

***Development of a Multidisciplinary
Treatment Program for the
Management
of HIV/HCV Co-infected Patients***

***Suffolk County Department of
Health Services (SCDHS)***

Technical Assistance provided by
HRSA

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The background of the slide is a solid blue color. In the lower half, there are several decorative elements consisting of concentric circles, resembling ripples in water, rendered in a lighter shade of blue. These ripples are scattered across the bottom, with a larger one on the right side and several smaller ones towards the left and center.

HCV and HIV



HCV Characteristics

- Family Flaviviridae¹
- Enveloped²
- Positive-sense single-stranded RNA (9.6 kb)^{1,3}
- 3000–amino acid polyprotein³
- No RNA polymerase proofreading ability⁴
– Quasispecies⁴
- Half-life: ≈2.7 hours²
- Daily production: 10 trillion (10^{12}) virions²

¹ Purcell R. NIH Consensus Conference on Hepatitis C. 1997.

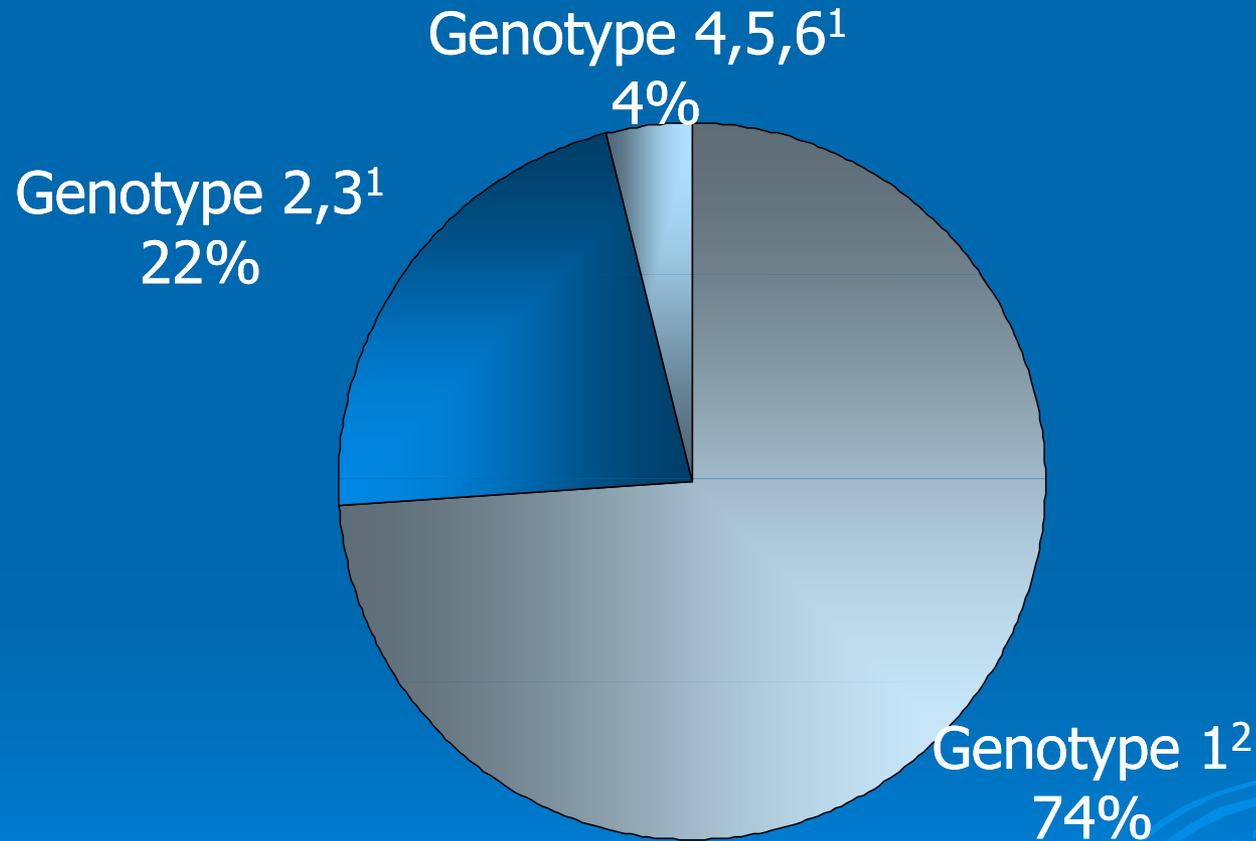
² Neumann A et al. *Science*. 1998;282:103-107.

³ Rosenberg S. *J Mol Biol*. 2001;313(3):451-464.

⁴ Lauer G et al. *N Engl J Med*. 2001;345(1):41-52.

Epidemiology of HCV

Genotype Distribution in the US*



*In Hepatitis C Monoinfection

¹Alter M et al. *N Engl J Med.* 1999;341(8):556-562.

²Blatt, L et al. *J Viral Hepatitis.* 2000;7:196-202.

