Starting Injectable buprenorphine in persons hospitalized with OUD & infections

Sandra A. Springer, Prerana Roth, Michelle Strong, Manesh Gopaldes, Alain Litwin, Nikhil Seval, Kathleen Brady, Frances Levin, Edward Nunes

April 15, 2023, ASAM 54th Annual Conference

Disclosure Information

- Presenter 1: Sandra A. Springer, MD
  - Presenter 1 Commercial Interests: Paid Scientific consultation from Alkermes Inc and received NIH and VA grant funding. Dr. Springer has received in-kind study drug donations from Alkermes Inc and Indivior Pharmaceutical Company for NIH-funded research including this study
- Presenter 2: Prerana Roth, MD
  - Presenter 2 Commercial Interests: No disclosures
- Presenter 3: Manesh Gopaldes, MD
  - Presenter 3 Commercial Interests: No Disclosures
- Presenter 4: Michelle Strong, PhD
  - Presenter 4 Commercial Interests: No disclosures
- Presenter 5: Alain Litwin, MD
  - Commercial interests: Advisory Board - Gilead Sciences and AbbVie Pharmaceuticals; Grant support - Gilead Sciences; Medication from Indivior

Learning Objectives (Suggested)

1. Participants will understand the common infections that patients with OUD present with in a hospital setting and how to rapidly screen & diagnose OUD and initiate Medication treatments for OUD while managing concurrent infections.
2. Participants will learn how to to safely initiate long-acting buprenorphine (LAB) in the hospital setting
3. Participants will learn the risk of overdose during COVID19 and how to improve education to include opioid overdose risk and improve MOUD initiation and naloxone prescription prior to discharge to reduce risk.
4. Participants will learn how Addiction Psychiatry/ Addiction Medicine and Infectious Disease can best collaborate on how to best serve patients hospitalized with OUD and infections.

Characteristics of patients presenting to the hospital with severe infections and OUD and management of MOUD including long-acting buprenorphine initiation during acute infectious disease management

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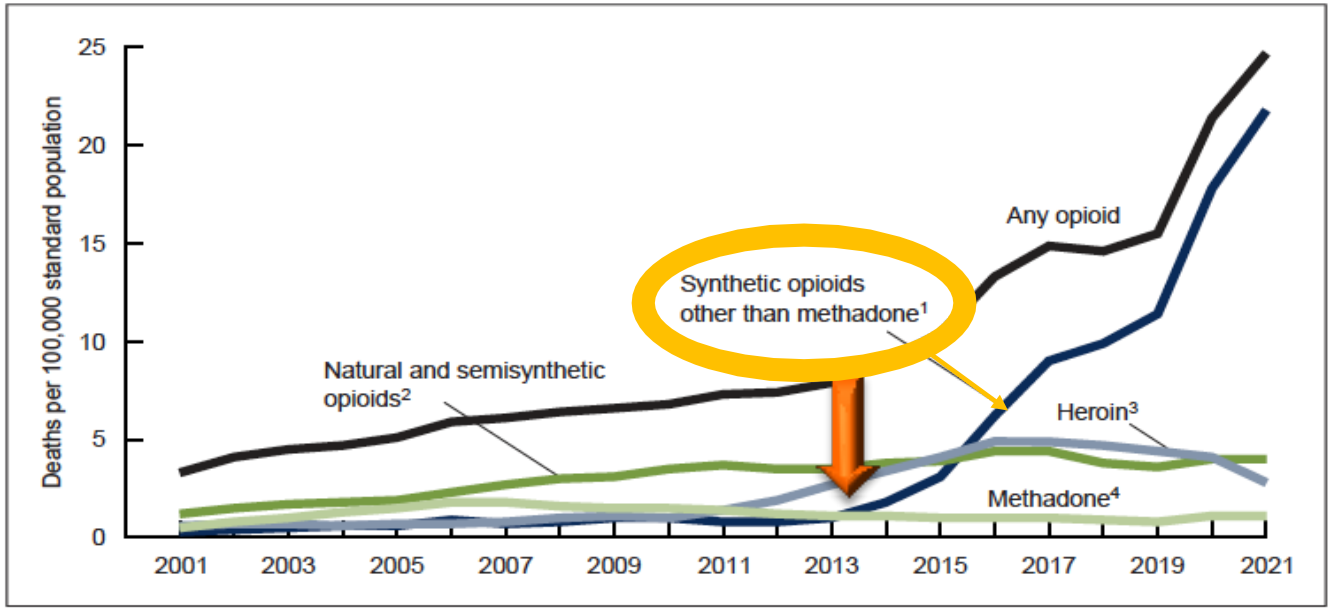
ASAM 54th Annual Conference, April 15, 2023

U.S. Opioid Overdose Deaths 2001-2021

Figure 4. Age-adjusted rate of drug overdose deaths involving opioids, by type of opioid: United States, 2001–2021



[1]Significant increasing trend from 2001 through 2021 with different rates of change over time, $p < 0.05$.
[2]Significant increasing trend from 2001 through 2010, then stable trend from 2010 through 2021, $p < 0.05$.
[3]Significant increasing trend from 2001 through 2015 with different rates of change over time, stable trend from 2015 through 2019, then significant decreasing trend from 2019 through 2021, $p < 0.05$.
[4]Significant increasing trend from 2001 through 2006 with different rates of change over time, significant decreasing trend from 2006 through 2019, then stable trend from 2019 through 2021, $p < 0.05$.
NOTES: Drug overdose deaths were identified using *International Classification of Diseases, 10th Revision* (ICD–10) underlying cause-of-death codes X40–X44, X60–X64, X85, and Y10–Y14. Among these deaths, the following ICD–10 multiple cause-of-death codes indicate the drug type(s) involved: T40.0–T40.4, T40.6, any opioid; T40.1, heroin; T40.2, natural and semisynthetic opioids; T40.3, methadone; and T40.4, synthetic opioids other than methadone. Age-adjusted death rates were calculated using the direct method and the 2000 U.S. standard population. Deaths involving more than one opioid category (a death involving both methadone and a natural or semisynthetic opioid, for example) were counted in both categories. The percentage of drug overdose deaths that identified the specific drugs involved varied by year, ranging from 75% to 79% from 2000 through 2013 and increasing from 81% in 2014 to 95% in 2021. Access data table for Figure 4 at: https://www.cdc.gov/nchs/data/databriefs/db457-tables.pdf#4.
SOURCE: National Center for Health Statistics, National Vital Statistics System, Mortality File.

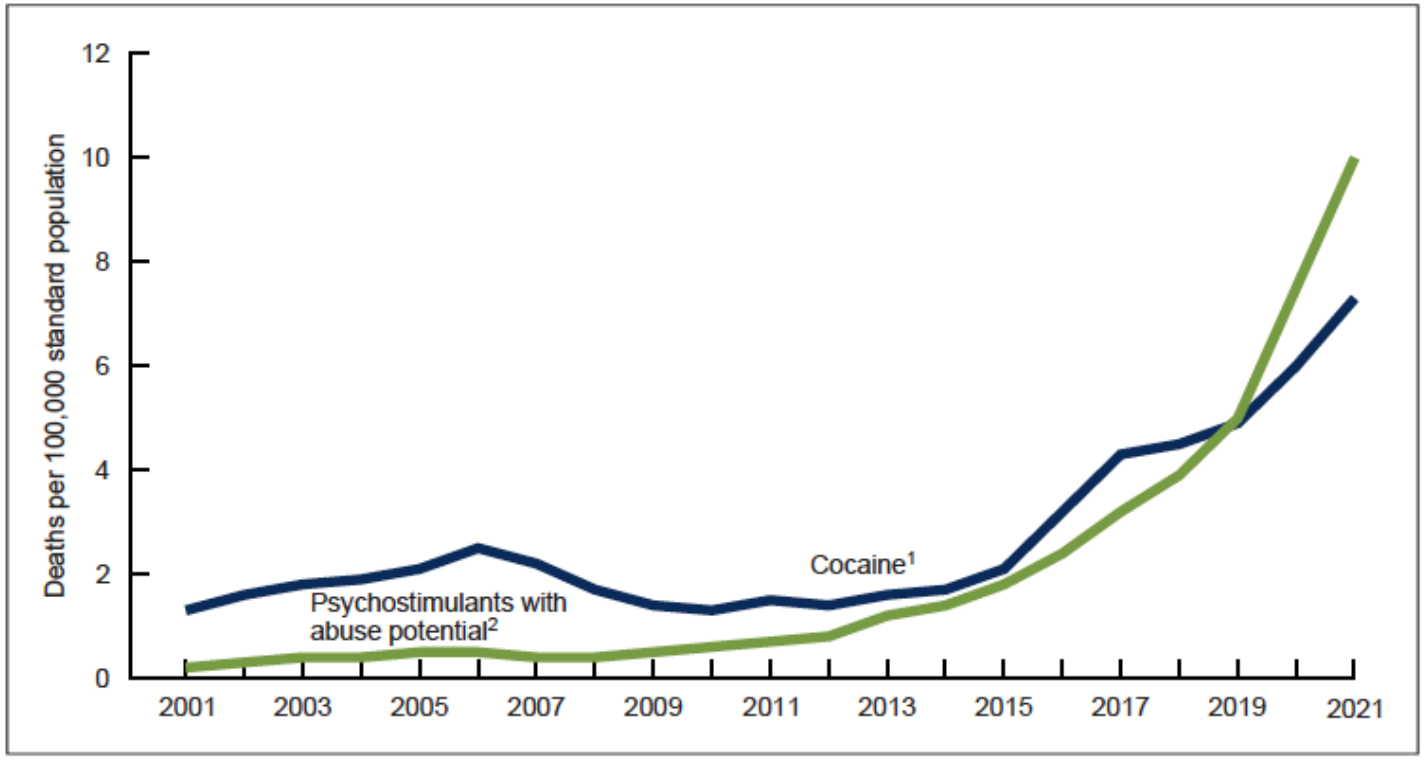
- 106,699 drug overdose deaths in 2021 (32.4/100,000 persons)
- Synthetic Overdose deaths
  ⬆ 22% (2020-2021)

Spencer MR, Miniño AM, Warner M. Drug overdose deaths in the United States, 2001–2021. NCHS Data Brief, no 457. Hyattsville, MD: National Center for Health Statistics. 2022. DOI: https://dx.doi.org/10.15620/cdc:122556.

Spencer et al. NCHS Data Brief no 457. Hyattsville, MD; National Center for Health Statistics 2022.

U.S. Stimulant Overdose Deaths 2001-2021

Figure 5. Age-adjusted rate of drug overdose deaths involving stimulants, by type of stimulant: United States, 2001–2021



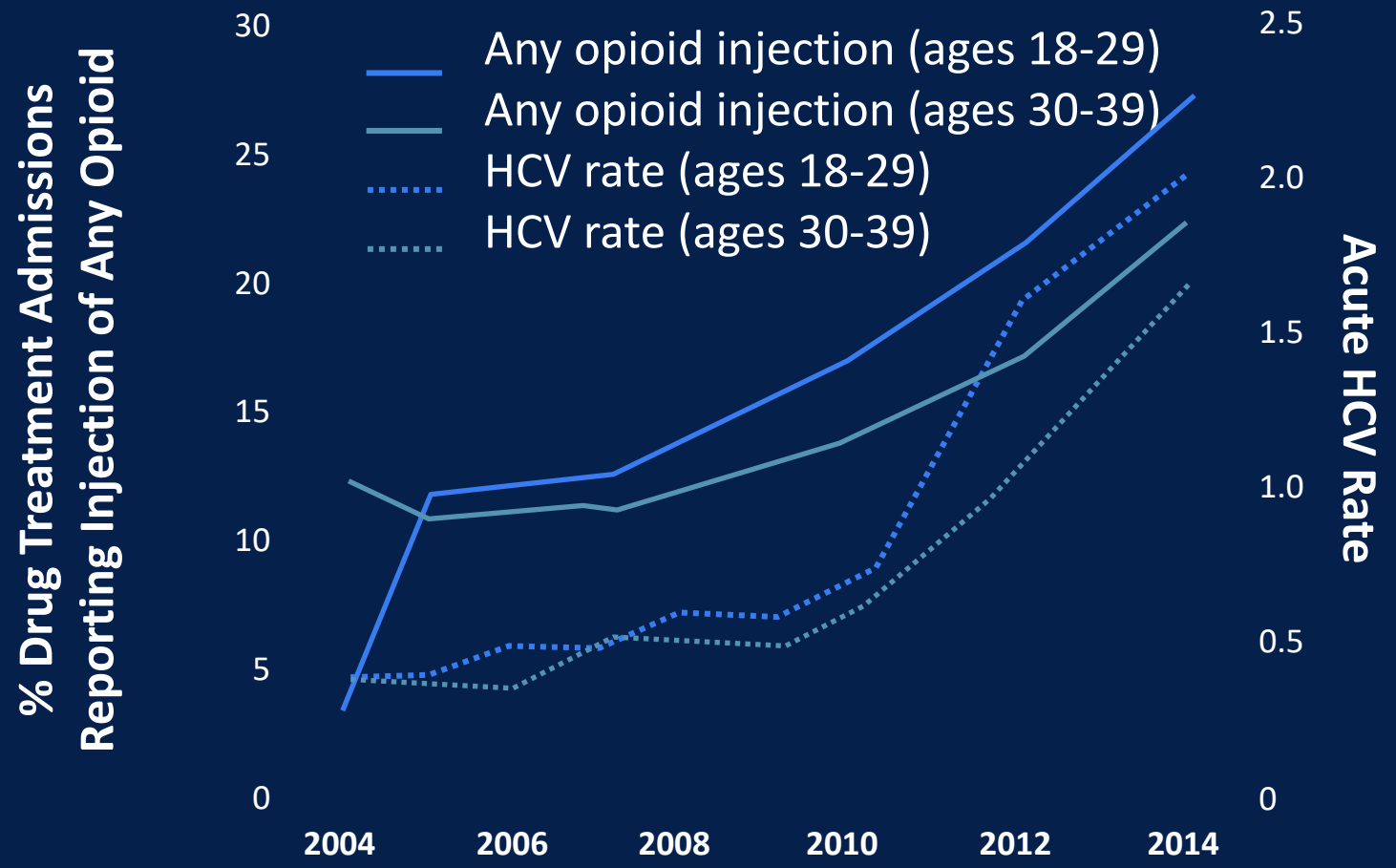
[1]Significant increasing trend from 2001 through 2006, significant decreasing trend from 2006 through 2011, then significant increasing trend from 2011 through 2021, $p < 0.05$.
[2]Significant increasing trend from 2001 through 2005, stable trend from 2005 through 2008, then significant increasing trend from 2008 through 2021 with different rates of change over time, $p < 0.05$.
NOTES: Drug overdose deaths were identified using *International Classification of Diseases, 10th Revision* (ICD–10) underlying cause-of-death codes X40–X44, X60–X64, X85, and Y10–Y14. Among these deaths, the following ICD–10 multiple cause-of-death codes indicate the drug type(s) involved: T40.5, cocaine; and T43.6, psychostimulants with abuse potential. Age-adjusted death rates were calculated using the direct method and the 2000 U.S. standard population. Deaths may involve more than one drug. The percentage of drug overdose deaths that identified the specific drugs involved varied by year, ranging from 75% to 79% from 2000 through 2013 and increasing from 81% in 2014 to 95% in 2021. Access data table for Figure 5 at: https://www.cdc.gov/nchs/data/databriefs/db457-tables.pdf#5.
SOURCE: National Center for Health Statistics, National Vital Statistics System, Mortality File.

From 2020-2021:

- Cocaine overdose deaths increased by 22%;
- Psychostimulants overdose deaths increased by 33% (methamphetamine, amphetamine etc)

Spencer MR, Miniño AM, Warner M. Drug overdose deaths in the United States, 2001–2021. NCHS Data Brief, no 457. Hyattsville, MD: National Center for Health Statistics. 2022. DOI: https://dx.doi.org/10.15620/cdc:122556.

Increase in HCV and Opioid Injection Among Younger Americans



CDC. https://www.cdc.gov/nchhstp/newsroom/2017/hepatitis-c-and-opioid-injection-press-release.html.

HIV Epidemics on the Rise in PWID

King County, WA. 27 HIV cases from IDU in 2018 (286% increase from 2017)

Scott County, IN 215 HIV cases from IDU in 2014-2015

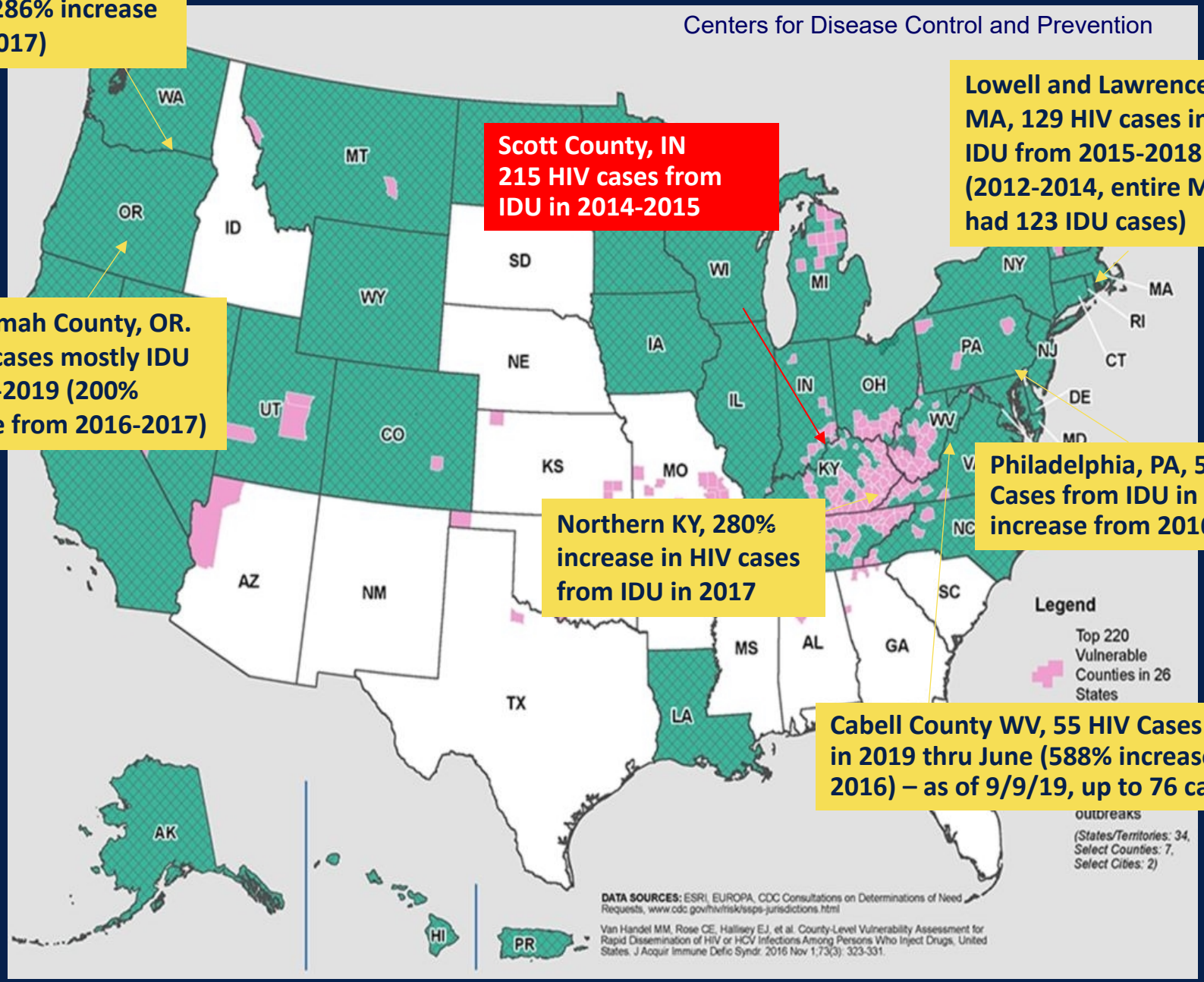
Lowell and Lawrence, MA, 129 HIV cases in IDU from 2015-2018 (2012-2014, entire Mass had 123 IDU cases)

Multnomah County, OR. 42 HIV cases mostly IDU in 2018-2019 (200% increase from 2016-2017)

Philadelphia, PA, 59 HIV Cases from IDU in 2018 (60% increase from 2016)

Northern KY, 280% increase in HIV cases from IDU in 2017

Cabell County WV, 55 HIV Cases from IDU in 2019 thru June (588% increase from 2016) – as of 9/9/19, up to 76 cases



Hospitalizations With Opioid Misuse and Related Serious Infection Have Increased: US Nationwide Estimates

Diagnosis (n)	2002 (N = 36,523,831)	2012 (N = 36,484,846)	*P* Value†
Opioid misuse/dependence	301,707	520,275	< .001
Opioid misuse/dependence with infection*	3421	6535	< .001
▪ **Endocarditis**	2077	3035	< .01
▪ **Osteomyelitis**	458	985	< .001
▪ **Septic arthritis**	729	1940	< .001
▪ **Epidural abscess**	411	1085	< .001

*Includes ≥ 1 of the infections listed in the table; †Differences between 2002 and 2012 evaluated using z-test.

