FAMILY HEALTH CENTERS OF SAN DIEGO

The HCV Treatment Revolution: A view from the Community Health Center

Christian B. Ramers, MD, MPH (ramers@uw.edu)
Assistant Medical Director, Director of Graduate Medical Education – Family Health Centers of San Diego
HIV/HCV Distance Education Specialist – NW AETC, University of Washington School of Medicine
PAETC – University of California, San Diego School of Medicine

UCSD AIDS Clinical Rounds
San Diego, CA – March 14, 2014

Disclosures

- **Speaker's Bureau:** Janssen Therapeutics (HIV), Gilead Sciences (HIV, HCV), AbbVie (HCV)
- **Scientific Advisor:** Gilead Sciences (HIV, HIV/HCV)
- **Grant/Research Support:** CDC/HRSA, Northwest AETC, Pacific AETC
- **Mention will be made of therapeutic combinations not fully evaluated/approved by the FDA (HCV pipeline, 'off-label' combinations)**

FAMILY HEALTH CENTERS OF SAN DIEGO

Learning Objectives

- Review HCV epidemiology and screening recommendations
- Highlight unique aspects of Community Health Center/FQHC environment
- Describe HepCareConnect HCV testing and linkage to care efforts to date
- Contrast HCV with HIV: focus on ‘When to Start?’
- Explore realities of implementing broad-based HCV treatment

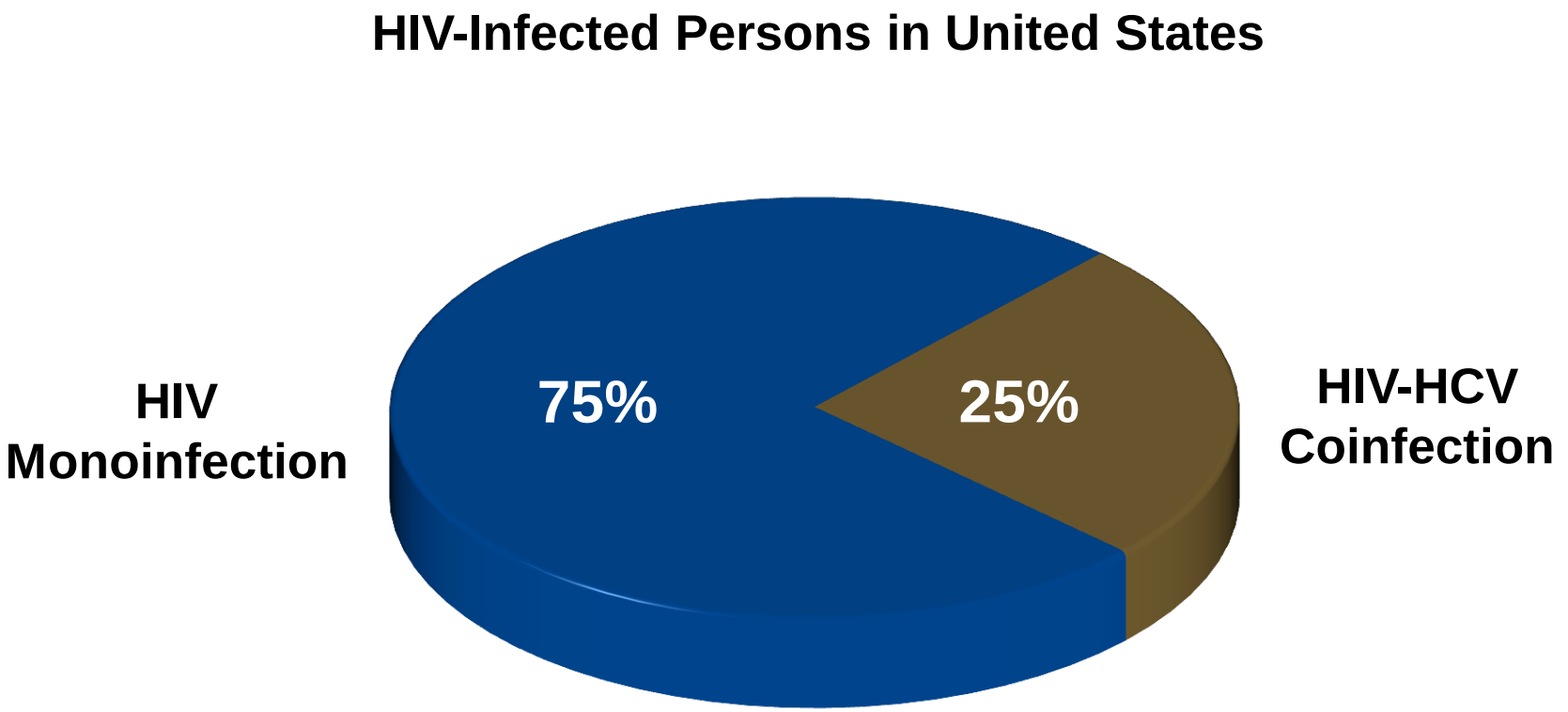
Hepatitis C Epidemiology

The unmet need of HCV screening

Risk Factors for Transmission of Hepatitis C

FAMILY HEALTH CENTERS
OF SAN DIEGO

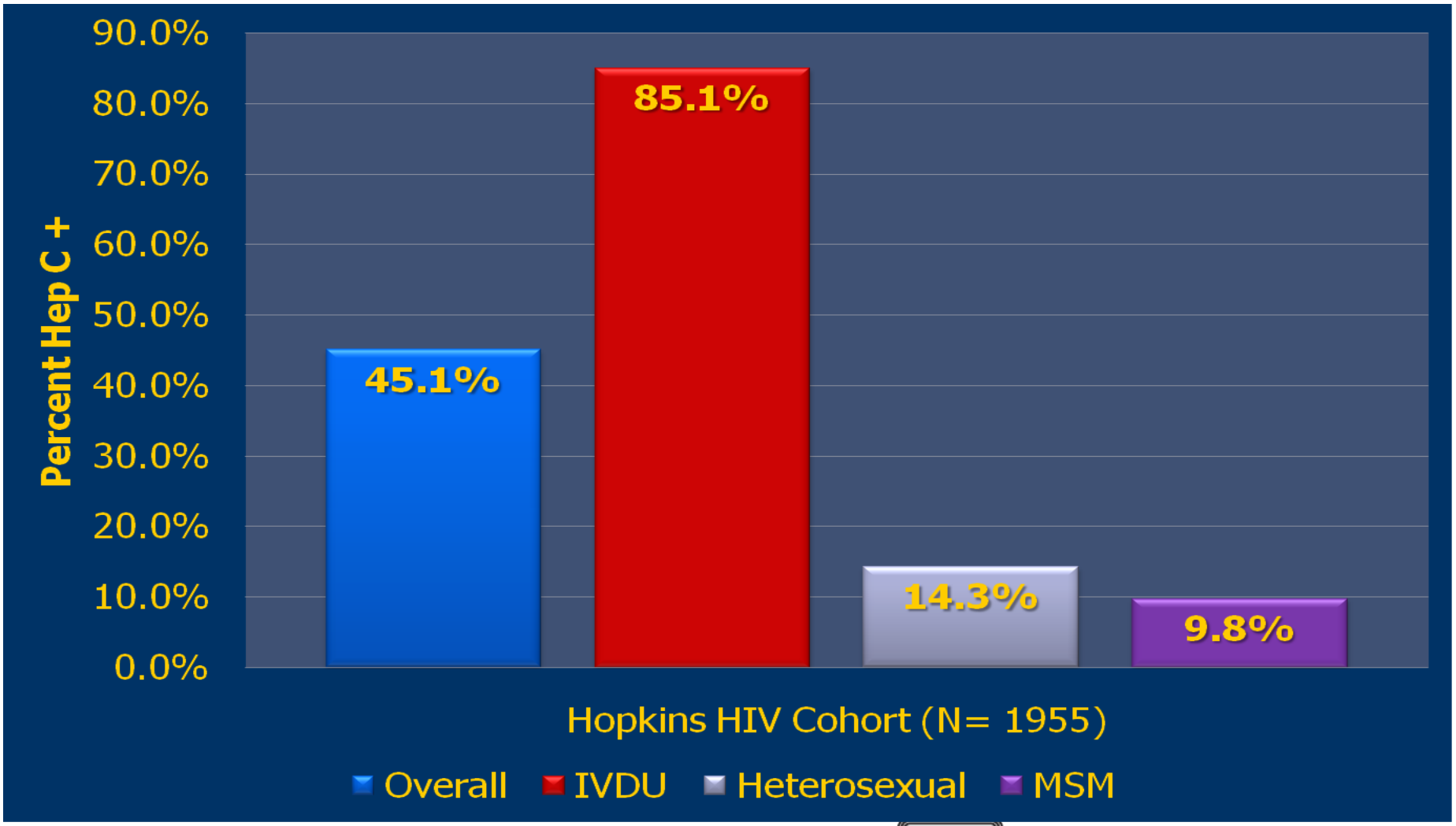
HCV-HIV Coinfection



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

FAMILY HEALTH CENTERS OF SAN DIEGO

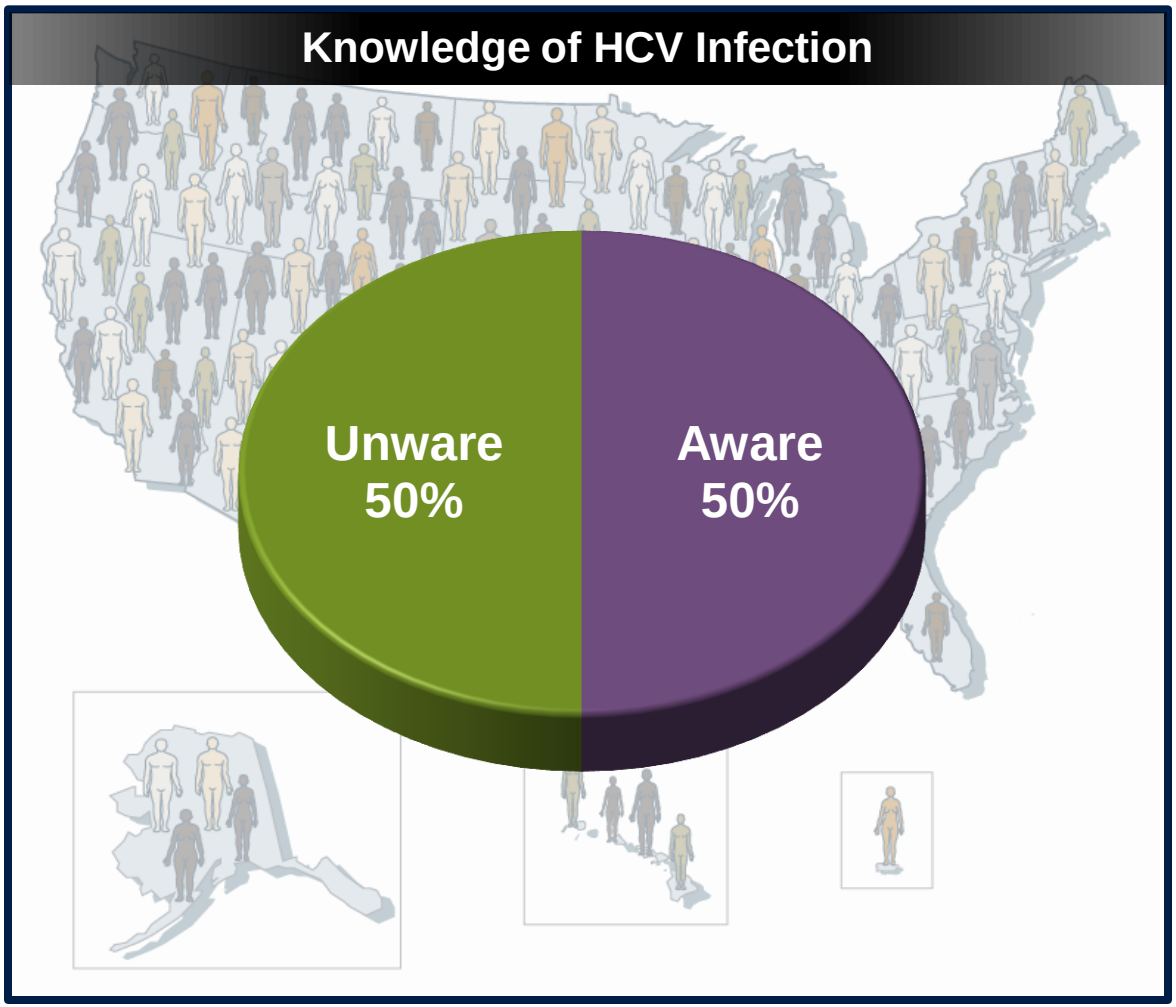
Hepatitis C Prevalence in HIV+ Patients



Sulkowski *et al Ann Int Med* 2003; 138: 197-207

FAMILY HEALTH CENTERS OF SAN DIEGO

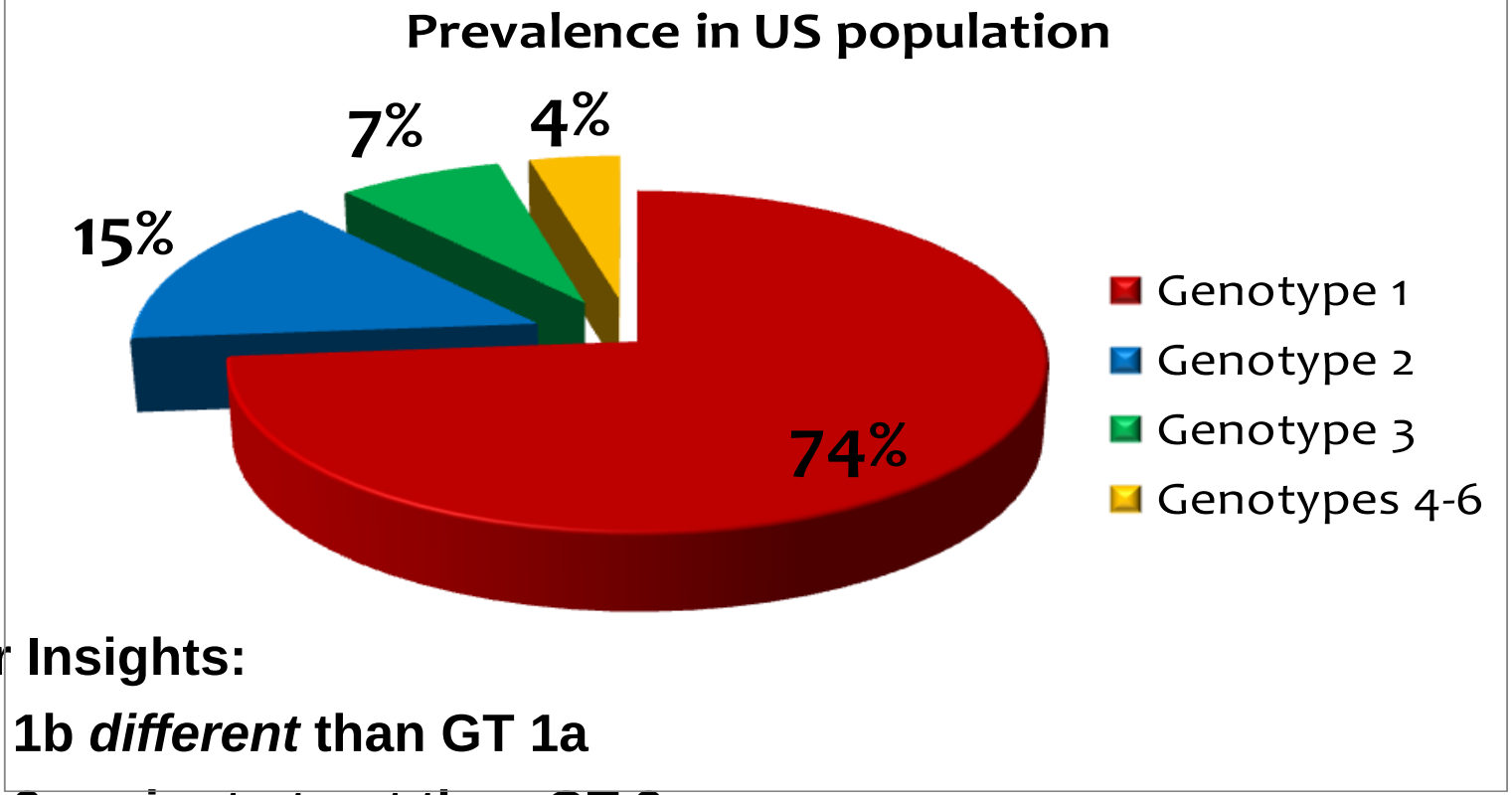
NHANES Survey, United States, 2001-2008
Awareness of HCV Infection Status



Source: Denniston M, et al. Hepatology. 2012:55:1652-61.

