Addressing SUD-related Comorbidities, such as Hepatitis, HIV, Depression, Anxiety, and PTSD

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  - Harm Reduction Counseling and Injectable Naltrexone in Homeless persons with Severe Alcohol Dep.
  - Preventing Addiction Related Suicide
  - PTSD Treatment in Persons with Severe Cannabis Dep
  - Contingency Management of Alcohol in Mentally Ill
  - Comparing CAMS to TAU after recent suicide attempts
- Dept of Defense
  - Suicide Prevention in Active Duty Soldiers

Medical co-occurring disorders: focus on Hepatitis C

Hepatitis C

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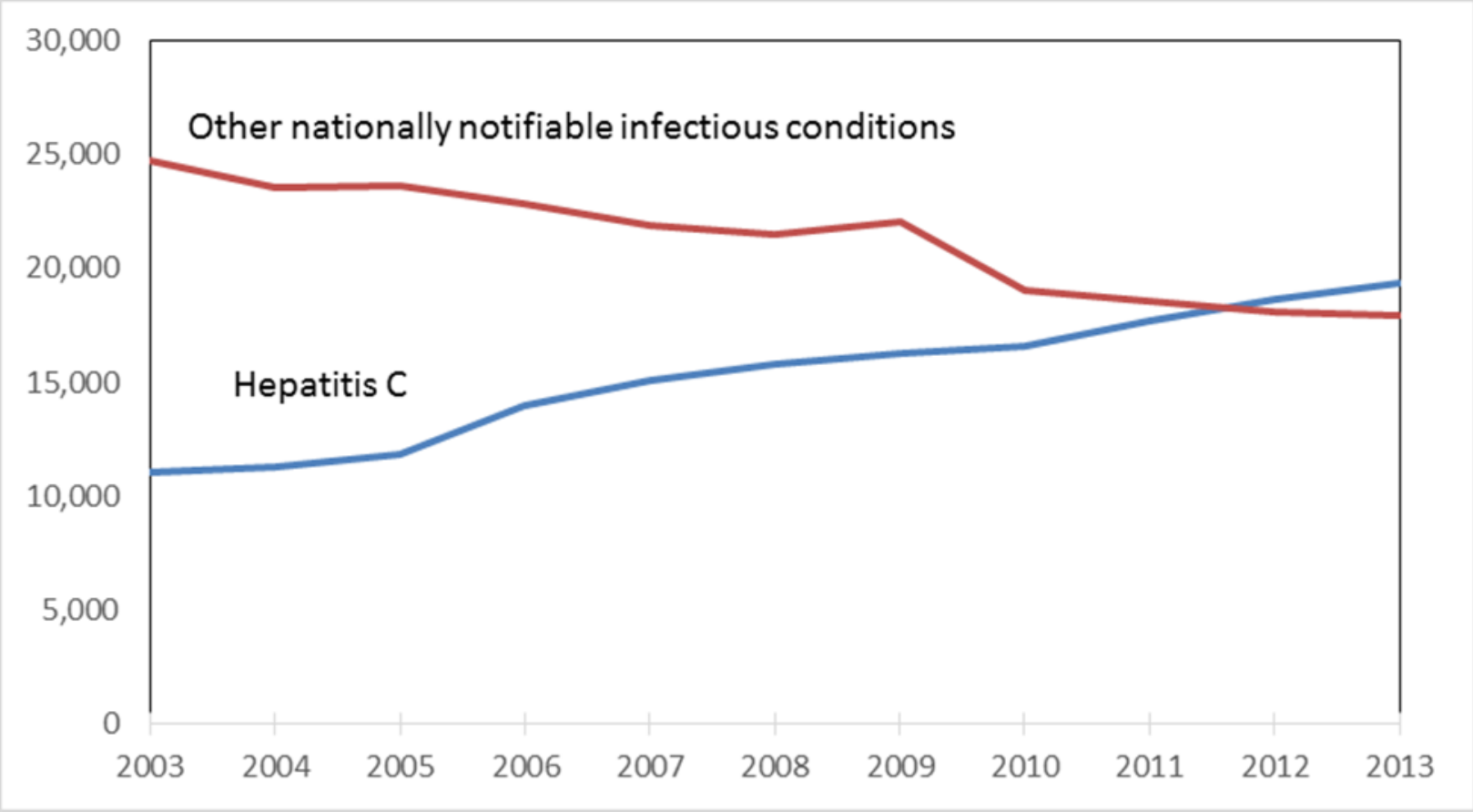
Learning Objectives

- Describe the epidemiology of HCV in the United States
- Interpret HCV testing
- Recognize the importance of addressing HCV in the primary care setting

HCV Deaths and Deaths from Other Nationally Notifiable Infectious Diseases,* 2003- 2013



* TB, HIV, Hepatitis B and 57 other infectious conditions reported to CDC

Holmberg S, et al. "Continued Rising Mortality from Hepatitis C Virus in the United States, 2003-2013"
Presented at ID Week 2015, October 10, 2015, San Diego, CA

