HCV Diagnostics
Market Intelligence Report 2017

First Report on Screening and Diagnosis Market Growth

Funded by Unitaid

Summary

In order to close the diagnosis gap and reduce barriers to accessing diagnostics in low- and middle-income countries (LMICs), the Foundation for Innovative Diagnostics (FIND) and the Clinton Health Access Initiative (CHAI), with support from Unitaid, surveyed 29 LMICs and worked closely with 44 suppliers and in-country partners worldwide to gain market intelligence insights into the hepatitis C virus (HCV) diagnostic landscape. Categories analyzed include program structure, trends in procurement, testing rates, national targets, and obstacles to scale-up. A five-year forecast of the total market need and the projected demand for HCV diagnostics was developed for the 29 LMICs representing 80% of absolute HCV viremic burden in LMICs, plus high relative prevalence countries with active HCV programs (see Appendix A for country list).

The total market need and demand for screening tests over the next five years is estimated to be respectively 826 and 178 million tests, of which 75% is driven by five countries (China, Pakistan, Egypt, Brazil and Morocco). While lab-based immunoassays (IAs) are mainly used for screening of HCV in middle-income countries, most low-income countries surveyed are shifting towards the use of rapid diagnostic tests (RDTs) as the main method of screening, primarily for cost and access reasons. The market for screening tests is highly fragmented, with an average of five RDT or IA brands being procured per country, although some of these tests, particularly RDTs, are of unknown quality. While the average price per test stays generally under $1 in the public and private sectors, there are some major disparities between countries and brands. These differences are heavily influenced by purchasing volumes, competition and local importation and taxation costs.

The total market need and demand for viral load tests over the next five years for high-burden LMICs is estimated at respectively 31 and 16 million tests, of which 79% is driven by four countries (China, Egypt, Pakistan and India). An increasing number of LMICs are adopting policies and guidelines to simplify their HCV diagnostic algorithms and are also exploring various service delivery models to account for the needs of different high-risk groups. The viral load testing market is rather consolidated: the two market leaders – Roche and Abbott – offer platforms used mainly by countries in centralized laboratory settings. Another fast-growing manufacturer, Cepheid, provides decentralized testing with its GeneXpert platform. The majority of countries have HCV assays from Roche and Abbott registered and available. Most countries have already or are in progress of registering and using GeneXpert HCV assays. The analysis has noted excess capacity on major platforms so that the integration of testing for HCV alongside other diseases such as HIV and TB is feasible. HCV viral load testing pricing remains high in most countries (from $15-$30 per test in the public sector to $60-$200 per test in the private sector) and was noted by survey respondents as a significant barrier to program scale-up.

Many stakeholders have been advocating for a shift to core antigen (cAg) testing - which may enable a one-step diagnosis more easily than nucleic acid testing (NAT) – and some global treatment guidelines have recommended it as an option for confirmatory testing. Considering a gradual scale-down of on-treatment monitoring tests and other factors, the total need for cAg testing over the next five years is projected to be 285 million tests. Very few cAg assays are available commercially and they range widely in quality. The Abbott ARCHITECT HCV cAg assay is one of the best performing options; however, most LMICs do not have the Abbott ARCHITECT 2000 platform in place to be able to conduct cAg testing. In the long-term, widespread adoption of cAg testing will require factors such

as more quality-assured supply options, competitive pricing to allow for use in screening, affordable, point-of-care (POC) cAg platforms, and/or greater availability of Architect platforms.

Six obstacles have been identified and need to be addressed in order to increase diagnostic coverage and help scale up HCV programs in LMICs. Firstly, despite a noticeable shift towards greater investment in HCV, a majority of countries still have inadequate funding to meet the WHO's 2020/2030 HCV elimination targets. Secondly, suboptimal device placement or inadequate testing capacity within laboratory networks prevents scale-up of HCV programs. Integration of HCV/HIV/TB testing on the existing platforms could be a solution although there are governance and systems challenges that must be addressed. Thirdly, lack of healthcare worker engagement on HCV due to lack of knowledge requires additional training resources, integration of HCV care into existing systems, and use of innovative models to target high-risk patients. Fourthly, most countries lack key data on HCV patients, impeding their ability to develop well-informed national strategies and engage with suppliers on pricing negotiations. Fifthly, very few countries have clear diagnostic targets or scale-up plans for HCV in line with the WHO's 2020/2030 HCV elimination targets. Identifying and setting such targets is crucial to advocating for HCV funding, planning for procurement, developing appropriate service delivery models tailored to the national context and locating sources of technical support and partnership. Finally, limited awareness of HCV in the general public is a key challenge: embarking on education and awareness programs in-country will lower stigma about HCV, stimulate demand for services, and increase case-finding.

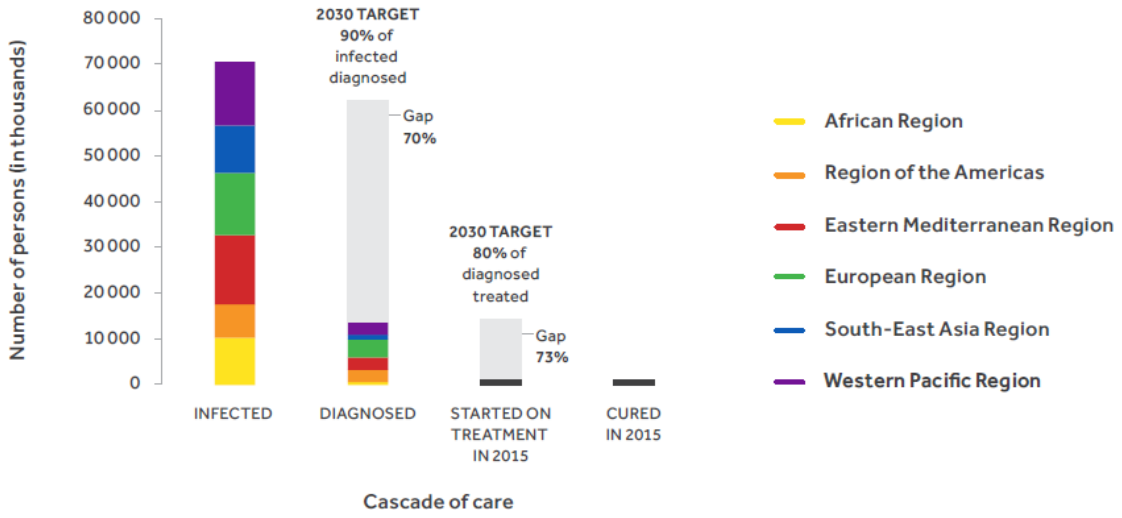
Acronyms

AASLD	American Association for the Study of Liver Diseases
CAGR	Compounded annual growth rate
cAg	Core antigen
CBO	Community-based organization
CHAI	Clinton Health Access Initiative
CoNE	Community Network for Empowerment (Manipur, India)
DAAs	Direct-acting antivirals
EASL	European Association for the Study of the Liver
FIND	Foundation for Innovative Diagnostics
GX	GeneXpert
HCV	Hepatitis C virus
HIV	Human immunodeficiency virus
IA	Immunoassay
LMIC	Low- and middle-income country
LTFU	Loss-to-follow-up
MDR-TB	Multidrug-resistant tuberculosis
MSF	Médecins sans Frontières
NAT	Nucleic acid testing
NGO	Non-governmental organization
NSP	Needle/syringe programs
OST	Opiate substitution therapy
PLHIV	People living with HIV
PWID	People who inject drugs
POC	Point-of-care
RDT	Rapid diagnostic test
SVR (SVR12)	Sustained virologic response (12 or more weeks after the end of treatment)
TB	Tuberculosis
VL	Viral load
WHO	World Health Organization

