ACTIVIST STRATEGIES

for Increasing Access to HCV Treatment in Low- and Middle-Income Countries

TAG

Treatment Action Group

HCV Webinar Series

Webinar #2:

Direct-Acting Antivirals Drastically Simplify HCV Diagnosis and Monitoring

Presenter: Dr. Teri Roberts, Senior Scientific Officer, Hepatitis and HIV, FIND (Foundation for Innovative New Diagnostics), Geneva

FIND

TAG HCV Webinar Series: Direct Acting Antivirals Drastically Simplify HCV Diagnostics and Monitoring

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10 December 2015

Introduction to FIND

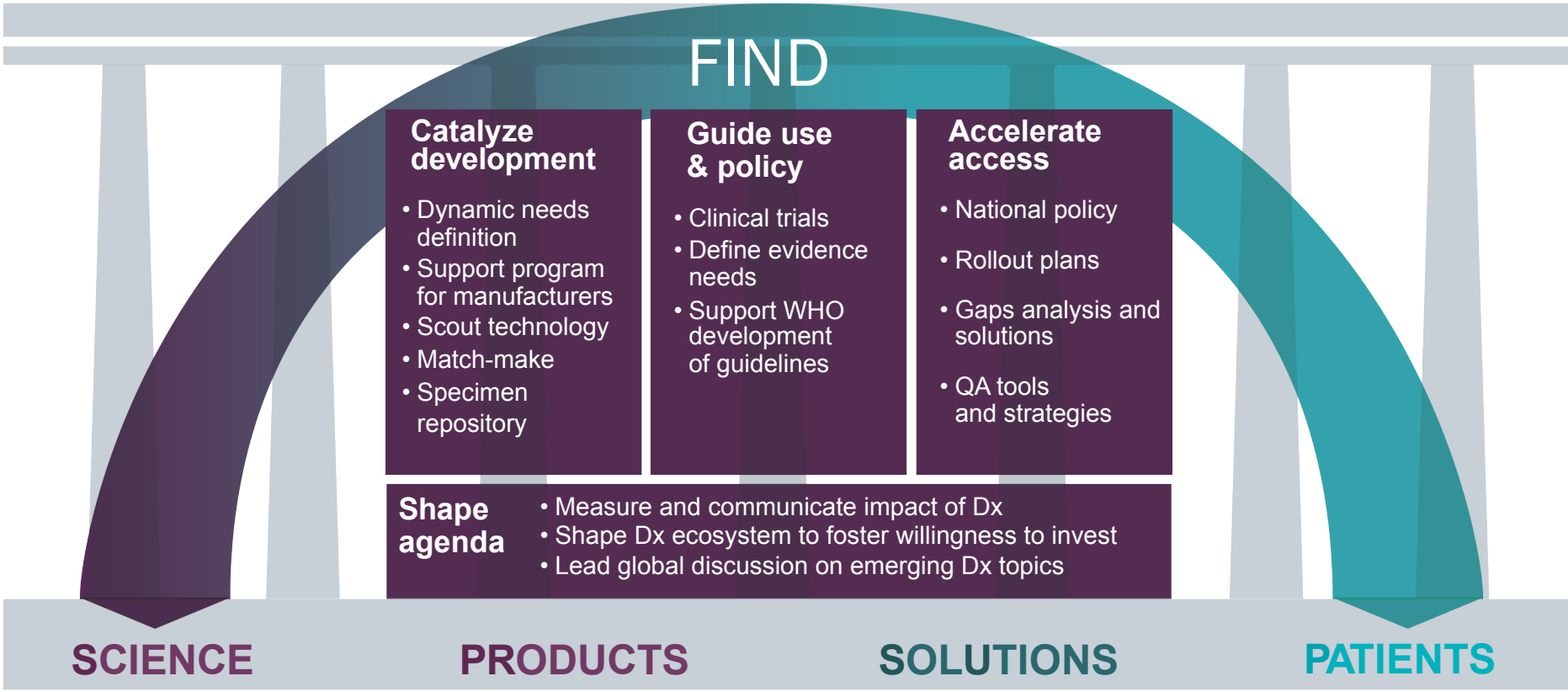
Why Diagnostics Matter

Diagnosis equals knowledge:
To enable accurate treatment, to target healthcare interventions, and to measure progress.

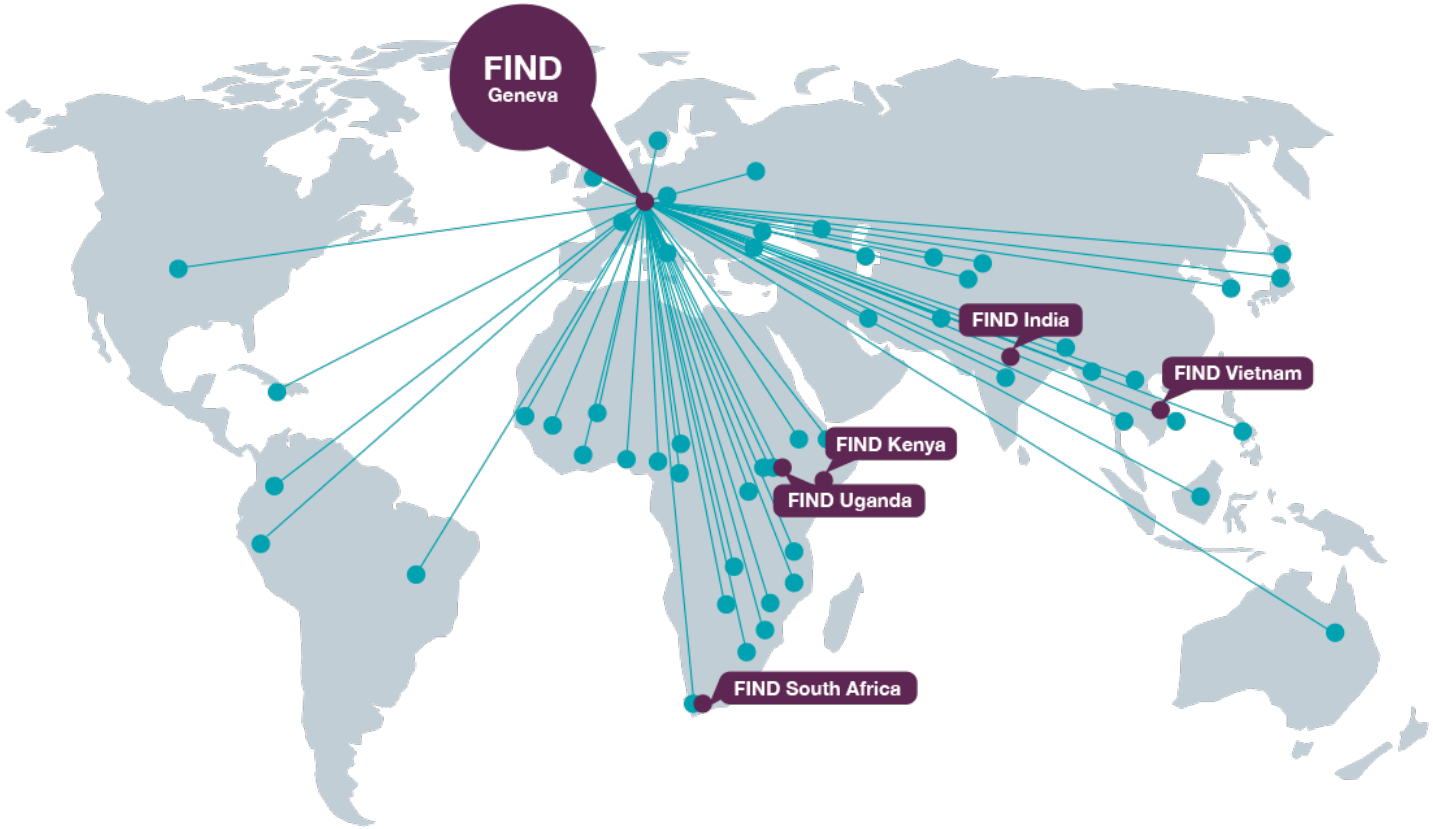
Enable control, elimination and eradication of diseases.

