Hepatitis C Infection and the Opportunity for Eradication

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Women in Government Healthcare Summit
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Disclosures

Advisory Boards: BMS, Gilead, Gilead FOCUS
Medical Advisory Boards: Hepatitis Foundation International, American Liver Foundation
Grant Funding: Gilead FOCUS (Testing and linkage to care)
Stock Ownership: various pharmaceuticals in managed discretionary account
Question

Which patient is likely infected with hepatitis C?

1. 19 year old white, female high school student in Indiana
2. 40 year old nurse in Chicago, Illinois, who received blood transfusions in the 1980s
3. 55 year old male professor of Anthropology, who did his thesis dissertation on the culture of Woodstock
4. 60 year old State Senator from .....
Chronic Hepatitis C Infection

- Epidemiology
  - Baby Boomer: Cost Effectiveness of Screening
  - Studies in Urban regions: Primary Care and ED
  - Cascade of Care
- Treatment Options
- Policy
  - States like NY: Mandatory Testing for Baby Boomers
  - HCV Guidelines
  - Recent CMS letter to Medicaid
  - AASLD Press Release
- Projections in Disease Burden
- Cost Effectiveness
- Common Misconceptions
HCV Epidemiology

• 180 million worldwide
• Incidence - not well known
  • Rising - risky sexual behavior; young IDUs
• Prevalence:
  • 4.1 (1.6%) million infected in US
  • 3.2 (1.3%) (80%) chronic HCV
  • Likely higher 5 – 7 million
  • NHANES 1999-2002
• Liver transplant in US
Global HCV Antibody Prevalence

HCV Transmission Factors

- Injection drug use
- Transfusion prior to 1992; clotting factors prior to 1987
- Hemodialysis
- Occupational exposure
- Sexual/Multiple sexual partners
- Vertical transmission
- Consider: tatoos, piercings, drug snorting
- And ....
Recommendations for the Identification of Chronic Hepatitis C Virus Infection Among Persons Born During 1945–1965
CDC HCV Testing Recommendations

- Adults born during 1945 through 1965 should be tested once for HCV infection without prior ascertainment of HCV risk factors
  - (strong recommendation, moderate evidence)
- If positive, brief alcohol screening and intervention, as well as referral for HCV care and treatment
  - (strong recommendation, moderate evidence)
- Screening is Cost Effective

MMWR, Aug 2012, Vol 61 (4)
CDC HCV Testing Recommendations

Why 1945 – 1965:

- 27% of population, 81% of all adult HCV US infx
- Prevalence 3.25%, 5x higher than other years
  - Non-hispanic black males 8%, non-hispanic white males 4% and Mexican-American 3.4%
- 73% of HCV related mortality
- 45% do not report any risk factors
- 31.5% do not have health insurance
- Alcohol use: 57% who drink, moderate to heavy

MMWR, Aug 2012, Vol 61 (4)
Effective Screening Programs

• National Committee on Prevention Priorities:
  • Birth cohort screen with *std treatment* v risk based screening ranks equivalent to:
    • Colorectal Cancer screening
    • Hypertension
    • Influenza vaccination > 50, pneumococcal > 65
  • Birth cohort screen with DAA ranks equivalent:
    • Below above, equivalent to cervical cancer or cholesterol

McGarry, Hepatology, 2012, 56
Additional Recommendations

• US Preventive Services Task Force (USPSTF)
  • June 2013
  • Grade B recommendation
    • Recommend testing as there is high certainty of moderate benefit OR moderate certainty of moderate to substantial benefit
• NYS Mandatory HCV testing in those born 1945-1965
  • January 2014
  • Inpatient or primary care testing; must be linked to a provider
  • Other states?
• Centers for Medicare and Medicaid
  • June 2014
  • In Primary care clinic for Birth Cohort
    • Def. integrated, accessible health care services addressing a large majority of personal health care needs
    • Not included: ED, inpatient amb surg, SNF, inpatient rehab, hospice
ED Testing: Birmingham, AL

