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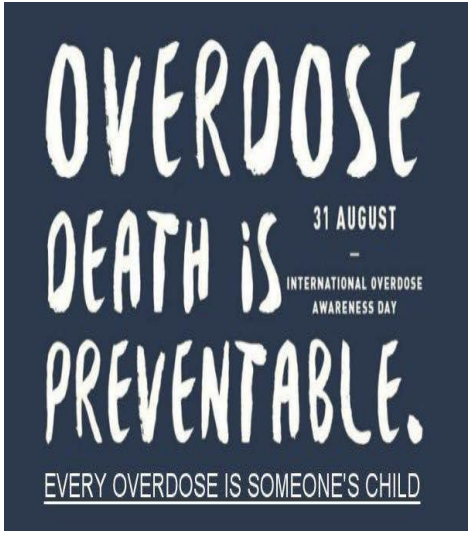

The Evidence for Overdose Prevention and Intervention Strategies
Harm Reduction Webinar #3, 5/19/22

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Chief of Medical Services

May 19, 2022

Disclosures

- Dr. Ramsey has no significant financial disclosures

Harm Reduction: Needle Exchange in Santa Cruz, CA, circa mid-1990s

Harm Reduction: Needle Exchange in Santa Cruz, CA, circa mid-1990s

Learning Objectives

- Discuss very briefly the current epidemiology of overdoses
- Discuss briefly the evidence for medication for opioid use disorder (MOUD)
- Discuss the evidence for naloxone
- Discuss the evidence for fentanyl test strips (FTS) and drug checking
- Discuss the evidence for syringe services programs (SSPs)
- Discuss the evidence for overdose prevention centers (OPCs)

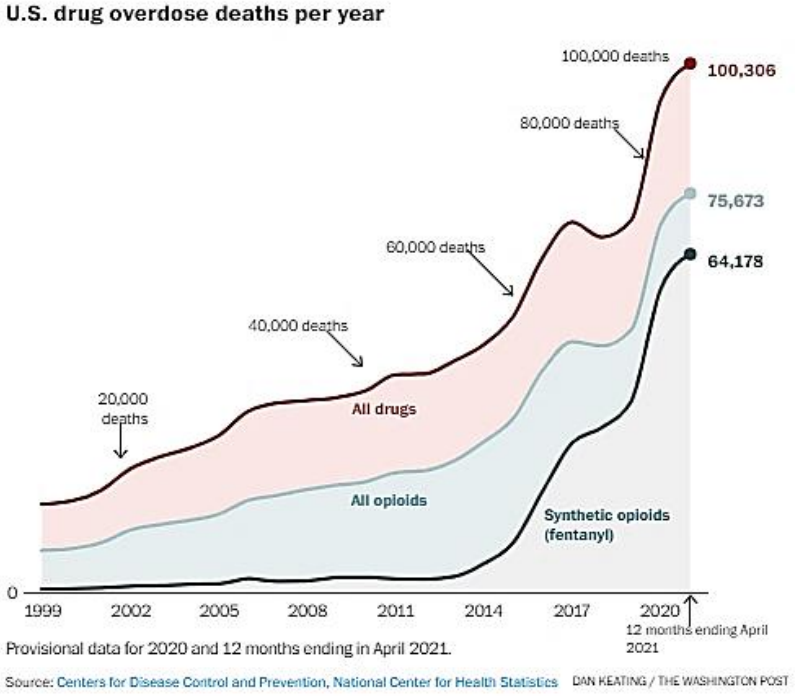
Evidence-Based Strategies for Preventing Opioid Overdose

1. Targeted Naloxone Distribution
2. Medications for opioid use disorder (MOUD)
3. Academic Detailing
4. Eliminating Prior-Authorization Requirements for MOUD
5. Screening for Fentanyl in Routine Clinical Toxicology Testing
6. 911 Good Samaritan Laws
7. Naloxone Distribution in Treatment Centers and Criminal Justice Settings
8. MOUD in Criminal Justice Settings and Upon Release
9. Initiating Buprenorphine-based MOUD in Emergency Departments
10. Syringe Services Programs

https://www.cdc.gov/drugoverdose/pdf/pubs/2018-evidence-based-strategies.pdf and https://www.cdc.gov/drugoverdose/featured-topics/evidence-based-strategies.html

Epidemiology of overdoses

Overdose Deaths in the US



Overdose Deaths Increased Again in 2019 (and 2020*)

	ALL DRUGS	HEROIN	NAT & SEMI - SYNTHETIC	METHADONE	SYNTHETIC OPIOIDS	COCAINE	OTHER PSYCHO-STIMULANTS (mainly meth)
September 2019*	70,036	14,548	12,136	2,832	34,758	15,389	15,600
March 2020*	75,687	14,145	12,349	2,837	40,756	17,465	18,033
September 2020*	90,237	14,201	13,649	3,501	53,877	19,952	22,791
Year end September 2019-September 2020 Change	+28.8%	-2.4%	+12.5%	+23.6%	+55.0%	+30.0%	+46.0%

*NCHS Provisional Drug Overdose Death Counts: https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm

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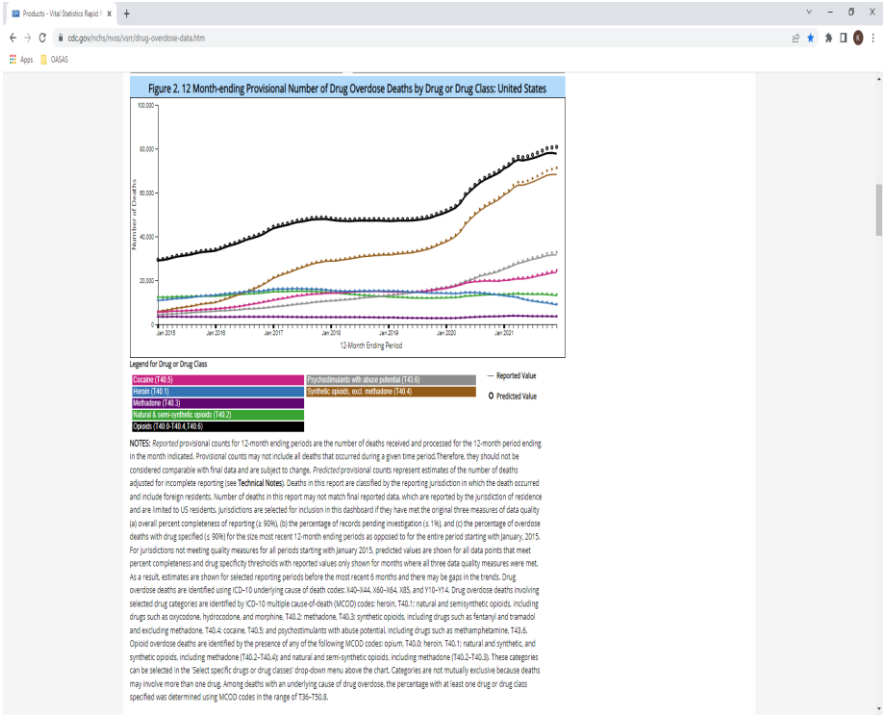
CDC Provisional Drug Overdose Death Counts 2021

Overdose by Substance Through December 2021



Total Estimated Overdose Deaths Through December 2021

Annual drug overdose deaths have reached another record high in the United States, as deaths from fentanyl and its analogues surge to unprecedented levels.

An estimated ***107,622 people*** died of a drug overdose in the 12-month period ending December 2021, according to provisional data published 5/11/2022 by the US Centers for Disease Control and Prevention's National Center for Health Statistics.

An overall 15% increase in deaths compared with 2020. About two-thirds of those deaths involved synthetic opioids such as fentanyl and its analogues. There were significant deaths due to methamphetamine use as well.

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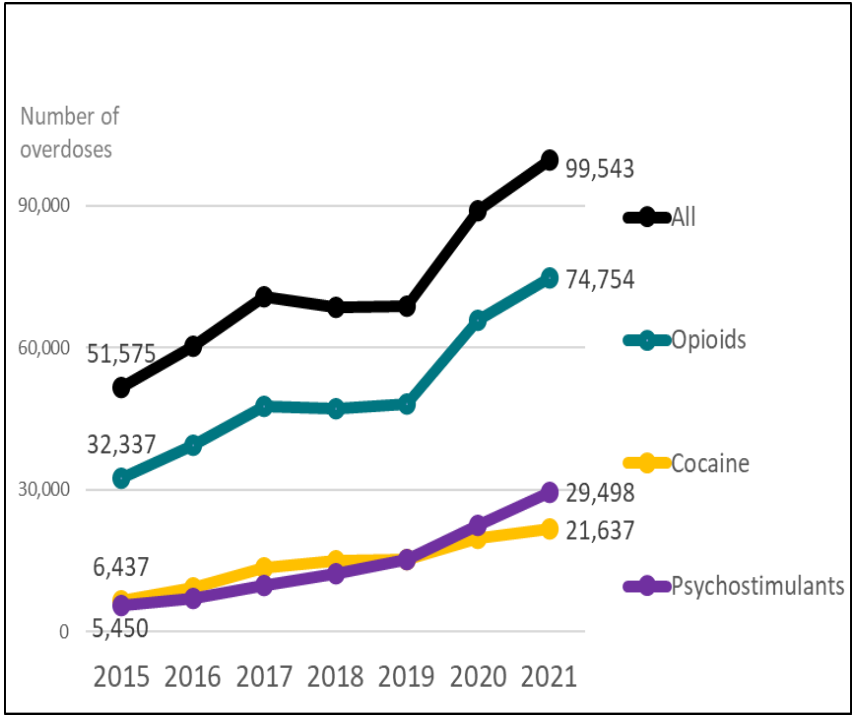
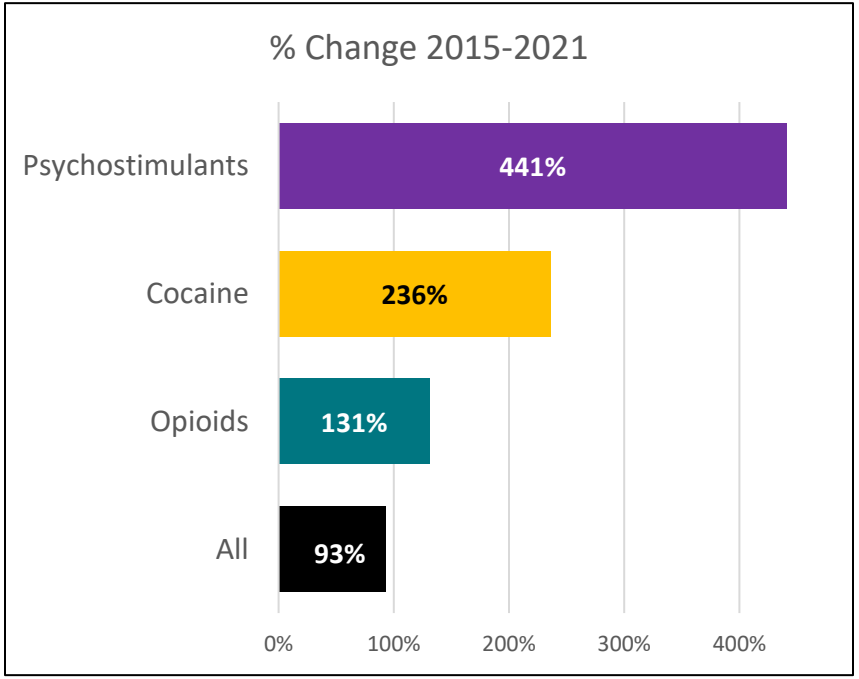
Overdose Deaths in the US by Drug Class





Source: Ahmad FB, et.al., National Center for Health Statistics. 2022

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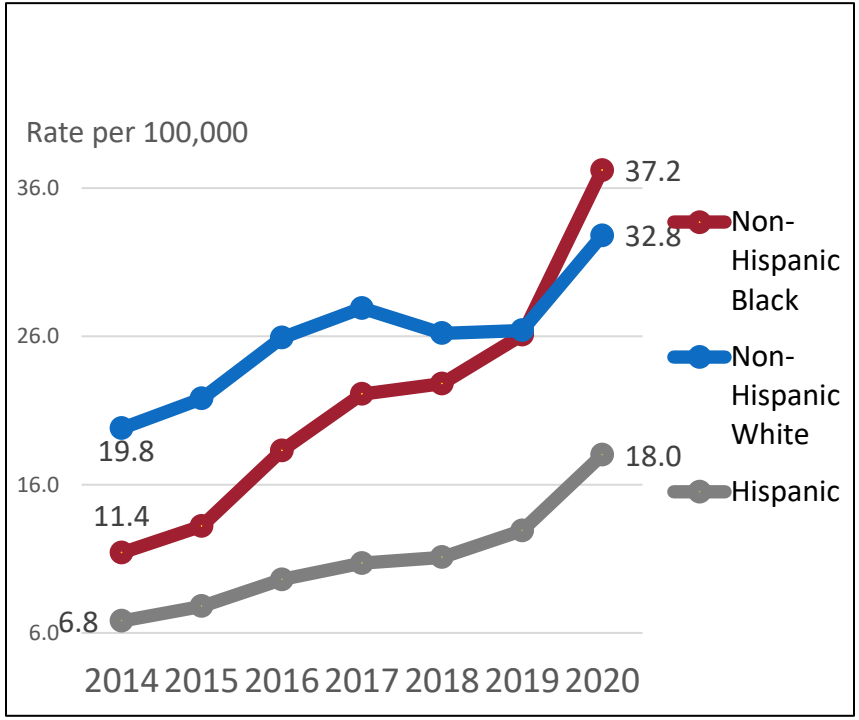
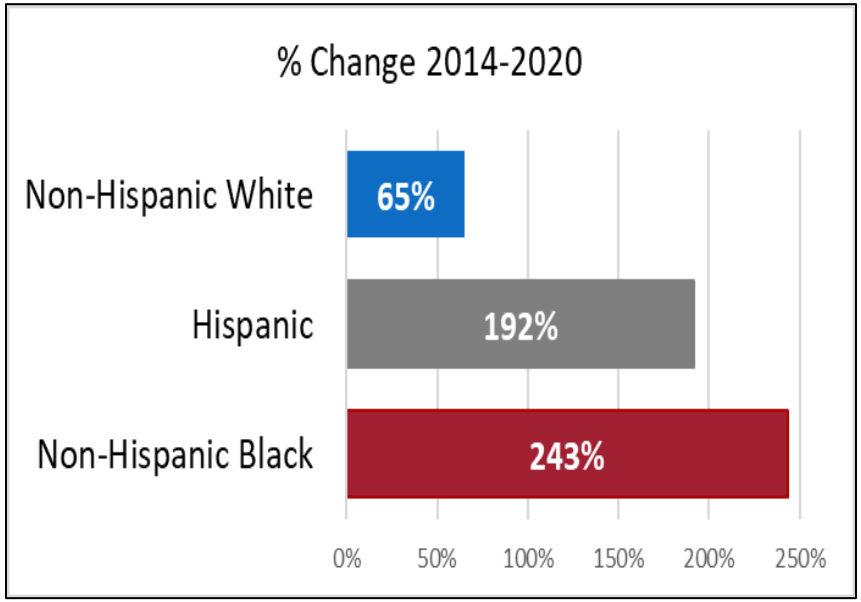
Overdose Deaths in the US by Race/Ethnicity





Source: CDC, National Center for Health Statistics, via WONDER 2021

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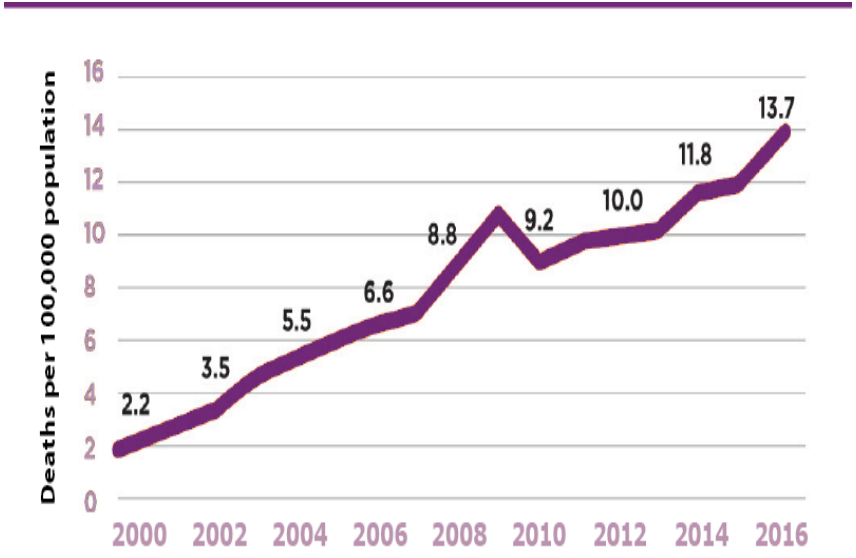
Opioid Overdose Deaths in the US among Native Americans and Alaskan Natives



Source: https://www.cdc.gov/injury/budget/opioidoverdosepolicy/TribalCommunities.html

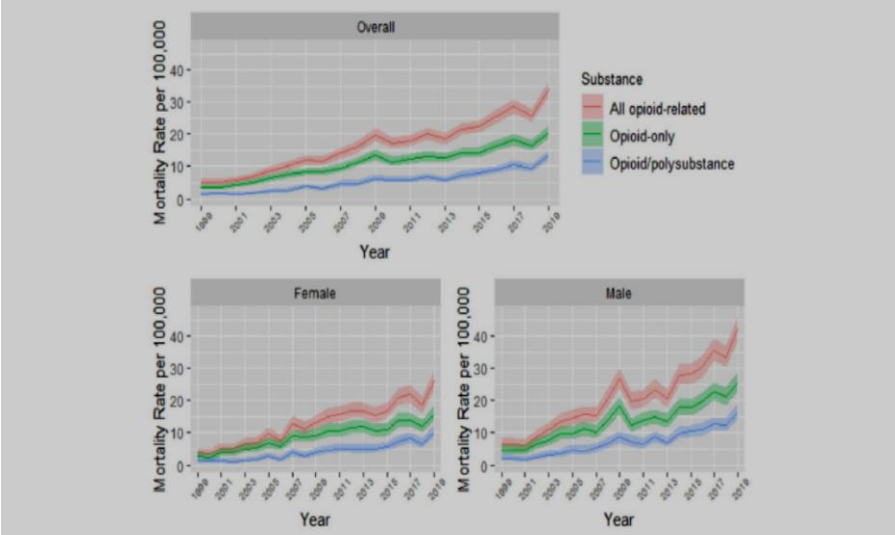
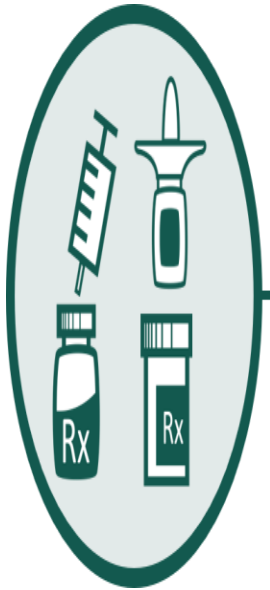


Figure 1 Trends in opioid death rates among US non-Hispanic American Indian/Alaska Native 12 and older by opioid-only (no other substances), opioid/polysubstance (opioids and at least one other substance) and all opioid-related cases (sum of opioid-only and opioid/polysubstance). Opioid-only (underlying: X40-44, X60-64, X85, Y10-Y14; multiple: T40.0, T40.1, T40.2, T40.3, T40.4, T40.6); opioid/polysubstance (underlying: R78.0, X40-45, X60-65, X85, Y10-Y15; multiple: T40.0, T40.1, T40.2, T40.3, T40.4, T40.6 and T40.5, T42.4, T43.6, T51.0, T51.1, T51.9); all-opioid related: sum of 'opioid-only' and 'opioid/polysubstance'.

