LIVER DISEASE
VIRAL HEPATITIS

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Liver Disease- Degree of the problem
Hepatitis B virus
Hepatitis C virus
What for Croydon patients?
Mortality in England & Wales
UK LIVER DISEASE CRISIS

Survival rates have improved for almost every disease of every organ in the last few decades, with one notable exception: liver disease.

What’s driving this?

1. The UK population changed their drinking habits reflecting the affordability of stronger alcohol at home...

...and the number of people admitted to hospital for alcohol-related liver disease has almost doubled in a decade.
The Lancet Commission on liver disease is a group of multi-disciplinary experts aiming to make firm recommendations to reduce the unacceptable premature mortality and disease burden from avoidable causes and to improve the standard of care for patients with liver disease in hospital.

**Summary of the ten key recommendations of the initial *Lancet* Commission report published in November, 2014**

- Strengthening detection of early liver disease and its treatment in primary care
- Improvement of support services in the community for screening of people at high risk
- A blueprint for improving care for acutely sick patients through establishment of liver units in district general hospitals and regional specialist centres
- A national review of liver transplantation services in the UK
- Strengthening the continuity of transitional care from child to adult services
- Scaling up of national action to reduce the country's overall consumption of alcohol
- Promotion of healthy lifestyles to address the current epidemic of obesity
- Eradication of hepatitis B and C virus infections by 2030
- Greater provision of medical training in hepatology and wider opportunities for all health professionals to increase knowledge of liver disease
- Launch of a national campaign to increase awareness of liver disease in the general population

Figure 3: Liver deaths in England and Wales (ONS DH2 and DR)
CROYDON CENTRAL
LIVER DISEASE PROFILE

BACKGROUND
Liver disease is the third most common cause of premature death in the UK and the national liver disease health outcomes are worse than in other western European countries.\(^1\)

Over the last decade, the number of liver disease-related hospital admissions in England has increased by half,\(^2\) placing an ever greater strain on the health service.

Liver disease disproportionately affects the poorest and the most vulnerable in society and is a major factor in generating socioeconomic health inequalities.\(^3\)

LIVER DISEASE IN NUMBERS
- Liver disease mortality rates in the UK increased 400% since 1970\(^1\)
- £2.1 billion per year spent on treating liver disease\(^3\)
- More than 1 million admissions to hospital per year as a result of alcohol-related disorders\(^1\)
- 62,000 years of working life lost to liver disease every year\(^1\)
- Care for patients who died of liver disease rated as less than good in more than half cases\(^5\)

LIVER DISEASE IN CROYDON CENTRAL

368 YEARS OF WORKING LIFE were lost in your constituency due to liver disease in 2012-14\(^6\)

That is more than the number of working years lost due to:
- Lung cancer
- Stroke
- Colorectal cancer

The liver disease MORTALITY RATE amongst under-75s in your local area is 15.7 per 100,000
This is lower than the national average (17.8 per 100,000)\(^7\)

The rate of hospital admissions due to liver disease in your local area is lower than the national average.\(^7\)

232 HOSPITAL ADMISSIONS due to liver disease in your constituency in 2014-15\(^8\)
Hepatitis B

- Hepadna(DNA) virus which is endemic worldwide but in some isolated communities, there is a very high carriage rate (upto 20%), particularly in South and East Asia, Africa, Southern and Eastern Europe and S America.

- 8 distinct genotypes which vary in pathogenicity and treatment susceptibility like A and B genotypes are more likely to achieve HBeAg and HBsAg loss with PEG IFN.

- Transmission
  - Sexual
  - Vertical, parenteral-unscreened blood pdts, sharing needles, syringes, occupational, non sterile acupuncture/tattoo needles
  - Sporadic – institutions for learning difficulties, children in countries of high background prevalence.
Hepatitis B

- Incubation period: 40-160 days

- Symptoms:
  - Asymptomatic (usually infants/children)
  - Prodormal illness: flu like symptoms. 3-10 days
  - Icteric illness: Jaundice (mixed hepatitis and cholestatic) - 1 to 3 weeks
  - Chronic carriers: usually asymptomatic but can have fatigue/loss of appetite

