The dollars of HCV: pay now or pay later

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AMMI CACMID April 18th, 2015
Disclosures:

In the past two years I have participated in research$^1$ or received consultation/speaking fees$^2$ from:

- Abbvie$^{1, 2}$
- Gilead$^2$
- Merck$^{1, 2}$
Objectives

(1) To review the health economic impact of untreated HCV

(2) To review the potential economic impact of increased treatment using novel HCV regimens.

(3) To discuss optimal models of care designed to evaluate clinical, epidemiologic, and economic impact in Atlantic Canada.
• The premise:

- That highly effective therapies for HCV while expensive offset significant (and greater) downstream costs related to complications of chronic untreated infection in Canada.

- That highly effective and well tolerated therapies represent a unique opportunity to access marginalized populations, which will ultimately achieve significant downstream savings through reduced transmission.
Poll the audience

HCV: Pay now or pay later?

(1) Treat everyone now to prevent complications and incident infections.

(2) Partial treatment access with Fibrosis restriction (F2).

(3) Focus on the sickest first then expand access to everyone.

(4) Treatment costs way to much, focus on prevention for now and pay later when complications occur.

(5) Give me a little more information and ask me again in 25 min.
Natural History of HCV Infection

HCV Exposure → Acute Infection → Chronic Infection

- Most Asymptomatic
- 20-25% of patients

- Viral eradication stops progression of liver disease and improves clinical outcomes

Cirrhosis → Liver Failure → HCC

- 1-4%/year

Liver Transplant or Death

- 1-4%/year

- $ \quad $ $ \quad $ $

- $ $ $ $ $ 

- $ $ $ $ $ $ $ $
Hepatitis C, of all infectious diseases, is responsible for highest increase in premature mortality.

Exhibit 3.5
Years of life lost due to premature mortality (YLL), year-equivalents of reduced functioning (YERF) and health-adjusted life years (HALYs) for the top 20 pathogens, ranked by disease burden.
HCV related mortality now exceeds that of HIV

Ly et al, Ann Intern Med 2012
Hepatitis C Medical Burden:

HCV increases all cause mortality.

Attainment of SVR associated with:

Reduced liver related and all cause mortality.

Reduced HCC and liver failure.

Van der Meer, JAMA 2012
HCC Incidence over time in F4 patients according to SVR status.

Median Follow up 10 years
Disease Progression and Comorbidities

**Disease progression in patients with chronic HCV**

- **Acute infection**
  - Fibrosis
- **Chronic infection**
  - F0
  - F1
  - F2
  - F3
  - F4 (cirrhosis)
- **Liver failure**
- **HCC**

**Morbidities associated with chronic HCV infection**
- Cirrhosis
- End stage liver disease
- Hepatocellular carcinoma
- Liver transplantation

**Major co-morbidities associated with chronic HCV infection**
- Coronary artery disease
- Diabetes

The coming Wave of Liver Disease

- Driven largely by chronically infected baby boomer population.
- HCV leading cause of hepatic adverse outcome including liver transplantation in North America.
- Curative well tolerated therapies will increase treatment demand and require global management plan with stratified access.

O’Leary et al, Gastroenterology, 2008; Myers et al, CJGH, 2014
2013-2030 Predictions

- Liver cirrhosis: 45% increase
- Decompensated cirrhosis: 35% increase
- Liver related death: 90% increase
- Hepatocellular carcinoma: 120% increase


Assumptions include:

- 70% of infected population diagnosed.
- 77% viremic.
- Modeled IFN/RBV treatment using historical data and treatment dispensing in Canada.

- Peak comp/decompensated cirrhosis in 2031 (36,210/3380 cases).
- Peak HCC 2035 at 2220 cases.
- Peak mortality 2034.
- 32,460 deaths 2013-2035 from liver related causes.