- The global community needs diagnostics to target interventions, identify outbreaks, and monitor progress towards goals.

Turning Complex Diagnostic Challenges Into Simple Solutions To Transform Lives



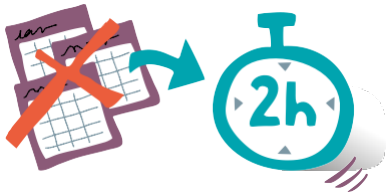
Working With 185 Partners Globally And Forming Coalitions, Always With The End In Mind



Universities and Research Institutes	Industry	Government/ multilateral agencies	Advocacy	Clinical Trial Sites	Implementing partners
• 44 partners	• 46 partners	• 35 partners	• 2 partners	• 32 partners	• 26 partners

Significant Progress Achieved In The Last 10 Years

TB

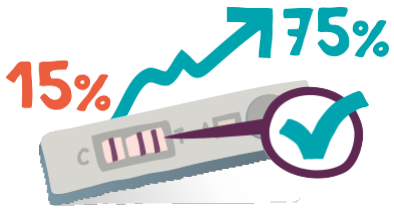


Patients can now get drug susceptibility testing in 2 hours at a district hospital. This used to take up to 120 days and was only available at national reference labs.

Sleeping sickness

The development of a rapid diagnostic test has helped make disease elimination a reality.

Malaria



Joint FIND-WHO efforts to assure the quality of rapid tests have increased the % of quality products in use from 15% to 75%.

HCV: High-priority target product profile for hepatitis C diagnosis in decentralized settings: Combined TPP for HCV diagnostics following consensus process

High-priority target product profile for hepatitis C diagnosis in decentralized settings:

Report of a consensus meeting

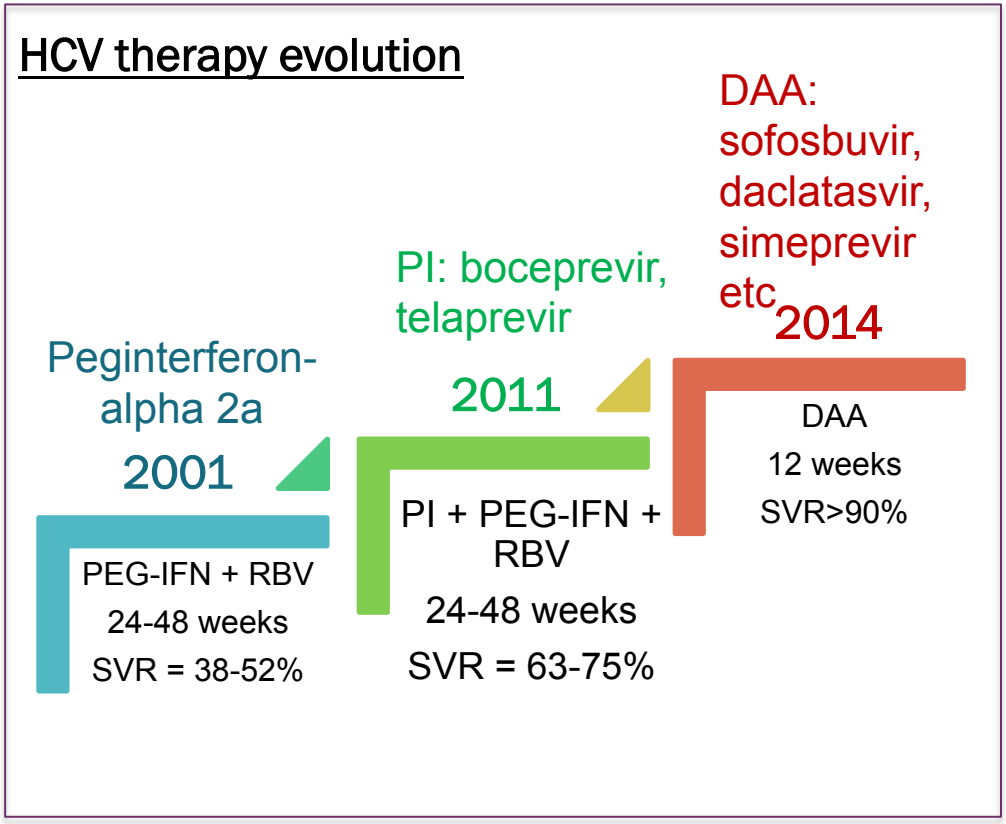
FIND
Because diagnosis matters

Forum for Collaborative HIV Research

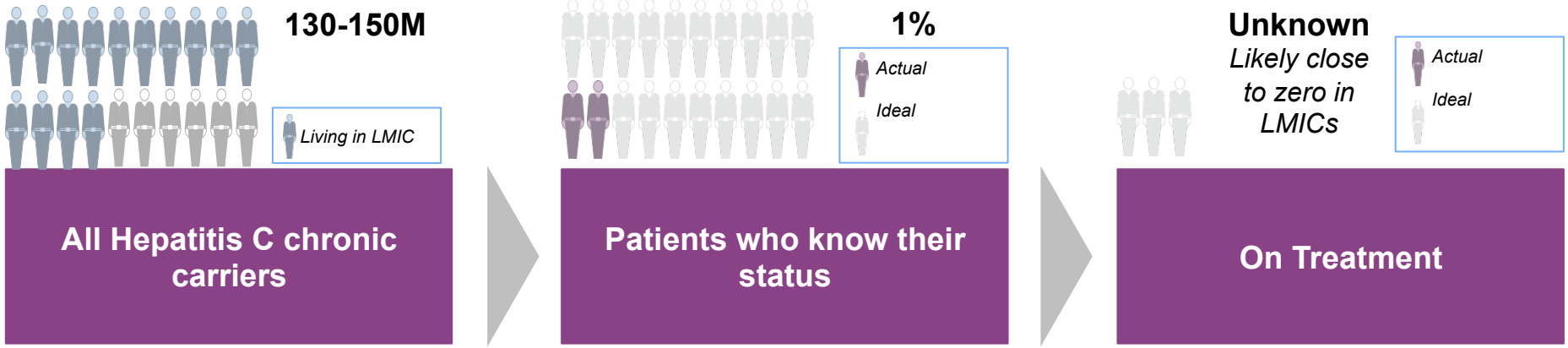
Why HCV diagnostics matters

HCV a significant global health problem with an opportunity to intervene

- 185M HCV-infected people worldwide; 130-150M of them are living in resource-limiting settings.
- Up to 85% of HCV-infected will develop chronic disease that leads to severe liver damages (such as liver cirrhosis and HCC).
- HCV causes an estimated 350,000-500,000 deaths/year.
- New highly efficient pan-genotypic, all-oral, IFN-free direct acting antiviral (DAA) drugs eliminate the virus in 12-weeks course.



Lack of simple and affordable HCV diagnostic solutions is a major barrier to large treatment access in LMIC



- World Health Assembly (WHA) resolution in 2014 specifically highlights the importance to improve HCV screening worldwide.
- WHO has HCV elimination as a goal.

India: "We need to tackle our hepatitis problem, both HBV and HCV, and this is the time to do it. India will drive the treatment availability like it did for HIV but we need to make diagnosis available on a larger scale to identify the patients to treat."

Mozambique: "As we are getting our HIV problem under better control, we see the impact of HCV that is threatening our achievements but it is a silent killer and people don't know they have it until it's too late."

Indonesia: "HCV is wiping out a whole generation of people who at some point in their lives used drugs or were unlucky to get a contaminated injection or blood product. We can and need to urgently intervene and diagnostics are the first step!"

Unmet Needs - HCV

Community health worker | Health post | Clinic | District hospital | Reference centre

A Passive & active screening with serological tests

B Core antigen test for POC diagnosis

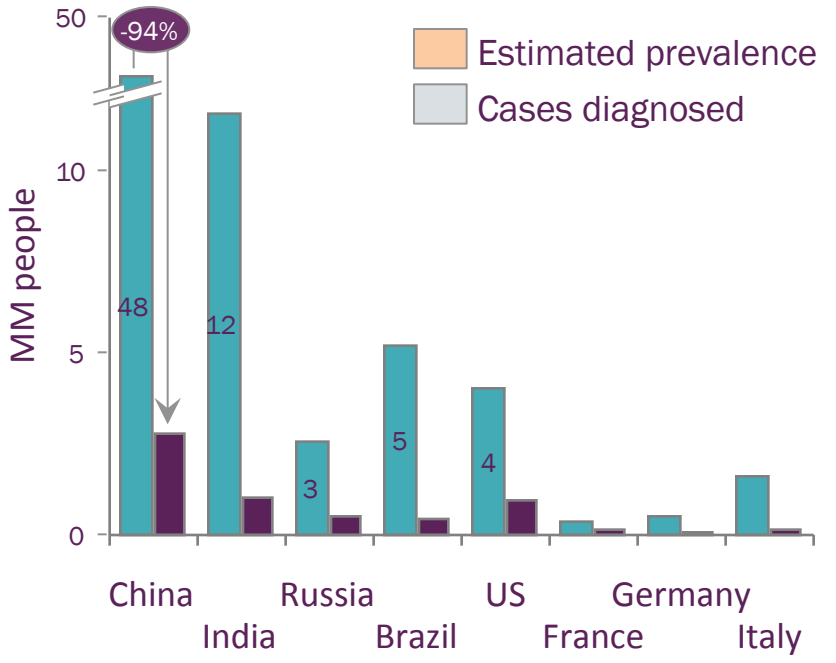
C Molecular tests for POC diagnosis

D Test of cure

eHealth and connectivity solutions

Today, HCV infection is severely under-diagnosed

<8% of cases diagnosed in MICs, <1%less in LICs



Lack of reliable data for LMICs. Available data suggests a major problem of under-diagnosis

Roots of under-diagnosis include lack of appropriate tools & delivery issues

- **Absence of policy, commitment and funding**
  - Lack of policy
  - Lack of funding from countries /donors
- **Diagnostics not suitable and too costly**
  - Algorithms for diagnosis too complex and costly
  - Limited developer investment due to unclear market/pathway to uptake
  - Serological tests of variable quality
  - NAAT-based Dx tools to confirm infection + monitoring can only be done at centralized labs
- **No market development in LMIC**
  - Low demand due to lack of awareness of disease burden & cost
  - Lack of demand aggregation and forecasting for pricing negotiations
- **Treatment regimens are complex and expensive**

Impossible for low-income countries to diagnose and treat patients at scale

1. Low & Middle Income Countries

Source: Decision resources; UNITAID: Hepatitis C Medicines and Diagnostics in the Context of HIV/HCV Co-Infection: A Scoping Report (October 2013)

