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Medications for Opioid Use Disorder and Hepatitis C: Access and Adherence Among People Who Inject Drugs

Dr. Judith Tsui, MD, MPH
University of Washington

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This Live activity, Medications for Opioid Use Disorders and Hepatitis C: Access and Adherence among People who Inject Drugs, with a beginning date of 06/26/2019, has been reviewed and is acceptable for up to 1.00 Prescribed credit(s) by the American Academy of Family Physicians. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

Today's Presenter

Dr. Judith Tsui, MD, MPH

- Board-certified physician, Harborview Medical Center
- Associate professor, UW General Internal Medicine
- Clinician investigator
  - Opioid Use Disorder
  - Pain
  - Hepatitis C and HIV

UNIVERSITY of WASHINGTON

Medications for Opioid Use Disorder and Hepatitis C: Access and Adherence Among People Who Inject Drugs

Judith Tsui, MD, MPH
Associate Professor of Medicine
Division of General Internal Medicine
University of Washington School of Medicine

Northwest ATTC Webinar
June 26, 2019

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*This PCORI-funded study accepts medication and funds for pharmacy dispensing from Gilead

Objectives

- Describe epidemiology of the opioid crisis and its overlap with hepatitis C virus (HCV)
- Review evidence that medications for opioid use disorder (OUD) can prevent HCV
- Highlight research showing that medications for HCV and OUD are under-utilized, and describe clinical programs that have been implemented at Harborview to address gaps
- Describe on-going research to improve OUD/HCV medication access and adherence

Patient Stories: T.S.*

- 60 yo man presenting for primary care
- h/o experimenting with heroin as young adult
- Back injury in his 40s, introduced to prescription opioids
- Receives high-dose opioids for chronic pain
- Multiple hospitalizations for “over-sedation”
- PCP discontinued opioids, subsequently lapsed to heroin
- Started on buprenorphine a year ago, doing well
- Recently diagnosed with HCV

*Patient is a composite of real patients

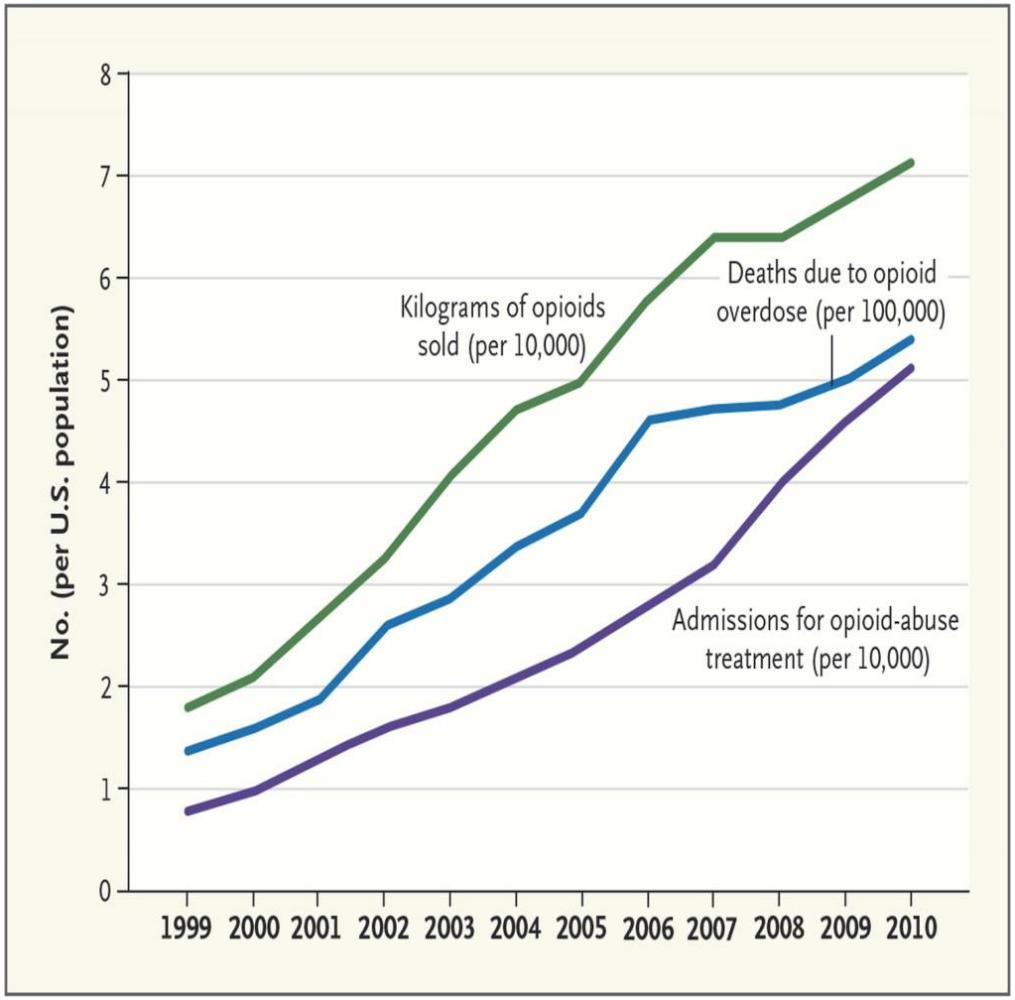
Patient Stories: C.L.*

- 28 yo woman, seen in ED for cellulitis
- H/o childhood physical and sexual trauma, PTSD
- Age 13 she had experimented with alcohol, cigarettes, marijuana
- Age 15 introduced to prescription opioids through a friend
- Age 17 started snorting heroin, within a year injecting
- Was on previously on methadone, but self-discontinued
- Currently homeless, trades sex for money and drugs
- Recently diagnosed with hepatitis C

*Patient is a composite of real patients

Concurrent Epidemics of Opioid Use Disorders and Hepatitis C

National Opioid Trends, 1999-2010



Volkow ND et al. *N Engl J Med.* 2014

Trends in Opioid Prescribing

- Opioid prescribing rate peaked in 2012, but remains high (59 prescriptions per 100 persons in 2017)[1,2]
- In 16% of U.S. counties, enough opioid prescriptions were dispensed for every person to have one[1]
- In a study of 140 patients who were seeking treatment for OUD (i.e. opioid addiction) in 2006-2009, **29% reported they were introduced to opioids through a physician**[3]

1. https://www.cdc.gov/drugoverdose/maps/rxrate-maps.html
2. Guy GP Jr. et al. *MMWR*. 2017
3. Tsui JI et al. *J of Subst Abuse Treat*. 2010

Origins of the Opioid Crisis

- Pharmaceutical company promotion
- Wide-spread prescribing of opioids for chronic pain
- Diversion and widespread non-medical use of opioids
- Increased availability, decreased cost of heroin

The New York Times

Purdue Pharma and Sacklers Reach $270 Million Settlement in Opioid Lawsuit

The agreement, negotiated with the state of Oklahoma, will allow the maker of OxyContin to avoid a televised courtroom trial.

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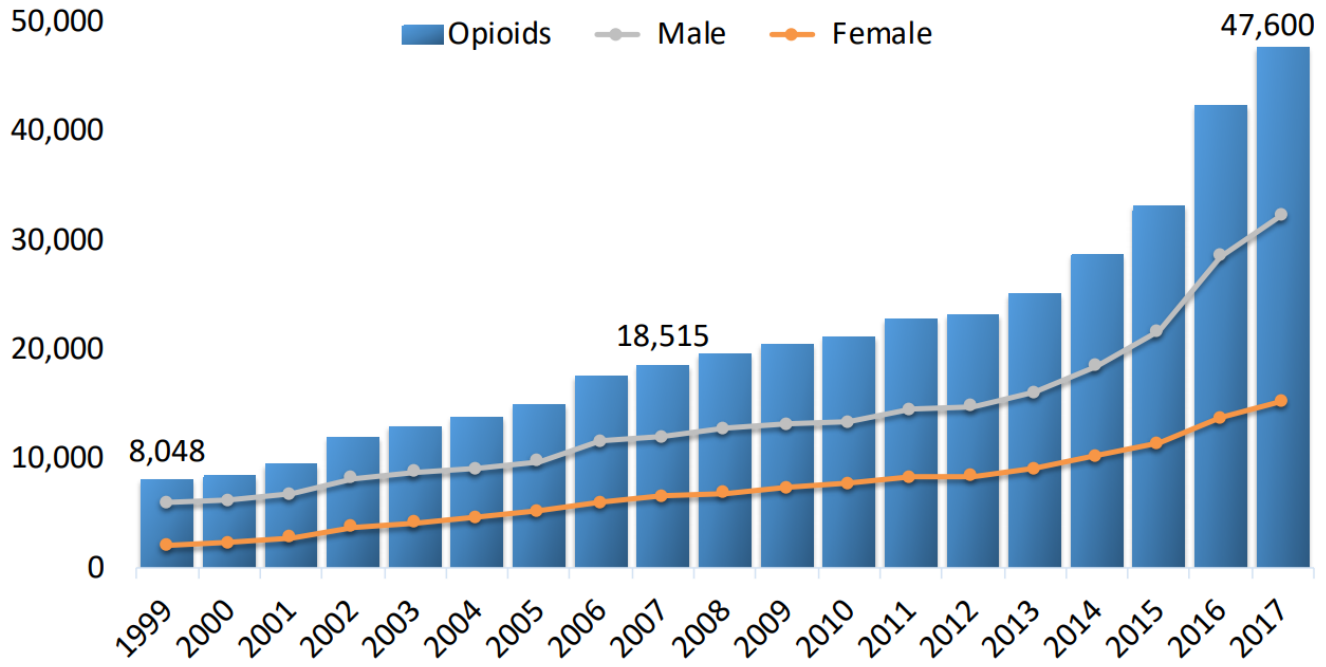
Lawsuit Details How The Sackler Family Allegedly Built An OxyContin Fortune

Dreamland: The True Tale of America's Opiate epidemic by Sam Quinones
https://www.nytimes.com/2019/03/26/health/opioids-purdue-pharma-oklahoma.html
https://khn.org/news/lawsuit-details-how-the-sackler-family-allegedly-built-an-oxycontin-fortune/

National Overdose Trends

Figure 3. **National Drug Overdose Deaths Involving Any Opioid,** Number Among All Ages, by Gender, 1999-2017



Source: : Centers for Disease Control and Prevention, National Center for Health Statistics. Multiple Cause of Death 1999-2017 on CDC WONDER Online Database, released December, 2018

Consequences of Opioid Crisis: Increasing Cases of HIV and HCV Associated with Injecting Drugs

- "Wake-up call": January 1, 2015 Indiana State Department of Health announced 11 confirmed cases of HIV in rural community[1]
  - Investigation found 181 HIV cases total, nearly all also HCV+
  - Outbreak was linked to injecting a prescription opioid (oxymorphone)
- Subsequent outbreaks among persons who inject drugs (PWID) reported in northeastern MA[4] and Seattle, WA[5]

1. Caitlin C et al. *MMWR*. 2015
2. Peters PJ et al. *NEJM.* 2016
3. Gonsalves GS. *Lancet HIV.* 2018
4. Cranston K et al. *MMWR*. 2019
5. Golden M et al. *MMWR*. 2019

Consequences of Opioid Crisis: Increasing Cases of HIV and HCV Associated with Injecting Drugs

Morbidity and Mortality Weekly Report (*MMWR*)

Outbreak of Human Immunodeficiency Virus Infection Among Heterosexual Persons Who Are Living Homeless and Inject Drugs — Seattle, Washington, 2018

Matthew R. Golden, MD[1,2]; Richard Lechtenberg, MPH[1]; Sara N. Glick, PhD[1,2]; Julie Dombrowski, MD[1,2]; Jeff Duchin, MD[1,2]; Jennifer R. Reuer, MPH[3]; Shireesha Dhanireddy, MD[2]; Santiago Neme, MD[2]; Susan E. Buskin, PhD[1]

Notes from the Field: HIV Diagnoses Among Persons Who Inject Drugs — Northeastern Massachusetts, 2015–2018