Source: Qeadan F, Madden EF, Mensah NA, *et al, 2022*

Evidence for MOUD



MEDICATIONS FOR OPIOID USE DISORDER:

- Reduce spread of infectious disease
- Reduce overdose
- Reduce mortality
- Reduce recidivism
- Increase likelihood of successful treatment

Goals for MOUD and MOUD Options

Goals for MOUD

- Decrease risk for fatal and nonfatal overdoses
- Eliminate opioid withdrawal syndrome (OWS)
- Decrease opioid cravings
- Increase patient functionality
- Normalize brain anatomy and physiology
- Decrease transmission/acquisition of viral infections (Hepatitis B Virus, Hepatitis C Virus, HIV) and infection complications (abscesses, cellulitis, endocarditis)

3 FDA Approved Medication Options

Methadone: opioid full agonist; must be dispensed from an OTP; associated with decreased mortality

Buprenorphine: opioid partial agonist; Schedule lll drug; requires DEA "X" waiver to prescribe; associated with decreased mortality

Naltrexone: opioid antagonist; not a controlled substance; not associated with decreased mortality

Evidence for the Use of MOUD: Inpatient Detox Outcomes Without the Use of MOUD

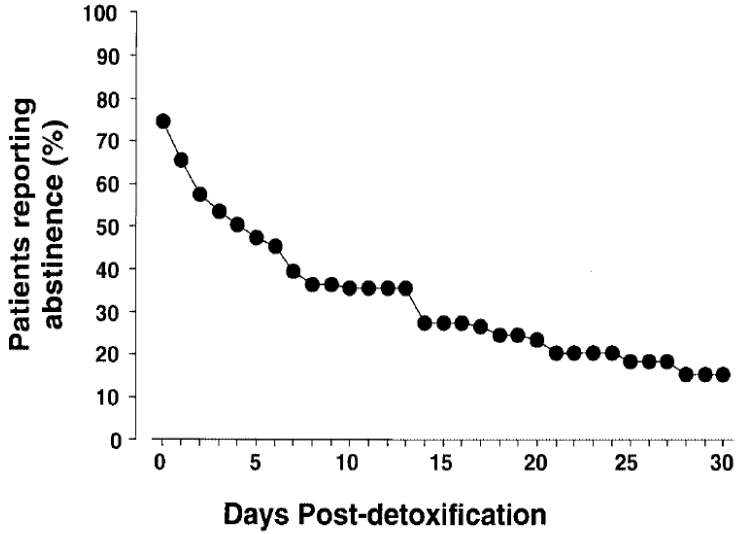


Figure 2. Abstinence from heroin. Percent of patients who remained abstinent from heroin (based on self-report) after a brief inpatient detoxification for opioid dependence. Data were collected 1 month postdetoxification. This variable was assessed during the latter half of the study with only a subset of the sample (n = 66 out of 116).

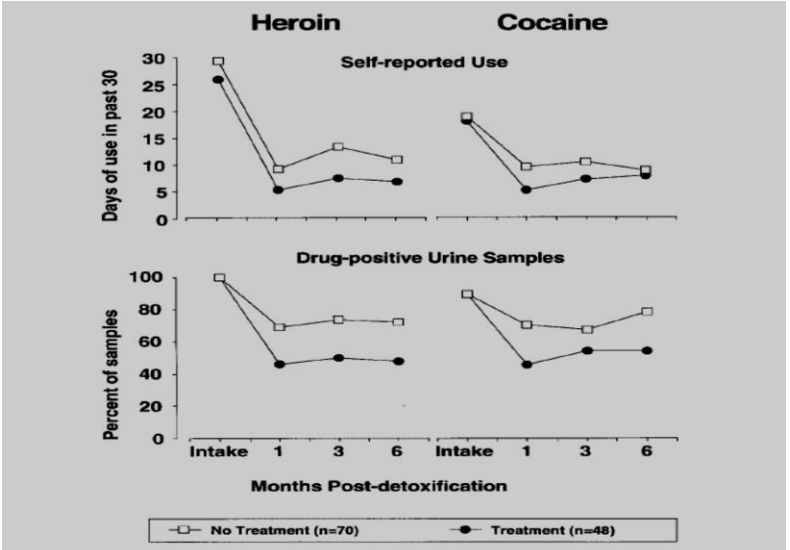
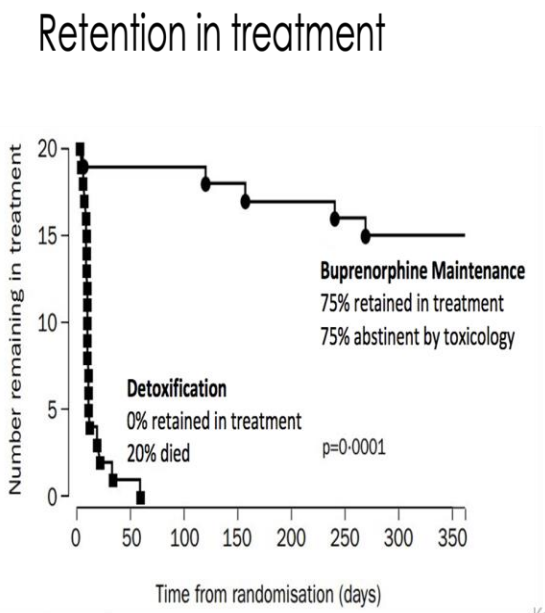


Figure 4. Self-report and urinalysis results for heroin (*left*) and cocaine (*right*). Data were collected at intake and 1, 3, and 6 months after brief inpatient opioid detoxification. Study participants were classified into two groups: treatment (engaged in ≥7 days of formal drug treatment) and no treatment (engaged in <7 days of formal treatment) after detoxification. Means for days of self-reported use were adjusted for missing data using PROC MIXED analysis. Cocaine self-report data showed no statistically significant group or time effects. Remaining variables depicted showed significant group and significant time effects, as did mean days of alcohol use and days detained or incarcerated (data not shown).

26% resumed heroin use on the day of discharge
61% resumed heroin use during the week after discharge
17% remained abstinent from heroin (by self-report) 30 days after discharge

Chutuape, et al, AJDAA, 2001

Evidence for the Use of MOUD



Kakko et al. Lancet 2003; 361: 662-8.

- **Methods:** 40 individuals aged older than 20 years, who met DSM-IV criteria for opiate dependence for at least 1 year but did not fulfil Swedish legal criteria for methadone maintenance treatment were randomly allocated either to daily buprenorphine (fixed dose 16 mg sublingually for 12 months; supervised daily administration for a least 6 months, possible take-home doses thereafter) or a tapered 6-day regimen of buprenorphine, thereafter, followed by placebo. All patients participated in cognitive-behavioral group therapy to prevent return to use, received weekly individual counselling sessions, and submitted 3x weekly supervised urine samples for analysis to detect illicit drug use. ***Our primary endpoint was 1-year retention in treatment and analysis was by intention to treat.***
- **Findings:** ***1-year retention in treatment was 75% and 0% in the buprenorphine and placebo groups, respectively (p=0·0001***; risk ratio 58·7 [95% CI 7·4–467·4]). ***Urine screens were about 75% negative for illicit opiates, central stimulants, cannabinoids, and benzodiazepines in the patients remaining in treatment.***

Evidence for the Use of MOUD

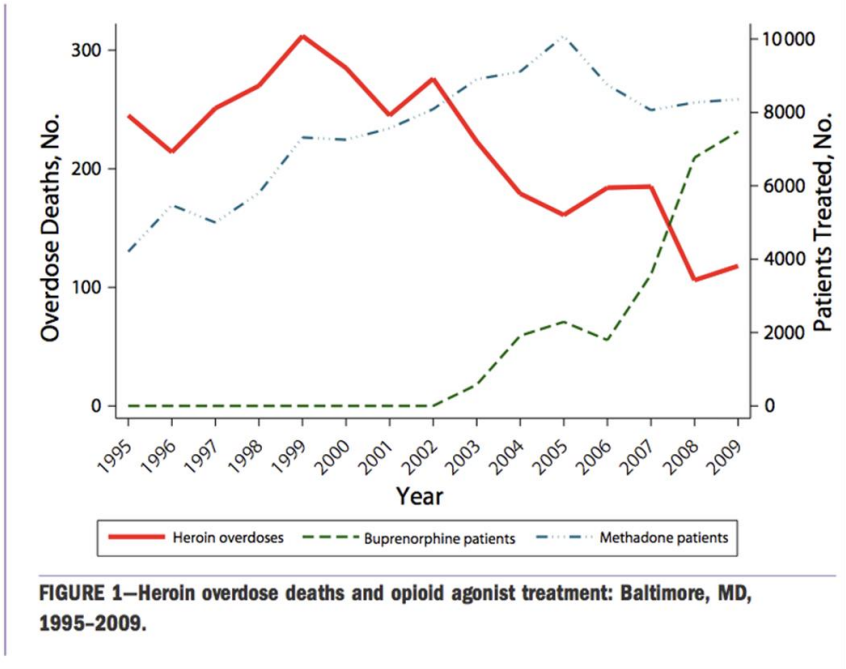
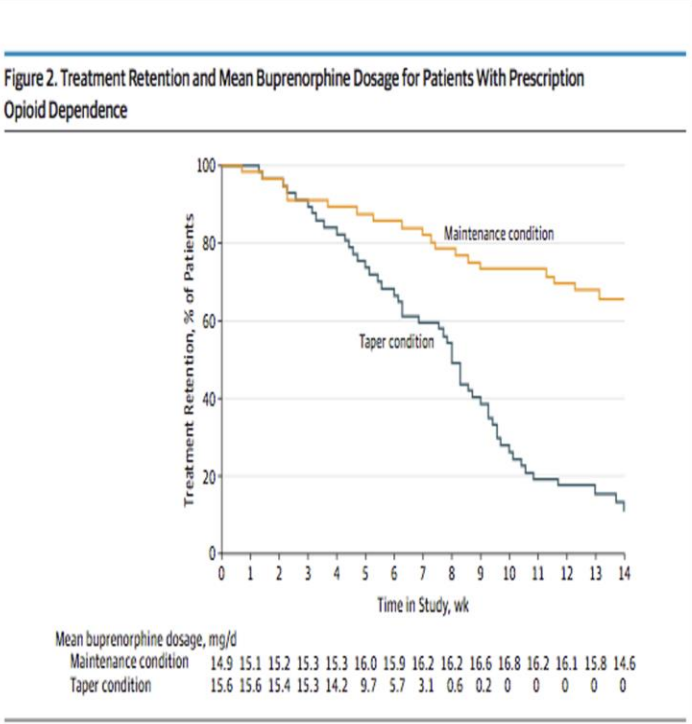


FIGURE 1—Heroin overdose deaths and opioid agonist treatment: Baltimore, MD, 1995–2009.

Source: Schwartz et al AJPH 2013

- In Baltimore, researchers found:
- A statistically significant inverse relationship between heroin OD deaths and patients treated with buprenorphine (P = .002)
- (Adjusting for heroin purity and # of methadone patients)

Evidence for the Use of MOUD



- **MAIN OUTCOMES AND MEASURES—**Illicit opioid use via results of urinalysis and patient report, treatment retention, and reinitiation of buprenorphine therapy (taper group only).
- **RESULTS—**During the trial, the mean percentage of urine samples negative for opioids was lower for patients in the taper group (35.2% [95% CI, 26.2%−44.2%]) compared with those in the maintenance group (53.2% [95% CI, 44.3%−62.0%]). Patients in the taper group reported more days per week of illicit opioid use than those in the maintenance group once they were no longer receiving buprenorphine (mean use, 1.27 [95% CI, 0.60–1.94] vs 0.47 [95% CI,0.19–0.74] days). Patients in the taper group had fewer maximum consecutive weeks of opioid abstinence compared with those in the maintenance group (mean abstinence, 2.70 [95% CI, 1.72–3.75] vs 5.20 [95% CI, 4.16–6.20] weeks). Patients in the taper group were less likely to complete the trial (6 of 57 [11%] vs 37 of 56 [66%]; P < .001). Sixteen patients in the taper group reinitiated buprenorphine treatment after the taper owing to return to use.
- **CONCLUSIONS AND RELEVANCE—*Tapering is less efficacious than ongoing maintenance treatment in patients with prescription opioid dependence who receive buprenorphine therapy in primary care.***

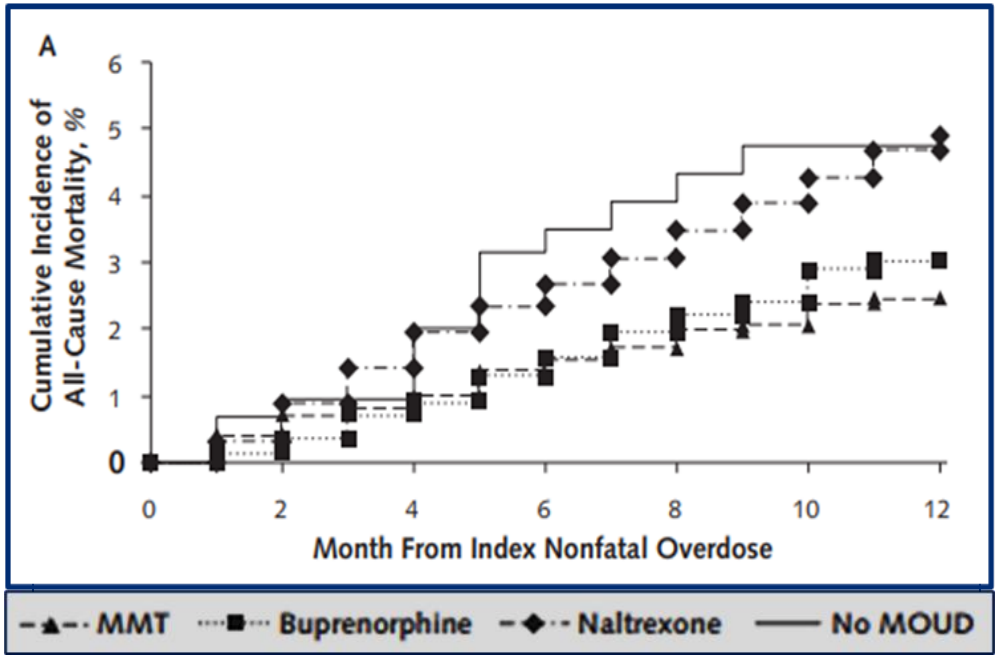
Fielin et al. JAMA 2014; 174(12): 1947-54.

Evidence for the Use of MOUD

- **Aims:**
- To compare the change in illicit opioid users' risk of fatal drug-related poisoning (DRP) associated with opioid agonist pharmacotherapy (OAP) and psychological support, and investigate the modifying effect of patient characteristics, criminal justice system (CJS) referral and treatment completion.
- **Design:**
- National data linkage cohort study of the English National Drug Treatment Monitoring System and the Office for National Statistics national mortality database. Data were analysed using survival methods.
- **Setting:**
- All services in England that provide publicly funded, structured treatment for illicit opioid users.
- **Participants:**
- Adults treated for opioid dependence during April 2005 to March 2009: 151 983 individuals; 69% male; median age 32.6 with 442 950 person-years of observation.
- **Measurements:**
- The outcome was fatal DRP occurring during periods in or out of treatment, with adjustment for age, gender, substances used, injecting status and CJS referral.
- **Findings:**
- There were 1499 DRP deaths [3.4 per 1000 person-years, 95% confidence interval (CI) = 3.2–3.6]. ***DRP risk increased while patients were not enrolled in any treatment [adjusted hazard ratio (aHR) = 1.73, 95% CI = 1.55–1.92]. Risk when enrolled only in a psychological intervention was double that during OAP (aHR = 2.07, 95% CI = 1.75–2.46). The increased risk when out of treatment was greater for men (aHR = 1.88, 95% CI = 1.67–2.12), illicit drug injectors (aHR = 2.27, 95% CI = 1.97–2.62) and those reporting problematic alcohol use (aHR = 2.37, 95% CI = 1.90–2.98).***
- **Conclusions:**
- ***Patients who received only psychological support for opioid dependence in England appear to be at greater risk of fatal opioid poisoning than those who received opioid agonist pharmacotherapy.***

Source: Pierce, M, et al, Addiction, 2016

Evidence for the Use of MOUD: Opioid Agonist Treatment is Associated with a Reduction in Mortality by ~50%



- **Results:** In the 12 months after a nonfatal overdose, 2040 persons (11%) enrolled in MMT for a median of 5 months (interquartile range, 2 to 9 months), 3022 persons (17%) received buprenorphine for a median of 4 months (interquartile range, 2 to 8 months), and 1099 persons (6%) received naltrexone for a median of 1 month (interquartile range, 1 to 2 months). Among the entire cohort, all-cause mortality was 4.7 deaths (95% CI, 4.4 to 5.0 deaths) per 100 person-years and opioid-related mortality was 2.1 deaths (CI, 1.9 to 2.4 deaths) per 100 person-years. **Compared with no MOUD, MMT was associated with decreased all-cause mortality (adjusted hazard ratio [AHR], 0.47 [CI, 0.32 to 0.71]) and opioid-related mortality (AHR, 0.41 [CI, 0.24 to 0.70]). Buprenorphine was associated with decreased all-cause mortality (AHR, 0.63 [CI, 0.46 to 0.87]) and opioid-related mortality (AHR, 0.62 [CI, 0.41 to 0.92]). No associations between naltrexone and all-cause mortality (AHR, 1.44 [CI, 0.84 to 2.46]) or opioid-related mortality (AHR, 1.42 [CI, 0.73 to 2.79]) were identified.**
- **Conclusion:** A minority of opioid overdose survivors received MOUD. ***Buprenorphine and methadone were associated with reduced all-cause and opioid-related mortality. Naltrexone was not associated with decreased mortality.***

MMT=Methadone maintenance treatment; MOUD=Medication for opioid use disorder
Source: Larochelle MR, et. al., Annals Int Med. 2018.

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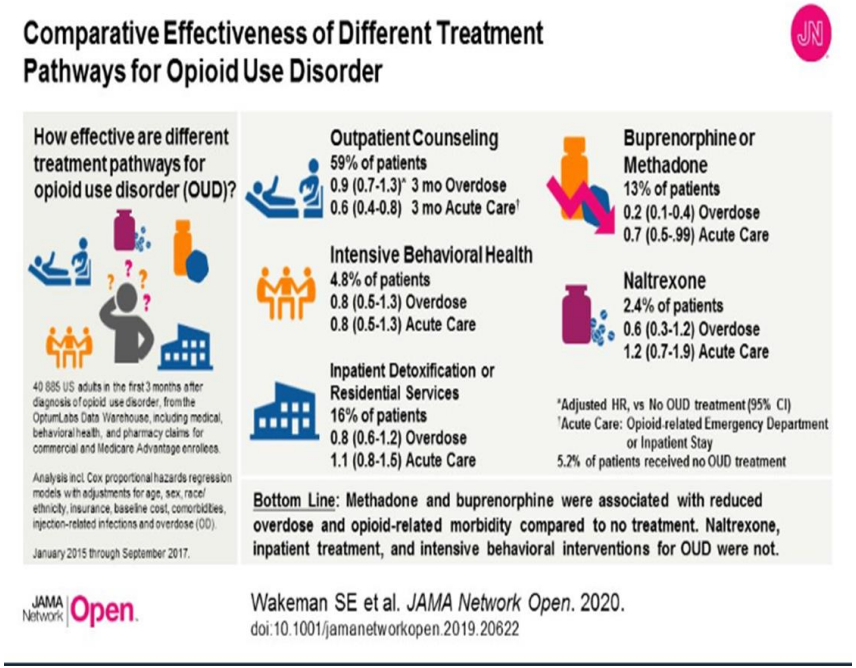
Evidence for the Use of MOUD



- **Key Points**
- **Question What is the real-world effectiveness of different treatment pathways for opioid use disorder?**
- **Findings:** *In this comparative effectiveness research study of 40 885 adults with opioid use disorder that compared 6 different treatment pathways, only treatment with buprenorphine or methadone was associated with reduced risk of overdose and serious opioid-related acute care use compared with no treatment during 3 and 12 months of follow-up.* ***Meaning Methadone and buprenorphine were associated with reduced overdose and opioid-related morbidity compared with opioid antagonist therapy, inpatient treatment, or intensive outpatient behavioral interventions and may be used as firstline treatments for opioid use disorder.***

Evidence for the Use of MOUD: MOUD Plus Access to Harm Reduction Services

JAMA Network | Open

Original Investigation | Substance Use and Addiction

Projected Estimates of Opioid Mortality After Community-Level Interventions

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Abstract

IMPORTANCE The United States is experiencing a crisis of opioid overdose. In response, the US Department of Health and Human Services has defined a goal to reduce overdose mortality by 40% by 2022.

