

Advances in HCV Therapy



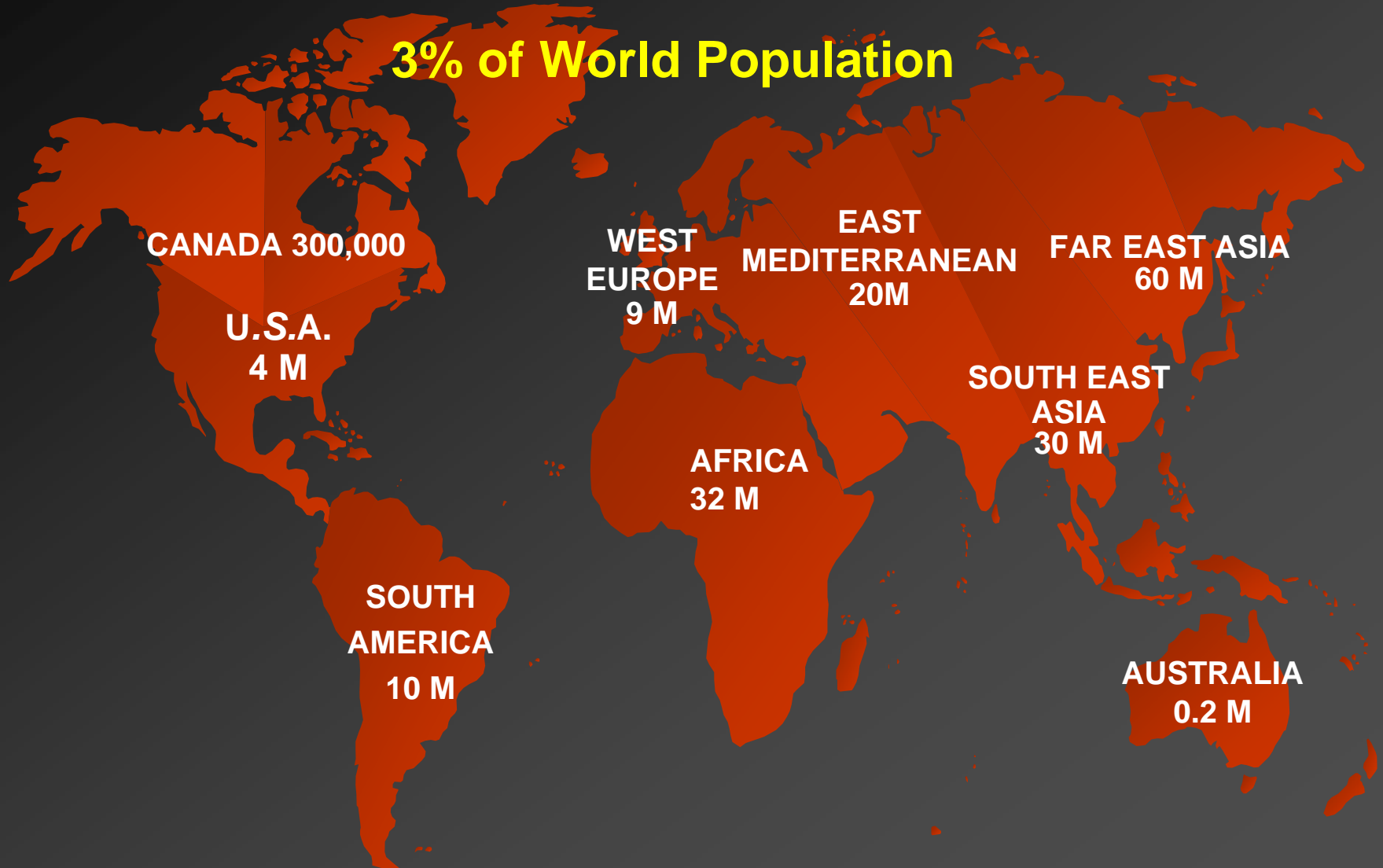
Hepatitis C Virus (HCV)

- Discovered in 1989 as a small RNA blood-borne virus with a large reservoir of chronic carriers worldwide
- Major cause of posttransfusion hepatitis prior to 1992
- Major cause of chronic liver disease, cirrhosis, and hepatocellular carcinoma worldwide
- Prevalence is 0.8% of the CDN population
- 1990-2015: estimated 4-fold increase in the number of patients diagnosed with HCV in Canada