FAMILY HEALTH CENTERS OF SAN DIEGO

Hepatitis C Genotypes



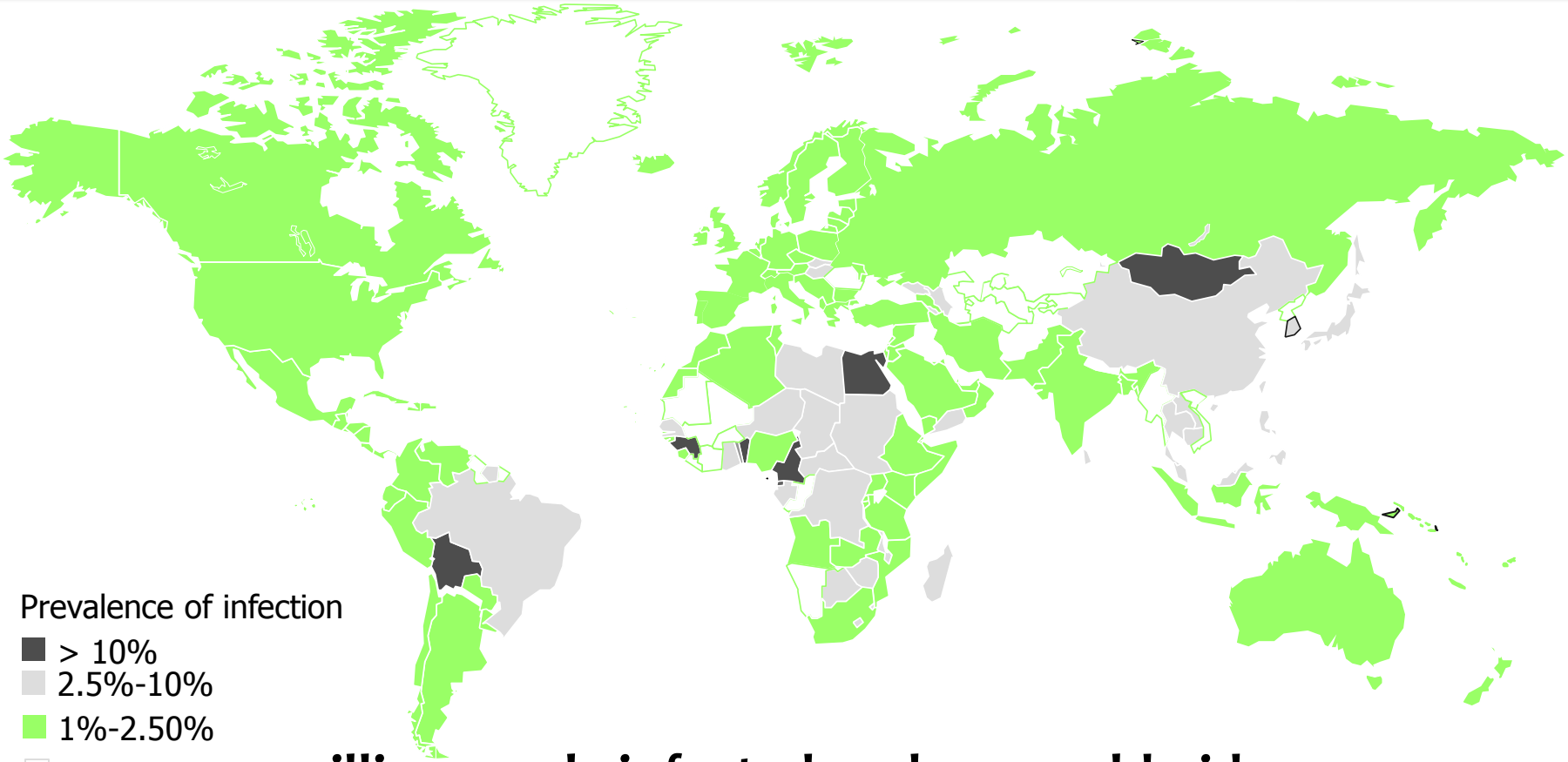
Newer Insights:

- **GT 1b *different* than GT 1a**
- **GT 2 easier to treat than GT 3**
- **GT 3 associated with higher mortality, steatohepatitis**
- **Genotypes tend to cluster in different populations**

Alter MJ *et al. N Engl J Med* 1999; 341:556-62

FAMILY HEALTH CENTERS OF SAN DIEGO

Hepatitis C is a Global Health Problem

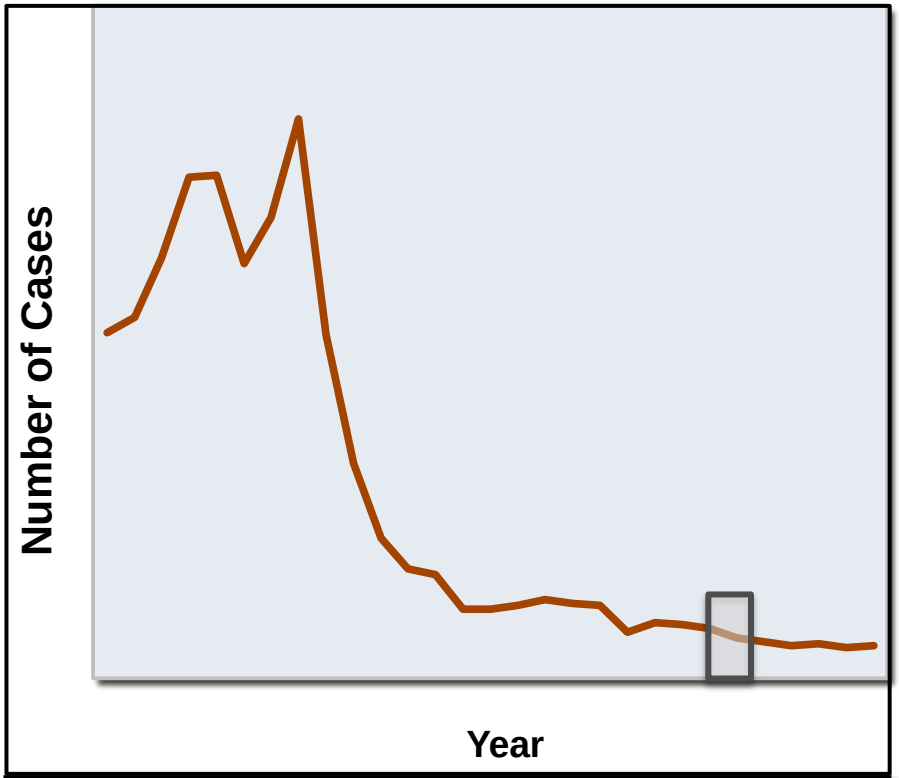


- **3-4 million newly infected each yr worldwide**
- **Over 170 million estimated infections worldwide**

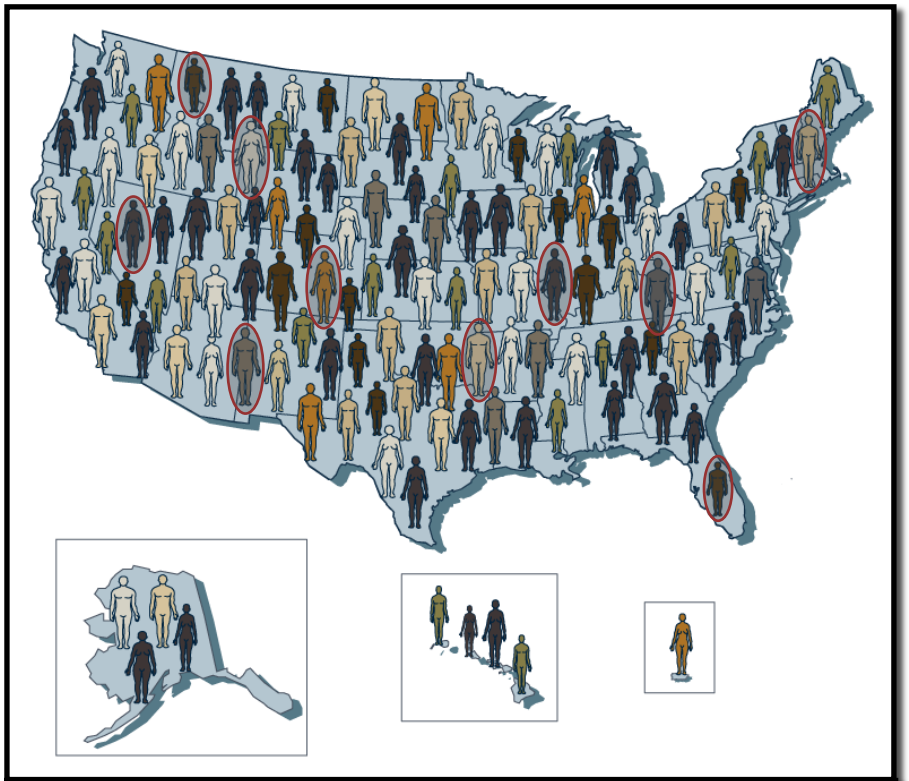
World Health Organization 2008 (http://www.who.int/ith/es/index.html)

FAMILY HEALTH CENTERS OF SAN DIEGO

Hepatitis C Incidence and Prevalence - US



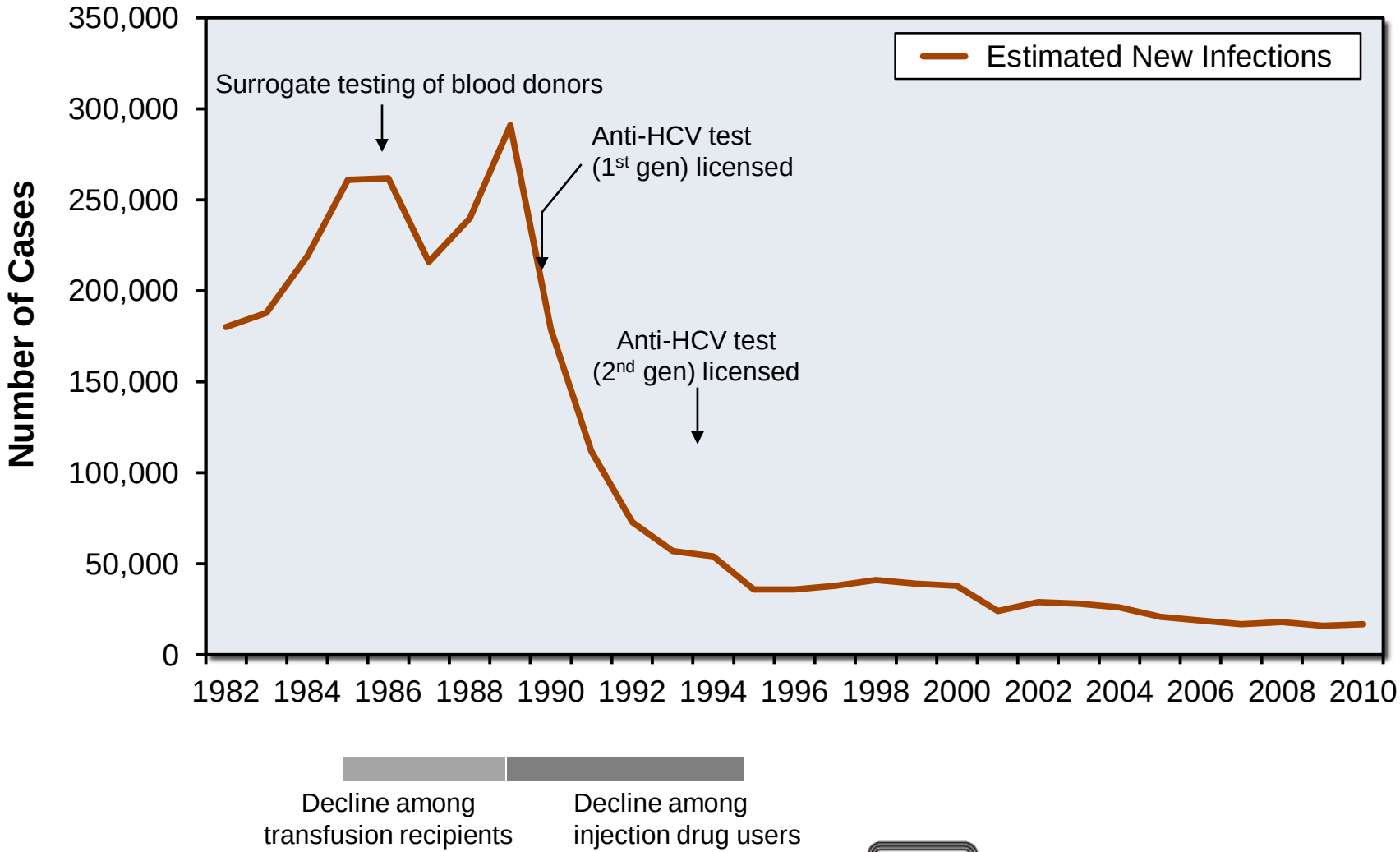
HCV Incidence. The number of people who become newly infected with HCV in a defined time period.



HCV Prevalence. The number of people living with HCV in a population at a point in time.

FAMILY HEALTH CENTERS OF SAN DIEGO

Hepatitis C Incidence in United States, 1982-2010



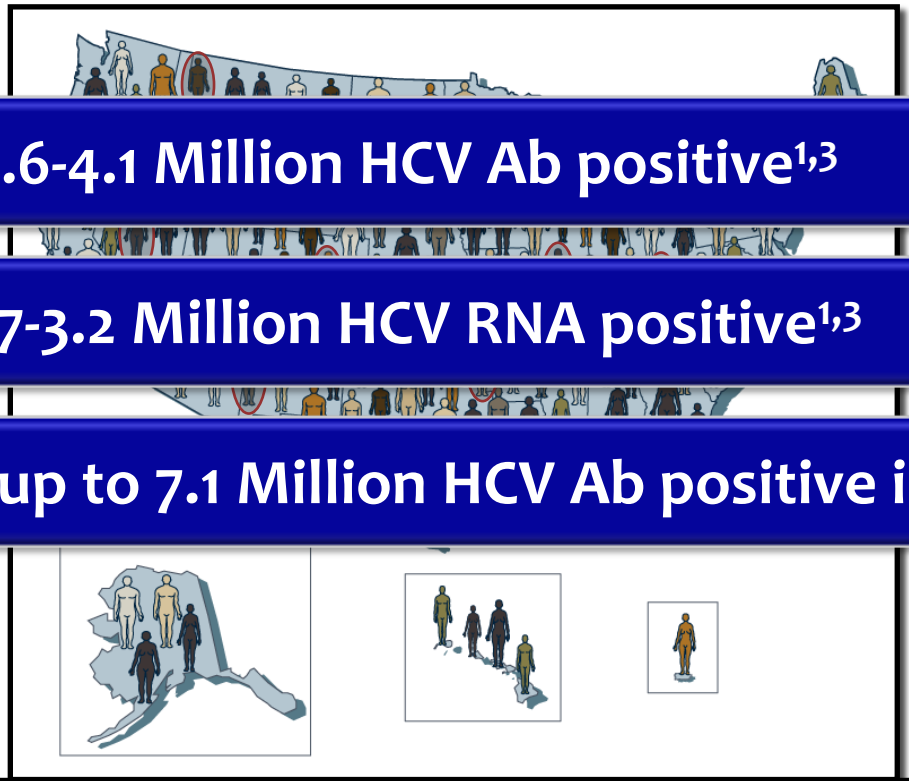
FAMILY HEALTH CENTERS OF SAN DIEGO

HCV Prevalence in the United States?