Weekly / March 15, 2019 / 68(10);253–254

Kevin Cranston, MDiv[1]; Charles Alpren, MBChB[2,3]; Betsey John, MPH[1]; Erica Dawson, PhD[3,4]; Kathleen Roosevelt, MPH[1]; Amanda Burrage, MD[3,5]; Janice Bryant[1]; William M. Switzer, MPH[4]; Courtney Breen, MA[1]; Philip J. Peters, MD[4]; Tracy Stiles, MS[1]; Ashley Murray, MPH[4]; H. Dawn Fukuda, ScM[1]; William Adih, PhD[4]; Linda Goldman, MBA, MSW[1]; Nivedha Panneer, MPH[4]; Barry Callis, MSW[1]; Ellsworth M. Campbell, MSc[4]; Liisa Randall, PhD[1]; Anne Marie France, PhD[4]; R. Monina Klevens, DDS[1]; Sheryl Lyss, MD[4]; Shauna Onofrey, MPH[1]; Christine Agnew-Brune, PhD[4]; Michael Goulart, MPH[1]; Hongwei Jia, PhD[4]; Matthew Tumpney, ScM[1]; Paul McClung, MD[4]; Sharoda Dasgupta, PhD[4]; Danae Bixler, MD[6]; Kischa Hampton, MSW[4]; Amy Board, DrPH[7]; Jenifer Leaf Jaeger, MD[2]; Kate Buchacz, PhD[4]; Alfred DeMaria Jr., MD[1] (View author affiliations)

1. Cranston K et al. *MMWR*. 2019
2. Golden M et al. *MMWR*. 2019

Changing Epidemiology of HCV

MAJOR ARTICLE

Emerging Epidemic of Hepatitis C Virus Infections Among Young Nonurban Persons Who Inject Drugs in the United States, 2006–2012

Anil G. Suryaprasad,[1] Jianglan Z. White,[1] Fujie Xu,[1] Beth-Ann Eichler,[2] Janet Hamilton,[2] Ami Patel,[3,4] Shadia Bel Hamdounia,[3] Daniel R. Church,[5] Kerri Barton,[5] Chardé Fisher,[6] Kathryn Macomber,[6] Marisa Stanley,[7] Sheila M. Guilfoyle,[7] Kristin Sweet,[8] Stephen Liu,[1] Kashif Iqbal,[1] Rania Tohme,[1] Umid Sharapov,[1] Benjamin A. Kupronis,[1] John W. Ward,[1] and Scott D. Holmberg[1]

Suryaprasad AG et al. *Clin Infect Dis*. 2014

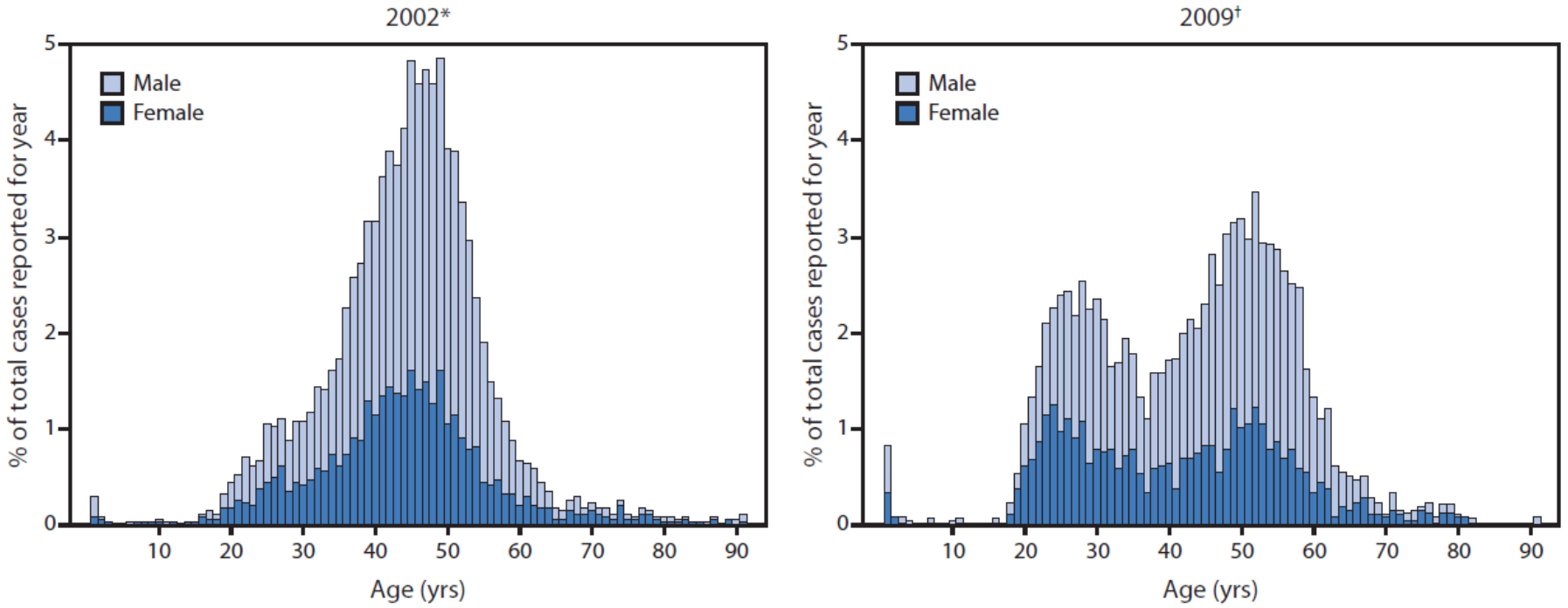
Emerging Epidemic of Hepatitis C Virus Infection Among Young Adult PWID

National surveillance data of acute HCV 2006-2012

- 7169 cases of acute HCV reported; 44% were ≤30 years old
- The majority (88%) of states reported increased incidence of HCV among young adults in 2012 compared to 2006
- Most cases were white (93%), non-Hispanic (92%)
- Approximately half female

Suryaprasad AG et al. *Clin Infect Dis.* 2014

Epidemiology of HCV in MA



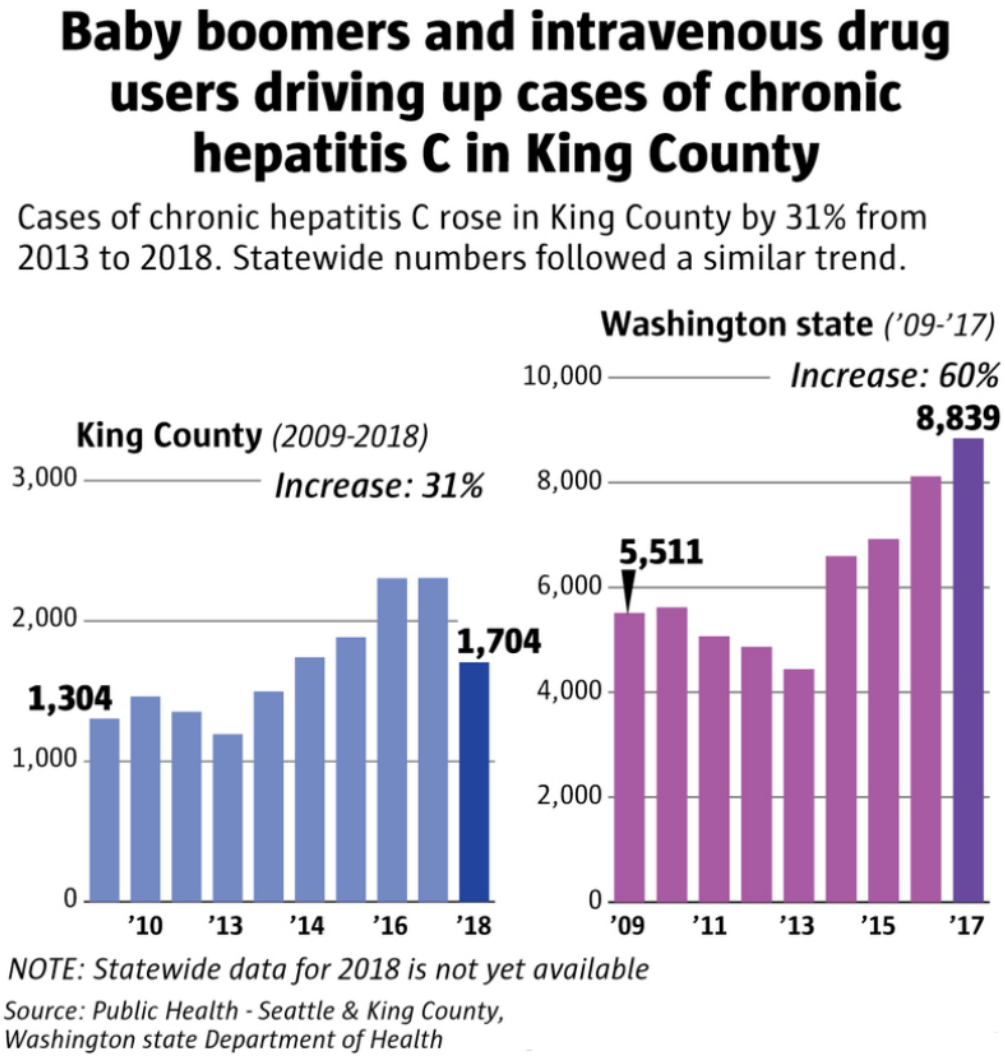
Age distribution of newly reported confirmed cases of hepatitis C virus infection --- Massachusetts, 2002 and 2009.

* N = 6,281; excludes 35 cases with missing age or sex information.

† N = 3,904; excludes 346 cases with missing age or sex information.

https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6017a2.htm#fig2

Epidemiology of HCV in WA State



https://www.seattletimes.com/seattle-news/health/whats-behind-the-increase-of-hepatitis-c-cases-in-washington-state/

A Crossroads…

The magnitude of the current opioid crisis and its infectious disease consequences have become abundantly clear… ***yet we have the tools to overcome the crisis.***

Medications for Opioid Use Disorder and Hepatitis C

The Good News: Effective Medications to Treat Opioid Use Disorders Exist

Medications to treat OUD include:

- Methadone (full opioid agonist)
- Buprenorphine (partial opioid agonist)
- Naltrexone (opioid antagonist)

Evidence from numerous studies demonstrate that medications can decrease[1-4]:

- Opioid craving/illicit use
- Overdose/mortality
- Injection drug use/HIV risk behaviors
- HIV and ***HCV incidence***

1. Mattick RP et al. Cochrane Database of Syst Rev. 2014
2. Schwartz R et al. AJPH 2012
3. Macarthur GJ et al. *BMJ*. 2012
4. Platt L et al. Cochrane Database Syst Rev. 2017

Original Investigation

Association of Opioid Agonist Therapy With Lower Incidence of Hepatitis C Virus Infection in Young Adult Injection Drug Users

Judith I. Tsui, MD, MPH; Jennifer L. Evans, MS; Paula J. Lum, MD, MPH; Judith A. Hahn, PhD; Kimberly Page, PhD, MPH

Tsui JI et al. *JAMA Intern Med*. 2014

Results: Sample Characteristics

- 552 participants were followed prospectively.
- Median age: 23 (IQR: 20-26); majority white males
- Median years injecting: 3.6 (IQR: 1.5-6.6); 60% reported heroin as drug of choice
- 82% reported no substance use treatment in the prior year

Incident HCV Infection in Young Adult Injectors

Table 2. Incident HCV Infection and Type of Drug Treatment Programs Attended in 552 Young Adult Injection Drug Users Followed Up in the UFO Cohort Study, San Francisco, California, 2000-2013

Baseline Characteristic	Incident HCV, No. of Participants	Person-years of Observation	Incidence per 100 Person-years (95% CI)[a]	RR (95% CI)	*P* Value
Overall	171	680	25.1 (21.6-29.2)	NA	NA
Drug treatment in past 3 mo[b]					
None	138	488	28.2 (23.9-33.4)	1 [Reference]	
Non-OA therapy	15	84	17.9 (10.8-29.6)	0.63 (0.37-1.08)	.09
OA detoxification	11	27	41.1 (22.8-74.2)	1.45 (0.80-2.69)	.23
Maintenance OA therapy[c]	7	81	8.6 (4.1-18.1)	0.31 (0.14-0.65)	.001

Abbreviations: HCV, hepatitis C virus; NA, not applicable; OA, opioid agonist; RR, rate ratio.

