School of Medicine
University of Dundee

Models of HCV screening & treatment: An evidence-based international perspective

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• Speakers Bureau: AbbVie, Bristol-Myers Squibb, Boehringer Ingelheim, Gilead Sciences, GlaxoSmithKline, Janssen, Merck Sharp & Dohme, Roche
Why change our Hospital based model of care
The continuum of viral hepatitis services and the retention cascade

The global cascade of care for chronic HCV infection in 2015

HCV Tayside 2003
SVR associated with reduced hazard for a range of hepatic and non-hepatic events in Scotland (N=3,385) (Innes et al. Hepatology 2015)

Reduced hazard for behavioural events is consistent with SVR patients leading healthier lives.
Excess risk of a liver-related hospital episode post-therapy in HCV patients, compared to general population

SVR associated with a 5-fold reduction in risk of liver-related morbidity

Excess risk remains in SVR patients despite clearance of infection. Cannot ignore the importance of addressing lifestyle factors.
Stigma, Barriers, fear, inflexibility, distance, travel costs, lack of self worth, nihilistic view of future, Ignorance

Loss of the benefits of HCV treatment engagement beyond liver health
If the Mountain of patients won’t come to treatment

We must take treatment to the patients to achieve elimination
Out Reach & In reach services

Shortening the distance
Moving conventional Out-patient services to Locality
→ Usually partial
→ Community health centres
→ Mobile vans
→ Sometimes collocated with addictions facilities
  → Still new faces
  → A new environment
Treatment - no one “best” model of care
The PRIME Study is a randomised trial assessing the optimal model of HCV care

Prime Study cascade of care – first 120 patients
What do you need to treat HCV?
What do you really need to cure HCV?
Current Tayside practice
But can be varied to suit the patient

1. Diagnosis made on DBS (HCV ab and PCR, HIV, HBV) or venepuncture by non specialist, referred by whoever did the test

2. Visit 1 Seen by Nurse specialist (or the Community Pharmacist who did the DBS)
   1. Protocol history (age and alcohol history)
   2. Bloods for FBC, LFTs, Fib 4, HCV PCR if not possible before,
      1. Genotype (only if cost difference)
      2. Start treatment

3. Visit 2 Start Treatment/pick up treatment if not already done so

4. Virtual review of results, decide if ultrasound/fibroscan/duration of treatment/follow up

5. Visit 2 SVR
How do you deliver addiction care

Wide variety of

→ 1. addictive substances and treatments
→ 2. models of care

Key questions

→ Where are the patients already attending
→ Who is already seeing them

They have already over come the barriers
General practices, community health centres, and pharmacies

Community health Centres- site for outreach
General Practice-family practioners, primary medical care
  Often in community health centres
Addictions treatment centres
  Pharmacies for dispensing
Needle exchanges
General Practice  
Telemedicine, MCNs, virtual MDTs

Marked geographical variation in HCV prevalence with deprivation status in a practice area, varying from 0.1 to 3%

Should approaches be tailored to local circumstances?

GPs who provide addictions services
General Practice Identified Rates of Hepatitis C

Rate of Patients with a previous diagnosis of Hepatitis C in Dundee CHP practices participating in the BBV program per 1,000 registered patients.
Addictions services and Pharmacies

Addictions treatment centres
A site for out reach, an opportunity for addictions specialists
Who are your addictions specialists, what background

Who dispenses OST and where
<table>
<thead>
<tr>
<th>Preference</th>
<th>Willing to Wait</th>
</tr>
</thead>
<tbody>
<tr>
<td>Own rather than other pharmacy</td>
<td>4.25 weeks</td>
</tr>
<tr>
<td>Own pharmacy rather than GP</td>
<td>2.11 weeks</td>
</tr>
<tr>
<td>Own pharmacy rather than drug worker</td>
<td>0.08 weeks</td>
</tr>
<tr>
<td>Treated with respect</td>
<td>7.42 weeks</td>
</tr>
</tbody>
</table>
Pharmacies providing OST Mr Andrew Radley
PWID defined as those who either (a) are currently injecting drugs, (b) have ever injected drugs and are currently on opioid substitute therapy, or (c) have ever injected drugs and are currently in prison.