Ronan. Health Aff (Millwood). 2016;35:832.

Why? Infectious Disease and Substance Use Treatment Have Been Siloed

- Integration of treatment for
  - Infectious Diseases &
  - Substance Use

  is KEY

VIEWPOINT

Integrating Responses to the Opioid Use Disorder and Infectious Disease Epidemics

A Report From the National Academies of Sciences, Engineering, and Medicine

JAMA 2020.

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Andrew P. Merluzzi, PhD, MPA
Health and Medicine Division, Board on Population Health and Public Health Practice, National Academies of Sciences, Engineering, and Medicine, Washington, DC.

Carlos del Rio, MD
Division of Infectious Diseases, Department of Medicine, Emory University School of Medicine, Atlanta, Georgia.

The United States is in the midst of an opioid use disorder (OUD) epidemic,[1] with more than 2.1 million persons affected and more than 700 000 deaths since 1999.[2] In October 2017, President Trump declared the opioid crisis a public health emergency, and a national response was initiated. However, it is estimated that only 1 in 10 people with OUD are receiving needed treatment. The opioid epidemic also has contributed to an increase in bacterial and fungal infections as well as new HIV[3] and hepatitis C virus[4] outbreaks across many parts of the country.[5]

To guide the response to these dueling epidemics, the Department of Health and Human Services (DHHS) Office of Infectious Disease and HIV/AIDS Policy requested that the National Academies of Sciences, Engineering, and Medicine (NASEM) convene a committee that would (1) identify, highlight, and review programs within the United States that are achieving integration of OUD and infectious disease (ID) services; (2) identify and highlight barriers to integration and to suggest strategies to overcome barriers; and (3) provide conclusions and recommendations to inform existing and future projects that pro-

Same-Day Billing Restrictions

Some states have implemented restrictions on billing for both behavioral and physical health care visits on the same day.[8] These restrictions are intended to contain costs but often force patients to return to medical centers on a different day or require that the medical center incur financial loss for providing same-day care. The committee recommended that all states amend their policies to allow greater access to treatment for patients who need it.

Inadequate Data Sharing That Limits Integrated Care

Title 42, Part 2 of the *Code of Federal Regulations* (42 CFR Part 2) is a federal regulation that places strong protections around patients' substance use information and prevents sharing this information without explicit patient consent. The committee recognized that there is a balance between confidentiality and sharing of patient information related to substance use[9,10] and recommended that the Substance Abuse and Mental Health Services Administration (SAMHSA) engage with patients, advocacy groups, the general public, and legal experts to determine the benefits and costs of changing 42 CFR Part 2 and aligning it with the Health Insurance

The Journal of Infectious Diseases

SUPPLEMENT ARTICLE

Federal and State Action Needed to End the Infectious Complications of Illicit Drug Use in the United States: IDSA and HIVMA's Advocacy Agenda

Sandra A. Springer,[1] Joshua A. Barocas,[2] Alysse Wurcel,[3] Ank Nijhawan,[4] Kinna Thakarar,[5,6] Ruth Lynfield,[7] Hermione Hurley,[8] Jessica Snowden,[9] Alice Thornton,[10] and Carlos del Rio,[11] on behalf of the Infectious Diseases Society of America and HIV Medicine Association's Infectious Diseases and Opioid Use Disorder Working Group.

[1]Yale School of Medicine, New Haven, Connecticut, USA, [2]Boston University, Boston, Massachusetts, USA, [3]Tufts Medical Center, Boston, Massachusetts, USA, [4]UT Southwestern Medical Center, Dallas, Texas, USA, [5]Maine Medical Center, Portland, ME, USA, [6]Tufts University School Of Medicine, Boston, Massachusetts, USA, [7]Minnesota Department of Health, St. Paul, Minnesota, USA, [8]Denver Health, Denver, Colorado, USA, [9]University of Arkansas for Medical Sciences, Little Rock, Arkansas, USA, [10]University of Kentucky, Lexington, Kentucky, USA, [11]Emory University, Atlanta, Georgia, USA

In response to the opioid crisis, IDSA and HIVMA established a working group to drive an evidence- and human rights-based response to illicit drug use and associated infectious diseases. Infectious diseases and HIV physicians have an opportunity to intervene, addressing both conditions. IDSA and HIVMA have developed a policy agenda highlighting evidence-based practices that need further dissemination. This paper reviews (1) programs most relevant to infectious diseases in the 2018 SUPPORT Act; (2) opportunities offered by the "End the HIV Epidemic" initiative; and (3) policy changes necessary to affect the trajectory of the opioid epidemic and associated infections. Issues addressed include leveraging harm reduction tools and improving integrated prevention and treatment services for the infectious diseases and substance use disorder care continuum. By strengthening collaborations between infectious diseases and addiction specialists, including increasing training in substance use disorder treatment among infectious diseases and addiction specialists, we can decrease morbidity and mortality associated with these overlapping epidemics.

Keywords. injection drug use; opioid epidemic; medications for treatment of opioid use disorder.

Clinical Infectious Diseases

VIEWPOINTS

Infectious Complications of Addiction: A Call for a New Subspecialty Within Infectious Diseases

David P. Serota,[1] Joshua A. Barocas,[2,3] and Sandra A. Springer[4]

[1]Department of Medicine, Division of Infectious Diseases, University of Miami Miller School of Medicine, Florida; [2]Department of Medicine, Section of Infectious Diseases, Boston Medical Center, and [3]Boston University School of Medicine, Massachusetts; and [4]Department of Internal Medicine, Section of Infectious Diseases, AIDS Program, Yale School of Medicine, New Haven, Connecticut

Open Forum Infectious Diseases

REVIEW ARTICLE

Beyond Antibiotics: A Practical Guide for the Infectious Disease Physician to Treat Opioid Use Disorder in the Setting of Associated Infectious Diseases

Nikhil Seval,[1] Ellen Eaton,[3] and Sandra A. Springer[1,2]

[1]Department of Internal Medicine, Section of Infectious Diseases, AIDS Program, Yale School of Medicine, New Haven, Connecticut, USA [2]Center for Interdisciplinary Research on AIDS, Yale University School of Public Health, New Haven, Connecticut, USA [3]Department of Medicine, Division of Infectious Disease, University of Alabama at Birmingham, Birmingham, Alabama, USA

Project COMMIT

- U01 Multi-site study funded by NIH's National Center for Advancing Translational Science (NCATS)
- Grant # U01TR002763

Coordinating Opioid Use Treatment Through Medical Management With Infection Treatment

Principal Investigators:

Sandra Springer, MD – Contact PI – Yale School of Medicine

Kathleen Brady, MD, PhD – Medical University of South Carolina

Edward Nunes, MD – Columbia University

Frances Levin, MD – Columbia University

Co- Investigators:

Alain Litwin, MD, MPH – Prisma Health, Greenville, South Carolina

Prerana Roth, MD - Prisma Health, Greenville, South Carolina

Meredith Schade, MD – Penn State Health

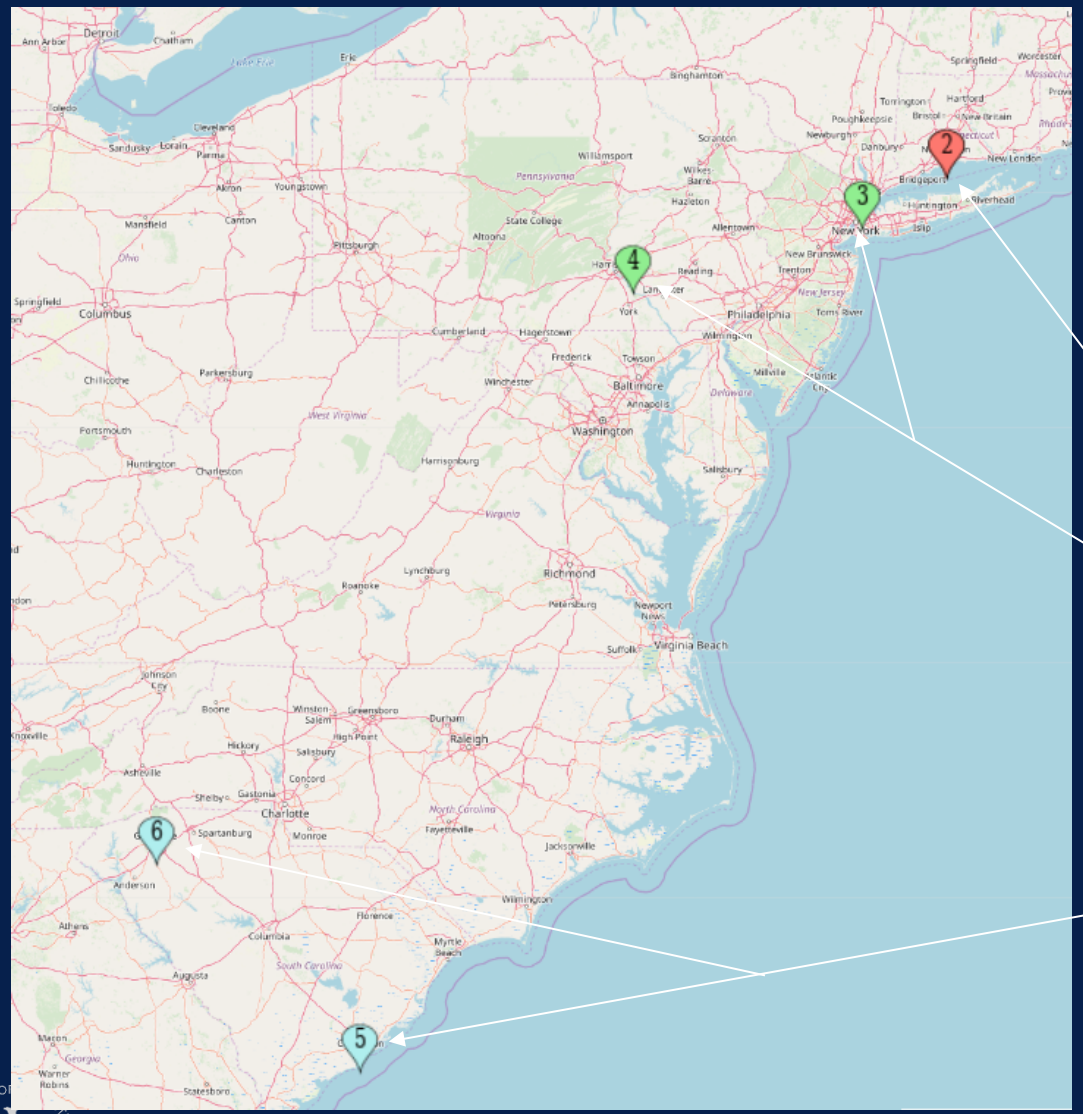
Study Aims

This study seeks to test a new model of care (ID/LAB) in which opioid use disorder (OUD) is managed by infectious disease (ID) specialists and hospitalists concurrent with management of the infections, using long-acting injectable buprenorphine (LAB), followed by referral as soon as possible after hospital discharge to community resources for long term treatment of OUD as compared to treatment as usual (TAU).

Specific Aims:

1. To evaluate which form of treatment (ID/LAB or TAU) improves enrollment/receipt of a medication at 12 weeks after randomization
2. To assess if the intervention as compared to TAU results in improved opioid use outcomes (lower days of opioid use, negative urine opioids)
3. To assess if ID/LAB results in higher rates of antimicrobial completion, decreased re-hospitalizations and ED presentations for ID or OUD at 12 weeks post randomization as compared to TAU

Project COMMIT: Where is it?



3 regions of the United States

and 3 sites:

- New England (Yale, Connecticut)
- Mid Atlantic (Columbia University & Penn State Hershey, Pennsylvania)
- South (MUSC & Greenville, South Carolina)

Eligibility

Inclusion

- ✓ Age ≥ 18 yo & English or Spanish speaking
- ✓ Hospitalized with infection or suspected infection not limited to:
  - ❑ Bacteremia, Candidal, Fungemia
  - ❑ Pneumonia
  - ❑ Osteomyelitis
  - ❑ Endophthalmitis
  - ❑ Septic Thrombophlebitis
  - ❑ Infected Pseudoaneurysm
  - ❑ Endocarditis
  - ❑ Skin/Soft Tissue Infection (SSTI)
  - ❑ Septic Arthritis
  - ❑ Viral (HIV/HCV/HBV) Infection
- ✓ Current DSM-5 moderate-to-severe OUD
- ✓ Willingness to participate in a trial

Exclusion

- × Severe medical or psychiatric disability making participation unsafe (e.g. imminent suicide risk)
- × Pregnancy, planning conception, or breast-feeding for female participants
- × Allergy, hypersensitivity or medical contraindication to buprenorphine
- × Moderate-severe liver impairment (Childs-Pugh Class C Cirrhosis)
- × Preexisting stable enrollment on methadone or buprenorphine maintenance (last 30 days taking daily)
- × Inability or unwillingness of subject to give informed consent.