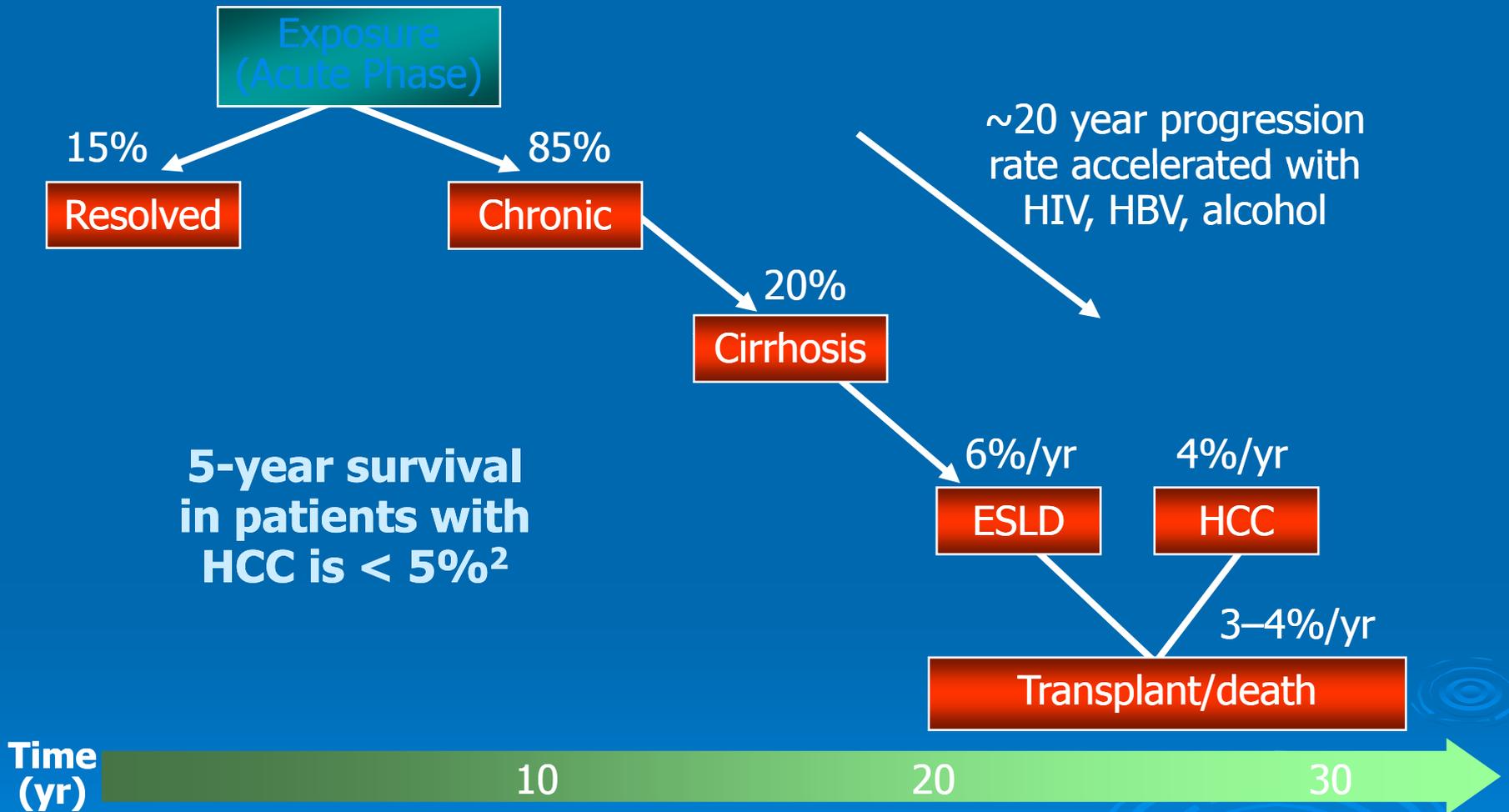
HCV Infection: Worldwide Genotype Distribution



Epidemiology: Quick Hits

- 5 million antibody positive
 - At least 4 Million have HCV RNA
 - CDC estimates may be as high as 7 million carriers
- 2.7 million are chronically infected with HCV
- Highest prevalence;
 - 30- to 54-year-olds
 - African American Males
- US disease burden and financial burden is steep
 - ~10,000 deaths per year attributed to CHC

Natural History of HCV Infection



HCC = hepatocellular carcinoma

ESLD = end-stage liver disease

Di Bisceglie A, et al. *Hepatology*. 2000;31:1014-1018.

Financial Burden of HCV-Related Liver Transplant

HCV-Related Liver Transplants Account for 40% of Total Transplants¹

Number ²	~2000/year
Procurement, Hospital/Physician Charges ³	~\$300,000
Evaluation, Follow Up ³	~\$100,000
Total Transplant Cost	~\$400,000
Immunosuppressant medication ³	~\$30,000/year
Total cost (transplant + immunosuppressant tx)	~\$430,000/ first year

¹Kim W et al. *Hepatology*. 2002;36:S30-S34.

²Available at: www.unos.org. Accessed March 13, 2006.

