortality within the country, infectious diseases such as diarrhoea, lower respiratory infections and tuberculosis are among the leading causes of years of life lost (YLL) in all regions [7]. However, the specific causes of death vary geographically. In the capital city, Addis Ababa, HIV/AIDS is the leading cause of age standardised YLLs, while tuberculosis is the leading cause in the Afar region. In addition to these infectious diseases, non-communicable diseases, particularly stroke, contribute significantly to mortality within the country. The already strained healthcare resources of the country were further challenged by the global COVID-19 pandemic [7].

Globally, 20 countries hold 75% of the hepatitis disease burden, with Ethiopia being one of these countries [8]. Although the country has developed national viral hepatitis guidelines and a revised strategic plan in 2021, Ethiopia currently does not have

a national survey on prevalence, incidence, or official measures of mortality for viral hepatitis. Furthermore, there are no economic studies focusing on viral hepatitis to inform the World Health Organization's (WHO) elimination targets by 2030.

The country did, however, launch its “Expanded Program on Immunization” in 1980 covering six different antigens. Today, it provides 12 vaccinations at no cost, including the combined HBV, Hib (*Haemophilus influenzae* type b) and DPT vaccine (diphtheria, tetanus and pertussis), which it started providing in 2007 [9]. Currently, Ethiopia's 3 dose infant HBV vaccination schedule is administered at 6, 10 and 14 weeks. As of 2022, 93% of infants receive the three doses of the HepB3 [4]. However, there is no ongoing HBV birth dose program in Ethiopia.

Therefore, the aim of this study is to analyse the burden of HBV and HCV in the country, provide stronger epidemiological data, as well as assess the economic burden of both diseases, prophylaxis coverage and the investment required for Ethiopia to achieve the WHO elimination targets by the year 2030.

2 | Methods

2.1 | Literature Review and Expert Consultation

Epidemiological and economic data were collected for Ethiopia from experts within the country and from the National Viral Hepatitis Technical Working Group for both HBV and HCV in meetings held from December 15, 2022, to August 31, 2023. A series of these meetings were held to discuss analyses performed based on the data gathered, adjusting inputs in response to expert consensus following a modified Delphi process. To supplement the previously published estimates by the Polaris Observatory and expert data collected, a literature search was done on PubMed to identify new literature published between January 1, 2020, and December 31, 2023, using the terms “hepatitis B AND prevalence AND Ethiopia” along with “hepatitis C AND prevalence AND Ethiopia.” [1, 5].

2.2 | HBV Disease Burden Model

To estimate HBV prevalence in Ethiopia, the PROGRESS model, a fully dynamic Markov disease burden model created in Microsoft Excel v16.83 (2024, Microsoft Corp., Redmond, WA), was utilised. This model has been previously published and validated [1]. To estimate disease burden, the model was populated with epidemiological data based on expert opinion and gathered from literature, along with observed and projected United Nations World Population Prospects (UN WPP) demographic data for population, mortality, births, and sex ratios at birth from 1950 to 2050 [10]. With these inputs, the model estimated hepatitis B surface antigen (HBsAg) prevalence by sex, age, viral load and disease stage—by taking into account age-, sex- and viral load-specific disease progression rates and spontaneous clearance. Both vertical and horizontal transmissions of HBV were calculated considering mother-to-child transmission rates of HBV, prophylaxis rates and age-specific HBV transmission patterns for the entire population (from age 0 to ages 85 and above). Epidemiological data inputs used within the

model include HBsAg prevalence by age and sex, hepatitis B e-antigen (HBeAg) prevalence among pregnant women, prophylaxis coverage schedules, diagnosis levels and treatment levels as outlined in Table 1. Disease burden outcomes were estimated within the model from 2015 to 2030.

2.3 | HCV Disease Burden Model

In order to estimate the HCV prevalence in Ethiopia, a Markov HCV disease progression model was used. The model was created in Microsoft Excel v16.83 (2024, Microsoft Corp., Redmond, WA) and has been reviewed and published previously [5]. The inputs used within the model include anti-HCV prevalence by age and sex, viremic rate, viremic diagnosed and treated as detailed in Table 1. These inputs were used to model HCV progression as patients move from acute infection to chronic infection to end-stage liver disease, to eventual liver-related mortality or cure. Like the HBV model, sex- and age-specific disease progression rates were employed to model the HCV-infected population and spontaneous clearance. Epidemiological data provided by experts and those found in the literature, along with observed and projected UN WPP population, mortality and fertility data from 1950 to 2050 were inputted [10]. The model used a previously published screening module utilising epidemiological input data, the estimated number of screens needed to find one HCV case and previous and current diagnosis and treatment schedules to quantify the population eligible for HCV antibody screening and the number of HCV antibody screens performed [18]. Disease burden outcomes were estimated from 2015 to 2030.

2.4 | Economic Burden and Inputs

The HBV and HCV disease burden models served as input to a previously published economic model for HBV and HCV, respectively [19, 20]. The economic impact of reaching elimination was analysed through 2035 to examine the costs of increasing intervention overtime. All price data used for both HBV and HCV were collected from Ethiopian experts and further converted to United States dollars. The goal of the economic analyses were to serve as a point of reference for the government and other stakeholders in Ethiopia working towards the elimination of HBV and HCV.