Study Design

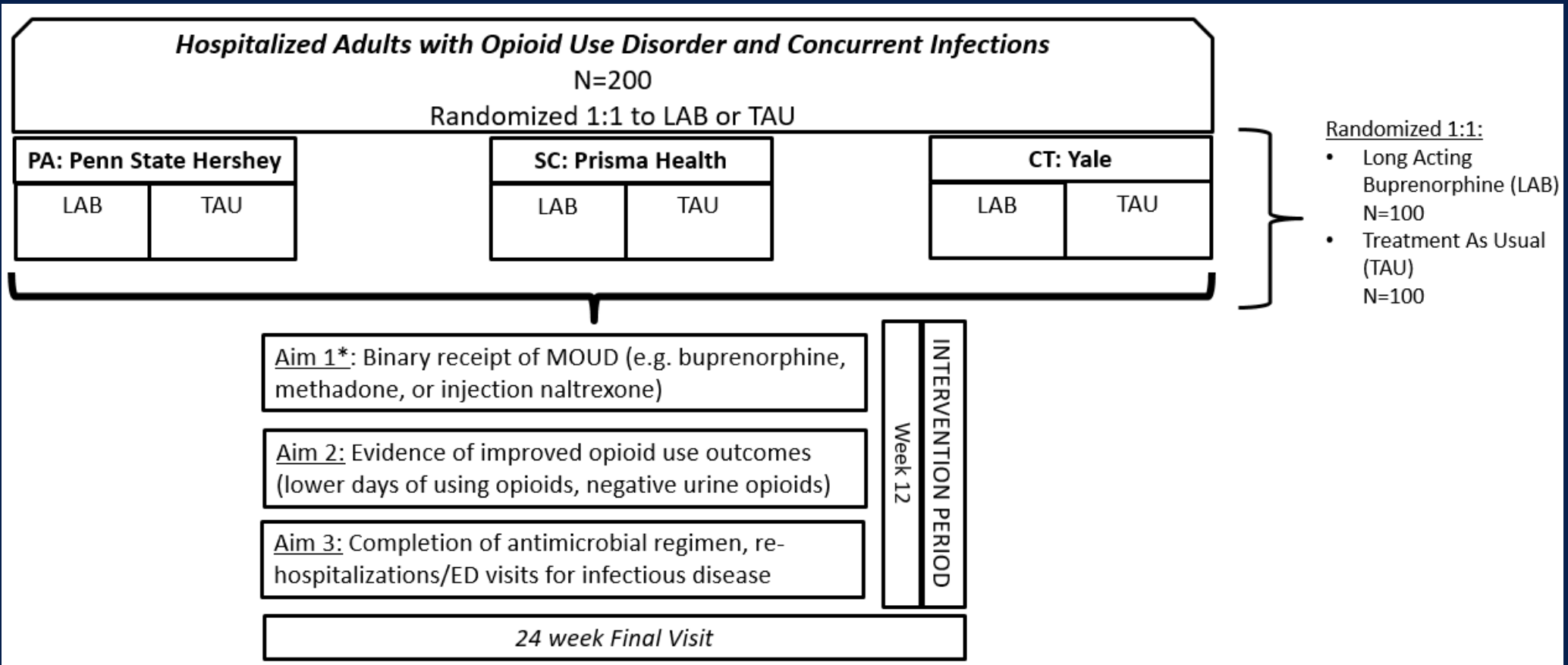


Figure 1. Study Design

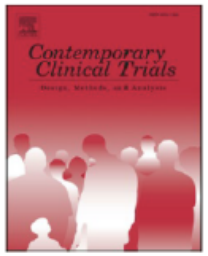
Protocol Paper

Contemporary Clinical Trials 105 (2021) 106394

Contents lists available at ScienceDirect

Contemporary Clinical Trials

journal homepage: www.elsevier.com/locate/conclintrial

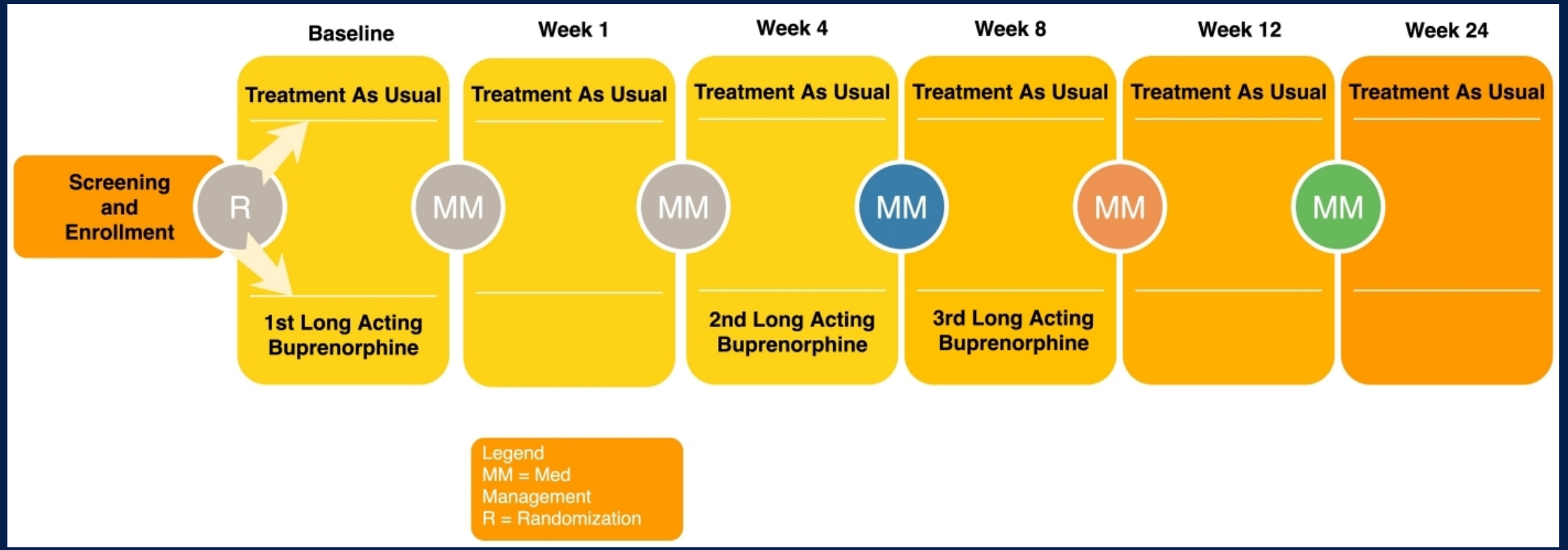


Check for updates

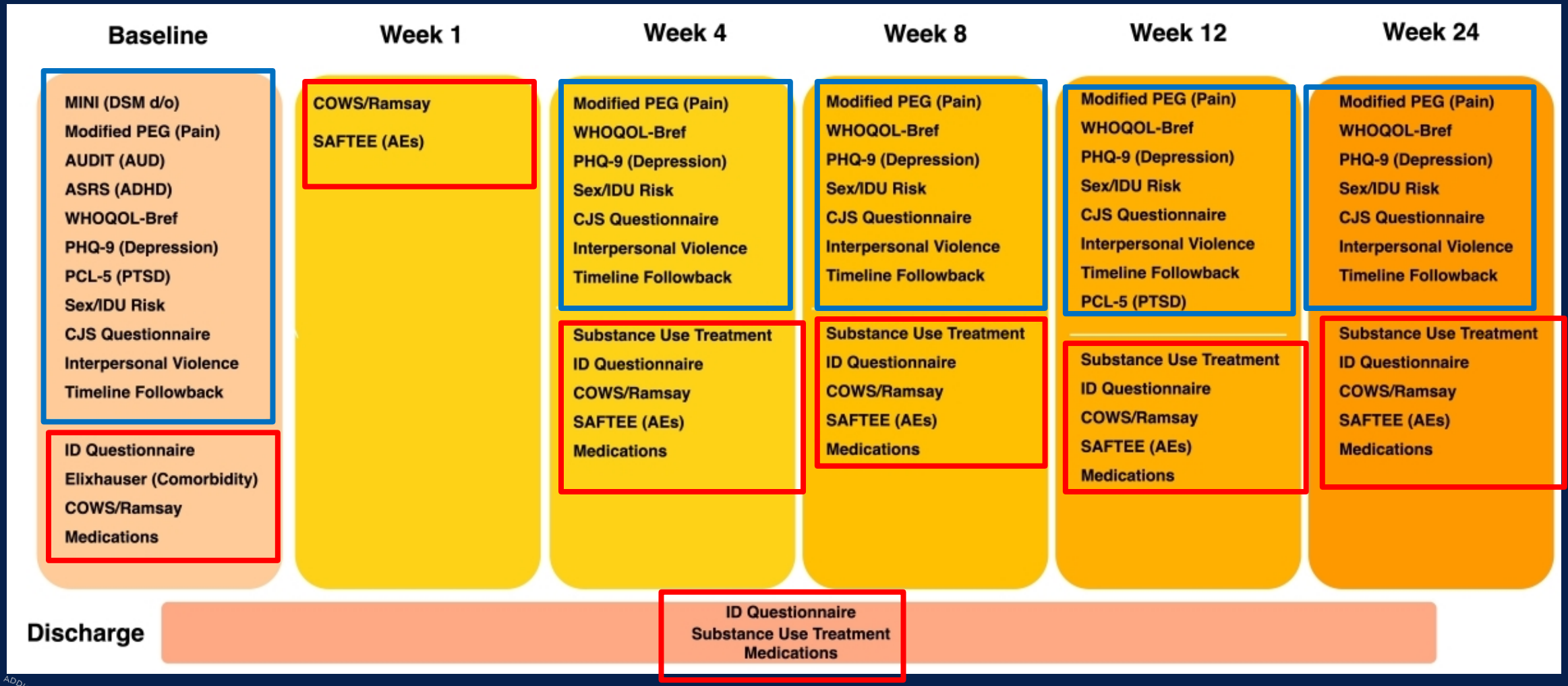
Design and methods of a multi-site randomized controlled trial of an integrated care model of long-acting injectable buprenorphine with infectious disease treatment among persons hospitalized with infections and opioid use disorder

Nikhil Seval [a], Cynthia A. Frank [a], Alain H. Litwin [c,d], Prerana Roth [c], Meredith A. Schade [g], Martina Pavlicova [f], Frances R. Levin [b], Kathleen T. Brady [e], Edward V. Nunes [b], Sandra A. Springer [a,*]

Study Flow


Baseline
Week 1
Week 4
Week 8
Week 12
Week 24
Screening and Enrollment
R
MM
MM
MM
MM
MM
Treatment As Usual
Treatment As Usual
Treatment As Usual
Treatment As Usual
Treatment As Usual
Treatment As Usual
1st Long Acting Buprenorphine
2nd Long Acting Buprenorphine
3rd Long Acting Buprenorphine
Legend
MM = Med Management
R = Randomization

Research & Clinical Assessments



Red = Clinical Researchers (CR)

Blue = Research Associates (RA)

Point of Care Labs

Timeline	Research Team	Chart Review/Requested From Hospital Team
Baseline	Point of Care: HIV, HCV, UDS, Urine Pregnancy Test	Hepatitis B panel and reflex HBV DNA viral load if positive; BMP, CBC, INR, LFTs HIV+: VL (HIV+), +CD4 Count HCV+: VL
Week 4	Point of Care: UDS, Urine pregnancy test	
Week 8	Point of Care: UDS, Urine pregnancy test	
Week 12	Point of Care: HIV, HCV, Urine Pregnancy Test Blood Draw (if not available from chart review): HIV+: VL (HIV+) HCV+: VL	Chart review, if available: HIV VL (HIV+), +CD4 Count (HIV+), HCV VL (HCV+), BMP, CBC, LFTs
Week 24	Point of Care: UDS, Urine Pregnancy Test	

Ab = Antibody Ag = Antigen	UDS = Urine drug screen VL = Viral Load

First- identifying patients with OUD

- OUD assessment is not standard process in all hospitals

-We created a detailed evaluation to find patients who may have OUD and have infections in the hospitals

-Utilized quick screen and validated diagnostic tool the Rapid Opioid Dependency Scale that non-clinicians could use (Research Assistants)

- Carefully coordinated with hospital teams to determine if safe to start buprenorphine and LAB

Identifying Eligible Patients

Run EMR reports to generate lists of potentially eligible patients

- Generated lists of patient names + hospital locations, link directly to full patient chart
- Study personnel perform in-depth chart review to confirm eligibility
- Checked multiple times daily

Uses ICD-10 codes related to eligibility criteria

Example:

- F11.9 – opioid use, unspecified
- I33.0 – infective endocarditis

Reports based on different interpretations of eligibility criteria

- Not just searching for explicit diagnosis of OUD
- Search for other terms that may indicate a SUD
  - Hx of overdose
  - Unintentional poisoning
  - HCV
  - Altered mental status

Rapid Opioid Dependence Screen (RODS)

- 8 questions created by Dr. Springer and used to assess opioid dependence, validated with the MINI[1]
- Used to safely initiate buprenorphine at time of release from prison or jail[1-3]
- Used to identify patients eligible to start extended-release naltrexone, long-acting buprenorphine in prison or jail **before** release[4,5]

Rapid Opioid Dependence Screen (RODS)

Instructions: [Interviewer reads] The following questions are about your prior use of drugs. For each question, please indicate "yes" or "no" as it applies to your drug use during the last 12 months.

1. Have you ever taken any of the following drugs?

a. Heroin	○ Yes	○ No
b. Methadone	○ Yes	○ No
c. Buprenorphine	○ Yes	○ No
d. Morphine	○ Yes	○ No
e. MS Contin	○ Yes	○ No
f. Oxycontin	○ Yes	○ No
g. Oxycodone	○ Yes	○ No
e. Other opioid analgesics (e.g., Vicodin, Darvocet, etc.)	○ Yes	○ No

If any drug in question 1 is coded "yes", proceed to questions 2 to 8.

If all drugs in question 1 are "no", skip to end and code "no" for opioid dependent.

2. Did you ever need to use more opioids to get the same high as when you first started using opioids?	○ Yes	○ No
3. Did the idea of missing a fix (or dose) ever make you anxious or worried?	○ Yes	○ No
4. In the morning, did you ever use opioids to keep from feeling "dope sick" or did you ever feel "dope sick"?	○ Yes	○ No
5. Did you worry about your use of opioids?	○ Yes	○ No
6. Did you find it difficult to stop or not use opioids?	○ Yes	○ No
7. Did you ever need to spend a lot of time/energy on finding opioids or recovering from feeling high?	○ Yes	○ No
8. Did you ever miss important things like doctor's appointments, family/friend activities, or other things because of opioids?	○ Yes	○ No

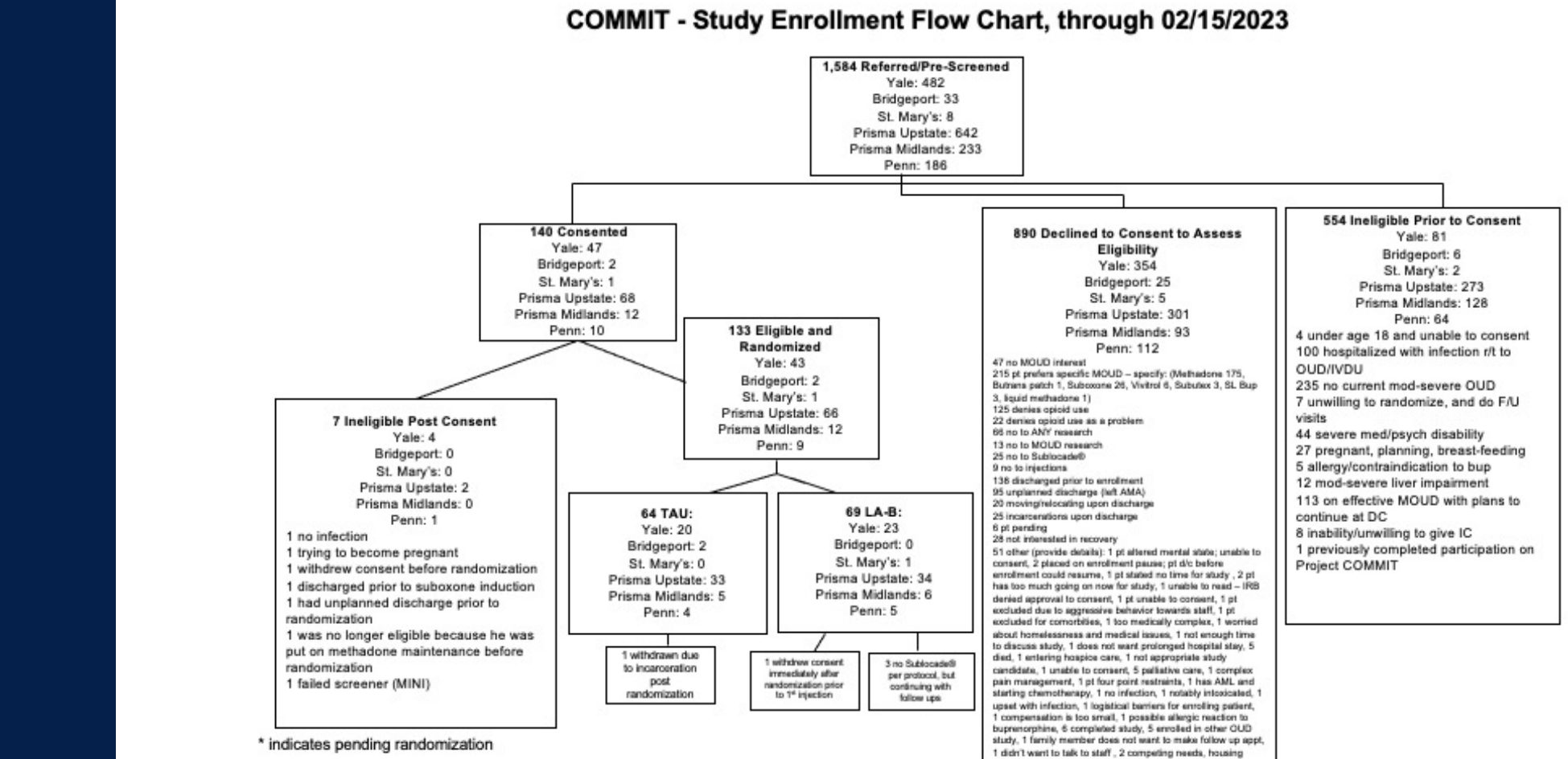
Scoring Instructions: Add number of "yes" responses for questions 2 to 8. If total is > 3, code "yes" for opioid dependent. If total is < 2, code "no" for opioid dependent.

Opioid Dependent: ○ **Yes** ○ **No**

Wickersham. J Correct Health Care. 2015;21:12. 2. Springer. J Urban Health. 2010;87:592. 3. Springer. PLoS One. 2012;7:e38335.

4.. Springer. J Acquir Immune Defic Syndr. 2018;78:43 5. DiPaola. Contemp Clin Trials. 2014;39:256.

Consort Diagram



Baseline Characteristics (N=133)

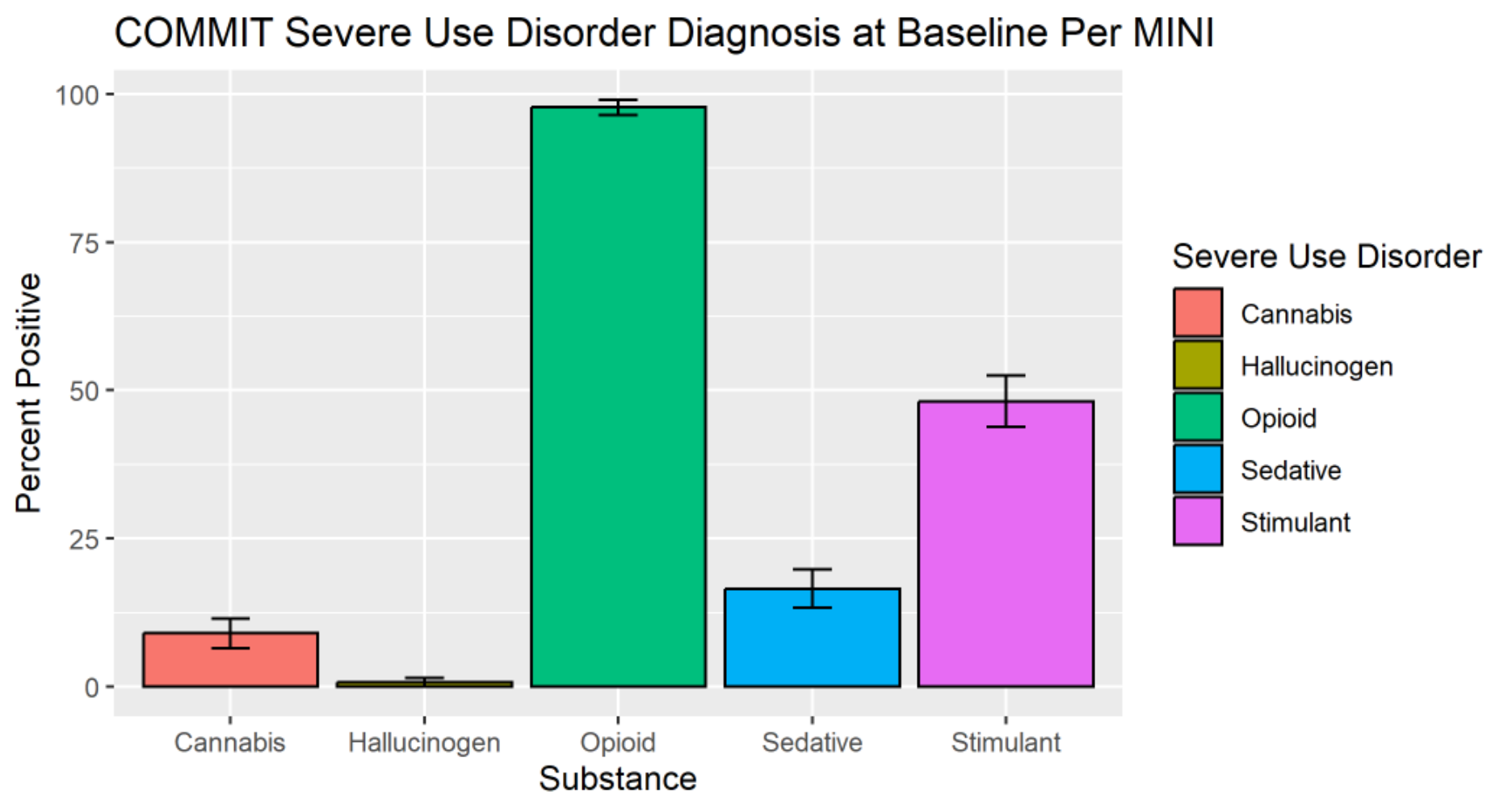
Baseline Participant Characteristics	N=133 n (%)
Female	63 (47.4%)
Hispanic Ethnicity	14 (10.5%)
White	108 (81.2%)
Black/African-American	10 (7.5%)
More than one race	5 (3.8%)
Other/Missing	2 (1.5%)
Age (mean, quartiles)	38.9 (32, 46)
Covered by insurance 30 days before interview	74 (55.6%)
Considered homeless in past 30 days	54 (40.6%)
Moderate to severe Depression per PHQ (10+ score)	72 (66.4)
PTSD - PCL Provisional Diagnosis (14+ score)	90 (67.6%)
ADHD Score (ASRS)	15.20 (5.67)
Pain Scale (PEG), mean (SD)	5.00 (4.00, 7.00)

