Can we eliminate Hepatitis C in NZ?

Ed Gane
NZ Liver Transplant Unit
Hepatitis C has become the silent global epidemic of the 21st Century

- Almost 180 million now infected
Health burden from hepatitis C is increasing as the infected population gets older

Liver transplant (ANZL TR)

Liver cancer (NZLTU)

Impact of improved treatment on disease burden of chronic hepatitis C in New Zealand

Edward Gane, Catherine Stedman, Cheryl Brunton, Sarah Radke, Charles Henderson, Chris Estes, Homie Razavi

Abstract

Background Chronic hepatitis C is an important cause of liver failure, liver cancer and liver-related deaths in New Zealand. Although these complications can be prevented by HCV eradication, current treatment uptake is <1% per annum. We describe the burden of HCV infection and estimate the effect of four different treatment strategies to reduce HCV-related morbidity and mortality.

Methods Baseline model parameters were based upon literature review and expert consensus, focusing on New Zealand data. Four scenarios were modelled: Scenario 1 estimated the impact of increased treatment efficacy, while Scenario 2 estimated the effect of increased treatment efficacy and gradual increases in numbers treated. Scenarios 3 and 4 estimated the impact of deferred introduction of new DAAs for either 1 or 2 years.

Results Prevalence of HCV infection peaked in 2010 (50,480 cases). Peak prevalence of cirrhosis and HCC will occur after 2030. Scenario 2 resulted in sizeable decreases in HCV-related morbidity and mortality. The impact of Scenario 1 was smaller. Deferring funding for new DAA treatments for a further 1 or 2 years resulted in an 18-36% increase in liver-related deaths in 2030.

Conclusions While prevalence of chronic HCV infection may have peaked, disease burden continues to grow. Increased treatment uptake and efficacy combined with efforts to reduce disease transmission, will help prevent advanced liver disease and deaths.
Objectives of Working Group

1. Update estimates on current incidence in PWID (to confirm reduction in high risk population).

2. Determine overall prevalence of HCV infection, incidence of HCC and liver-related mortality.

3. Determine age distribution and proportion with cirrhosis (data from current pilots).

4. Use updated assumptions of prevalence and disease progression to develop a new model for projecting disease burden over next 20 yrs.
### Assumptions in Modeling HCV in NZ

<table>
<thead>
<tr>
<th></th>
<th>Historical</th>
<th>Year</th>
<th>2013 (Est.)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HCV Infected Cases</strong></td>
<td>65,000 (39,000–82,000)</td>
<td>2013</td>
<td>65,000</td>
</tr>
<tr>
<td>Anti-HCV Prevalence</td>
<td>1.4% (0.9%–1.8%)</td>
<td></td>
<td>1.4%</td>
</tr>
<tr>
<td><strong>Total Viremic Cases</strong></td>
<td>50,000 (30,000–63,000)</td>
<td>2013</td>
<td>50,000</td>
</tr>
<tr>
<td>Viremic Prevalence</td>
<td>1.1% (0.7%–1.4%)</td>
<td></td>
<td>1.1%</td>
</tr>
<tr>
<td>Viremic Rate</td>
<td>76.5%</td>
<td></td>
<td>76.5%</td>
</tr>
<tr>
<td><strong>HCV Diagnosed (Viremic)</strong></td>
<td>20,000</td>
<td>2013</td>
<td>20,000</td>
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<tr>
<td>Viremic Diagnosis Rate</td>
<td>39.6%</td>
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<td>40.0%</td>
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<tr>
<td><strong>New Infections</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Annual Newly Diagnosed</td>
<td>910</td>
<td>2013</td>
<td>910</td>
</tr>
<tr>
<td><strong>Treated</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number Treated</td>
<td>900</td>
<td>2011</td>
<td>900</td>
</tr>
<tr>
<td>Annual Treatment Rate</td>
<td>1.8%</td>
<td></td>
<td>1.8%</td>
</tr>
<tr>
<td><strong>Risk Factors</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Active IDU with HCV</td>
<td>10,300</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Percent Active IDU</td>
<td>20.7%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Previous Blood Transfusion</td>
<td>1,800</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Percent Previous Blood Transfusion</td>
<td>3.6%</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Genotype</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>G1/other</td>
<td>58%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>G2/3</td>
<td>42%</td>
<td></td>
<td></td>
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<tr>
<td><strong>SVR Rate</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Base Case</td>
<td>65%</td>
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</tr>
<tr>
<td>G1/other</td>
<td>60%</td>
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<tr>
<td>G2/3</td>
<td>70%</td>
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What is the TRUE Diagnosis rate in NZ?

