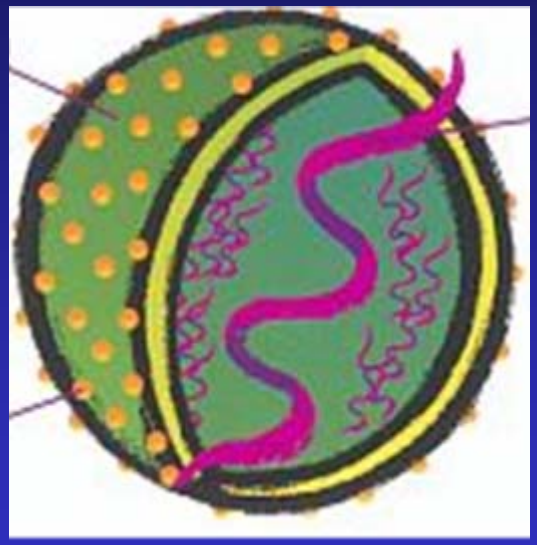
Clinical and Educational Tools for Managing Hepatitis C



CDC National Viral Hepatitis Prevention Conference

December 7, 2005

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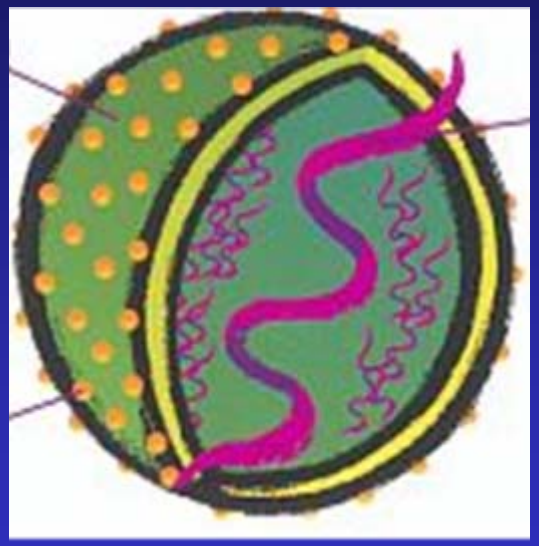
Department of Veterans Affairs Hepatitis C Resource Centers



Peter Hauser, MD[1]

Helen Yee, PharmD[2]

Betsy Zucker, FNP[1]

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Julie Nelligan, PhD[1]

[1]Portland VA Medical Center

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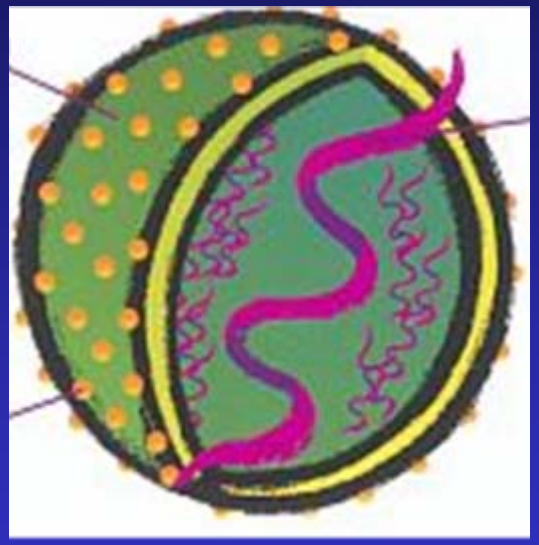
Hepatitis C Management & Care
Why the VA?



Peter Hauser, MD

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Hepatitis C & the U.S.

- U.S. Prevalence: 1.8%
  (approx 3-4 million)
- Leading cause for liver transplantation
- Complications from HCV increasing
  (ESLD, liver cancer)

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Hepatitis C & U.S. Veterans

- 5.4% National Prevalence (2004)
  - only vets who use VA facilities
  - 3x rate in general population (2004)
- 6% VISN 20 (Pacific NW) Prevalence (2003)

- Due to high prevalence in 1998, the VA created a National Hepatitis C Program
  - Mandated screening, testing, education, treatment
- As a result, the VA treats more HCV than any other healthcare organization

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The VA Hepatitis C Resource Centers

- 4 VA Hepatitis C Resource Centers (HCRCs) funded in January 2002.
- Psychiatric and substance use co-morbidty is one of five focus areas of the HCRC.
- Purpose: To increase access to care for those who have been historically excluded from antiviral therapy.
- WHY? Vast majority of veterans with hepatitis C have co-morbid psychiatric and substance use disorders.

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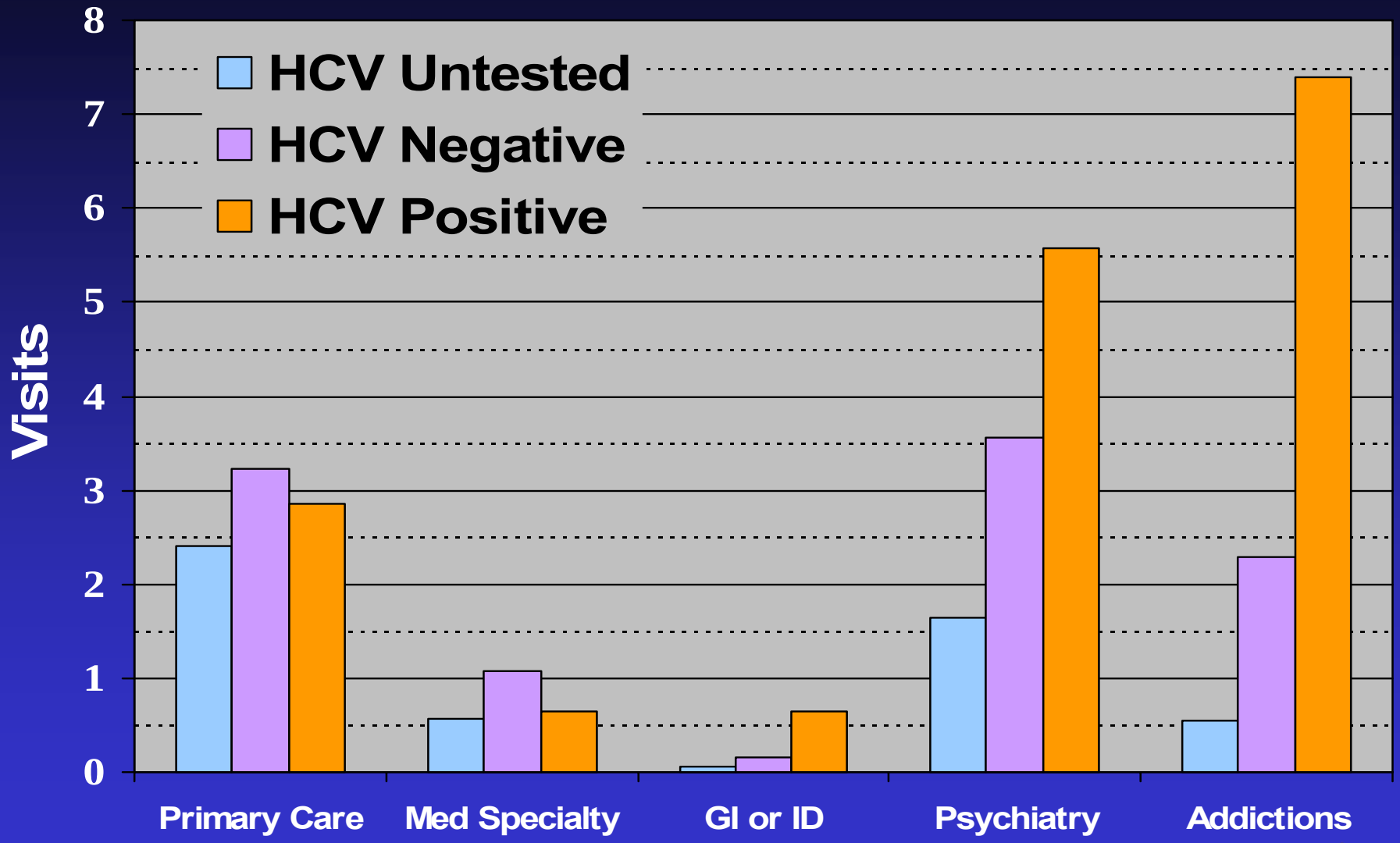
VISN 20 Outpatient Clinic Use



Sloan, Puget Sound VAMC, unpublished data, 2003

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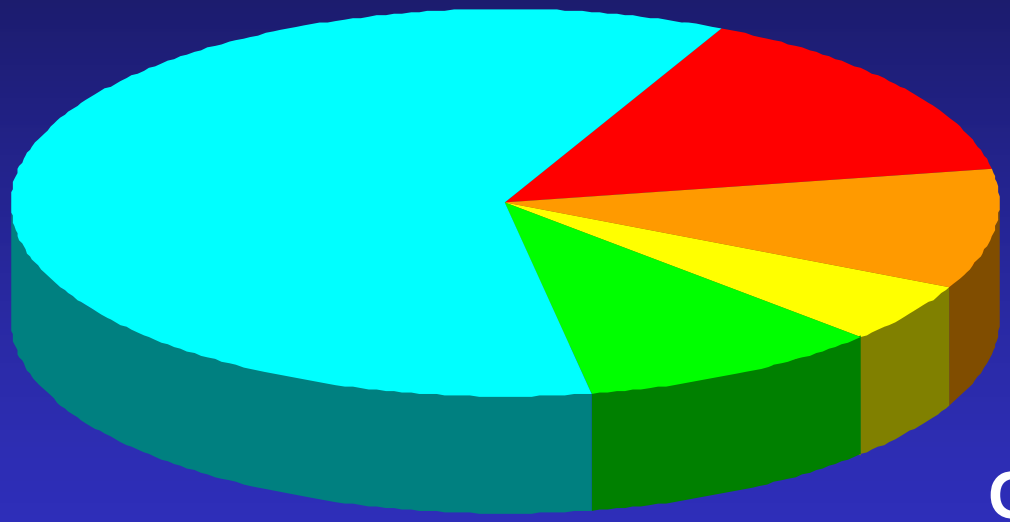
Hep C Source of Infection



*Nosocomial; Health-care work; Perinatal

Source: Centers for Disease Control and Prevention

CDC
Centers for Disease Control and Prevention

Multidisciplinary Approach in HCV Management

- HCV screening and education in SA & MH clinics
- Evaluation of liver disease & HAV/HBV vaccination
- SA & MH screening in HCV care clinics
- Referral of HCV pts for SA & MH care
- SA/MH evaluation & preparation for IFN/RBV tx
- Treatment decision
- Co-management of SA & MH during IFN/RBV tx

The VA experience offers a Co-Management Model suitable for community care programs

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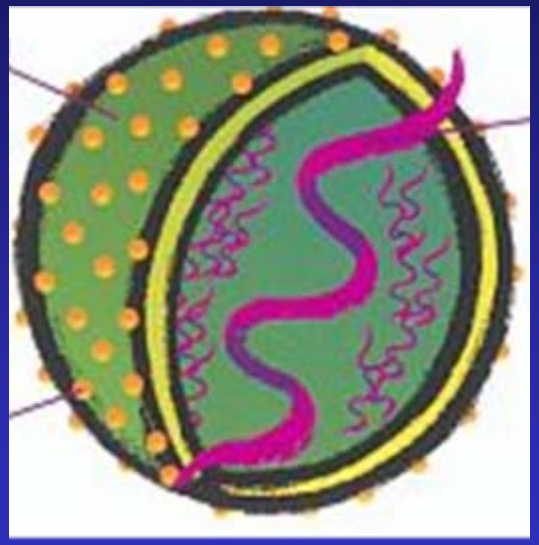
Hepatitis A & B Vaccinations



Helen Yee, PharmD

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Evaluating Universal Hepatitis A and B Vaccination in Patients with Chronic Hepatitis C

Helen S. Yee, PharmD,[1,2] Sue L. Currie, MA,[1,2]
Michael K. Chapko, PhD,[3,4] Teresa L. Wright, MD[1,2]

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Rationale for Hepatitis A and B Vaccination in Chronic HCV Patients

- Prevent further hepatic injury and reduce mortality
  - Mortality increases by 23 fold with acute HAV and chronic liver disease
  - Cirrhosis and HCC risk increases with HBV/HCV coinfection
  - Mortality increases by 5 fold with HBV/HCV coinfection
- Higher risk for acquiring HBV
- Guidelines recommend vaccinating all patients with chronic liver disease
  - NIH, WHO, CDC, ACIP

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Hepatitis A and B Screening and Vaccination in Chronic HCV Patients

- Despite recommendations, screening for immunity and referral for vaccination varies
  - HAV antibody testing at 24 VA sites (n=4,338)
    - 51.5% tested for HAV immunity
    - Site variation: 14-90% testing rate
    - 68.3% of those tested were susceptible to HAV
- Limited data on HAV/HBV vaccine efficacy in veterans with chronic HCV
  - Seroconversion with HAV vaccine occurs in 66-98% of patients with chronic liver disease
  - Seroprotection with HBV vaccine occurs in 69-100% of chronic HCV patients

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Screening for Hepatitis A and B Immunity and Vaccine Referrals in Chronic HCV Veterans

Methods

- Retrospective review of 2,317 chronic HCV veterans accessing VASF outpatient services
  - ≥1 clinic visit between 2002-2003
  - Chronic HCV confirmed by lab data and ICD coding
- Data collection using the Veterans Health Information Systems dating back to Jan 1997
  - Demographics
  - Hepatitis A and B serologies prior to vaccination
  - Documentation of vaccine administration

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Screening for Hepatitis A and B Immunity

Chronic HCV Patients Accessing VASF Services

(n=2,317)

HAV Antibody Testing

75.2%

(n=1,742)

HBV Surface Antibody Testing

75.6%

(n=1,753)

