

# Hepatitis C: A Rapidly Evolving Paradigm

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**Arizona Infectious Disease Conference**  
**Black Canyon Conference Center**  
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# Objectives

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- To understand the epidemiology and clinical sequelae of chronic HCV infection
- To understand the current and future management strategies for HCV infection
- To understand how direct acting antiviral drugs have and will alter the treatment of HCV-infected patients.

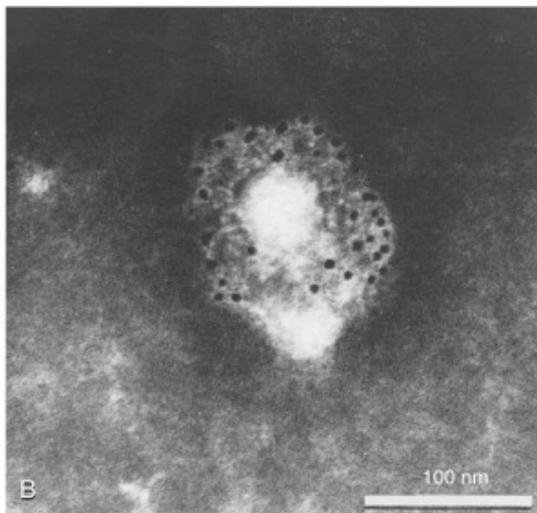
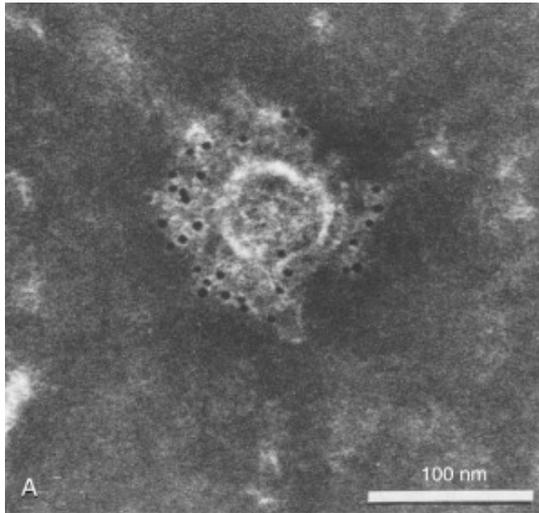
# HCV Infection

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- 200 million Chronic Infections Worldwide
  - 2% of worlds population
  - 75% of people unaware of status

# HCV Virus

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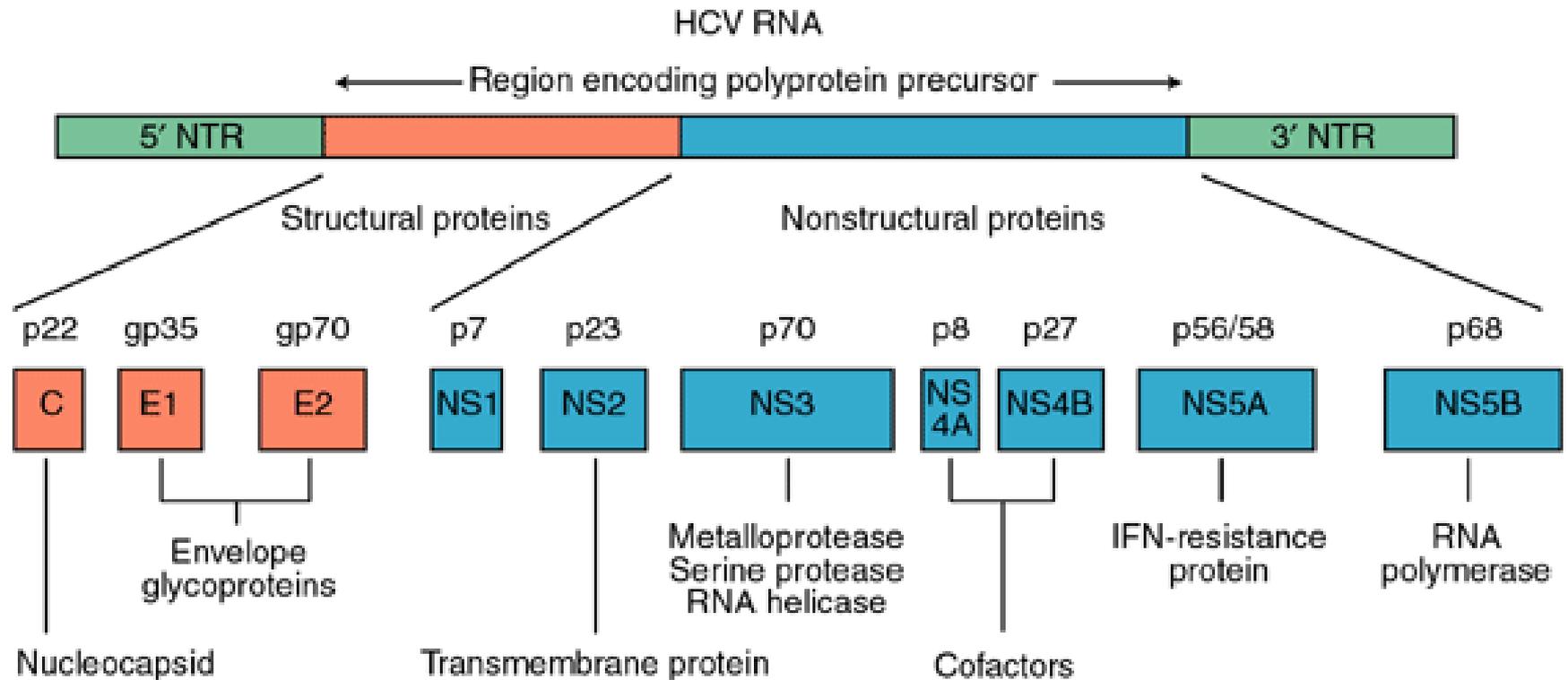
- RNA virus
  - Positive strand
  - 55nm diameter
  - Family Flaviviridae, Genus Hepacivirus
    - Related genus Flavivirus- Dengue, Yellow Fever
  - In vivo replication: liver and lymphocytes

A and B, Electron microscopic images of hepatitis C virus (HCV) virions concentrated from human plasma by high-speed centrifugation. The virions are identified by staining with gold-labeled antibodies to the HCV envelope proteins.

