The Northwest & Pacific Southwest ATTCs and the CTN Western States Node present:

Evidence to Consider When Advising Patients on Buprenorphine Treatment Duration for Opioid use Disorder

Thank you for joining us! The webinar will begin shortly.

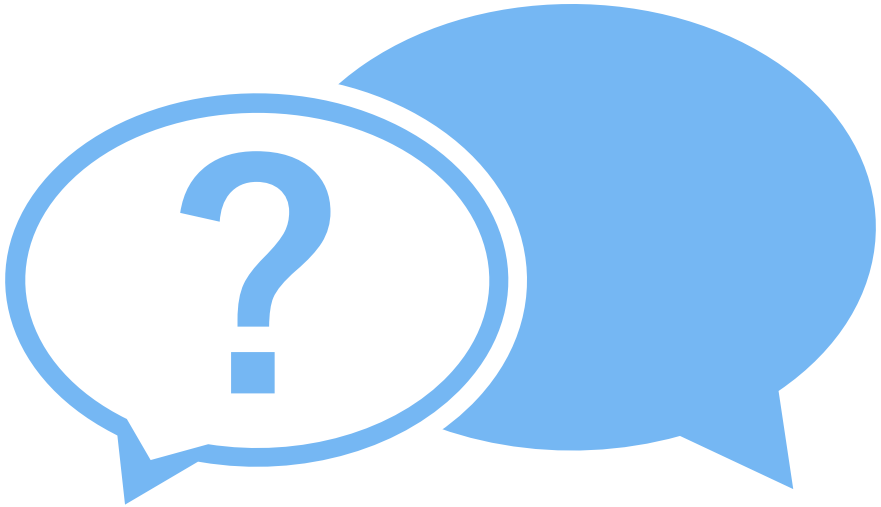
- **You are muted with camera off.** Attendees are automatically muted with their cameras off for the webinar. **Please type questions in the chat box!**

- **This webinar is being recorded** and will be made available on our website tomorrow at attcnetwork.org/northwest

SAMHSA
Substance Abuse and Mental Health Services Administration

Q&A

Questions? Please type them in the chat box!



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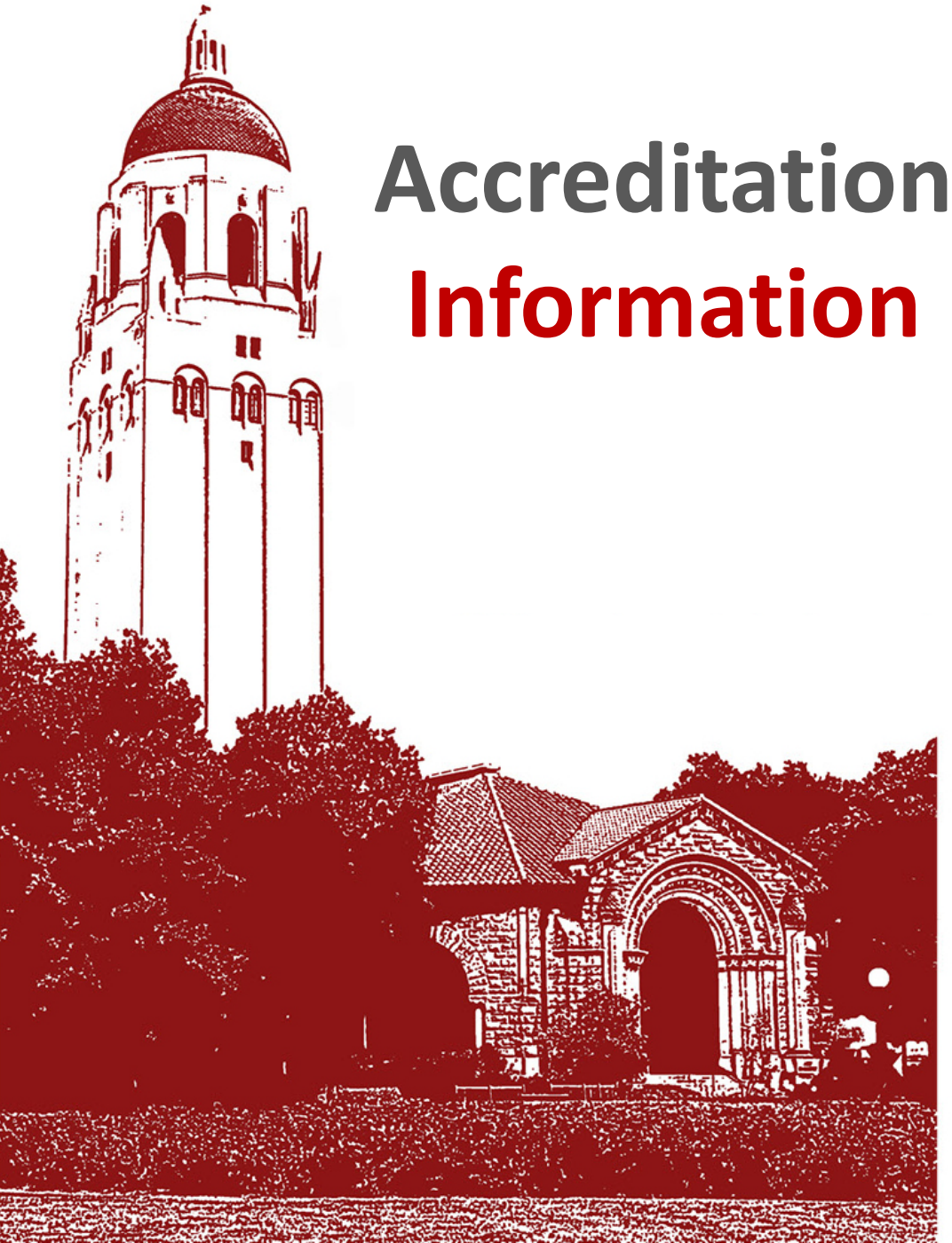
We greatly appreciate your feedback! Every survey we receive helps us improve and continue offering our programs.



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- Following the web training, LMFTs, LCSWs, and SUD counselors will receive an email from **Brandy Oeser** with the links to two different brief online CE course evaluations.
- Once you submit your CE evaluation form, a CE Certificate will be emailed to you within **6-8 weeks**

- Reach out to **Brandy** with questions (BOeser@mednet.ucla.edu)

Certificate of Attendance

If you requested a “certificate of attendance” rather than specific CME/CE, you will receive that certificate from the Northwest ATTC automatically via email within a week.

Evidence to Consider when Advising Patients on Buprenorphine Treatment Duration for Opioid Use Disorder

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Objectives

- Understand the evidence for buprenorphine effectiveness in mortality reduction
- Be able to identify common barriers to buprenorphine retention
- Communicate the results of research on length of treatment exposure and mortality in people who stop buprenorphine treatment
- Consider how to counsel patients who want to stop medications

Retention outcomes in randomized controlled trials of buprenorphine

- >30 studies of sublingual (SL) buprenorphine (or buprenorphine/naloxone)
  - Intervention durations of 2 to 52 weeks
  - Compared SL buprenorphine to methadone, extended-release (XR) naltrexone or placebo
  - Buprenorphine had higher retention than placebo, with dose response
  - Methadone had higher retention rates than SL buprenorphine
  - Similar retention for SL buprenorphine and XR naltrexone
- Extended-release subcutaneous buprenorphine vs. SL buprenorphine
  - Similar retention
  - 24-week retention with fentanyl use (60%) similar to without fentanyl (57%) at 24 weeks

Lee, et al. Lancet. 2018; Mattick, et al. Cochrane Database Syst Rev. 2014; Degenhardt et al Lancet Psych 2023; Nunes et al. JAMA Netw Open, 2024; Lofwall, et al., JAMA Intern Med, 2018; *and others*

Rates of buprenorphine discontinuation variable by setting but generally high

Medicaid: 28% discontinued before 30 days

VA: 38% discontinued within 1 year, 68% within 3 years

Privately insured: 55% discontinued within 1 year

Office-based collaborative treatment: Emerging adults (18-25): 57% at 3 months vs. 22% for older adults

Manhapra A, et al., Am J Addict. 2017; Samples H, et al., J Subst Abuse Treat. 2018.
Manhapra A, et al, Psychiatr Serv. 2018; Meinhofer A, et al. JSAT. 2019; Schuman-Olivier Z et al., JSAT. 2014: 47: 202-212.