Baseline Characteristics	N=133 n (%)
AUDIT - Hazardous Drinking	30.0 (22.6%)
Opioid Craving Scale, mean (SD)	4.0 (2.62)
COWS Score, mean (SD)	1.82 (2.02)
Received MOUD in 30 days prior to hospitalization	
Buprenorphine	18.0 (13.5%)
Methadone	10.0 (7.5%)
Injectable Naltrexone	1.0 (0.8%)

Index Infectious Diseases

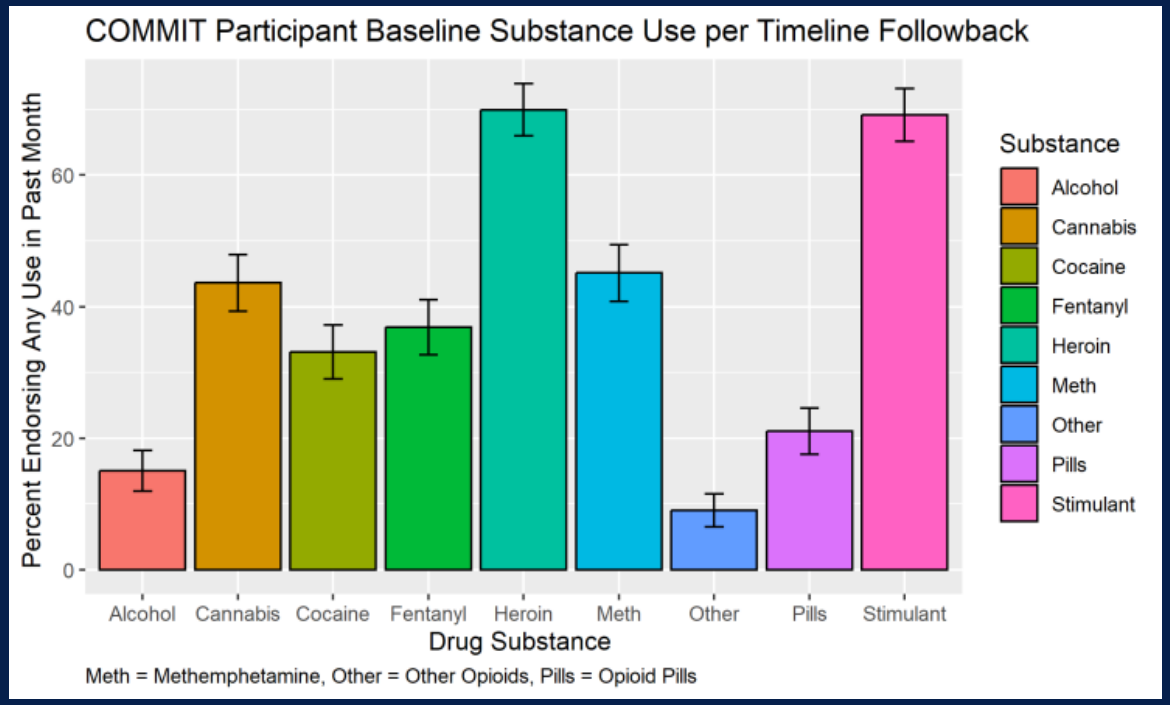
Infections at Baseline	
Bacteremia	61 (45.9%)*
Endocarditis	29 (21.8%)*
Fungemia	2 (1.5%)
HBV	1 (0.8%)
HCV	58 (43.6%)*
HIV	3 (2.3%)
Joint septic arthritis/infection	22 (16.5%)
Osteomyelitis	23 (17.3%)
Pneumonia (not related to HIV)	11 (8.3%)
Skin/soft tissue infection (SSTI/NSTI)	25(18.8%)
Abscess	43 (32.3%)*
Covid-19	6 (5.6%)
Other/Suspected	29 (21.8%)

DSM-5 Severe SUDs at Baseline

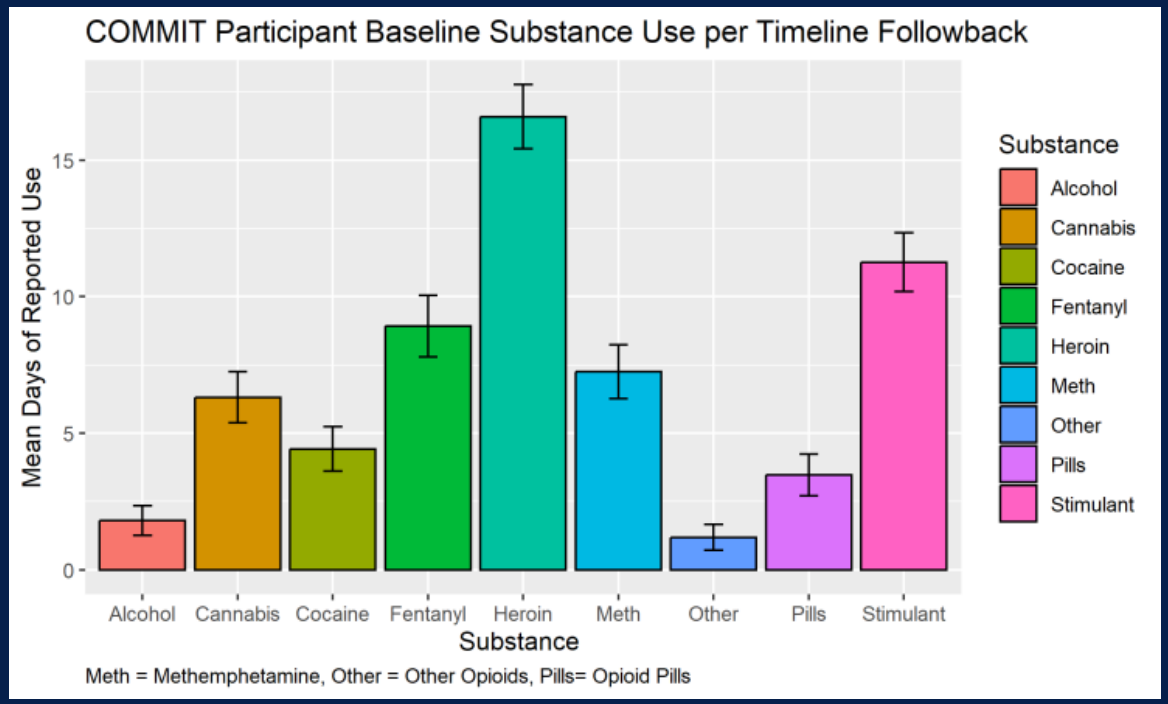


Self-reported Substance use via Timeline Follow Back

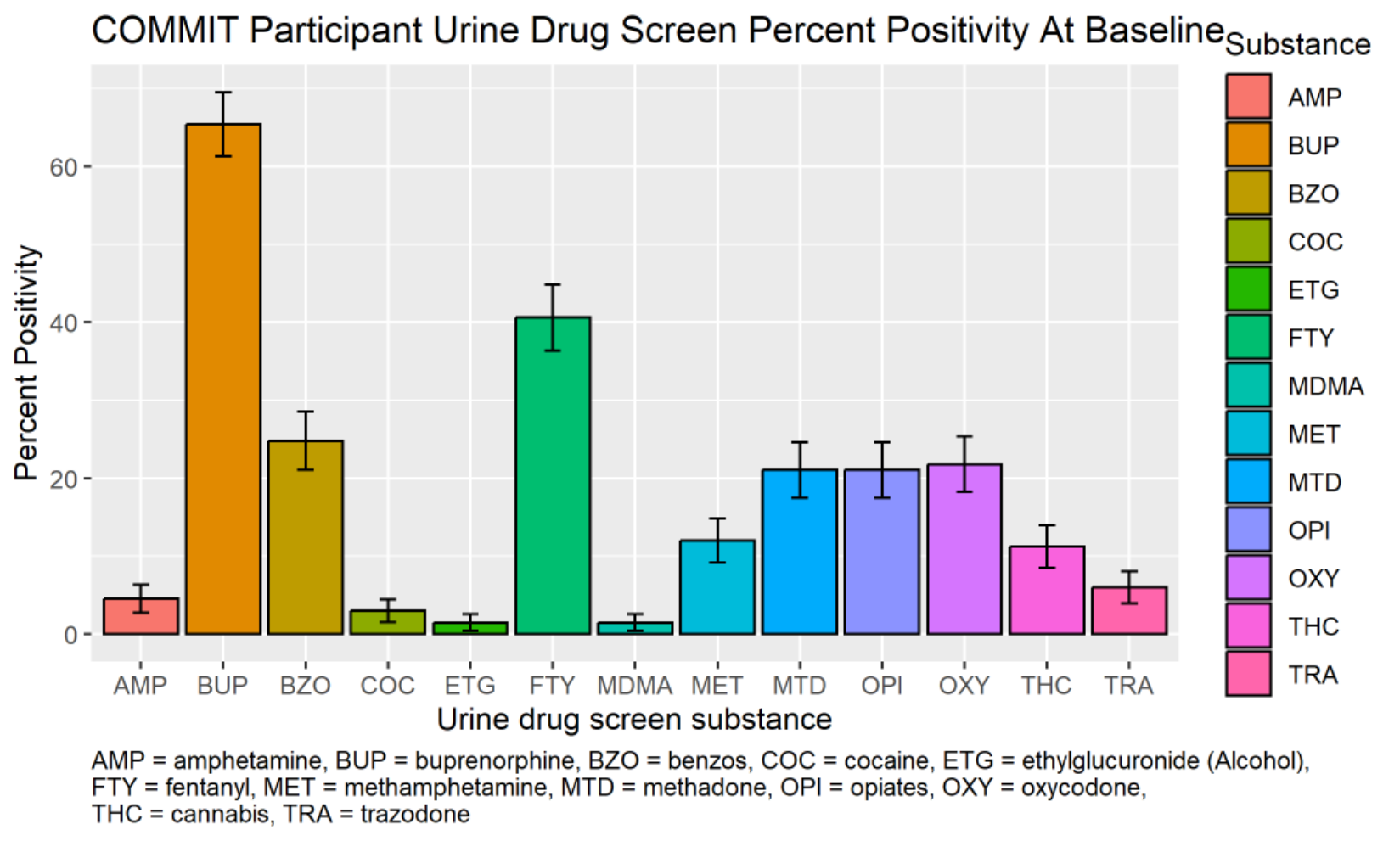
Any Use in past 30 days



Mean Days of Use in past 30 days

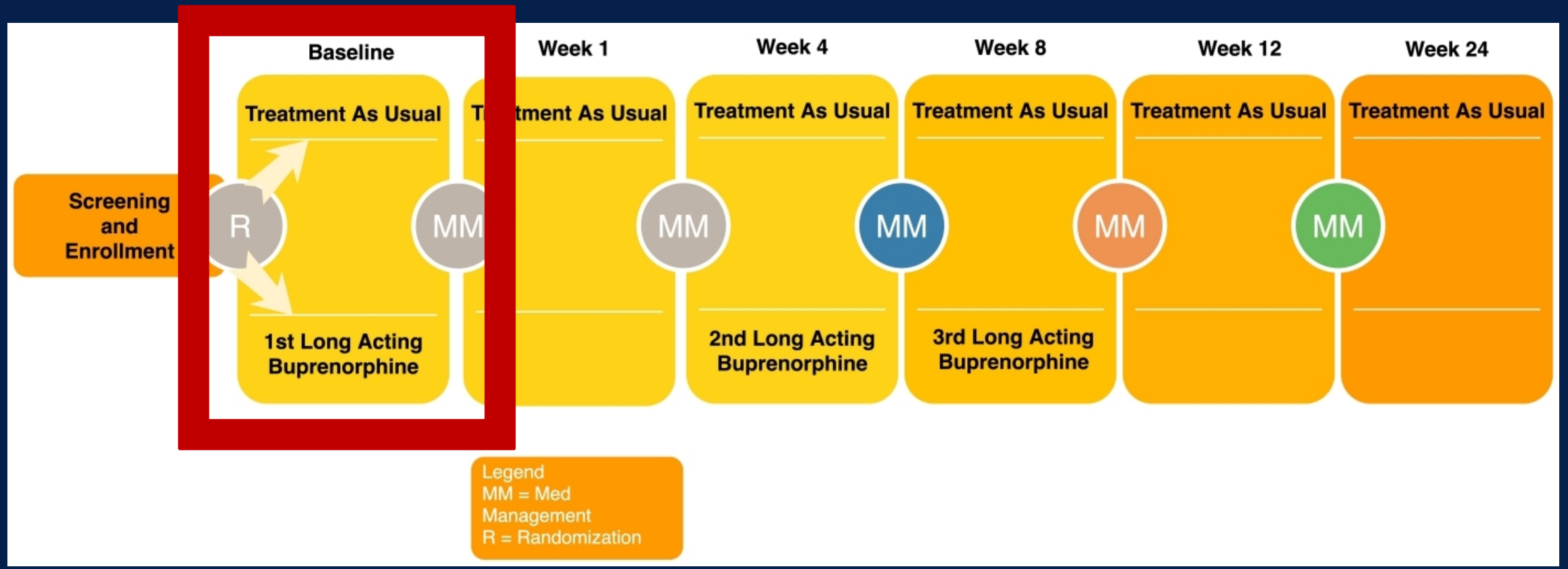


Baseline Urine Toxicology Data



*Not all participants recruited at time of initial hospitalization -some were already started on buprenorphine

Randomization : LAB or TAU



Study Design

- Randomized controlled trial of adults with OUD admitted to the hospital infections or suspected infections (bacterial, viral, fungal)
- **Randomized 1:1 to two models of care:**
  1. **ID/LAB** – long-acting buprenorphine (LAB) (Sublocade®) and integrated care (ID specialists , hospitalists etc.)
  2. **Treatment As Usual (TAU)- enhanced**
     - Determined by primary hospital team

All receive: Diagnosis of OUD, general recommendation for MOUD (buprenorphine (including LAB)/methadone/extended-release naltrexone) initiation, OEND, safe injection information, linkage to outpatient addiction care- assertive discharge planning, needs assessment, Nurse led Medical Management calls weekly

Educational Materials Given to All Participants

What is medication for opioid use disorder (MOUD)?

- MOUD is a medication treatment for opioid use disorder (OUD). When used as prescribed, it can decrease your chance of overdose, death, or getting infections related to drug use.
- MOUD is a proven life-saving treatment for opioid addiction.
- MOUD works by treating withdrawal symptoms and reducing cravings.
- MOUD can be used in combination with counseling and therapy to help you stop using opioids.

- Methadone prevents withdrawal and decreases cravings
- Daily pill, liquid, or wafer
- Dose adjusted based on your needs
- Can only get at Opioid Treatment Program (also known as a 'Methadone Clinic')

- Naltrexone blocks the effects of opioids
- Monthly injection
- If you take opioids or heroin, you won't feel high
- You must be free from opioids for at least 7-10 days before starting Naltrexone
- It is also used to treat alcohol use disorder
- Before stopping, please talk to your provider

Buprenorphine

- Buprenorphine blocks the effects of other opioids or heroin, prevents withdrawal and decreases cravings
- Can be prescribed at addiction treatment centers or by some primary care providers
- Types of buprenorphine:

Subutex
- Contains only buprenorphine
- Sublingual (under the tongue) pill

Suboxone
- Contains buprenorphine AND naloxone
- Pill or film

Sublocade
- Monthly injection
- Don't have to remember to take a pill every day
- Must be on stable sublingual (under the tongue) dose before starting

Naloxone (Narcan)

- Can be used to reverse an opioid overdose
- Must be administered within a few minutes of overdose
- Nose spray or muscle injection
- You can get it from a local Walgreens or other pharmacy with Medicaid, Medicare, or other insurance
- Has no effect on someone who does not have opioids in their system

Identifying an Opioid Overdose

- Person doesn't wake up after you shout, shake their shoulders, or firmly rub the middle of their chest
- Breathing is very slow, irregular or has stopped
- Pupils are very small, "pinpoint"

How to deliver Naloxone (Narcan)

1. **Call 911.** Keep in mind that Connecticut Good Samaritan Laws protect you from arrest while giving assistance even if you have drugs or paraphernalia on you.

2. Tilt the person's head back, support their neck
3. Insert the device into one nostril
4. Push up quickly on the plunger with your thumb
5. Move person into recovery position
6. Give another dose if there is no response after 2-3 minutes

https://www.narcan.com/static/NARCAN-Quick-Start-Guide.pdf

Guidance and Services

For Persons with Opioid Use Disorder

- Luis Ojeda - 860-305-3289
- Barbara Valdes - 860-573-3271
- Katie McNamara - 203-494-3093

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IF POSSIBLE, DO NOT INJECT ALONE

Why should needles only be used once?

- Using a needle more than once increases risk for infection (i.e. HIV or Hep C) even if you're not sharing
- The tip of a needle becomes duller and rugged after each use
- Should not share or reuse supplies

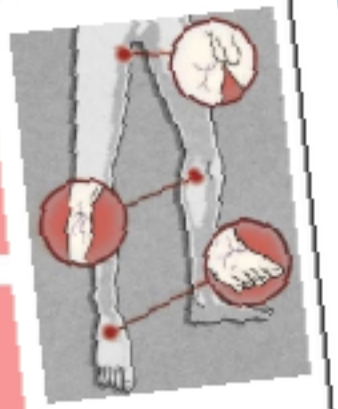
If I must reuse, can I clean it?