In analysing the economic burden of HBV, the cost of the implementation of universal birth dose was estimated. The number of annual births, as reported by the UN WPP, was included along with the price of each dose regimen, gathered from expert opinion (Table 1) [10]. The cost of elimination was estimated by considering the direct medical costs (screening, diagnosis, treatment, staging, vaccination and healthcare costs of all stages of liver disease). DALYs (disability-adjusted life years), were calculated to understand the years of life lost to disease. Additionally, an incremental cost-effectiveness ratio (ICER) was determined by dividing the cost difference between the elimination scenario and base case by the difference in DALYs between the two unique scenarios as outlined in prior studies [21]. To determine whether elimination is cost-effective, the ICER was compared to the gross national income (GNI) per capita in Ethiopia, \$960

USD. Price data associated with HBV management per the status quo is outlined in Table 1. In the elimination scenario, it was assumed that there would be price decreases due to the scale up of interventions and industry negotiations. Prices used for elimination modelling are highlighted in Table 1.

When estimating the cost of HCV elimination in Ethiopia, the direct medical costs (screening, diagnosing, treatment, and healthcare costs of all stages of liver disease) were assessed. The same methodology as described above was applied to the HCV DALYs. All price data associated with HCV management under the status quo is also outlined in Table 1. In the elimination scenario, it was assumed that there would be price decreases due to scale up and negotiations. Prices used for elimination modelling are highlighted in Table 1.

2.5 | Model Scenarios

Scenarios were created to analyse different outcomes against the status quo or “base” for each disease as outlined below. The data used for all scenario inputs is detailed in Table 2 for HBV and Table 3 for HCV. A probabilistic sensitivity analysis (PSA) was conducted to generate 95% uncertainty intervals (UIs) on various modelled outputs for both HBV and HCV using Crystal Ball v11.1.3708.0 (2014, Oracle Corp., Austin, TX), a Microsoft Excel add-in. All uncertain assumptions used in the models were assumed beta-PERT-distributed, and 1000 Monte Carlo simulations were performed. Country specific uncertain variables are shown in Table 1, others for progression rates of HBV along with prophylaxis coverage were assessed at their mean value as previously described in the appendix of prior published work [1].

2.6 | Historical Base HBV

The base in Ethiopia for HBV looked at the most recent data available as described above. These data indicated that 400 patients were diagnosed annually along with 1320 patients on treatment. Under current guidelines within the country, patients are eligible for HBV treatment if they are clinically diagnosed with cirrhosis, have an aspartate aminotransferase to platelet ratio index (APRI) greater than 0.7, have an alanine aminotransferase (ALT) greater than 40 U/L along with a viral load greater than 2000 IU/mL, or have a first-degree relative with HCC and a viral load greater than 2000 IU/mL [22]. For prophylaxes, in 2022 there was 93% coverage of the three-dose vaccine regimen for infants before the age of 1 year. These values were assumed to remain constant in the future.

2.7 | Historical Base HCV

The status quo in Ethiopia for HCV looked at the most recent data available as detailed above. These data indicated that starting in 2014, 3160 patients were diagnosed annually with 1170 patients treated in 2022. In 2015, Ethiopia removed treatment restrictions based on fibrosis stage along with introducing direct acting antiviral (DAA) regimens with expected SVR of 95% denoted by expert input. These values were assumed to remain constant in the future.

TABLE 1 | HBV and HCV model inputs for disease and economic burden.

Category	Item	Year	Value	Source
HBV disease burden	HBsAg ⁺ prevalence	2015	9.4% (8.3%–10.7%)	[11]
	HBsAg ⁺ prevalence: age and sex distribution	2015	—	[12]
	HBeAg ⁺ among HBsAg ⁺ WoCBA	2014	5%	[13] and EC
	HBeAg ⁺ HVL			
	HBeAg ⁺ LVL			
	Total diagnosed	2015–2023	3600	EC
	Newly diagnosed	2015	400	
	Treated	2023	1319	
	Historical treatment	2010–2022	10,850	
	HepB3 dose coverage	2015	93%	[14]
	HBIG coverage (infants born to HBsAg ⁺ mothers)	2019	2%	EC
	HCV disease burden	Anti-HCV prevalence	1994	0.97% (0.6%–1.2%)
Anti-HCV prevalence: age and sex distribution		1994	—	[15]
Viremic rate		2014	75%	[16]
Viremic diagnosed		2014	3156	[17]
Treated		2022	1167	EC
HBV public costs (cost per test/cost per dose)—USD	HBsAg	2024	\$1.93	EC
	Viral load testing		\$47.37	
	ALT testing		\$0.70	
	AST testing		\$0.70	
	Birth dose regimen		\$0.20	
	Antiviral treatment 3 months		\$63.15	
HCV public costs (cost per test)—USD	Anti-HCV test	2024	\$1.90	EC
	Viral load testing		\$47.37	
	Treatment per month		\$105.26	
	Staging		\$250	
	Genotyping		\$70	
HBV elimination costs (cost per test/cost per dose)—USD	HBsAg	2024	\$1.00	EC
	Viral load testing		\$20	
	ALT testing		\$0.70	
	AST testing		\$0.70	
	Birth dose regimen		\$0.20	
	Antiviral treatment 3 months		\$7.50	
HCV elimination costs (cost per test)—USD	Anti-HCV test	2024	\$0.65	EC
	Viral load testing		\$20	
	Treatment per month		\$20	
	Staging		\$0	
	Genotyping		\$0	

Note: EC—expert consensus was gathered around this data point.