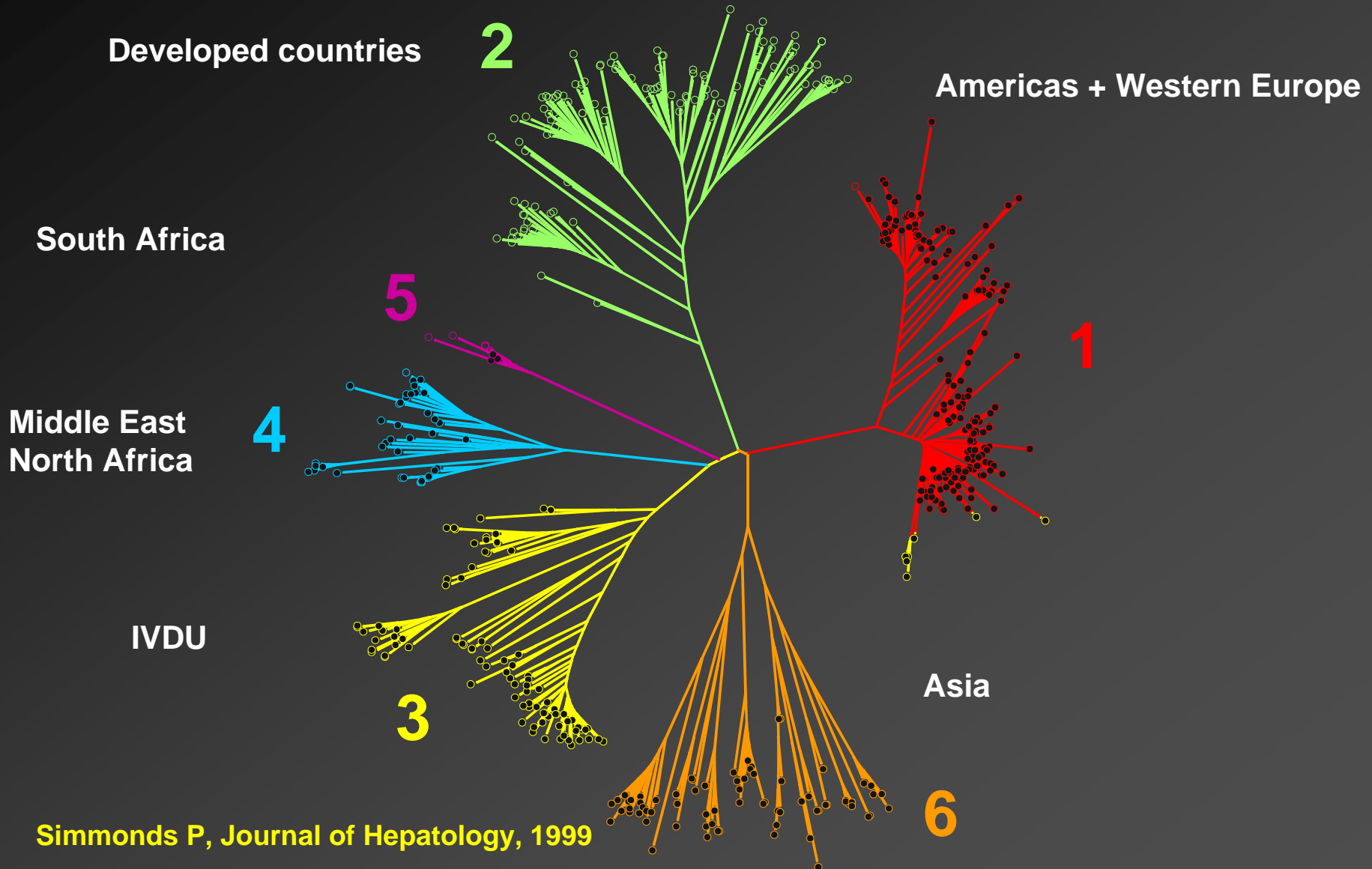
HCV: A Global Health Problem

170 Million Carriers Worldwide, 3 - 4 MM new cases/year

3% of World Population



HCV Genotypes and Subtypes



Simmonds P, Journal of Hepatology, 1999

Acute Hepatitis C Clinical Presentation and Natural History

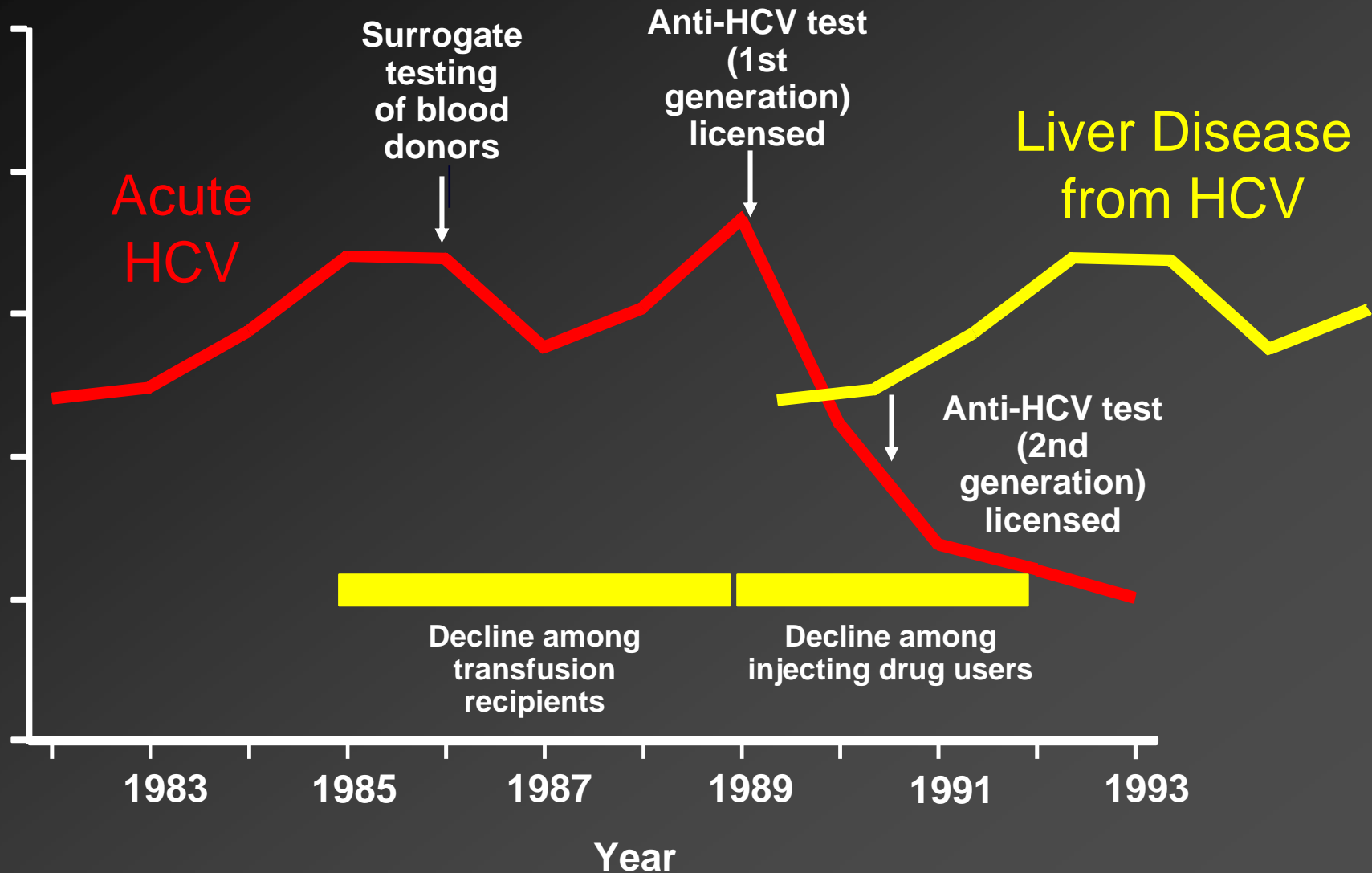
- HCV RNA can be detected in blood within 1-3 weeks after exposure
- Implications for Healthcare Workers
- Average time from exposure to seroconversion is 8-9 weeks
- Average time from exposure to symptoms period 6-7 weeks
- Liver injury (elevations in ALT) with 4-12 weeks
- Symptoms develop in only of 20% of patients
 - Nonspecific 10%-20%
 - Jaundice in only 20%-30%

CDC. MMWR. 1998; 47(No. RR-19):1-39.

Hoofnagle JH Hepatology. 1997;26 (suppl 1): 15S-20S

NIH Consensus Development Conference Panel Statement Management of Hepatitis C, 2002

Incidence of HCV: Infection vs Disease*



*Adapted from Brown RS. Epidemiology and Natural History of Hepatitis C. Presented at an ACG Clinical Implications meeting April 6, 2000 in Dallas, TX.

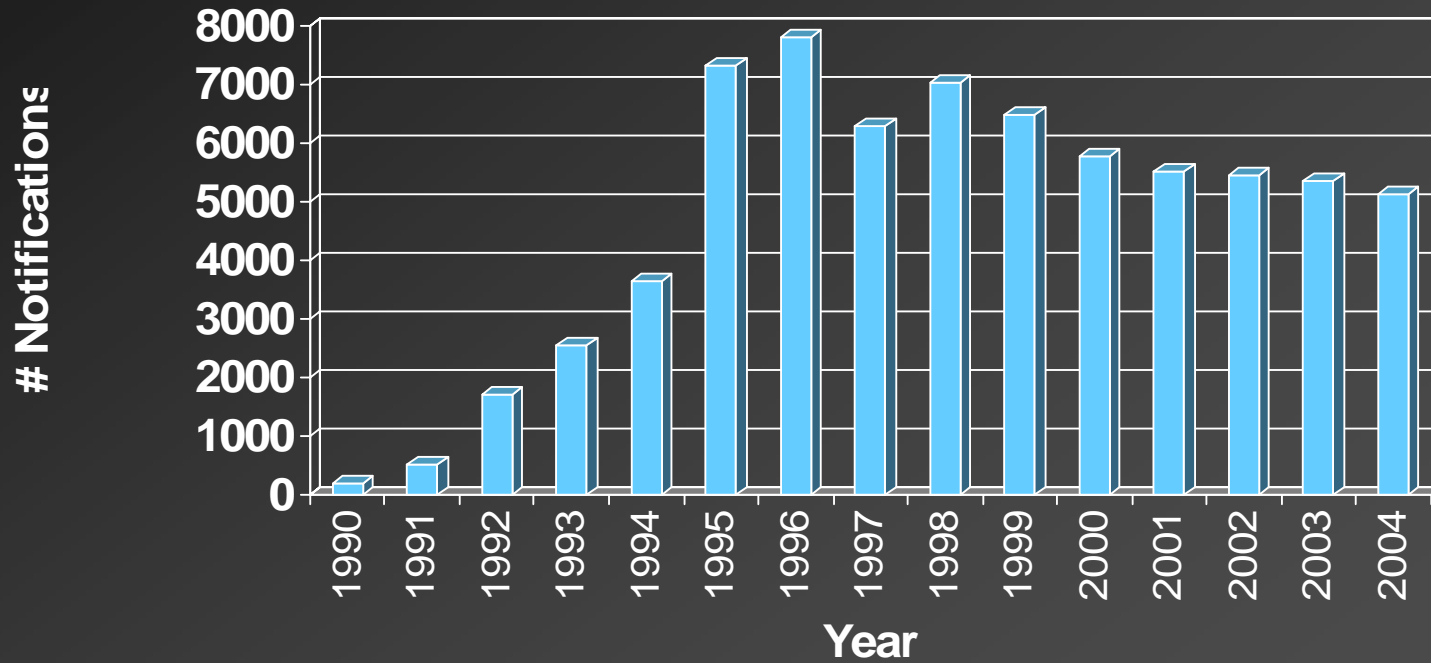
Source: CDC Sentinel Counties Study of Acute Viral Hepatitis