[a] Incidence was calculated using behavior or characteristic at the last period that patient was seronegative for HCV (uninfected during follow-up) or the first HCV-seropositive risk period (incident infections).

[b] For participants in wave 1, time frame is past year at baseline and past 3 months at follow-up; for participants in wave 2, past week; and for participants in wave 3, past 3 months.

[c] Includes OA therapy unspecified for wave 2 only.

Tsui JI et al. *JAMA Intern Med*. 2014

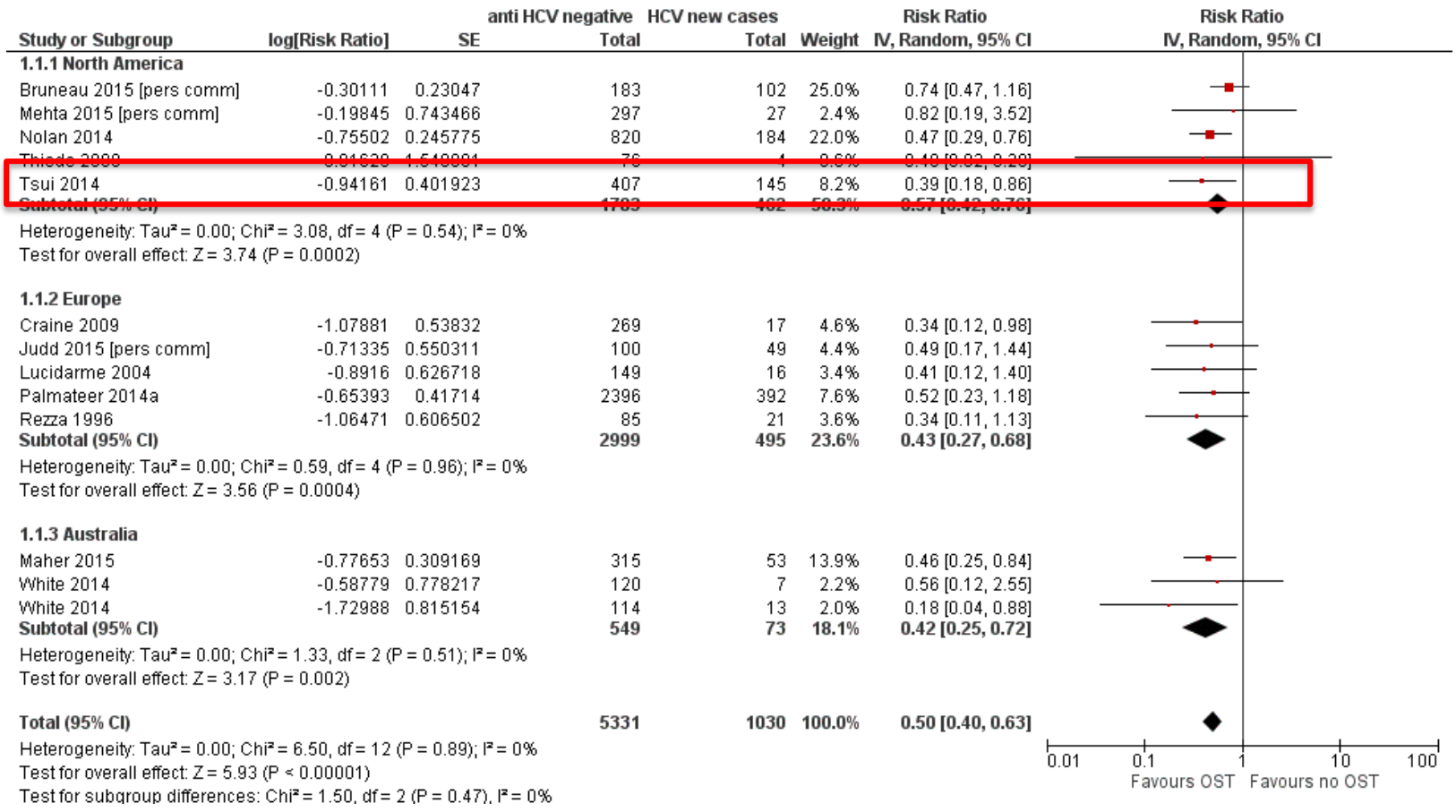
Adjusted Relative Hazards for Incident HCV Infection in Young Adult Injectors

Table 3. Multivariate Cox Proportional Hazards Regression Model of Independent Predictors of Incident HCV Infection in 552 Young Adult Injection Drug Users Followed Up in the UFO Cohort Study, San Francisco, California, 2000-2013

Characteristic	AHR (95% CI)[a]	*P* Value
Drug treatment in past 3 mo[b]		
None	1 [Reference]	NA
Non-OA therapy	0.71 (0.41-1.20)	.20
OA detoxification	1.39 (0.73-2.67)	.32
Maintenance OA therapy[c]	0.39 (0.18-0.87)	.02
Age, y	0.99 (0.94-1.04)	.66
Duration of injection drug use, y	1.03 (0.98-1.07)	.24
Sex		
Male	0.72 (0.52-1.00)	.05
Female	1 [Reference]	
Race/ethnicity		
White	1 [Reference]	.37
Nonwhite	1.17 (0.82-1.67)	
Homeless in past 3 mo		
No	1 [Reference]	.26
Yes	1.22 (0.86-1.74)	
Incarcerated in past 3 mo		
No	1 [Reference]	<.01
Yes	1.58 (1.12-2.23)	

Tsui JI et al. *JAMA Intern Med*. 2014

Cochrane 2017 Systematic Review: OAT for Prevention of HCV



Study or Subgroup	log[Risk Ratio]	SE	anti HCV negative Total	HCV new cases Total	Weight	Risk Ratio IV, Random, 95% CI
1.1.1 North America						
Bruneau 2015 [pers comm]	-0.30111	0.23047	183	102	25.0%	0.74 [0.47, 1.16]
Mehta 2015 [pers comm]	-0.19845	0.743466	297	27	2.4%	0.82 [0.19, 3.52]
Nolan 2014	-0.75502	0.245775	820	184	22.0%	0.47 [0.29, 0.76]
Thiede 2008	-0.91629	1.540891	76	4	0.6%	0.40 [0.02, 8.29]
Tsui 2014	-0.94161	0.401923	407	145	8.2%	0.39 [0.18, 0.86]
Subtotal (95% CI)			**1783**	**462**	**58.3%**	**0.57 [0.42, 0.76]**
Heterogeneity: Tau² = 0.00; Chi² = 3.08, df = 4 (P = 0.54); I² = 0%						
Test for overall effect: Z = 3.74 (P = 0.0002)						
1.1.2 Europe						
Craine 2009	-1.07881	0.53832	269	17	4.6%	0.34 [0.12, 0.98]
Judd 2015 [pers comm]	-0.71335	0.550311	100	49	4.4%	0.49 [0.17, 1.44]
Lucidarme 2004	-0.8916	0.626718	149	16	3.4%	0.41 [0.12, 1.40]
Palmateer 2014a	-0.65393	0.41714	2396	392	7.6%	0.52 [0.23, 1.18]
Rezza 1996	-1.06471	0.606502	85	21	3.6%	0.34 [0.11, 1.13]
Subtotal (95% CI)			**2999**	**495**	**23.6%**	**0.43 [0.27, 0.68]**
Heterogeneity: Tau² = 0.00; Chi² = 0.59, df = 4 (P = 0.96); I² = 0%						
Test for overall effect: Z = 3.56 (P = 0.0004)						
1.1.3 Australia						
Maher 2015	-0.77653	0.309169	315	53	13.9%	0.46 [0.25, 0.84]
White 2014	-0.58779	0.778217	120	7	2.2%	0.56 [0.12, 2.55]
White 2014	-1.72988	0.815154	114	13	2.0%	0.18 [0.04, 0.88]
Subtotal (95% CI)			**549**	**73**	**18.1%**	**0.42 [0.25, 0.72]**
Heterogeneity: Tau² = 0.00; Chi² = 1.33, df = 2 (P = 0.51); I² = 0%						
Test for overall effect: Z = 3.17 (P = 0.002)						
Total (95% CI)			**5331**	**1030**	**100.0%**	**0.50 [0.40, 0.63]**
Heterogeneity: Tau² = 0.00; Chi² = 6.50, df = 12 (P = 0.89); I² = 0%						
Test for overall effect: Z = 5.93 (P < 0.00001)						
Test for subgroup differences: Chi² = 1.50, df = 2 (P = 0.47), I² = 0%						

Platt L et al. Cochrane Database Syst Rev. 2017

Cochrane 2017 Systematic Review: OAT for Preventing HCV

- Review concluded that ***OAT reduces the risk of HCV acquisition by 50%***
  - Based on 12 observational studies (N=6361); no RCTs therefore quality of evidence is low[1]
  - Subsequent study suggested there may be an attenuated effect in females compared to males[2]

1. Platt L et al. Cochrane Database Syst Rev. 2017
2. Geddes L, Iversen J, Wand H, Esmaeili A, Tsui J, et al. *Clin Infect Dis*. 2019

Costs of OAT v. DAAs

- Methadone treatment: $126.00 per week or **$6,552** per year
- Buprenorphine: $115.00 per week or **$5,980** per year
- Gilead priced its first new hepatitis C drug, sofosbuvir, at $1,000 per pill, or **$84,000** for a three-month course of treatment

https://www.drugabuse.gov/publications/research-reports/medications-to-treat-opioid-addiction/how-much-does-opioid-treatment-cost

A Revolution in HCV Treatment

- The emergence of direct-acting antivirals (DAAs) has radically changed the HCV treatment paradigm
  - Sofosbuvir licensed 2013
  - Now multiple regimens, including pan-genotypic

- ***Nearly all patients (>90%) can be cured of HCV with 8-12 weeks of oral medications with few side effects***

http://www.hcvguidelines.org/full-report/when-and-whom-initiate-hcv-therapy

Treatment for HCV Pre and Post-DAA

THEN

- Treat for 24-48 weeks
- Weekly shots plus pills BID
- Risk of many side effects:
  - Depression, suicidality
  - Flu-like symptoms
  - Fatigue
  - Hair loss
  - Severe anemia
  - Immunosuppression
  - Rashes
  - Thyroid disease
- Only ~50% chance of getting cured.