Galbraith, et al, unpublished
<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Total HCV Ab Tests Performed</th>
<th>HCV Ab Positive</th>
<th>HCV RNA Positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>2276 (100)</td>
<td>169 (7.4)</td>
<td>93/147 (63.2)</td>
</tr>
<tr>
<td>Age (mean ± SD)</td>
<td>58.6 +</td>
<td>60.3 +</td>
<td>59.9 +</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>1477 (64.9)</td>
<td>80 (47.3)</td>
<td>41 (44.1)</td>
</tr>
<tr>
<td>Men</td>
<td>799 (35.1)</td>
<td>89 (52.6)</td>
<td>52 (55.9)</td>
</tr>
<tr>
<td>Race/Ethnicity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-Hispanic, black/African American (b/AA)</td>
<td>1901 (83.5)</td>
<td>153 (90.5)</td>
<td>86 (56.2)</td>
</tr>
<tr>
<td>b/AA (Women/Men)</td>
<td>1249 (65.7)</td>
<td>73 (47.7)</td>
<td>39 (45.3)</td>
</tr>
<tr>
<td></td>
<td>652 (34.3)</td>
<td>80 (52.3)</td>
<td>47 (54.7)</td>
</tr>
<tr>
<td>Intragroup b/AA Women/Men</td>
<td>73/1249 (5.8)</td>
<td>80/652 (12.3)</td>
<td>39/73 (53.4)</td>
</tr>
<tr>
<td></td>
<td>65/146 (44.5)</td>
<td>40/65 (61.5)</td>
<td></td>
</tr>
<tr>
<td>Insurance</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Public</td>
<td>1466 (64.4)</td>
<td>129 (76.3)</td>
<td>70 (75.3)</td>
</tr>
<tr>
<td>Private</td>
<td>807 (35.5)</td>
<td>40 (23.7)</td>
<td>23 (24.7)</td>
</tr>
<tr>
<td>IVDU (Reported Post Test)</td>
<td>65/146 (44.5)</td>
<td>40/65 (61.5)</td>
<td></td>
</tr>
</tbody>
</table>
WHC Fibrosis Scores at Initial Visit

Advanced Fibrosis or Cirrhosis: 42%

Geboy, HCV Summit, APHA 2015
Global HCV Antibody Prevalence

Redefining the HCV Cascade of Care

Screening & Testing

Linkage and Retention in Care

Liver Staging, HCC Screening, Vaccinating, Harm Reduction Discussions

Addressing Socioeconomic Needs

Improving Other Medical Outcomes

Antiviral Treatment

Cure

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Liver Staging, HCC Screening, Vaccinating, Harm Reduction Discussions

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Screening & Testing

Linkage and Retention in Care
Barriers to Care

- **Patient Barriers**
  - Transportation Barriers
  - Family/Social Barriers
  - Education and Awareness Barriers
  - Housing Barriers

- **Provider & Facility Barriers**
  - Education and Awareness Barriers
  - missing appointments
  - not following through with orders for xray, blood work, etc.
  - Lack of continuity, scheduling different providers

- **Systemic Barriers**
  - Treatment access and Policy
Advances in SVR Rates in GT1

![Graph showing SVR rates for different HCV treatment regimens from 1991 to 2015](image-url)

**HCV Treatment Regimen**
- IFN 24
- IFN 48
- IFN/RBV 24
- IFN/RBV 48
- PEG-IFN/RBV
- DAARGT
- IFN Free

**SVR Rate (%)**
- 1991: 2%
- 2011: 95%
- 2015: 95%
Current Approved HCV Therapy
Cure > 90%

- **Genotype 1:** 8-24 wks
  - Harvoni: ledipasvir/sofosbuvir
  - Viekira: Paritaprevir (150)/r/ Ombitasvir (25), + Dasabuvir (250) bid +/- ribavarin
  - Olysio (simeprevir) + Sovaldi (sofosbuvir)
- **Genotype 2:** 12 weeks
  - Sovaldi (sofosbuvir) and RBV
- **Genotype 3:** 24 weeks
  - Sofosbuvir and RBV +/- Interferon
  - Daclinza (daclatasvir) + Sovaldi (sofosbuvir)
- **Genotype 4:** Technivie
- Response varies especially with cirrhosis and prior treatment
- Insurance Issues: May lose treating providers
HCV Therapeutics: Cure > 90%

FDA Approved 2013

FDA Approved 2014

FDA Approved 2015

ZEPATIER (Elbasvir/grazoprevir)

FDA To be Approved 2016
Based on expanded “real-world” experience with the tolerability and efficacy of newer HCV medications, the section on “When and in Whom to Initiate HCV Therapy” no longer includes tables that offer recommendations on how to prioritize patients for treatment.

“However, the goal is to treat all patients as promptly as feasible to improve health and to reduce HCV transmission” said panel co-chair Henry Masur, MD.