Epidemiology

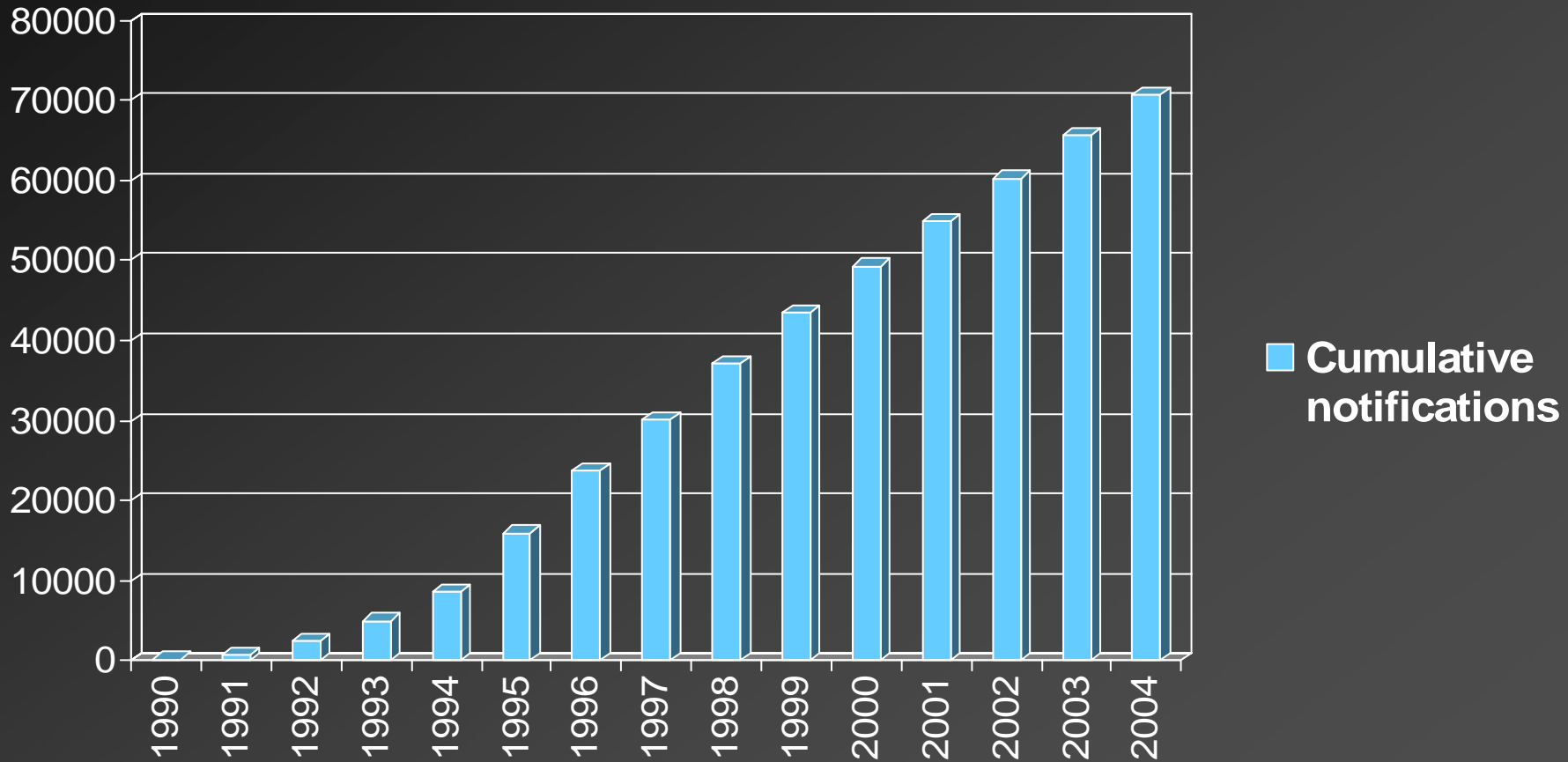
- Estimated number infected
 - 0.8% anti HCV positively, > % male
 - 250,000-300,000
 - Majority between 25 and 45 years of age
- Estimated number diagnosed (2001)
 - 100,000-120,000
 - 2nd most frequently reported disease
 - 8000 new infections per year
 - 2000 acute