(From Kaito M, Watanabe S, Tsukiyama-Koham K, et al. Hepatitis C virus particle detected by immunoelectron microscopic study. J Gen Virol. 1994;75:1755-1760.)

# HCV genome

## b Proteins encoded by the HCV genome



Hepatitis C virus (HCV): model structure and genome organisation

Expert Reviews in Molecular Medicine ©2003 Cambridge University Press

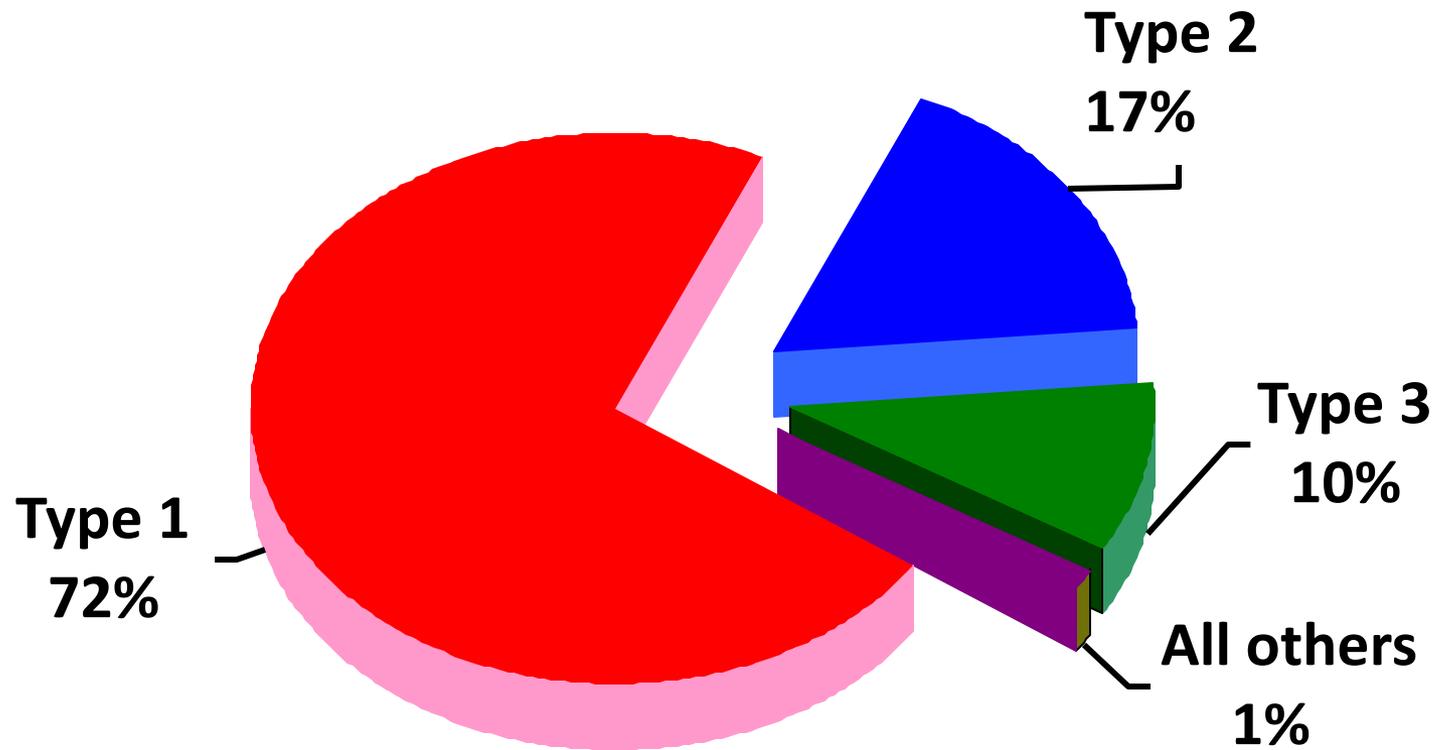
# Hepatitis C Has High Viral Diversity

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- HCV replicates at high levels (>10 trillion virions/day)
- Lack of error correction leads to drift
- Drift is observed in two forms
  - Quasispecies
  - Genotypes (1-7)