TABLE 2 | Modelled scenario inputs for HBV disease elimination.

Year(s)	Treated	Newly diagnosed	HepB3 (%)	Birth dose (%)
Historical base HBV				
2023	1320	400	93	0
2024	1320	400	93	0
2025	1320	400	93	0
2026	1320	400	93	0
2027	1320	400	93	0
2028–2030	1320	400	93	0
WHO elimination				
2023	1320	400	93	0
2024	68,890	892,030	96	90
2025	220,200	892,030	96	90
2026	375,370	892,030	96	90
2027	519,190	892,030	96	90
2028	649,830	892,030	96	90
2029	771,410	892,030	96	90
2030	821,420	892,030	96	90
Universal birth dose vaccine				
2023	1320	400	93	0
2024	1320	400	96	95
2025	1320	400	96	95
2026	1320	400	96	95
2027	1320	400	96	95
2028–2030	1320	400	96	95

2.8 | HBV Elimination

To reach WHO elimination targets for HBV by 2030, there would need to be a 90% diagnosis coverage, an 80% treatment coverage and a prevalence of $\leq 0.1\%$ in children aged 5 and younger by 2030 as outlined in the WHO HBV elimination guidelines [23]. To achieve HBV elimination, the model estimated that 892,000 patients need to be diagnosed annually and 821,400 eligible patients need to be treated by 2030. The 93% coverage of the three-dose vaccine regimen would remain constant along with having a 90% coverage of birth dose through 2030.

2.9 | HCV Elimination

In order to reach the WHO elimination targets for HCV by 2030, there would need to be a 90% reduction in new HCV infections, a 90% diagnosis coverage, an 80% treatment rate and a 65% reduction in liver-related mortality by 2030 as outlined in the WHO HCV elimination guidelines [23]. To achieve HCV elimination,

TABLE 3 | Modelled scenario inputs for HCV disease elimination.

Year(s)	Treated	Fibrosis stage	Newly diagnosed	SVR (%)
Historical base HCV				
2015	2000	$\geq F0$	3160	95
2020	620	$\geq F0$	3160	95
2022	1170	$\geq F0$	3160	95
2023	1170	$\geq F0$	3160	95
2024	1170	$\geq F0$	3160	95
2025–2030	1170	$\geq F0$	3160	95
WHO elimination				
2015	2000	$\geq F0$	3160	95
2020	620	$\geq F0$	3160	95
2022	1170	$\geq F0$	3160	95
2023	1170	$\geq F0$	3160	95
2024	41,400	$\geq F0$	79,200	95
2025–2030	74,340	$\geq F0$	79,200	95

the model estimated that 79,200 patients need to be diagnosed and 74,340 patients need to be treated annually.

2.10 | Universal Birth Dose

The implementation of a universal birth dose vaccination program against HBV for the annual 3.9 million births was analysed to understand what the impact would be on disease burden. The screening of all pregnant women was also included under this proposed program.

3 | Results

3.1 | HBV Disease Burden

The model estimated that at the end of 2023, there were 7,606,710 (95% UI: 6,873,260–8,558,780) people living with HBV infection in Ethiopia, corresponding to a prevalence rate of 6.01% (95% UI: 5.43%–6.76%). HBV infection accounted for an estimated 32,900 (95% UI: 22,610–49,410) incident hepatocellular carcinoma (HCC) cases, 1940 (95% UI: 860–3120) incident decompensated cirrhosis cases, and 34,180 (95% UI: 24,160–50,460) liver-related deaths in 2023. Among children 5 years and younger, the HBsAg-positivity rate was 0.65% in 2023. If no additional interventions were implemented, it was estimated that this prevalence rate would drop to 0.57% by 2030. The total number of HBV infections were estimated to decrease by 5% by 2030 due to the current vaccination program and mortality. In the same time frame, the number of new cases of HBV-related decompensated cirrhosis would increase

