

Review Article

A Path to Ending Hepatitis C in Ethiopia: A Phased Public Health Approach to Achieve Micro-Elimination

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Abstract. Ethiopia's hepatitis C virus (HCV) prevalence is predicted to rise by 2030. To halt this increasing trend, a suitable approach to the elimination of HCV is needed. This review explores the current status, challenges, and opportunities and outlines a strategy for the micro-elimination approach in Ethiopia. I searched PubMed and EMBASE using combined Medical Subject Heading databases for the literature on HCV micro-elimination. A phased public health approach to HCV micro-elimination, including preparation/capacity building (phase I), implementation (phase II), and rollout and scale-up (phase III), targeting people living with HIV, prisoners, chronic hepatitis and cancer patients, blood donors, and pregnant women is a pragmatic strategy to Ethiopia. This can be implemented at general and tertiary care referral hospitals with a future scale-up to district hospitals through task-shifting by training general practitioners, nurses, laboratory technologists, and pharmacists. Availability of the highly effective direct-acting antivirals (DAAs) can be ensured by expanding the existing program that provides highly subsidized DAAs through an agreement with Gilead Sciences, Inc. and eventually aiming at domestic generic manufacturing. The significant enablers to HCV micro-elimination in Ethiopia include the control of healthcare-associated HCV infection, blood safety, access to affordable testing and pan-genotypic DAAs, task-shifting, multisectoral partnership, and regulatory support. General population-based HCV screening and treatment are not cost-effective for Ethiopia because of high cost, program complexity, and disease epidemiology.

INTRODUCTION

In sub-Saharan Africa in 2016, 2.98% of people lived with hepatitis C virus (HCV) infection, with an extensive regional and national variation.¹ In Ethiopia, most studies of HCV infection are limited to subpopulations in the healthcare setting. Although the prevalence of HCV infection from a few clinic-based surveys is low in Ethiopia, the prevalence has significantly increased from 0.1% in 2014 to 0.7% in 2017.² It is estimated that there will be 655,000 viremic HCV infections, 3,800 hepatocellular carcinoma cases, 8,800 decompensated and 80,300 compensated cirrhosis cases, and 4,200 liver-related deaths in Ethiopia by 2030.³

The most frequent risk factors for HCV transmission in Ethiopia are the transfusion of infected blood, unsafe medical procedures, such as surgery and injections, and healthcare worker parenteral exposure.^{1,4} Besides, healthcare waste handling and traditional community practices, including tooth extraction, circumcision, and tattooing, contribute to HCV transmission. In children, vertical transmission is the dominant risk factor.⁵

The prevalence of HCV infection is predicted to rise in Ethiopia with the current state of screening, diagnosis, and treatment.³ As a result, there is a need to scale-up HCV screening and treatment using cost-effective approaches. Although the emergence of highly efficient treatments for HCV infection that result in a virologic cure in most of the treated patients creates a golden opportunity for the elimination of the virus from different geographical areas, an effective approach to ensure access to screening and treatment adapting to national financial resources, workforce, and healthcare infrastructure is required.

GLOBAL AND REGIONAL APPROACHES TO HEPATITIS C ELIMINATION

The Global Health Sector Strategy states the elimination of viral hepatitis as a significant public health threat by 2030. Its targets are to reduce viral hepatitis infections from between six and 10 million to one million and hepatitis-related deaths from 1.4 million to 500,000 by 2030.⁶

The viral hepatitis elimination strategy for Africa aims at 30% reduction in new cases of chronic viral hepatitis C infections and 10% reduction in viral hepatitis C-related deaths by 2020 through country ownership, partnership and multi-sectoral cooperation, universal health coverage, integration, and a public health approach based on simplified and standardized interventions.⁷

Micro-elimination is a pragmatic approach that breaks national elimination goals into smaller goals for subpopulation groups and enables the delivery of treatment and prevention interventions more quickly and efficiently.⁸ It is manageable by policymakers and facilitates better participation of subpopulations in the program, which is useful to create better access to treatment.⁸ Micro-elimination could be a very suitable approach to countries such as Ethiopia for being less intricate, less costly, less overwhelming, and more inspiring by building success compared with a full-scale, country-level initiative to eliminate HCV.⁹

Many countries promote the HCV micro-elimination approach to be effective,⁸ but the evidence is scarce on the situation in Ethiopia. Moreover, there were no studies that explored the gap in the implementation of HCV elimination and outlined future directions. This review examines the current status, challenges, and opportunities for HCV control and proposes a micro-elimination approach taking into consideration the healthcare system, epidemiology of HCV infection, and risk factors in Ethiopia.

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METHODS

This review examines the status, challenges, and opportunities of HCV elimination in Ethiopia. PubMed and EMBASE databases were searched using combined Medical Subject Heading terms and keywords for hepatitis C, control, elimination, micro-elimination, and Ethiopia using Boolean operators “AND” and “OR.” The relevance of articles was examined by reading the title and abstract. Studies that focus on HCV control and elimination in the context of low-income countries, particularly sub-Saharan Africa, including Ethiopia, were read, and the concepts were organized into this review. Figure 1 shows the selection process using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses flowchart (Figure 1).

