CLINTON HEALTH ACCESS INITIATIVE

HCV Market Intelligence Report

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Includes First-Ever Preliminary Insights on Harm Reduction Commodities Market

Photo credit: Olivier Mugwiza

Disclaimer: The data sources primarily used for analysis in the report include the India Import Export data, CHAI country teams, Ministry of Health counterparts, and stakeholder (NGO and civil society partners) conversations. CHAI has taken precautions to verify the information shared on the report. However, the analysis in the report is not exhaustive, and the responsibility for the interpretation and use of the material lies with the reader. The mention of specific companies or supplier products does not imply that CHAI is endorsing or recommending them.

Contents

CHAI Hepatitis Market Reports

CHAI routinely collects and publishes market intelligence highlighting trends in the hepatitis C virus (HCV) and hepatitis B virus (HBV) markets. These reports provide updates on diagnostic and treatment markets including the supplier landscape, volume, and pricing trends mainly across LMICs. This report intends to build market visibility and transparency by:

- improving visibility into high-quality diagnostic and treatment products at affordable prices, particularly for stakeholders in high-burden LMICs
- highlighting key drivers and barriers related to scaling diagnostic and treatment commodities as countries commit to viral hepatitis programming
- providing an outlook on emerging market trends and innovations that could improve HCV care for patients

In July 2022, CHAI published the Hepatitis C Market Memo, a brief covering the latest trends in the HCV diagnostics and treatment markets from January 2021 to April 2022. CHAI published its first and second editions of the HCV Market Intelligence Report in May 2020 and August 2021 covering market updates for 2019 and 2020, respectively. CHAI also published the Hepatitis B Market Report 2022 which expands upon CHAI's preliminary HBV market insights first published in August 2021 and provides additional updates.

It is worth noting that this report focuses primarily on high-burden LMICs across Asia and Africa and high-burden countries in Latin America. Products highlighted in the report have World Health Organization prequalification (WHO PQ) or are Expert panel reviewed (ERP) products as they meet quality assurance standards and have been declared bioequivalent to the innovator products. While CHAI supports the use of products approved by stringent regulatory authorities (SRA) such as the US Food and Drug Administration (FDA) or European Medical Agencies (EMA), and WHO PQ, pricing information in the report also accounts for locally approved products which have not been assessed against global quality standards but meet local quality standards, as these products are used in several LMICs.

Acknowledgments

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- Global partners who contributed invaluable insights to inform the harm reduction analyses including Harm Reduction International (HRI), International Network of People Who Use Drugs (INPUD), Network of Asian People who use Drugs (NAPUD), Indian Drug users Forum (IDUF), Asian Harm Reduction Network (AHRN), Butabika National Referral Hospital, Infectious Diseases Institute, Uganda, The AIDS Support Organization (TASO), and Uganda Harm Reduction Networks.
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Acronyms

Ag	Antigen
ASLM	African Society for Laboratory Medicine
cAg	Core Antigen
CE	Conformitè Europëenne
CGHE	Coalition for Global Hepatitis Elimination
CHAI	Clinton Health Access Initiative
CPT	Carriage Paid To
DAA	Direct Acting Antivirals
DAP	Delivery At Place
DBS	Dried Blood Spot
DCV	Daclatasvir
EMA	European Medicines Agency
EOI	Experssions of Interest
ERP	Expert Review Panel
ERPD	Expert Review Panel for Diagnostics
EXW	Ex-Works Price
FCA	Free Carrier
FDA	U.S. Food and Drug Administration
FDC	Fixed Dose Combination
FOB	Freight on Board
G/P	Glecaprevir/Pibrentasvir
GAP	Global Access Program
GFATM	The Global Fund to Fight AIDS, Tuberculosis and Malaria
HBV	Hepatitis B Virus
HCV	Hepatitis C Virus
HCVST	Hepatitis C Virus Self-Testing
HDSS	High Dead-Space Syringes
HIC	High Income Countries
HRI	Harm Reduction International
INCB	International Narcotics Control Board
IVD	In-vitro Diagnostics
LAB	Long-Acting Buprenorphine
LAC	Latin America and the Caribbean
LDSS	Low Dead-Space Syringes
LFA	Lateral Flow Assay
LMICs	Low- and Middle-Income Countries
MMT	Methadone Maintenance Therapy
MOUD	Medications for Opioid Use Disorder
MPP	Medicines Patent Pool
NA	Not Available
NSEP	Needles and Syringe Exchange Program
NSPs	Needles and Syringes Programs
OAMT	Opioid Agonist Maintenance Therapy
OTC	Over-The-Counter
PAHO	Pan American Health Organization
PEPFAR	US President's Emergency Plan for AIDS Relief
POC	Point-of-Care
PQ	Prequalification
PQ'd	Prequalified
QA	Quality Assured
RDT	Rapid Diagnostic Test
RUO	Research Use Only
SOF	Sofosbuvir
SOF + DCV	Sofosbuvir and Daclatasvir used in combination
SOF/DCV	Sofosbuvir/Daclatasvir
SOF/DCV FDC	Sofosbuvir/Daclatasvir Fixed Dose Combination
SOF/LDV	Sofosbuvir/Ledipasvir
SOF/VEL	Sofosbuvir/Velpatasvir
SRA	Stringent Regulatory Authorities
SSPs	Syringe Service Programs
TE	Transient Elastography
UNDP	United Nations Development Programme
UNODC	United Nations Office on Drug and Crime
US$	US Dollars
USD	US Dollars
VL	Viral Load
WHA	World Hepatitis Alliance
WHO	World Health Organization
WHO EML	WHO Model List of Essential Medicines

Market Report At a Glance

Overview of HCV Diagnostic Market

There is an evolving and expanding market for quality-assured, affordable HCV diagnostic products

- Several rapid diagnostic tests (RDTs), laboratory-based immunoassays, and viral load (VL) assays have maintained WHO PQ, and additional products have been added to PQ including two RDTs and one HCV VL intended for use on point-of-care (POC) platforms
- Three additional HCV diagnostic products are under assessment to achieve WHO PQ
- RDTs are widely procured for decentralized, POC screening in LMICs with procurement of RDTs up to 24 times higher than laboratory-based immunoassays

Major suppliers offer Global Access Program (GAP) pricing agreements for HCV VL assays

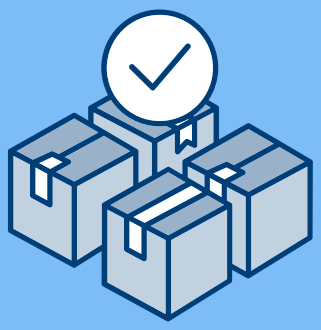
- GAP agreements have been negotiated by CHAI, with support from partners, for public sector buyers to access essential diagnostics in LMICs based on various eligibility criteria
- Pricing agreements vary based on terms, conditions, volumes, platforms, and device placements resulting in variations in final landing costs across countries
- Despite GAP agreements, multiple cost components add to the final cost paid by countries highlighting the need to improve price transparency and enable programs to effectively negotiate terms and conditions

Emerging HCV diagnostic innovations can continue to simplify HCV care

- Innovative diagnostic technologies such as near POC VL testing, HCV self-testing, multi-disease RDTs, dried blood spot sampling, and HCV core antigen testing can simplify HCV testing
- These approaches save time and generate cost savings making testing more affordable, convenient, and accessible
- Technologies such as self-testing can expand access in settings beyond traditional healthcare structures
- Several HCV self-test products are in advanced stages, with manufacturers considering development

Overview of HCV Treatment Market

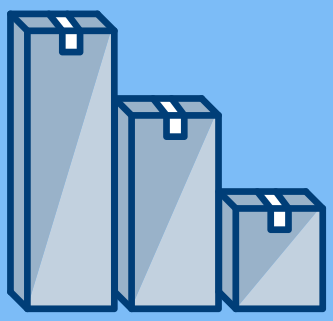
Although some suppliers have not retained WHO PQ status, the supplier landscape for pan-genotypic direct acting antivirals (DAAs) remains robust



- Maintaining WHO PQ status is costly and some suppliers have chosen not to retain it due to low returns on sales
- Lack of program scale-up in HCV and low demand visibility in LMICs pose challenges for market stability

1.31 million patients have received treatment with generic sofosbuvir (SOF) and daclatasvir (DCV) since 2016

- Medicines Patent Pool (MPP) estimates 3.93 million packs of generic DCV were supplied from 2016 to March 2023; this translates to about 1.31 million people receiving treatment on SOF paired with DCV



DAA demand has tapered over the last few years, highlighting the need for resource mobilization and political commitment

- Except for India and Pakistan, procurement levels are lower than pre COVID-19 pandemic levels
- Buyers are concentrated to a few countries that are contributing to the majority of procurement
- Irregular procurement patterns and low demand in most LMICs threaten supply security and make demand-based forecasting challenging

Breakthrough ceiling price agreement has made DAAs more affordable than ever

- CHAI and The Hepatitis Fund signed agreements with leading generic manufacturers, Viatris and Hetero, to establish a ceiling price for a 12-week course of treatment at US$60 Ex Works (EXW) to public programs (read details here)
- This represents a price reduction of over 90 percent since 2015 and a 20 percent reduction from the Global Fund negotiated reference price as in May 2023

Need for a sustainable demand for DAAs

- Governments, international stakeholders, and donors need to work together to develop and foster a long-term, sustainable market for HCV commodities
- Stewardship at the global, regional, and country levels is required to develop plans, leverage partnerships, and allocate resources effectively to drive the uptake of DAAs and implement high-impact interventions

Preliminary Insights into Harm Reduction Market

Need for market transparency and increased resource commitment to harm reduction to effectively implement HCV prevention strategies

- An estimated 15.2 percent of people who inject drugs have HIV infection, 38.8 percent have HCV infection, and 8.4 percent have HBV infection. Globally, 43 percent of new HCV infections are attributed to injection drug use with regional variations
- Implementing comprehensive harm reduction programs among people who inject drugs that include prevention interventions, alongside diagnosis and treatment for hepatitis, is key to addressing the health needs of these communities and reaching global hepatitis elimination goals
- The current market for prevention commodities used in opioid agonist maintenance therapy (methadone and buprenorphine), overdose reversal (naloxone), and needles and syringe programs within LMICs remains nascent and opaque
- The market for prevention commodities faces three main challenges: (1) the absence of public programming, (2) insufficient financial resources, and (3) lack of market transparency
- This report aims to serve as a market intelligence resource for prevention commodities

Strategies for Sustainable and Affordable Access to HCV Diagnostics and Treatment in LMICs

Optimizing and sustaining the HCV diagnostic and treatment markets will require joint efforts between policy makers, country governments, donors, and suppliers to ensure access to high-quality, affordable drugs and diagnostics and to increase uptake of HCV testing and treatment commodities across LMICs. To achieve this goal, the following recommendations are proposed:

Commit to HCV Management in Public Healthcare Systems

Prioritize diagnosis and treatment of HCV by developing national plans, leveraging partnerships, securing commitments, and allocating resources to implement highly impactful viral hepatitis programs. Country plans should include a community mobilization strategy to ensure heightened awareness and increased access to services, consequently fueling demand.

Ensure Patient Savings and Access to Global Access Pricing for HCV Commodities

Leverage negotiated global access pricing for diagnostic and treatment commodities to ensure savings are realized and enable enhanced value for money procurement. Additionally, stakeholders should aim to improve price transparency and mitigate the risk of in-country cost markups to lower out-of-pocket expenses and ensure that the savings due to procurement of commodities via global access pricing agreements are passed on to patients. Programs could take the suggested steps to leverage diagnostic and treatment global access price agreements:

- **Amplify communications related to pricing agreements** to all stakeholders, particularly procurement divisions
- **Enhance price transparency and challenge in-country markups** by seeking clarity on components of additional costs, finding opportunities to streamline, and encourage distributors to provide greater transparency
- **Accelerate scale-up of hepatitis services** and drive demand for services to sustain the accessibility and affordability of hepatitis drugs and diagnostics, overall market health, and to achieve elimination

Improve Procurement Practices

Improve procurement practices in LMICs to ensure that there is a sustainable and consistent demand and supply for HCV diagnostics and treatment commodities. This could be done by establishing long-term contracts with suppliers or implementing a centralized procurement system.

Optimize Existing Resources through Integration

Identify high-value investments that can improve the delivery of HCV testing, treatment, and programs in LMICs. This could be done through an integrated program strategy that provides all services in a coordinated manner and establishes partnerships between diagnostic facilities and treatment providers. This approach can improve patient coverage, increase demand for HCV services, and lead to better patient outcomes through early diagnosis and treatment, improved adherence, and reduced healthcare costs.

Develop Market Projections

Develop accurate and evidence-based demand forecasts of HCV commodities to quantify market size on a global scale, increase market visibility and inform production planning.

Establish Public-Private Partnerships

Leverage partnerships between government and private sector, including private healthcare providers and laboratory networks, to improve access to services.

Introduction

Significant progress has been made in recent years towards the global agenda of eliminating HCV. Access to testing has improved tremendously with the introduction of affordable RDTs and the increasing availability of affordable and effective DAAs from generics making HCV treatment more accessible in LMICs. Despite this, in 2019 an estimated 58 million people were still living with chronic HCV infection globally, accounting for around 290,000 deaths annually. HCV continues to remain a major health challenge, with over 1.5 million new infections each year. In 2019, it is estimated that only 21 percent (around 15.2 million people) were aware of their status and of those that were diagnosed, only 16 percent (9.4 million people) were treated with DAAs by the end of 2019.[1] This highlights the urgent need to strengthen testing and treatment programs for HCV to reach the millions of undiagnosed and untreated people living with HCV.

WHO's Global Health Sector Strategies on Viral Hepatitis aims to reduce new hepatitis infections by 90 percent and deaths by 65 percent, with the goal of eliminating viral hepatitis as a public health by 2030. To achieve this elimination goal, WHO has set coverage targets to diagnose 90 percent and cure 80 percent of people living with HCV by 2030.[2]

There are only 14 countries on track towards achieving impact and program targets by 2030, and another 12 countries by 2030-2050. However, there are still 91 countries that are not on track for achieving impact or programmatic targets by 2050,[3] highlighting that significant progress is yet to be made to achieve HCV elimination. Of these, around 70 percent are classified as LMIC. Progress towards sustainable public programming for HCV is hampered by key factors including inadequate healthcare infrastructure in resource-limited settings and lack of resources from national governments to prioritize viral hepatitis as a public health concern. A gap in financing poses a major barrier for HCV, resulting in limited implementation of prevention, testing, and treatment programs. Viral hepatitis remains an underfunded public health area with minimal centrally earmarked domestic budgets and a limited funding pool from donors. Targeted funding from The Global Fund to Fight AIDS, Tuberculosis and Malaria (GFATM) is supporting catalytic services for some vulnerable populations and an initial round of funding from The Hepatitis Fund has supported complementary funding for countries well positioned to scale hepatitis programming. However, this funding is insufficient to match efforts needed towards global elimination targets.

The diagnostics section of the report provides key insights into the supply landscape, pricing, and volume trends of focal HCV diagnostic commodities including RDTs, laboratory-based immunoassays, viral load technologies, and liver function tests. In addition, the report covers and expands upon emerging trends in HCV diagnostic innovations including HCV self-testing, multi-disease RDTs, DBS technologies, and HCV core antigen.

The treatment section of the report provides insights into the latest DAA market trends including pricing and volume trends and market gaps. The section also highlights progress in newer areas such as the pediatric treatment market.

The new section on HCV prevention covers preliminary insights into harm reduction as a tool for HCV prevention and management, with a focus on buprenorphine and methadone (opioid agonist maintenance therapy commodities), which are recommended by the WHO's consolidated guidelines on HIV, viral hepatitis, and STI prevention, diagnosis, treatment, and care for key populations. The section also touches upon naloxone, which is used for overdose reversal, and needles and syringes that are distributed as a part of harm reduction programs. CHAI has compiled and analyzed available data and market insights to showcase broad trends and the landscape of these harm reduction commodities.

To achieve HCV elimination, action must be taken now. This report aims to support the global hepatitis community by serving as a resource for various stakeholders, including country governments and health programs, donors and funders, manufacturers and distributors, and other civil society organizations. Sharing market intelligence has enabled countries to advocate and secure better pricing for diagnostics and drugs. With political will, modest financing, and affordable commodities, hepatitis programs can be more accessible, paving a way towards elimination. As market access for HCV drugs and diagnostics improves, this report serves as a call to action for the global community to prioritize the elimination of HCV as a public health threat.

Guidelines Update

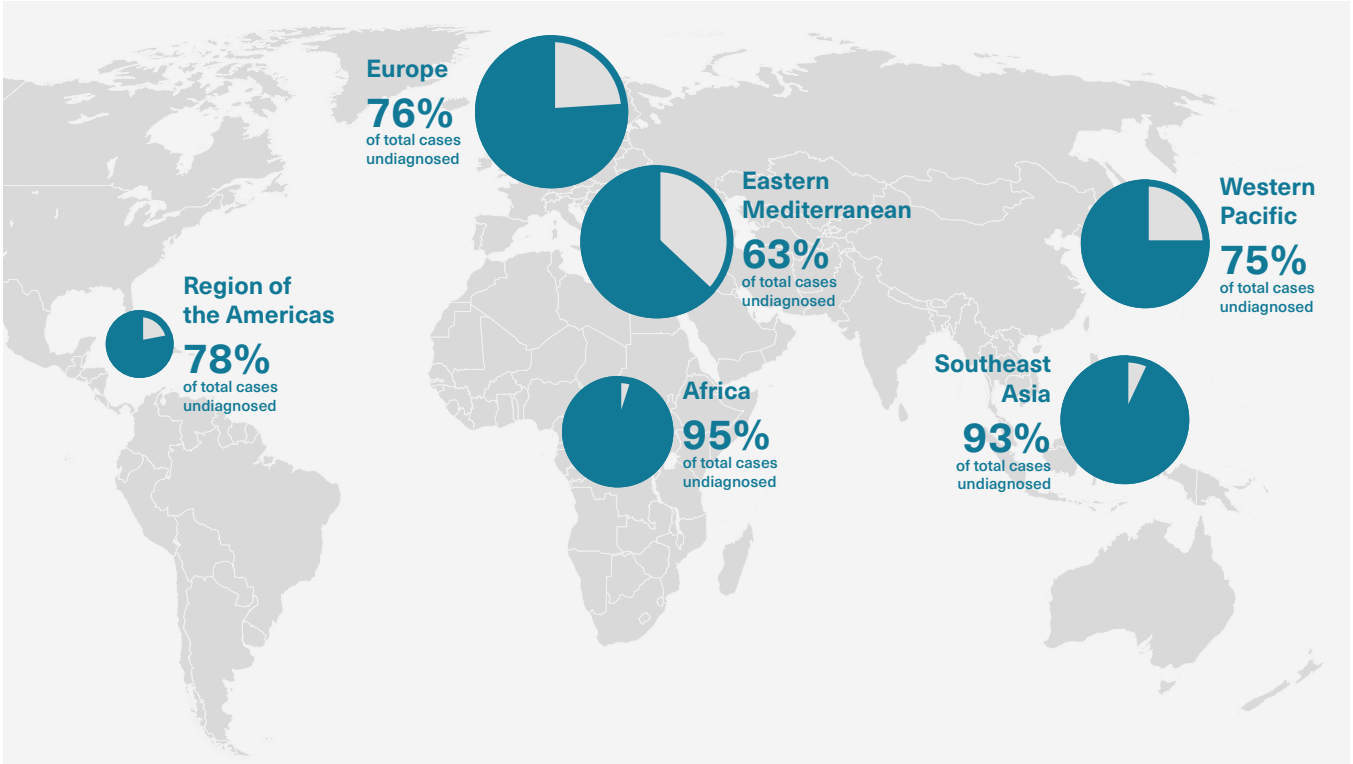
In 2022, WHO released the *Updated recommendations on treatment of adolescents and children with chronic HCV infection, and HCV simplified service delivery and diagnostics*.[4] The latest algorithm can be found in Appendix 1.

1 WHO. Hepatitis C Factsheet. Updated July 2023; WHO is expected to release latest data in October 2023
2 WHO. Global health sector strategies on, respectively, HIV, viral hepatitis and sexually transmitted infections for the period 2022-2030. (July 2022).
3 CDA Foundation; Countries/Territories Achieving Relative or Absolute Impact and Programmatic Targets for HCV. Accessed 14 December 2023.
4 WHO. Updated recommendations on treatment of adolescents and children with chronic HCV infection, and HCV simplified service delivery and diagnostics. Published 17 October 2022.

Diagnostics

Globally, the Eastern Mediterranean and Europe regions have the highest burden of HCV with 12 million chronically infected, followed by Southeast Asia and the Western Pacific (10 million people), Africa (nine million), and Latin America with five million chronically infected people[5]. Gaps in diagnosis continue to persist, highlighting the urgency for stakeholders to invest now in effective screening programs with high-quality and affordable diagnostics to accelerate progress towards HCV elimination. Globally, 79 percent of the total burden remains undiagnosed with LMIC-dominant regions having the greatest gaps. An estimated 9.12 million (76 percent) remain undiagnosed in Europe, 7.56 million (63 percent) in the Eastern Mediterranean, 7.5 million (75 percent) in the Western Pacific, 9.3 million (93 percent) in Southeast Asia, 8.55 million (95 percent) in Africa, and 3.9 million (78 percent) in the Region of the Americas (see Exhibit 1).

EXHIBIT 1 Percent of HCV Individuals Undiagnosed at the End of 2019



Source: WHO 2021 Report on Accelerating access to hepatitis C diagnostics and treatment. Link.

5 WHO. Hepatitis C Factsheet. Updated July 2023.

Supply Landscape

Quality-Assured Rapid Diagnostic Tests[6] and Laboratory-Based Immunoassays

RDTs offer a convenient and accessible method to screen populations and can enable same day test-and-treat models of care for chronic hepatitis C.

Based on WHO guidance, the first step in the testing and treatment algorithm (see Appendix 1) is to identify exposure to HCV through the use of a screening test to detect HCV antibodies. This step is commonly done through either a non-laboratory based RDT or a laboratory-based immunoassay. Within the market there are several quality assured options which have WHO PQ status and/or have been approved by other SRAs, enabling countries to use donor funding to procure.

The list of WHO PQ'd screening products for RDTs has seen the addition of two new assays, while the list of laboratory-based immunoassay has remained the same since 2022 (see Exhibit 2). Furthermore, there are additional screening products which meet other global quality standards as highlighted by GFATM's quality assurance policy[7] (see Exhibit 3) that countries can procure. The options for HCV RDTs with WHO PQ may continue growing as several manufacturers have products under assessment[8], including newer versions like the INSTI HCV Antibody test (bioLytical Laboratories, Inc.), which has a CE mark and offers result availability in just one minute.