Hepatitis C Prevalence in the United States

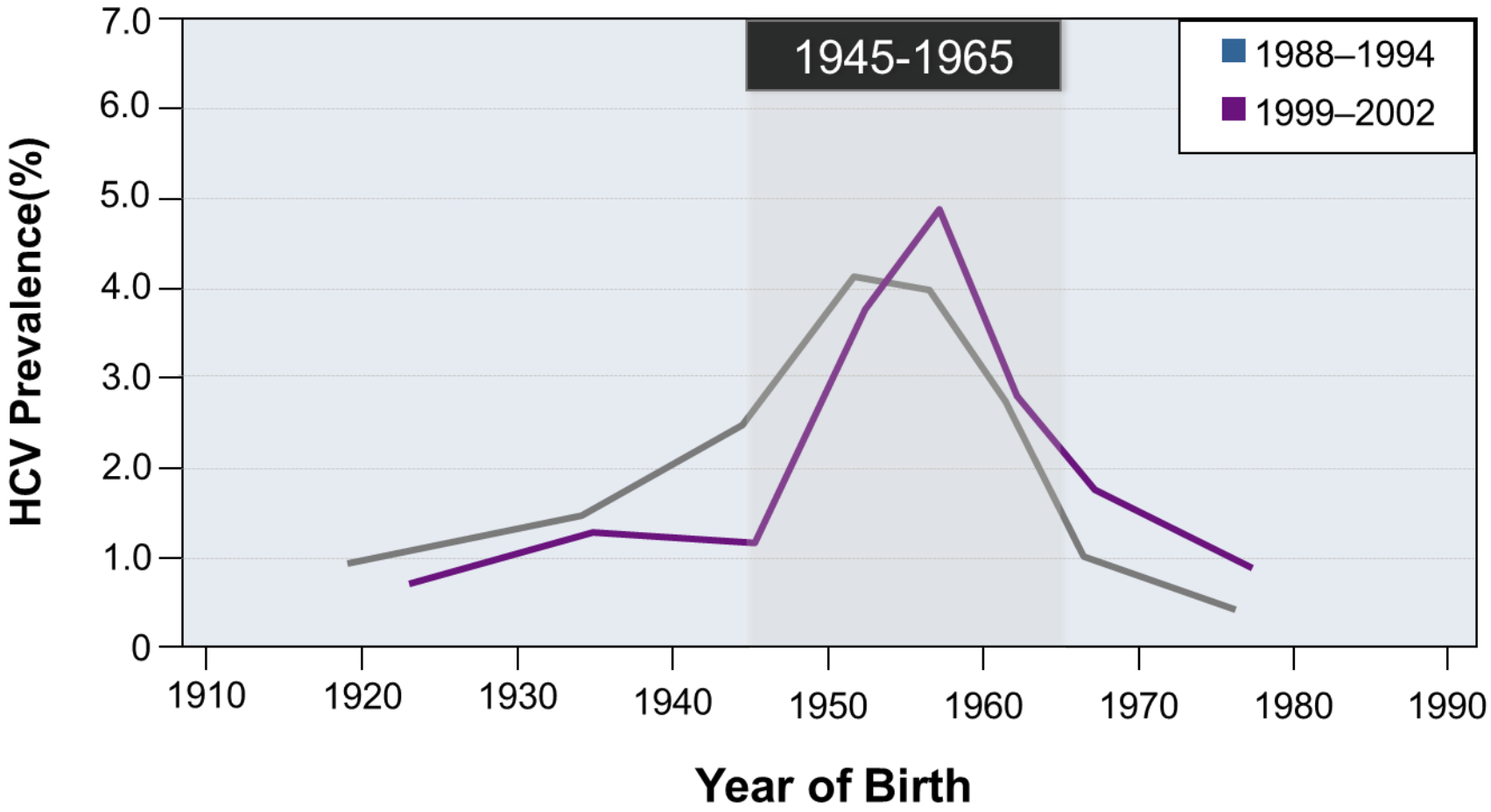
- NHANES (2003-2010)
  - 3.6 million chronically infected (anti-HCV)
  - 2.7 million currently infected (82% of anti-HCV positive)
- Populations not included in NHANES:

Population	Estimated Size	Prevalence (anti-HCV, %)	Number Chronically Infected
Incarcerated	2,186,230	23.1	505,350
Homeless	691,899	32.1	222,100
Hospitalized	478,054	15.6	74,576
Nursing homes	1,446,959	4.5	65,113
Active-duty military	1,404,060	0.5	7,020
Indian reservations	1,069,411	11.5	123,224
Total			**997,384**

Denniston, Ann. Int. Med. 2014, Edlin, Hepatology 2015; Armstrong GL, Ann Int. Med. 2006;144:705-14

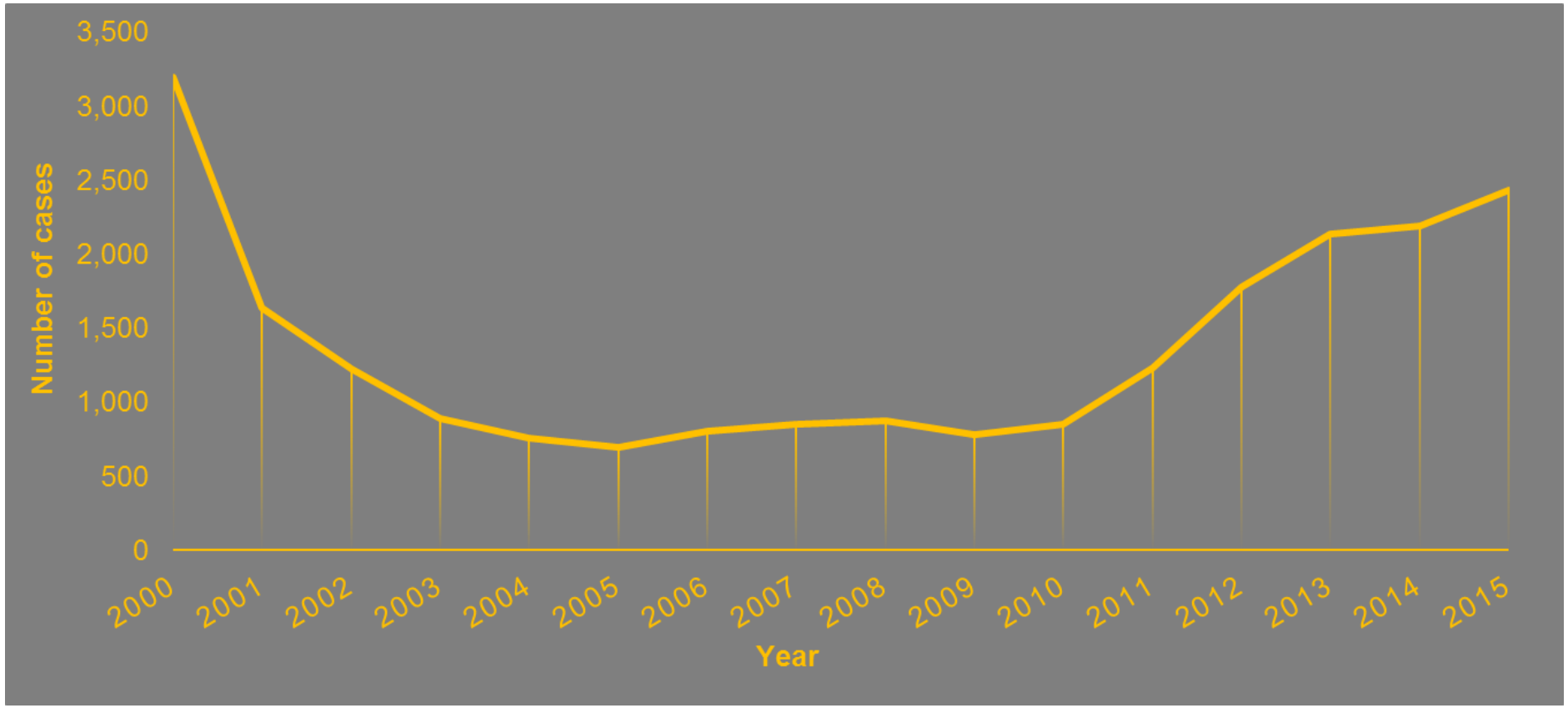
NHANES SURVEY: UNITED STATES, 1988-1994 AND 1999-2002

