Simplified HCV Diagnostics

Viral Hepatitis Elimination Meeting
Amsterdam
2016
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For Dr Teri Roberts
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MSF SAMU and Access Campaign
Speaker Disclosure

No conflicts to report
MSF AND HCV
MSF HCV Projects

- **Unitaid HCV grant**: “Ensuring access to the HCV treatment revolution for HCV/HIV co-infected patients in Low and Middle Income Countries”

- **Sites** (Unitaid (co-infection) and MSF (mono-infection) funded):
  - **PWID**: India, Kenya, Uzbekistan
  - **Generalised**: Myanmar (incl PWID, GT6) Mozambique (GT5, also HBV), Pakistan, Cambodia (GT6), South Africa (GT5)
  - (Increased demand for HCV treatment programmes within TB programmes in Eastern Europe)

- **Studies**:
  - Multi-centric longitudinal cohort to evaluate HCV treatment effectiveness in HIV co-infected people
  - Evaluation of the performance of HCV RDTs among HCV/HIV co-infected people
  - Cost-effectiveness (with Bristol University)
MSF HCV DAA Tx to date

• In MSF HIV programmes (different types of cohorts):
  HCV prevalence Asia/Middle East >> east/southern Africa

• % RNA+
  – Nairobi (Kibera): 0.04%; Mozambique (Maputo): 1%; Uganda (Mbarara): 0.07%
  – Cambodia (Phnom Penh): 4%; India (Manipur): 6.8%; Myanmar (Yangon): 6.5%; Myanmar (Dawei): 8%
  – Pakistan (Karachi): 37%; Armenia (Yerevan): 13%

• Actively treating: India, Pakistan, Kenya
• Few treatments: Uganda
• Recently started: Uzbekistan, Cambodia, Myanmar

• DAAs: SOF + DAC generic and originator
• In countries where there are patents, obliged to use originator or generics part of VL
HCV DX SIMPLIFICATION: (TYPE OF TESTS AND FREQUENCY OF TESTING)
Why simplified HCV Dx is important

~70 million (56M – 90M) people are infected with HCV (viraemic), a 2016 prevalence of 1% (0.8%-1.2%)

Source: Polaris Observatory
http://www.polarisobservatory.com/

- As there are few comprehensive screening programmes in LMICs, few people know their status
- The diagnostic package needed for IFN-based therapy was complex but can now be drastically simplified with pan-genotypic, all oral DAA-based therapy
- Two current barriers to simplification: 1. no pan-genotypic regimen in WHO guidelines, 2. eligibility criteria still used (cost, minimal access to Tx, no FDC)
One vs two step Dx strategy
(depending on prevalence, cost, ease-of-use, LTFU etc)

TWO-STEP DIAGNOSIS

RDT for HCV antibodies
Screening: high sensitivity, low specificity

ONE-STEP DIAGNOSIS

HCV virological test
POC test: high sensitivity, high specificity

Source: FIND
Sensitivity - What is good enough?

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% of 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
- Therefore unlikely to need very sensitive tests because clinically relevant sensitivity is >1,000 IU/mL, which means testing using small blood volumes (e.g. fingerstick blood) or core antigen is much more feasible

E.g. Abbott Architect HCV Ag assay: LOD 3fmol/L (sensitivity of 1000-3000 IU/mL)
- BUT current guidelines (e.g. EASL, AASLD) recommend <25 IU/mL analytical sensitivity → needs revising for appropriate clinical sensitivity so that POC and core Ag tests can be used
Systematic review: core Ag detection for the diagnosis of HCV

- Freiman et al Hepatitis C Core Antigen Testing for Diagnosis of Hepatitis C Virus Infection, Ann Intern Med. doi:10.7326/M16-0065

- HCV core Ag assays can perform with high sensitivity (>90%) and specificity (>98%) compared with RNA assays
- HCV core Ag can conceivably reach a lower cost (based on cost of goods analysis); <10USD
- **Access:**
  - POC suitability versus centralized testing: possibly equal for both RNA/core Ag tests
  - DBS for core Ag: Lamoury et al (Kirby Institute) - good accuracy of core Ag DBS at the 10th Australian Viral Hepatitis Conference
- Well-performing core Ag tests could serve as a replacement for RNA for HCV detection, particularly if they are more accessible and affordable than RNA tests
Overview of the programmatic experience of using DBS

• **DBS used by associations:**
  – "Hepatitis C Trust" in UK
  – le “Réseau Hépatites LR” in France
  – by community pharmacists in UK

• **France: cited and discussed but not recommended**
  – "CheckPoint-Paris from the Kiosque” is a VCT service in France that has offered rapid tests for screening and DBS for confirmation since 2010
  – guidelines from the “Haute Autorité Sanitaire” and AFEF-ANRS underlined that DBS tests have good performance and are an alternative to venous blood tests
  – ANRS: DBS frequently used for research studies