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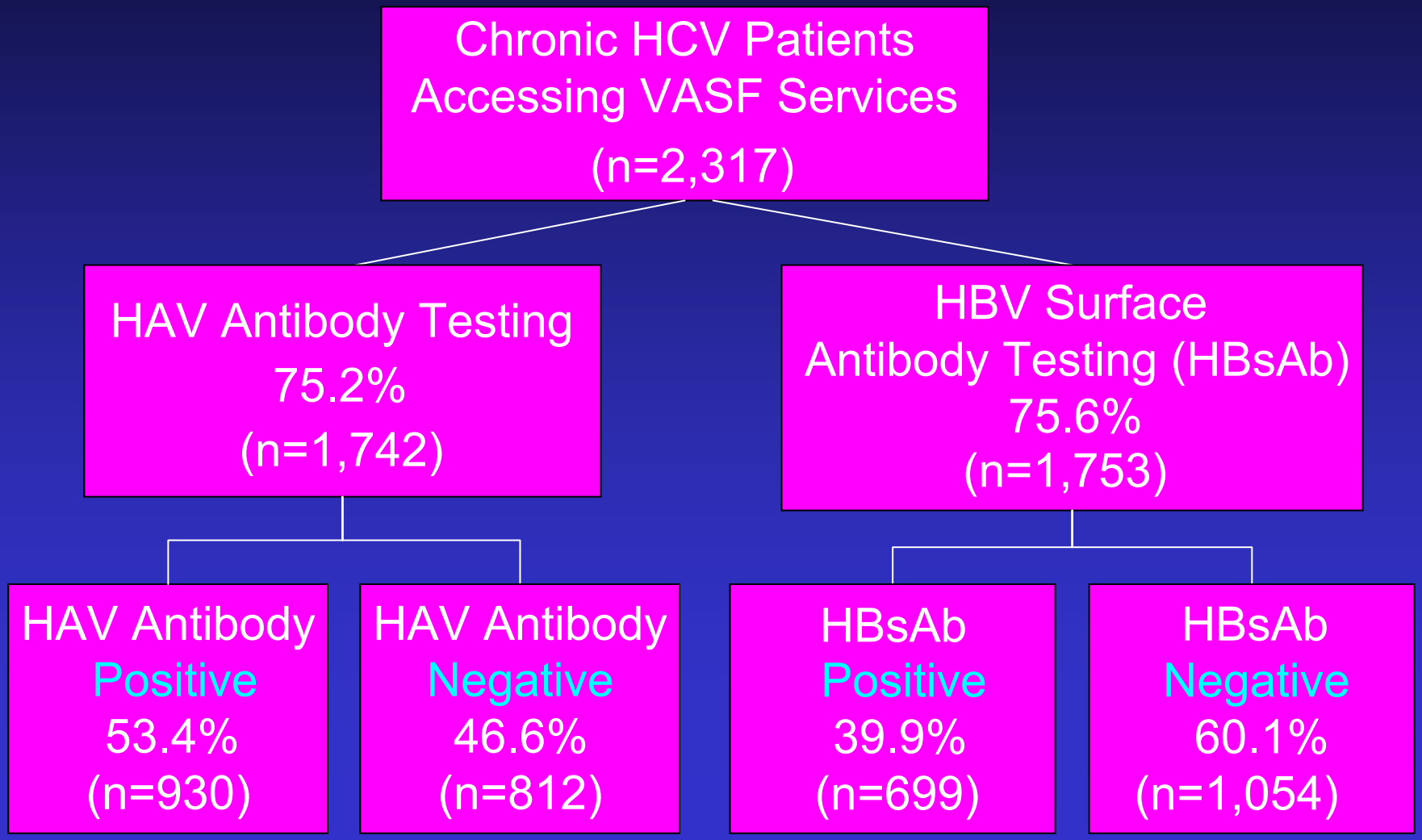
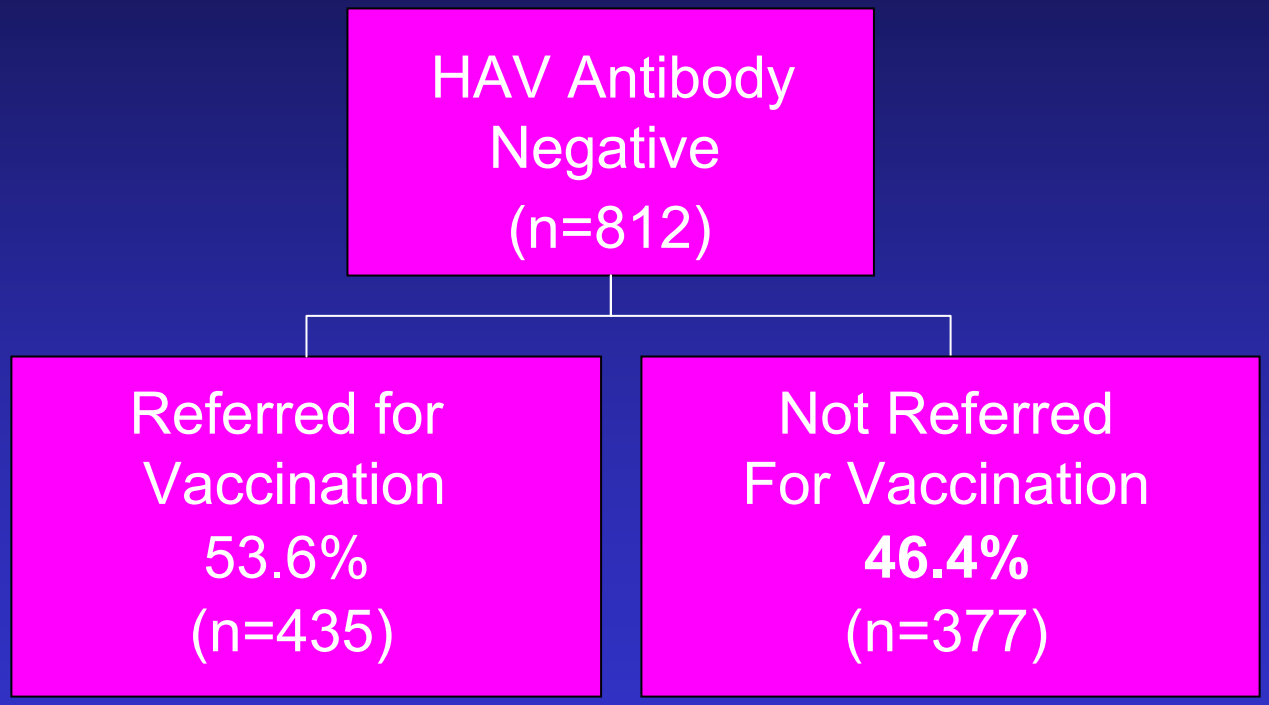
Seroprevalence of Hepatitis A and B Antibodies Prior to Vaccination



Referrals for Hepatitis A Vaccination



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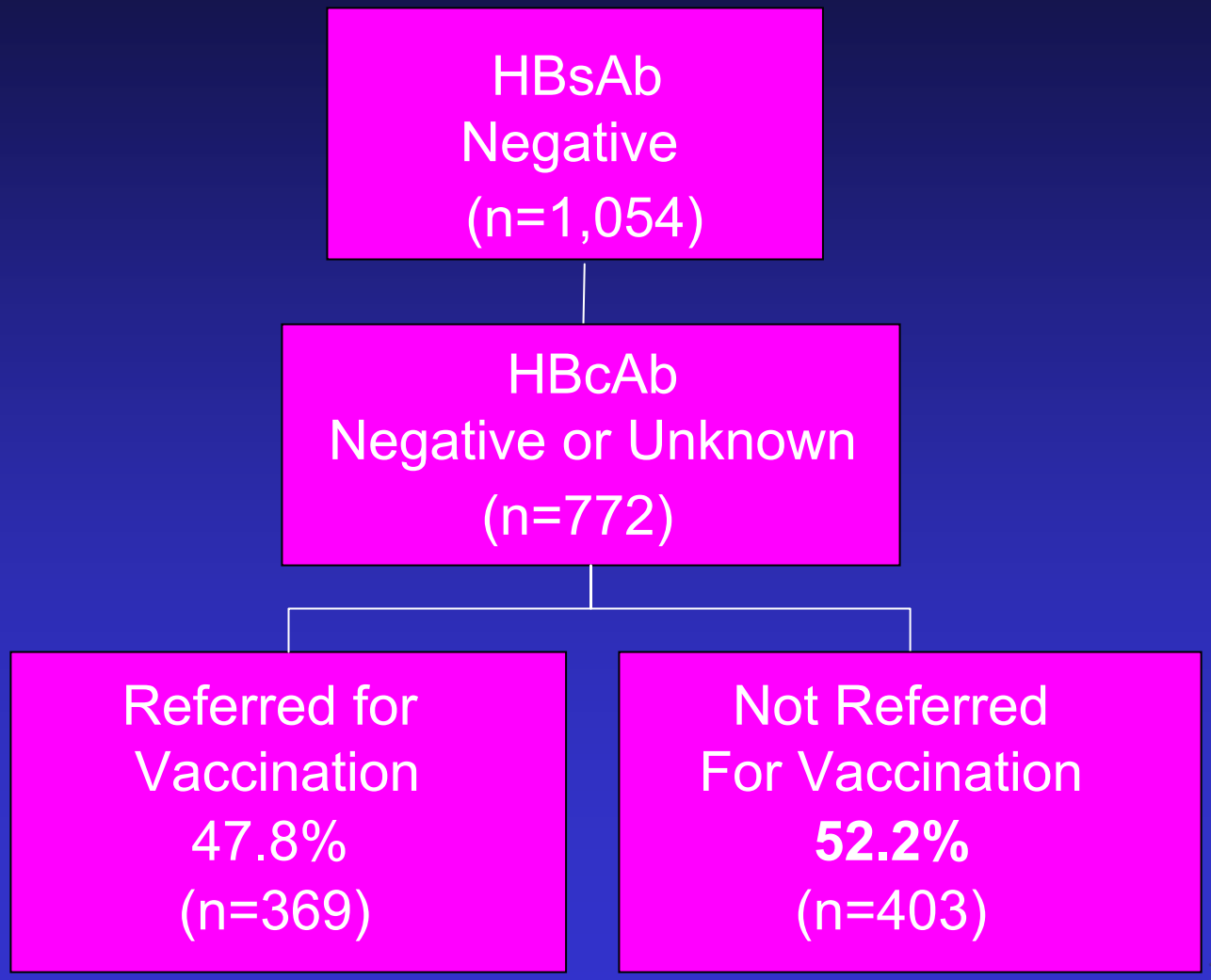
Referrals for Hepatitis B Vaccination



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Missed Opportunities for Hepatitis A or B Vaccination

HAV Susceptible
(n=812)

Not Referred
For Vaccination
46.4%
(n=377)

Median visits/yr: 9

HBV Susceptible
(n=772)

Not Referred
For Vaccination
52.2%
(n=403)

Median visits/yr: 10

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Summary
Hepatitis A and B Screening and Vaccine Referrals in Chronic HCV Veterans

- HAV/HBV antibody testing was better than vaccine referrals
  - Over 75% tested for HAV and HBV antibodies
  - 46% susceptible to HAV
  - 44% susceptible to HBV
  - Approx 50% referred for HAV/HBV vaccination
- Target efforts to improve testing and vaccine referrals
  - Increase provider education and awareness
  - Develop systematic mechanisms

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Evaluating Hepatitis A and B Vaccine Response in Chronic HCV Veterans

Methods

- Retrospective chart review of 399 patients
- Inclusion criteria
  - Chronic HCV confirmed by positive HCV RNA
  - Accessing VASF outpatient services
  - HAV or HBV susceptible
  - Completed appropriate vaccine series
  - HAV/HBV antibody status performed pre- and post-vaccination
- Exclusion criteria
  - Organ transplant recipient
  - End-stage renal disease
  - Malignancy
  - Immunosuppressive therapies within 6 mo prior to vaccination

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Hepatitis A and B Vaccine Response of VASF Veterans with Chronic HCV Demographics (N = 185)

Median Age	55.2 years
Male Gender	98.9%
Ethnicity	
– Caucasian	61.6%
– African American	18.9%
– Latino	4.3%
– Other	15.2%
Followed by Liver Clinic	96.2%
Primary provider at VASF	69.7%

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Hepatitis A and B Vaccine Response of VASF Veterans with Chronic HCV Clinical Characteristics

Alcohol use	79.8% (146/183)
Tobacco use	77.8% (140/180)
Non-IV illicit drug use	77.2% (139/180)
Injection drug use	63.6% (117/184)
High-risk sex	68.3% (112/164)
Psychiatric disease	74.6% (138/185)
Advanced liver disease	43.8% (67/153)
HIV coinfection	12.1% (17/140)

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Hepatitis A Vaccination Serological Response

Pre-Vaccination
HAV Antibody Negative
(n=119)

Post-Vaccination
HAV Antibody Positive
74.8% ($p \leq 0.001$)*
(n=89)

Post-Vaccination
HAV Antibody Negative
25.2%
(n=30)

*Chi-square analysis compared to 98% response rate

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Hepatitis A Vaccination Serological Response By Factors

	n	Responders vs Nonresponders
Age >50	119	76% vs 83%
Alcohol use	117	81% vs 76%
Advanced liver disease (stage 3 or 4)	105	48% vs 43%
African Americans	119	29% vs 47%
HIV/HCV	95	10% vs 25% (p=0.07)

No statistical difference by independent T-test at 95% confidence level

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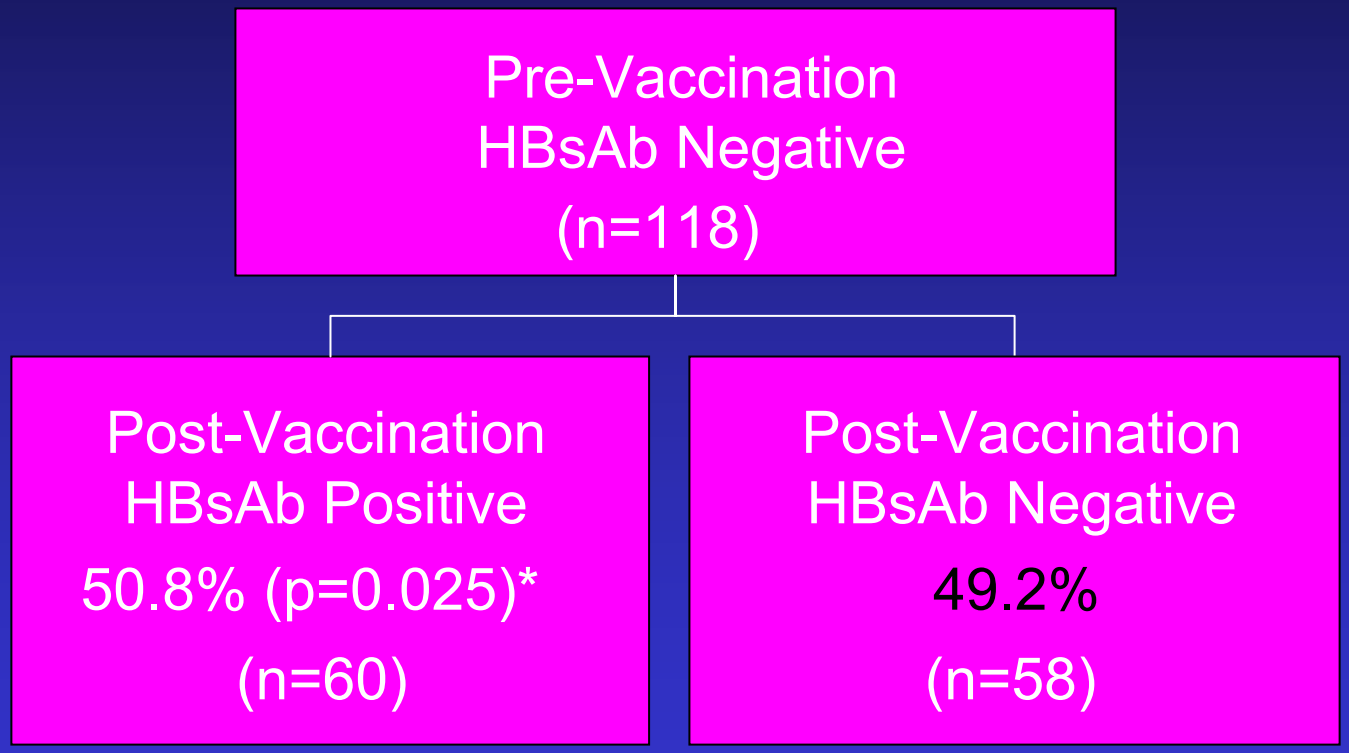
Hepatitis B Vaccination Serological Response



*Chi-square analysis compared to 69% response rate

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Hepatitis B Vaccination Serological Response By Factors

	n	Responders vs Nonresponders
Age >50	119	85% vs 72%
Alcohol use	117	75% vs 88% (p=0.08)
Advanced liver disease (stage 3 or 4)	95	44% vs 40%
African Americans	118	30% vs 34%
HIV/HCV	82	5% vs 7%

No statistical difference by independent T-test at 95% confidence level

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Summary
Hepatitis A and B Vaccination in Chronic HCV Veterans

- All susceptible chronic HCV patients should be vaccinated against hepatitis A and B
  - Vaccine response was not associated with
    - age >50
    - alcohol use
    - advanced liver disease
    - HIV/HCV coinfection
    - African American race
- High seroprevalence of HAV/HBV antibodies
  - Cost benefit analysis to evaluate testing for immunity versus universal vaccination
    - Model should account for seroprevalence HAV/HBV antibodies and risk for infection

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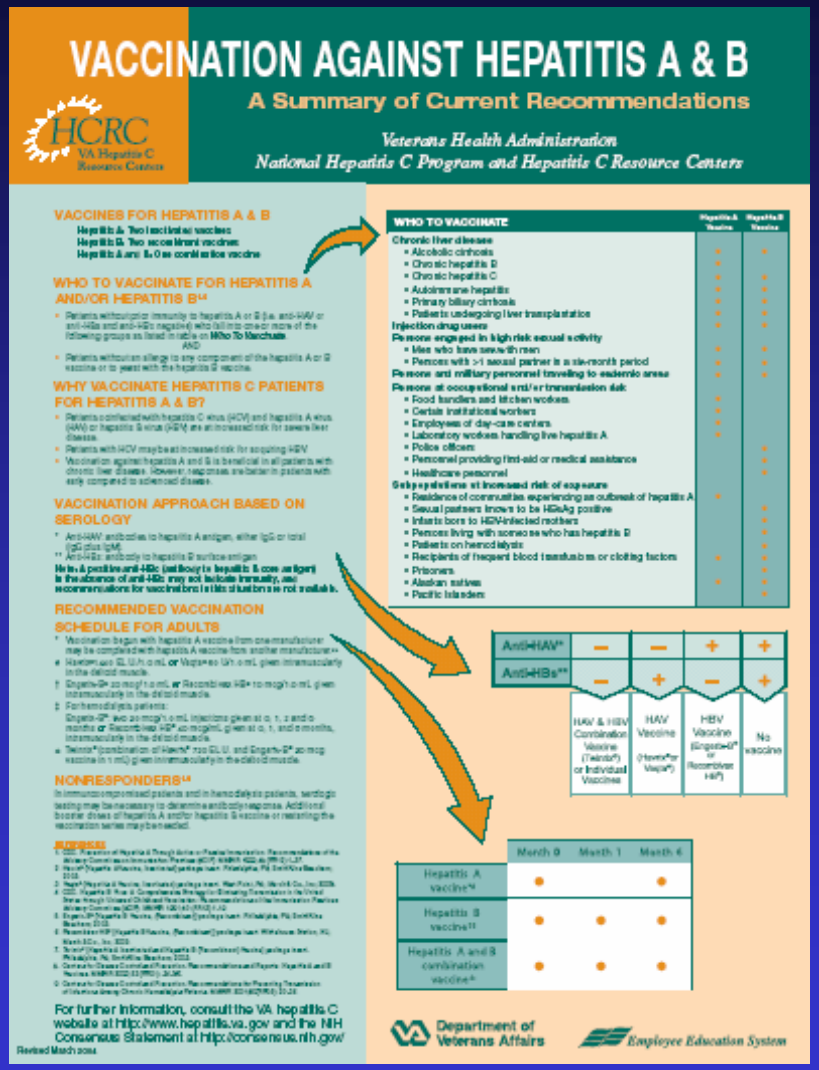
Summary
Hepatitis A and B Vaccination in Chronic HCV Veterans

- Improve HAV/HBV testing and vaccine referrals
  - Increase provider education and awareness
  - Develop systematic mechanisms
- Additional studies on HAV/HBV vaccine response needed
  - Identify factors for poor response
  - Evaluate need for post-vaccination serology testing
  - Evaluate need for booster doses or revaccinating in nonresponders

HAV/HBV Vaccination Guidelines: Poster & Pocket Card



VACCINATION AGAINST HEPATITIS A & B

A Summary of Current Recommendations

Veterans Health Administration
National Hepatitis C Program and Hepatitis C Resource Centers

HCRC VA Hepatitis C Resource Centers

VACCINES FOR HEPATITIS A & B

WHO TO VACCINATE FOR HEPATITIS A AND/OR HEPATITIS B

WHY VACCINATE HEPATITIS C PATIENTS FOR HEPATITIS A & B?

