ACCEPT

Addiction & Co-morbid Conditions: Enhancing Prevention & Therapeutics

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Session Date: Friday, August 19, 2022

Didactic Topic and Presenter:
Prevention Services for People Who Inject Drugs: Wisconsin Rural Opioid Initiative

Ryan Westergaard, MD, PhD, MPH
Infectious Disease Physician
Associate Professor at UW Madison
Principle Investigator on the WI Rural Opioid project
Chief Medical Officer for the WI Bureau of Communicable Diseases (DHS)
Content Experts:
Ritu Bhatnagar, MD; Lindsey Peterson, MS, CRC; Sheila M. Weix, MSN, RN, CARN

- 12:15 PM: Attendance text-in – Introductions
- 12:25 PM: Case Presentation and Discussion
    - Presenter: Caroline Hensley, MD/MPH - PGY-3, UW Department of Family Medicine & Community Health
- 1 PM: Didactic Presentation
    - Presenter: Ryan Westergaard, MD, PhD, MPH

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- 1:15 PM End of Session

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School of Medicine and Public Health
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University of Wisconsin

ECHO ACCEPT
Addiction & Co-morbid Conditions: Enhancing Prevention & Therapeutics
2022-2024
Prevention Services for People Who Inject Drugs: Wisconsin Rural Opioid Initiative
8/19/2022
Didactic Presenter: Ryan Westergaard, MD, PhD, MPH
Case Presenter: Caroline Hensley, MD/MPH

Provided by the University of Wisconsin–Madison Interprofessional Continuing Education Partnership (ICEP)

Intended Audience:

Nurses, Nurse Practitioners, Pharmacists, Physicians, Physician Assistants, Pharmacy Technicians, Psychologists, Social Workers, Patient/Caregivers, Students

Objectives:

As a result of this educational regularly scheduled series, learners as members of the healthcare team will be able to:

1. Summarize how rural communities face unique challenges for preventing overdose and infectious disease-related harms of injection drug use
2. Discuss findings from a large cross-sectional survey of rural-dwelling people who inject drugs (PWID) in 65 rural counties across the U.S.
3. Explain the emerging strategies that support harm reduction and promote drug user health in rural communities

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Randall Brown	RSS Chair	No relevant financial relationships to disclose	Yes	2/15/2022
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Ritu Bhatnagar	Planner	No relevant financial relationships to disclose	Yes	2/13/2022
Paul Hutson	Planner	No relevant financial relationships to disclose	Yes	2/15/2022
Susan Mindock	Planner	No relevant financial relationships to disclose	No	2/15/2022
Lindsey Peterson	Planner	No relevant financial relationships to disclose	No	2/28/2022
Sheila Weix	Planner	No relevant financial relationships to disclose	No	2/18/2022
Kellene Eagen	Planner	No relevant financial relationships to disclose	No	2/14/2022
Joseph Galey	Planner	No relevant financial relationships to disclose	Yes	6/23/21
Ryan Westergaard	Presenter	No relevant financial relationships to disclose	No	6/20/2022

Caroline Hensley	Presenter	No relevant financial relationships to disclose	No	8/15/2022

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Case Presentation

Caroline Hensley, MD/MPH, PGY-3

UW Department of Family Medicine & Community Health

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For this educational activity there are no reported conflicts of interest

Case Introduction

- 7 day old female born at 37 weeks and 1 day to now G3P3 being seen in clinic for newborn exam s/p 5 day admission for neonatal opioid withdrawal syndrome.
- Now with minimal newborn symptoms of withdrawal, but significant maternal guilt surrounding need for suboxone during pregnancy.
- Dad requests MD “explain neonatal abstinence syndrome to mom”.

Primary question for discussion:

- How could this family have been better supported during the perinatal period to build parents' confidence in the newborn period?

Opioid use disorder in pregnancy

- Opioid agonist pharmacotherapy is the recommended treatment by American College of OB/Gyn
- Medically supervised withdrawal is associated with high relapse rates → worse pregnancy outcomes

Intrauterine exposure to opioids

- Infants should be monitored for neonatal opioid withdrawal syndrome
- Breastfeeding should be encouraged in birthing parents who are stable on their opioid agonist, not using illicit substances, no other contraindications (ie HIV)

Eat, Sleep, Console Method

Non pharmacologic interventions to address:

- Is the baby feeding
- Is the baby able to sleep?
- Can the baby be consoled within 10 minutes of crying

Reduces use of morphine and length of hospitalization

*low stimulation environment, rooming-in, swaddling, and on-demand feedings

Back to the case…

Mom's Medical & Behavioral Health Diagnosis:	Mom's Current Medications:
• Opioid use disorder, in remission • Anxiety and depression with suicidal ideation • Chronic pain • History of methamphetamine use	• Buprenorphine-naltrexone (Suboxone) 24-6 mg daily • Fluoxetine 20 mg daily & • Pregabalin 100 mg three times daily • Prenatal vitamin

Mom's Social History:	Mom's Family History:
• Currently staying at family friend's house with plans to move to family shelter when bed available • In a relationship with father of baby. Denies safety concerns. He does not use substances. • Does have custody of 2nd child, same father of this baby • Does not have custody of 1st child, lives with father	Unknown

Prenatal care

1/11/2022 - Phone call to OB reporting pregnancy

1/24/2022 - Phone call to PCP for pregabalin refill, refill denied given pregnancy and need for office visit to discuss

2/9/2022 - PCP visit for refill of pregabalin, reports positive home pregnancy test and plans to establish with OB, doesn't want to discuss pregnancy further

6/27/2022 - ED visit for constipation, found to be 32 weeks pregnant, notes Suboxone provider aware of her pregnancy and stable on Suboxone, denies other substance use

Maternal urine drug screen at 32 weeks

Component Ref Range & Units	1 mo ago
Amphetamines,UR NEG Comment: (SCREENING @ 500 ng/mL)	NEG
Barbiturates,UR NEG Comment: (Screening at 200 ng/mL)	NEG
Benzodiazepines,UR NEG Comment: (Screening at 200 ng/mL)	NEG
Cannabinoids,UR NEG Comment: (SCREENING @ 20 ng/mL) Screening results intended for medical use only. If clinically indicated, additional confirmatory testing may be requested by contacting the laboratory.	POS !
Cocaine,UR NEG Comment: (SCREENING @ 150 ng/mL)	NEG
Opiates,UR NEG Comment: (SCREENING @ 300 ng/mL) Opiate screen method will not detect Oxycodone or Methadone.	NEG
Oxycodone Screen,UR NEG Comment: (Screening at 300 ng/mL) ML urine oxycodone should be used for clinical purposes only. Drug or metabolite detection may not indicate intoxication. A more specific method such as GC/MS must be used for analytical confirmation.	NEG
Methadone Screen, UR NEG Comment: (Screening at 300 ng/mL)	NEG
Creatinine Check,UR 20 - 1000 mg/dL Comment: Testing performed at Meriter Laboratories, 36 S Brooks St Madison, WI 53715, unless otherwise stated in result.	53.30

*buprenorphine not tested via this hospital's standard UDS

Birth hospitalization

8/2/2022 - Admitted for labor at 37 weeks 1 day & baby born!

8/4/2022 - Mom discharged, but remains admitted, breastfeeding

8/5/2022 - Mom brought by baby's nurse to ED with c/f delusional thoughts, no SI/HI, left prior to MD evaluation

8/7/2022 - Baby discharged after 5 days of monitoring for neonatal opioid withdrawal syndrome via eat sleep console protocol

Infant urine drug screen @ 2 days of life

Component Ref Range & Units	11 d ago
Amphetamines,UR NEG Comment: (SCREENING @ 500 ng/mL)	NEG
Barbiturates,UR NEG Comment: (Screening at 200 ng/mL)	NEG
Benzodiazepines,UR NEG Comment: (Screening at 200 ng/mL)	NEG
Cannabinoids,UR NEG Comment: (SCREENING @ 20 ng/mL)	NEG
Cocaine,UR NEG Comment: (SCREENING @ 150 ng/mL)	NEG
Opiates,UR NEG Comment: (SCREENING @ 300 ng/mL) Opiate screen method will not detect Oxycodone or Methadone.	NEG
Oxycodone Screen,UR NEG Comment: (Screening at 300 ng/mL) ML urine oxycodone should be used for clinical purposes only. Drug or metabolite detection may not indicate intoxication. A more specific method such as GC/MS must be used for analytical confirmation.	NEG
Methadone Screen, UR NEG Comment: (Screening at 300 ng/mL)	NEG
Creatinine Check,UR 20 - 1000 mg/dL	43.40

*buprenorphine not tested via this hospital's standard UDS

Mom's strengths & protective factors:	Risk factors:
• Remained engaged on MOUD throughout pregnancy, insight to know she needs these medications • Breastfeeding • Two parents involved • Same PCP for mom & baby	• Limited prenatal care • Lack of communication between suboxone prescriber/PCP/OB • Lack of confidence in parenting skills • Guilt surrounding need for medication • Discord between parents

Mom's Goals & Motivations for Treatment

- Stability of mental health and opioid use disorder
- Healthy baby

Proposed Diagnoses

For mom:

- Maternal opioid use disorder, on suboxone

For baby:

- Intrauterine exposure to opioids
- Mild neonatal opioid withdrawal syndrome

Proposed Treatment Plan

- Social support of family
- Family education surrounding utility of and recommendation for MOUD in pregnancy
- Continuation of breastfeeding while mom continues suboxone
- Discussion of postpartum birth control

Discussion:

- Primary question: How could this family have been better supported during the perinatal period to build parents' confidence in the newborn period?

My takeaways

- De-stigmatization of MOUD
- Counseling for parents around what to expect in neonatal opioid withdrawal syndrome
- Better communication between providers

DSM-5 Substance Use Disorder ("Addiction")

- Tolerance
- Withdrawal

} Physical Dependence ≠ Use Disorder

- Larger amts/longer periods than intended
- Persistent desire/failed attempts to quit/control use
- Much time obtaining/using/recovering
- Important activities sacrificed
- Continued use despite known adverse effects
- Failure to fulfill major obligations
- Recurrent hazardous use
- Craving
- Ongoing use despite interpersonal problems

2-3 = mild
4-5 = moderate
≥ 6 = severe

References

- https://publications.aap.org/pediatrics/article/147/1/e2020007393/33461/Evaluating-Definitions-for-Neonatal-Abstinence

- https://www.acog.org/clinical/clinical-guidance/committee-opinion/articles/2017/08/opioid-use-and-opioid-use-disorder-in-pregnancy

The Wisconsin Rural Opioid Initiative

Providing Evidence to Understand the Fourth Wave of the Opioid Crisis

Ryan Westergaard, MD, PHD, MPH
Associate Professor of Medicine

Acknowledgements

Tulane University:
David Seal

UWSMPH:
Wajiha Akhtar
Rebecca Miller
Alexandria Moellner
Katy Mijal
Sarah Dietz
Randy Brown
Marlon Mundt
James Sosman
Rachel Gicquelais
Amelia Baltes
Queila Griffen
Jacob Schleicher
Andrew Hagmeier

Vivent Health:
Kristen Grimes
Mikaela Becker
Sarah Krechel
Laura Runchey
Callie Barribeau
Kailey Wood
Amanda Tennyson
Leanne Eisenhauer

WI DHS & WSLH
TJ Whyte
Kailynn Mitchell
Sheila Guilfoyle
Kelsa Lowe
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Jenkins *et al.*
Addiction Science & Clinical Practice (2022) 17:38
https://doi.org/10.1186/s13722-022-00322-5

Addiction Science & Clinical Practice

RESEARCH Open Access

The Rural Opioid Initiative Consortium description: providing evidence to Understand the Fourth Wave of the Opioid Crisis

Richard A. Jenkins[1], Bridget M. Whitney[2], Robin M. Nance[2], Todd M. Allen[3], Hannah L. F. Cooper[4], Judith Feinberg[5], Rob Fredericksen[2], Peter D. Friedmann[6], Vivian F. Go[7], Wiley D. Jenkins[8], P. Todd Korthuis[9], William C. Miller[10], Mai T. Pho[11], Abby E. Rudolph[12], David W. Seal[13], Gordon S. Smith[5,18], Thomas J. Stopka[14], Ryan P. Westergaard[15], April M. Young[16], William A. Zule[17], Joseph A. C. Delaney[18], Judith I. Tsui[2] and Heidi M. Crane[2*] on behalf of the Rural Opioid Initiative

Abstract

Objective: To characterize and address the opioid crisis disproportionately impacting rural U.S. regions.