RESULTS

The epidemiology of HCV infection in Ethiopia. There are no nationally representative HCV prevalence data in Ethiopia. Available studies are clinic-based and represent different subpopulations. Two general population-based studies in northwest (2015)¹⁰ and southern (2018)¹¹ Ethiopia found the

prevalence of HCV infection to be 1.0% and 1.9%, respectively. The prevalence of HCV infection in blood donors ranges from 0.3%² to 1.3%,¹² with wider variations among different cities. Studies on the burden of HCV in healthcare workers ranges from 0.4% (in healthcare professionals)¹³ to 0.7% (in medical students and healthcare waste handlers).^{4,5} The highest HCV prevalence reported so far was in people living with HIV (PLHIV) (6.6%),¹⁴ chronic liver disease patients (3.6%),¹⁵ and prisoners (2.6%).¹⁶ Table 1 summarizes HCV prevalence in different subpopulation groups, settings, and years of study (Table 1). The HCV genotype (G) 4 (77.6%), the most prevalent in Ethiopia comprised seven subtypes, with 4d (34.7%), 4r (34.7%) being the most frequent, followed by G2 (12.2%) is predominant subtype), G5, and G1.¹⁷

Current status of HCV control and elimination in Ethiopia. Ethiopia recognizes HCV infection-related chronic liver disease and liver cancer as a significant cause of morbidity and mortality. To date, HCV elimination plan is not in place in Ethiopia, but the National Cancer Control Plan of the Federal Ministry of Health, Ethiopia,¹⁸ stated national viral hepatitis strategy is being developed. Nevertheless, Ethiopia’s Health Sector Transformation Plan sets the target of 10%

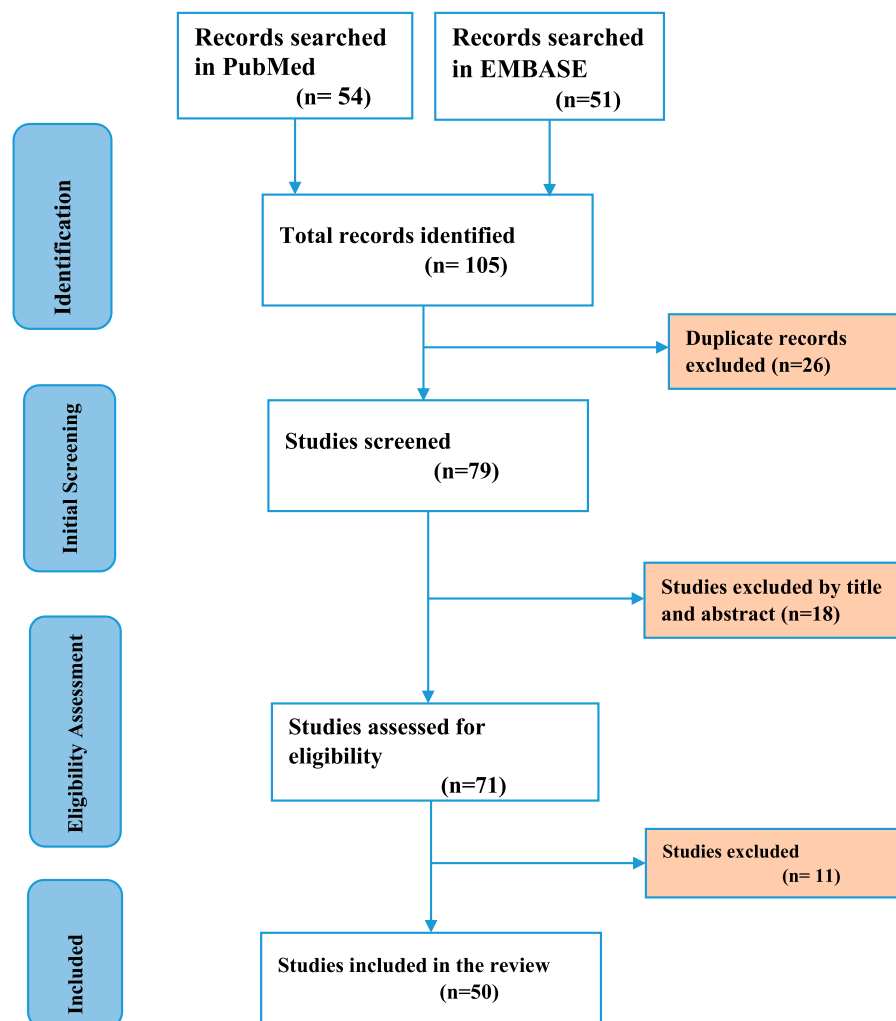


FIGURE 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses flowchart showing the selection of articles reporting on hepatitis C control or elimination, identifying the key population, enabling factors to hepatitis C virus elimination, and major challenges in the context of low-income and middle-income countries. This figure appears in color at www.ajtmh.org.

TABLE 1
Prevalence of hepatitis C virus infection in different subpopulations in Ethiopia

Study	Population type	Sample size	Study design	Setting	Region	Study year	Hepatitis C virus prevalence (%)
Degefa, 2018	Blood donors	10,728	Retrospective chart review	Blood bank	Tigray	2011–2014	1.33
Atsbaha, 2016	People living with HIV	302	Comparative cross-sectional	Health facility	Tigray	2014	6.6
Demsis, 2018	Healthcare workers	408	Cross-sectional	Education institution	Amhara	2017	0.7
Amsalu, 2016	Medical waste handlers	152	Cross-sectional	Health facility	SNNPR*	2014–2015	0.7
Hebo, 2019	Healthcare workers	240	Cross-sectional	Health facility	Oromia	2015–2016	0.42
Molla, 2015	Pregnant women	384	Cross-sectional	Health facility	Amhara	2013–2014	0.26
Kebede, 2017	Prisoners	156	Cross-sectional	Prison	Oromia	2016	2.6
Taye, 2014	Chronic hepatitis patients	578	Retrospective chart review	Health facility	Oromia	2012–2013	3.6
Abera, 2017	General population	481	Cross-sectional	Community	Amhara	2015	1.0
Woldegiorgis, 2019	General population	625	Cross-sectional	Community	SNNPR*	2018	1.9