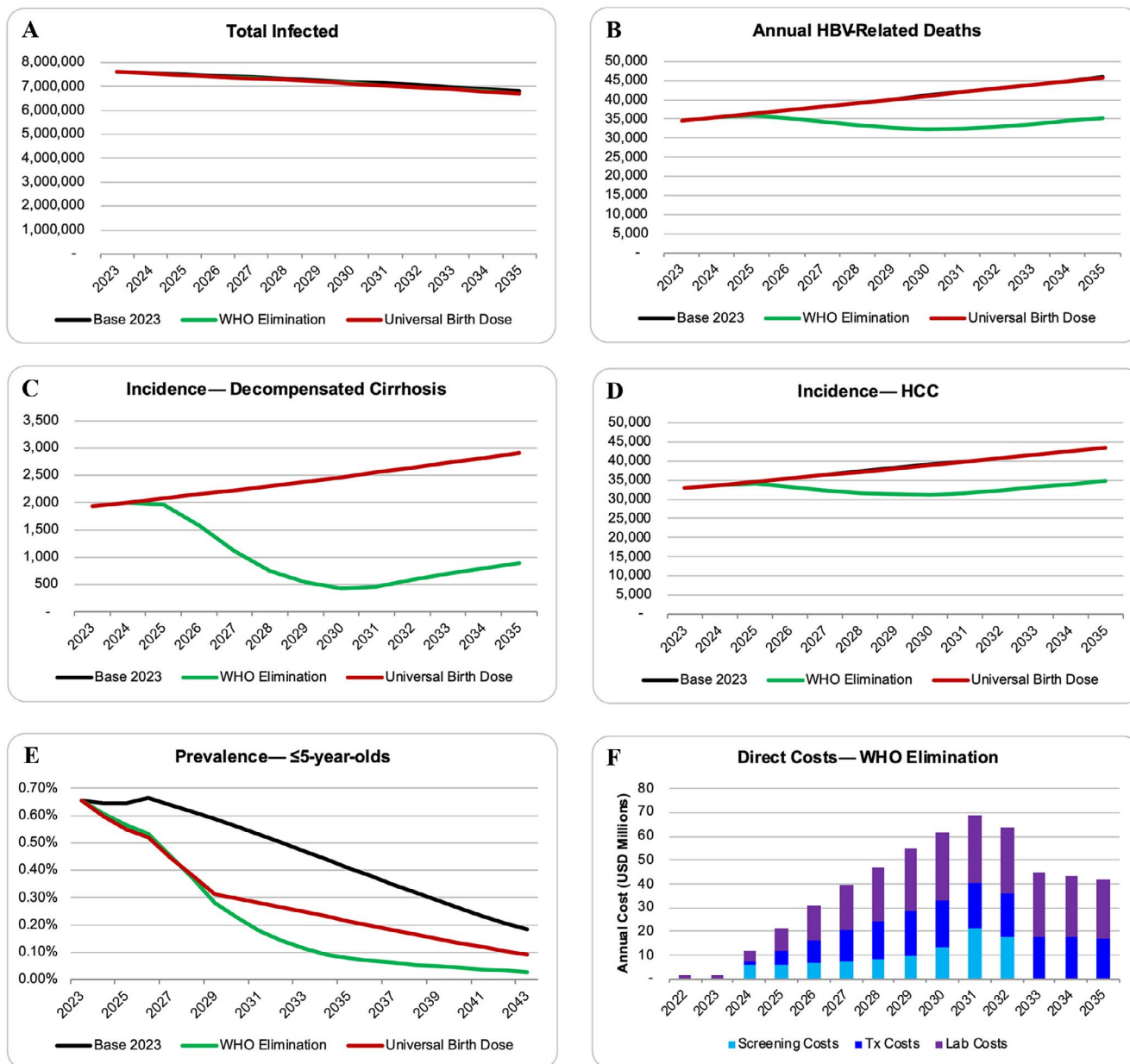


FIGURE 1 | Hepatitis B disease burden outcomes defined by each scenario from 2023 to 2035. (A) The total number of HBV infections in Ethiopia. (B) The total number of HBV-related deaths. (C) Incident cases of decompensated cirrhosis. (D) Incident cases of hepatocellular carcinoma. (E) The prevalence of children aged 5 years and younger until 2043, when the WHO elimination target could be met. (F) The cost of eliminating HBV in Ethiopia from 2024 to 2035 separated by screening costs, treatment costs and lab costs.

by 27% and new cases of HBV-related liver cancer would increase by 19%. The overall HBV-related mortality would also increase by 19% (Figure 1).

To reach HBV elimination, the model highlighted the need to increase interventions. The model estimated there would be 7,126,800 (95% UI: 6,388,900–8,026,610) people living with HBV infection by 2030 with a minimum of 892,000 individuals diagnosed annually and 821,400 eligible patients treated by 2030. The higher number of HBV infections under this scenario is predicted as result of higher treatment rate which would result in lower overall mortality. The impact of an elimination program corresponded to a decrease of 75% in new infections between 2023 and 2030 (Figure 1). Compared to the historical base scenario,

this scenario averted 7240 cases of decompensated cirrhosis and 26,990 cases of HCC, while saving 28,560 lives. To reach 0.1% prevalence for children aged 5 and younger, birth dose vaccination coverage would have to reach 90% and the three-dose vaccine regimen would require continued high coverage of 93% or greater.

A scenario was also created to look at the implementation of a universal birth dose vaccination program along with screening all the pregnant women. With only the introduction of 95% birth dose vaccination coverage, there would be a 38% decrease in new infections, and the total number infected would decrease by 6%. The number of new cases of decompensated cirrhosis would increase by 27% with new cases of HBV-related HCC increasing

by 19%. These values are the same as those reported in the base scenario as increasing birth dose vaccination, does not impact those already infected. By 2030, HBsAg-positivity among children under 5 years of age would decrease to 0.3% (Figure 1). This program would meet the WHO prevalence elimination target ($\leq 0.1\%$ in < 5 -year-olds) by 2043 while averting 6800–8600 new HBV infections per year.

3.2 | HCV Disease Burden

At the end of 2023, the model estimated that there were 690,000 (95% UI: 510,710–806,450) viremic HCV infected individuals corresponding to a 0.53% (95% UI: 0.39%–0.62%) HCV prevalence in Ethiopia. A total of 45,300 (7%) patients were diagnosed and 1200 (0.2%) were treated (Figure 2). There were

an estimated 3200 newly diagnosed HCV infections in 2023. HCV infection accounted for an estimated 2730 (95% UI: 2020–3190) incident HCC cases, 2130 (95% UI: 1580–2490) incident decompensated cirrhosis cases, and 3790 (95% UI: 2790–4430) liver-related deaths. Without any additional interventions, by 2030, it was estimated that the total number of infections would decrease by 2%, with the number of new infections decreasing by 3%. In the same time frame, the number of new cases of decompensated cirrhosis would increase by 28% and new cases of HCV-related HCC would increase by 27%. The overall HCV-related mortality would increase by 30%.