# Hepatitis C Virus *Genotypes in the USA*

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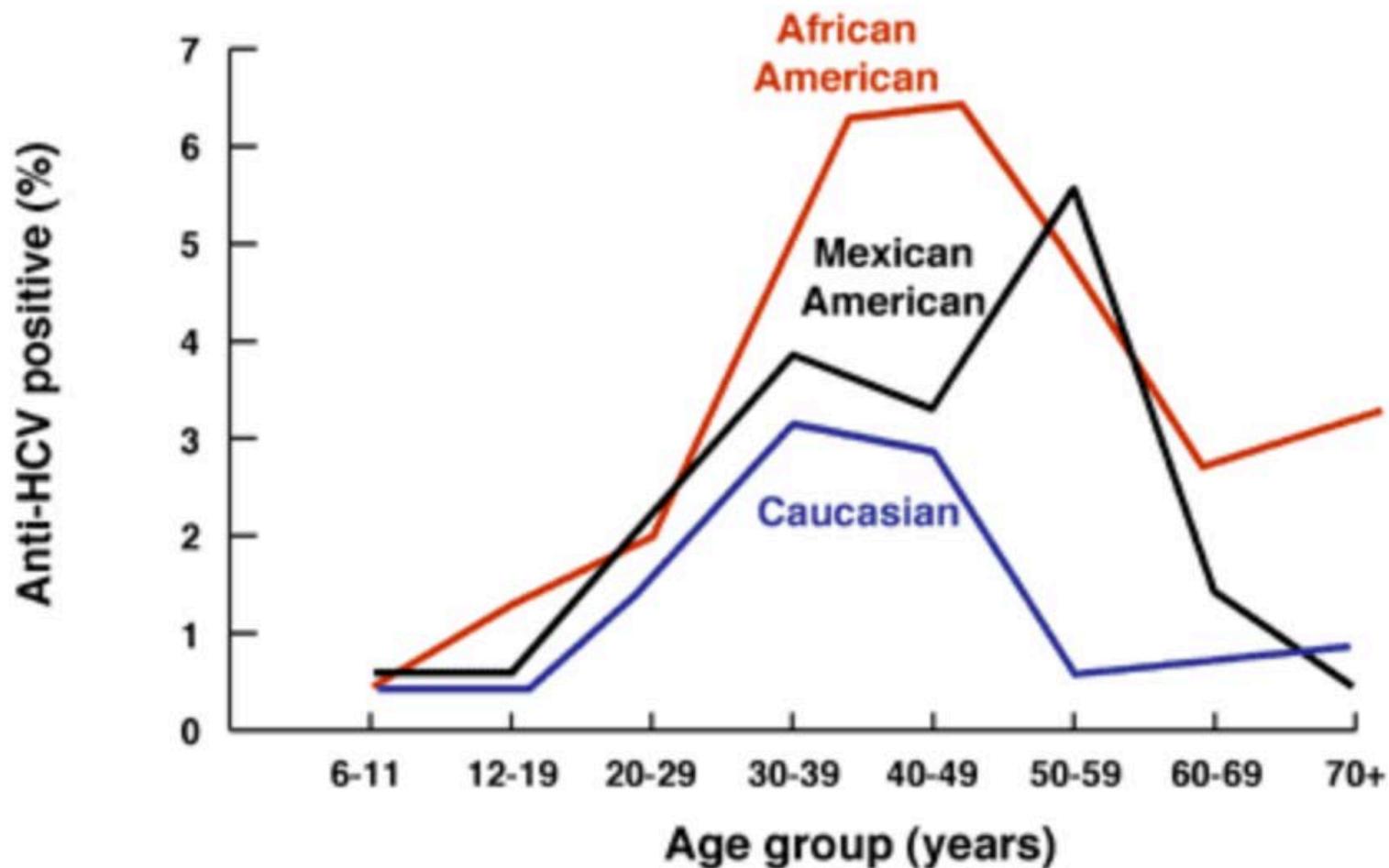


# HCV Testing and Linkage to Care

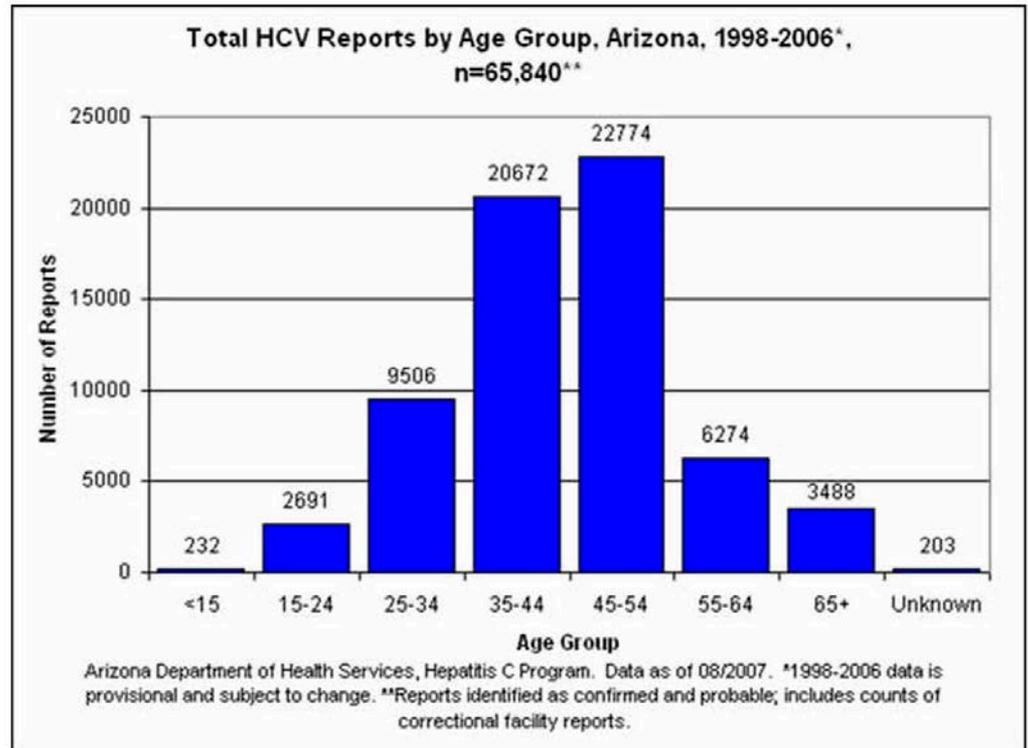
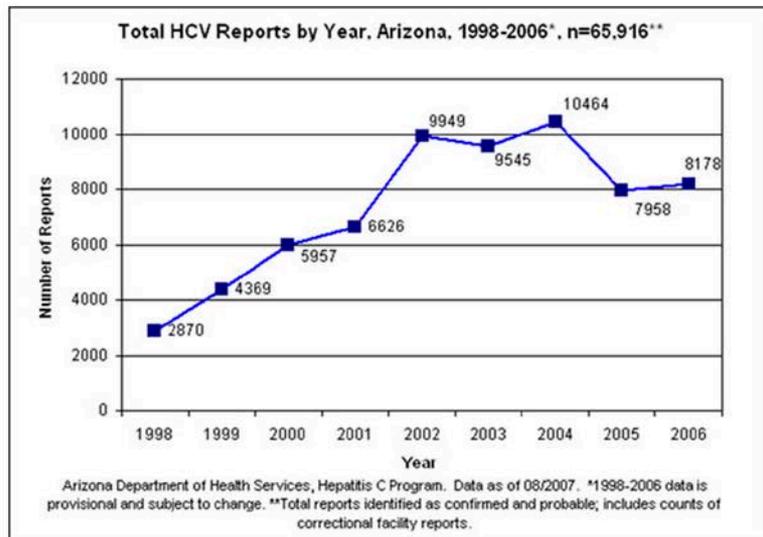
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- **2.7-3.9 millions Americans infected with HCV**
- **45-85% are unaware they are infected**