- Yes, clean with bleach.
  - Fill needle and syringe with distilled bleach and keep full for at least 2 minutes. Rinse several times with clean, cold water (sterile or boiled)
  - If you have to use water from a toilet, use from the tanks not the bowl

To avoid reusing, visit a local confidential syringe service (203-996-0162)

Which veins are safer to inject into?

Injecting in the arm or hand is safer



Avoid injecting in the neck, groin, legs, or feet

Avoid skin or muscle popping

https://www.drugs.ie/resourcefiles/guides/rapi_safer_injecting_guide.pdf

If you accidemly hit an artery call 911 or go to ED, untie, pull out, and apply pressure to wound for 10 minutes.

Local Services

- APT Foundation
  - **Treatment**
  - 1 Long Wharf Drive, New Haven
  - 203-781-4600
- Community Health Care Van
  - **Syringe services**
  - 270 Congress Avenue, New Haven
  - Call or text Angel: 203-996-0162
- A Place to Nourish your Health (APNH)
  - **Testing and social services**
  - 1302 Chapel Street, New Haven
  - 475-441-7031

To find a provider near you, visit **suboxcade.com/find-a-treatment-provider**

Other safety tips

- Wash your hands with soap and water before handling supplies
- Use alcohol pads to clean the skin at the injection site
- Carry Narcan with you and know how to use it (see back of this pamphlet for more info)

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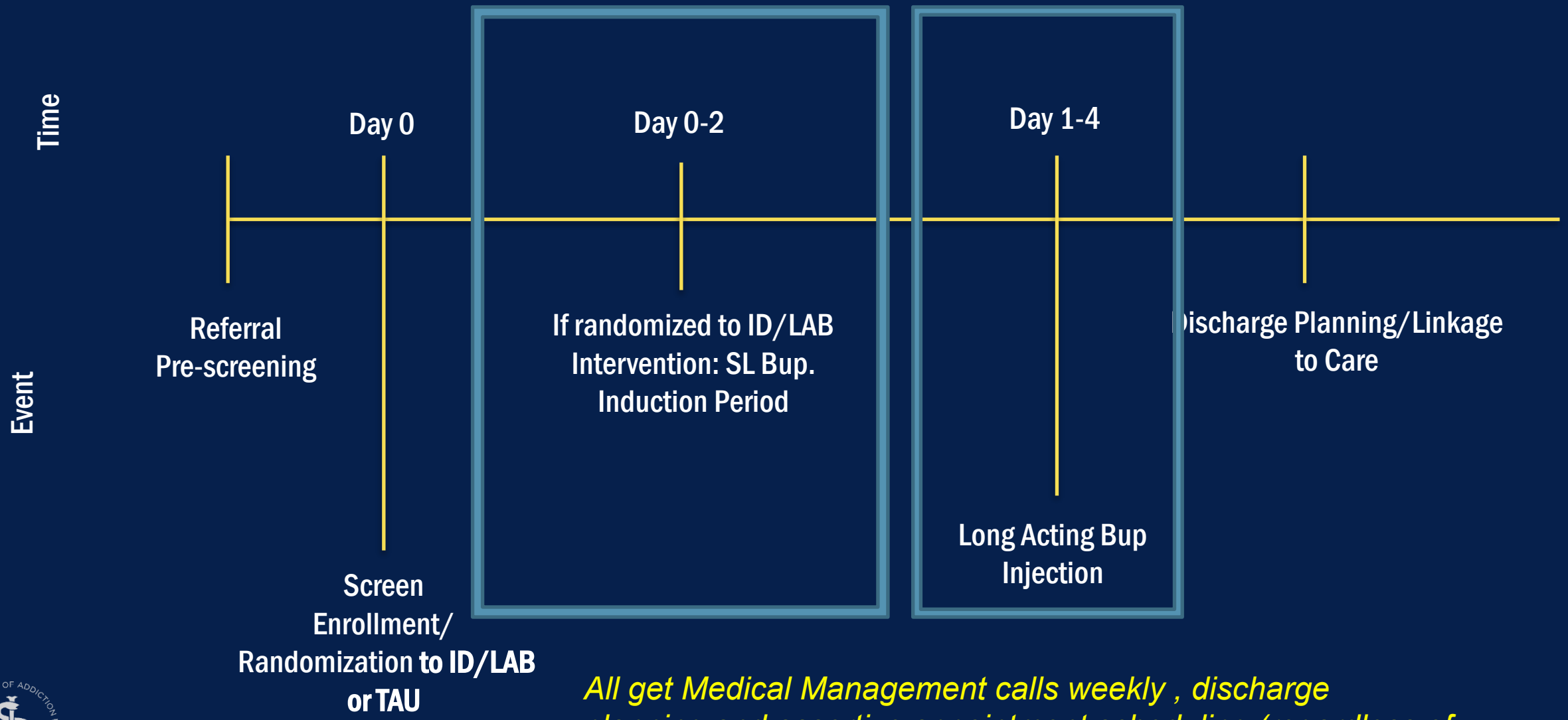
Treatment As Usual (TAU)

1. Formal diagnosis of OUD

2. Recommendation for MOUD as standard of care

Same counselling (Med Management), discharge planning, and visit schedule as those in the ID/LAB arm

LAB Treatment Arm



All get Medical Management calls weekly , discharge planning and assertive appointment scheduling (regardless of arm)

Clinical Safety Sheet: published in COMMIT protocol paper.

COMMIT Clinical Safety Checklist

Last updated 11/19/2020
Created by Sandra A. Springer, MD

Visit Date: ____/____/____ Injection #: _____

Consent Given: ☐Yes ☐No Study Site: _____ ID #: _____

Visit Location: ☐Hospital ☐Outpatient ☐Other: _____

Clinician Name: _____ Start Time: ____ : ____ End Time: ____ : ____

Randomization Group: _____

Planned Surgery? If yes, describe what the surgery is for and when it is scheduled. ***Consult a research clinician:***

_____

_____

_____

Precautionary Medication Check (Check all that apply):

CYP Inhibitors	CYP Inducers	QTc prolonging medications
Amiodarone Fluoroquinolones (Ciprofloxacin, levofloxacin, etc) Cobicistat Fluconazole Isoniazid Itraconazole Ranitidine Ritonavir Valproic acid Voriconazole	Carbamazepine Efavirenz Oxcarbazepine Phenytoin Rifabutin Rifampin St Johns wort Topiramate	Macrolides Fluoroquinolones Anti-emetics (ondansetron, metoclopramide) Antipsychotics (e.g. haloperidol, quetiapine, etc)
Antihypertensives ACE Inhibitors (e.g. lisinopril, captopril) Angiotensin II Receptor Blockers (ARBs; e.g. losartan, Olmesartan, etc) Diuretics (e.g. hydrochlorothiazide, furosemide, etc) Calcium channel blockers (e.g. amlodipine, nifedipine, etc)	Sedatives Benzodiazepines	Non-Opioid Withdrawal Treatment Alpha-2 agonists (e.g. clonidine, tizanidine)

Note: XR-B Drug must be out of the fridge for 15 minutes PRIOR to administration

COMMIT Clinical Safety Checklist

Last updated 11/19/2020
Created by Sandra A. Springer, MD

Sublingual Buprenorphine Dosing History:

1. Date: ____/____/____ Time: ___ : ___ am / pm Dose: _____ mg
2. Date: ____/____/____ Time: ___ : ___ am / pm Dose: _____ mg
3. Date: ____/____/____ Time: ___ : ___ am / pm Dose: _____ mg
4. Date: ____/____/____ Time: ___ : ___ am / pm Dose: _____ mg
5. Date: ____/____/____ Time: ___ : ___ am / pm Dose: _____ mg
6. Date: ____/____/____ Time: ___ : ___ am / pm Dose: _____ mg
7. Date: ____/____/____ Time: ___ : ___ am / pm Dose: _____ mg
8. Date: ____/____/____ Time: ___ : ___ am / pm Dose: _____ mg

Add Any Additional date fields at end of form

Does participant have acute pain? ☐No ☐Yes, consult a research clinician.

When was the last opioid use? Date: ____/____/____ Type of opioid: _____
Route: ☐IV ☐Intranasal ☐Oral

☐Yes ☐No Current prescribed opioid use ***consult a research clinician***

☐Yes ☐No Active opioid withdrawal (COWS > 4) ***consult a research clinician***

☐Yes ☐No Anticipated need for opioids to treat a medical problem ***consult a research clinician***

☐Yes ☐No Maintained on SL buprenorphine for at least 48 hours ***consult a research clinician***

Blood cultures: Last Positive- ____/____/____ Last Negative- ____/____/____

**Blood cultures negative for < 48 hours, consult a research clinician

UTOX: Date collected- ____/____/____

Opiates:	☐Positive ☐Negative	
Methamphetamine:	☐Positive ☐Negative	
Amphetamine:	☐Positive ☐Negative	
Cocaine:	☐Positive ☐Negative	
Benzodiazepines:	☐Positive ☐Negative	
THC:	☐Positive ☐Negative	
Oxycontin:	☐Positive ☐Negative	
BUP assay	☐Positive ☐Negative	
Fentanyl	☐Positive ☐Negative	
Tramadol	☐Positive ☐Negative	
Opioids	☐Positive ☐Negative	
Methadone	☐Positive ☐Negative	

Note: XR-B Drug must be out of the fridge for 15 minutes PRIOR to administration

COMMIT Clinical Safety Checklist

Last updated 11/19/2020
Created by Sandra A. Springer, MD

Urine HCG:	☐Positive ☐Negative	(Note: Must be negative to administer any study med)

Labs: Date collected- ____/____/____

INR: _____ Creatinine: _____

BUN: _____ GFR: _____

Bilirubin: _____ Albumin: _____

Ascites: ☐Absent ☐Slight ☐Moderate

AST: ☐Abnormal ☐Normal ** if > 5 x ULN, consult a research clinician

ALT: ☐Abnormal ☐Normal ** if > 5 x ULN, consult a research clinician

Encephalopathy: ☐Absent ☐Grade 1-2 ☐Grade 3-4

Child-Pugh C = 10 to 15 points, consult a research clinician

Bilirubin (Total) • <2 mg/dL (<34.2 µmol/L) (+1) • 2-3 mg/dL (34.2-51.3 µmol/L) (+2) • >3 mg/dL (>51.3 µmol/L) (+3)	Ascites • Absent (+1) • Slight (+2) • Moderate (+3)
Albumin • >3.5 g/dL (>35 g/L) (+1) • 2.8-3.5 g/dL (28-35 g/L) (+2) • <2.8 g/dL (<28 g/L) (+3)	Encephalopathy • No Encephalopathy (+1) • Grade 1-2 (+2) • Grade 3-4 (+3)
INR • <1.7 (+1) • 1.7-2.2 (+2) • >2.2 (+3)	

Vitals: Date Collected- ____/____/____

Temperature: _____ > 100.4, consult research clinician	BP: ____/____, Systolic BP < 90, consult research clinician	RR: _____ < 12, consult research clinician	RAMSAY: _____ > 3, consult research clinician
HR: _____ < 55, consult research clinician	O2 Sat: _____ < 94% on RA, consult research clinician	COWS: _____ > 3, consult research clinician	

Administration: Date of Injection: ____/____/____ Time of Injection: ____:____ am / pm

Injection delivered? ☐Yes ☐No, why? _____

Abdominal? (XR-B)			
☐Quad 1	☐Quad 2	☐Quad 3	☐Quad 4

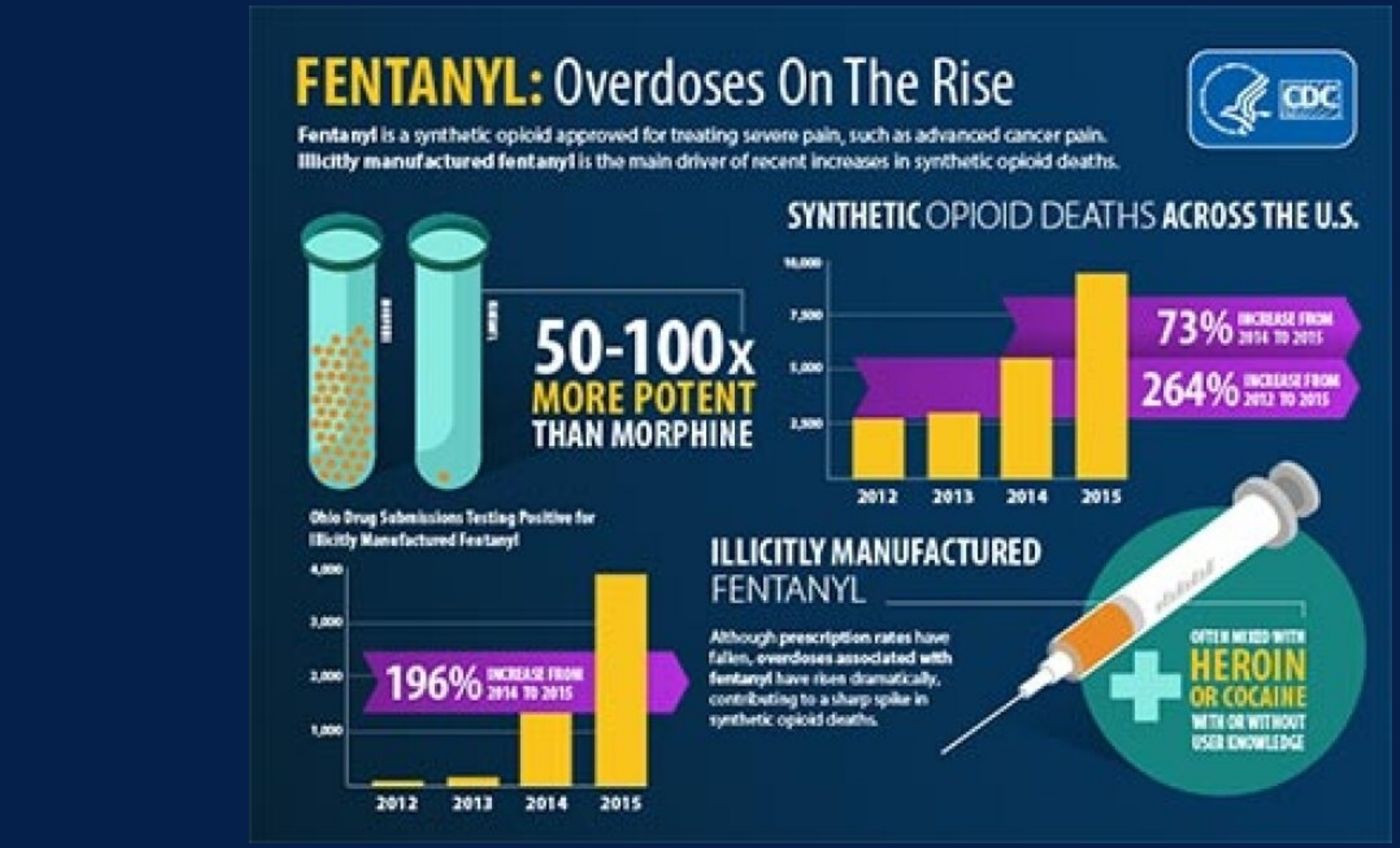
Immediate sensitivity reaction (assessed after 10min)? ☐No ☐Yes, describe: _____

Note: XR-B Drug must be out of the fridge for 15 minutes PRIOR to administration

LAB Induction

- Every person that is randomized to LAB could safely start LAB in 1-3 days (FDA IND to rapidly start- FDA)
  - Those that were already started on buprenorphine could be started on LAB
    - A few could be given LAB in one day , even on day of discharge
- All LAB patients are monitored (per request from FDA) for 2 hours after first dose every 30 minutes to do COWS and Ramsey Assessments
- No precipitated withdrawal in any participants

The Challenges of LAB Initiation in Persons Taking Full Opioid Agonists



Patient case

- 35-year-old man with a past medical history of:
  - severe OUD (intermittently adherent to high dose methadone),
  - Injecting fentanyl/ heroin daily
  - benzodiazepine use disorder (on prescribed benzos),
  - chart history of PTSD/anxiety/depression,
- Presents with bilateral upper extremity cellulitis in setting of IV drug use.
- He is started on IV antibiotics and
- restarted on his 115 mg of methadone.
- He undergoes bilateral bedside I&Ds of upper extremity abscesses;
- he is on standing and PRN oxycodone for pain.
- He is interested in the trial – he is enrolled in COMMIT and randomizes to the LAB arm.

How would you induct this patient onto buprenorphine?