EXHIBIT 2 WHO Prequalified HCV RDTs and HCV Laboratory-based Immunoassays

HCV ANTIBODY RDTS			
Product Name	**Manufacturer**	**Sample Type**	**Time to Result**
Bioline HCV	Abbott	plasma, serum, whole blood	5-20 minutes
STANDARD Q HCV Ab Test	SD Biosensor, Inc.	plasma, serum, whole blood	10 minutes
Rapid Anti-HCV Test	InTec PRODUCTS, INC	plasma, serum, whole blood	15 - 20 minutes
OraQuick HCV Rapid Antibody Test Kit	OraSure Technologies, Inc.	plasma, serum, whole blood, oral fluid	20 minutes
First Response HCV Card Test	Premier Medical Corporation	plasma, serum, whole blood	15 – 20 minutes
Hepatitis C Virus Rapid Test Device	ABON Biopharm	plasma, serum, whole blood	10 minutes

HCV ANTIBODY LABORATORY-BASED IMMUNOASSAYS				
Product Name	**Manufacturer**	**Sample Type**	**Time to Result**	**Instrumentation**
Monolisa HCV Ag-Ab ULTRA V2	Bio-Rad	plasma, serum	NA	Microplate Reader (Spectrophotometer)
INNOTEST HCV Ab IV*	Fujirebio Europe NV	plasma, serum	180 minutes	Microplate Reader (Spectrophotometer)
INNO-LIA HCV Score*	Fujirebio Europe NV	plasma, serum	NA	Auto-LIA (Immunoassay Analyzer)

Source: WHO List of Prequalified In Vitro Diagnostic Products
**Both assays can be used to identify the detection of antibodies to human hepatitis C virus in serum or plasma, however the INNO-LIA HCV Score is intended for use as a supplementary test for those found to be reactive using anti-HCV screening*

6 "Rapid diagnostic tests" (RDTs) refer to diagnostics categorized by performance characteristics (short performance time and availability of results to enable management at the point of care), rather than the specific test platform. For the purposes of this report, the term "RDT" refers to immunochromatographic assays, which may include vertical flow and lateral flow assays (LFA)

7 Based on the GFATM Quality Assurance Policy for Diagnostic Products, grant funds can be used to procure select HCV diagnostic products which meet base global quality standards. These criteria include (1) products that have been WHO prequalified, (2) diagnostic products that have been authorized by regulatory authorities of the founding members of the Global Harmonization Task Force (GHTF) (EU, US, Canada, Australia, and Japan), or (3) products that have been determined acceptable for procurement by GFATM based on the advice of the WHO Expert Review Panel (ERP).

8 WHO. HCV In vitro diagnostics (IVDs) Under Assessment. Accessed 17 September 2023. Link.

EXHIBIT 3 Additional Quality-Assured HCV Antibody Products (Approved for Procurement by GFATM)

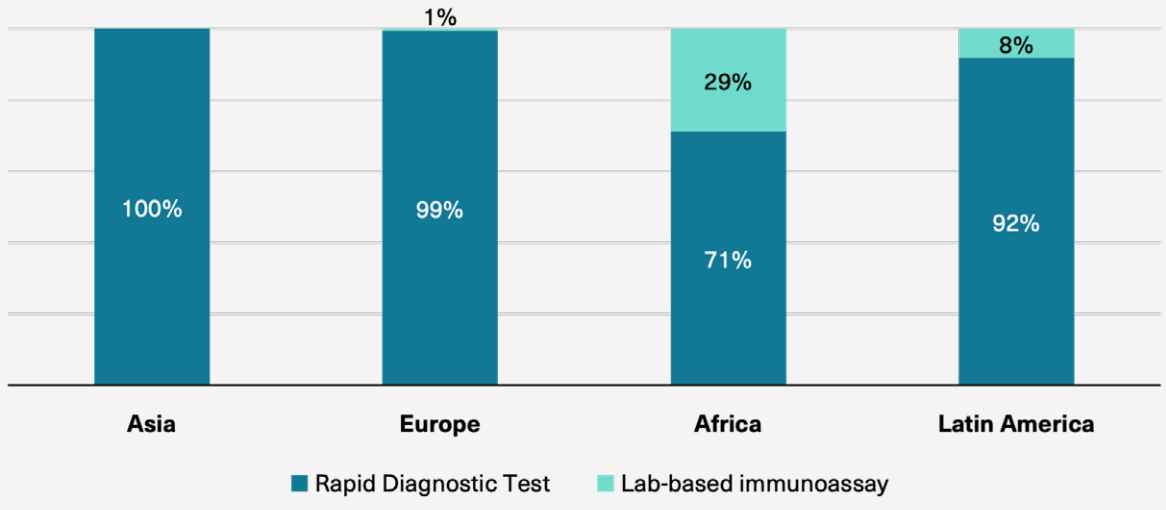
HCV ANTIBODY RDTS			
Product Name	**Manufacturer**	**Sample Type**	**Time to Result**
INSTI HCV Antibody Test	BioLytical	plasma, serum, whole blood	1 minute

HCV ANTIBODY LABORATORY-BASED IMMUNOASSAYS				
Product Name	**Manufacturer**	**Sample Type**	**Time to Result**	**Instrumentation**
Murex anti-HCV Version 4	DiaSorin	plasma, serum	120 minutes	Microplate Reader (Spectrophotometer)
Elecsys Anti-HCV II	Roche	plasma, serum	18 minutes	cobas e 411 analyzer, cobas e 601 / cobas e 602 modules, cobas e 402 and cobas e 801 analytical units (Immunoassay Analyzer)

Source: GFATM List of HIV Diagnostic Test Kits and Equipment Classified According to the Quality Assurance Policy

Although there is limited market visibility into the non-donor funded market in LMICs, procurement data from donors such as the GFATM suggests a preference for RDTs compared to laboratory-based immunoassays (Exhibit 4). RDTs are more accessible and can be easily adopted for decentralized models of care in LMICs, expanding coverage of their national screening programs. Based on publicly available data from country procurement reports, procurement of RDTs was up to 24 times more than laboratory-based immunoassays from 2016 to 2022.

EXHIBIT 4 HCV screening assay type procured through the Global Fund and publicly reported, by region (2016-2022)



Source: GFATM Price Reference Report (non-exhaustive data from a sample of 43 countries which was available through publicly available procurement reports)

Increased uptake in the use of RDTs may be related to several considerations. RDTs offer a more convenient and accessible method to screen populations and enable potential same day test-and-treat models of care for chronic HCV. In comparison, laboratory-based immunoassays require formal laboratory infrastructure, instrumentation, and training, which are obstacles for many resource-limited settings (see Exhibit 5).

EXHIBIT 5 Programmatic and Cost Considerations Between RDTs and Laboratory-Based Immunoassays

	Rapid Diagnostic Tests	Laboratory-Based Immunoassays
Sample type	Whole blood, serum, plasma, and/or oral fluid	Serum, plasma
Access to testing	Sample collection and testing can be decentralized to community and primary health care settings	Sample collection can be performed at sites and facilities offering phlebotomy services and connected to sample transport systems, while testing requires technical training, laboratory equipment, laboratory infrastructure, and cold chain
Logistic requirements	Requires minimal to no technical training, laboratory infrastructure, equipment, sample transport system, and cold chain; sample types require minimal preparation for testing	Requires settings to have well established sample collection, storage, and transportation networks, in addition to technical training, laboratory equipment (e.g., a microplate reader or automated immunoassay analyzer), and infrastructure; sample types require preparation for both transport and testing
Price (US$)	US$0.80 – US$1.10 per test (EXW)[9]	Unit cost average US$0.65 – US$5.17[10], and may include additional costs such as phlebotomy and cold chain
Time to result and linkage to confirmation	Results are available in 20 minutes or less. Potential to design clinic-based reflex algorithm and workflow whereby an additional sample can be collected for VL at time of positive result	Varies dependent on sample transport, laboratory processing, and result return and reporting. Offers opportunity for laboratory-based reflex testing, whereby a single sample can be collected to conduct both the HCV antibody test as well as the viral load test. Requires reliable result return system and client notification

The government of **Rwanda** has achieved universal HCV screening by leveraging WHO's simplified approach to HCV programming and wide use of HCV RDTs for screening. The country has successfully been able to scale up and decentralize HCV services to peripheral level facilities making HCV screening, diagnosis, and treatment widely available to all. Since the program started in 2014, **the country has been able to screen seven million people and initiated over 60,000 patients on treatment.**

Quality-Assured Viral Load Assays

Near point-of-care (POC) HCV VL technology presents an opportunity to improve testing access for countries by decentralizing testing to all levels of a healthcare system.

According to the WHO testing and treatment algorithm, all individuals who are HCV antibody positive should receive supplementary HCV VL testing to determine if they are chronically infected with the disease and require further liver staging assessment, treatment, and care. Confirmatory VL testing can be done on both centralized laboratory-based devices (using serum or plasma samples) and near POC devices (using serum, plasma, and capillary or venous whole blood samples). There are five HCV VL assays across three suppliers which have WHO PQ status (see Exhibit 6). Based on the GFATM's quality assurance policy for diagnostics, additional quality assured HCV VL assays which are not WHO PQ'd can be procured through grant funds (see Exhibit 7).

9 GFATM PPM Reference Pricing RDTs. Updated September 2023.
10 Estimates based on GFATM's Price Reference Report

EXHIBIT 6 WHO PQ'd HCV VL Assays (Centralized and Near POC)

Product Name	Manufacturer	Platform	Sample Type	Time to Result	Price Per Test (US$)*	Incoterm**
CENTRALIZED LABORATORY-BASED PLATFORMS						
Abbott RealTime HCV	Abbott	m2000 System (m200sp and m2000rt)	serum, plasma, dried blood spot (DBS)	96 results/8 hours	9.60 – 17.05	FCA
Alinity m HCV		Alinity m Instrument	serum, plasma	115 minutes	9.60 – 17.05	FCA
cobas HCV	Roche	cobas 4800	serum, plasma	384 results/8 hours	7.90	CPT
		cobas 5800	serum, plasma	144 results/8 hours		
		cobas 6800	serum, plasma	384 results/8 hours		
		cobas 8800	serum, plasma	1,056 results/8 hours		
NEAR POINT-OF-CARE PLATFORMS						
Xpert HCV VL Fingerstick	Cepheid	Cepheid GeneXpert Instruments	capillary and venous whole blood	75 minutes	14.90	EXW
Xpert HCV Viral Load		Cepheid GeneXpert Instruments	serum, plasma	105 minutes		

**African Society for Laboratory Medicine (ASLM) Molecular Supplier Pricing Database updated in May 2023 (see here); these prices reflect reagents and consumables only*
***International commercial term defines who is responsible (seller or buyer) for paying of various activities throughout the trade process including loading charges, delivery, export duty, taxes, custom clearance, etc.*

EXHIBIT 7 Additional Quality-Assured HCV VL Products (Approved for Procurement by GFATM)

Product Name	Manufacturer	Platform	Sample Type	Time to Result	Regulatory Status	Price Per Test (US$)	Incoterm
CENTRALIZED LABORATORY-BASED PLATFORMS							
Aptima HCV Quant Dx Assay	Hologic	Panther System	serum, plasma	2hr 40min to 1st 5 results, followed by 5 results/ 5 mins	CE Mark and US FDA	11.28*	DAP
AccuPower HCV Quantitative RT-PCR Kit	Bioneer	ExitStation Universal Molecular Diagnostic System	serum, plasma	NA	CE Mark	NA	NA
artus HCV RG RT-PCR Kit	Qiagen	Rotor-Gene Q or Rotor-Gene Instrument	plasma	NA	CE Mark	16.00**	FCA

**African Society for Laboratory Medicine (ASLM) Molecular Supplier Pricing Database updated in May 2023 (see here)*
*** Price reported by manufacturer; Total cost reflects both extraction and detection steps*

Near Point-of-Care Viral Load Technology

Innovative technologies such as near POC testing can improve linkages to VL testing and enable same day test-and-treat models, reducing the risk of patients being lost to follow up from screening to diagnosis. POC VL testing can improve access to HCV testing by decentralizing services to all levels and facilities within a national healthcare system. Furthermore, evidence has demonstrated a growing opportunity to leverage existing multi-disease POC platforms to integrate HCV testing and utilize unused and available testing capacity across several disease areas, including HIV, tuberculosis, and COVID-19. Depending on country context and other factors, near POC platforms may offer several programmatic benefits (see Exhibit 8).

EXHIBIT 8 Considerations for Near POC Platforms and Centralized Laboratory-Based Platforms

	Near Point-of-Care Platforms	Centralized Laboratory-Based Platforms
Sample type	Venous or capillary whole blood, serum, plasma	Serum, plasma
Logistic requirements	Lower throughput machines which require some formal laboratory infrastructure with controlled conditions (temperature, humidity, dust), require less training for laboratory staff Sample collection via fingerstick possible, or may require phlebotomy and sample processing, depending on assay used	High throughput machines which require formal laboratory infrastructure and laboratory trained staff All assays require serum or plasma samples, which require phlebotomy, sample processing, and potentially storage and stability for transport
Access to testing	Offer an opportunity to perform on-site testing nearby where a patient accesses care (district hospital or high-volume health center), facilitating same day test-and-treat	Samples require cold-chain transport and well-established sample storage, and transportation networks
Assay run time	~1-2 hours	~6-8 hours
Test Turnaround Time	Hours - Days	Days - Weeks

The market for quality assured HCV POC VL technology is smaller than for screening. Most recently, Cepheid's Xpert HCV VL fingerstick assay received WHO PQ status in 2022. The market is dominated by one major supplier of POC HCV VL technology (refer to Exhibit 6) with a large global footprint in at least 142 countries. The near POC platforms are primarily for tuberculosis with increasing use across other diseases (e.g., HIV, COVID-19, HCV, and HPV). Other suppliers such as Molbio (Truenat HCV assay priced at US$12 per test EXW[11]) are entering the market with a growing global presence, presenting an opportunity for greater access to near HCV POC VL testing. Currently, the Molbio near POC platform is available in 35 countries primarily in Asia, Africa, and Europe. Furthermore, suppliers with near POC platforms with HCV assays in the pipeline include SD Biosensor and Bioneer.

As the market grows, global recommendations continue to favor decentralization, integration, and task sharing. In updated guidance on simplified service delivery and diagnostics for HCV, the WHO recommended the use of HCV POC VL testing as an alternative approach to laboratory-based HCV VL testing to diagnose HCV viremic infection and/or to complete test of cure for sustained virological response at 12 or 24 weeks of treatment completion.[12] Evidence for this recommendation was supported by systematic reviews of literature highlighting several key advantages as compared to laboratory-based VL testing including shorter turnaround time between antibody testing and treatment initiation (19 versus 64-67 days), higher treatment uptake (77-81 versus 53 percent), improved access, particularly in remote and rural settings, and strong diagnostic performance.[13]

11 African Society for Laboratory Medicine (ASLM) Molecular Supplier Pricing Database updated in May 2023 (see here)
12 World Health Organization. Updated recommendations on simplified service delivery and diagnostics for hepatitis C infection. (June 2022).
13 Tang W, Tao Y, Fajardo E, et al. Diagnostic Accuracy of Point-of-Care HCV Viral Load Assays for HCV Diagnosis: A Systematic Review and Meta-Analysis. Diagnostics (Basel). 2022;12(5):1255. Published 2022 May 18. doi:10.3390/diagnostics12051255

The government of **Nigeria** piloted a model to understand the impact of HCV VL integration onto existing near POC platforms at a tertiary hospital[14]. The model evaluated the uptake of diagnostic services with integration of HCV confirmatory testing and uptake of treatment for viremic patients following HCV VL testing.

During the pilot phase, an analysis evaluated device capacity on multi-disease POC platforms prior to integration; results found that with adjustments made to lab work hours, there was **47 percent of unused capacity** to test for both TB and HCV in a proposed integration scenario compared to a scenario without integration.

Pilot results for six months highlighted that integration **did not affect TB testing volumes** and **significantly improved median result turnaround times for HCV from 90 days to one day**.

The pilot model was expanded across six district hospitals, **demonstrating between 22 and 54 percent unused spare capacity to integrate**.

Overall, the integration pilot highlighted **expanded access to testing, an 84 percent decrease in cost to access VL test for a patient, faster result turnaround times, and increased uptake of viremic patients initiated on treatment**.

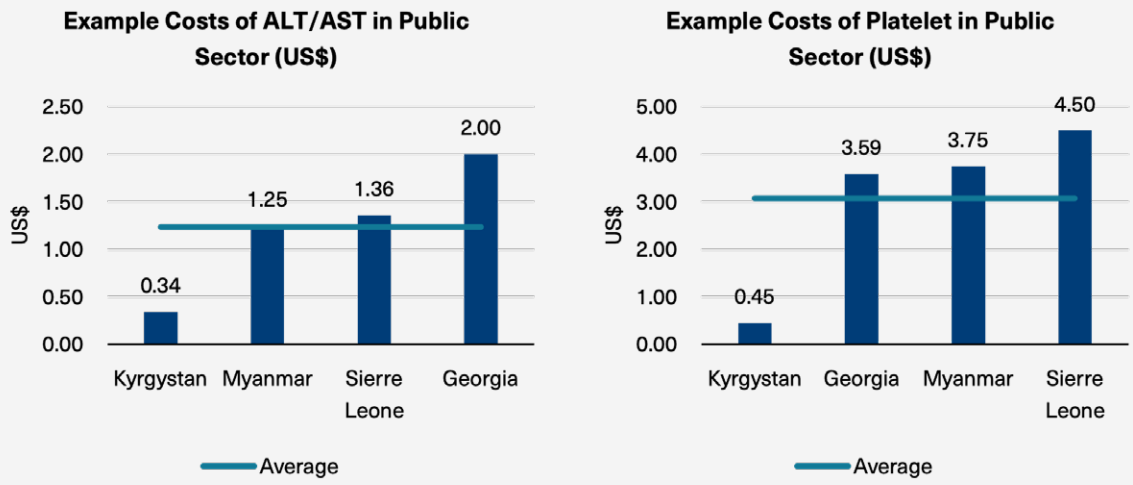
The successful pilot and model contributed to the scale up of integrated diagnostic testing leveraging POC and near POC devices in country.

Liver Staging

Standard chemistry blood tests, which can be used to determine liver fibrosis, are more accessible and less costly in the public sector compared to transient elastography (TE), which is not as widely available in the public sector in LMICs.

Individuals who test positive for HCV RNA should undergo a liver staging assessment to examine the degree of liver disease (i.e., liver fibrosis, cirrhosis). Non-invasive methods such as Aspartate Aminotransferase-to-Platelet Ratio Index (APRI) and Fibrosis-4 (FIB4) are more accessible and less costly and continue to be the most widely used approach in LMICs. APRI and FIB-4 are indirect scoring indices which rely on standard laboratory tests such as Aspartate Aminotransferase (AST) and/or Alanine Transaminase (ALT) and platelet count. A sample of high-burden countries demonstrated that the cost of ALT/AST in the public sector could range between US$0.34 and US$2.00, while the cost of platelet count test could range anywhere between US$0.45 – 4.50 (see Exhibit 9).

EXHIBIT 9 Public Sector Price of ALT/AST and Platelet in Sample of High-Burden HCV Countries (US$)



Source: Pricing data reported from CHAI Country Teams and external partners such as FIND, MSF, and WHA; a midpoint cost was used for countries where a range of prices was provided

14 ASLM Lab Community of Practice (LabCop). Achieving Integrated Hepatitis Testing through Decentralization: A Nasarawa Case Study

Other methods such as TE use ultrasound technology to measure liver stiffness. This method requires significant up-front investment in the platform, as well as specific training and expertise to deploy. The most widely used elastography technology globally is FibroScan (Echosens). There is limited data on uptake and availability of TE in LMICs as it is relatively expensive compared to other non-invasive methods and not widely available in the public sector. In a sample of high-burden HCV countries, TE was generally not available in the public sector. However in the case of two countries, the cost of TE in the public sector ranged from US$31 - 80, significantly higher than the cost of routine blood-based liver enzyme and platelet tests.

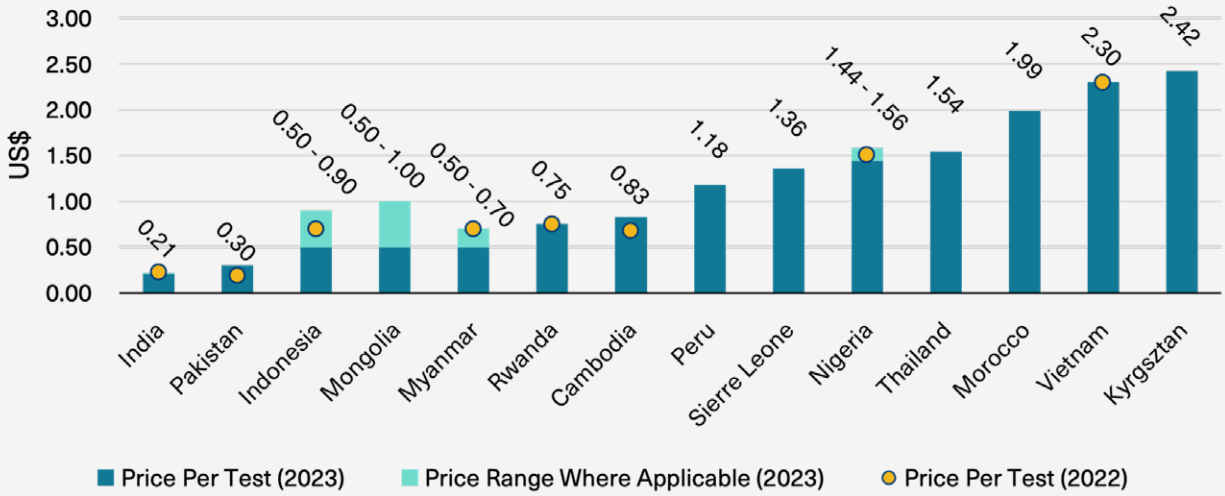
Pricing Trends

Cost of HCV Antibody RDTs Paid by Country

The total price paid per RDT varies across countries from the low-end at US$0.21 in India to the high-end at US$2.42 in Kyrgyzstan.

Procurement of key diagnostic products such as rapid tests are available through donors such as the GFATM, PAHO, and UNDP. The GFATM's Pooled Procurement Mechanisms pricing for RDTs indicates that HCV RDTs aim to be delivered at US$0.80-1.10 EXW.[15] However, when considering the total price paid per test (including shipping, handling, fees, etc.), these prices vary across a sample of high-burden countries (see Exhibit 10). Since last reported in 2022, the prices of RDT have generally remained consistent. It should be noted that the cost of RDTs for governments to procure can be priced higher or lower across countries and is largely dependent on other considerations such as procurement mechanisms used by the government. For example, whether procured directly from suppliers using national or domestic budget or through donor funds vis-à-vis third-party procurement service agents. Furthermore, countries such as India, Indonesia, and Pakistan are now able to locally manufacture and register their own anti-HCV RDT kits in country, enabling and simplifying the procurement process.