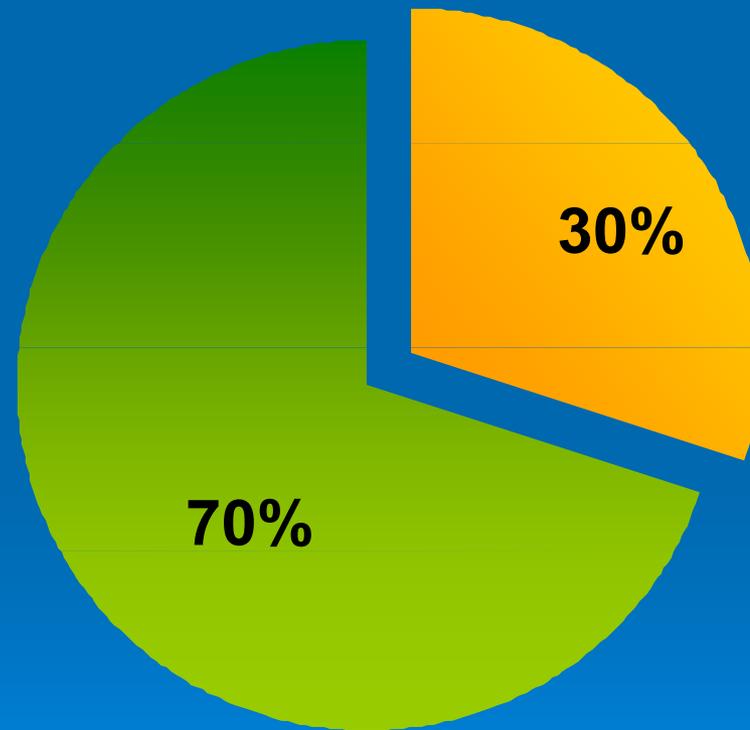
³Ortner N. *2005 US Organ and Tissue Transplant Cost Estimates and Discussion*, June 2005, 1-28.

HIV/HCV Co-infection



Overall Prevalence of HCV Among HIV-Infected Persons in the US

■ HCV/HIV Coinfected ■ HIV Monoinfected



¹Sulkowski M, et al. *Ann Intern Med.* 2003;138:197-207.

²Thomas D. *Hepatology.* 2002;36:S201-S209.

Impact of HCV on HIV Disease Progression

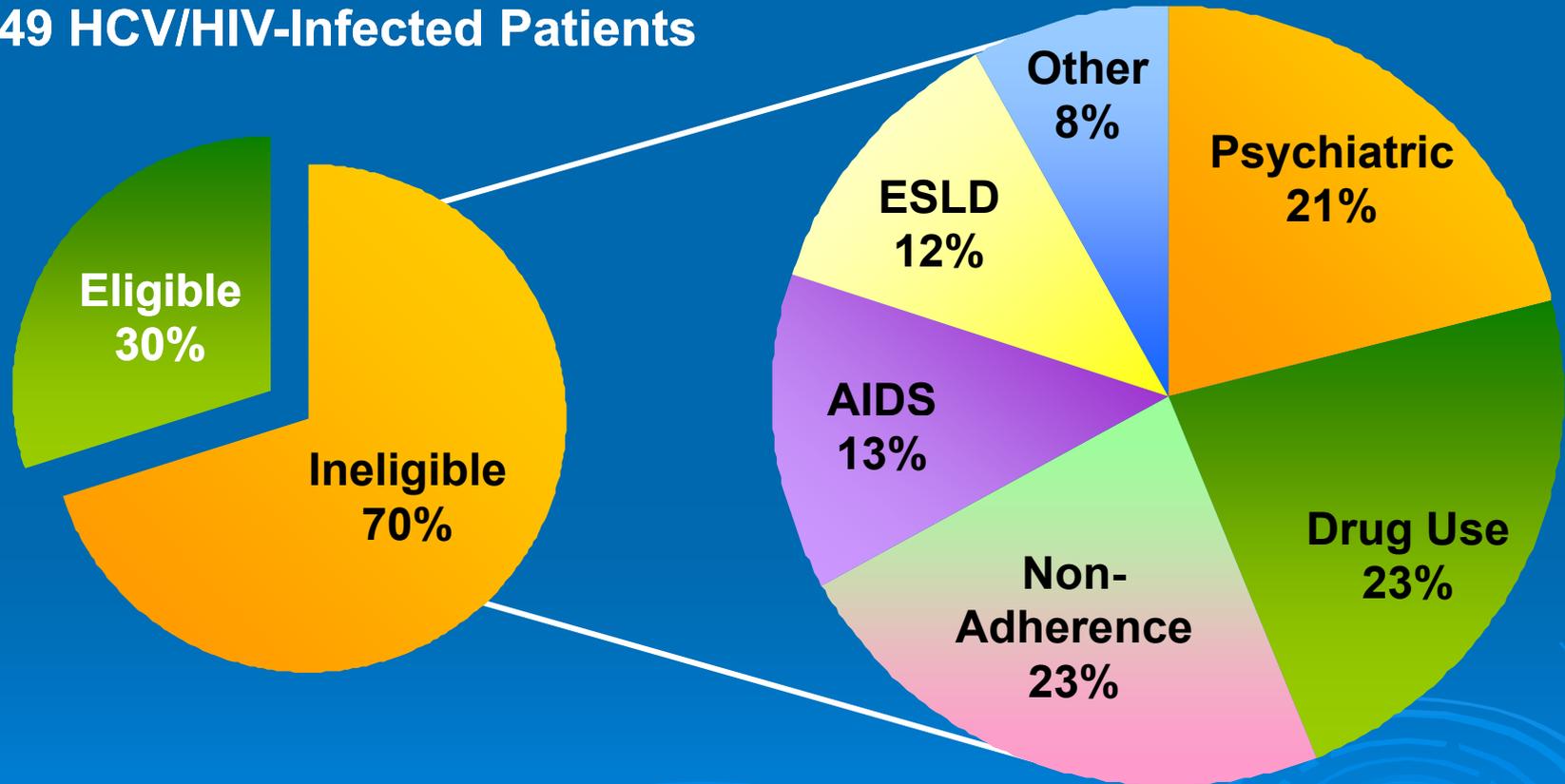
- Prospective cohort study of 3111 patients on HAART between 6/96 to 5/99
- 37% were HCV+
- HIV-related progression and death higher in active IVDU with HCV infection
- HCV associated with blunted CD4 recovery
- Deaths from liver disease 3-fold higher