WHO 2014 WHA resolution, strategy and targets

- 67th WHA 2014, Hepatitis Resolution reaffirming:
  - Hepatitis as a global public health problem
  - Need for governments and and populations to to take action to prevent, diagnose and treat viral hepatitis
  - Need to WHO to develop and implement comprehensive global strategy to support these efforts
  - Concern at slow pace of implementation
- WHO HCV Strategy:
  - Priorities include: HBV vaccination – childhood coverage; PMTCT of HBV – incl birth dose vaccination; safe injection, blood and med procedures; harm reduction for PWID; HBV Tx (lifelong); HCV Tx (cure)
- First ever WHO targets for elimination of viral hepatitis (2015 baseline):
  - Reduction in new cases of chronic hepatitis B and C by 30% (2020) / 90% (2030)
  - Reduction in hepatitis B and C deaths by 10% (2020) / 65% (2030)
  - 80% of treatment eligible persons with chronic hepatitis B and C infections treated by 2030

Dramatic diagnostic simplification possible with new DAAs

Potential for dramatic simplification of HCV diagnosis in the mid- to long-term

Current

Cost

- Screening – RDT/ELISA — $17-55
- Quantitative molecular – for confirmation of active infection — $17-80
- Genotype — $20-478
- Biomarker/Imaging/Biopsy – for staging — $100-1,625
- +/- IL28B - for prognosis — $300
- Quantitative molecular - Test of treatment response — $17-320
- Quantitative molecular - Test of cure — $17-80

Short-term

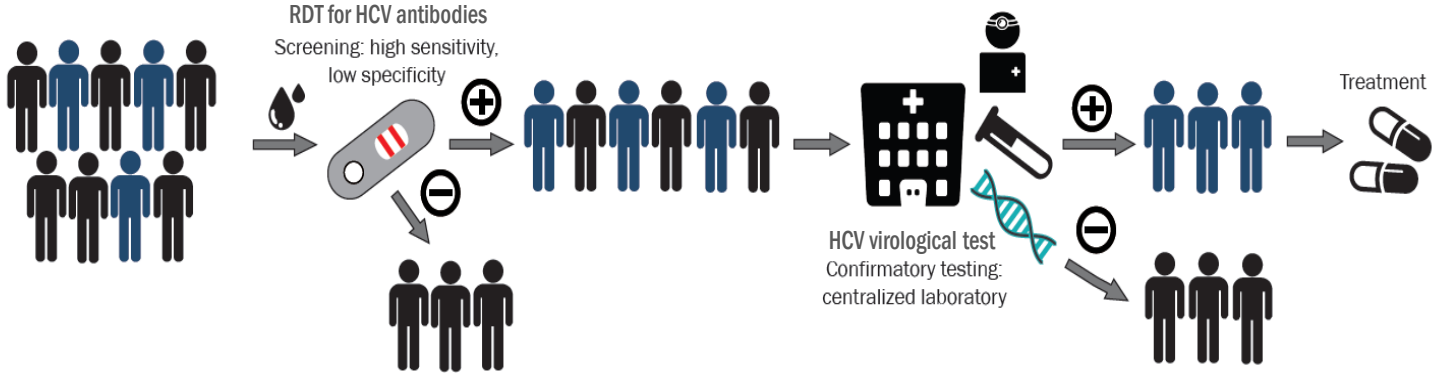
- Screening – RDT
- Quantitative molecular – for confirmation of active infection
- Biomarker/Imaging/Biopsy – for staging
- Quantitative molecular - Test of treatment response
- Quantitative molecular - Test of cure

Mid-term

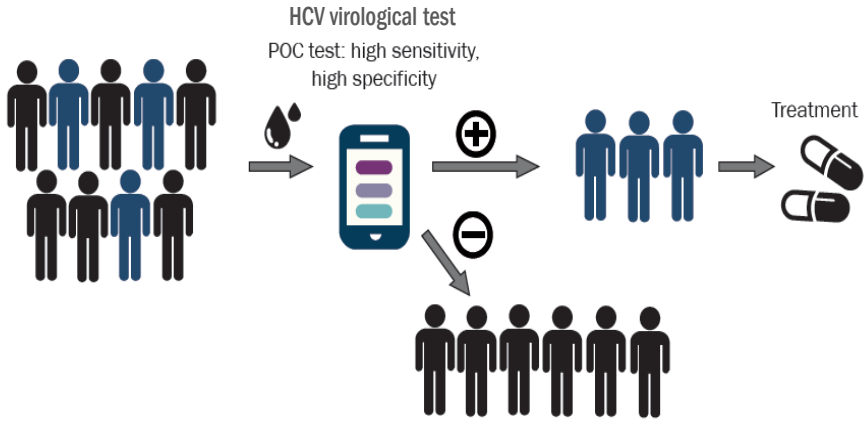
- ~~Screening – RDT~~
- Qual/Quant– for confirmation of active infection — <$20
- Biomarker – Cirrhosis versus no cirrhosis — <$3
- Qual/Quant molecular - Test of cure — <$20

One vs two step Dx strategy (depending on prevalence, cost, ease-of-use, LTFU etc)

TWO-STEP DIAGNOSIS



ONE-STEP DIAGNOSIS



The current standard of HCV monitoring during HCV treatment with PEG-IFN-alpha

Source: EASL Clinical Practice Guidelines: 2013 revised version. Clinical practice guidelines to optimize the management of hepatitis C virus infection.

	Pre-treatment	Baseline	Week 4	Week 12	End of treatment (week 24)	SVR12	SVR24
Antibody screening	x						
Virological confirmation	x						
Liver staging		x					
IL-28B		x					
Genotype		x					
Viral load		x	x	x	x	x	x
Complete blood count with differential		x	x	x			x
Thyroid stimulating hormone		x	x	x			
Clinical chemistry and haematology		x	x	x			x
Alpha-fetoprotein		x					
Lipids panel		x					

