Relative Risk of Opioid-Involved Death Following Exposure to Treatments for Opioid Use Disorder, Connecticut, 2017.

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December 2023

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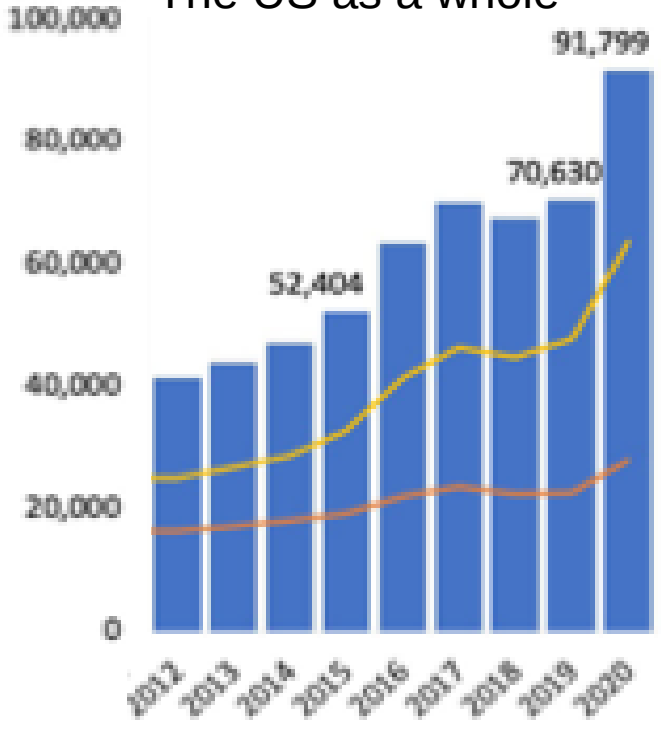
Outline

- Background and Purpose
- Study Design
- Methods: Data Elements, Sources, and Estimates
- Results: Estimation of Incidence and Relative Risk
- Conclusions
- Limitations
- Policy Implications and Recommendations

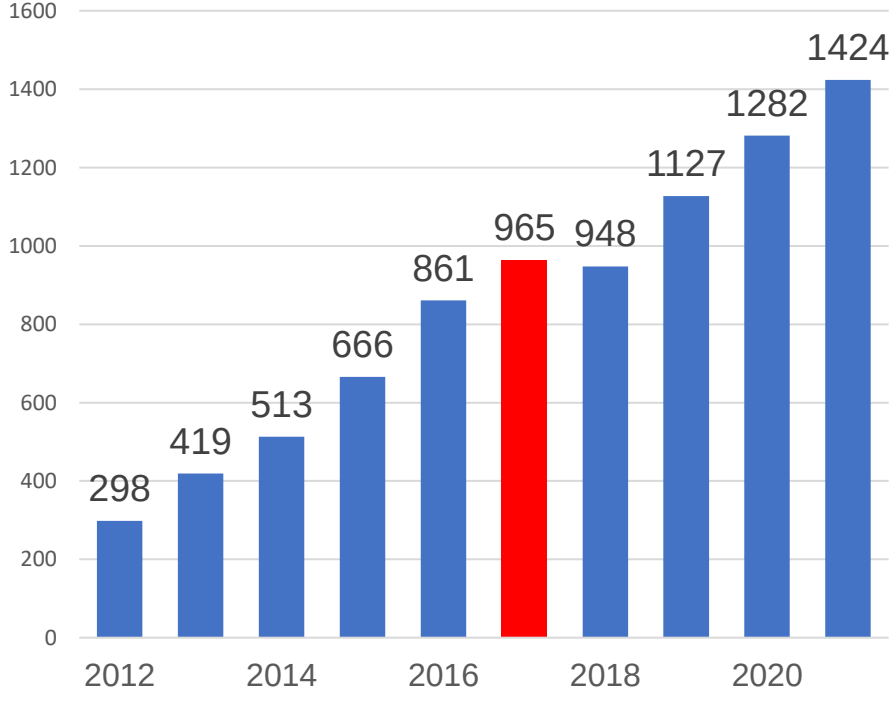
Background – 1

- Overdose trends in CT mirror those in the US, but deaths are about 40% higher

The US as a whole



Opioid-involved fatal ODs in CT



Background – 2

- Treatment for opioid use disorders has not kept pace with increases in fatalities