Overview

Approximately 71 million people worldwide are chronically infected with HCV, establishing it as **one of the world's most common infectious diseases**.[i] More than 80% of these people live in LMICs. Over the last fifteen years, mortality has steadily increased to over 400,000 deaths annually, in stark contrast to the declining number of deaths seen for other infectious diseases such as HIV, TB and malaria.[ii] Despite its high prevalence, morbidity and mortality, **only 20% of HCV-infected persons have been diagnosed and only 7% have received treatment worldwide.**[iii] In LMICs, rates of diagnosis and treatment are even lower.[iv]

Figure 1: Cascade of care for HCV infection, by WHO region, 2015



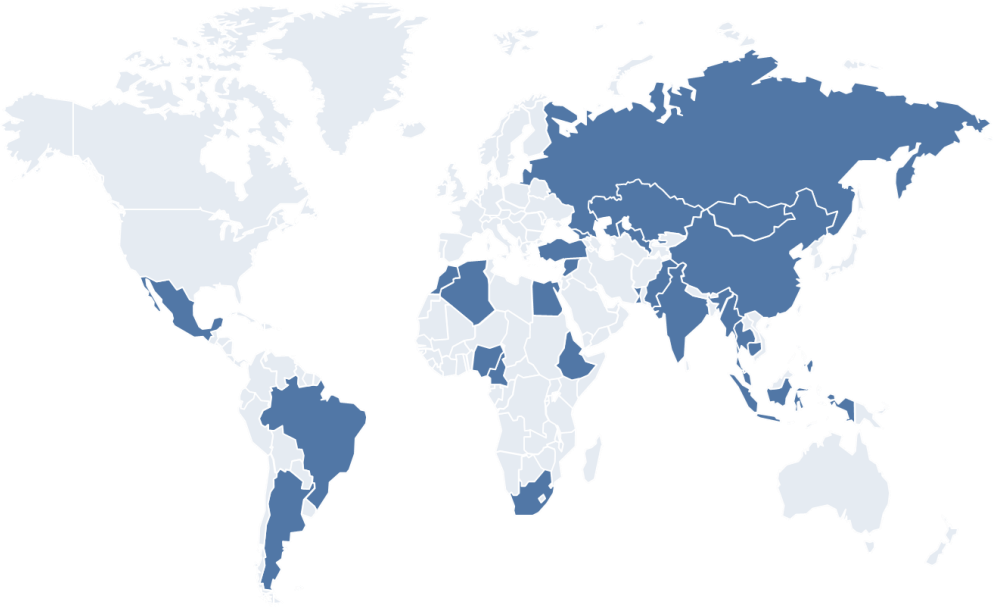
Closing the diagnosis gap is crucial for countries to achieve the 2030 elimination targets they committed to at the 2016 World Health Assembly. However, rates of diagnosis and the diagnostic access barriers in LMICs have not been well-characterized to date. As a result, investment in improved tools and commitment from suppliers to lower prices has been limited despite the release of the WHO guidelines[v] on testing, strategic diagnostic approaches, solving access barriers, and linking patients to treatment. To address these information gaps, FIND and CHAI, with support from Unitaid, sought to develop a first-ever HCV diagnostic market forecast for LMICs and analyze the enablers and barriers to growth with the aim of providing adequate market transparency to stimulate investment in HCV diagnostics at the supplier level while identifying concrete actions to improve access in local markets. This report highlights the key findings and insights from this analysis for HCV screening, viral load/core antigen testing, overall market growth potential, and barriers to scale.

Methodology

CHAI and FIND, with the support of Unitaid, surveyed 29 countries and 44 partners/suppliers worldwide to gain market intelligence insights into the HCV diagnostic landscape, including program structure, trends in procurement, testing rates, national targets, and obstacles to scale-up. CHAI built

a five-year need and demand forecast to project the total market need for HCV diagnostics and the actual projected demand for the highest-burden HCV countries globally. This market intelligence assessment covers low- and middle-income countries that represent 80% of the total global HCV burden, in addition to several other high prevalence countries that are currently contributing a disproportionate amount of diagnostic volumes due to their ambitious public programs, even though their relative absolute burden is small, such as Georgia. See Appendix A for list of these countries.

Figure 2: Countries selected for market assessment



The approach to data collection included:

1. Supplier surveys to determine actual diagnostics platform capacity/footprint and past and future orders data
2. Market intelligence survey shared with 44 partners to better understand country programs, procurement, funding, algorithms, and future scale-up plans
3. Partner interviews, surveys, and data requests in key geographies
4. An in-depth desk review of all published data and policy documents to assess available information on country-level HCV programs
5. Extensive assessments of the HCV program in 5 countries, including stakeholder interviews

The 5-year HCV need forecast leveraged Polaris Observatory country data on existing/new HCV infections and patients diagnosed/treated to calculate the total number of patients requiring diagnosis each year to meet the WHO targets of 30% diagnosed by 2020 and 90% diagnosed by 2030. The number of screening and viral load tests was calculated factoring in chronicity rates, prevalence, testing algorithm, and false negative rates.

The 5-year demand forecast was defined as the number of tests likely to be consumed by the market and represents assumptions and expectations in light of currently available information. This forecast is based on a number ofs factors relating to a country's capacity to scale up HCV testing, and it thus involves uncertainty. The innovative demand forecasting approach is based on a number of analogue

countries which were identified to represent a range of scale-up scenarios. Forecasts were then developed using available data for the analogue countries. The remaining countries were mapped to analogue scale-up scenarios according to a scoring index that included factors such as prevalence, guidelines/strategic plans, level of government commitment to HCV, level of HCV financing and general health funding, existing lab capacity, price of diagnostics, and planned procurements. Table 1 gives details of these scoring index factors.

Table 1: *Index factors for country mapping*

Policy		Funding and procurement		Program capacity	
Index factors	**Max score**	**Index factors**	**Max score**	**Index factors**	**Max score**
Viremic prevalence	8	Financing availability	18	Level of lab capacity	6
Strength of advocacy	4	HCV funding	16	HIV VL program maturity	2
DAAs in guidelines	4	Diagnostics procurement levels	8	HCV diagnostics cost	4
DAAs in use	8			GeneXpert approval	2
National Strategic Plan	4				
Active screening	8				
Demand generation	8				
Subtotal	**44**	**Subtotal**	**42**	**Subtotal**	**14**

TOTAL INDEX FACTORS MAX = 100

Growth rates for analogue countries in each category were then applied to the remaining countries to deduce global estimates. Furthermore, forecasts were developed for the highest-burden countries individually when data was available in order to increase projection accuracy. Table 2 provides details of 10 analogue countries that were selected due to the availability of enough data for more robust predictions and the countries that were mapped to the analogue countries.