OBJECTIVE To identify specific combinations of 3 interventions (initiating more people to medications for opioid use disorder [MOUD], increasing 6-month retention with MOUD, and increasing naloxone distribution) associated with at least a 40% reduction in opioid overdose in simulated populations.

DESIGN, SETTING, AND PARTICIPANTS This decision analytical model used a dynamic population-level state-transition model to project outcomes over a 2-year horizon. Each intervention scenario was compared with the counterfactual of no intervention in simulated urban and rural communities in Massachusetts. Simulation modeling was used to determine the associations of community-level interventions with opioid overdose rates. The 3 examined interventions were initiation of more people to MOUD, increasing individuals' retention with MOUD, and increasing distribution of naloxone. Data were analyzed from July to November 2020.

MAIN OUTCOMES AND MEASURES Reduction in overdose mortality, medication treatment capacity needs, and naloxone needs.

RESULTS No single intervention was associated with a 40% reduction in overdose mortality in the simulated communities. Reaching this goal required use of MOUD and naloxone. Achieving a 40% reduction required that 10% to 15% of the estimated OUD population not already receiving MOUD initiate MOUD every month, with 45% to 60%% retention for at least 6 months, and increased naloxone distribution. In all feasible settings and scenarios, attaining a 40% reduction in overdose mortality required that in every month, at least 10% of the population with OUD who were not currently receiving treatment initiate an MOUD.

CONCLUSIONS AND RELEVANCE In this modeling study, only communities with increased capacity for treating with MOUD and increased MOUD retention experienced a 40% decrease in overdose mortality. These findings could provide a framework for developing community-level interventions to reduce opioid overdose death.

Key Points

Question Using simulated urban and rural communities, what evidence-based practices are associated with a reduction in opioid overdose mortality of at least 40% by 2022?

Findings In this decision analytical model using simulated urban and rural communities, no single intervention or approach was associated with a 40% reduction in overdose mortality in any community. Achieving a 40% reduction required increasing capacity for treating with medications for opioid use disorder, improving retention on medications, and increased naloxone distribution.

Meaning These findings suggest that reducing opioid overdose may require substantial, coordinated effort with a focus on improving initiation with medications, retention in care, and increased naloxone distribution.

+ Invited Commentary
+ Multimedia
+ Supplemental content

Author affiliations and article information are listed at the end of this article.

- ➔ Achieving a 40% reduction in opioid overdose mortality required *increasing capacity for treating with* ***medications for opioid use disorder (MOUD)****, improving* ***retention*** *on medications, and* ***increased naloxone distribution****.*

Source: Linas, BP, et al, JAMA, 2021

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Evidence for the Use of MOUD

- Methadone and buprenorphine remain the gold standard of care for OUD; naltrexone is considered second tier treatment
- ***"The use of opioid agonist medications to treat opioid use disorders has always had its critics. Many people, including some policymakers, authorities in the criminal justice system, and treatment providers, have viewed maintenance treatments as 'substituting one substance for another' and have adhered instead to an abstinence-only philosophy that avoids the use of medications, especially those that activate opioid receptors. Such views are not scientifically supported; the research clearly demonstrates that opioid agonist therapy leads to better treatment outcomes compared to behavioral treatments alone. Moreover, withholding medications greatly increases the risk of relapse to illicit opioid use and overdose death. Decades of research have shown that the benefits of opioid agonist therapy greatly outweigh the risks associated with diversion."*** – Facing Addiction in America: The Surgeon General's Spotlight on Opioids, HHS, September 2018
- *"Scientific research has firmly established that the treatment of opioid use disorder with medication reduces OUD and related criminal activity more effectively and at far less cost than incarceration."* - Legal Action Center, 2011

Source: U.S. Department of Health and Human Services (HHS), Office of the Surgeon General, Facing Addiction in America: The Surgeon General's Spotlight on Opioids. Washington, DC: HHS, September 2018.

Evidence for the Use of MOUD: Decreased Suicide Mortality, External-cause Mortality, and All-cause Mortality

TABLE 3. Crude and adjusted hazard ratios for suicide mortality, external-cause mortality, and all-cause mortality for each MOUD agent[a]

	Unadjusted		Adjusted for Age, Gender, and Race		Further Adjusted for Medical and Psychiatric Comorbidities		Further Adjusted for Health Care Utilization	
Measure and Agent	Hazard Ratio	95% CI	Hazard Ratio	95% CI	Hazard Ratio	95% CI	Hazard Ratio	95% CI
Suicide mortality								
Buprenorphine	0.37	0.24, 0.56	0.33	0.22, 0.49	0.34	0.22, 0.51	0.34	0.23, 0.52
Methadone	0.38	0.17, 0.85	0.43	0.19, 0.95	0.47	0.21, 1.06	0.47	0.21, 1.08
Naltrexone	1.45	0.77, 2.76	1.38	0.73, 2.63	1.30	0.68, 2.48	1.28	0.67, 2.44
External-cause mortality								
Buprenorphine	0.27	0.23, 0.32	0.25	0.21, 0.29	0.26	0.22, 0.31	0.27	0.23, 0.31
Methadone	0.45	0.34, 0.59	0.49	0.37, 0.64	0.53	0.40, 0.71	0.53	0.40, 0.71
Naltrexone	0.98	0.75, 1.28	0.96	0.73, 1.25	0.90	0.69, 1.18	0.88	0.67, 1.15
All-cause mortality								
Buprenorphine	0.25	0.23, 0.28	0.26	0.23, 0.29	0.27	0.24, 0.30	0.27	0.24, 0.30
Methadone	0.51	0.43, 0.60	0.49	0.42, 0.58	0.52	0.44, 0.61	0.51	0.43, 0.60
Naltrexone	0.71	0.58, 0.88	0.67	0.55, 0.83	0.64	0.52, 0.79	0.64	0.52, 0.79

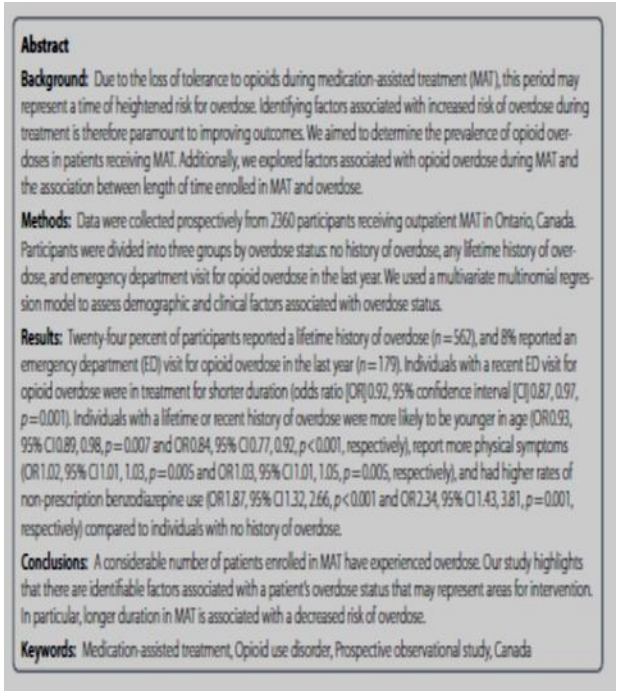
[a] MOUD=medications for opioid use disorder. Reference period is off MOUD.

Watts, et al, Am J Psychiatry, April 2022

- **MOUD start associated with decreased suicide mortality, though less so than individuals on stable MOUD**
- **MOUD cessation associated with increased suicide mortality, external-cause mortality, and all-cause mortality**
- ***Buprenorphine was associated with a >65% decrease in suicide mortality***
- ***Naltrexone showed no indication of a reduced risk of suicide mortality***
- Methadone's effect on suicide risk was unclear; persons who received methadone in this study had far more mental health contacts than those on buprenorphine or naltrexone, which may have diminished the effects in this study of methadone's effect on the decrease of suicide mortality

Evidence for the Use of MOUD: How Long Should Persons Remain on MOUD?

- LONG ENOUGH...!!! ***As long as the patient receives benefit from taking the medication, the patient should stay on the medication***
- It is different for every patient, but...***return to use and fatal overdose rates are higher for shorter courses of treatment and for no treatment***
- At a minimum, patients should remain on MOUD for 6-12 months; but, in reality, MOUD is often much longer, and, often chronic
- Per one study, the average duration on buprenorphine treatment is 8-9 years
- OUD is a CHRONIC medical condition, and, like other chronic medical conditions, may require medication CHRONICALLY (think long term v. lifetime, but NOT short term); like a person with diabetes mellitus needing insulin for life to manage their diabetes mellitus



Abstract

Background: Due to the loss of tolerance to opioids during medication-assisted treatment (MAT), this period may represent a time of heightened risk for overdose. Identifying factors associated with increased risk of overdose during treatment is therefore paramount to improving outcomes. We aimed to determine the prevalence of opioid overdoses in patients receiving MAT. Additionally, we explored factors associated with opioid overdose during MAT and the association between length of time enrolled in MAT and overdose.

Methods: Data were collected prospectively from 2360 participants receiving outpatient MAT in Ontario, Canada. Participants were divided into three groups by overdose status: no history of overdose, any lifetime history of overdose, and emergency department visit for opioid overdose in the last year. We used a multivariate multinomial regression model to assess demographic and clinical factors associated with overdose status.

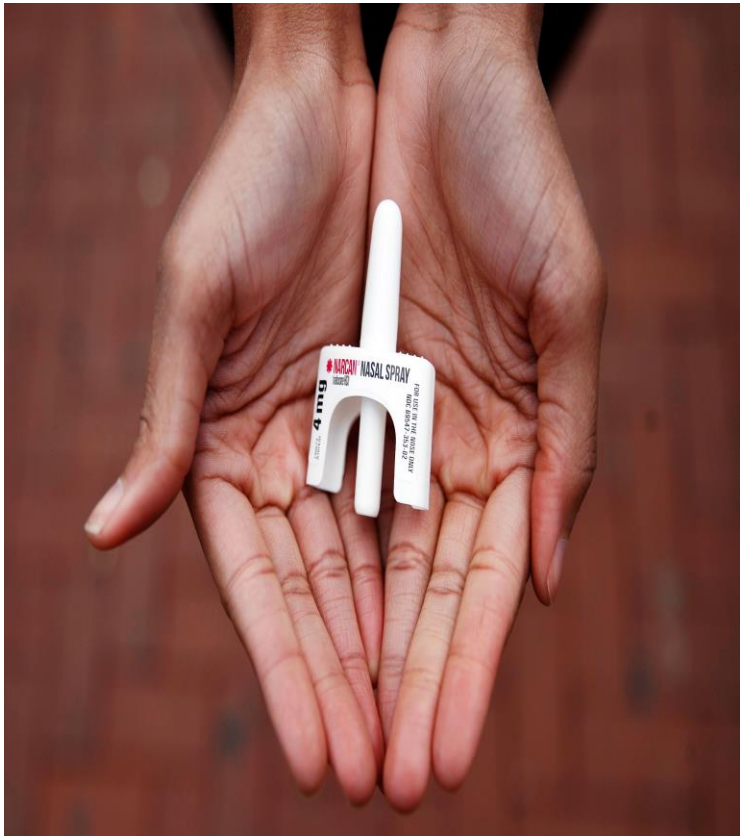
Results: Twenty-four percent of participants reported a lifetime history of overdose ($n = 562$), and 8% reported an emergency department (ED) visit for opioid overdose in the last year ($n = 179$). Individuals with a recent ED visit for opioid overdose were in treatment for shorter duration (odds ratio [OR] 0.92, 95% confidence interval [CI] 0.87, 0.97, $p = 0.001$). Individuals with a lifetime or recent history of overdose were more likely to be younger in age (OR 0.93, 95% CI 0.89, 0.98, $p = 0.007$ and OR 0.84, 95% CI 0.77, 0.92, $p < 0.001$, respectively), report more physical symptoms (OR 1.02, 95% CI 1.01, 1.03, $p = 0.005$ and OR 1.03, 95% CI 1.01, 1.05, $p = 0.005$, respectively), and had higher rates of non-prescription benzodiazepine use (OR 1.87, 95% CI 1.32, 2.66, $p < 0.001$ and OR 2.34, 95% CI 1.43, 3.81, $p = 0.001$, respectively) compared to individuals with no history of overdose.

Conclusions: A considerable number of patients enrolled in MAT have experienced overdose. Our study highlights that there are identifiable factors associated with a patient's overdose status that may represent areas for intervention. In particular, longer duration in MAT is associated with a decreased risk of overdose.

Keywords: Medication-assisted treatment, Opioid use disorder, Prospective observational study, Canada

Source: Au, VYO, et al, Harm Reduction Journal, 2021

Evidence for naloxone



Overview: Evaluations of Opioid Overdose Education and Naloxone Distribution Programs

Feasibility

- Piper et al. Subst Use Misuse 2008: 43; 858-70.
- Doe-Simkins et al. Am J Public Health 2009: 99: 788-791.
- Enteen et al. J Urban Health 2010:87: 931-41.
- Bennett et al. J Urban Health. 2011: 88; 1020-30.
- Walley et al. JSAT 2013; 44:241-7. (Methadone and detox programs)

Increased knowledge and skills

- Green et al. Addiction 2008: 103;979-89.
- Tobin et al. Int J Drug Policy 2009: 20; 131-6.
- Wagner et al. Int J Drug Policy 2010: 21: 186-93.

No increase in use, increase in entrance to SUD treatment

- Seal et al. J Urban Health 2005:82:303-11.
- Doe-Simkins et al. BMC Public Health 2014 14:297.

Reduction in overdose in communities

- Maxwell et al. J Addict Dis 2006:25; 89-96.
- Evans et al. Am J Epidemiol 2012; 174: 302-8.
- Walley et al. BMJ 2013; 346: f174.

Cost-effective $438 (best) $14,000 (worst) per quality-adjusted life year gained

Coffin and Sullivan. Ann Intern Med. 2013 Jan 1;158(1):1-9.

Evidence for naloxone

Proof of Concept

Table. Large and established naloxone prescription programs in the United States (February 2006).

City	Year of Establishment	Number of Trainings/ Prescriptions	Number of Reported Overdose Reversals
Chicago	1999	4,600	416
New Mexico	2001	1,312	222
San Francisco	2003	650	141
Baltimore	2004	951	131
New York City	2005	938	73

Chicago: D. Bigg, written communication, March 2006; New Mexico: P. Fiuty, written communication, March 2006; San Francisco: E. Huriaux, written communication, March 2006; Baltimore: M. Rucker, written communication, March 2006; New York: S. Stancliff, written communication, March 2006.

Proof of Concept

- Death from a heroin overdose most commonly occurs at home in the company of other people and most commonly occurs one to three hours after injection.
- Numerous communities have taken advantage of this opportunity for treatment by implementing overdose prevention education to active heroin users as well as prescribing naloxone for home use.
- ***Naloxone is a specific opioid antagonist with no agonist properties and no potential for misuse. It is inexpensive, non-scheduled and readily reverses the respiratory depression and sedation caused by heroin as well as causing transient opioid withdrawal symptoms.***
- Program implementation considerations, legal ramifications, and research needs for prescription naloxone are discussed.

Sporer, et al, Annals of Emergency Medicine, 2/2007

Evidence for naloxone

Trained v. Untrained Rescuers: no difference in OD reversal success rates

Abstract

Background: One approach to preventing opioid overdose, a leading cause of premature, preventable mortality, is to provide overdose education and naloxone distribution (OEND). Two outstanding issues for OEND implementation include 1) the dissemination of OEND training from trained to untrained community members; and 2) the concern that OEND provides active substance users with a false sense of security resulting in increased opioid use.

Methods: To compare overdose rescue behaviors between trained and untrained rescuers among people reporting naloxone rescue kit use; and determine whether heroin use changed after OEND, we conducted a retrospective cohort study among substance users in the Massachusetts OEND program from 2006 to 2010. We used chi square and t-test statistics to compare the differences in overdose management characteristics among overdoses managed by trained versus untrained participants. We employed Wilcoxon signed rank test to compare median difference among two repeated measures of substance use among participants with drug use information collected more than once.

Results: Among 4,926 substance-using participants, 295 trained and 78 untrained participants reported one or more rescues, resulting in 599 rescue reports. We found no statistically significant differences in help-seeking ($p = 0.41$), rescue breathing ($p = 0.54$), staying with the victim ($p = 0.84$) or in the success of naloxone administration ($p = 0.69$) by trained versus untrained rescuers. We identified 325 OEND participants who had drug use information collected more than once. We found no significant overall change in the number of days using heroin in past 30 days (decreased 38%, increased 35%, did not change 27%, $p = 0.52$).

Conclusion: Among 4926 substance users who participated in OEND, 373(7.6%) reported administering naloxone during an overdose rescue. We found few differences in behavior between trained and untrained overdose rescuers. Prospective studies will be needed to determine the optimal level of training and whether naloxone rescue kits can meet an over-the-counter standard. With no clear evidence of increased heroin use, this concern should not impede expansion of OEND programs or policies that support them.

Keywords: Overdose, Opioids, Bystander naloxone, Rescue, People who use drugs

Doe-Simkins, et al, BMC Public Health, 2014

Access to naloxone did not change substance use patterns

Table 3 Change in substance use among overdose education and naloxone distribution program participants between first and second enrollment- number of days and substances used, past 30 days

N = 325	Increased	Decreased	No change	p-value*
Heroin	115 (35%)	122 (38%)	88 (27%)	0.52
Methadone	84 (26%)	70 (22%)	171 (52%)	0.72
Buprenorphine	73 (22%)	66 (20%)	186 (58%)	0.31
Other opioids	59 (18%)	62 (19%)	205 (63%)	0.51
Cocaine	83 (26%)	96 (30%)	146 (44%)	0.41
Alcohol	69 (21%)	70 (22%)	186 (57%)	0.86
Benzo/Barbiturate	99 (30%)	74 (23%)	152 (47%)	0.004
Number of substances** used	131 (40%)	125 (38%)	69 (21%)	0.65

*Wilcoxon signed rank test which compares the median difference between two repeated measures among the repeat enrollers.
**Participants were asked about use of heroin, methadone, buprenorphine, other opioids, cocaine, alcohol, benzodiazepine/barbiturate and methamphetamine.

