4th International Symposium on Hepatitis Care in Substance Users

Sydney Oct 7-9
Interventions to Enhance Testing & Diagnosis of HCV Infection among PWID

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Health Protection Scotland
University of Glasgow

Disclosures: Honoraria from Abbvie, BMS, Gilead, Janssen, Merck

Global estimate: 10 million PWID with anti-HCV

W. Europe: 0.7M  E. Europe: 2.3M

Canada & US: 1M

Asia: 3.1M

Sub-Saharan Africa: 0.8M
How effective are we at diagnosing infection?

- Sweden
- France
- Denmark
- Germany
- Scotland
- Belgium
- Spain
- Switzerland
- Austria
- England
- Portugal
- Czech

Estimated % infected population diagnosed

Razavi et al J Viral Hepat. 2014
## EASL Recommendations
### Hepatitis C 2015
#### Treatment Prioritisation

<table>
<thead>
<tr>
<th>HCV Disease</th>
<th>Treatment Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver Failure</td>
<td>Urgent</td>
</tr>
<tr>
<td>Cirrhosis/pre-cirrhosis</td>
<td>Prioritised</td>
</tr>
<tr>
<td>Significant Extrahepatic disease</td>
<td>Prioritised</td>
</tr>
<tr>
<td>Any + Active PWID and others who might transmit infection</td>
<td>Prioritised</td>
</tr>
<tr>
<td>Moderate liver fibrosis</td>
<td>Justified</td>
</tr>
<tr>
<td>No or mild liver disease</td>
<td>Individualised</td>
</tr>
</tbody>
</table>
WHO Guidelines for the Screening, Care and Treatment of Persons with Hepatitis C Infection

- Guidelines Development Group
  - Chairs: Bryce Smith, Yngve Falck-Ytter

- External Peer Review Group
  - Chairs: Jude Byrne et al

- Steering Committee
  - Chairs: Stephan Wiktor et al

- Temporary Advisors
  - Margaret Hellard (Lead), Joe Doyle (Senior Reviewer), Sharon Hutchinson, Esther Aspinall, David Goldberg

Eligibility Criteria

Population: H/O risk behaviours/exposure

Intervention: Targeted HCV Ab testing

Comparison/control: No intervention or just routine practice

Outcomes: Ab tests, Ab positive results, Specialist referrals, Treatment commencement, SVR.
# Study Selection and Characteristics

<table>
<thead>
<tr>
<th>Category</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full text articles reviewed</td>
<td>279</td>
</tr>
<tr>
<td>Studies eligible</td>
<td>16</td>
</tr>
<tr>
<td><strong>Outcome Indicator Completeness:</strong></td>
<td></td>
</tr>
<tr>
<td>Tests</td>
<td>16</td>
</tr>
<tr>
<td>Pos Results</td>
<td>14</td>
</tr>
<tr>
<td>Referrals</td>
<td>4</td>
</tr>
<tr>
<td>Treatment Commencement</td>
<td>4</td>
</tr>
<tr>
<td>SVR</td>
<td>2</td>
</tr>
<tr>
<td><strong>Intervention Type</strong></td>
<td></td>
</tr>
<tr>
<td>Practitioner-based targeting</td>
<td>12</td>
</tr>
<tr>
<td>Media/Information-based targeting</td>
<td>4</td>
</tr>
</tbody>
</table>
## Study Characteristics