Methods: The Rural Opioid Initiative (ROI) is a two-phase project to collect and harmonize quantitative and qualitative data and develop tailored interventions to address rural opioid use. The baseline quantitative survey data from people who use drugs (PWUD) characterizes the current opioid epidemic (2018–2020) in eight geographically diverse regions.

Results: Among 3,084 PWUD, 92% reported ever injecting drugs, 86% reported using opioids (most often heroin) and 74% reported using methamphetamine to get high in the past 30 days; 53% experienced homelessness in the prior 6 months; and 49% had ever overdosed. Syringe service program use varied by region and 53% had ever received an overdose kit or naloxone prescription. Less than half (48%) ever received medication for opioid use disorder (MOUD).

Conclusions: The ROI combines data across eight rural regions to better understand drug use including drivers and potential interventions in rural areas with limited resources. Baseline ROI data demonstrate extensive overlap between opioid and methamphetamine use, high homelessness rates, inadequate access to MOUD, and other unmet needs among PWUD in the rural U.S. By combining data across studies, the ROI provides much greater statistical power to address research questions and better understand the syndemic ofinfectious diseases and drug use in rural settings including unmet treatmentneeds.

Keywords: Opioids, Methamphetamine, Rural, Substance use, Injection drug use, Overdose

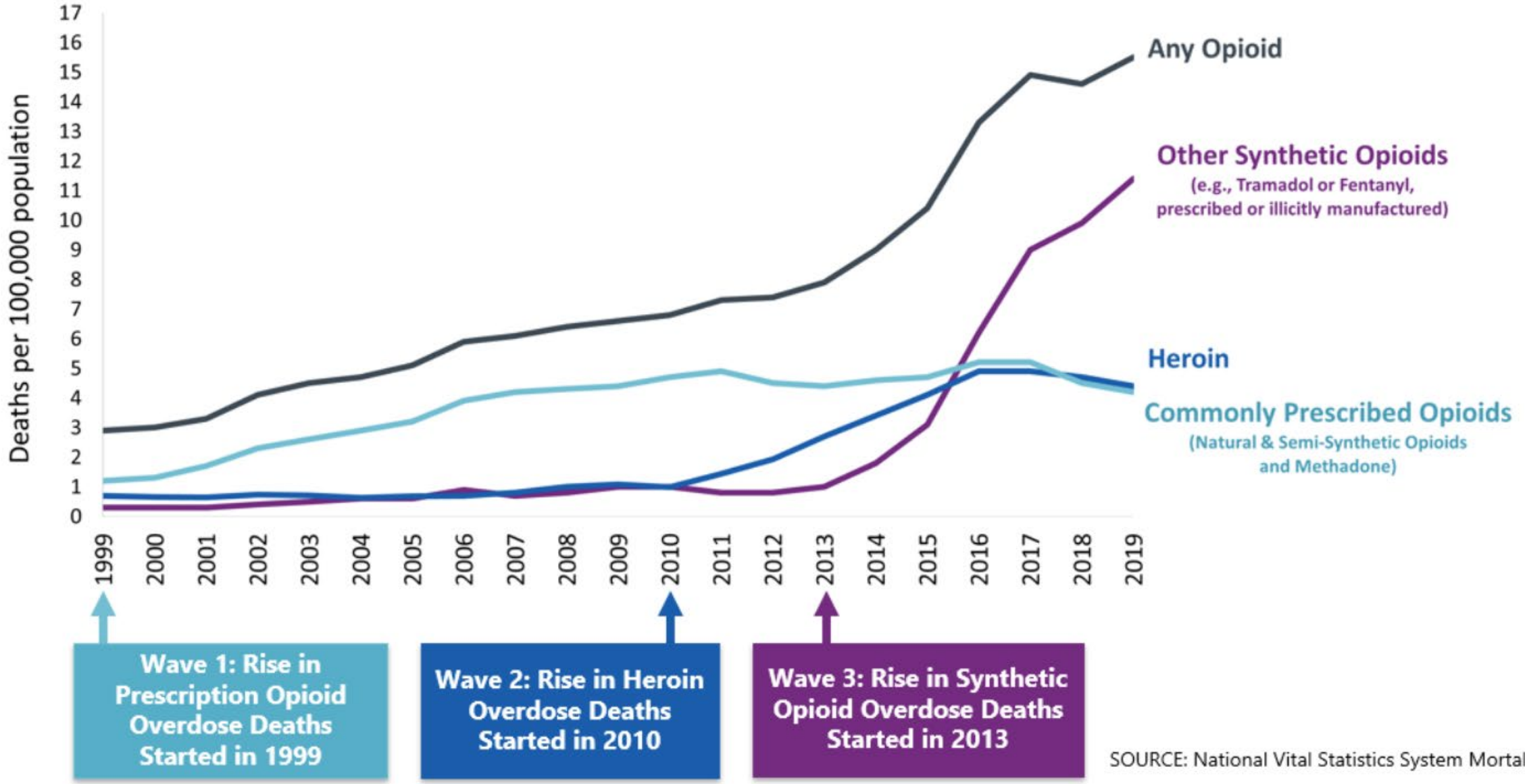
Learning Objectives

1. Understand how rural communities face unique challenges for preventing overdose and infectious disease-related harms of injection drug use

2. Review findings from a large cross-sectional survey of rural-dwelling people who inject drugs (PWID) in 65 rural counties across the U.S.

3. Look forward to emerging strategies to support harm reduction and promote drug user health in rural communities

Three Waves of the Rise in Opioid Overdose Deaths



SOURCE: National Vital Statistics System Mortality File.

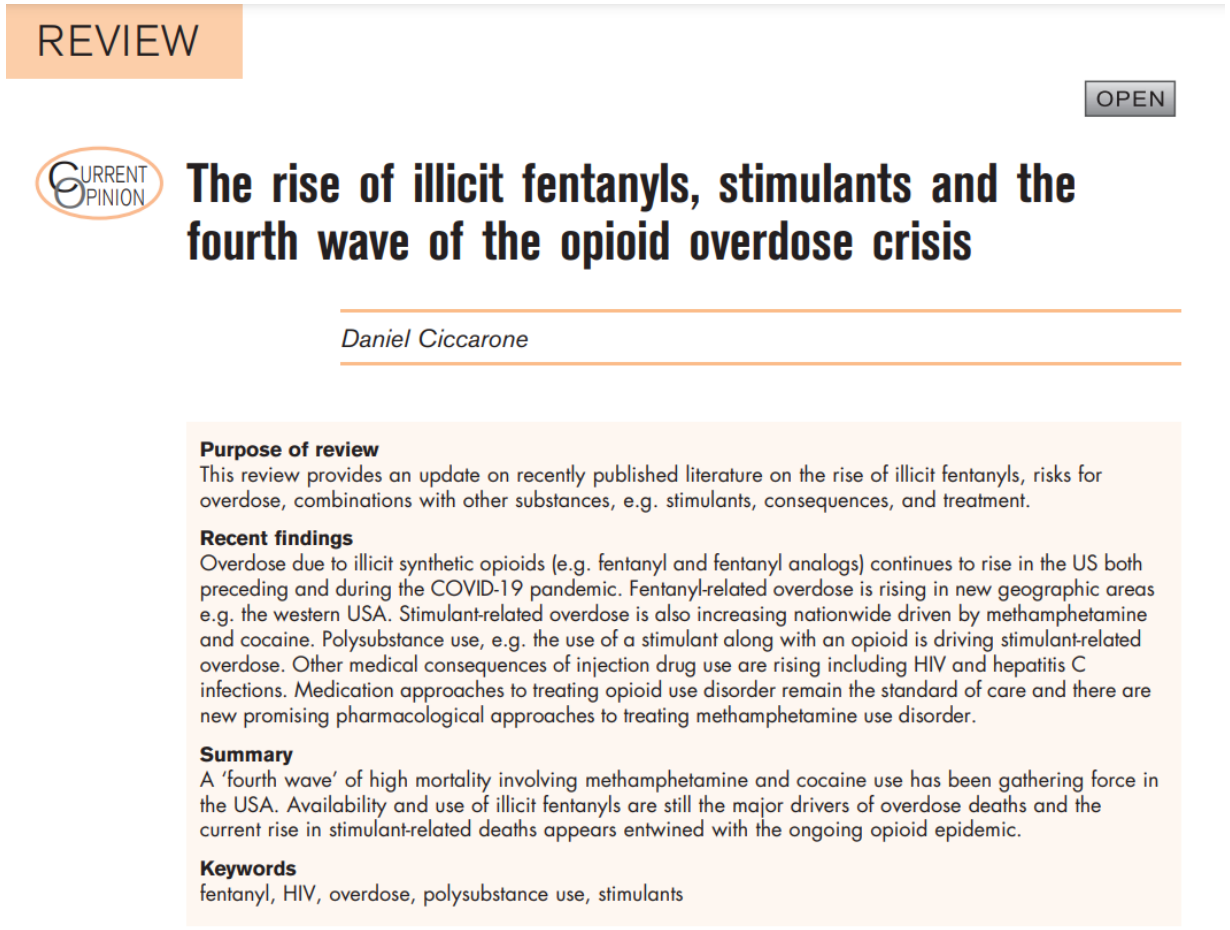
Fourth Wave?

Wave 1 (1990s): Resulting from over-prescription of opioid analgesics

Wave 2 (2010): Rapid increase in overdose deaths involving heroin.

Wave 3 (2013): Rise of synthetic fentanyl analogues

Wave 4 (2017): Polysubstance use involving stimulants



REVIEW

OPEN

CURRENT OPINION

The rise of illicit fentanyls, stimulants and the fourth wave of the opioid overdose crisis

Daniel Ciccarone

Purpose of review
This review provides an update on recently published literature on the rise of illicit fentanyls, risks for overdose, combinations with other substances, e.g. stimulants, consequences, and treatment.

Recent findings
Overdose due to illicit synthetic opioids (e.g. fentanyl and fentanyl analogs) continues to rise in the US both preceding and during the COVID-19 pandemic. Fentanyl-related overdose is rising in new geographic areas e.g. the western USA. Stimulant-related overdose is also increasing nationwide driven by methamphetamine and cocaine. Polysubstance use, e.g. the use of a stimulant along with an opioid is driving stimulant-related overdose. Other medical consequences of injection drug use are rising including HIV and hepatitis C infections. Medication approaches to treating opioid use disorder remain the standard of care and there are new promising pharmacological approaches to treating methamphetamine use disorder.

Summary
A 'fourth wave' of high mortality involving methamphetamine and cocaine use has been gathering force in the USA. Availability and use of illicit fentanyls are still the major drivers of overdose deaths and the current rise in stimulant-related deaths appears entwined with the ongoing opioid epidemic.

Keywords
fentanyl, HIV, overdose, polysubstance use, stimulants

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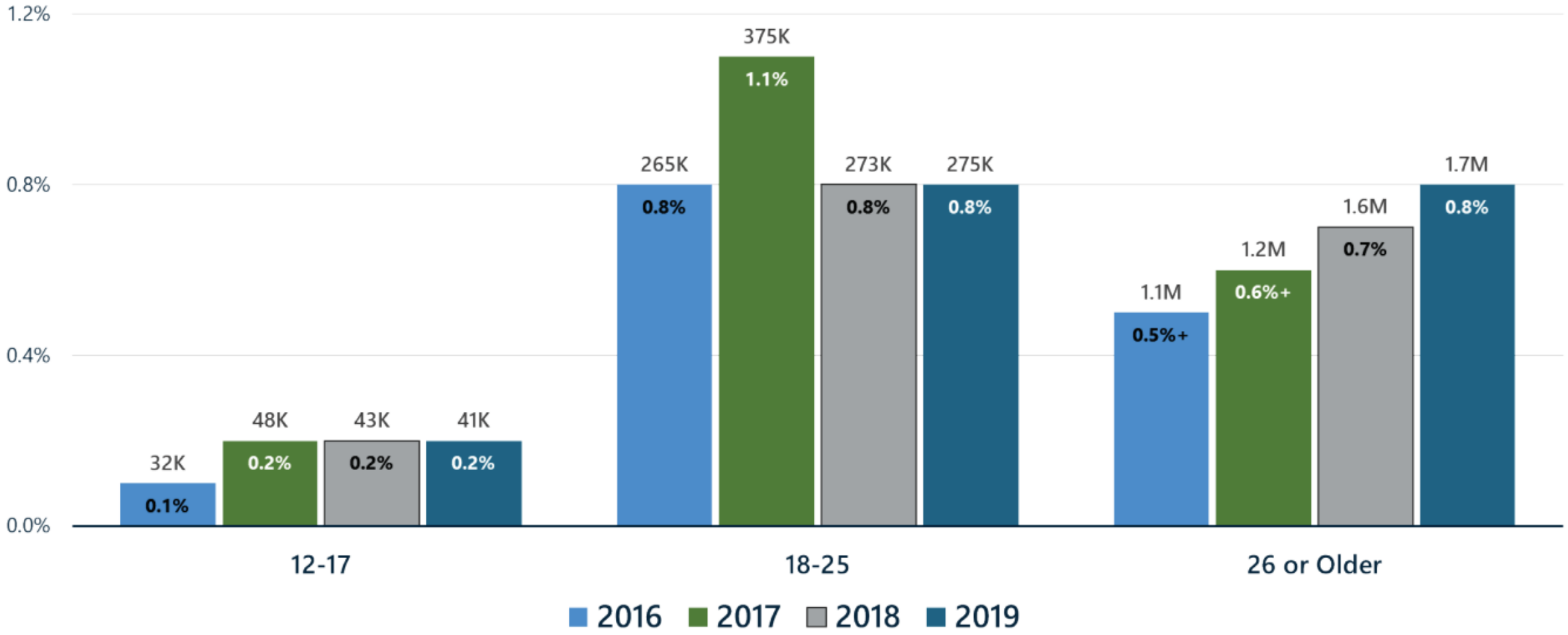
Methamphetamine Use

PAST YEAR, 2016-2019 NSDUH, 12+



+ Difference between this estimate and the 2019 estimate is statistically significant at the .05 level.