EXHIBIT 10 Total Price Paid for HCV Antibody RDTs in Public Programs within a Sample of High-Burden Countries (US$)



Source: Pricing data reported by CHAI Country Teams and through the support of external partners such as FIND, MSF, and WHA
Notes on Pricing: Prices in Vietnam are per the national health insurance policy. Previously reported prices for HCV RDTs ranged from US$2 - 6 for public programs and included additional mark-ups by private service providers who also participate in the national health insurance scheme. In Myanmar, the range for prices reflects differences in the official exchange rate and the market exchange rates.

15 As noted in the GFATM PPM Reference Pricing for RDTs: *Actual prices achieved for a grant will depend on how early the orders are placed by Principal Recipients - and additionally the achievement of certain volume thresholds through the pooled volumes to enable [GFATM] to achieve negotiated prices through the mechanism. Actual prices achieved will be charged to the grant.*

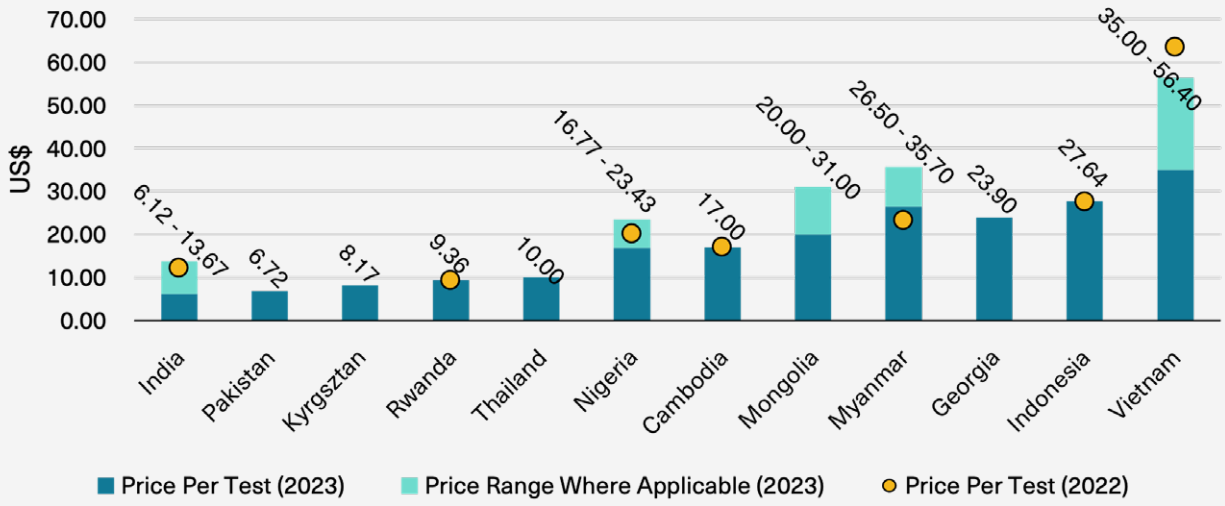
Cost of HCV VL Paid by Country

Global access program (GAP) pricing agreements offered by select HCV VL suppliers ensure that molecular tests for HCV are made available at affordable base prices

These prices may be negotiated on a country-by-country basis and depend on several conditions such as the number of device placements, test volumes, service and maintenance, and distribution details.[16] Through the support of regional diagnostic consortiums, these prices continue to be made public to ensure government purchasers have visibility to supplier pricing. The African Society for Laboratory Medicine (ASLM) published the Molecular Diagnostic Pricing Database to facilitate comparison of supplier pricing and offerings across a number of components including disease areas, commodities, logistics, and services. This initiative provides an opportunity to convene stakeholders including suppliers, distributors, country governments, donors, and investors alike to allow better clarity and transparency around diagnostic procurement.

Despite GAP pricing agreements, the final price paid for HCV VL to the public sector has varied by country due to differences in pricing inclusivity, incoterms, and the supplier-distributor relationship. In 2023, the cost of HCV VL to the public sector ranges from US$6.12 on the low end in India to US$56.40 on the high end in Vietnam (see Exhibit 11). Some countries, such as Indonesia and Vietnam, continue to experience high prices for HCV VL. This may be attributed to several factors. For example, a single distributor may have a monopoly over the market contributing to high added markup costs for specific products. Over the years, the average cost of HCV VL to the public sector has varied by country. Several countries, including Rwanda, Cambodia, and Myanmar indicate ability to access HCV VL at steady, consistent prices as evinced from 2020 to 2023 (see Exhibit 12). Other countries such as Nigeria, Indonesia, and India have seen a steady reduction in the cost of HCV VL over the past years, which might be attributed to factors such as volume commitments, negotiations of distributor/supplier agreements, or lower costs of locally produced tests.

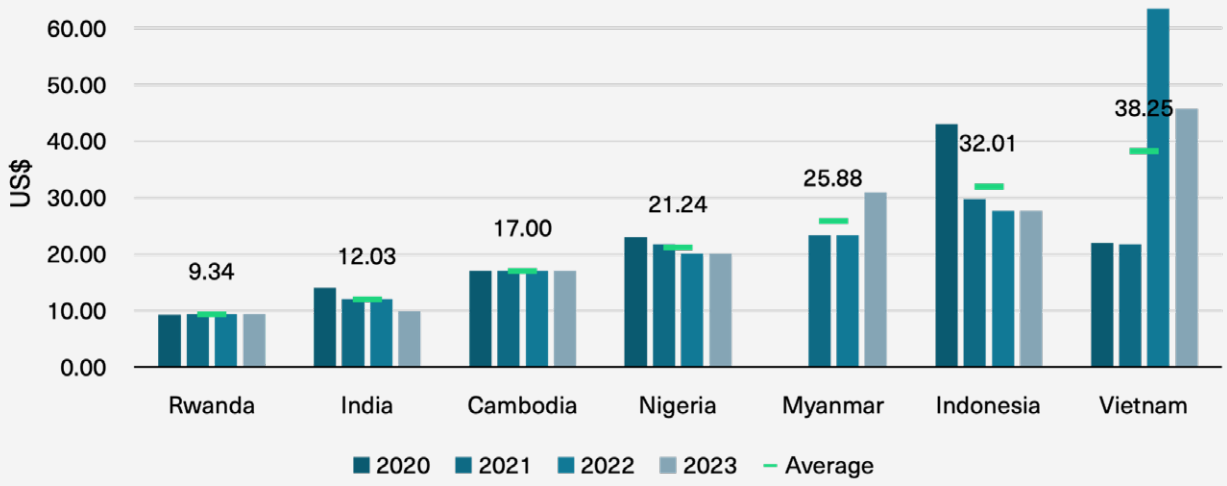
EXHIBIT 11 Costs of HCV VL in Public Programs within a Sample of High-Burden Countries in 2023 (US$)



Source: Pricing data reported by CHAI Country Teams and external partners such as FIND, MSF, and WHA
Prices in Vietnam are per the National Health Insurance policy. Previously reported prices for HCV VL tests ranged from US$37 - 90 for public programs and reflected additional mark-ups by private service providers who also participate in the National Health Insurance scheme
In Myanmar, the range for prices reflects differences in the official exchange rate and the market exchange rates

16 See most recent CHAI HBV Market Report 2022 for GAP Pricing Agreement details, including geographic coverage by supplier (see Exhibit 7).

EXHIBIT 12 Changes in Public Sector Prices of HCV VL Across Sample of High-Burden Countries from 2020-2023 (US$)



Source: Pricing data reported from CHAI-Supported Country Teams; midpoint price used when range reported

Volume Trends

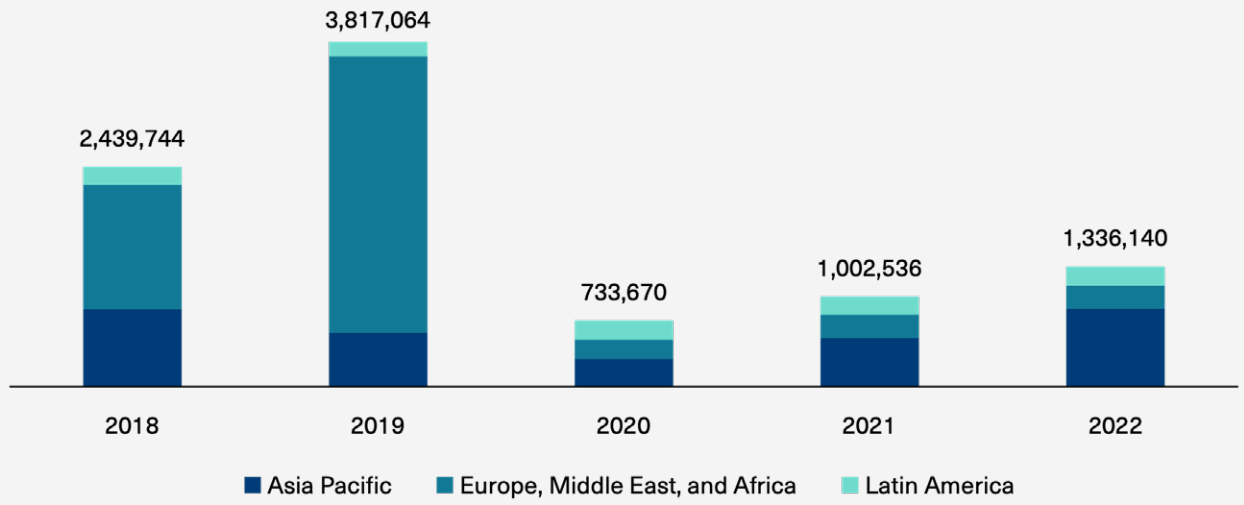
Sale volumes of HCV VL across molecular suppliers demonstrate that procurement remains significantly smaller compared to the potential market need.

Despite the growing availability of quality assured, affordable diagnostics, there remain critical gaps to fill to find the remaining millions undiagnosed people living with HCV. Closing this gap will require concerted efforts across stakeholders—governments and diagnostic suppliers in particular must work to enable expanded access to screening and improve linkages to confirmatory viral load testing.

Hepatitis remains a growing public health priority with limited awareness and infrastructure compared to other high-burden diseases across LMICs. To this end, there is limited visibility on quantifiable, aggregated uptake, market share, and procurement of key diagnostic commodities, which could be used to inform future procurement decisions and inform government approaches to public hepatitis programming, more generally.

Historically, procurement sale volumes across suppliers have demonstrated significantly smaller volumes in comparison to potential market need. Non-exhaustive data collected across VL suppliers demonstrates that sale volumes reached a peak of over three million tests sold in 2019 (see Exhibit 13). Following 2019, sale volumes significantly dropped, which may be attributed to governments deprioritizing investments into hepatitis programming because of the COVID-19 pandemic in addition to high-burden elimination champion countries, such as Egypt, nearing targets. Overall, most sales for HCV VL tests were in the Europe, Middle East, and Africa regions (55 percent) compared to smaller volumes in the Asia Pacific region (34 percent), and substantially lower volumes in Latin America (10 percent).

EXHIBIT 13 Sale Volumes of HCV VL Assays from 2018-2022 Across Select Countries and Suppliers in GAP Pricing Agreement Countries (Non-Exhaustive)



Notes on Methodology: The data is representative of estimated HCV VL sale volumes across four major molecular suppliers; HCV VL sales volume data was shared across regions, however regional groupings varied among suppliers; The data does not account for country-level sales volume data; The data above is representative of estimated HCV VL volumes across regions eligible for GAP pricing agreements and represents only public sector buyers

Emerging Diagnostic Innovations

Additional opportunities to expand HCV diagnostic market innovations, commercialize cost-effective solutions, and simplify testing approaches for low-resource settings.

With the increasing availability of affordable and quality of WHO PQ'd HCV diagnostics, there is growing opportunity for high-burden LMICs to continue investing in public hepatitis programming. This will ensure that key populations—inclusive of people living with HIV (PLHIV), people who inject drugs, migrants, prisoners—have access to the appropriate technologies, simplifying the continuum of care, and thereby enabling faster uptake of treatment and eventually cure. Alternative cost-effective approaches may be best suitable to reach key populations in low-resource settings.

The development and introduction of **multiplex or combination RDTs** provides an opportunity for public sector HCV programs to integrate screening across multiple disease areas, providing comprehensive diagnosis for patients. Preliminary research undertaken in Thailand on the uptake and acceptability of a 3-in-1 blood self-test for HIV, HBV, and HCV demonstrated that 99 percent of users reported high satisfaction with the testing process and that it simplified and streamlined the service delivery process.[17] Furthermore, a systematic review studied the cost effectiveness of implementing a combined testing and treatment approach for blood-borne viruses such as HIV, HCV, and HBV. Results found that if combined testing was implemented on a global scale, for every one individual diagnosed with HIV, an additional five would be diagnosed with HBV and an additional three would be diagnosed with HCV.[18]

Professional use RDTs which are typically used by trained healthcare workers for HCV screening can be adapted to meet the needs of end-users. With increasing emphasis on self-care strategies, diagnostic tools such as **HCV self-tests** are increasingly becoming popular, particularly among hard-to-reach and key populations. WHO guidance recommends HCV self-testing or peer-testing as an alternative approach to traditional professional use antibody rapid testing in facility.[19] A growing body of evidence suggests that HCV self-testing is usable, acceptable, and preferred among key populations (see Exhibit 14). Settings may consider pilot demonstrations to highlight the diagnostic accuracy and assess feasibility, acceptability, uptake, clinical impact, and cost-effectiveness of self-tests. In fact, multiple pilot demonstrations are ongoing with the STAR HepC Consortium. FIND has ongoing randomized control trials in Malaysia, Pakistan, and Georgia to assess the impact of HCV self-testing compared to the standard of care; preliminary results from these suggests that HCV

17 Salvadori N, Achalapong J, Boontan C, et al. Uptake, acceptability and interpretability of 3-in-1 rapid blood self-testing for HIV, hepatitis B and hepatitis C. J Int AIDS Soc. 2022;25(12):e26053. doi:10.1002/jia2.26053
18 Mascolini, Mark (Jul. 2023) Triple Test and Treat for HIV/HBV/HCVSimple Way to Slow Hep Epidemics? IAS 2023. Link.
19 World Health Organization. Recommendations and guidance on hepatitis C virus self-testing. July 2021.

self-testing increases uptake of HCV antibody testing 19 to 65 percent[20]. Furthermore, economic modeling demonstrated that the cost-per-diagnosis for HCV self-testing compared to facility-based testing services may be more cost-effective in populations with high prevalence.[21] There are a number of suppliers with products in the pipeline available for research use only (see Exhibit 15), however, plans to enter the market at scale for commercial use are dependent on other factors, including WHO PQ, regulatory approvals, pricing, and ongoing research and clinical trials.

EXHIBIT 14 Evidence on Acceptability, User Preferences on HCV Self-Testing

Acceptability and Usability of HCV Self-Testing

- Observational study conducted in Vietnam to assess the acceptability and usability of HCV Self-Test prototype among key populations showed that acceptability was 92 percent among people who inject drugs and 98 percent among men who have sex with men (MSM) [1]
- Similar results found in Egypt through an observational study conducted in two hospitals in the Nile Delta region found that 72 percent of participants completed all testing steps without any assistance and interpreted the test results correctly [2]
- A study in Kenya found high acceptability of oral fluid HCV self-testing among people who inject drugs [3]

Values and Preferences of HCV Self-Testing

- Qualitative research in Rwanda among public and healthcare workers found that HCV self-testing is perceived to be an acceptable method to increase HCV testing [4]
- A qualitative study in Kyrgyzstan to assess values and preferences of HCV self-testing within people who inject drugs, found that acceptability may increase if HCV self-testing is delivered in pharmacies or by harm reduction associations; was free of charge, included instructions with images and clear information on test accuracy [5]

Sources: [1] Acceptability and Usability of HCV Self-Testing in High Risk Populations in Vietnam (February 2021)
[2] Usability and acceptability of self-testing for hepatitis C virus infection among the general population in the Nile Delta region of Egypt (June 2021)
[3] Usability and acceptability of oral fluid hepatitis C self-testing among people who inject drugs in Coastal Kenya: a cross-sectional pilot study (September 2022)
[4] Values and preferences for hepatitis C self-testing among the general population and healthcare workers in Rwanda (October 2021)
[5] Values and preferences for hepatitis C self-testing among people who inject drugs in Kyrgyzstan (June 2021)

EXHIBIT 15 HCV Self-Tests Available for Research Use

Product	Manufacturer	Sample Type
OraQuick HCV Rapid Antibody Self-Test	OraSure Technologies	Oral Fluid
First Response HCV Card Test (Self-Test)	PMC	Whole blood (fingerstick)
Wondfo HCV Self-Test	Wondfo	Whole blood (fingerstick)
HCV Self-Test	bioLytical	Whole blood (fingerstick)

Techniques such as collection of **dried blood spot (DBS) specimens** make it possible to easily collect and transport samples. They are ideal for decentralized models of testing because they require fingerstick samples rather than phlebotomy, and can be stored and/or transported for weeks without needing cold chain; therefore, they can be conveniently used in remote areas. The Abbott RealTime HCV assay has WHO PQ including for use with whole blood spotted on DBS cards. These can be performed on the m2000 platform, which many countries are already using for HIV VL testing using DBS. DBS sampling techniques can be used for both serological and molecular testing. As demonstrated by a study in Brazil, DBS was used to detect anti-HCV.[22] The results indicated promising diagnostic performance with sensitivity ranging from 87.5 - 100 percent in subgroups (98 percent overall) and specificity above 99.2 percent. Molecular DBS presents an opportunity for use in places without access to phlebotomy or reliable cold chain transport systems, which is encouraging because many countries already use platforms such as the Abbott m2000 for HIV VL testing that can be re-used for HCV testing.

20 Population Services International (PSI). Hepatitis C Self-Testing: Updates on Country Pilots, WHO Guidance and Products Webinar. Link.
21 Walker, Josephine G et al. "Cost-effectiveness of Hepatitis C virus self-testing in four settings." PLOS global public health vol. 3,4 e0001667. 5 Apr. 2023, doi:10.1371/journal.pgph.0001667
22 Villar, L.M., de Lima, M.P., Cruz, H.M. et al. Feasibility of dried blood spot for hepatitis C diagnosis in vulnerable subjects and people living in remote areas from Brazil. BMC Infect Dis 22, 804 (2022). https://doi.org/10.1186/s12879-022-07717-4

HCV core antigen (cAg) can be used as an alternative to HCV RNA confirmatory testing where there is limited access to RNA testing. Core antigen can show up within the bloodstream within two weeks of infection and persists in cases with HCV viremia. Evidence demonstrating HCV cAg as an alternative for diagnosing HCV infections shows that cAg performs comparably well to traditional PCR-based approaches.[23] There are several limitations however, including that HCV cAg is dependent on centralized laboratory systems which require strong appropriate laboratory infrastructure and equipment. There are few quality-assured products in the market, with newer products that allow simultaneous antibody and antigen testing; however evidence and experience on using and adopting these assays is needed in LMIC contexts (see Exhibit 16).

EXHIBIT 16 Landscape for HCV Core Antigen Products (Non-Exhaustive)

HCV core antigen (cAg)				
Product	**Manufacturer**	**Sample Type**	**Time to Result**	**Regulatory Approval**
Elecsys HCV Duo* (Qualitative)	Roche	plasma, serum	27 minutes	CE-IVD
ARCHITECT HCV Ag assay (Quantitative)	Abbott	plasma, serum	36 minutes	WHO PQ

**HCV Duo combines an HCV core antigen test with an anti-HCV test*

23 Sadeghimehr M, Bertisch B, Negro F, et al. Hepatitis C core antigen test as an alternative for diagnosing HCV infection: mathematical model and cost-effectiveness analysis. PeerJ. 2021;9:e11895. Published 2021 Sep 10. doi:10.7717/peerj.11895

Treatment

Supplier Landscape

While the supplier landscape for pan-genotypic DAAs remains robust with at least one generic PQ'd product, a few suppliers have exited the WHO PQ market because of low product uptake.

Licensing

Historically, originators of the key HCV drugs (DAAs) such as Gilead, Bristol Myers Squibb (BMS), and AbbVie each have licensing agreements that continue to allow generics to manufacture and sell these drugs in many LMICs.

Sofosbuvir (SOF) and SOF- based fixed-dose combinations, Sofosbuvir/Ledipasvir (SOF/LDV), Sofosbuvir/Velpatasvir (SOF/VEL): Gilead continues its sublicensing agreements with 11 Indian suppliers to produce and/or sell generic versions of sofosbuvir (SOF), ledipasvir (LDV), velpatasvir (VEL), and voxilaprevir (VOX) in 105 countries. Additionally, two suppliers in Egypt and one in Pakistan have sublicensing agreements to manufacture and sell in their local markets.

Daclatasvir (DCV): The daclatasvir patent initially held by BMS has expired enabling suppliers to manufacture and distribute the generic product. BMS announced in early 2020 that the marketing authorizations and resulting patent protection for its originator product would be withdrawn or allowed to lapse in countries where the product is no longer routinely prescribed or where there are other therapeutic options available. As of December 2021, generic DCV can be supplied to at least 143 countries[24].

Glecaprevir/Pibrentasvir (G/P): The licensing agreement between AbbVie (originator) and Medicines Patent Pool (MPP) enables quality-assured manufacturers to develop and sell generic medicines containing G/P in 96 LMICs. The list of countries can be found here. However, the licensing agreement excludes India, which has a large HCV burden and is a major market for DAAs.

Quality-Assured Generics

The generic supplier landscape for DAAs has expanded significantly since their introduction in 2016. Several generic suppliers manufacture DAAs, and a few have WHO PQ for their products or have been reviewed by the Expert Review Panel (ERP). At least one generic supplier has received WHO PQ across key pan-genotypic treatment DAA regimens.

A few suppliers have decided not to retain WHO PQ for specific DAAs and continue to supply non-WHO-PQ products. The high cost of maintaining WHO PQ coupled with low sales volumes of the products may have contributed to this withdrawal. While the supply of quality-assured generics remains robust for all pan-genotypic regimens, decisions not to retain WHO PQ for DAAs signal dwindling supplier confidence in the future demand outlook of the DAA market.