VACCINATION APPROACH BASED ON SEROLOGY

RECOMMENDED VACCINATION SCHEDULE FOR ADULTS

NONRESPONDERS

WHO TO VACCINATE	Hepatitis A Vaccine	Hepatitis B Vaccine
Chronic liver disease		
• Alcoholic cirrhosis	+	+
• Chronic hepatitis B	+	+
• Chronic hepatitis C	+	+
• Autoimmune hepatitis	+	+
• Primary biliary cirrhosis	+	+
• Patients undergoing liver transplantation	+	+
Injection drug users	+	+
People engaged in high-risk sexual activity		
• Men who have sex with men	+	+
• Persons with >1 sexual partner in a six-month period	+	+
People and military personnel traveling to endemic areas	+	+
People at occupational and/or transmission risk		
• Food handlers and kitchen workers	+	
• Certain institutional workers	+	
• Employees of day-care centers	+	
• Laboratory workers handling live hepatitis A	+	
• Police officers		+
• Personnel providing first-aid or medical assistance		+
• Healthcare personnel		+
Subpopulations at increased risk of exposure		
• Residence of communities experiencing an outbreak of hepatitis A	+	
• Sexual partners known to be HBsAg positive		+
• Infants born to HBsAg-infected mothers		+
• Persons living with someone who has hepatitis B		+
• Patients on hemodialysis		+
• Recipients of frequent blood transfusions or clotting factors	+	+
• Prisoners	+	+
• Alaskan natives	+	+
• Pacific Islanders	+	+

Anti-HAV*	–	–	+	+
Anti-HBs**	–	+	–	+
	HAV & HBV Combination Vaccine (Twinrix®) or Individual Vaccines	HAV Vaccine (Havrix® or Vaqta®)	HBV Vaccine (Engerix-B® or Recombivax HB®)	No vaccine

	Month 0	Month 1	Month 6
Hepatitis A vaccine*	•		•
Hepatitis B vaccine**	•	•	•
Hepatitis A and B combination vaccine*	•	•	•

For further information, consult the VA hepatitis C website at http://www.hepatitis.va.gov and the NIH Consensus Statement at http://consensus.nih.gov/

Revised March 2004

Department of Veterans Affairs — Employee Education System

WHY VACCINATE HEPATITIS C PATIENTS FOR HEPATITIS A AND B?

- Patients coinfected with hepatitis C virus (HCV) and HAV or HBV are at increased risk for severe liver disease.
- Patients with HCV may be at increased risk for acquiring HBV.
- Vaccination against hepatitis A and B is beneficial in all patients with chronic liver disease. However, responses are better in patients with early compared to advanced disease.

VACCINATION APPROACH BASED ON SEROLOGY

Anti-HAV*	–	–	+	+
Anti-HBs**	–	+	–	+
	HAV & HBV Combination Vaccine (Twinrix®) or Individual Vaccines	HAV Vaccine (Havrix® or Vaqta®)	HBV Vaccine (Engerix-B® or Recombivax HB®)	No vaccine

* Anti-HAV: antibodies to hepatitis A antigen, either IgG or total (IgG plus IgM).

** Anti-HBs: antibody to hepatitis B surface antigen

Note: A positive anti-HBc (antibody to hepatitis B core antigen) in the absence of anti-HBs may not indicate immunity, and recommendations for vaccinations in this situation are not available.

www.hepatitis.va.gov/vahep?page=tp04-02-01-01

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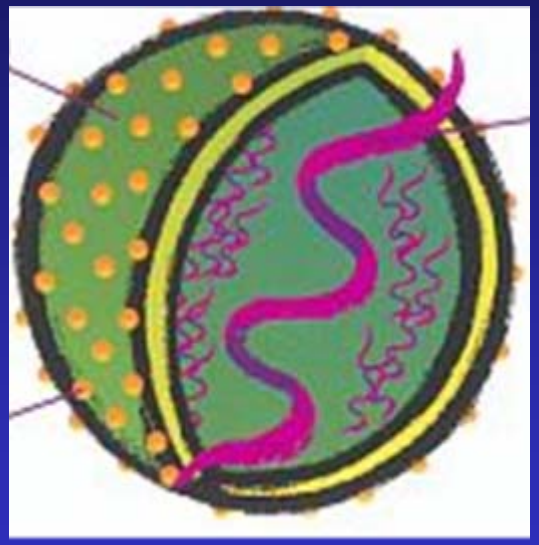
Psychiatric & Substance Abuse Co-Morbidities



Peter Hauser, MD

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Psychiatric and SU Disorder Co-morbidity

National VA Database of 1.9 million veterans hospitalized between 1992-1999.

- Of these, 33,824 Hep C- infected (1.77%)
  - 85% had at least 1 past or present psychiatric or substance use disorder.
  - 78% had a past or present substance use disorder.
    - Cocaine use 69%, opioids 48%
    - 85% co- morbid depression, 30% co-morbid bipolar
    - 71% co-morbid anxiety disorder excluding PTSD
    - 43% PTSD
    - 42% co-morbid psychotic disorders

El-Serag, et al, Gastroenterology 2002;123:476-82

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Hepatitis C in the Seriously Mentally Ill

	Sample size	% tested	odds ratio*
Total	293,355		
Controls	244,597	30.1%	1.00
SUD only	39,922	63.0%	3.95
SUD and SMI	4,192	72.3%	6.04
SMI only	4,644	47.5%	2.10

* Compared with controls

Huckans et al., *Psychiatric Services*, in press, 2005

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Hepatitis C in the Seriously Mentally Ill

	% HCV +*	odds ratio**
Controls	5.1%	1.00
SUD only	27.0%	6.64
SUD and SMI	31.1%	8.12
SMI only	9.9%	1.98

* Of those tested; ** compared with controls

Huckans et al., *Psychiatric Services*, in press, 2005

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‘Special Populations’

- 1997 NIH Consensus Conference on Hep C
  - Excluded patients with psychiatric illness from IFN therapy
  - IFN treatment of patients with substance use disorder contingent on at least 6 months abstinence
- 2002 NIH Consensus Conference on Hep C
  - Selected psychiatric diagnoses eligible for IFN therapy
  - Patients with active substance use disorders not automatically excluded from IFN therapy

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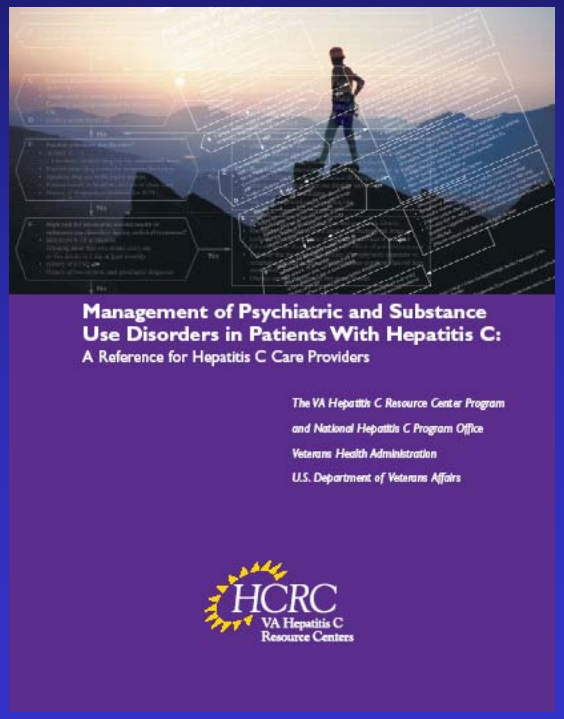
How do we develop a better model of care for patients with hepatitis C?

- Integrate mental health care into existing clinics.
- The focus is on:
  - Universal screening for psychiatric and substance use disorders.
  - Single session Patient Education Group.
- In the Portland VA over 900 patients screened of 3000 patients with hepatitis C.

Loftis & Hauser, *Current Hepatitis C Reports*, 2003;2(3):93-100



www.hepatitis.va.gov/vahep?page=tp03-gd-01

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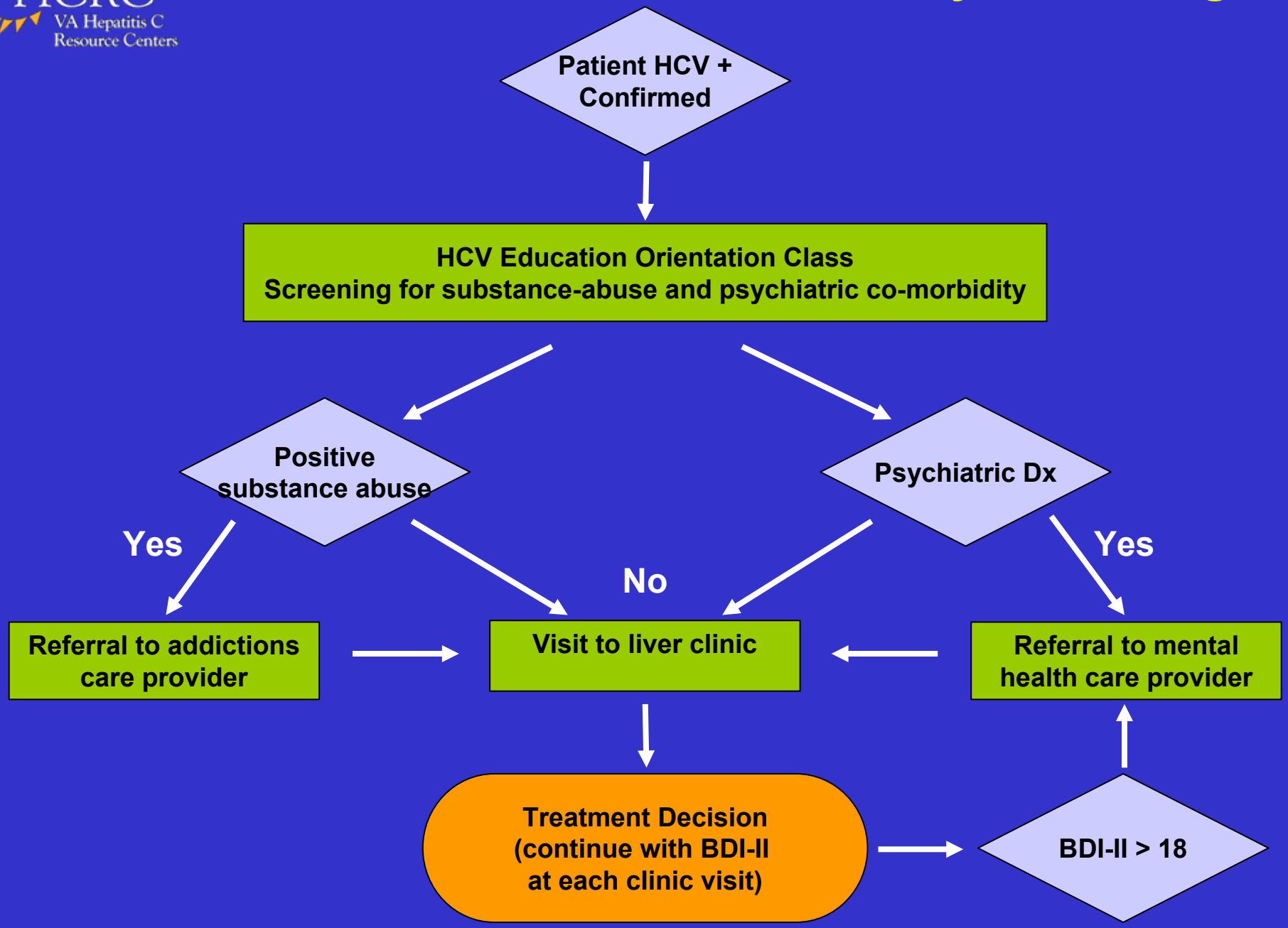
HCV Education & Co-morbidity Screening



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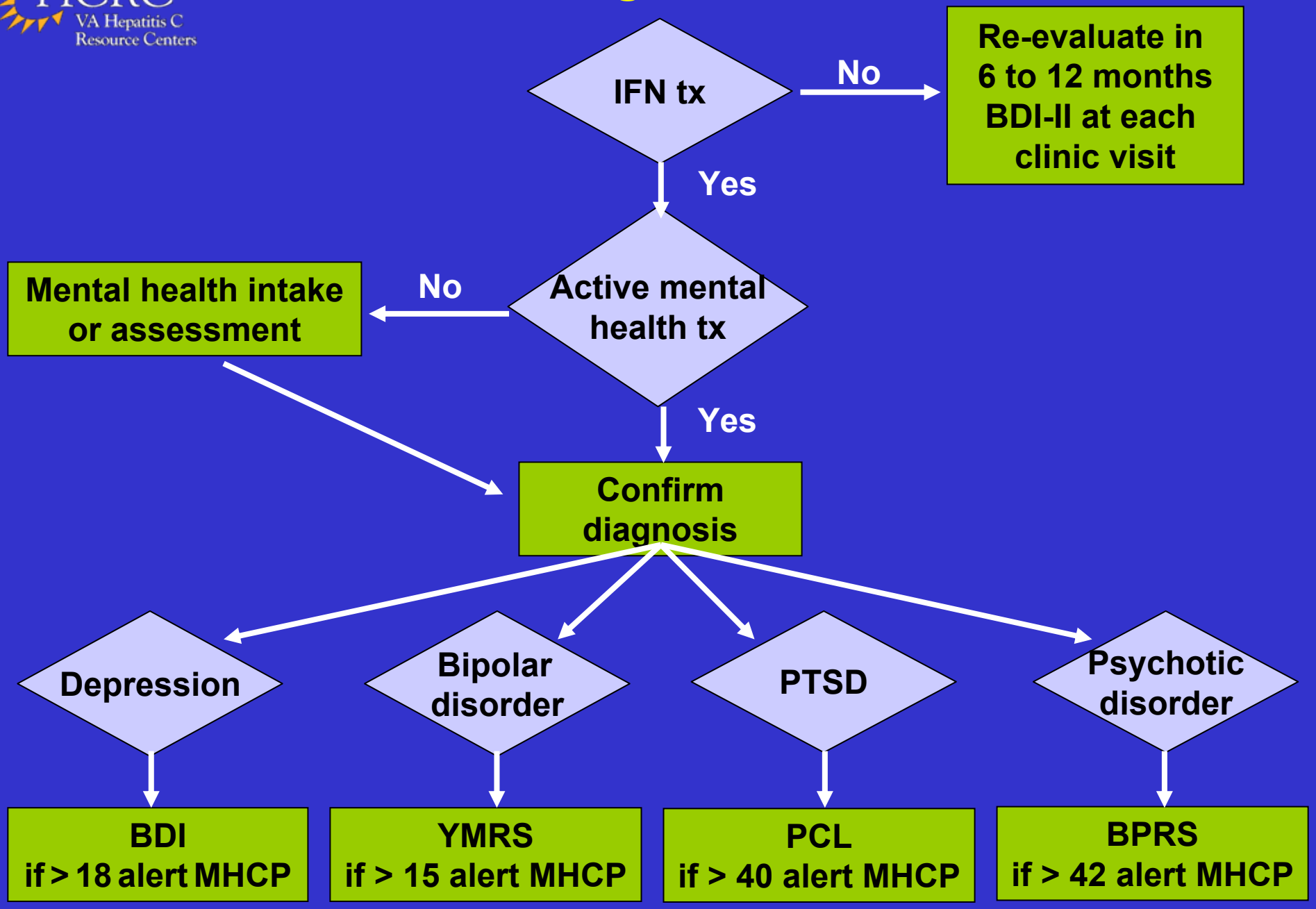
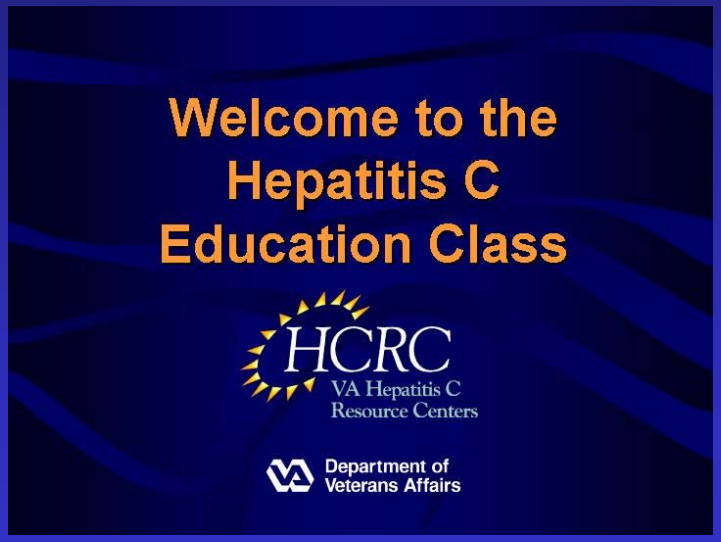
HCV Integrated Care