Factors associated with buprenorphine discontinuation

- Medication factors: lower dose and days supply
- Comorbidities: other substance use disorders, higher comorbidity score, chronic pain, hepatitis C
- Higher utilization: Inpatient care, psychiatric hospitalization, emergency dept. visits

Manhapra A, et al., Am J Addict. 2017; Samples H, et al., J Subst Abuse Treat. 2018.
Manhapra A, et al, Psychiatr Serv. 2018; Meinhofer A, et al. JSAT. 2019; Schuman-Olivier Z et al., JSAT. 2014: 47: 202-212.

Factors associated with buprenorphine retention

- Older age
- Outpatient psychotherapy
- Antidepressant use

Manhapra A, et al., Am J Addict. 2017; Samples H, et al., J Subst Abuse Treat. 2018.
Manhapra A, et al, Psychiatr Serv. 2018; Meinhofer A, et al. JSAT. 2019; Schuman-Olivier Z et al., JSAT. 2014: 47: 202-212.

Patient preferences and program/policy requirements

- At onset of treatment, >25% do not want to stay on buprenorphine longer than 6 months
- Barriers to retention
  - Life obligations
  - Dissatisfaction with the medication
  - Conflicts with program staff
  - Difficulty adhering to program requirements
  - Incarceration
  - Substance use
- Prior authorization associated with lower treatment duration

Gryczynski J, et al. JSAT 2014; Gryczynski J, et al. JSAT 2013; Stein MD, et al., JGIM 2005; Landis et al, DAD 2022

Evidence suggests buprenorphine retention improves survival

- Overdose and all-cause mortality lower during treatment than off treatment
- Longer retention associated with lower use rates and improved survival
- First 4 weeks off treatment riskier than remaining time (>4 weeks) off treatment

Cornish, et al. BMJ. 2010; Mattick, et al. Cochrane Database Syst Rev. 2014; Lee, Nunes, Novo, et al., Lancet. 2018.; Sordo, et al. BMJ 2017; Larochelle MR, et all, Ann Intern Med. 2018; 169:137–45; Hayes CJ et al, Addiction, 2026

Can we honor patient preferences for buprenorphine discontinuation while maximizing positive outcomes?

- Respect autonomy while avoiding harm?
- Need evidence to inform conversations with patients about buprenorphine discontinuation, particularly those who have already decided to do so – When? How? With what support?
- Difficult to study in a randomized trial: is there equipoise?
- But numerous potential confounders in observational studies

Aim

Examine the association between buprenorphine treatment length and mortality and overdose risk

(Is there an optimal period after which patients can safely discontinue buprenorphine treatment?)

Glanz JM, Binswanger IA, Clarke CL, et al., The association between buprenorphine treatment duration and mortality: a multi-site cohort study of people who discontinued treatment. Addiction. 2023 Jan;118(1):97-107

Opioid Registry
Eight Participating Health Systems

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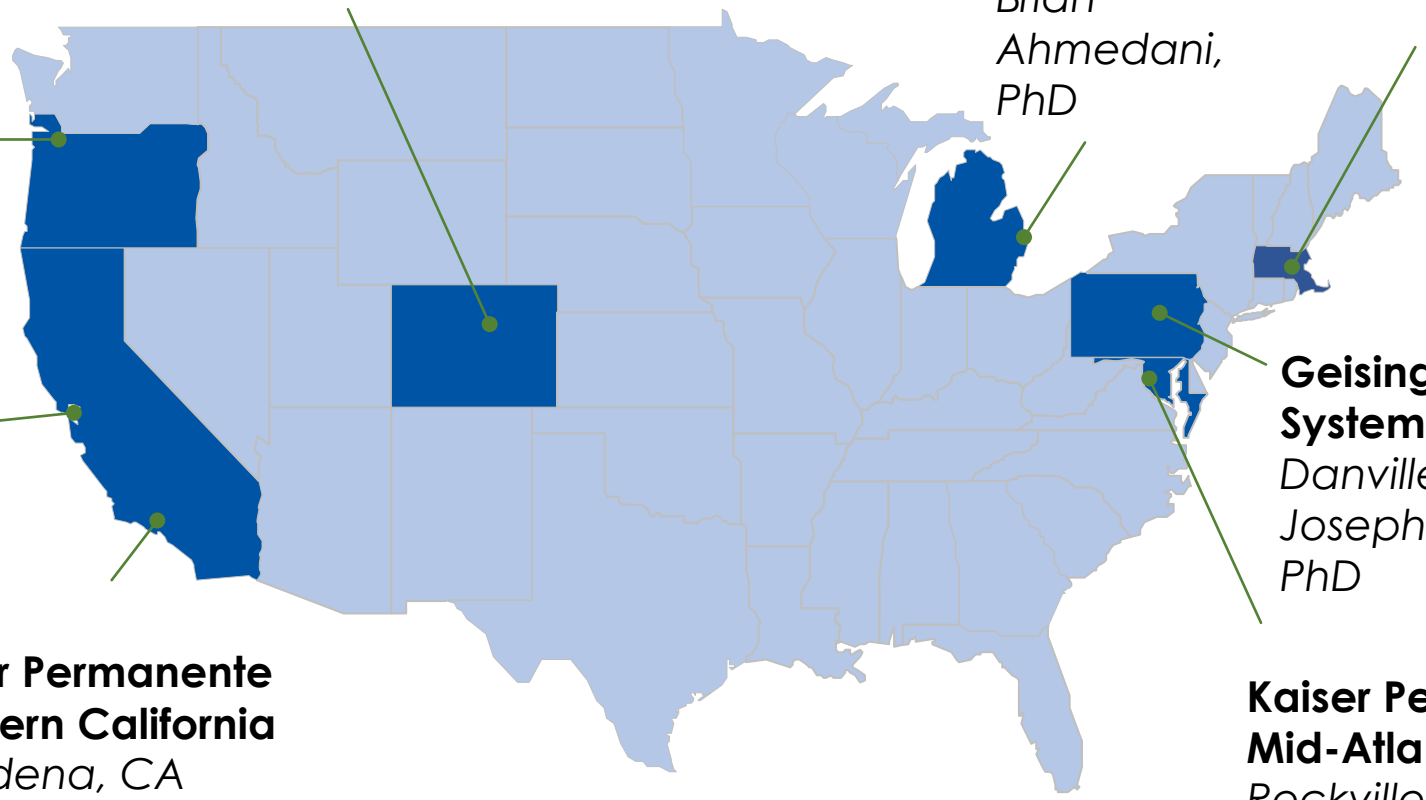