EXHIBIT 17 Availability of Quality-Assured Generic DAA Products (As of November 2023)

DAA	WHO PQ	Suppliers that did not retain WHO PQ
SOF (400 mg)	Viatris, Hetero, European Egyptian Pharmaceutical Industry (Pharco), Strides Pharma	Cipla
DCV (30mg)	Hetero, Cipla, Laurus Lab	Viatris
DCV (60mg)	Hetero, Cipla, and Laurus Lab, Viatris	
SOF/DCV FDC (400 mg/60 mg)	Viatris	

24 DCV license

DAA	WHO PQ	Suppliers that did not retain WHO PQ
SOF/VEL (400mg/100mg)	Viatris	
SOF/LDV (SOF/LDV) (400mg/90mg)	None	Viatris
SOF/VEL/VOX (400 mg /100 mg /100 mg)	SOF/VEL/VOX, which is recommended by WHO for retreatment of HCV, currently does not have a generic product in the market due to small and fragmented retreatment market.	
G/P (300 mg/120 mg)	In 2022, G/P was included in WHO's Expression of Interest for product evaluation to the WHO PQ,[25] delineating a clear regulatory pathway for MPP licensees to file their generic formulations with WHO, if the product evaluation concludes in favor of G/P. Currently, there are no generics G/P products available in the market.	

Source: The WHO List of Finished Pharmaceutical Products (FPPs) that have received WHO PQ as of November 2023.

In-country Supplier Registrations

The availability of different quality-assured generic products promotes increased competition and helps lower prices, thereby increasing access to medications and ensuring the sustainability of public health programs. This can be particularly important for patients with chronic conditions who may need to take medications for extended periods of time.

Eight out of 33 countries, from high-burden countries or LMICs that are the focus of the report (Appendix 2), did not have any registered generic suppliers of quality-assured products. Out of these, registration of quality-assured generics in seven countries is restricted by Gilead's licensing agreement for SOF. In South Africa, regulatory barriers restricted generic DAA registration as originator products were not yet registered in the country. During 2022, the South African Health Products Regulatory Authority (SAHPRA) registered Gilead's sofosbuvir/velpatasvir (Epclusa), allowing for generic companies to seek registration in the country. However, the registration of generic versions of sofosbuvir/daclatasvir (the most affordable DAA product) is unlikely in South Africa. This is because the originator version of daclatasvir has not been registered in the country. Generics are typically registered in reference to an already registered originator product.[26]

A few countries which aren't included in Gilead's licensing territory have opted for compulsory licensing for SOF under certain conditions. Compulsory licensing refers to the use of a patent without the authorization of the patent holder and is one of the flexibilities in the field of patent protection included in the World Trade Organization's agreement on intellectual property for public goods.[27] It allows countries to locally manufacture or import generic versions of the treatment without the patent holder's consent.

- Brazil granted patents related to manufacturing processes of SOF in 2021, which allowed for generic production through public-private partnerships, even though legal challenges on Intellectual Property still persist.
- China does not have access to WHO PQ'd generic products. It is included in the countries eligible under MPP/BMS license for DCV but not in Gilead's licensing agreement for SOF. China procures locally manufactured/developed DAAs or originator products. Some of the DAA products have also been added to the National Reimbursement Drug List, which is a list of drugs fully or partially reimbursed by the national basic health insurance.

DAA Volume Trends

Except for India and Pakistan, procurement volumes across most LMICs haven't recovered to the COVID-19 pre-pandemic level.

Methodology

Visibility into DAA volume trends remains limited due to the lack of robust and reliable publicly available data sources. We focus primarily on India's generic export market[28], MPP's data on DCV sales reported by sublicensees, and public sector program data, for which data is robust and encompassing of sales to LMICs. Where possible, we also add insight into the generic-inaccessible market based on CHAI analysis and publicly available data. This methodology is limited as it doesn't account for the use or export of DAAs manufactured outside India, such as in Egypt, and China, among other countries. It

25 WHO 5th EOI for HCV and HBV products
26 In-depth: Breakthrough hepatitis C cures slowly becoming more widely available in South Africa
27 Wong H. The case for compulsory licensing during COVID-19. J Glob Health. 2020
28 As a majority of generic manufacturers that have the license from Gilead to manufacture SOF are based in India.

also does not include sales or donations by local manufacturers. These limitations may lead to underestimating the volume of drugs procured across LMICs shown in Exhibit 18.

An overview of the CHAI analyses and methodologies used in this section is provided in Appendix 3.

Volume Trends for First-line treatment DAAs

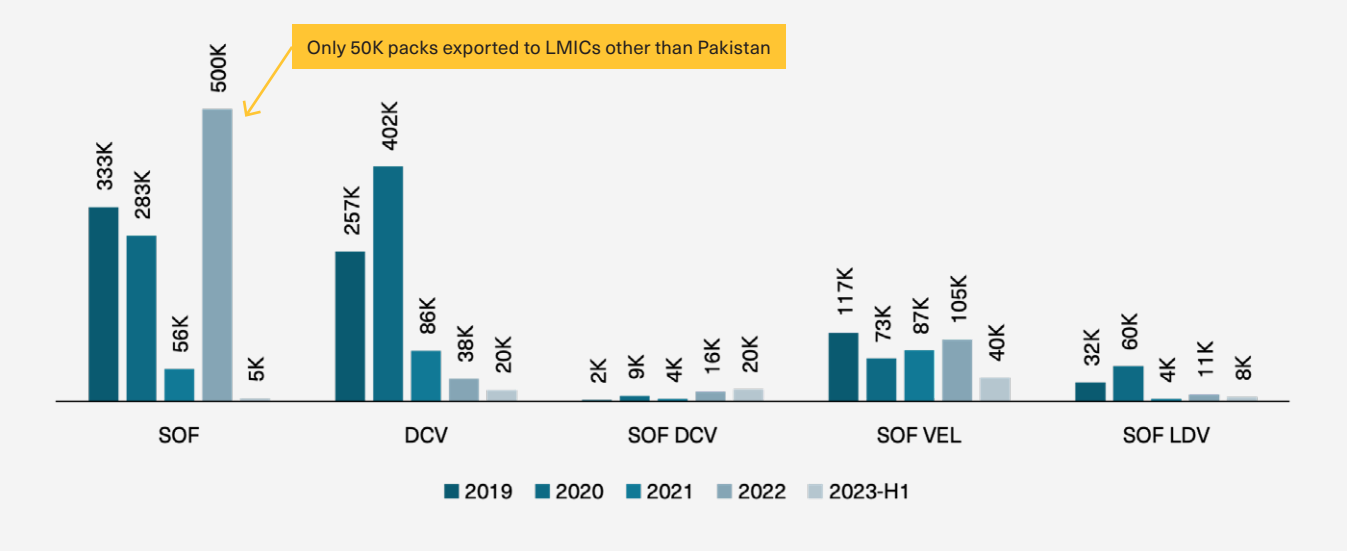
Takeaways from DAA procurement analysis:

1. Except for India and Pakistan, procurement levels across many countries are lower than pre-COVID-19 pandemic levels

Annual DAA exports from Indian generics to LMICs increased by 183 percent between 2021 and 2022. This increase was primarily driven by Pakistan which has procured nearly 450,000 SOF packs. Notably, Pakistan's SOF orders alone accounted for 67 percent of total export in 2022. Conversely, DCV exports from Indian generics to Pakistan remained minimal as it pairs locally sourced DCV with SOF.

However, when excluding exports to Pakistan, the overall DAA export volumes in 2022 were approximately half pre-pandemic level, average export volumes i.e., export volume between 2016 and 2020. A contributing factor to the declining procurement trend is the lower demand from countries such as Rwanda that are progressing towards elimination. Exhibit 18 also shows a total of 93,000 packs were exported in the first half of in 2023.

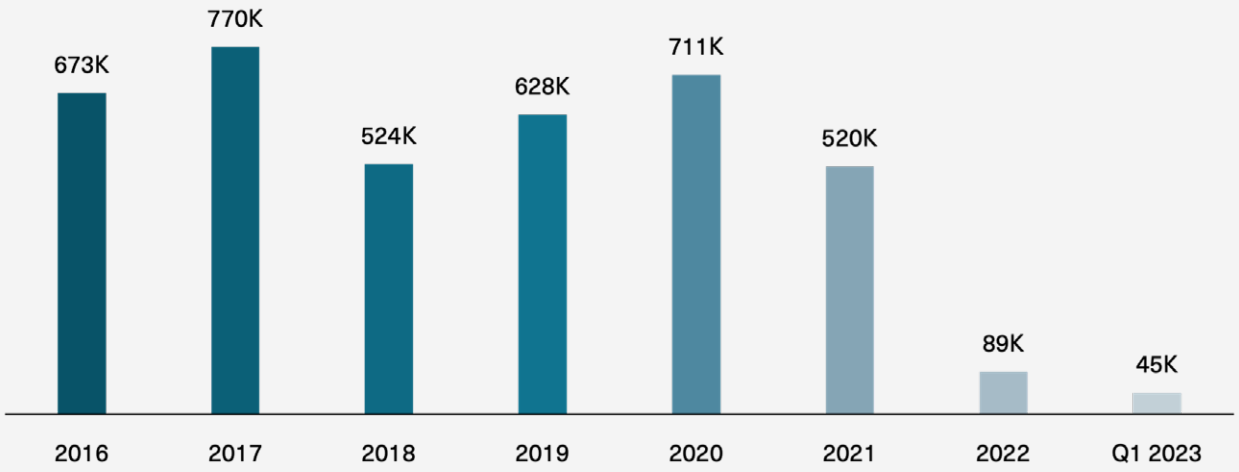
EXHIBIT 18 Export of DAAs from India to LMICs (# of packs) from 2019 to H1-2023



This is corroborated by DCV sales data reported by generics to MPP. Overall, as of Q1 2023, generic daclatasvir reached approximately 1.3 million patients via this licensing agreement with MPP[29] (note that MPP reported sales include sales within India). However, the sales volume significantly dropped in 2022 by 83 percent from 2021. **Stagnating volumes threaten supply security, as existing suppliers may exit the market due to low volumes and/or new suppliers are discouraged from entering the market.**

29 Reported by MPP

EXHIBIT 19 Sales of DCV 60mg and DCV 30mg via MPP-license[30]



Source: Data shared by MPP with CHAI as of Q1 2023

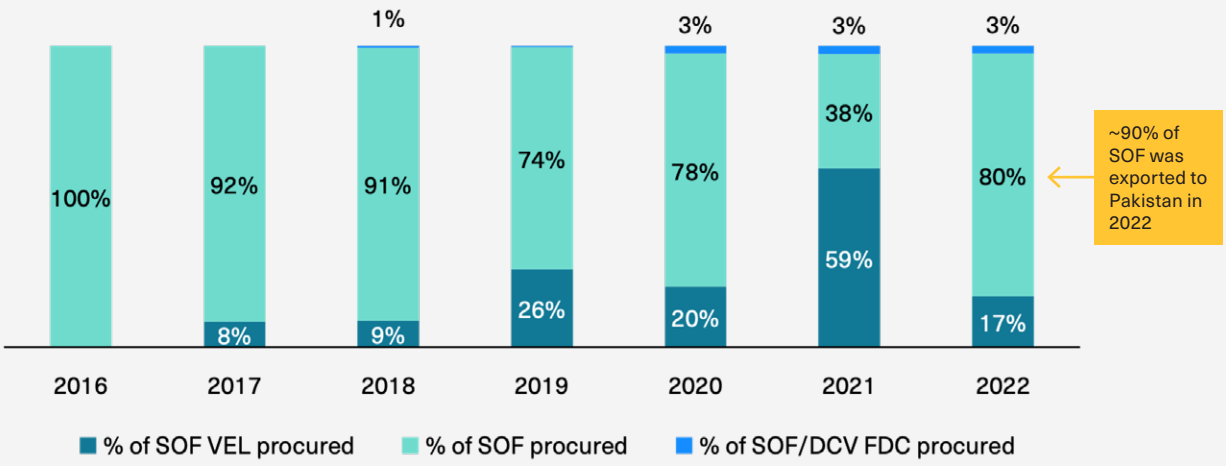
2. SOF and DCV remain the preferred first-line treatment regimen, with a few countries opting to procure SOF/VEL

Between 2016 and 2020, India exported larger quantities of SOF compared to the combination of SOF/VEL. This export trend was primarily driven by the significantly higher cost of SOF/VEL regimen as compared to SOF and DCV and by significant SOF demand from countries such as Egypt, Pakistan, Vietnam, and Ukraine, among others. However, as the cost of SOF/VEL reduced and certain elimination programs matured and approached their targets, the commodity mix of DAAs exported from India started to shift. Countries started opting for SOF/VEL regimens to treat patients with compensated cirrhosis or patients who fail treatment on SOF/DCV, while some newer programs also started opting for SOF/VEL to treat all HCV patients including non-cirrhosis.

Exhibit 20 shows increasing SOF/VEL procurement by countries compared to SOF and SOF/DCV FDC. The procurement of SOF/VEL, SOF, and SOF/DCV FDC is calculated as a percentage of the total procurement of these regimens yearly. SOF volumes are used as a proxy for SOF and DCV regimen volumes. DCV volumes have not been included in the calculation of total exports for this graph as SOF and DCV are drugs prescribed as a combination treatment. While export data may not show a 1:1 procurement of SOF and DCV, the countries using these regimens for HCV treatment will be procuring them in equal quantities either from India or from other non-Indian suppliers.

30 MPP sales data contains sales in India and other markets that may not be covered in the India-export data shown in Exhibit 19. Hence, these numbers are not conducive for direct comparison.

EXHIBIT 20 **SOF, SOF/VEL and SOF/DCV FDC exported from India since 2016 as a percentage of total export (SOF volumes are used as a proxy for SOF and DCV regimen volumes. DCV volumes have not been included in calculation of total exports for this graph as SOF and DCV are drugs prescribed as a combination treatment)**



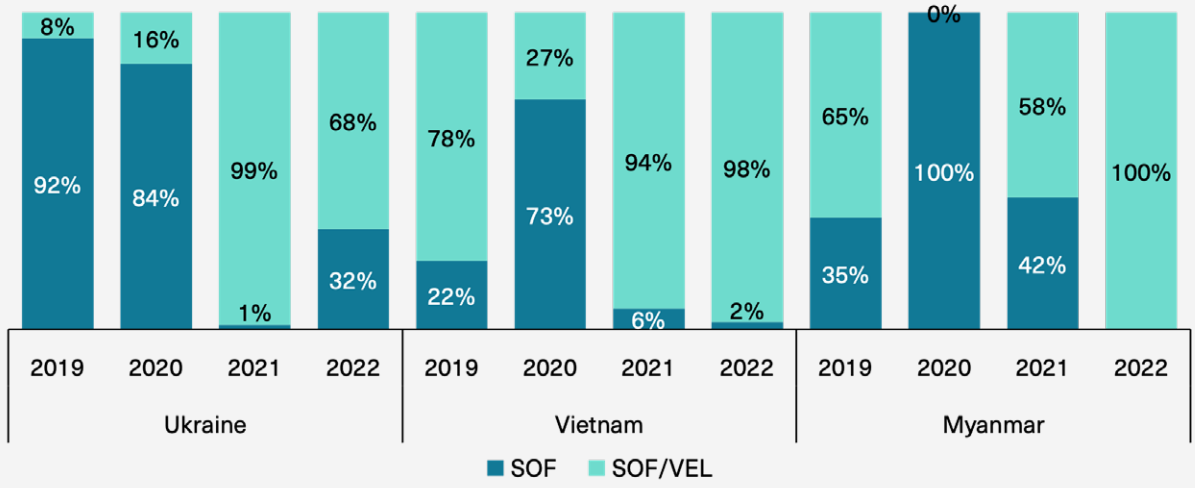
In recent years, some countries opted to import SOF/VEL instead of individual drugs like SOF and DCV from Indian generics (Exhibit 21) as the data shows. This change in preference for specific DAA combinations further influenced the shifting dynamics of India's DAA exports.

SOF/VEL exports increased by 21 percent in 2022 driven by demand in Georgia, Myanmar, Ukraine, and Vietnam. These countries showed a preference for purchasing more packs of SOF/VEL as opposed to SOF and DCV singles. Vietnam, for instance, imported 44 times more SOF/VEL than SOF, while Ukraine imported twice as much SOF/VEL than SOF. Additionally, Georgia and Myanmar exclusively imported SOF/VEL in 2022.

The choice of SOF/VEL over other DAA combinations in countries is influenced by national guidelines. For instance, Myanmar's national guidelines recommend the use of SOF/VEL for individuals with and without cirrhosis in HCV treatment[31]. Similarly, Georgia's National Guidelines endorse the use of SOF/VEL for patients with or without cirrhosis[32]. In India, SOF/VEL is recommended for patients with compensated cirrhosis, and SOF/VEL based regimens are advised for retreatment[33]. Although there are instances where guidance does not exclusively recommend SOF/VEL, some countries, like Vietnam, Kyrgyzstan, and Ukraine, have predominantly imported SOF/VEL from India.

31 National Simplified Treatment Guidelines of Viral Hepatitis C Infection 2019; It is of note that there is no strict preference for SOF/VEL in the public sector
32 National Guidelines received from National Center for Disease Control and Public Health, Georgia
33 National Guidelines for Diagnosis & Management of Viral Hepatitis

EXHIBIT 21 SOF and SOF/VEL exported from India to Ukraine, Vietnam and Myanmar between 2019 – 2022

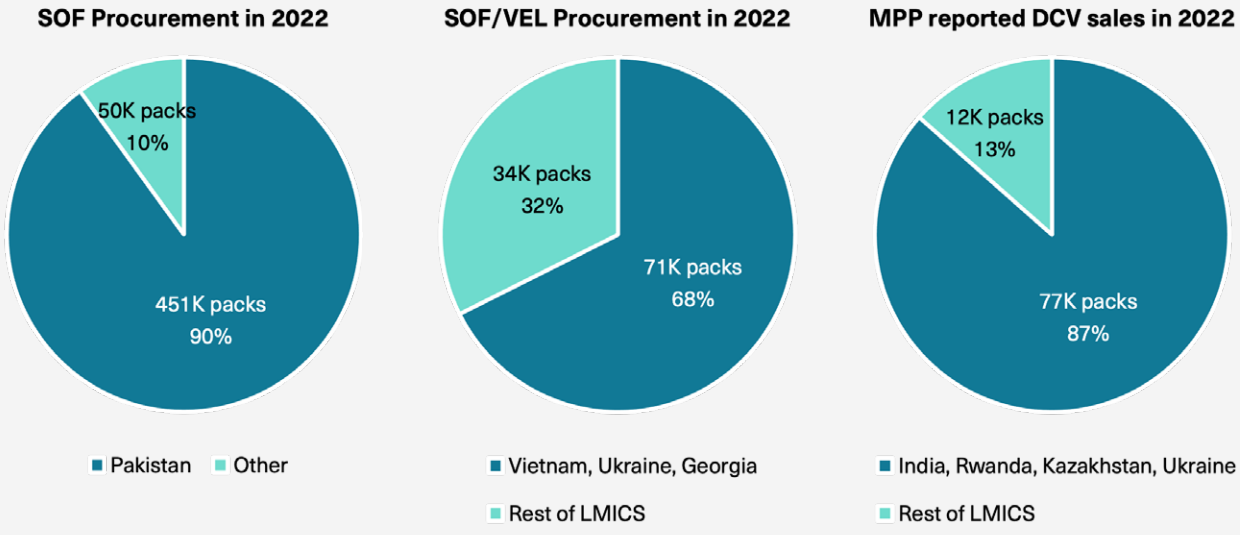


Except for a few countries which have shown preference for procuring SOF/VEL, SOF and DCV remains the preferred regimen for HCV treatment across LMICs.

3. Buyer Concentration: Procurement driven by select countries

The DAA market exhibits a recurring trend of buyer concentration with a few countries accounting for most of the DAA procurement over the years. Exhibit 22 indicates the concentration of demand for SOF/VEL exported by Indian generics in three countries in 2022. Similarly, with SOF singles exports (Exhibit 22), Pakistan accounted for 90 percent of the demand for the drug in 2022. MPP-licensed DCV 60mg sales data for 2022 also shows that four countries were responsible for over 86 percent of DCV 60mg procurement in 2022. Such concentration makes it difficult for suppliers and other stakeholders to plan for demand efficiently and leads to longer lead times, and shortages.

EXHIBIT 22 Buyer concentration of DCV 60mg, SOF/VEL, and SOF (Singles) procurement in 2022



This high buyer concentration of a few countries indicates an asymmetry in the market and unpredictable demand in the medium to long term. Further, irregular, and non-linear procurement patterns also make forecasting potential DAA demand a challenge, especially for suppliers.

In conclusion, DAA volumes across LMICs, except for India and Pakistan, are lagging below pre-pandemic levels with demand driven by a few countries. While for countries such as Rwanda that are progressing towards elimination, tapering demand is expected; limited resources towards hepatitis care in most countries is responsible for the low uptake of products.

Some countries have taken steps to scale hepatitis programs in recent years. Cambodia for example in 2022 allocated US$1 million for the country's hepatitis program, the majority of which is for the procurement of HCV commodities, including DAA regimens for over 4,300 patients. Through the advocacy of key stakeholders, and strong political will, the government committed to scaling up of hepatitis testing and treatment services in the country. Such efforts are needed across LMICs to achieve HCV elimination targets.

DAA Pricing Trends

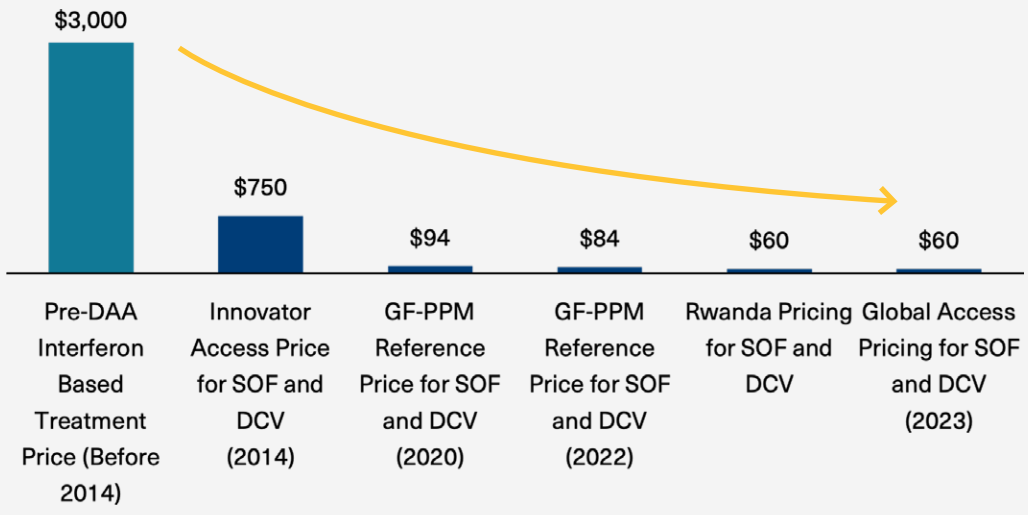
DAA prices have fallen significantly since 2014. In 2023 CHAI partnered with The Hepatitis Fund and leading DAA generic manufacturers, Hetero and Viatris, to achieve a historic access pricing of US$60 for a 12-week treatment course of quality-assured SOF and DCV.