# Prevalence of HCV Infection by Age and Race/Ethnicity in the United States, 1988-1994



# Prevalence of HCV Infection by Year and Age in the Arizona, 1988-2008





# IDENTIFICATION OF PERSONS INFECTED WITH HCV: *Populations at Risk*

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- **Transfusion of blood products before 1992**
- **Intravenous drug use**
- **Nasal inhalation of cocaine**
- **Chronic renal failure on dialysis**
- **Incarceration**
- **Occupational exposure to blood products**
- **Transplantation of an organ/tissue graft from an HCV-positive donor**
- **Body piercing and potentially tattoo**

# IDENTIFICATION OF PERSONS INFECTED WITH HCV: *Universal Screening of Persons Born 1945-65*

**TABLE 1. Number and prevalence of persons born during 1945–1970 positive for anti-HCV and with chronic HCV infection, by birth cohort — National Health and Nutrition Examination Survey, United States, 1999–2008**

Birth cohort	U.S. population (in millions)*	Anti-HCV		Chronic HCV infection	
		No. (in millions)	(Weighted %) <sup>†</sup>	No. (in millions) <sup>§</sup>	(%)
1945–1965	84.2	2.74	(3.25)	2.06	76.6
1950–1970	89.2	2.89	(3.24)	2.17	80.6
1945–1970	105.1	3.15	(3.00)	2.36	87.3
1950–1965	68.3	2.47	(3.61)	1.85	69.9
1950–1960	45.6	1.83	(4.01)	1.37	52.3
1945–1949	13.2	0.21	(1.58)	0.16	6.7
1966–1970	20.9	0.41	(1.94)	0.30	10.8

**Abbreviations:** HCV = hepatitis C virus; anti-HCV = antibody to hepatitis C virus.

# HCV Testing and Linkage to Care

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- **US Preventive Services Task Force Guidelines expanded screening**

HCV testing is recommended at least once for persons born between 1945 and 1965.

Rating: Class I, Level B



**Accounts for 75% of all HCV infections**

Other persons should be screened for risk factors for HCV infection, and one-time testing should be performed for all persons with behaviors, exposures, and conditions associated with an increased risk of HCV infection.