* SNNPR = Southern Nations, Nationalities, and People's Region.

reduction in the prevalence of viral hepatitis in Ethiopia by 2020, which implies reducing HCV prevalence from the 2015 baseline 2.5% to 2.3%. In addition, the plan sets out to increase the proportion of HCV patients diagnosed by 50% by 2020.¹⁹

The diagnosis and treatment of HCV infection in Ethiopia occur mainly during blood donation or as part of the clinical work-up of patients who present with complications of chronic viral hepatitis.²⁰ General hospitals and tertiary hospitals are capable of diagnosing HCV infection. The diagnosis follows the WHO algorithm and includes the HCV rapid antibody test, followed by RNA testing and viral load for those who turned positive. The decision on treatment duration is based on prior treatment history, cirrhosis status, and baseline viral load.²¹ Following the inclusion of HCV control in the national health sector strategy, the viral hepatitis treatment program was initiated in 25 government hospitals across the country and screened 17,579 persons; of whom, 346 patients were treated for HCV infection in 2015.²²

There is no generic DAA manufacturing in Ethiopia. Moreover, the National Essential Medicines List²³ of Ethiopia does not include direct-acting antivirals (DAAs), and cost subsidies by the government are not available. The current antiviral treatment in Ethiopia is provided through agreement with Gilead Sciences developing countries access program²⁴ with highly reduced prices of 1,200 USD per person for the 12-week treatment using ledipasvir–sofosbuvir, which the patient shall pay out-of-pocket.

Despite these steps undertaken by the Ministry of Health, a specific plan responsive to the global or sub-Saharan African initiatives for HCV elimination is not yet in place in Ethiopia. As a result of this, Ethiopia is not currently at the right position to meet global and African targets of eliminating HCV as a public health problem by 2030.²⁵

Opportunities for HCV elimination in Ethiopia. One of the opportunities that positively support future HCV elimination initiatives is the low prevalence of the infection in the population, although data came from sparse reports of subpopulation-based studies.^{2,4,10,26} The implication of having low burden in the country is that the limited healthcare resources could be directed toward screening and treatment of HCV infection in most at-risk populations. An expert review identified that injecting drug use is low in Ethiopia.³ This means HCV burden and transmission in hard-to-reach populations could be low, placing the healthcare system in an excellent position to detect and treat persons with HCV infection, thereby ensuring more comprehensive access to treatment.

Besides, Ethiopia has a vast experience of multisectoral collaboration from the HIV/AIDS epidemic during which the country achieved global targets to control HIV infection by working with global and local partners, proper financing, and integration of HIV care into major programs.²⁷ This experience of collaboration, integration, and partner engagement can be partly applied to HCV elimination in the country.

Challenges to HCV elimination in Ethiopia. The lack of population-based data on new HCV infections and the epidemiology of HCV in the country make informed decision-making difficult. There was no nationwide survey that measured the burden of HCV infection in different socioeconomic, geographic, and demographic subgroups. The only available studies are meta-analyses and surveys limited to specific population groups at the blood bank sites and healthcare facilities.²⁸ Data from such studies are representative of only the subpopulations they are sampled from, making planning and monitoring progress challenging. Moreover, HCV infection is not included in Ethiopia's Integrated Disease Surveillance and Response system, making monitoring of the disease from regular healthcare reports difficult.²⁹

Although rapid anti-HCV antibody testing is cheaper, these screening test kits are not available in most hospitals in Ethiopia mainly because of financial limitations. The shortage of highly qualified personnel and setups to perform advanced laboratory testing such as polymerase chain reaction and viral load is an important issue.^{30,31}

Last, the widespread healthcare-associated risk factor for HCV transmission in Ethiopia's health facilities, which helps perpetuate the transmission of HCV in the population, remains an essential barrier to be dealt with for elimination to be a reality. In Ethiopia, the blood transfusion system depends mainly on replacement donation than the volunteer-based donation of reserve blood units. This might lead to low-sensitivity detection because of inadequate time for screening, which has a high chance of missing infections in the window period.^{32,33} Unsafe medical procedures, such as surgical and dental operations, and the slow transition in infection prevention at Ethiopia's health facilities are still outstanding problems that may pose a considerable challenge to HCV elimination initiatives aimed at achieving morbidity and mortality reduction targets in the near future.³³

Recommended approach to hepatitis C micro-elimination in Ethiopia. A phased public health approach to the micro-elimination of HCV in Ethiopia is proposed taking into consideration the success stories of the country's health system,

current opportunities in HCV treatment coverage and success, and the prevailing challenges to healthcare in the country. The suggested micro-elimination approach is aimed to eliminate HCV through the elimination in subpopulation groups, including chronic hepatitis patients, PLHIV, prisoners, pregnant women, healthcare workers, and blood donors identified based on the burden or higher risk of HCV. The proposed approach considers the wide gap in access to DAAs, availability of sensitive, low-cost diagnostic tests, and the need for significant reduction in healthcare-associated infections.³⁴ It also considers criteria that need to be addressed in developing the micro-elimination initiative.⁹

Figure 2 presents the phased public health approach to implement HCV micro-elimination in Ethiopia. The three phases of the micro-elimination approach include preparation and capacity building (phase I), implementation (phase II), and rollout and scale-up (phase III). Based on existing data, the micro-elimination focuses on key populations including chronic hepatitis patients, PLHIV, prisoners, pregnant women, healthcare workers, and blood donors. It starts with the screening, treatment, and monitoring of these population groups and moves forward by expanding to other population groups.