DAA Pricing Evolution

The price of HCV treatment has fallen significantly since 2014 with the introduction of more effective treatment and the expansion of the generic landscape for DAAs. For instance, countries like Rwanda and India have been able to access DAA at some of the lowest prices globally in recent years. Global reference pricing from international procurement mechanisms has also declined over the years.

However, pricing remains varied across countries and the effect of globally decreasing DAA prices has not translated evenly and enabled a proportional decrease in final prices accessed by public program/patients in countries.

EXHIBIT 23 Evolution of DAA pricing trends 2014-2023



In 2023, CHAI partnered with The Hepatitis Fund and leading DAA generic manufacturers, Hetero and Viatris, to achieve an access pricing deal of US$60[34] for a 12-week treatment course of SOF and DCV. This price will apply to the public sector[35], including governments, NGOs, and organizations that purchase products on behalf of the public sector across licensed territories. These agreements were announced at an inaugural Global Hepatitis Resource Mobilization Conference, in Geneva on May 17, 2023[36]. The access pricing deal is the first-of-its-kind for hepatitis treatment commodities and comes at a crucial time to help countries make strides towards hepatitis elimination.

34 US$60 EXW price for 12 weeks of the treatment course of WHO PQ'd SOF+DCV; Minimum order quantity is 2,500 packs from Viatris and 3,500 packs from Hetero: Press Release
35 Territories as per the agreement with Gilead and MPP
36 Inaugural Global Hepatitis Resource Mobilization Conference

FOB Pricing Trends

EXHIBIT 24 Weighted average FOB price for 12 weeks of treatment with DAAs in LMICs from 2019 to H1-2023

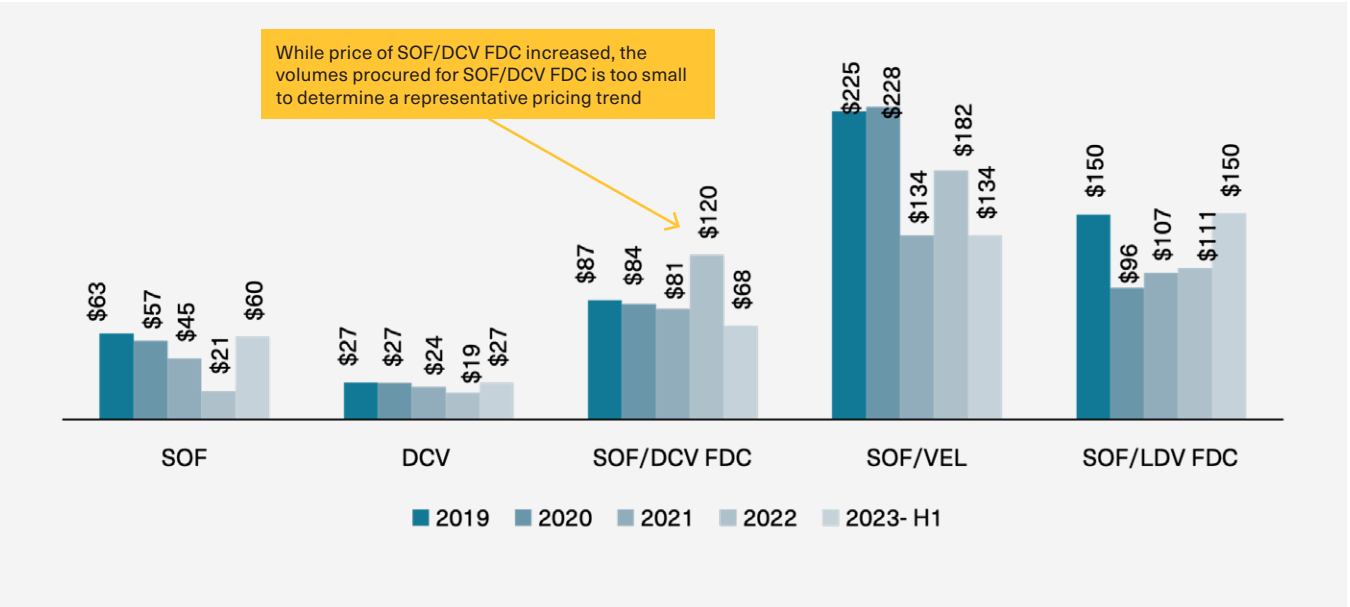


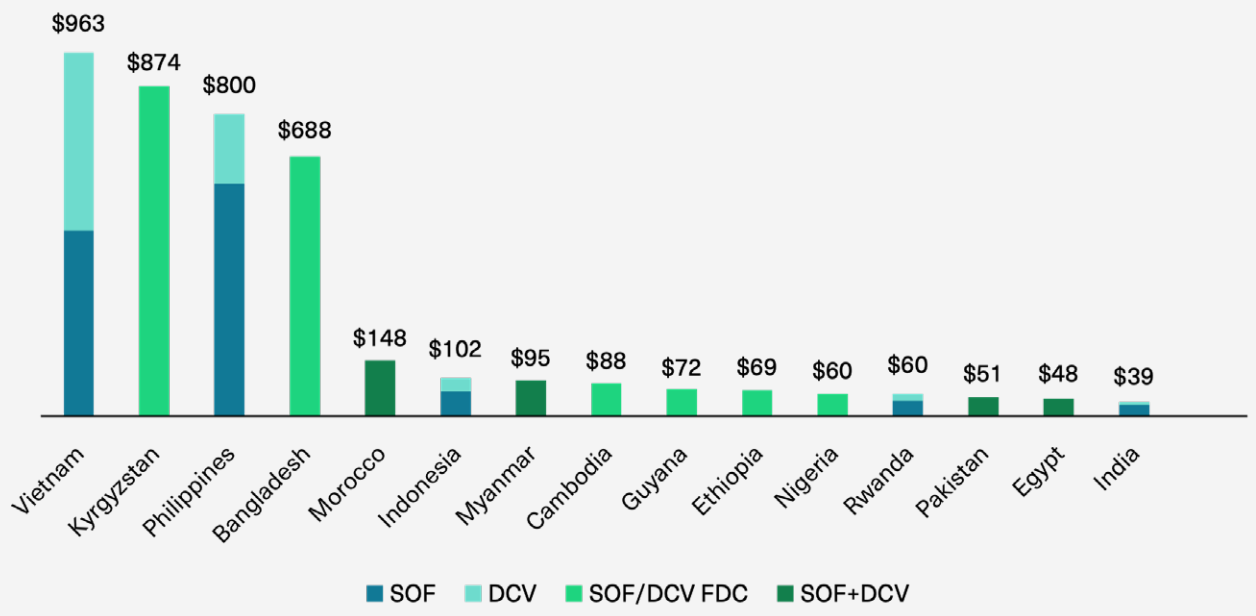
Exhibit 24 summarizes the weighted average price for a 12-week DAA treatment course in LMICs. Prices are shown in 'Freight on Board' (FOB) or EXW terms. These are prices at which generic suppliers export drugs from India. They do not include shipping, customs, storage, distributor-associated costs, and other additional costs. Usually, there are in-country costs added to the FOB price, resulting in a higher final price to the public procurement division, public hospitals, and private retail market.

Overall, FOB prices of all DAAs except SOF/VEL exported by Indian generics remained similar or declined from 2021 FOB prices. The decrease in FOB prices of SOF by over 50 percent was driven by large procurements of the drug at a lower price by Pakistan. While the price of SOF/DCV FDC increased, the volumes procured for SOF/DCV FDC were too small to determine a representative pricing trend.

The FOB price of SOF/VEL increased by 35 percent from US$45 to US$61 between 2021 and 2022. While most countries procured SOF/VEL at prices similar to previous years, Ukraine, and Vietnam (which made up a large volume of the procurement) procured the drug at higher prices than before, contributing to this increase.

In-country Pricing Trends

EXHIBIT 25 In-country Prices of SOF and DCV course for 12 Weeks Treatment Course (US$)



Source: CHAI analysis; Ministries of Health and CHAI Partners
Notes: [1] In-country prices mentioned are public sector prices paid by the government in each country, if available, or the lowest identified private sector price if a public sector price is not available. The most recent possible pricing has been reflected. [2] Price for the Philippines and Kyrgyzstan is from second edition of Hepatitis C Market Report. [3] Public program in Kyrgyzstan only procured SOF/VEL regimen from 2019 onwards. The latest price of the SOF/VEL regimen procured by the country is reflected in Exhibit 26. [4] Price for Nigeria is accessed by Nasarawa State. [5] Price for Myanmar is the average price accessed by the public program in 2022; The range of prices accessed by the public program is US$80.8 – US$109. The range reflects differences in the official exchange rate and the market exchange rates in Myanmar

While DAA prices have fallen significantly due to the expansion of the competitive landscape of generic DAAs and the increase in demand, there is significant variability in prices accessed across LMICs driven by fragmented demand, sub-optimal procurement practices, and geo-political instability in some regions.

Rwanda continued to procure WHO PQ'd SOF and DCV at US$60 for a 12-week treatment course, setting a price benchmark for WHO PQ'd DAA regimens. Rwanda has procured retreatment regimen SOF/VEL/VOX at a cost of US$1,000[37] for a 12-week treatment course. This price corresponds to originator product as there are no generics of SOF/VEL/VOX in the market as yet.

Countries such as India and Pakistan continue to procure DAAs at some of the lowest prices globally at US$39 and US$28 respectively. It is worth noting that they are procuring locally approved products, which can be manufactured at a lower cost than WHO PQ'd products. Additionally, DAA prices in Pakistan recently increased due to the devaluation of the local currency and inflation in the economy.

In 2021, Nasarawa state in Nigeria secured a price of US$60 (55 percent reduction) for a 12-week course of the SOF/DCV FDC through continuous state government investment in the scale-up of hepatitis care, optimization of in-country margins, and collaboration with suppliers and other key stakeholders. Nasarawa state continued to access this price in 2022.

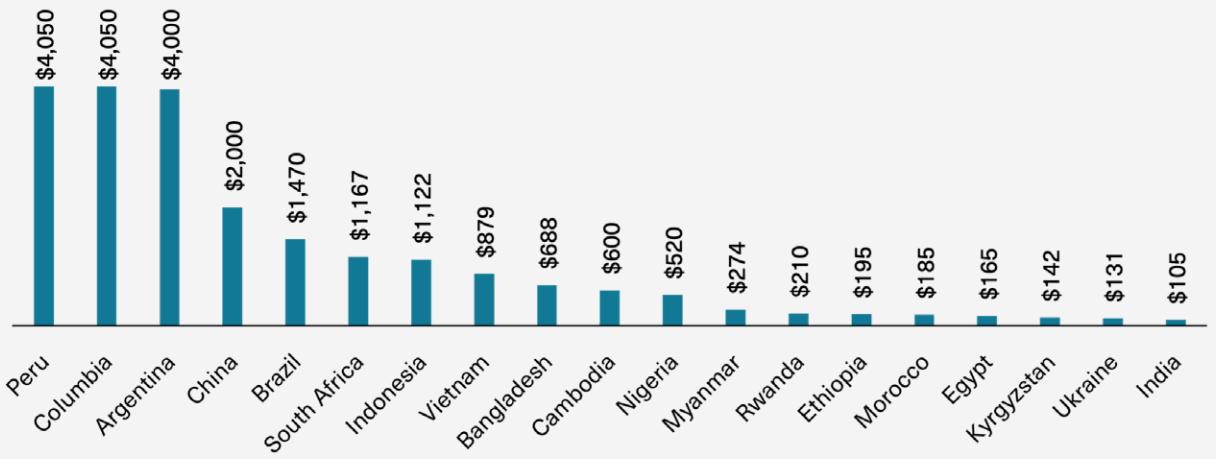
In Vietnam, the price shown above (Exhibit 25) is the lowest bidding price from public health facilities in 2022. The data is publicly available on Drug Administration, Vietnam website. These prices slightly decreased from 2021.

Vietnam's national HIV/HCV co-infection program, led by the Vietnam Administration for HIV/AIDS Control and supported financially by the GFATM and National Social Health Insurance, also procured over 3,700 12-week treatment courses of SOF and DCV at US$90 (inclusive of fees) in 2023. This price decreased from US$100 at which over 16,000 of the same treatment courses were procured in 2021-2022. The program expects to continue providing treatment for an additional 18,000 co-infected individuals until 2026. As the price is not representative of the overall market and only applicable to procurement by for the GFATM supported co-infection program, we have not reflected this price.

It is also of note that some countries in Latin America and The Caribbean (LAC) are eligible to procure DAAs under license agreements and are able to access DAAs at globally competitive prices. For example, Guyana procures a 12-week course of SOF/DCV FDC at US$72 (EXW) prices.

37 Cost per bottle of SOF/VEL/VOX is 420,000 Rwandan Franc; Exchange rate used is Rwandan Franc/USD = 1/ 0.00079

EXHIBIT 26 In-Country prices of SOF/VEL drug for 12 weeks treatment course (US$)



Source: CHAI analysis; Ministries of Health and CHAI Partners
Notes: [1] In-country prices mentioned are public sector prices paid by the government in each country, if available, or the lowest identified private sector price if a public sector price is not available. The most recent possible pricing has been reflected. [2] Price for Egypt, China is from second edition of Hepatitis C Market Report. [3] Price for Cambodia and Myanmar is from private sector; In Myanmar the price accessed for SOF/VEL in-country is between US$233.20 – US$314.30. The range reflects differences in the official exchange rate and the market exchange rates in Myanmar

Prices for SOF/VEL vary significantly across LMICs. India continues to access SOF/VEL at the lowest price in the set of countries in Exhibit 26. Note that the price of SOF/VEL is generally higher than the price of SOF and DCV, as it is more expensive to manufacture due to higher input cost.

In South Africa, Gilead Sciences recently launched EPCLUSA which is their SOF/VEL drug at a price of ~US$389 per pack to the public sector. The medicine has recently (July 2023) been included in the Tertial/ Quaternary Hospital Essential Medicines List and a national tender is planned.

Global Reference Pricing

GFATM revised its reference prices for hepatitis drugs in 2023 with a marginal reduction in prices of DAAs.

International and regional organizations such as GFATM, the United Nations Development Programme (UNDP), and the Pan American Health Organization (PAHO) Strategic Fund have implemented central mechanisms to pool procurement orders to help negotiate lower prices with suppliers (Exhibit 27). Member states can purchase DAAs through these organizations.

GFATM's reference pricing decreased slightly for treatment courses of SOF/DCV FDC and SOF and DCV singles combination. Pricing from other global procurement mechanisms remained similar to that of 2021.

PAHO has agreements from both generics (through a partnership with GFATM) and with Gilead for countries that are unable to procure from a generic sources. Agreement with generics is restricted to supply within licensing territory. When buying through PAHO, and hence it is possible to import WHO PQ generic products without registration to any licensed territory.

EXHIBIT 27 Negotiated Prices by GFATM, UNDP & PAHO for 12 Weeks of Treatment

Mechanism	Eligible countries	DAAs	Price for 12-week treatment (EXW price)
GFATM	List	SOF+DCV	US$63
		SOF/DCV FDC	US$60
		SOF/VEL FDC	US$174
		SOF/LDV FDC	Not included in April 2023

Mechanism	Eligible countries	DAAs	Price for 12-week treatment (EXW price)
PAHO	List	SOF/DCV FDC	US$72
		SOF+DCV	US$57
		SOF/VEL FDC	US$4,050 (Innovator product price)[3] US$174 (Generic product price)
UNDP	105 Member states	SOF/DCV FDC	US$74.55
		SOF/VEL FDC	US$202.50

Source: GFATM; PAHO.
Note: 1. DAAs offered through these organizations are from WHO PQ/ERP-reviewed suppliers.; 2. Countries can access generic DAAs if they are eligible under patents by originators Gilead (SOF and SOF Compounds) and BMS (DCV compounds). In case they are not eligible under these patents, they have to procure originator products.; 3. This is a negotiated reference price that includes reductions based on volume and includes freight and insurance

High In-Country Prices

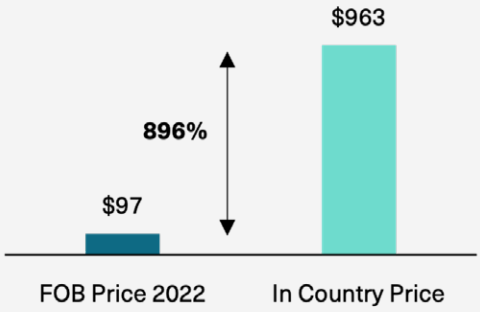
DAAs cost across some LMICs continue to be exorbitantly high due to one or a combination of the following reasons: 1. In-country price mark-ups, 2. Fragmented procurement, and 3. Lack of generic competition due to licensing and patent barriers.

In-country Price Markups

Despite a significant reduction in DAA prices, the final price to program/patients remains high and unaffordable in some countries.

Exhibit 28 showcases how FOB prices compare to in-country prices and provides an overview of potential price distortion. Price distortion and high in-country margins are common across countries that do not employ centralized procurement or have high regulatory barriers.

EXHIBIT 28 Vietnam in-country price mark-up for 12-week treatment course of DAAs (indicative example)



In Vietnam's example, there is an over 800 percent markup on the FOB price for SOF and DCV 12-week treatment course. Such price markups, which typically include insurance costs, in-country taxes and duties, logistic costs, and distributor margins, result in large increases over the FOB price. More affordable pricing may be achieved by identifying components of in-country mark-ups and devising strategies to optimize them.

Volume-Based Pricing

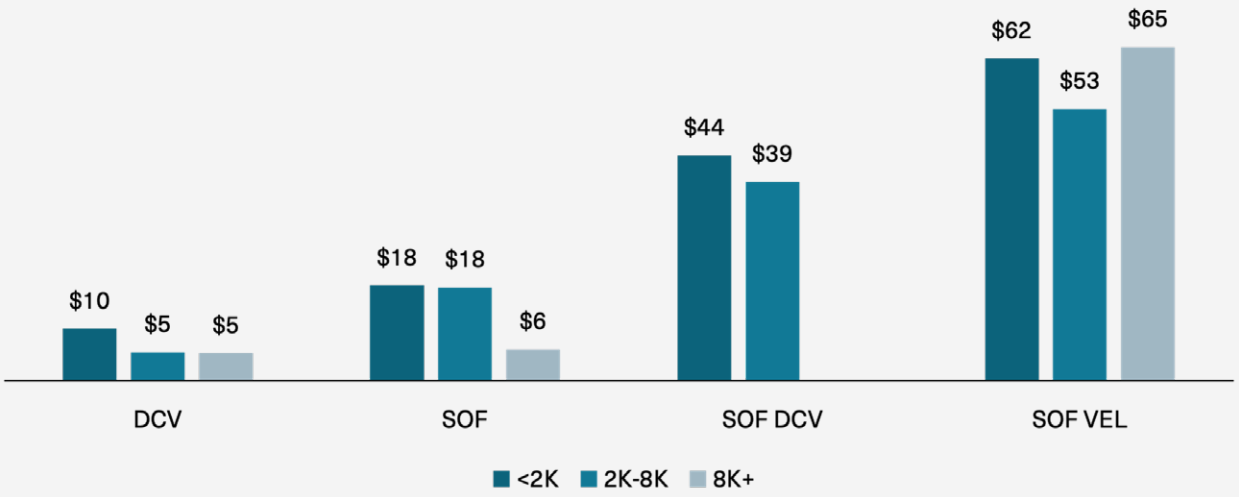
Large orders allow drug suppliers to efficiently manufacture the product and manage the supply chain, which in turn can lead to lower prices for buyers. However, the data shows (Exhibit 29) that most orders placed in 2022 were under 2,000 packs per order.

EXHIBIT 29 Number of orders placed by order size in 2022

Drug/Order Size	<2K	2K-5K	5K+	Total
DCV 60 mg	28	2	3	33
SOF	33	2	9	44
SOF/DCV	7	3		10
SOF/LDV	35	3		38
SOF/VEL	126	9	6	141
Total	**229**	**19**	**18**	**266**

On average, the unit price for small and fragmented orders was 45-65 percent more than that of larger orders (Exhibit 30). An exception to this was the trend observed for SOF/VEL. This trend can be explained by a large procurement of close to 18,000 packs by Vietnam at an average weighted price of US$84 per pack which increased the weighted average price. The other procurement transactions in this category were in the price range of US$48-US$57 per pack, which is in line with volume-based pricing.

EXHIBIT 30 Average weighted FOB price per 12 weeks treatment in 2022 by Order Size



Due to fragmented procurement and inconsistent demand, suppliers may find it difficult to achieve economies of scale in their production and inventory management processes, resulting in higher production costs. These are further inflated by the additional costs of processing and fulfilling small orders. As a result, suppliers may be forced to pass on these costs to customers in the form of higher prices, reducing their competitive advantage and potentially further limiting market demand. For buyers, the small order sizes and fragmented demand can also lead to reduced bargaining power and potentially higher costs.

Countries should instead plan their procurement strategically, including centralizing procurement, to reap the benefits of volume-based pricing. Such an approach will help countries meet the required minimum order quantity for accessing low global pricing agreements for SOF and DCV. For instance, India pools the demand for DAAs from across states and has procured DAAs in large quantities over the years. Such large volumes have allowed India to negotiate some of the lowest prices of DAAs in the world at US$39 for a 12-week treatment course of SOF and DCV in 2022.

Lack of Generic Competition Due to Licensing and Patent Barriers

Countries in the LAC region with valid patents still encounter relatively high prices for cost-effective DAAs, in contrast to many other LMICs despite regional efforts. This discrepancy arises primarily because these countries are not part of licensing agreements. For instance, Gilead's patent restrictions impact the availability of generic SOF and SOF/VEL in several LAC countries, including Colombia, Brazil, Chile, Peru, and Argentina. Consequently, these nations acquire DAAs at high prices. For instance, Brazil procured a treatment course of SOF/VEL for US$1400 (as a result of a national competitive tender with significant volumes and commitment) while others with no generic access are procuring the same medicines for approximately US$4000. These countries only have access to limited DAA regimens reducing their choice of products and prices. In 2021, Brazil granted a secondary patent to SOF, which allowed for generic production through public-private partnerships despite ongoing legal challenges related to Intellectual Property. Nevertheless, even if prices are more competitive than innovator sources, the price of SOF from these partnerships in Brazil is far from international generic sources. For countries without patents, the drugs in the region are accessible and available.