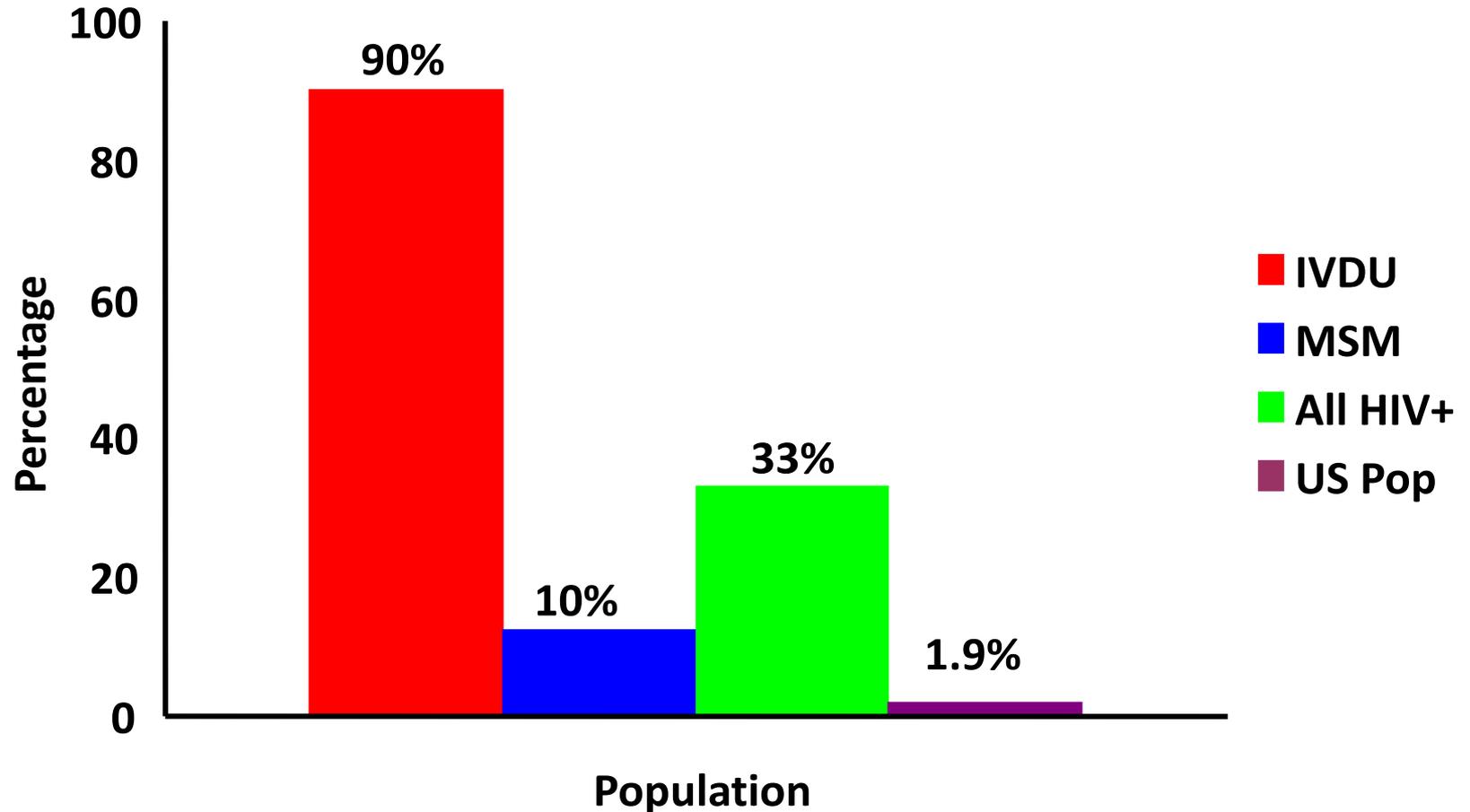
Rating: Class I, Level B

Annual HCV testing is recommended for persons who inject drugs and for HIV-seropositive men who have unprotected sex with men. Periodic testing should be offered to other persons with ongoing risk factors for exposure to HCV.

Rating: Class IIA, Level C

# Prevalence of HCV/HIV Co-infection

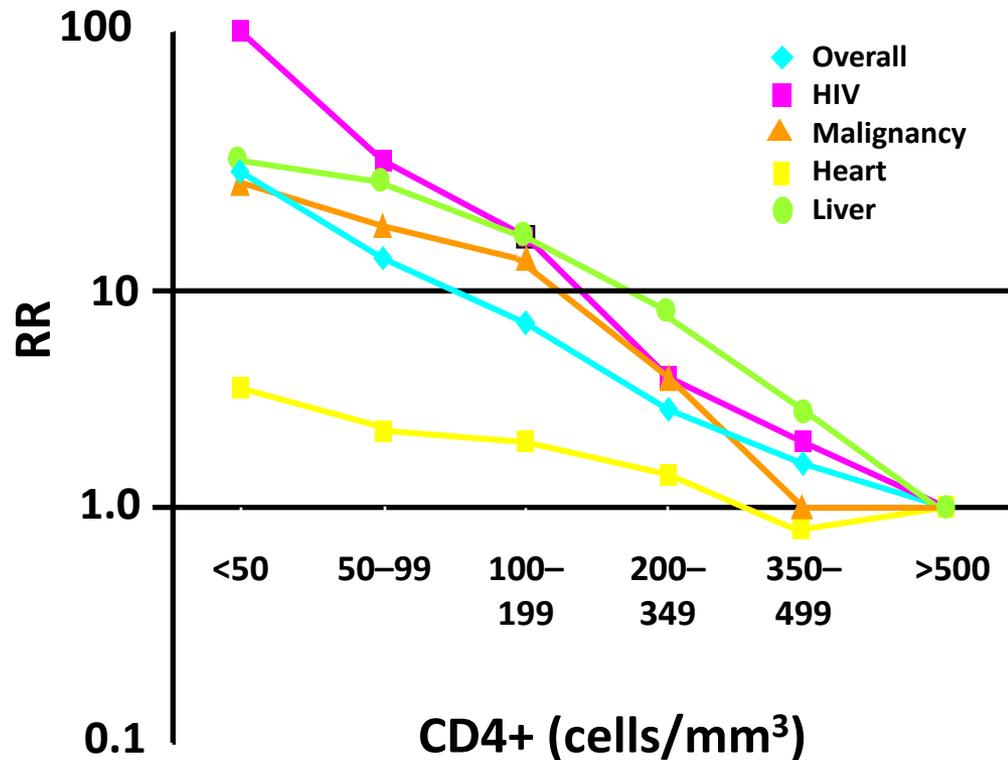
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# Risk of Death in HIV-Infected (D:A:D Study)