Table 1: Annual Exposures to OUD Treatment, CT, 2015-19*

	2015	2016	2017	2018	2019
Methadone	19,203	20,886	21,518	21,257	21,651
Buprenorphine	20,879	21,709	23,500	25,821	28,941
Non-MOUD Treatment	24,728	24,587	24,442	23,498	22,152
Short-term	21,312	21,350	21,331	20,220	18,907
Long-term	6,791	6,271	6,285	6,572	6,462

*Numbers are for unique individuals receiving each treatment type

Background – 3

- In 2016, in response to rising opioid OD rates, a CT Opioid Response (CORe) Plan was developed by Yale researchers at Governor Malloy's request following consultations with stakeholders statewide.
- The six CORe Plan strategies were (and remain):
  - Expand access to treatment with medications
  - Reduce overdose risk, especially among those individuals at highest risk
  - Promote improved prescriber adherence to guidelines
  - Expand access to naloxone
  - Increase data sharing across relevant agencies and organizations to monitor and facilitate responses
  - Increase community understanding of opioid use disorder and its treatment to decrease stigma.

Purpose

- This study seeks to use administrative data from state agencies and combine it with data from other sources to determine the influence of exposure to different forms of treatment on subsequent opioid-involved accidental fatalities.
- Use the findings to advise state officials and inform the general public about the relative effective of these treatments in preventing fatal overdoses.

Design

- Case-control study to determine risk of death following recent exposure to MOUD or non-MOUD treatment modalities.
- **Outcome** – opioid-involved deaths reported to CT Office of the Chief Medical Examiner (OCME) in 2017
- **Cases** – Exposure to medical treatments for OUD during the six months prior to death (July 1, 2016-December 31, 2017)
- **Controls** – No treatment exposure

Methods

Data Source for Fatal Opioid Overdoses

- CT Office of the Chief Medical Examiner reviews all accidental deaths, collects names and demographic data including date of birth, conducts site investigations, performs post-mortem toxicology, and assigns causality – accidental, suicide, or undetermined
- All opioid-involved accidental deaths among CT residents from 2017 (N = 965) are included in this analysis

Data Sources for Treatment Exposures

- All individuals receiving methadone treatment at accredited opioid treatment programs in CT reported to the CT Dept. of Mental Health & Addiction Services (DMHAS), with demographic data including date of birth
- All individual receiving non-MOUD treatment including out-patient, in-patient, and residential services at accredited treatment facilities in CT reported to DMHAS, with demographic data including date of birth
- All individuals prescribed buprenorphine and filling prescriptions reported to the CT Prescription Monitoring & Reporting System (CPMRS) maintained by the CT Dept. of Consumer Protection (DCP)

Determining Total Treatment Exposures

- DMHAS provided the number of unique individuals receiving methadone treatment or non-MOUD treatment in 2017
- Non-MOUD treatments in 2017 were categorized as short-term (aka detox) if ≤14 days and longer-term (aka rehab) if >14 days
- DCP did not provide data on the number of unique individuals filling buprenorphine prescriptions

Estimating Total Buprenorphine Exposures

- DEA's ARCOS Drug Retail Summary Reports for total amount dispensed at CT pharmacies used to estimate number of individuals prescribed buprenorphine in 2017 – 56.87 kilograms
- Assumptions to estimate number of patients treated:
  - average dose = 20 mg/day
  - average duration in treatment = four months
  - annual dispensing per patient = 2.42 grams pver 4 months
- Estimated number of patients receiving buprenorphine: **23,500** in 2017

Estimating Total Unexposed to Treatment

- There is no roster or census of people with untreated OUD, so we used recent efforts to determine the proportion of people who are receiving no treatment exposure in 6 months
- Applied two approaches to estimate this number
  - Jones & McCance-Katz used NSDUH data to conclude that 34.5% sought any OUD treatment at any time.[1] Thus, for our six-month window period, the estimate of individuals unexposed in 2017 = [(# in treatment over 6 month / 0.345) – # in treatment over 6 months]
  - Keyes et al.[2] used two multiplier methods to calculate the burden of OUD in the US at 6.7-7.6 million. For CT, the estimate = [7.15 million x 0.0108 (CT proportion of US population x 1.42 (relative rate of fatal ODs CT compared to the US)] - # in treatment over 6 months