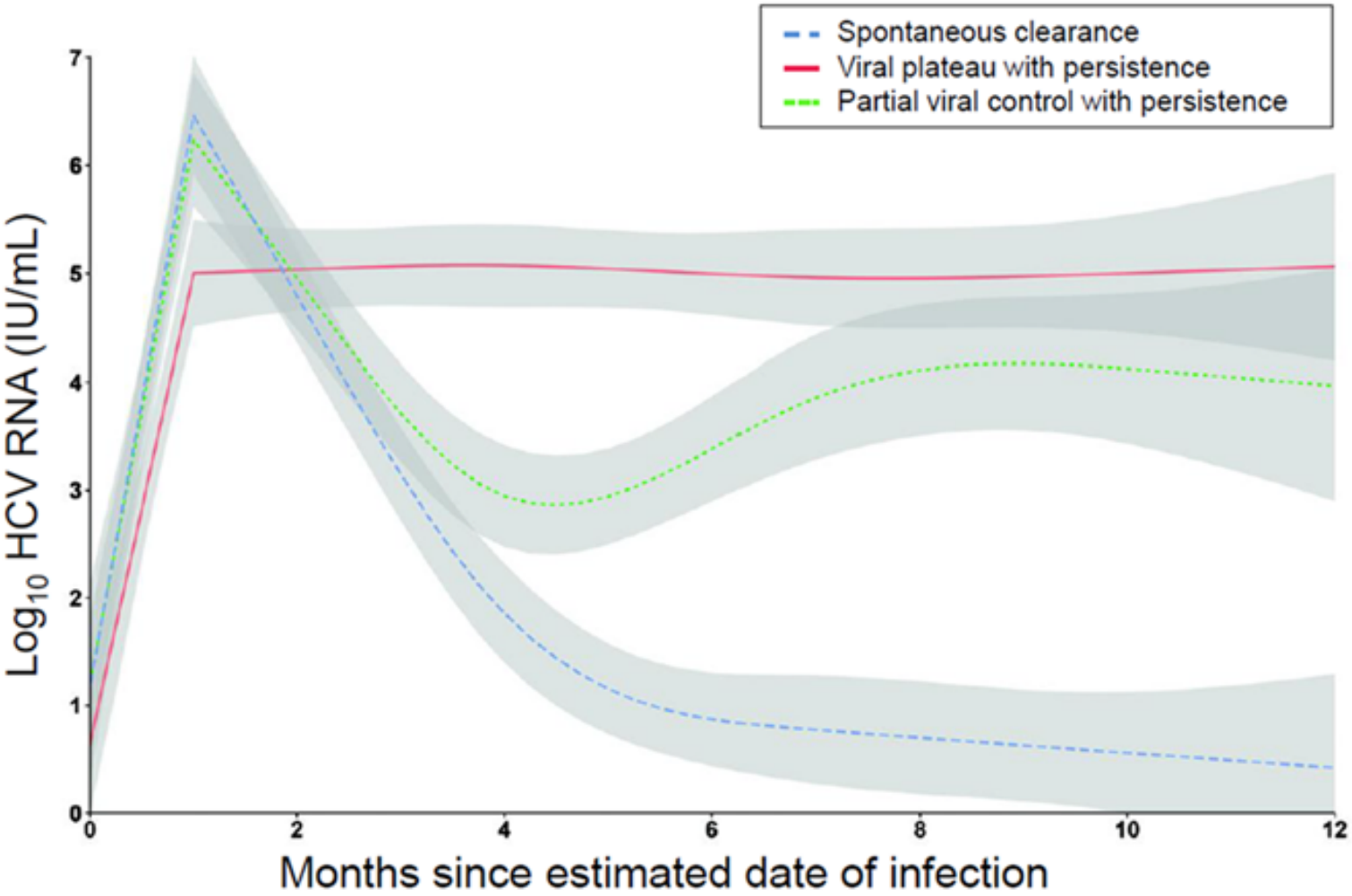
The proposed standard of diagnostic monitoring with an ideal, all oral, pan-genotypic regimen

	Pre-treatment	Baseline	Week 4	End of treatment (week 12)	SVR12
HCV core antigen or RNA (qualitative)	x				x
Alanine transaminase		x	x	x	
Creatinine		x	x	x	
Haemaglobin		x	x	x	

Source: Cohn J, Roberts T, Amorosa V, et al. Simplified diagnostic monitoring for Hepatitis C, in the era of Direct Acting Antiviral treatment. Curr Opin HIV AIDS. 2015;10:369–373.

Patterns of HCV RNA levels in individuals with well-characterized acute HCV infection in the InC3 study

(total n = 162); source: Hajarizadeh PLOS one 2015



Sensitivity - What is good enough?

- **~ 95% individuals have HCV RNA> 10,000 IU/ml in chronic infection**
- Subset of patients with persistent infection have **partial viral control** and drop to at least >1,000 IU/mL temporarily (several months) but then go back to a viral load >100,000 IU/mL between months 10 and 12
- Abbott Architect: sensitivity of 1000-3000 IU/ml
- Therefore unlikely to need very sensitive tests, which means testing using small blood volumes (e.g. fingerstick blood) or core antigen is much more feasible
- Awaiting systematic review of the evidence (Q2 2016) to confirm acceptable sensitivity for diagnosis and SVR12

Hajarizadeh PLOS one 2015
Hajarizadeh J Med Virol 2014
Glynn Transfusion 2005

Products available

Serological antibody screening tests

- Only one regulatory approved RDT for HCV: OraQuick HCV Rapid Antibody Test
  - Good performance, even in HIV co-infected
  - Around USD17 in developing countries
  - MSF get the lowest price at <USD8
  - FDA approved: fingerstick whole blood
  - CE marked: oral fluid, serum, plasma and fingerstick whole blood
  - Oral fluid test useful for self-testing
  - Manufactured in the US so freight can significantly increase cost
  - Awaiting approval of other tests by WHO prequalifcation but mostly low quality tests submitted so unlikely to pass PQ
  - Only EIAs (lab-based) WHO PQed so far: http://www.who.int/diagnostics_laboratory/evaluations/PQ_list/en/
  - Donors and large procurers e.g. GFATM, PEPFAR have strict quality stds for procurement eligibility but HCV is largely domestically funded so countries often make a choice on price, not quality = no incentive for manufacturers to invest in better quality tests

There may be other CE marked tests but this has been difficult to confirm e.g. MP Biomedicals MULTISURE HCV (most likely first to receive WHO PQ)

Point-of-care virological tests (HCV RNA)

SUPPLIER	CD4	HIV EID	HIV VL	HCV VL
Alere	Pima Analyser			
BD	FACSPresto			
Millipore	Muse Auto CD4/CD4% system			
Omega Diagnostics	Visitect CD4			
Sysmex Partec	CyFlow miniPOC			
Alere		q HIV 1/2 Detect		
Cepheid		Xpert HIV-1 qual	Xpert HIV-1 Viral Load	Xpert HCV Viral Load
Diagnostics for the Real World		SAMBA HIV-1 Qual Test SAMBA II HIV-1 Qual Whole Blood Test	SAMBA HIV-1 Semi Q Test SAMBA II HIV-1 Semi Q Plasma Test	
Molbio Diagnostics			Truelab/Truenat HIV	Truelab/Truenat HCV
Northwestern Global Health Foundation / Quidel		LYNX HIV p24 Antigen Test	Savanna Quantitative RealTime HIV-1 Assay	Not yet available