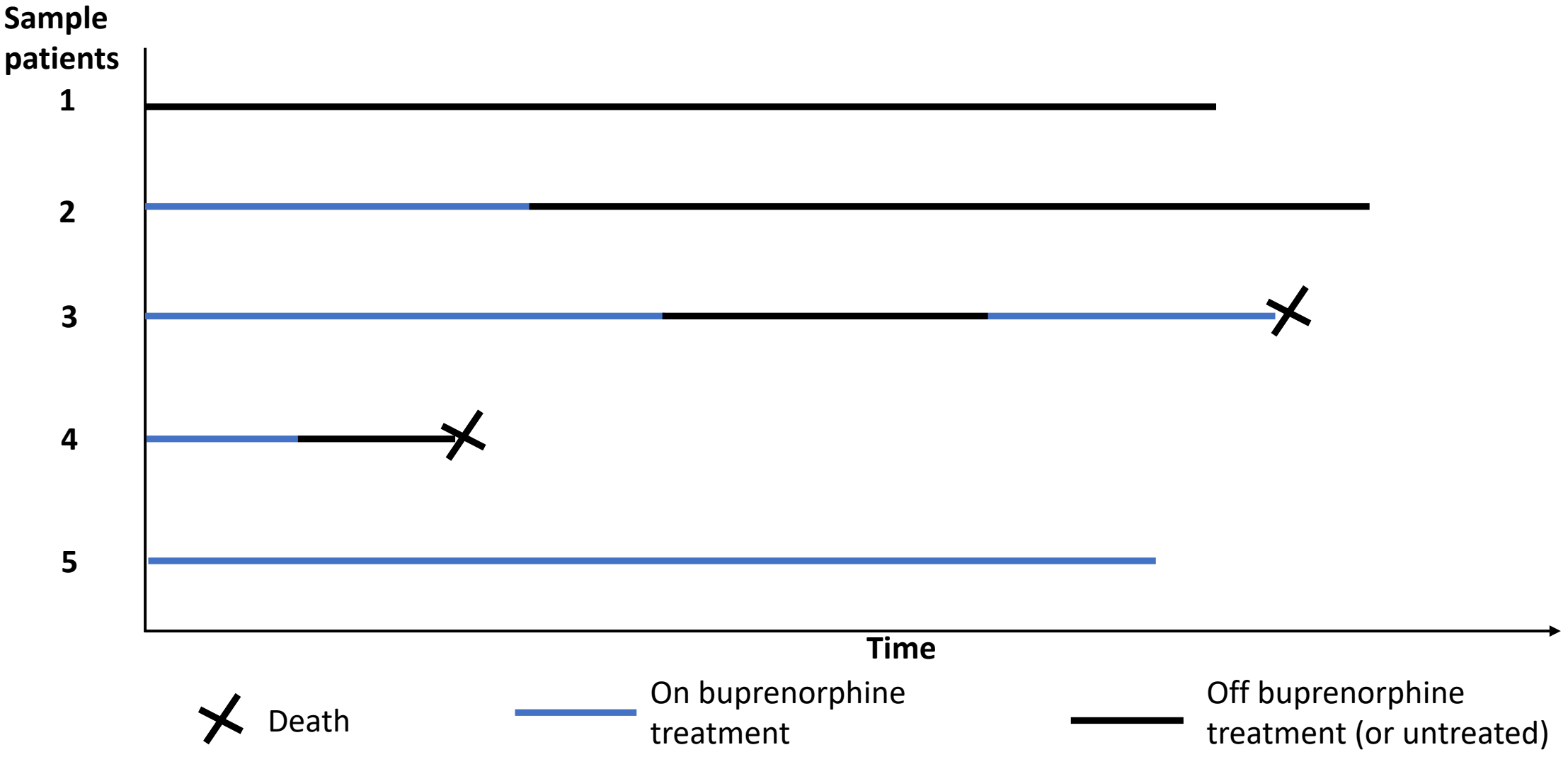
Settings

- Eight integrated health systems representing an insurance plan and care delivery system serving between 270,000-4.7 million people
- OUD care delivered through internal or contracted specialty treatment programs or primary care including:
  - Sublingual buprenorphine or buprenorphine/naloxone
  - XR naltrexone
  - Referral to methadone

Data in the Opioid Registry

- Based on any opioid dispensation or diagnosis of OUD for years 2012-2018
- Demographics
- Medications: Opioid prescriptions, medications for OUD, benzodiazepines
- Diagnoses: Pain, opioid use disorder, non-opioid substance use disorder, comorbid diagnoses
- Health services utilization
- Overdose and mortality

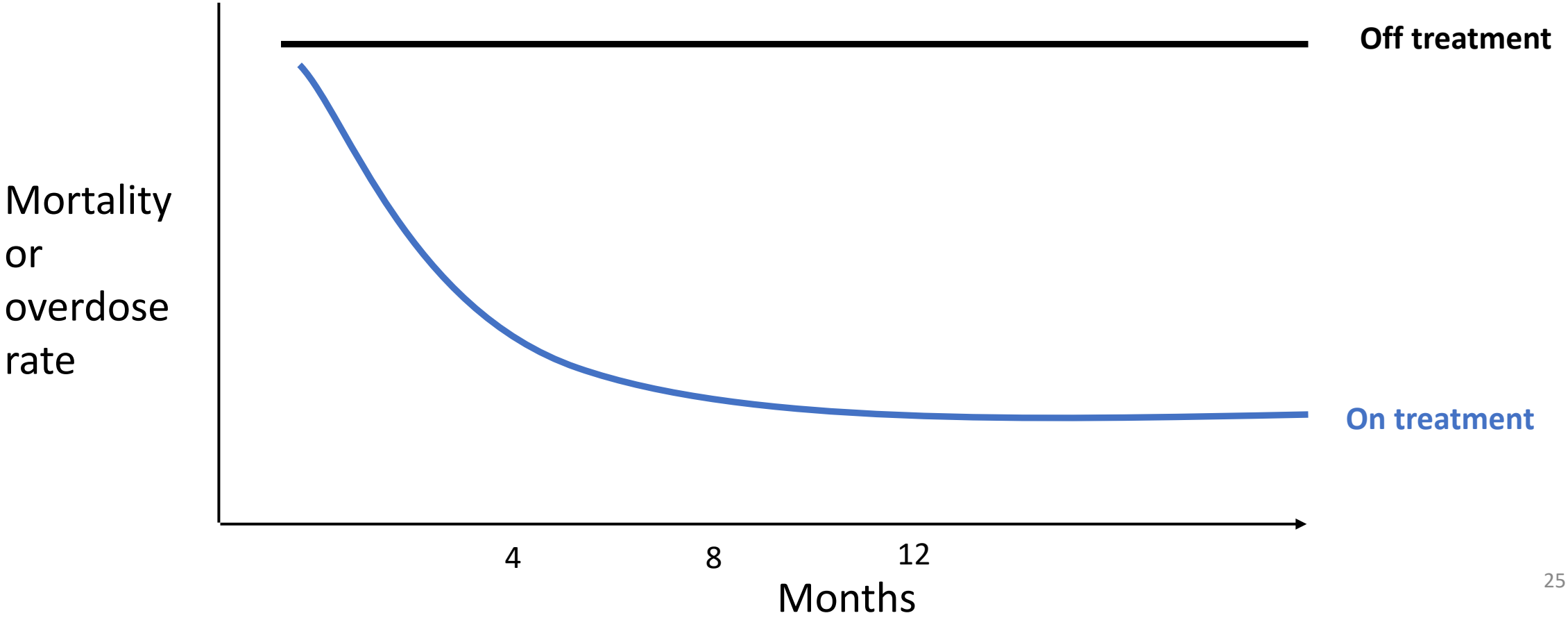
Classic cohort design to examine the association between buprenorphine retention and mortality



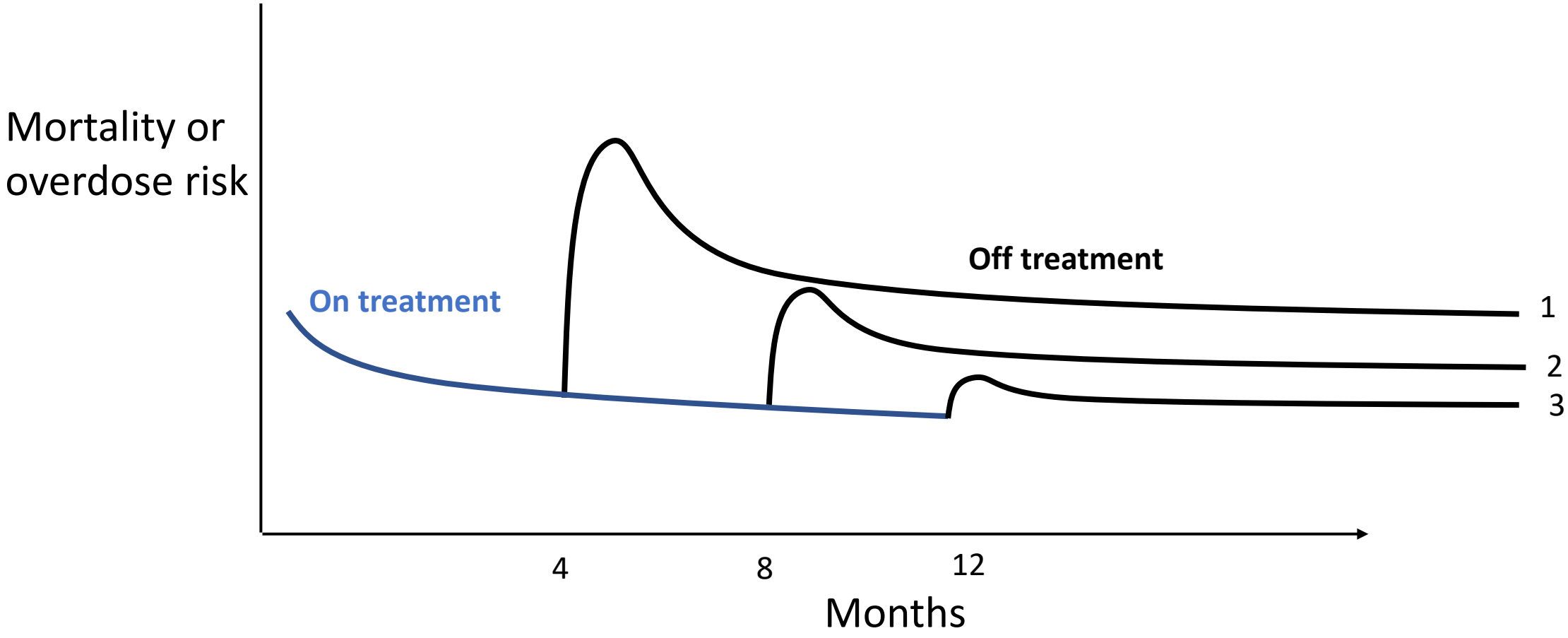
Two assessments of buprenorphine effectiveness

1. How long does one have to stay on buprenorphine treatment to see a mortality or overdose benefit relative to being off treatment (or alternative treatments)?
2. How long does one have to stay on treatment to see a reduction in mortality or overdose risk after discontinuing treatment?