Buprenorphine Induction Considerations

Issues	Standard Buprenorphine Induction	COMMIT Cohort
Pain	Requires cessation period from all full agonist opioids	Pain from underlying infection, necessary surgeries
Pre-Induction Withdrawal	Require COWS >5 prior to first buprenorphine dose	Baseline discomfort, risk for unplanned discharge, WD aversion
Precipitated Withdrawal	Possible increased likelihood with fentanyl use	Baseline discomfort, risk for unplanned discharge, WD aversion

Buprenorphine Induction Considerations

Issues	Standard Buprenorphine Induction	COMMIT Cohort	Low Dose Buprenorphine Induction
Pain	Requires cessation period from all full agonist opioids	Pain from underlying infection, necessary surgeries	Can continue agonist opioids for analgesia
Pre-Induction Withdrawal	Require COWS >5 prior to first buprenorphine dose	Baseline discomfort, risk for unplanned discharge, WD aversion	No withdrawal required for initiation
Precipitated Withdrawal	Possible Increased likelihood with fentanyl use	Baseline discomfort, risk for unplanned discharge, WD aversion	Theoretically lower

Case Series from COMMIT

ORIGINAL RESEARCH

Inpatient Low-dose Transitions From Full Agonist Opioids Including Methadone Onto Long-acting Depot Buprenorphine: Case Series From a Multicenter Clinical Trial

Nikhil Seval, MD, Johnathan Nunez, MD, Prerana Roth, MD, Meredith Schade, MD, Michelle Strong, MSN, FNP-BC, Cynthia A. Frank, PhD, Alain H. Litwin, MD, MPH, MS, Frances R. Levin, MD, Kathleen T. Brady, MD, PhD, Edward V. Nunes, MD, and Sandra A. Springer, MD

Seval et al. Journal of Addiction Medicine. 2023. Jan 26. PMID: 36701748
DOI: 10.1097/ADM.0000000000001136

Table 1: Patient Characteristics

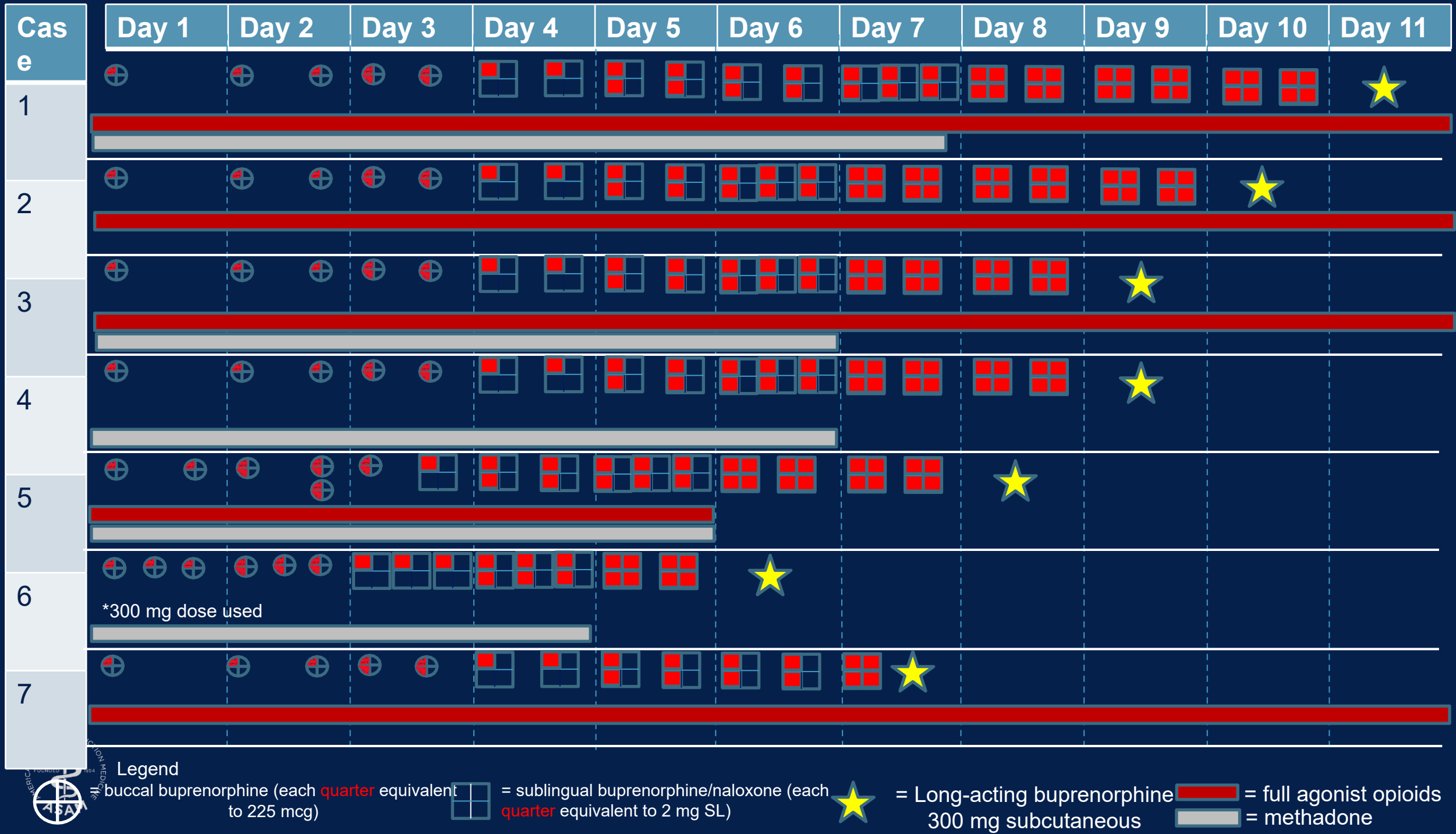
Case	Patient	Substance Use Dx per MINI	Day of Randomization and Length of Stay	Infectious Syndrome	Surgery
1	35 y/o female	Severe OUD, severe cocaine UD	Day 6 of hospitalization LOS: 42d	Enterococcal aortic valve/mitral valve prosthetic endocarditis	Redo aortic valve/mitral valve replacement (d8) pacemaker placement (d11)
2	31 y/o female	Severe OUD *Prescribed benzodiazepine and dextroamphetamine use*	Day 29 of hospitalization LOS: 43d	MSSA native tricuspid valve endocarditis	Tricuspid valve replacement + pacemaker placement (d10)
3	39 y/o male	Severe OUD	Day 7 of hospitalization LOS: 17d	MSSA bacteremia + chronic ulnar osteomyelitis	*n/a*
4	35 y/o male	Severe OUD, severe benzodiazepine UD	Day 7 of hospitalization LOS: 15d	Bilateral upper extremity abscesses	*n/a*
5	67 y/o male	Severe OUD	Day 8 of hospitalization LOS: 16d *(premature discharge)*	MRSA septic arthritis of knee	knee arthroscopic irrigation and debridement (d2)
6	44 y/o male	Severe OUD Severe cocaine UD	Day 2 of hospitalization LOS: 8d	Severe covid 19 pneumonia	*n/a*
7	29 y/o male	Severe methamphetamine UD, severe OUD, severe cocaine UD, severe cannabis UD	Day 5 of hospitalization LOS: 13d	Polymicrobial mitral native valve endocarditis	Mitral valve replacement (d2)

Key : COWS = Clinical Opioid Withdrawal Scale; d/c = discharge; IV = intravenous; IR = Immediate release; LAB = Long-acting buprenorphine; LOS = Length of Stay; MINI = Mini-International Neuropsychiatric Interview; MOUD = Medications for opioid use disorder; MRSA = Methicillin Resistant Staphylococcus Aureus; MSSA = Methicillin Susceptible Staphylococcus Aureus; MS-ER = morphine sulfate extended-release; po = By mouth; q day = Each day; UD = Use disorder (e.g. OUD = opioid use disorder); WD = withdrawal

All hospitalization days (e.g. d1, d2) given in terms of day of hospitalization

Pain

- Pain, Enjoyment of Life and General Activity (PEG) Scale
  - 0 to 10 rating scale, 3 question assessment including ‘Past Week Pain’
  - Single question added (modified PEG) to assess pain at time of assessment
- COMMIT baseline PEG score= 5.0
  - (No difference in pain scale between LAB and TAU (5.50 versus 5.00)
- Case series cohort: Average past week pain: 8.2 (range: 5-10)
  - Average pain at time of question: 5.7 (range 3-7)

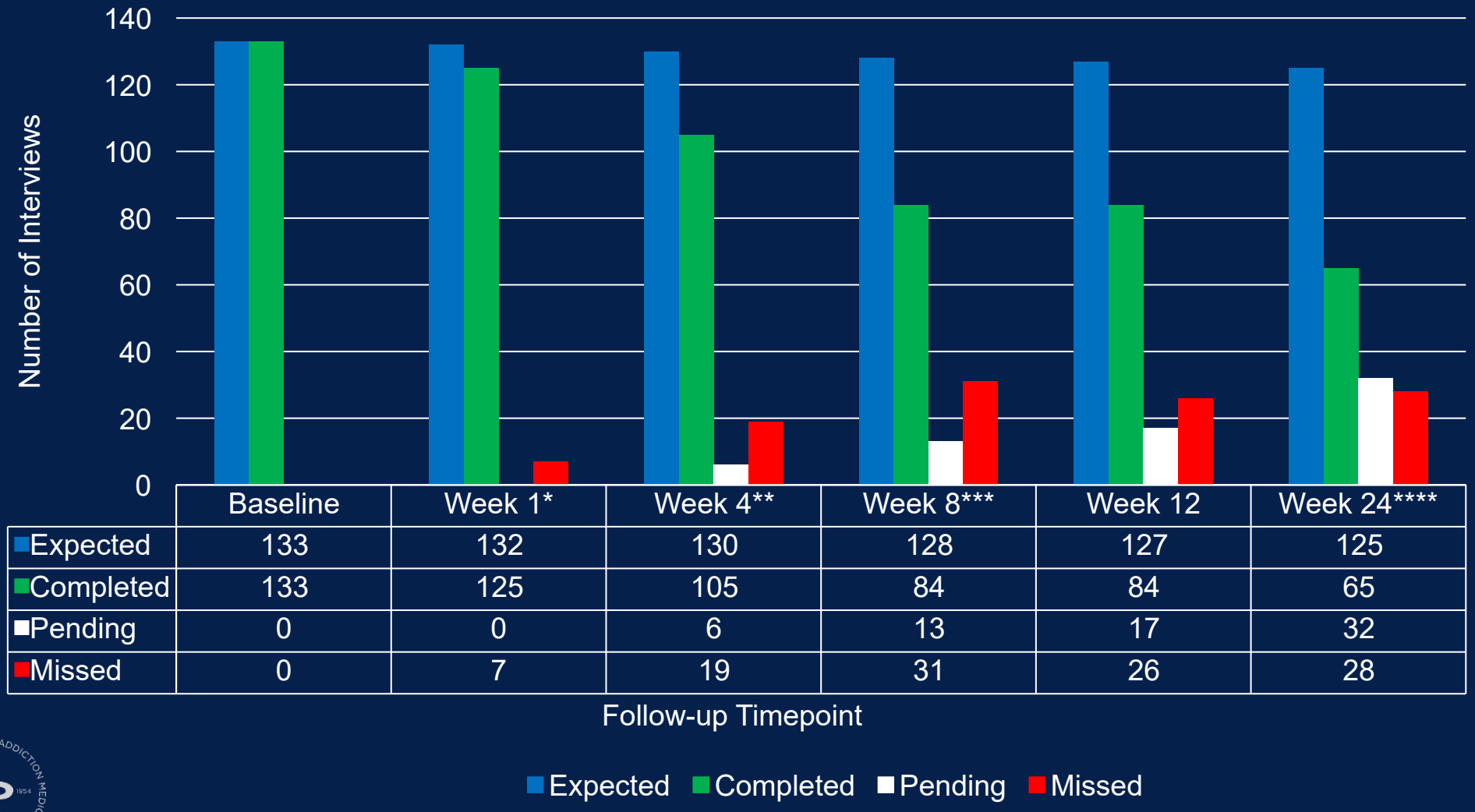

Case
Day 1
Day 2
Day 3
Day 4
Day 5
Day 6
Day 7
Day 8
Day 9
Day 10
Day 11
1
2
3
4
5
6
7
*300 mg dose used
Legend
buccal buprenorphine (each quarter equivalent to 225 mcg)
= sublingual buprenorphine/naloxone (each quarter equivalent to 2 mg SL)
= Long-acting buprenorphine 300 mg subcutaneous
= full agonist opioids
= methadone

COWS Scores after LAB Administration

Case	COWS at LAB Injection
1	1 – immediately prior 0 – immediately after 0 – q30 mins for 2 hours
2	1 – immediately prior 0 – immediately after 0 to 1 – q30 mins for 2 hours
3	1 – immediately prior 1 – immediately after 0 to 1 – q30 mins for 2 hours
4	1 – immediately prior 3 – immediately after 1 – q30 mins for 2 hours
5	1- immediately prior 1- immediately after 0 to 1- q30 mins for 2 hours
6	4- immediately prior 2- immediately after 0-1 – q30 mins for 2 hours
7	2 – immediately after and q30 mins for 2 hours

**For full cohort N=133, No difference in COWS score at baseline: LAB 1.72 vs . TAU 1.92*

Retention Through 02/15/2023 (N=133)



	Baseline	Week 1*	Week 4**	Week 8***	Week 12	Week 24****
Expected	133	132	130	128	127	125
Completed	133	125	105	84	84	65
Pending	0	0	6	13	17	32
Missed	0	7	19	31	26	28

Interview Completion Rates:

- 100% Baseline
- 94.7% Week 1
- 84.7% Week 4
- 73.0% Week 8
- 76.4% Week 12
- 69.9% Week 24

* Week 1: One withdrew consent prior to week 1

** Week 4: One died prior to week 4

*** Week 8: One died prior to week 8

**** Week 24: One died prior to week 24

Serious Adverse Events

- 84 SAEs as of 02.20.23
- MOST COMMON :
  - Endocarditis N=12
  - Skin/Soft Tissue Infections N=11
    - (none related to LAB injection)
  - Suicidal Ideation N=6
- 13 SAEs Unexpected
- 2 SAEs possibly- related to study intervention (1 anemia, 1 PE)

Serious Adverse Events: 3 Deaths

Event	Expectedness	Index Infection	Intervention	Study Arm
Death: cause undetermined	Yes	Unrelated	Unrelated	TAU
Death: respiratory failure	Yes	Unrelated	Unrelated	LAB
Death: respiratory failure	No	Unrelated	Unrelated	TAU

Key Takeaways

- Infectious Diseases are increasing in persons who use drugs leading to increased hospitalizations and higher morbidity and mortality
- Integration of screening , diagnosis and treatment of OUD in persons hospitalized with infections could improve morbidity and mortality
- Preliminary data from a multisite randomized clinical trial of a new integrated model of care of OUD treatment with long-acting buprenorphine with nurse care discharge planning and continued treatment in the community could improve retention on MOUD and reduce overdose and improve infectious disease treatment
- Preliminary data of this ongoing trial demonstrate high acceptability and feasibility with minimal adverse events

References

1. Spencer et al. NCHS Data Brief no 457. Hyattsville, MD; National Center for Health Statistics 2022.
2. Ronan. Health Aff (Millwood). 2016;35:832.
3. Springer et al. JAMA. 2020.
4. Seval N et al. OFID. 2019.
5. Wickersham et al. J Correctional Health Care. 2015.
6. Seval N et al. Contemporary Clinical Trials. 2021
7. Seval et al. Journal of Addiction Medicine. 2023. Jan 26. PMID: 36701748
8. CDC. https://www.cdc.gov/nchhstp/newsroom/2017/hepatitis-c-and-opioid-injection-press-release.html.

Impact of COVID-19 on Overdose Risk and Healthcare-Seeking Behavior among Hospitalized Persons with Opioid Use Disorder

Manesh Gopaldas, MD

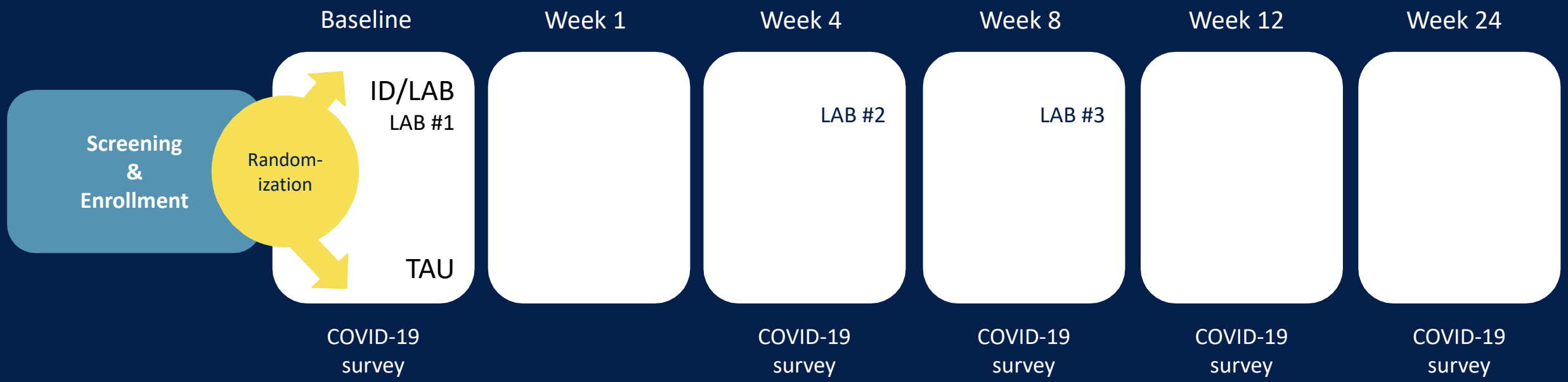
What we (don't) know

- Drug overdose deaths continue to climb
  - Exacerbated by the COVID-19 pandemic
    - Disrupted access to substance use treatment
    - Social isolation and stress
    - Increases in drug use and using drugs alone

- Opportunity to examine the **pandemic's impact on overdose risk and healthcare-seeking behavior** among a ***vulnerable, complex population with opioid use disorder (OUD)***.

Friedman 2021, Cartus 2022, Galarneau 2021, Seval 2021

Study flow and assessment timepoints



- COVID-19 survey administered to all participants enrolled in COMMIT trial.
  - This sub-study included data through 02/15/2023.
    - Analysis included all 5 timepoints.

COVID-19 survey

9 questions covering 5 domains:

- **COVID-19 testing and diagnosis**
- **COVID-19 risk behavior**
  - *Social distancing*
- **Healthcare-seeking behavior**
  - *Seeking infectious disease care*
  - *Seeking addiction care*
  - *Receiving medications for OUD (MOUD)*
- **Overdose risk behavior**
  - *Purchasing drugs*
  - *Using drugs alone*
- **Overdose risk**

- Survey responses assessed on 5-point Likert scale
  - Converted to 3 categories
    - ***Less Likely***
    - ***No Change***
    - ***More Likely***

Study questions

- What is the perceived impact of the pandemic on overdose risk and healthcare-seeking behavior among hospitalized persons with OUD?
- Does overdose risk perception change over time?