SAMHSA
Substance Abuse and Mental Health Services Administration

Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Weekly / Vol. 69 / No. 34
August 28, 2020

Nonfatal Drug and Polydrug Overdoses Treated in Emergency Departments — 29 States, 2018–2019

Stephen Liu, PhD[1]; Lawrence Scholl, PhD[1]; Brooke Hoots, PhD[1]; Puja Seth, PhD[1]

TABLE 2. Annual change in rates per 100,000 emergency department (ED) visits for suspected unintentional and undetermined intent nonfatal overdoses* of cocaine,† amphetamines,§ benzodiazepines¶ co-involving opioids, by sex, age, U.S. Census region, and county urbanization level — 29 states,†† 2018 to 2019**

ED patient/ visit characteristic	Rate change from 2018 to 2019§§					
	Opioids and cocaine		Opioids and amphetamines		Opioids and benzodiazepines	
	Relative (%)	Absolute	Relative (%)	Absolute	Relative (%)	Absolute
All	**4.4**	**0.1**	**37.3¶¶**	**0.4¶¶**	**2.6**	**0.1**
U.S. Census region* **						
Northeast	−1.4	0.0	116.3¶¶	0.4¶¶	5.2	0.1
South	6.1	0.1	33.3¶¶	0.4¶¶	−0.6	0.0
Midwest	19.2	0.2	21.1	0.1	3.0	0.1
West	−13.7	−0.1	26.7¶¶	0.7¶¶	2.6	0.1

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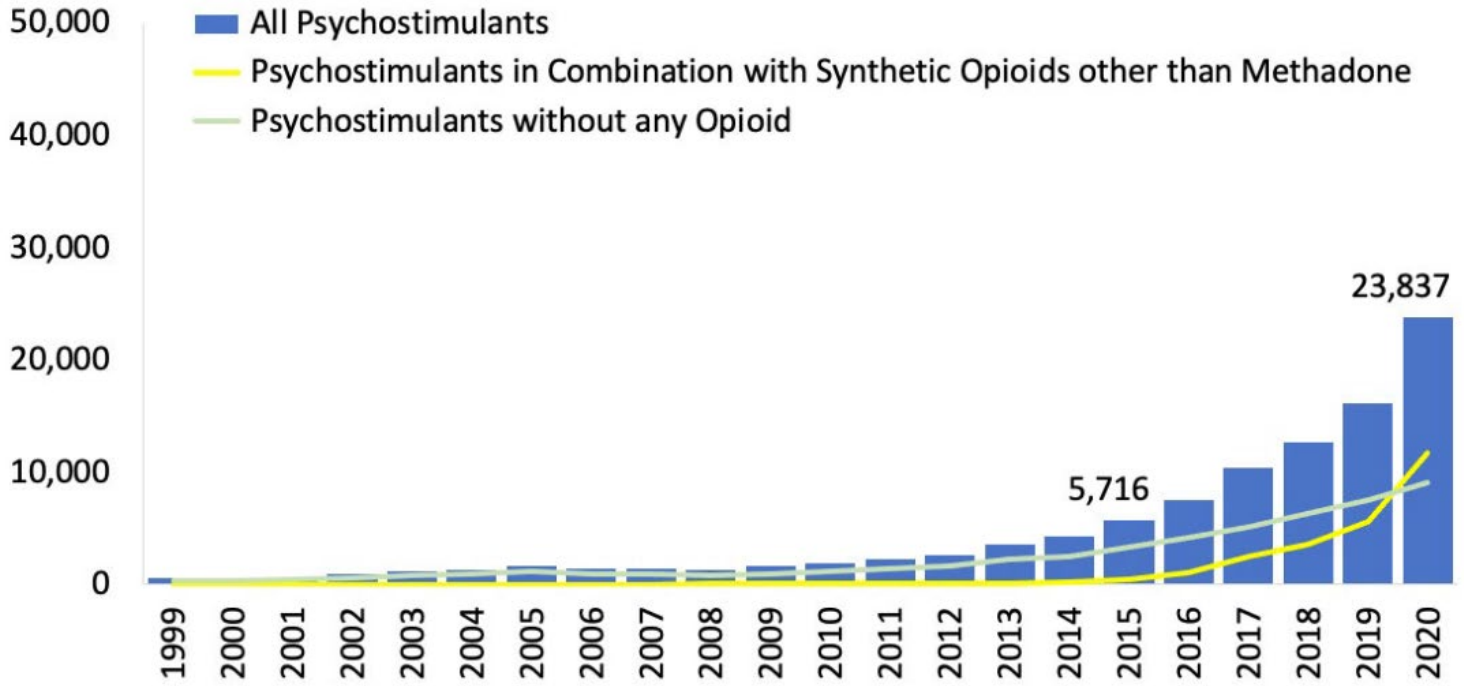
Figure 6. National Overdose Deaths Involving Psychostimulants with Abuse Potential (Primarily Methamphetamine)*, by Opioid Involvement

Number Among All Ages, 1999-2020



*Among deaths with drug overdose as the underlying cause, the psychostimulants with abuse potential (primarily methamphetamine) category was determined by the T43.6 ICD-10 multiple cause-of-death code. Abbreviated to *psychostimulants* in the bar chart above.
Source: Centers for Disease Control and Prevention, National Center for Health Statistics. Multiple Cause of Death 1999-2020 on CDC WONDER Online Database, released 12/2021.

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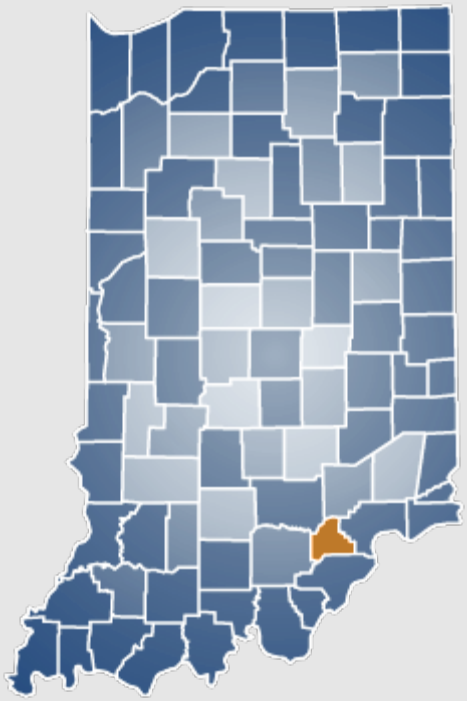
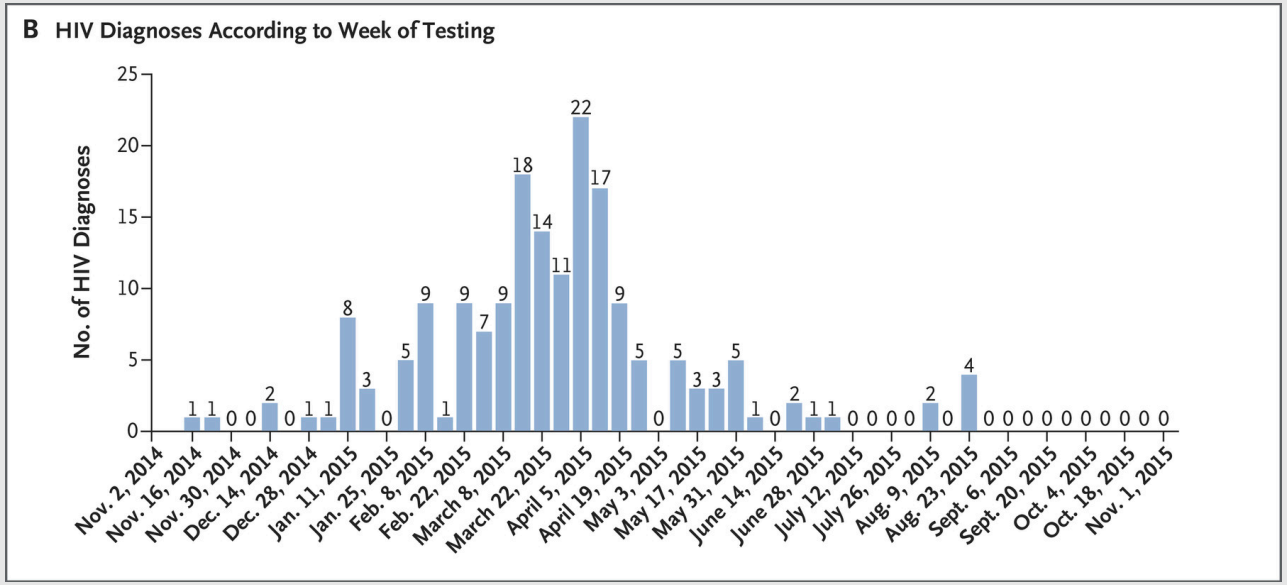
Scott County, Indiana, 2014-15

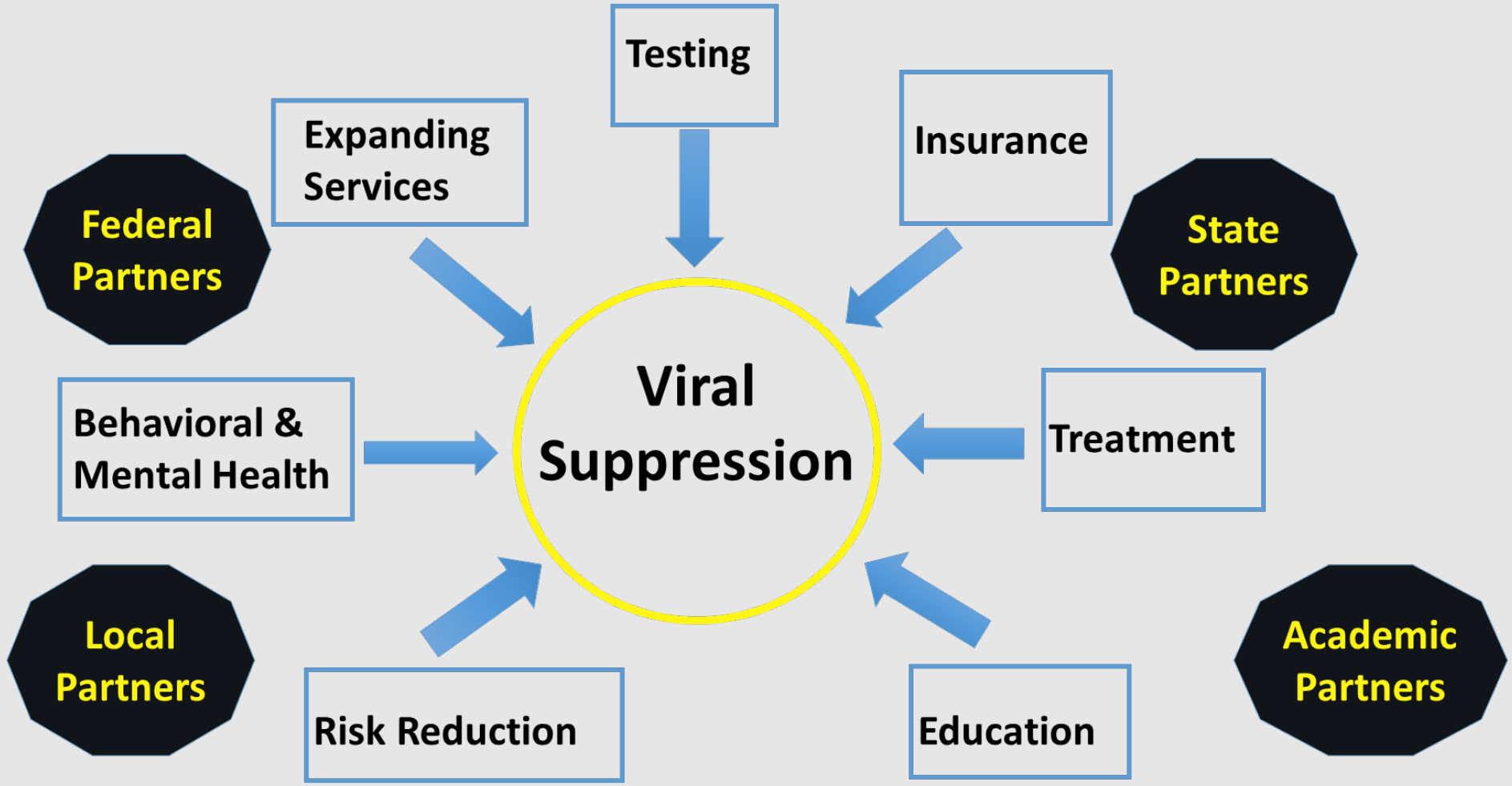


- **On Jan 23, 2015, the Indiana State Department of Health began investigating a cluster of 11 newly diagnosed HIV infections.**
  - **Only 5 HIV infections had been diagnosed from 2004-2013**
  - **All 11 HIV-infected persons reported having injected prescription opioid oxymorphone.**