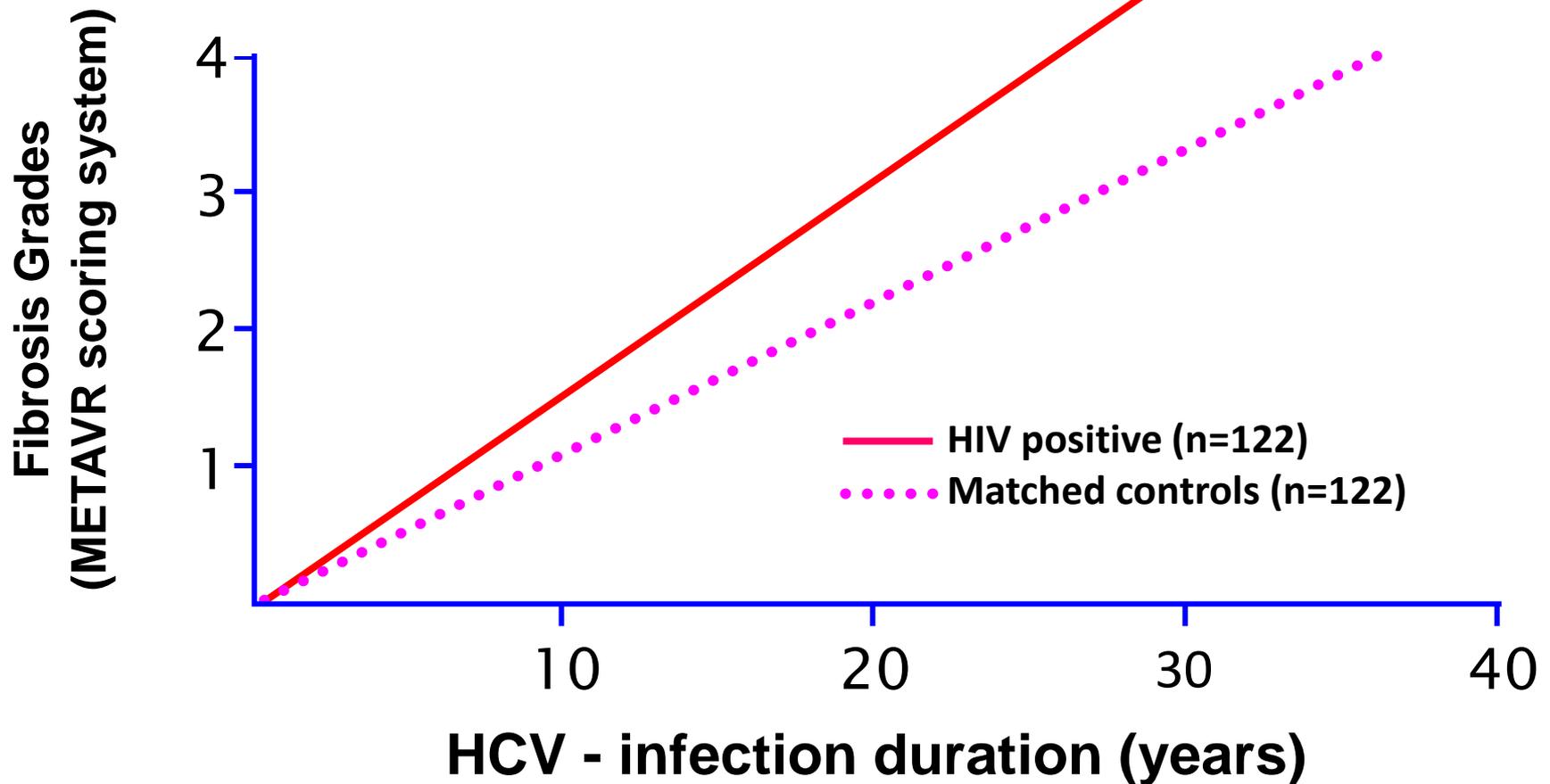
- Cohort study of >23,000 patients in Europe, Australia, and the USA
- 1248 (5.3%) deaths 2000–2004 (1.6/100 person-years)
  - Of these, 82% on ART
- Leading causes of death
  - AIDS (30%)
  - **Liver disease (14%)**
  - Heart disease (9%)
  - Malignancy (8%)
- Predictors of liver-related death:
  - Age (RR: 1.3 per 5 years older)
  - IDU (RR: 2 vs MSM)
  - CD4+ (RR: 1.23 per halving of CD4)
  - **Anti-HCV+ (RR: 6.7)**
  - HBsAg+ (RR: 3.7)

RR of death according to immune function and specific cause



# HIV Coinfection Accelerates Liver Fibrosis Progression Rate

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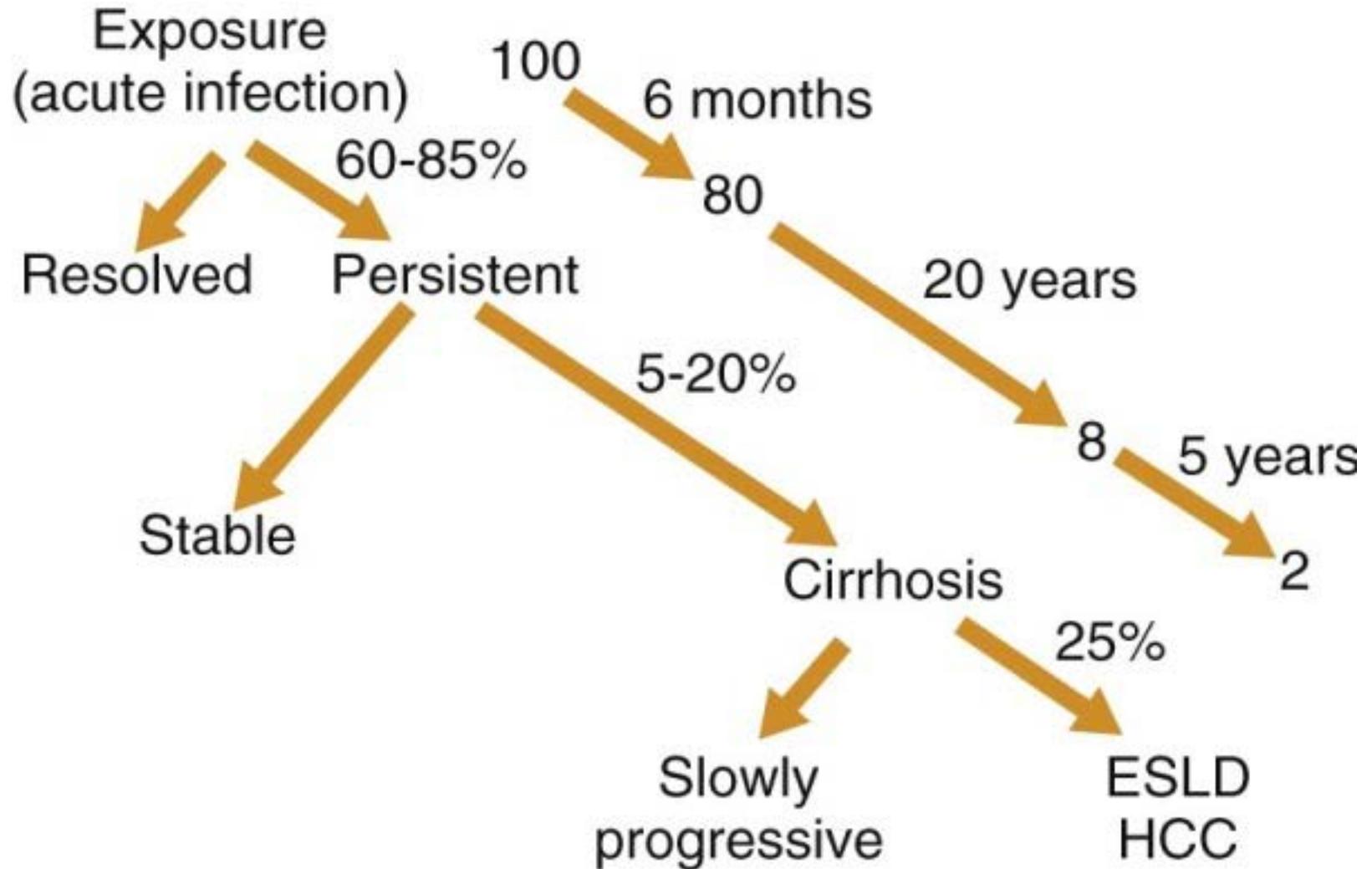