What is the best estimate for chronic HCV (Ab and RNA +) prevalence in the United States?

A. 1.2 million
B. 2.7 million
C. 3.2 million
D. 7.1 million

Hepatitis C Prevalence – NHANES estimates



3.6-4.1 Million HCV Ab positive[1,3]

2.7-3.2 Million HCV RNA positive[1,3]

Possibly up to 7.1 Million HCV Ab positive in US[2]

HCV Prevalence**.** The number of people living with HCV in a population at a point in time.

1. Armstrong GL, et al. Ann Intern Med. 2006;144:705-14.
2. Chak E, et al. *Liver Int.* 2011;31:1090-1101
3. Denniston MM et al Ann Intern Med. 2014; 160:293-300

FAMILY HEALTH CENTERS OF SAN DIEGO

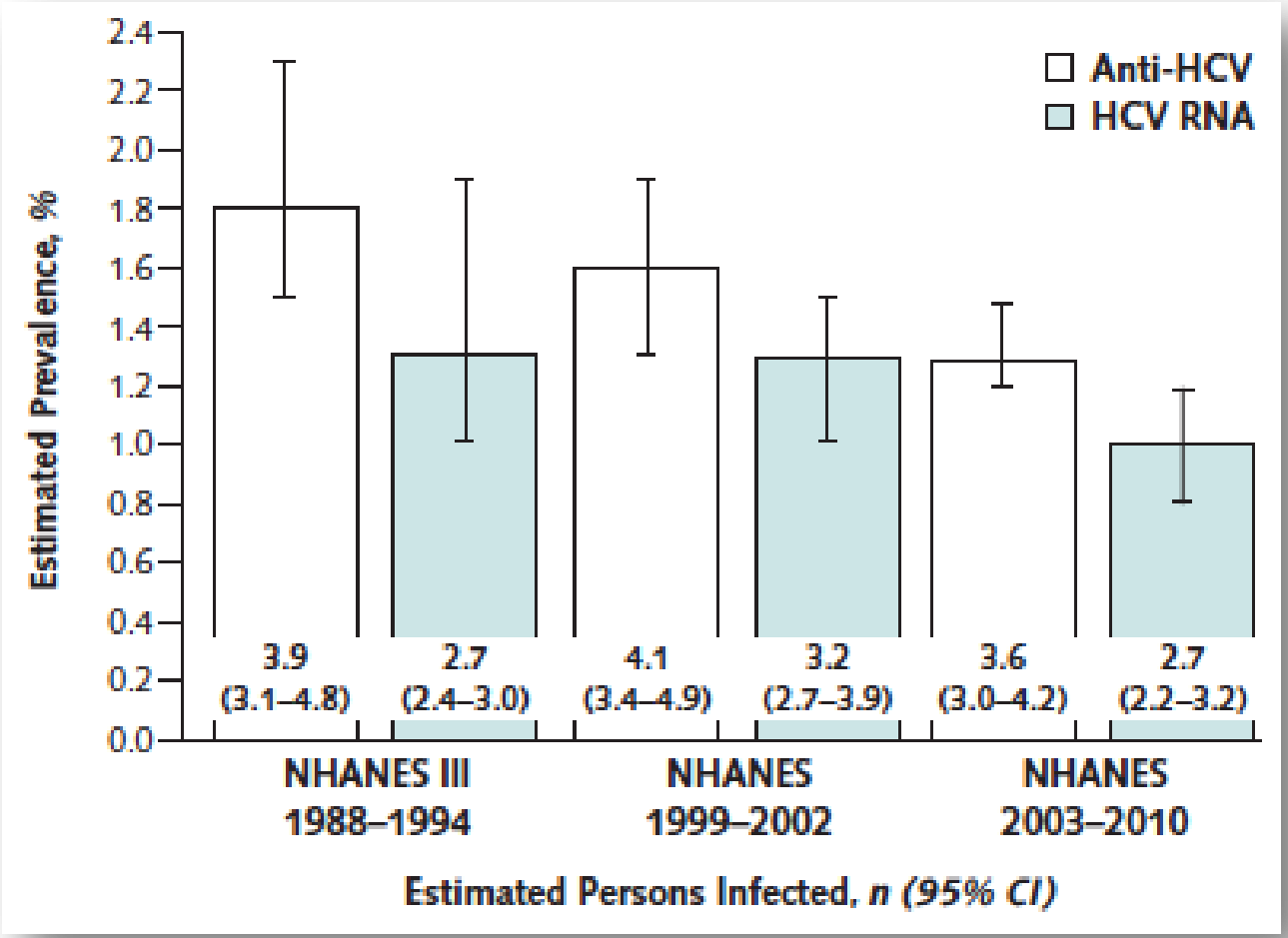
National Health and Nutrition Examination Survey

- Stratified probability sampling of demographic, nutritional, behavioral, and serologic info 5,000 Americans/yr
- **Includes**: non-institutionalized civilians
- **Excludes**: active duty military, inpatient, prisoners, homeless +/- veterans
- HCV Ab testing included since 1980's, RNA added since NHANES III
- N = 30,074 for latest analysis from 2003-2010

1. Armstrong GL, et al. Ann Intern Med. 2006;144:705-14.
2. Denniston MM et al Ann Intern Med. 2014; 160:293-300

Annals of Internal Medicine | ORIGINAL RESEARCH

Chronic Hepatitis C Virus Infection in the United States, National Health and Nutrition Examination Survey 2003 to 2010



Declining Prevalence of HCV Ab (1.3%) AND HCV RNA (1.0%)

Denniston MM et al *Ann Intern Med*. 2014; 160:293-300

FAMILY HEALTH CENTERS OF SAN DIEGO

What does the declining HCV Ab+ and RNA+ prevalence indicate?

A. Better HCV prevention through syringe exchange programs
B. Much higher rates of Sustained Virologic Response (SVR) with newer treatments
C. Expected pattern of high prevalence, low incidence with relatively constant treatment
D. Deaths in Baby Boomers due to liver-related disease

Annals of Internal Medicine | ORIGINAL RESEARCH

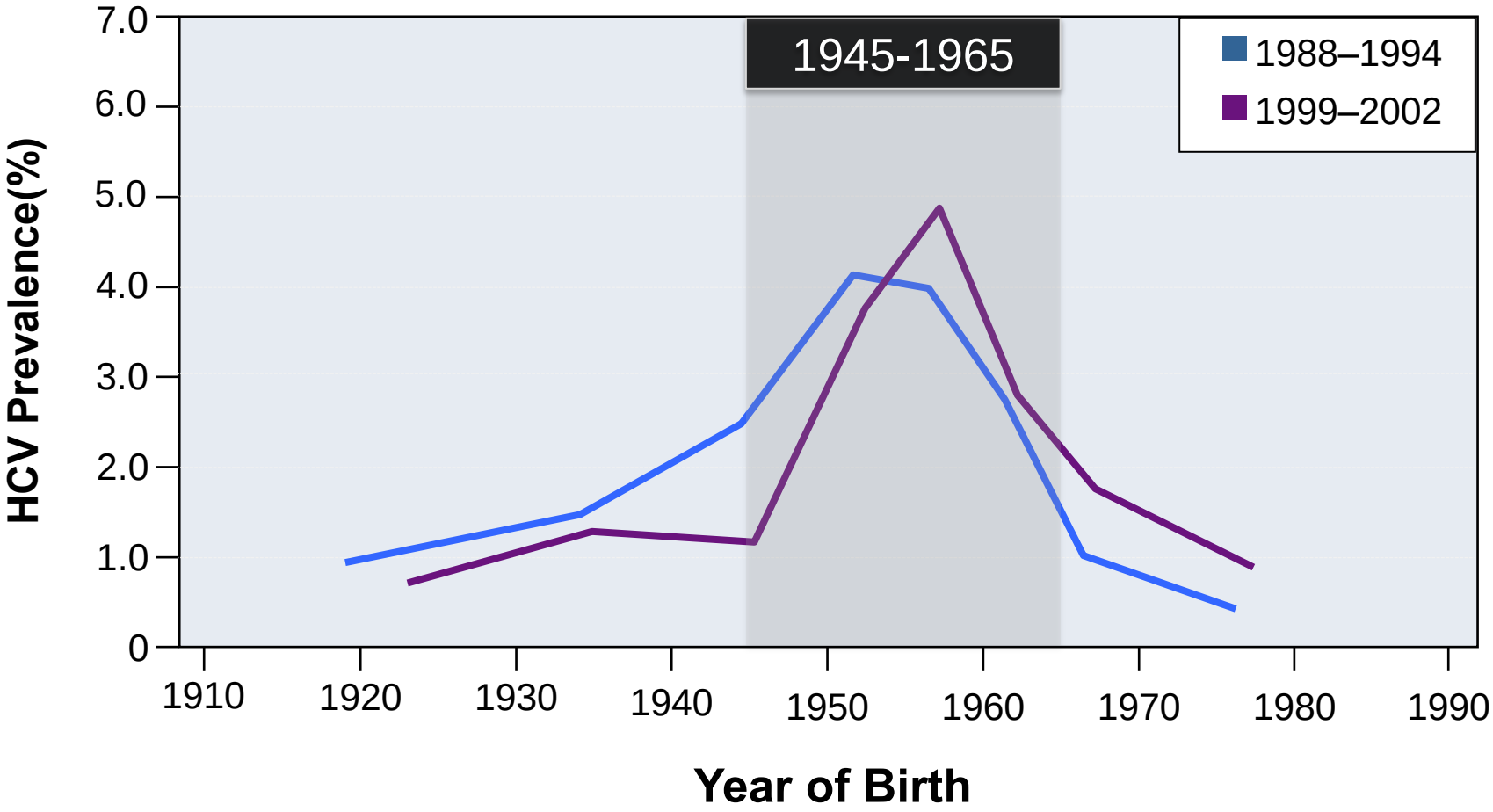
Chronic Hepatitis C Virus Infection in the United States, National Health and Nutrition Examination Survey 2003 to 2010

"Our analysis suggests decreases in prevalence that probably reflect increasing mortality from HCV-related conditions. That these deaths largely occur in the age group born between 1945 and 1965 underscores the urgency of addressing this underappreciated national epidemic"

Denniston MM et al *Ann Intern Med*. 2014; 160:293-300

NHANES Survey: United States, 1988-1994 and 1999-2002

Prevalence of HCV Antibody, by Year of Birth



Source: Armstrong GL, et al. Ann Intern Med. 2006;144:705-14.

FAMILY HEALTH CENTERS OF SAN DIEGO

Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Recommendations and Reports / Vol. 61 / No. 4
August 17, 2012

Recommendations for the Identification of Chronic Hepatitis C Virus Infection Among Persons Born During 1945–1965

1998 – CDC Risk-Based HCV Screening Recommendations

HCV screening based on risk for infection:

- Persons who ever injected illegal drugs
- Persons with selected medical conditions, including
  - receipt of clotting factor concentrates produced before 1987;
  - ever on chronic (long-term) hemodialysis; and
  - persistently abnormal alanine aminotransferase levels
- Prior recipients of transfusions or organ transplants (before July 1992)

HCV screening based on recognized exposure:

- Healthcare, emergency medical, and public safety workers after needle sticks, sharps, or mucosal exposures to HCV-positive blood
- Children born to HCV-positive women

Source: CDC and Prevention.

FAMILY HEALTH CENTERS OF SAN DIEGO

2012 CDC Birth Cohort HCV Testing Recommendations

In addition to testing adults of all ages at risk for hepatitis C virus:

- Adults born during **1945 to 1965** should receive 1-time testing for HCV without prior ascertainment of HCV risk.
- All persons identified with HCV infection should receive:
  - A brief alcohol screening and intervention as clinically indicated,
  - Referral to appropriate care and treatment services for HCV infection,
  - Post-test counseling

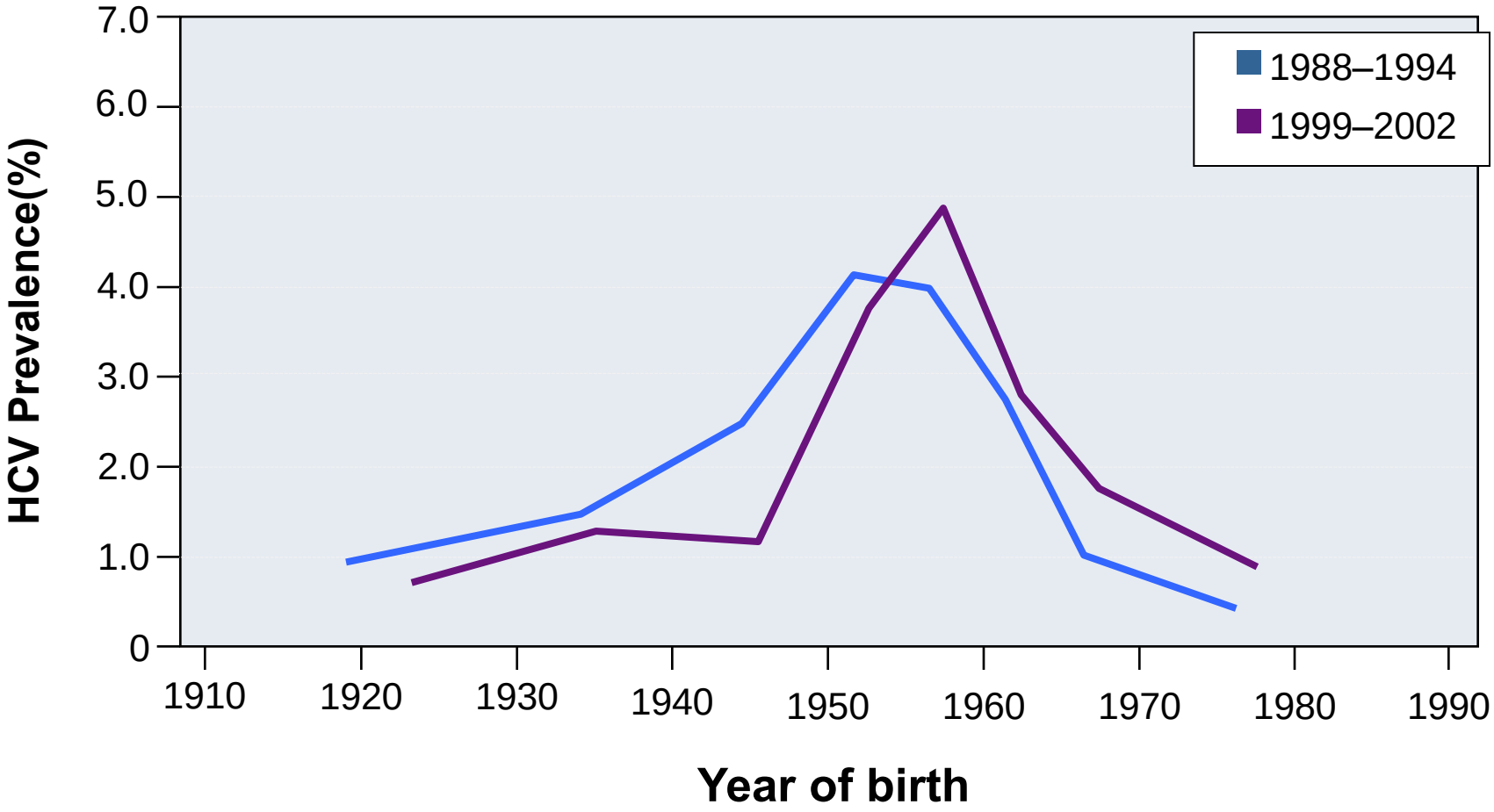
USPSTF – Grade 'B' Endorsement

Source: Source: CDC and Prevention. MMWR. 2012:RR61:1-32.