- Signs: Icteric phase:
  - Cholestatic jaundice with probable tender liver
Acute hepatitis B infection

- Acute liver failure occurs in 1% of symptomatic cases

- Mortality is less than 1% for acute cases

- Increased risk of miscarriage / premature labour in acute infection

- There is evidence that anti-viral agents can prevent Acute Liver Failure, improve morbidity and mortality in patients with severe acute infection
CHRONIC HBV INFECTION

- 350 million people worldwide with CHB
- >600,000 deaths per year
- 80% of deaths in those infected at birth/early childhood
- 25% of those infected in childhood develop cirrhosis or HCC
CHRONIC HBV INFECTION

**Diagram:**
- **Entry:** Virion binds to receptor(s) and enters the cell.
- **Endocytosis:** Virion is taken up by endocytosis.
- **Cytoplasm:** Virion enters the cytoplasm.
  - **cccDNA Formation:**cccDNA is formed.
  - **cccDNA Amplification:** cccDNA is amplified.
- **Nucleus:**
  - **Minichromosome Transcription:** Transcription of minichromosome.
    - 3.5kb
    - 2.4kb
    - 2.1kb
    - 0.7kb
  - **Pre-genomic RNA Transcription:** Transcription of pre-genomic RNA.
- **Endoplasmic Reticulum (ER):**
  - **Envelope Proteins:**Envelope proteins are synthesized.
  - **Budding:** Virions bud from the ER.
  - **Plus Strand DNA Synthesis:** Plus strand DNA is synthesized.
  - **Reverse Transcription:** Reverse transcription of RNA to DNA.
  - **Encapsidation:** Enveloped virions are formed.
  - **Secretion:** Virions are secreted outside the cell.
CHRONIC HBV INFECTION

NUC therapy target
CHRONIC HBV INFECTION

Ideal therapy target

NUC therapy target
NATURAL HISTORY OF HBV

HBsAg +

HBeAg +

HBeAg - / anti-HBe +

HBV-DNA

ALT

Immunotolerant phase

Immunoactive phase

Inactive carrier state (resolved hepatitis B (HBsAg - /anti-HBs +))

Reactivation
<table>
<thead>
<tr>
<th>Stage of infection</th>
<th>Surface antigen (HBsAg)</th>
<th>'e' antigen (HBeAg)</th>
<th>IgM anti-core antibody</th>
<th>IgG anti-core antibody</th>
<th>Hepatitis B virus DNA</th>
<th>Anti-HBe</th>
<th>Anti-HBs</th>
<th>ALT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute (early)</td>
<td>+</td>
<td>+</td>
<td>+*</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>↑↑↑↑</td>
</tr>
<tr>
<td>Acute (resolving)</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>+/-</td>
<td>-</td>
<td>↑↑</td>
</tr>
<tr>
<td>Chronic (immune tolerant)</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>++</td>
<td>-</td>
<td>-</td>
<td>N**</td>
</tr>
<tr>
<td>Chronic (immune active)</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>↑</td>
</tr>
<tr>
<td>Chronic (eAg Neg.)</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>+/-</td>
<td>-</td>
<td>↑</td>
</tr>
<tr>
<td>Chronic (inactive carrier)</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>N</td>
</tr>
<tr>
<td>Resolved (immune)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>+/-</td>
<td>+/-</td>
<td>N</td>
</tr>
<tr>
<td>Successful vaccination</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>N</td>
</tr>
</tbody>
</table>
NICE Clinical Guideline 165; Hepatitis B (chronic); June 2013
Treatment sequence in CHB

- PegIFN x 48 weeks (1\textsuperscript{st} line)- contraindicated in those with liver cirrhosis, autoimmune ds, uncontrolled psychiatric ds, uncontrolled seizures, severe cardiac ds and cytopenias

- Tenofovir (2\textsuperscript{nd} line treatment) NICE TA guidance (2009)- Nucleotide analogue that works by blocking enzyme reverse transcriptase which is responsible for viral replication.