# Clinical Manifestations of HCV

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# Natural History of HCV

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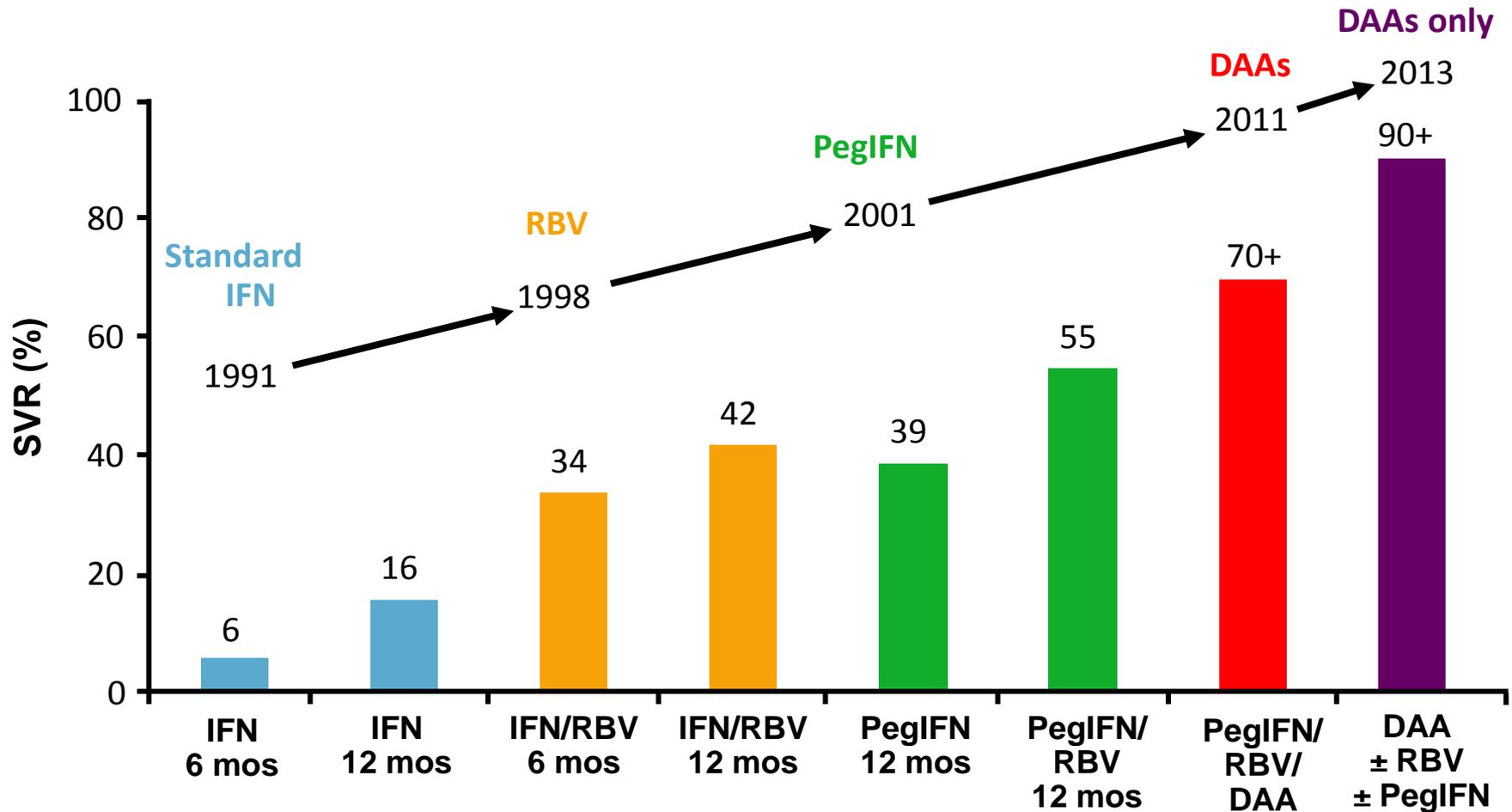