Hepatitis C in Ontario

HCV notifications by year

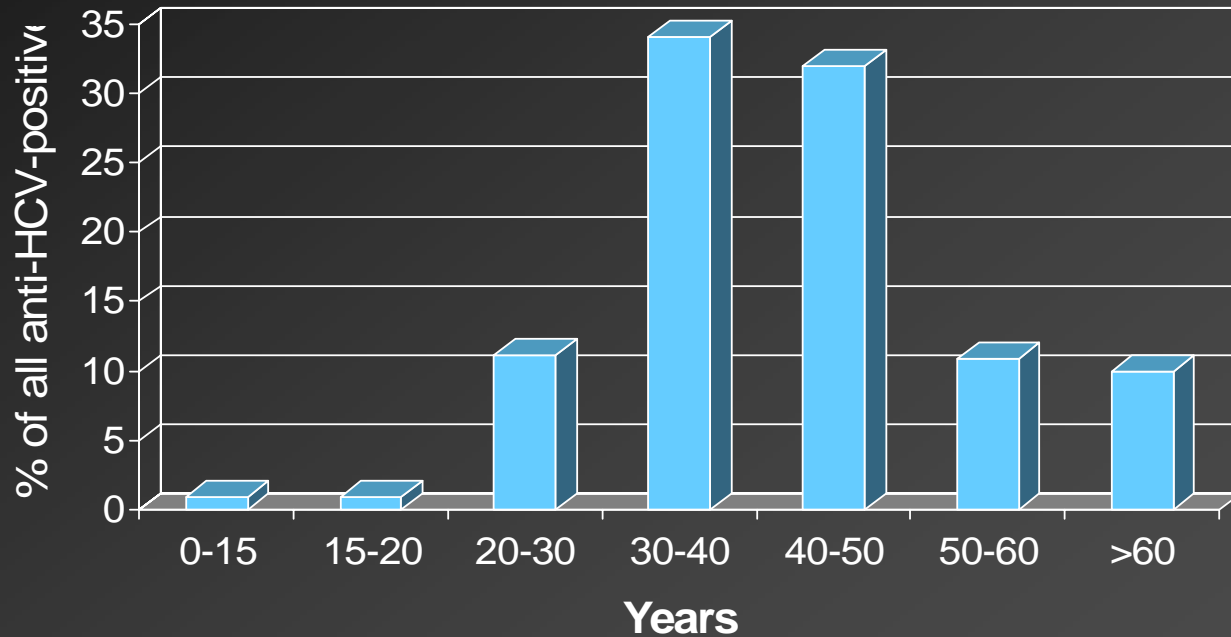


Hepatitis C in Ontario



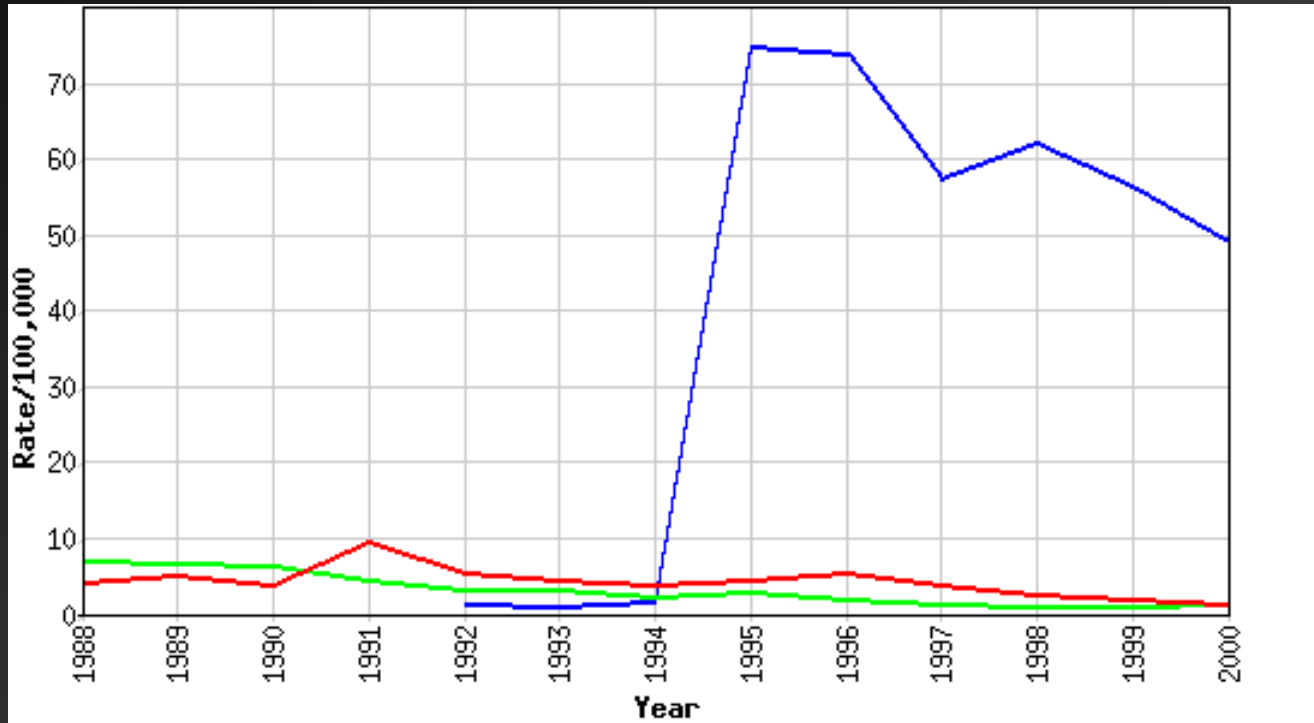
Hepatitis C in Ontario

Age distribution of positive anti-HCV results



Hepatitis C - Incidence over Time

Both Sexes Combined, All Ages, Ontario, 1988-2000
Rate per 100,000



		1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000
Hepatitis A	—	4.43	5.21	4.00	9.73	5.53	4.64	3.93	4.52	5.54	4.00	2.75	2.15	1.33
Hepatitis B, Viral	—	7.20	6.75	6.37	4.73	3.19	3.19	2.47	2.86	2.16	1.56	1.22	1.22	1.28
Hepatitis C	—					1.47	1.16	1.61	75.09	73.98	57.53	62.24	56.56	49.30

Chronic Hepatitis C

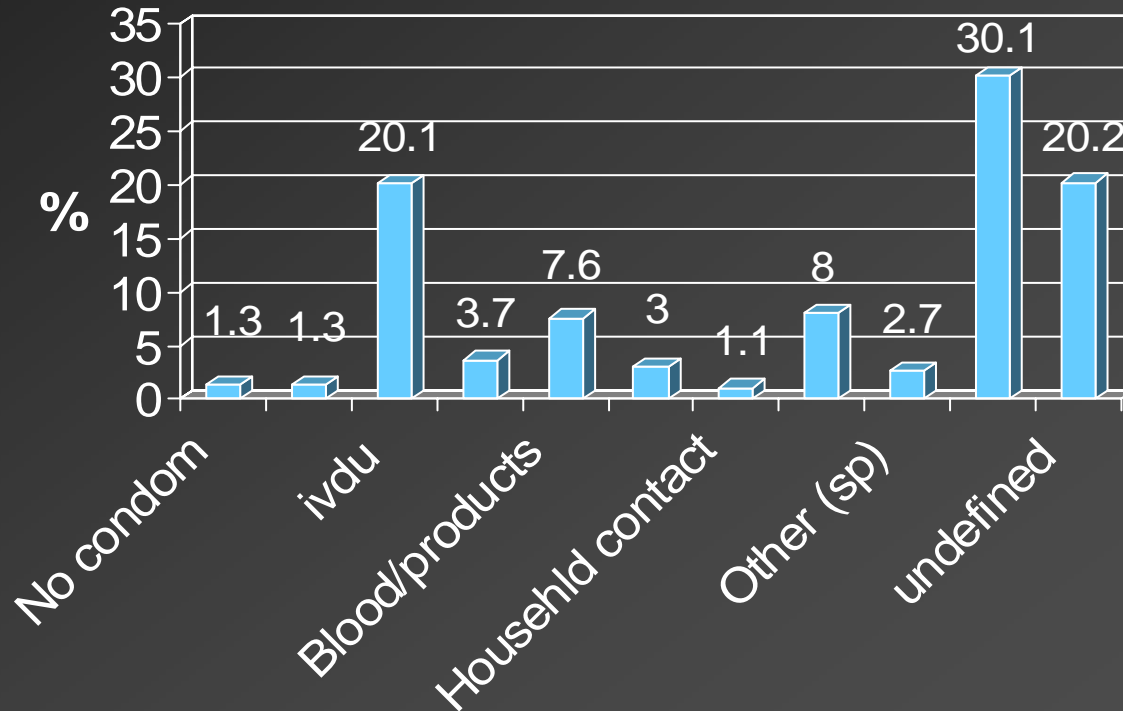
- A leading cause of cirrhosis in the Canada
- 1,000-2,000 deaths/yr
 - This number expected to triple in the next 10 to 20 years (*without therapy*)
- Associated with an increased risk of liver cancer
- Most common reason for liver transplantation in Canada

Epidemiology of Hepatitis C

- How many patients are there in Ontario?
 - Remis estimate
 - 100,000-130,000 patients
- Who are they (estimates)?
 - Ex/current IDU
 - Immigrants from endemic areas
 - Recipients of blood/blood products
 - Others
 - ? Sexual, ? cocaine, ? tattoos, etc

Hepatitis C in Ontario

% anti-HCV-positive by risk factor (last 5 years)



Risk Factors for HCV

- Intravenous drug use (even one-time use)
- High risk country of origin
- Transfusions of blood or blood products before 1992
- Current recipients of multiple blood transfusions
- Hemophiliacs given clotting factors
- Sexual partners of intravenous drug users
- Intranasal cocaine use
- Tattooing or body piercing
- Medical procedures in other countries
- Long-term hemodialysis
- History of imprisonment
- High risk sexual contact, patients with multiple sexual partners
- Occupational exposure to blood or blood products
- Receiving an organ, graft, or tissue transplant from an HCV-positive donor
- Health-care workers exposed to needle-stick and sharp injuries
- Patients with sexually transmitted diseases, HIV, HBV

HCV Infection: Extrahepatic Manifestations

Hematologic

- Mixed cryoglobulinemia
- Aplastic anemia
- Thrombocytopenia
- Non-Hodgkin's β -cell lymphoma

