Hepatitis C
The NHS Model

Professor Graham R Foster
Professor of Hepatology
Barts Liver Centre
QMUL
The NHS Approach

• Background

• The strategy

• Tactics
The NHS Approach

• Background

• The strategy

• Tactics
NHSE

• Single provider of health care in England

• Multiple different commissioning groups (local clinical, local council and national)

• Single provider allows central negotiation and planning

• Multiple local providers introduces innovation and local prioritisation
NHSE

• Equity is key

• If anyone can get it, everyone gets it

• Discrimination on any grounds, overt or covert is strictly forbidden
HCV in England – the aim is to eliminate
How many?

• ~ 120,000 infected
• ~ 25% of liver transplants
• ~ 1000 deaths per year
In England, 50% of people who inject drugs (PWID) are thought to be infected. 16% of PWID share needles.

- 68,000 don’t know they have HCV
- 16,600 are likely F3/F4
- 8,660 are F3
- 8660 F4
- 13,000 F3
- 68,000 F0-F2

About 20% have symptoms related to HCV.

End Stage Liver Disease
1810 prevalence. NHS England Clinical Policy from April 2014

The total number of patients with Hepatitis C is circa 160K but 95% uncertainty is a range from 120-225K.

Advanced Fibrosis
Circa 1650 from this group develop cirrhosis each year. NICE TA for oral drugs for all this group. The data of the size of this group is uncertain. Many of those newly tested will already have fibrosis so this cohort may rise significantly.

Risk in numbers as we do not know how many of prevalence will come forward.

NICE oral drug access if GT1. GT3 access if interferon based treatments have failed.

10-20,000 expected to come forward for treatment each year.

Many patients won’t come forward because they don’t access healthcare with chaotic lives. Some in this group are most likely to cause cross infection.

Men who have sex with men

Immigrant

Blood products

Public Health England focus on increased testing, opt out testing in prisons. Strategies to reduce transmission.

4 main genotypes of HCV

- GT1 47%
- GT3 44%
- GT2
- GT4

All F3/F4 patients have access to new drugs. F0-2 patients have access if they have failed PEGI.

All this group have access to new drugs regardless of disease severity.

The data of the size of this group is uncertain. Many of those newly tested will already have fibrosis so this cohort may rise significantly.

Many patients won’t come forward because they don’t access healthcare with chaotic lives. Some in this group are most likely to cause cross infection.

Cirrhosis
8,660 prevalence
NHS England Clinical Policy from May 2015

20-30% will develop cirrhosis over 20 years.

68,000 prevalence. NHS England Clinical Policy from April 2014

The total number of patients with Hepatitis C is circa 160K but 95% uncertainty is a range from 120-225K.

Cirrhosis
8,660 prevalence
NHS England Clinical Policy from May 2015

Risk in numbers as we do not know how many of prevalence will come forward.

Advanced Fibrosis
Circa 1650 from this group develop cirrhosis each year. NICE TA for oral drugs for all this group. The data of the size of this group is uncertain. Many of those newly tested will already have fibrosis so this cohort may rise significantly.

Risk in numbers as we do not know how many of prevalence will come forward.

NICE oral drug access if GT1. GT3 access if interferon based treatments have failed.

10-20,000 expected to come forward for treatment each year.

Many patients won’t come forward because they don’t access healthcare with chaotic lives. Some in this group are most likely to cause cross infection.

Cirrhosis
8,660 prevalence
NHS England Clinical Policy from May 2015

Risk in numbers as we do not know how many of prevalence will come forward.

Advanced Fibrosis
Circa 1650 from this group develop cirrhosis each year. NICE TA for oral drugs for all this group. The data of the size of this group is uncertain. Many of those newly tested will already have fibrosis so this cohort may rise significantly.

Risk in numbers as we do not know how many of prevalence will come forward.

NICE oral drug access if GT1. GT3 access if interferon based treatments have failed.

10-20,000 expected to come forward for treatment each year.

