Current Status of HCV in the United States

The Chronic Hepatitis Cohort Study (‘CHeCS’)
Why do we need a cohort study of chronic hepatitis? (or, why aren’t all studies controlled, blinded trials?)

- Questions about a disease spectrum require study of many patients over a long period
- Effects of drugs, good and bad, can often not be discerned in 24-, 48- or even 96- wk clinical trial
- Questions of public health, policy and epidemiology require population-based study
- Many questions cannot be answered by clinical trials methods because they would be too expensive, impossible, and/or unethical
The **Chronic Hepatitis Cohort Study (CHeCS)**:

**Public health/policy/burden objectives:**
- Health burden and mortality;
- Spectrum and natural history of disease;
- Characteristics of persons in care;
- Modes of transmission and ongoing risk behaviors;
- Use/effectiveness of recommended screening/care practices;
- Access to testing, care and treatment

**Clinical epidemiology/treatment issues/population basis:**
- Types of therapy in use, the benefits and risks/adverse effects associated with therapy, and factors influencing outcome of therapy
- Costs and potential savings of care and treatment;
CHeCS--operational elements:

- Each site(s) has/have data manager(s).
- Data collected from integrated electronic medical systems (clinic, hospital, ERs, lab, pharmacy).
- Some data (e.g., liver biopsy, treatment) manually collected and entered.
- Survey of patient behaviors important (ETOH, cigs, etc).
- Study is run by an Executive Committee comprised of CDC staff and PIs (Cooperative Agreement model).
Funding

• CHeCS has been generously funded by a CDC Foundation Grant:
  – Vertex Pharmaceuticals
  – Janssen/Johnson & Johnson
  – Abbvie/Abbott
  – Genentech/Roche (2010-2013)

• The CDC Foundation acts as a “firewall” to avoid both reality and appearance of commercial bias to CHeCS findings
CHeCS since March 2010: Patients retrospectively and prospectively identified*

<table>
<thead>
<tr>
<th>Site</th>
<th>2006- present † HBV</th>
<th>HCV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Henry Ford Health System (Detroit MI) ‡</td>
<td>1 135</td>
<td>5 422</td>
</tr>
<tr>
<td>Geisinger Health (Danville PA)</td>
<td>267</td>
<td>2 092</td>
</tr>
<tr>
<td>Kaiser- HI (Honolulu HI)</td>
<td>952</td>
<td>1 309</td>
</tr>
<tr>
<td>Kaiser -Northwest (Portland OR)</td>
<td>1 090</td>
<td>3 447</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>3 444</strong></td>
<td><strong>12 270</strong></td>
</tr>
</tbody>
</table>

* Only patients meeting stringent inclusion criteria
† Patients collected ‘retrospectively’ 2006-2008 and ‘prospectively’ 2009-present
‡ Main site
Baseline Characteristics and Mortality Among People in Care for Chronic Viral Hepatitis: The Chronic Hepatitis Cohort Study

- Anne C. Moorman, Stuart C. Gordon, Loralee B. Rupp, Philip R. Spradling, Eyasu H. Teshale, Mei Lu, David R. Nerenz, Cynthia C. Nakasato, Joseph A. Boscarino, Emily M. Henkle, Nancy J. Oja-Tebbe, Jian Xing, John W. Ward, and Scott D. Holmberg; for the Chronic Hepatitis Cohort Study Investigators

*Clinical Infectious Diseases* 2013; 56 (1 January):40-50
### Selected Characteristics of the First 11,000 Hepatitis B and C Patients in the CHeCS

<table>
<thead>
<tr>
<th></th>
<th>HBV (N= 2,202)</th>
<th>HCV (N= 8,810)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Received antiviral therapy (by 2010)</td>
<td>15%</td>
<td>37%</td>
</tr>
<tr>
<td>Underwent liver biopsy, 2001-2010</td>
<td>22%</td>
<td>38%</td>
</tr>
<tr>
<td>Most recent HBV DNA levels:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>“undetectable”</td>
<td>47%</td>
<td>___</td>
</tr>
<tr>
<td>&gt; 2,000 IU/ml</td>
<td>34%</td>
<td>___</td>
</tr>
<tr>
<td>HCV RNA levels &gt; 100,000 IU/µl</td>
<td>___</td>
<td>67%</td>
</tr>
<tr>
<td>Hospitalized, 2001-2010</td>
<td>38%</td>
<td>44%</td>
</tr>
<tr>
<td>Died, 2006-2010</td>
<td>9%</td>
<td>14%</td>
</tr>
</tbody>
</table>
Hepatitis B and C Virus Infection Among 1.2 Million Persons With Access to Care: Factors Associated With Testing and Infection Prevalence

• Philip R. Spradling, Loralee Rupp, Anne C. Moorman, Mei Lu, Eyasu H. Teshale, Stuart C. Gordon, Cynthia Nakasato, Joseph A. Boscarino, Emily M. Henkle, David R. Nerenz, Maxine M. Denniston, Scott D. Holmberg, for the Chronic Hepatitis Cohort Study (CHeCS) Investigators

• Clinical Infectious Diseases, 2012; 55 (15 October) 1047-55
Spradling et al: some conclusions

• Calculating how many were diagnosed compared with expected, it appears that 50% or more of HCV and 30% or more of HBV patients at the 4 health care organizations have **not** been diagnosed.

• Only 70% had evidence of follow-up care.