Dermatologic

- Porphyria cutanea tarda
- Lichen planus
- Cutaneous necrotizing vasculitis

Renal

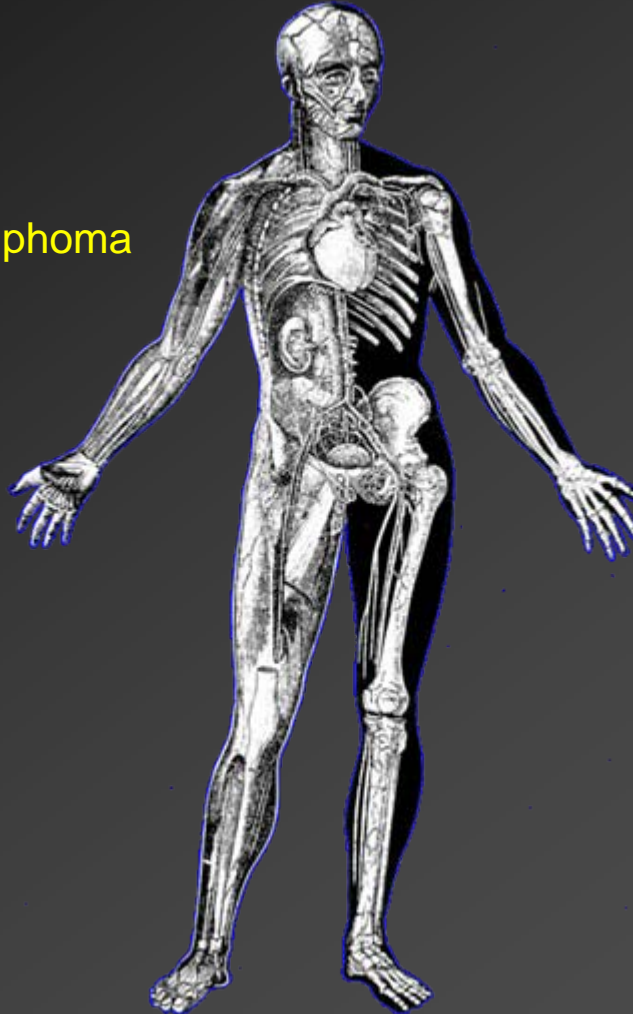
- Glomerulonephritis
- Nephrotic syndrome

Endocrine

- Anti-thyroid antibodies
- Diabetes mellitus

Salivary

- Sialadenitis



Ocular

- Corneal ulcer
- Uveitis

Vascular

- Necrotizing vasculitis
- Polyarteritis nodosa

Neuromuscular

- Weakness/myalgia
- Peripheral neuropathy
- Arthritis/arthralgia

Autoimmune Phenomena

- CREST syndrome

HEPATITIS C AROUND THE WORLD

WHO Region	Total Population (Millions)	Hepatitis C prevalence Rate %	Infected Population (Millions)
Africa	602	5.3	31.9
Americas	785	1.7	13.1
Eastern Mediterranean	466	4.6	21.3
Europe	858	1.03	8.9
South-East Asia	1 500	2.15	32.3
Western Pacific	1 600	3.9	62.2
Total	5 811	3.1	169.7

**Who is At-Risk in Your
Community?**

□ Audience Poll

- **In your clinical practice, what percentage of your patients are Canadian immigrants?**

1.<10%

2.11-20%

3.21-30%

4.31-40%

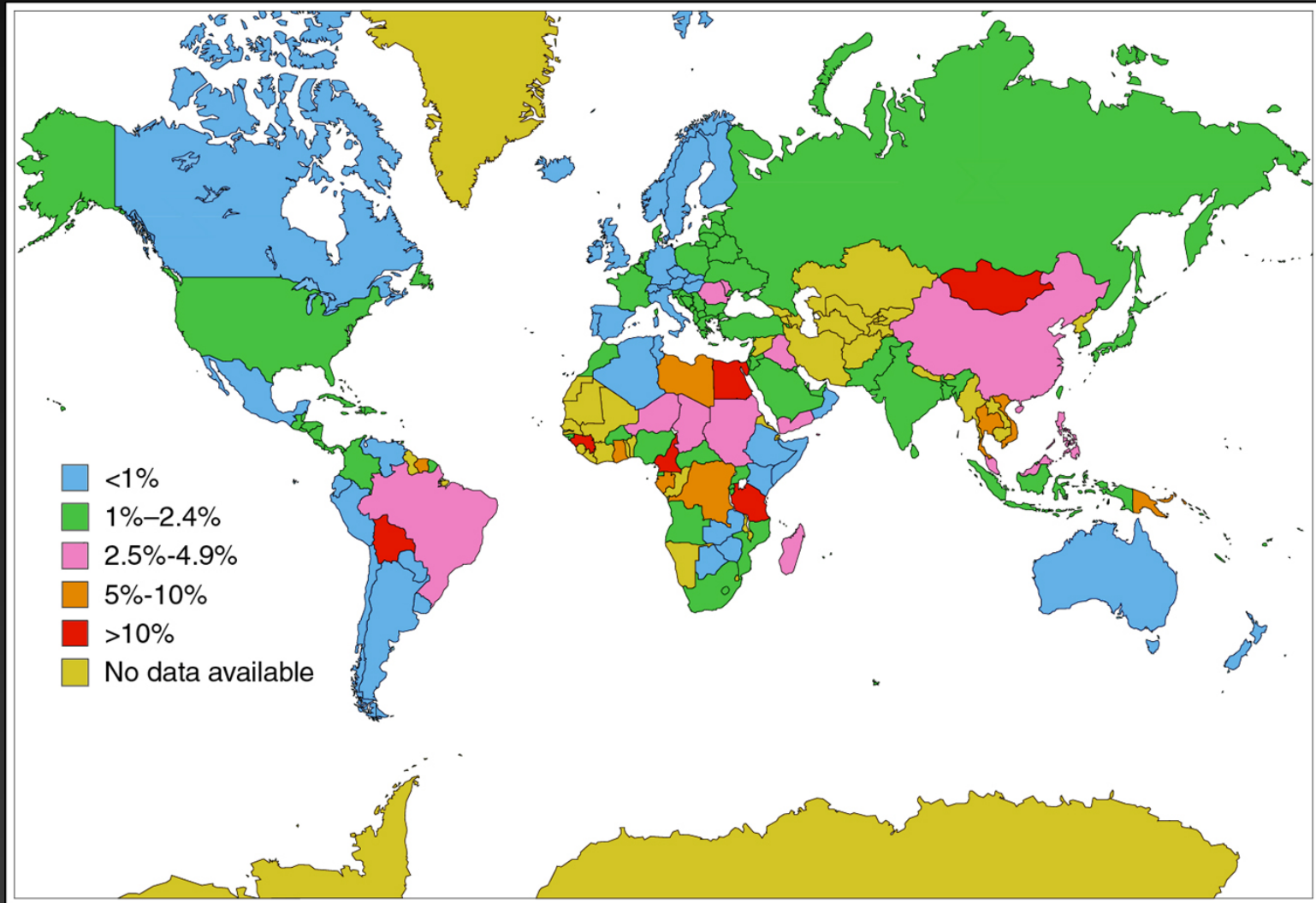
5.>40%

HEPATITIS C IN IMMIGRANTS

COUNTRY	RATE (%)	COUNTRY	RATE (%)
ITALY	0.5	INDIA	1.8
GREECE	1.5	PAKISTAN	2.4
EGYPT	18.1	PHILLIPINES	3.6
SOMALIA	0.9	RWANDA	17.0
HONG KONG	0.5	VIETNAM	6.1
ROMANIA	4.5	RUSSIA	2.0
KOREA	1.7	POLAND	1.4

Worldwide Prevalence

Hepatitis C Virus Infection



HEPATITIS C TRANSMISSION IN ITALY

- PREVALENCE OF HEPATITIS C IN A SOUTHERN ITALIAN TOWN
 - 488 SUBJECTS
 - 1.2% PREVALENCE IN UNDER 30'S
 - 42.1% PREVALENCE IN > 60'S
 - MULTIVARIATE ANALYSIS
 - ASSOCIATION WITH USE OF NON-DISPOSABLE GLASS SYRINGES