Phase I: Preparation/capacity building. One of the critical activities in the initial phase is awareness creation to the general public (with priority to key populations) on HCV burden, transmission, and the prevention methods.²⁵ Improved public awareness not only increases uptake of HCV screening

and treatment adherence but also reduces community practices such as tooth extraction, uvulectomy, and circumcision that contribute to HCV transmission in Ethiopia.

Second, training healthcare workers on HCV infection risk factors and prevention is equally important.³⁵ Focused training of healthcare workers plays a crucial role to the reduction in healthcare-associated HCV infection in the population through breaking the chain of transmission and help reduce work-related risk of acquiring HCV among healthcare workers themselves.

A population-based survey, which is integrated into the hepatitis B virus (HBV) national survey and the Demographic and Health Survey, is vital to know the actual distribution of and risk factors for HCV infection in different geographic locations and population groups. This is a critical step in the evidence-based planning of HCV elimination and development of implementation guidelines.^{1,36} In addition, monitoring the progress using routine testing and treatment data from hospitals of key populations is a useful and resource-saving scheme.

The development of national strategy customized to the Health Sector Transformation Plan and WHO African Region targets materializes the preparation for HCV micro-elimination. The national viral hepatitis guideline, being developed, helps to standardize screening, diagnosis, and referral and improves the quality of these services. More importantly, this will be useful to develop a national elimination plan.

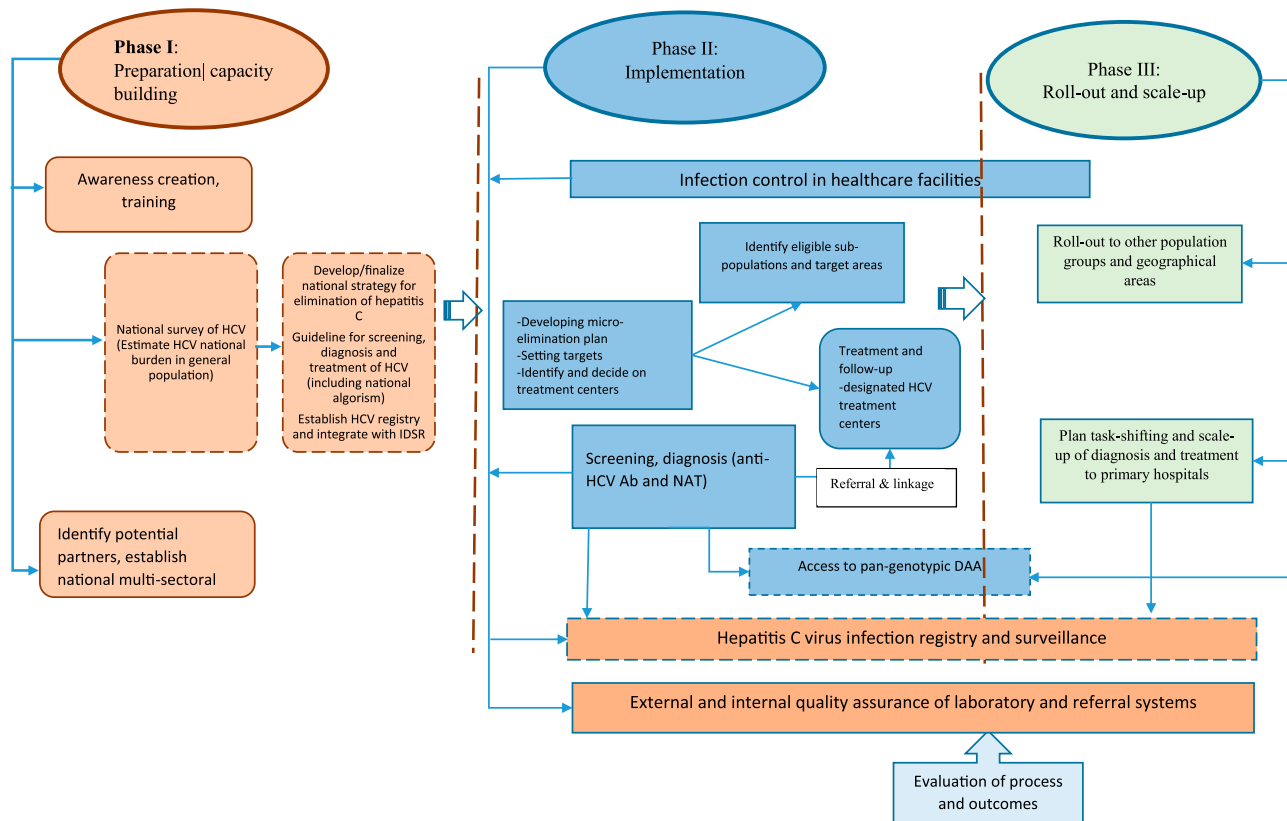


FIGURE 2. Hepatitis C virus micro-elimination pathway in the context of Ethiopia. It includes the oval-shaped boxes comprising the three linked phases of elimination activities. The gray-colored shapes show activities for preparation to initiate capacity building. This is connected with the blue-colored boxes that depict the actual implementation activities. The light green-colored boxes represent scale-up activities with geographic and population expansion. The boxes in orange color are registry and surveillance and quality assurance and monitoring activities. This figure appears in color at www.ajtmh.org.