NOW

- Treat for 8-12 weeks
- Daily pill(s)
- Side effects are rare and minor
- >90% chance of being cured

New HCV Elimination Directive

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Inslee: Erase hepatitis C in Washington by 2030

Originally published September 28, 2018 at 2:09 pm | *Updated September 28, 2018 at 9:48 pm*

1 of 6

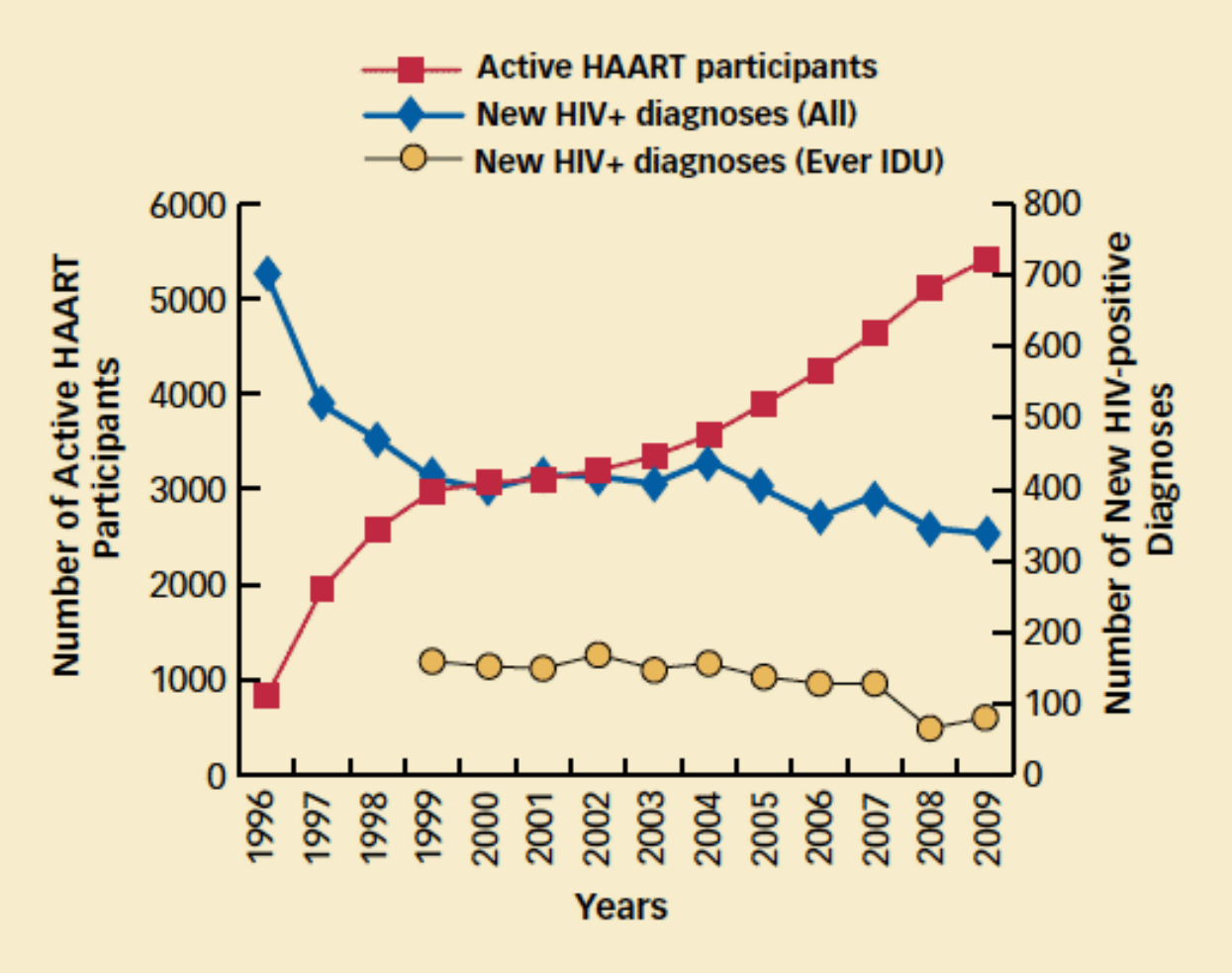
Gov. Jay Inslee, right, speaks with Alfonso Adinolfi of West Seattle about hepatitis C. They were at Harborview's Hepatitis and Liver Clinic in Seattle on Friday. Adinolfi, 66, contracted hepatitis C at the... (Ellen M. Banner / The Seattle Times) **More**

HCV Elimination Goal and Treatment of Persons Who Inject Drugs

- Elimination of HCV is now a global, national and state priority
  - WHO goal of elimination by 2030
  - "Hep C Free WA" initiative announced fall 2018
- Treating HCV among persons who inject drugs (PWID) is essential to achieve elimination
  - Treating "baby-boomers"→ reduces immediate complications (cirrhosis, liver cancer)
  - Treating young PWID→ reduces incidence and lowers prevalence over time ("treatment as prevention")

WHO Advocacy Brief 2016
Eliminating the Public Health Problem of Hepatitis B and C in the United States: Phase One Report. National Academies Press; 2016
https://www.cdc.gov/hepatitis/nasemreports.htm

Treatment as Prevention



Montaner, J. *The Lancet.* 2010

Rationale for HCV "Treatment as Prevention" among PWID

- DAA medications are highly effective and studies to date demonstrate nearly equivalent cure rates among DAA treated PWID[1] (including active drug users[2])
- Re-infection is believed to be relatively uncommon
  - 2.2 per 100 person-years (95% CI: 0.9-6.1) pre-DAA[3]
  - 4.6 per 100 person-years in recent study of DAA in drug users (C-EDGE CO-STAR[2])
- Re-infections may be preventable with syringe service programs and OAT access

1. Grebely J. *CID.* 2016
2. Dore G. *Annal Int Med*. 2016
3. Aspinall EJ. *CID*. 2013

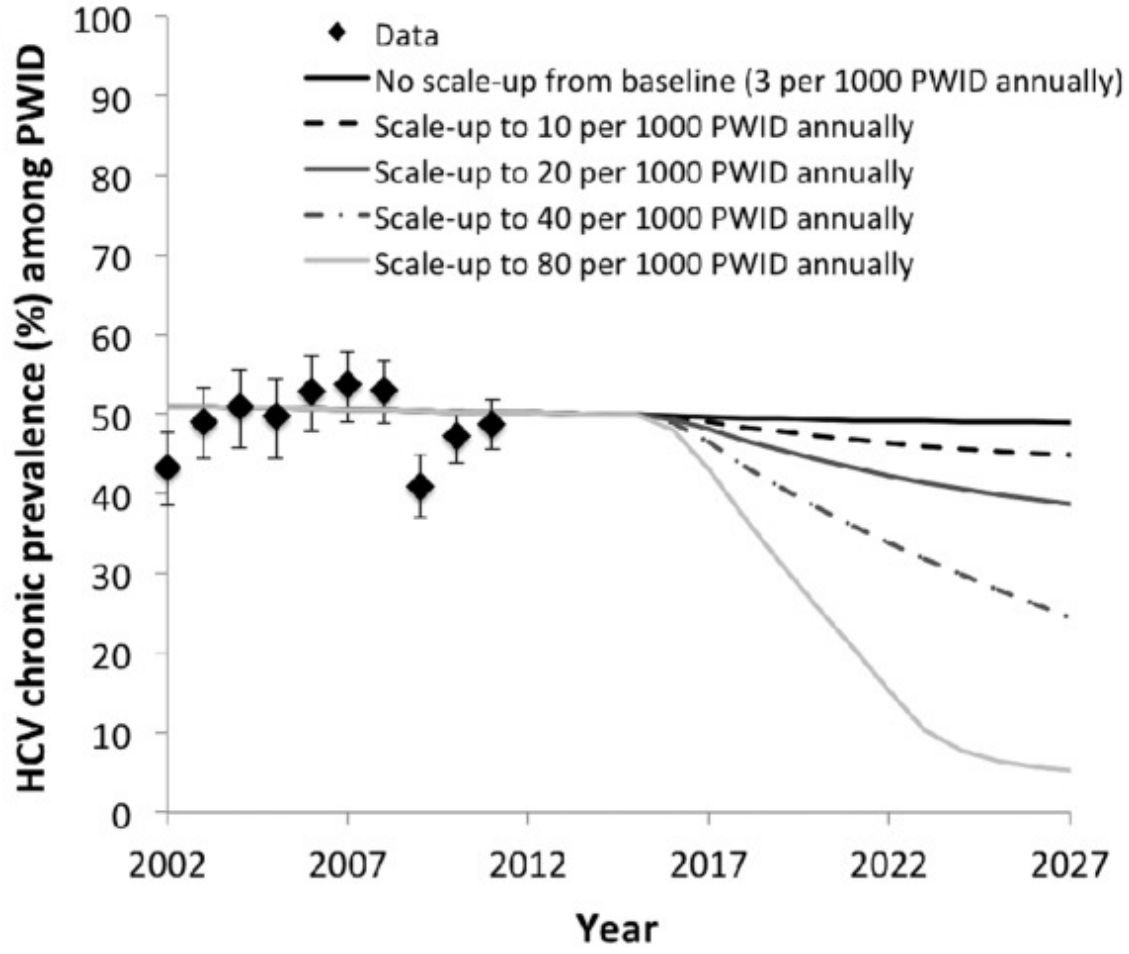
AASLD/IDSA Guidelines for Treatment of Hepatitis C

"HCV treatment is indicated for all patients with chronic HCV… "

"Scale up of HCV treatment in persons who inject drugs is necessary to positively impact the HCV epidemic in the US and globally."

http://www.hcvguidelines.org/full-report/when-and-whom-initiate-hcv-therapy

Treatment/Cure as Prevention for HCV among PWID: Mathematical Modeling



Martin NK et al. *Hepatology*. 2013

Treatment Delivery Gaps for Medications for Opioid Use Disorders and HCV

SUBSTANCE ABUSE
2018, VOL. 39, NO. 1, 83–88
https://doi.org/10.1080/08897077.2017.1363844

Taylor & Francis
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ORIGINAL RESEARCH

Check for updates

Utilization of buprenorphine and methadone among opioid users who inject drugs

Judith I. Tsui, MD, MPH[a], Richard Burt, PhD[b], Hanne Thiede, DVM, MPH[b], and Sara N. Glick, PhD, MPH[c]

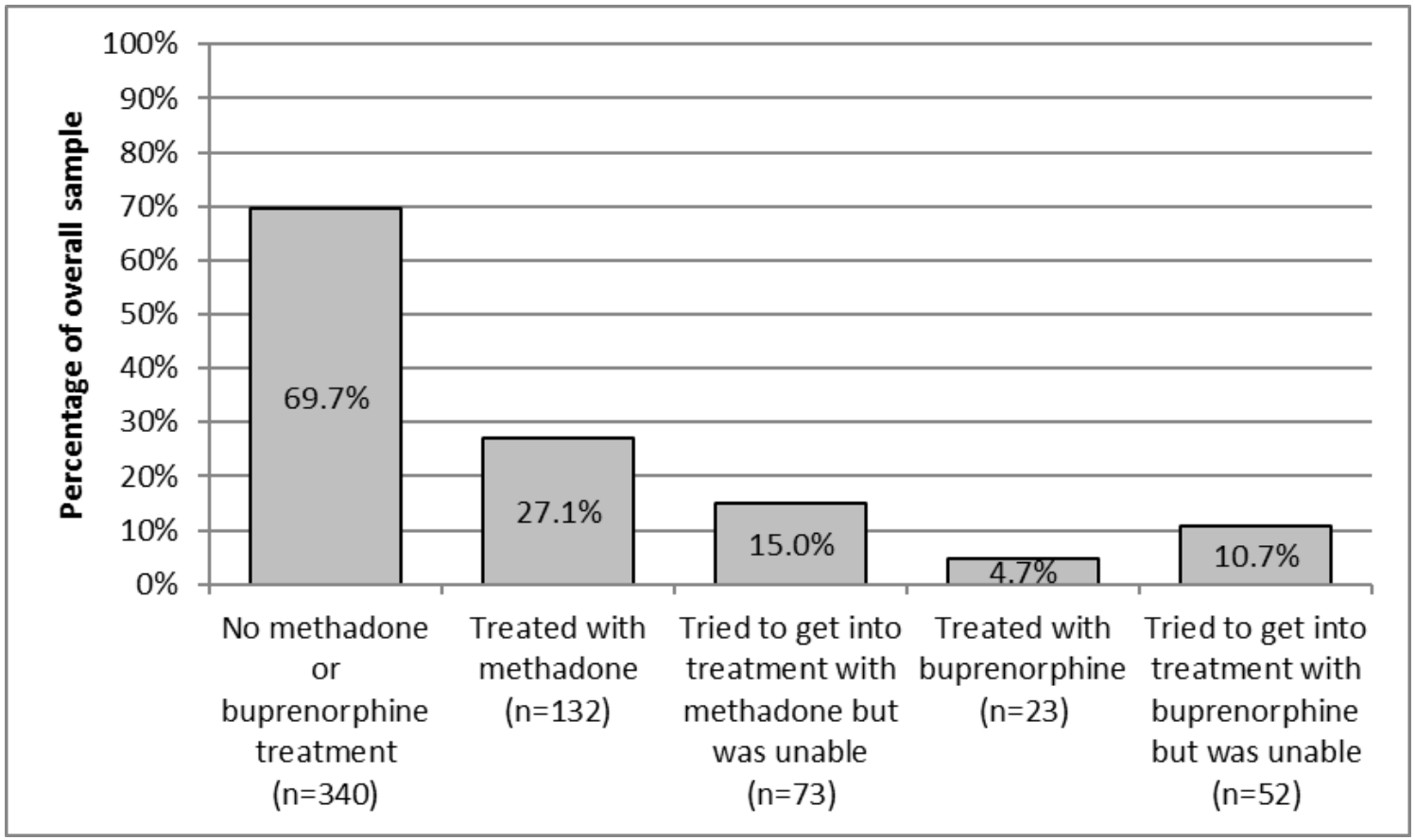
[a]Division of General Internal Medicine, Department of Medicine, University of Washington, Seattle, Washington, USA; [b]Public Health–Seattle & King County, HIV/STD Program, Seattle, Washington, USA; [c]Division of Allergy and Infectious Diseases, Department of Medicine, University of Washington, Seattle, Washington, USA