  - Achieves viral replication in 76% for Hep BeAg +ve patients and 90% for Hep BeAg –ve pts.
  - £225 for a 30 day pack; with 30% discount 2016 per patient per year. Becomes generic(-80%) in 2017 – estimated £403 per pt per yr
  - Tenofovir Alafenamide (pro-drug of tenofovir disoproxil)-just been approved by the European Medicines Agency- lesser bone mineral density loss and renal side effects
Entecavir (alternative 2\textsuperscript{nd} line for those who cannot tolerate Tenofovir or contraindicated)

- NICE TA guidance(2008)- Nucleoside analogue that works by blocking the viral DNA polymerase which is responsible for viral replication.
- Achieves viral suppression in 70-83\% HepBeAg +ve pts and 91-98\% in HepBeAg -ve pts.
- £378 for a 30 daypack. Entacavir becomes generic in UK in 2017
Every little helps

Global Hepatitis B epidemic can be treated at cost of £24 per person per year

Entecavir for Hepatitis B
one year's supply (0.18g)

There must be something wrong!!
1. Testing and vaccination for hepatitis B

2. Referral for specialist care

3. Referral of HBsAg+ pregnant women from antenatal screening

4. Complete course of neonatal hepatitis B vaccination and blood testing at 12 months
Flow chart for Hepatitis B screening using serum HBsAg

- **HBsAg**
  - **Negative**
    - **anti-HBc**
      - **Negative**
        - No previous exposure to hepatitis B. Do anti-HBs test if previously vaccinated
      - **Positive**
        - Patient naturally immune to hepatitis B
        - If Anti-HBe/s-ve, give vaccine booster
  - **Positive**
    - Acute or Chronic hepatitis B Carrier: test for IgM anti-HBc, HBeAg, HBeAb (+/-HBV-DNA)
Pregnancy
Why is it important to refer to a hepatologist?

NICE clinical guideline (CG165) states:

- Pregnant women who are found to have hepatitis B infection during antenatal testing are assessed by a specialist within 6 weeks of receiving the screening test result.

Rationale: In the absence of intervention, vertical transmission occurs in 90% of pregnancies where the mother is Hepatitis eAntigen +ve and in about 10% of HBsAg +ve but HBeAg –ve mothers and >90% infected infants become chronic carriers.

- HBIG (200IU I/M) reduces vertical transmission by 90%
- Consider Tenofovir monotherapy for pregnant women with HBV DNA >10⁷ IU/ml in the third trimester to reduce the risk of transmission of HBV to baby.
- Hepatitis B activity may increase following pregnancy, but is seldom associated with clinical consequences.
Pregnancy and Breast feeding

- Only antivirals studied are lamivudine, Telbuvidine and Tenofovir

- Stop Antiviral therapy at 3 months post-partum (unless mother meets criteria for long term treatment) and the women should be monitored for ALT flares upto 6 months

- Breastfeeding is NOT contraindicated.

- C-section is not indicated owing to insufficient data to support benefit
KPI target set by NHSE is 90% for HBsAG +ve pregnant women to be seen by a specialist within 6 weeks

CUH achieved 46.7% in Q3 2014-15

HIGH DNA rate at King’s liver unit for these antenatal clinic
Prophylactic treatment during immunosuppressive therapy

- Immunosuppressive therapy for autoimmune diseases, chemotherapy, bone marrow or solid organ transplantation

- Should start before the chemotherapy and be continued for 6 months after stopping immunosuppressive therapy or HBV levels undetectable

- HBsAg +ve and HBV DNA >2000 IU/ml
  - Offer prophylaxis with Tenofovir or Entacavir

- HBsAg +ve and HBV DNA <2000 IU/ml
  - Lamuvudine if chemotherapy <6/12
  - Tenofovir/Entacavir if chemotherapy >6/12
Prophylactic treatment during immunosuppressive therapy

- HBsAg -ve; Anti-HBc positive starting rituximab or B- cell depleting therapies: Offer prophylaxis with Lamuvidine

- HBsAg –ve; Anti-HBc positive and Anti-HBs negative who are not taking rituximab or B cell depleting therapies: monitor HBV DNA monthly and offer prophylaxis if HBV DNA becomes detectable

- HBsAg –ve; Anti-HBc positive and Anti- HBs positive: NO prophylaxis if not taking Rituximab/B cell depleting therapies
5. Personalised care plan