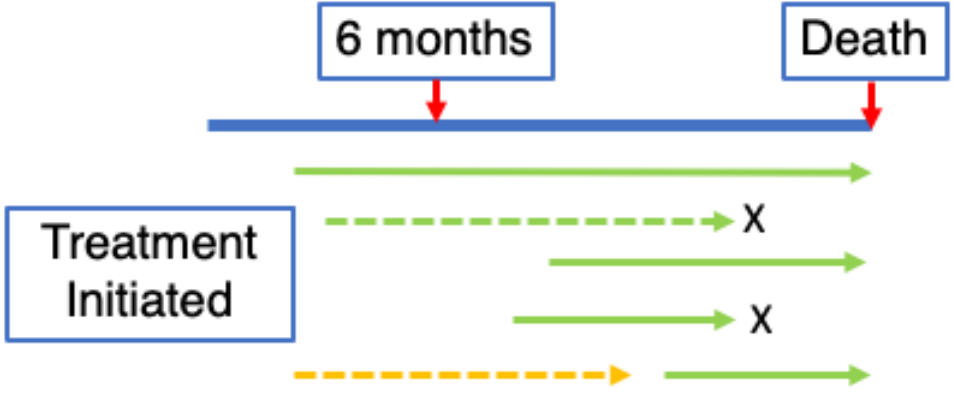
1) Jones & McCance-Katz. Drug Alc Depend, 2019; 197:78-82. 2) Keyes et al. DAD Reps, 2022; 3:100052

Summary of Data Sources

Table 2: Linkage of deaths to exposures and total exposed

	Deaths	Total Exposed
Methadone	OCME matched to DMHAS	DMHAS
Buprenorphine	OCME matched to CPMRS	*Estimated*
Non-MOUD Treatment	OCME matched to DMHAS	DMHAS
Short-term	OCME matched to DMHAS	DMHAS
Long-term	OCME matched to DMHAS	DMHAS
		Total Not Exposed
No Exposure	OCME minus those exposed	*Estimated*

Matching Opioid ODs to Exposures



- DMHAS matched decedents in 2017 to rosters of individuals receiving methadone or non-MOUD treatment
- DCP matched decedents to the CPMRS
- For those with multiple exposures, we determined the treatment closest to the date of death
- All unmatched individuals were considered without exposure to treatment

Results

Individuals with Exposure to Treatment in a 6 Month Period, 2017

Table 3: Exposures to OUD Treatment, CT, 2017[1]

	Annual Exposure	Treatment Duration	6-Month Exposure[1]
Methadone	21,518	Avg. 8-months [2]	14,375
Buprenorphine	23,500	Avg. 3.3 months[3]	11,750
Non-MOUD Treatment	24,442[4]	< 6 months	12,221
Short-term	21,331	< 6 months	10,666
Long-term	6,285	< 6 months	3,143

1) We assume that treatment demand is constant across 12 months
2) While average treatment is 6 months nationwide, the best programs in CT have a ~90% retention rate at 6 months (see Madden LM et al. Addiction, 2018; 113:1450-1458)
3) For buprenorphine, average treatment duration is ~100 days (Olfson M et al. JAMA, 2020; 323:276-277; Thomas CP et al. Drug Alc Depend, 2017; 181:213-218) or less (Morgan JR et al., J Subst Abuse Treat, 2018; 85:90-96)
4) Total is less than the sum since some individual transition from short-term to long-term

Individuals with No Exposure to Treatment

Table 4A: Estimation based on Jones & McCance-Katz

Number in Treatment	Adjustment Factor	Total with Treatment Need	Total Not Exposed to Treatment
38,441	0.345	111,423	**72,982**

Table 4B: Estimation based on Keyes et al.