Study Design/Methods

- Study utilized local data from the CDC's National HIV Behavioral Surveillance (NHBS) system conducted in 2015
  - Conducted annually; every 3 years among PWID
- Sample: adults aged ≥18 years in the Seattle metropolitan area who injected drugs in the past year and reported opioid use
- The primary outcome of interest was self-report of receiving treatment with either methadone or buprenorphine in the past 12 months
  - National survey asked "any treatment for addiction"

Tsui JI, Burt R, Thiede H, Glick S. *Subst Abus*. 2018

Results from NHBS 2015: Percentage Reporting Past-Year OAT, or Attempts, Among Seattle Area PWID with Opioid Use (N=487)



Tsui JI, Burt R, Thiede H, Glick SN. *Subst Abus*. 2018

ELSEVIER

Drug and Alcohol Dependence

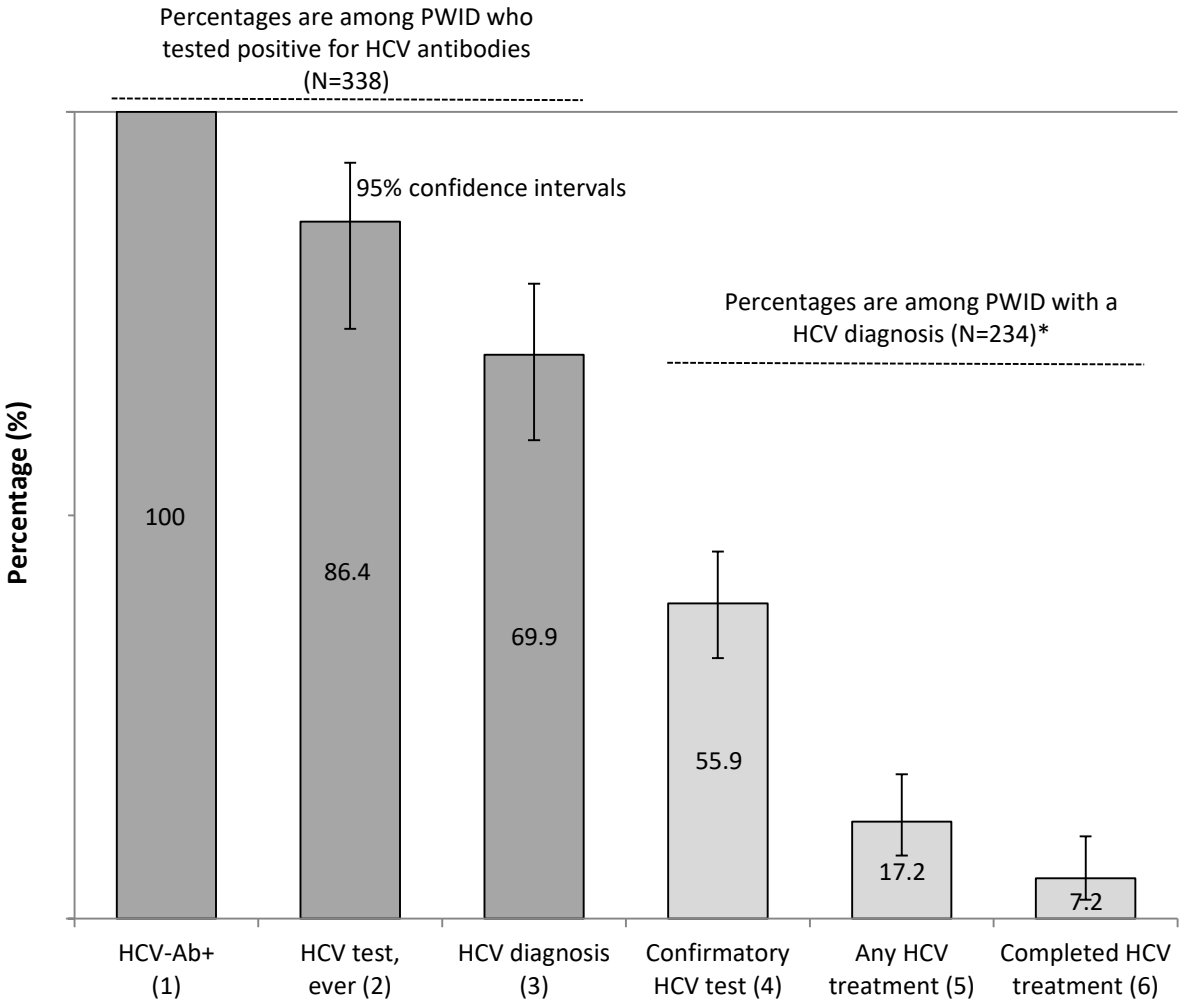
Volume 195, 1 February 2019, Pages 114-120

Full length article

Hepatitis C continuum of care and utilization of healthcare and harm reduction services among persons who inject drugs in Seattle

Judith I. Tsui [a], Claire M. Miller [a], John D. Scott [b], Maria A. Corcorran [b], Julia C. Dombrowski [b], Sara N. Glick [b]

HCV Care Continuum among Seattle PWID, National HIV Behavioral Surveillance Survey, 2015



Contents lists available at ScienceDirect

Journal of Substance Abuse Treatment

Hepatitis C Virus Testing and Treatment Among Persons Receiving Buprenorphine in an Office-Based Program for Opioid Use Disorders

Katelyn J. Carey, M.P.H. [a,*], Wei Huang, M.P.H., Ph.D. [b], Benjamin P. Linas, M.D., M.P.H. [a,b,c], Judith I. Tsui, M.D., M.P.H. [c,1]

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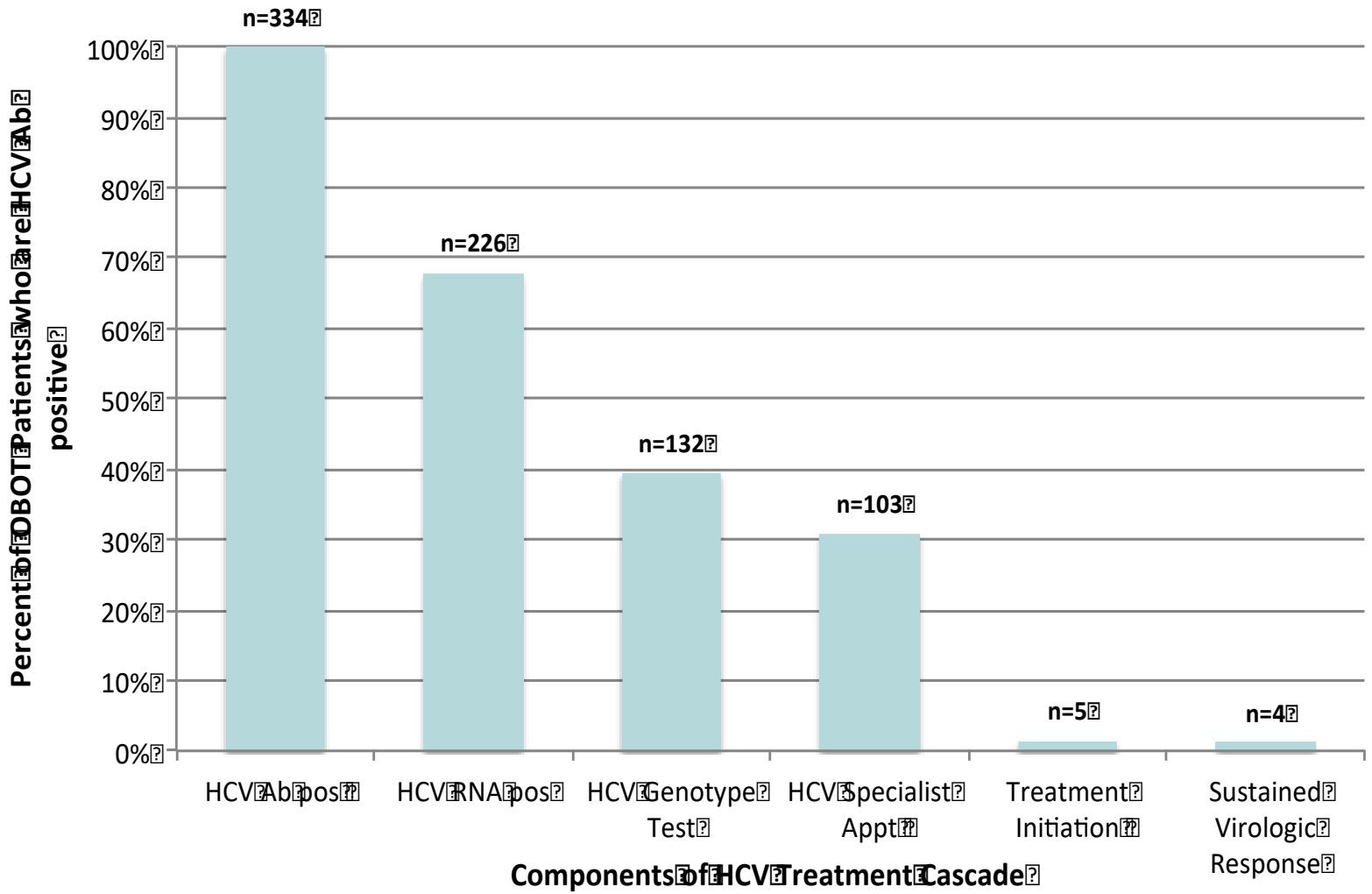
[c] Boston Medical Center, 850 Harrison Ave, Dowling 3N, Boston, MA 02118, USA

Journal of Substance Abuse Treatment 66 (2016) 54–59

Figure 1: Completion Rates for Components of the HCV Treatment Cascade Among DOBOT Patients Who Were HCV Ab Positive (n=334)



Current Programs to Address OUD Treatment Gaps

Reasons for OUD Medication Treatment Gap: Provider Factors

- Insufficient number of buprenorphine waivered providers
  - Waiver is barrier
  - Prescribing authority historically limited to physicians, typically addiction specialists
  - Lack of training among medical students and residents
  - Stigma of OUD
- Waivered providers not prescribing
  - Lack of time and clinic support [1]
  - Fear of patient diversion of medication[2,3]

1. Walley AY et al. *J Gen Intern Med*. 2008
2. Lin L et al. *Drug Alcohol Depend*. 2018
3. Andrilla CHA et al. *Ann Fam Med*. 2017

SUBSTANCE ABUSE
https://doi.org/10.1080/08897077.2018.1449176

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LETTER TO THE EDITOR

Check for updates

Interest in prescribing buprenorphine among resident and attending physicians at an urban teaching clinic

Jocelyn R. James, MD, Leah M. Gordon, MD, MPH, Jared W. Klein, MD, MPH, Joseph O. Merrill, MD, MPH, and Judith I. Tsui, MD, MPH

Division of General Internal Medicine, Department of Medicine, University of Washington, Seattle, Washington, USA