Scott County, Indiana, 2014-15

Multi-pronged, coordinated response to HIV



From DM Janowicz, MD, at Atlanta, GA: April 8, 2016, IAS-USA.

Rural Opioid Initiative, NIDA/CDC/SAMHSA

- **Identify best practices that can be disseminated to address the particular need of communities confronting the opioid epidemic**
- **Conduct community assessments**
- **Use these assessments to design plans for implementing evidence-based practices to address:**
  - **Opioid Overdose**
  - **HIV/AIDS,**
  - **Hepatitis C,**
  - **Other related comorbidities**
- **Evaluate implementation of these plans**

NIH National Institute on Drug Abuse

CDC Centers for Disease Control and Prevention

ARC Appalachian Regional Commission

Substance Abuse and Mental Health Services Administration SAMHSA www.samhsa.gov • 1-877-SAMHSA-7 (1-877-726-4727)

ROI Research Consortium (www.ruralopioid.org)

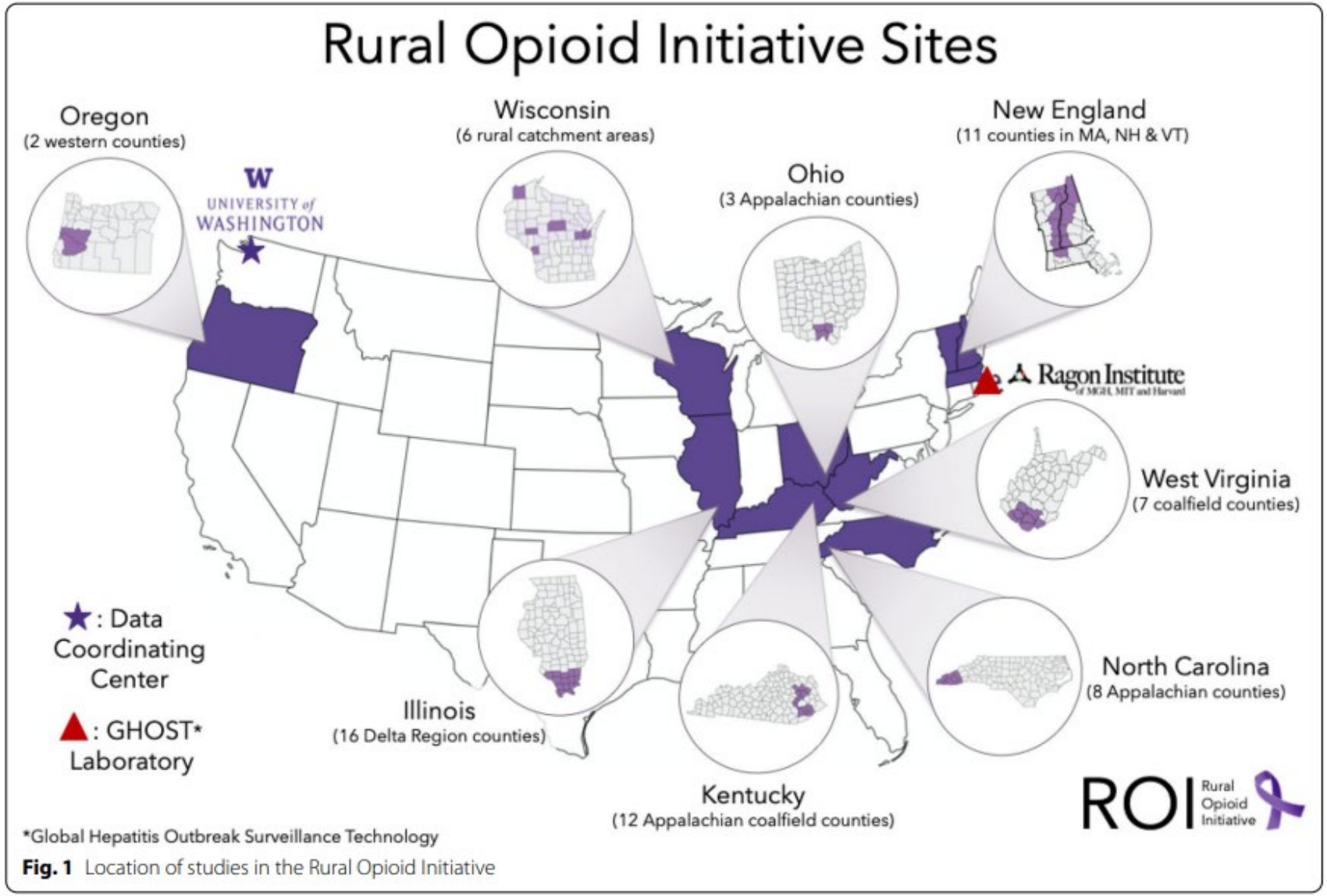


Fig. 1 Location of studies in the Rural Opioid Initiative

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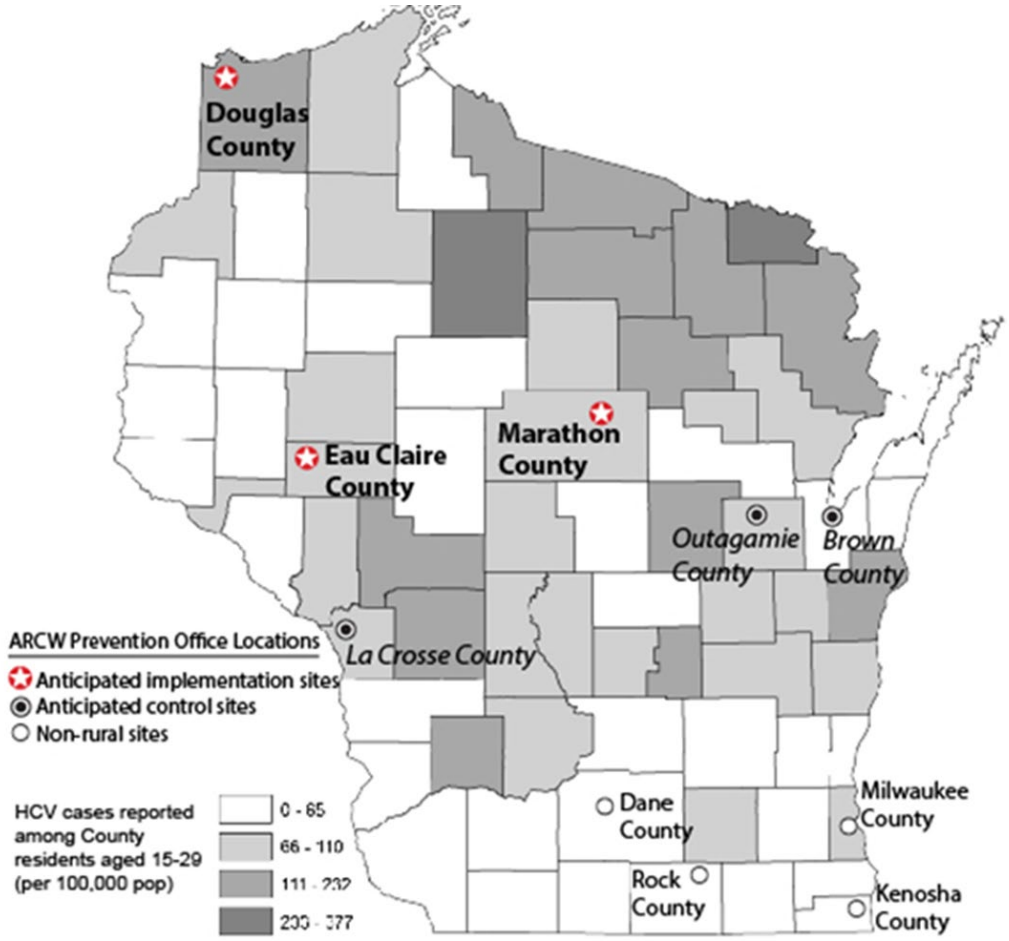
Wisconsin Rural Opioid Initiative

"Community-based, client-centered prevention homes to address the rural opioid epidemic"



vivent health

World Health Organization (2016)

Essential Services for People who Inject Drugs

- Needle/syringe programmes
- Opioid substitution therapy
- HIV testing and counselling
- HIV treatment and care
- Condom access
- Behavioural interventions
- Treatment of viral hepatitis
- Sexual and reproductive health interventions
- Provision of naloxone and training on overdose prevention for PWID community

HIV Medical Homes

Our HIV Medical Home ensures patients receive innovative care to support them in acheiving optimal health outcomes.

Our HIV Medical Home has received recognition from:

HEALTHCARE EQUALITY INDEX 2018 LGBTQ HEALTHCARE EQUALITY LEADER

RECOGNIZED NCQA PATIENT-CENTERED MEDICAL HOME

CMS CENTERS FOR MEDICARE & MEDICAID SERVICES

Wisconsin Department of Health Services

MEDICAL HOME PATIENTS

MEDICAL

High quality, comprehensive primary care and HIV treatment is provided to all patients, uniquely integrated with health and social services to ensure the best clinical outcomes.

LEGAL

Direct representation in appeals of the denial of public and private benefits, cases of discrimination, advance directives and other legal matters.

DENTAL

A full range of dentistry services to restore the health, smiles and confidence of our patients.

HOUSING

Transitional and long-term residential housing, rent and utility assistance, and counseling to assure no one with HIV is homeless.

BEHAVIORAL HEALTH

Individual and group therapy, psychiatry, drug treatment and neuropsychological testing are provided to assure wellness.

FOOD

Healthy and delicious food to assure good nutrition and support overall health.

PHARMACY

All prescriptions for patients, regardless of ability to pay, are filled along with in-depth education, adherence counseling, financial assistance and home delivery.