1. Population seroprevalence surveys
2. Linkage studies: % HCC cases with previous dx of HCV

(a) % HCC cases detected through surveillance of HCV-cirrhotics

- YES, n=128 (44%)
- NO, n=160 (56%)

(b) Years between HCV diagnosis and HCC diagnosis

- >10 yrs, 37%
- 5-10 yrs, 28%
- 2-5 yrs, 17%
- nil, 12%
- 1-2 yr, 6%
The NZ HCV+ Population: Age and Sex

- Age and Sex Distribution (Hepatitis Foundation of NZ, Christchurch Community Clinic)

The NZ HCV+ Population: Ethnicity

1. Hepatitis Foundation Pilots cf. 2013 Census

Bay of Plenty

<table>
<thead>
<tr>
<th></th>
<th>Pilot</th>
<th>Census</th>
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<tr>
<td>European</td>
<td>21</td>
<td>17</td>
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<tr>
<td>Maori</td>
<td></td>
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<tr>
<td>PI</td>
<td></td>
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<tr>
<td>Asian</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
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Wellington Region

<table>
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<tr>
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<th>Pilot</th>
<th>Census</th>
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<tbody>
<tr>
<td>European</td>
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<tr>
<td>Maori</td>
<td></td>
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<tr>
<td>Asian</td>
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<td></td>
</tr>
<tr>
<td>Other</td>
<td></td>
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</tbody>
</table>
NZ Injecting Drug User Population: Ethnicity

2. Christchurch NEX 2013

Charles Henderson, Personal communication
The NZ HCV+ Population: Genotype

- Genotype Distribution (from 6130 patients genotyped at LabPlus between 2005 and 2014)

99% are GT-1, 2, or 3

- GT1a
- GT1b
- GT3
- GT4
- GT5
- GT6

The NZ HCV+ Population: Cirrhosis

- HCV Pilots in Bay of Plenty and Wellington
  - 788 Fibroscans performed in community

16% have established cirrhosis
25% have at least severe fibrosis
The HCV disease burden model

Modeled Disease Progression

- Number of Patients at Each Disease Stage

Assumptions for Model

- Number of Patients at Each Disease Stage

<table>
<thead>
<tr>
<th></th>
<th>2013</th>
<th>2030</th>
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<tbody>
<tr>
<td>Infected</td>
<td>50,480</td>
<td>39,950</td>
</tr>
<tr>
<td>Cirrhosis</td>
<td>3700 (8%)</td>
<td>8500 (21%)</td>
</tr>
<tr>
<td>Decompensated*</td>
<td>380</td>
<td>900</td>
</tr>
<tr>
<td>HCC</td>
<td>120</td>
<td>360</td>
</tr>
<tr>
<td>Death</td>
<td>140</td>
<td>340</td>
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*Numbers are cumulative numbers for patients in both Child-Pugh B or C and assume no one returns to compensated state.
...What will it take to truly eradicate HCV?

Effective treatment

- Efficacy
- Optimal therapeutic tool to eradicate HCV
- Safety
- Adherence
Increasing SVR Rates (HCV GT 1)

- 1986: IFN 6 mo
- 1998: IFN 12 mo
- 2001: IFN/RBV 12 mo
- 2004: PEG-IFN/RBV 12 mo
- 2011: TVR/BOC PEG/RBV 6-12 mo
- 2013: SMV/PEG/RBV 6 mo
- 2014: SOF/RBV 3 mo
- 2015: SOF/PEG/RBV 3 mo
- 2013: SOF/SMV 3 mo
- 2014: SOF/LDV 3 mo
- 2015: ABT450r/ABT333/ABT267/RBV 3 mo
SVR12 (%)