FAMILY HEALTH CENTERS OF SAN DIEGO

NHANES Survey: United States, 1988-1994 and 1999-2002

Prevalence of HCV Antibody, by Year of Birth

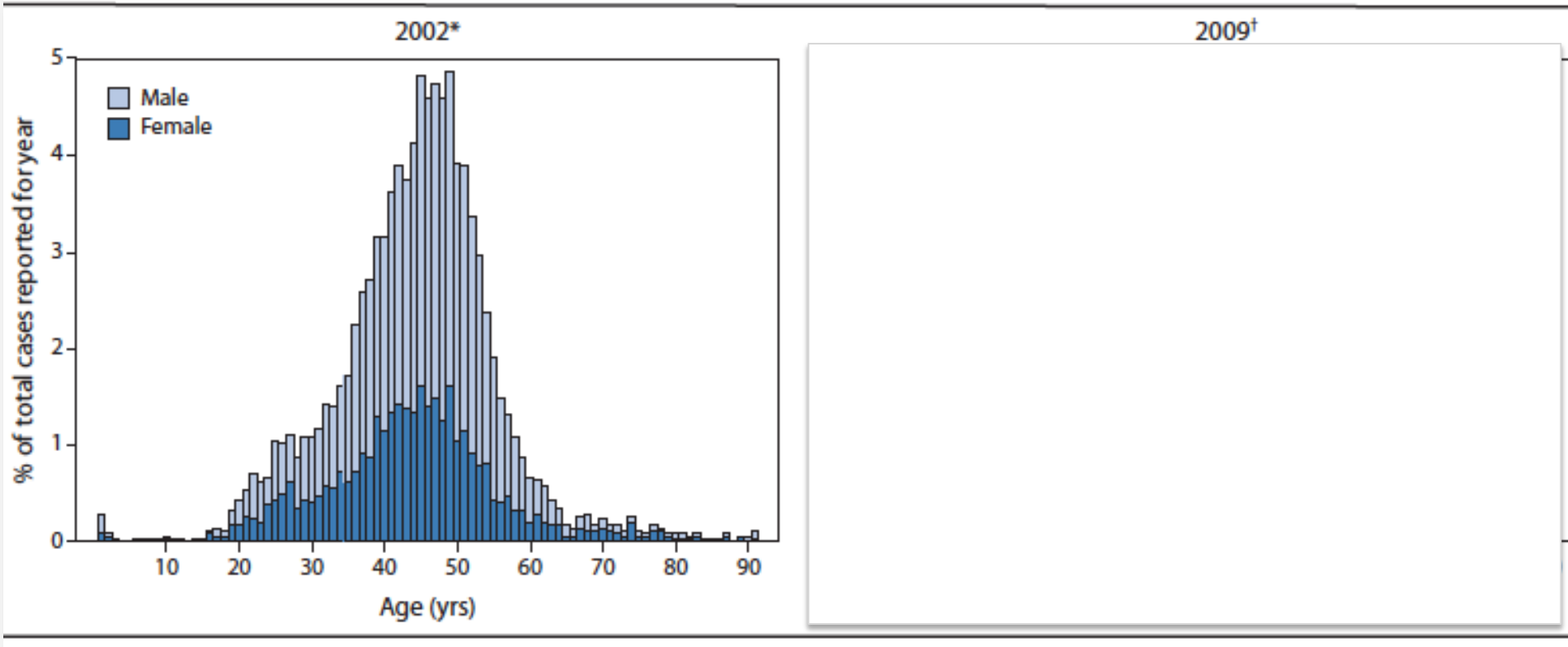


Source: Armstrong GL, et al. Ann Intern Med. 2006;144:705-14.

FAMILY HEALTH CENTERS OF SAN DIEGO

High Incidence of HCV in Young IDU's

FIGURE 2. Age distribution of newly reported confirmed cases of hepatitis C virus infection — Massachusetts, 2002 and 2009



MMWR. May 6, 2011:60; 17:537-541.

FAMILY HEALTH CENTERS OF SAN DIEGO

Liver INTERNATIONAL
OFFICIAL JOURNAL OF THE INTERNATIONAL ASSOCIATION FOR THE STUDY OF THE LIVER

REVIEW ARTICLE

Hepatitis C virus infection in USA: an estimate of true prevalence

Eric Chak[1], Andrew H. Talal[2], Kenneth E. Sherman[3], Eugene R. Schiff[4] and Sammy Saab[5]

Abstract

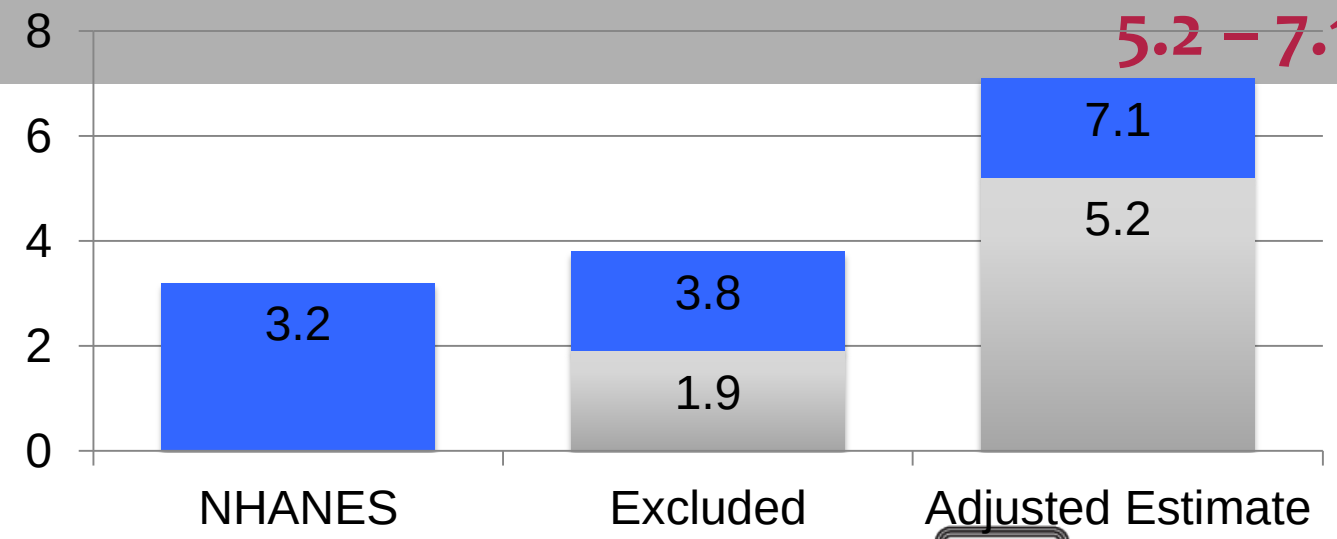
The recent National Health and Nutrition Examination Survey (NHANES) sampled only the civilian, non-institutionalized population of USA and may have underestimated the prevalence of hepatitis C virus (HCV) in this country. We searched the database MEDLINE, the Bureau of Justice Statistics, Center for Medicare and Medicaid and individual states Department of Corrections for all epidemiological studies regarding the prevalence of HCV in populations not sampled by the NHANES survey namely the incarcerated, homeless, nursing home residents, hospitalized and those on active military duty. Because of their relatively low frequency in the NHANES sample, we also expanded our search to include healthcare workers and long-term dialysis

Chak E et al Liver International 2011; 1090-1101

FAMILY HEALTH CENTERS OF SAN DIEGO

Chak E et al - True Prevalence of HCV

Population	N	Estimated Prevalence	Total HCV Ab + Patients
General Population	260 million	1.6-1.8%%	4,100,000
Homeless	643,067	19.0-69.1%	142,761 - 337,610
Incarcerated	1,613,656	23.1-41.2%	372,754 - 664,826
Active Military	1,417,747	0.48%	6805
TOTAL			**5.2 – 7.1 million**



Chak E et al Liver International 2011: 1090-1101

FAMILY HEALTH CENTERS OF SAN DIEGO

HCV Prevalence in San Diego?

What is the best estimate for HCV prevalence in San Diego County?

A. 13,000
B. 35,000
C. 50,000
D. 60,000

FAMILY HEALTH CENTERS OF SAN DIEGO

San Diego - True Prevalence of HCV

Population	N	Estimated Prevalence*	Total HCV Ab + Patients
General Population	3,177,000	1.6-1.8%	50,832 – 57,186
Homeless	6,363	22.2-69.1%	1,399 – 4,396
Incarcerated	4,841	34.3-41.2%	1,660 – 1,994
Active Military	110,700	0.48%	531
TOTAL			**54,422 – 64,107**

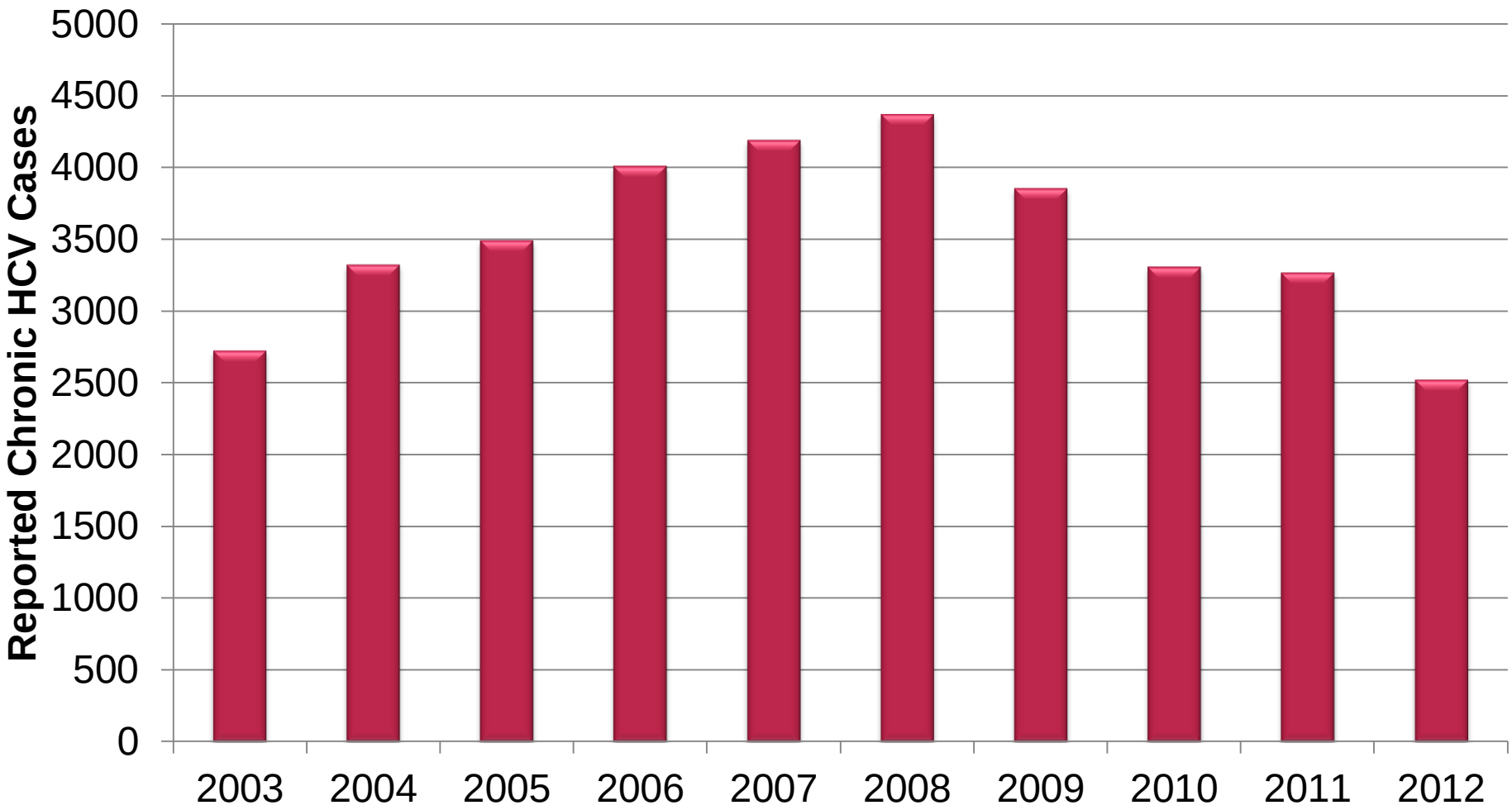
*Estimated prevalence ranges taken from review of literature in Chak E et al Liver International