HCV/HIV Coinfection: An Area Of High Medical Need

- One third of HIV patients are coinfecting with HCV¹
 - Among HIV-infected IVDU, this rises to 50% - 90%²
- HCV viral load higher in HCV/HIV vs. HCV patients³
- HIV accelerates clinical course of HCV-related liver disease
 - Time to cirrhosis is significantly reduced⁴
 - Liver disease is now a leading cause of death in hospitalized AIDS patients⁵
- HCV may also impact the course of HIV disease
 - Increases risk of ART-related hepatotoxicity⁶
 - Apparent reduction in CD4 count responsiveness to ART⁷

Barrier to HCV Treatment in an Urban HCV/HIV Clinic

149 HCV/HIV-Infected Patients



ESLD, end stage liver disease

Fleming C, et al. *Clin Infect Dis*. 2003;36:97-100.

Barriers to Treatment of HCV/HIV Coinfected Individuals

Conclusions

- HCV/HIV coinfecting patients are less likely to be treated for HCV than those with HCV mono-infection¹
- Primary Barriers
 - Low physician referral rates
 - High no-show rates
- Additional reasons of ineligibility for HCV treatment²
 - Non-adherence
 - Psychiatric illness
 - Relapsed drug or alcohol use
- Strategies to overcome these barriers are needed

¹ Shim, et al. AASLD 2004, Oct. 29-Nov. 1, Boston, MA. Abstract 386.

² Fleming C, et al. *Clin Infect Dis*. 2003;36:97-100.

Practice Guidelines Regarding HCV/HIV Coinfection

- 2004 AASLD Practice Guidelines, endorsed by the IDSA, recommend¹:
 - All HIV-infected individuals should be screened for HCV antibodies in serum or plasma
 - Including those previously diagnosed with HIV
- Recommendations endorsed by the CDC, NIH, HIVMA, and IDSA, based on safety and efficacy demonstrated in PEGASYS Trials²:
 - Antiviral treatment should be considered for all HIV patients coinfecting with chronic hepatitis C infection

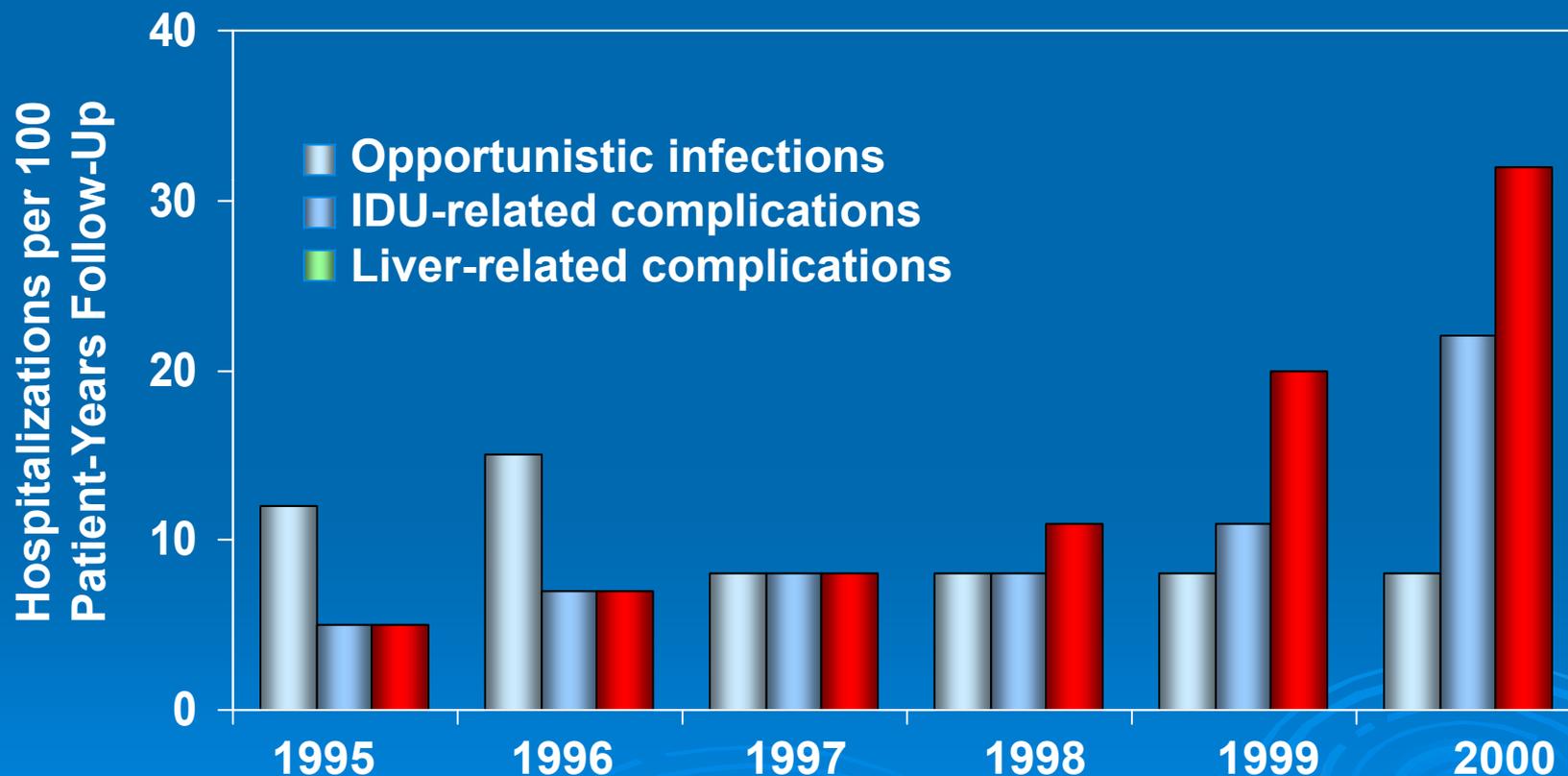
Guidelines may not necessarily reflect the approved labeling for Pegasys and Copegus