Emerging Market Trends: Adolescents and Pediatric Market

There are an estimated 3.26 million children living with chronic HCV infection globally, with 20 countries accounting for 80 percent of all cases in patients 0-18 years of age. CHAI conducted a market sizing exercise highlighting that countries with robust adult HCV programs, including Rwanda, India, Pakistan, Egypt, Mongolia, Ukraine and Georgia, could be focal countries for the expansion of pediatric HCV treatment in the next three to five years. Among these seven countries, there is an addressable market of approximately 500,000 children requiring HCV pediatric formulations. CHAI's market sizing analysis and assessment of DAA generic supplier status highlighted the importance of aligning treatment regimens for adults and children, providing the opportunity for lower pricing, streamlined procurement, and simplified service delivery. For more information please refer to the HCV Market Intelligence Report 2021 and Preliminary HBV Market Insights and Hepatitis C Market Memo 2022.

Over recent years, there have been several developments to address the access gap in pediatric treatment:

- In September 2021, 200 mg of SOF was included on the WHO Model List of Essential Medicines for Children. While 200 mg of SOF is the recommended dose in younger children, due to the challenges that small children face with swallowing tablets, a regimen comprising two 100 mg SOF tablets rather than a single 200 mg SOF tablet is preferred. Development of the preferred 100 mg SOF tablets from generics is needed to treat children with HCV. Resources will be required to support development of this product.
- In June 2022, WHO released updated guidelines on HCV testing and treatment which expanded the DAA market by recommending pan genotypic DAA regimens for adolescents and children aged 3 years and above with HCV infection, regardless of the stage of the disease. Treatment of children less than 3 years old is not recommended due to the significant occurrence of spontaneous viral clearance in young children.
- In October 2022, WHO invited manufacturers and suppliers of medicinal products for the treatment of hepatitis B and C to submit Expressions of Interest (EOI) for product evaluation to the WHO Prequalification Unit: medicines. The WHO EOI invited expressions of interest for antivirals as single-ingredient formulations for use in children, including pediatric formulations of the following DAAs:
    - DCV, tablet 30mg (preferably dispersible)
    - Ribavirin, syrup, 40mg/ml (oral)
    - SOF, tablet 100mg (preferably dispersible)
- The WHO Guideline SOF and DCV recommendation for adolescents (400/60 mg dosing if >26 kg) presents an opportunity for immediate, rapid scale-up of HCV services for this age group and weight band as the available adult formulations are accessible and affordable across a majority of LMICs. To fully capitalize on the advantages brought by WHO's guideline change, countries need to undertake several key actions. These include updating their hepatitis guidelines to align with the latest WHO updates, implementing screening programs specifically designed for young populations, integrating HCV care into existing pediatric services, and establishing robust referral networks to clinicians comfortable treating HCV in adolescents. By implementing these proactive measures, countries can successfully bring the adolescent cohort into the cascade of HCV care, close the gap in treatment options for younger children and enhance health outcomes for all.

Conclusion and Way Forward:
Diagnostic and Treatment Markets

Accessing quality and affordable diagnostic and treatment commodities is crucial to achieving global HCV elimination. This will continue to require collaborative efforts among various stakeholders, including governments, donors, and suppliers, to ensure the availability and accessibility of appropriate commodities in all LMIC settings, prioritizing populations in urgent need. The global landscape of HCV commodities presents a combination of challenges and opportunities.

The emergence of quality-assured, affordable, easy-to-use screening RDTs has improved access to decentralized testing, bringing screening closer to the point of patient care. With multiple WHO prequalified RDT options, an increasing number of suppliers are also entering the market, providing more options for simple, cost-effective, time saving RDT solutions. Despite this, the cost of RDTs per unit varies by country. Global reference pricing for RDTs indicates that the cost per test can range anywhere between US$0.80 to 1.10 (EXW) cost of RDTs. However, prices in-country can vary from US$0.21 on the low end to US$2.42 on the high end.

Access to confirmatory viral load testing remains a gap to identifying the remaining chronic HCV cases worldwide. However, GAP pricing agreements can address pricing barriers for public sector buyers to access essential diagnostics. GAP prices can range from US$9.60 to 14.90 per test (with varying terms and conditions), however, countries continue to procure tests up to US$53 on the high end, per test, due to additional cost components. The market for viral load testing is also evolving, with potential for increased access through near POC technologies, and integrating testing across disease-specific programs with multi-disease testing platforms.

The HCV diagnostic market highlights a growing body of research on emerging diagnostic technologies and approaches that have the potential to improve and simplify access to testing in resource-limited settings. Alternative approaches such as HCV cAg have the potential to simplify testing, while DBS sampling approaches may streamline the sample collection process, particularly for people living in remote areas or with difficult venous access. Furthermore, the design of professional-use screening RDTs can now be adapted to reach vulnerable populations and move health systems towards more sustainable, integrated service delivery models via HCV self-tests, peer testing, and combination RDTs, which can screen multiple diseases, a particularly useful advance in integrated settings such as in antenatal clinics.

The treatment market has experienced some wins and losses over recent years. The market for HCV DAAs remains fragmented. With demand for HCV DAAs lower than pre-pandemic levels in most LMICs, increasing uptake remains a priority. The WHO PQ market for DAAs has experienced supplier exits in recent years, indicating a potential supply security risk. While the availability of pan-genotypic regimens remains robust for now, trends must be monitored to prevent further supplier exits.

In 2023, global access pricing agreements for SOF and DCV by CHAI and the Hepatitis Fund presented a significant milestone in addressing the pricing barrier for accessing DAAs. Global access pricing enables countries to procure a 12-week course of WHO PQ'd SOF and DCV at a cost of US$60. We anticipate global access pricing agreements to encourage uptake by LMICs and enable supply security in the WHO PQ'd DAAs market. Governments must prevent high in-country cost mark-ups on drugs to allow the gains of reduced costs to transfer to the patients to widen the net of HCV treatment.

In 2022, WHO published updated treatment recommendations for all patient cohorts. These recommendations, incorporating adolescents and pediatric treatment, have created opportunities for expanding the HCV DAA market. Since the regimen recommended for adolescents >26 kg is the same as that for adults, governments must take steps to bring the adolescent cohort under the net of HCV services. Eligible adolescents must be put on SOF and DCV regimen for treatment, which is now widely available at affordable prices. Suppliers must also be encouraged to develop pediatric formulations of SOF.

To effectively address HCV, it is imperative for countries to commit to HCV diagnosis, and treatment within their public healthcare systems by developing comprehensive plans, securing partnerships, and allocating resources to implement highly impactful viral hepatitis programs. Additionally, efforts should focus on improving procurement practices, optimizing existing resources through integration, developing accurate projections, and leveraging public-private partnerships. By implementing these recommendations, countries can strengthen their healthcare systems, improve access to HCV services, and work towards achieving the global elimination targets.

Overall, HCV commodities are more affordable and cost-effective than ever before, giving governments and donors an opportunity to maximize investments and put more patients on treatment. With political will and modest financing, programs can ensure that these commodities reach patients in need to realize viral hepatitis elimination by 2030.

Preliminary Insights on Commodities Utilized for Harm Reduction Interventions

Introduction

Globally, an estimated 14.8 million people inject drugs, and are at significant risk of contracting blood-borne viruses like HCV, HBV, and HIV through sharing of needles and injecting equipment.[38] Approximately 15.2 percent of people who inject drugs have HIV infection, 38.8 percent have HCV infection, and 8.4 percent have HBV infection[39] representing a significant opportunity for screening and treatment, as well as to interrupt onward transmission through harm reduction and prevention efforts. Globally, 43 percent of new HCV infections are attributed to injection drug use with regional variations.[40] People who use drugs and/or inject drugs require a basket of services and approaches for harm reduction. Given the high rates of HCV among people who inject drugs, identifying and managing HCV is central to the provision of harm reduction services. Ensuring access to comprehensive prevention interventions, alongside diagnosis and treatment for hepatitis, is key to addressing the health needs of these communities, preventing transmission, and reaching global hepatitis elimination goals.

Harm Reduction International (HRI)[41] defines harm reduction as "policies, programs, and practices that aim to minimize the negative health, social and legal impacts associated with drug use, drug policies and drug laws. Harm reduction is grounded in justice and human rights. It focuses on positive change and on working with people without judgement, coercion, discrimination, or requiring that people stop using drugs as a precondition of support." WHO recommends a comprehensive package of interventions[42], which includes the provision of disease-specific diagnosis, treatment, and prevention interventions to reduce the risk of transmission and reinfection. This approach focuses on positive change and working with people without judgment, coercion, or discrimination.

Often, harm reduction services for individuals who inject drugs are either lacking or inaccessible due to stigma, financial burden, and discrimination.[43] These barriers can be further magnified for women in low-resource settings, who are often disproportionately affected by these challenges.

According to WHO[44], global coverage of harm reduction interventions is extremely low – nearly 100 percent (99+ percent) of people who inject drugs live in settings with insufficient, low-coverage of services. Additionally, the effectiveness of harm reduction heavily relies on the consistent availability of needed commodities in adequate doses and/or quantities. Within resource-constrained and politically regulated environments, programs, affected communities, and other stakeholders often lack visibility into commodity pricing dynamics, competitive advantages, and leverage points.

Such challenges hinder efforts to increase access and make harm reduction services more widely available to those who need them. Addressing these issues is essential for optimizing harm reduction interventions and improving outcomes for all stakeholders involved.

Scope: Range of Products Addressed in this Report

There are a variety of commodities used as part of harm reduction services and employed in syringe service programs and in the treatment of opioid use disorder. This preliminary report covers:

38 Epidemiology of injecting drug use, prevalence of injecting related harm, and exposure to behavioural and environmental risks among people who inject drugs: a systematic review
39 Epidemiology of injecting drug use, prevalence of injecting related harm, and exposure to behavioural and environmental risks among people who inject drugs: a systematic review
40 The contribution of injection drug use to hepatitis C virus transmission globally, regionally, and at country level: a modelling study; The Lancet Gastroenterology & Hepatology, Volume 4, Issue 6, 2019
41 https://hri.global/what-is-harm-reduction/
42 Consolidated guidelines on HIV, viral hepatitis and STI prevention, diagnosis, treatment and care for key populations
43 Women and harm reduction, HRI 2018
44 WHO Global HIV, Hepatitis and STIs Programs: People who inject drugs

1. Medications for Opioid Use Disorder[45] (MOUD) Commodities: Methadone and buprenorphine

Methadone and buprenorphine are medications that can help treat opioid use disorder by reducing withdrawal symptoms, cravings and reduce and preventing non-medical opioid use. They are typically given in a clinical setting and can support an individual to reduce injection drug use. WHO recommends that key populations who are dependent on opioids should be offered these products[46] as part of Opioid Agonist Maintenance Therapy (OAMT).

2. Overdose Reversal Commodity: Naloxone

Naloxone is an opioid antagonist that can reverse an opioid overdose. It is often utilized as an emergency response to an overdose and should be provided to people who use drugs as a key element of harm reduction. WHO recommends that people who are likely to witness an opioid overdose should be given naloxone to help reverse potentially fatal opioid overdoses.

3. Additional Harm Reduction Commodities: Needles & Syringes

Providing sterile needles and syringes to people who inject drugs can reduce sharing of injecting equipment, and therefore, reduce the risk of spreading blood-borne diseases such as HCV. WHO recommends that key populations who inject drugs should have access to sterile injecting equipment through Needle and Syringes Programs (NSPs), also known as Syringe Service Programs (SSPs) and Needles and Syringe Exchange Program (NSEP). Under WHO's 2030 hepatitis elimination targets, each person who injects drugs should be given 300 sterile needles and syringes per year.[47]

> In addition to needles and syringes, other injecting-related equipment may also be provided, including alcohol swabs, vials of sterile water, filters, tourniquets, mixing vessels (e.g., spoons or "cookers"), and acidifiers (e.g., ascorbic acid or citric acid powders) to assist with dissolving the substance to be injected. However, these products are not covered in this report as the market for these commodities is nascent and there is limited reliable market data available to understand market trends. It is worth noting that advocacy efforts with stakeholders and donors are underway for the inclusion of these products in funding policies. We aim to publish market intel for these products in a subsequent market reports.

The following sections present preliminary understanding of the markets for harm reduction commodities, including pricing, supplier landscape, and global manufacturing and consumption patterns.

OAMT Commodities Market Landscape: Methadone and Buprenorphine

The goal of OAMT is to minimize withdrawal symptoms, reduce opioid cravings and mitigate the risk of overdose among people who use opioids. It involves the use of medications that are agonists at the mu opioid receptor such as methadone and buprenorphine. Another example of a MOUD is the full opioid antagonist naltrexone, however use of this agent is more difficult and nuanced, requires a lead-in period of full abstinence to all opioids, and is not covered in this report. Various products are available for OAMT; however, this section focuses on products recommended by WHO for OAMT, i.e., methadone and buprenorphine.

Formulations Recommended

In the WHO Model List of Essential Medicines (EML), the following are included as 'medicines for disorders due to psychoactive substance use'[48]:

Methadone	**Concentrate for oral liquid**: 5 mg/mL; 10 mg/mL (hydrochloride). **Oral liquid**: 5 mg/5 mL; 10 mg/5 mL (hydrochloride). *The medicines should only be used within an established support program.*
Buprenorphine is recommended as a therapeutic alternative to methadone.	

45 As per 2009 WHO Guidelines for the Psychosocially Assisted Pharmacological Treatment of Opioid Dependence Opioid-use disorders are a group of conditions associated with the use of opioids. In the International Classification of Diseases (10th Edition), section F11.0–9 ("Mental and behavioural disorders due to psychoactive substance use (opioids)") contains a wide variety of disorders of different severity and clinical form, all having in common the use of opioids, which may or may not have been medically prescribed. The clinical states that may occur include acute intoxication, harmful use, dependence syndrome, withdrawal syndrome (or withdrawal state), withdrawal state with delirium, psychotic disorder, late-onset psychotic disorder, and amnesic syndrome.

46 Individuals can choose to OAMT voluntarily.

47 Interim guidance for country validation of viral hepatitis elimination (who.int)

48 WHO model list of essential medicines - 22nd list, 2021 (WHO 2021)

In addition to the formulations mentioned in the WHO EML, other formulations are also available for these products (Exhibit 31). Buprenorphine is available in several different formulations as a long-acting injectable, a newer and more innovative formulation. These products are designed as a slow-release formulation that can release steady concentrations of medication from nearly one week up to one month at a time, removing the need for daily administration. Available formulations of methadone and buprenorphine are captured in Exhibit 31.

EXHIBIT 31 Available formulation of methadone and buprenorphine[49]

Commodity	Formulation
Methadone	Oral Tablets, Sublingual Tablets, Dispersible Tablets, Oral Solution, Injectable solution, Buccal film, Powder
Buprenorphine	Sublingual tablets, Long-Acting Injectable (Injectable Weekly and Monthly), Transdermal patches, Sublingual film, Buccal film, Implant

Buprenorphine is also available in strips or tablets co-formulated with the opioid antagonist naloxone as an abuse deterrent formulation. These products are available in high-income countries and deter misuse due to the dominant action of the antagonist naloxone if these products are to be melted down and injected. As the current report is the first look at generic and widely available formulations of buprenorphine, these combination products will not be covered in this edition.

It is of note that not all formulations mentioned above are used for OAMT. For instance, buprenorphine's transdermal formulation is typically used for pain management and methadone injectable solution is not used for OAMT.

Choice of Commodity: WHO Guidelines for the Psychosocially Assisted Pharmacological Treatment of Opioid Dependence

The 2022 WHO Consolidated guidelines on HIV, viral hepatitis and STI prevention, diagnosis, treatment, and care for key populations recommends offering OAMT to key populations who are dependent on opioids. The guidelines cite the 2009 WHO Guidelines for the Psychosocially Assisted Pharmacological Treatment of Opioid Dependence[50] for further guidance on products that can be used for OAMT. It should be noted that these guidelines were published in 2009 and have not been updated since then. A summary of recommendations and findings is below:

The guidelines suggest methadone as the first line OAMT commodity and buprenorphine as the second line commodity. Reasons for buprenorphine use may include previous response to buprenorphine or lack of response to methadone, interaction between methadone and other medications taken, specific adverse effects of methadone, treatment availability, and patient preference for subjective effects of buprenorphine compared to methadone. It is also recommended that both commodities should be available and offered for OAMT.

The guidelines recommend the following doses for methadone and buprenorphine:

Methadone	On average, methadone maintenance doses should be in the range of 60–120 mg per day.	Strength of recommendation – strong Quality of evidence – low
Buprenorphine	On average, buprenorphine maintenance doses should be at least 8 mg per day.	Strength of recommendation – standard Quality of evidence – very low

These guidelines also underscore the ethical principles of autonomy and the highest standard of health, emphasizing individuals' freedom to choose participation in treatment. The WHO guidelines highlight key criteria for valid consent, including the importance of the individual's competence, freedom from coercion, and comprehensive disclosure of treatment details. People who inject drugs should be offered choices, informed in a clear and understandable manner, and have the right to refuse or stop treatment, with awareness of the consequences. Documentation of consent in medical records is essential, and the right to refuse treatment must be respected if the patient is deemed competent. Ideally, treatment choice would be individualized, as the differences between buprenorphine and methadone are nuanced. A recent systematic review[51] found higher retention rates and lower alcohol use and hospitalization in patients taking methadone. However, buprenorphine was associated with higher patient satisfaction rates, lower cravings, lower cocaine use and cardiac dysfunction. For these reasons, WHO guidelines state that it is a best practice for programs to offer both buprenorphine and methadone for opioid agonist maintenance and opioid withdrawal.

49 This list is not exhaustive
50 Guidelines for the psychosocially assisted pharmacological treatment of opioid dependence (who.int)
51 Degenhardt, Louisa et al. "Buprenorphine versus methadone for the treatment of opioid dependence: a systematic review and meta-analysis of randomised and observational studies." The Lancet. Psychiatry vol. 10,6 (2023)

Supplier Landscape

While methadone and buprenorphine do not have WHO PQ'd products in the market, SRA-approved products are available.

WHO-recommended OAMT commodities methadone and buprenorphine are not WHO PQ'd as there is no WHO PQ process, but some formulations do have SRA-approved products. Quality-assured generic products are not available across all formulations (Exhibit 32).

EXHIBIT 32 OAMT Products: WHO PQ and SRA Generics Status

Commodity	Formulation	Originator	WHO PQ	FDA/EMA-approved products
Methadone	Tablet	Dolophine	Not eligible for PQ	Products from generic are available
	Oral Solution/ Concentrate	Methadose	Not eligible for PQ	Products from generic are available. Some FDA-approved generics include[52]: Hikma SpecGX Vistapharm
Buprenorphine	Sublingual	Subutex	Not eligible for PQ	Products from generic are available. Some FDA-approved generics include[53]: Ethypharm Rhodes Pharms Sun Pharma Hikma
	Injectable long acting	Sublocade	Not eligible for PQ	US FDA approval for the originator product (Indivior); No generic product available
	Injectable long acting	Brixadi	Not eligible for PQ	US FDA approval for originator received in May 2023 (Braeburn); No generic product available

Long-Acting Buprenorphine

Long-acting buprenorphine (LAB) is an extended-release formulation that could provide a valuable alternative option for clients who wish to switch from daily dosing of the oral formulation. The cost of monthly injectable LAB in high-income markets, which has been available since 2018, is prohibitively high at over US$1,500 per month. Furthermore, no LAB product has WHO PQ status.[54] Two LAB products are available in high-income countries and have SRA approval (as shown in Exhibit 32). The long-acting formulation is not widely utilized in LMICs, apart from limited use in Ukraine.[55]

Often, individuals who inject drugs face challenges in adhering to the required frequency of taking methadone or buprenorphine daily doses because of high out-of-pocket expenses, police harassment, homelessness and difficulty protecting personal supplies, or discrimination. The demanding nature of daily jobs and routines can pose difficulties for people who inject drugs in maintaining consistent schedules to visit an OAMT center. For women in low-resource settings, household responsibilities and limited disposable income for travel fares can restrict the ability to attend an OAMT clinic frequently. The use of long-acting formulations could provide more convenience and sustainability of treatment. Long-acting formulations could help overcome barriers to medication adherence, ultimately improving the effectiveness and accessibility of OAMT for individuals, particularly women. However, to achieve this goal, market shaping efforts are necessary. Generic and more affordable LAB products need to be developed and made available in LMIC settings to enable greater access.

52 US FDA Drug Database; Accessed November 2023
53 US FDA Drug Database; Accessed November 2023
54 No WHO PQ process exists for the commodity
55 UNITAID Harm Reduction Investment

Manufacturing and Export of Methadone and Buprenorphine

Manufacturing and export of both commodities is concentrated in HICs; India is the only major manufacturer in LMICs.

Methodology

To estimate volumes, manufacturing, and consumption trends of OAMT commodities, the India Export database and International Narcotics Control Board's (INCB) reports on Psychotropic and Narcotic Substances were used.

Please also note that both products are sold in various dosages and are used in both pain management and OAMT settings. Due to a lack of details to clearly segregate the data, this report only comments on trends for the total value of products. It is not possible to discern what percentage of these products were used in OAMT settings from the export data alone.

Countries are not obligated to report data for buprenorphine to INCB, therefore, this data is self-reported. For further details on the data published by INCB, please refer to their website.

The India export data only includes the export of commodities from India to the rest of the world. It does not showcase the export of commodities from other countries and hence may underrepresent global exports of these formulations.

INCB presents data on methadone and buprenorphine manufactured in the form of kilograms manufactured each year. For this analysis a calculation of the number of patient courses manufactured in a year was done. The minimum dosing recommended in WHO's 2009 Guidelines for the psychosocially assisted pharmacological treatment of opioid dependence, has been taken for methadone and buprenorphine, specifically 60 mg for methadone, and 8 mg for buprenorphine. These are understood as standardized, minimum doses and may not be reflective of individual patient doses according to their clinical need. In clinical practice, the doses of methadone or buprenorphine are individually tailored, based on ongoing opioid use, presence or absence of concomitant chronic pain, withdrawal symptoms between doses and adverse effects. Additionally, they are administered under clinical supervision.

Methadone

Between 2015 to 2020, global methadone manufacturing was dominated by HICs at nearly 94 percent. USA and Switzerland accounted for 80 percent of these volumes. Among LMICs, India was the only country that manufactured a significant amount of reported total global production of methadone; however, this represents only about 6 percent of total methadone manufactured. No other LMICs manufactured any significant amount of methadone.

Buprenorphine

Similar to methadone, 96 percent of total buprenorphine reported between 2015 and 2020 was manufactured in HICs; the United Kingdom and the United States manufactured 70 percent of total buprenorphine. India is the only LMIC that manufactured a significant amount of buprenorphine globally at 4 percent of reported total global production. No other LMIC produced any significant amount of buprenorphine.

India's Export of OAMT Commodities in 2022[56]

Methadone. Indian generics exported methadone to eight countries for a total value of US$781,000 in 2022. These countries were Algeria, Bangladesh, Costa Rica, Kenya, Maldives, Mauritius, Saudi Arabia, and Uganda. At least 66 percent of total generics was exported to HICs and the remaining 34 percent was exported to LMICs. Mauritius and Costa Rica alone accounted for approximately 53 percent of total LMIC procurement in 2022.