Table 2: *Country mapping to analogue countries under different scenarios*

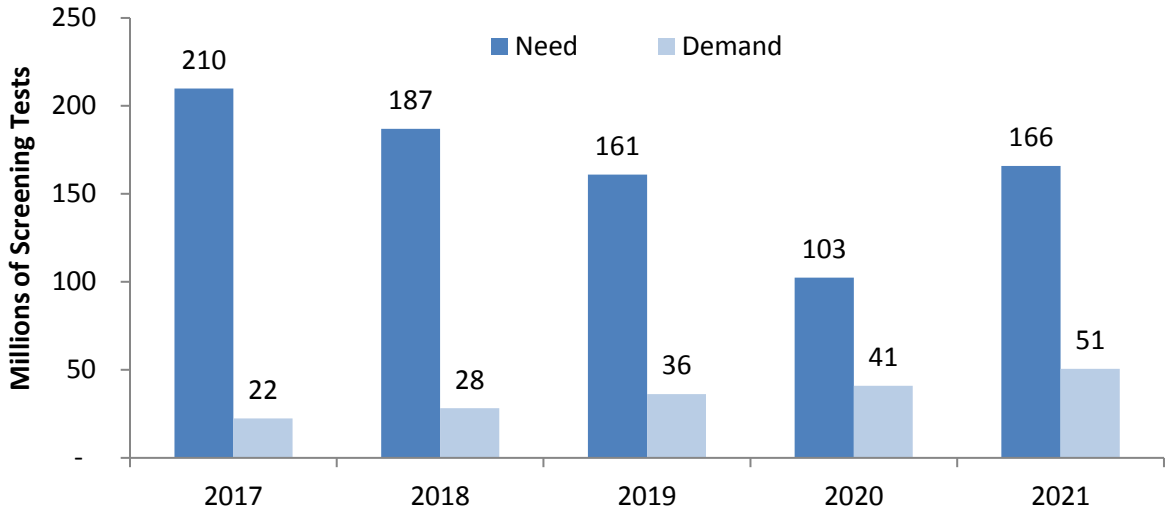
	Scenario 1	Scenario 2	Scenario 3	Scenario 4	Scenario 5
Country description	Limited access to funding or political will to scale program	Initial public program progress, but limited in scale	Significant scale-up to date, but not yet on elimination track	Upper middle income countries who may be constrained by drug pricing	Countries on elimination track
Index score range	5 – 25	26 – 39	40 – 55	56 – 75	76 - 100
Analogue countries	**Ethiopia**	**Myanmar**	**Punjab (India)**	**Brazil**	**Georgia**
	Cameroon	**Colombia**	China	**Thailand**	**Mongolia**
Other countries	Philippines	Nigeria	Pakistan	Russia	Egypt
	Syria	Indonesia	India	Romania	
	Ghana	Algeria	Uzbekistan	Mexico	
	Cambodia	South Africa	Turkey	Argentina	
			Malaysia	Morocco	
			Kazakhstan		

Screening

Screening forecast

The total market need for screening tests over the next five years for high-burden LMICs is estimated to be 826 million tests. The total projected demand for screening tests over the next five years for LMICs is 178 million tests, which accounts for a number of factors relating to a country's capacity to scale up HCV testing. Three quarters (75%) of screening test demand was driven by five countries (China, Pakistan, Egypt, Brazil, Morocco). It is important to note that the total market need for screening tests trends downward as it approaches 2020 and countries get closer to meeting the WHO target of 30% diagnosed, hence a negative total compounded annual growth rate (CAGR) of -4.6% over the five years. The market need returns to a positive trajectory when the WHO diagnosis target changes to 90% in 2020. The forecasted demand projection for screening tests, however, increases at a CAGR of 7.2% over the five years, highlighting that countries are increasing screening activities for HCV but not at the pace required to meet the WHO target for diagnosis. The gap between need and demand is influenced by low rates of active screening, and the difference between theoretical and actual tests needed to find the target number of patients. However, the need forecast does not take into account whether countries are screening for high-risk populations, so countries doing prioritized screening may reach WHO targets with far fewer screening tests than estimated here.

Figure 3: *Estimated Annual Need to Meet WHO's 2030 Elimination Targets vs. Annual Demand for Screening Tests 2017-2021*



Screening policy

Most surveyed countries have guidelines which recommend RDTs as an acceptable method of screening for HCV in addition to lab-based IAs. Historically, IAs have been more commonly used in most countries where HCV programs are limited to large tertiary care facilities with hepatology services. However, a shift to primarily using RDTs is being seen in many low-income countries as they expand their programs geographically while contending with less developed laboratory infrastructure. Several CHAI hepatitis program countries have recently started or completed RDT validations for this reason, and noted using RDTs for cost and access reasons.

This trend of screening with RDTs is expected to accelerate as countries look to expand screening. With the challenges of underdeveloped laboratory networks, low levels of infrastructure, high transportation costs, unequal access to laboratory facilities, and a dearth of skilled laboratory technicians, countries are gravitating towards the ease of using RDTs to avoid long turnaround times and patient loss-to-follow-up (LTFU). RDTs will prove to be particularly useful as countries actively begin screening patients for HCV infection, focusing on high-risk populations that may be hard to reach (e.g., PWID). In middle-income countries, IA platforms are still being used extensively due to their relatively stronger existing laboratory capacity, infrastructure, health workforce, and transportation networks.

To achieve diagnosis targets, programs will need to find patients who are asymptomatic, requiring active screening strategies such as provider-initiated screening, risk-based screening, index tracing, and systematic screening of high-risk groups, and general population campaigns. However, the number of high-burden countries that are actively screening patients or targeting high-risk populations for prioritized screening remains low. In most countries, the patients being diagnosed with HCV are presenting to clinics with acute symptoms or advanced illness. Only 10 out of 29 analyzed countries (35%) had active screening programs in place, and all were middle- or lower-middle income countries.

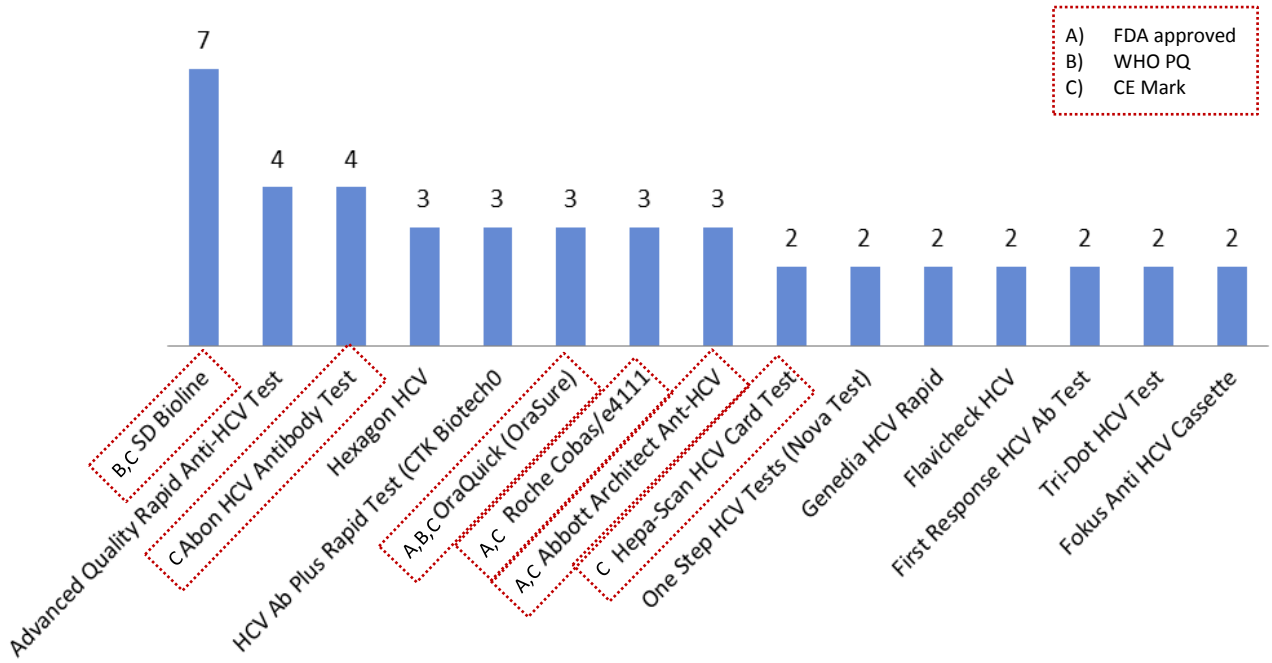
The Rwanda Biomedical Center pursued active screening through campaigns targeting risk groups. In 2016, RBC screened 65% of its HIV population in care over 6 months, identifying more than 4% of its ART cohort as antibody-positive. In 2017, follow-up campaigns were conducted in prisons, targeting people over age 40, which are two other risk groups.[ix]