¹Strader D et al. *Hepatology*. 2004;39(4):1147-1171.

²MMWR, Dec. 17, 2004. Treating opportunistic infections among HIV-infected adults & adolescents. Available at: <http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5315a1.htm>

Hospital Admissions Among HIV-Infected Patients

5 Fold Increase in Liver Complications From 1995–2000



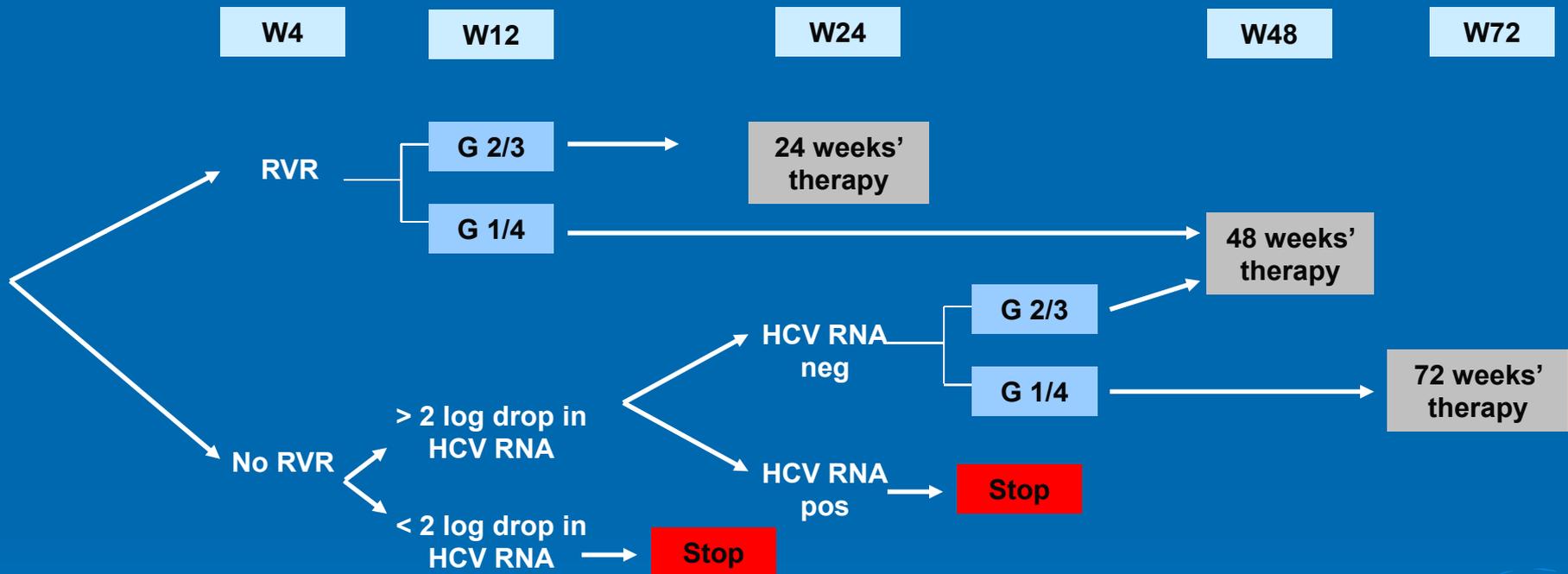
2007 Updated Recommendations From the HCV-HIV International Panel

- Optimal dosages of Peginterferon and RBV*
 - Current treatment of HCV in HIV+ should be pegylated interferon at standard doses plus weight-based RBV:
 - 1,000 mg/day if < 75 kg
 - 1,200 mg/day if > 75 kg

*Proposed RBV dosing is not reflective of current Copegus product labeling

Approved Copegus dosing is 800mg for HIV/HCV co-infected patients

Proposed Optimal Duration of Hepatitis C Therapy in HCV/HIV Coinfection Patients[§]



Weight-based Ribavirin[§]: 1,000 mg/day if < 75 kg and 1,200 mg/day if > 75 kg

[§] Proposed duration of therapy is not reflective of current Pegasys/Copegus labeling. Please see complete prescribing information for details

Approved Copegus dosing is 800mg for HIV/HCV co-infected patients

* In patients with baseline low viral load and minimal liver fibrosis

W = week; neg = negative; pos = positive; G = genotype

Soriano V, et al. *AIDS*. 2007;21:1073-1089.