<table>
<thead>
<tr>
<th>Treatment history</th>
<th>Subtype</th>
<th>GT1</th>
<th>GT1a</th>
<th>GT1b</th>
<th>GT1a</th>
<th>GT1b</th>
<th>GT1a</th>
<th>GT1b</th>
<th>GT1a</th>
<th>GT1b</th>
<th>GT1a</th>
<th>GT1b</th>
<th>GT1a</th>
<th>GT1b</th>
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<tbody>
<tr>
<td>Overall</td>
<td>Naive</td>
<td>96</td>
<td>95</td>
<td>98</td>
<td>96</td>
<td>96</td>
<td>97</td>
<td>100</td>
<td>99</td>
<td>100</td>
<td>97</td>
<td>100</td>
<td>97</td>
<td>97</td>
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<tr>
<td></td>
<td>Experienced</td>
<td>297</td>
<td>173</td>
<td>123</td>
<td>210</td>
<td>207</td>
<td>88</td>
<td>91</td>
<td>100</td>
<td>205</td>
<td>97</td>
<td>90</td>
<td>97</td>
<td>90</td>
</tr>
<tr>
<td>Cirrhotic</td>
<td>Naive</td>
<td>473</td>
<td>322</td>
<td>151</td>
<td>297</td>
<td>173</td>
<td>123</td>
<td>210</td>
<td>207</td>
<td>88</td>
<td>91</td>
<td>100</td>
<td>205</td>
<td>92</td>
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<tr>
<td></td>
<td>Experienced</td>
<td>322</td>
<td>151</td>
<td>297</td>
<td>173</td>
<td>123</td>
<td>210</td>
<td>207</td>
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<td>91</td>
<td>100</td>
<td>205</td>
<td>92</td>
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Gilead Harvoni™ in HCV GT 1-6

48 weeks
48 weeks

8-12 weeks
TIME TO BURY PEG-IFN?
Total number of HCV infections will decrease, but HCV related morbidity & mortality will increase

Increasing SVR without increase in number treated will have small impact on morbidity & mortality

Increasing SVR and increasing number treated from 1 to 5% (i.e. 4000 p.a.) could eliminate HCV

We run out of patients by 2031!!

75% reduction

70% reduction

72% reduction

Delivering access will have a negative impact on morbidity, mortality and total infections.

Cost of not funding DAAs:
Until 2017: 377 deaths
Until 2020: >1000 deaths
ALL PREVENTABLE

Gane E, et al. NZ Med J 2014; Dec
...What will it take to truly eradicate HCV?

Effective treatment

Efficacy

Optimal therapeutic tool to eradicate HCV

Safety

Adherence

Change in treatment priorities?

Patients at greatest risk of morbidity and mortality
Risk of future complications is linked to severity of liver fibrosis

CHeCS: Chronic Hepatitis Cohort Study – clinical outcomes after baseline biopsy

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Mild fibrosis</th>
<th>Mod fibrosis</th>
<th>Cirrhosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transplant</td>
<td>1.1</td>
<td>1.7</td>
<td>5.2</td>
</tr>
<tr>
<td>Liver Cancer</td>
<td>1</td>
<td>4.6</td>
<td>11.3</td>
</tr>
<tr>
<td>Death</td>
<td>6</td>
<td>10.8</td>
<td>23.1</td>
</tr>
<tr>
<td>Decompensate</td>
<td>3.8</td>
<td>11.9</td>
<td>28.6</td>
</tr>
</tbody>
</table>

n=810  n=461  n=364

Moorman AC, et al. AASLD 2014; Oral #174

DAA: direct-acting antiviral agent; LTx: liver transplant
What would it take to reduce the health burden associated with chronic hepatitis C?

- **Reduce liver-related complications**
  - Funding of DAA therapy only for all cirrhotics
  - Capacity to treat 2%/year
  - Need increased community diagnosis or we will run out of cirrhotics to treat
  - Need access to **Fibroscan** to identify cirrhotics
Liver biopsy

- Day off work in 100%
- Pain, tenderness in 100%
- Haemorrhage in 1%
- Bile leak in 0.5%
- Admission in 5%
- Surgery in 1%
- Death in 0.3%

Fibroscan

- No days off work
- Non-invasive
  - No pain
  - No admissions
  - No deaths
- Performed in clinic
- Immediate result
- Inexpensive
- Reproducible
Eradicating HCV in patients at high risk of transmission

How should we prioritize HCV treatment?

With new DAA therapies, viral eradication is possible in patients at high risk of transmission, therefore reducing the number of new HCV infections and HCV prevalence.
...What will it take to truly eradicate HCV?