Finally, establishing national HCV registry and integration to the existing Integrated Diseases Surveillance and Response system, using the indicators from every health facility of the number of all cases of HCV, number of PLHCV treated with DAAs, and deaths due to HCV-related complications, will facilitate case notification and monitoring the progress of implementation.^{37,38} Development of monitoring and evaluation indicators at this stage is essential to the success of the program. These include infrastructure for HCV testing, harm reduction and injection safety, testing, treatment and success of therapy, and incidence and mortality from HCV infection.³⁹ Detailed explanation for the monitoring and evaluation is presented in Figure 3.

Phase II: Implementation: Screening, treatment, and monitoring. After the required inputs are secured, implementation starts by identifying target population groups, geographical areas, and the health facilities to be involved in screening, diagnosis, and treatment of HCV infection. Although utilization of population-based data may provide a clearer picture of the population groups to start the micro-elimination, our review shows that PLHIV, prisoners, chronic liver disease patients, blood donors, pregnant women at antenatal care centers, and healthcare workers are the key population to be targeted.

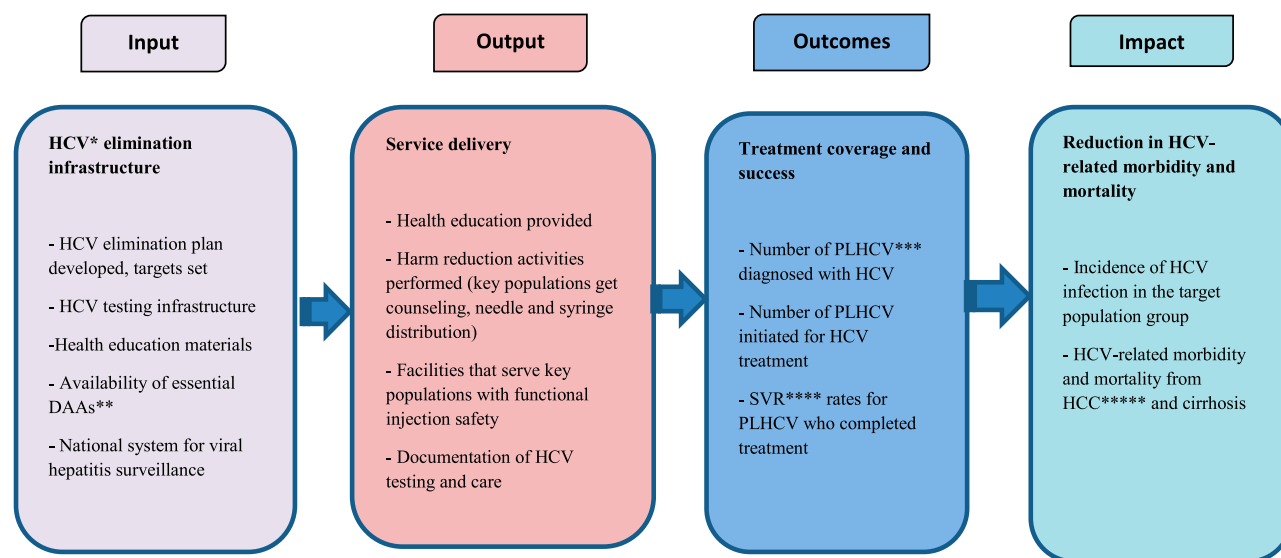
Screening, diagnosis, and treatment for these subpopulations can be initiated in all regional states, including city administrations. Hepatitis C virus testing is feasible at district, general, and tertiary hospitals. Connecting patients to treatment centers at general and tertiary hospitals where internists, and in some areas gastroenterologists, are available for treatment initiation and follow-up by integrating to the existing referral network of the three-tier health system creates a smooth transfer of patients.

Moreover, the long-standing lessons learned from national HIV control program could be adapted to shape the integrated HCV elimination activity.²⁷ There is an existing initiative to ensure access to DAAs by patients at highly reduced prices through an agreement with the Gilead Sciences, Inc. More effort is needed to make sure that there is enough supply of pan-genotypic DAAs for the expected growing number of eligible PLHCV through extended agreements and generic manufacturing within Ethiopia, of the fixed-dose combination pan-genotypic DAAs. As evaluated in other countries' experiences, Ethiopia can aim at using pan-genotypic regimens for the treatment of chronic HCV infection including sofosbuvir plus velpatasvir, sofosbuvir plus daclatasvir, glecaprevir plus pibrentasvir, and sofosbuvir plus velpatasvir plus voxilaprevir.⁴⁰

As the implementation is carried out, it is important that performance evaluation is done using the short- and long-term indicators to address the challenges in specific settings and enhance progress in subsequent scale-up to other subpopulations and areas.

Phase III: Rollout and scale-up. Once the initial round of implementation is underway for some time, it is crucial to expand the elimination activities to more subpopulations with a broader geographical coverage depending on monitoring and evaluation results of the phase-I and phase-II implementation activities. Scale-up builds on the lessons learned, challenges faced, and success stories from the initial implementation. This approach ensures the success of the subsequent expansion of screening and treatment to other subpopulation groups and areas.