+ source: Regional Task force on Homeless

$ source: San Diego Military Economic Impact Study

FAMILY HEALTH CENTERS OF SAN DIEGO

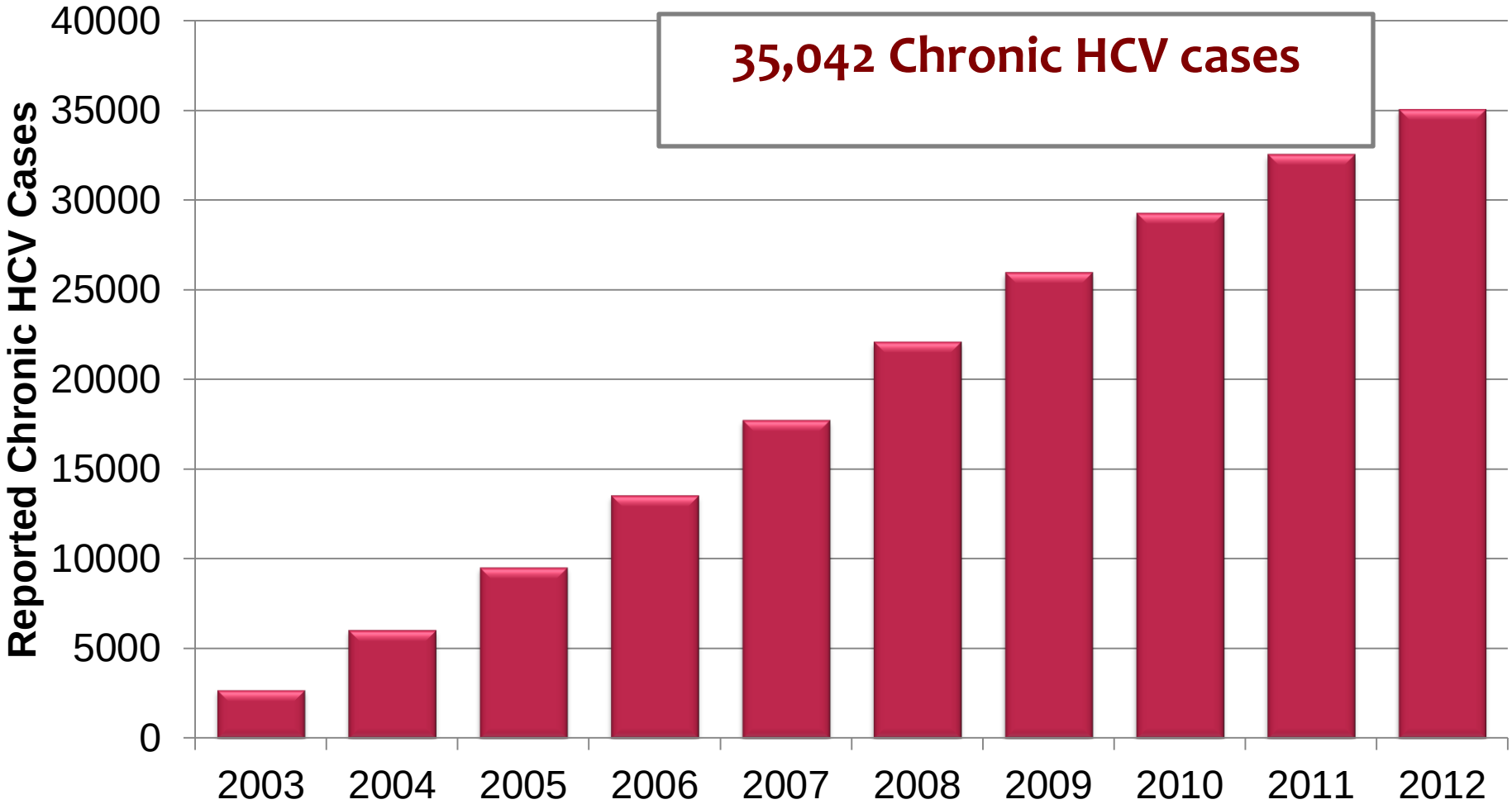
Reported HCV Cases/yr - SD County, 2003-12



*SD County Communicable Disease Report 2007, 2013

FAMILY HEALTH CENTERS OF SAN DIEGO

Cumulative Chronic HCV Cases – SD County, 2008-12

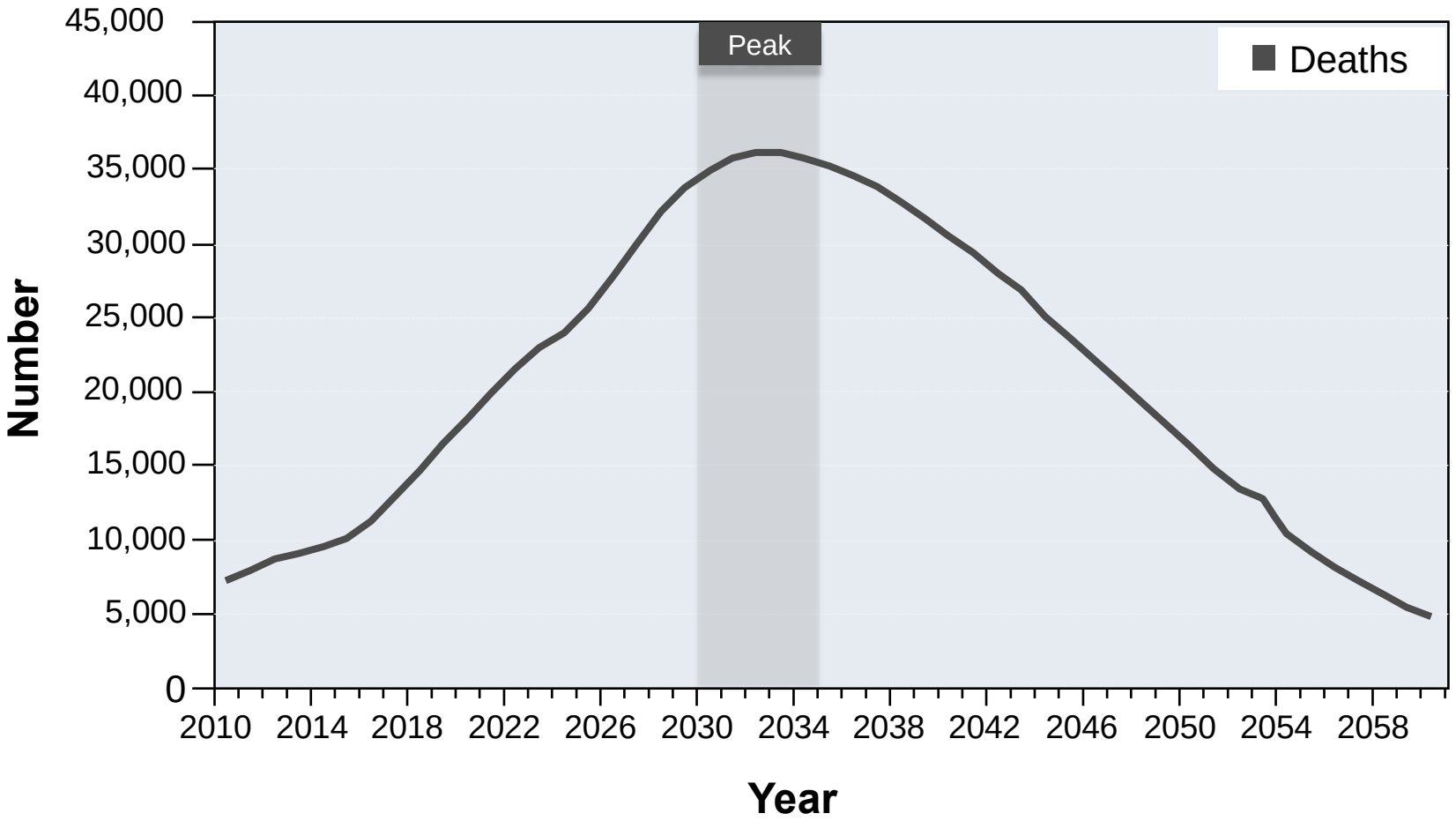


*SD County Communicable Disease Report 2007, 2013

FAMILY HEALTH CENTERS OF SAN DIEGO

Forecasted 2010-2060 Annual HCV-Related Deaths in the US

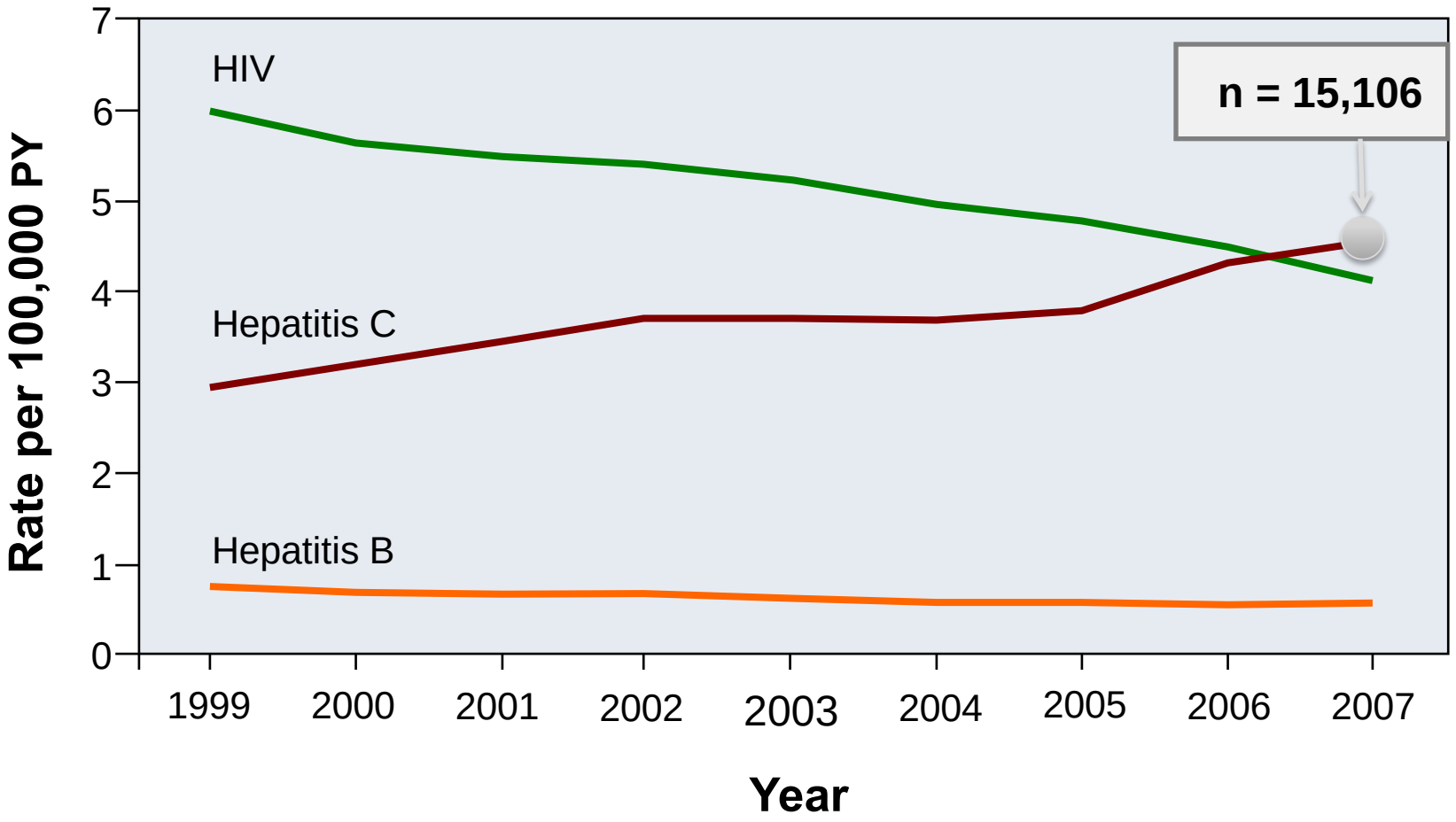
Persons with Chronic Hepatitis C and no Cirrhosis in 2005



Source: Rein DR, et al. Dig Liver Dis. 2011:43:66-72.

FAMILY HEALTH CENTERS OF SAN DIEGO

Age-Adjusted Mortality Rates* from HBV, HCV, & HIV United States, 1999-2007



*Mortality Rates = HBV, HCV, HIV listed as cause of death

Source: Ly KN, et al. Ann Intern Med. 2012:156:271-8.

FAMILY HEALTH CENTERS OF SAN DIEGO

Hepatitis C Epidemiology – Summary

- Hepatitis C transmission is primarily through IDU and blood transfusions before 1992
- CDC recommends risk-based AND birth cohort screening (probably only 50% diagnosed)
- Likely ~3-7 million in US chronically infected, with measurable liver-related mortality now
- Likely ~50,000 chronic HCV cases in SD County

The View From the CHC/FQHC

Specialty Care in the Medical Home

Family Health Centers of San Diego - Overview

Mission

FHCSD is dedicated to providing caring, affordable, high quality healthcare and supportive services to everyone, with a special commitment to the uninsured, low-income and medically underserved persons

FAMILY HEALTH CENTERS OF SAN DIEGO

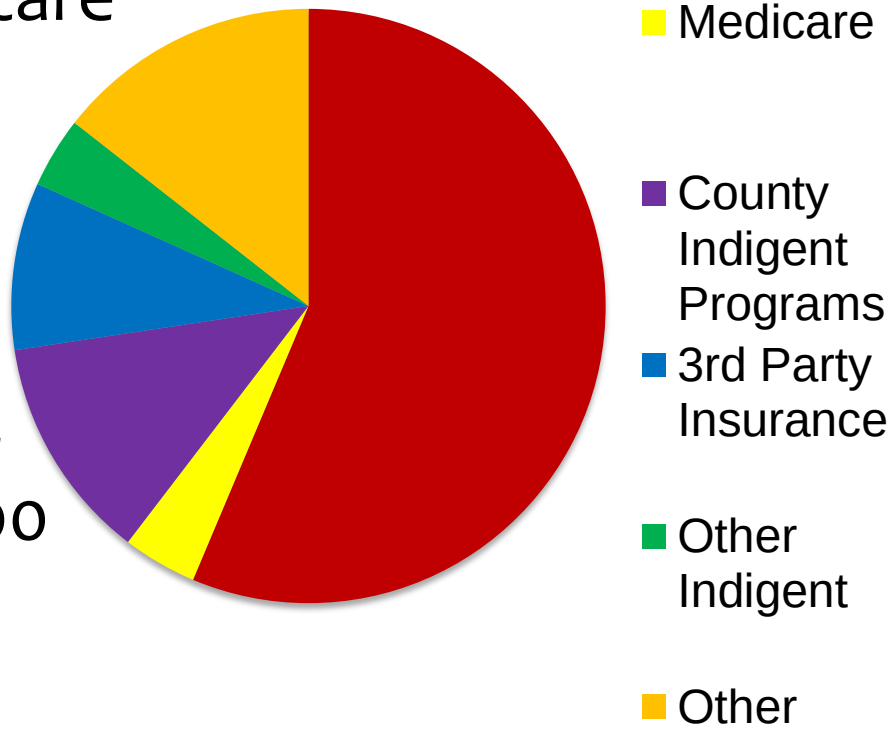
Family Health Centers of San Diego - History

- Founded in Barrio Logan in 1970 by community activists
- Grown to 34 sites including 18 Health Centers throughout SD County
- Served homeless since inception, HRSA Healthcare for the Homeless grantee since 1989

FAMILY HEALTH CENTERS OF SAN DIEGO

FHCSD – Patient Payer Mix - 2012

- 173,000 unique patients served through 650,000 encounters
- Largest provider of health care to the uninsured in US
- 87% of pts income <200% of Federal Poverty
- In 2012, served more than 22,000 unduplicated homeless patients through 90,000 encounters



FAMILY HEALTH CENTERS OF SAN DIEGO

FHCSD – Healthcare for the Homeless

KidCare Express
Mobile Medical Units

Elm Street
Family Health Center

- One of 200 grantees through federal Bureau of Primary Health Care (BPHC)
- Elm/SD Rescue Mission
- Mobile Medical Units (19 subcontracted partners)
- Downtown Connections
- Clean Syringe Exchange

FAMILY HEALTH CENTERS OF SAN DIEGO

HepCareConnect – HCV testing & linkage

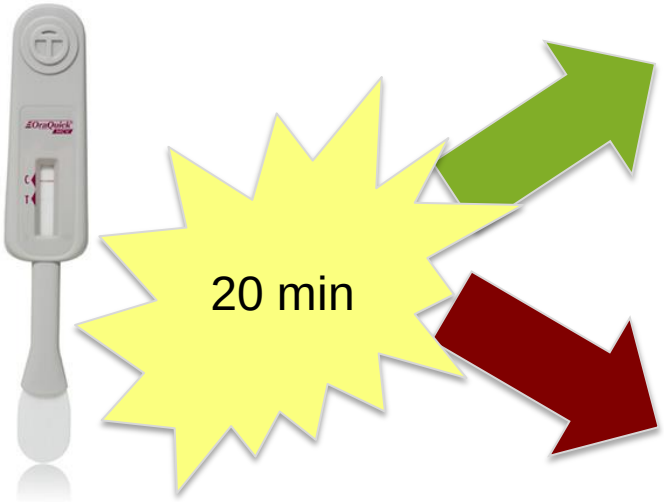
An Academic-Community Partnership

FHCSD HepCareConnect Testing Algorithm

FHC
Elm St, Logan, DT Connections, City Heights

HIV Testing
Syringe Exchange

MMUs
ADS sites



HCV Ab Negative

- LIHP/ACA info
- Risk Reduction counseling

HCV Ab Positive

- Plasma HCV RNA
- LIHP/ACA info
- EtOH intervention
- Linkage to care (appt within 4 weeks)