1. How long does one have to stay on buprenorphine treatment to see a mortality or overdose benefit relative to being off treatment or alternative treatments?

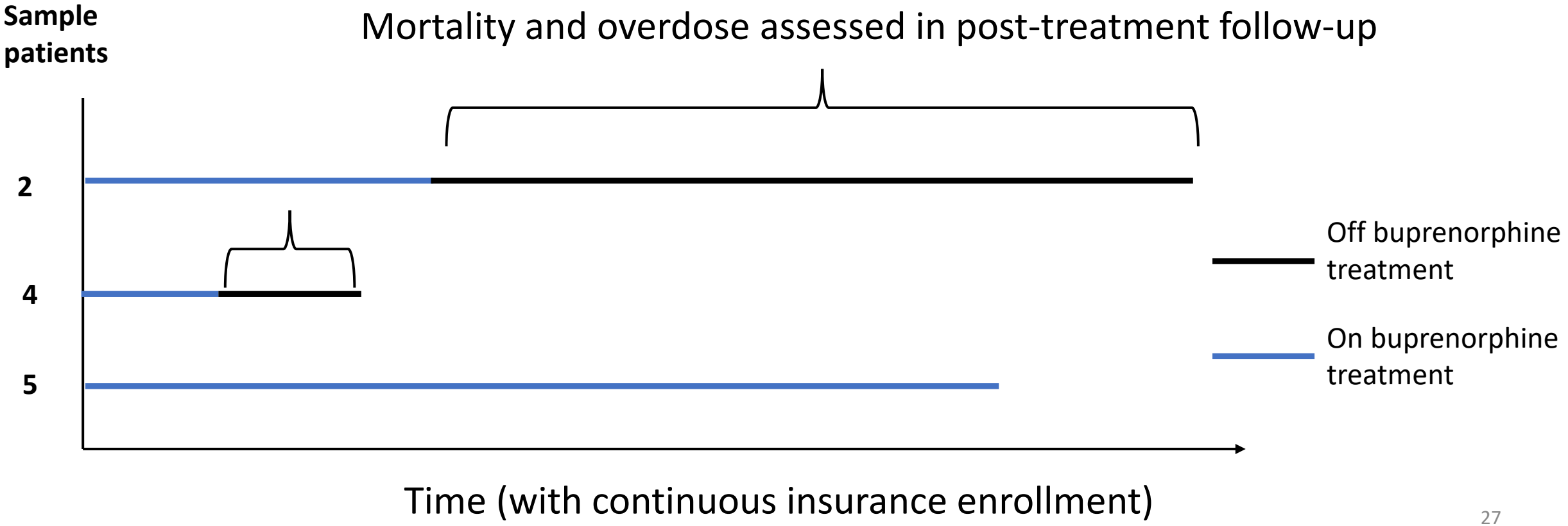


2. How long does one have to stay on treatment to see a reduction in mortality or overdose risk after discontinuing treatment?



For #2, need adequate post-treatment follow-up

- Outcomes assessed during insurance enrollment after treatment ends
- Length of post-treatment insurance enrollment affects statistical power



Cohort

1. In the opioid registry, identified adults (> 18 years) who
   - Started buprenorphine between 1/1/2012 and 12/31/2017
   - Stopped buprenorphine treatment prior to 12/31/2018
   - Had at least 1 day of post-treatment insurance enrollment
2. Excluded patients with <90 days pre-treatment enrollment, in hospice, with cancer, or without pharmacy insurance

Cohort

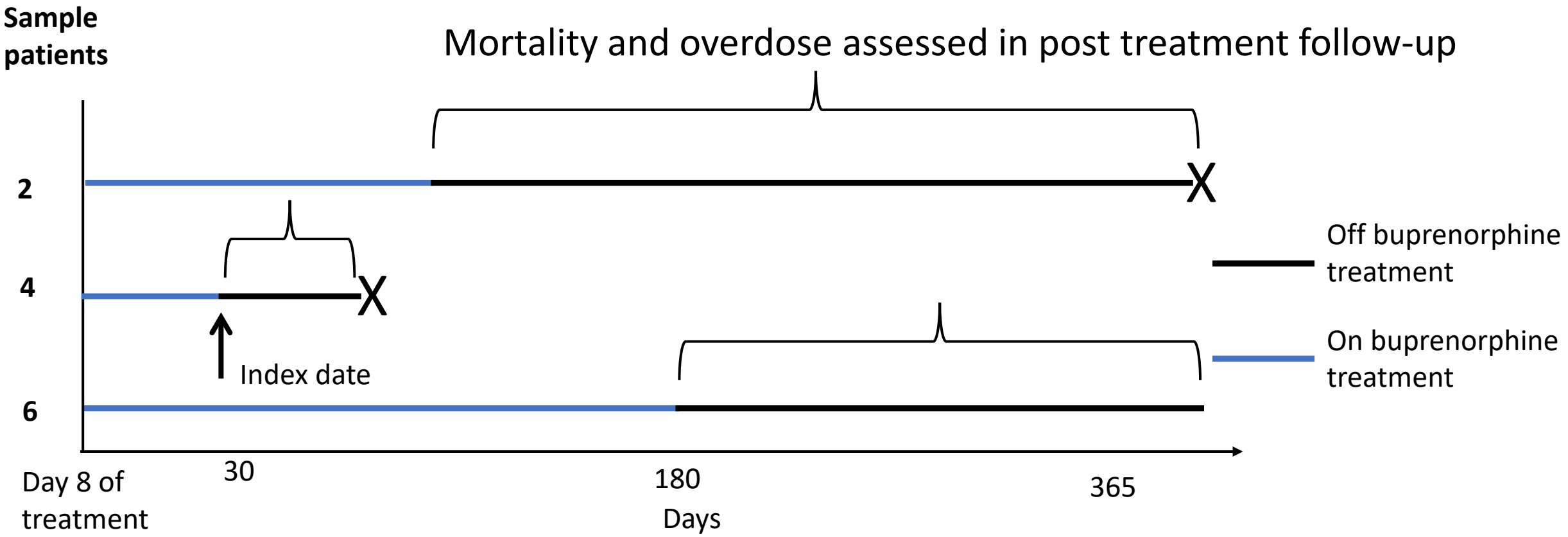
3. Assessed final treatment episode if there was more than one episode
    - New treatment episode occurred after a gap in treatment > 28 days
    - Excluded treatment episodes of <8 days (induction failure)
    - Most patients had one episode but wide range: median = 1 episode (IQR 1 to 2 episodes; range 1 to 17 episodes)
4. Sensitivity analysis for all treatment episodes