Evidence for naloxone

OD Education and Nasal Naloxone Distribution

- **Objective:** To evaluate the impact of state supported overdose education and nasal naloxone distribution (OEND) programs on rates of opioid related death from overdose and acute care utilization in Massachusetts.
- **Design:** Interrupted time series analysis of opioid related overdose death and acute care utilization rates from 2002 to 2009 comparing community-year strata with high and low rates of OEND implementation to those with no implementation.
- **Setting:** 19 Massachusetts communities (geographically distinct cities and towns) with at least five fatal opioid overdoses in each of the years 2004 to 2006.
- **Participants:** OEND was implemented among opioid users at risk for overdose, social service agency staff, family, and friends of opioid users.
- **Intervention:** OEND programs equipped people at risk for overdose and bystanders with nasal naloxone rescue kits and trained them how to prevent, recognize, and respond to an overdose by engaging emergency medical services, providing rescue breathing, and delivering naloxone.
- **Main outcome measures:** Adjusted rate ratios for annual deaths related to opioid overdose and utilization of acute care hospitals.
- **Results:** Among these communities, OEND programs trained 2912 potential bystanders who reported 327 rescues. Both community-year strata with 1-100 enrollments per 100 000 population (adjusted rate ratio 0.73, 95% confidence interval 0.57 to 0.91) and community-year strata with greater than 100 enrollments per 100 000 population (0.54, 0.39 to 0.76) had significantly reduced adjusted rate ratios compared with communities with no implementation. Differences in rates of acute care hospital utilization were not significant.
- **Conclusions:** ***Opioid overdose death rates were reduced in communities where OEND was implemented. This study provides observational evidence that by training potential bystanders to prevent, recognize, and respond to opioid overdoses, OEND is an effective intervention.***

Walley, et al, BMJ, January 2013

Unadjusted unintentional opioid related overdose death rates in 19 communities with no, low, and high enrollment in overdose education and nasal naloxone distribution program in Massachusetts, 2002-09

Figures

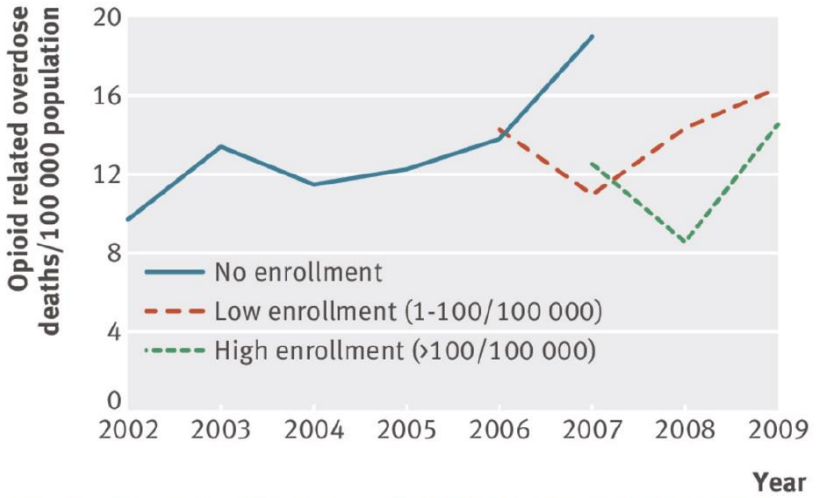


Fig 1 Unadjusted unintentional opioid related overdose death rates in 19 communities with no, low, and high enrollment in overdose education and nasal naloxone distribution program in Massachusetts, 2002-09

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Evidence for naloxone: Are take home naloxone programs effective?

- **Background and Aims:** Fatal outcome of opioid overdose, once detected, is preventable through timely administration of the antidote naloxone. Take-home naloxone provision directly to opioid users for emergency use has been implemented recently in more than 15 countries worldwide, albeit mainly as pilot schemes and without formal evaluation. This systematic review assesses the effectiveness of take-home naloxone, with two specific aims: (1) to study the impact of take-home naloxone distribution on overdose-related mortality; and (2) to assess the safety of take-home naloxone in terms of adverse events.
- **Methods:** PubMed, MEDLINE and PsychINFO were searched for English-language peer-reviewed publications(randomized or observational trials) using the Boolean search query: (opioid OR opiate) AND overdose AND prevention. Evidence was evaluated using the nine Bradford Hill criteria for causation, devised to assess a potential causal relationship between public health interventions and clinical outcomes when only observational data are available.
- **Results:** A total of 1397 records (1164 after removal of duplicates) were retrieved, with 22 observational studies meeting eligibility criteria. Due to variability in size and quality of the included studies, meta-analysis was dismissed in favor of narrative synthesis. From eligible studies, we found take-home naloxone met all nine Bradford Hill criteria. The additional five World Health Organization criteria were all either met partially (two) or fully (three). Even with take-home naloxone administration, fatal outcome was reported in one in 123 overdose cases (0.8%; 95% confidence interval = 0.4, 1.2).
- **Conclusions: Take-home naloxone programs are found to reduce overdose mortality among program participants and in the community and have a low rate of adverse events.**

McDonald, et al, Addiction, 2016

Evidence for naloxone: naloxone use among OD prevention trainees in NYC

Naloxone use among OD prevention trainees in NYC: A longitudinal cohort study

- **Background:** Providing naloxone to laypersons who are likely to witness an opioid overdose is now a widespread public health response to the national opioid overdose epidemic. Estimating the proportion of individuals who use naloxone can define its potential impact to reduce overdose deaths at a population level. We determined the proportion of study participants who used naloxone within 12 months following training and factors associated with witnessing overdose and naloxone use.
- **Methods:** We conducted a prospective, observational study of individuals completing overdose prevention training (OPT) between June and September 2013. Participants were recruited from New York City's six largest overdose prevention programs, all operated by syringe exchange programs. Questionnaires were administered at four time points over 12 months. Main outcomes were witnessing or experiencing overdose, and naloxone administration.
- **Results:** Of 675 individuals completing OPT, 429 (64%) were approached and 351 (52%) were enrolled. Overall, 299 (85%) study participants completed at least one follow-up survey; **128 (36%) witnessed at least one overdose. Of 312 witnessed opioid overdoses, naloxone was administered in 241 events (77%); 188 (60%) by the OPT study participant. Eighty-six (25%) study participants administered naloxone at least once. Over one third of study participants (30, 35%) used naloxone 6 or more months after training.**
- **Conclusions: Witnessing an overdose and naloxone use was common among this study cohort of OPT trainees. Training individuals at high risk for witnessing overdoses may reduce opioid overdose mortality at a population level if sufficient numbers of potential responders are equipped with naloxone.**

Table 2
Bivariable and multivariable results: factors associated with witnessing an overdose.[a]

	OR (95% CI)[b]	p-value	AOR (95% CI)[i]	p-value
Age	1.00 (0.97–1.02)	0.71	0.99 (0.96–1.02)	0.39
Gender[h]				
Male	Ref	Ref	Ref	Ref
Female	0.94 (0.58–1.53)	0.8	1.21 (0.68–2.18)	0.52
Race/Ethnicity				
Hispanic/Latino	Ref	Ref	Ref	Ref
White	1.55 (0.70–3.43)	0.28	0.80 (0.31–2.08)	0.65
Black/African American	1.20 (0.72–2.00)	0.49	**2.41 (1.22–4.76)**	**0.01**
Other	–	–	–	–
Education				
Less than high school	Ref	Ref	Ref	Ref
High school or GED	1.38 (0.80–2.37)	0.25	1.18 (0.62–2.22)	0.62
Some college or college graduate	**2.30 (1.27–4.17)**	**0.01**	**2.54 (1.21–5.32)**	**0.01**
Drug services participation				
Methadone Maintenance (MMTP) only	Ref	Ref	Ref	Ref
Syringe exchange (SEP)[c]	**2.04 (1.17–3.53)**	**0.01**	1.82 (0.92–3.59)	0.08
No SEP or MMTP	**0.36 (0.17–0.76)**	**0.01**	0.41 (0.14–1.26)	0.12
Housing				
Stable permanent[d]	Ref	Ref	Ref	Ref
Temporary[e]	1.56 (0.93–2.62)	0.09	1.29 (0.70–2.38)	0.42
Unstable[f]	**2.01 (1.00–4.05)**	**0.05**	1.55 (0.67–3.55)	0.3
Criminal justice involvement	1.58 (0.96–2.60)	0.07		
Receives public benefits	0.91 (0.48–1.74)	0.78		
Has health insurance	1.16 (0.54–2.50)	0.71		
Has primary care physician	0.70 (0.42–1.15)	0.16		
Employed	1.21 (0.60–2.44)	0.59		
Medication/substance use during study period				
Medication use[g]				
Prescription painkillers	1.05 (0.66–1.68)	0.83		
Benzodiazepines	**1.81 (1.14–2.89)**	**0.01**	1.12 (0.61–2.04)	0.71
Methadone	**2.21 (1.31–3.70)**	**< 0.01**	1.88 (0.79–4.47)	0.16
Buprenorphine	1.41 (0.66–3.02)	0.38		
Substance use				
Heroin	**1.68 (1.05–2.67)**	**0.03**	1.09 (0.59–2.00)	0.79
Cocaine/crack	1.55 (0.96–2.51)	0.07		
Alcohol	1.16 (0.73–1.85)	0.52		
Injected within year prior to OPT	1.59 (0.98–2.57)	0.06		
Overdose history				
Witnessed OD in lifetime[j]	**4.94 (2.45–9.96)**	**< 0.01**		
Witnessed OD in 3 months prior to baseline	**6.56 (2.87–15.02)**	**< 0.01**	**4.96 (1.99–12.41)**	**< 0.01**
Personal OD in lifetime	**1.81 (1.12–2.94)**	**0.02**	1.28 (0.71–2.31)	0.41
Personal OD in 3 months prior to baseline	3.81 (0.76–19.20)	0.11		

Siegler, et al, Drug and Alcohol Dependence, October 2017

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Evidence for naloxone: Myth of ‘naloxone resistance’

Why might naloxone not be effective?

- Severe hypercapnia
- Hypoglycemia
- Non-opioid ingestion (mimic) e.g., atypical antipsychotic, clonidine/guanfacine, xylazine, alcohol/sedatives
- Polydrug OD involving opioid and other sedating drugs*
- Anoxic injury present
- Head injury/seizure
- Administration technique poor
- Other?

slide courtesy of Timothy Wiegand, MD

Evidence for naloxone: In the era of illicitly manufactured fentanyl, is an increased amount of naloxone needed?

- ***Background*:** Illicitly manufactured fentanyl (IMF) prevalence has increased. However, there is uncertainty about naloxone dose(s) used by nonmedical bystanders to reverse opioid overdoses in the context of increasing IMF.
- ***Methods*:** We used community naloxone distribution program data about naloxone doses and fatal opioid overdoses from the Allegheny County Medical Examiner. From January 2013 to December 2016, staff interviewed participants who administered naloxone in response to 1072 overdoses. We calculated frequencies, percentages, and conducted a 1-way analysis of variance (ANOVA).
- ***Results*: *Despite increases in fentanyl-contributed deaths, there were no statistically significant differences between any of the 4 years (2013-2016) on average number of naloxone doses used by participants to reverse an overdose*** (*F* = 0.88; *P* = .449).
- ***Conclusion*: Even though IMF is more potent than heroin and is a rapidly increasing contributor to drug overdose deaths in Allegheny County, the average dose of naloxone administered has not changed.** Our findings differ from studies in different areas also experiencing increasing IMF prevalence. Additional investigations are needed to clarify the amount of naloxone needed to reverse opioid overdoses in the community caused by new synthetic opioids.

Bell, A, et al, Substance Abuse, 2019

- **Introduction:** Illicitly manufactured fentanyl (IMF) is responsible for a growing number of deaths. Some case series have suggested that IMF overdoses require significantly higher naloxone doses than heroin overdoses. Our objective was to determine if the naloxone dose required to treat an opioid overdose is associated with the finding of fentanyl, opiates, or both on urine drug screen (UDS).
- **Methods:** A retrospective chart review was conducted at a single emergency department and its affiliated emergency medical services (EMS) agency. The charts of all patients who received naloxone through this EMS from 1/1/2017 to 6/15/2018 were reviewed. The study included patients diagnosed with a non-suicidal opioid overdose whose UDS was positive for opiates, fentanyl, or both. Data collected included demographics, vital signs, initial GCS, EMS and ED naloxone administrations, response to treatment, laboratory findings, and ED disposition. The fentanyl-only and fentanyl + opiate groups were compared to the opiate-only group using the stratified (by ED provider) variant of the Mann-Whitney U test.
- **Results:** Eight hundred and thirty-seven charts were reviewed, and 121 subjects were included in the final analysis. The median age of included subjects was 38 years and 75% were male***. In the naloxone dose analysis, neither the fentanyl-only (median 0.8 mg, IQR 0.4–1.6; p = 0.68) nor the fentanyl + opiate (median 0.8 mg, IQR 0.4–1.2; p = 0.56) groups differed from the opiate only group (median 0.58 mg, IQR 0.4–1.6).***
- **Conclusion:** ***Our findings refute the notion that high potency synthetic opioids like illicitly manufactured fentanyl require increased doses of naloxone to successfully treat an overdose. There were no significant differences in the dose of naloxone required to treat opioid overdose patients with UDS evidence of exposure to fentanyl, opiates, or both.*** Further evaluation of naloxone stocking and dosing protocols is needed.

Carpenter, et al, J Med Toxicol, Jan 2020

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Evidence for naloxone: In the era of illicitly manufactured fentanyl, is an increased amount of naloxone needed?

CASE 1 Naloxone dosing by UDS

- No differences in dose by UDS result
- Top Graph
  - Fentanyl+ (blue)
  - Opiate + (red)
  - Fentanyl + Opioid +
- Bottom Graph (Fentanyl groups combined)
  - Opiate (red)
  - Fentanyl involved (fentanyl + fentanyl + opiate)

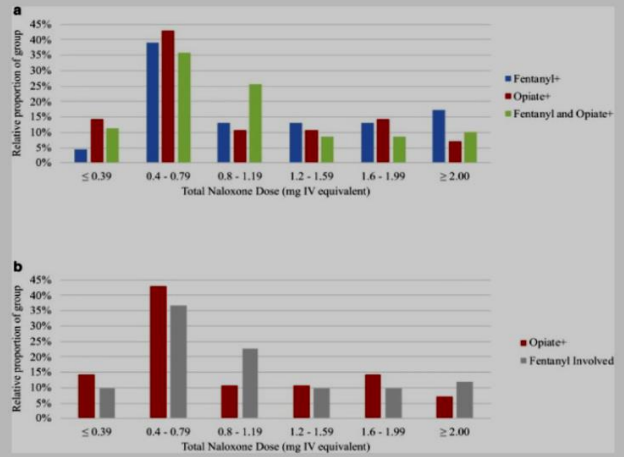

Fig. 2.

Distribution of naloxone dosing by UDS results. **a** Comparing fentanyl+, opiate+ and fentanyl and opiate+ cases. **b** Fentanyl+ and fentanyl and opiate+ groups are combined to form the fentanyl-involved group

slide courtesy of Timothy Wiegand, MD

Evidence for naloxone: Is high dose naloxone needed?

- **Background:** Advocates for more powerful opioid antagonists often cite two retrospective studies which found that emergency medical services (EMS) providers responding to a suspected opioid overdose were more likely to administer multiple doses of naloxone in 2015 (18.2%) compared to 2012 (14.5%) (Faul et al., 2017) and in 2016 (21.4%) compared to 2013 (15.0%) (Geiger, Smart, & Stein, 2020). However, these studies did not describe the route or dose of these administrations. IN naloxone administrations were likely rare as trained clinicians often prefer to carefully titrate IV dosing and may also administer IM. The significance of a modest increase in multiple administrations of unknown IV and IM doses is difficult to ascertain. ***Given widespread news reports describing the increased prevalence of potent synthetic opioids, often accompanied by alarmist misinformation about passive exposure risk, it is plausible that the increase in multiple naloxone administrations among EMS is an artifact of availability bias with multiple doses of naloxone administered out of an abundance of caution rather than based on clinical signs and symptoms. Patients treated for a suspected opioid overdose may also appear to need more naloxone due to intentional concomitant use of opioids and other sedating drugs (e.g., alcohol, benzodiazepines) and contamination of the illegal opioid supply with non-opioid depressants (e.g., xylazine, barbiturates).***

- Three other studies, two in emergency departments and one in a syringe services program, provide superior insight regarding the hypothesized need for more powerful opioid antagonists. ***An analysis of prehospital and emergency department naloxone administration was conducted in Atlanta from 2017 to 2018 (Carpenter et al., 2020). This study included naloxone dosing information and urine drug screen results, and it found that the median dose of naloxone administered in successful reversals did not differ significantly based on the presence or absence of fentanyl (0.8 mg IV vs 0.56 mg IV, p = 0.79).*** A study conducted in Boston from 2017 to 2018 compared blood fentanyl concentrations to naloxone doses administered among patients experiencing a non-fatal opioid-related overdose (Krotulski et al., 2021). All 20 subjects reported use of heroin, and fentanyl was detected in 19. ***No relationship between blood fentanyl concentration and naloxone dose administered was identified***. Data collected from clients of a syringe services program in Pittsburgh, Pennsylvania from 2013 to 2016 corroborate these results (Bell, Bennett, Jones, Doe-Simkins, & Williams, 2019). ***While the proportion of opioid overdose deaths testing positive for fentanyl in the county increased from 3.5% to 68.7% during this timeframe, the reported naloxone doses used by clients to effectively reverse opioid overdoses did not change. Notably, the program distributed relatively low-dose 0.4 mg vials for IM administration, and a mean of only 1.56 doses per reversal were required.***

Hill, et al, International Journal of Drug Policy, 2022

Evidence for naloxone: Is high dose naloxone needed?

- **Unintended Consequences:** ***The proliferation of powerful opioid antagonists could have unintended consequences that are counterproductive to efforts to prevent opioid-related overdose deaths. Precipitated opioid withdrawal is a known risk of naloxone for opioid-tolerant individuals, producing symptoms such as hyperalgesia, diarrhea, and vomiting, particularly at higher doses (Purssell et al., 2021). Aversion to being administered naloxone and experiencing opioid withdrawal symptoms was thoroughly documented in an ethnographic study conducted in Scotland from 1997 to 1999 (Neale & Strang, 2015).*** Nearly all subjects who were familiar with naloxone described it negatively and indicated it should be avoided, and many expressed mistrust of health professionals' judgment regarding when to administer it. Notably, while this study included interviews with 200 people who use opioids, it occurred in an environment of relatively low-dose naloxone administration and poor awareness of naloxone among the subjects. Thus, it is worthwhile to consider the findings of two recent studies describing naloxone wariness among people who use opioids in the U.S.

- In one study, 10 adults reporting to an emergency department in Boston with an opioid-related chief complaint were interviewed (Lai et al., 2021). All were familiar with naloxone and had received training in its administration, and they generally reported positive perceptions of it. ***However, the eight subjects who had previously received naloxone each reported experiencing severe opioid withdrawal symptoms they were eager to avoid in the future. In another study, 20 adults who use opioids in New York were interviewed to identify reasons they do or do not carry naloxone (Bennett, Freeman, Des Jarlais, & Aronson, 2020).*** A major reported theme from these interviews was a fear of misrecognizing the need for naloxone and inducing or experiencing prolonged opioid withdrawal symptoms. ***Significantly, an 8 mg naloxone product has not yet been marketed, so these qualitative findings are in the context of 4 mg IN being the highest single-dose naloxone product available. The introduction of an 8 mg IN naloxone product and the potential future introduction of a similarly potent nalmefene product with longer duration of action could plausibly lead some people who use opioids to avoid carrying it.***

Hill, et al, International Journal of Drug Policy, 2022

Overdose Prevention: Naloxone

Naloxone

- An opioid antagonist: reverses opioid overdose; effective against fentanyl and fentanyl analogues, may require additional naloxone doses administered due to its potency
- Easy to administer
- Inert when opioids not on board; no drug-drug interactions with other medications, no contraindications with any co-morbid medical or psychiatric conditions
- ***It is imperative that naloxone is in the hands of PWUD (who actually experience/witness/do the most reversals)***
- ***Overdose education should be done with all patients regardless of substance use disorder diagnosis, last date of use, and intended substance of use***
- **Naloxone prescribing:**
  - **Intranasal** (**naloxone** 2 mg/2 mL) Sig: **Spray** 1 mL (one-half of total dose) into each nostril upon signs of opioid overdose. Call 911. May repeat once if no response within 2-3 minutes. Refills: up to 99.