HEPATITIS C TRANSMISSION IN ITALY

- RISK FACTORS FOR HEPATITIS C INFECTION IN THE ELDERLY
 - 11.1-11.8% PREVALENCE
 - ASSOCIATED WITH ANTI-HBs
- SUGGESTS PARENTERAL TRANSMISSION
- SUGGESTS EPIDEMIC DURING AND AFTER WWII

HEPATITIS C TRANSMISSION IN ITALY

- GENOTYPE DISTRIBUTION IN ITALY
- GENERAL POPULATION
 - GENOTYPE 1 - 74%
- IVDU'S
 - GENOTYPE 3 - 49%

HEPATITIS C IN CANADA

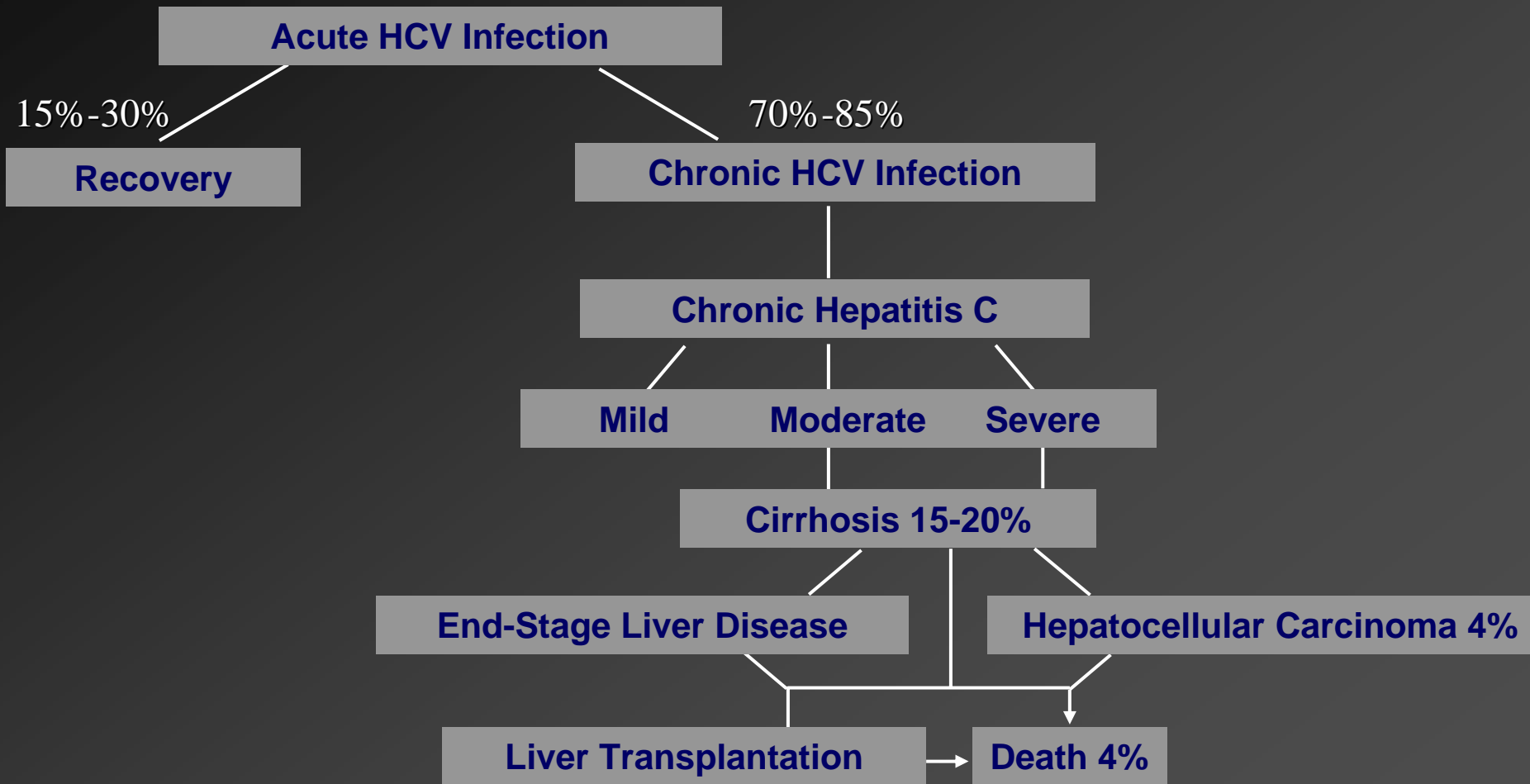
- IMPLICATIONS OF HEPATITIS C IN THE IMMIGRANT POPULATION
 - GENERATION OF MIDDLE-AGED/ELDERLY MEDITERRANEANS AT RISK FOR CIRRHOSIS AND LIVER CANCER
 - INFLUX OF IMMIGRANTS OF ALL AGES FROM HIGH ENDEMIC AREAS WILL DEVELOP CIRRHOSIS AND HCC OVER NEXT 20-30 YEARS

NATURAL HISTORY OF HEPATITIS C INFECTION

■ ACUTE INFECTION

- >90 % ASYMPTOMATIC
 - (POST TRANSFUSION)
- 20-30% “RECOVER” SPONTANEOUSLY
 - MAY HAVE PERSISTENT HCV RNA IN LIVER
- 70-80% DEVELOP CHRONIC INFECTION