MH & SA Screening in Patient Group HCV Education

- Patient education class - single session
  - 45-minute PowerPoint slide presentation
  - Also available as a narrated slide show
- Information on
  - Hep C transmission & risk factors
  - Hep C symptoms & natural history
  - Evaluation
  - Healthy living
  - Treatment



www.hepatitis.va.gov/vahep?page=tp05-01-01-91

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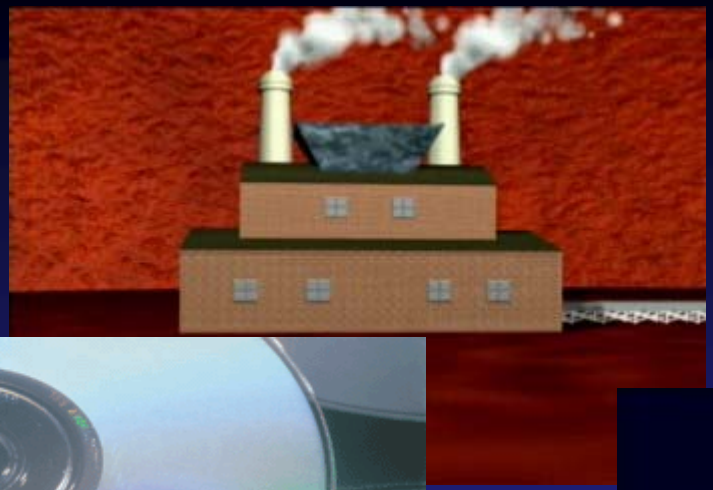
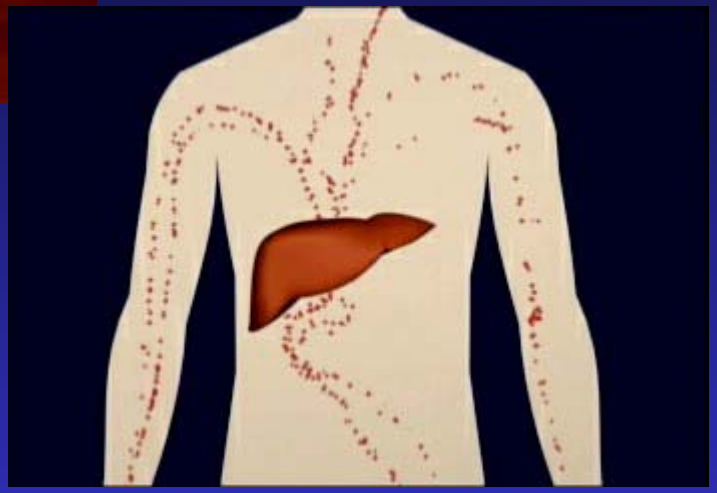
Patient HCV Education Video





- 4 Short Segments
- Narrated “Nova” Format
- Web, DVD, & VHS Formats

www.hepatitis.va.gov/vahep?page=pt-video

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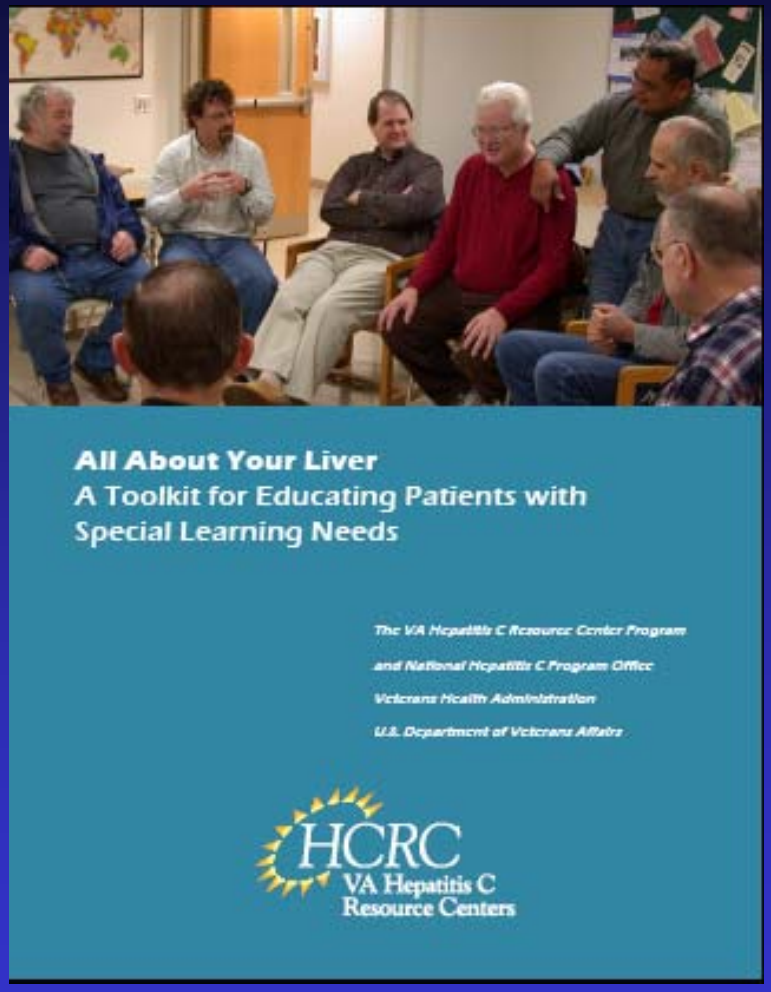
HCV Education Class Guides



Coming soon! to www.hepatitis.va.gov

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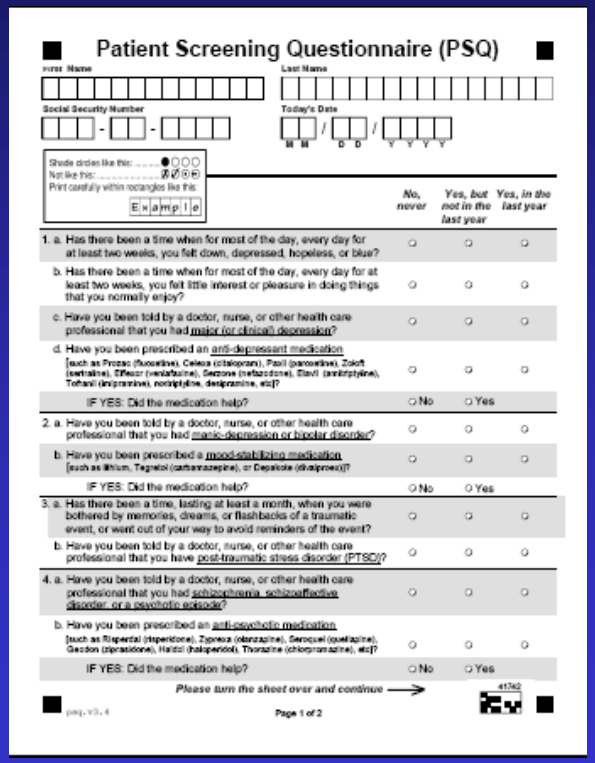
Screening Tool

- Patient Screening Questionnaire (PSQ): 2-page pt-rated instrument that screens for
  - Depression - 2 item screen
  - PTSD - PCL
  - Substance use disorders - AUDIT-C
  - Psychotic disorders
  - Prior/current psychotropic meds and in/out-pt treatment



Patient Screening Questionnaire (PSQ)

First Name | Last Name

Social Security Number | Today's Date

Shade circles like this: ●○○○
Not like this: ✗✓⊙⊙
Print carefully within rectangles like this:
Example

	No, never	Yes, but not in the last year	Yes, in the last year
1. a. Has there been a time when for most of the day, every day for at least two weeks, you felt down, depressed, hopeless, or blue?	○	○	○
b. Has there been a time when for most of the day, every day for at least two weeks, you felt little interest or pleasure in doing things that you normally enjoy?	○	○	○
c. Have you been told by a doctor, nurse, or other health care professional that you had major (or clinical) depression?	○	○	○
d. Have you been prescribed an anti-depressant medication [such as Prozac (fluoxetine), Celexa (citalopram), Paxil (paroxetine), Zoloft (sertraline), Effexor (venlafaxine), Serzone (nefazodone), Elavil (amitriptyline), Tofranil (imipramine), nortriptyline, desipramine, etc]?	○	○	○
IF YES: Did the medication help?	○ No	○ Yes	
2. a. Have you been told by a doctor, nurse, or other health care professional that you had manic-depression or bipolar disorder?	○	○	○
b. Have you been prescribed a mood-stabilizing medication [such as lithium, Tegretol (carbamazepine), or Depakote (divalproex)]?	○	○	○
IF YES: Did the medication help?	○ No	○ Yes	
3. a. Has there been a time, lasting at least a month, when you were bothered by memories, dreams, or flashbacks of a traumatic event, or went out of your way to avoid reminders of the event?	○	○	○
b. Have you been told by a doctor, nurse, or other health care professional that you have post-traumatic stress disorder (PTSD)?	○	○	○
4. a. Have you been told by a doctor, nurse, or other health care professional that you had schizophrenia, schizoaffective disorder, or a psychotic episode?	○	○	○
b. Have you been prescribed an anti-psychotic medication [such as Risperdal (risperidone), Zyprexa (olanzapine), Seroquel (quetiapine), Geodon (ziprasidone), Haldol (haloperidol), Thorazine (chlorpromazine), etc]?	○	○	○
IF YES: Did the medication help?	○ No	○ Yes	

Please turn the sheet over and continue →

psq.v3.4 Page 1 of 2 41742

www.va.gov/portland/Mood-Disorders-Center/documents/psq.v3.4.pdf

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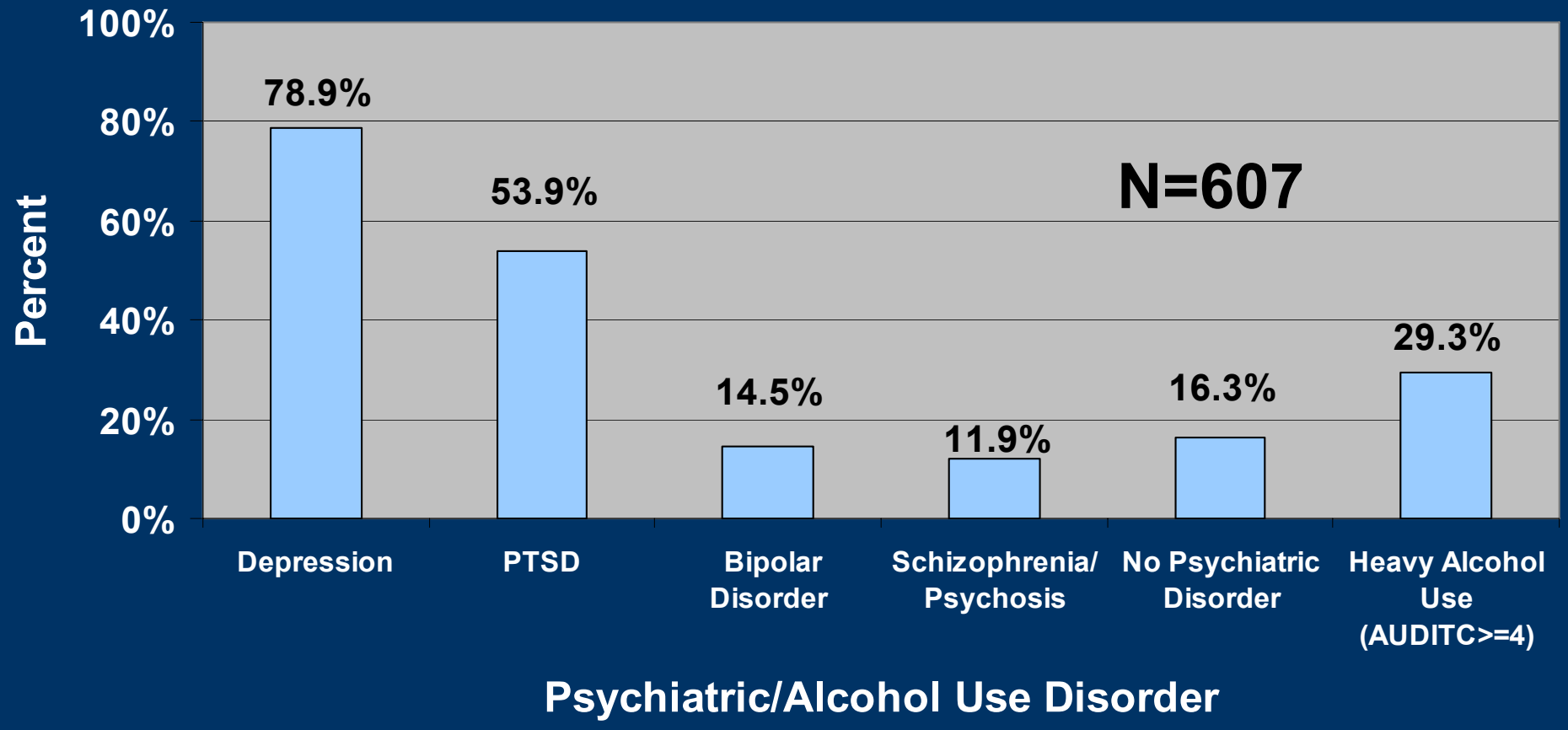
Psychiatric & Substance Abuse Screening of HCV Patients at HCV Education Group



Note: Patients can screen positive for more than one diagnosis

NWHCRC, unpublished data, 2005
updating Fireman et al, Clinical Infectious Diseases 2005;40:s286-91.