Hepatitis C virus elimination scale-up can be effectively implemented through task-shifting⁴¹ in which mid-level healthcare workers at general hospitals are involved in screening and treatment. The program benefits from expanded



Abbreviations: *HCV=Hepatitis C virus; **DAAs=direct-acting antivirals; ***PLHCV=People living with hepatitis C;

****HCC=hepatocellular carcinoma; *****SVR=sustained virologic response

FIGURE 3. Monitoring and evaluation process for hepatitis C virus elimination activities. The gray-colored box comprises the inputs required to initiate micro-elimination; the pink-colored box refers to service delivery as a process of elimination activities; the blue-colored box shows outcomes of the program in terms of treatment coverage and success; the last box in green color represents the final impact of the program. This figure appears in color at www.ajtmh.org.

training of healthcare workers, including nurses, laboratory technologists, pharmacists, general practitioners, and internists (in selected topics) focusing on both detection and treatment of HCV infection, and reduction in healthcare-associated HCV transmission (Figure 2).

Priority subpopulation groups for HCV micro-elimination in Ethiopia. In Ethiopia, a practical approach to establish screening and treatment for HCV micro-elimination is a risk factor-based testing by identifying high-risk subpopulation groups from surveys.¹ Implementing a micro-elimination approach in subpopulations is preferred to a full-scale, general population-based initiative. This is because the program is manageable by policymakers,⁸ and it is less intricate, less costly, and inspires the health system from the developing success stories in a reasonably shorter period of time.^{9,42} General population-based screening, however, is not a pragmatic approach because of financial, human resource, test kit, and treatment shortages and program complexity. The HCV micro-elimination is proposed for Ethiopia to be implemented in subpopulations such as chronic hepatitis patients, prisoners, PLHIV, blood donors, pregnant women, and healthcare workers for their higher HCV burden, their high risk for HCV infection, and their engagement with the healthcare system. The inclusion of people who are already engaged in the health system for another reason into HCV elimination has been effective in previous studies.⁴³⁻⁴⁵

People living with HIV. The burden of HCV infection is high in PLHIV, and they are at increased risk of getting the disease because of their repeated hospitalization and blood transfusion. In Ethiopia, about 610,000 people lived with HIV in 2017,⁴⁶ and the HIV/HCV coinfection rate in Ethiopia is 3.1%,⁴⁷ ranging from 0.4%¹⁰ to 15.1%.⁴⁸ A comparative study of HCV prevalence in HIV-positive and HIV-negative persons showed a higher rate of HCV infection in PLHIV (4.5%) and is attributed to transfusion and unsafe injections.⁴⁹ A high HCV/HIV coinfection rate of 3.6% was found from a study in central Ethiopia.³¹

Increasing life expectancy with multimorbidity of PLHIV leads to an increased risk of developing HCV infection because of their frequent hospital admission, multiple transfusions, injections, and other medical procedures. History of hospitalization, tooth extraction, and blood transfusion is a known risk factor for the higher prevalence (6.6%) of HCV in PLHIV.¹⁴

The higher concentration of HCV infection in PLHIV means the screening and treatment of the disease at chronic HIV care clinics and elimination in this group could be effective. Integrating HCV screening and treatment into HIV care clinics will not only prove to be a cost-effective micro-elimination approach but also creates the opportunity to use existing referral and follow-up experiences from the long-standing HIV program.

Prisoners. Prisoners are at high risk of HCV infection because of a high potential for sharing sharps and the high rate of injection drug use. The prevalence of HCV is more elevated in prisoners than the general population. In Ethiopia, the prevalence of HCV infection in prisoners was 2.6%, more than two times higher than that in the general population.¹⁶

They cannot be accessed by regular health services and targeted interventions benefit in HCV elimination initiative. However, HCV elimination activities can be performed through integration with special programs such as prison health services, where HCV screening and treatment can be

implemented. Testing and treatment with DAAs in the prison setting can produce a significant reduction in HCV infection in the prison population, thereby reducing the spillover effect of HCV transmission from prison to the community.⁵⁰

Chronic liver disease and cancer patients. Patients who primarily present as chronic hepatitis cases have a high burden of HCV infection. For example, a greater than three times higher prevalence of HCV infection (3.6%) was found from an institution-based study of 578 chronic hepatitis patients.¹⁵ Another study found a 1.3% HCV prevalence in these patients.⁵¹

Hepatitis C virus infection in chronic hepatitis patients is a source of healthcare-associated HCV infection between patients, healthcare workers, and other susceptible individuals. Diagnosis and treatment of HCV infection in this population is vital to improve the quality of life and disease progression of the patients themselves. In addition, it is believed to play a pivotal role in eliminating the infection in these patients and breaking the transmission cycle at the healthcare and household settings.

Pregnant women. Pregnant women are priority populations to HCV elimination because of their increased risk of HIV infection (premature rupture of membranes, operative delivery, and blood transfusion), vertical transmission of HCV to their newborns, and their engagement to the healthcare system that enables a better access to testing and treatment.^{52,53} Dental procedures, household contact with the HCV-infected person, multiple sexual exposures, and delivery assisted by traditional birth attendants are risk factors associated with HCV infection in pregnant women that must be addressed by the healthcare facilities during the course of the elimination initiative.⁵⁴ As a result of this, targeting pregnant women at antenatal clinics is critical to increasing access to HCV screening and treatment to women.

Healthcare workers. Healthcare workers, including physicians, nurses, midwives, environmental health professionals, health science students, anesthetists, and medical waste handlers, are at risk of getting HCV infection because of their professional exposure to HCV-infected patients.⁴ Needlestick injuries, suboptimal infection prevention practices, poor healthcare waste handling practices, exposure to surgical and medical procedures, and, in some cases, inadequate knowledge of the transmission of HCV are important risk factors challenging healthcare workers.^{4,5}

Regular testing and treatment of healthcare workers is an indispensable element of the HCV elimination strategy because of their day-to-day contact with PLHIV, and other patients and communities. Focused training, improved utilization of personal protective equipment, screening, and treatment are feasible and help break the chain of HCV transmission at the healthcare setting. Strengthening universal and disease-based infection prevention practices at health facilities is an integral part of this activity.