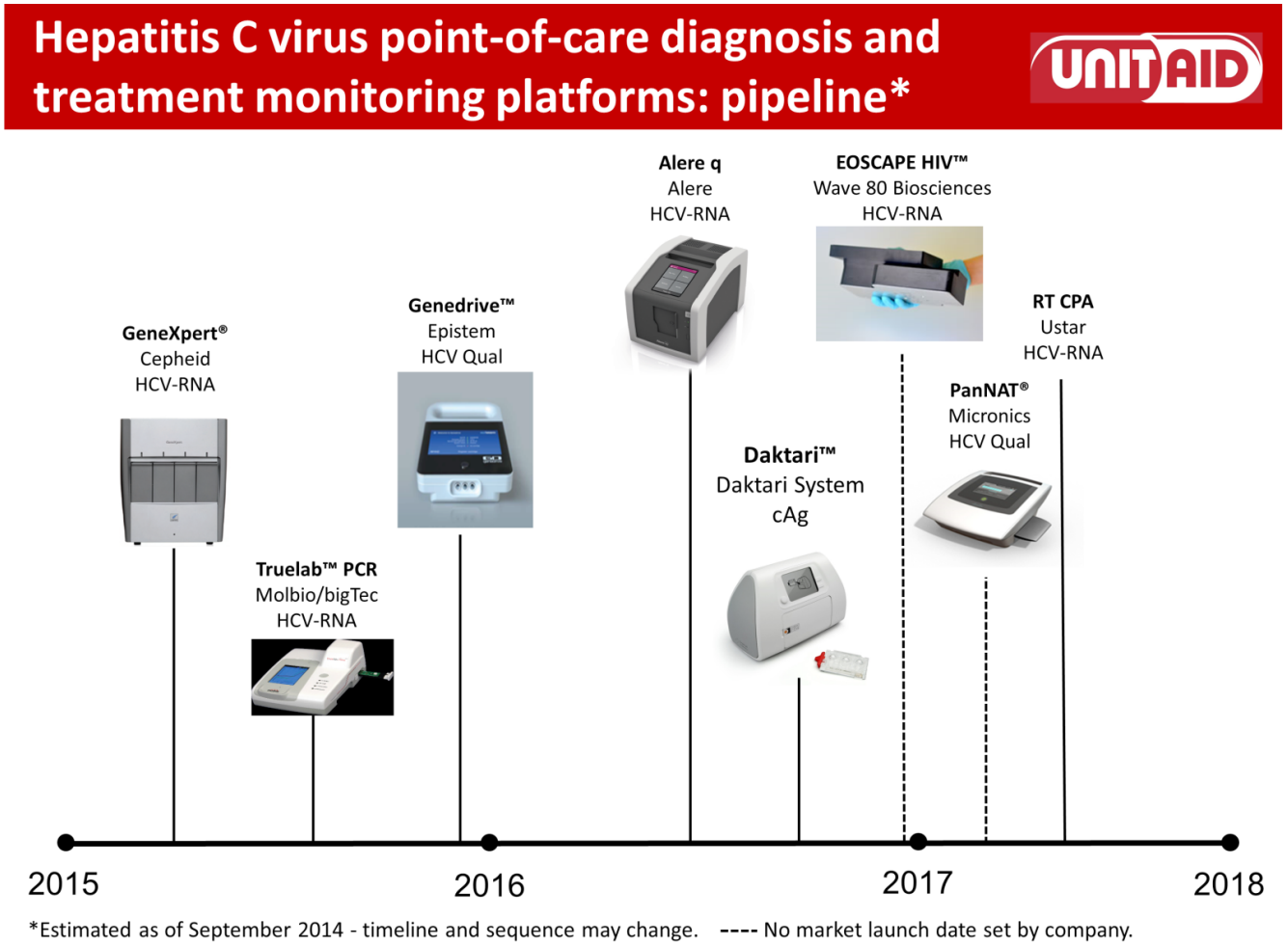
Source: http://msfaccess.org/HIV-HCV-diagnostic-product-guide-2015

Lab-based virological tests (HCV RNA and core antigen, GT)

SUPPLIER	HIV EID	HIV VL	HCV VL	HCV CORE ANTIGEN	HCV GENOTYPING
Abbott	RealTime HIV-1 Qualitative	RealTime HIV-1	RealTime HCV	ARCHITECT HCV Ag	RealTime HCV Genotype II
Biocentric	Generic HIV DNA Cell	Generic HIV Charge Virale	Generic HCV Charge Virale		
bioMérieux		NucliSENS EasyQ HIV-1			
Cavidi		ExaVir Load			
Hologic		Aptima HIV-1 Quant Dx Assay	Aptima HCV Quant Dx Assay		
Qiagen		artus HI Virus-1 RG RT-PCR artus HI Virus-1 QS-RGQ	artus HCV RG RT-PCR artus HCV QS-RGQ		
Roche Molecular Diagnostics	CAP/CTM HIV-1 Qualitative	CAP/CTM HIV-1	CAP/CTM HCV Qualitative and CAP/CTM HCV		
Sacace Biotechnologies		HIV Real-TM Quant Dx	HCV Real-TM Quant Dx		HCV Genotype Plus Real-TM
Siemens		VERSANT HIV-1 RNA Assay	VERSANT HCV RNA Assay		VERSANT HCV Genotype 2.0 Assay

Source: http://msfaccess.org/HIV-HCV-diagnostic-product-guide-2015

Point-of-care tests in the pipeline
(optimistic)



Source: http://unitaid.org/images/marketdynamics/publications/UNITAID-HCV_Diagnostic_Landscape-1st_edition.pdf

FIND and HCV

FIND's strategy is focused on addressing challenges around diagnosis to meet global goals

Long-term vision

Enable a world free of Hepatitis C

5-year goal

To support the Global Hepatitis Programme in its goals: to reduce transmission, reduce the morbidity and mortality, and reduce the socio-economic impact of viral hepatitis at individual, community and population levels

Strategy objectives

1. Enable affordable and fit-for-purpose diagnosis
2. Enable access to diagnosis
3. Support the prevention of infection
4. Demonstrate the need and benefit of interventions for HCV