### Population:
- PWID : 4
- At risk of PWID : 5
- Any Risk Factor : 6
- High prevalence country risk : 1

### Country of Study
- UK : 4
- US : 4
- France : 4
- Netherlands : 2
- Ireland : 1
- Australia : 1

### Year of Publication
- 2000-06 : 2
- 2007-12 : 14
## Study Characteristics: Target Population “At Risk of PWID”

<table>
<thead>
<tr>
<th>Author</th>
<th>Country</th>
<th>Design</th>
<th>Population</th>
<th>Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anderson</td>
<td>UK</td>
<td>Non-Randomised CT</td>
<td>V deprived area, 30-54 GP attendees</td>
<td>Counsellor based in General Practice</td>
</tr>
<tr>
<td>Lacey</td>
<td>Australia</td>
<td>Before &amp; After</td>
<td>Psychiatric In-patients</td>
<td>Leaflet &amp; Research Assistant</td>
</tr>
<tr>
<td>Litwin</td>
<td>US</td>
<td>Before &amp; After</td>
<td>Primary Care clinics in deprived area</td>
<td>“Ask about Risk” sticker on case notes</td>
</tr>
<tr>
<td>Sahajian</td>
<td>France</td>
<td>Cluster RCT</td>
<td>Homeless in hostels</td>
<td>Group info seminars &amp; referral to H. Centre</td>
</tr>
<tr>
<td>Author</td>
<td>Country</td>
<td>Design</td>
<td>Population</td>
<td>Intervention</td>
</tr>
<tr>
<td>----------</td>
<td>-----------</td>
<td>-----------------</td>
<td>----------------------------</td>
<td>-------------------------------------------------------</td>
</tr>
<tr>
<td>Cullen</td>
<td>Ireland</td>
<td>Cluster RCT</td>
<td>Methadone (GP)</td>
<td>Liaison Support Nurse</td>
</tr>
<tr>
<td>Cullen</td>
<td>UK</td>
<td>Non-Randomised CT</td>
<td>PWID 30-54 (GP)</td>
<td>GPs paid and trained</td>
</tr>
<tr>
<td>Helsper</td>
<td>Netherlands</td>
<td>Before &amp; After</td>
<td>“Hard” Drug Users</td>
<td>Training of addiction professionals &amp; meetings for HDU</td>
</tr>
<tr>
<td>Hickman</td>
<td>UK</td>
<td>Cluster RCT</td>
<td>Current PWID, attending drug clinics &amp; prisoners</td>
<td>Specialist nurses &amp; DBS</td>
</tr>
</tbody>
</table>
## Pooled effect of Interventions on Outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>*Studies</th>
<th>Effect size</th>
<th>(95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tested</td>
<td>16</td>
<td>2.9</td>
<td>(2.0-4.2)</td>
</tr>
<tr>
<td>HCV positive</td>
<td>14</td>
<td>1.7</td>
<td>(1.3-2.2)</td>
</tr>
<tr>
<td>Specialist Referral*</td>
<td>1</td>
<td>3.0</td>
<td>(1.8-5.0)</td>
</tr>
<tr>
<td>Attendance at Specialist*</td>
<td>1</td>
<td>3.7</td>
<td>(1.9-7.0)</td>
</tr>
<tr>
<td>Commenced Treatment</td>
<td>4</td>
<td>3.2</td>
<td>(1.1-10.0)</td>
</tr>
<tr>
<td>SVR</td>
<td>2</td>
<td>1.4</td>
<td>(0.3-7.1)</td>
</tr>
</tbody>
</table>

*Analysis restricted to one study
# HCV Ab Positive Cases Detected by Study Type

<table>
<thead>
<tr>
<th>Study Type</th>
<th>Studies</th>
<th>Effect size</th>
<th>(95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Media/Information Studies</td>
<td>4</td>
<td>1.3</td>
<td>(1.0-1.6)</td>
</tr>
<tr>
<td>Practitioner Based Studies</td>
<td>10</td>
<td>2.2</td>
<td>(1.4-3.5)</td>
</tr>
<tr>
<td>PWID</td>
<td>3</td>
<td>3.1</td>
<td>(1.4-7.1)</td>
</tr>
<tr>
<td>At risk of PWID</td>
<td>5</td>
<td>1.8</td>
<td>(0.9-3.6)</td>
</tr>
<tr>
<td>All HCV Risk Groups</td>
<td>6</td>
<td>1.3</td>
<td>(1.1-1.6)</td>
</tr>
<tr>
<td>All</td>
<td>14</td>
<td>1.7</td>
<td>(1.3-2.2)</td>
</tr>
<tr>
<td>Author</td>
<td>Study arm</td>
<td>Eligible</td>
<td>Accepted</td>
</tr>
<tr>
<td>---------------------</td>
<td>-----------------------------------------------</td>
<td>----------</td>
<td>----------</td>
</tr>
<tr>
<td>Anderson 2009 ¹ (Scotland)</td>
<td>Targeting people aged 30–54 at GP practices</td>
<td>584</td>
<td>117</td>
</tr>
<tr>
<td></td>
<td>Routine practice</td>
<td>458</td>
<td>0</td>
</tr>
<tr>
<td>Lewis 2012 ² (England)</td>
<td>Targeting patients of South Asian ethnicity at GP practices</td>
<td>1163</td>
<td>229</td>
</tr>
<tr>
<td></td>
<td>Routine practice</td>
<td>1134</td>
<td>17</td>
</tr>
<tr>
<td>Cullen 2012 ³ (Scotland)</td>
<td>Targeting PWID aged 30-54 at GP practices</td>
<td>485</td>
<td>105</td>
</tr>
<tr>
<td></td>
<td>Routine practice</td>
<td>528</td>
<td>36</td>
</tr>
<tr>
<td>Cullen 2006 ⁴ (Ireland)</td>
<td>Targeting PWID using GP methadone services</td>
<td>104</td>
<td>51</td>
</tr>
<tr>
<td></td>
<td>Routine practice</td>
<td>92</td>
<td>25</td>
</tr>
</tbody>
</table>

1. Anderson et al, Scottish Medical Journal, 2009
2. Lewis et al, EASL Conference, 2012
WHO Recommendation Stemming from the Systematic Review & Meta-Analysis

• “...interventions are effective in increasing uptake of testing, identifying HCV infected individuals & referring them to care. However the approaches...were different...Therefore the GD Group could not recommend a specific intervention to increase the uptake of HCV testing.”