Many patients won’t come forward because they don’t access healthcare with chaotic lives. Some in this group are most likely to cause cross infection.
The NHS Approach

• Background

• The strategy

• Tactics
Fig. 4

Cumulative subhazard for cirrhosis

Time since infection
Fig. 4

Cumulative subhazard for cirrhosis vs. time since infection.
These people transmit

These people die
HCV in England
The numbers

• Eventually most people with HCV will need treating

• Only very sick people need treating immediately

• (Drug prices always come down)
NHSE Strategy

• Immediate therapy for decomp cirrhosis

• Early therapy for cirrhosis (reduce mortality)

• Priority expansion of access in drug services/prisons (cut off transmission)
In England 50% of people who inject drugs (PWID) are thought to be infected. 16% of PWID share needles.

68,000
F0-F2

About 20% have symptoms related to HCV

20-30% will develop cirrhosis over 20 years

Risk in numbers as we do not know how many of prevalence will come forward

Advanced Fibrosis
Circa 1650 from this group develop cirrhosis each year. NICE TA for oral drugs for all this group. The data of the size of this group is uncertain. Many of those newly tested will already have fibrosis so this cohort may rise significantly.

NICE oral drug access if GT1. GT3 access if interferon based treatments have failed

10-20,000 expected to come forward for treatment each year

Many patients won’t come forward because they don’t access healthcare with chaotic lives. Some in this group are most likely to cause cross infection

GT1 47%
GT2
GT3 44%
GT4

Public Health England focus on increased testing, opt out testing in prisons. Strategies to reduce transmission

The total number of patients with Hepatitis C is circa 160K but 95% uncertainty is a range from 120-225K

End Stage Liver Disease
1810 prevalence. NHS England Clinical Policy from April 2014

Immigrant
Men who have sex with men
Blood products

Don’t know they have HCV

GT1
GT2
GT3
GT4

4 main genotypes of HCV

All F3/F4 patients have access to new drugs. F0-2 patients have access if they have failed PEGI

All this group have access to new drugs regardless of disease severity

Public Health England

Men who have sex with men

About 20% have symptoms related to HCV

10,000 extra patients diagnosed each year

NHS England Clinical Policy from May 2015

Cirrhosis
8,660 prevalence

NHS England Clinical Policy from April 2014

End Stage Liver Disease
1810 prevalence. NHS England Clinical Policy from April 2014

Cirrhosis
8,660 prevalence

NHS England Clinical Policy from May 2015

Cirrhosis
8,660 prevalence

NHS England Clinical Policy from May 2015

Cirrhosis
8,660 prevalence
The NHS Approach

• Background

• The strategy

• Tactics
NHSE Tactics

• Regional networks with responsibility for the region – clinically led
8. Leicester

* Below average population size
* More than 10% of population of South Asian ethnicity
* Below average estimated number of chronic HCV infections
* The majority of infections (77%) are in those that have ever injected drugs
* 15.0% of chronic infections are estimated to be in never-injectors of South Asian ethnicity
* As with most areas, the number of people initiating injecting drug use is estimated to have fallen since the 1990s
* The proportion of HCV-infected PWID is estimated to be below average (21%)
* The estimated proportion of those infected living with cirrhosis is above average (13.3%)
This is due to an earlier epidemic of injecting drug use and older infected population
* Likely under-reporting of ESLD/HCC in pre-2011 period
* 32% of the ever-infected population in 2017 are estimated to have achieved SVR

Prevalence estimates (end of 2017)

<table>
<thead>
<tr>
<th>Risk group</th>
<th>Risk group size</th>
<th>Chronic infections</th>
<th>% prevalence</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>PWID</td>
<td>3,060</td>
<td>640</td>
<td>20.9%</td>
<td>Depends on UAM survey and NTA estimates</td>
</tr>
<tr>
<td>Ex-PWID</td>
<td>9,810</td>
<td>1,310</td>
<td>13.4%</td>
<td>Dependent on progression rates and HES data</td>
</tr>
<tr>
<td>S. Asian never injectors</td>
<td>182,200</td>
<td>380</td>
<td>0.21%</td>
<td>Based on limited 2005 data and no temporal trend</td>
</tr>
<tr>
<td>White/other never injectors</td>
<td>1,580,000</td>
<td>210</td>
<td>0.01%</td>
<td>No direct data and no temporal trends</td>
</tr>
<tr>
<td>Total population</td>
<td>1,775,070</td>
<td>2,550</td>
<td>0.14%</td>
<td>Dependent on all assumptions</td>
</tr>
</tbody>
</table>