*Versus 2013, increase in compensated cirrhosis, decompensated cirrhosis, HCC and liver related deaths 89%, 80%, 205%, and 160%*
Average annual all-cause healthcare costs are increased with HCV (US):

<table>
<thead>
<tr>
<th>Patient Population</th>
<th>Mean per person annual healthcare cost (2010 USD²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCV uninfected¹</td>
<td>9979</td>
</tr>
<tr>
<td>HCV+, non-cirrhotic²</td>
<td>17,277</td>
</tr>
<tr>
<td>HCV+, compensated cirrhotic²</td>
<td>22,752</td>
</tr>
<tr>
<td>HCV+, ESLD²</td>
<td>59,995</td>
</tr>
<tr>
<td>HCV+, HCC²</td>
<td>112,537</td>
</tr>
<tr>
<td>HCV+, OLT²</td>
<td>145,045</td>
</tr>
</tbody>
</table>

US Insurance claims data > 50,000 persons 2002-2010

Cost 247% higher with ESLD versus non cirrhotic independent of age or other comorbidities (>93% ambulatory, inpatient, and pharmacy).

¹ McAdam-Marx, J Manag Care Pharm, 2011; ² Gordon et al, Hepatology, 2012
Prevalence of HCV decreases while cost increases due to treatment of late complications.
Hepatitis C: Significant Burden of Disease\textsuperscript{1,2}

Hepatitis C is the main cause of liver transplantation. In 2012:
- 494 people received liver transplants
- 492 people remained on the transplant list
- 62 people died waiting for a transplant\textsuperscript{4}

\textsuperscript{1} Mühlberger et al 2009; \textsuperscript{2} Gordon et al 2012; \textsuperscript{3} Myers et al. 2014; \textsuperscript{4} Transplantation data from Canadian Institutes for Health Information, 2013.
Indirect costs exceed direct medical costs

- **Egypt:**
  - Modelling of direct/indirect costs 2013.
  - Direct costs for each disease state from national government hospital.
  - Indirect costs by WHO DALY template.

- YLD from chronic cirrhosis (F0-F3), compensated cirrhosis, HCC and EHM (DM, NHL).
- YLL due to decompensated cirrhosis, HCC, and EHM.

Indirect cost: $2,575 M (2013 USD).
Total 3.1 Billion (1.4% GDP).
SVR12 = improved Quality of Life (QOL) and Patient reported Outcomes (PRO)

<table>
<thead>
<tr>
<th>Study/Regimen</th>
<th>Measurement</th>
<th>Outcome</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>VALENCE (SOF/RBV)¹</td>
<td>SF-36, FACIT-F, CLDQ-HCV, WPAI-SHP</td>
<td>SVR12 = improved general health, fatigue, emotional well being, SF-36 physical component summary</td>
<td>Additional 12w of therapy did not affect PRO.</td>
</tr>
<tr>
<td>SOF containing regimes (NEUTRINO, FUSION)²</td>
<td>SF-36, FACIT-F, CLDQ-HCV</td>
<td>SVR12 = improved fatigue using all measurements (P &lt; 0.0001.)</td>
<td></td>
</tr>
<tr>
<td>QUEST 1/2, PROMISE (SMV/PR)³</td>
<td>FSS, WPAI-HCV, EQ-5D</td>
<td>Versus PR alone reduced fatigue, depression, impairment of daily activities and work productivity, QOL.</td>
<td></td>
</tr>
<tr>
<td>Aviator (3D)⁴</td>
<td>SF-36, EQ-5D, HCV-PRO</td>
<td>Minimal PRO impact during treatment, all PRO’s improved over baseline at post treatment week 24</td>
<td></td>
</tr>
</tbody>
</table>

Indirect cost savings: SVR12 improves PRO and QOL even with advanced Fibrosis

CHANGE OF PRO SCORE
SVR12 vs. BL

SF-36: PCS
SF-36: MCS
FACIT-F: fatigue
FACIT-F: total
CLDQ-HCV
Work...
Activity

SF-36: PCS
SF-36: MCS
FACIT-F: fatigue
FACIT-F: total
CLDQ-HCV
Work productivity
Activity