To become a NYS DOH OOPP: https://www.health.ny.gov/diseases/aids/general/opioid_overdose_prevention/

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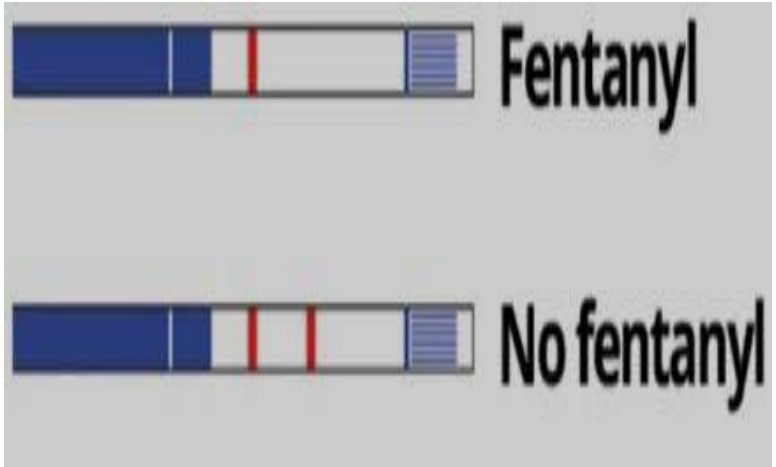
Overdose Prevention: N-CAP

Many pharmacies dispense naloxone, either under a standing order or by prescription

- N-CAP: Funded by NYS, covers **up to $40** in naloxone co-payments with health insurance coverage

NEW YORK STATE | Office of Addiction Services and Supports

Evidence for FTS and Drug Checking



Overdose Prevention: Fentanyl Test Strip Pilot Project, San Francisco, 2017-2018

Background

- In August 2017, in response to an increase in fentanyl in the drug supply in San Francisco, the DOPE Project partnered with the Syringe Access Collaborative (SAC) to pilot a fentanyl test strip monitoring survey.
- The SAC includes the San Francisco AIDS Foundation's Syringe Access Services, Glide Harm Reduction Services, St. James Infirmary, SF Drug Users Union and the Homeless Youth Alliance—all of which are DOPE Project naloxone distribution sites in addition to syringe access service providers.
- The strips are provided to SF syringe access programs through the California Supply Clearinghouse, supported by the California Department of Public Health.

Findings

- Test strips are a useful engagement tool to foster discussion with people who use drugs (PWUD around practicing universal precautions and anticipating the presence of fentanyl in their drug supply.
- Test strips are easy for PWUD to use with minimal instruction, and the response from PWUD about their availability has been extremely positive.
- Test strips are detecting positives in various drug supplies in SF and indicate that we have an increasingly frequent presence of fentanyl.
- Test strips allow PWUD to be more informed about the drugs they are buying and using, leading to behavior change and the adoption of increased harm reduction measures, including sharing information among peers.
- Test strips allow providers to better engage with non-injectors and non-opioid users around overdose prevention and resulted in an increase in naloxone trainings with non-opioid users.
- PWUD demonstrate a high likelihood of implementing one or more harm reduction strategies when learning that their drugs are positive for fentanyl.
- Test strip use has increased general awareness and understanding of fentanyl among PWUD and providers at SAC sites.

https://harmreduction.org/issues/fentanyl/fentanyl-test-strip-pilot/

Note: federal funds now can be used to purchase fentanyl test strips

Overdose Prevention: Fentanyl Test Strip Pilot Project, San Francisco, 2017-2018, Key Findings

Finding 1

Fentanyl testing strips had the lowest detection limit and the highest sensitivity and specificity for fentanyl of the technologies assessed.

TECHNOLOGY	DETECTION LIMIT	SENSITIVITY		SPECIFICITY	
		Rhode Island Lab	Baltimore Lab	Rhode Island Lab	Baltimore Lab
BTNX Fentanyl Testing Strips (immunoassay)	0.13 micrograms/ml	96%	100%	90%	98%
TruNarc (Raman Spectroscopy)	25 micrograms/ml	4% (61% with SERS kit)	4% (39% with SERS kit)	100% (92% with SERS kit)	98% (92% with SERS kit)
Bruker Alpha (FTIR Spectroscopy)	3-4% weight, which is comparable to TruNarc	83%		90%	

https://harmreduction.org/issues/fentanyl/fentanyl-test-strip-pilot/

Note: federal funds now can be used to purchase fentanyl test strips

Finding 2

The vast majority of people who use drugs have a high degree of concern about fentanyl in the drug supply.

- ***84% of respondents were concerned about the drugs they use having fentanyl in them.*** Of 256 respondents who thought they had consumed fentanyl, 85% said they wished they had known beforehand. Contradicting the idea that people who use drugs are actively looking for fentanyl, only about one in four (26%) stated a preference for drugs with fentanyl.

Overdose Prevention: Fentanyl Test Strip Pilot Project, San Francisco, 2017-2018, Key Findings

Finding 3

The vast majority of people who use drugs are interested in fentanyl checking as a product safety measure.

- ***Of all respondents, 85% desired to know about the presence of fentanyl before using drugs, with 73% expressing moderate to high interest. Drug checking was viewed as an important means of overdose prevention, with 89% agreeing that it would make them feel better about protecting themselves from overdose***. Interest in drug checking was associated with having witnessed an overdose and recently using a drug thought to contain fentanyl. ***In addition to the presence or absence of fentanyl, a large majority of respondents were interested in knowing the amount of fentanyl (86%) and the presence of other substances (87%).***

Finding 4

The majority of people who use drugs would modify their drug use behaviors if their drugs tested positive for fentanyl.

- ***Across all sites, 70% of respondents reported that knowing that their drugs contained fentanyl would lead them to modify their behavior. This could include not using the drugs, using the drugs more slowly, or using the drugs with others who have naloxone. It could also include changing their purchasing behaviors***.

https://harmreduction.org/issues/fentanyl/fentanyl-test-strip-pilot/

Note: federal funds now can be used to purchase fentanyl test strips

Overdose Prevention: Fentanyl Test Strip Pilot Project, San Francisco, 2017-2018, Key Findings

Finding 5

Key informants support the concept of drug checking with the goals of providing needed information to people who use drugs and serving as a point for greater engagement in services, including syringe services programs and treatment for substance use disorder.

- Service providers supported drug checking as a way to connect with people who use drugs, provide education, and potentially engage them in other services, including syringe services programs and treatment for substance use disorder. They were enthusiastic about the ease of use of the test strips, the potential for incorporating drug checking into existing harm reduction services, and even allowing people who use drugs to use the strips themselves.

https://harmreduction.org/issues/fentanyl/fentanyl-test-strip-pilot/

Note: federal funds now can be used to purchase fentanyl test strips

Finding 6

Key informants have questions about the legality and logistics of drug checking.

- Key informants identified additional issues about the implementation of drug checking services, including the potential legal liability and possible security risks of performing the drug checking (such as attracting law enforcement), especially at the point of service

Overdose Prevention: Fentanyl Test Strip Pilot: The FORECAST Study, April-November 2017, Recommendations

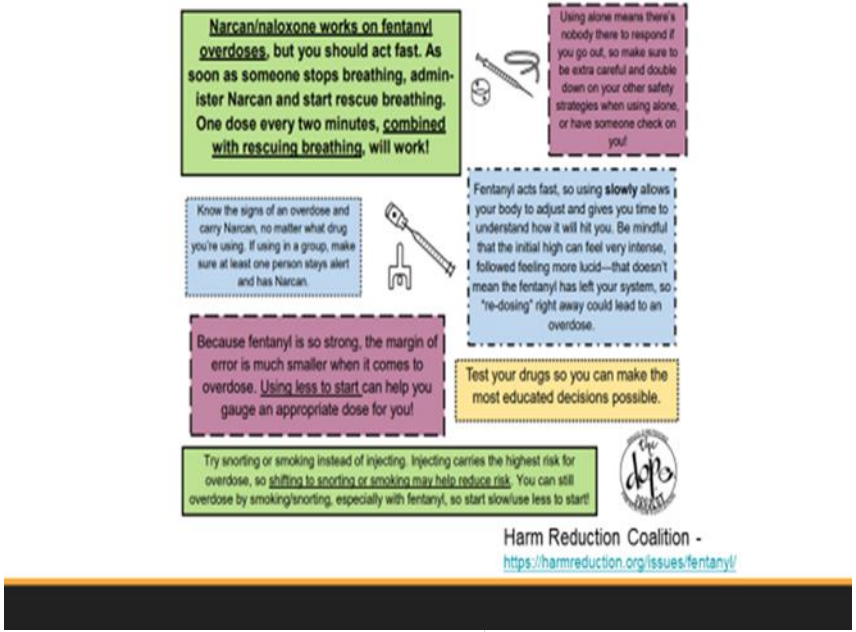
- Recommendation 1: Public health and harm reduction agencies should address logistical questions and implement anonymous drug checking as part of a public health strategy to save lives from fentanyl.
- Recommendation 2: Harm reduction counseling, health education and connection to services including treatment for substance use disorder should be part of any drug checking program.
- Recommendation 3: Research, philanthropic, syringe service programs and overdose prevention agencies should support pilot programs seeking to test, evaluate and scale-up drug checking services as part of a comprehensive approach to addressing the opioid and overdose epidemic.
- Recommendation 4: Entities in the private sector should continue to develop mobile technologies for effective drug checking.
- Recommendation 5: Public health surveillance efforts should include information about local trends in the drug supply, such as those available through drug checking, to inform timely and accurate responses.

Perspectives on rapid fentanyl test strips as a harm reduction practice among young adults who use drugs: a qualitative study

- **Background:** In 2016, drug overdose deaths exceeded 64,000 in the United States, driven by a sixfold increase in deaths attributable to illicitly manufactured fentanyl. Rapid fentanyl test strips (FTS), used to detect fentanyl in illicit drugs, may help inform people who use drugs about their risk of fentanyl exposure prior to consumption. This qualitative study assessed perceptions of FTS among young adults.
- **Methods:** From May to September 2017, we recruited a convenience sample of 93 young adults in Rhode Island (age 18–35 years) with self-reported drug use in the past 30 days to participate in a pilot study aimed at better understanding perspectives of using take-home FTS for personal use. Participants completed a baseline quantitative survey, then completed a training to learn how to use the FTS. Participants then received ten FTS for personal use and were asked to return 2–4 weeks later to complete a brief quantitative and structured qualitative interview. Interviews were transcribed, coded, and double coded in NVivo.
- **Results:** ***Of the 81 (87%) participants who returned for follow-up, the majority (n = 62, 77%) used at least one FTS, and of those, a majority found them to be useful and straightforward to use. Positive FTS results led some participants to alter their drug use behaviors, including discarding their drug supply, using with someone else, and keeping naloxone nearby.*** Participants also reported giving FTS to friends who they felt were at high risk for fentanyl exposure.
- **Conclusion:** ***These findings provide important perspectives on the use of FTS among young adults who use drugs. Given the high level of acceptability and behavioral changes reported by study participants, FTS may be a useful harm reduction intervention to reduce fentanyl overdose risk among this population.***

Goldman, JE, et al, Harm Reduct J, 2019

Fentanyl Test Strips



www.harmreduction.org/issues/fentanyl and www.harmreduction.org

Note: federal funds now can be used to purchase fentanyl test strips

BTNX Fentanyl Test Strip Instructions

Rapid Response

Single Drug Test Strip
(Urine)
Product Insert

For forensic use only.

INTENDED USE

The Rapid Response ™ Single Drug Test Strip is a rapid visual immunoassay for the qualitative, presumptive detection of Fentanyl in human urine specimens at the cut-off concentrations listed below:

Parameter	Calibrator	Cut-off (ng/mL)
FYL (Fentanyl)	Fentanyl	20

INTRODUCTION

Fentanyl is a synthetic opioid related to the phenylpiperidines. Fentanyl is approximately 100 times more potent than morphine. This agent is highly lipid soluble and rapidly cross the blood-brain barrier. This is reflected in the half-life for equilibration between the plasma and cerebrospinal fluid of approximately 5 minutes for fentanyl. The levels in plasma and cerebrospinal fluid decline rapidly owing to redistribution of fentanyl from highly perfused tissue groups to other tissues, such as muscle and fat. As saturation of less well-perfused tissue occurs, the duration of effect of fentanyl and sufentanil approaches the length of their elimination half-lives of between 3 and 4 hours. Fentanyl undergoes hepatic metabolism and renal excretion. Therefore, with the use of higher doses or prolonged infusions, fentanyl becomes longer acting.

PRINCIPLE

The Rapid Response ™ Single Drug Test Strip detects Fentanyl through visual interpretation of color development on the strip. Drug conjugates are immobilized on the test region of the membrane. During testing, the specimen reacts with antibodies conjugated to colored particles and precoated on the sample pad. The mixture then migrates through the membrane by capillary action, and interacts with reagents on the membrane. If there are insufficient drug molecules in the specimen, the antibody-colored particle conjugate will bind to the drug conjugates, forming a colored band at the test region of the membrane. Therefore, a colored band appears in the test region when the urine is negative for the drug. If drug molecules are present in the urine above the cut-off concentration of the test, they compete with the immobilized drug conjugate on the test region for limited antibody binding sites. This will prevent attachment of the antibody-colored particle conjugate to the test region. Therefore, the absence of a colored band at the test region indicates a positive result. The appearance of a colored band at the control region serves as a procedural control, indicating that the proper volume of specimen has been added and membrane wicking has occurred.

REAGENTS

Each test consists of a reagent strip. The amount of each antigen and/or antibody coated on the strip is less than 0.001 mg for antigen conjugates and goat anti-rabbit IgG antibodies, and less than 0.0015 mg for antibody components.
The control zone of each test contains goat anti-rabbit IgG antibody. The test zone of each test contains drug-bovine protein antigen conjugate, and the conjugate pad of each test contains monoclonal anti-drug antibody and rabbit antibody-colored particle complex.

MATERIALS

Materials Provided

- Test strips (individually pouched or in canisters)
- Package insert

Materials Required but Not provided

- Positive and negative controls
- Timer
- Centrifuge

PRECAUTIONS

- For forensic use only.
- Do not use after the expiration date indicated on the package. Do not use the test if the foil pouch or canister is damaged. Do not reuse tests.
- This kit contains products of animal origin. Certified knowledge of the origin and/or sanitary state of the animals does not completely guarantee the absence of transmissible pathogenic agents. It is therefore, recommended that these products be treated as potentially infectious, and handled by observing usual safety precautions (e.g., do not ingest or inhale).
- Avoid cross-contamination of specimens by using a new specimen collection container for each specimen obtained.
- Read the entire procedure carefully prior to testing.
- Do not eat, drink or smoke in the area where specimens and kits are handled. Handle all specimens as if they contain infectious agents. Observe established precautions against microbiological hazards throughout the procedure and follow standard procedures for the proper disposal of specimens. Wear protective clothing such as laboratory coats, disposable gloves and eye protection when specimens are assayed.
- Humidity and temperature can adversely affect results.
- Used testing materials should be discarded in accordance with local regulations.

STORAGE AND STABILITY

- The kit should be stored at 2-30°C until the expiry date printed on the sealed pouch.
- The test must remain in the sealed pouch or closed canister until use.
- **Do not freeze.**
- Kits should be kept out of direct sunlight.
- Care should be taken to protect the components of the kit from contamination. Do not use if there is evidence of microbial contamination or precipitation. Biological contamination of dispensing equipment, containers or reagents can lead to false results.

SPECIMEN COLLECTION AND STORAGE

- The Rapid Response ™ Single Drug Test Strip is intended for use with human urine specimens only.
- Urine collected at any time of the day may be used.
- Urine specimens must be collected in clean, dry containers.
- Turbid specimens should be centrifuged, filtered, or allowed to settle and only the clear supernatant should be used for testing.
- Perform testing immediately after specimen collection. Do not leave specimens at room temperature for prolonged periods. Urine specimens may be stored at 2-8°C for up to 2 days. For long term storage, specimens should be kept below -20°C.
- Bring specimens to room temperature prior to testing. Frozen specimens must be completely thawed and mixed well prior to testing. Avoid repeated freezing and thawing of specimens.
- If specimens are to be shipped, pack them in compliance with all applicable regulations for transportation of etiological agents.

PROCEDURE

Bring tests, specimens, buffer and/or controls to room temperature (15-30°C) before use.

1. Remove the test from its sealed pouch, or remove one strip from the canister, and use it as soon as possible. For best results, the assay should be performed within one hour. Canisters should be closed tightly after removing strips.
2. Hold the strip by the end, where the product name is printed. To avoid contamination, do not touch the strip membrane.
3. Holding the strip vertically, dip the test strip in the urine specimen for at least 10-15 seconds. Do not immerse past the maximum line (MAX) on the test strip.
4. After the test has finished running, remove the strip from the specimen and place it on a non-absorbent flat surface. Start the timer and wait for the colored band(s) to appear. The result should be read at 5 minutes. Do not interpret the result after 10 minutes

INTERPRETATION OF RESULTS

POSITIVE: Only one colored band appears, in the control region (C). No apparent colored band appears in the test region (T).
NEGATIVE: Two colored bands appear on the membrane. One band appears in the control region (C) and another band appears in the test region (T).
INVALID: Control band fails to appear. Results from any test which has not produced a control band at the specified read time must be discarded. Please review the procedure and repeat with a new test. If the problem persists, discontinue using the kit immediately and contact your local distributor.
NOTE:

1. The intensity of color in the test region (T) may vary depending on the concentration of analytes present in the specimen. Therefore, any shade of color in the test region should be considered negative. Note that this is a qualitative test only, and cannot determine the concentration of analytes in the specimen.
2. Insufficient specimen volume, incorrect operating procedure or expired tests are the most likely reasons for control band failure.

QUALITY CONTROL

- Internal procedural controls are included in the test. A colored band appearing in the control region (C) is considered an internal positive procedural control, confirming sufficient specimen volume and correct procedural technique.
- External controls are not supplied with this kit. It is recommended that positive and negative controls be tested as a good laboratory practice to confirm the test procedure and to verify proper test performance.

LIMITATIONS

1. The Rapid Response ™ Single Drug Test Strip is for forensic use and should be only used for the qualitative detection of Fentanyl.
2. This assay provides a preliminary analytical test result only. A more specific alternative chemical method must be used in order to obtain a confirmed analytical result. Gas chromatography/mass spectrometry (GC/MS) has been established as the preferred confirmatory method by the National Institute on Drug Abuse (NIDA). Clinical consideration and professional judgment should be applied to any test result, particularly when preliminary positive results are indicated.
3. There is a possibility that technical or procedural errors as well as other substances and factors may interfere with the test and cause false results.
4. Adulterants, such as bleach and/or alum, in urine specimens may produce erroneous results regardless of the analytical method used. Therefore, please preclude the possibility of urine adulteration prior to testing.
5. A positive result indicates the presence of a Fentanyl only, and does not indicate or measure intoxication.
6. A negative result does not at any time rule out the presence of Fentanyl in urine, as they may be present below the minimum detection level of the test.
7. This test does not distinguish between Fentanyl and certain medications.

PERFORMANCE CHARACTERISTICS

A. Accuracy

The accuracy of the Rapid Response ™ Single Drug Test Strip was compared and checked against commercially available tests with a threshold value at the same cut-off levels. Urine samples taken from volunteers claiming to be non-users were examined under both tests. The results were >99.9% in agreement.

B. Reproducibility

The reproducibility of the Rapid Response ™ Single Drug Test Strip was verified by blind tests performed at four different locations. Samples with Fentanyl concentrations at 50% of the cut-off were all determined to be negative, while samples with Fentanyl concentrations at 200% of the cut-off were all determined to be positive.

C. Precision

Test precision was determined by blind tests with control solutions. Controls with Fentanyl concentrations at 50% of the cut-off yielded negative results, and controls with Fentanyl concentrations at 150% of the cut-off yielded positive results.

D. Specificity

The following tables list the concentrations of compounds (ng/mL) above which the Rapid Response ™ Single Drug Test Strip identified positive results at 5 minutes.