EXHIBIT 33 Methadone manufactured in LMICs and HICs between 2015-2020 calculated as number of patient courses

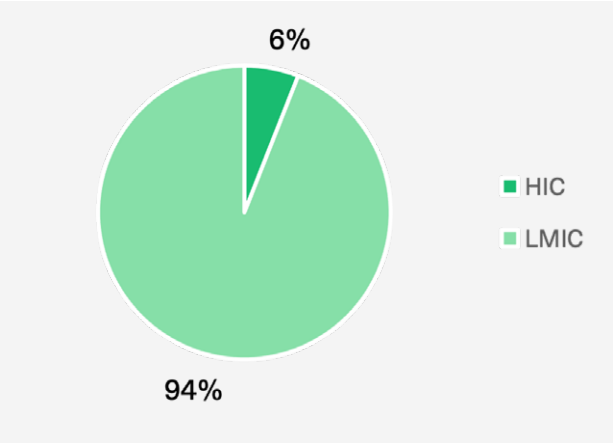
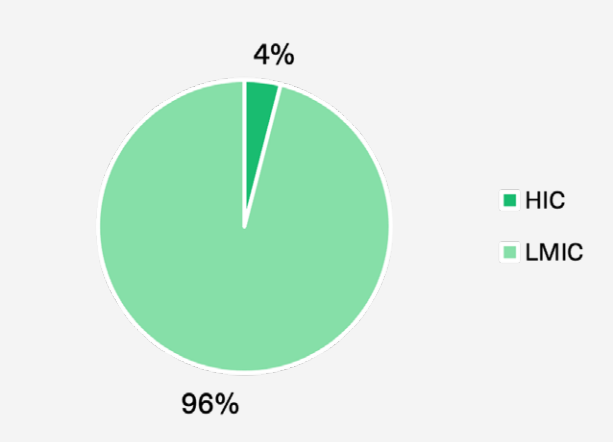


EXHIBIT 34 Buprenorphine manufactured in LMICs and HICs between 2015-2020 calculated as number of patient courses



56 Percentage of procurement by LMICs and HICs based on total value of shipments

Generics exported to these countries include three types of formulation: tablet, injectable, and concentrate. At least 85 percent of overall methadone procurement was oral concentrate formulation. This is a formulation typically used in harm-reduction settings. LMICs bought only oral concentrate while HICs bought all three formulations.

Buprenorphine. Indian generics exported buprenorphine to 8 countries for a total value of US$2.03 million in 2022. These countries were Bhutan, Cayman Islands, Germany, Hungary, Kenya, Sri Lanka, Uganda, and the USA. At least 93 percent of total procurement was to HICs and the remaining 7 percent was exported to LMICs.

Two types of formulations - tablets and patches - were exported by Indian generics in 2022 across countries. Nearly 100 percent of procured were buprenorphine tablets, and of this, 93 percent was procured by HICs. The USA accounted for 77 percent of total procurement.

Consumption of Methadone and Buprenorphine

Consumption of these commodities is disproportionately higher in HIC as opposed to LMICs; methadone consumption is two times larger than buprenorphine consumption in LMICs.

Methodology

INCB presents data on methadone and buprenorphine consumed in the form of kilograms consumed each year. For this analysis a calculation of the number of patient courses consumed in a year was done. The minimum dosing recommended in WHO's 2009 Guidelines for the psychosocially assisted pharmacological treatment of opioid dependence, has been taken for methadone and buprenorphine, specifically 60 mg for methadone, and 8 mg for buprenorphine. These are understood as standardized, minimum doses and may not be reflective of individual patient doses according to their clinical need. In clinical practice, the doses of methadone or buprenorphine are individually tailored, based on ongoing opioid use, presence or absence of concomitant chronic pain, withdrawal symptoms between doses and adverse effects. Additionally, they are administered under clinical supervision.

Exhibit 35 shows the consumption of methadone calculated as number of patient courses. About 87 percent of methadone was consumed in HICs, while 13 percent was consumed in LMICs. LMICs that consumed the highest doses of methadone were Iran, Vietnam, Myanmar, and Ukraine. They accounted for 93 percent of total consumption in LMICs from 2015-2020.

Similarly, 97 percent of buprenorphine was consumed in HICs and 3 percent in LMICs. In LMICs, India consumed the highest number of 8mg patient courses. This accounted for approximately 93 percent of total buprenorphine consumed in LMICs. It should be noted that data shows LMICs consume nearly two times more methadone than buprenorphine.

EXHIBIT 35 Consumption of methadone and buprenorphine between 2015-2020 calculated as number of patient courses

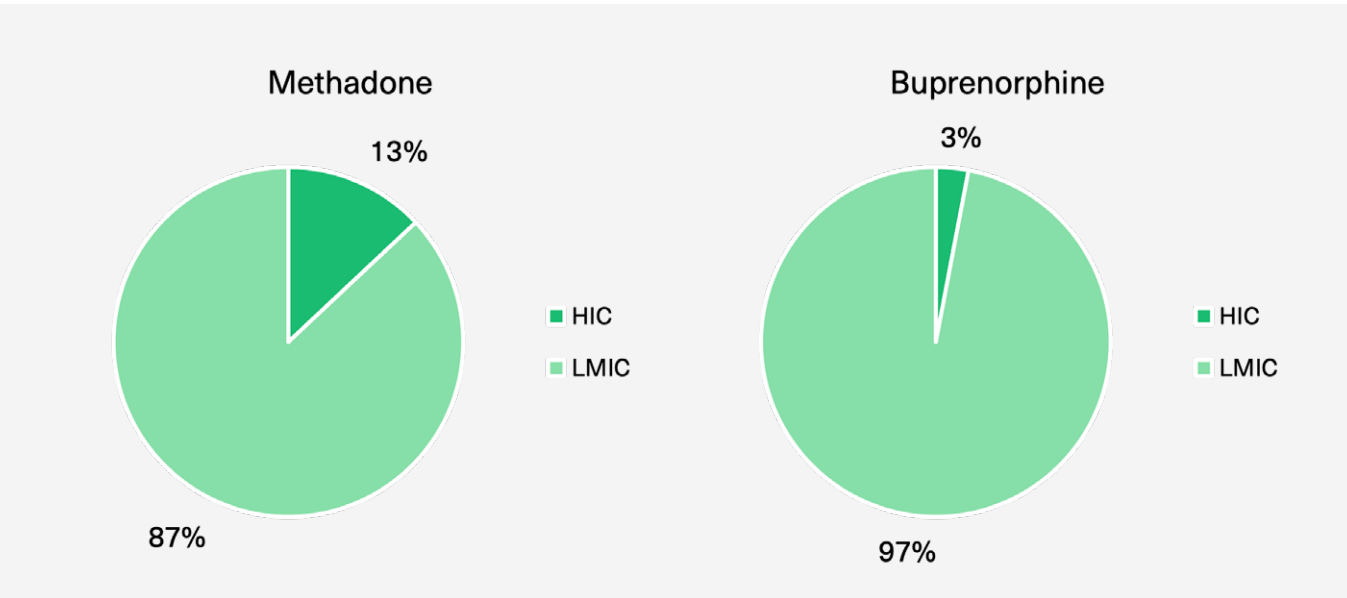


EXHIBIT 36 In-Country Pricing of Methadone & Buprenorphine (indicative)

Country	Cost of Methadone	Minimum cost per person who injects drugs per day (60 mg dosage)[57]	Cost of Buprenorphine	Minimum cost per person who injects drugs per day (8 mg dosage)[58]
India	NA	NA	Cost is ~US$0.06 per tab for 2mg buprenorphine[59]	US$0.30 per 8 mg dose
Indonesia	1000 ml bottle of 50 mg/5 ml Methadone is US$19.20	US$0.10 per 60mg dose	NA	NA
Myanmar	Methadone has been procured at ~US$16 per 1000 ml 10 mg/ml bottle	US$0.10 per 60 mg dose	NA	NA
South Africa	The Single exit price[60] of 100ml bottle of methadone 10mg/ml solution is US$22-32.	US$1-2 per 60mg dose[61]	Single exit price[62] of a Buprenorphine 2mg tablet (Subutex) is US$1.44-2.26.	US$6-9 per 8mg dose
Uganda	Cost for Methadone Hydrochloride Oral Concentration BP (5mg/ml) is US$23.55 per litre (R-Meth®)[63].	US$0.30 per 60mg dose	Buprenorphine tablets are also available at the cost of US$68.8 for a 28-tablet pack.	US$9.80 per 8mg dose

A note on the above calculation and dosing of commodities used in OAMT

For the above calculation, the minimum dosing recommended in WHO's 2009 Guidelines for the psychosocially assisted pharmacological treatment of opioid dependence has been taken for methadone and buprenorphine, specifically 60 mg for methadone, and 8 mg for buprenorphine. These are understood as standardized, minimum doses and may not be reflective of individual patient doses according to their clinical need. In clinical practice, the doses of methadone or buprenorphine are individually tailored, based on ongoing opioid use, presence or absence of concomitant chronic pain, withdrawal symptoms between doses and adverse effects. Additionally, they are administered under clinical supervision.

Overdose Reversal Products

Naloxone, the recommended commodity for overdose reversal is typically used in injectable formulations in LMICs; The scale of overdose reversal services remains low in LMICs with some countries only providing key commodities at the hospital level.

The WHO Key Populations Guidelines recommends that people likely to witness an opioid overdose should have access to naloxone and be instructed in its use for emergency reversal of suspected opioid overdose. Naloxone is a potentially lifesaving medication that can rapidly reverse an opioid overdose and is available in a variety of formulations, including injectable, intranasal, and more novel formulations such as auto-injectors pre-filled syringes.

The WHO Model List of Essential Medicines includes naloxone under essential antidotes and substances used in poisonings, with a recommended formulation of 400 micrograms in a 1 ml ampoule for injection[64]. Available formulations of naloxone are mentioned in Exhibit 37. Some formulations are suitable to be used by the general public—these include intra-nasal spray.

57 As per Guidelines for the psychosocially assisted pharmacological treatment of opioid dependence (who.int), on average, methadone maintenance doses should be in the range of 60–120 mg per day.
58 As per Guidelines for the psychosocially assisted pharmacological treatment of opioid dependence (who.int), average buprenorphine maintenance doses should be at least 8 mg per day.
59 Rate contract by Government of Rajasthan, India.
60 The single exit price (SEP) mechanism in South Africa lists the maximum price that a medicine can be charged in the private (non-government) sector. Dispensers may charge an additional dispensing fee depending on the price of the medicine. Price includes VAT and dispensing fees.
61 Please note that Methadone is registered for use for OAMT, but in the public health sector, its indication on the Essential Medicine List is limited to detoxification, not for use in OAMT.
62 The single exit price (SEP) mechanism in South Africa lists the maximum price that a medicine can be charged in the private (non-government) sector. Dispensers may charge an additional dispensing fee depending on the price of the medicine. Price includes VAT and dispensing fees.
63 Procurement of Methadone (2011 – 2019), Drug treatment in Myanmar
64 WHO model list of essential medicines - 22nd list, 2021 (WHO 2021)

EXHIBIT 37 Available formulations of Naloxone

Commodity	Formulation
Naloxone	Injectable solution, pre-filled syringe, intranasal spray

Access to naloxone varies widely. In many regions, naloxone is only available via prescription and only in medical settings, and in certain regions, naloxone availability is even limited to specific medical settings, e.g., ambulances.[65] In LMICs, take-home naloxone programs are not widespread, thereby potentially delaying lifesaving intervention by peers during an overdose.

Despite the benefits of naloxone and the need for wider access, an analysis of 199 countries[66], found that only about 10 LMICs have take-home naloxone available and 78 percent of countries did not have a naloxone peer distribution program in operation.[67]

In some countries, mainly HICs, naloxone has been introduced as an over-the-counter (OTC) medication and proactive dissemination in communities to healthcare workers, first responders, and general public has been initiated. For instance, U.S. Food and Drug Administration has approved naloxone nasal spray for OTC, non-prescription, use.[68] However, evidence of such options in LMICs is scarce.

India's Export for Naloxone

Access to naloxone is critical for managing opioid overdoses and preventing deaths. However, access to naloxone varies widely across different regions and countries.

In 2022, Indian generics exported US$2.63 million worth of Naloxone across 55 countries. However, only 4 percent of these exports were to LMICs that mostly procure injectable formulations of naloxone. The data indicated that there is limited uptake of nasal sprays and pre-filled syringes formulations by LMICs. This lack of uptake is a significant barrier to scaling up take-home naloxone or peer distribution programs in LMICs, potentially delaying lifesaving intervention during an overdose. This highlights the need for wider availability and uptake of naloxone formulations, including the exploration of new distribution channels, such as over-the-counter access in certain settings.

EXHIBIT 38: In-Country Pricing of Naloxone (indicative)

Country	Cost of Naloxone
India	Cost for injectable 1 ml ampoules of 0.4mg/ml Naloxone is US$0.50-0.70[69]
Indonesia	Injectable solution of 0.4mg/ml is typically procured at a cost of US$4.50 per 2ml vial
Nigeria	Cost for injectable 1 ml ampoules of 0.4mg/ml Naloxone is ~US$1.33
South Africa	Injectable formulation of Naloxone is available in 0.02 mg/1 ml and 0.4 mg/1 ml formulations at ~US$0.50[70]
Uganda	Naloxone injectable solution 0.4mg is available at the cost of US$9.10 per ampule. [71]

65 Community management of Opioid Overdose (WHO 2014)
66 Global State of Harm Reduction 2022 (Harm Reduction International 2022)
67 Peer distribution programs distribute naloxone to peers of injecting drug users, who may witness an overdose
68 US FDA Approves First Over-the-Counter Naloxone Nasal Spray Press Release
69 Indonesia E-Katalog
70 South Africa Master Heath Product List December 2022
71 CHAI Uganda; Butabika Mental Health Referral Hospital, Uganda

Needles & Syringes Ecosystem

Choice of needles and syringes used in harm reduction programs varies across countries and may be specific to different settings; there is a need for over three billion needles and syringes globally to reach high coverage[72] out of which only nearly 17 percent has been met.[73]

The WHO Key Populations guidelines recommend the following:

1. All individuals from key populations who inject drugs should have access to sterile injecting equipment through NSPs (strong recommendation, low certainty of evidence).
2. It is suggested that NSPs also provide low dead-space syringes (LDSSs), along with information about their preventive advantage over conventional syringes (this recommendation is conditional on local acceptability and resource availability).

UNAIDs estimates the cost of Needle–Syringe Exchange Programmes at US$23–71[74] per person per year. Considering the reduction of HIV and HCV infections through less transmission through needle-sharing, and the benefits from distribution of life-saving naloxone to reverse overdoses, such programs are cost-effective.

The choice of needles and syringes for country programs varies across countries and is dependent on factors like drug use patterns and community acceptability. Product selection should be tailored to local population needs and preferences as 'one type of syringe will not fit all needs.' Therefore, a variety of locally preferred options may need to be provided to serve the local community.

Various types of needles and syringes exist in the market that primarily differ on three design aspects: barrel capacity, needle type (detachable/attached needle, sharpness, gauge, and length), and dead space.

For instance, the Standard Operating Procedures published by India's National AIDS Control Agency (NACO) along with United Nations Office on Drug and Crime (UNODC)[75] mention that 24 and 26 gauge needles should be a part of the NSEP along with 1 ml, 2 ml, 5 ml, and 10 ml syringes. Similarly, it is expected that product recommendations and procurement will vary across countries even though there is limited information available on product choices and procurement trends of countries. Additionally, limited data on needles and syringes market prohibits further analysis.

WHO recommends that NSPs also provide low dead-space syringes (LDSSs), contingent on local preferences.

> **Low-dead space syringes and needles**
>
> LDSS and needles are recommended to reduce the transmission risk of blood-borne viruses such as HIV and viral hepatitis for community members who share injecting devices. LDSS is designed to reduce the amount of blood remaining in the syringe after completely depressing the plunger. However, local user preferences and acceptability must be considered by programs and will influence demand for such products.
>
> LDSS commonly have a non-detachable needle, which directly connects with the syringe barrel itself. This design is most commonly seen in a 1 ml syringe type and is less common in 3 ml, 5 ml, and 10 ml or larger syringes. In contrast, high dead space syringes (HDSS) consist of a detachable needle connected to a syringe.

Currently, WHO does not have any mechanism to provide prequalification to needles and syringes and these products are typically approved by local regulators and procured in accordance.

Needles and syringes are accessible at various price points in many countries. In Indonesia a unit of needle and syringe costs nearly US$0.181. In India and Myanmar, the same product costs US$0.006 and US$0.15 – 1, respectively[76]. CHAI observed that pricing in most cases is not a barrier to accessing needles and syringes.

---

72 High: >200 syringes per person who injects drugs per year; UNAID classification
73 Global coverage of interventions to prevent and manage drug-related harms among people who inject drugs: a systematic review
74 Do No Harm; Health, Human Rights and People Who Use Drugs (UNAIDS 2016)
75 Standard Operating Procedures for Needles and Syringe Exchange Program; NACO and UNODC
76 Myanmar: Needle and syringe are provided free of charge by harm reduction programs (Procurement price is not disclosed). US$0.15 – 1 is the prices accessed by the patients at private pharmacies where NSP service is not available; India: price has been extracted from the E-Aushadhi Portal.

Demand Gap

WHO recommends the following as targets for needle and syringe exchange programs:

- **WHO targets**: >200-300 sterile needles-syringes distributed per person who injects drugs per year.
- **WHO VH elimination targets**: 300 sterile needles and syringes annually per person who inject drugs.
- **2021-2026 Global AIDS Strategy target**: access to comprehensive harm reduction at 90 percent by 2025.

A report published by HRI suggests that only 92 of the 199 countries (46 percent of countries) had at least one operational NSP[77].

Another published study[78] on global coverage of interventions to prevent and manage drug-related harms among people who inject drugs highlighted globally that on average 35 needles and syringes are distributed per person who injects drugs per year. This indicates that most countries have low coverage of OAMT and NSPs, leaving most persons who inject drugs without access to these essential harm-reduction services.[79] and by definition, setting up conditions in which they are more likely to re-use and share needles and syringes.

These reports indicate an unfulfilled demand gap in the market which suppliers can leverage. Globally, 518 million needles and syringes were distributed through NSP sites within 12 months[80], but there is a need for over three billion needles and syringe distribution annually through these NSP sites to achieve high coverage.

It is worth noting that, market intelligence for these products being used and procured for harm reduction programs remains restricted as there is a lack of insight into country-level needles and syringe volume data, appropriate guidance on the quality status and requirements for these commodities, and availability of the most appropriate product designs for use in NSP across countries.

Country Wise Market Intel Snapshot

CHAI collected quantitative and qualitative information regarding harm reduction programs funding, size of target population and availability and accessibility of OAMT commodities, needles and syringes distribution, and overdose reversal commodities across select countries. These countries were selected based on the availability of commodities within their healthcare systems and access to information.

Several countries beyond the seven showcased in the table are in the process of initiating harm reduction programs. For instance, Ethiopia is actively working towards launching harm reduction initiatives and is currently in the resource mobilization phase to establish these services. In 2023, Ethiopia's government unveiled the HIV/AIDS National Strategic Plan 2023-2027, which includes a focus on harm reduction as one of its key components. This plan outlines strategies for the implementation and scaling of harm reduction services for various key populations, including people who inject drugs. The strategic plan encompasses a range of services, such as medically assisted therapy, including opioid substitution therapy, drug overdose treatment, needle and syringe distribution through private pharmacies and social marketing, and integration with HIV, HCV, and sexual and reproductive health services.

The following table showcases a snapshot of services and commodity market intel available across several countries. The information was collected with the support of several in-country stakeholders and CHAI country teams.

77 Global State of Harm Reduction 2022 (Harm Reduction International 2022)
78 Global coverage of interventions to prevent and manage drug-related harms among people who inject drugs: a systematic review
79 Low: <100 syringes per person who injects drugs per year; Medium: 100–200 syringes per person who injects drugs per year ; High: >200 syringes per person who injects drugs per year; UNAID classification
80 Global coverage of interventions to prevent and manage drug-related harms among people who inject drugs: a systematic review

EXHIBIT 39: Country Wise Market Intel Snapshot

Country	People who Inject Drugs	Program Funding	OAMT Commodities		Needles and Syringes Distribution	Overdose Reversal
			Methadone	Buprenorphine	Needles and Syringes	Naloxone
Cambodia	3,200[81]	• GFATM supports NSP in Cambodia. • The government of Cambodia provides funding support for supports methadone maintenance therapy (MMT).	• Currently methadone based OAMT is available in two public hospitals in Phnom Penh. • Cost of methadone in country was unavailable.	• Use of buprenorphine for OAMT was not observed.	• High dead space syringe with detachable needles are used in the program. The unit cost for 1cc/3cc needle and syringe is US$0.03 per unit[82]. • NSP program plans to increase coverage to 4 needles and syringe per person, per day. This will amount to 1,400 needles and syringes per person per year.	• Overdose management services are not available in the public sector yet. • Plans for the introduction of Naloxone in public health settings are currently underway.
India[83]	177,000+	• Harm reduction program is domestically funded by the government.	• Methadone is used in OAMT settings in India, however, not at scale. • Cost of commodity was not available.	• Buprenorphine is widely used in OAMT program. • Cost of Buprenorphine per 2mg tablet is US$0.06[84].	• Needles and syringes are provided to persons who inject drugs. • Cost of commodities is approximately US$0.006 needle and US$0.016 syringe[85].	• Naloxone is used for Overdose reversal/ management in the country. • Cost for injectable 1 ml ampoules of 0.4mg/ml Naloxone is US$0.50-0.70[86].
Indonesia	27,000[87]	• The funding for harm reduction services mainly comes from the GFATM, and the government of Indonesia.	• Methadone is the primary commodity used for OAMT in Indonesia and MMT is offered in several areas including in prisons via 92 MMT sites. • Methadone is procured by the Ministry of Health and provided for free. In some cases when clients may not have national insurance, a fee of ~US$0.5 as administration fee. • A 1000 ml bottle of 50mg/5ml Methadone is US$19.2[88].	• Buprenorphine tablets in combination with Naloxone (Suboxone) are provided as part of OAMT. • While single tablets for Buprenorphine have been available in the country for over a decade, there are currently restrictions on who can provide it as misuse of buprenorphine has been reported. • Buprenorphine cost was unavailable.	• The needles and syringes now recommended for distribution are of size 1 mL (26G X ½ inch) and needles of size 26G X ½ inch and 24G X 1 inch. • One unit of a needle and syringe costs ~US$0.181[89].	• Naloxone injection is typically used for the same and provided by public hospitals. • A 2ml Naloxone injectable solution ampoule (0.4mg/ml) is typically procured for US$4.5 per vial[90].