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Universal Screening Facilitates Interdisciplinary Model

- Of 752 veterans in the hepatitis C registry:
  - 101 (13.3) had a consult to mental health
    - For pre –IFN therapy consult
    - For treatment of psychiatric/SU disorder- 61 for MDD
  - 23 (3%) had a mood disorders consult
  - 69 (9.2%) had substance abuse treatment consult
  - Total of 193/752 (25.6%) had a mental health consultation

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NW Hepatitis C Resource Center Clinical Care

- Multidisciplinary HCV case conference
  - Twice monthly
- Mental health & substance abuse screening & referrals in Hep C class and Liver Clinic
- Pre-interferon mental health evaluations
- Mental health & substance abuse monitoring and support for patients during HCV tx

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NW Hepatitis C Resource Center

- Education
  - Hep C Classes
  - Materials: brochures, videos, library, more!
- Monthly Support Groups
  - HCV, Tx (IFN/RBV)
- Hepatitis C Product Development
  - Educational, guidelines, best practices
- Research, esp. related to HCV & mental health

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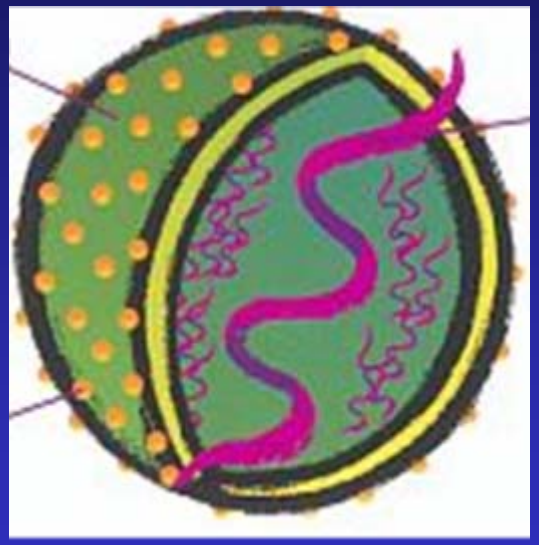
Integrated Care



Betsy Zucker, FNP

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HCV Education

- TRANSMISSION: (blood to blood)
- NATURAL HX: chronic infection
  - 80% never develop cirrhosis
  - 20% develop cirrhosis or complications
- SYMPTOMS may not correlate with severity of liver disease
- HEPATITIS A & B
- ALCOHOL

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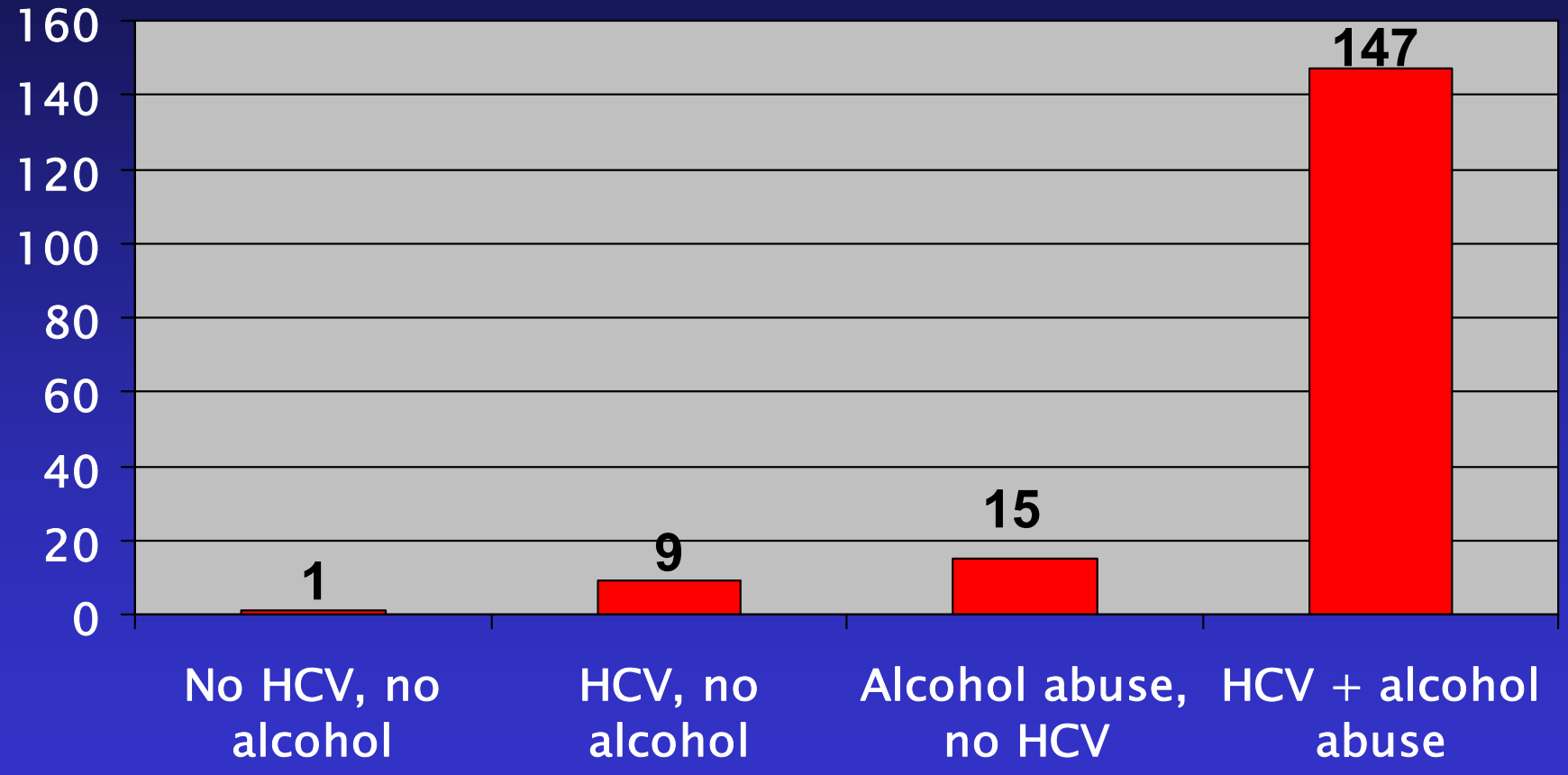
Alcohol Abuse Greatly Increases Risk of Developing Cirrhosis



Corrao & Aricò, *Hepatology*, 1998;27:914-9.

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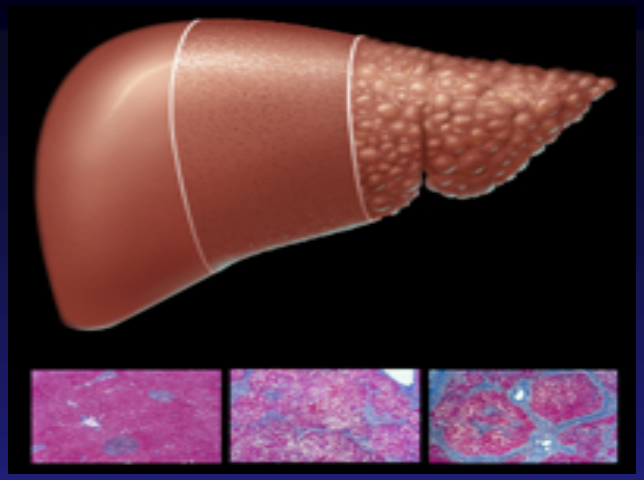
Hep C – Work-up



- HISTORY –
  - including MH & SA screening
- PHYSICAL EXAM
- LABWORK :
  - Liver enzymes: ALT, AST
  - Hepatitis function: bilirubin, platelets, albumin, INR
  - Hep A & Hep B status (sometimes)
  - R/O other common liver dx: ferritin, Hep B
  - Hep C genotype & viral load if tx candidate

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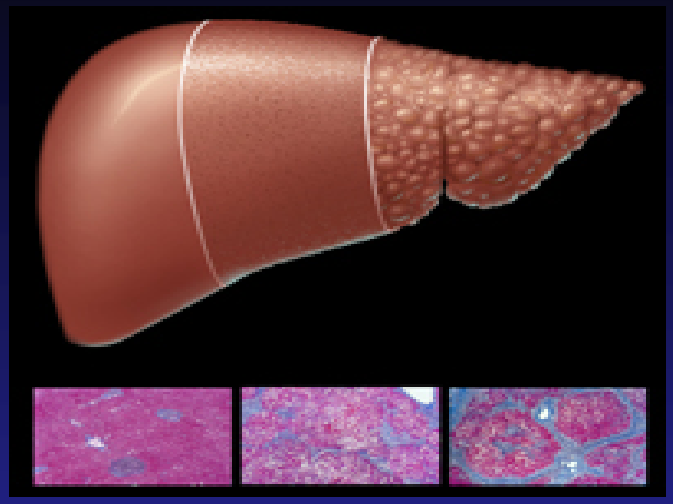
Hep C Work-up



- TREATMENT CANDIDATE?
- Liver biopsy:
  - Inflammation: Grade 0-4 (none to severe)
  - Fibrosis: Stage 0-4 (4 = cirrhosis)
  - Biopsy not always necessary

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Hepatitis C Treatment

- IFN/RBV
  - Peg-IFN alfa-2a or 2-b: weekly injection
  - Ribavirin – twice daily oral med.
- Approx 50% success rate (improved treatments in the last 10 yrs)
- 6-12 month treatment
- Difficult to tolerate

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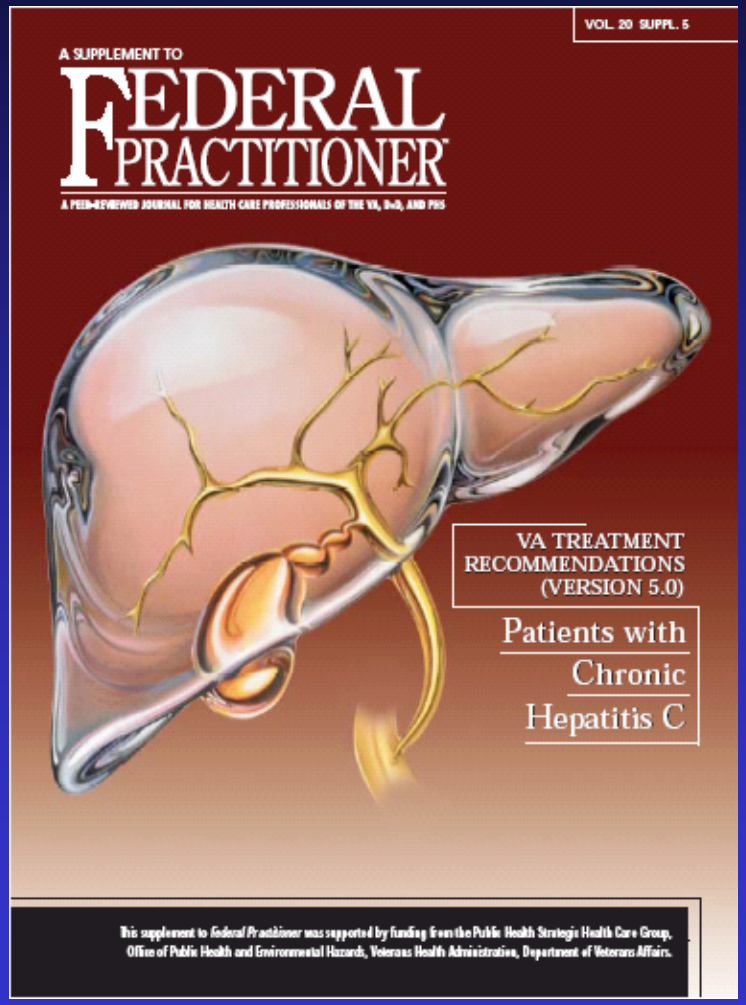
Treatment Recommendations

www.hepatitis.va.gov/vahep?page=tp03-01-04-01



Also available as
Hepatititis C Quicknotes for PDAs

www.hepatitis.va.gov/vahep?page=tp06-ct-02-01

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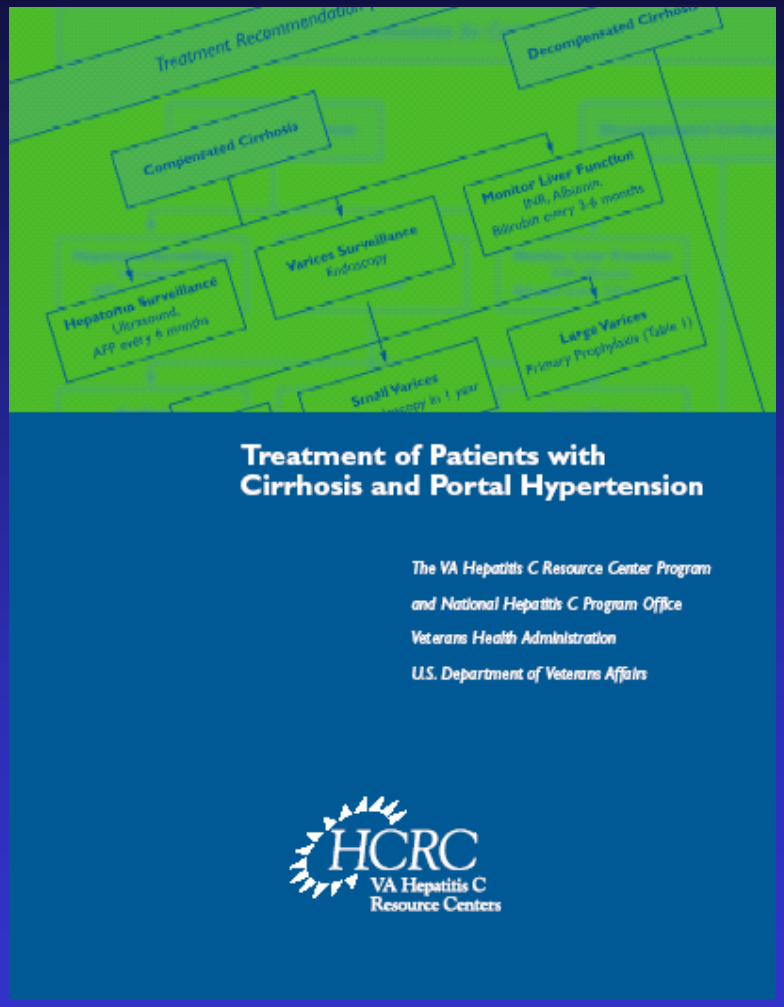
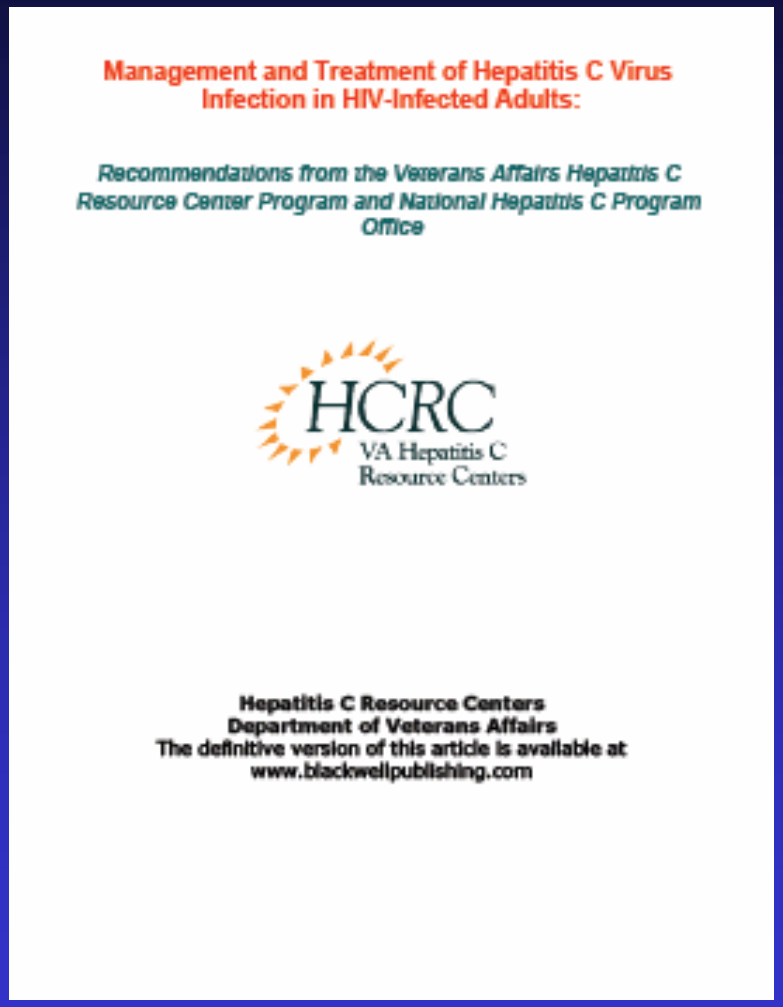
Treatment Recommendations