Fentanyl related compounds	Concentration (ng/ml)
Fentanyl and Fentanyl metabolites	20
Fentanyl	200
Norfentanyl	>10,000

The following compounds yielded negative results up to a concentration of 100 µg/mL:

(-)-Ephedrine	Chlorpheniramine	Oxalic Acid
(+)-Naproxen	Creatine	Penicillin-G
(+/-)-Ephedrine	Dextromethorphan	Pheniramine
4-	Dextrorphan tartrate	Phenothiazine
Acetaminophen	Dopamine	Procaine
Acetone	Erythromycin	Protonix
Albumin	Ethanol	Pseudoephedrine
Amitriptyline	Furosemide	Quinidine
Ampicillin	Glucose	Ranitidine
Aspartame	Guaiacol Glyceryl Ether	Sertraline
Aspirin	Hemoglobin	Tyramine
Benzocaine	Ibuprofen	Vitamin C (Ascorbic
Bilirubin	Imipramine	Trimeprazine
b-Phenylethyl-amine	Isoproterenol	Venlafaxine
Caffeine	Lidocaine	
Chloroquine	Methadone	

LIERATURE REFERENCES

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2. Hawks RL, Chiang CN, eds. Urine Testing for Drugs of Abuse. Rockville: Department of Health and Human Services, National Institute on Drug Abuse; 1986.
3. Substance Abuse and Mental Health Services Administration. Mandatory Guidelines for Federal Workplace Drug Testing Programs. 53 Federal Register; 1988.
4. McBay AJ. Drug-analysis technology--pitfalls and problems of drug testing. Clin Chem. 1987 Oct; 33 (11 Suppl): 33B-40B.
5. Gilman AG, Goodman LS, Gilman A, eds. Goodman and Gilman's The Pharmacological Basis of Therapeutics. 6th ed. New York: Macmillan; 1980.

GLOSSARY OF SYMBOLS

	Consult instructions for use	REF	Catalogue #	LOT	Lot Number
	Store between 2°C to 30°C		Use by	2	Do Not Reuse

BTNX, Inc.
870 Hood Rd, Unit 23
Markham, ON, L3R 4G7, Canada
Technical Support: 1-888-338-9864

BTNX INC.

Number: 1110027120
REV 1.0/ Effective date: 2019-03-12
Rev06-10082018

https://www.btnx.com/Product?id=16940 and https://www.btnx.com/Product?id=2005

NEW YORK STATE | Office of Addiction Services and Supports

Fentanyl Test Strip Instructions

Fentanyl Test Strips

1. Add sterile water to your **empty** baggie or the **cooker you just prepped** – mix well!

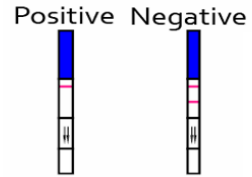
   **Load your shot FIRST! Only test your rinse water!

2. **Dip the test strip** in the water, in up to the first line & **hold for 15 seconds**

3. **Place test strip** on sterile surface or across top of cooker.

One line POSITIVE

Two lines NEGATIVE



NEW YORK STATE Office of Addiction Services and Supports

BTNX Fentanyl Test Strip Instructions

Using Fentanyl Test Strips

These strips are not guaranteed to detect all forms of fentanyl. You could overdose even if the strip says there is no fentanyl in your heroin, cocaine, or other street drugs.

Testing For Fentanyl

- Prepare your shot and draw it into a syringe leaving several drops in the cooker. Do not shoot up yet!
- Set the loaded syringe aside and empty a 5ml. ampule of sterile water into the cooker.
- Stir the mixture.
- Holding a test strip by the blue end, insert it into the solution (don't go past the blue line) and leave it there for about 15 seconds.
- Wait a full minute for the test strip to process.
- Throw the cooker, and any remaining liquid away. Any remaining solution is now toxic.

One red line = positive for fentanyl

Two red lines = negative for fentanyl

A wide variety of street drugs can be laced with fentanyl. While it is advisable to test street drugs for fentanyl, there are no well-researched, established recommendations on how to test drugs with the test strips we provide. People who use fentanyl test strips provided by NOSS accept all responsibility for any injury, or death that could occur after taking drugs, whether they have been tested, or not tested, for fentanyl.

NOSS Northwest Ohio Syringe Services

Mental Health & Recovery Services Board of Lucas County

Toledo-Lucas County Health Department

UT Medical Center Ryan White Program

https://www.btnx.com/files/Fentanyl_Test_Strips_Instructions.pdf

New York State Office of Addiction Services and Supports

High concentrations of illicit stimulants and cutting agents cause false positives on fentanyl test strips

- **Background:** The opioid epidemic has caused an increase in overdose deaths which can be attributed to fentanyl combined with various illicit substances. Drug checking programs have been started by many harm reduction groups to provide tools for users to determine the composition of their street drugs. Immunoassay fentanyl test strips (FTS) allow users to test drugs for fentanyl by either filling a baggie or cooker with water to dissolve the sample and test. The antibody used in FTS is very selective for fentanyl at high dilutions, a characteristic of the traditional use of urine testing. These street sample preparation methods can lead to mg/mL concentrations of several potential interferents. We tested whether these concentrated samples could cause false positive results on an FTS.
- **Methods:** 20 ng/mL Rapid Response FTS were obtained from BTNX Inc. and tested against 4 different pharmaceuticals (diphenhydramine, alprazolam, gabapentin, and naloxone buprenorphine) and 3 illicit stimulants [cocaine HCl, methamphetamine, and 3,4-methylenedioxymethamphetamine (MDMA)] in concentrations from 20 to 0.2 mg/mL. The FTS testing pad is divided into 2 sections: the control area and the test area. Control and test area signal intensities were quantified by ImageJ from photographs of the test strips and compared to a threshold set by fentanyl at the FTS limit of detection.
- **Results:** ***False positive results indicating the presence of fentanyl were obtained from samples of methamphetamine, MDMA, and diphenhydramine at concentrations at or above 1 mg/mL. Diphenhydramine is a common cutting agent in heroin. The street sample preparation protocols for FTS use suggested by many online resources would produce such concentrations of these materials. Street samples need to be diluted more significantly to avoid interference from potential cutting agents and stimulants.***
- **Conclusions:** Fentanyl test strips are commercially available, successful at detecting fentanyl to the specified limit of detection and can be a valuable tool for harm reduction efforts. Users should be aware that when drugs and adulterants are in high concentrations, FTS can give a false positive result.

Lockwood, TLE, et al, Harm Reduction Journal, 2021

High concentrations of illicit stimulants and cutting agents cause false positives on fentanyl test strips

- ***When testing methamphetamine or MDMA for fentanyl, you must dilute the sample you are testing down to 2mg/ml. This is about one teaspoon of water for every 10mg of powder or crystals. If it's more concentrated, you may get a false positive result.***
- If it's more dilute, the strips may not be able to detect fentanyl or its analogues. A set of instructions has been going around telling methamphetamine users to add a few milligrams of meth into half a cup of water. **This is way too dilute!**
- As you can see, the D isomer of methamphetamine (symbolized by the plus signs) triggered a false positive at 10mg/ml and 5mg/ml, but not at 2.5mg/ml. What this means is that you only need to dilute meth down to 2.5mg/ml to avoid false positives. In our instructions we recommend 2mg/ml just to be a little extra cautious. And this dilution comes to only one teaspoon for every 10mg of meth, far lower than 118 teaspoons for 2mg of baggie residue.

Interference Testing	BTNX 20
heroin 10 µg/mL	NEG
6-acetylcodeine 10 µg/mL	NEG
quinidine 10 µg/mL	NEG
cocaine at 25 mg/mL	NEG
ketamine at 25 mg/mL	NEG
diphenhydramine 50 mg/mL	NEG
diphenhydramine 100 mg/mL	POS
diphenhydramine 150 mg/mL	POS
lidocaine 25 mg/mL	NEG
lidocaine 50 mg/mL	NEG
lidocaine 100 mg/mL	POS
lidocaine 150 mg/mL	POS
(-) methamphetamine at 25 mg/mL	NEG
(+) methamphetamine at 2.5 mg/mL	NEG
(+) methamphetamine at 5 mg/mL	POS
(+) methamphetamine at 10 mg/mL	POS
MDMA at 25 mg/mL	NEG
MDMA at 50 mg/mL	POS

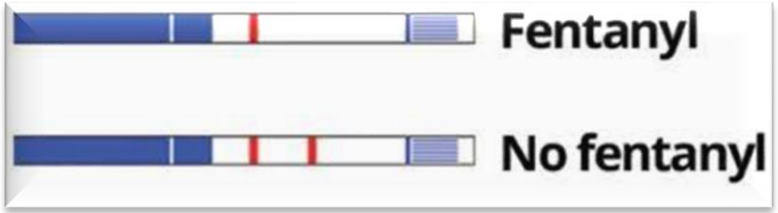
https://dancesafe.org/wp-content/uploads/2019/02/2019-fent-strips.pdf and https://dancesafe.org/what-is-drug-checking/ and https://dancesafe.org/you-may-be-using-fentanyl-testing-strips-incorrectly

Where Can I Get Fentanyl Test Strips?

- Federal funds may now be used to purchase fentanyl test strips (FTS)
- It is recommended that programs purchase and dispense FTS to all persons using illicit substances
- FTS cannot be prescribed
- For programs who intend to dispense FTS:
  - FTS cost ~$1/FTS
  - Programs may purchase FTS at several sites on the internet, including:
    - https://dancesafe.org/product/fentanyl-test-strips-box-of-100/
    - https://www.btnx.com/Product?id=2005
- For PWUD who would like to access FTS:
  - Refer to an SSP
  - PWUD (outside of NYC and those without access to a SSP) can order FTS confidentially: https://nextdistro.org/

Drug Checking

- In addition to fentanyl test strips,
- Pilot project with Gas Chromatography/Mass Spectrometry (GC-MS) machines in the Drug User Health Hubs and other sites



Drug Checking and Its Potential Impact on Substance Use

What Is Drug Checking?

- ***Drug-checking services provide individuals who use drugs with information on the chemical content of their drugs as well as advice, and, sometimes, counseling or brief interventions.*** Service priorities vary and may include information collection, harm reduction, and early warning. The analytical techniques used also vary from sophisticated technology that is able to provide information on strength and content of a wide variety of substances, such as high-performance liquid chromatography and Fourier transform infrared spectroscopy, to methods that simply show the presence or absence of a particular drug, such as thin-layer chromatography and reagent test kits.
- ***The sites at which testing occurs include drop-in services with fixed laboratories, where individuals and organizations can submit drugs for testing (with results days later), and mobile laboratories at festivals, clubs or drug consumption rooms, which provide almost immediate results.***
- ***An important aspect of drug-checking services is how the results are communicated to individuals and whether this is accompanied by harm reduction advice and brief interventions.***

What Is Known About the Effectiveness of Drug Checking?

- ***Drug-checking services remain controversial in some EU countries. They have provided a valuable contribution to early warning systems and the monitoring of drug availability in the European Union. However, evidence of their impact on risk behaviors remains limited. Advocates argue that information from drug-checking services has had a positive public health impact and that drug checking can potentially reduce harm by engaging with people who use drugs recreationally, who would otherwise remain unreachable; identifying drugs that contain unwanted or unknown chemicals allowing an early public health response; and helping avoid overdose or deaths by providing information on potency or adulteration. On the other hand, critics suggest that drug checking may give a false feeling of safety because the reliability of some of the testing approaches used is questionable or limited;*** may give the impression that drug taking is normal and acceptable behavior, potentially undermining prevention efforts; and that clients will go ahead and use their drugs regardless of results.
- Any assessment of the arguments, either those set forth by advocates or critics, is hampered by the lack of robust studies and the difficulties in generalizing given the very different approaches and models used. Nevertheless, given the growing importance of synthetic drugs in the European market, including high potency synthetic opioids, any response that may reduce risks merits careful consideration and evaluation.

Drug Checking as a Harm Reduction Intervention

- **The concept of drug checking was introduced in the early 1990s as a new strategy to reduce harms associated with the use of novel and sometimes hazardous synthetic psychoactive drugs at party settings across Europe.**
- The first harm reduction-focused drug checking program was established in the Netherlands in 1992 when the Dutch government commissioned the Drug Information and Monitoring System (DIMS) to monitor the country's recreational drug markets with respect to dose, composition, adulterants, and availability.
- Different modifications of the Dutch drug checking system were established in many European countries including France, Switzerland, Spain, and Portugal during the 1990s and 2000s.
- **In addition to communicating analysis results to service users, these drug checking networks maintain up-to-date databases of new and existing psychoactive drugs. These data serve as a guiding factor in policymaking and harm reduction activities on a population scale.**

https://www.bccsu.ca/wp-content/uploads/2017/12/Drug-Checking-Evidence-Review-Report.pdf

Drug Checking and Its Potential Impact on Substance Use

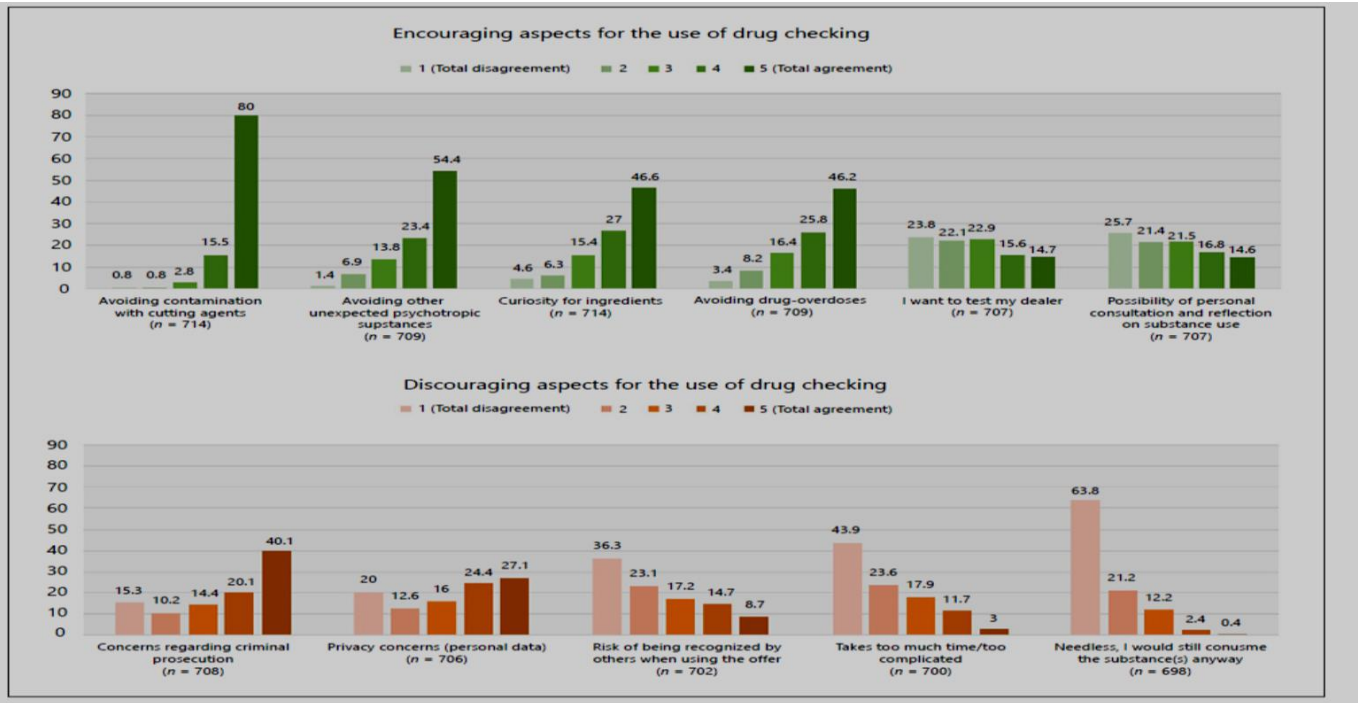


Fig. 1. Encouraging and discouraging aspects for the use of drug checking. Distribution of answers ranging from total disagreement to total agreement is presented as percent.

Betzler, F, et al, Eur Addict Res, 2021

NEW YORK STATE Office of Addiction Services and Supports

Drug checking as a harm reduction tool for recreational drug users: opportunities and challenges

Figure 1
European drug-checking services in existence in 2017

Figure 3
Ways in which drug checking services can vary

Technique	Colormetric reagents	High-performance liquid chromatography	Gas chromatography	Mass spectrometry
Timing				
Testing for	Presence or absence of a component	Information on whole range of substances present	Quantitative information about all compounds	
Setting	At home	On-site/mobile	Remote site	
Who	Individuals	Professionals		
Results	Drug content	Public health alerts	Harm reduction information	Brief interventions
Use of results	Individual harm reduction	Public health action	Market monitoring	

https://www.emcdda.europa.eu/document-library/drug-checking-pill-testing-harm-reduction-tool-recreational-drug-users-opportunities-and-challenges_en

Drug Checking as Strategy for Harm Reduction in Recreational Contests: Evaluation of Two Different Drug Analysis Methodologies

- **Introduction:** Drug checking as a part of drug harm-reduction strategies represents an essential aspect of public health policies. It focuses on rapid identification of drugs that individuals intend to use during night events, in order to implement health-protective behaviors. Chemical drug analysis techniques vary considerably, from simple colorimetric reagents to advanced forensic methods such as gas chromatography/mass spectrometry (GC/MS).
- **Materials and Methods:** In 2019, drug-check services were offered at some night events in Umbria (Central Italy). One hundred and twenty attendees directly delivered unidentified substances to a harm-reduction worker, who collected a few milligrams of the substances on ceramic plates and added a drop of colorimetric reagent. Multiple reagents were used to increase the diagnostic capacity of a substance, which may react with a specific drug or a few drugs. Later, a fraction of the samples was analyzed by GC/MS. The concordance of the results obtained using these two methodologies and the intended behaviors of consumers after being informed of the test result was evaluated.
- **Results: We analyzed 120 samples** by colorimetric test: 32 MDMA, 25 ketamine, 10 amphetamine, 11 cocaine, 8 heroin, and 4 LSD samples. **The results were inconclusive for 29 samples**. The GS/MS analysis confirmed MDMA in 84%, ketamine in 78%, amphetamine in 91%, cocaine in 92%, heroin in 88%, and LSD in 100% of the samples. The results of samples with inconclusive results were as follows: 2, MDMA; 7, ketamine; 2, amphetamine; 2, cocaine; 2, heroin; 2, mephedrone; 6, mixes; 1, debris; and 5, adulterants as the main component**. Twenty-one of 29 participants reported that they had no intention of consuming the unidentified substance.**
- **Discussion: The high percentage of individuals who claimed no intention of consuming the unidentified drugs indicates that drug checking is viable as a part of drug harm-reduction strategies.** Overall, colorimetric reagents showed a good performance with regard to samples being unadulterated (LSD) or minimal in quantity but failed to identify mixtures of substances and the adulterants present in them. Therefore, the use of more discriminatory on-site methods such as Raman or infrared spectrometry is strongly recommended.