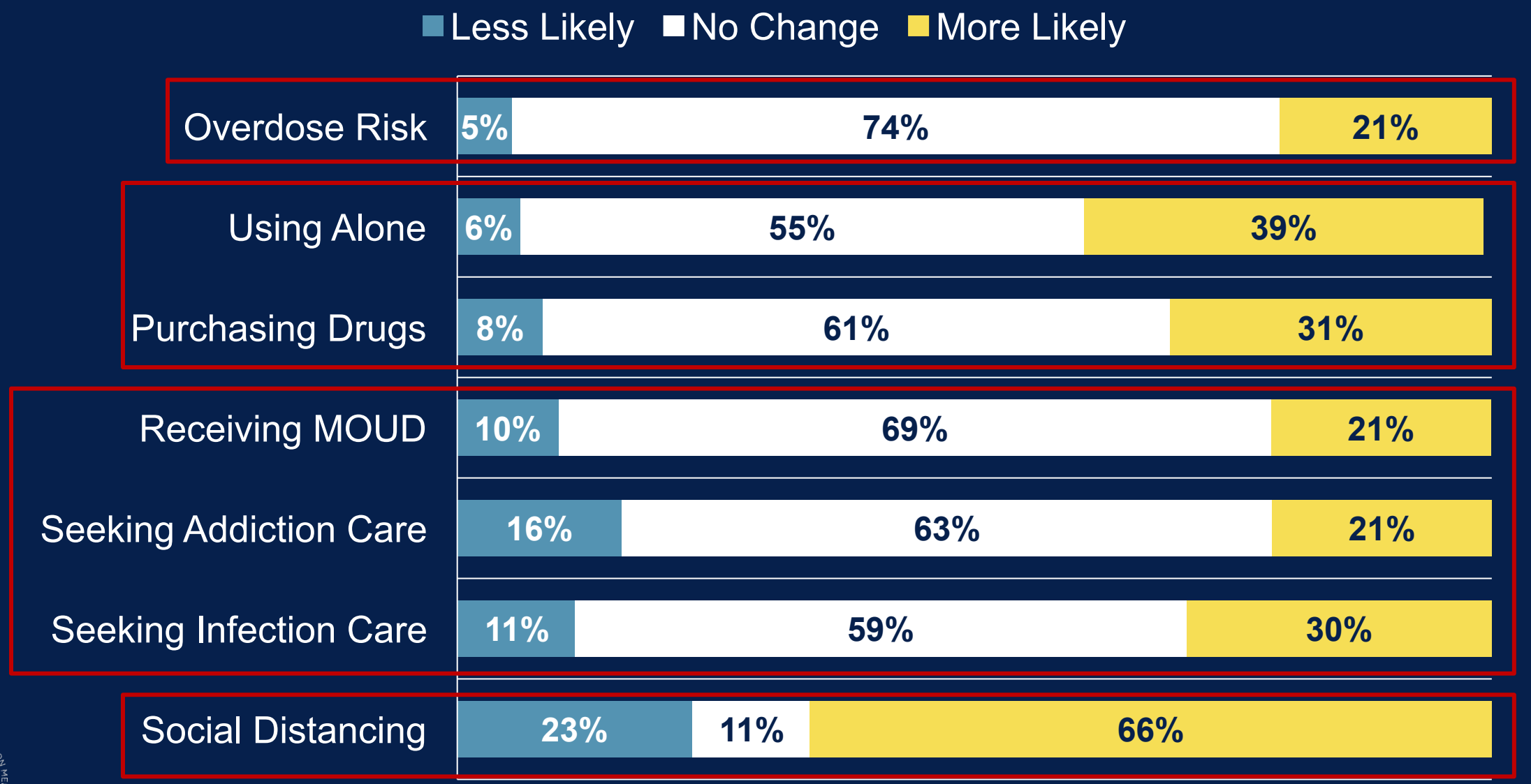
Study questions

- **What is the perceived impact of the pandemic on overdose risk and healthcare-seeking behavior among hospitalized persons with OUD?**
- Does overdose risk perception change over time?

COVID-19 testing and diagnosis at baseline, *N*=132

- Tested for COVID-19: 96%
- Tested positive for COVID-19: 29%

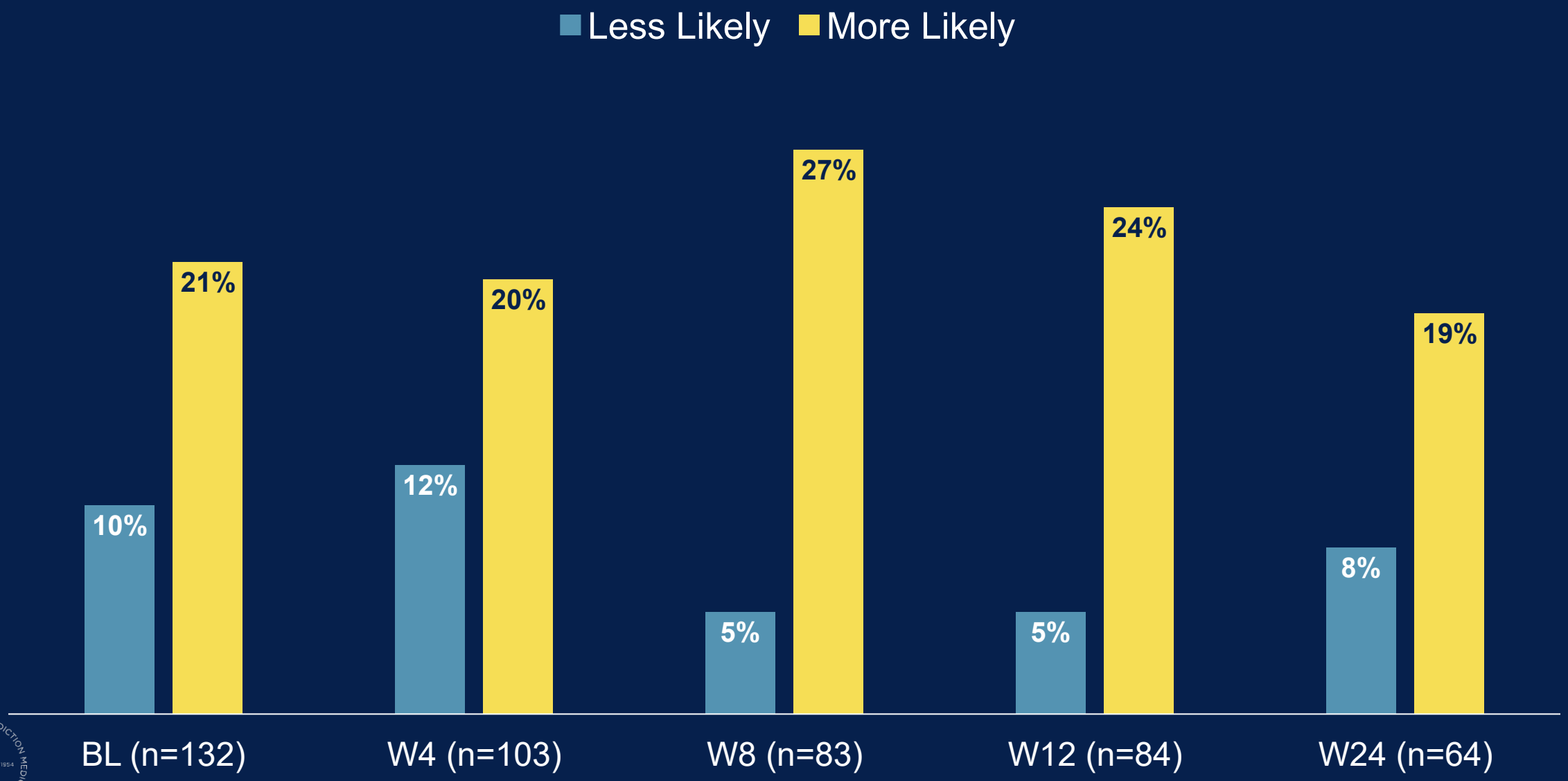
Relative frequencies of survey responses at baseline, *N*=132



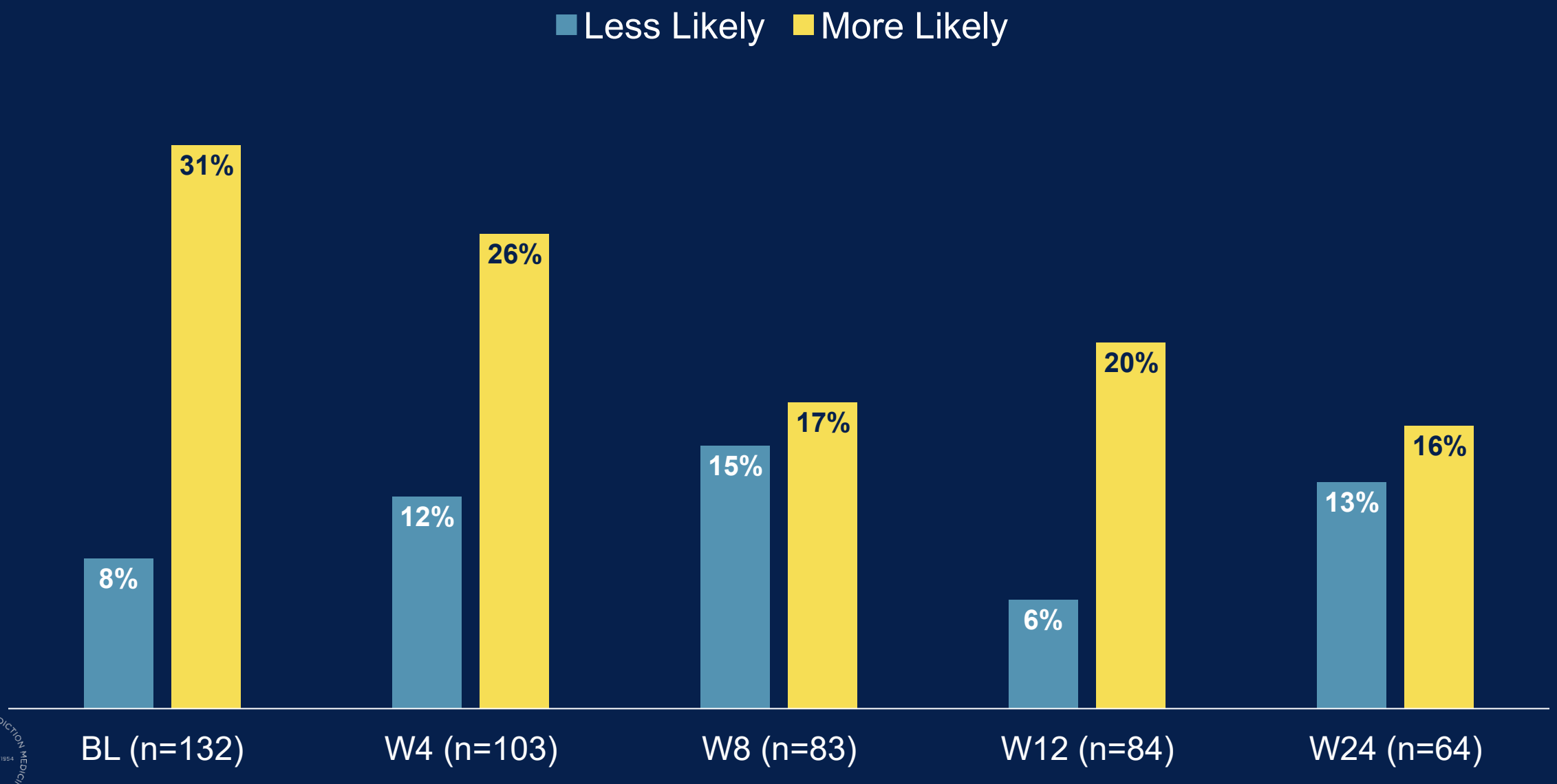
Study questions

- What is the perceived impact of the pandemic on overdose risk and healthcare-seeking behavior among hospitalized persons with OUD?
- **Does overdose risk perception change over time?**

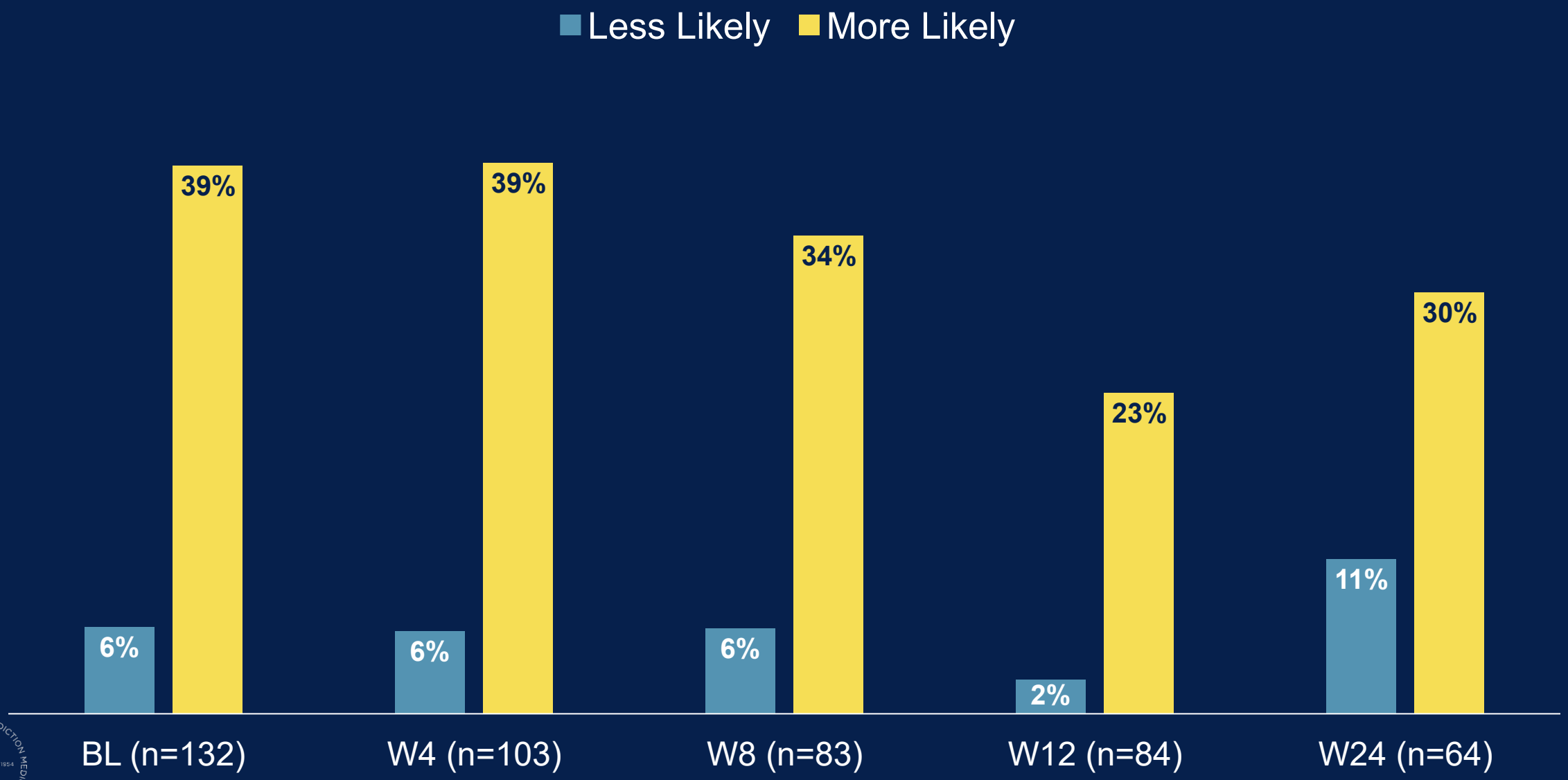
Perceived Impact of Pandemic on ***Receiving MOUD***



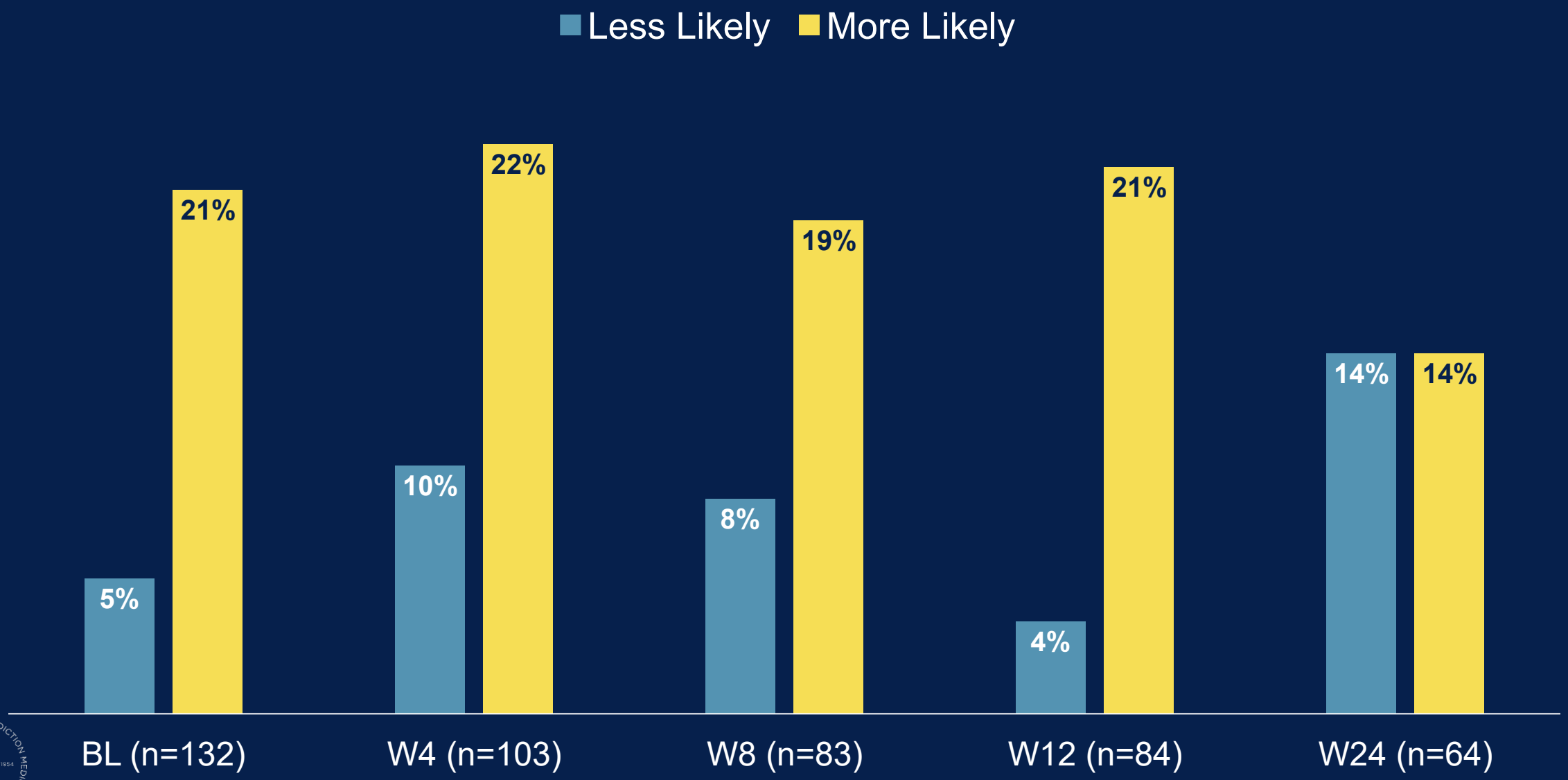
Impact of Pandemic on *Purchasing Drugs*