Standard HCV testing and treatment to all at risk of HCV

- Primary/secondary care
  - At risk patients offered venous blood test by physician
  - HCV therapy provided in secondary care by specialist nurse-led clinics in 1 hospital and 18 outreach clinics

Enhanced HCV testing and treatment service targeting PWID

- Pharmacies
  - OST clients offered DBS test by pharmacist
  - HCV therapy provided by specialist nurse-led or pharmacist-led clinics

- Drug treatment centres
  - OST clients offered DBS test by trained addiction worker
  - HCV therapy provided by specialist nurse-led clinics

- Prisons
  - Prisoners offered test on admission by prison nurse
  - HCV therapy provided by specialist nurse-led clinics at the 4 fixed site needle exchange sites

- Needle exchange
  - Clients offered DBS test by trained needle exchange staff
  - HCV therapy provided by specialist nurse-led clinics

DBS: dried blood spot; OST: opioid substitution therapies; POC: point of care; PWID: people who inject drugs
Empirical social network of PWID

200 %
SVR

8,100 %
SVR
Needle exchanges

Eradicate HCV project: a pilot of treatment as prevention in PWID

Treat
In the needle exchange
20–40 very active PWID/year
Collecting needles and injecting
Not required to change anything
Treatment with
→ PEG-IFN + RBV and telaprevir

Endpoints
• Year 2 numbers in treatment and SVR
• Year 5, 7 and 10 HCV population prevalence
→ NESI, needle exchange, entering methadone

Recruit
From needle exchange
→ Bring a friend, mine the vein
→ Contingency management
→ Low threshold methadone

Ahmad F, et al. EASL 2015; Abstract #P0801; Unpublished data

NESI: Network for Education and Support in Immunisation;
NHS: National Health Service
Eradicate HCV project: success is possible!

- Engage PWID at needle exchange centres in Tayside
- Incentivise suitable participants to comply with treatment
- 42 months into project; 105/125 eligible patients agreed to participate

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consented</td>
<td>105</td>
</tr>
<tr>
<td>Received treatment</td>
<td>94</td>
</tr>
<tr>
<td>Spontaneous resolver</td>
<td>3</td>
</tr>
<tr>
<td>Lost to follow-up</td>
<td>4</td>
</tr>
<tr>
<td>Stabilised drug use</td>
<td>2</td>
</tr>
<tr>
<td>Died prior to treatment</td>
<td>1</td>
</tr>
<tr>
<td>Prison prior to treatment</td>
<td>1</td>
</tr>
</tbody>
</table>

SVR12: sustained virological response 12 weeks after the end of treatment

Dillon JF. Unpublished data

Genotype 1: 88%
Genotype 2 and 3: 93%
10 YEAR RELATIVE PREVALENCE REDUCTIONS WITH COMBINING OST/NSP/TREATMENT: NO BASELINE COVERAGE OF OST/NSP AND USING DAAs

Martin NK, Hickman M, Hutchinson SJ, Goldberg DJ, and Vickerman P. Combination interventions to prevent HCV transmission among people who inject drugs: modelling the impact of antiviral treatment, needle and syringe programmes, and opiate substitution therapy. Clinical Infectious Diseases 2013
Challenges for TasP strategies

• Society is looking for treatment
  – Prevention of transmission

• Patient not prioritising treatment
  – Society needs most patients to agree to treatment
    • Or be coerced

• Treatment most effective if delivered to most risky patients
  – Not waiting for stabilisation
  – Not requiring behaviour change
  – Reaching out and encouraging