HEPATITIS C SPECTRUM OF DISEASE

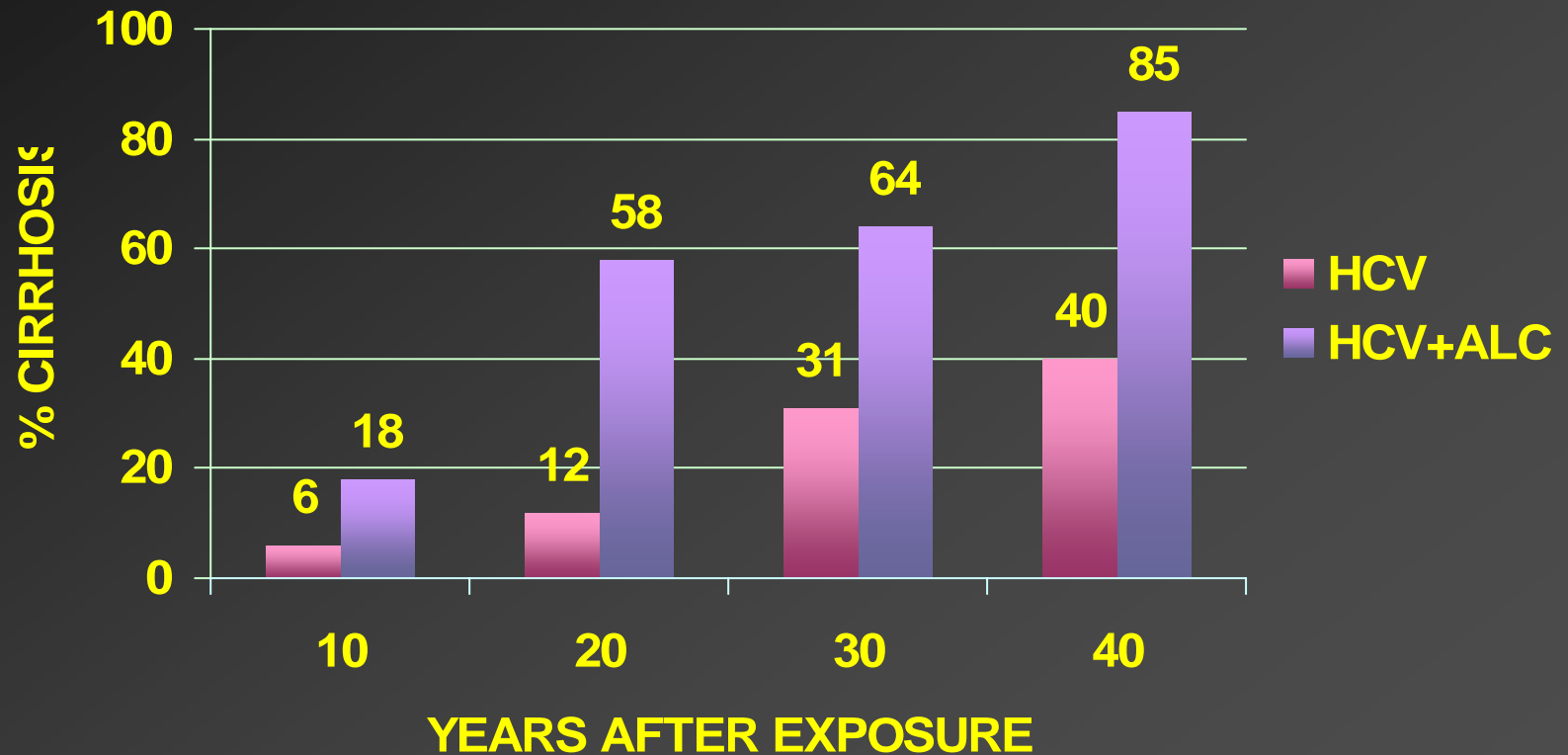


NATURAL HISTORY OF HEPATITIS C

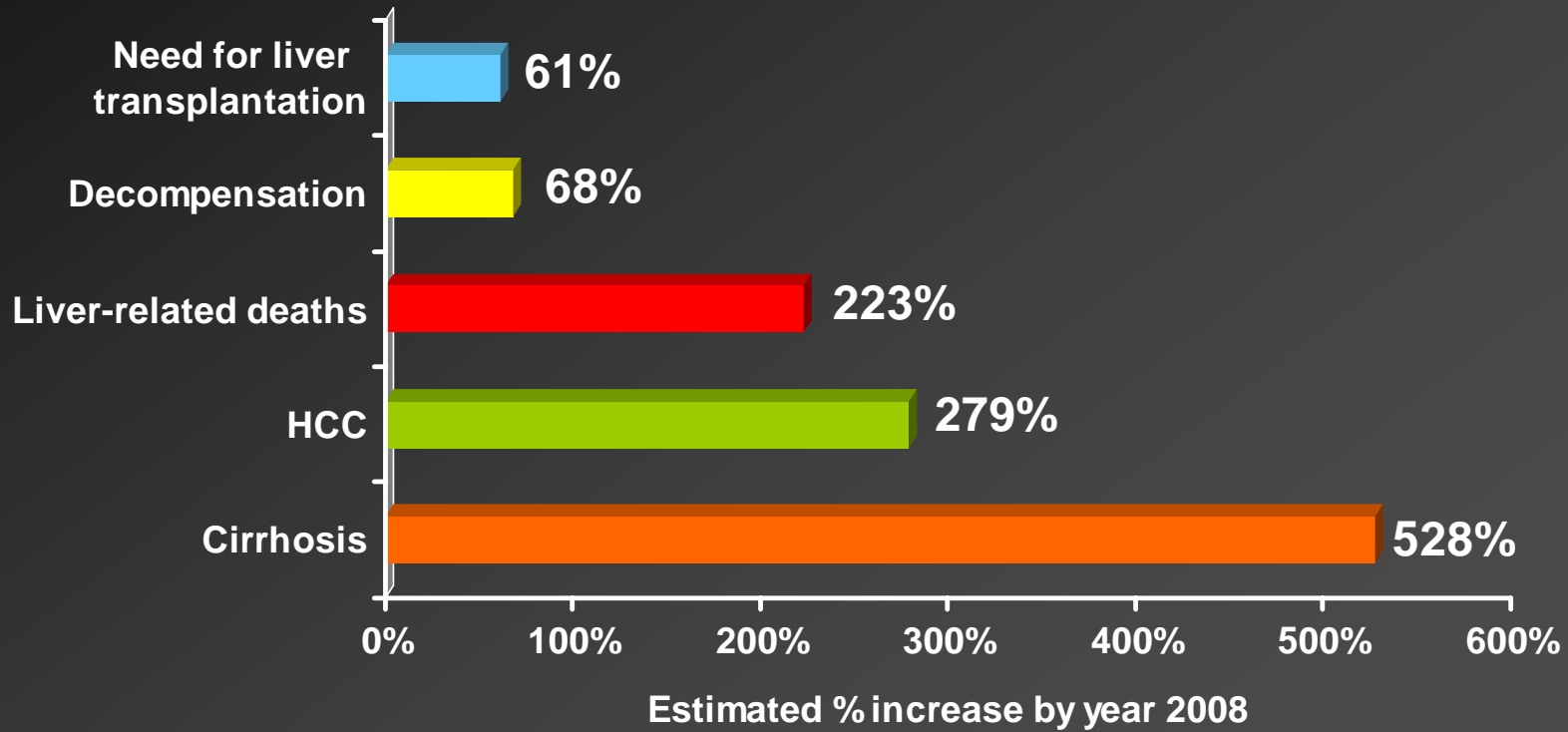
- DETERMINANTS OF PROGRESSION TO CIRRHOSIS
 - Disease duration
 - Comorbid conditions
 - Male, alcohol use, HIV/HBV coinfection
 - Grade of Inflammation