# HCV Therapy and Goals

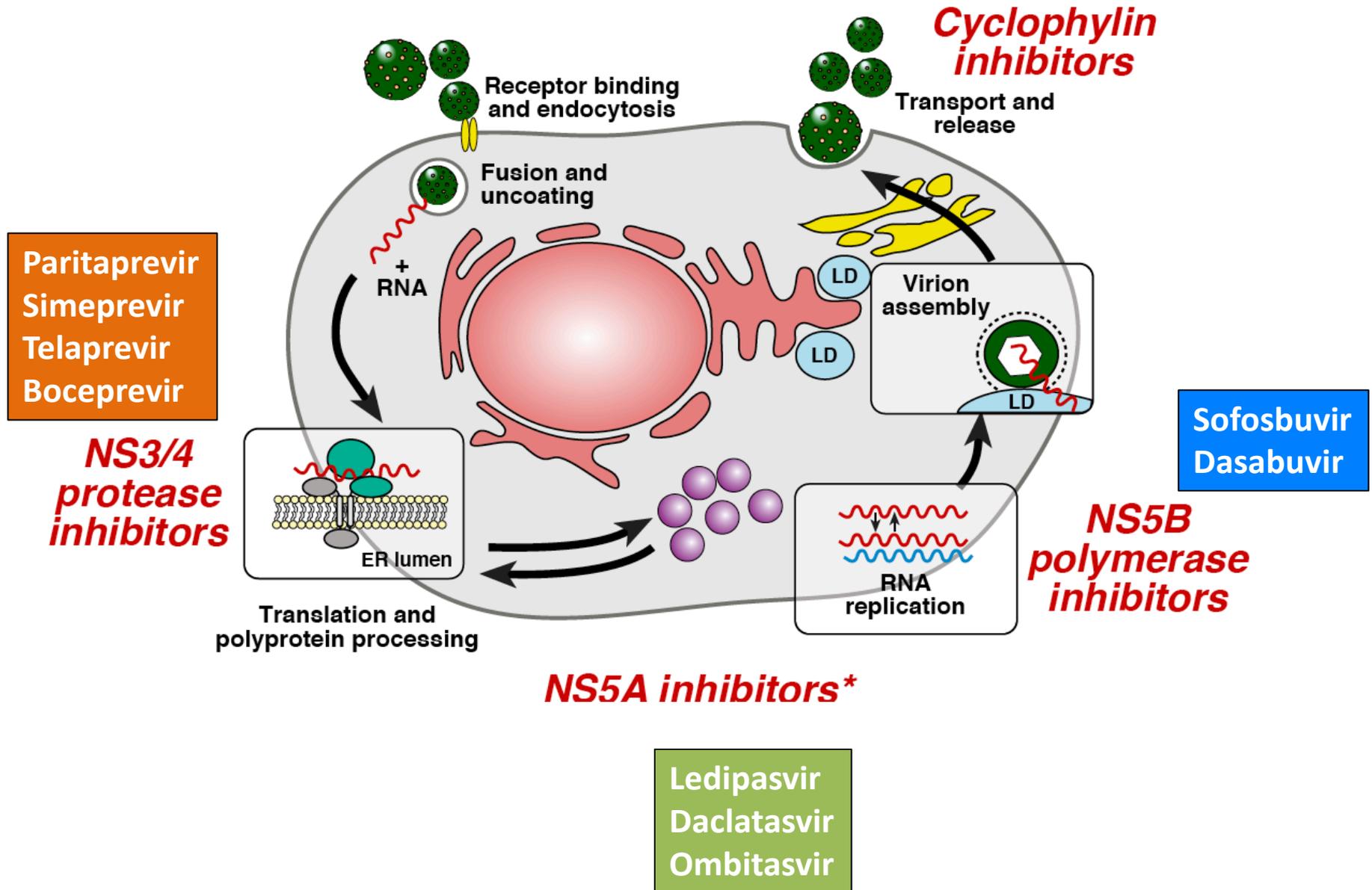
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- **Eradicate HCV**
- **Improve liver histology**
- **Improved clinical outcomes**
  - **Decreased Decompensation**
  - **Decreased Esophageal Varices**
  - **Decreased Hepatocellular carcinoma**
  - **Decreased Mortality**

# Changing Treatment Paradigms for HCV



# DAA Targets



# IDSA/AASLD Guidelines Overview

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AMERICAN ASSOCIATION FOR  
THE STUDY OF LIVER DISEASES



## **HCV Guidance: Recommendations for Testing, Managing, and Treating Hepatitis C**



- 1. HCV Testing and Linkage to Care**
- 2. When to Treat**
- 3. Initial Treatment**
- 4. Retreatment**
- 5. Monitoring Patients On or PostTherapy**
- 6. Unique Patient Populations**
- 7. Management of Acute HCV Infection**

# Important Points When Interpreting HCV Guidelines

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- **Treatment for HCV is rapidly changing with the development and approval of directly acting antivirals (DAAs)**
- **Guidance provides up-to-date recommendations and are up dated regularly**

# Important Points When Interpreting HCV Guidelines

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- **Most patients can be cured with 8-24 weeks of all oral therapy.**
  - **>90% cure rates**
- **Cost of medications is high (~94,000)**
  - **Many restrictions by insurers on types of patients that can be treated**

# Strategy for HCV Cure

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## Emerging HCV Therapy

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graph TD; A[Emerging HCV Therapy] --> B[High cure rate<br/>All oral therapy<br/>Low pill burden<br/>Shorter course<br/>Fewer side effects]; A --> C[Reinfection<br/>Resistance<br/>Screening<br/>Linkage to care<br/>Economics];
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**High cure rate**  
**All oral therapy**  
**Low pill burden**  
**Shorter course**  
**Fewer side effects**

**Reinfection**  
**Resistance**  
**Screening**  
**Linkage to care**  
**Economics**

# Eradication of Hepatitis C a Possibility

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To Your Health

## Eradication of hepatitis C on the horizon

-Washington Post 2014

### Global Eradication of Hepatitis C Virus: A Herculean Task

Rajinder M Joshi\*

Nuclear Medicine and Laboratory Center, Yiacco Medical Co. Al Adan Hospital, Kuwait

*Antiviral Res.* 2014 Oct;110:79-93. doi: 10.1016/j.antiviral.2014.07.015. Epub 2014 Aug 7.

#### Can hepatitis C be eradicated in the United States?

Edlin BR<sup>1</sup>, Winkelstein ER<sup>2</sup>.

### Hepatitis C: only a step away from elimination?

-Lancet 2015

## Gilead uses Georgia as free-drug testbed for hepatitis C elimination

LONDON | BY BEN HIRSCHLER

# Eradication of Hepatitis C a Possibility

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- **Sensitive and specific disease detection**
  - **Simple therapies with high cure rates and tolerability**
  - **No animal reservoir**
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- **Political and Social Will Required!**

# Conclusions

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- **Treatment for hepatitis C has evolved rapidly in the past 3 years to simple, all oral regimens with high cure rates**
- **Increased screening and linkage to care is required as most patients with hepatitis C do not know they are infected**
- **Political and social will required to improve patient access to drugs**
- **Possibilities ahead for global eradication/elimination, with pilot projects being done**

Thank you