www.hepatitis.va.gov/vahep?page=tp03-03-02-01





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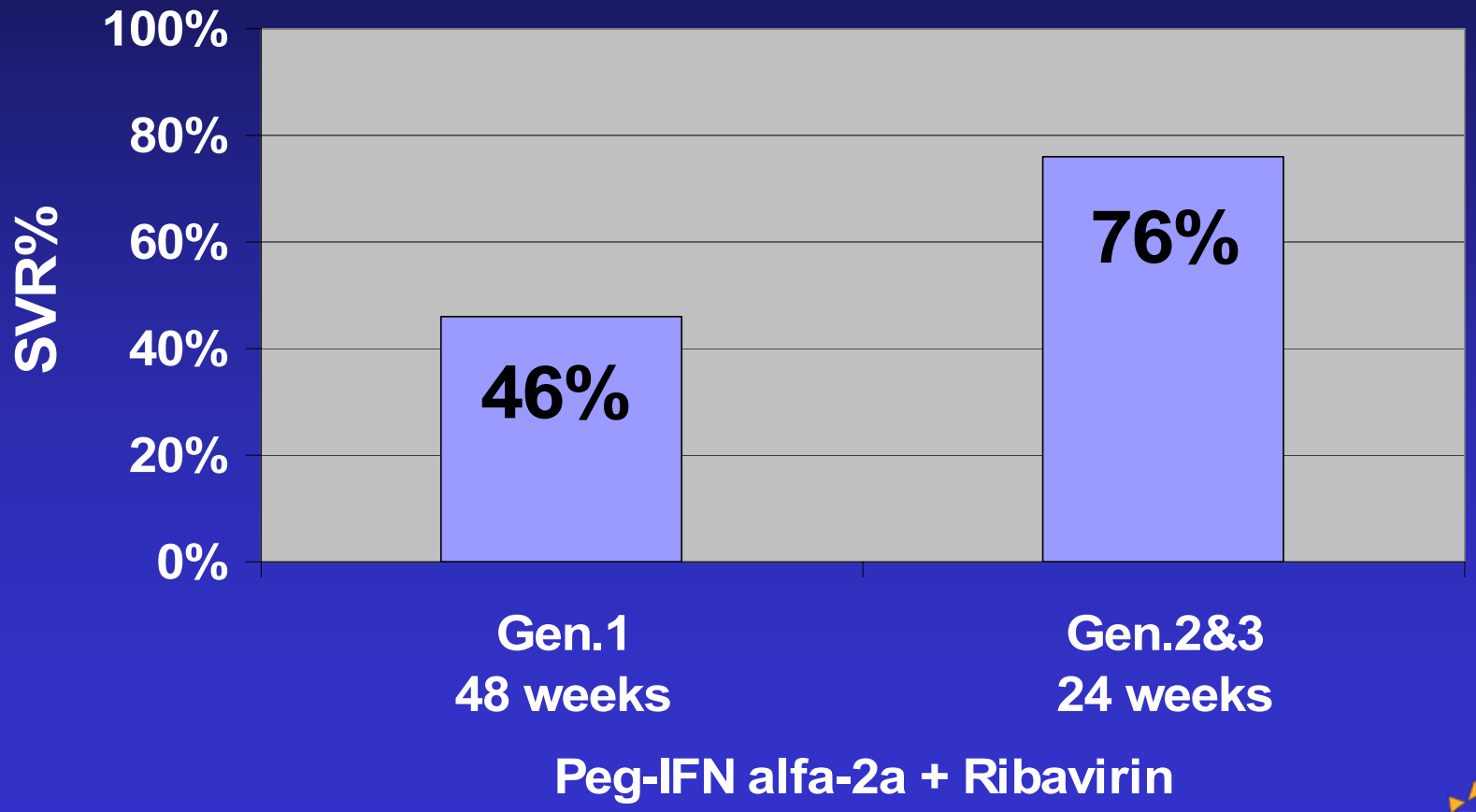
www.hepatitis.va.gov/vahep?page=tp04-gd-01

HCV Genotype

Best Predictor of Treatment Response



Fried, *NEJM*, 2002

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HCV Treatment Side Effects

- Flu-like symptoms - common
- Neuropsychiatric Side Effects (<50%)
  - irritability, anxiety, insomnia
  - depression, triggering of PTSD
- Cytopenias (drops in blood counts)
  - anemia etc; worse in cirrhotics
- Thyroid, other autoimmune
- GI S/E

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HCV Treatment: Negative Prognostic Indicators

- Increased liver fibrosis
- Advanced age, male gender, obesity
- African American race
- HCV Genotype 1
  - (MOST common in US)
- If genotype 1, high viral load
- Ongoing alcohol use

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HCV Treatment Candidacy

- Is Antiviral Treatment Likely to be Successful?
- How Severe is the Person's Liver Disease?
- Are there contraindications to treatment, either medical or psychsocial?

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Hep C Treatment Candidacy

- MH/SA Consults can help:
  - Tx decisions are not urgent:
  - Determine appropriateness for tx (pre-IFN Eval)
  - Prepare patients thru tx of MH or SA issues
  - Monitor MH & SA sx and support patients thru tx
- Planning & Preparation:
  - Timing, Finances
  - 6 months abstinence from substances

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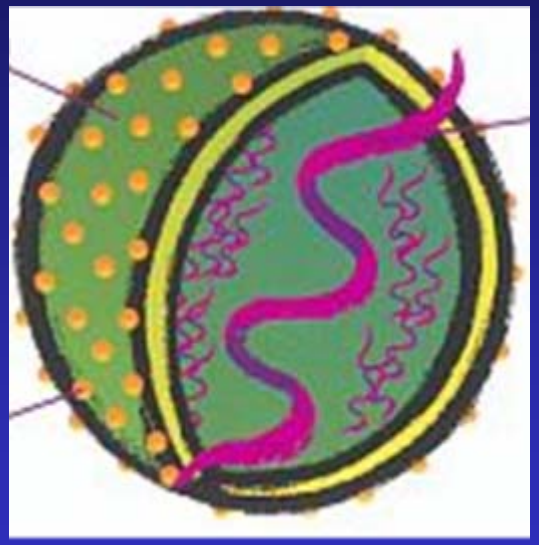
VA Integrated Care: A Model for Hep C Treatment

- With proper staffing, psychiatric and substance abuse problems need not be a barrier to HCV antiviral tx

Neuropsychiatric Side Effects of Interferon Therapy



Julie Nelligan, PhD

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Neuropsychiatric Events

PSYCHIATRIC SYMPTOMS	peg IFN-α 2a N= 223 No. (%)	IFN-α 2b + RBV N= 443 No. (%)	peg IFN-α 2a + RBV N= 451 No. (%)
Total Pts with at least 1 AE	107 (48)	261 (59)	222 (49)
IRRITABILITY	**56 (25)**	**123 (28)**	**109 (24)**
DEPRESSION NOS	**44 (20)**	**131 (30)**	**95 (21)**
ANXIETY	18 (8)	60 (14)	51 (11)
NERVOUSNESS	6 (3)	23 (5)	17 (4)
MOOD SWINGS	5 (2)	16 (4)	12 (3)
AGGRESSION	1 (<1)	9 (2)	6 (1)
MOOD ALTERATION	2 (1)	7 (2)	4 (1)
PANIC REACTION	--	7 (2)	2 (<1)
SUICIDE ATTEMPT	1 (<1)	4 (1)	2 (<1)
DEPRESSION AGGRAVATED	1 (<1)	3 (1)	2 (<1)

Fried MW et al., DDW, 2001; see also Fried MW et al., *NEJM*, 2002

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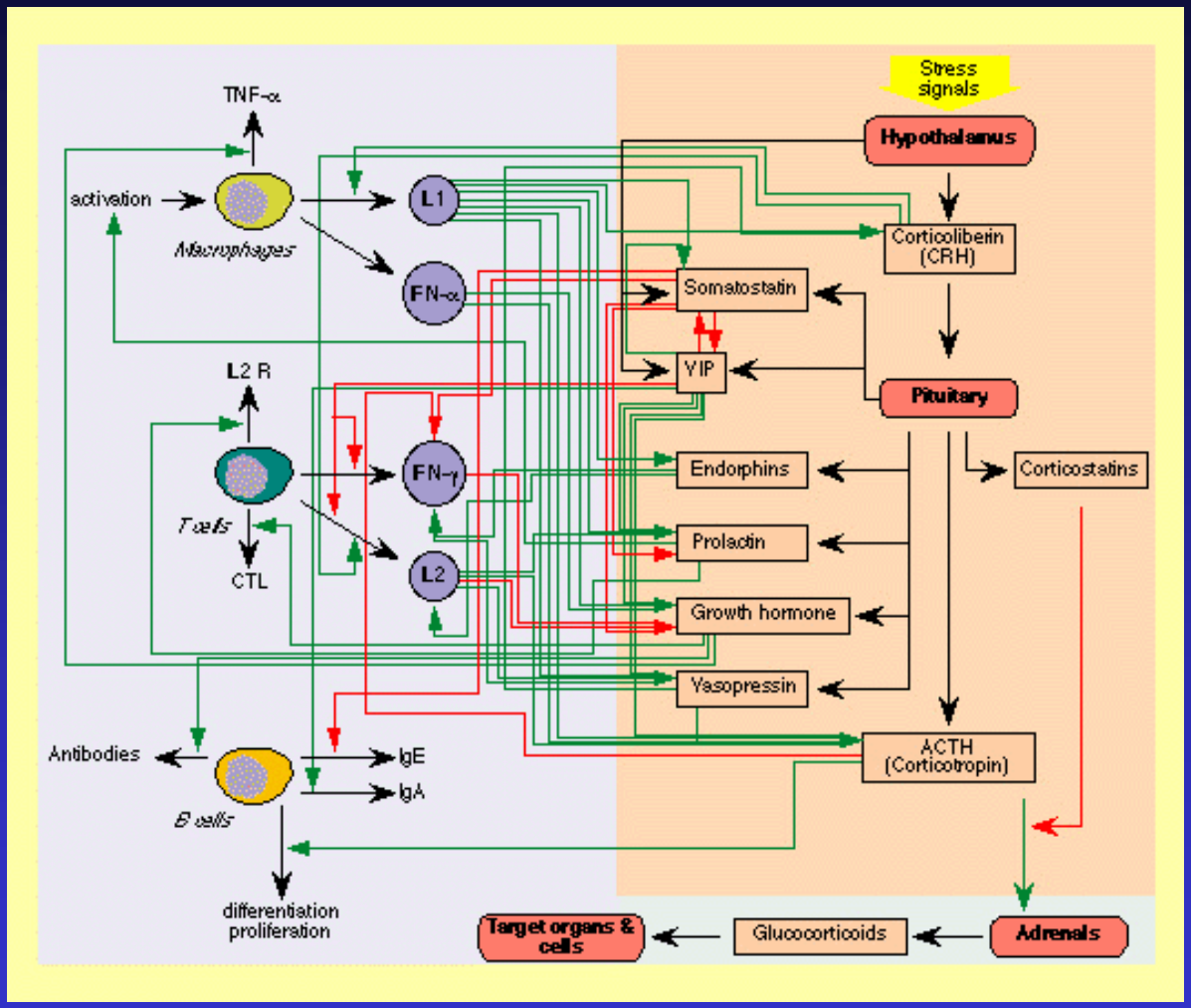
What are cytokines?



- Signaling molecules of the immune system
- Released in response to…
  - Tissue injury
  - Infection
  - Inflammation
  - Stress

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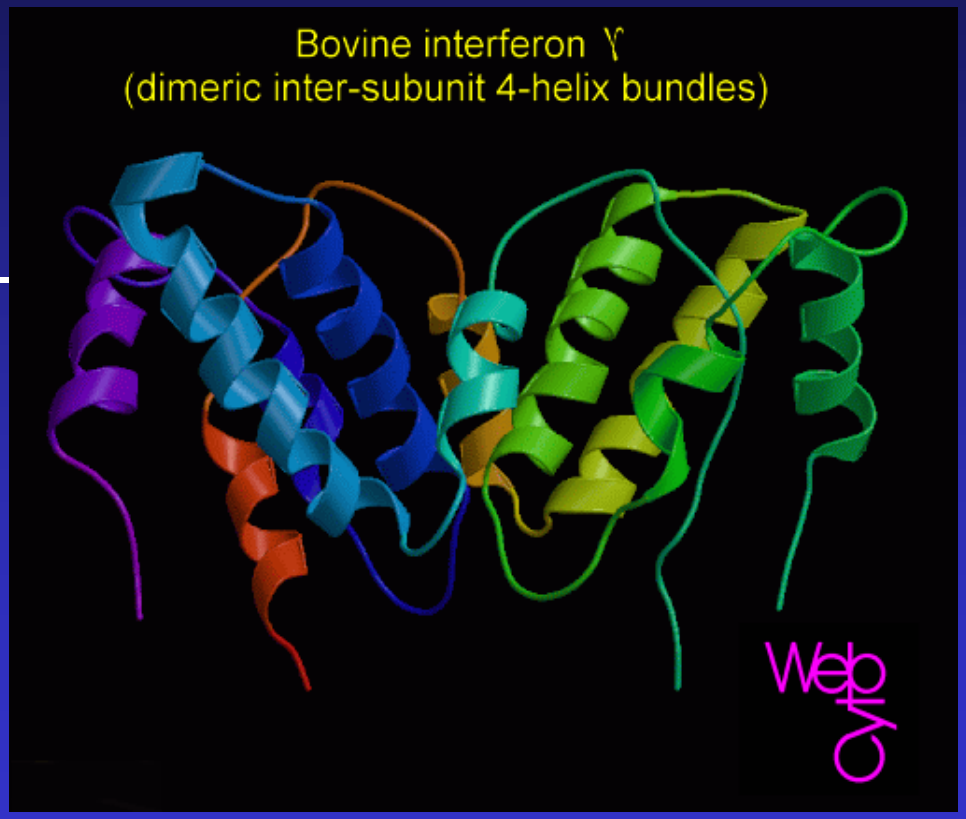
Some Cytokines Relevant to Psychiatry

- IFN-α, IFN-β, IFN-γ
- TNF-α, TNF-β
- Erythropoietin
- Granulocyte colony-stimulating factor
- IL-1α, IL-1β
- IL-2 thru IL-6
- IL-8
- IL-10
- IL-12



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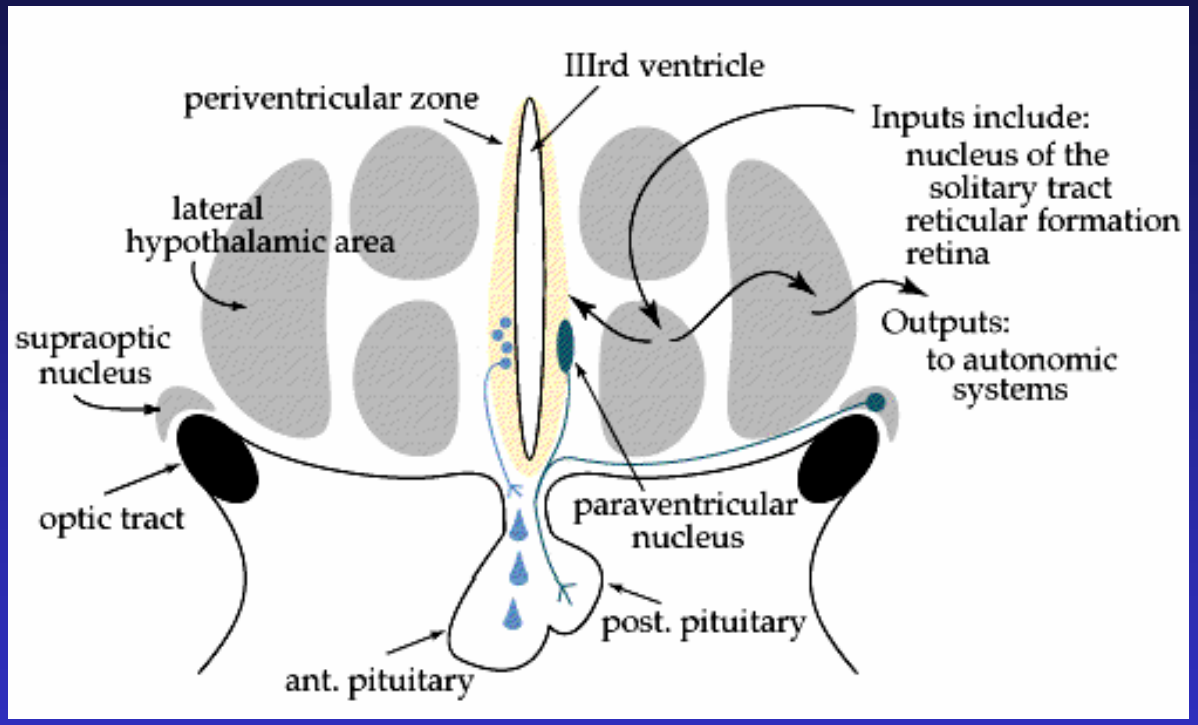
Cytokines Affect the CNS and Can…

- Modulate neurotransmitter systems
- Play a role in…
  - Sleep
  - Food intake
  - Body weight regulation
  - Temperature regulation
  - Cognition
  - Behavior



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Evidence Relating Cytokines and Depression

- Severely depressed patients have elevated cytokine levels
- Cytokines induce neurotransmitter changes similar to changes seen in depression
- Proinflammatory cytokines promote depressive symptoms, which can be reduced through antidepressant medications
- Immunotherapy (e.g., IFN tx) promotes depressive symptoms, which can be reduced by antidepressant medications.