PREVALENCE OF HCV ANTIBODY, BY YEAR OF BIRTH



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

Reported Number of Acute Hepatitis C cases — United States, 2000–2015

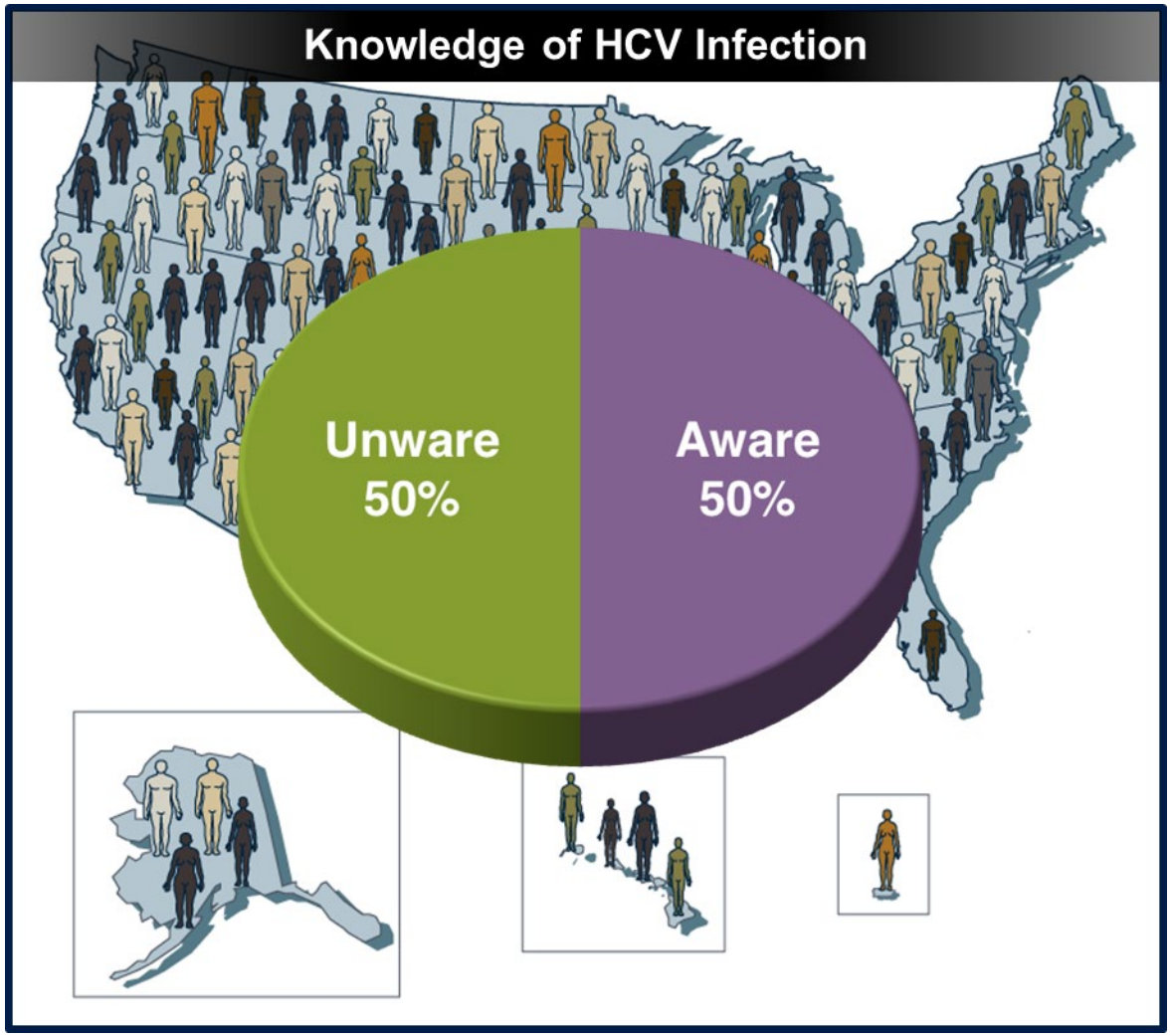


Source: National Notifiable Diseases Surveillance System (NNDSS

Role of the Primary Care Clinician in HCV

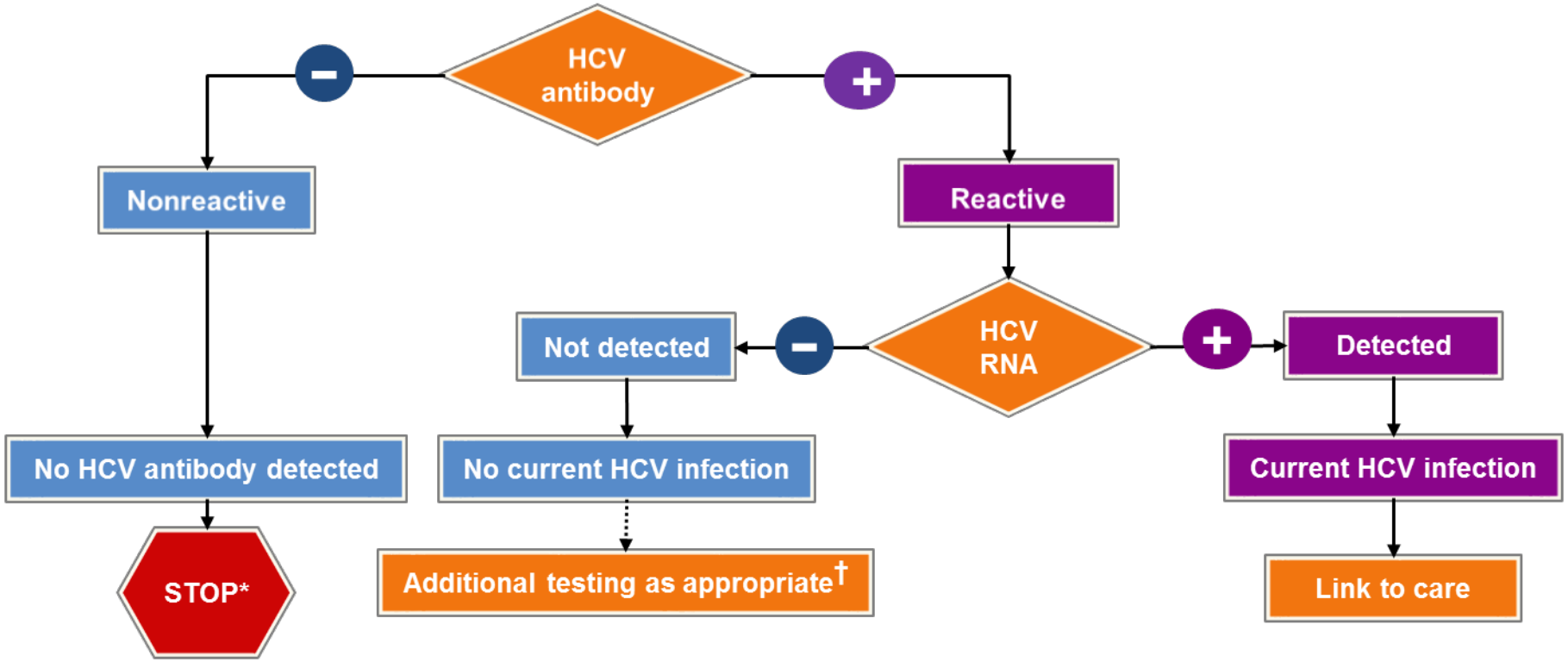
- Screening for HCV
- Counseling on modifiable risk factors important in disease progression
- Staging of liver disease
- HCC surveillance
- Recognition of extra-hepatic manifestations