To achieve HCV elimination targets set by the WHO, Ethiopia would need to diagnose a minimum of 79,200 patients annually and treat 74,340 patients annually. This would leave 309,150 (95% UI: 133,440–422,710) individuals with viremic HCV

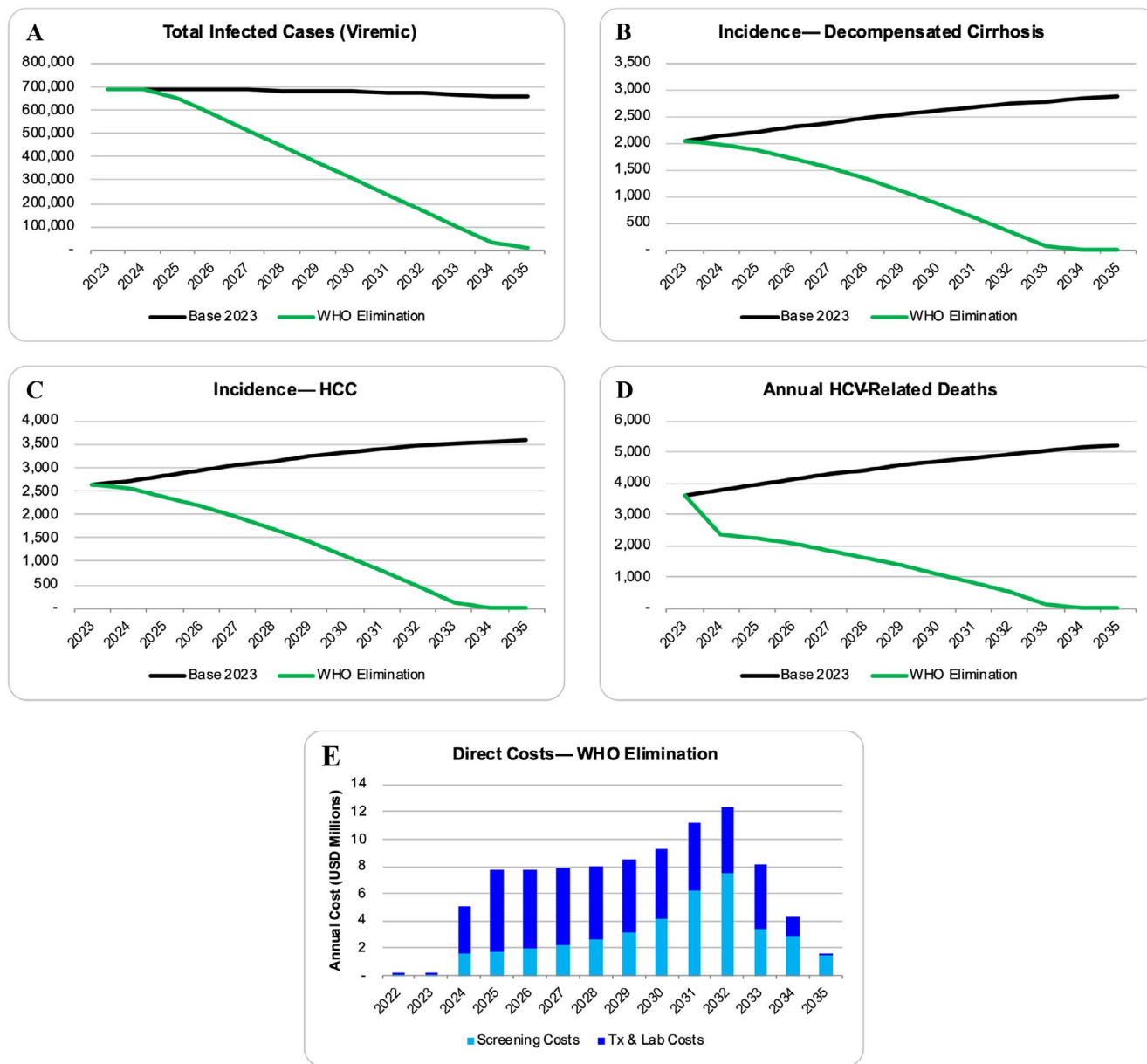


FIGURE 2 | Hepatitis C disease burden outcomes defined by each scenario from 2023 to 2035. (A) The total number of HCV infections in Ethiopia. (B) Incident cases of decompensated cirrhosis. (C) Incident cases of hepatocellular carcinoma. (D) The total number of HCV liver-related deaths. (E) The cost of eliminating HCV in Ethiopia from 2024 to 2035 separated by screening costs, treatment costs and lab costs.

infections at the start of 2030, a 55% decrease from the base, with a corresponding 56% decrease in new infections between 2023 and 2030 (Figure 2). Compared to the historical base scenario, an elimination scenario would avert 6270 cases of decompensated cirrhosis and 7970 cases of HCC, while saving 17,230 lives.