Blood donors. Blood donors' chances of being an entry point to the transmission of HCV infection to their recipients make them the key populations in elimination efforts. In addition, in Ethiopia, the rate of replacement blood donation is very high, in some cases up to 79.1%,³² which leads to hasty testing procedures and affects the sensitivity and specificity of blood screening for HCV infection including missing HCV detection during the window period.

The largest HCV survey of blood donors conducted on 56,885 donors in five regional blood banks found HCV prevalence of 0.5%.²⁶ In other studies elsewhere in Ethiopia, HCV prevalence in blood donors ranges from 0.2% to 1.3%.^{2,5,55–57} A 6-year retrospective study of 11,382 blood donors from 2008 to 2015 found a significant increase in HCV prevalence (P -value for linear trend = 0.001).³³ Universal screening and treatment for HCV infection of all blood donors will ensure access to HCV treatment, which in turn accentuates micro-elimination.

Enabling factors for the HCV micro-elimination. *Control of healthcare-associated HCV infection.* Unsafe blood supply is an essential contributor to HCV transmission in Ethiopia, and blood screening at the blood banks using WHO-accredited test kits with increased utilization of confirmatory nucleic acid tests will reduce the transmission.¹ In the Ethiopian context, efforts must be made to ensure donor-based transfusion as the primary source of blood transfusion than replacement transfusion,³² which currently dominates. This can be made through the expansion of voluntary donation sites by working with the national blood bank agency. This gives the opportunity not only to conduct high-quality HCV screening but also to detect HCV in the window period.

Utilization of affordable testing and access to pan-genotypic DAAs. The use of rapid tests for initial screening plus nucleic acid test for the detection of active infection, which is relatively cost-effective, will be the most feasible approach for detection of HCV infection in Ethiopia.^{1,38,58} The use of dried blood spots for the screening, diagnosis, and monitoring the treatment of HCV infection has been effective in many countries, and this would be a sensible approach in the context of Ethiopia.³⁸

The country has initiated a subsidized pan-genotypic DAA (sofosbuvir/ledipasvir) through an agreement with the Gilead Sciences developing countries access program, but the cost of the full treatment course is high for most patients. Ultimately, generic production of DAAs, with the expansion of the fixed-dose combination treatment options, including sofosbuvir plus velpatasvir, glecaprevir plus pibrentasvir, and sofosbuvir plus velpatasvir plus voxilaprevir,⁴⁰ would alleviate the cost and availability challenges that patients experience. These second-generation drugs could not only cover the different genotypes that are present in Ethiopia but also abolish the need to conduct costly genotyping tests during the pre-treatment preparation, unavailable in most settings in Ethiopia.⁵⁸ It also creates a cost-efficient opportunity to procure similar drugs that cover all genotypes present in the country. There is a promising global initiative which targets large-scale manufacture of a low-cost two to three drug combination regimen for the 12-week treatment course. This realizes the highly demanded access to HCV treatment in low- and middle-income countries.^{59,60}

Task-shifting. Ethiopia has a few gastroenterologists/hepatologists.⁶¹ Involvement of nurses and general medical practitioners, along with internists and gastroenterologists/hepatologists, will be a cost-effective approach to reach the intended HCV elimination targets.⁶² The participation of nongastroenterology specialists, general medical practitioners, and nurses with compact informative training could substantially increase the availability of providers at general and district hospitals, thereby bridging the gap in the continuum of care for patients with HCV infection.⁴¹ Alike, other studies revealed training general practitioners and nurses in

the diagnosis and treatment of HCV infection increases patient reach, improves primary care of PLHCV, and reduces the workload of specialists.^{25,62}

Task-shifting through the utilization of district and general hospitals by training resident healthcare workers to expand HCV diagnosis and treatment services can be effectively implemented by referral to tertiary hospitals where gastroenterologists or trained internists can handle complex cases. External and internal quality assurance schemes can be established by linking with the accredited, high-quality diagnostic centers at the Ethiopian Public Health Institute and regional health research laboratories, where a wealth of experience in the quality assurance network in the HIV and malaria diagnostic programs can be transferred.^{63–65}