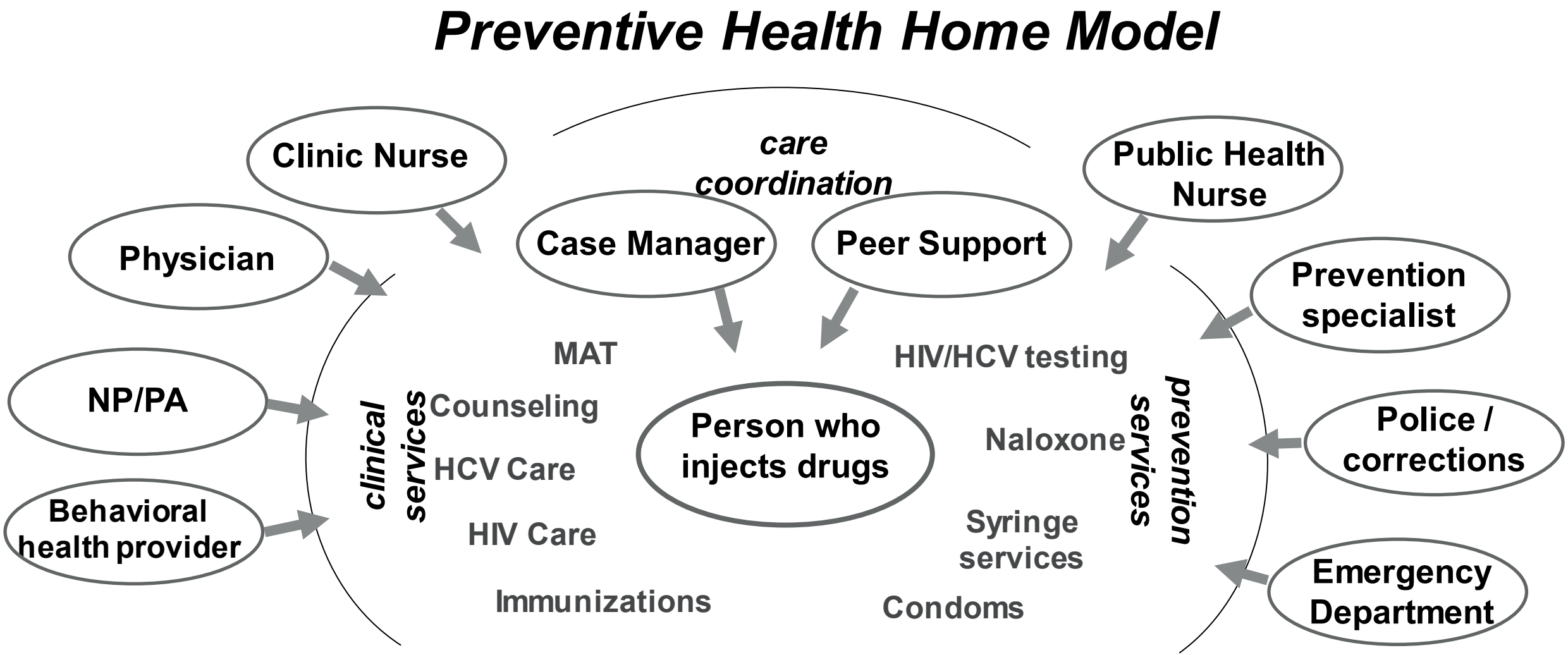
CASE MANAGEMENT

Assists patients and clients with enrollment in benefit programs to help them access and remain in care.

Key Performance Indicators

	Our outcomes	National average of HIV specialty clinics
Patients retained in care	94%	86%
Patients who have been prescribed HIV medications	99%	91%
Patients who are virally suppressed	91%	72%

Needed: A new model of care for people who use drugs



Wisconsin Rural Opioid Initiative

Phase 1 (UG3): Sep 2017-Aug 2018

- HIV/HCV seroprevalence study
- Community needs assessment through stakeholder interviews
- Client survey assessing health behaviors and health care access

Eligibility Criteria

1. 15 years or older
2. Injected drugs the past 30 days
3. Reside in a rural community

Enrollment

1. Rapid HIV, HCV, and syphilis test
2. 25-30 minutes ACASI style survey
3. Confirmatory testing (if needed)

Phase 2 (UH3): Sep 2019-Aug 2022

- Implementation of Client Centered Prevention Home Model at ARCW office in 3 rural communities

Qualitative Data ⟷ Qualitative Data

Respondent Driven Sampling

1. Participants receive three coupons to recruit their peers
2. Receive $10 for each eligible recruit that enrolls into the study

Participant Interviews

1. Enrolled participants may be asked to participate in an interview
2. Receive $30 for their time (1-2 hours).

Results:

Wisconsin Rural Opioid Initiative (UG3 Phase)

1. Early Findings from Multi-Site Survey
2. WI-specific findings related to Hepatitis C

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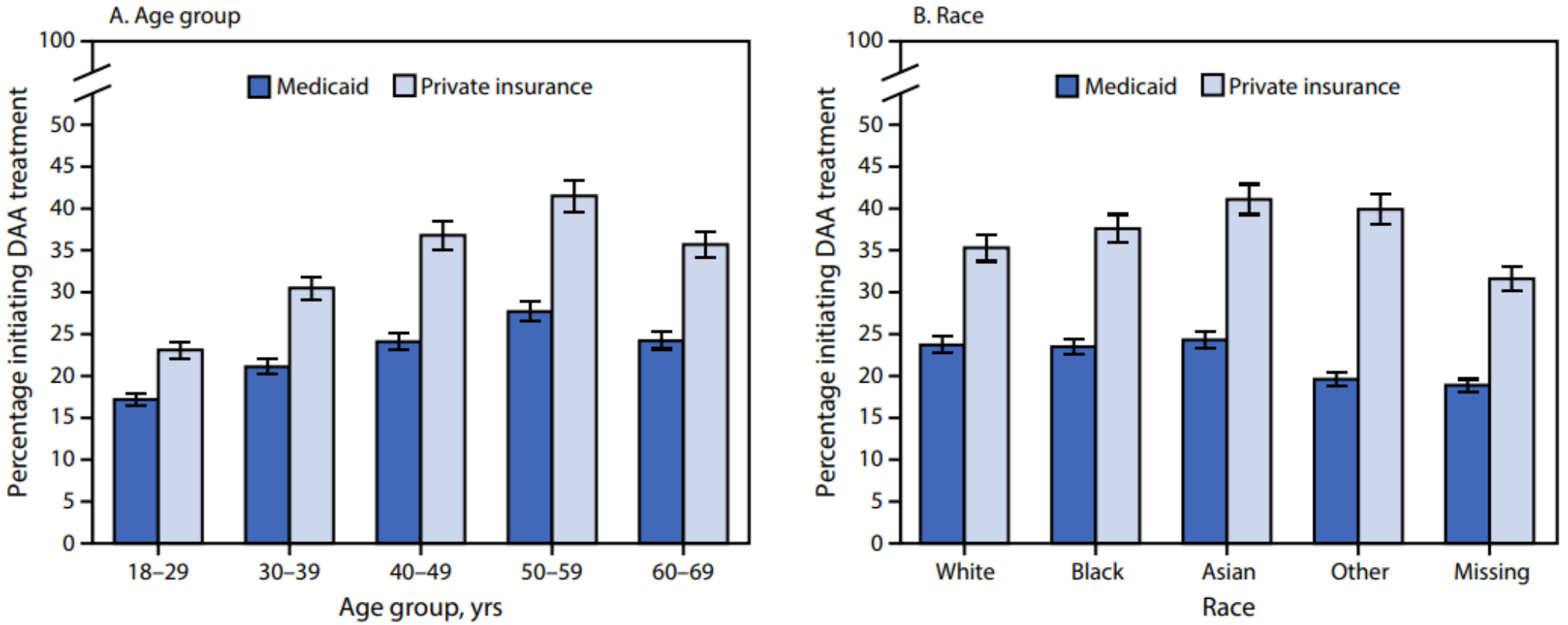
Vital Signs: Hepatitis C Treatment Among Insured Adults — United States, 2019–2020

William W. Thompson, PhD[1,*]; Hasan Symum, PhD[2,*]; Amy Sandul, DHSc[1]; Neil Gupta, MD[1]; Priti Patel, MD[1]; Noele Nelson, MD, PhD[1]; Jonathan Mermin, MD[2]; Carolyn Wester, MD[1]

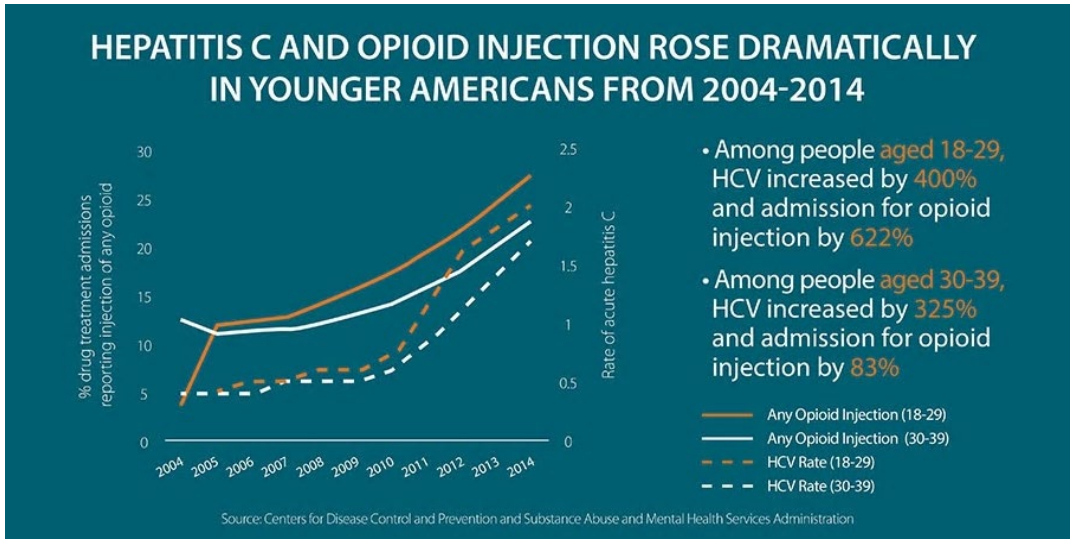
On August 9, 2022, this report was posted as an MMWR *Early Release on the* MMWR *website (https://www.cdc.gov/mmwr).*

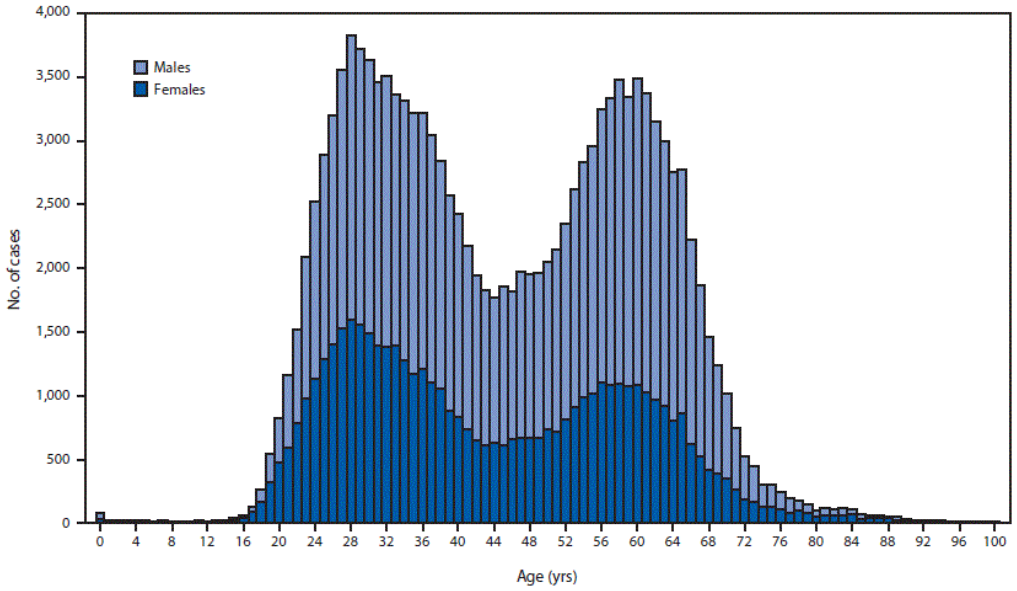
FIGURE 2. Percentage of adults* with hepatitis C initiating direct-acting antiviral treatment, by insurance type, age group (A), and race (B) — United States, 2019–2020