6. Monitoring patients with CHB who do not meet treatment criteria for antiviral therapy

7. Six monthly surveillance testing for HCC in patients with CHB and advanced fibrosis/cirrhosis
Surveillance testing for Hepatocellular carcinoma for those with chronic hepatitis B infection with significant liver fibrosis or cirrhosis

- Significant liver fibrosis/cirrhosis is a risk factor for HCC and those with Chronic hepatitis B are at INCREASED risk
- HCC can be asymptomatic and can develop quickly
- Regular surveillance can lead to early detection, which can lead to earlier treatment and improve chances of survival
- Treatment with antivirals does not eliminate the risk of HCC and therefore surveillance should continue in these patients.
- In chronic HBV, there is high risk of HCC development in some groups of non-cirrhotic patients which includes African patients >20 yrs old; Asian males > 40 yrs old; Asian females >50 yrs old and those with a positive family history of HCC.
Hepatitis C is an often asymptomatic, infectious liver disease caused by HCV

- Chronic HCV infection is a leading cause of chronic liver disease, end-stage cirrhosis and HCC\(^1\)
- An estimated 175 million people are chronically infected worldwide but most are unaware of their infection\(^1\)
- Incidence is projected to increase, particularly in developing countries\(^1\)
- Prevalence rates varying from 1% in Europe to 4% in North Africa and Middle east
- Approx 215000 HCV infected in UK (90% are genotype 1 and 3)
- HCV is usually transmitted through blood-to-blood contact\(^2\)

Hepatitis C

- Flaviviridae family (RNA virus)
- Transmission in UK
  - Parenteral
  - Sexual: extremely unlikely in heterosexual relationships (<0.1%/10 yrs)
  - Vertical: about 5%
- Incubation period: 4 to 20 weeks
- Symptoms: >60% are asymptomatic
- Signs: as in Hepatitis B
Hepatitis C

- Acute fulminant hepatitis is rare (<1%)
- Approx 50-85% of infected pts become chronic carriers
- Serology
  - Anti-HCV seroconverts to positive may take several months after acute infection but a test for HCV RNA will be positive after 2 weeks
- Chronic Hepatitis C- infected >6 months- rarely resolves spontaneously (0.02%/year)
  - Upt to 30% carriers will progress to severe liver disease after 14-30 yrs infection, with an increased risk of liver cancer (approx. 14% for all patients and 33% for those with cirrhosis)
Hepatitis C in Pregnancy and Breast feeding

- There is no clearly demonstrated intervention to reduce HCV transmission from mother to child
- Treatment of HCV is not recommended
- Women should be informed of the small potential risk of transmission in pregnancy
- Breast feeding: No firm evidence of ‘additional’ risk of transmission

» NO AVAILABLE VACCINE
NICE guidelines for Chronic hepatitis C

- 23 September 2016

NICE has decided that the development of a hepatitis C clinical guideline should continue to be paused until there is stability in the availability of treatments and the cost to the NHS of the drugs. Registered stakeholders will be alerted if the guideline restarts its development.

EASL guidelines for Hepatitis C – published Sept 2016
Treat Acute Hepatitis C or not?

- Clear evidence that treatment given during the acute phase reduces progression and will reduce the rate of chronicity.
- Treatment in the acute phase has significantly higher success rates than treatment in the chronic phase*

4.8.4 Figure: Summary of NEAT Algorithm for the management of Acute HCV[183]

- **Initial presentation acute HCV**
  - **Week 4**
    - Decay HCV-RNA
      - $< 2 \log_{10}$
        - Treatment
      - $\geq 2 \log_{10}$
        - HCV-RNA
          - **Week 12**
            - HCV-RNA
              - positive
                - Treatment
              - negative
                - wait: cont’d monitoring for 48 weeks

*Cronic infection*
HCV therapy aims to eradicate HCV infection to avoid future complications

What is the goal of therapy?

To eradicate HCV infection (to prevent cirrhosis, decompensation, HCC and death), as evidenced by an SVR (undetectable HCV RNA, ie <15 IU/mL at 12 and 24 weeks after the end of treatment)\textsuperscript{1–3} A1

Who should be treated?