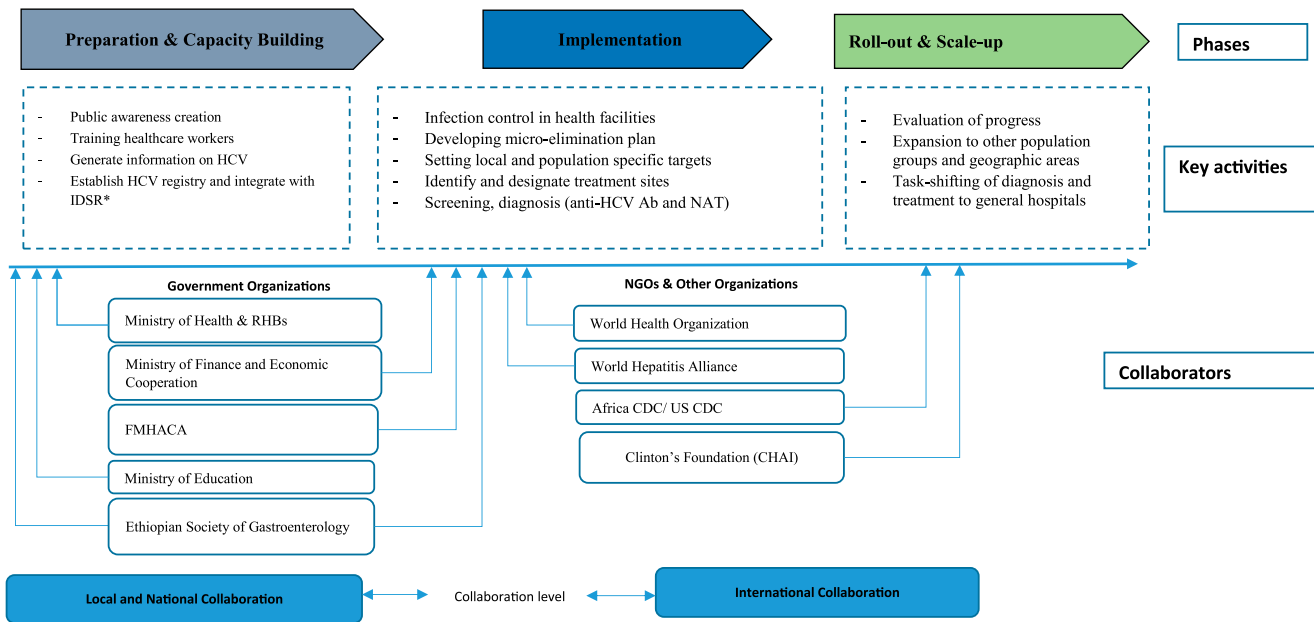
Multisectoral partnership. Collaboration and coalition building across sectors in the government and outside the government are recommended for successful implementation of HCV elimination led by the Ministry of Health.^{7,36} Only a collaborative effort built between different ministries in the country, partner organizations working on hepatitis and other diseases, and international agencies will make the national elimination targets to be achieved.^{60,66}

National partners working with Ethiopia's health system shall be identified and engaged starting from the planning process. The regulatory authorities in the country and the Ministry of Finance will help solve the challenges in the availability of HCV treatment in hospitals by improving the international procurement process.²⁵ Finally, working with the Central Statistical Agency, Ethiopian Public Health Institute, and regional public health institutes/health research centers virtually complements the evidence gap that exists to date and helps in monitoring and evaluation of progress. Among the international agencies, for example, the WHO, World Hepatitis Alliance, and United States CDC, the Africa CDC could have significant contributions to implement a successful program for HCV elimination.⁶⁶ Figure 4 shows a sketch map of multisectoral collaboration that could help the coordinated response toward HCV control (Figure 4).

Regulatory support. Besides the existence of the national health policy, it is critical that HCV elimination targets are set within the 5-year strategic plan. This gives a better opportunity to secure budget, train human resource, and avail laboratory and other diagnostic infrastructures.^{25,36,58,67} Similarly, regulatory support helps the procurement of DAAs essential to treat HCV by enabling the acquisition of pan-genotypic regimens to ensure access to the broader population.^{27,34,59}

CONCLUSION

Ethiopia has comparably low, but rising HCV burden. The country recognizes HCV infection as a public health problem and initiated control programs. The emergence of and recently increased access to highly efficient DAAs create an opportunity to eliminate chronic HCV infection as a public health problem in Ethiopia. The realization of this goal requires cost-effective and sustainable approaches. The micro-elimination approach is proven to be efficient, manageable, and can be scaled-up. General population-based screening and treatment programs are not cost-effective for countries such as Ethiopia because of the high cost and program complexity, given the existence of other competing healthcare needs.



*RHB: Regional Health Bureaus; IDSR: Integrated Disease Surveillance and Response; NAT: Nucleic Acid Test; CDC: Centers for Disease Prevention and Control; NGO: Non-Government Organization; CHAI: Clinton's Health Access Initiative; FMHACA: Food, Medicine and Health Care Administration and Control Authority of Ethiopia

FIGURE 4. Sketch map of multisectoral collaboration. The boxes at the top show the different phases of the hepatitis C virus micro-elimination from preparation and actual implementation to scale-up of activities. The boxes with broken lines show the activities to be performed under each phase, which is actually not limited to the respective phase but may continue throughout the process. The hardline boxes in two columns show the potential domestic and international collaborators that act at the national and international level. It includes the primary national agencies and societies and the international organizations that had previous experience of collaborating with Ethiopia. This figure appears in color at www.ajtmh.org.

Therefore, a public health approach to micro-elimination of HCV infection, led by the Ministry of Health, which uses the existing three-tier referral system integrated to the HBV, HIV, and other control programs, is recommended. Phase I is the preparation and capacity building to ensure necessary inputs are in place; phase II is the training, testing, treatment, and follow-up; and phase III will be the rollout and scale-up of activities to other subpopulation groups and geographic areas based on evaluation and feedback. The micro-elimination could target high-risk subpopulation groups, including PLHCV, prisoners, chronic liver disease patients, healthcare workers, pregnant women, and blood donors.

The micro-elimination initiative can be implemented at general and tertiary care hospitals with further expansion to district hospitals via a task-shifting approach by training nongastroenterology specialists, general practitioners, nurses, laboratory technologists, and pharmacists. The performance of expansion to the primary care can be realized through referral and feedback of complex cases and external quality assurance of diagnosis and treatment.

The major enablers to HCV micro-elimination in Ethiopia include significant reduction in healthcare-associated HCV infection, blood safety, utilization of affordable testing, use of pan-genotypic DAAs, task-shifting, multisectoral partnership, and regulatory support to the procurement of DAAs.

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