However, countries are moving towards active screening, as evidenced in changes to recent guidelines which list key populations for screening. Of CHAI hepatitis program countries, 100% of the countries list PLHIV and PWID as populations prioritized for screening. Of profiled countries, 60% prioritized prisoners and hemodialysis patients and 40% focused on pregnant women, children born to HCV-infected mothers, people with a history of blood transfusions, and/or people with tattoos or surgical procedures conducted in places with weak infection control procedures under priority population for HCV screening. Only 20% of surveyed countries included healthcare workers and female sex workers as key populations prioritized for HCV screening.

Procurement

Few countries surveyed provided detailed screening test procurement or consumption data and very few provided a breakdown between the use of laboratory-based IAs versus RDTs. In many of the countries surveyed, screening test procurement is a hospital-level responsibility and procurement/consumption data is not reported to national hepatitis programs. Where data was available, volumes were inconsistent from year-to-year in most countries, concordant with a passive approach to case finding. Furthermore, few national programs have provided direction or guidance on product selection, which may hinder procurement of high-quality, cost-efficient screening tests. As a result, screening test procurement is highly fragmented (a significant number of countries have more than five RDTs registered) and test performance is highly variable. Nine LMICs were analyzed in a previous internal study by CHAI and were found to be using 46 different RDTs for HCV screening collectively. A subset of these tests and the number of countries using each test is shown below.

Figure 4: *Number of surveyed countries procuring RDT/IA Brands*

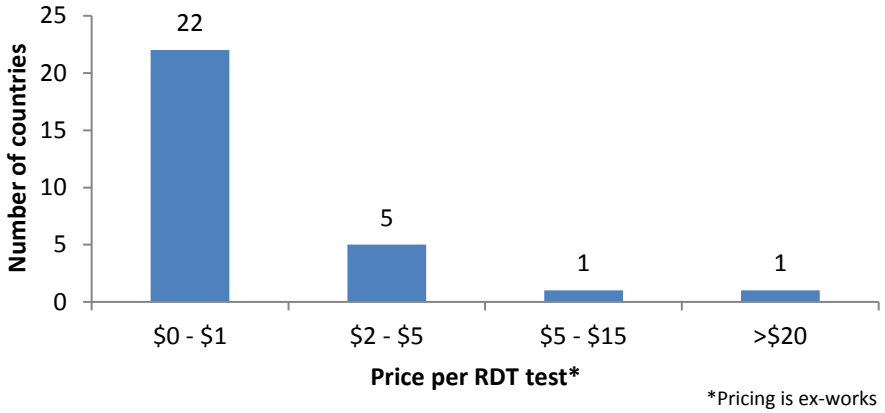


Forecasting procurement of screening tests was also difficult as many countries have not set HCV screening targets, even though they may have treatment targets. Absence of historical antibody positivity rates captured by data systems made it difficult to forecast the number of screening tests needed to hit treatment targets.

Payment and pricing

Pricing for screening tests is generally low but can vary significantly country-by-country depending on the test brand. The price paid to distributors by public or private purchasers is generally quite low, although it is heavily influenced by purchasing volumes, competition and local importation and taxation costs. Where patients pay for testing, the price fluctuates depending on whether the patient goes to a public or private clinic for treatment, cold chain storage needs, sample type, and sample transportation. There is currently only one oral-fluid test that is commercially available in the surveyed countries (OraQuick/OraSure), which is priced much higher than blood-based RDTs. FIND has purchased RDTs for $1 for many of its country programs. The graph below highlights the range of prices to the patient for RDTs.

Figure 5: *Number of surveyed countries in various RDT price per test ranges*



Demand for screening tests is heavily influenced by whether the patient must pay out-of-pocket. Few countries offer systematic free testing for their populations in the public sector. Among CHAI hepatitis program countries, only one country offers free screening to public sector patients and only in some regions while two countries offer free screening only for patients covered under national health insurance. A third country offers free testing to high-risk populations (PLHIV, PWID, prisoners, pregnant women) only through certain demonstration pilots, not nationally. In some countries, screening is covered under insurance programs, but limited to patients who are either admitted to the hospital or who exhibit symptomatic disease. Where countries have begun to provide testing free-of-charge, this is often still limited to a small number of hospitals or entry points within hospitals.

Partner involvement

NGOs and CBOs are catalyzing countries to conduct wider screening and actively seek out HCV-infected patients. NGOs have a significant role to play in galvanizing and re-allocating funding for HCV efforts, tracking screening volumes and yields, corralling stakeholders for HCV efforts, and advocating to the government for crucial policy and strategy changes in HCV diagnosis and treatment. Organizations that were found to be actively supporting screening across a number of countries include Médecins du Monde, that screening injecting drug users in Côte d'Ivoire, Georgia, Kenya and Vietnam; MSF, that is running demonstration projects in Cambodia, India, Mozambique and Myanmar, and Coalition Plus, that supports a diverse group of CBOs in Colombia, India, Indonesia, and Morocco.

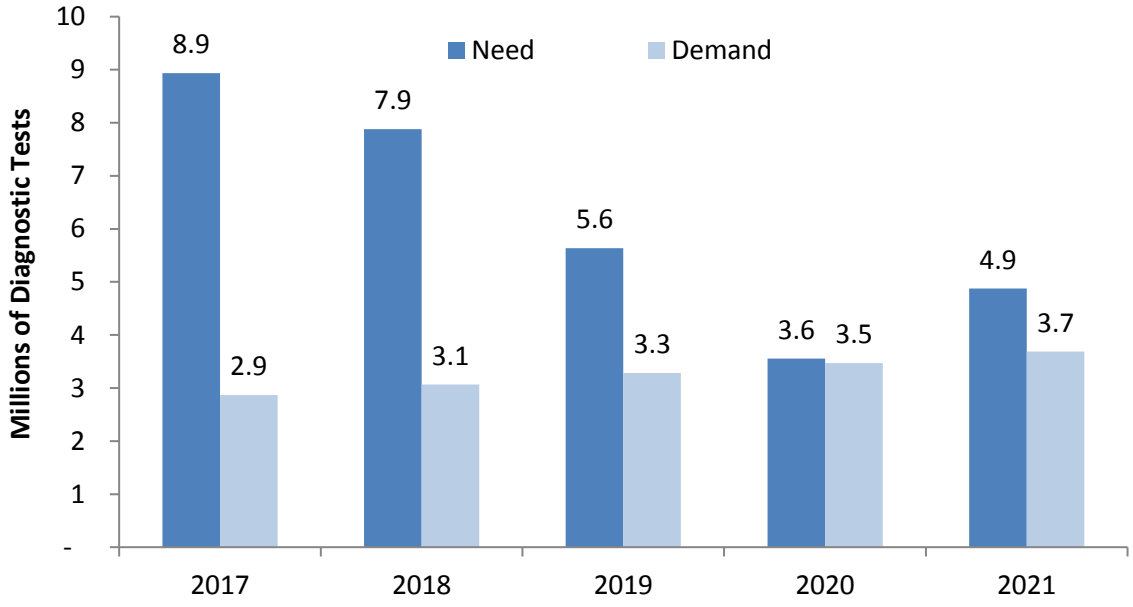
The Community Network for Empowerment (CoNE) in India collaborated with the government and pharma companies to screen over 1,000 high risk individuals at 13 sites, supported by road shows to generate disease awareness. They found 494 antibody-positive patients who were subsequently linked to confirmatory diagnosis and treatment.

