Recommendation for the Identification of Hepatitis C Virus (HCV) Infection among Persons Born from 1945-1965

Rebecca L. Morgan, MPH

Centers for Disease Control and Prevention
Division of Viral Hepatitis
August 30, 2011

National Center for HIV/AIDS, Viral Hepatitis, STD & TB Prevention
Division of Viral Hepatitis

Agenda

- Morbidity and mortality of HCV infection
- Two-stage process for HCV screening recommendations
- Scope of the screening recommendations
- Research question
- HCV prevalence among birth cohort
- Outcome variables
- Consultation
- Reflections and implications
- Next steps

2

MORBIDITY AND MORTALITY OF HCV INFECTION

3

Morbidity and Mortality related to Hepatitis C Virus

- HCV Mortality has increased significantly from 1999-2007 and more people died from HCV than from HIV in 2007 (~15,000 vs. ~13,000)[2]
- HCV is the leading cause of hepatocellular carcinoma in the U.S.[3]
- HCV is the leading indication for liver transplantation in the U.S. [4]
- Chronic HCV all-cause mortality is 2.4 times higher than HCV negative persons[1]
- Estimated 2.9M persons with chronic HCV infection in U.S.
- Implementing a birth cohort screening strategy (persons born from 1945-1965) would identify up to 1.9M persons who are unaware of their HCV status

1. Ly, K., et al., The growing burden of mortality from viral hepatitis in the U.S., 1999-2007. Under review. 2. Velazquez, R.F., Et al., Prospective analysis of risk factors for hepatocellular carcinoma in patients with liver cirrhosis. Hepatology, 2003. 3. Ghany, et al., Diagnosis, Management, and Treatment of Hepatitis C: An Update. 2009. 4. El-Kamary, S., All-cause, liver-related, and non-liver-related mortality among HCV-injected individuals in the general US population. Clinical Infectious Diseases, 2011.

4

TWO-STAGE PROCESS FOR HCV SCREENING RECOMMENDATIONS

5

CDC Update of HCV Screening Policy Two Stages

- **Birth Cohort Recommendations (expected in 2012)**
  - Systematic review focusing on birth cohort (1945-1965)
  - Including brief reiteration of 1998 recommendation
- **Comprehensive Recommendations (expected in 2013)**
  - Systematic review of all other areas (e.g., ALT, IDU, transfusion, etc.)
- **Both Recommendations together will comprise the update of the 1998 Recommendations, combining targeted prevalence and risk-based strategies**

6

SCOPE OF THE HCV SCREENING RECOMMENDATIONS

7

Recommendation Scope

- Reason for update
- Target audience
- Date of completion
- Funding available
- Existing guidelines
  - AASLD Practice Guidelines, 2009;
  - CDC STD Guidelines, 2010;
  - SIGN, 2006;
  - Finnish Medical Society Duodecim: Viral Hepatitis Guidelines, 2008;
  - Gilson & Brook: UK screening and testing guidelines for hepatitis A, B, C, 2006
- Internal/external involvement
- Final document format

Internal/External Involvement

- **Steering Committee**
  - Leads the development of the recommendations
- **Internal Work Group**
  - Representatives from the Division of Viral Hepatitis
- **External Work Group**
  - Representatives from:
    - Federal Partners, Practice Implementation Groups, Community/Advocacy Groups, Expert Groups, Content Experts (Gastroenterologists, Hepatologists, Corrections, Modeling, Methodologists)
  - Input:
    - 6 conference calls to review process and methodology
    - Attendance at a consultation in Atlanta to discuss the findings
    - Review of the draft recommendations document