3.3 | HBV Economic Impact

In order to reach HBV elimination in Ethiopia, there would need to be a peak investment of \$69 million USD annually by 2031 to cover the increase in diagnosis, screening, treatment and prophylaxis (Figure 1). If Ethiopia were to implement a universal birth dose program at a rate of \$0.20 USD per dose, a peak investment of \$742,000 USD annually would need to be made to fund the vaccines with an additional peak annual investment of \$4.12 million USD to support the screening of all pregnant women (Figure 3). Solely implementing a universe birth dose program would correspond to \$83–\$109 USD per infection averted (Figure 3). With an elimination strategy, over time, direct costs such as healthcare costs associated with advanced

disease as well as indirect costs such as years lost to disability will steadily decrease, making this a cost-effective program, with the cost per DALYs averted equalling \$472 USD in 2030.

3.4 | HCV Economic Impact

As it currently stands, Ethiopia spends almost \$15 million USD annually on direct costs related to HCV such as healthcare costs associated with advanced disease. To work towards HCV elimination in Ethiopia, there would need to be an annual investment of a maximum of \$12 million USD in 2032 decreasing to \$2 million by 2035 (Figure 2). This total also assumed that a 3-month course of treatment would decrease in cost from \$315.80 to \$60 USD, accounting for price negotiations and time. This investment would cover screening, lab tests and treatment. With an elimination strategy, over time, direct costs such as healthcare costs associated with advanced disease as well as indirect costs such as years lost to disability will steadily decrease, making this a cost saving (and therefore cost-effective) program, with \$4 million USD in cost savings.

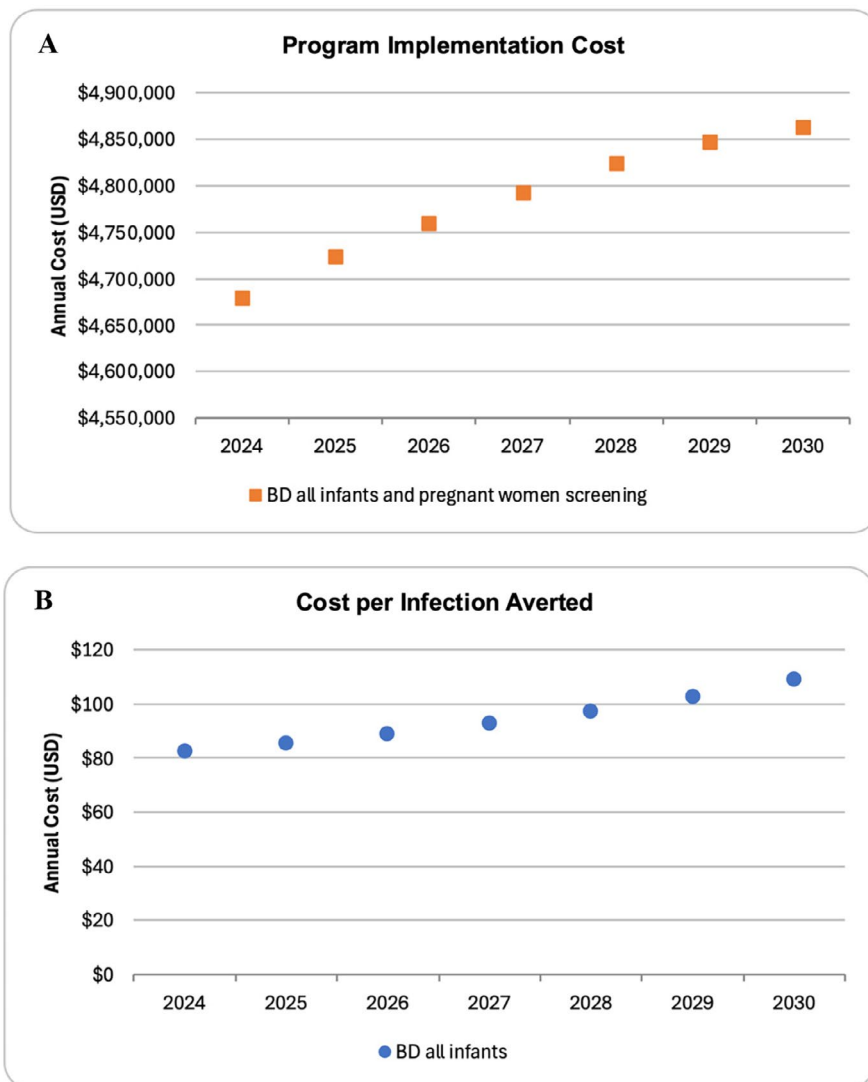


FIGURE 3 | The cost of a universal birth dose vaccination and pregnant women screening program in Ethiopia from 2024 to 2030. (A) The annual cost of implementing a birth dose program. (B) The cost per infection averted with implementing only a universal birth dose program.

4 | Discussion

With an estimated 7,606,710 people living with HBV infection in Ethiopia, interventions are needed to work towards easing the disease burden. The modelled universal birth dose vaccine scenario is an option not only to make steps towards elimination, but more importantly to save future lives by averting 6800–8600 infections per year. This would also meet the WHO early childhood prevalence target by 2043. While this is a great step in the right direction, increasing prophylaxis coverage will not help the 7.6 million people living with HBV infection in the country currently. With only 5% of infections diagnosed and less than 1% of those eligible for treatment being treated, there is a great need to increase intervention in these areas in addition to implementing a universal birth dose vaccination program. To reach the WHO elimination targets, it would require 892,000 newly diagnosed patients and 821,400 eligible patients to be treated by 2030. While this would take a peak investment of \$69 million USD annually, as compared to \$4.86 million annually for a universal vaccination and pregnant women screening program, up to 28,560 lives would be saved through 2030 and would provide a cost-effective program for Ethiopia.