• **UK (NICE public health guidance): recommended to promote and offer testing to people at increased risk of infection**
  – Prison services and drug services
  – People with poor venous access / no phlebotomy services
  – Consider extending pilot programmes (pharmacists providing DBS)
  – In Scotland, **19% of new HCV diagnoses during 2011-2013 were made in specialist drug service where DBS testing has been introduced**

Source: Edouard Tuaillon (Montpellier University)
DBS in HCV – Scotland 2009

- DBS testing introduced into specialised drug services during 2009
- Test for HCV Antibody testing

- Drug services referred 16% of new HCV diagnosed in Scotland during 2009-13 (compared to <1% during 2003-08)

McLeod A et al. J Epidemiol Community Health 2014
HCV TESTS AVAILABLE
Serological antibody screening tests

- Only one known strictly regulatory approved RDT for HCV: OraQuick HCV Rapid Antibody Test
  - Good performance
  - At least USD10 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 RDTs by WHO prequalification
  - Only EIAs (lab-based) have WHO PQ 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 as no database exists
# Point-of-care virological tests (HCV RNA)

<table>
<thead>
<tr>
<th>SUPPLIER</th>
<th>CD4</th>
<th>HIV EID</th>
<th>HIV VL</th>
<th>HCV VL</th>
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<tbody>
<tr>
<td>Alere</td>
<td>Pima Analyser</td>
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<td>BD</td>
<td>FACSPresto</td>
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<td>Millipore</td>
<td>Muse Auto CD4/CD4% system</td>
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<td>Omega Diagnostics</td>
<td>Visitect CD4</td>
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<td>Sysmex Partec</td>
<td>CyFlow miniPOC</td>
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<tr>
<td>Alere</td>
<td></td>
<td>q HIV 1/2 Detect</td>
<td>Xpert HIV-1 Viral Load</td>
<td>Xpert HCV Viral Load</td>
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<td>Cepheid</td>
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<td>Diagnostics for the Real World</td>
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<td>SAMBA HIV-1 Semi Q Test</td>
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<td>SAMBA II HIV-1 Qual Whole Blood Test</td>
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<td>Molbio Diagnostics</td>
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<td>Truelab/Truenat HIV</td>
<td>Truelab/Truenat HCV</td>
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<td>Northwestern Global Health Foundation / Quidel</td>
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<td>LYNX HIV p24 Antigen Test</td>
<td>Savanna Quantitative RealTime HIV-1 Assay</td>
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</tbody>
</table>

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

<table>
<thead>
<tr>
<th>SUPPLIER</th>
<th>HIV EID</th>
<th>HIV VL</th>
<th>HCV VL</th>
<th>HCV CORE ANTIGEN</th>
<th>HCV GENOTYPING</th>
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<tr>
<td>Abbott</td>
<td>RealTime HIV-1 Qualitative</td>
<td>RealTime HIV-1</td>
<td>RealTime HCV</td>
<td>ARCHITECT HCV Ag</td>
<td>RealTime HCV Genotype II</td>
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<td>Biocentric</td>
<td>Generic HIV DNA Cell</td>
<td>Generic HIV Charge Virale</td>
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<td>Hologic</td>
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<td>Qiagen</td>
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<td>artus HI Virus-1 QS-RGQ</td>
<td>artus HCV RG RT-PCR artus HCV QS-RGQ</td>
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<td>Roche Molecular Diagnostics</td>
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<td>CAP/CTM HIV-1</td>
<td>CAP/CTM HCV Qualitative and CAP/CTM HCV</td>
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<td>cobas HCV GT</td>
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<td>HCV Real-TM Quant Dx</td>
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<td>HCV Genotype Plus Real-TM</td>
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<td>Siemens</td>
<td>VERSANT HIV-1 RNA Assay</td>
<td>VERSANT HCV RNA Assay</td>
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<td>VERSANT HCV Genotype 2.0 Assay</td>
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Point-of-care tests in the pipeline

Hepatitis C virus point-of-care diagnosis and treatment monitoring platforms: pipeline

*Estimated as of September 2014 - timeline and sequence may change. ---- No market launch date set by company.

KEY RESOURCES
MSF Access Campaign Report

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

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 Access Campaign Product Guide
(will be updated in 2017)


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
FIND Target Product Profile

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

KEY ADVOCACY AREAS
Lessons Learnt

• **Delay in HCV screening** due to lack of in-country policy, guidelines and programmes
• **Unknown quality of serological screening** where counties use cheaper RDTs of unknown manufacturing quality and performance; **HIV co-infection** may cause false positives (polyclonal) and false negatives (immunosuppression)
• **DAAs are allowing for diagnostic simplification and decentralisation** but guidelines and models of care are 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 – same for Dx) 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 guidelines will be released this year
  – 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
  – Establish best policy for pharma funding/partnerships/donations to ensure sustainability

• 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 facilitate 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
THANK YOU

HEPATITIS C TREATMENT:
149.75 MILLION PEOPLE
STILL WAITING...

your number is
149,750,000