Fregonese, M, et al, Front. Psychiatry, 22 February 2021

Drug Checking as a Harm Reduction Intervention: Comparative Summary of Device Specifications

Table 1. Comparative summary of device specifications

Technology	Detect a wide variety of compounds	Ability to detect fentanyl and other opioids	Ability to detect multiple compounds at once	Specificity	Sensitivity	Quantitative analysis	Can identify unknown compounds	Speed per sample	Cost	Suitable drug checking settings
Colorimetric Reagent Testing[6,17,20-23]	Moderate	Low	Low	Low	Low	No	No	<6 min	$	Stationary, Mobile
Fourier-transform Infrared Spectroscopy (FTIR)[24-27]	High	Moderate	High	High	High	Low	No	<2 min	$$	Stationary, Mobile
Thin Layer Chromatography (TLC) with UV detection[6,20,23-25]	Moderate	Weak	Moderate	Moderate	Moderate	Low	No	30 min, multiple at once	$$	Stationary
Capillary Electrophoresis (CE) with UV detection[23,24,26-28]	High	Moderate	Moderate	Moderate	Moderate	Moderate	No	<2min*	$$	Stationary
High Performance Liquid Chromatography (HPLC) with UV detection[6,17,23,24,29-31]	High	High	High	High	High	High	No	15 min	$$	Stationary, Mobile
High Performance Liquid Chromatography (HPLC) with MS detection[6,17,24,32-34]	Highest	Very high	Very high	Very high	Highest	Highest	Yes	7.5 min*	$$$$	Stationary**
Gas Chromatography (GC) with MS detection[6,17,24,33,35,36]	Very high	Very high	Very high	Very high	Very high	Very high	Yes	14.5 min*	$$$$	Stationary
Ion Mobility Spectrometry[37-42]	Moderate	Moderate	Moderate	Low	High	Moderate	No	<1 min*	$$	Stationary, Mobile
Ion Mobility with MS detection37-41	High	High	Very high	High	Very high	High	Yes	20-30min*	$$$$	Stationary

*These durations are estimates based on machine-specific run times alone, and do not include collection, preparation, report generation, or consultation.
** While this technology has also been used in mobile lab-in-a-van settings, but the equipment is not considered portable.

https://www.bccsu.ca/wp-content/uploads/2017/12/Drug-Checking-Evidence-Review-Report.pdf

Drug Checking as a Harm Reduction Intervention: Gas Chromatography-Mass Spectrometry (GC-MS)

- Gas chromatography mass spectrometry (GC-MS) involves the separation of compounds by gas chromatography, followed by detection using a mass spectrometer (measuring mass to charge ratio). This method of identification and quantification of compounds has been widely used for many years in both the pharmaceutical industry and law enforcement.
- Evidence for the use of GC-MS in drug checking is limited.
- **Technical Selectivity:** GC-MS is capable of identifying unknown compounds. However, the range of compounds it can identify is limited. This is because compounds must be readily able to evaporate and be stable at high temperatures.
- **Sensitivity:** The minimum detection limit for GC-MS varies between methods and has been reported as 3ppm for impurities in cocaine and 2ppm for impurities in heroin.
- **Speed:** GC-MS was used in the Netherlands with a run time of 14.5 minutes per sample.
- **Possible settings:** To date, there are no known examples of GC-MS being used as a portable method for drug checking. The Netherlands utilizes this method in their stationary sample testing service, where samples are sent in and the results are available for the consumer within one week. This method is only operable by highly trained laboratory technicians.
- **Cost:** GC-MS may be prohibitive due to the high cost of equipment.
- **Summary of advantages and disadvantages: GC-MS is an established instrument for impurity profiling for heroin and cocaine.** The amount of sample required for testing is quite small, potentially increasing the likelihood of consumers using this service. **GC-MS sample preparation is generally complicated and slow, which renders it unsuitable for drug checking in high-traffic settings.** Additionally, if the goal is to build up a database on new drug adulterants alongside drug checking, GC-MS selects for a smaller range of drugs compared to other methods.

https://www.bccsu.ca/wp-content/uploads/2017/12/Drug-Checking-Evidence-Review-Report.pdf

Third party drug checking: accessing harm reduction services on the behalf of others

- **Background:** Drug checking uses chemical analytical technologies to analyze drugs from the unregulated market to reduce substance use-related risks. We aim to examine the frequency of third-party use of a community drug checking service to explore the potential for harm reduction to extend beyond the individual into the community, increase service accessibility, and to contribute to upstream interventions in the supply.
- **Methods:** Over 31 months, data were collected from a point-of-care drug checking service operated in Victoria, Canada. Through the implementation of survey questions at the intake of the service, data were collected about whether the drug check was for the individual, to sell, and/or for others.
- **Results:** ***Just over half (52%) of service users were checking for reasons that extended beyond individual use. When checking for others, friends were the most common response, representing 52% of responses, and outreach/support workers checking for others was the second most at 32%. Twelve percent of service users reported checking to sell or for a supplier.***
- **Conclusions: Third party checking is a frequent, and important aspect of drug checking services, which through facilitating community engagement and increasing accessibility, has expanded the reach of interventions beyond individuals to reduce risks within the unregulated market. Therefore, drug checking as an overdose response should be responsive and accessible for those using the service on the behalf of others.**

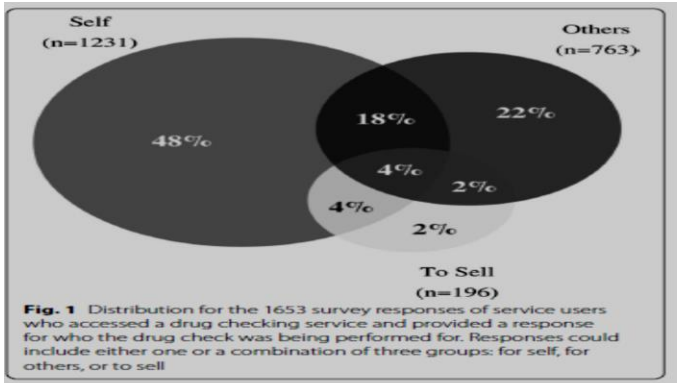


Fig. 1 Distribution for the 1653 survey responses of service users who accessed a drug checking service and provided a response for who the drug check was being performed for. Responses could include either one or a combination of three groups: for self, for others, or to sell

Table 1 Cross-tabulation of the frequency of 345 service users who were checking for others, or in a combination of for others with self or to sell, that further specified who the third party was according to the general categories of friends, outreach, family, supplier or other

Specified other	Checking for others			Total	*N* (%)
	Other only	Other & Self	Other & To Sell		
Friends	57	116	18	179	52%
Outreach	91	11	7	104	30%
Family	38	17	1	56	16%
Suppliers	4	9	3	13	4%
Other	10	8	1	11	3%
Total	190	146	26		
N (%)	55%	42%	8%		

Multiple responses could be selected per service user; therefore, responses are not mutually exclusive and percentages do not add to 100%

Larnder, A, et al, Harm Reduction Journal, 2021

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Drug Checking as a Harm Reduction Intervention: Evidence Summary

- ***A dominant and largely evidence-based argument supporting the efficacy of drug checking as a harm reduction program is that it serves as a real-time, consumer-centered surveillance tool facilitating regulatory intervention in the illegal drug market.***
- The Trans European Drug Information Project (TEDI), a shared database of substances analyzed by participating drug checking labs across Europe, has analyzed over 45,000 samples between 2008 and 2013 and provided valuable insight about the emergence of new and dangerous substances in the European drug market on the 'street' level. These findings have been used for issuing numerous public warnings and taking various harm reduction actions.
- ***Furthermore, it has been suggested that drug users' direct access to knowledge regarding the contents of the substances they purchase may gradually shift the unregulated illegal drug market and make it difficult for dealers to knowingly or unwittingly sell unknown or hazardous substances.*** It should be noted, however, that the benefits of public warnings in the literature on drug checking is discussed exclusively in the context of occasional non-dependent drug use and may not be generalizable to those who use drugs daily. In a qualitative study of the impact of public warnings regarding high-potency heroin and increases in fatal overdose rates in Vancouver, BC, Kerr et al (2013) found that these campaigns had little effect on the perceptions and behaviors of participating heroin injectors. Although the warnings had effectively reached their audience, the majority of study participants reported no change in their substance use behavior, while some reported seeking out the high-potency heroin that had prompted the warning campaigns.
- ***Published evaluations of drug checking found no adverse effect on recreational drug using populations, refuting early arguments that these services may increase drug use in this population by fostering a false sense of confidence.*** However, the literature also emphasizes that drug checking should be utilized as one component of a more comprehensive harm reduction program tailored to specific target populations. While acknowledging that drug checking is supported by relatively meager evidence at this time, a set of practice standards published by the Nightlife Empowerment and Well-being Implementation Project (NEWIP) funded by the EU Health Program argues that this service can be an effective addition to existing health promotion strategies if it is designed, implemented, and evaluated according best practice principles.

https://www.bccsu.ca/wp-content/uploads/2017/12/Drug-Checking-Evidence-Review-Report.pdf

Drug Checking as a Harm Reduction Intervention: Evidence Summary

- There are over a dozen government-supported drug checking services operating around the world***. By combining a range of sample collection modalities, chemical analysis technologies, and modes of communication with service users and the public, a range of hybrid drug checking services have evolved to inform and complement harm reduction strategies in various communities.***
- **Evidence Summary:** ***There are no clinical trials examining the direct impact of drug checking services on the substance use behaviors or health outcomes of service users.*** In the absence of concrete evidence, steadily increasing patronage and service users' self-reported intentions to discard dangerous drugs based on drug checking results are commonly cited as an indicator the effectiveness of drug checking as a harm reduction intervention. ***For example, in a survey of the Checkit! service users in Vienna, two out of three participants reported that they would not use a drug that tests positive for unusual or hazardous contents.*** Similarly, 50% of the drug checking service users surveyed at the 2013 Shambhala festival in British Columbia reported that they would discard the substance if it tested positive for a "high hazard compound." Data reported by ANKORS, the organization that provides the drug checking service at the Shambhala, indicates that in the 2015 festival 31% of checked drugs that contained hazardous substances were discarded. ***Preliminary information from Insite's drug checking pilot project suggests that people who use opioids regularly at the SCS do not tend to dispose of their drugs following a positive result for fentanyl, but they are 10 times more likely to reduce their dose, and those who inject reduced doses are 25% less likely to overdose.***
- Regardless of whether drug checking can influence the service users' immediate drug use behaviors, studies viewed the opportunity for communication with an otherwise invisible population of drug users as a harm reduction measure. Hungerbuehler et al's 2011 analysis of the sociodemographic features of people who use Zurich's drug checking services revealed that these facilities are the first point of access to any substance use-related service for the majority of service users. ***Furthermore, studies show that young people who use drugs find factual one-on-one information about their drug purchase more trustworthy than general government-issued information and are more likely to disseminate individually-obtained facts within their social environments.***

https://www.bccsu.ca/wp-content/uploads/2017/12/Drug-Checking-Evidence-Review-Report.pdf

Myths about Fentanyl in the Media

Inhalation Exposure Risk for Fentanyl:

"At the highest airborne concentration encountered by workers, an unprotected individual would require nearly 200 minutes of exposure to reach a dose of 100 mcg of fentanyl." – American College of Medical Toxicology

Dermal Exposure Risk for Fentanyl:

"Transdermal delivery systems (patches) take 3-13 hours to produce a therapeutic serum fentanyl concentration and 35 hours to reach peak concentration… if bilateral palmar surfaces were covered with fentanyl patches, it would take ~ 14 minutes to receive 100 mcg of fentanyl."

In addition, fentanyl patches are optimized material matrix to absorb to the skin vs powdered drug sitting on skin – it is unlikely that unintentional skin exposures to tablets or powders cause rapid toxicity

Fentanyl in the Street Marijuana Supply: This has been debunked multiple times. Positive tests have typically been field tests by police with cross contamination being the problem. When retested in the lab under sterile conditions, the tests have been negative.

https://www.forbes.com/sites/chrisroberts/2021/11/18/is-this-the-first-for-real-case-of-fentanyl-tainted-marijuana-in-the-us/?sh=16e66bdd5633

https://www.buzzfeednews.com/article/danvergano/marijuana-laced-fentanyl-myth

Evidence for SSPs

Syringe Services Programs are Safe, Effective, and Cost-saving

- Syringe services programs (SSPs) are proven and effective community-based prevention programs that can provide a range of services, including access to and disposal of sterile syringes and injection equipment, vaccination, testing, and linkage to infectious disease care and substance use treatment.
- SSPs reach people who inject drugs, an often hidden and marginalized population. ***Nearly 30 years of research has shown that comprehensive SSPs are safe, effective, and cost-saving, do not increase illegal drug use or crime, and play an important role in reducing the transmission of viral hepatitis, HIV and other infections.***
- ***Research shows that new users of SSPs are five times more likely to enter drug treatment and about three times more likely to stop using drugs than those who don't use the programs.***
- SSPs that provide naloxone also help decrease opioid overdose deaths. SSPs protect the public and first responders by facilitating the safe disposal of used needles and syringes. – CDC Summary on SSPs

Source: https://www.cdc.gov/ssp/syringe-services-programs-summary

Syringe Services Programs are Safe, Effective, and Cost-saving

Proof of Concept

- **Amsterdam, 1984:** The exchange of used syringes for new, sterile ones was first carried out in Amsterdam in 1984 to reduce the spread of hepatitis B among people who inject drugs (PWID). An evaluation of this first syringe exchange found that
  - **1) it did not increase drug use;**
  - **2) it diminished the sharing of syringes;**
  - **3) it did not result in increased needle sticks among the general public;**
  - **4) it stabilized the transmission of HIV; and 5) it decreased the transmission of hepatitis B.**
- **San Francisco, 1987-1992:** An evaluation of one of the first syringe exchanges (SEP) in the United States, an underground operation in San Francisco, found that the median frequency of injections per day more than halved between 1987 and 1992, and participation in the SEP was found to be positively correlated with the non-sharing of syringes.
- **CDC, 1993:** A comprehensive summary of the public health impact of the early syringe exchange efforts in the United States and abroad was funded by the CDC in 1993; its findings were overwhelmingly supportive of syringe exchange as a means of addressing the HIV epidemic among IDUs.
- **NYS Report, 2005:** In spite of the Federal ban on funds directly supporting syringe exchange---a decision not based on science but rather on political exigencies---public health experts, including those in the Federal government have examined the research identified access to sterile syringes as a component of a comprehensive HIV prevention strategy to reduce HIV infections among injectors.

Early NYS Data

- **HIV seroincidence began to fall following the introduction of syringe exchange, as indicated by 10 studies conducted from 1992 through 1997.**
- **HIV seroprevalence also declined markedly among IDUs in New York City.**
  - From 1991 to 1996, seroprevalence decreased from 53% to 36% in the Beth Israel Medical Center (BIMC) detoxification program;
  - From 45% to 29% in a blinded seroprevalence study of entrants in BIMC methadone maintenance programs; from 44% to 22% in a research storefront on the Lower East Side;
  - From 48% to 21% in a research storefront in Harlem; and
  - From 30% to 21% in STI clinics.

Syringe Services Programs are Safe, Effective, and Cost-saving

- In this overview of systematic reviews examining the effectiveness of needle and syringe programs (NSP) for PWID in reducing blood-borne infection transmission and injecting risk behaviors, the authors identified 13 systematic reviews contributing with 133 unique studies, which were mostly observational. Nine reviews reported outcome data on HIV prevalence/incidence, eight on HCV, and six on injection risk behaviors (IRB). Meta-analysis was performed in four of these reviews.
- **Our interpretation of the findings is that the overall results of the included systematic reviews are supportive of the**:
  - ***Effectiveness of NSP in reducing HIV transmission and IRB among PWID, as well as in reducing HCV infection, although the latter to lesser extent. The overall quality of the evidence is higher for HIV transmission and IRB than for HCV infection. However, for HCV infection, the strength of the evidence increases (because studies' results are more consistent) if the intervention under consideration is not solely NSP, but includes other components such as MOUD, in a strategy of full harm reduction intervention.***
- Furthermore, it is well known that sharing other injecting equipment (e.g., cottons, cookers, water, and filters) is an important route of transmission of blood-borne infections, particularly in the case of HCV. ***This overview did not identify any studies evaluating the effects of paraphernalia distribution at reducing the incidence or prevalence of HCV. One further aspect is that individual NSP intervention studies are prone to selection (volunteer) bias, as these exchange programs attract and retain higher-risk PWID. Taken together, these aspects may have contributed to some mixed results reported in the systematic reviews and individual studies addressing HCV infection.***
- To sum up, aspects of NSP provision may be relevant, including structural-level NSP (i.e., high-level coverage), and multi-component programs including full harm reduction seem to benefit all outcomes more than individual NSP.

Source: Fernandes RM, et. al., BMC Public Health. 2017.

What Happens When SSPs Are Not Operational?

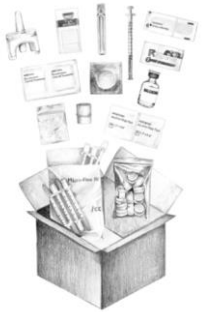
- In early 2015, Scott County, Indiana, was in the midst of one of the worst drug-related HIV (and HCV) outbreaks in US history. As HIV surged in southeastern Indiana, the county's response was inhibited due to Indiana's prohibition of syringe services programs (SSPs).
- State lawmakers eventually reversed course and legalized a local SSP. The results were remarkable.
  - The county's drug-related overdose deaths plunged 20 percent in 2019, and its HIV transmission rate plummeted to just a single case in 2020.
  - Research models further suggest that Indiana may have mitigated—and even prevented—its HIV outbreak had it implemented an evidence-based response that included a syringe services program before the county's transmission rate skyrocketed.

Source: https://www.healthaffairs.org/do/10.1377/forefront.20210817.592015 and https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6192548/pdf/nihms-989814.pdf

Syringe Services Programs

Innovations to Increase Access

- NEXT Distro: mail order supplies directly to the homes of PWUDs
- Expand to emergency departments
- Vending machines (NYC DOHMH pilot project)
- Sharps boxes in public areas
- Naloxone boxes (“nalox boxes”) in public areas



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Sources: www.NEXTDistro.org; WBUR 3/14/18

Expanding Access to Syringes (NYS ESAP)

- **Syringe services programs**
- **Expanded syringe access program (ESAP)**
  - Pharmacies & medical providers: NYS Law (signed 10/2021) eliminates the10-syringe limit, but NYS DOH regulation hasn't been updated yet to reflect this change
- **Secondary syringe exchange:** PWID engage in secondary syringe exchange (SSE), meaning that one PWID (a "provider") obtains syringes at an SSP to distribute to other PWID ("recipients")
- **Drug User Health Hubs:**
  - Increase accessibility
  - Culturally responsive
  - Low threshold
  - Harm reduction framework
  - 12 drug user health hubs around NYS

https://www.health.ny.gov/diseases/aids/consumers/prevention/

Expanding Access to Syringes (NYS ESAP)

What the Law Says

- **Licensed pharmacies, health care facilities, and health care practitioners who can otherwise prescribe hypodermic needles or syringes may register with the New York State Department of Health to sell or furnish hypodermic needles or syringes to persons 18 years of age or older. (The previous limit of 10 syringes has been eliminated)**
- **Persons who are age 18 years or older may legally obtain and possess hypodermic needles and syringes through ESAP- without a medical prescription.**
- **Pharmacies may not advertise availability of hypodermic needles or syringes without a prescription, and they must keep them in a manner that makes them available only to pharmacy staff (i.e., not openly available to customers).**
- Registered providers must cooperate in a program to assure safe disposal of used hypodermic needles or syringes.
- Hypodermic needles and syringes provided through ESAP are accompanied by a safety insert explaining proper use, risk of blood borne diseases, proper disposal, dangers of injection drug use, how to access drug treatment as well as information about HIV/AIDS.
- An independent evaluation conducted in consultation with the New York State AIDS Advisory Council, was submitted to the Governor and the Legislature on January 15, 2003. It assessed the impact of ESAP on needle and syringe sharing, substance use, pharmacy practice, criminal activity, accidental needle sticks among law enforcement, sanitation and other personnel, syringe disposal, and various methods of education on safe use and proper disposal.
- **10/2021: possession of and sale of needles and syringes is decriminalized in NYS**

What the Regulations Say

- Eligible providers must register with the NYSDOH to sell, furnish or accept for disposal hypodermic needles and/or syringes. Pharmacies, clinics, and health care practitioners that wish to accept household sharps under ESAP will have to register for this program component. Hospitals are already required to accept household sharps. Providers that accept needles and syringes for disposal must comply with state and local laws regarding the disposal of regulated medical waste.
- Registration is limited to providers in good standing. It requires completion of a registration that includes information regarding the provider; an attestation that the provider will abide by applicable laws and regulations; an explanation of how the provider will participate in safe disposal; and an authorized signature.
- Registered providers must notify the NYSDOH of any changes to the registration information, including notification to withdraw from the program.
- Registration information may be included in a resource directory or registry for use by consumers and providers.
- Registration may be suspended for a period up to one year, upon the finding of a violation of Section 80.137 or when the provider is found to be no longer in good standing.
- **Individuals aged 18 or older may legally obtain and possess hypodermic syringes and needles obtained pursuant to this regulation.**

Evidence for OPCs

Figure 1. Mock-up of supervised injection services waiting room.

What Are Overdose Prevention Centers (OPCs)?

Definition:

- **Overdose Prevention Centers (OPC):** ***a facility that allows people to consume pre-obtained substances under the supervision of trained staff in a clean, safe space.*** The facilities are designed to reduce the public health (morbidity and mortality associated with substance use) and public order (public use, litter, crime) issues often associated with public substance use.