• One or even two abnormal ALT levels triggered viral hepatitis testing in half or fewer of patients with such abnormal values.
National Health and Nutrition Examination Survey (NHANES)*

- 30,140 randomly interviewed and tested persons in the US 2001-2008
- Corroborating data from deeper interview of 170 recently discovered HCV patients:
  - ½ knew previously about their HCV infection;
  - Of them, 77% had f/u for their infection; and
  - 13% had received antiviral treatment.

Putting this all together: Current Status of HCV in the US

- U.S. population with chronic HCV infection: 3.2 million
- HCV detected: 1.6 million (50%)
  - Referred to care: 1.0 - 1.2 million (32%-38%)
    - HCV RNA test: 630,000 - 750,000 (20%-23%)
    - Liver biopsy: 380,000 - 560,000 (12% - 18%)
      - Treated: 220,000 - 360,000 (7% - 11%)
        - Successfully Treated: 170,000 - 200,000 (5%-6%)
The growing burden of morbidity and mortality from HCV

• Why we need to get more people tested (early), into care, and treated
From national mortality/death certificate data*, updated through 2008:

* Ly K et al, Ann Intern Med 2012; 156:271-8
CHeCS: Annual Rate of Length of Stay (days/year) by FIB4 score*, 2006-2010

*FIB4, calculated from ALT, AST, platelet count and patient age, increases with worsening fibrosis; values ≥ 5.88 indicate cirrhosis and end-stage liver disease.
HCV-infected persons in CHeCS: Mortality rates also increasing*

<table>
<thead>
<tr>
<th>Year</th>
<th>Mortality rate (per 100 py)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2006</td>
<td>1.4</td>
</tr>
<tr>
<td>2007</td>
<td>2.1</td>
</tr>
<tr>
<td>2008</td>
<td>2.8</td>
</tr>
<tr>
<td>2009</td>
<td>3.2</td>
</tr>
<tr>
<td>2010</td>
<td>4.4</td>
</tr>
</tbody>
</table>

*From: AC Moorman et al, Abstract submitted to IDWeek 2013*
Other, recent findings*

- Despite high death rates, preliminary analysis suggests that only 19% of confirmed chronic HCV patients in CHeCS had HCV infection noted on their death certificate; only 30% even of those dying with liver-related conditions.

- This suggests that even if all HCV-infected patients are identified before death—clearly, not the case—actual mortality in them exceeds 75,000/yr.

- Whatever the listed cause of disease, HCV-infected persons die 15 years younger than everyone else.

CHeCS: The Future

- CHeCS has recruited over 3,500 chronic HBV and 13,000 chronic HCV patients drawn from a pool of > 1.6 M adults at four integrated health systems.
- Ongoing data collected from CHeCS will permit longitudinal assessments of HBV and HCV infection co-morbidities, access to care, and treatment adherence and outcome.
- We are now trying to get poised to evaluate population impact of new drugs as they come on line.
- Challenges, essentially:
  - Shrinking funding;
  - Burgeoning cohort size and complexity.
CHeCS Executive Committee

● CDC:
  - Scott Holmberg, MD
  - Anne Moorman, MPH
  - Phil Spradling, MD
  - Eyasu Teshale, MD

● Henry Ford Hosp/Detroit
  - Stuart Gordon, MD
  - David Nerenz, PhD
  - Lora Rupp, MPH
  - Mei Lu, PhD

● Kaiser/ Hawaii
  - Vinutha Visayaja, MD

● Geisinger/ central Penn
  - Joe Boscarino, PhD

● Kaiser NW/Portland, OR
  - Mark Schmidt, PhD

● Alaska Native Tribal Health/ Anchorage (ancillary site)
  - Brian McMahon, MD
Special thanks to external partners who have been funding CHeCS through the CDC Foundation

• Vertex Pharmaceuticals
• Janssen/Johnson & Johnson
• Abbvie/Abbott
• Genentech/Roche (2010-2013)
Additional Slides
Some submitted and in press articles

• Holmberg S, Lu M, Rupp B, Lamerato L, Moorman A, Vijayadeva V, Boscarino J, Henkle E, Gordon S, for the CHeCS Investigators. Use of non-invasive serum markers for staging hepatitis C virus (HCV) in the Chronic Hepatitis Cohort Study (CHeCS). Clin Infect Dis; in press


Some submitted and in press articles


- Teshale E, Lu M et al. Noninvasive serum markers to stage fibrosis in patients with chronic hepatitis B infection.
Manuscripts submitted January-March 2013


• Henkle E, et al. Hepatitis A and B vaccination and immunity in a cohort of chronically-infected hepatitis B and C patients in four health care systems. Submitted
Initial Findings (Performance Measure per AASLD/AGA/PCPI)- 1

- Of the 1.6 million adults from whom the CHeCS cohort was drawn, the actual number of HBV and HCV infections was substantially less than predicted (two-thirds less for HBV and one-half less for HCV). [0393**]
- Only half of those with ≥2 abnormal ALT received HBV/HCV testing.
- About 45%-65% of those with HCV Ab+ had NAT testing (indicative of follow-up) [0395]
- Among patients with chronic HCV, 35% were neither tested nor vaccinated for hepatitis A [0399], and 32% were neither tested nor vaccinated for hepatitis B. [0400]
- Very high hospitalization and mortality rates were observed among persons with HBV and HCV, even in those (66%) who are relatively young (aged 45-65 years).