US OUD burden	CT pop. as % of US pop	Adjustment factor for fatal OD rates	Total treatment need	Exposed to treatment	Not Exposed to treatment
6.7-7.6 x 10^6	1.08	1.42	109,652	38,441	**71,211**

- The two calculations provide remarkably close estimates of treatment need
- For calculating incidence, we will use **72,000** people with OUD not exposed to treatment

Matching Fatal Overdoses to Treatment Exposures

Table 5: Matching the 965 accidental opioid-involved fatalities to DMHAS treatment rosters and CPRMS

Treatment Modality	Matched Fatal Overdoses
Methadone	70
Buprenorphine	74
Non-MOUD Treatment	110
Short-term Treatment	71
Long-term Treatment	26
No Treatment Exposure	711

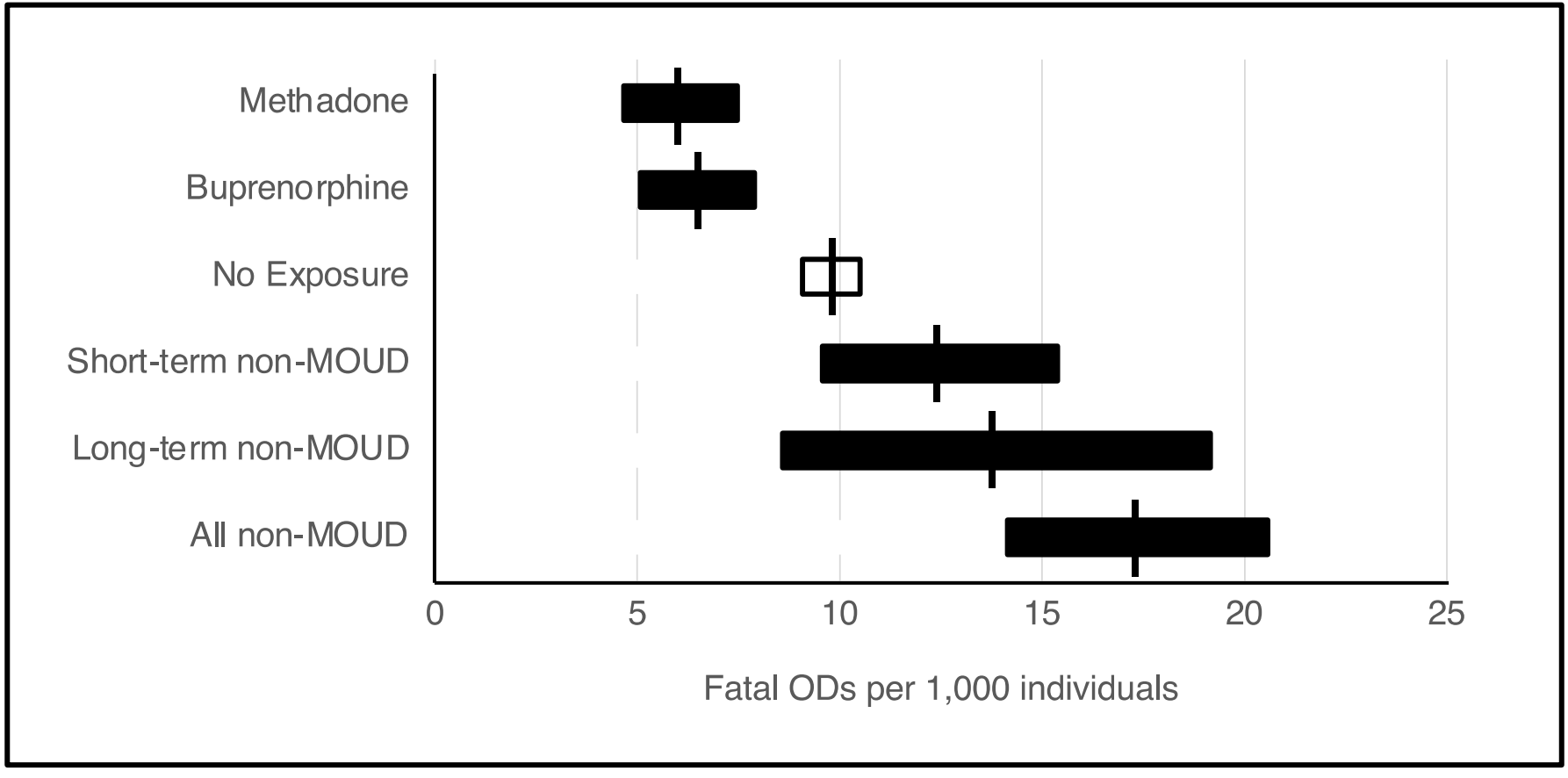
Incidence of Fatal Overdoses – 1

Table 6: Incidence of Fatal Overdose by Treatment Exposure

	Deaths	Total Exposed	Incidence
Methadone	70	11,551	6.1/1,000
Buprenorphine	74	11,358	6.5/1,000
Non-MOUD Treatment	110*	6,335	17.4/1,000
Short-term	71	5,693	12.5/1,000
Long-term	26	1,875	13.9/1,000
No Treatment Exposure	711	72,586	9.8/1,000

* Any non-MOUD includes 13 opioid overdose deaths exposed to non-MOUD treatment, but it was unclear which modality was the one proximal to death.

Incidence of Fatal Overdoses – 3



Relative Risk of Death – 1

- We used no treatment exposure as the referent category

Table 7A: Relative Risk of Death by Exposure Category

	Relative Risk	95% CI	p-value
Methadone vs. No Treatment	**0.62**	0.607 - 0.947	<0.001
Buprenorphine vs. No Treatment	**0.66**	0.723 – 1.133	<0.001
Non-MOUD vs. No Treatment	**1.74**	1.706 – 3.346	<0.0001
Short-term vs. No Treatment	**1.25**	1.275 – 1.851	0.051
Long-term vs. No Treatment	**1.39**	1.995 – 3.302	0.080

Relative Risk of Death – 2