- Early fibrosis (F0-F2)
- Advanced fibrosis (F3-F4)
Indirect costs substantial with traditional therapy

**Graphs:**
- **PRO with PR:** SOF+PR
- **PRO with RBV-ONLY:** SOF+RBV
- **PRO in IFN/RBV-FREE:** LDV/SOF

- **Normalized FACIT-F**
- **Normalized FACIT-FS**
- **TREATMENT PERIOD**
- **EoT** F/U w4 F/U w12
- **Week**

**Source:** Younossi ZM, AASLD, 2014, Poster #77
• So let's start treating then. But these new drugs are pretty expensive?
Evaluation of Healthcare Costs in HCV Patients by Liver Disease Severity and Treatment Status

Covariates adjusted for in the analysis included age, sex, geographical region, index year, baseline comorbidities, and baseline treatment for HCV.

PPP$=\text{per-patient-per-month}$; NCD=non-cirrhotic disease; CC=compensated cirrhosis; ESLD=end-stage liver disease

Gordon et al, Aliment Pharmacol Ther 2013
Cost of treatment is increasing but cost per SVR is decreasing.

- Cost per SVR in cirrhotic patient, **direct drug cost** only (Canadian list prices).

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Cost/regimen</th>
<th>SVR (%)</th>
<th>HCV drug cost/G1 SVR</th>
</tr>
</thead>
<tbody>
<tr>
<td>PR 48 weeks + BOC 44 weeks</td>
<td>$66,200</td>
<td>55</td>
<td>66,200/0.55 = $120,364</td>
</tr>
<tr>
<td>PR 48 weeks + TVR 12 weeks</td>
<td>$55,000</td>
<td>62</td>
<td>55,000/0.62 = $88,710</td>
</tr>
<tr>
<td>PR + SOF 12 weeks</td>
<td>$60,000</td>
<td>80</td>
<td>60,000/0.80 = $75,000</td>
</tr>
<tr>
<td>SOF + LDV 12 weeks</td>
<td>$67,000</td>
<td>94</td>
<td>67,000/0.94 = $71,277</td>
</tr>
<tr>
<td>3D/RBV 12 weeks</td>
<td>$55,000</td>
<td>92</td>
<td>55,000/0.92 = $59,782</td>
</tr>
</tbody>
</table>

*Modified from Shafran et al, CJGH, February 2015, with Poordad, NEJM, May 2014*
Real world experience and cost

• TVR: registration trials 64-75% SVR

• Real world experience: HCV TARGET\(^1\), 90 centers, > 2000 patients, **overall SVR 54%**, 90% with AE leading to treatment change, serious AE in >10%.

• Real world median cost of SVR in 147 patients 189,338 (2012 USD), with close to 10% of cost spent on AE management\(^2\).

Program considerations
The treatment cascade: comprehensive HCV programming is essential

2.7-3.9 Million

50%

32-38%

7-11%

Infected
Detected
Referred
Treated

Asrani, Curr Gastroentrol Rep, 2014
Screening and Treatment are Cost-Effective in Canada

<table>
<thead>
<tr>
<th>Age Group Screened</th>
<th>Strategy</th>
<th>ICER ($)</th>
<th>HCV Deaths Prevented (per 10,000 screened)</th>
</tr>
</thead>
<tbody>
<tr>
<td>25-64</td>
<td>Screen and treat with PegIFN/RBV</td>
<td>38,117</td>
<td>9</td>
</tr>
<tr>
<td></td>
<td>Screen and treat with DAA</td>
<td>34,783</td>
<td>18</td>
</tr>
<tr>
<td>45-64</td>
<td>Screen and treat with PegIFN/RBV</td>
<td>34,359</td>
<td>9</td>
</tr>
<tr>
<td></td>
<td>Screen and treat with DAA</td>
<td>35,562</td>
<td>21</td>
</tr>
</tbody>
</table>

Wong W et al. CMAJ, Jan 2015
Defining ‘Highest’ or ‘High’ Priority HCV Patients for Treatment in the Chronic Hepatitis Cohort Study (CHeCS)

Retrospective study by CDC to identify how many patients in CHeCS database fall into the ‘Highest’ or ‘High’ Priority classification as defined by AASLD/IDSA treatment guidelines in the real-world.