FAMILY HEALTH CENTERS OF SAN DIEGO

FHCSD HepCareConnect Testing sites

- 8 → 16 ADS sites
- Syringe Exchange

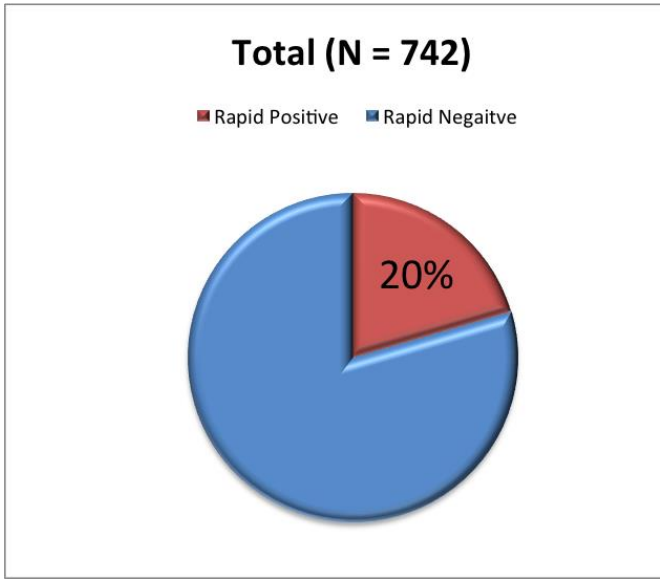
Elm Street
Family Health Center

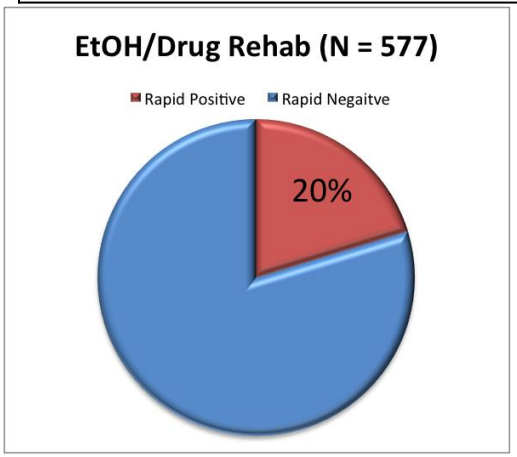
Downtown Family Health Center
at Connections

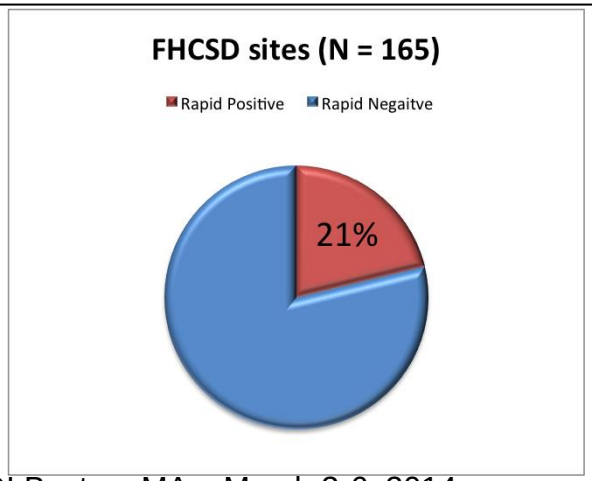
FAMILY HEALTH CENTERS
OF SAN DIEGO

HCV testing at FHCSD – Results 4/13-11/13

(as of 9/5)	Tests	Rapid +	% Rapid +	PCR+	%PCR+
FHC clinic	165	35	21.2%	28	80%
ADS sites	577	117	20.3%	74	63%
Total	742	152	20.5%	102	67%



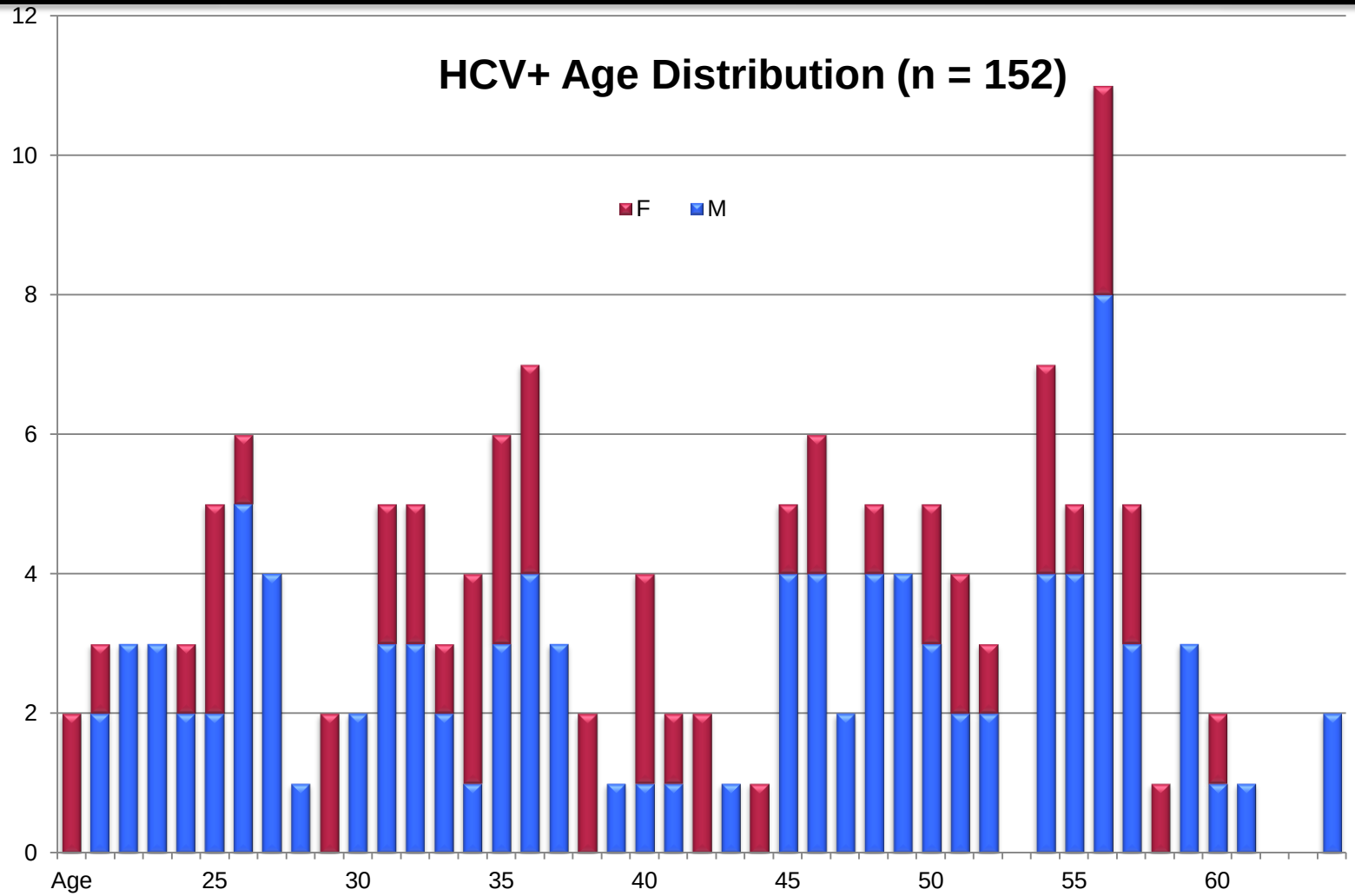




Ramers C et al – Abstract #670 CROI Boston, MA – March 3-6, 2014

FAMILY HEALTH CENTERS OF SAN DIEGO

HCV testing at FHCSD – 6 month Results



Ramers C et al CROI abstract #670– Boston, MA March 3-6, 2014

FAMILY HEALTH CENTERS OF SAN DIEGO

HCV testing at FHCSD – 7 month Results

Table 1. Sociodemographic Characteristics of Participants: Hepatitis C Screening		
(N = 152)	N	%
Baby Boomer		
Yes	58	38.2%
No	94	61.8%
Gender		
Male	99	65.1%
Female	51	33.6%
Transgender	2	1.3%
Education		
< High school	42	27.6%
High school	46	30.3%
Some college	21	13.8%
College/Post graduate	7	4.6%
Marital status		
Married/cohabitating	19	12.5%
Single	105	69.1%
Divorced/separated/widowed	20	13.2%
Race		
White	103	67.8%
Black/African American	17	11.2%
Multi-racial	15	9.9%
Ethnicity		
Hispanic/Latino	62	40.8%
Non-Hispanic/Latino	84	55.3%
Insurance Status		
Insured	52	34.2%
Uninsured	100	65.8%

- HCV Ab + cohort is:
  - **Young**
  - **65% male**
  - **Uneducated**
  - **69% single**
  - **40% Latino**
  - **17% African American**
  - **66% Uninsured**

Ramers C et al CROI abstract #670– Boston, MA March 3-6, 2014

FAMILY HEALTH CENTERS OF SAN DIEGO

Care Setting

What is the most appropriate setting for treatment of these patients

A. Teaching Hospital/Clinic
B. Liver Transplant Center
C. Community GI office
D. Primary Care Physician Office
E. Primary Care Physician Office + specialist support (e.g. via telehealth)

Treating Provider

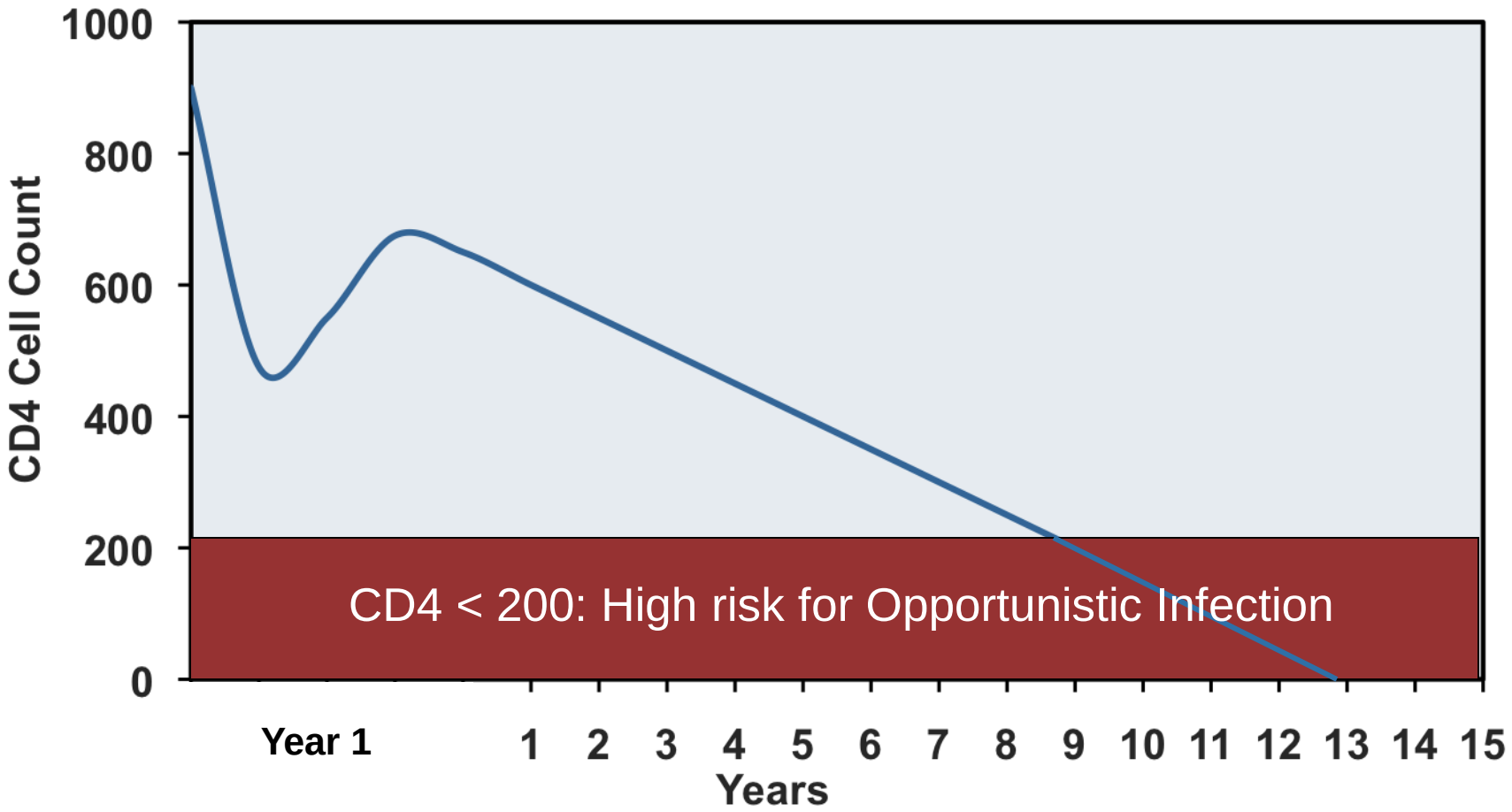
Who should be managing treatment decisions

A. Gastroenterologist
B. Hepatologist
C. Infectious Disease
D. Primary Care Provider (IM, FP, NP, PA)

When to Start?