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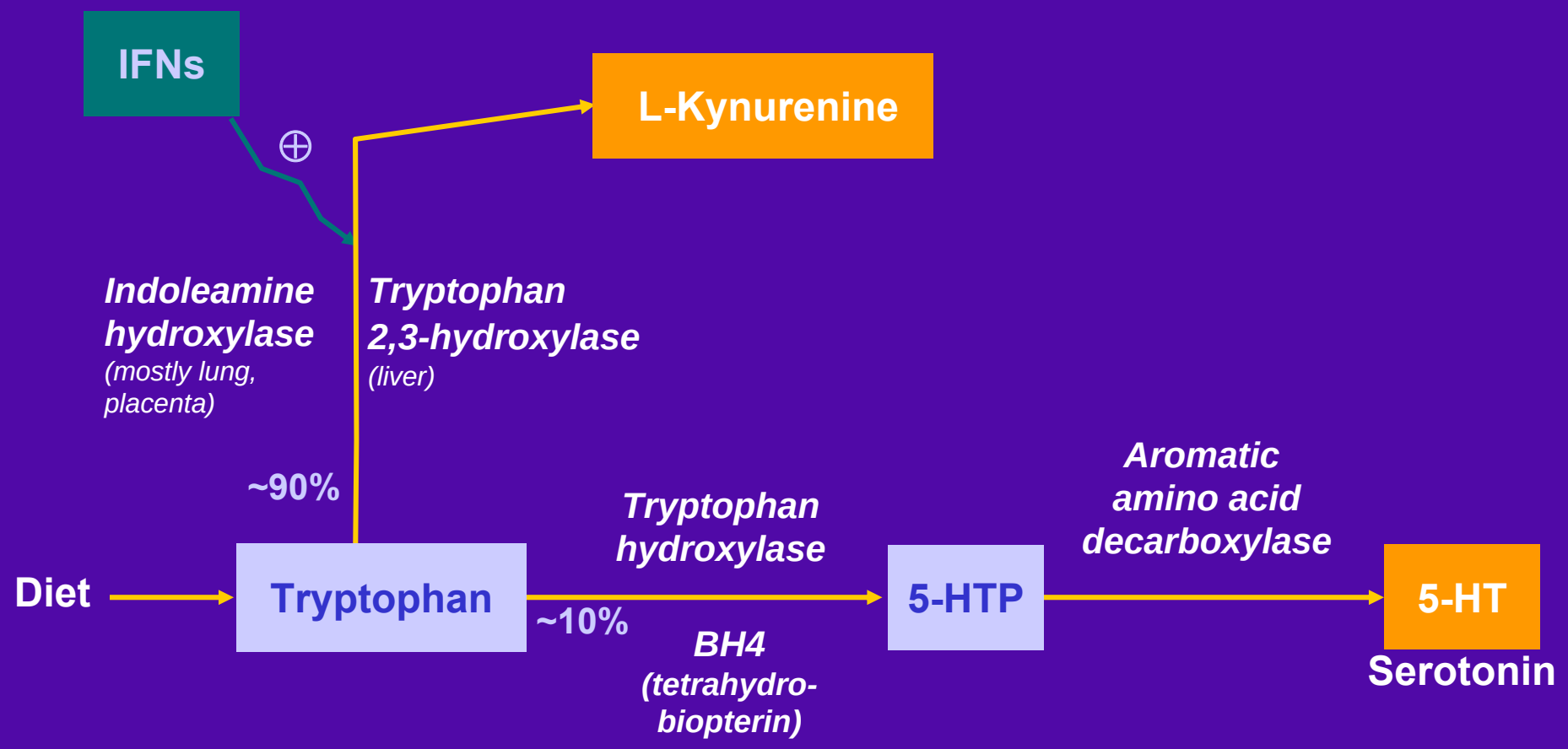
Etiology of IFN-Induced Depression: Tryptophan/Serotonin Depletion?



Tryptophan Metabolic Pathway

Bonaccorso et al. *J Clin Psychopharmacol*. 2002;22:86-90.
Capuron et al. *Mol Psychiatry*. 2002;7:468-73.

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Cytokines & Depression

The mechanisms by which cytokines may mediate depressive symptoms

- remain unclear,
- and are most probably
  - multifactorial, and
  - dependent on patient-specific factors.

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Depression Rates in Patients Treated for Hepatitis C

Author, Year	Sample size	Depression Rate
Otsubo, 1997	85	37%
Miyaoka, 1999	66	44%
Keefe, 1998	632	18%-26%
Farrel, 1997	1071	12%-14%
Hunt, 1997	26	12%
Renault, 1987	58	12%
Okanoue, 1996	677	3%
Davis, 1998	172	6%
McHutchison, 1998	456	25%-37%
Fried, 2002	1121	20%-30%

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Post-Traumatic Stress Disorder

- Irritability is just as prevalent as depression
- PTSD symptoms may be exacerbated by IFN
  - Sleep disturbances (hyperarousal, nightmares)
  - Irritability/Anger (hyperarousal)
  - Guilt and self-blame (also seen in depression)
- Maunder et al., 1998
  - Case study of 3 patients
  - One patient developed hyperstartle despite no trauma history or PTSD diagnosis

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Treating IFN-Induced Depression

- Few studies specific to HCV patients
  - Case reports
  - Prospective study
  - Citalopram, Sertraline, Paroxetine, Fluoxetine, Nortriptyline
- SSRIs can be used safely
- *Prophylactic treatment?*
  - Effective in Melanoma patients on IFN

Gleason OC et al. Psychosomatics. 1999; Hauser P et al. Molecular Psychiatry. 2002; Schramm TM et al. Medical J Australia. 2002; Carvajal et al. J Clinical Psychiatry, 2002; Kraus MR et al. Aliment Pharmacol Ther. 2002; Gleason et al. J. Clinical Psychiatry, 2002

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Future Directions

- Prophylactic antidepressant studies
  - Non-specific
  - SSRIs and IFN share some side effects
- Targeted SSRI treatment
  - Administer SSRI if BDI score crosses a threshold, but before full blown depression
- Biochemical markers (tryptophan pathway)
- Genetic markers
  - Serotonin transport polymorphisms
  - IFN-α receptor polymorphisms

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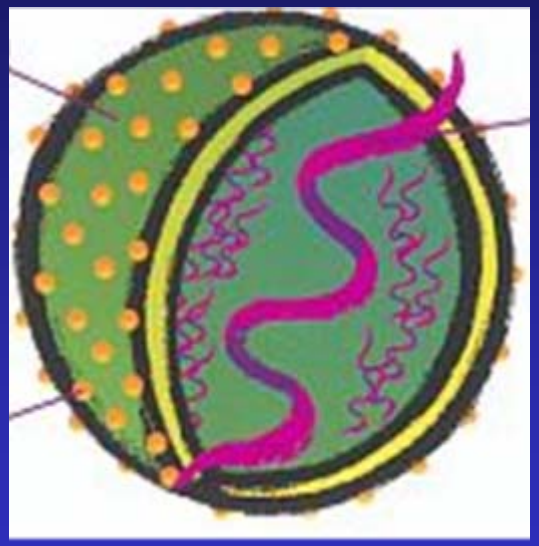
Acknowledgements



Jennifer Loftis, PhD

J.E.N.S. Lab, Portland VA Medical Center

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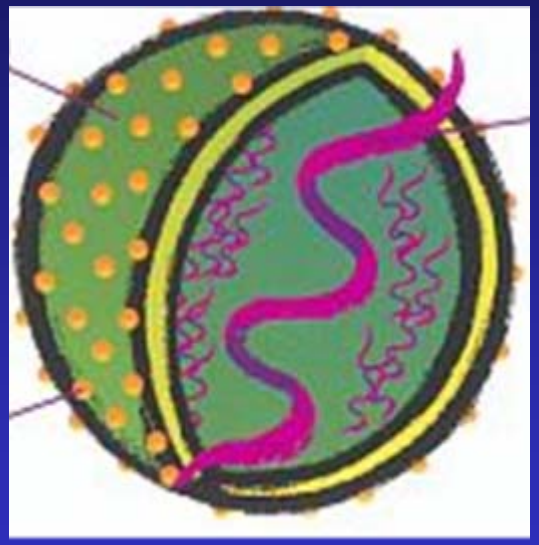
Treatment Issues



David Indest, PsyD

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MH & SA Roles in HCV Care

- Primary & secondary prevention
- Co-morbidity screening
- Education & support (patients & family)
- Evaluation & preparation for INF/RBV tx
- Compliance & side-effect management

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Co-management

- Multidisciplinary case staffing
- Ongoing consultation with patient, support network, and other professionals
- Standardized ongoing MH/SA screening
- Groups: education, HCV support, HCV tx support

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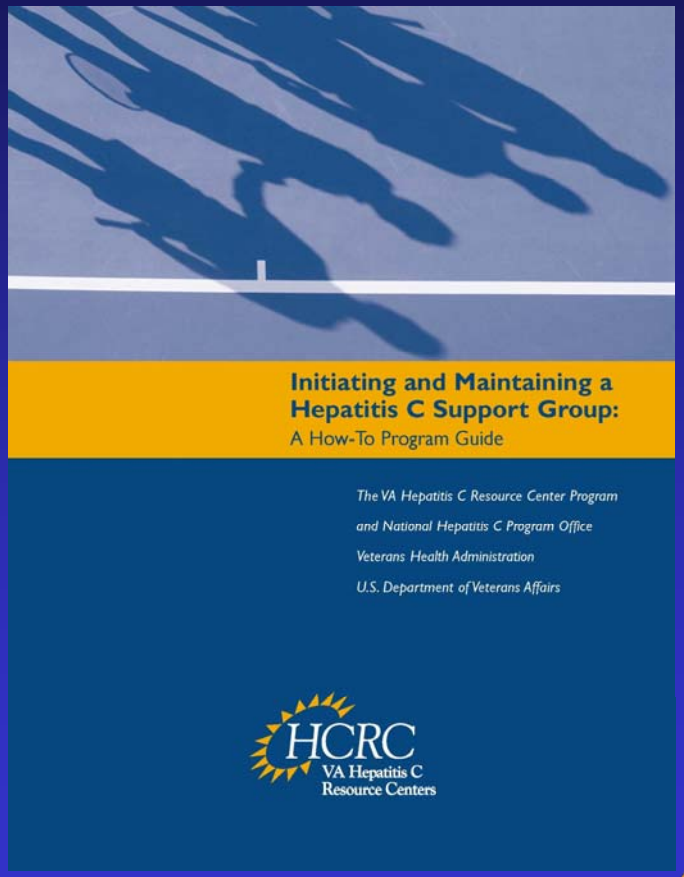
HCV Support Group Toolkit

- A “How To” Guide
- Everything you need to get started
- Designed for any provider new to doing a support group
- Practical pointers
- Logistics



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Selecting & Preparing Treatment Candidates: Pre-IFN/RBV Evaluation

Planning for 6-12 mos of disability, work loss, financial hardship, emotional & physical distress

- Does Pt have *unmanaged* MH or SA issues that may be worsened by tx?
  - PTSD, irritability, anger, anxiety, mania, depression
  - Pd of sobriety, trigger & craving awareness, relapse plan, sponsor/support, injection issues
  - Past OR present
  - Beware of waking the sleeping dragon (subclinical sx)

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Pre-IFN/RBV Evaluation

- Social Support
  - Material – cooking, cleaning, transportation….
  - Emotional – misery loves company
  - Family dynamics – system for/against the sick role, family discord, caretaking responsibilities
- Financial
  - Income – contingent on being able to work?
  - Insurance – contingent on work?
  - Contingency plans – What if Pt can't work? What if primary income falls through?

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Pre-IFN/RBV Evaluation

- Timing & Planning – upcoming family life events, transitions, stressors
  - Pregnancy
  - Changing jobs
  - Moving
  - Vacations, weddings, graduations, etc.
  - Any upcoming needs to be at full capacity

  - URGENCY – Why now?
    - What will be different 1-3 years from now?
    - Opportunity to educate Pt about disease progression

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HCV Treatment Eligibility

- There are NO data to support excluding patients with prior MH/SA from HCV treatment
- Patients with MH/SA dx can be treated for HCV if the conditions are stable and monitored
- Active substance abuse:
  - No longer an *absolute* contraindication.
    - Alcohol use risks cirrhosis
    - Is the impact the substance or tx compliance?

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Brief Alcohol Intervention (BAI)

- Motivational Interviewing
- Work WITH the Pt's goals not against them
- Primary Care & other settings
- Any and all providers

Coming soon! to www.hepatitis.va.gov

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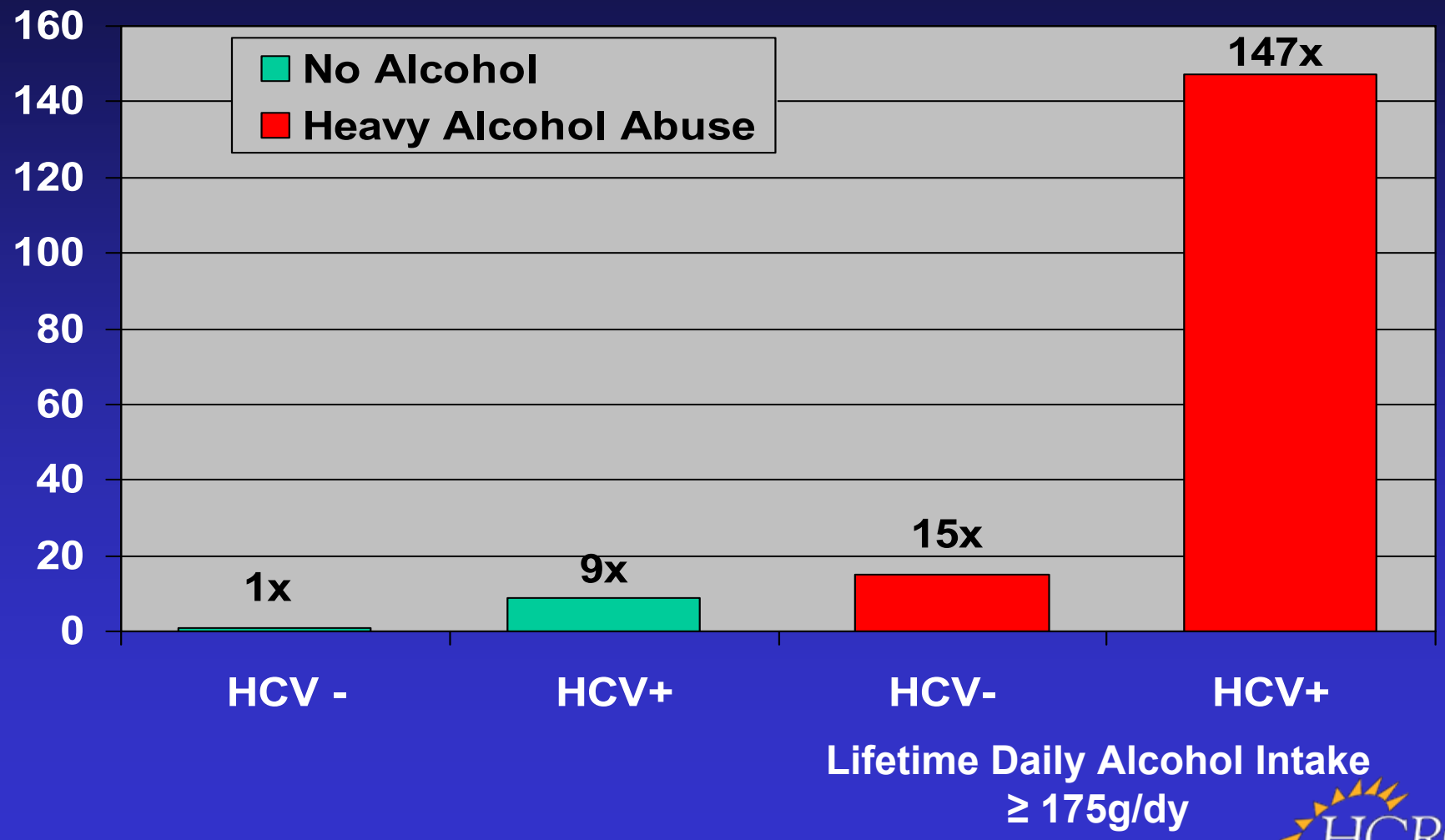
Alcohol Abuse Greatly Increases Risk of Developing Cirrhosis



Corrao & Aricò, *Hepatology*, 1998;27:914-9.