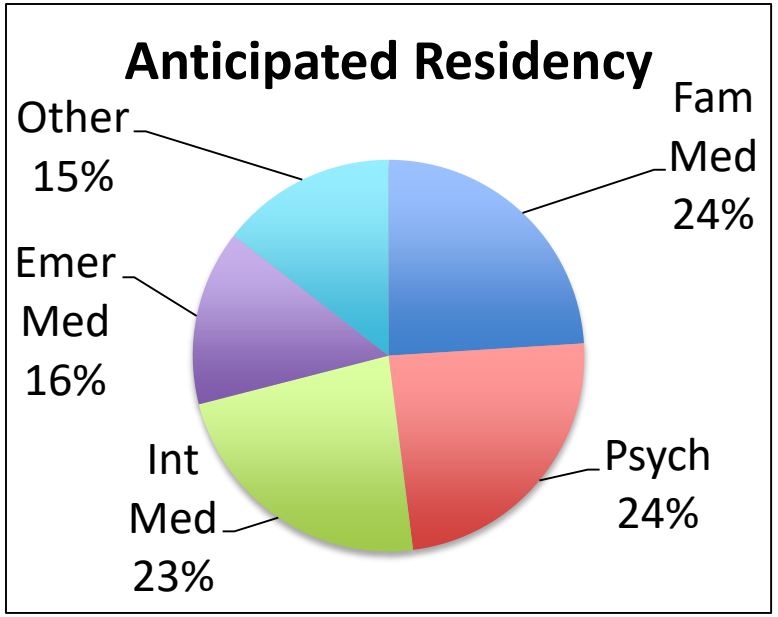
Interest in Prescribing Buprenorphine Among Residents

- Survey of attending and resident physicians at HMC Adult Medicine Clinic in 2016[1]
  - 44 respondents; 27 residents, 17 attendings
- ***39 (89%) were not waivered to prescribe buprenorphine***
- 26/39 (67%) reported "high interest" in becoming waivered (higher than prior study reporting 36%[2])
  - Those with "higher interest" were younger in age (p=0.007) and strongly believed in buprenorphine effectiveness (p=0.023)

1. James JR, Gordon LM, Klein JW, Merrill JO, Tsui JI. *Subst Abus.* 2018
2. Cunningham CO et al. *Fam Med*. 2016

Training UW Medical Students to Prescribe Buprenorphine

- Year 1:
  - Medical student didactic trainings completed May 2019 (n=60)
  - Resident trainings scheduled for July-August 2019
- Medical Student results:
  - Confidence in treating OUD increased from 21% to 90%
  - 97% plan to obtain buprenorphine waiver
  - 85% would like a paired mentor



Case Study: Harborview Adult Medicine Clinic Office-Based Opioid Treatment (OBOT) Program

- Partnered with WA State and Evergreen Treatment Services for "Medication-Assisted Treatment-Prescription Drug and Opioid Addiction" (MAT-PDOA) grant from SAMHSA (PI: Funai)
- Funded implementation of Collaborative Care/MA-model for office-based buprenorphine treatment (OBOT) in HMC Adult Medicine Clinic
  - Model creates care team centered around Nurse Care Manager, leverages MD time; demonstrated effectiveness in >20 clinics in MA[1]
  - 3 year grant→ subsequent SAMHSA funding for "Hub and Spoke" expansion of OBOT programs (PI: Merrill)

1. LaBelle C et al. *JSAT*. 2016

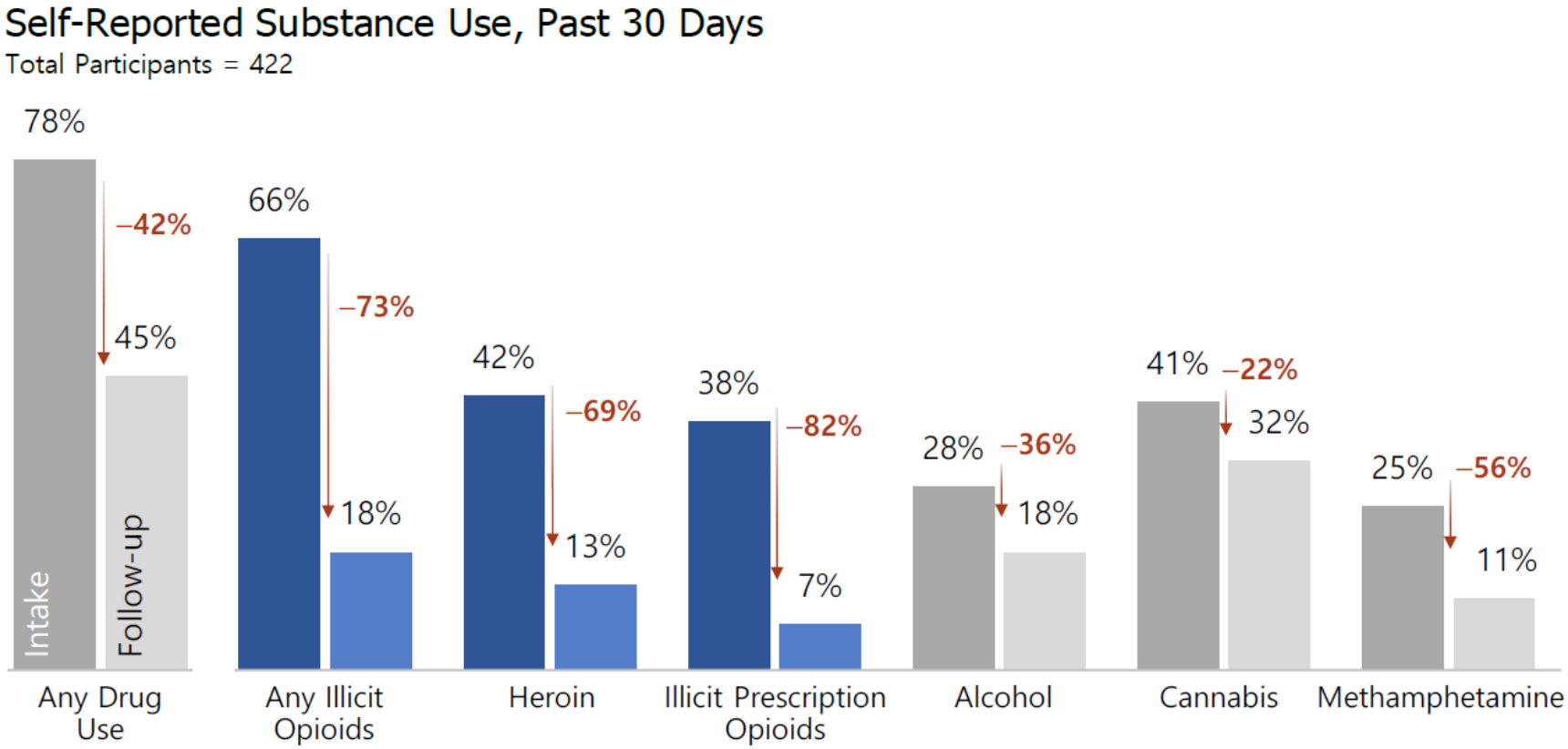
MA Nurse Care Manager Model

Table 3–Continued

Model	Summary	Components				
		Pharmacologic	Education/ Outreach	Coordination/ Integration of Care	Psychosocial	Other
Massachusetts nurse care manager model	A primary care–based model that teams nurse care managers with primary care physicians; nurse care managers generally perform initial screening, intake, education, observed/ supports induction, follow-up, maintenance, stabilization, and medical management with the physician and team	Primarily buprenorphine–naloxone, with recent addition of extended-release naltrexone	A training program exists to get more physicians (especially residents) and faculty on board. The Department of Public Health trains staff on best practices. Nurse care managers receive 8 h of training in MAT, shadowing in model MAT site, site visits, e-mail and telephone support, case review, quarterly training, and an addiction listserv	Nurse care managers (registered nurses or family NPs) manage 100 to 125 patients alongside primary care clinicians, with assistance from a medical assistant. Alternatively, care partners (usually persons with a master's degree) assist the primary care staff with screening, brief intervention, and referral to treatment	Psychological services are integrated on-site or nearby	Patients who require a higher level of care can be expedited into an OTP, assistance with transfers of care, and day-support programs

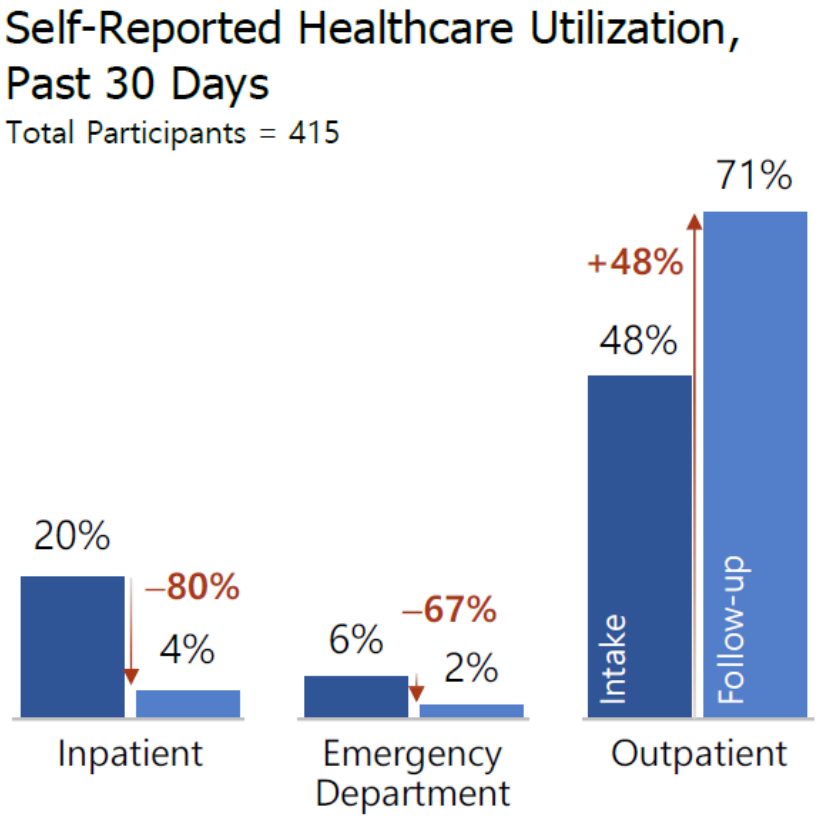
Korthuis PT, et al. *Ann of Intern Med.* 2016

Substance Use at Baseline v. 6 months: WA State MAT-PDOA 2015-2017 Outcomes



https://www.dshs.wa.gov/sites/default/files/SESA/rda/documents/research-4-102.pdf

Healthcare Utilization at Baseline v. 6 months: WA State MAT-PDOA 2015-2017 Outcomes



https://www.dshs.wa.gov/sites/default/files/SESA/rda/documents/research-4-102.pdf

Reasons for OUD Medication Treatment Gap: Patient Factors

- ***Most patients with substance use disorders are not "treatment seeking"***
  - In national survey <10% with SUD perceive need for treatment[1]
- Treatment needs to be offered in unconventional settings where patients with OUD are seen for non-addiction care
  - Emergency Department
  - Hospital In-patient

1. https://www.samhsa.gov/data/report/2017-nsduh-annual-national-report

Original Investigation

Buprenorphine Treatment for Hospitalized, Opioid-Dependent Patients
A Randomized Clinical Trial

Jane M. Liebschutz, MD, MPH; Denise Crooks, MPH; Debra Herman, PhD; Bradley Anderson, PhD; Judith Tsui, MD, MPH; Lidia Z. Meshesha, BA; Shernaz Dossabhoy, BA; Michael Stein, MD

Original Investigation

Emergency Department–Initiated Buprenorphine/Naloxone Treatment for Opioid Dependence
A Randomized Clinical Trial

Gail D'Onofrio, MD, MS; Patrick G. O'Connor, MD, MPH; Michael V. Pantalon, PhD; Marek C. Chawarski, PhD; Susan H. Busch, PhD; Patricia H. Owens, MS; Steven L. Bernstein, MD; David A. Fiellin, MD

Liebschutz JM et al. *JAMA Intern Med*. 2014
D'Onofrio G et al. *JAMA*. 2015

Study Methods

- Recruited hospitalized patients with opioid use disorders (heroin or prescription opioids) who were NOT already in addiction treatment
- Study patients randomized to either:
  - **Linkage**: Induction with buprenorphine/naloxone followed by prescription to bridge to an outpatient OBOT program appointment
  - **Detox**: Induction with buprenorphine/naloxone to manage acute withdrawal, followed by taper over 5 day