- HCV treatment (with mentoring) or referral

NHANES SURVEY, UNITED STATES, 2001-2008
AWARENESS OF HCV INFECTION STATUS



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

Recommended Testing Sequence for Identifying Current Hepatitis C Virus (HCV) Infection



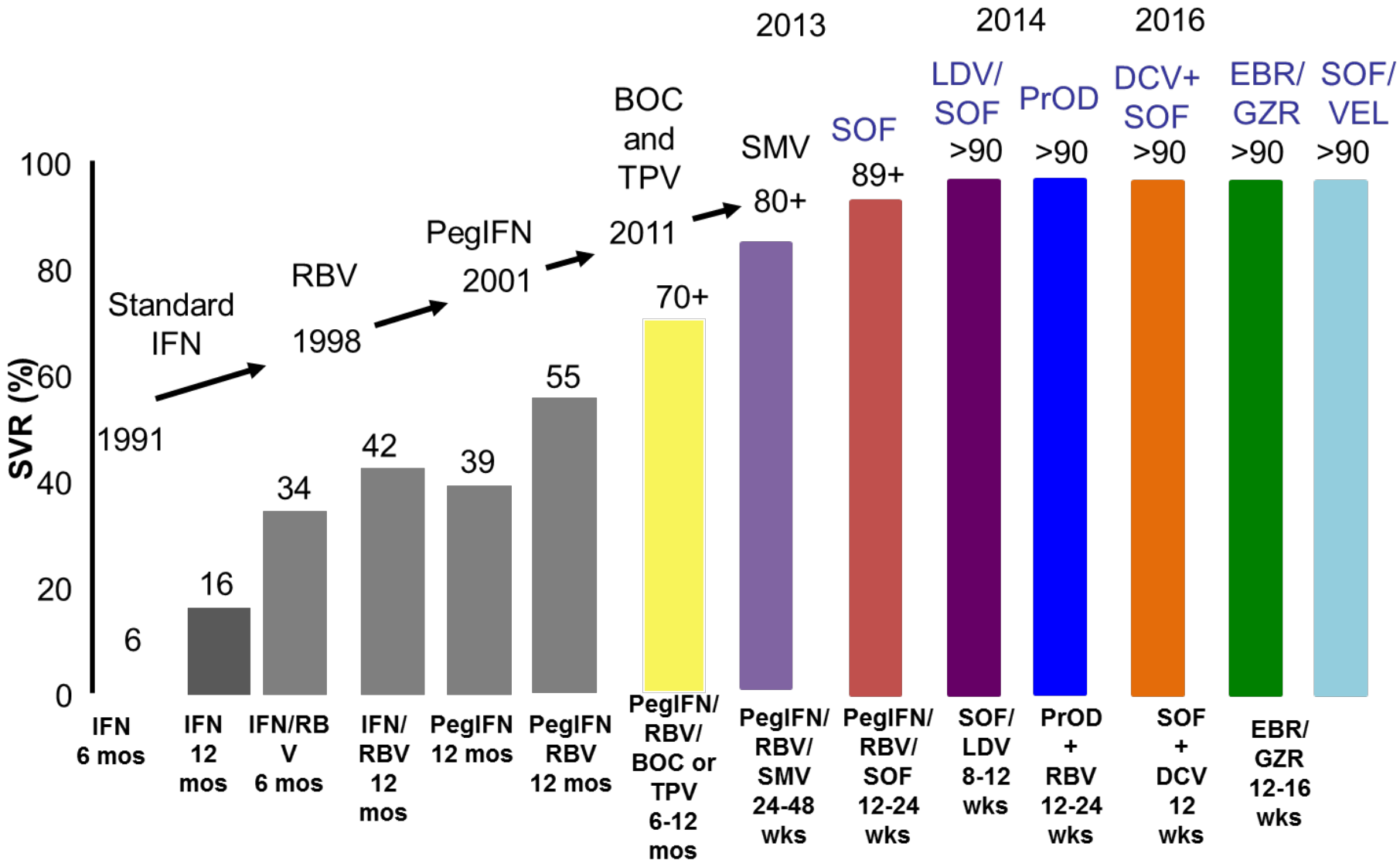
* For persons who might have been exposed to HCV within the past 6 months, testing for HCV RNA or follow-up testing for HCV antibody is recommended. For persons who are immunocompromised, testing for HCV RNA can be considered.