“A good relationship between doctor and patient is crucial to achieving the best outcomes with direct-acting therapies. The physician needs to make an assessment of a patient’s understanding of the treatment goals and provide education on the importance of adherence to the therapy and follow-up care,” added panel co-chair Gary Davis, MD.
Current HCV Therapy

“Successful hepatitis C treatment results in sustained virologic response (SVR), which is tantamount to virologic cure, and as such, is expected to benefit nearly all chronically infected persons. Evidence clearly supports treatment in all HCV-infected persons, except those with limited life expectancy (less than 12 months) due to non–liver-related comorbid conditions. Urgent initiation of treatment is recommended for some patients, such as those with advanced fibrosis or compensated cirrhosis.”
CMS Letter: November 5, 2015
ASSURING MEDICAID BENEFICIARIES ACCESS TO HEPATITIS C (HCV) DRUGS

• Concern: some states are restricting access to DAA HCV drugs contrary to the statutory requirements in section 1927 of the Act
  – imposing conditions for coverage that may unreasonably restrict access to these drugs. (eg, programs are limiting treatment for metavir fibrosis score F3 or even F4)

• CMS shares states’ concerns regarding budgetary impact
  – However, more therapeutics allow for price competition and states can negotiate FFS and managed care pricing, driving down costs

• Manufacturers also have a role and letter sent from CMS to provide information on value-based purchasing arrangements so that states might participate

Center for Medicaid and CHIP service, No 172, 11/5/15
Incidence of Absolute Denial of DAA Therapy, By Insurance (n=2,321*)

*Excludes 21 patients with incomplete prior authorization after 60 days

Lo Re, etal, LB 5, AASLD Nov, 2015
• “There is no medical evidence to justify that position and much to justify treating all patients.”
• “AASLD endorses treating patients with HCV as the standard of care. “
• “HCV treatment that leads to a cure is the only evidence-based intervention to prevent liver disease progression.”
• “Inaction is harmful to patients.”
• “Failure to treat leads to other medical problems.”
• “Access to curative therapies is the most effective way to eliminate the virus at a population level. “
Cost Effectiveness

• New DAAs are cost effective in the U.S.
  – QALY (quality adjusted life years) and ICER (incremental cost effectiveness ratio):
    • HCV GT1 cost saving (less than $0) to $31,452 per QALY gained, depending on the presence or absence of cirrhosis. [(Chatwal, 2015); (Najafzadeh, 2015); (Linas, 2015); (Younossi, 2015a)]
    • Harder to treat: $84,744 to $178,295 per QALY gained IFN-experienced with fibrosis who are being retreated using an IFN-free regimen. [(Chatwal, 2015)]
  • Cost effectiveness does not equal affordability

HCVGuidelines.org August 2015
Potential Impact on Future Burden of HCV

Impact on Mortality

Ward, J, CROI 2013, CDC
Hepatocellular Carcinoma in the Era of DAAs

Jagpreet Chhatwal, et al, AASLD, 2015
Liver-Related Deaths in the Era of DAAs

Jagpreet Chhatwal, et al, AASLD, 2015
HCV-Associated Disease Burden (2015–2050)

- **Liver-related Death**:
  - No Treatment: 767,000
  - Pre-DAA Era: 317,000
  - DAA Era: 198,000

- **HCC**:
  - No Treatment: 407,000
  - Pre-DAA Era: 154,000
  - DAA Era: 63,000

- ** Decomp. Cirrhosis**:
  - No Treatment: 651,000
  - Pre-DAA Era: 198,000
  - DAA Era: 31,000

- **Liver Transplants**:
  - No Treatment: 198,000
  - Pre-DAA Era: 63,000
  - DAA Era: 31,000

50–70% reduction in HCV-associated disease burden

Jagpreet Chhatwal, et al, AASLD, 2015
Patient Quotes

“In the beginning they were like fish out of water. You have to remember there was a big stigma and there was no cure at that time. They offered interferon but I just couldn’t take another treatment I was so exhausted…”

-Patient Partner for study development

“I’ve been infected for 30 years, and that whole time I just felt “dirty” living with the infection and the stigma, even though I know this not to be true.”

-Patient Partner

“I’ve lived in complete silence of my disease for over 20 years, I was so ashamed. It was not until I got treated with the new medications, that I was willing to come to support groups and even be on camera. I want to be able to help others now.”

-Support Group Member
Common Misconceptions

• Treating this disease is expensive and it will never go away
  – False: There is a cure and there is NO other disease where we can cure, eliminate and eradicate
  – Treatment is Cost Effective (though it is costly)

• But treatment doesn’t work and it’s toxic
  – False: Treatment CURES! And it’s safe!
  – Patients WANT to be treated
Common Misconceptions

• Hepatitis C is only a disease of drug users
  – False: Baby boomer data
• Urban problem
  – False: New rural epidemics
• The price is $1,000 per pill
  – False: Payer negotiations; need for transparency
  – States CAN negotiate price; Feds cannot
  – Population is aging into Medicare
  – Price does not equal Cost
  – Paradigm for industry is different due to curing and not treating a disease chronically
Common Misconceptions

• Current & former drug users can not adhere to medication
  – False – recent Merck data
  – Patients want to be empowered

• Alcohol use reduces efficacy
  – False: But it can increase severity of liver disease

• Only alcohol causes liver cirrhosis
  – False: So does hepatitis C!
Take Home Points