Liebschutz JM et al. *JAMA Intern Med*. 2014

Study Results

- Study enrolled 139 subjects, 6 month follow-up
- Patients in linkage arm (v. detox) were:
  - More likely to enter outpatient treatment (72% v. 12%, p<.001),
  - Retained at 6 months (17% v. 3%, p=0.007)
  - Less likely to be using illicit opioids at 6 months (incidence rate ratio, 0.60; 95% CI, 0.46-0.73; p < .01)

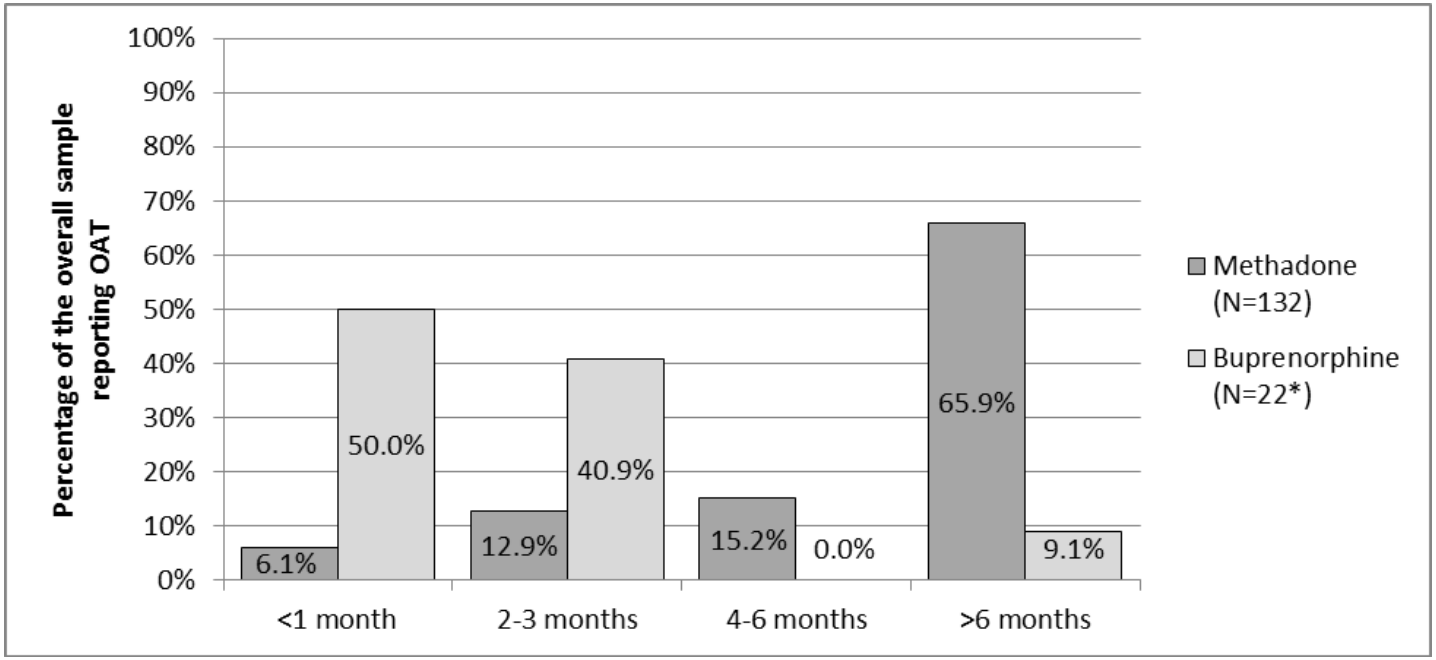
Liebschutz JM et al. *JAMA Intern Med*. 2014

Reasons for OUD Medication Treatment Gap: Patient Factors

- Most patients with substance use disorders are not "treatment seeking"
  - <10% with SUD perceive need for treatment[1]
- ***Retention and adherence to medications are sub-optimal***
  - Retention better for methadone compared to buprenorphine[2]

1. https://www.samhsa.gov/data/report/2017-nsduh-annual-national-report
2. Hser Y et al. *Addiction*. 2014

Duration of OAT Among PWID with Opioid Use Who Reported Past Year Treatment (N=154)



*One participant on buprenorphine did not answer the duration question.

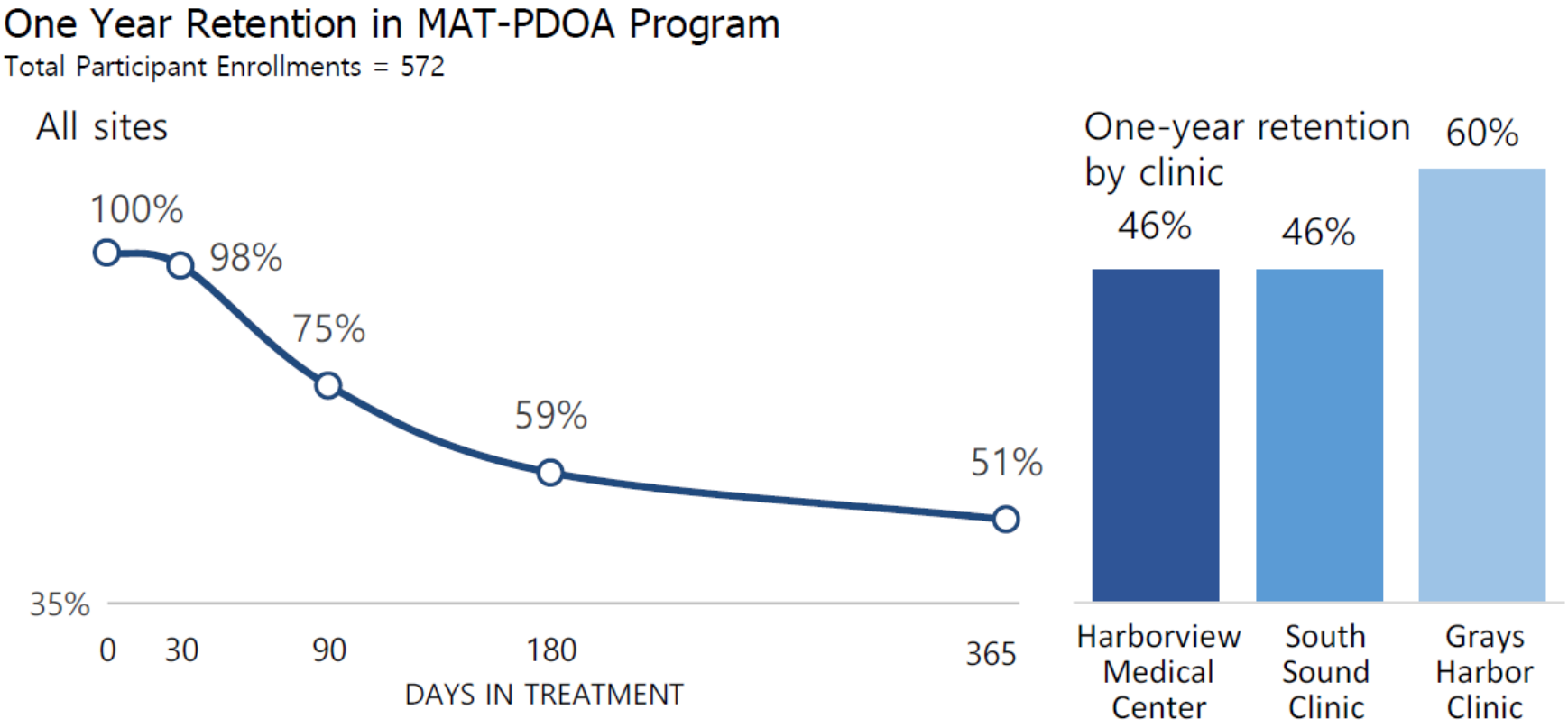
Tsui JI, Burt R, Thiede H, Glick SN. *Subst Abus*. 2018

Reasons for OUD Medication Treatment Gap: Patient Factors

- Most patients with substance use disorders are not "treatment seeking"
  - <10% with SUD perceive need for treatment[1]
- ***Retention and adherence to medications are sub-optimal***
  - Retention better for methadone compared to buprenorphine[2]
  - ~50% drop-out of buprenorphine treatment by one year[3-4]

1. https://www.samhsa.gov/data/report/2017-nsduh-annual-national-report
2. Hser Y et al. *Addiction*. 2014
3. Weinstein ZM et al. *J Subst Abuse Treat*. 2017
4. Bhatraju EP et al. *Addict Sci Clin Pract*. 2017

Retention on Buprenorphine Treatment



Research on Innovative Healthcare Delivery Interventions to Improve Treatment Adherence and Outcomes for HCV and OUD

ORIGINAL RESEARCH

Annals of Internal Medicine

Intensive Models of Hepatitis C Care for People Who Inject Drugs Receiving Opioid Agonist Therapy

A Randomized Controlled Trial

Matthew J. Akiyama, MD, MSc; Brianna L. Norton, DO, MPH; Julia H. Arnsten, MD, MPH; Linda Agyemang, MPH; Moonseong Heo, PhD; and Alain H. Litwin, MD, MS, MPH

Akiyama MJ et al. Annals Int Med 2019

Study Methods

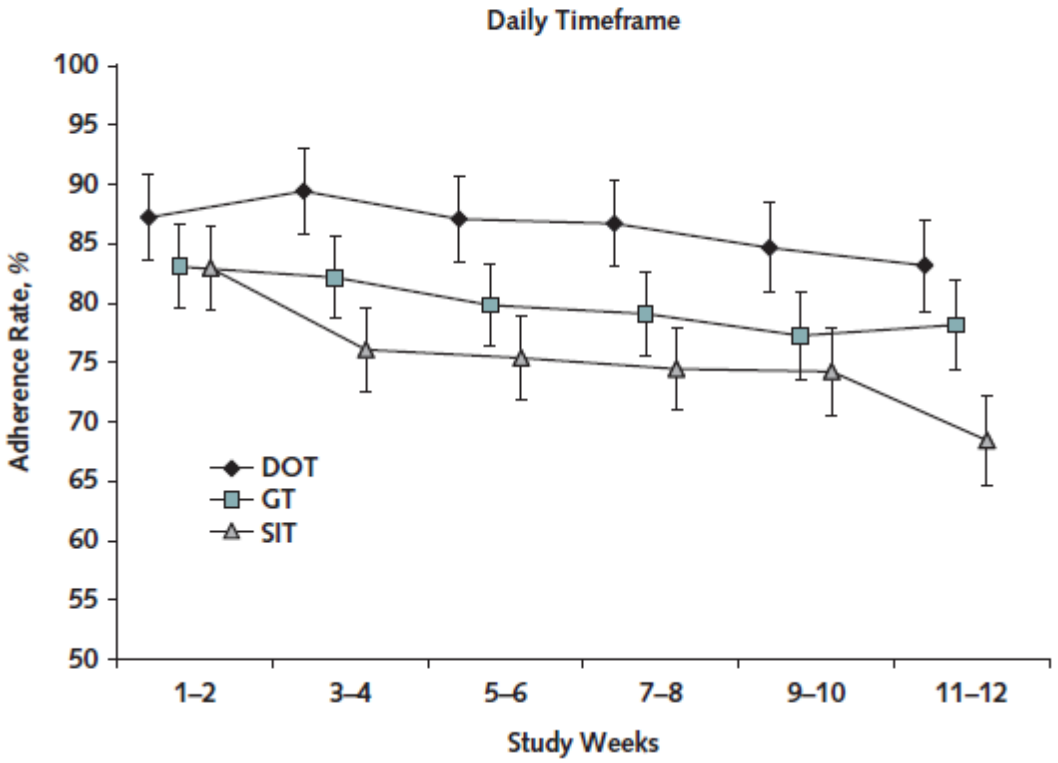
- Recruited HCV+ adults in 3 OAT programs in Bronx, NY
- Study patients randomized to either:
  - Directly Observed Therapy (DOT)
  - Group Therapy (GT)
  - Self-administered Individual Treatment (SIT)

- Adherence to medication measured through use of electronic blister packs

Akiyama MJ et al. Annals of Int Med 2019

Results: Adherence

Figure 2. Adherence rates over time.