† To differentiate past, resolved HCV infection from biologic false positivity for HCV antibody, testing with another HCV antibody assay can be considered. Repeat HCV RNA testing if the person tested is suspected to have had HCV exposure within the past 6 months or has clinical evidence of HCV disease, or if there is concern regarding the handling or storage of the test specimen.

Slide courtesy AASLD Curriculum & Training

Source: CDC. Testing for HCV infection: An update of guidance for clinicians and laboratorians. *MMWR.* 2013;62(18).

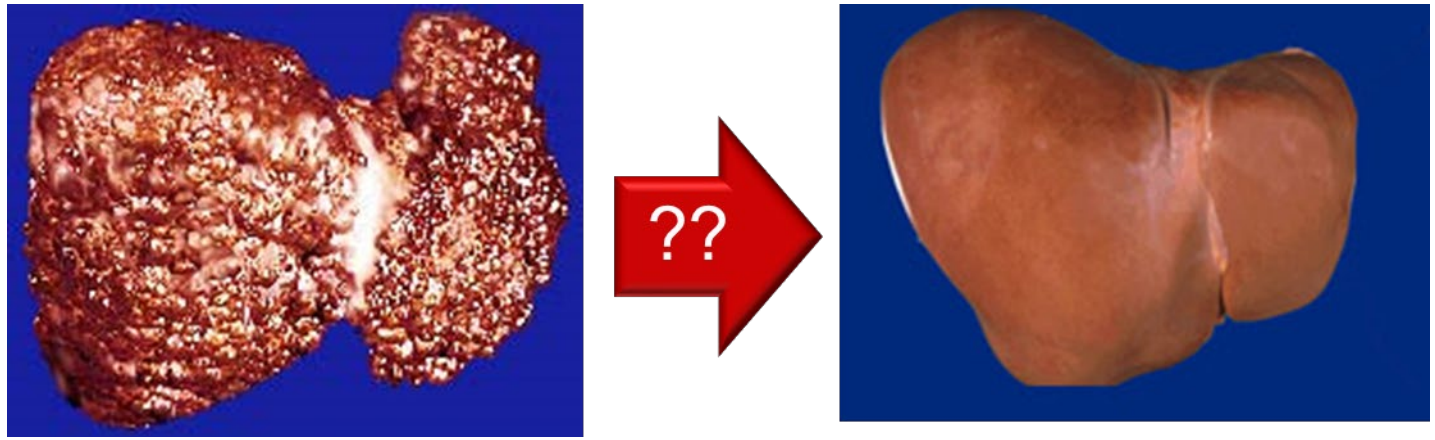
The Evolution of Highly Effective Treatment



WHAT DO WE GET WITH HCV TREATMENT?