Cohort

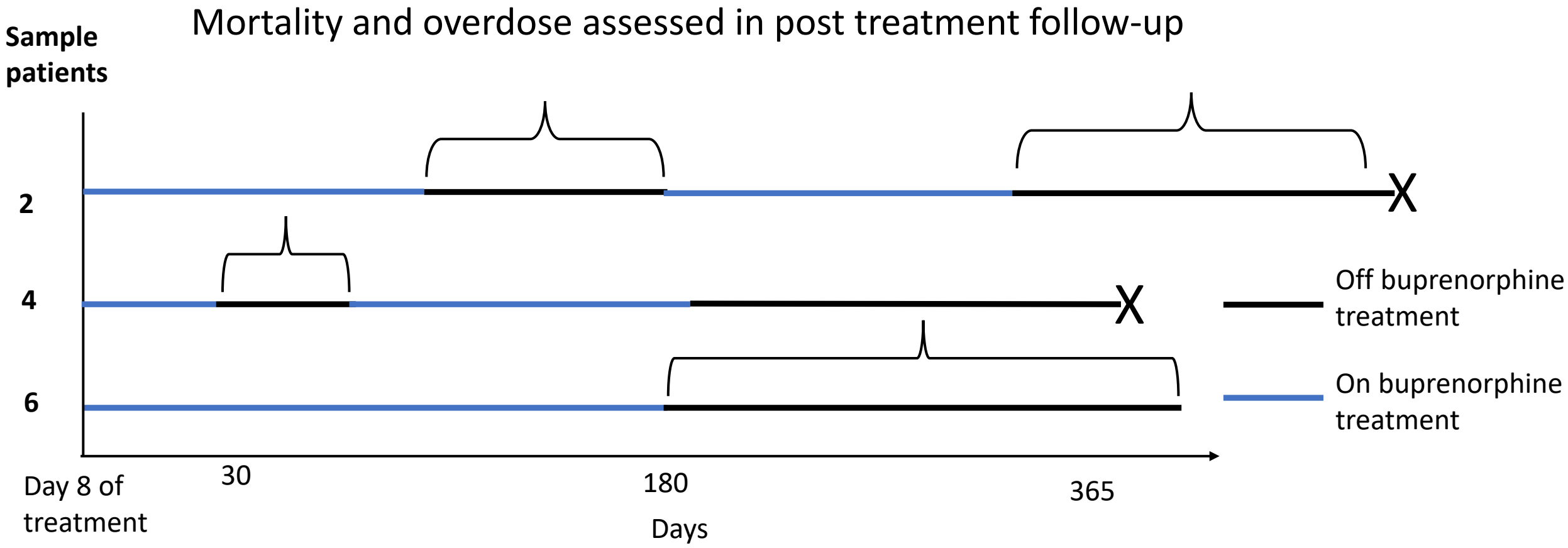
5. Categorized final treatment episode into 5 groups (exposure)
    - 8-30 days (post-induction month 1)
    - 31-90 days (months 2-3)
    - 91-180 days (months 4-6)
    - 181-365 days (months 7-12)
    - >365 days (referent, greater than a year)

6. Censored at death, overdose, disenrollment, switching to another treatment, or end of study (12/31/2018)

Cohort study design with post-treatment all-cause mortality or overdose (time-to-event)



Cohort study design with multiple treatment episodes



Outcomes

1. All-cause mortality – 8 sites: deaths in electronic health records (emergency department or hospital or reported) for 4 sites, state vital records for 4 sites
2. Non-fatal and fatal drug overdose -- data from EHR and state vital records with cause-of-death available for 4 sites
3. Non-fatal and fatal opioid overdose from EHR and state vital records at 4 sites

Covariates considered (potential confounders)

- Age
- Race and ethnicity
- Year of final treatment episode
- Number of treatment episodes
- Other medication use in 6 months prior to starting the final episode of treatment (antidepressants, z-drugs, gabapentin, benzodiazepines)
- Prior drug overdose
- Indicators of injection drug use (HIV/AIDS, Hep C or related infections)
- Alcohol use disorder
- Other drug use disorders
- Mental health disorder diagnosis
- Charlson comorbidity Index
- Number emergency department visits
- Opioid dispensings in 30 days prior to final treatment episode
- OUD severity
- Maximum dispensed buprenorphine dose

Analysis

Aim: Examine the association between buprenorphine treatment length and mortality/overdose risk among people who have discontinued

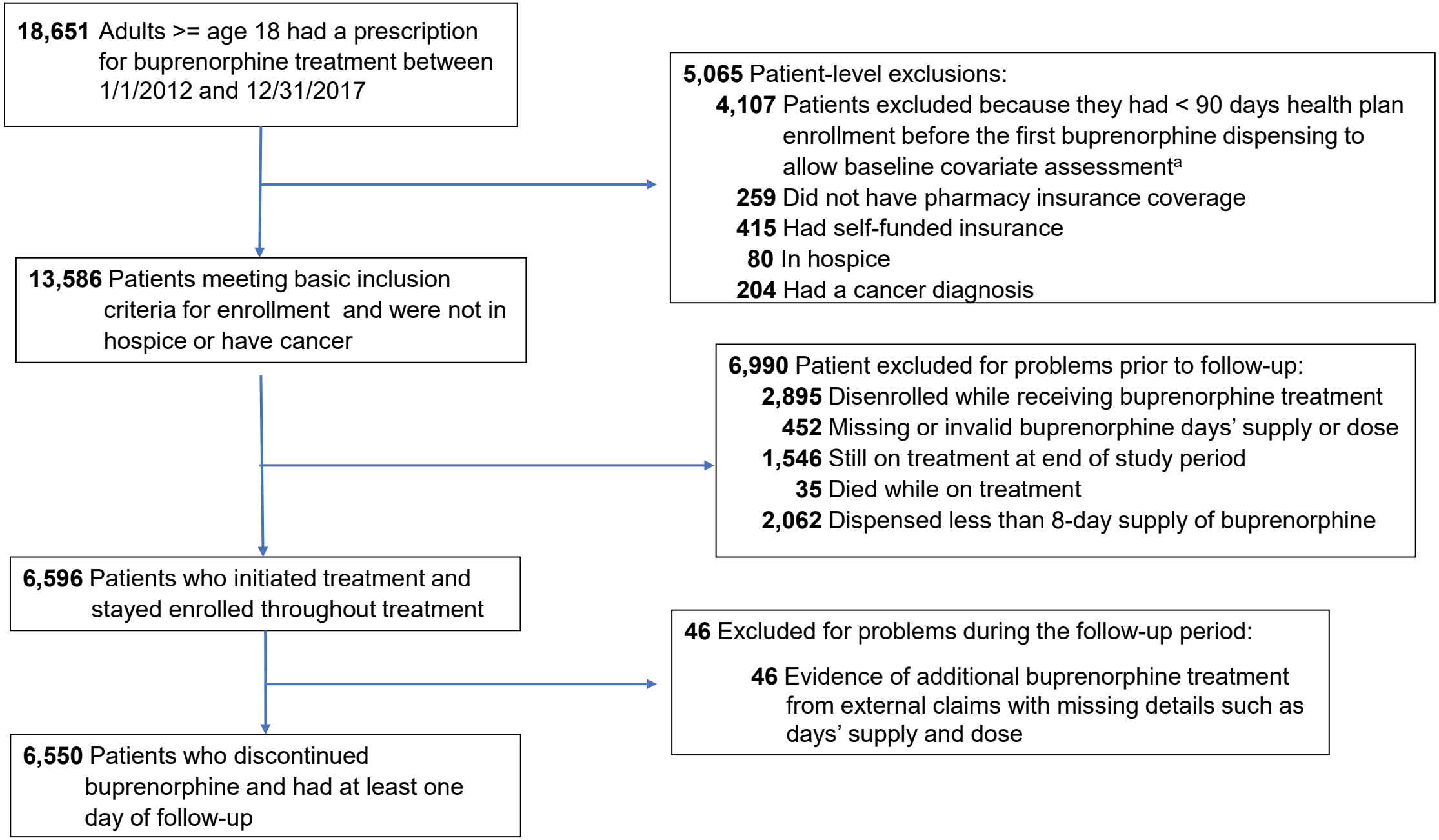
1. Propensity score analysis to control for confounding with inverse probability weighting
2. Frailty regression to analyze time-to-death or overdose post-treatment, adjusted for covariates via propensity score weighting
   - Three models – all-cause mortality and fatal/nonfatal overdose and opioid overdose as outcomes
   - Study site included in models as a random effect
   - Pairwise comparisons
3. Frailty regression with individual patients as a random effect to account for clustering of multiple treatment episodes

Propensity score analysis

1. Assess associations between baseline characteristics (covariates) and treatment and between covariates and outcome
   - Univariate multinomial logistic regression with treatment length as dependent variable and each baseline covariate as independent variable
   - Univariate Cox proportional hazards regression with death as outcome and each baseline covariate as independent variable
   - Identify baseline covariates associated with both treatment and outcome (confounders)
2. Build multivariable multinomial logistic regression model with treatment length as dependent variable and baseline confounders as independent variables