• Tackling groups
• Re-infection
### The Maths of TasP in Tayside

<table>
<thead>
<tr>
<th>Description</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total population of Tayside</td>
<td>397,000</td>
</tr>
<tr>
<td>PWID total</td>
<td>2761 (2360, 3174)</td>
</tr>
<tr>
<td>PWID recent/current</td>
<td>1595 (1343, 1887)</td>
</tr>
<tr>
<td>Number in contact with NSP</td>
<td>1151 (775, 1607)</td>
</tr>
<tr>
<td>OST</td>
<td>2198 (1838, 2568)</td>
</tr>
<tr>
<td>Number OST-only</td>
<td>1164 (784, 1523)</td>
</tr>
<tr>
<td>Proportion of PWID in NX</td>
<td>0.72 (0.51, 0.94)</td>
</tr>
<tr>
<td>Proportion NX on OST</td>
<td>0.65 (0.56, 0.73)</td>
</tr>
<tr>
<td>Proportion not NX on OST</td>
<td>0.67 (0.47, 0.81)</td>
</tr>
<tr>
<td>Chronic HCV infection rate in current PWID</td>
<td>28.8% (22-35)</td>
</tr>
<tr>
<td>Number PWID recent/current with chronic HCV</td>
<td>459 (387-544)</td>
</tr>
</tbody>
</table>

University of Dundee
Epitope and E-rapid in NHS Tayside

We will treat 450 active PWID in two years
Which is projected to reduce chronic HCV prevalence from 29% to less than 5%
This should reduce HCV incidence from 6-10% to less than 1%
This should prevent significant onward transmission
MCNs-lifesaving interventions for hepatitis C patients

Environment
System
→ Free for all at point of care
Drug workers- statutory/3rd sector
→ HCV awareness and diagnosis part of core work
→ Used as lever for behaviour change
→ Empowered to refer for treatment
→ Co-supervision of treatment

Pharmacists testing and treating OST

HCV treatment staff
→ Out-reach to locality
→ Embedded in drug services
→ Prison medical services

Patients HCV repeatedly on the agenda
→ Treated when patient wants to

Cohort study, prospectively collected data
A 22 year study 1994 and 2014 with follow up till 2016
Over 3,100 patients
Comparing the effectiveness of 4 care pathways
For all HCV antibody positive individuals tested in a geographical region.
Date of diagnosis defined pathway exposure despite subsequent pathway changes
<table>
<thead>
<tr>
<th>Care Pathway</th>
<th>Time period</th>
<th>Nature of pathway</th>
</tr>
</thead>
</table>
| Subgroup A  | Pre July 1999 | - HCV testing commenced in region  
- Limited access to treatment  
- No specialist nursing input available |
| Subgroup B  | July 1999 - June 2004 | - Specialist nursing support given at HCV treatment clinic  
- Clinic at main city hospital only  
- Treatment offered, interferon and ribavirin |
| Subgroup C  | July 2004 - June 2009 | - Development of managed care network  
- Appointment of part time Nurse specialist  
- New referral pathway- referrals open to all health care professionals including drug workers and prison nurses  
- Outreach clinics established locally and in drug and prison centres throughout region  
- Treatment interferon and ribavirin |
| Subgroup D  | July 2009 - June 2014 | - Routine dry blood spot testing in drug services and needle exchanges  
- Appointment of full time nurse specialist  
- Increase in outreach clinics across region  
- Treatment use of Direct Acting Antivirals (DAAs) in treatment regimen |
## Results