While the burden of HCV is not as high as that of HBV, this study highlights how HCV elimination does require a large up-front investment for screening, diagnosis and treatment, but over time can become a cost saving investment. With approximately 3780 people dying in 2024 due to HCV-related liver complications increasing to over 5000 after 2033, there is a need for increased intervention measures. Without further intervention, healthcare costs alone required to tackle HCV-related morbidity can reach upwards to \$14 million USD annually. With a peak investment of \$12 million USD, Ethiopia can reduce HCV-associated healthcare costs down to \$1 million USD in 2035 while having to only invest another \$1 million in the same year for screening, reducing the cost burden and saving up to 17,230 lives through 2030.

The projected improvements in healthcare costs and reaching the WHO elimination goals for viral hepatitis by 2030 will only be achieved if aggressive and concerted efforts are started immediately. These need to include a scale-up of HBV birth dose programs across the country, wide scale screening, and linkage to treatment centres, while also focusing on the implementation of the existing strategic plan for viral hepatitis. Innovative solutions should also be considered to work with already in place HIV programmes to support infrastructure as well as considering PrEP or pre-exposure prophylaxis, a tenofovir-based antiviral therapy, as a means for HBV patients eligible for treatment. For HCV, stronger efforts are needed to link patients to care after diagnosis. Without the implementation of stronger programs, Ethiopia will not reach the WHO elimination targets for either HBV or HCV by 2030. The country has the opportunity to build upon successful lessons from the screening and treatment of care models from other African countries that are working to wards or on track for hepatitis elimination, such as Rwanda or Egypt.

There are multiple limitations within the scope of this analysis. Due to the nature of this study being based on mathematical modelling, the estimated modelled outputs will only be

as strong as the data inputs. With the assistance of Ethiopian experts and the technical working group, the inputted data were strengthened, since many of the inputs are from older published studies or come from unpublished work. With this collaboration effort, we were able to gather cost data, population data and epidemiological data to improve modelled outcomes and generate a potential plan towards elimination efforts. When looking at the treatment of HBV, the model assumes that a successful treatment course would halt any disease progression outside of the transition to HCC. This could potentially mean that the model is underestimating the impact HBV treatment can have as fibrosis regression has been shown to occur. The HBV treatment rate in Ethiopia may also have been underestimated as 2% of the HBV positive individuals are potentially HIV positive and are already receiving treatment through HIV programs [24]. Further, the full disease burden impact and cost-effectiveness of the HBV universal birth dose vaccine will not be fully realised for 5 to 6 decades after the last birth cohort included in the analysis has been born. Previous analyses have shown this to be the case [25]. Both disease analyses attempted to take into consideration the COVID-19 pandemic since data were provided by experts for the years 2020 and 2021. Finally, when looking at the economic impact for both diseases, the model assumes there will be no advancements in treatment for either HBV or HCV, affecting the total costs from a societal lens.

In conclusion, there is an opportunity to work towards both HBV and HCV elimination in Ethiopia. By taking strategic steps for one or both diseases, there is a huge potential for saving lives and reducing future healthcare costs caused by the two diseases. For HBV, by implementing a universal birth dose vaccination strategy, Ethiopia can avoid 6800–8600 new HBV infections per year. Furthermore, if measures to scale-up diagnosis and treatment for HBV were created, up to 28,560 lives could be saved through 2030. Similarly, if an elimination strategy was instated for HCV, up to 17,230 lives could be saved through 2030. Achieving the elimination goals in Ethiopia will require large investments in preventative, diagnostic and therapeutic measures over the coming years.

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Conflicts of Interest

A.S.V., I.G., D.R.-S. and H.R. are employees of the CDA Foundation. The CDA Foundation has received research funding from Gilead, Assembly Biosciences, AbbVie, Boehringer Ingelheim, Intercept, Merck, Novartis, Pfizer, and Roche for projects unrelated to this work. All other authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