Definitions of Virologic Response to Antiviral Therapy for Hepatitis C

Response	Definition
RVR Rapid Virologic Response	HCV-RNA negative at 4 weeks as defined by HCV-RNA < 50 IU/mL
EVR Early Virologic Response	HCV-RNA negative or > 2 log ₁₀ drop at week 12
<ul style="list-style-type: none"> • Complete EVR (cEVR) • Partial EVR (pEVR) <ul style="list-style-type: none"> – Slow partial responder – Partial responder 	<p>No RVR but HCV-RNA negative (< 50 IU/mL) at week 12</p> <p>No RVR and detectable but ≥ 2 log₁₀ drop in HCV-RNA at week 12</p> <p>≥ 2 log₁₀ drop in HCV-RNA at week 12 but not HCV RNA negative until week 24</p> <p>≥ 2 log₁₀ drop in HCV-RNA at week 12 but HCV RNA positive at week 24</p>
SVR Sustained Virologic Response	HCV-RNA negative 24 weeks after end of treatment
Relapse	HCV-RNA negative at end of treatment but HCV-RNA positive after treatment stopped

Ferenci P, et al. Presented at EASL 2006, April 26-30, Vienna, Austria. Abstract 8.

Marcellin P, et al. AASLD 2007, Oct. 2-6, Boston, MA. Poster 1308.

Sánchez-Tapias JM, et al. EASL 2007, April 11-15, Barcelona, Spain. Poster 641.

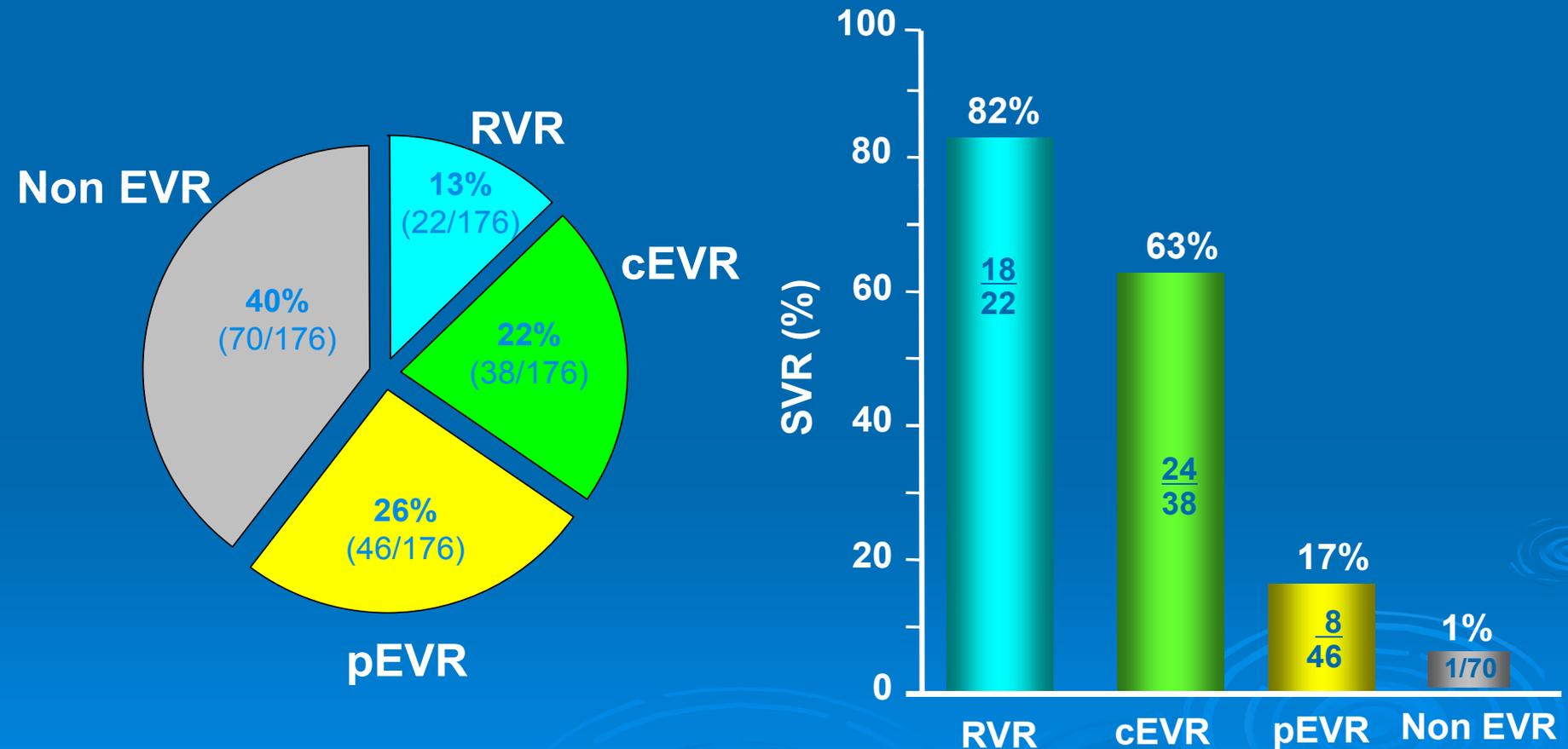
Paulon E, Naoumov NV. *Eur J Gastroenterol Hepatol.* 2006;18(4):321-325.

Pawlotsky JM. *Hepatology.* 2002;36(suppl 1):S65-S73.