### Demographics

<table>
<thead>
<tr>
<th></th>
<th>Subgroup A (n=688)</th>
<th>Subgroup B (n=634)</th>
<th>Subgroup C (n=593)</th>
<th>Subgroup D (n=1207)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Tester</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>General Practitioner</td>
<td>227 (32.9%)</td>
<td>265 (41.7%)</td>
<td>222 (37.4%)</td>
<td>276 (22.8%)</td>
</tr>
<tr>
<td>Prison Services</td>
<td>150 (21.8%)</td>
<td>131 (20.6%)</td>
<td>118 (19.8%)</td>
<td>174 (14.4%)</td>
</tr>
<tr>
<td>Hospital inpatient/outpatient</td>
<td>111 (16.1%)</td>
<td>76 (11.9%)</td>
<td>85 (14.3%)</td>
<td>195 (16.1%)</td>
</tr>
<tr>
<td>Other</td>
<td>84 (12.2%)</td>
<td>98 (15.4%)</td>
<td>82 (13.8%)</td>
<td>120 (9.9%)</td>
</tr>
<tr>
<td>HIV Specialist Team</td>
<td>56 (8.1%)</td>
<td>24 (3.7%)</td>
<td>21 (3.5%)</td>
<td>9 (0.7%)</td>
</tr>
<tr>
<td>Drug services</td>
<td>31 (4.5%)</td>
<td>36 (5.6%)</td>
<td>64 (10.4%)</td>
<td>433 (35.8%)</td>
</tr>
<tr>
<td>Haematology</td>
<td>29 (4.2%)</td>
<td>4 (0.6%)</td>
<td>1 (0.1%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td><strong>Median age at diagnosis (Age range)</strong></td>
<td>34.9 years</td>
<td>35.5 years</td>
<td>36.8 years</td>
<td>35.8 years</td>
</tr>
<tr>
<td><strong>Risk Factor</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blood products</td>
<td>50 (7.2%)</td>
<td>18 (2.8%)</td>
<td>25 (4.2%)</td>
<td>21 (1.7%)</td>
</tr>
<tr>
<td>Intravenous drug use</td>
<td>496 (72.0%)</td>
<td>501 (81.0%)</td>
<td>450 (75.8%)</td>
<td>1009 (87.5%)</td>
</tr>
<tr>
<td>From high prevalence country</td>
<td>14 (2.0%)</td>
<td>15 (2.3%)</td>
<td>38 (6.4%)</td>
<td>81 (5.0%)</td>
</tr>
<tr>
<td>No risk factors known</td>
<td>55 (7.9%)</td>
<td>36 (5.6%)</td>
<td>38 (6.4%)</td>
<td>52 (4.3%)</td>
</tr>
<tr>
<td>Other (sexual, tattoo, needle stick)</td>
<td>32 (4.6%)</td>
<td>35 (5.5%)</td>
<td>36 (6.1%)</td>
<td>42 (3.4%)</td>
</tr>
<tr>
<td>Not documented</td>
<td>37 (5.4%)</td>
<td>29 (4.7%)</td>
<td>2 (0.3%)</td>
<td>2 (0.1)</td>
</tr>
<tr>
<td><strong>Non Resident/moved</strong></td>
<td>103 (14.9%)</td>
<td>93 (14.6%)</td>
<td>58 (9.7%)</td>
<td>40 (3.3%)</td>
</tr>
<tr>
<td><strong>Death before access to care</strong></td>
<td>181 (26.3%)</td>
<td>82 (12.9%)</td>
<td>39 (6.5%)</td>
<td>22 (1.8%)</td>
</tr>
<tr>
<td><strong>No Trace</strong></td>
<td>19 (2.7%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>4 (0.3%)</td>
</tr>
</tbody>
</table>
## Numbers of deaths by subgroup

<table>
<thead>
<tr>
<th>Number diagnosed with HCV</th>
<th>Subgroup A (n=688)</th>
<th>Subgroup B (n=634)</th>
<th>Subgroup C (n=593)</th>
<th>Subgroup D (n=1207)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dead before access to care</td>
<td>181 (26.3%)</td>
<td>82 (12.9%)</td>
<td>39 (6.5%)</td>
<td>22 (1.8%)</td>
</tr>
<tr>
<td>Died after access to care</td>
<td>51 (7.4%)</td>
<td>57 (8.9%)</td>
<td>36 (6.1%)</td>
<td>33 (2.7%)</td>
</tr>
<tr>
<td>Total deaths</td>
<td>232 (33.7%)</td>
<td>139 (21.9%)</td>
<td>75 (12.6%)</td>
<td>55 (4.5%)</td>
</tr>
</tbody>
</table>
Kaplan-Meier curves of survival (all-cause mortality)