81 Key Populations Atlas from UNAIDS
82 CHAI Country Team Analysis
83 National AIDS Control Organization (2022). Sankalak: Status of National AIDS Response (Fourth Edition, 2022). New Delhi: NACO, Ministry of Health and Family Welfare, Government of India
84 Indian State Government Rate Contract Price: Rajasthan Government Rate Contract
85 Pricing in e-aushidi portal of the Government of India
86 Indian State Government Rate Contract Price: Rajasthan Government Rate Contract
87 Key Populations Atlas from UNAIDS
88 Indonesia E-Katalog price for Jakarta
89 CHAI Country Team Analysis
90 Indonesia E-Katalog price for Jakarta

Country	People who Inject Drugs	Program Funding	OAMT Commodities		Needles and Syringes Distribution	Overdose Reversal
			Methadone	Buprenorphine	Needles and Syringes	Naloxone
Myanmar	~93,000	• The funding for harm reduction services mainly comes from GFATM, the government of Myanmar contributes US$15 million annually with expected increment of US$1 million per year for investments in antiretroviral therapy commodities and methadone[91]. • Some other donors are also supporting the harm reduction program in Myanmar.	• Methadone is the only OAMT commodity used in the country and was introduced in early 2006 as part of MMT services. • A 1000ml bottle of 10mg/ml Methadone has been procured at ~US$16 per bottle.	• The government in Myanmar has plans to introduce Buprenorphine to 3% of OAMT patients and gradually scale up to 10% of the patients.	• Myanmar also operates an extensive needles and syringes exchange program through which 44.2 million sterile needles and syringes were distributed across seven states and regions in 2021. • This is equivalent to an average of 463 needles and syringes per person who inject drugs per year, which is above defined targets. • Cost of needles and syringes is US$0.15 – 1[92].	• Myanmar currently provides overdose management services using naloxone in hospitals, drug treatment centres (DTCs), and community-based drop-in centres. • Commodity cost was not available.
Nigeria[93]	~80,000[94]	• Program funding for harm reduction is primarily from GFATM and ViiV Healthcare. • Both organizations are supporting scale up of harm reduction services with combined investments of over US$2.5 million[95].	• Methadone is included in the country guidelines for medication assisted treatment for opioid dependence. However, implementation of medication assisted treatment currently unavailable in-country[96].	• Buprenorphine is included as part of medically assisted treatment however roll out of services yet to commence in-country[97].	• Implementation of the Needle Syringe Program in country commenced in 2021 following pilots by partners in country from 2019-2020. • There are ongoing efforts to scale up the NSP to additional states in country. • Cost of 1 unit of 1ml needles and syringes is ~ US$0.003.	• Naloxone is recommended for overdose reversal in the country guidelines however access and availability are limited. • Cost for injectable 1 ml ampoules of 0.4mg/ml Naloxone is ~US$1.33.

91 National Strategic Plan on HIV and AIDS, Myanmar (2021 – 2025)
92 Myanmar: Needle and syringe are provided free of charge by harm reduction programs (Procurement price is not disclosed). US$0.15 – 1 is the prices accessed by the patients at private pharmacies where NSP service is not available.
93 Exchange Rate used: 750 Naira/USD
94 UNODC Drug Use in Nigeria Survey, 2018
95 HRI Financing Landscape Analysis in Nigeria, 2022
96 FMOH National Guidelines for the Treatment of Substance Use Disorders for Nigeria
97 HRI Financing Landscape Analysis in Nigeria, 2022

Country	People who Inject Drugs	Program Funding	OAMT Commodities		Needles and Syringes Distribution	Overdose Reversal
			Methadone	Buprenorphine	Needles and Syringes	Naloxone
South Africa[98]	82,500[99]	• Currently there are no major OAMT services provided in the public healthcare system. • GFATM and PEPFAR/CDC are the major funders of Harm Reduction services, which are implemented by civil society organisations. • One municipality funds a harm reduction programme with co-funding from PEPFAR/CDC. • PATH is preparing for the implementation of a UNITAID-funded project for the Prevention of hepatitis C among people who inject drugs. This includes work around the introduction of long-acting depot buprenorphine and low dead-space syringes[100].	• Methadone is registered for use for OAMT, but in the public health sector, its indication on the Essential Medicine List is limited to detoxification, not for use in OAMT. • The single exit (non-government/ private sector) price[101] of 100ml bottle of methadone 10mg/ml solution is US$22-32 and for a 1000ml bottle of 10mg/ml methadone is US$225-250[102,103].	• Buprenorphine is registered in RSA and available, but it is not on the public sector Essential Medicines List. • This impedes the public sector from procuring and using buprenorphine for OAMT services. • Single exit price[104] of Buprenorphine 2mg[105] tablet (Subutex) is US$1.44-2.26.	• Even though funding from GFATM for implementing NSP has increased, program coverage is low at only ~30% of the WHO target of 200 per person per year[106]. • Single-use Insulin syringes with barrel capacities of 1ml and needle gauges 29Gx1/2 are used in NSPs.	• There is no formal community distribution of the naloxone program in RSA. • Naloxone is available in harm reduction service centers and emergency units; limited take-home naloxone service in one site. • In RSA, the injectable formulation of Naloxone is available in 0.02 mg/1 ml and 0.4 mg/1 ml formulations. • These formulations are available at a price of ~US$0.50[107].

98 Exchange Rate used: 0.056 Rand/USD
99 UNAIDS Key Populations Atlas
100 PATH work in South Africa
101 The single exit price (SEP) mechanism in South Africa lists the maximum price that a medicine can be charged in the private (non-government) sector. Dispensers may charge an additional dispensing fee depending on the price of the medicine. Price includes VAT and dispensing fees.
102 Single Exit Price RSA: MPR (Medicine Price Registry) - (medicineprices.org.za)
103 Due to dispensing regulations the 100ml methadone bottle of the 10mg/ml formulation is typically used
104 The single exit price (SEP) mechanism in South Africa lists the maximum price that a medicine can be charged in the private (non-government) sector. Dispensers may charge an additional dispensing fee depending on the price of the medicine. Price includes VAT and dispensing fees.
105 Single Exit Price RSA: MPR (Medicine Price Registry) - (medicineprices.org.za)
106 HRI Financing Landscape Analysis in South Africa
107 South Africa Master Heath Product List December 2022

Country	People who Inject Drugs	Program Funding	OAMT Commodities		Needles and Syringes Distribution	Overdose Reversal
			Methadone	Buprenorphine	Needles and Syringes	Naloxone
Uganda	~7,356	• Program funding comes primarily from donors. • GFATM, PEPFAR/CDC, and USAID are the main donors involved in providing assistance for procuring harm reduction commodities including needles and syringes.	• Methadone suspension (5mg/ml) is used in OAMT. This are supplied in 1000ml bottles, dispensed using a machine called Methameasure. • Cost for Methadone Hydrochloride Oral Concentration BP is US$23.55 per litre (R-Meth®).	• Buprenorphine is also used in OAMT setting in Uganda. • Buprenorphine tablets are also available at the cost of US$68.80 for a 28-tablet pack.	• Civil Society Organizations play a key role in providing needles and syringe distribution services in Uganda. • Typically, auto-disable needles and syringes of 2ml and insulin needles and syringes are distributed as part of NSP. Commodity prices were not available however, they were reported to be cheap.	• Overdose reversal is offered across all facility levels, up to community if available. • Civil society organisation in the harm reduction space are permitted to provide overdose reversal using Naloxone through trained personnel. • Naloxone injectable solution 0.4mg is available for overdose reversal at the cost of US$9.10 per ampule.
Brazil[108]	~406,000	• There is limited understanding of the funding landscape in Brazil. • There is no public program for OAMT in the country[109]. • Doctors in the public health system may prescribe OAMT. Services in the public health system are provided free-of-cost to the patients.	• Methadone and buprenorphine have been incorporated into the Public Health System, however, used mostly for the management of chronic pain. It is not clear how much of the procured products are utilized for OAMT. • Methadone suspension (10mg/ml, 1ml vial) is priced at US$2.83 per vial on average, and Methadone in tablet form (5mg and 10mg) is priced at US$0.21 per 10mg tablet and US$0.60 per 5mg tablet on average.	• Buprenorphine is available in the public sector in Brazil, but there is limited understanding of its use in OAMT. • Buprenorphine is available in transdermal patches of 5mg, 10mg and 20mg. • Buprenorphine patches are priced at US$14 on average, with negligible price differentiation amongst the different drug concentrations.	• There is no needle and syringe distribution program[110] in the country.	• Naloxone is available in 0.4mg/ml and a 1ml vial costs US$1. • Use of Naloxone is restricted to hospitals in the country. There is no take-home naloxone program in country[111].

Source: CHAI Analysis, CHAI Country Teams; Butabika Mental Health Referral Hospital, Uganda, Infectious Diseases Institute, Uganda and Ministry of Health AIDS Control Program, Uganda; Andrew Scheibe, TB HIV Care and University of Pretoria; Treatment Action Group, PAHO
Note: Information captured in the table is indicative.

108 Treatment Action Group, PAHO
109 Global State of Harm Reduction 2022 (Harm Reduction International 2022)
110 Global State of Harm Reduction 2022 (Harm Reduction International 2022)
111 Global State of Harm Reduction 2022 (Harm Reduction International 2022)

Conclusion & Way Forward

Harm reduction can help reduce the overall burden of HCV in the community. By preventing new infections and improving the health outcomes of people living with HCV and those at risk, harm reduction strategies can contribute to the global goal of eliminating HCV as a public health threat. It is imperative, especially within the scope of HCV prevention, to improve the availability and accessibility of harm reduction commodities to LMICs over the next decade[112].

Key Barriers to the Provision of Harm Reduction Services in LMICs

The current state of the harm reduction market is characterized by three significant problems: inadequate harm reduction services in countries, market opacity, and insufficient program funding.

Globally, harm reduction services are not available at the level and scale required. Limited political commitment, challenging policy environments and a lack of prioritization within the healthcare system pose a challenge to harm reduction programming globally.[113] This gap in harm reduction programming across LMIC is hindering the achievement of global elimination agendas for diseases like hepatitis which disproportionately affect people who inject drugs.

Market transparency and an understanding of market dynamics play a key role in effective harm reduction programming and helps in the identification of opportunities for market shaping. While harm reduction commodities are not widely accessible and can be expensive in some settings, there is a limited understanding on in-country market barriers. Many countries only provide limited supplies and product options of essential harm reduction commodities used in OAMT and NSPs. Access to overdose reversal commodities is often limited to medical settings, despite guidelines[114] recommending wider access and peer-friendly naloxone and training for those likely to witness an opioid overdose. These gaps in accessibility and sometimes affordability of products are addressable, but the lack of market intelligence hinders this process.

In 2021, HRI published a report on the 'Failure to Fund: the continued crisis for harm reduction funding in low- and middle-income countries' highlighting that funding for harm reduction is at 5 percent of the level required by LMICs[115]. Where harm reduction programming exists, it is often funded through a mix of domestic and donor budgets. Among donors in 2019, GFATM accounted for 60 percent of funding. To increase the coverage and access of harm reduction, greater investments will be needed. The GFATM latest policy supports countries to implement comprehensive harm reduction including OAMT, sterile needles and syringes, overdose prevention (naloxone), hepatitis screening and treatment and other elements of the WHO recommended package. Other funders include the US President's Emergency Plan for AIDS Relief (PEPFAR) and Open Society Foundation.

HCV Prevention and Harm Reduction Services Are Urgently Needed

Across LMICs, governments have committed to eliminating diseases like viral hepatitis. However, without providing adequate harm reduction services at scale and removing major implementation and access barriers, eliminating viral hepatitis will not be possible. With the right market intelligence to inform market shaping efforts, existing and newer innovative commodities can be introduced or scaled in LMICs to ensure that people who inject drugs have access to affordable products.

Access to harm reduction must be in accordance with community priorities, preference, and needs. It is also crucial that service access and availability be looked at from a gender lens. Women are subject to health inequities including limited access to harm reduction services[116]. Lack of gender-sensitive policies can leave women underserved and the specific issues they may face poorly understood[117]. Such elements must be taken into consideration with the implementation of harm reduction programs.

Suppliers should be encouraged to enter access markets. Governments must also improve demand estimation and procurement planning to meet the needs of the target population consistently. These practices enable governments to access products at affordable rates, avoid procurement delays, and stockouts.

This report serves as a crucial initial step towards achieving greater market transparency for harm reduction commodities and facilitating the development of programs that can effectively address the challenges in this domain. Further research and analysis are necessary to gain a comprehensive understanding of market trends in this area.

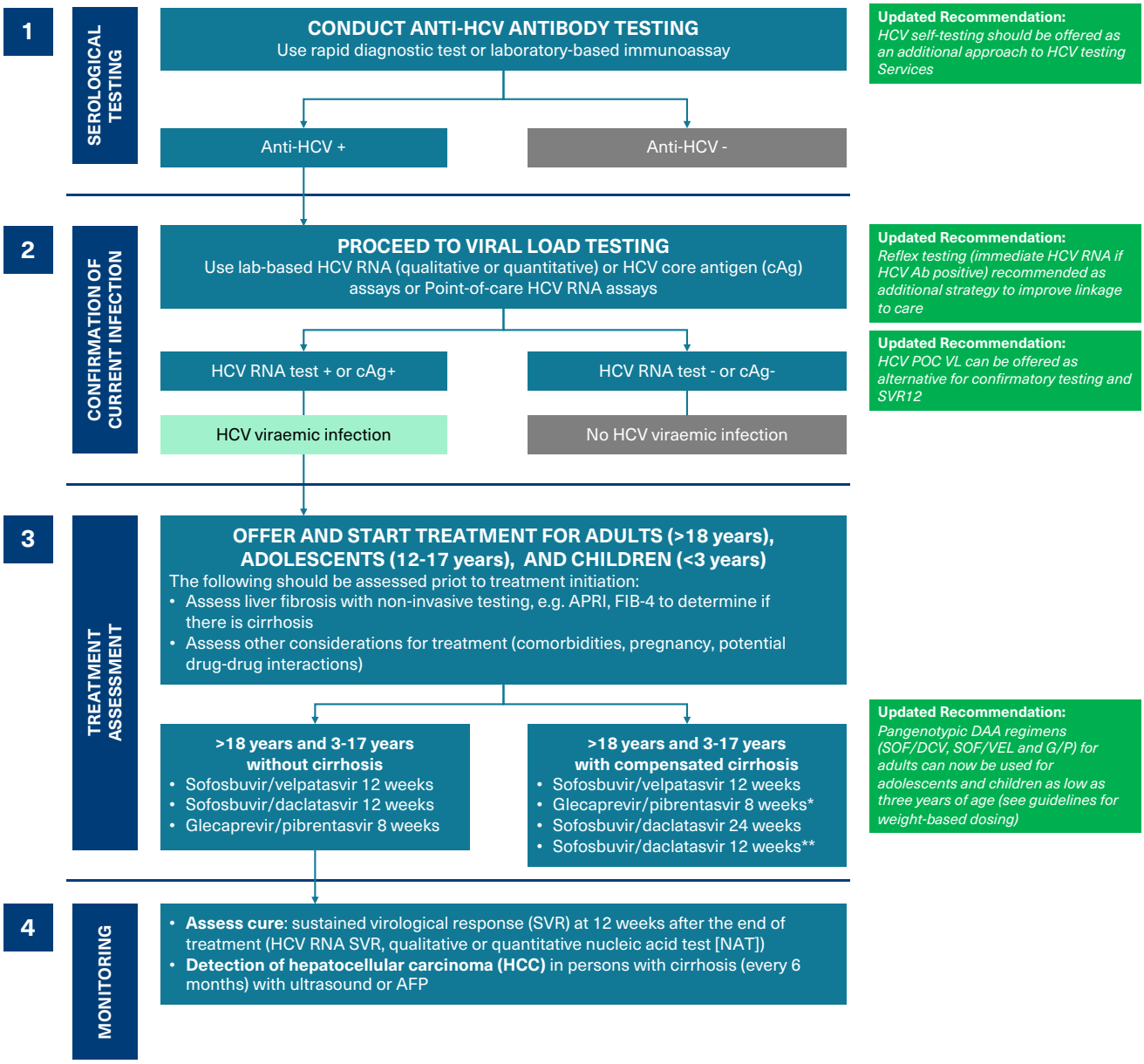
Moreover, to effectively address the challenges identified in this report, it will be necessary to formulate interventions on the back of greater market transparency, specifically in the context of LMICs. Investments in further country landscaping and analysis can support a better understanding of the market dynamics, identification of gaps and opportunities, and development of strategies to drive impact.

112 WHO's goal of eliminating viral hepatitis by 2030
113 The Global State of Harm Reduction 2022
114 WHO Key Populations Guidelines 2022
115 https://hri.global/wp-content/uploads/2022/10/HRI-FAILURE-TO-FUND-REPORT-LOWRES.pdf
116 Women and barriers to harm reduction services: a literature review and initial findings from a qualitative study in Barcelona, Spain
117 HRI: Women and harm reduction

Appendix

Appendix 1: Summary of WHO recommended HCV guidelines

At the time of publication, the updated WHO HCV testing and treatment algorithm can be found in the Updated recommendations on simplified service delivery and diagnostics for hepatitis C infection (see here). The algorithm below has been adapted to reflect updated changes.



** Persons who failed prior therapy with interferon, ribavirin, and/or sofosbuvir with HCV genotype 1, 2, 4-6 with cirrhosis should be treated for 12 weeks, and with HCV genotype 3 with or without cirrhosis should be treated for 16 weeks.*

Diagnostics Algorithm

The WHO recommends a simplified, two-step algorithm to diagnose HCV. First, a blood test to screen for HCV antibodies, using either a RDT or lab-based immunoassay (IA) is performed. A positive antibody result indicates that the individual has been exposed to the pathogen. While someone may have antibodies against the pathogen due to exposure, their immune system may have successfully cleared the virus from their body.

> ***NEW***: In July 2021, WHO published recommendations and guidance on hepatitis C virus self-testing (see here). The updated recommendations states that HCV self-testing should be offered as an additional approach to HCV testing services (strong recommendation, moderate-certainty evidence.

A subsequent RNA nucleic acid VL test is therefore performed for individuals who screen positive for HCV antibodies to confirm active viremia prior to initiating treatment. When RNA testing is not available, detection of HCV core antigen (HCV cAg) may serve as confirmation of viremia. Twelve weeks after completing a full treatment course, a VL test is recommended to provide a confirmation of HCV cure. Due to the sensitivity required for SVR12 however, HCV cAg testing is not recommended for confirmation of cure. The need to maintain VL testing for SVR12 is therefore essential and cannot be replaced solely through the use of quantification of cAg in the diagnostics cascade. In targeting elimination as set by the WHO, testing needs to be cost-effective and streamlined. Screening using rapid antibody tests and confirmation of viremia and cure by VL is therefore the method most often employed in elimination programs.

> ***NEW***: In July 2022, WHO published recommendations stating the use of HCV point-of-care (POC) viral load NAT assays can be an alternative approach to laboratory-based HCV RNA NAT assays to diagnose HCV viremic infection. Furthermore POC HCV RNA assays with comparable limit of detection to laboratory-based assays can be used as an alternative approach for the test of cure (i.e. SVR12).

> ***NEW***: In July 2022, WHO recommends the use of reflex testing in those individuals with positive HCV antibody test results as an additional key strategy to promote linkage to care and treatment. Reflex testing can be laboratory-based whereby a single sample is collected and used for both antibody and HCV RNA testing or clinic-based whereby two samples are collected in the same session/clinic visit and used to conduct an antibody test and link, if results are positive, to a HCV RNA test.

Previous diagnostic guidelines recommended the use of viral load monitoring at week four and required the determination of the viral genotype to enable appropriate treatment. The current diagnostics cascade, recommended by WHO in 2018, is simplified from the previous guidance. Assessing viral load at week four has been eliminated due to the lack of evidence correlating viral load at week four with those who achieve cure. In addition, when pangenotypic DAAs are utilized in treatment, genotyping is not required, thereby significantly reducing the cost and complexity of testing.

> ***NEW***: In July 2022, WHO recommends the use of pangenotypic DAA regimens for the treatment of all adults, adolescents and children ages 3 years and above with chronic hepatitis C infection, regardless of stage of disease:
>
> - Adults (≥18 years)1: strong recommendations; moderate certainty of evidence
> - Adolescents (12–17 years)2 : strong recommendation; moderate/low certainty of evidence
> - Older children (6–11 years): strong recommendation; moderate/very low certainty of evidence
> - Younger children (3–5 years): conditional recommendation; very low certainty of evidence

Appendix 2:
List of HCV High-Burden/Low- and Middle-Income Countries

Ukraine	Ethiopia	Armenia
Georgia	Uganda	Myanmar*
Uzbekistan	Tanzania	Nepal
Kyrgyzstan	Zimbabwe	India*
Mongolia	South Africa	Rwanda*
China	Cameroon	Mexico**
Cambodia*	Nigeria*	Brazil**
Thailand	Sierra Leone	Pakistan
Philippines	Morocco	Malaysia
Vietnam*	Egypt	
Indonesia*	Colombia**	
Peru**	Argentina**	

**CHAI Program Countries*
***LATAM Countries*
Note: This report focuses primarily on high-burden LMICs across Asia and Africa and high-burden countries in Latin America.

Appendix 3: India export data analysis methodology

The India Export Database has been used for analysis of export of treatment and harm reduction commodities by Indian manufacturers. It can be accessed via a license.

The database provides details on the volumes and prices of drugs exported from India to the rest of the world. The data has relevant details on date of export, importer name, the product exported and the country to which it was exported, size of the export order, and the freight on board price. FOB prices are the prices at which the supplier exports the drug from the country. These prices do not include shipping, customs, storage, and distributor-associated costs. Usually, there are in-country costs added to the FOB/EXW price, resulting in a higher final price to the buyer.

Database Limitations

1. Does not account for the use or export of drugs manufactured outside India including sales or donations by originators.
2. The transaction data is not available in a standardised manner and is sometimes incomplete. Certain assumptions and judgement need to be exercised to clean the data for analysis.
3. The database has several identical transactions.

These limitations may lead to underestimating the volume of drugs procured across LMICs.

Brief on the methodology used to perform analysis of India export data:

1. Commodity volume for each transaction is sorted and standardised to represent number of packs. Any further analysis is done for one pack.
2. Entries that are identical are removed to avoid data duplication.
3. Entries with abnormally low pricing or low volume are not considered for the analysis.
4. Weighted average prices per pack are calculated to ensure a more accurate representation of the mean and avoid distortion.
5. Triangulate aggregated analyses with other sources such as MPP data on daclatasvir sales reported by sublicensees.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