Principal of FIND development work

Prioritization & TPP dvlpt with consensus process; advocacy

Landscaping & opportunity description & partner building

Drive project to success: inform R&D; accelerate trial pathway; country rollout


High-priority target product profile for hepatitis C diagnosis in decentralized settings:

Report of a consensus meeting

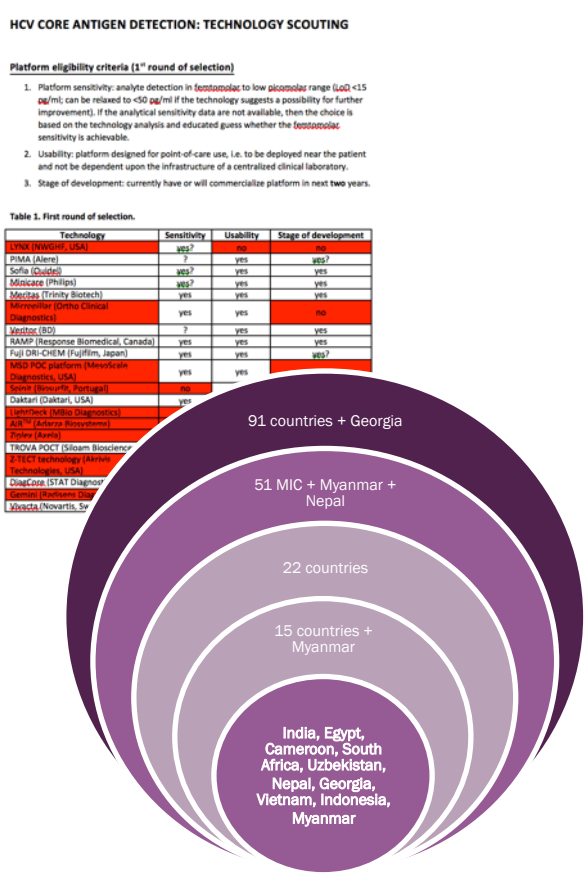
22 April 2015
Vienna, Austria

FIND
Because diagnosis m

Correspondence

Diagnostics for hepatitis C: an urgent need for action

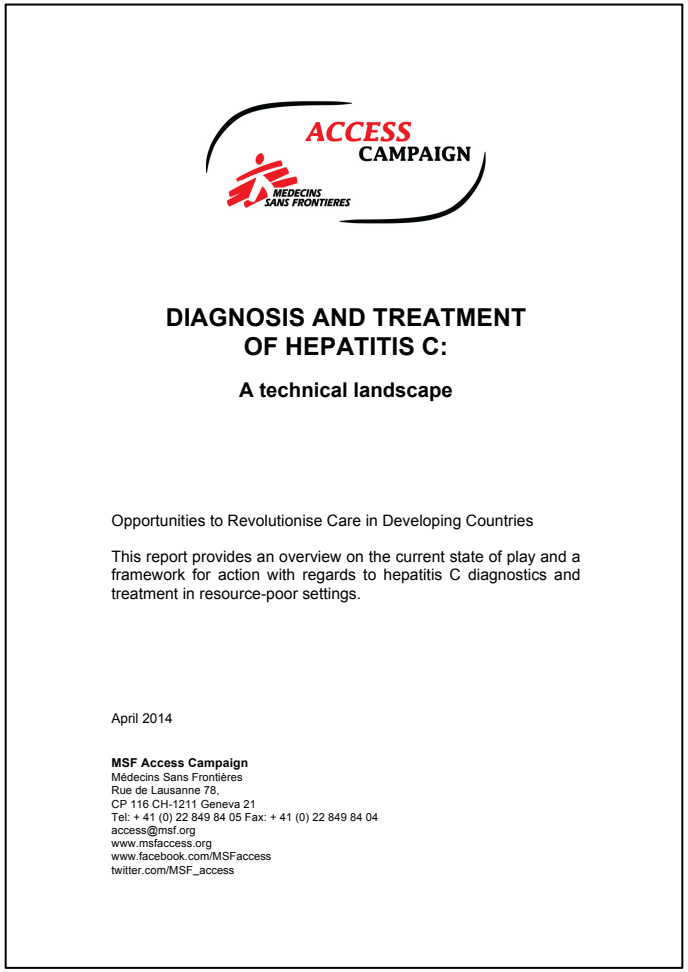
Claudia M Denkinger, Mark Kessel



Key resources

MSF Access Report

http://www.msfaccess.org/content/diagnosis-and-treatment-hepatitis-c-technical-landscape



ACCESS CAMPAIGN

MEDECINS SANS FRONTIERES

DIAGNOSIS AND TREATMENT OF HEPATITIS C:

A technical landscape

Opportunities to Revolutionise Care in Developing Countries

This report provides an overview on the current state of play and a framework for action with regards to hepatitis C diagnostics and treatment in resource-poor settings.

April 2014

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MSF Product Guide

http://msfaccess.org/HIV-HCV-diagnostic-product-guide-2015

PUTTING HIV AND HCV TO THE TEST

A PRODUCT GUIDE FOR POINT-OF-CARE CD4 AND LABORATORY-BASED AND POINT-OF-CARE VIROLOGICAL HIV AND HCV TESTS

July 2015

www.msfaccess.org

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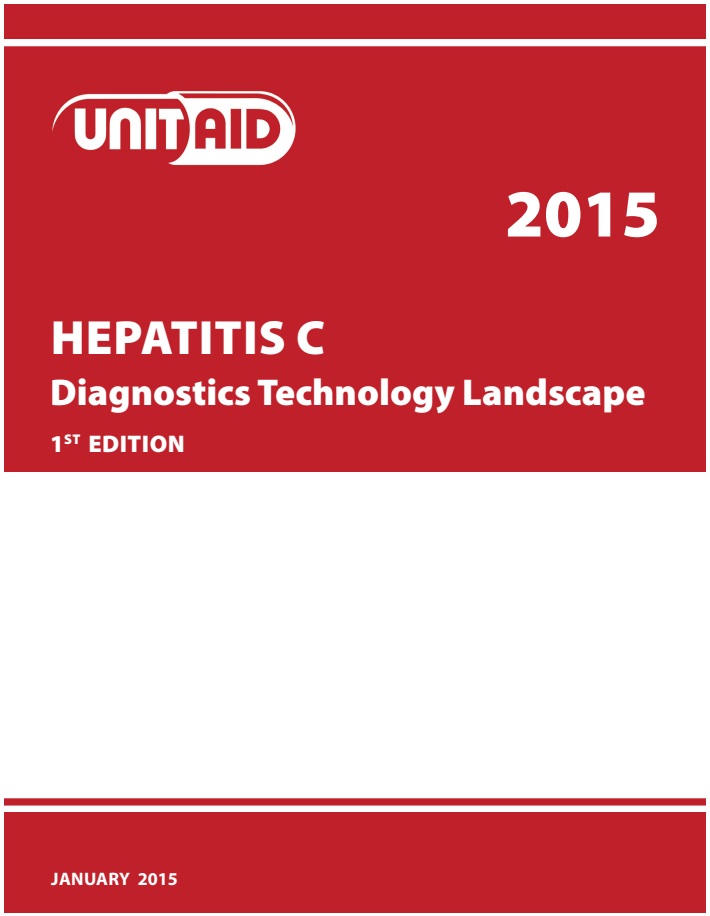
MEDECINS SANS FRONTIERES