Adapted from <http://www.hepatitis.va.gov/vahep?page=prtop04-wp-03> accessed January 4th, 2008

RVR, cEVR, SVR in HIV/HCV Co-infection: *Genotype 1 Virologic Responses*

Pegasys 180 µg/week plus RBV 800 mg/day for 48 weeks



Community Health Center Network

- SCDOHS operates 9 community health centers
- Strategically located throughout Suffolk County
- Most patients do not have access to regular preventive care anywhere else



Health Center Patients

➤ Patient Volume

- Approximately 60,000 unduplicated patients seen annually
- Approximately 280,000 annual visits

➤ Gender

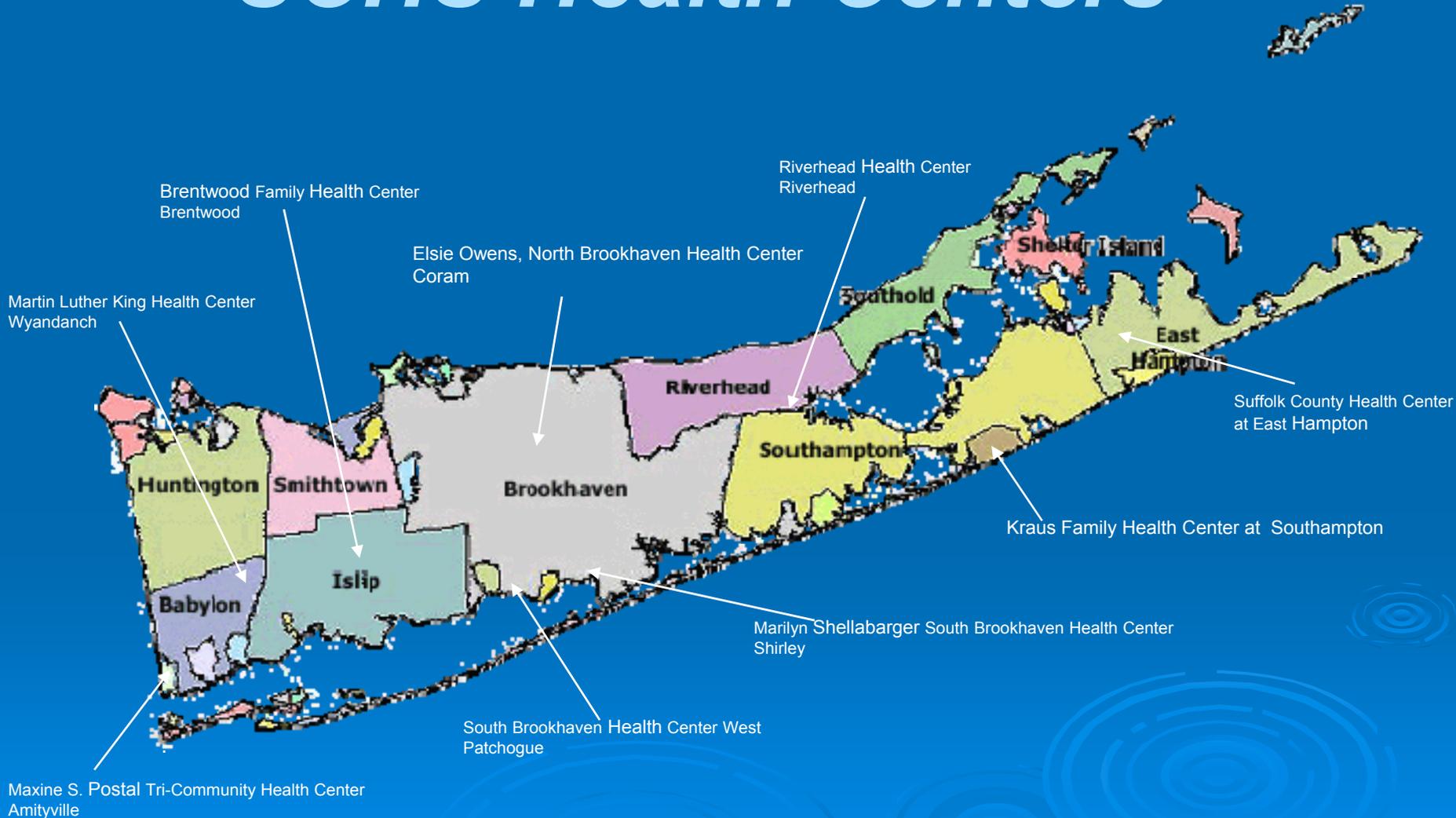
- Male -37.7%
- Female - 62.3%



SUFFOLK COUNTY (NY)

Pop: 1,504,947 Area: 912 sq. miles

SCHS Health Centers



Health Center Locations



- **Amityville** – The Maxine S. Postal Tri-Community Health Center
- **Brentwood** – Brentwood Family Health Center
- **Coram** – Elsie Owens North Brookhaven County Health Center
- **East Hampton** – The Suffolk County Health Center at East Hampton
- **Patchogue** – South Brookhaven Family Health Center, West
- **Riverhead** – Riverhead Health Center
- **Shirley** – Marilyn Shellabarger South Brookhaven Family Health Center, East
- **Southampton** – Kraus Family Health Center at Southampton
- **Wyandanch** – Martin Luther King, Jr. Community Health Center

Health Center HIV Positive Patients

- Approximately 500 HIV positive patients receive comprehensive primary care services at the health centers.
- 121 of these patients are HIV/HCV co-infected
- Each health center has an HIV Care Team (HIV specialist, HIV Nurse Coordinator, Case Manager/Social Worker) to take care of the HIV positive patients.