The majority of CHC patients in the USA fall within the ‘highest’ and ‘high’ treatment priority designation.

Restricting treatment to only patients with advanced fibrosis will deprive a large percentage of patients from needed treatment.

<table>
<thead>
<tr>
<th>Patient Characteristics</th>
<th>% TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients Staged by Biopsy or FIB-4 Score (N=8,504)</td>
<td></td>
</tr>
<tr>
<td><strong>HIGHEST PRIORITY</strong></td>
<td></td>
</tr>
<tr>
<td>F3 (biopsy staged F3 or higher or FIB-4 score ≥2.5)</td>
<td>32.9</td>
</tr>
<tr>
<td>Less than F3 with chronic kidney disease</td>
<td>30.0</td>
</tr>
<tr>
<td><strong>HIGH PRIORITY</strong></td>
<td></td>
</tr>
<tr>
<td>F2 (biopsy stage F2 of FIB-4 score ≥1.6 but &lt;2.5)</td>
<td>22.7</td>
</tr>
<tr>
<td>Less than F2 with HIV co-infection</td>
<td>0.7</td>
</tr>
<tr>
<td>Less than F2 with HBV co-infection</td>
<td>0.2</td>
</tr>
<tr>
<td>Less than F2 with NASH</td>
<td>0.4</td>
</tr>
<tr>
<td>Less than F2 with Diabetes</td>
<td>4.9</td>
</tr>
<tr>
<td><strong>NOT MEETING ‘HIGHEST OR HIGH’ PRIORITY CRITERIA</strong></td>
<td>38.1</td>
</tr>
</tbody>
</table>
F4 prioritization decreases cost and liver complications

Markov HCV simulation model to model if phased fibrosis dependent treatment offers health economic value in screened baby boomers.

McEwan et al, Hepatology, 2013
Prioritization of treatment to those at highest risk of liver adverse event.

Recognize capacity issues associated with increased treatment demand.

Ultimately provide access to all those requiring treatment.
## Birth Cohort Stratification

<table>
<thead>
<tr>
<th>Phase 1 (Short term, years 1-2, highest risk of hepatic adverse event or complication):</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cirrhosis with documented Fibrosis F3/F4.</td>
</tr>
<tr>
<td>Extra hepatic manifestation of chronic HCV infection.</td>
</tr>
<tr>
<td>HIV Positive</td>
</tr>
<tr>
<td>At discretion of HCV expert.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Phase 2 (incorporates lower risk patients):</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cirrhosis with documented Fibrosis F2/F3/F4.</td>
</tr>
<tr>
<td>Extra hepatic manifestation of chronic HCV infection.</td>
</tr>
<tr>
<td>Patient with HCV infection &gt; 10 years.</td>
</tr>
<tr>
<td>At discretion of HCV expert.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Phase 3 (incorporates most patients):</th>
</tr>
</thead>
<tbody>
<tr>
<td>All remaining patients at discretion of HCV expert.</td>
</tr>
</tbody>
</table>
Targeting core transmitters

- Persons who inject drugs (PWID) account for 70-80% of incident infections in Canada.
- 50-80% will be seropositive after one year of IVDU.
- Estimated that average PWID will infect 20 persons, with majority of transmission event taking place in the first two years.
- 42.14% of opioid dependent persons in New Brunswick methadone maintenance clinic HCV+.