Viral load

Viral load forecast

The total need for viral load tests over the next five years for high-burden LMICs is estimated at 31 million tests. Need was calculated in a similar manner for screening tests, using the 2020 and 2030 WHO targets for diagnosing HCV patients. The total projected demand for viral load tests over the next five years for LMICs is 16 million tests, which factors in planned procurement data, historical demand, funding, country targets, and a number of other aspects relating to a country's capacity to scale up HCV testing. Of the projected demand for viral load tests, 79% was driven by four countries (China, Egypt, Pakistan, India), with Egypt driving the most significant portion of total demand (36%). Like the need forecast for screening tests, the need forecast for viral load tests shares a similar downward trajectory (CAGR of -11.4%) as countries approach the 30% diagnosis target in 2020 and moves upward as the targets change to 90% for diagnosis in 2030. The viral load need forecast's CAGR decreases at a greater pace than that for screening tests as it accounts for countries reducing the number of viral load tests in their algorithm down to 2 tests by 2021. The viral load demand forecast grows at a CAGR of 5.1% over the next five years, demonstrating a steady increase as countries set their sights on diagnosing more patients.

Figure 6: *Annual need for WHO's 2030 elimination targets vs. annual demand for confirmation and monitoring tests 2017-2021*



Viral load policy

An increasing number of countries, specifically low- and lower-middle income countries, are adopting policies and guidelines to simplify their HCV diagnostic algorithms. This includes decreasing the total number of viral load tests to diagnose and monitor patients (down to 2 in total), as well as shifting away from requiring genotyping prior to HCV treatment initiation. These trends can be a catalyst for program scale-up and rapid growth, and reflect the increasing availability of direct-acting antivirals that are effective across all genotypes.

Until 2017, Nasarawa State in Nigeria had no access to nucleic acid testing for any disease. In partnership with HealthLine and Cepheid, Nigeria is piloting an HCV/TB integration strategy on Cepheid's GeneXpert platform.

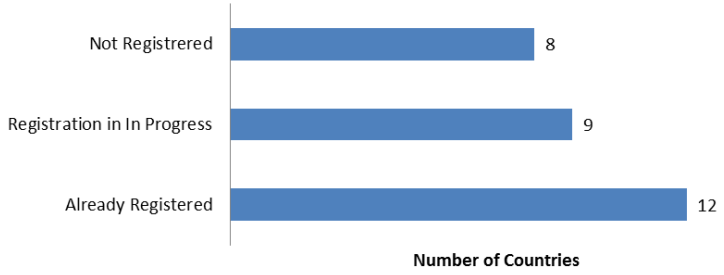
NAT platforms

Only a few companies worldwide market HCV nucleic acid testing, of which Roche and Abbott are the two main suppliers of viral load tests for HCV in both low- and middle-income countries. Roche is the market leader in sales, followed by Abbott, although Cepheid is gaining market share since the launch of its HCV cartridge for GeneXpert in 2015. Roche and Abbott platforms tend to be found in laboratories in the private sector and in tertiary or district hospital-level laboratories in the public sector, where they have often been placed for use by HIV programs. Cepheid platforms tend to be more decentralized and have been placed by TB programs historically to screen PLHIV for TB and those suspected to have MDR-TB. Most countries surveyed noted available capacity on HIV and TB testing platforms, which could also accommodate HCV testing on existing devices. However, the challenges on how to make this integration possible and acceptable across programs, given the situation around governance, funding, and oversight still remains to be addressed in most countries.

Total viral load testing capacity on major platforms in 25 out of 29 LMICs included in the forecast is estimated to be over 17 million tests per year. The highest projected annual need for HCV testing is 8.9 million viral load tests (2017) and the highest projected demand is 3.7 million viral load tests (2021), indicating there likely is excess capacity available on existing platforms to accommodate HCV testing. An internal analysis by CHAI of 2017 Cepheid TB sales data indicates that 83 out of 120 countries (69%) are using less than 25% of their GeneXpert installed base capacity. Additionally, Cepheid's 2017 TB sales data indicate that 111 out of 120 countries (92%) are using less than 50% of their installed base capacity. This analysis further indicates there is ample available capacity to integrate HCV testing on existing GeneXpert platforms in LMICs.

Countries expanding their HCV programs have made different decisions about which platforms to use according to their context. Sites with lower expected testing volumes or where there is a mismatch between the location of a centralized platform and the HCV disease burden have opted to use Cepheid GeneXpert devices. Where integration of testing on existing platforms has proven politically challenging, countries have found purchasing new GeneXpert devices to be the most financially feasible option for expansion of diagnosis. Other countries have found it most feasible to integrate HCV testing into their existing sample transport networks for testing at centralized laboratories on Abbott or Roche platforms. All of the 29 countries surveyed had in-country registration of HCV assays from Roche or Abbott and 21 countries had already registered or were in the process of registering GeneXpert's HCV assay.

***Figure 7**: Status of registration of GeneXpert use for HCV Viral load testing in high burden countries*



Some middle- or lower-middle income countries such as China, Georgia, and India are also using open source viral load testing platforms, which be lower priced and can potentially use reagents from multiple suppliers. However, use of open source VL testing platforms often requires increased training and rigorous quality assurance to ensure consistent provision of accurate test results. Open source platforms also create more complexity in a country's supply chain due to the need to procure various commodities from multiple suppliers.

Service delivery models

A number of service delivery models are in place for HCV viral load testing. As countries continue to explore integration of HCV testing into their existing systems and deal with changing disease demographics, these service delivery models may shift or merge in the future. It is noteworthy that WHO and other partners strongly advocate for differentiation of service delivery models as the needs of the general population can differ from high-risk groups, and even within diverse high-risk groups there are significant differences. Countries are testing different models, depending on their device throughput and current diagnostic systems structure.

The Mukht Mantri Hepatitis C Relief Fund in Punjab State, India, covers the cost of treatment for all citizens of the state. The government has negotiated a deal with private sector laboratories to charge patients $30 for their two viral load tests (prior to and upon completion of treatment).