All patients with chronic HCV infection\textsuperscript{1–3}
Priority should be given to those at high risk for complications (A1) and those with high transmission risk (C2a)

What about patients with cirrhosis?

Treatment is strongly recommended. Viral eradication reduces the rate of decompensation and HCC. Surveillance should continue\textsuperscript{1} A1

SVR, sustained virological response

Improvements in treatment regimens are substantially improving patient care

**Efficacy**
- Increased cure rates (SVR)
- Expanded genotypic activity

**Safety and tolerability**
- Decreased adverse events
- Fewer dose reductions
- Fewer drug–drug interactions
- Decreased discontinuations

**Adherence**
- Decreased length of therapy
- Improved convenience

**Patient eligibility**
- Increased proportion of patients eligible for therapy (IFN-ineligible / -intolerant, non-responders, liver fibrosis, elderly, co-infected)
Evolution of HCV treatment landscape: increased cure rates in genotype 1 patients

*In genotype 1b patients.

DAA, direct-acting antiviral; PegIFN, pegylated interferon; PI, protease inhibitor RBV, ribavirin

Evolution of HCV treatment landscape: shortened treatment duration


*In genotype 1b patients.
Evolution of HCV treatment landscape: expanded genotype coverage


*In genotype 1b patients.
Evolution of HCV treatment landscape: simplified injection-free dosing regimen


*In genotype 1b patients.
Daclatasvir, a first-in-class HCV NS5A replication complex inhibitor, and sofosbuvir is a nucleotide analogue HCV NS5B polymerase inhibitor, together used in naïve and previously not responding to Protease inhibitors patient for 12 weeks therapy

Results: 98% with genotype 1; 92% with genotype 2 and 89% with genotype 3 achieved Sustained Virological response (SVR) a the end of 12 weeks
Treatment with the all-oral combination of the nucleotide polymerase inhibitor sofosbuvir and the NS5A inhibitor ledipasvir resulted in high rates of sustained virologic response among previously untreated patients with hepatitis C virus (HCV) genotype 1 infection- 99%
Table 6. Treatment recommendations for HCV-monoinfected or HCV/HIV coinfected patients with chronic hepatitis C without cirrhosis, including treatment-naive patients and patients who failed on a treatment based on pegylated IFN-α and ribavirin (treatment-experienced, DAA-naive patients).

<table>
<thead>
<tr>
<th>Patients</th>
<th>Treatment-naive or -experienced</th>
<th>Sofosbuvir/ledipasvir</th>
<th>Sofosbuvir/velpatasvir</th>
<th>Ombitasvir/paritaprevir/ritonavir and dasabuvir</th>
<th>Ombitasvir/paritaprevir/ritonavir</th>
<th>Grazoprevir/elbasvir</th>
<th>Sofosbuvir and dadastavir</th>
<th>Sofosbuvir and simeprevir</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genotype 1a</td>
<td>Treatment-naive</td>
<td>8-12 wk, no ribavirin</td>
<td>12 wk, no ribavirin</td>
<td>12 wk with ribavirin if HCV RNA ≤800,000 (5.9 log) IU/ml or 16 wk with ribavirin if HCV RNA &gt;800,000 (5.9 log) IU/ml</td>
<td>No</td>
<td>12 wk, no ribavirin if HCV RNA ≤800,000 (5.9 log) IU/ml</td>
<td>12 wk, no ribavirin if HCV RNA ≤800,000 (5.9 log) IU/ml</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>Treatment-experienced</td>
<td>12 wk with ribavirin</td>
<td>12 wk with ribavirin</td>
<td>12 wk with ribavirin if HCV RNA ≤800,000 (5.9 log) IU/ml</td>
<td>No</td>
<td>12 wk, no ribavirin if HCV RNA ≤800,000 (5.9 log) IU/ml</td>
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<td>Genotype 1b</td>
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<td>12 wk, no ribavirin</td>
<td>8-12 wk, no ribavirin</td>
<td>No</td>
<td>12 wk, no ribavirin</td>
<td>12 wk, no ribavirin</td>
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<td></td>
<td>Treatment-experienced</td>
<td>12 wk, no ribavirin</td>
<td>12 wk, no ribavirin</td>
<td>12 wk, no ribavirin</td>
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<tr>
<td></td>
<td>Treatment-experienced</td>
<td>12 wk with ribavirin</td>
<td>12 wk with ribavirin</td>
<td>12 wk with ribavirin if HCV RNA ≤800,000 (5.9 log) IU/ml</td>
<td>No</td>
<td>12 wk with ribavirin if HCV RNA ≤800,000 (5.9 log) IU/ml</td>
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<td>12 wk with ribavirin if HCV RNA ≤800,000 (5.9 log) IU/ml</td>
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<tr>
<td></td>
<td>Treatment-experienced</td>
<td>12 wk with ribavirin</td>
<td>12 wk with ribavirin</td>
<td>12 wk with ribavirin if HCV RNA ≤800,000 (5.9 log) IU/ml</td>
<td>No</td>
<td>12 wk with ribavirin if HCV RNA ≤800,000 (5.9 log) IU/ml</td>
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<td>No</td>
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</tr>
<tr>
<td></td>
<td>Treatment-experienced</td>
<td>12 wk with ribavirin</td>
<td>12 wk with ribavirin</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
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</table>