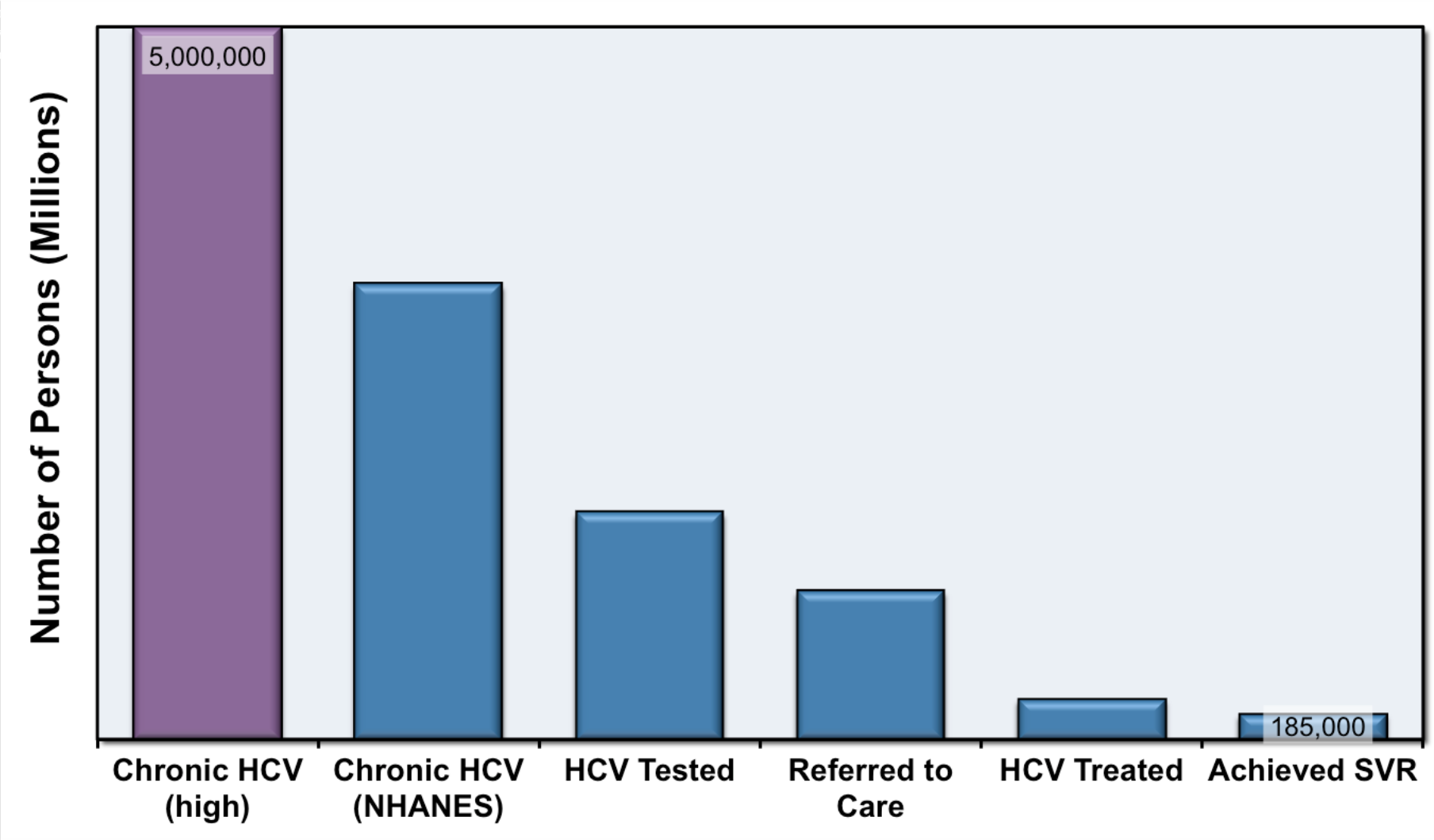
SVR (cure) of HCV is associated with:

- 70% Reduction of Liver Cancer
- 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

HEPATITIS C CASCADE OF CARE IN UNITED STATES



Source: Holmberg SD, et al. N Engl J Med. 2013;368:1859-61.

HCV Treatment in PWID

- Treatment of HCV in PWID has been very limited
  - Stigma
  - Drug use status as a criterion for treatment exclusion
  - Incarceration in prisons where treatment is limited
  - Concern for HCV reinfection
- Current AASLD/IDSA HCV Treatment Guidelines recommend HCV treatment for all persons including PWID
- PWID can be successfully treated for HCV on-site in an opioid treatment program rather than being referred

Mehta et al., 2008;Grebely, Oser, Taylor, & Dore, 2013; Oramasionwu, Moore, & Toliver, 2014; Wolfe et al., 2015; Butner, 2017.

Co-Occurring Psychiatric and Substance Use Disorder in OUD

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Questions for Co-Occurring Disorders in Primary Care Settings

- Are psychiatric symptoms present only during substance use disorder?

  →Likely psychiatric disorder due to substance

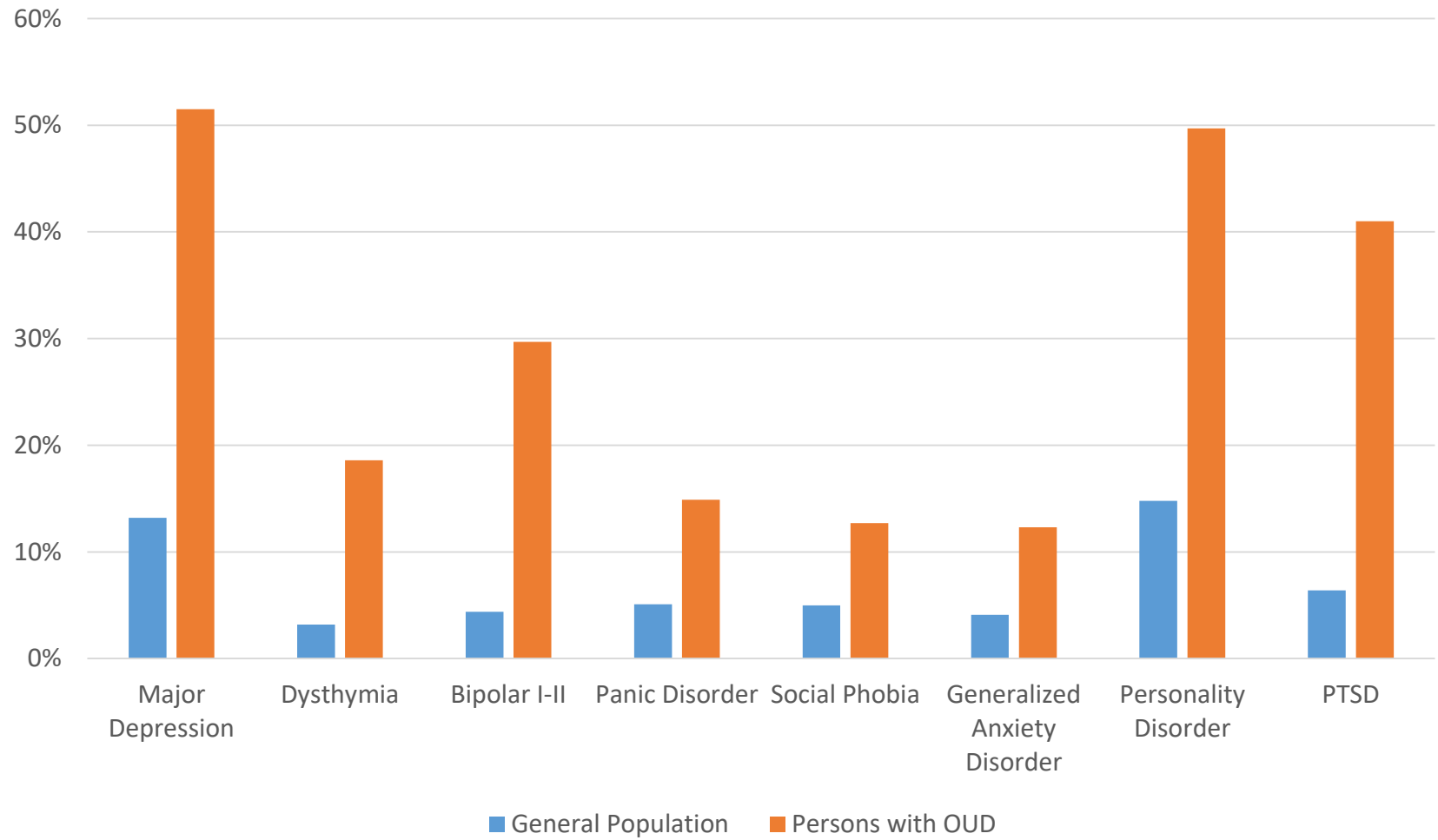
- Are psychiatric symptoms present before substance use disorder, and/or during extended periods of sobriety?