- ***Facility staff members do not assist directly in substance use or handle any substances brought in by clients but are present to provide sterile injection and other supplies, answer questions on safe injection practices, administer first aid if needed, and monitor for overdose (with oxygen and naloxone on hand).***

- ***There has not been a single overdose fatality at any OPC worldwide. Facility staff also offer general medical advice and referrals to substance use disorder treatment, medical treatment, and other social support programs. These facilities are intended to complement, not replace, existing prevention, harm reduction, and treatment services.***

https://drugpolicy.org/issues/supervised-consumption-services

Other names for OPC include:

- Supervised/Safe Injection Facilities (SIF)
- Supervised/Safe Injection Sites (SIS)
- Drug Consumption Rooms (DCR)
- Harm Reduction Centers (HRC)
- Supervised/Safe Consumption Spaces (SCS)
- Medically Supervised Injection Centers (MSIC)

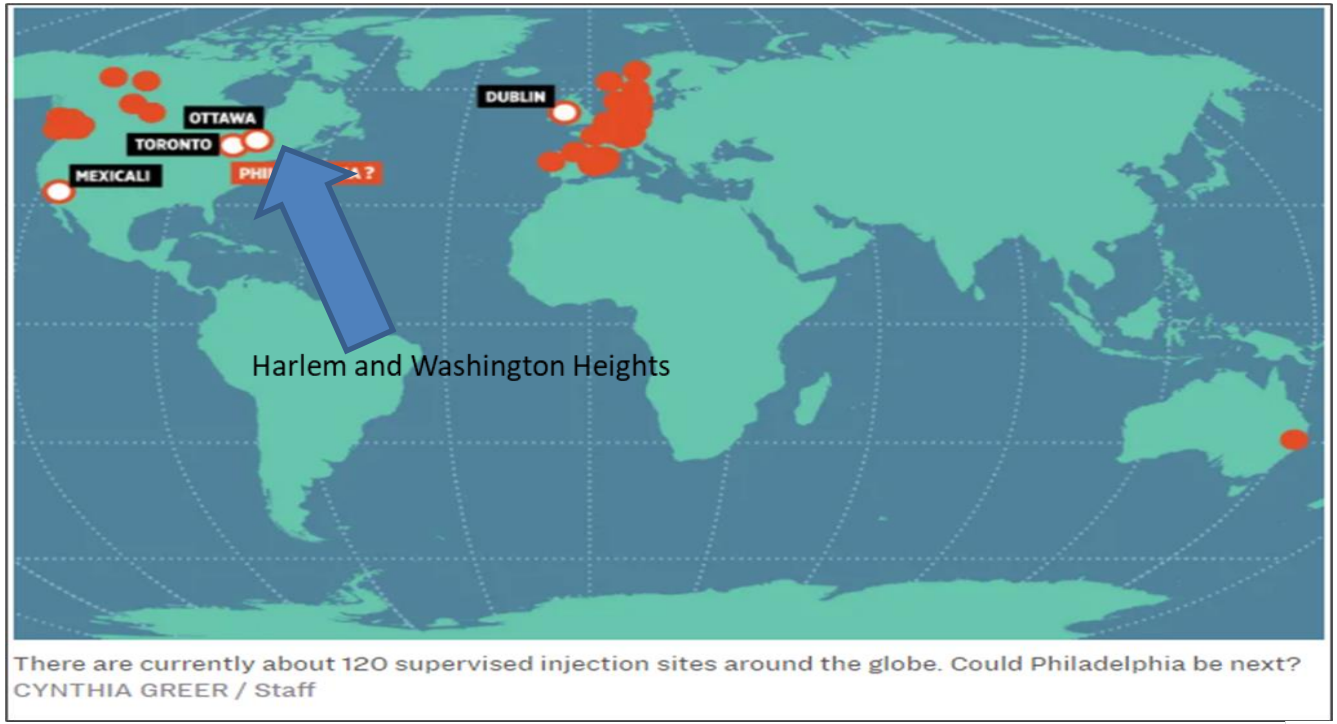
Background/History of OPCs

- The first professionally staffed service where injection substance use was accepted emerged in the Netherlands during the early 1970s as part of the "alternative youth service" provided by the St. Paul's church in Rotterdam. The first modern OPC, actually a café, was opened in Berne, Switzerland in 1986. An injection room was not originally conceived; however, people who use drugs (PWUD) began to use the facility for this purpose. After discussions with the police and the legislature, the café was turned into the first legally sanctioned OPC provided that no one under the age of 18 was admitted.

- **There are approximately 122 OPCs currently operating in > 60 cities in ten countries around the world (Australia, Canada, Denmark, France, Germany, Luxembourg, the Netherlands, Norway, Spain, Switzerland, and the US: NYS).** Underground OPCs have operated in the United States (US) since 2014. In July 2021, Rhode Island became the first state in the US to authorize a two-year pilot program to establish OPC (termed HRC in their legislation) where people can consume pre-obtained substances under the supervision of trained staff. **In November 2021, two OPCs opened in Manhattan (in Harlem and Washington Heights).**

https://jamanetwork.com/journals/jama/fullarticle/2724457
https://en.wikipedia.org/wiki/Supervised_injection_site#:~:text=Supervised%20injection%20sites%20(SIS)%20are,by%20location%20and%20political%20jurisdiction

Where Are the OPCs?



There are currently about 120 supervised injection sites around the globe. Could Philadelphia be next?
CYNTHIA GREER / Staff

https://www.inquirer.com/opinion/commentary/safe-injection-sites-philadelphia-dublin-ottawa-toronto-mexicali-20190629.html

Overdose Prevention Centers (OPCs) in NYC

Gotham Gazette, 3/14/22

- 2 OPCs opened in NYC in November 2021
  - Operated by a harm reduction organization (On Point); privately funded
  - Numerous social and medical services on-site
  - No public funding or oversight
- Outcomes in first 3 months
  - Reversed nearly 200 overdoses
  - Used >10,000 times

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Overdose Prevention Centers (OPCs)

- **Endorsed by AMA, APHA, ASAM**
- **ASAM Recommendations, July 2021:**

Considering the rapidly rising rates of overdose deaths and currently available data on overdose prevention sites (OPS), ASAM recommends:

1.Pilot OPS should be developed and implemented in communities where there is perceived need and local support by PWUD and other community members. Pilot programs should be designed, monitored, and evaluated to generate data to inform policymakers on the feasibility, effectiveness, and legal aspects of OPS in reducing harms and health care costs related to drug use.

1. Pilot OPS should be considered a health service for PWUD that is integrated with a larger continuum of health services, including evidence-based SUD treatment.
2. OPS staff should be trained to forge trusting relationships with PWUD and to help link them to a range of services, including evidence-based SUD treatment.

2.The federal, state and local governments should take action to ensure state- or locality-sanctioned pilot OPS can operate without fear of prosecution.

3.State and local health departments should provide regulatory oversight of any established OPS to ensure that best practices are implemented and maintained, and that outcomes are continuously measured.

4.Studies of OPS should seek to answer the following questions:

1. Are international outcomes replicable in the United States (for example impact on fatal and non-fatal overdoses; emergency service calls; injection use behaviors; crime rates in surrounding area)?
2. How does the establishment of an OPS impact the community's health care system and what are the best models for integration of services with area health care systems including emergency services (EMS/Emergency Department), hospitals and health care systems?
3. What staffing models (e.g., healthcare professionals, peer coaches, etc.) and available services (e.g., linkages to housing or employment support, other healthcare services, etc.) lead to the best outcomes based on the metrics above?

5.Funding for OPS should not reduce resources that support effective evidence-based treatment and social services needed by program participants.

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What is the evidence for OPCs?

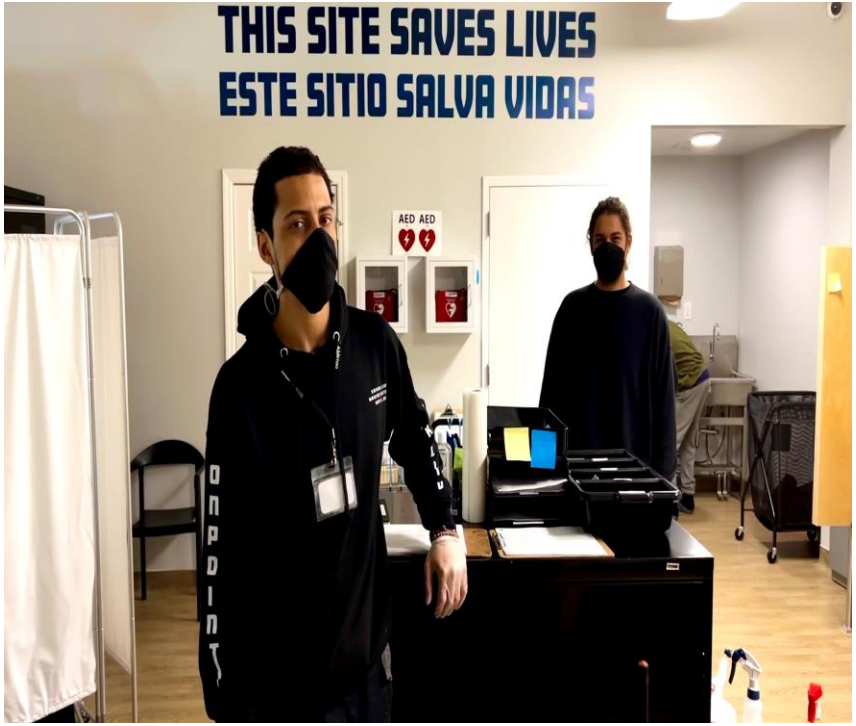

Photo Courtesy of OnPoint NYC

Finally, we note that, although the research on SCSs is largely limited in its type and design, many SCSs have been around for 15 to 30 years and have survived multiple changes in local and national governments. Of course, persistence does not imply effectiveness; however, it seems unlikely that these programs—which were initially controversial in many places—would have such longevity if they had serious adverse consequences for their clients or for their communities. There are researchers and advocates who believe that during an emergency such as the present opioid crisis in the United States, the absence of a large downside risk for a program that has strong face validity may be sufficient for some policymakers to proceed, rather than

Kilmer et al. RAND 2018

Reduction in overdose mortality

Reduction in overdose mortality after the opening of North America's first medically supervised safer injecting facility: a retrospective population-based study

Brandon D L Marshall, M-J Milloy, Evan Wood, Julio S G Montaner, Thomas Kerr

Summary

Background Overdose from illicit drugs is a leading cause of premature mortality in North America. Internationally, more than 65 supervised injecting facilities (SIFs), where drug users can inject pre-obtained illicit drugs, have been opened as part of various strategies to reduce the harms associated with drug use. We sought to determine whether the opening of an SIF in Vancouver, BC, Canada, was associated with a reduction in overdose mortality.

Methods We examined population-based overdose mortality rates for the period before (Jan 1, 2001, to Sept 20, 2003) and after (Sept 21, 2003, to Dec 31, 2005) the opening of the Vancouver SIF. The location of death was determined from provincial coroner records. We compared overdose fatality rates within an a priori specified 500 m radius of the SIF and for the rest of the city.

Findings Of 290 decedents, 229 (79·0%) were male, and the median age at death was 40 years (IQR 32–48 years). A third (89, 30·7%) of deaths occurred in city blocks within 500 m of the SIF. The fatal overdose rate in this area decreased by 35·0% after the opening of the SIF, from 253·8 to 165·1 deaths per 100 000 person-years (p=0·048). By contrast, during the same period, the fatal overdose rate in the rest of the city decreased by only 9·3%, from 7·6 to 6·9 deaths per 100 000 person-years (p=0·490). There was a significant interaction of rate differences across strata (p=0·049).

Interpretation SIFs should be considered where injection drug use is prevalent, particularly in areas with high densities of overdose.

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Lancet 2011; 377: 1429–37
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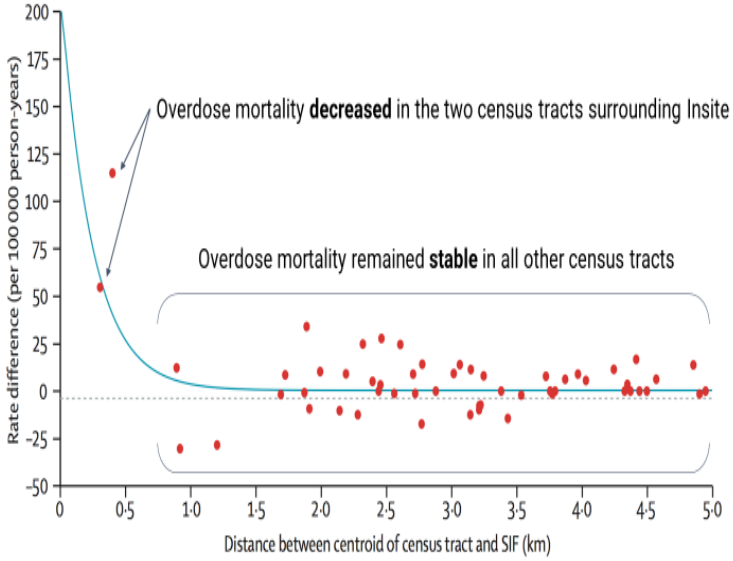
See Comment page 1385

British Columbia Centre for Excellence in HIV/AIDS (B D L Marshall PhD, M-J Milloy MSc, E Wood PhD, Prof J S G Montaner MD, T Kerr PhD), Faculty of Medicine (E Wood, J S G Montaner, T Kerr), School of Population and Public Health, University of British Columbia (M-J Milloy), Vancouver, BC, Canada; and Department of Epidemiology, Mailman School of Public Health, Columbia University, New York, NY, USA (B D L Marshall)

Correspondence to Thomas Kerr, Urban Health Research Initiative, BC Centre for Excellence in HIV/AIDS,

Marshall et al. *Lancet*, 2011

Results



Source: Marshall et al. *Lancet*, 2011

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No fatal overdoses ever at any OPC

Table 1. Injections, Opioid-Involved Overdoses, and Overdose Deaths at an Unsanctioned Safe Consumption Site, 2014 through 2019.*

Year	Injection Events	Opioid Overdoses	Overdoses per 1000 Injections	Overdose Deaths
2014	350	0	0.00	0
2015	1,076	1	0.93	0
2016	1,536	1	0.65	0
2017	1,759	3	1.71	0
2018	2,867	13	4.53	0
2019	2,926	15	5.13	0
Total	10,514	33	3.14	0

* The data are from an unsanctioned safe consumption site in an undisclosed city in the United States.

Kral et al. *NEJM*, 2020

Evidence of Efficacy of OPCs

Over 100 evidence-based, peer-reviewed studies have consistently proven the positive impacts of OPCs, including:

- **Increasing entry into substance use disorder (SUD) treatment; at Insite, an OPC in Vancouver, Canada, 42% of a select group of substance users followed over time entered SUD treatment between 2003-2005; another study of Insite clients found that 57% had entered SUD treatment during the study period**
- **Reducing the amount and frequency that clients use substances; in one study, 75% of Insite clients reported a change in injecting behavior because of receiving services; another study found that 23% of Insite clients had stopped injecting during the study period**
- **Reducing public disorder and public injecting without increasing substance use or crime in the vicinity of the OPC; an OPC in Barcelona, Spain reported a decrease in discarded syringes from 13,000 in 2004 to 3,000 in 2012; public injecting in the surrounding 10 blocks around Insite decreased by 50% in the first 3 months it was operational**
- **Reducing HIV and Hepatitis C risk behavior (i.e., syringe sharing, unsafe sex); in one study among OPC clients, syringe sharing decreased from 37% in 1996 to 2% in 2011**
- **Successfully managing frequent on-site overdoses and reducing drug-related overdose death rates, particularly in the vicinity of the OPC; an OPC in Barcelona, Spain reported a 50% reduction in overdose mortality in the vicinity from 1991 (1833 deaths) to 2008 (773 deaths)**
- **Saving costs due to a reduction in disease, overdose deaths, and need for emergency medical services; near Insite, there was a 67% reduction in EMS calls for overdoses; among Insite clients, there was a reduction in hospitalizations for cutaneous injection-related infections, such as endocarditis, osteomyelitis, and abscesses, from 27% to 9% over 4 years, and the length of hospitalization decreased from an average of 12 days to 4 days**
- **Increasing the delivery of medical and social services; in one study, among Insite clients, 94% accessed non-medical services on site, 44% accessed medical services on site, and 24% indicated that they would not have accessed these services if they had not been available on site**

https://jamanetwork.com/journals/jama/fullarticle/2724457
https://www.ohtn.on.ca/Pages/Knowledge-Exchange/Rapid-Responses/Documents/RR83-Supervised-Injection-Effectiveness.pdf
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5685449/
https://dbhids.org/wp-content/uploads/2018/01/OTF_LarsonS_PHLReportOnSCF_Dec2017.pdf

The Cost Effectiveness of OPCs

- It is more challenging to determine the costs to operate OPC. Many of the referenced costs are dated and done in the context of single-payor health care systems. Conceptually, it is challenging (not impossible but challenging) to think about billable services at OPCs as persons may prefer to use services at the OPC anonymously.

- **Most of the information published on cost as related to OPC is around cost effectiveness and cost savings due to averted infections (HIV; HCV; injection-related infections: skin and soft tissue infections, endocarditis, osteomyelitis) and averted hospitalizations.**

- **Using data from Insite in Vancouver, focusing on the base assumption of decreased needle sharing as the *only* effect of an OPC, the OPC was associated with an incremental net savings of almost $14 million and 920 life-years gained over 10 years**.

- When also considering the health effect of increased use of safe injection practices, the incremental net savings increased to more than $20 million and the number of life-years gained increased to 1070. Results took into consideration the frequency of injecting, the risk of HIV transmission through needle sharing, the frequency of safe injection practices among clients of the OPC, the costs of HIV-related care, the cost of operating the OPC, and the proportion of clients who inject in the facility. Insite has been associated with improved health and cost savings, even with conservative estimates of efficacy.

- **Another study found an average of $17.6 million in lifetime medical expenses saved for each year that Insite is operational. The estimates of savings greatly exceed Insite's annual operating cost of $3 million.**

- The average per-capita operating cost of government sanctioned OPCs in Canada is reported to be CAD$600 (US$475) per unique client. Mathematical modeling showed cost to benefit ratios of $1 spent ranging from $1.50-$4.00 in benefit. The certainty of cost-effectiveness is monitored with longitudinal studies.

Modeling of cost savings for a hypothetical OPC in Philadelphia found the following:

- Reduced costs related to hospitalization for skin and soft tissue infections (SSTI) were estimated to between $1.5 and $1.8 million per year
- The estimated total value of overdose deaths averted was between $12.5 and $74.8 million annually
- The estimates for the impact on health care costs annually were:
  - A reduction of ~$123,000 from ambulance costs
  - ~$280,000 savings from a reduction in hospital emergency department utilization
  - ~$247,000 savings from reduced hospitalizations

https://dbhids.org/wp-content/uploads/2018/01/OTF_LarsonS_PHLReportOnSCF_Dec2017.pdf

- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2582765/
- https://www.ohtn.on.ca/Pages/Knowledge-Exchange/Rapid-Responses/Documents/RR83-Supervised-Injection-Effectiveness.pdf
- https://en.wikipedia.org/wiki/Supervised_injection_site#:~:text=Supervised%20injection%20sites%20(SIS)%20are,by%20location%20and%20political%20jurisdiction
- https://dbhids.org/wp-content/uploads/2018/01/OTF_LarsonS_PHLReportOnSCF_Dec2017.pdf

Conclusions: Harm Reduction:
The Evidence for Overdose Prevention and Intervention Strategies

- There is robust data with respect to evidence-based harm reduction strategies for overdose prevention and intervention.
- MOUD, naloxone education and distribution, FTS (and less so, other drug checking strategies), SSPs, and OPCs all have evidence-based research to support their use with PWUD to decrease the high morbidity and mortality related to unintentional overdose.

Questions?

- Kelly.Ramsey@oasas.ny.gov
- Thanks!