Impact of Pandemic on *Using Alone*



Impact of Pandemic on ***Overdose Risk***



Key takeaways

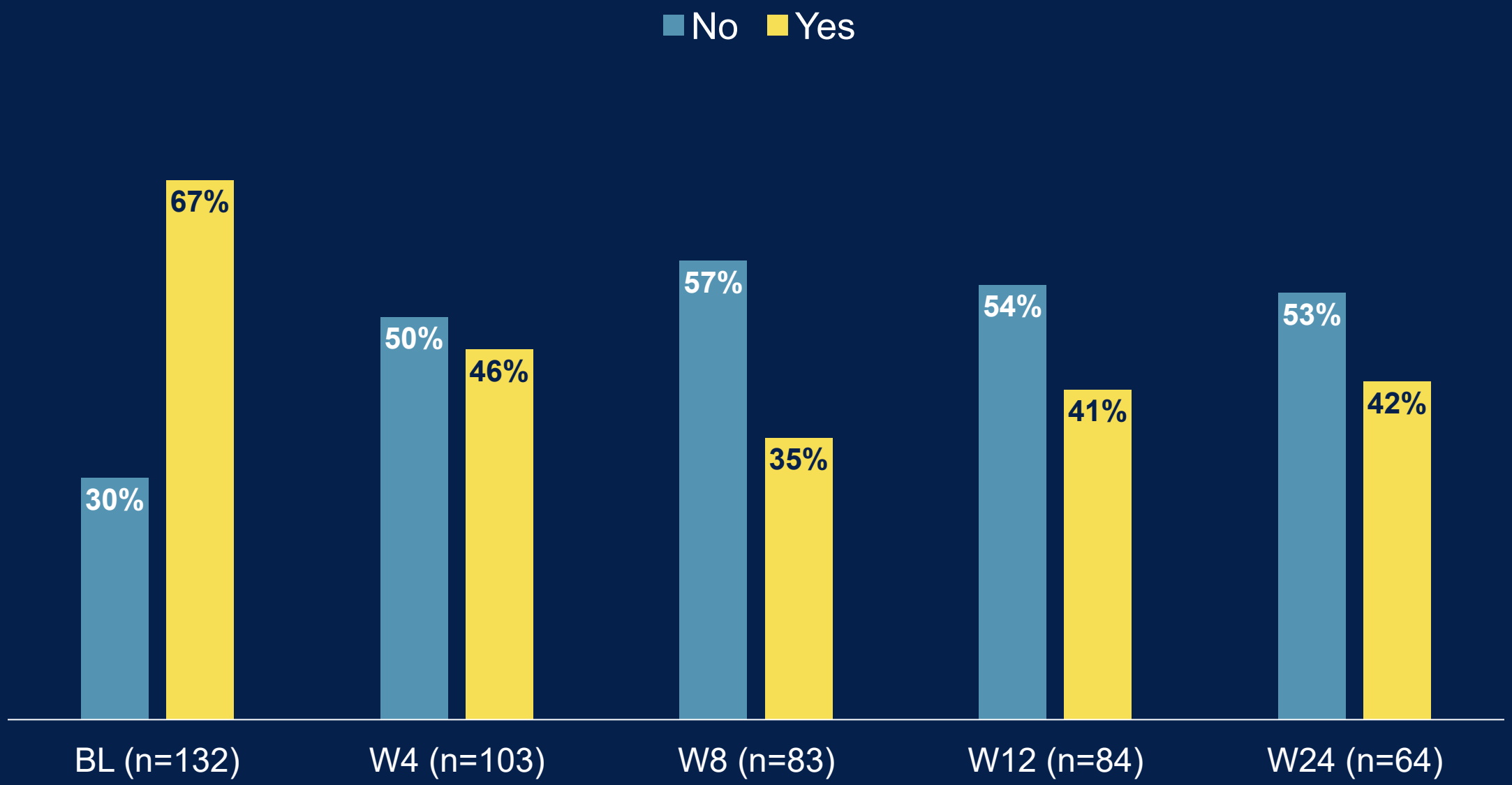
- Compared to pre-pandemic ratings, hospitalized persons with OUD rated themselves as being at **higher risk for purchasing drugs, using drugs alone, and overdose** since the onset of the pandemic.
- Limited variability in overdose risk perception and healthcare-seeking behavior, and **responses remained relatively stable over time**.
- Perceived impact of pandemic among COMMIT participants might have been offset by clinical trial.

Future directions

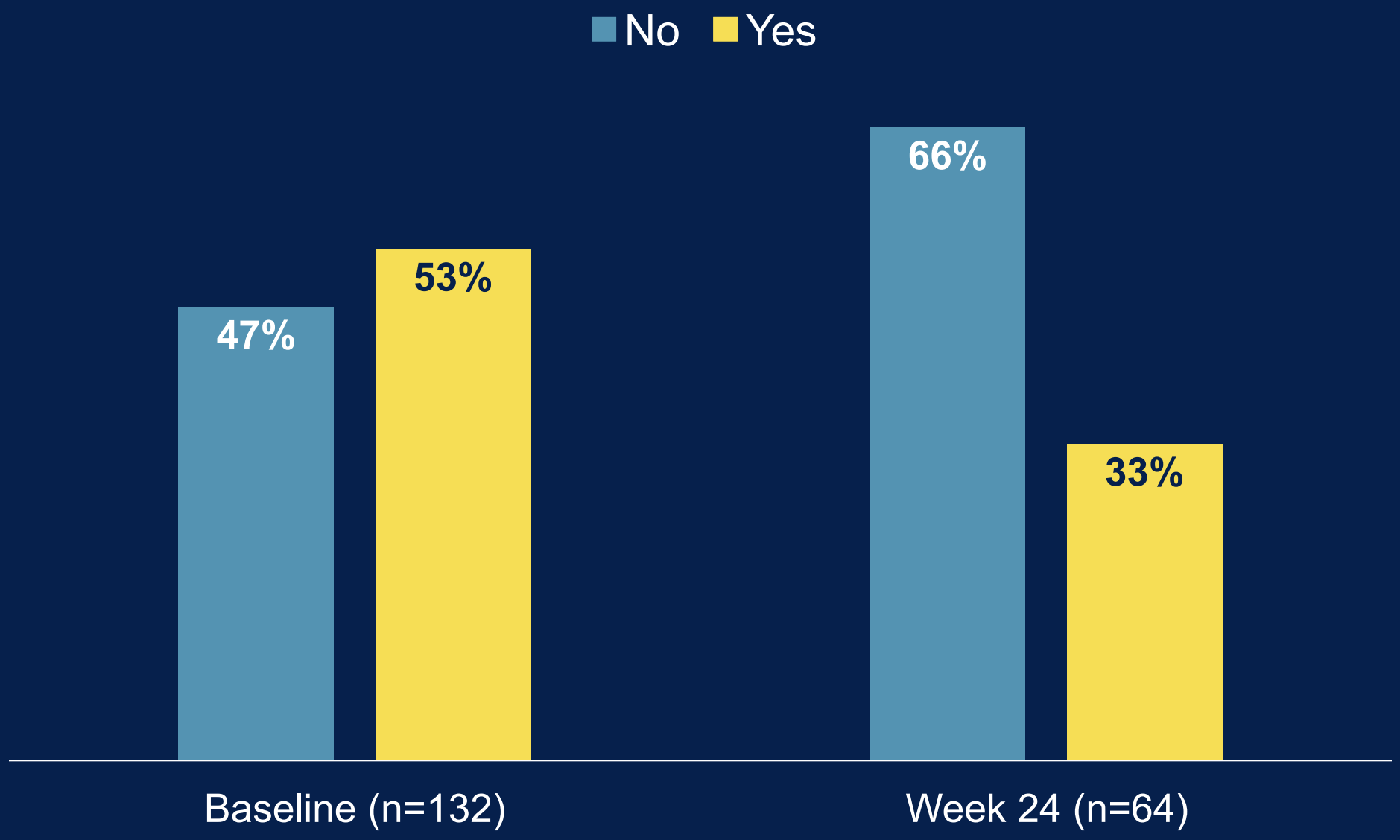
- Data collection is ongoing
  - Patterns may change as sample size increases
- Examine the impact of MOUD on risk and health-seeking behavior
  - Perceived risk (COVID-19 survey) vs. actual risk (adverse events log)
- Examine individual- and group-level differences among participants on negative trajectories
  - Do survey responses differ by treatment arm?
  - Can we identify characteristics predictive of study retention vs. dropout?

Importance of Mental Health Care Integration

Depression (PHQ-9) of at least moderate severity over time



PTSD (PCL-5) diagnosis at baseline and week 24



Key takeaways

- **High rates of co-occurring mental illness** among hospitalized persons with severe OUD-related infections
  - 67% with clinically significant depression at baseline
  - 53% had provisional PTSD diagnosis at baseline
- **<u>OUD treatment can have a substantial impact on mental health suffering</u>**
- Importance of **mental health care integration**
  - Make it easier for our patients to access treatment
  - Unmet mental health needs affect retention in care

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Clinical Considerations: Lessons Learned Through the COMMIT Trial

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Alain Litwin, MD, MPH

Patient Complexity

- Hospitalized
  - Severe Infections
    - MRSA/MSSA bacteremia with complications such as endocarditis, epidural abscess, osteomyelitis, necrotizing fasciitis, septic emboli
      - Surgical intervention and lengthy antibiotic course often indicated
    - Hepatitis C – acute and chronic
  - Social Situation
    - Unstable housing
    - Unstable employment
    - Unfunded/self-pay
    - Outstanding legal issues
    - Minimal support network
    - Co-occurring mental health diagnoses

Reasons for Not Enrolling

- Desire for MOUD choice
- No interest in changing use patterns
- No interest in medication
- No interest in research
- More important personal concerns
  - Housing
  - Family challenges
  - Concern for pending legal issues

Case 1: Elevated Liver Enzymes

- 35 y.o. F with a history of IVDU admitted with back pain, found to have MRSA bacteremia and
  - Tricuspid valve endocarditis and septic emboli
  - L sacroiliac septic arthritis
  - L iliacus muscle pyomyositis and intramuscular abscess
- Abscess was drained and plan was to complete 6 weeks of IV daptomycin
- **COMMIT TAU** : Patient started on SL buprenorphine during hospitalization
- HCV Ab positive with RNA quant 11 million
- LFTs normal 8/2021, elevated on admission 9/2021 and continued to worsen after SL buprenorphine started
  - AST 100s → 800s
  - ALT 200s → 800s
  - T.bili normal
- Concern for liver injury from SL buprenorphine vs Acute Hepatitis C
- Workup included liver biopsy which showed chronic hepatitis with rare granulomas
- Buprenorphine dosing was decreased during hospitalization while DILI workup was completed and was able to be escalated when results were reassuring

Patient Stigma

Case Study

History of Present Illness: [redacted] a 35 y.o. female who presents with back pain. Patient refuses to provide history, she claims she is very tired and as she would speak to order doctors so history was obtained from emergency room physician and charts.
Patient has had multiple hospitalizations since August this year and usually signed out AMA, she is shuttling between this hospital and Spartanburg Medical Center, known to have infective endocarditis, septic emboli, history of IV drug abuse, she has not been able to complete therapy, she had a positive blood culture for MRSA, now she coming in with lower back pain radiating to left thigh and buttocks. MRI lumbar spine and sacrum showed left sacroiliac joint septic arthritis with adjacent pyomyositis including an intramuscular abscess in the left iliac us muscle. There is also nonspecific edema and enhancement involving the right aspect of the T1 vertebral body and adjacent first rib.
Her urinalysis is positive for UTI
He does have leukocytosis, no documented fever
She received IV vancomycin and Zosyn in the ER
She is very noncooperative and difficult"

MRSA Bacteremia, Septic Arthritis, Vertebral Osteomyelitis, Endocarditis- known hx untreated MRSA bacteremia secondary to IVD use. Has had multiple admissions between here and Spartanburg, always leaves AMA. Often uncooperative with care. Seems more motivated to stay this AM. She acknowledged that she would need to remain hospitalized at least 6 weeks. I think starting suboxone as below gives her the best chances, she understands. Continue IV vancomycin for now. Noted ?septic emboli on prior CTA. Will ask ID to weigh in today. Needs repeat blood cultures tomorrow.

IVD Abuse- active heroin use. Addiction medicine following, started on suboxone which is helping her a lot. Appreciate assistance. HIV neg.

Bacteremia/septic arthritis/vertebral osteomyelitis/endocarditis
With Hx of untreated MRSA bacteremia 2/2 IVDU, Hx of medical noncompliance
Multiple admission between Prisma health and Spartanburg
Repeated BCx NGTD on 9/16. Started on cephalexin, decreased dose on 9/23 d/t transaminase-follow by GI, ID and addiction team and appreciate them
Determined to complete treatment this admission, continue to encourage
PICC line placed 9/24. Continue IV Vanc as per ID rec, **EOT 10/28**-no change 9/25

Patient seen at bedside today - plan still in place for discharge tomorrow. Patient will discharge directly to Phoenix Center Residential Treatment Program. Second bottle of Epclusa delivered to patient bedside yesterday - reports no side effects, HCV labs checked this AM. ROS otherwise negative.

Medication Interactions

Clinical readiness assessment for Sublocade administration

CYP Inhibitors
Amiodarone
Fluoroquinolones
Cobicistat
Fluconazole
Isoniazid
Itraconazole
Ranitidine
Ritonavir
Valproic acid
Voriconazole

CYP Inducers
Carbamazepine
Efavirenz
Oxcarbazepine
Phenytoin
Rifabutin
Rifampin
St Johns wort
Topiramate

QTc prolonging medications
Macrolides
Fluoroquinolones
Anti-emetics (ondansetron, metoclopramide)
Antipsychotics (haloperidol)

Antihypertensives
ACE Inhibitors and ARBs
Diuretics (furosemide)
Calcium channel blockers

Sedatives
Benzodiazepines

Non-Opioid Withdrawal Treatment
Alpha-2 agonists (clonidine, tizanidine)

Cases 2 & 3: LAB Administration Fluconazole Treatment Delays

- 32 y.o. M with a history of IVDU admitted with 5 days of fever and malaise, found to have both MSSA bacteremia and fungemia with Candida parapsilosis. TEE was negative. Patient got 2 weeks of IV cefazolin followed by a dose of dalbavancin to treat for 2 more weeks. For candidemia, he was initially started on caspofungin but completed the 4-week course with PO fluconazole. First dose of LAB received 7 days post discharge and fluconazole end date. Second and third LAB doses missed.

- 40 y.o. M with a history of IVDU presented with 1 week of neck and shoulder pain and was found to have C spine discitis and septic arthritis with severe central canal stenosis. Blood cultures were positive for Candida parapsilosis and Enterobacter. Treatment plan for was for cefepime + fluconazole for 6 weeks which would end 11/8. Surgery for C spine was planned for 11/16. Pt was randomized to LAB, but LAB was delayed until after fluconazole and surgery were completed. Pt was lost to follow-up post discharge.

- Fluconazole can cause a 2-5-fold increase in levels of buprenorphine through inhibiting its metabolism
- No data for effect of fluconazole on long-acting buprenorphine levels

Discharge Challenges

- Insurance status impacting medication choices
  - Less than 5 patients continued Sublocade after study due to cost barriers
- Self pay cost of care
  - Medication
  - Patient visit cost
- Housing options that allow for MOUD
- Access to Transportation

Why the X Waiver Removal Is Not Enough

GENERIC SUBUTEX

AVERAGE RETAIL: $456.19

PRICES ON GOODRX.COM
PLEASE USE COUPON

Prices are for 8mg buprenorphine 90 sublingual tablets in **Greenville SC**

This equates to a 1 month supply for patients on 24mg dosage.

- **CVS Pharmacy** $173.02
- **Costco** $142.19
- **Harris Teeter** $124.02
- **Kroger Pharmacy** $124.02
- **Publix** $69.99
- **Walgreens** $25.83

GENERIC SUBOXONE TABLET

AVERAGE RETAIL: $802.51
PRICES ON GOODRX.COM
PLEASE USE COUPON

Prices are for 8mg/2mg buprenorphine/naloxone 90 sublingual tablets in **Greenville SC**.

This equates to a 1 month supply for patients on 24mg dosage.

- **Walgreens** $231.69
- **CVS Pharmacy** $221.08
- **Costco** $161.92
- **Harris Teeter** $131.14
- **Publix** $82.55

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Need for Non-punitive/Holistic Care

- Conversations with patients driven by data/information
  - UDS
  - Timeline follow back
- Frequent touch points to establish further care
- Support for pending legal challenges
- Harm reduction resources and education
  - Sexual Risk/Injection Risk

In the past 30 days have you injected drugs?	o No o Yes
In the past 30 days, did you share works with anyone?	o No o Yes
In the past 30 days, how many people did you share works with?	_____ people
In the past 30 days, how many persons with WHO WERE HIV POSITIVE OR WERE OF UNKNOWN HIV STATUS did you share works with?	_____ people
In the 30 days prior to this evaluation, when you injected, did you inject with others without sharing works?	o No o Yes
How frequently did you inject with others without sharing works?	o Never o Rarely o Sometimes o Always o Don't know

Sexual risk

During the 30 days prior to this interview, how many people did you have sex with?	
During the 30 days prior to the interview, did you have condomless vaginal/anal sex?	o No o Yes
How many sexual partners did you have condomless vaginal or anal sex with in the last 30 days?	_____ people
How many of the sexual partners in the last question were HIV positive or unknown status?	_____ people
About how many times have you had condomless vaginal or anal sex during this time? (Please make your best estimation or guess)	_____ times
About how many times have you had condomless vaginal or anal sex during the last 30 days WITH A PARTNER WHO IS HIV POSITIVE OR OF UNKNOWN HIV STATUS? (Please make your best estimation or guess)	_____ times

Integrated Care

- Shared decision making in choice of medication (TAU patients)
  - Type of medication desired (if at all)
  - Medication cost
  - Access to care at discharge
- Co-management with surgery/pain/trauma teams
  - Low Dose Inductions onto Buprenorphine (LAB and TAU patients)
    - Not an option to pull off their full agonist
    - Post surgical patients
    - Uncontrolled pain

Reachable Moments

Hepatitis C

- 60/79 Randomized pts were HCV Ab Positive at Baseline
- 37/60 HCV Ab positive had detectable VL at Baseline
- Only 2/60 HCV Ab positive had received treatment prior to study participation and had undetectable VL at baseline

Pre-exposure Prophylaxis to Prevent HIV (PrEP)

- 0 patients on PrEP when enrolled in study
- 1 patient started PrEP during study with a community provider (MSM with previous experience on PrEP)

Safe Use Practices

- Community syringe service programs

Overdose Education/Narcan

- Prescription at discharge
- Community Narcan distribution

Key Takeaways

- More collaborations are needed across hospital teams to provide integrated SUD/ OUD care
- Holistic care that provides non-punitive assistance in treatment of substance use disorders, prevention of overdose is necessary
- Hospitals provide a reachable moment to identify , treat as well as prevent infections like HIV, HCV , HBV and substance use disorders

Questions & Discussion

Sandra A. Springer, MD

Final Takeaways/Summary (Suggested)

- Infections are increasing along with overdose deaths in this country leading to an increase in hospital admissions
- Hospitals provide a reachable moment to screen and diagnose OUD/ SUD and offer SUD and ID treatment and prevention services
- LAB is possible to start in hospitalized patients with OUD even with serious life-threatening infections
- Proactive harm reduction services should be offered and administered prior to discharge (Naloxone, PrEP, SSPs, Fentanyl Test Strips)
- Careful needs assessments should be conducted to provide pro-active discharge planning and follow-up including assistance with transportation, housing , and cell phone assistance to ensure patients can continue to receive care after discharge .

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