Akiyama MJ et al. Annals of Int Med 2019

Results: SVR

Appendix Table 1. SVR, by Group, for Study Participants Overall and for Those Receiving a Combination DAA Regimen*

Group	Overall			Combination DAA Regimen		
	Patients, *n*	SVR, *n* (%)	SVR, 95% CI, %	Patients, *n*	SVR, *n* (%)	SVR, 95% CI, %
Overall						
DOT	51	50 (98)	90 to 100	36	36 (100)	90 to 100
GT	48	45 (94)	83 to 99	40	38 (95)	83 to 99
SIT	51	46 (90)	79 to 97	39	35 (90)	76 to 97
Total	150	141 (94)	89 to 97	115	109 (95)	89 to 98
		Difference in SVR (95% CI), *percentage points*			**Difference in SVR (95% CI), *percentage points***	
Comparison						
DOT vs. GT	–	4 (−7 to 16)		–	5 (−8 to 18)	
DOT vs. SIT	–	8 (−4 to 20)		–	10 (−4 to 25)	
GT vs. SIT	–	4 (−10 to 17)		–	5 (−10 to 21)	

DAA = direct-acting antiviral; DOT = directly observed therapy; GT = group treatment; SIT = self-administered individual treatment; SVR = sustained virologic response.

* No significant differences in SVR were found across the 3 groups ($P = 0.152$) among all participants or among those receiving combination DAA treatment ($P = 0.056$), on the basis of multivariable exact logistic regression adjusting for site and the 3 stratifying variables. No missing data were observed for this analysis.

Akiyama MJ et al. Annals of Int Med 2019

Conclusions

- DOT was associated with slightly better rates of adherence
- Adherence was significantly associated with likelihood of cure
- HOWEVER, all models of care (even SIT) resulted in high rates of cure (90-98%)
  - Overall adherence was 78% and 94% were cured, suggesting lower adherence may be tolerated

Akiyama MJ et al. Annals of Int Med 2019

OUD Medication Adherence

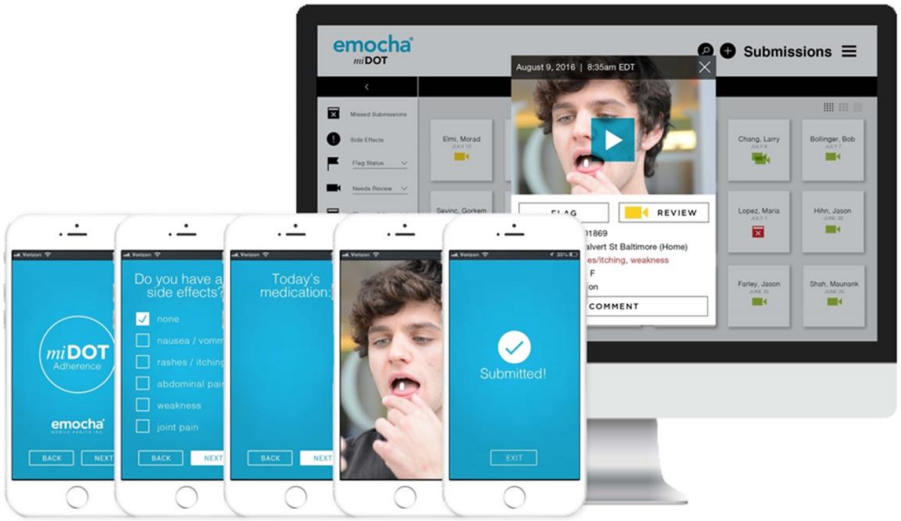
- Retention and adherence to medications are sub-optimal
  - Retention better for methadone compared to buprenorphine[2]
  - **Studies suggest non-adherence to 30% of buprenorphine treatment doses[3]**
  - Non-adherence correlated with illicit opioid use

1. https://www.samhsa.gov/data/report/2017-nsduh-annual-national-report
2. Hser Y et al. *Addiction*. 2014
3. Feillin DA et al. *NEJM*. 2006

TAAB Study

Trial of Adherence App for Buprenorphine treatment Study (R44DA044053 PIs: Seiguer/Tsui)

- NIDA SBIR grant to assess mHealth tool to improve buprenorphine adherence
- **Phase I: Qualitative study and pilot feasibility study**
- Phase II: 2-site RCT conducted at Harborview and Boston Medical Center (n=80)
- Video DOT vs TAU
- Outcomes: % weekly urine drug tests +opioids; retention in treatment



UNIVERSITY of WASHINGTON

Godersky *et al. Addict Sci Clin Pract* (2019) 14:11
https://doi.org/10.1186/s13722-019-0139-3

Addiction Science & Clinical Practice

RESEARCH Open Access

Provider and patient perspectives on barriers to buprenorphine adherence and the acceptability of video directly observed therapy to enhance adherence

Margo E. Godersky[1], Andrew J. Saxon[2], Joseph O. Merrill[1], Jeffrey H. Samet[3], Jane M. Simoni[4] and Judith I. Tsui[1*]

Patient Perspectives on Buprenorphine Adherence

"Sometimes I have [forgotten], in the afternoon, when you're busy and not really thinking about it …There has been times that I have just said throughout the day, 'Hey, I forgot to take my Suboxone (sic)'."

Godersky ME, et. al. *Addiction Science and Clinical Practice* 2019

Patient Perspectives on Buprenorphine Adherence

"It's just because us addicts, whether everyone else wants to admit it or not, we like to get high. And taking the medicine, we can't get high if we're taking it like we should…That's why I wouldn't want to take it all the time."

Godersky ME, et al. *Addiction Science and Clinical Practice* 2019

Patient Perspectives on Video Directly Observed Therapy for Buprenorphine

"… the Suboxone program in general relies on a lot of trust and communication between the patient and provider, or providers, you know... So I think that [video-DOT] would be good. Everybody could be on the same page. They feel good about it, especially when you're changing doses or have had maybe problems in the past staying on the program. I think it would help hold people accountable."

Godersky ME, et al. *Addiction Science and Clinical Practice* 2019

Results of Phase I Feasibility Study

- All participants but one (13/14; 93%) were able to successfully upload videos
- 10/14 participants reported they were “satisfied” or “very satisfied” with using the app; 2/14 were neutral; none were “dissatisfied”.
- For those using the app, daily buprenorphine treatment was confirmed through videos most (**73%**) of the time.
- Results suggest that use of a smartphone app to allow at-home video directly observed therapy of buprenorphine treatment is **feasible and acceptable.**

Godersky ME, Klein JW, Merrill JO, Blalock KL, Saxon AJ, Samet JH, Tsui JI. Acceptability and feasibility of a mobile health application for video directly observed therapy of buprenorphine for opioid use disorders in an office-based setting. AMERSA 2018, San Francisco, CA.

TAAB Study

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- NIDA SBIR grant to assess mHealth tool to improve buprenorphine adherence
- Phase I: Qualitative study and pilot feasibility study
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- **Video DOT vs TAU**
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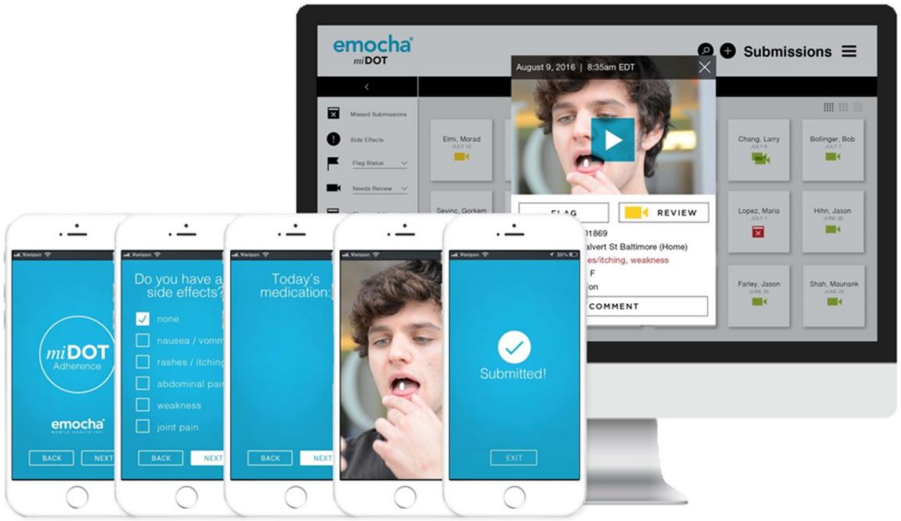


Summary/Conclusions

- The epidemics of opioid use disorder (OUD) and hepatitis C virus (HCV) are closely intertwined.
- Elimination of HCV is a state, national and global priority and requires treating persons who inject drugs.
- Efficacious medications exist for both OUD and HCV, and yet are under-utilized by patients.
- Numerous programs have been developed at UW/HMC to address OUD and HCV treatment gaps; on-going research is testing whether an mHealth intervention for video DOT can improve outcomes.

Acknowledgements: Community Partners and Patient Participants

ADAI
ALCOHOL & DRUG ABUSE INSTITUTE
UNIVERSITY of WASHINGTON

Evergreen Treatment Services

PHRA
PEOPLES HARM REDUCTION ALLIANCE

HEP
HEPATITIS EDUCATION PROJECT

UW Medicine
HARBORVIEW MEDICAL CENTER

Public Health
Seattle & King County

Acknowledgements: OBOT Team

Surveys

Look for our surveys in your inbox!

We'll send two short surveys:
one now, and
one in a month.

We greatly appreciate your feedback! Every survey we receive helps us improve and develop our programming.

Reminder: Certificates

Certificates of Attendance and CME credit available for live viewers!

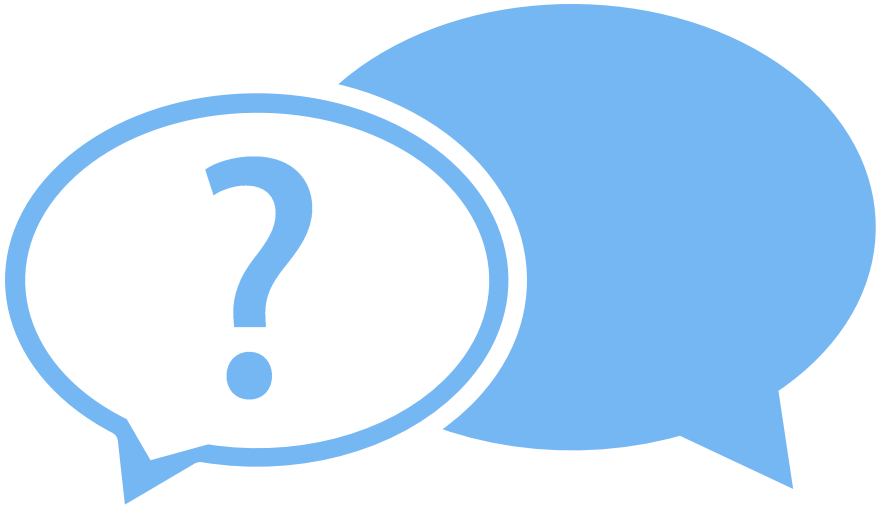
Viewing Groups:
Please send each individual's **name** and **email address** to northwest@attcnetwork.org within 1 business day.

You will be emailed your certificate in a few weeks.

This Live activity, Medications for Opioid Use Disorders and Hepatitis C: Access and Adherence among People who Inject Drugs, with a beginning date of 06/26/2019, has been reviewed and is acceptable for up to 1.00 Prescribed credit(s) by the American Academy of Family Physicians. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

Q&A

Questions? Please type them in the chat box!



Upcoming Events

Join us for our next webinar!

Methamphetamine Use Trends and Consequences in the Northwestern United States

Sarah Glick, PhD

July 31, 2019, 12-1pm


gracias cảm ơn bạn ধন্যবাদ 고맙습니다
شكرا جزيلا salamat благодарю вас 谢谢
Dziękuję Ci Thank you! ευχαριστώ
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धन्यवाद danke asante grazie
hík'wu? merci תודה obrigado ขอบคุณ
ありがとうございました спасибі mahalo