Credible interval for total chronic infections: **2,100 - 3,160**

Uncertainty is conditional on model assumptions

**Note:** sums of subgroup estimates do not necessarily match total (see Technical details)

<table>
<thead>
<tr>
<th>Disease stage breakdown</th>
<th>Mild</th>
<th>Moderate</th>
<th>Cirrhosis</th>
<th>% cirrhosis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1,750</td>
<td>780</td>
<td>360</td>
<td>12.5%</td>
</tr>
</tbody>
</table>

**Notes:** estimates depend strongly on progression rates

Sums of subgroup estimates do not necessarily match total (see Technical details)
NHSE Tactics

• Each region must set its own priorities
  • (Everyone prioritised cirrhosis first but great differences in second priorities)

• Each region must set up out-reach clinics with signed agreements in prisons, addiction units etc

• Each region must set up a laboratory link to report all infected patients
NHSE Tactics

• Choice of drug is determined nationally based on a six month tender (lowest acquisition cost is awarded the tender)

• Clinicians must use lowest acquisition cost treatment unless there is a compelling clinical reason

• All patients must be discussed at a central meeting

• Data on everything is recorded (prescriptions, national registry)
NHSE Tactics

• Each network given a treatment target with financial incentives for reaching the target
  
• (Initially targets prioritised patients and only priority patients were treated, very soon targets drove case-finding as hospitals ‘ran out’ of patients)
NHSE Tactics

• What did they achieve?
Impact of therapy on mortality

Deaths from HCV or HCC in patients with HCV (PHE report on HCV 2016)

Transplants for HCV
The English Registry

Gender

Liver disease stage
- No fibrosis
- Mild fibrosis
- Moderate fibrosis
- Compensated cirrhosis
- Decompensated cirrhosis

Number of patients

Age

Liver disease stage
- No fibrosis
- Mild fibrosis
- Moderate fibrosis
- Compensated cirrhosis
- Decompensated cirrhosis

Gender
- Female
- Male

Age (years)

Number of patients
HCV – the registry delivers

Note major differences in referral source (GP/hospital excluded for clarity)
NB – most referrals from GP/Hospital is there consistent coding?
NHSE HCV Registry

Total entries 35,634

Adults 35,435

Age unknown: 131
Age under 16 years: 68

Treated adults 27,360

No treatment: 7,659
Invalid treatment: 416

Treated adults with cirrhosis (local diagnosis): 8,070
Treated adults with fibrosis (defined by Fibroscan): 14,895

No disease stage: 4,395
National SVR12 rate is 95.16% (94.81%-95.49%)
Impact on price

• The price has plummeted

• NHSE agreed to re-invest price reductions in more treatments

• The run rate has increased substantially
Impact of NHSE Tactics

• Rapid reduction in waiting lists
• Access to ‘welcoming’ services achieved

BUT

• Testing rates have not kept pace with treatment rates
• Non-engaged services remain disengaged
NHSE Future Tactics

• We need to expand access and testing
NHSE Future Tactics

• We need to expand access and testing

Plan

• Partner with pharma to find and treat patients
• New deal offered to pharma with funding dependent on finding and treating patients
Moving to elimination

NHS England hopes England will be first country to eliminate Hepatitis C

Press Association  29 January 2018

The NHS is planning for England to be the first country in the world to eliminate Hepatitis C. Health leaders have called on the pharmaceutical industry to work with them to provide best value for money for treatments so that the NHS can commit to eliminating Hepatitis C in England at least five years earlier than the World Health Organisation goal of 2030.