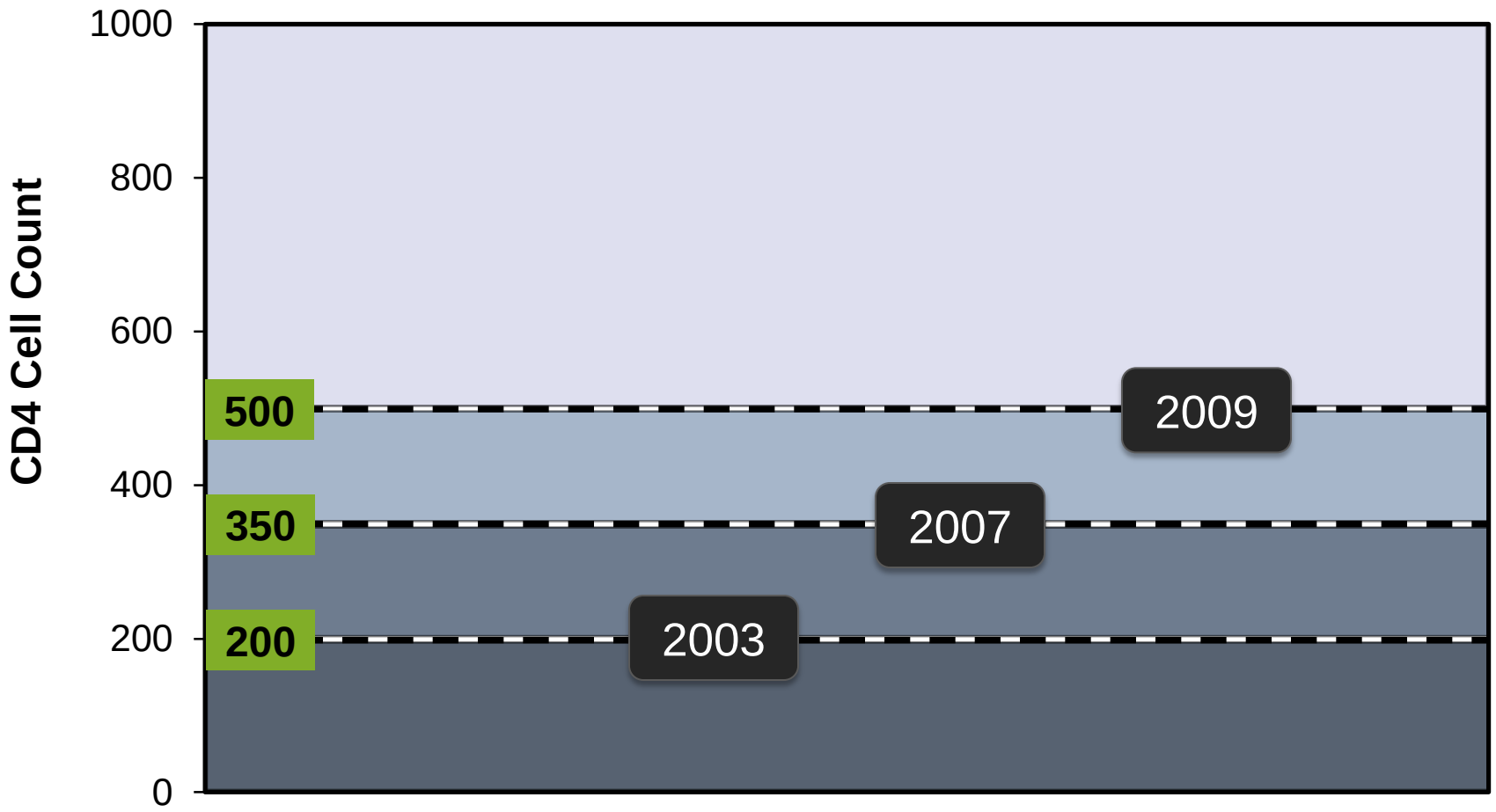
Contrasting the HIV & HCV Epidemics

Natural History of Untreated HIV Infection



FAMILY HEALTH CENTERS OF SAN DIEGO

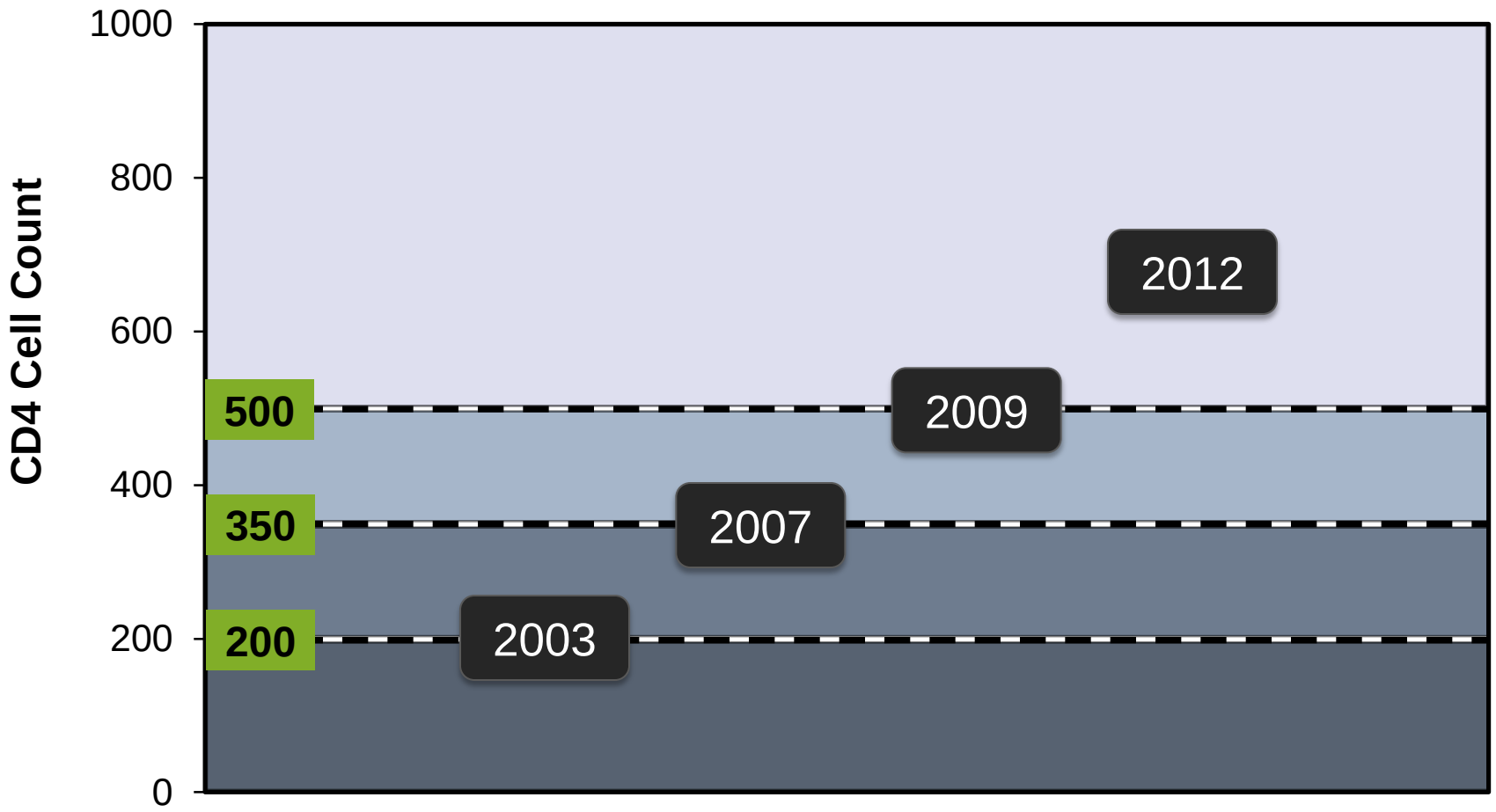
Initiating Antiretroviral Therapy in Treatment-Naïve Patients
Change in CD4 Threshold in DHHS Guidelines



DHHS Antiretroviral Therapy Guidelines. (aidsinfo.nih.gov)

FAMILY HEALTH CENTERS OF SAN DIEGO

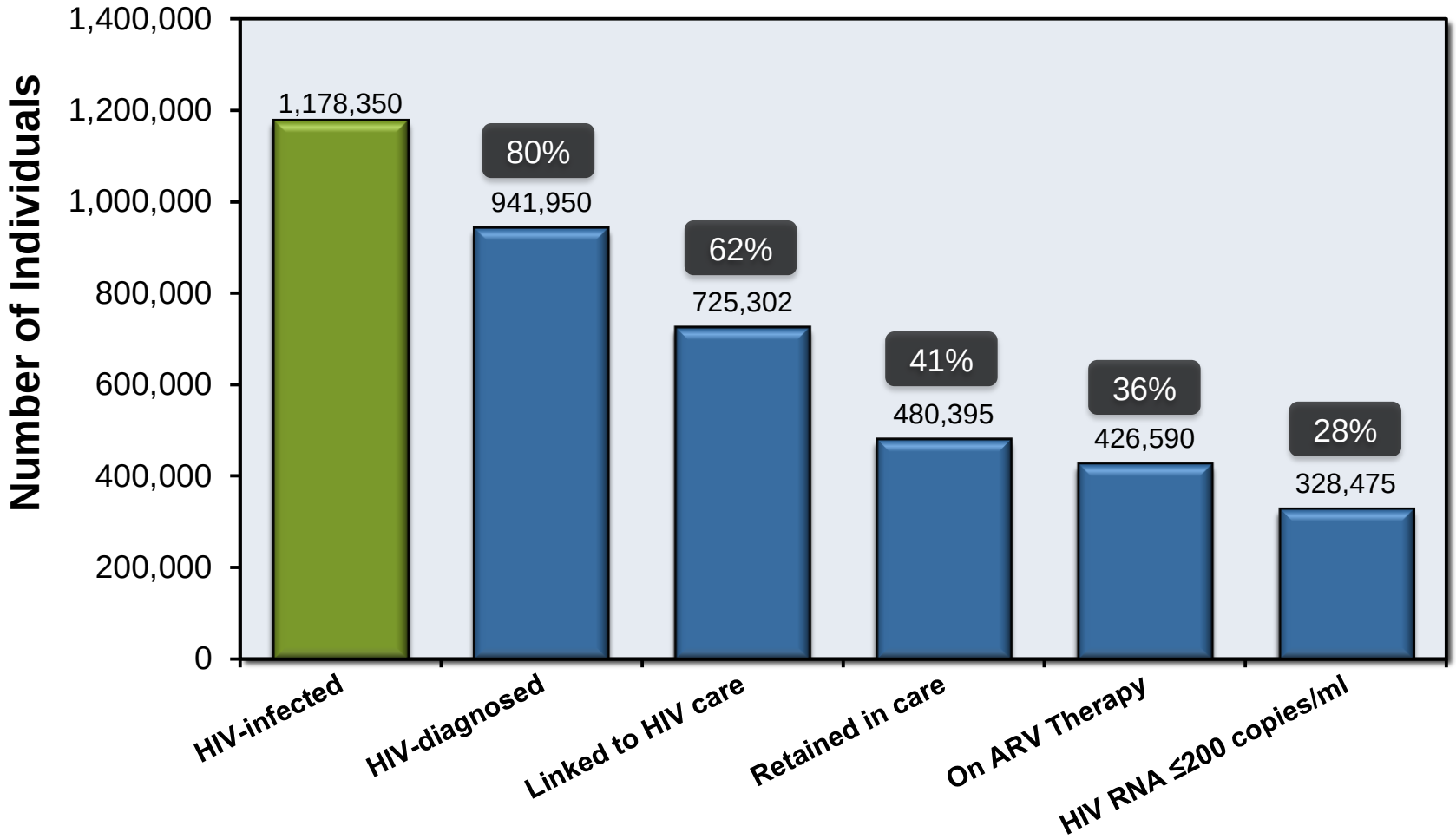
Initiating Antiretroviral Therapy in Treatment-Naïve Patients
Change in CD4 Threshold in DHHS Guidelines



DHHS Antiretroviral Therapy Guidelines. (www.aidsinfo.nih.gov)