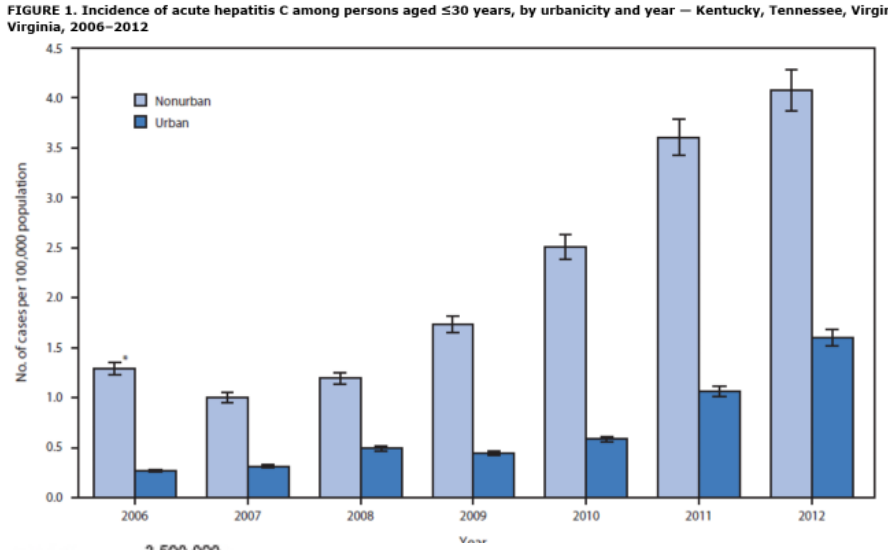


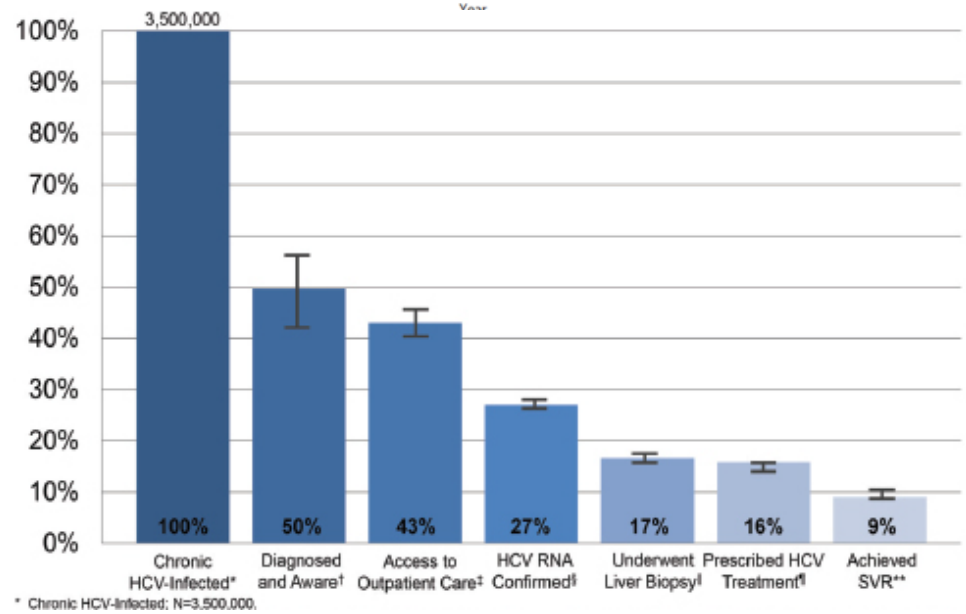
Abbreviation: DAA = direct-acting antiviral.
* With 95% CIs shown by error bars.

Hepatitis C Attributed to Injection Drug Use









Source: Centers for Disease Control and Prevention

Molecular Epidemiological Investigation

A large HCV transmission network enabled a fast-growing HIV outbreak in rural Indiana, 2015

Sumathi Ramachandran • Hong Thai • Joseph C. Forbi • Romeo Regi Galang • Zoya Dimitrova • Guo-liang Xia • et al. Show all authors • Show footnotes

Open Access • Published: November 14, 2018 •

A B S T R A C T

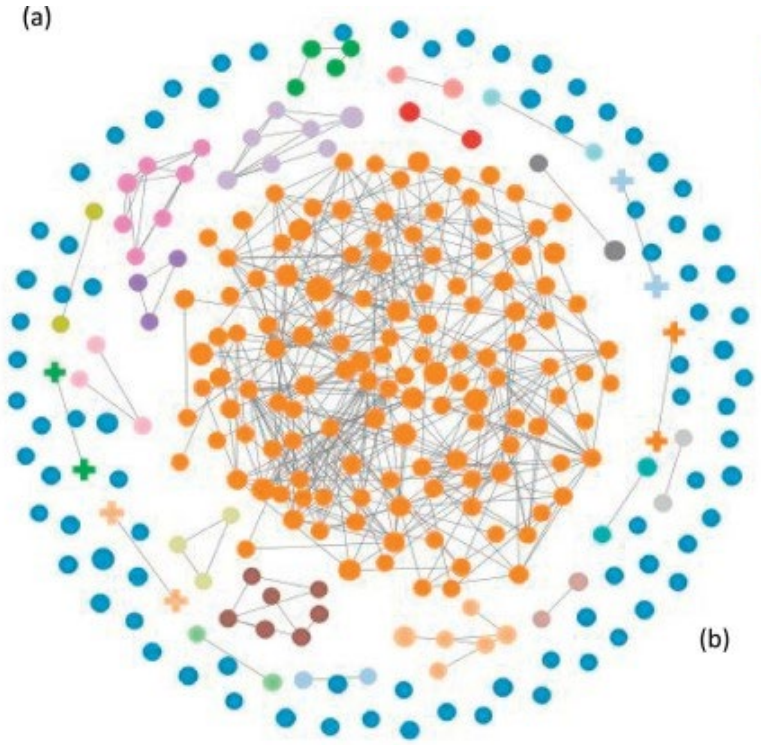
Background: A high prevalence (92.3%) of hepatitis C virus (HCV) co-infection among HIV patients identified during a large HIV outbreak associated with injection of oxymorphone in Indiana prompted genetic analysis of HCV strains.

Methods: Molecular epidemiological analysis of HCV-positive samples included genotyping, sampling intra-host HVR1 variants by next-generation sequencing (NGS) and constructing transmission networks using Global Hepatitis Outbreak and Surveillance Technology (GHOST).

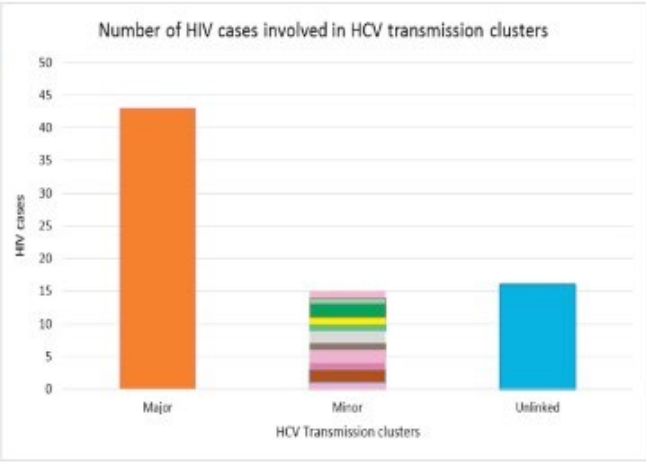
Findings: Results from the 492 samples indicate predominance of HCV genotypes 1a (72.2%) and 3a (20.4%), and existence of 2 major endemic NS5B clusters involving 49.8% of the sequenced strains. Among 76 HIV co-infected patients, 60.5% segregated into 2 endemic clusters. NGS analyses of 281 cases identified 826,917 unique HVR1 sequences and 51 cases of mixed subtype/genotype infections. GHOST mapped 23 transmission clusters. One large cluster (n = 130) included 50 cases infected with ≥2 subtypes/genotypes and 43 cases co-infected with HIV. Rapid strain replacement and superinfection with different strains were found among 7 of 12 cases who were followed up.

Interpretation: GHOST enabled mapping of HCV transmission networks among persons who inject drugs (PWID). Findings of numerous transmission clusters, mixed-genotype infections and rapid succession of infections with different HCV strains indicate a high rate of HCV spread. Co-localization of HIV co-infected patients in the major HCV clusters suggests that HIV dissemination was enabled by existing HCV transmission networks that likely perpetuated HCV in the community for years. Identification of transmission networks is an important step to guiding efficient public health interventions for preventing and interrupting HCV and HIV transmission among PWID.

Fund: US Centers for Disease Control and Prevention, and US state and local public health departments.

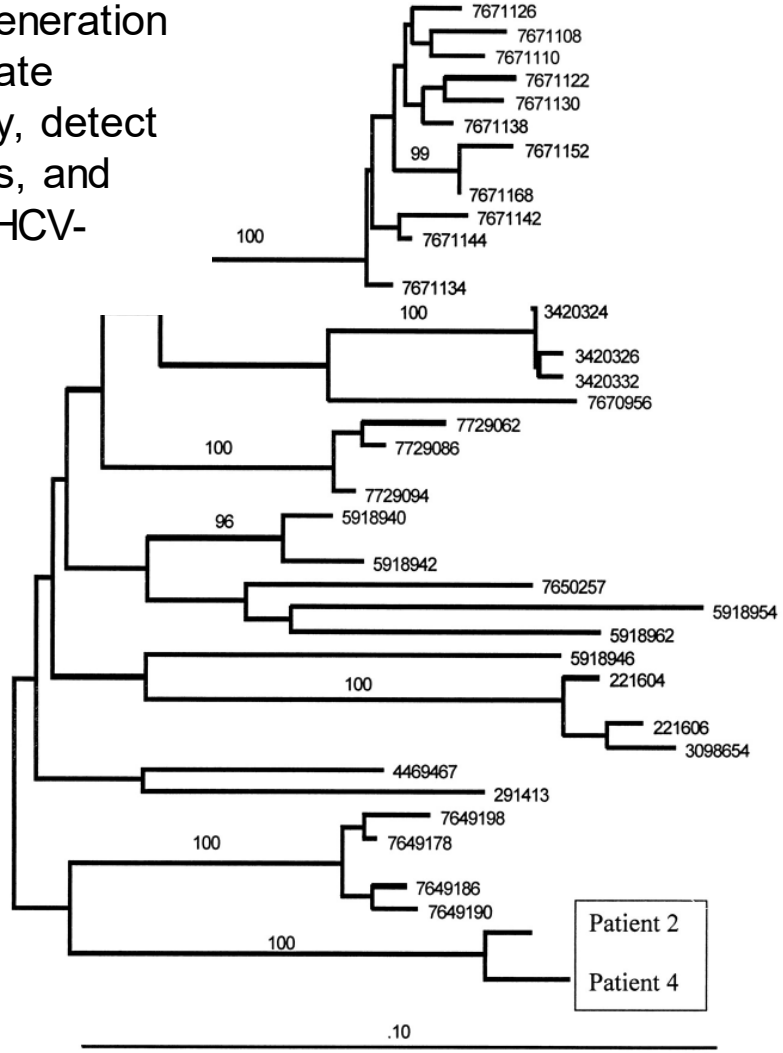


HCV Groups	Clusters	Cases	%
Related cases as clusters	23	198	70.46
Unrelated	0	83	29.54
Total	23	281	100



Global Hepatitis Outbreak Surveillance Technology

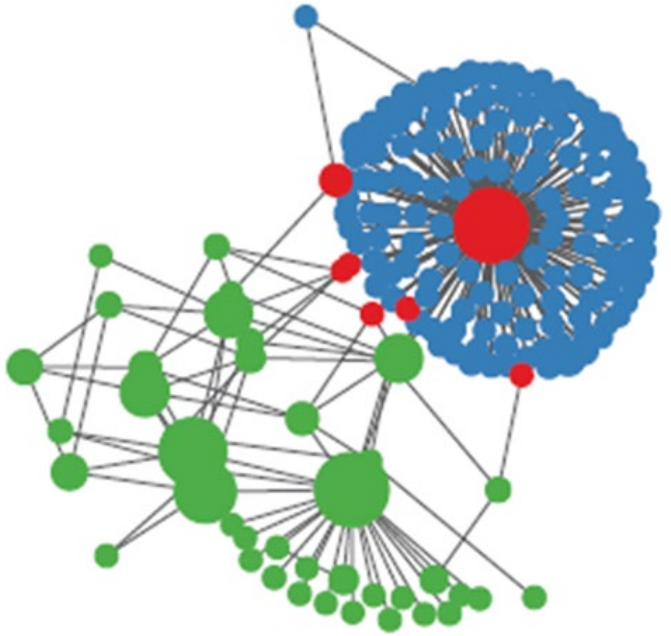
GHOST uses next generation sequencing to calculate genetic heterogeneity, detect transmission linkages, and identify networks of HCV-infected individuals



DOI: 10.1128/JCM.40.4.1541-1545.2002

Example of a K-step Network: A Network Diagram Showing the Genetic Distances among all HCV Variants for Two Linked Individuals

	Number of variants found within the sample
Shared*	9
Subject 1	134
Subject 2	41



Hepatitis C in Wisconsin: Increase Among Young PWID

FIGURE 1.

The number of acute HCV cases has increased over the past 10 years in Wisconsin, and remained high in 2017. Most reported injecting drugs.