A round of procurement launching in February is the single largest medicine procurement done by the NHS, and NHS England expects to see more new treatments curing more patients by October.
NHS Tactics
Future schemes

• A number of initiatives to find and treat patients are under way

• We envisage that some of the schemes will be adopted and become standard practice
Finding and treating
The ‘old positives’

• Schemes to re-engage previously diagnosed patients are under way
  (10-20% attendance in first few months)

• 60,000 old patients diagnosed since 2000

• Data on ALL old diagnosed patients to be made available in April
Finding and treating

Immigrants

• HepFREE trial of 90,000 immigrants in primary care identifies techniques to test and treat
• (bribe GPs, test the right patients)
Testing rates in HepFREE

Control Practices
Total Eligible 31,738
- Tested = 543 (1.7%)
- Not Tested = 31,195

Intervention Practices
Total Eligible 58,512
- Tested = 11,386 (19.5%)
- Not Tested = 47,126

INCIDENCE RATIO 3.7
p-Value 0.014

Flanagan et al Lancet Gastro Hep 2019
### Who tested positive for Viral Hepatitis?

<table>
<thead>
<tr>
<th></th>
<th>Tested</th>
<th>+ve</th>
<th>% +ve</th>
<th>HBsAg +ve</th>
<th>HBsAg +ve (%)</th>
<th>HCV Ab +ve</th>
<th>HCV Ab +ve (%)</th>
<th>RNA +ve</th>
<th>RNA +ve (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TOTAL</strong></td>
<td>11,929</td>
<td>237</td>
<td>2.0%</td>
<td>127</td>
<td>1.06%</td>
<td>111</td>
<td>0.93</td>
<td>36</td>
<td>0.3%</td>
</tr>
<tr>
<td>Afro/Cari</td>
<td>657</td>
<td>11</td>
<td>1.7%</td>
<td>9</td>
<td>1.37%</td>
<td>2</td>
<td>0.30</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Indian SC</td>
<td>8,991</td>
<td>166</td>
<td>1.8%</td>
<td>70</td>
<td>0.78%</td>
<td>96</td>
<td>1.06</td>
<td>34</td>
<td>0.38%</td>
</tr>
<tr>
<td>Other</td>
<td>2,281</td>
<td>69</td>
<td>2.63%</td>
<td>48</td>
<td>2.1%</td>
<td>13</td>
<td>0.57</td>
<td>2</td>
<td>0.09%</td>
</tr>
</tbody>
</table>

|                |         |      |       |           |               |            |               |         |            |
| **GENDER**     |         |      |       |           |               |            |               |         |            |
| Male           | 6,841   | 104  | 1.5%  | 41        | 0.60%         | 63         | 0.92          |         |            |
| Female         | 5,087   | 133  | 2.6%  | 86        | 1.69%         | 48         | 0.94%         |         |            |

|                |         |      |       |           |               |            |               |         |            |
| **AGE GROUP**  |         |      |       |           |               |            |               |         |            |
| <40            | 5,522   | 95   | 1.7%  | 52        | 0.94%         | 43         | 0.78%         |         |            |
| >40            | 6,407   | 142  | 2.2%  | 75        | 1.17%         | 68         | 1.1%          |         |            |

- **<40 years:** 1.72% prevalence
- **>40 years:** 2.21% prevalence
Finding and treating

Prisoners

• Point of care Cepheid machines are being tested in reception prisons with instant access to pan-genotypic medication

• ‘Blitz Clean’ is being tried where all prisoners on a wing are tested and treated
Finding and treating PWIDs in methadone programmes

- Testing rates vary from 5% – 90%
- Studies examining the barriers are in progress
- Staff attitudes may be key, peer workers to improve engagement may help
Finding and treating

PWIDs in needle exchange programmes

• Testing in needle exchange pharmacies is being introduced

• Schemes with point of care instant access to treatment, incentivised referrals and peer supporters are being tried
Lessons learned
What worked?

• Regional clinical leads, local multi-disciplinary meetings enabled local control and devolution of responsibility

• Enforcing collaboration and out-reach was key

• The national registry allows monitoring and supervision

• Single drug tender reduced prices without clinical compromise
Lessons learned

What did not work?

• Access to many institutions (prisons, drug services) was limited by factors beyond doctor’s control

• Testing rates in key groups remains low
NHS and HCV
70 years old and still innovating