Propensity score analysis

3. Calculate propensity scores (PS) = patients' predicted probability of receiving treatment given their characteristics
4. Create weights = 1/PS for treated, 1/(1-PS) for untreated
5. Check balance of covariates
   - Population standardized mean differences
6. Estimate treatment effect using Cox proportional hazards regression, adjusted for covariates via propensity score weighting


18,651 Adults >= age 18 had a prescription for buprenorphine treatment between 1/1/2012 and 12/31/2017
5,065 Patient-level exclusions:
4,107 Patients excluded because they had < 90 days health plan enrollment before the first buprenorphine dispensing to allow baseline covariate assessment[a]
259 Did not have pharmacy insurance coverage
415 Had self-funded insurance
80 In hospice
204 Had a cancer diagnosis
13,586 Patients meeting basic inclusion criteria for enrollment and were not in hospice or have cancer
6,990 Patient excluded for problems prior to follow-up:
2,895 Disenrolled while receiving buprenorphine treatment
452 Missing or invalid buprenorphine days' supply or dose
1,546 Still on treatment at end of study period
35 Died while on treatment
2,062 Dispensed less than 8-day supply of buprenorphine
6,596 Patients who initiated treatment and stayed enrolled throughout treatment
46 Excluded for problems during the follow-up period:
46 Evidence of additional buprenorphine treatment from external claims with missing details such as days' supply and dose
6,550 Patients who discontinued buprenorphine and had at least one day of follow-up

Cohort characteristics (N=6550)

Characteristic	Mean (SD) or %
Age at start of treatment, y	37 (15)
Male gender	61%
Race and Ethnicity	
Non-Hispanic Black	5%
Hispanic	13%
Non-Hispanic White	73%
Non-Hispanic Asian, Pacific Islander, Native American, and other groups	3%
Unknown	6%

Cohort characteristics (N=6550)

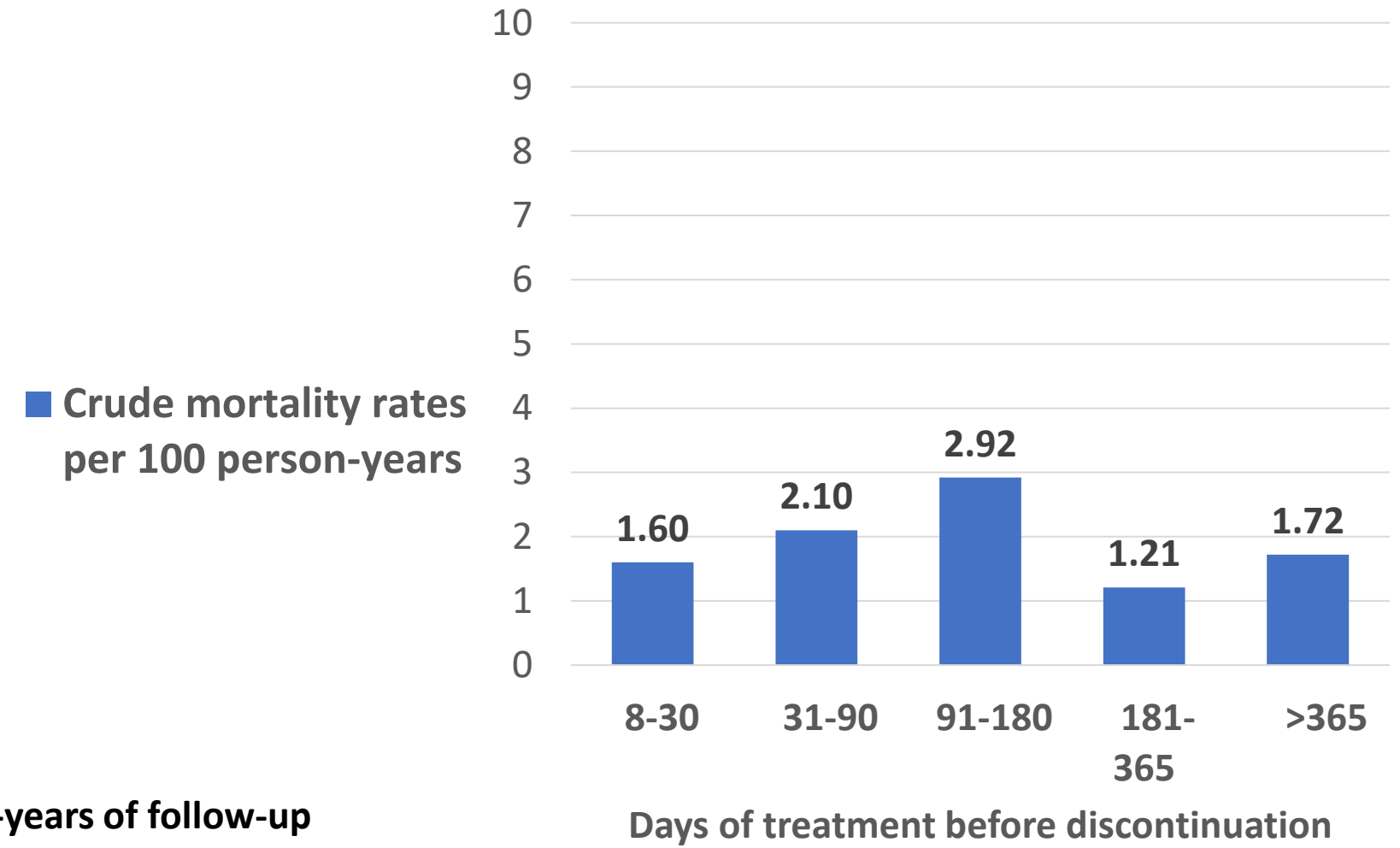
Characteristic	% or median (IQR)
Opioid dispensed in 30 days prior to treatment episode	29%
Alcohol use disorder	18%
Injection drug use related infection	5%
Mental health disorder	55%
Drug overdose	10%
Charlson co-morbidity	0 (0-1)
Emergency department utilization, 6 months	0 (0-1)

*Also examined year treatment episode started, past 6 month medications (Z-drugs, antidepressants, gabapentin, benzodiazepines), OUD severity coding

Cohort characteristics (N=6550)