References

1. Polaris Observatory Collaborators, O. C. Polaris, "Global Prevalence, Cascade of Care, and Prophylaxis Coverage of Hepatitis B in 2022: A Modelling Study," *Lancet Gastroenterology & Hepatology* 8, no. 10 (2023): 879–907.
2. World Health Organization, *Global Hepatitis Report 2024: Action for Access in Low- and Middle-Income Countries* (Geneva: World Health Organization, 2024).
3. H. J. Kabore, X. Li, M. M. Alleman, et al., "Progress Toward Hepatitis B Control and Elimination of Mother-to-Child Transmission of Hepatitis B Virus—World Health Organization African Region, 2016–2021," *Morbidity and Mortality Weekly Report* 72, no. 29 (2023): 782–787.
4. WHO/UNICEF, "Estimates of National Immunization Coverage 1990–2023," (2024), <https://www.who.int/teams/immunization-vaccines-and-biologicals/immunization-analysis-and-insights/global-monitoring/immunization-coverage/who-unicef-estimates-of-national-immunization-coverage>.
5. S. Blach, N. A. Terrault, F. Tacke, et al., "Global Change in Hepatitis C Virus Prevalence and Cascade of Care Between 2015 and 2020: A Modelling Study," *Lancet Gastroenterology & Hepatology* 7, no. 5 (2022): 396–415.
6. The World Bank, "World Development Indicators," (2023), <https://datacatalog.worldbank.org/dataset/world-development-indicators>.
7. Y. B. S. Lakew, G. Davey, T. Tilahun, et al., "Trends in Mortality and Years of Life Lost Across Regions in Ethiopia: A Systematic Subnational Analysis in Global Burden of Disease Study 1990–2019," *Ethiopian Journal of Health Development* 37, no. 2 (2023): 1–28.
8. G. S. Cooke, B. Flower, E. Cunningham, et al., "Progress Towards Elimination of Viral Hepatitis: A Lancet Gastroenterology & Hepatology Commission Update," *Lancet Gastroenterology & Hepatology* 9 (2024): 346–365.
9. T. Kidane, A. Yizaw, Y. Sahilemariam, et al., "National EPI Coverage Survey Report in Ethiopia, 2006," *Ethiopian Journal of Health Development* 22, no. 2 (2008): 148–157.
10. Population Division of the Department of Economic and Social Affairs of the United Nations, "The 2022 Revision and World Urbanization Prospects," (2022), <https://population.un.org/wpp/>.
11. A. G. Weldemariam, "Nationwide Seroprevalence of Hepatitis B Virus Infection in Ethiopia: A Population- Based Cross-Sectional Study," *Infectious Diseases Suppl.* 1 (2020): 19–20.
12. Institute EPH, "National Seroprevalence of Hepatitis B Virus Infection in Ethiopia," EPHI, ed2017.
13. A. Abebe, D. J. Nokes, A. Dejene, F. Enquselassie, T. Messele, and F. T. Cutts, "Seroepidemiology of Hepatitis B Virus in Addis Ababa, Ethiopia: Transmission Patterns and Vaccine Control," *Epidemiology and Infection* 131, no. 1 (2003): 757–770.
14. "Estimates of National Immunization Coverage 2015–2022," accessed January 29, 2024, <https://www.who.int/teams/immunization-vaccines-and-biologicals/immunization-analysis-and-insights/global-monitoring/immunization-coverage/who-unicef-estimates-of-national-immunization-coverage>.
15. W. Ayele, D. J. Nokes, A. Abebe, et al., "Higher Prevalence of Anti-HCV Antibodies Among HIV-Positive Compared to HIV-Negative Inhabitants of Addis Ababa, Ethiopia," *Journal of Medical Virology* 68, no. 1 (2002): 12–17.
16. E. Kassa, A. Bane, and H. Kefene, "Common Genotypes and Treatment Outcomes of HCV Infection Among Ethiopian Patients: A Prospective Study," *Ethiopian Medical Journal* 54, no. 1 (2016): 1–7.
17. W. Ayele, A. B. Workneh, A. Bane, and B. Redae, "Clinicians Survey, Unpublished," Addis Ababa, Ethiopia 2015.
18. L. A. Kondili, I. Gamkrelidze, S. Blach, et al., "Optimization of Hepatitis C Virus Screening Strategies by Birth Cohort in Italy," *Liver International* 40, no. 7 (2020): 1545–1555.
19. S. Ezzat, I. Gamkrelidze, A. Osman, et al., "Impacts of the Egyptian National Screening and Treatment Programme for Viral Hepatitis C: A Cost-Effectiveness Model," *Liver International* 43 (2023): 1417–1426.
20. Y. S. Lim, S. H. Ahn, J. J. Shim, H. Razavi, D. Razavi-Shearer, and D. H. Sinn, "Impact of Expanding Hepatitis B Treatment Guidelines: A Modelling and Economic Impact Analysis," *Alimentary Pharmacology & Therapeutics* 56 (2022): 519–528.
21. E. Mooneyhan, R. A. De la Torre, D. B. Serrano, et al., "Cost-Effectiveness and Economic Investment to Eliminate Chronic Hepatitis C in Mexico," *Journal of Viral Hepatitis* 30 (2023): 551–558.
22. A. Johannessen, L. T. Gebremedhin, and H. Desalegn, "New WHO Hepatitis B Treatment Guidelines: Look to Ethiopia," *Lancet Global Health* 10, no. 12 (2022): e1711–e1712.
23. World Health Organization, *Global Health Sector Strategy on Viral Hepatitis 2016–2021 Towards Ending Viral Hepatitis* (Geneva, Switzerland: World Health Organization, 2016).
24. Y. Tassachew, T. Abebe, Y. Belyhun, et al., "Prevalence of HIV and ITs co-Infection With Hepatitis B/C Virus Among Chronic Liver Disease Patients in Ethiopia," *Hepatic Medicine: Evidence and Research* 14 (2022): 67–77.
25. M. J. de Villiers, I. Gamkrelidze, T. B. Hallett, S. Nayagam, H. Razavi, and D. Razavi-Shearer, "Modelling Hepatitis B Virus Infection and Impact of Timely Birth Dose Vaccine: A Comparison of Two Simulation Models," *PLoS One* 15, no. 8 (2020): e0237525.