Issues and Barriers to Treatment of HIV /HCV Co-Infected Patients

- Shortage of specialists in the area
- Co-infected patients could not obtain appointments in timely fashion and treatment for HCV was delayed
- Lack of adequate transportation

Solution

- January 2009, HRSA consultant provided in-depth training on treatment of co-infected patients to the SCDHS HIV Care Teams
- Patient assessment and audit tools developed
- All HIV + patients screened for HCV and placed into one of five categories

Patient Assessment at Baseline

Liver Evaluation if Needed	Clinical Evaluation	
HCV Genotype	PHQ9 Depression Screen	
HCV RNA	Weight Evaluation	
Liver Biopsy	Adverse Events	
Liver Sono	ETOH counseling	
AFP	Cardiac Eval/EKG	
Lab Tests	Hep A serology	
WBC	Hep B serology	
PLT	Hep A vaccination	
ANC	Hep B vaccination	
Hgb/Hct	Pneumococcal vaccine	
ALT	Flu Vaccine	
Bilirubin	HIV Markers	
Pregnancy test	HIV RNA	
Cr	CD ₄	
Glu		
TSH		
ANA		

Assessment:

- Patient is a candidate for HCV treatment or not; if not, what is the reason
- Treatment deferred at this time with the reason

Hepatitis C Treatment Audit Tool

Health Center _____ Patient _____ MR# _____

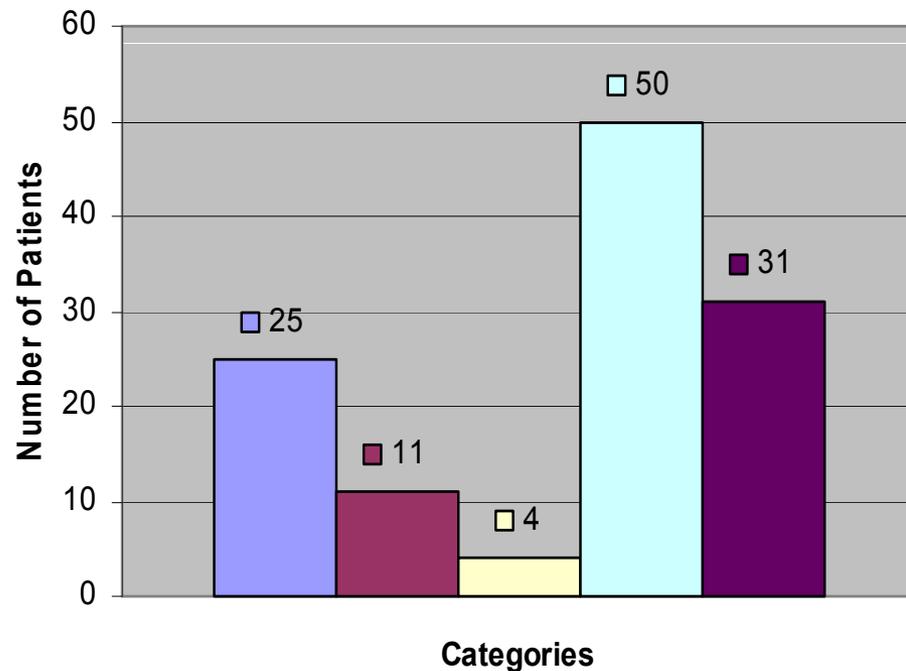
	DATE					
CD ₄						
HEP C VL						
HEP GENOTYPE						
DEPRESSION SCREEN (PHQ9)						
ETOH EVALUATION						
HEP A SEROLOGY						
HEP B SEROLOGY						
HEP A VACCINE (if indicated)						
HEP B VACCINE (if indicated)						
PNEUMOCOCCAL VACCINE						
FLU VACCINE						
EKG						
Sonogram						
AFP						
PREGNANCY TEST						

Patient is a candidate for treatment Yes _____ No _____

Treatment Success _____ Treatment Failure _____

Client Categories

Hepatitis C - Co-infected HIV Client Categories



- Category 1: Patient is Hep C+, yet has cleared virus, previous exposure - no active infection (self cured, +HepC AB no virus detected)
- Category 2: Patient with previous treatment, treatment failure in the past.
- Category 3: Patient with previous treatment and cure.
- Category 4: Patient who has active current barriers to treatment (low CD4, ETOH abuse, thrombocytopenia, etc.).
- Category 5: Patient in the process of pre-treatment, target date for treatment initiation is to be determined, or in current active Hepatitis C treatment.

Results

- Candidates for treatment (Category 5) underwent screening, education and counseling on treatment options and side effects
- HRSA consultant remained available by telephone for questions
- Follow up visit by HRSA consultant in May 2009 to review and discuss cases of screened patients

Where We Are Now

- A total of 9 patients began treatment
- The first patient began treatment in July 2009
- Treatment takes extended time and patients need support of entire team
- HRSA consultant made a return visit in July 2010 to meet with the HIV Care Team to discuss patient management issues
- In the process of analyzing additional data

Lessons Learned

- Primary care providers can be effectively trained to become self sufficient in providing the prevention education and treatment to HIV/HCV co-infected patients, with technical assistance from agencies like HRSA
- Appropriate leadership is essential for the success of the program
- In future mono infected patients may be treated using the same model