NATURAL HISTORY OF CHRONIC HEPATITIS C

RELATIONSHIP BETWEEN CIRRHOSIS AND YEARS AFTER EXPOSURE



Future HCV Disease Burden in the North America

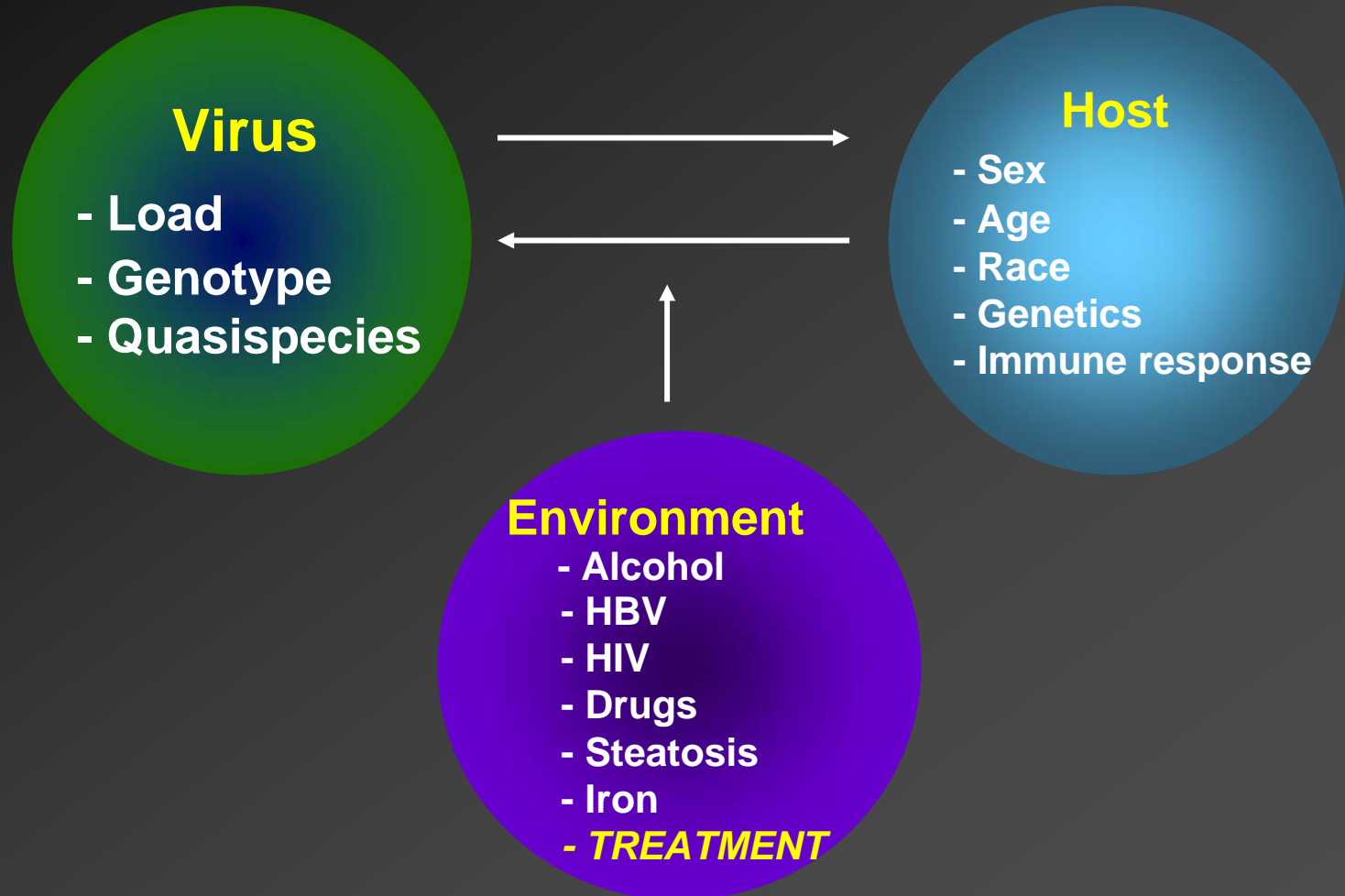


Predictions for 2010-2019

US Numbers

- 193,000 HCV deaths
 - 720,700 million years of advanced liver disease
 - 1.83 million years of life lost
- \$11 billion in direct medical care costs
- \$21.3 and \$54 billion societal costs from premature disability and mortality
- Divide by 10 for canadian equivalent

Factors Which Might Influence The Outcome Of Hepatitis C



Alcohol



Are you sure he said we
can only have one?

Hepatitis C Screening and Diagnosis

Diagnosis of Chronic Viral Hepatitis

Serologic Testing

- ALT levels may be intermittently normal in a significant number of patients who have chronic hepatitis C
- Patients should be tested if they:
 - Have known risk factors for viral hepatitis
 - Indicate possible risk factors for hepatitis
 - Have elevated liver enzymes

Hepatitis C Antibody (Anti-HCV) Test

- EIA test for detection of hepatitis C antibodies
- Sensitivity over 99%
- Detection of anti-HCV following infection averages 12 weeks
- Positive test usually diagnostic in patients with elevated levels of liver enzymes and presence of risk factors
- False negatives in Immunosuppressed and Chronic Dialysis Patients

Hepatitis C Virus RNA Tests

- Determine the presence of actual virus, not anti-HCV antibodies
- Helpful in difficult cases, when antibody tests inconclusive
- *Genotype and viral load necessary pre-Rx.*
- Sensitivity may vary between labs; depends on type of assay

Liver Biopsy

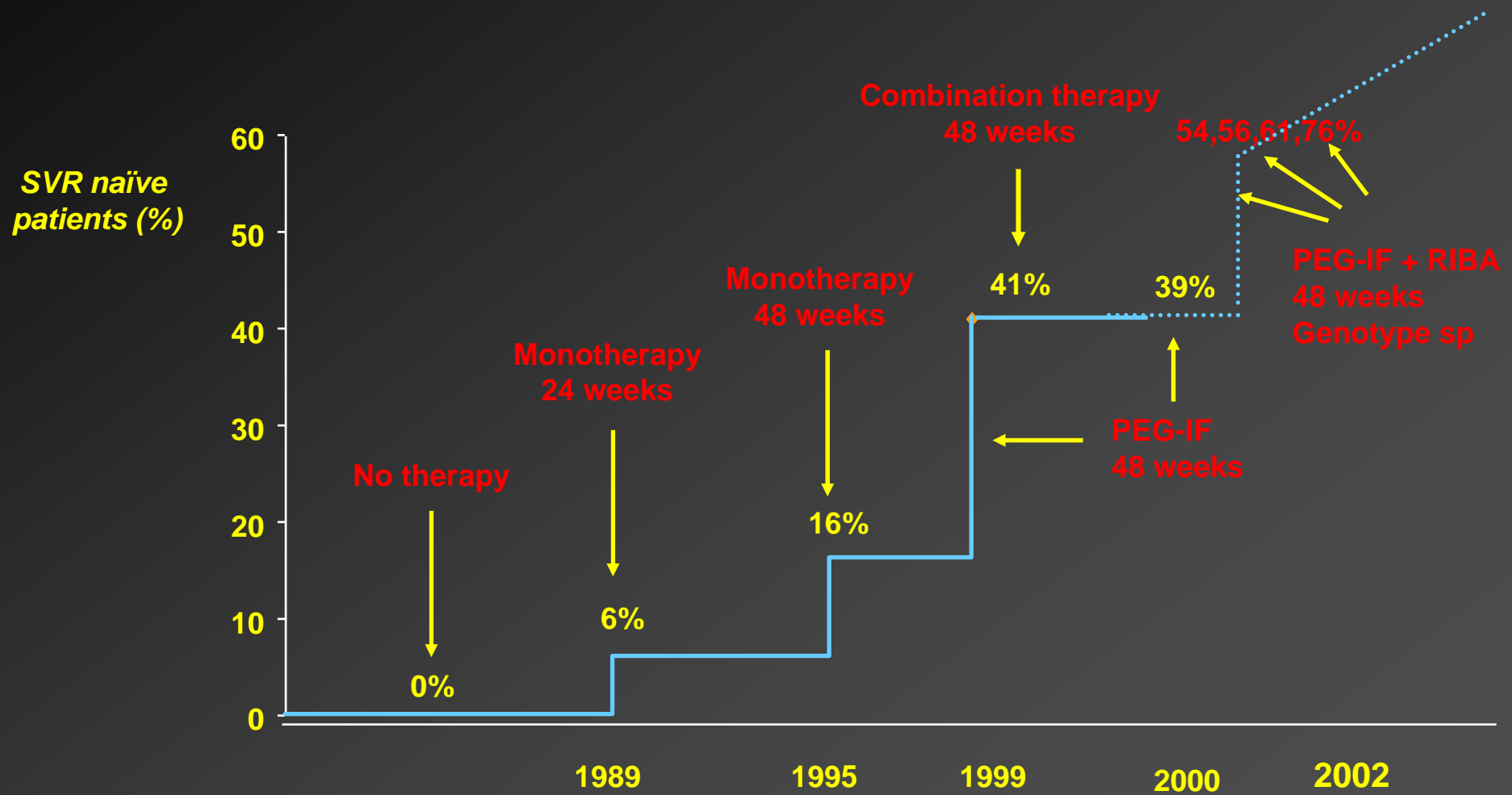
- May be guided by CT or ultrasound
- Provides information regarding
 - Degree of inflammation
 - Disease severity
 - Tissue damage
 - Presence/absence of cirrhosis
- Helps determine
 - Degree of disease progression
 - Cause of liver disease
 - Need for treatment / Patient Motivation
 - Estimate chance of response

Patient Management

- When chronic hepatitis C is diagnosed:
 - Immunize against hepatitis A and hepatitis B
 - Advise patient to avoid alcohol consumption
 - Review all medications, including vitamins, OTC, and herbal medications

Treatment of Hepatitis C

Standard Therapy for HCV



Combined data : Poynard et al (1998), McHutchison et al (1998), Zeuzem et al (2000), Fried et al (2002)

Keys

- Spend time before, during and after Rx.
- Educate patient on Side effects
- Include caregivers
- Stress the positive
- Team approach
- Individualize therapy

Factors that Improve Adherence

- Education and support of the patient
- Ease of dosing
- Management of side effects
- Positive Reinforcement
- Close Follow – Up: *CONTACT*

HCV Summary

- 300,000 Canadian with HCV and growing
- 100,000 in Ontario
- Diagnosis and treatment vital
- Need a high index of suspicion
- Treatment effective
- Health and Economic impact immense

- Only treat those you know!