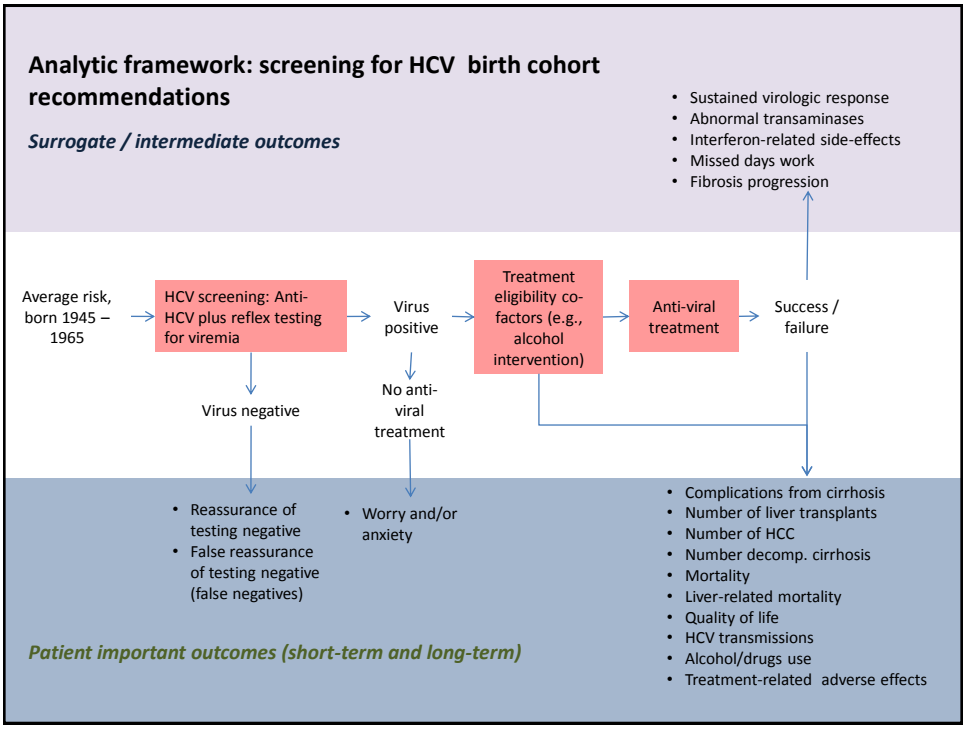
RESEARCH QUESTION

10

Research Question

- **PICO Question: To assess the effects of screening and care against the standard of care (i.e., risk-based screening) for HCV infection among persons born from 1945 to 1965 living in the U.S.**
  - **Population**: Persons born from 1945 to 1965, who are unaware of their HCV status
  - **Intervention**: Screening and care (e.g., response, work-up as needed, etc.)
  - **Comparator**: No screening (e.g., standard of care or risk-based screening)
  - **Outcome(s):** Any outcome that is patient important

Analytic framework: screening for HCV birth cohort recommendations



Ranked Outcomes and Surrogates

Importance of Outcomes		Outcome	←	Surrogate
Critical for decision making	9	All-cause Mortality	←	Sustained Virologic Response (SVR)
				Complications from Advanced Fibrosis
				Liver Transplants
		Hepatocellular Carcinoma (HCC)		
	9-8	Sustained Virologic Response (SVR)		
	8-7	Quality of Life	←	Missed Days of Work
				Worry and/or Anxiety
				Stigma/Discrimination After Testing Positive
	7	Insurability		
		Barriers to Accessing Care/Treatment		
		HCV Transmission		
		Treatment-related Adverse Effects	←	Interferon-related Suicide
Important, but not critical for decision making	6	Substance Use (e.g., Alcohol, Drugs)		

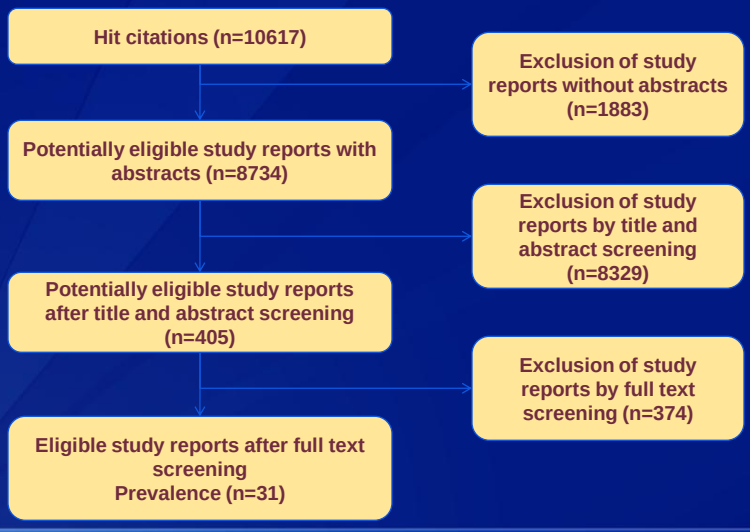
HCV PREVALENCE AMONG PERSONS BORN FROM 1945 TO 1965

14

Evidence Review

- **Search criteria:**
  - Years: 1995 – May 2011
  - Language: English
- **Search strategy:**
  - Hepatitis C or HCV
  - Prevalence or frequency
  - Epidemiological study designs: cohort or cross-sectional
- **Databases searched:**
  - Pubmed/Medline
  - Embase
  - Sociological Abstracts
  - Cochrane (e.g., Database of Systematic Reviews, Central Register of Controlled Trials, Economic Evaluation Database)
  - CINAHL
  - Database of Abstracts of Reviews of Effects
  - New York Academy of Medicine (grey literature)

HCV birth cohort recommendations study screening flow chart



Modified: June 24, 2011

Characteristics of Prevalence Studies

- **Inclusion Criteria**
  - U.S.-based prevalence data
  - Age-group prevalence data that includes birth cohort
- **Findings**
  - 2 nationally-representative studies
  - 29 city- and state-specific studies
- **Benefits**
  - Many studies (n=31)
  - Prevalence projected across various populations and settings
- **Limitations**
  - Birth cohort definition not standardized
  - Age groups ranged from 18-≥60 years
  - Unequal study population (e.g., all male)
  - Not nationally representative