A Cost-Effectiveness Analysis for Prioritizing PWID / non-PWID Subpopulations for HCV Treatment

- HCV transmission and progression cost-effectiveness model to inform prioritization of HCV treatment; prioritizing cirrhotic patients was compared to prioritizing patients with IV drug use (PWID) and ex/non PWID with mild/moderate disease.

- In scenarios with low or medium HCV prevalence in PWID, it is cost-effective to prioritize treatment to PWID at earlier disease stages
  - These strategies likely prove to be cost-effective due to the substantial prevention benefits accrued by treating patients at an earlier stage of disease.

![Graph showing mean incremental costs and QALYs for different scenarios.](image-url)
RECAP model of care

- Centre for Research, Education and Clinical Care of At-Risk Populations (RECAP).
- Nurse practitioner-led, interprofessional model of care for patients who are HCV-positive or at-risk of HCV acquisition.
- After optimization of clinical, mental, and social status, and with consideration to other comorbidities, it is determined whether the patient is a candidate for HCV treatment.
- Saint John based demonstration of model to ensure clinical effectiveness with planned expansion to other areas in NB.
HCV Utilization Management Plan

Identification and patient referral

Patient Stratification Plan for Birth Cohort

Patient Stratification Plan for At Risk/High Risk

Improved Models of Care for High Risk Groups

Education and Evaluation

Treatment

Inclusive registration of all treated patients

Voluntary evaluation/linkage to direct and indirect healthcare costs

Mechanism for outcomes measurement and program improvement

Education and Evaluation

HCV Management Plan
HEAR Database
(Hepatitis C Positive and At-Risk Prospective Patient Database)
### HEAR Database

*Hepatitis C Positive and At-Risk Prospective Patient Database*

<table>
<thead>
<tr>
<th>Demographic</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>63.0%</td>
</tr>
<tr>
<td>Median Age</td>
<td>37.0 years</td>
</tr>
<tr>
<td>Other Comorbidities</td>
<td>60.3%</td>
</tr>
<tr>
<td>No Primary Care Provider</td>
<td>44.8%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>HCV-Risk Factor (Historical or Current)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Intravenous Drug Use</td>
<td>62.1%</td>
</tr>
<tr>
<td>Shared Drug Paraphernalia</td>
<td>57.8%</td>
</tr>
<tr>
<td>High-Risk Sexual Activity</td>
<td>37.9%</td>
</tr>
<tr>
<td>Incarceration</td>
<td>60.3%</td>
</tr>
<tr>
<td>Tattoos/Piercing (Jail/Street)</td>
<td>40.5%</td>
</tr>
</tbody>
</table>

![HEAR-Database - Hepatitis C Genotype Distribution (n=67)](image)
Areas requiring further research

• Prospective evaluation of health economic impact of new DAA’s.

• Health economics of reinfection. Paying now and paying later?

• High risk population feasibility studies including incarcerated persons, First Nations, and immigrants.
Summary

- While disease prevalence is decreasing, complications of untreated chronic HCV will increase over the next two decades, as will healthcare expenditure.

- Cost of therapy is increasing, however cost of an SVR is decreasing.

- Versus rigid “F” restriction, maximal economic impact can be attained through dynamic programming which initially targets those with more advanced liver disease and core transmitters.

- Patient registries and outcome measures in the context of new therapies are essential to gauge real world clinical and health economic experience.
Poll the audience

HCV: Pay now or pay later?

(1) Treat now to prevent complications and incident infections.

(2) Partial treatment access with Fibrosis restriction (F2)

(3) Focus on the sickest first then expand access to everyone.

(4) Treatment costs way to much, focus on prevention for now and pay later when complications occur.

(5) Still not sure. Have they refilled the giant vat of coffee yet?
• Thanks!

- Dr. Duncan Webster
- Stefanie Materniak
- Dr. Lisa Barrett
- Dr. Greg German
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- Dr. Jeremy Beck
- Dr. Connie Hoare
- Dr. Meaghan O’Brien
- Dr. Morris Sherman
- Dr. Lamont Sweet
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- Lisa Frachette
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