![Graph showing Kaplan-Meier curves for different subgroups. The x-axis represents time from the first test (years), while the y-axis represents survival probability. Different subgroups are indicated by distinct colors: Subgroup A (black), Subgroup B (red), Subgroup C (green), and Subgroup D (blue).]
<table>
<thead>
<tr>
<th>Cause of death in all cohorts</th>
<th>Access to HCV care</th>
<th>No access to HCV care</th>
<th>PCR Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol related Cirrhosis Of Liver</td>
<td>17</td>
<td>13</td>
<td>3</td>
</tr>
<tr>
<td>Assault</td>
<td>3</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Drug related death</td>
<td>57</td>
<td>69</td>
<td>20</td>
</tr>
<tr>
<td>Falling jumping or pushed from high place</td>
<td>0</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Drug related death/known cirrhosis</td>
<td>5</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>HIV related death</td>
<td>10</td>
<td>58</td>
<td>6</td>
</tr>
<tr>
<td>Liver cirrhosis</td>
<td>9</td>
<td>8</td>
<td>0</td>
</tr>
<tr>
<td>Liver cirrhosis died from other serious illness</td>
<td>4</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Liver cirrhosis with liver cancer</td>
<td>26</td>
<td>14</td>
<td>1</td>
</tr>
<tr>
<td>Mental and behavioural disorders due to alcohol dependence syndrome</td>
<td>8</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Not known</td>
<td>7</td>
<td>11</td>
<td>8</td>
</tr>
<tr>
<td>Other cancer not liver related</td>
<td>7</td>
<td>14</td>
<td>6</td>
</tr>
<tr>
<td>Other serious illness resulting in death</td>
<td>23</td>
<td>51</td>
<td>16</td>
</tr>
<tr>
<td>Other specified viral hepatitis without mention of hepatic coma</td>
<td>10</td>
<td>14</td>
<td>4</td>
</tr>
<tr>
<td>Suicide</td>
<td>10</td>
<td>18</td>
<td>4</td>
</tr>
<tr>
<td>Total died</td>
<td>196</td>
<td>284</td>
<td>69</td>
</tr>
<tr>
<td>Total in subgroup</td>
<td>1629</td>
<td>545</td>
<td>651</td>
</tr>
<tr>
<td>% of deaths per subgroup</td>
<td>12.0%</td>
<td>52.1%</td>
<td>10.5%</td>
</tr>
</tbody>
</table>
Multivariate Cox regression analysis for the time from the first test to all-cause mortality

<table>
<thead>
<tr>
<th>Covariates</th>
<th>Multivariate HR (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at the first test</td>
<td>1.05 (1.04 – 1.05)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Gender Male vs. Female</td>
<td>1.28 (1.04 – 1.56)</td>
<td>0.018</td>
</tr>
<tr>
<td>HIV Yes vs No</td>
<td>4.35 (3.40 – 5.56)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Subgroup B vs A</td>
<td>0.85 (0.69 – 1.05)</td>
<td>0.128</td>
</tr>
<tr>
<td>Subgroup C vs A</td>
<td>0.79 (0.61 – 1.02)</td>
<td>0.074</td>
</tr>
<tr>
<td>Subgroup D vs A</td>
<td>0.53 (0.40 – 0.71)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>
What’s the point of doing a HCV test in People Who Inject Drugs

Having a HCV test positive
Having someone to talk to about
Perhaps having treatment for it
Reduces the risk of death for all cause mortality before liver disease mortality

It saves Lives
Acknowledgements
The Team- Jan Tait, Brian Stephens, Dianne Knight, Farsana Ahmed, Andrew Radley, Linda Johnston, Shirley Cleary, Christian Sharkey, Morgan Evans, Sarah Inglis, Lewis Beer, Chris Bryne, Amy Malaguti, Steve McSwiggan, James Flood, Donna Thain, Ann Eriksen
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