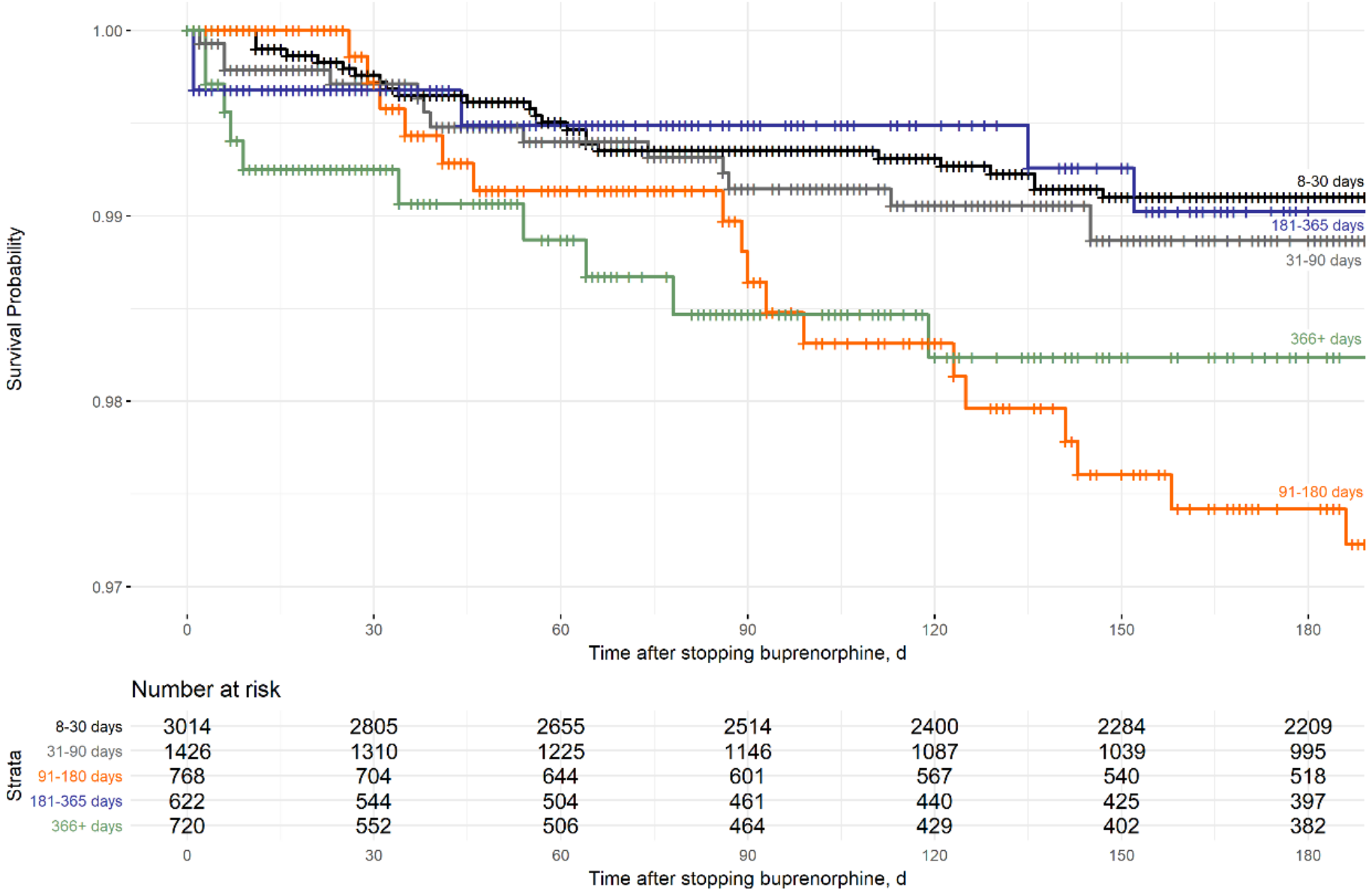
Characteristic	Mean (SD) or median (IQR) or %
Mean time on treatment, days	181 (290)
Median time on treatment, days	60 (27-203)
Time on treatment in groups	
8-30 days	46%
31-90 days	22%
91-180 days	12%
181-365 days	10%
>365 days	11%
Number of treatment episodes	1 (1-2)
Follow-up post treatment cessation, days	392 (120-875)
Median maximum buprenorphine dose (mg/day)	12 (8-16)
Switch to naltrexone or methadone after episode	11%

Crude mortality rates (CMR) after stopping treatment by length of time on treatment



N=191 deaths
10,471 person-years of follow-up

Survival curves for first 180 days of treatment



8-30 days

181-365 days

31-90 days

>365 days

91-180 days

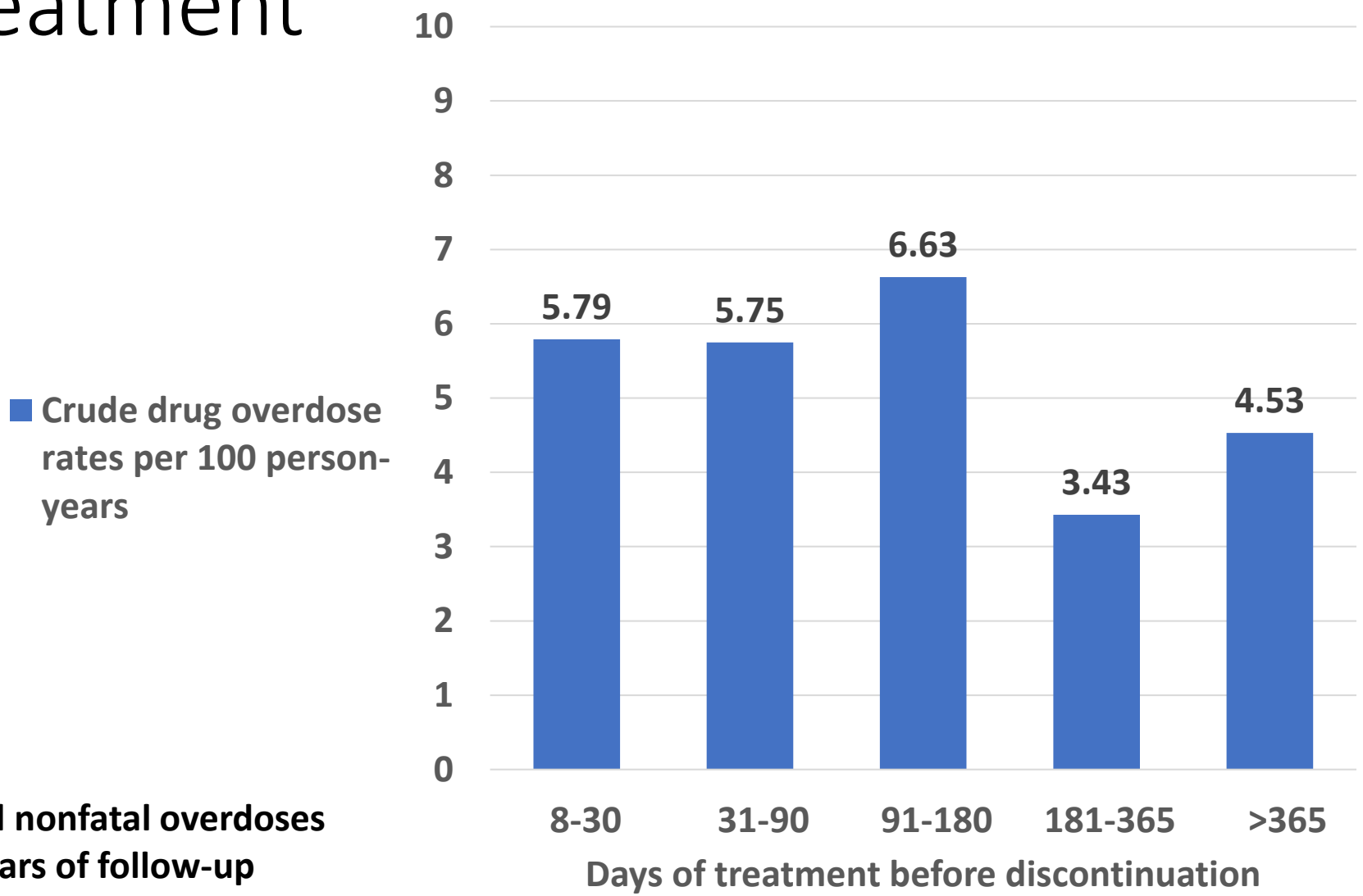
Adjusted and propensity-weighted model for the association between length of buprenorphine treatment and all-cause mortality

Length of buprenorphine treatment	Hazard Ratio (95% CI)
8-30 days	1.25 (0.68, 2.31)
31-90 days	1.59 (0.85, 2.98)
91-180 days	1.93 (1.00, 3.71)
181-365 days	0.79 (0.35, 1.82)
> 365 days	1.00

Model contrasts for all-cause mortality

Contrasts	Hazard ratio (95% CI)
8-30 vs. 31-90 days	0.79 (0.55, 1.13)
8-30 vs. 91-180 days	0.65 (0.42, 1.01)
8-30 vs. 181-365 days	1.57 (0.80, 3.08)
31-90 vs. 91-180 days	0.83 (0.52, 3.98)
31-90 vs. 181-365 days	**2.00 (1.01, 3.98)**
91-180 vs. 181-365 days	**2.42 (1.19, 4.95)**

Crude drug overdose rates by length of time on treatment



N=160 fatal and nonfatal overdoses
5892 person-years of follow-up

Adjusted and propensity-weighted model for the association between length of buprenorphine treatment and drug overdose