Table 3: *Details of different service delivery models for HCV VL testing*

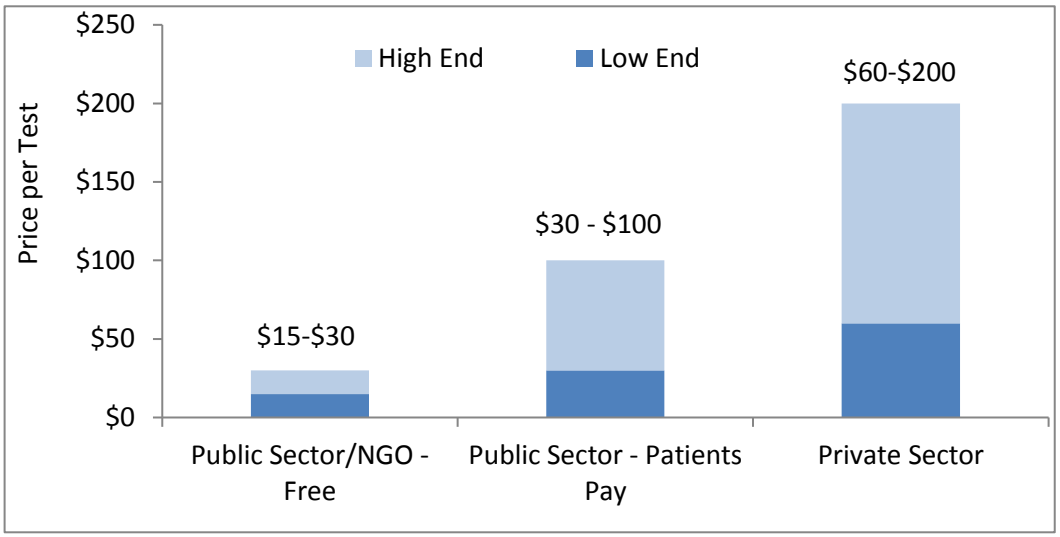
Service delivery model	Country example	Description	Advantages	Disadvantages
Testing at centralized laboratories	Nigeria, Vietnam	Patients are screened at lower-level health facilities and then are referred to the laboratory at the central hospital for testing	Consolidation of testing; ability to use higher throughput machines	High travel time and expense for patients; limited access to testing for many patients
Decentralized sample collection	India, Pakistan	Patients drop off samples at collection points near their homes; samples are then transported to a centralized facility for processing	Leverages existing sample transport networks	Long turnaround times for results delivery can be an issue
Centralized GeneXpert (GX) testing	Myanmar	Patient samples are sent to central laboratories for testing on dedicated GX platforms	Potential to scale HCV testing quickly; no integration challenges	Volumes limited by small number of devices, potential overcapacity in the lab system, long turnaround time
Decentralized and integrated GX testing	Indonesia, Nigeria pilots	Patients are tested on GX platforms at lower-level health facilities shared with HIV and TB programs	Leverages already-deployed GXs; higher utilization of machines	If platforms and HR are already near capacity, ability to leverage existing systems may be limited

Payment and pricing

HCV viral load testing pricing remains high in most countries and was noted by survey respondents as a significant barrier to program scale-up. Despite the small selection of platforms, reagent pricing was found to be highly variable, differing not only greatly across geographies but also within countries according to where services are being offered (NGOs, public, or private sector) and who is paying for the tests. Where free testing is available in the public sector or testing is offered through donor or NGO-funded programs, funders were paying between $15 and $30 per test, although middle-income countries faced higher pricing. Variation is both due to in-country customs, taxes, and distribution costs, as well as low and uncertain purchase volumes which impede negotiations for price reductions.

Where payment in the public sector was out-of-pocket for patients, countries reported testing costs in the $40-$100 range. The higher price largely seems to be explained by hospital margins and the need to incorporate small batch sizes and uncertain demand into final prices. Private sector pricing was more variable, with pricing as high as $200 for one viral load test. These prices often exceed the disposable income available to patients, preventing patients from accessing confirmatory diagnosis and initiating treatment.

Figure 8: *Reported pricing structure by industry segment for HCV Viral load testing in high burden countries*



A number of countries surveyed have started publicly-funded HCV treatment programs, but still require patients to pay for their viral load tests. Additionally, some health insurance programs limit reimbursement of viral load testing to those who are admitted for inpatient care. These restrictions will continue to hamper demand for diagnosis services and impede countries from reaching their treatment targets.

The cost of HCV diagnostics and treatment is a significant factor in whether patients present for confirmatory testing, start treatment, complete treatment, and return for the final SVR test. In particular, several countries, including Egypt, Georgia and the state of Punjab in India have reported challenges in having patients return for their SVR12 test. Striving for the provision of free HCV diagnostics in the public sector will be a key to reducing patient LTFU.

Core antigen

Need forecast

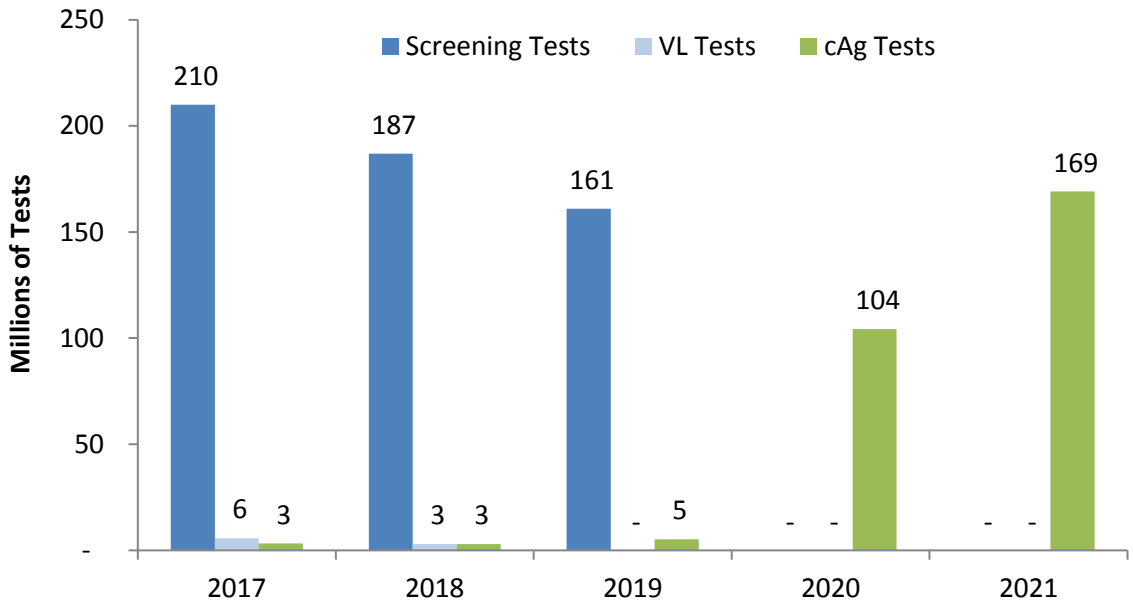
Many stakeholders have been advocating for a shift to core antigen (cAg) testing, which may enable a one-step diagnosis more easily than nucleic acid testing. This strategy could be of particular value for centralized testing settings or in countries focused on elimination and implementing of a test-and-treat strategy for HCV. Clinical data on the feasibility, accuracy and cost of cAg needed to justify a one-step testing strategy is still needed. Given the uncertainty on whether normative guidance (EASL, AASLD or WHO) would recommend this testing approach, a five-year need forecast was modeled for cAg testing based on WHO targets, including a gradual scale-down of on-treatment monitoring tests, and based on the assumption that the algorithm evolves as outlined in Table 4.

To implement this algorithm, the total need for cAg tests over the next five years is projected to be 285 million tests. The need increases significantly in 2020 once the algorithm incorporates core antigen for one-step diagnosis and also factors in the further increase in WHO diagnosis targets.