• Current therapy is pushing 100% CURE rates
  • Highly efficacious, low toxicity and short duration
• Testing & linkage to care and cure can lead to HCV *ELIMINATION* and *ERADICATION*
  • People need to be tested and aware of infection
  • Rates in the Birth Cohort, new younger epidemic
• Implementation into practices is now key
• Data being generated should drive policy
• New paradigm for industry given cure NOT chronicity
• Competition in therapeutics can drive price
• Efforts should be made to eliminate at a state level
• All HCV infected persons deserve to be treated
Additional Slides
Additional Slides
2.5% = 16,450 HIV+

2.5% = 16,450 HCV+
(92% African American)
<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Risk Based &amp; PR</th>
<th>Birth Cohort &amp; DAA</th>
<th>Differences</th>
</tr>
</thead>
<tbody>
<tr>
<td># of antibody tests</td>
<td>14,793,816</td>
<td>60,404,514</td>
<td>45,610,698 more tests</td>
</tr>
<tr>
<td># positive tests</td>
<td>262,260</td>
<td>1,070,840</td>
<td>808,580 more cases</td>
</tr>
<tr>
<td># patients treated</td>
<td>135,089</td>
<td>551,800</td>
<td>416,711 more treated</td>
</tr>
<tr>
<td># SVR</td>
<td>53,160</td>
<td>310,855</td>
<td>257,695 more SVR</td>
</tr>
<tr>
<td># compensated cirrhosis</td>
<td>994,291</td>
<td>791,053</td>
<td>203,238 cirrhosis cases averted</td>
</tr>
<tr>
<td># decompensated cirrhosis</td>
<td>360,388</td>
<td>286,699</td>
<td>73,689 DCC cases averted</td>
</tr>
<tr>
<td># HCC</td>
<td>230,784</td>
<td>183,595</td>
<td>47,189 HCC cases averted</td>
</tr>
<tr>
<td># transplant</td>
<td>75,752</td>
<td>60,268</td>
<td>15,484 transplants averted</td>
</tr>
<tr>
<td># HCV-related deaths</td>
<td>591,172</td>
<td>470,293</td>
<td>120,879 deaths averted</td>
</tr>
</tbody>
</table>

HCV Life Cycle and Targets

Adapted from Manns MP, Nat Rev Drug Discov. 2007

- **NS3/4 protease inhibitors**
- ** Cyclophylin inhibitors**
- **NS5B polymerase inhibitors**
- **NS5A inhibitors**

*Role in HCV lifecycle not well defined*
Outcomes of DAA Prescriptions, Including Reasons for Absolute Denial

- Prescription filled
- Lack of medical necessity
- Incomplete data to determine medical need
- Drug or alcohol use
- Non-preferred DAA
- Unknown, no denial letter received

Percent of Patients

US Medicaid (n=503) 95%

US Medicaid (n=795) 90%

Commercial Insurance (n=1,023)
## Incidence of Denials, By Insurance

<table>
<thead>
<tr>
<th>Type of Denial, n (%)</th>
<th>Overall (n=2,321)</th>
<th>Medicaid (n=503)</th>
<th>Medicare (n=795)</th>
<th>Commercial (n=1,023)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any denial</td>
<td>690 (30%)</td>
<td>356 (71%)</td>
<td>143 (18%)</td>
<td>191 (19%)</td>
</tr>
<tr>
<td>Denial, but filled</td>
<td>313 (14%)</td>
<td>123 (24%)</td>
<td>103 (13%)</td>
<td>87 (8%)</td>
</tr>
<tr>
<td>Absolute denial</td>
<td>377 (16%)</td>
<td>233 (46%)</td>
<td>40 (5%)</td>
<td>104 (10%)</td>
</tr>
<tr>
<td>No denial</td>
<td>1,631 (70%)</td>
<td>147 (29%)</td>
<td>652 (82%)</td>
<td>832 (81%)</td>
</tr>
</tbody>
</table>
Disease Burden Projections

- Increase treatment capacity
  - Decompensated cirrhosis
  - Hepatocellular carcinoma
  - Liver related deaths
  - Liver transplant
- DAA treatment and HCC
- DAA treatment and liver related deaths
- DAA treatment and disease burden
Reduction in Disease Burden by Increasing the Treatment Capacity

- DC, decompensated cirrhosis
- HCC, hepatocellular carcinoma
- LRD, liver-related deaths
- LT, liver transplants

Jagpreet Chhatwal, et al, AASLD, 2015
Resources

• MMWR, Recommendations for the identification of Chronic HCV infection among people born between 1945 and 1965; August, 2012, 61 (4)

• www.cdc.gov/hepatitis/

• http://www.hhs.gov/ash/initiatives/hepatitis/


• AASLD and IDSA Guidelines
  • HCVguidelines.org