- We included only conditions with known (not estimated) denominators and used methadone exposure as the referent category

Table 7B: Relative Risk of Death by Exposure Category

	Relative Risk	95% CI	p-value
Non-MOUD vs. Methadone	**2.87**	2.13 – 3.86	<0.0001
Short-term vs. Methadone	**2.06**	1.48 – 2.86	<0.0001
Long-term vs. Methadone	**2.29**	1.43 – 3.58	<0.001

Conclusions

- **Exposure to methadone or buprenorphine in the prior 6 months was protective, even for those whose treatment ended before death.**
- **Exposure to non-MOUD treatments does not reduce the risk on a fatal opioid overdose and may actually increase the risk.**
- **Long-term non-MOUD treatments seem to be especially risky.**

Limitations – 1

- Assumptions are needed to estimate number of individuals exposed to buprenorphine and having no exposure.
- Total number in treatment may be an overestimate if people receive multiple modalities in the 6-month window period.
- Not all opioid-involved fatalities or treatment episodes are captured in state agency databases.
- Data are from 2016-17. Needs to be repeated with more recent data and with cooperation from all relevant state agencies.

Limitations – 2

- We matched deaths to individuals in the DMHAS database who had received treatment for an OUD diagnosis. We excluded those who received treatment for any other SUD diagnosis. Approximately 90 individuals who had received treatment following other diagnoses also experienced a fatal opioid overdose within 6 months of treatment. Including these decedents would have non-MOUD treatments even riskier.
- Incarceration may interfere with treatment and increase risk. We are working to find out if any decedents treated with methadone or buprenorphine had an incarceration episode that interrupted or ended their medication.