Table 4: *Assumed algorithm to model need forecast for core antigen testing and total cAg tests needed*

	2017	2018	2019	2020	2021
Assumed cAg algorithm	• RDT/IA screening; • cAg diagnosis; • NAT SVR12	• RDT/IA screening; • cAg diagnosis; • cAg SVR12	• RDT/IA screening; • cAg diagnosis; • cAg SVR12	• cAg diagnosis; • cAg SVR12	• cAg diagnosis; • cAg SVR12
Total of cAg tests needed	**3,247,156**	**2,905,211**	**5,269,993**	**104,225,897**	**169,077,660**

Figure 9: *Annual HCV diagnostic needs 2017-2021, with adoption of cAg testing*



Uptake

Core antigen testing has been recommended in some global treatment guidelines as an option for confirmatory diagnosis only, as evidence is still emerging on its accuracy to confirm cure post-treatment. However, its use is not yet widespread. Very few cAg assays are available commercially and they vary in quality. The Abbott ARCHITECT HCV cAg assay is one of the best options, but is run on a high-throughput ARCHITECT 2000 platform, which is not widely available in LMICs. A few countries noted only 1-2 platforms available nationally. Although experts predict that core antigen pricing could be lower than viral load pricing in the future, more favorable pricing has yet to be seen, making this a key barrier to cAg uptake. Several countries, such as Cameroon and Georgia, are piloting cAg testing to streamline the HCV diagnostic algorithm to one-step diagnosis. In the short-term, countries with existing ARCHITECT platforms and who are using IA-based screening are likely to be the first to use cAg testing. Longer term, widespread adoption of core antigen testing would require competitive cAg pricing for general screening, the development of less expensive and more

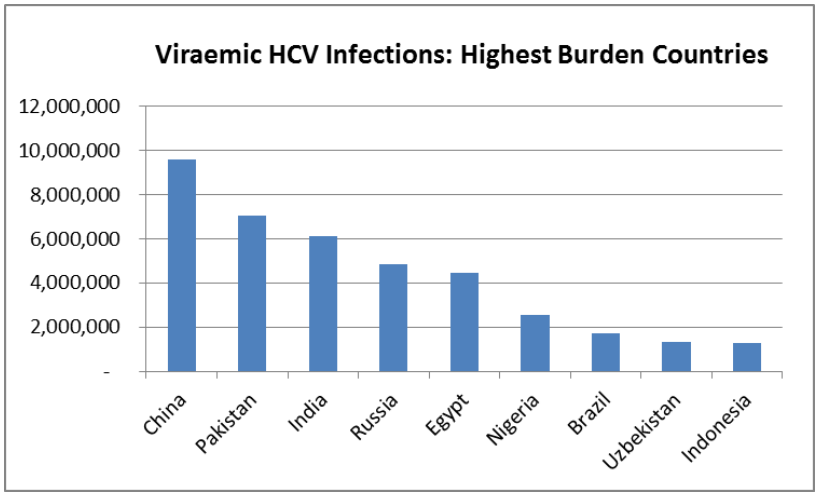
point-of-care platforms[vi]. Besides, the availability of new pan-genotypic, highly-effective DAAs could allow countries to further simplify their testing algorithms if they have not already (e.g. elimination of genotyping, or even SVR12). Adoption of HCV cAg as single step diagnosis might be the next frontier of diagnostic simplification.

Market growth potential

Increasing demand and coverage

A large portion of the HCV-infected population lives in a small number of high prevalence lower-middle income countries, which have high potential to fund increased diagnostic coverage for HCV patients. As China, Pakistan, India, Egypt, Nigeria, Russia, Brazil, Indonesia, and Uzbekistan are estimated to have the highest numbers of viraemic HCV infections,[vii] there is significant potential for these countries to leverage their existing healthcare infrastructure and financing to grow HCV diagnosis and treatment.

The country of Georgia has developed a public-private partnership where Gilead contributes DAAs and the government covers the cost of screening, diagnosis and SVR12 for patients, with technical assistance from the CDC.



Countries in Eastern Europe (Russia, Romania, Turkey), South America (Brazil, Mexico, Argentina), and Asia (Thailand and Malaysia) are also well positioned to make HCV diagnosis and treatment more accessible to their citizens. Although their absolute demand may be lower than higher burden countries, they have strong health systems, networks of hospitals and laboratories, and a relatively high level of health financing. Increasing demand for HCV care and treatment will be most challenging in low-income countries with low to moderate rates of prevalence, where garnering the political will, public commitment, and financing to scale up their programs will be difficult without donor support. However, these countries will benefit from economies of scale in diagnostic pricing achieved by larger markets, which will continue to make diagnosis and treatment more affordable.

Obstacles to growth

Despite the growth potential of the diagnostics market for HCV, the analysis identified six key obstacles to growth that will limit scale-up of HCV programs and the coverage of diagnostics in LMICs if left unaddressed. Additionally, potential interventions to address each obstacle have been recognized.

Funding

Only five out of 29 countries had high levels of funding for HCV, characterized by the presence of a dedicated national HCV budget which was estimated to be sufficient to meet or exceed the WHO 2020 targets. Almost 60% of countries were assessed as having low levels of funding for HCV. Almost all funding was domestic, although some countries are currently benefitting or plan to benefit from Unitaid-funded projects with MSF and FIND, and a few countries have small amounts of funding for HIV/HCV co-infected patients through the Global Fund. Several countries also benefit from DAA donations from originator companies. With domestic funding, treatment has often been prioritized over diagnostics. Pricing for HCV drugs in countries without access to generics remains high, serving to curtail interest from governments in providing widespread free diagnostic services for an illness if they can only afford to treat a few patients. Treatment pricing in generic-accessible countries is coming down rapidly, stimulating the launch of new programs, although the financial ability to scale up is still in question. Some low-income countries are constrained by small health budgets and lack of national health insurance systems, but many lower-middle income countries may have adequate fiscal space to allocate increased funding to diagnostics and treatment for HCV, especially in light of possible cost savings.

There has been a shift towards greater investment in HCV by a number of partners and governments, with a number of countries promising separate budget allocations for HCV funding in the near future. Of CHAI hepatitis program countries, one country has committed over $7 million for treating and diagnosing HCV patients in 2018. Another country expressed a desire to expand their HCV program and bring more public funding to the table and benefits from a robust partner/NGO network that has helped galvanize funding for HCV. A third country is looking to expand national health insurance benefits to include HCV testing and treatment. A fourth country covers testing for free but only for patients exhibiting symptoms, so many NGOs and partners in-country have committed to developing business cases to show the benefits of expanding HCV services and including HCV commodities in the national insurance program. A fifth country has a large number of partners and the government has committed to including HCV as a separate budget item in 2018. While these commitments and plans have not yet translated into measurable funding, they speak to the increasing interest of donors, implementing partners, and governments in investing more in covering HCV services for citizens.

Given the high annual morbidity and mortality from cirrhosis or liver cancer in high-prevalence countries, cost-benefit analyses have been useful in persuading country leadership, such as in Egypt and Pakistan, to dedicate funding for HCV. Building advocacy coalitions between NGOs, civil society organizations, and other stakeholders will be paramount to achieving inclusion of HCV drugs and diagnostics into health insurance systems and essential commodities lists and will also help to destigmatize the population affected by HCV.

	Potential interventions
1	Ensure government HCV budgets and health insurance packages include the costs of screening and diagnosis; ensure screening is widely covered for citizens
2	Seek novel and feasible mechanisms for integrating HCV screening into existing activities to reduce costs and develop public-private partnerships for expanding screening
3	When possible, leverage HIV or TB budgets to strengthen cross-cutting systems that would benefit HCV programs
4	Support investment case processes in countries
5	Consolidate negotiations on a national or regional level to increase purchasing power for HCV diagnostics and to advocate for lower DAA pricing

Platform availability and capacity

Limited laboratory networks are a barrier to scaling up HCV diagnostics and treatment in many high-burden countries. Actual testing capacity on machines is less of a limiting factor; most constraints result from suboptimal device distribution and insufficient numbers of health workers and lab technicians to perform tests. Low levels of human resource capacity in 31% of surveyed countries and moderate capacity in 48% of countries reduce the potential for rapid scale-up of HCV programs in high-burden countries. Integration of HCV testing with HIV/TB on the same NAT platforms can be a solution, although systems challenges must be addressed. Political sensitivities often exist around testing integration and local governments may have concerns about meeting HIV or TB testing demand if existing platforms share testing capacity for HCV patients. Vertical donor funding or in-country program organization often exacerbate disparate disease testing and present hurdles that need to be addressed to incorporate HCV testing into current diagnostic systems and platforms. Strong advocacy about operational benefits of integration and collaboration across national HIV, TB and hepatitis programs is imperative to overcome this barrier. Current pricing structures for diagnostics also favor separate devices for individual diseases. A shift towards a more harmonized procurement and transparent pricing across disease programs would help overcome these barriers. The lack of sample transportation between HCV screening and referral sites is also a factor that limits the demand of HCV testing. More integrated referral networks could help address this problem, but will require greater coordination between programs.