  → Likely co-occurring psychiatric disorder

- Are psychiatric symptoms present before substance use disorder, and/or during extended periods of sobriety, as well as during substance use disorder?

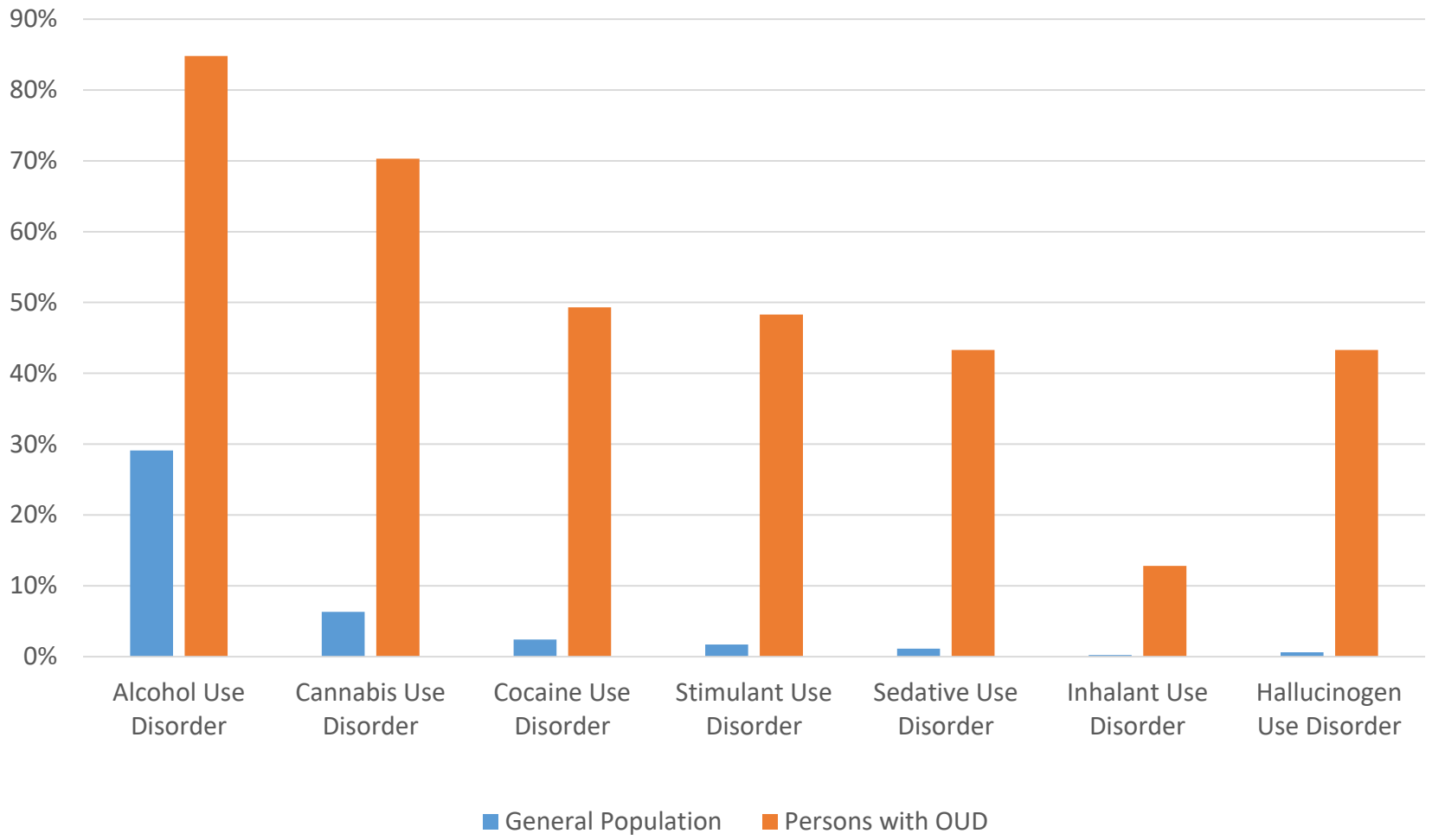
  → Likely co-occurring psychiatric disorder, +/- psychiatric disorder due to substance

Lifetime Prevalence of Psychiatric Disorders: General Population vs OUD



Grant et al 2004, Grella et al 2009, Hasin et al 2015, Mills et al 2004

Lifetime Prevalence of Substance Use Disorders: General Population vs OUD



Grant et al 2004, Grant et al 2016, Grella et al 2009, Hasin et al 2015

Psychiatric Disorders and Opioid Dependence Reciprocally Increase Risk

- Pre-existing psychiatric disorders:
  - Generalized anxiety disorder: 11x risk of developing opioid dependence
  - Bipolar I disorder: 10x risk of developing opioid dependence
  - Panic disorder: 7x risk of developing opioid dependence
  - Major depression: 5x risk of developing opioid dependence