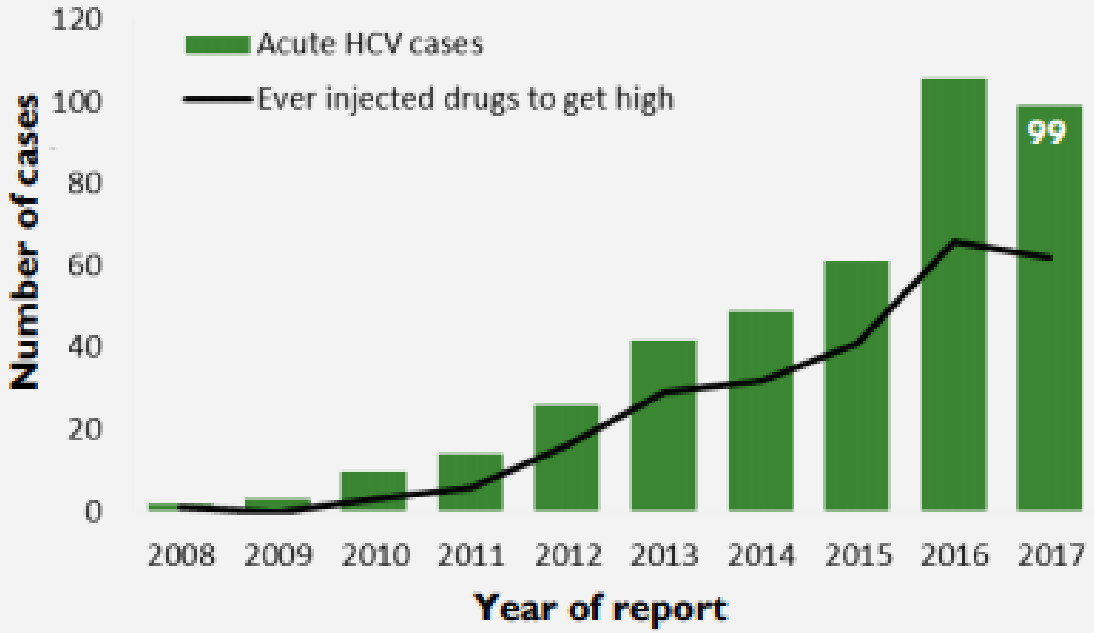
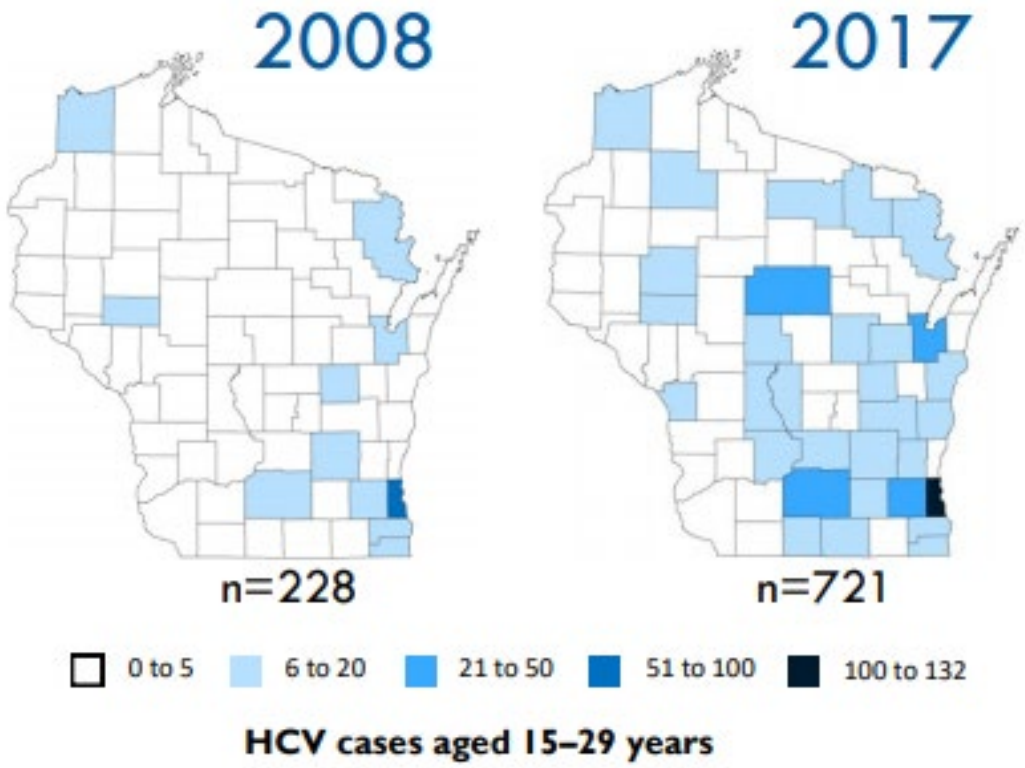


FIGURE 2.

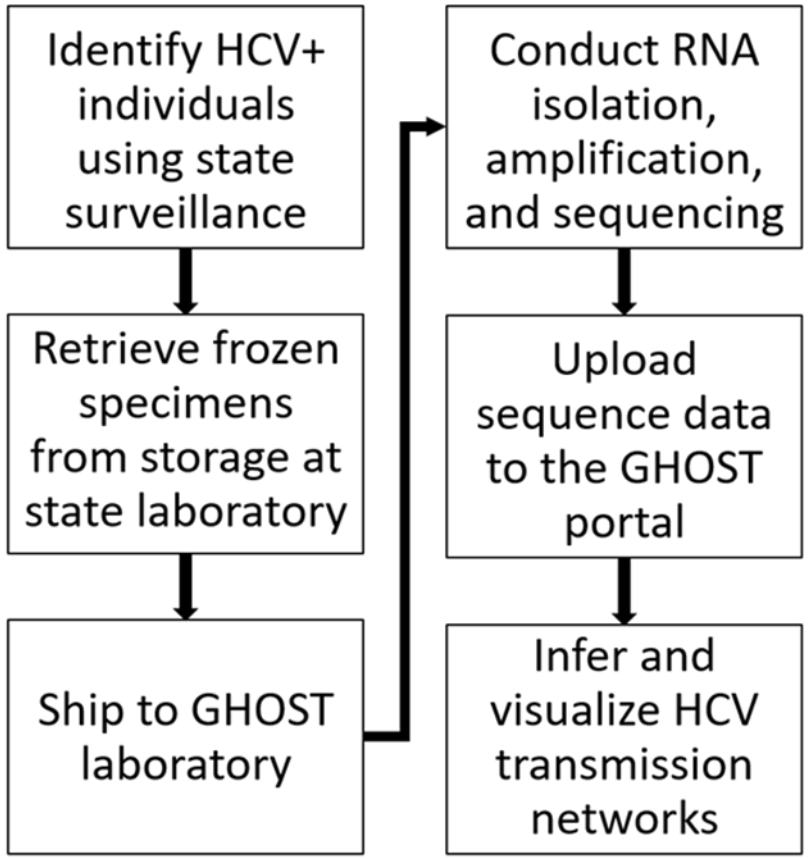
Over the past 10 years, the number of new HCV cases among young people aged 15–29 years has more than tripled, and more Wisconsin counties are reporting cases.



Wisconsin Hepatitis C Program. https://www.dhs.wisconsin.gov/publications/p02322.pdf

Identifying Individuals Key to the Spread of HCV in Wisconsin

- Laboratory Infrastructure in WI
  - Blood samples collected for HCV RNA confirmatory testing at sites supported by DPH are analyzed and stored at the WSLH
  - 18% of all confirmed HCV cases reported to the WEDSS represent individuals who underwent fee-exempt confirmatory RNA testing through the WSLH
  - These instances typically reflect testing done in public health settings such as SSPs and correctional facilities, and not traditional health care settings
  - This results in a sample that is enriched for younger people with a history of injection drug use



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WISCONSIN DEPARTMENT of HEALTH SERVICES

Ragon Institute of MGH, MIT and Harvard

Patient Demographic Characteristics and Risk Behaviors

- We identified 459 Wisconsin residents who were confirmed to have an HCV RNA+ sample analyzed at WSLH during 2016-17 and were likely to represent recent or acute infections
- Residual serum specimens corresponding to these 424 (92%) cases were retrieved from WSLH and shipped to the GHOST laboratory
- Of these, 379 specimens (89.4%) were successfully amplified, sequenced, and passed GHOST quality control metrics.

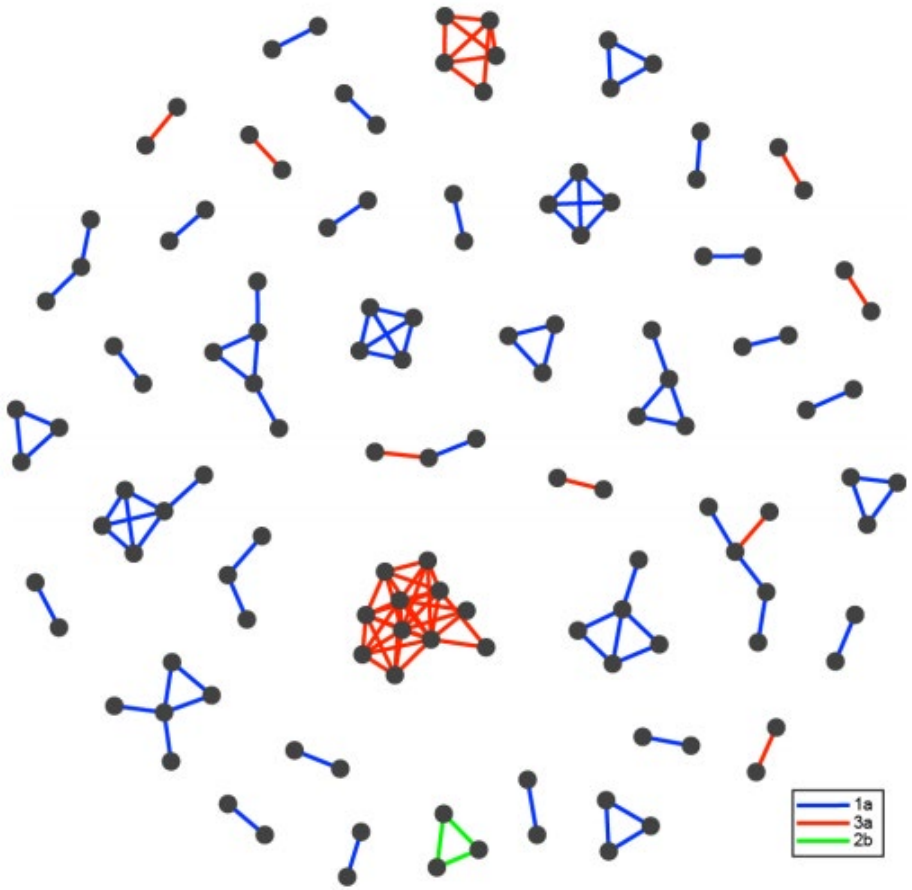
Table 1. Demographics and risk factor information, by type of testing facility, for all 379 persons tested for HCV while in public health or correctional settings, Wisconsin, USA, 2016–2017*

		Setting of first HCV-positive test result			
	Overall	Syringe Service Program	Corrections setting	Local health department	Other
Variable	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)
Total	379 (100)	119 (31.4)	154(40. 6)	38 (10.0)	68 (17.9)
Year first reported to WEDSS					
2016	222 (58.6)	68 (57.1)	87 (56.5)	22 (57.9)	45 (66.2)
2017	157 (41.4)	51 (42.9)	67 (43.5)	16 (42.1)	23 (33.8)
Age, y					
18–29	190 (50.1)	57 (47.9)	77 (50.0)	19 (50.0)	37 (54.4)
30–39	154 (40.6)	39 (32.8)	75 (48.7)	16 (42.1)	24 (35.3)
>40	35 (9.2)	23 (19.3)	2 (1.3)	3 (7.9)	7 (10.3)
Race/ethnicity					
Non-Hispanic white	318 (83.9)	103 (86.6)	127 (82.5)	34 (89.5)	54 (79.4)
Hispanic or Latino	18 (4.8)	4 (3.4)	7 (4.6)	2 (5.3)	5 (7.4)
American Indian or Alaska Native	21 (5.5)	7 (5.9)	9 (5.8)	1 (2.6)	4 (5.9)
Asian	2 (0.5)	0	1 (0.7)	0	1 (1.5)
Non-Hispanic black or African American	12 (3.2)	4 (3.4)	5 (3.3)	1 (2.6)	2 (2.9)
Other/Unknown	8 (2.1)	1 (0.8)	5 (3.3)	0	2 (2.9)
Sex					
F	93 (24.5)	44 (36.9)	14 (9.1)	13 (34.2)	22 (32.3)
M	286 (75.5)	75 (63.0)	14 (90.9)	25 (65.8)	46 (67.7)
Ever inject drugs					
Yes	177 (46.7)	98 (82.4)	16 (10.4)	32 (84.2)	31 (45.6)
No or unknown	202 (53.3)	21 (17.7)	138 (89.6)	6 (15.8)	37 (54.4)
Ever share works					
Yes	145 (38.3)	88 (74.0)	10 (6.5)	29 (76.3)	18 (26.5)
No, unknown, or not applicable	234 (61.7)	31 (26.1)	144 (93.5)	9 (23.7)	50 (73.5)
MSM					
Yes	8 (2.1)	4 (3.4)	0	2 (5.3)	2 (2.9)
No or unknown	371 (97.9)	115 (96.6)	154 (100)	36 (94.7)	66 (97.1)
Ever incarcerated					
Yes	335 (88.4)	92 (77.3)	154(100)	34 (89.5)	54 (79.7)
No or unknown	44 (11.6)	27 (22.7)	0	4 (10.5)	14 (20.6)

*MSM, man who has sex with men; WEDSS: Wisconsin Electronic Disease Surveillance System.