> Punjab State, India, overcame limited public sector diagnostic capacity by outsourcing viral load testing to the private sector. Patients drop off samples at one of the many sample collection sites throughout the state and receive notification to return to their doctor for results.

	Potential interventions
1	Map currently available platforms and projected capacity to identify excess/available capacity for HCV testing use
2	Conduct integration pilots to demonstrate feasibility of integration in both centralized and decentralized networks
3	Map sample transport networks to determine how HCV testing can fit into existing systems
4	Negotiate platform rental, maintenance and pricing agreements to favor platform integration
5	Identify opportunities to leverage HIV, TB or other cross-cutting programs to expand services

Health care worker capacity

Another critical capacity constraint is the limited number of healthcare professionals in LMICs who are knowledgeable on HCV and trained to screen and diagnose the disease. In many countries, screening for HCV has largely been limited to internal medicine or hepatology departments or through donor-funded screening in high-risk groups. HCV is often not included in pre-service training programs for clinicians. As a result, few frontline health care workers are assessing patients for risk of HCV and referring for appropriate diagnosis. Training more healthcare professionals, particularly on screening and diagnosing HCV, and using innovative models, such as Project ECHO[viii], can help build the technical capacity and comfort of health workers to care for HCV patients. Decentralizing HCV testing and treatment to primary care settings can also reduce stigma, enhance active case-finding, and

increase access to services. Integrating HCV care into existing programs targeting populations at high risk of HCV, such as harm reduction services (OST and NSP), can also reach those who are at risk but who may not have access to health care through other channels, at a low additional investment. Many countries also reported chronic shortages of laboratory staff, which impedes their ability to conduct HCV testing even when significant additional testing capacity is theoretically available on existing platforms. Continued efforts to expand the workforce and improve laboratory work flow will be critical to galvanize uptake of diagnostic testing without long backlogs and subsequent patient LTFU.

	Potential interventions
1	Develop training packages on viral hepatitis aimed at health care workers at lower tier facilities, targeting risk factors, signs and symptoms of HCV, and referral for viral load testing
2	Train additional laboratory staff on laboratory testing for HCV
3	Train staff at central lab with high-throughput NAT platforms on patients workflow, optimization of lab resources and laboratory management
4	Evaluate current laboratory workflow practices and identify modifications for more samples to be processed weekly
5	Extend HCV screening, diagnosis and treatment to harm-reduction centers and primary care facilities with trained health care workers
6	Leverage existing patient reminder and tracking systems for HCV to reduce LTFU and ensure linkage to treatment

Inadequate data

Most countries are not tracking the volume or yields of screening or viral load tests at a national level, impeding the development of well-informed country strategies, the proper use of diagnostic commodities, and effective price negotiations with suppliers. Where testing is documented, test volumes are rarely differentiated between RDTs or IAs, and not necessarily delineated between tests done in the public sector, the private sector, or by NGOs/partner organizations. Full screening data is rarely recorded. Without this information, it is harder for countries to plan procurement, identify national targets, and decide where to screen. Furthermore, accurate screening data demonstrating the burden of disease would be useful to advocate for expanding programs and increasing funding. With fragmented procurement and weak data, governments cannot monitor or assess the effectiveness of current screening strategies or resource allocation. Whilst viral load test volume data is more frequently available than screening, few programs are delineating between confirmatory, monitoring, and SVR tests. This makes it difficult for countries to measure program performance along the cascade of care and diagnose challenges around lab turnaround time and patient retention.

	Potential interventions
1	Provide screening registers at all key entry points in health facilities and collect and analyze the data regularly through national M&E systems
2	Adapt existing reporting systems to include HCV, with data reported at all critical steps of the care continuum
3	Synchronize screening and VL databases to report cascade of care numbers on national dashboards
4	Adapt laboratory information management systems to include HCV and provide information on the number of confirmatory, monitoring and SVR12 tests, as well as turnaround time data
5	Integrate HCV into national surveillance systems to monitor the epidemic and adapt programs

Diagnostic strategy

Few countries have concrete diagnostic targets or scale-up plans for HCV that operationalize the WHO targets of diagnosing 30% of HCV-infected patients by 2020 and 90% by 2030. While almost 60% of analyzed high-burden or high-prevalence countries had national strategic plans for viral hepatitis, almost none had defined diagnostic goals for the near future. Identifying and setting national targets is crucial to fueling the process for advocating for HCV funding, planning for procurement, developing appropriate service delivery models tailored to the national context, and locating sources of technical support and partnership.

	Potential interventions
1	Ensure strategic and operational plans and budgets include targets for screening and diagnosis, including retention rates throughout the cascade
2	Develop specific operational plans that map how HCV fits into the overall country's laboratory strategic goals
3	Provide decision support models to countries that evaluate the optimal mix of diagnosis and treatment commodities to procure
4	Evaluate different diagnostic service delivery models for different target populations
5	Develop and implement active screening strategies

Patient awareness

Limited awareness of HCV was noted as a key challenge by countries included in the analysis. Embarking on education and awareness programs in-country will improve the general public's knowledge and reduce stigma associated with HCV, leading to increased demand for testing and improved case-finding.

	Potential interventions
1	Train local NGOs to provide disease awareness education to local communities and high-risk groups
2	Support targeted information, education, and communication efforts to expand population knowledge about HCV
3	Implement advocacy and campaigning efforts to reduce stigma about HCV

Conclusion

While these obstacles do represent barriers to growth for nascent HCV programs, countries, partners, and suppliers can work together to increase investment in HCV diagnosis and treatment and implement these programmatic recommendations to improve the diagnostic system in LMICs. Collaboration, committed financing, and increased support at the country level will significantly advance the global fight against HCV and reduce unnecessary morbidity and mortality for patients all over the world.

Appendices

Appendix A: List of countries in scope for need and demand forecast

1. Algeria*
2. Argentina
3. Brazil
4. Cambodia*
5. Cameroon*
6. China
7. Colombia
8. Egypt*
9. Ethiopia*¤
10. Georgia*
11. Ghana*
12. India*¤
13. Indonesia*¤
14. Kazakhstan
15. Malaysia
16. Mexico
17. Mongolia*
18. Morocco*
19. Myanmar*¤
20. Nigeria*¤
21. Pakistan*
22. Philippines*
23. Romania
24. Russia
25. South Africa*
26. Syria*
27. Thailand
28. Turkey
29. Uzbekistan*

* Country that can access generic pricing for HCV treatment
¤ CHAI hepatitis program country

Endnotes

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[ii] Global Health Estimates 2015: Deaths by Cause, Age, Sex, by Country and by Region, 2000-2015. Geneva, World Health Organization; 2016

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[vi] High-priority target product profile for hepatitis C diagnosis in decentralized settings: Report of a consensus meeting, FIND; 2016

[vii] Polaris Observatory Data

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