REVIEW OF OUTCOMES

18

Ranked Outcomes and Surrogates

Importance of Outcomes		Outcome	←	Surrogate
Critical for decision making	9	All-cause Mortality	←	Sustained Virologic Response (SVR)
				Complications from Advanced Fibrosis
				Liver Transplants
		Hepatocellular Carcinoma (HCC)		
	9-8	Sustained Viral Response (SVR)		
	8-7	Quality of Life	←	Missed Days of Work
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		Barriers to Accessing Care/Treatment		
		HCV Transmission		
		Treatment-related Adverse Effects	←	Interferon-related Suicide
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Outcome Variables

- **Search strategy:**
  - Targeted searches of systematic reviews and meta-analyses
  - Conducted searches of primary research when systematic reviews and meta-analyses were not available
- **Inclusion criteria**
  - English language
  - 1995 – July 2011
  - Worldwide

CONSULTATION

21

Consultation

- **2-day consultation in Atlanta**
- **Reviewed prevalence data**
- **Presented summary of findings table**
- **Discussed:**
  - Quality of the evidence
  - Balance of benefits vs. harms and burdens
  - Values and preferences
  - Resource implications

Question: Should HCV screening followed by antiviral treatment (PR) vs. no screening (no or failed treatment) be used in birth cohort?[1]

Bibliography: Own meta-analyses; and from: Brok et al., 2010; Spiegel et al., 2005; Awad et al., 2010; Backus et al., 2011.

Quality assessment							Summary of Findings				
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With No screening (no or failed treatment)	With HCV screening followed by antiviral treatment (PR)		Risk with No screening (no or failed treatment)	Risk difference with HCV screening followed by antiviral treatment (PR) (95% CI)
mortality in HCV population (CRITICAL OUTCOME[3]; assessed with: death certificate)											
16868 (1 obs. study) 3.8 years[6]	no serious risk of bias[4]	no serious inconsistency	no serious indirectness	no serious imprecision	undetected	⊕⊕⊖⊖ **LOW**[4]	1126/9434 (11.9%)	409/7434 (5.5%)	**HR 0.7** (0.59 to 0.83)[5]	**119 deaths per 1000**	**34 fewer deaths per 1000** (from 19 fewer to 47 fewer)
hepatocellular carcinoma (CRITICAL OUTCOME; assessed with: imaging, pathology)											
29575 (37 obs. studies)	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	undetected	⊕⊕⊕⊖ **MODERATE**[2] due to large effect	1605/20150 (8%)	201/9425 (2.1%)	**RR 0.29** (0.24 to 0.35)	**80 HCC per 1000**	**57 fewer HCC per 1000** (from 52 fewer to 61 fewer)
HRQOL associated with SVR - vitality sub-score (CRITICAL OUTCOME; measured with: SF-36; range of scores: 4-24; Better indicated by higher values)											
0 (7 studies)	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	undetected	⊕⊕⊖⊖ **LOW**	-	0[7]	-		The mean hrqol associated with svr - vitality sub-score in the intervention groups was **6.6 higher**[8]
failure of SVR (CRITICAL OUTCOME; assessed with: PCR negative at 24 weeks post treatment)											
9146 (60 RCTs)	no serious risk of bias	no serious inconsistency	no serious indirectness[9]	no serious imprecision	undetected	⊕⊕⊕⊕ **HIGH**[2]	3471/4055 (85.6%)	3137/5091 (61.6%)	**RR 0.75** (0.71 to 0.79)	**Birth cohort** **999 per 1000**[12]	**Not estimable**
adverse effects leading to treatment discontinuation[10] (CRITICAL OUTCOME[11])											
4941 (11 RCTs)	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	undetected	⊕⊕⊕⊕ **HIGH**	303/2970 (10.2%)	187/1971 (9.5%)	**RR 0.79** (0.51 to 1.23)	**Birth cohort** **0/1000**	**Not estimable**

REFLECTIONS AND IMPLICATIONS

24

Reflections and Implications

- GRADE methodology accepted by Internal and External Work Group members
- Teleconferences and consultation provided opportunities for knowledge sharing and discussion between internal and external stakeholders
- Involvement of external stakeholders and methodologists increases the acceptability and transparency of final product

NEXT STEPS

26

Next Steps

- Vote on strength of the recommendations
- Draft recommendations document
- Submit for a peer review of methods
- Share for external public comment
- Enter into CDC clearance
- Submit to MMWR for publication

Thank you!

Questions?

Rebecca L. Morgan, evf5@cdc.gov, +1 404 639 6108

For more information please contact Centers for Disease Control and Prevention
1600 Clifton Road NE, Atlanta, GA 30333
Telephone, 1-800-CDC-INFO (232-4636)/TTY: 1-888-232-6348
E-mail: cdcinfo@cdc.gov Web: www.cdc.gov