**Effective treatment**

- **Efficacy**
  - Optimal therapeutic tool to eradicate HCV
- **Safety**
- **Adherence**

**Change in treatment priorities?**

- Patients at greatest risk of morbidity and mortality
- Patients at high risk of transmission

**Widespread diagnosis**

- Low rates of diagnosis and treatment remain significant barriers to reducing the disease burden
Estimated HCV Diagnosis and Treatment Rates

![Graph showing estimated HCV diagnosis and treatment rates across different countries. Geometrically, the Netherlands and Luxembourg have the highest treatment rates, over 5%. Russia, South Africa, and Mongolia have the lowest treatment rates, less than 0.5%. The diagnosis rates range from 0% to 100%, with some countries showing a high correlation between diagnosis and treatment rates.]
What would it take to eliminate Hep C?

We can eliminate HCV by 2030 if

- Funding of DAA therapy for ALL HCV infected
- Capacity to treat >5%/year
- Treat PWID and prisoners to stop transmission
- Widespread uptake of community testing
Towards a **NATIONAL** approach to addressing hepatitis C in New Zealand

Outcomes of the Hepatitis C Pilot

July 2012 - June 2014
The NZ hepatitis C pilot programme

• **Two year pilot programme**
  – July 2012 to June 2014
  – 4 DHBs (BOP; Capital and Coast, Hutt, Wairarapa)
  – Covers 16% of adult population in NZ

• **Collaborative**
  – involved key stakeholders (GPs, practice nurses, CADS, NEX, Gastroenterologists, ID Physicians, Hepatitis Nurse Specialists) to provide coordinated pathway of care

• **Developmental**
  – Assess a number of strategies and improve or discard those not sustainable or cost effective
Pilot Activities

1. Education and public awareness
2. Targeted testing and identification
3. Community-based testing and support delivered by the Hepatitis Foundation nurses
4. Improved disease surveillance and data collection (BUT NOT a national database)
Community Assessment and Support (CAS)

- Integrated shared care
- Community hepatitis nurse
- FibroScan assessment and triage
- Multidisciplinary meetings

**Flowchart Diagram:**

1. **Identify previously diagnosed**
2. **Testing** → **Referral** → **Community assessment and FibroScan** → **Multidisciplinary Meetings** → **Secondary care**

**Collaboration with:**
- PHOs
- GPs
- CADS
- Sexual health
- Corrections
- Secondary care
- Needle Exchanges
- Other Services

**Additional Text:**

- Education and support

**Logo:** Hepatitis C - Know it. Test it. Treat it.
Pilot Referrals 2012-2014
915 referrals diagnosed with hepatitis C

Pilot HCV Diagnosed Referrals

<table>
<thead>
<tr>
<th>Quarter</th>
<th>Number</th>
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<tbody>
<tr>
<td>Q3 2012</td>
<td>89</td>
</tr>
<tr>
<td>Q4 2012</td>
<td>106</td>
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<tr>
<td>Q1 2013</td>
<td>163</td>
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<td>Q2 2013</td>
<td>183</td>
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<tr>
<td>Q3 2013</td>
<td>127</td>
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<tr>
<td>Q4 2013</td>
<td>98</td>
</tr>
<tr>
<td>Q1 2014</td>
<td>70</td>
</tr>
<tr>
<td>Q2 2014</td>
<td>79</td>
</tr>
</tbody>
</table>

Hepatitis C. Know it. Test it. Treat it.
Learnings from the Pilots

• Excellent patient and primary care satisfaction
• Widespread support for national roll-out
• Future needs will include:
  – Increased testing and assessment in high-risk populations – Needle Exchange, CADS, Prisons
  – Increased treatment uptake
    • Initially secondary care
    • Eventually primary care
    • Will be driven by the new DAA therapies
• Consider DHB-funded Primary Care model
ONE SIZE FITS ALL

• Pan-genotypic
• High barrier to resistance
• No toxicity; IFN and RBV-free
• Safe in advanced liver disease

SIMPLE REGIMEN

• 1-3 pills/day for 6 or 8 weeks
• No baseline testing for predictors
• No on-treatment monitoring

↑ Treatment uptake
New models of care

↓ Health burden

HCV ERADICATION