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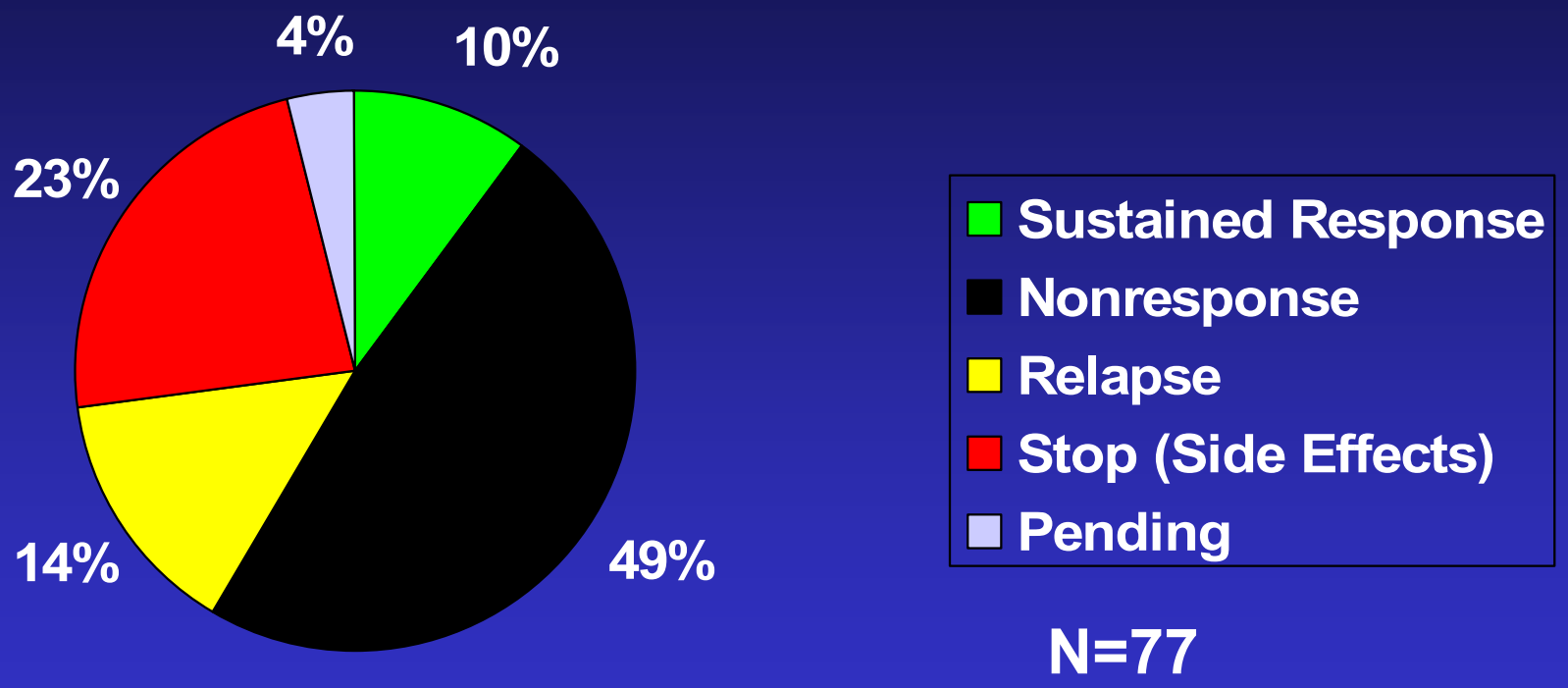
IFN/RBV Tx Outcomes – St Louis VA



41 on IFN/ribavirin combination therapy

Cawthorne et al., *Am J Gastroenterol*, 2002;97:149-55

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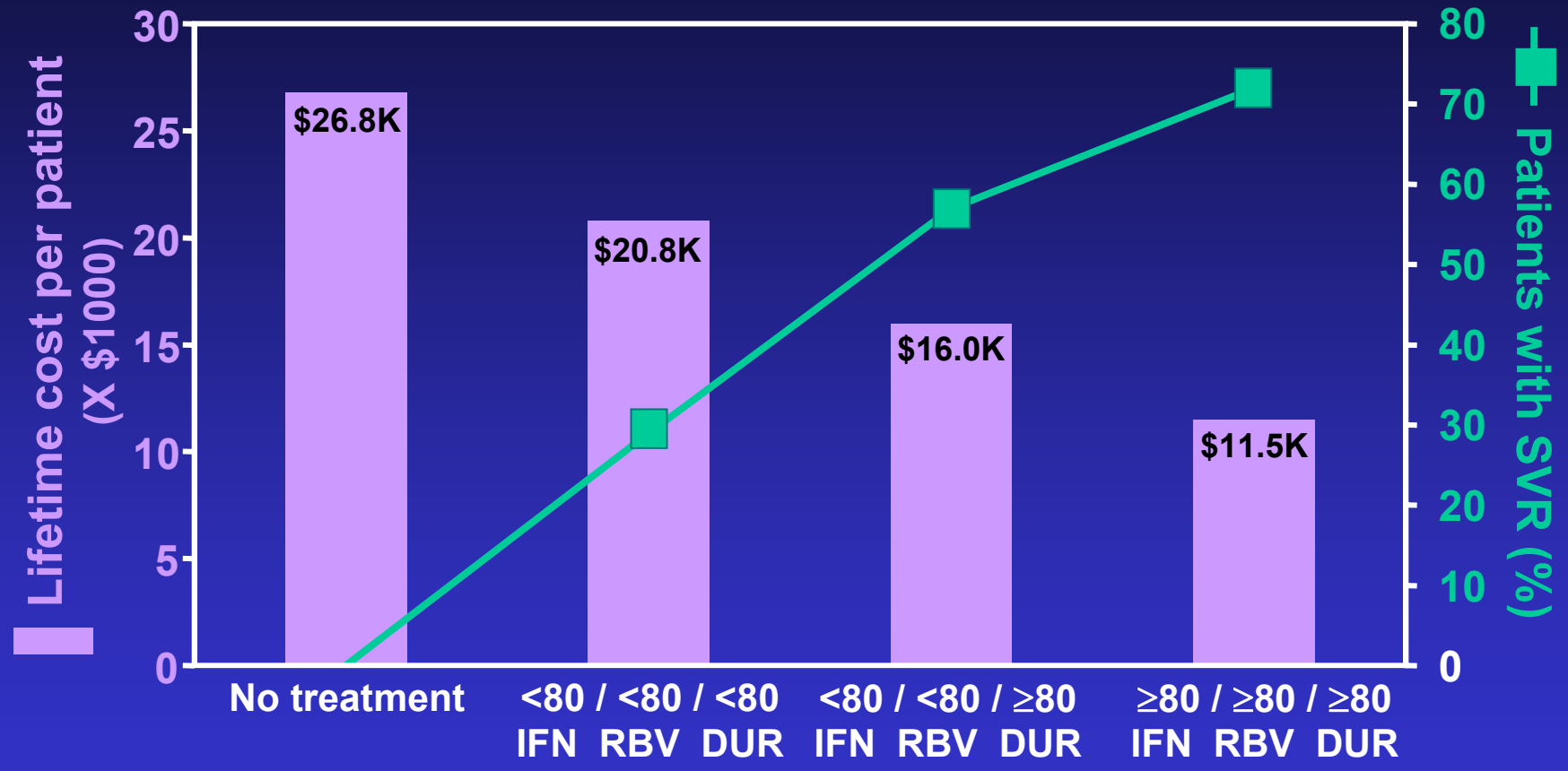
Adherence to PEG-IFN/RBV Therapy

Impact on Lifetime Cost Based on a Cohort Simulation Model – United States



PEG-IFN alfa-2b 1.5 μg/kg/wk; RBV >10.6 mg/kg/d
DUR = duration of treatment (48 weeks)

Wong et al., AASLD, 2002

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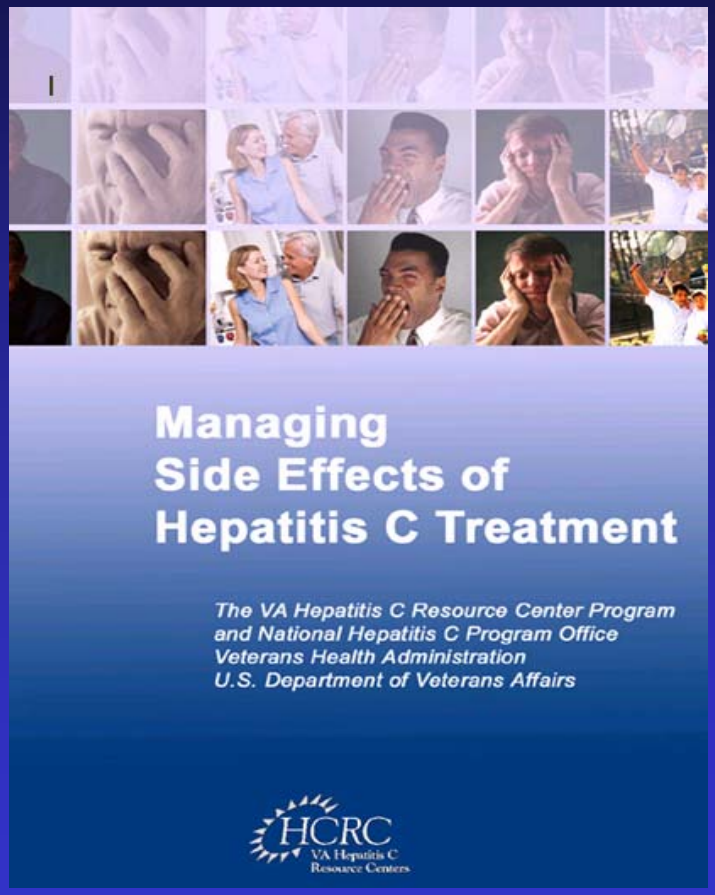
Managing IFN/RBV Side Effects



- Education on Pros & Cons
- Managing expectations
- Self-management
- “Virtual” support
- Questions & notes
- Inspirational

Coming soon! to www.hepatitis.va.gov

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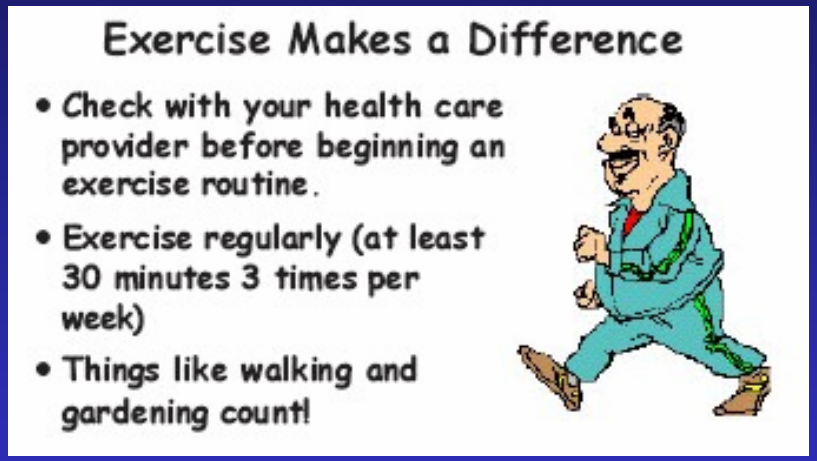
Patient Wallet Cards



- Healthy living
  - HCV & general
- Alcohol
- Testing
- Transmission
- HAV & HBV

www.hepatitis.va.gov/vahep?page=pt-01-02

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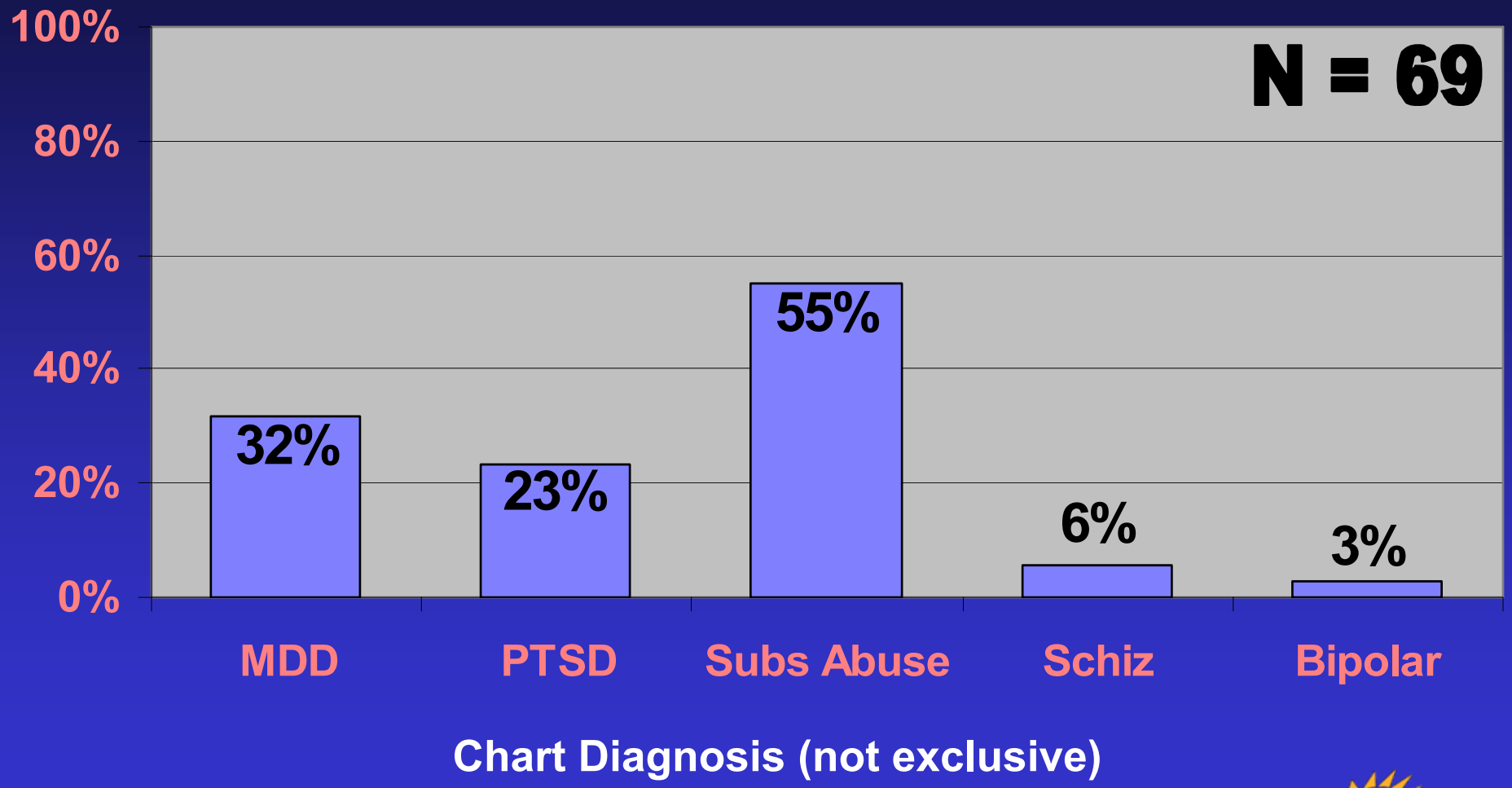
Interdisciplinary Model in Action: HCV+ Veterans Who Received IFN



NW HCRC, PVAMC, unpublished data.

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HCV on the Web

- VA National Hepatitis C Program - Info for patients & providers

  www.hepatitis.va.gov
  - Documents, video & tools for streaming & download
- Northwest HCRC, Portland

  www.va.gov/portland/Mood-Disorders-Center/ifn.htm#hcrc
- Centers for Disease Control & Prevention

  www.cdc.gov/ncidod/diseases/hepatitis/c/
- Hepatitis C Advocate

  www.hcvadvocate.org
- American Liver Foundation

  www.liverfoundation.org

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