Policy Implications

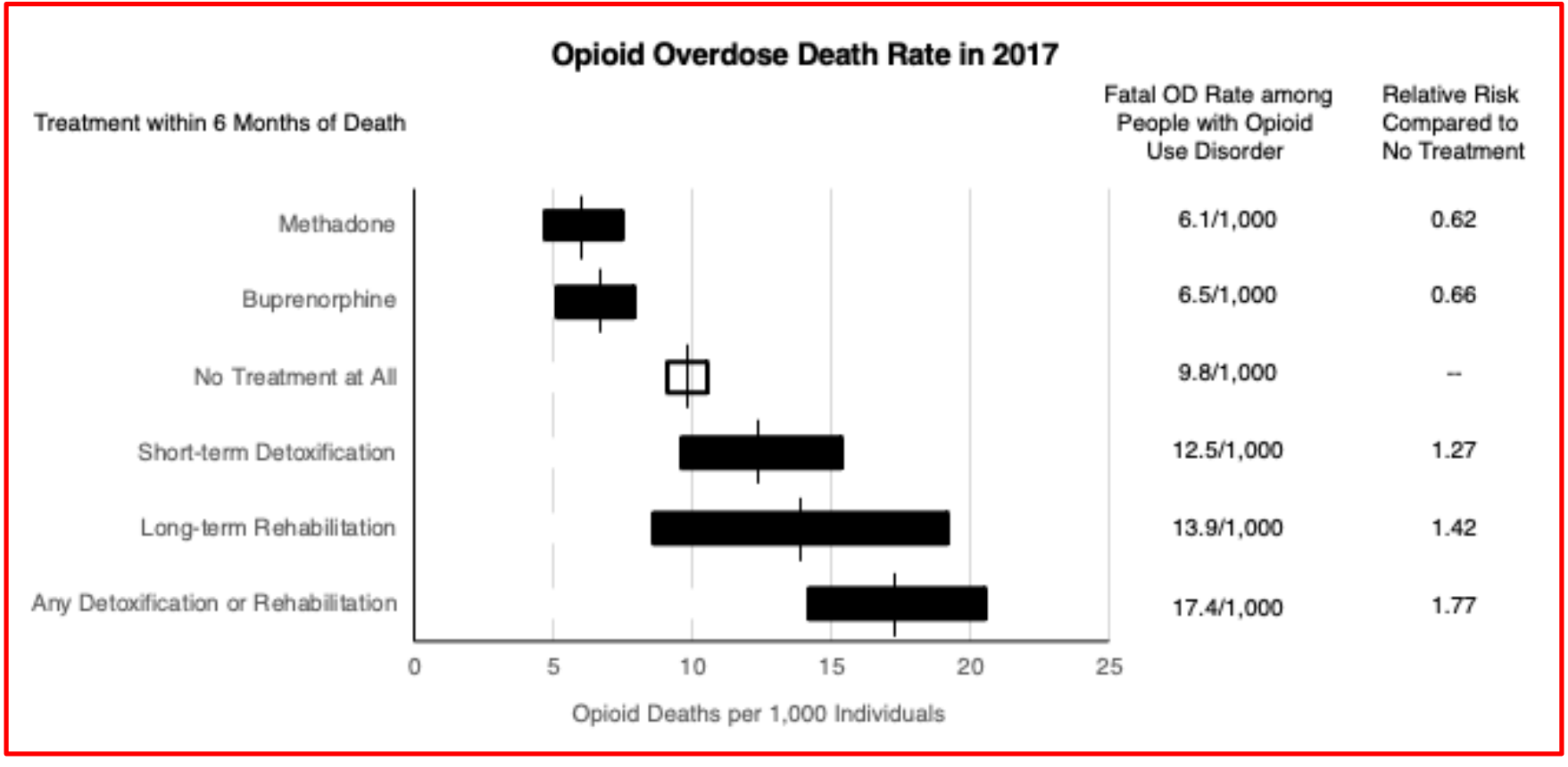
- Results are consistent with existing data on the relative benefit of MOUD and heightened risk of non-MOUD treatment for people with OUD.
  - A century of data on high relapse rates following all manner of abstinence-based approaches
  - Nearly sixty years of evidence on the benefits on methadone to treat OUD
  - Twenty years of data on the benefits of buprenorphine to treat OUD
- Stigma against MOUD and restrictive regulations remain the greatest barriers to reducing opioid-involved fatalities.

Policy Recommendations

- Expand number of people receiving long-acting agonist medications
  - Reduce burdens on providers and patients
  - Increase take-home dose allowance
  - Promote mobile prescribing and dispensing
  - Activate efforts to reduce stigma directed at people who use drugs and at programs that provide medications
- Clinical trials of short-acting agonist medications
  - Hydromorphone has proven effective, especially for those failing treatment with long-acting agonists
- Reduce funding for and increase restrictions on non-MOUD treatments
  - “Meds not beds” as the funding priority as new revenue streams to support treatment become available
  - Restrict non-MOUD treatment to adolescents and initial treatment episodes

Take Home Image

- If a picture is worth a thousand words:



Questions and Comments

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