*Add ribavirin only in patients with RASs that confer high-level resistance to NS5A inhibitors at baseline if RAS testing available.

*Prolong to 16 weeks and add ribavirin only in patients with RASs that confer resistance to elbasvir at baseline if RAS testing available.
Evolution of HCV treatment landscape: improved tolerability

Effective HCV treatment results in virological cure

- Achieving an SVR following treatment is indicative of successful therapy and is synonymous with a cure\(^1,2\)

Achieving an SVR is associated with multiple lifelong benefits

Biochemical / virological
- Negative HCV RNA for life in >99% of cases
- Disappearance of HCV RNA in the liver and peripheral blood mononuclear cells
- Negative detection of anti-HCV
- Normalization of aminotransferases
- Platelet increase in patients with thrombocytopenia

Liver histology
- Reversion to regular liver contours
- Reduction in portal vein diameter in the case of portal hypertension
- Disappearance of lymph nodes near the hepatic hilum and splenomegaly
- Normalization of Fibroscan® values

Clinical events
- Reduced risk of progression to cirrhosis, decompensated liver disease and liver cancer, and recurrence after transplantation
- Reversion of cirrhosis in some cases

Extrahepatic involvement
- Improvement of extrahepatic manifestations

Wellbeing, quality of life
- Improved quality of life (disappearance of asthenia, fatigue, general wellbeing)
- Reduced psychological impact (anxiety/depression)
- Reduced personal, family and social stigma

Survival
- Reduced risk of mortality by any cause

Transmission
- Elimination of transmission risk (sexual, injection drug users and perinatal)
- Public health benefits

Economic
- Cost-effectiveness of treatment
- Decreased health insurance premiums, and immediate and long-term healthcare costs

Marinho RT et al. J Gastrointestin Liver Dis 2014;23:85–90
Once SVR is achieved, lifetime virological cure is expected in >99% of patients

<table>
<thead>
<tr>
<th>Study reference*</th>
<th>Achieved SVR†, n</th>
<th>Late relapse, %</th>
<th>Follow-up, months (range)</th>
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<tbody>
<tr>
<td>Toccaceli *F et al. J Viral Hepat 2003;10:126</td>
<td>87</td>
<td>0</td>
<td>NR (36–76)</td>
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<tr>
<td>McHutchison *JG et al. Hepatol 2006;46:S275</td>
<td>492</td>
<td>1</td>
<td>Mean: 65 (NR)</td>
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<tr>
<td>Desmond *CP et al. J Viral Hepat 2006;13:311</td>
<td>147</td>
<td>0.7</td>
<td>Mean: 28 (4–124)</td>
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<td>Chavalitdhamrong *D et al. World J Gastroenterol 2006;12:5532</td>
<td>171</td>
<td>0</td>
<td>Mean: 35 (13–57)</td>
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<td>Moreno *M et al. J Viral Hepat 2006;13:28</td>
<td>132</td>
<td>0</td>
<td>Mean: 42 (12–156)</td>
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<tr>
<td>Torres-Ibarra *R et al. J Hepatol 2007;46:S247</td>
<td>75</td>
<td>0</td>
<td>NR (36–108)</td>
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<tr>
<td>Koh *C et al. J Hepatol 2010;52:S436</td>
<td>103</td>
<td>0</td>
<td>Median: 91 (6–264)</td>
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<tr>
<td>Giannini *EG et al. Aliment Pharmacol Ther 2010;31:502</td>
<td>231</td>
<td>0.9</td>
<td>Median: 38 (32–42)</td>
</tr>
<tr>
<td>Swain *MG et al. Gastroenterology 2010;139:1593</td>
<td>1343</td>
<td>0.9</td>
<td>Mean: 47 (10–85)</td>
</tr>
</tbody>
</table>