Unitaid diagnostics landscape

(updated every 6 months)

http://unitaid.org/images/marketdynamics/publications/UNITAID-HCV_Diagnostic_Landscape-1st_edition.pdf



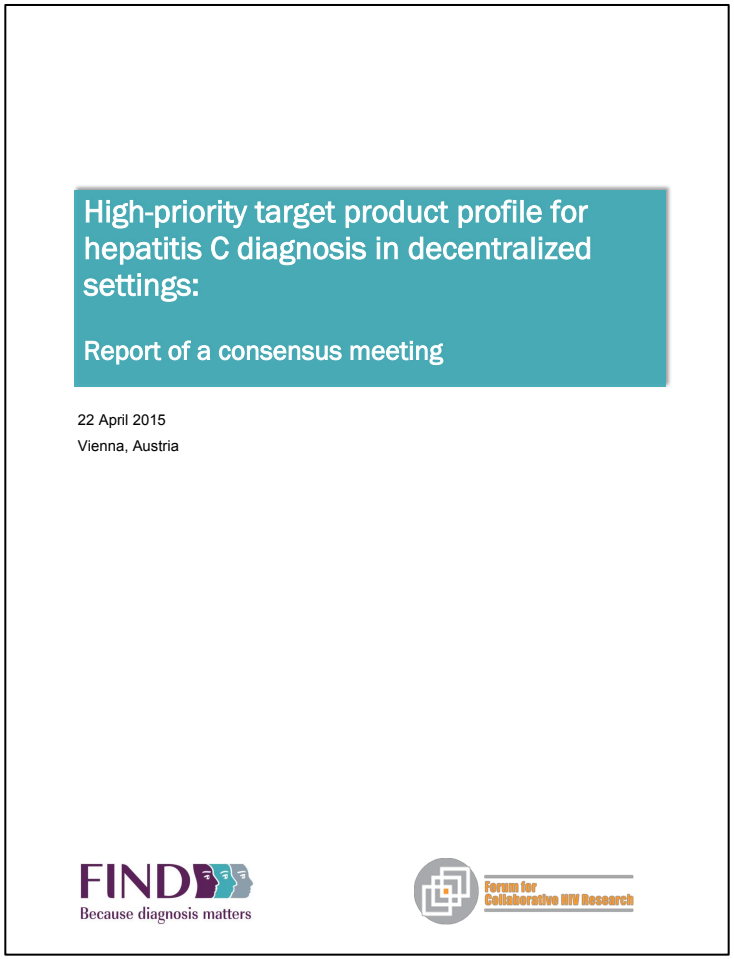
FIND HCV Strategy

http://www.finddiagnostics.org/export/sites/default/resource-centre/reports_brochures/docs/FIND_strategies/FIND_HepatitisC_Strategy_21Nov14.pdf

FIND Target Product Profile

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

http://www.finddiagnostics.org/programs/hepC/target-product-profile/



Key advocacy areas

Lessons learnt in 2015

- Delay in HCV testing due to lack of in-country guidelines or strategies on who to screen and how
- Poor quality of testing where counties use cheaper RDTs of unknown manufacturing quality and performance (OraQuick is the only approved test but expensive at USD17)
- DAAs are allowing for diagnostic simplification and decentralisation but guidelines and models of care haven't caught up with this yet (still very conservative)
- Delay in access to DAA treatment in countries due to slow registration and companies having no incentive to apply for WHO prequalification (no donor purchasing of drugs therefore no quality policy) means delay in implementing HCV programming overall
- Reliance on external stakeholders and political will but no dedicated international funding available; preferential pricing normally not extended to MICs, and LMICs are struggling to pay everything domestically, means manufacturers are not convinced of a viable market

Key messages

First WHO hepatitis testing will be released in Q2 2016 (HCV & HBV)

- Encourage countries to take them up!
- They include a public health approach to testing including high risk groups, RDTs, dried blood spots and uptake of testing, linkage to care and community-centric strategies

Lack of large donor funding for R&D and commodity purchasing

- Encourage large, classical donors to fund HCV (not just in the context of HIV co-infection)
- Work on innovative domestic financing e.g. social impact bonds/loans, other ideas?
- Establish best policy for pharma funding/partnerships/donations e.g. from Gilead, Merck and Abbott

Lack of affordable quality assured HCV RDTs for screening

- Key requirements for a POC RDT for use in resource- limited settings are a test that is **accurate** (close to 100% sensitivity and high negative predictive value, and equally accurate in HCV/HIV co-infection)**; simple** (with minimal training requirements and no cold chain); **reliable** (WHO-prequalified, CE marked or FDA approved); and **cheap**, at <$2 per test
- Increased procurement by large, classical donors will provide incentive for quality RDTs
- Large procurers can also faciliate pooled procurement, increased volumes and competition for price reductions
- Countries should strengthen their quality policies for diagnostics in general (tender systems should be based on quality and performance, not just price)
- Ramping up of country HCV programmes will lead to price reductions due to increased volumes and competition

Advocacy

- Ramped up advocacy is needed for increased awareness for importance of HCV testing & funding
- Diagnosis is the first step to treatment!

Acknowledgements

- HCV slide credits to: Claudia Denkinger and Elena Ivanova (FIND)

Thank you/ Danke / Merci

We believe

Simple, rapid, robust and affordable diagnostic solutions bring game-changing possibilities above and beyond their immediate benefit.

We believe

Our work can spark real progress in the health of lower and middle income countries and their populations.

We believe

With improved health comes greater hope: individuals empowered to support their families, revive businesses, and thrive in school.