FAMILY HEALTH CENTERS OF SAN DIEGO

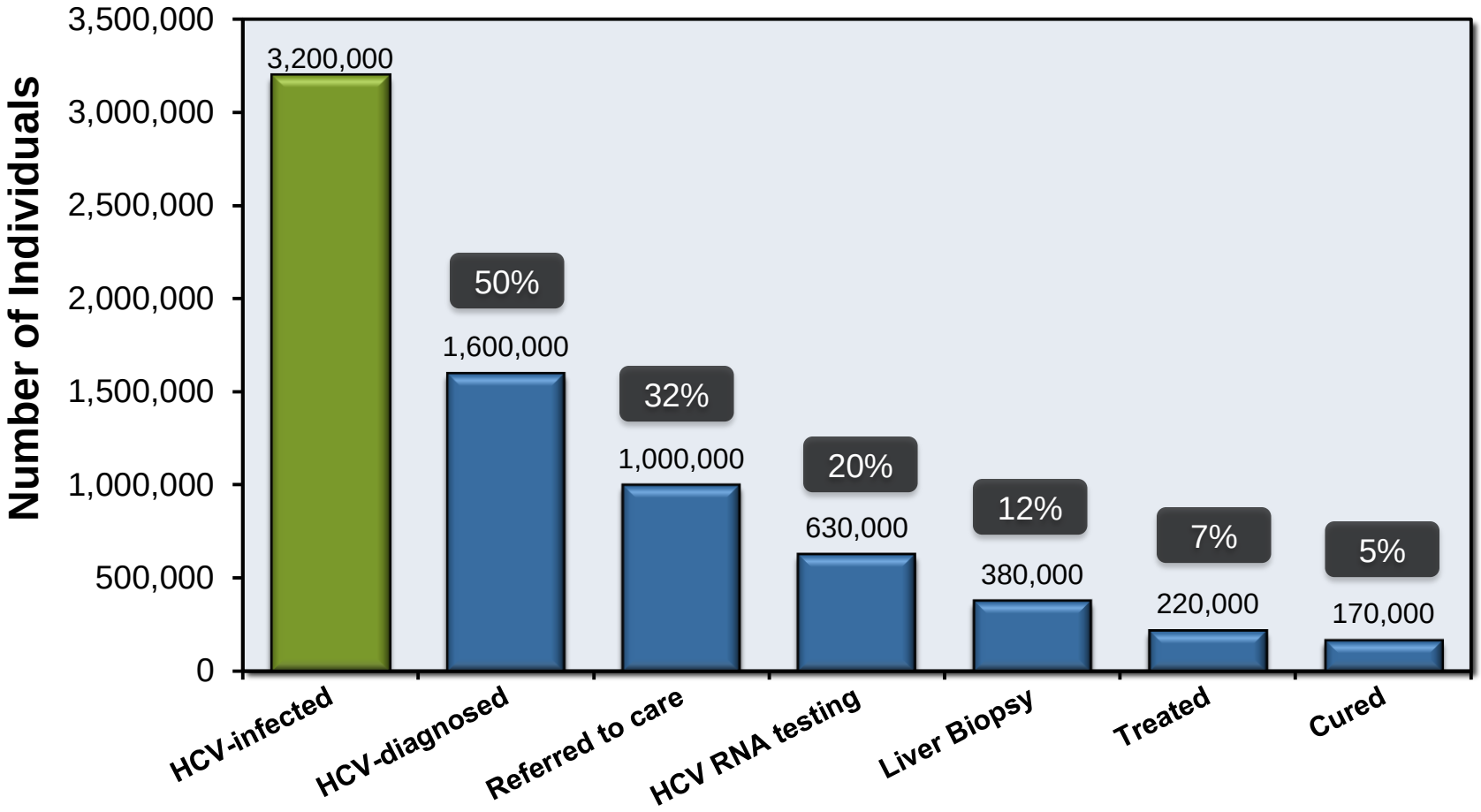
HIV Cascade of Care – United States



Cohen SM, et al. MMWR. 2011;60:1618-23

FAMILY HEALTH CENTERS OF SAN DIEGO

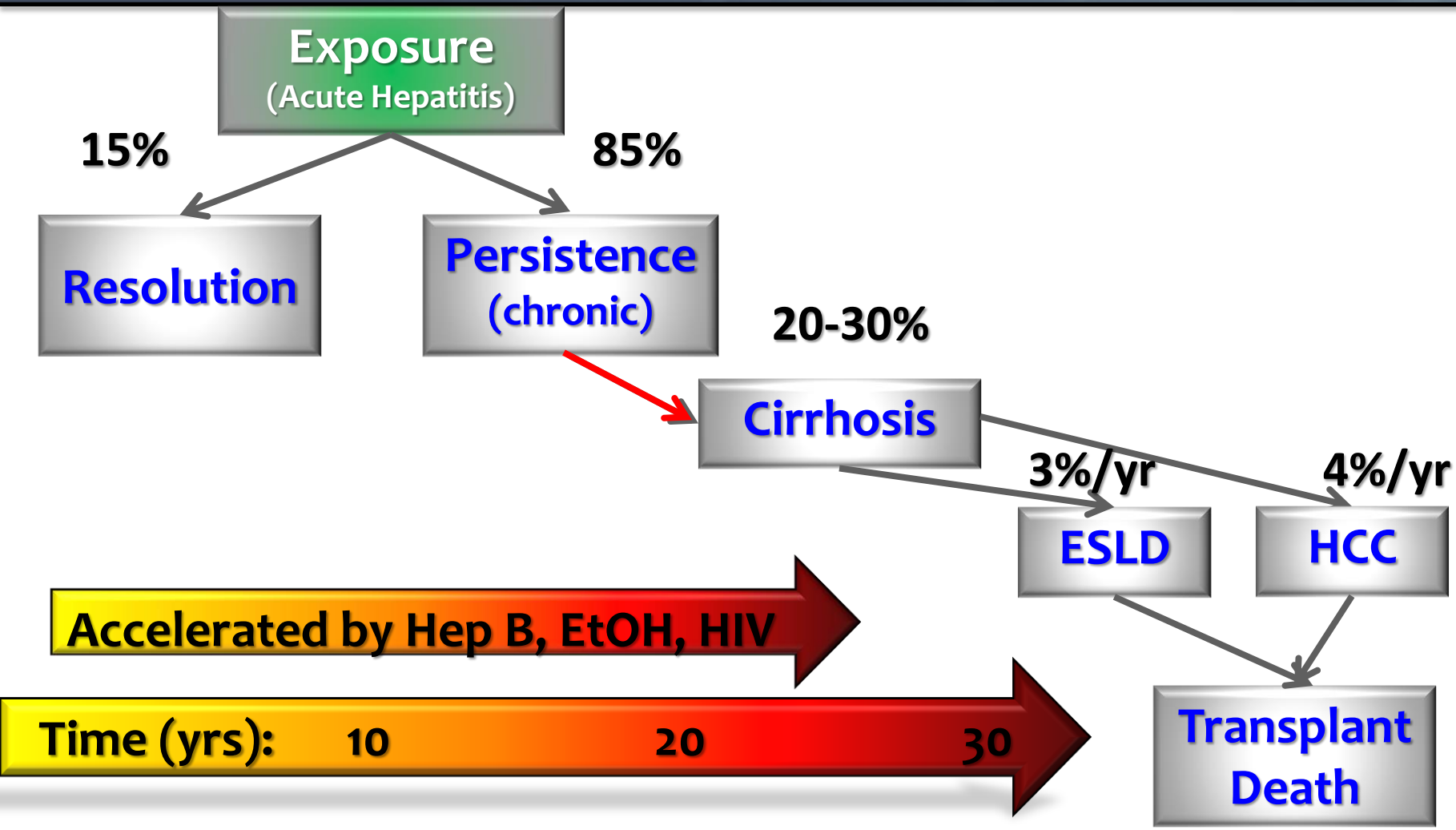
HCV Cascade of Care – United States



Source: Holmberg S, et al. NEJM. 2013;368:201859-61 .

FAMILY HEALTH CENTERS OF SAN DIEGO

Natural History of Hepatitis C

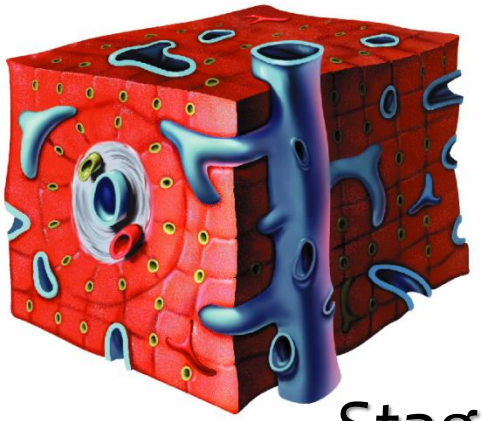


Mandell: Principles & Practice of Infectious Disease, 7th Ed;

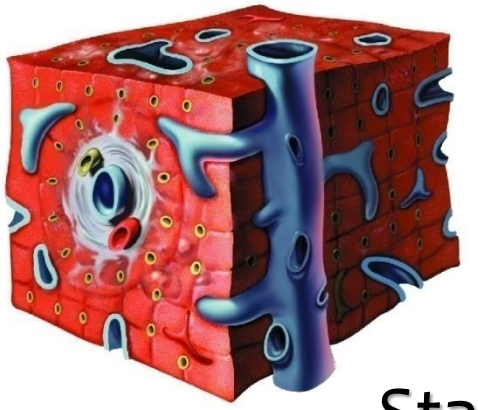
FAMILY HEALTH CENTERS OF SAN DIEGO

Histologic Staging - METAVIR

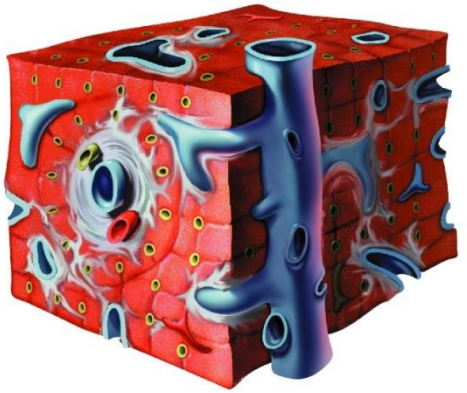
Stage 0



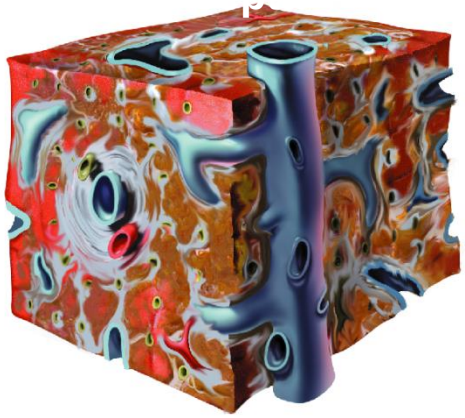
Stage 1



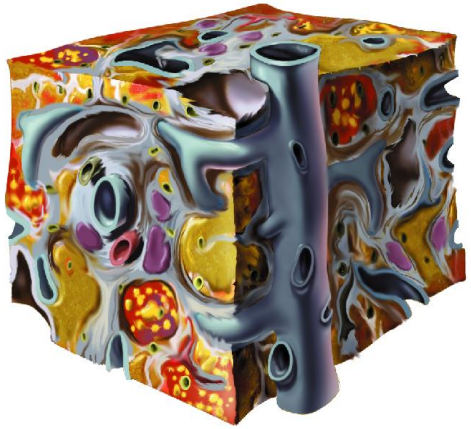
Stage 2



Stage 3

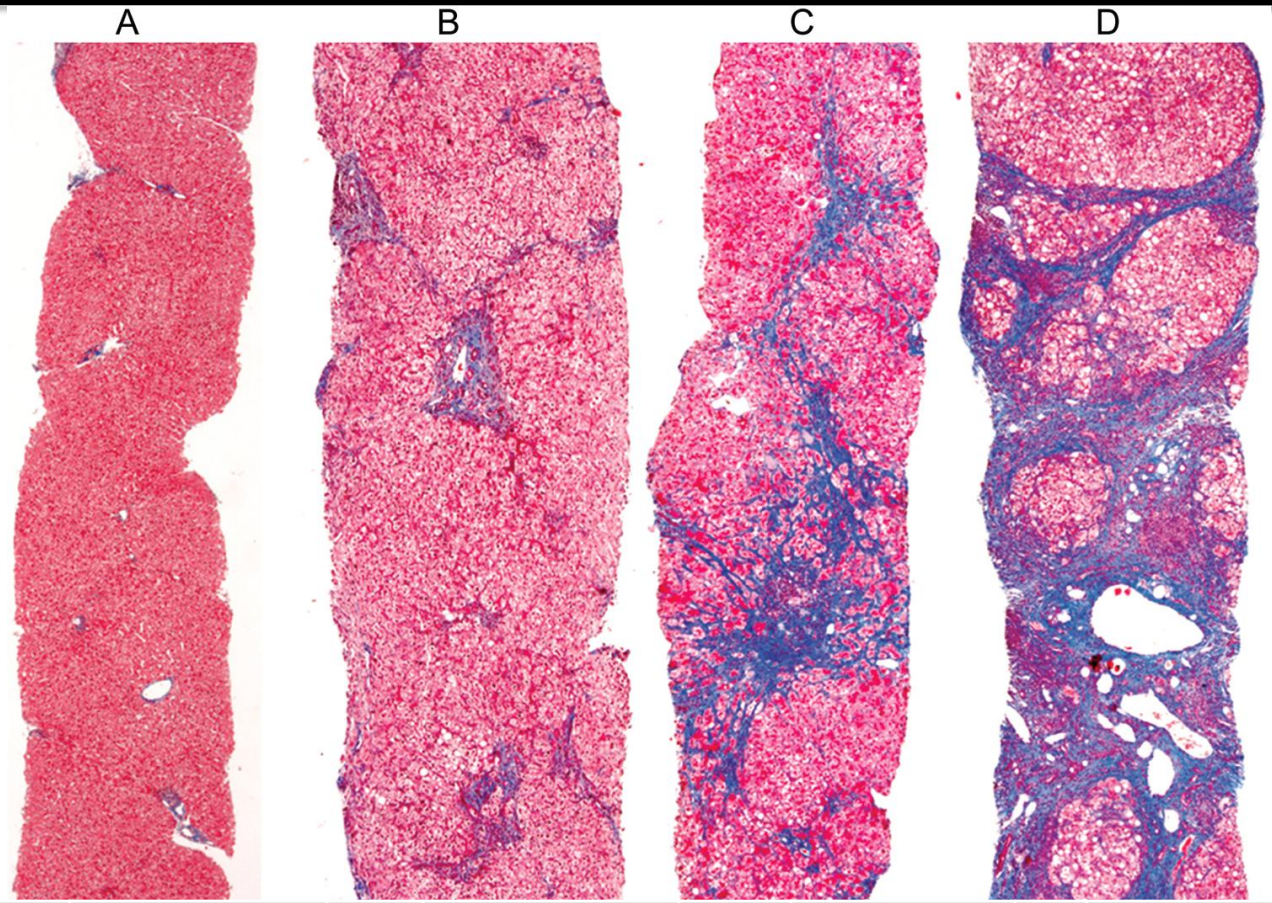


Stage 4



FAMILY HEALTH CENTERS OF SAN DIEGO

Histologic Staging – Ishak vs. METAVIR



Ishak	0	1	2	3	4	5	6
Metavir	0	1	1	2	3	4	4

Brau N, Clin Infect Dis 2013; 56(6): 853-60

FAMILY HEALTH CENTERS OF SAN DIEGO

Alternatives to Liver biopsy

- **APRI score** = (AST/40)/Plts*100
- **Fib-4 score** = (AST*Age)/(Plts*√(ALT))
- **Fibrosure** – blood test
- **Fibroscan** – augmented U/S test
- **MRE** – Magnetic Resonance Elastography

Progression to Cirrhosis

Normal Liver

- Filters/processes gut nutrients
- Produces proteins
- Detoxifies drugs and waste products (ammonia)
- Processes bile

Cirrhosis

- **Portal Hypertension**
- **Malnutrition**
- **Esophageal Varices**
- **Ascites/Edema**
- **Encephalopathy & Mental Slowness**
- **Jaundice**

FAMILY HEALTH CENTERS OF SAN DIEGO

Burden of disease related to HCV

Outcome	Key Facts
Cirrhosis	• Develops in **20-30%** of those who are chronically infected with HCV over 20-30 years
Decompensated Cirrhosis	• High risk of mortality from ruptured esophageal varices, bacterial peritonitis, hepatorenal syndrome/renal failure, encephalopathy
Hepatocellular Carcinoma	• Fastest growing Cancer in the US • **76%** associated with chronic HCV infection • **4%** annual incidence in those with cirrhosis
Liver Transplantation	• HCV responsible for **65%** of liver transplants worldwide
HCV Mortality	• Estimated at 16,000/year • Likely to peak ~2030

Burden of Liver disease expected to triple in next 10-20 yrs

Source: WHO Hepatitis C Fact Sheet
http://www.who.int/immunization/topics/hepatitis_c/en/index.html

FAMILY HEALTH CENTERS OF SAN DIEGO

What do we get with HCV Treatment?

- SVR (cure) of HCV is associated with:
  - **70% Reduction of Hepatocellular CA**
  - **50% Reduction in all-cause mortality**
  - **90% Reduction in Liver Failure**

Lok A. NEJM 2012; Ghany M. Hepatol 2009; Van der Meer AJ. JAMA 2012

FAMILY HEALTH CENTERS OF SAN DIEGO

Who Deserves Treatment?

Who should be treated for HCV?

A. Only patients with Decompensated Cirrhosis
B. Only patients with F3-F4 fibrosis by liver bx or non-invasive measure
C. Only patients with good insurance
D. Every patient is a candidate since it is a curable chronic infectious disease

The HCV Treatment Revolution

An Equity-based view

Case #1 - Lauren

- 32 yo woman 6 months clean from IDU (heroin). Graduated from Salvation Army program → moves into own apt in Pt. Loma, fully employed at recovery non-profit
- Requests HCV treatment
- Genotype 1A; VL 2.2 million IU/mL
- Liver U/S normal
- CBC: plts 215; CMP: AST/ALT 63/53

APRI = 0.7; Fib-4 = 1.29

Case #2 - Richard

- 56you man with h/o IDU (heroin), last use 2008 currently homeless, staying at SVDP. Very focused on taking care of his HCV, willing to take Interferon.
- Genotype 1A; VL: 2,545,050 IU/mL
- Liver U/S: sl increased echogenicity
- CBC: plts 199; CMP: AST/ALT 47/86

APRI = 0.59; Fib-4 = 1.45

Case #3 - William

- 48 you man with h/o IDU (meth), HIV co-infection. Has moved through sober living to independent housing, now w/ GF and daughter
- Prior HIV care at Owen Clinic, GF HIV+ and delivered healthy HIV – daughter
- On FTC/TDF/EFV but fell out of care
- Presented to Ciaccio with VL 16,227; CD4 85 (9%)
- Genosure MG: M184V, K103N, K65R

Case #3 – William (cont)

- HCV Genotype 1A; VL 852,100 IU/mL
- CBC: plts: 133; CMP: AST/ALT: 160/126
- Abd U/S: coarse echotexture, spleen 14 cm
- Liver Biopsy = Stage IV fibrosis (Cirrhosis)

- On DTG + DRV/r = VL undetectable; CD4 329 (27%)

APRI = 3.008; Fib-4 = 5.14

Who should be first in line?

- **Lauren**
- **Richard**
- **William**

FAMILY HEALTH CENTERS OF SAN DIEGO

Who should be first in line?

- **Lauren** — United Healthcare — Simeprevir + Sofosbuvir
- **Richard** — LIHP → Care 1st Medi-Cal — Sofosbuvir + Pegasys + Ribavirin
- **William** — Molina — "Thre is no evidence the patient has failed formulary alternatives Boceprevir or Telaprevir"

FAMILY HEALTH CENTERS OF SAN DIEGO

wp OPINIONS

The global AIDS response can help in fighting hepatitis C

By Paul Farmer, Published: February 12

Paul Farmer is a professor at Harvard University and an infectious disease physician with the Brigham and Women's Hospital in Boston. He co-founded Partners in Health.

"*The idea that some lives matter less is the root of all that's wrong with the world.*"

—DR. PAUL FARMER
Chief Strategist & Co-founder

Partners In Health

FAMILY HEALTH CENTERS OF SAN DIEGO

Final Thoughts

- The Hepatitis C Epidemic is upon us:
  - 3-5 million chronically infected
  - Rapidly rising liver-related mortality
- Testing and linkage to care are needed
  - Still only 50% estimated diagnosed
- Rational triage *must* occur
  - Look for non-invasive measures of fibrosis
- HCV treatments are improving rapidly
  - Costs may be prohibitive to allow equitable access

Questions?