Patients with SVR did not experience HCV infection recurrence even after 18 years

*All patients received IFN-based therapies including standard interferon alpha; leukocyte interferon-α; lymphoblastoid interferon and PegIFN.
†Assay sensitivities were between 5 and 50 IU/mL or 10 and 10,000 copies/mL.
NR, not reported
Achieving SVR is protective against HCC development

Retrospective analysis of 1371 HCV-treated patients with a median follow-up of 10 years: all patients

- Did not achieve SVR
- Achieved SVR

HCC incidence (%) vs. Time (years)

P < 0.0001

Purevsambuu T et al. J Hepatol 2014;60:S52 abstract 0125
SVR significantly reduces risk of developing HCC even in cirrhotic patients

Retrospective analysis of 1371 HCV-treated patients with a median follow-up of 10 years: patients with fibrosis stage F4

- Patients with fibrosis stage F4, did not achieve SVR
- Patients with fibrosis stage F4, achieved SVR

HCC incidence (%)

Time (years)

P=0.0009

Purevsambuu T et al. J Hepatol 2014;60:S52 abstract 0125
Resource implications

- Screening tests for Hepatitis (e.g., Anti-HBc, HBsAg, Anti-HCV) cost £10-20 each
- HBV DNA and HCV RNA PCR viral load cost in the range of £30-40 each
- HCV genotyping and HBV genotyping cost around £50
- Vaccination costs are in range of £10-20 per dose for monodose vaccines
South Thames Hepatitis Network (STHepNet) Agreement

- STHepNet is a commissioned operational delivery network (ODN) for delivery of Hepatitis C for all patients in the South London area.
- Comprises of the following organisations:
  - Covers 12 CCGs covering a population of 3.4 million with estimated 22,000 cases
    - Kings College Hospital and St George’s Hospital (Joint Lead centres) - “the Hub”
    - Lewisham and Greenwich NHS Trust – spoke
    - Guy’s and St Thomas NHS Trust - spoke
    - Kingston Hospital
    - St Helier Hospital
- Aim: To increase the number of patients who are treated and cured of HCV using the most clinically appropriate and cost effective options in accordance with NICE TAs and the NHS England policy
South Thames Hepatitis Network (STHepNet) Agreement

- Since August 2015, all patients who were prescribed the new DAA’s drug regimes must have been discussed at the hub MDT prior to commencing treatment.
- 2 weekly MDT meetings at St George’s to cover SW and King’s to cover SE.
  - Comprises of hub hepatologists, a hub hepatitis specialist pharmacist, hub hepatitis and co-infection CNS’s and similar representation from the spokes.
  - Does support videoconferencing.
- The Network manager will have oversight of the functioning of both the MDTs, facilitated by 2 MDT co-ordinators.
South Thames Hepatitis Network (STHepNet) Agreement

- Spoke authorisation process: It will be the devolved responsibility of the ODN hubs to assess the suitability for the spoke to prescribe and treat. Once authorised, the hub will inform NHS England.
- Hub responsibilities
- Spoke responsibilities
- Data Requirements: Spokes are expected to complete the standard monitoring and outcomes dataset and provide to the hub.
- Accountability: Clinical responsibility of the patients will lie with the supervising consultant at the treating site, unless the patient is transferred to the lead centre.
- The STHepNet management group meets quarterly.
I HOPE YOU HAVE FUN WHILE SOME OF US HAVE TO WORK OVERTIME!