- Pre-existing opioid dependence:
  - 9x risk of developing panic disorder
  - 5x risk of developing major depression
  - 5x risk of developing bipolar I disorder
  - 4x risk of developing generalized anxiety disorder

Martins et al 2009

Co-Occurring Psychiatric Disorders: Treatment Goals

- Acute Phase: 1-3 months
  - Non-response: <25% reduction in symptoms
  - Partial response: 25-50% reduction in symptoms
  - Response: >50% reduction in symptoms
  - Remission: no symptoms, e.g. PHQ-9 <5
- Continuation Phase: 3-12 months
  - Prevent relapse: another episode within 6 months of remission
- Maintenance Phase: 1-3 years
  - Prevent recurrence: another episode after 6 months of remission
- Treatment Goal: Durable remission

Co-Occurring Depressive Disorders

- Co-occurring depressive disorders treatment in OUD
  - Positive RCTs in methadone MAT: imipramine, doxepin
  - Negative RCTs in methadone MAT: imipramine, doxepin, bupropion, sertraline, fluoxetine
  - No RCTs in bup MAT
- Bup has empirical support as antidepressant outside OUD
- Lifetime major depression correlates positively with abstinence during bup MAT for OUD
- Depressive symptoms in OUD
  - Bup and methadone MAT equally improve depressive symptoms in patients with OUD – ~50% reduction
  - Naltrexone MAT does not appear to worsen depressive sx

Co-Occurring Depressive Disorders: Treatment

- Recommend first stabilizing OUD on MAT for ~6 weeks
- Depressive disorder remits?
  - Continue MAT as treatment of OUD and depressive disorder
- Depressive disorder persists?
  - Treat depressive disorder per established guidelines
    - Measurement based care: track and respond to depression using serial PHQ-9s
    - Shared decision making and patient activation: educated patient choses treatment direction, team uses behavioral activation
    - Systematic follow up: team contacts patient proactively to address symptoms and concerns
    - Stepped care: proactive treatment titration, consultation with behavioral health in resistant illness
    - Treat to target: remission defined as PHQ-9 score <5

Dean et al 2004, Dreifuss et al 2013, Fava et al 2016, Krupitsky et al 2016, Nunes et al 2004

Co-Occurring Major Depression: Treatment

- Major Depressive Disorder
  - Psychotherapy, e.g.: IPT, CBT, Behavioral Activation
  - Medication
  - Psychotherapy plus medication
  - General treatment sequence: Psychotherapy → SSRI → SNRI → Bupropion → Mirtazapine → TCA → rTMS → ECT → MAOI

Huhn et al 2014, Rush et al 2006

Co-Occurring Anxiety Disorders: Treatment

- Panic Disorder
  - Psychotherapy
  - Medication
  - General treatment sequence: Psychotherapy → SSRI → SNRI → Imipramine
- Social Phobia
  - Psychotherapy
  - Medication
  - General treatment sequence: Psychotherapy → SSRI → SNRI
- Avoid benzos in MAT: 2x risk of all-cause mortality
- Avoid MAOIs in MAT: risk of serotonin syndrome

Huhn et al 2014, Abrahamsson et al 2017

Co-Occurring Anxiety Disorders: Treatment

- Generalized Anxiety Disorder
  - Psychotherapy
  - Medication
    - Pregabalin
    - Hydroxyzine
    - SNRI or SSRI
    - Buspirone
  - General treatment sequence: Psychotherapy → Hydroxyzine → SNRI → SSRI → Pregabalin → Buspirone
- Avoid benzos in MAT: 2x risk of all-cause mortality
- Caution pregabalin in MAT: 3x risk of overdose death

Huhn et al 2014, Hidalgo et al 2007, Abrahamsson et al 2017

Co-Occurring PTSD: Treatment

- Psychotherapy, e.g.: CBT, PE, EMDR, SS
  - Positive RCT of PE for PTSD in methadone MAT
  - CBT for PTSD in buprenorphine MAT reduces positive urines
- Medication
  - Prazosin reduces nighmares and hyper-arousal assoc w PTSD
  - Note: prazosin only studied as augmentation of other PTSD treatment
- General treatment sequence: Psychotherapy → SSRI → SNRI → Prazosin Augmentation → TCA

Huhn et al 2014, Sunders et al 2015, Schiff et al 2015, Seal et al 2016, Peirce et al 2016

Insomnia

- Reported in up to 21% of patients on buprenorphine MAT
  - Central sleep apnea demonstrated in 33%
  - Nocturnal hypoxemia demonstrated in 39%
  - No RCTs examining insomnia treatment in buprenorphine MAT
- Reported in up to 84% of patients on methadone MAT
  - Central sleep apnea in up to 60%
  - Positive RCTs of insomnia treatment in methadone MAT
    - Cognitive behavioral therapy for insomnia (CBTI)
    - Suan Zao Ren Tang (sour jujube concoction) *GABA-ergic
    - Acupuncture
  - Negative RCTs of insomnia treatment in methadone MAT
    - Trazodone

Robabeh et al 2015, Farney et al 2013; Chan et al 2015; Li et al 2012

Insomnia: Treatment

- Assess for sleep disordered breathing and treat!

- Psychotherapy
  - CBT-I: stimulus control, sleep restriction, sleep hygiene, relaxation, cognitive restructuring
- Medication

- General treatment sequence: Psychotherapy → Doxepin → Ramelteon → Trazodone → Melatonin

- Caution z-drugs in MAT: 1.6x risk of overdose death

Sateia et al 2017, Smith et al 2002; Schutte-Rodin et al 2008, Abrahamsson et al 2017

Summary

- Psychiatric disorders strikingly common in OUD
- Psychiatric disorders and OUD reciprocally increase risk
- Limited direct literature on psychiatric disorders treatment in OUD or MAT
- Stabilize OUD with MAT
- Psychotherapy first line in major depression, anxiety disorders, PTSD, and insomnia
- Medication first line in dysthymia
- Caution pregabalin, z-drugs
- Avoid benzos

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