HCV Transmission Linkages

GHOST detected 42 clusters comprising 126 individuals for an overall clustering rate of 33%.



- Each node represents a HCV-infected individual.
- A transmission link is denoted as a line connecting individuals where the minimal hamming distance between sequences is smaller than the previously validated genetic threshold of 3.77%.
- The transmission networks were composed of mostly dyads (n=23, 54.8%), followed by groups of 3 (n=9, 21.4%), 4 (n=3, 9%), 5 (n=6, 14.3%), and 11 (n=1, 2.4%).
- Among the 379 persons, 171 (45.1%) resided in the rural catchment area, of which 67 (39.2%) clustered; 54 (14.3%) resided in the nonrural catchment area, of which 14 (25.9%) clustered; and 154 (40.6%) resided in correctional facilities, of which 45 (29.2%) clustered.
- Among the 171 rural persons, women were significantly more likely to cluster (49%) than men (33%) ($p = 0.04$), and persons who clustered were significantly younger (mean age 28.7 years) than persons who did not cluster (mean age 34.1 years) ($p = 0.0001$).

Publisher: CDC; Journal: Emerging Infectious Diseases
Article Type: Research; Volume: 27; Issue: 2; Year: 2021; Article ID: 20-2957
DOI: 10.3201/eid2702.202957; TOC Head: Research

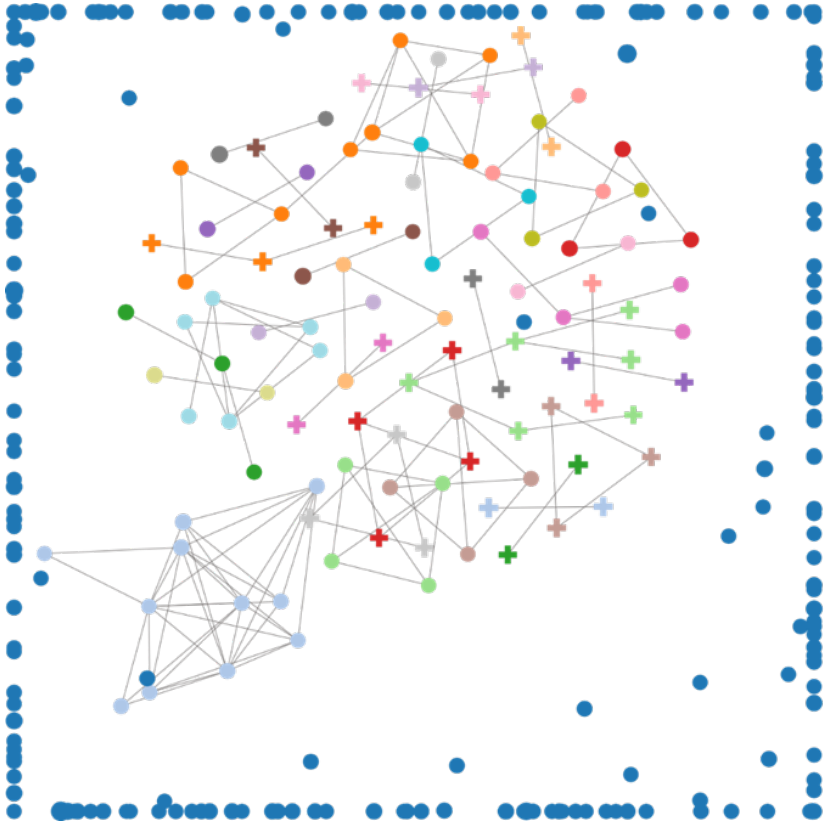
Transmission Clusters of Hepatitis C Virus in Public Health and Correctional Settings, Wisconsin, USA, 2016–2017[1]

Karli R. Hochstatter,[2] Damien C. Tully,[2] Karen A. Power, Ruth Koepke, Wajiha Z. Akhtar, Audrey F. Prieve, Thomas Whyte, David J. Bean, David W. Seal, Todd M. Allen,[3] Ryan P. Westergaard[3]

Prospectively Identifying Individuals Key to the Spread of HCV in Wisconsin

- Specimens from individuals testing HCV+ at needle and syringe exchange programs in Wisconsin are being analyzed by GHOST and added to this cohort prospectively as part of a larger study (Co-PIs: Ryan Westergaard and David Seal, NIDA Grant)
- Additional information from these individuals, as well as from those who test HCV-, that is not available in the public health surveillance system can be used to further understand network characteristics

Preliminary Results: Combined Retrospective + Prospective Cohorts



Strengths and limitations of molecular surveillance

- Strengths
  - Unbiased biological data
  - Includes hard-to-reach individuals
  - Can inform targeted public health interventions
- Limitations
  - Missing persons
  - Missing attribute data
  - Cannot identify source, directionality, or recency of infection

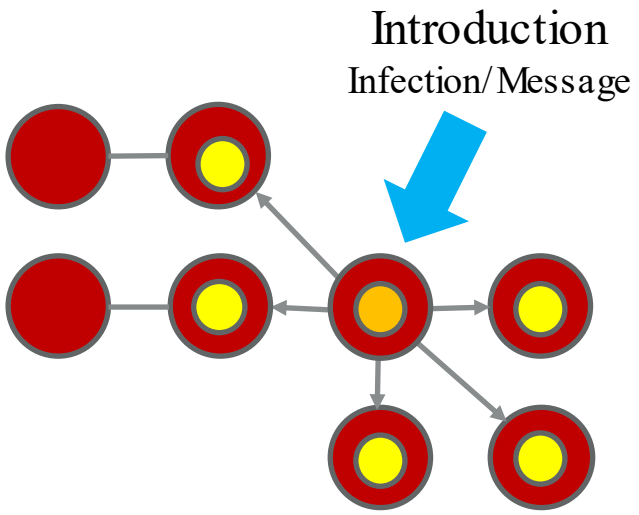
Summary

- Incorporating GHOST into routine laboratory and surveillance practices may enhance the ability of public health departments to detect individuals and networks contributing most to HCV transmission in their communities and intervene efficiently.

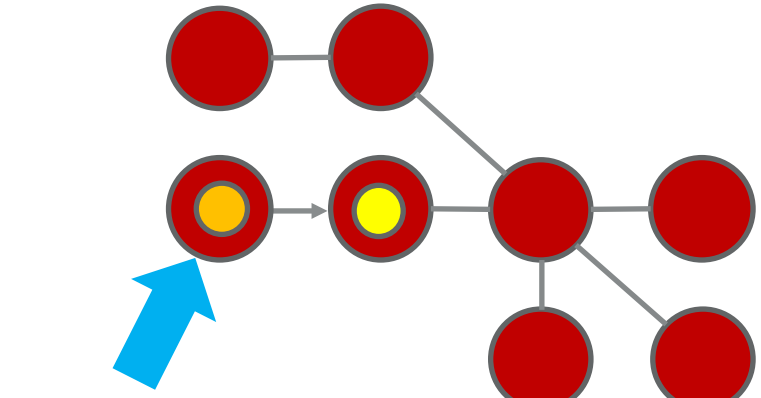
What's next?
Targeted treatment among PWID

Understanding network structure affects spread of infection and public health information/education

The availability of this web-based analytics tool can advance prevention efforts by facilitating the ability of health departments to conduct molecular surveillance and efficiently allocate limited resources.



Strong effect



Weak effect

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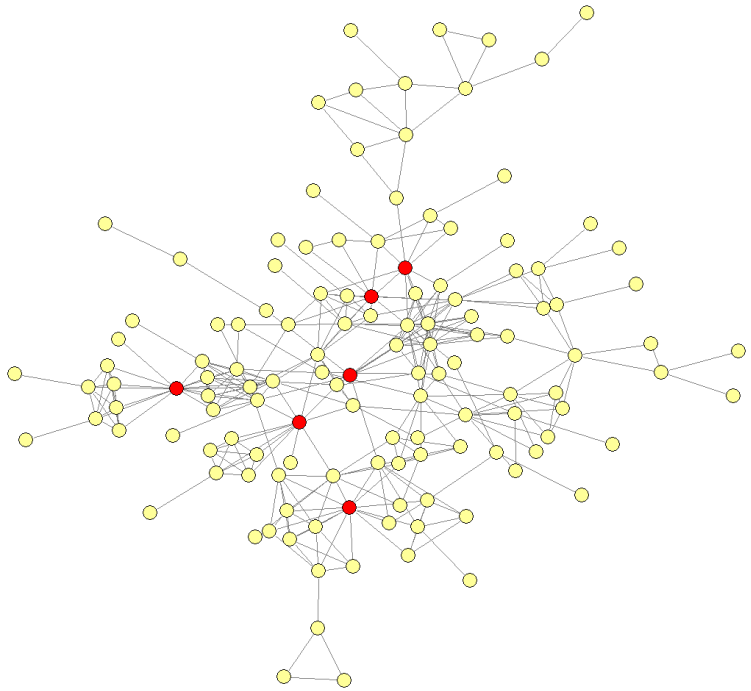
Targeted Network-Based Interventions (TNI) – Intelligent Network DisRuption Analysis (INDRA)

- Detects transmission networks in a near-real time
- Guides most efficient and cost-effective intervention
- Provides new instant measures for monitoring efficiency of public health intervention
- Personal/Community benefits: rapid reduction of probability to be infected with HCV



INDRA: Ranking Nodes for Interventions

ID	Rank	Efficiency
IN373	1	0.820151
INR6360	2	0.694935
IN136	3	0.603052
IN084	4	0.537548
IN365	5	0.490244
IN384	6	0.451528
….	….	….

Local Health Departments have/had infrastructure for community level disease control

Strategies for TB Prevention and Control

This report reemphasizes the importance of three priority strategies for TB prevention and control that have been well established for decades:

1. Identification of and completion of treatment for persons with active TB disease to render their condition noninfectious
2. Finding and screening persons who have had contact with TB patients to determine
    - whether they have active TB disease themselves;
    - whether they have been infected with *M. tuberculosis;* or
    - for children and other persons at high risk, whether they require window prophylaxis (preventive treatment of presumed TB infection during the time that it would normally take for a tuberculin skin test [TST] or interferon gamma-release assay [IGRA] to become positive after exposure) and whether to administer treatment
3. Screening, testing, and treatment of other selected persons and populations at high risk for latent TB infection (LTBI) and subsequent active TB disease to detect persons who can most benefit from treatment for LTBI, which is essential for TB elimination because of new immunosuppressive drugs and therapies used for different illnesses, immigration from areas where TB is endemic, and diminished knowledge and reduced recognition of TB by clinicians as a result of decreased incidence

Although the three priority strategies focus on individual patients, they serve broader epidemiologic functions because they reduce current and future transmission of *M. tuberculosis* in the community.

Local public health departments have existing infrastructure to treat HCV among people who inject drugs (preCOVID) and a trusted relationship with local syringe exchange programs

- Can we assess whether a local health department can leverage information from GHOST to prioritize and treat people who inject drugs for HCV to decrease future transmission of HCV to their peers?

- Stakeholder engagement is required to provide feedback and guidance on protocol development and collaborate on how such an intervention can be implemented in their community.

Specific Aims

- Aim 1: Comprehensively describe attitudes for HCV diagnoses, transmission clusters, molecular surveillance, community level public health implications, and strategies for HCV treatment among people who inject drugs.

- Aim 2: Assess legal, ethical, and policy barriers in using molecular surveillance for community level HCV micro-elimination strategies.

Explainify Video -

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Thank you


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