• “The GD Group recommended testing individuals belonging to populations of known high prevalence”
  – i.e. targeted & general population screening using bespoke approaches (depending on the problem, resources & existing services)

• Knowing status trumps any potential disbenefit
Review

The effect of introducing point-of-care or dried blood spot analysis on the uptake of hepatitis C virus testing in high-risk populations: A systematic review of the literature

Josh T. Coats *, John F. Dillon

Medical Research Institute, University of Dundee, Ninewells Hospital and Medical School, Dundee DD1 9SY, UK
The effect of introducing PoC or DBS analysis on the uptake of HCV testing in high-risk populations: a systematic review.

Eligibility Criteria

Population : All PWID
Intervention : DBS or PoC
Comparison/Control : non-DBS/PoC in context of routine practice
Outcomes : Ab tests
            Ab positive results
DBS/PoC Systematic Review Findings

- 6 DBS & 0 PoC studies met eligibility criteria
- All UK
- Published 2008-14
- All DBS in drug clinic, prison settings
- 2 cluster RCT, 2 cohort, 1 ecological & 1 audit
- All DBS interventions associated with other interventions e.g. staff training
- All except 1 study demonstrated increase in testing (effect size: from 6-fold to 1.4.5%)
- Conclusion: the DBS approach may increase HCV testing uptake in high risk populations.
Dried Blood Spot Testing
(introduced into specialist drug services in Scotland during 2009)

Annual number of people tested for HCV in specialist drug services across Scotland’s 4 largest NHS Boards

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

McLeod et al. JECH (2014)
### Estimates of HCV chronic population by disease stage

#### All Chronic (N=37,100)
- **0%**: 21,500
- **20%**: 5,200
- **40%**: 7,800
- **60%**: 2,600
- **80%**: 1,000
- **100%**: 0

#### Ever Diagnosed & Never in Specialist Care (N=10,300)
- **0%**: 6,700
- **20%**: 1,100
- **40%**: 1,900
- **60%**: 600
- **80%**: 1,100
- **100%**: 0

#### Ever in Specialist Care (N=10,000)
- **0%**: 5,600
- **20%**: 1,000
- **40%**: 1,800
- **60%**: 1,600
- **80%**: 1,000
- **100%**: 0

#### Treatment experienced (N=2,000)
- **0%**: 920
- **20%**: 220
- **40%**: 340
- **60%**: 520
- **80%**: 100
- **100%**: 0

#### Undiagnosed (N=16,800)
- **0%**: 9,200
- **20%**: 3,100
- **40%**: 4,100
- **60%**: 400
- **80%**: 400
- **100%**: 0

#### Treated each year (N=1,000)
- **0%**: 590
- **20%**: 110
- **40%**: 140
- **60%**: 160
- **80%**: 100
- **100%**: 0

(40% not seen for at least 1 year)
Research paper

Liver disease knowledge and acceptability of non-invasive liver fibrosis assessment among people who inject drugs in the drug and alcohol setting: The LiveRLife Study

A.D. Marshall a*, M. Micallef a, A. Erratt a, J. Telenta b, C. Treloar c, H. Everingham d, S.C. Jones b, N. Bath d, D. How-Chow c, J. Byrne f, P. Harvey g, A. Dunlop h,i, M. Jauncey f, P. Read a,j, T. Collie k, G.J. Dore a, J. Grebely a

aThe Kirby Institute, UNSW Australia, NSW, Australia
bCentre for Health and Social Research, Australian Catholic University, VIC, Australia
cCentre for Social Research in Health, UNSW Australia, NSW, Australia
dNSW Users and AIDS Association, Inc., NSW, Australia
eSt Vincent's Hospital Sydney, NSW, Australia
fAustralian Injecting and Illicit Drug Users League, ACT, Australia
gHepatitis NSW, Australia
hUniversity of Newcastle, Newcastle, NSW, Australia
iDrug and Alcohol Clinical Services, Hunter New England Local Health District, Newcastle, NSW, Australia
jKirketon Road Centre, NSW, Australia
kCoffs Harbour Drug and Alcohol Service, NSW, Australia
Conclusion

• Intervention works! And the more investment and targeting, the better.
• DBS testing highly acceptable.
• No intervention panacea exists but incentivisation
• Targeting current & former PWID is straightforward but requires effort & resources
• Non or very limited intervention for PWID is unjustifiable – but need to get best value for money
• New therapies render the existing evidence base less meaningful ...and their high cost means prioritisation, while undesirable, is a reality.
• It’s not just about diagnosis – but also “rediagnosis”