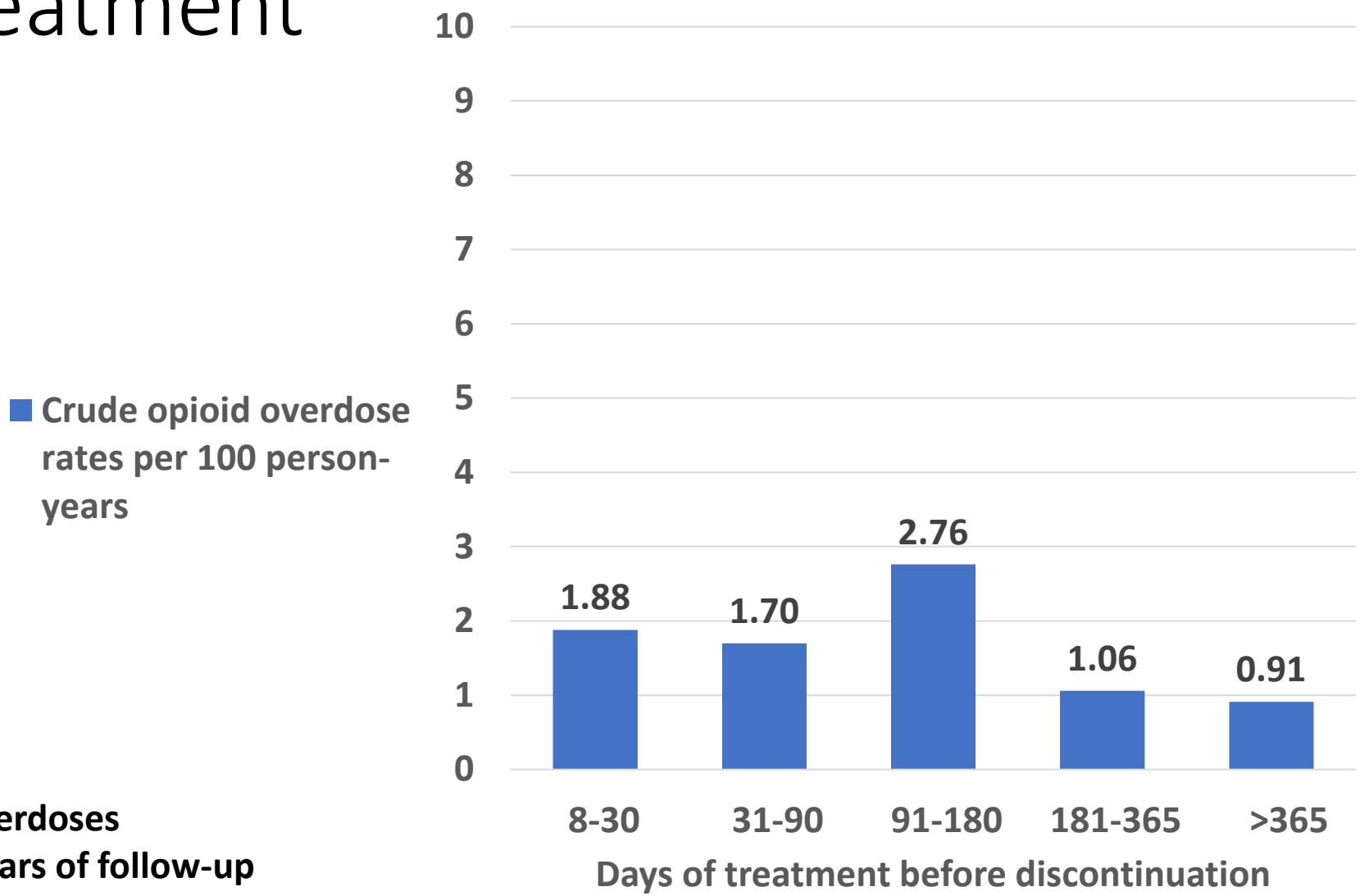
Length of buprenorphine treatment	Hazard Ratio (95% CI)
8-30 days	1.39 (0.89, 2.16)
31-90 days	1.30 (0.82, 2.07)
91-180 days	1.48 (0.91, 2.42)
181-365 days	0.74 (0.41, 1.36)
> 365 days	1.00

*Overdose fatalities available from 4 of 8 sites

Model contrasts for fatal and nonfatal drug overdose

Contrasts	Hazard ratio (95% CI)
8-30 vs. 31-90 days	1.07 (0.80, 1.41)
8-30 vs. 91-180 days	0.93 (0.67, 1.31)
8-30 vs. 181-365 days	**1.86 (1.14, 3.04)**
31-90 vs. 91-180 days	0.88 (0.61, 1.27)
31-90 vs. 181-365 days	**1.75 (1.05, 2.91)**
91-180 vs. 181-365 days	**1.99 (1.17, 3.40)**

Crude opioid overdose rates by length of time on treatment



N=54 opioid overdoses
6112 person-years of follow-up

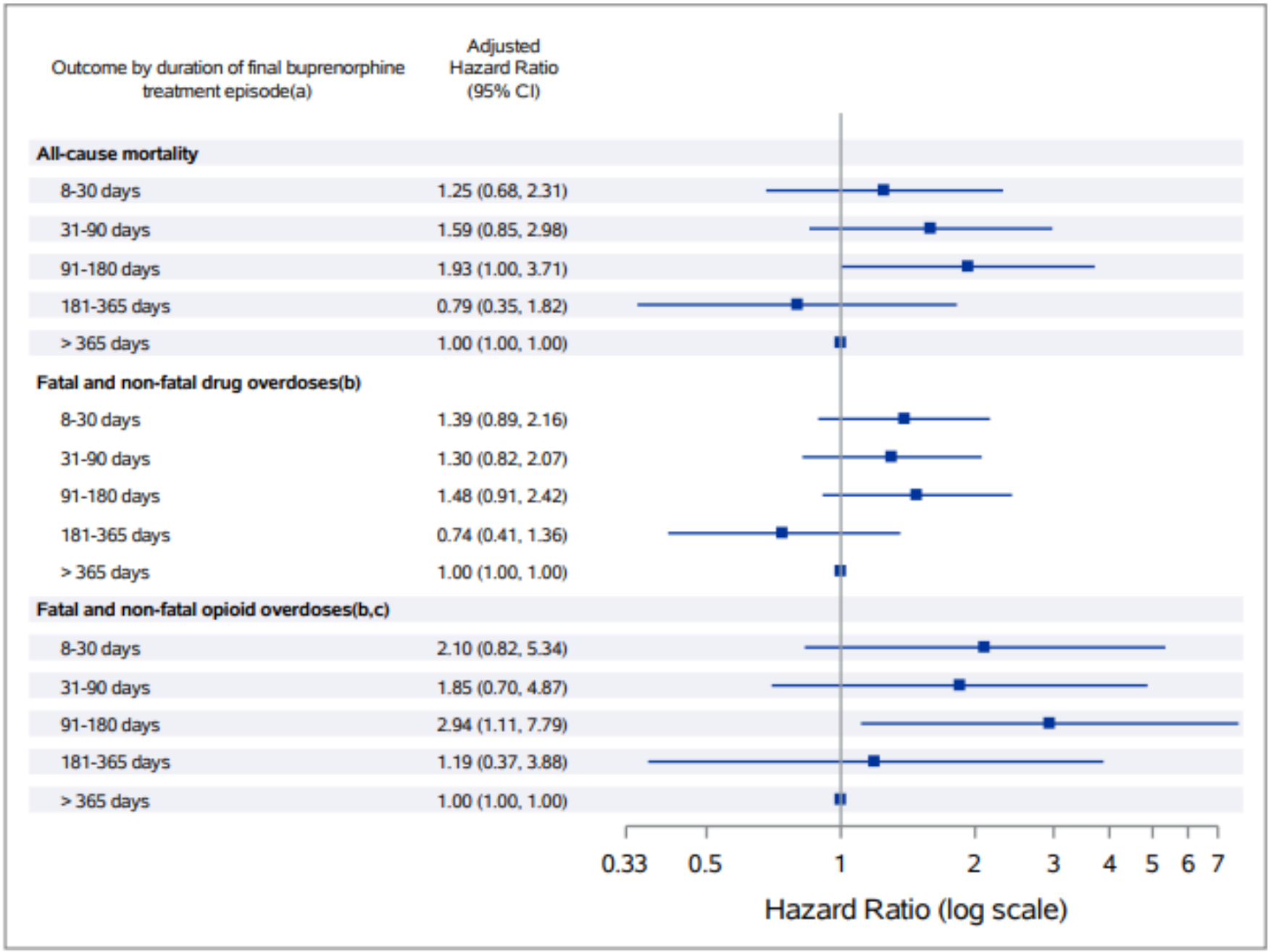
Adjusted and propensity-weighted model for the association between length of buprenorphine treatment and opioid overdose

Length of buprenorphine treatment	Hazard Ratio (95% CI)
8-30 days	2.10 (0.82, 2.16)
31-90 days	1.85 (0.70, 2.07)
91-180 days	**2.94 (1.11, 7.79)**
181-365 days	1.19 (0.37, 3.88)
> 365 days	1.00

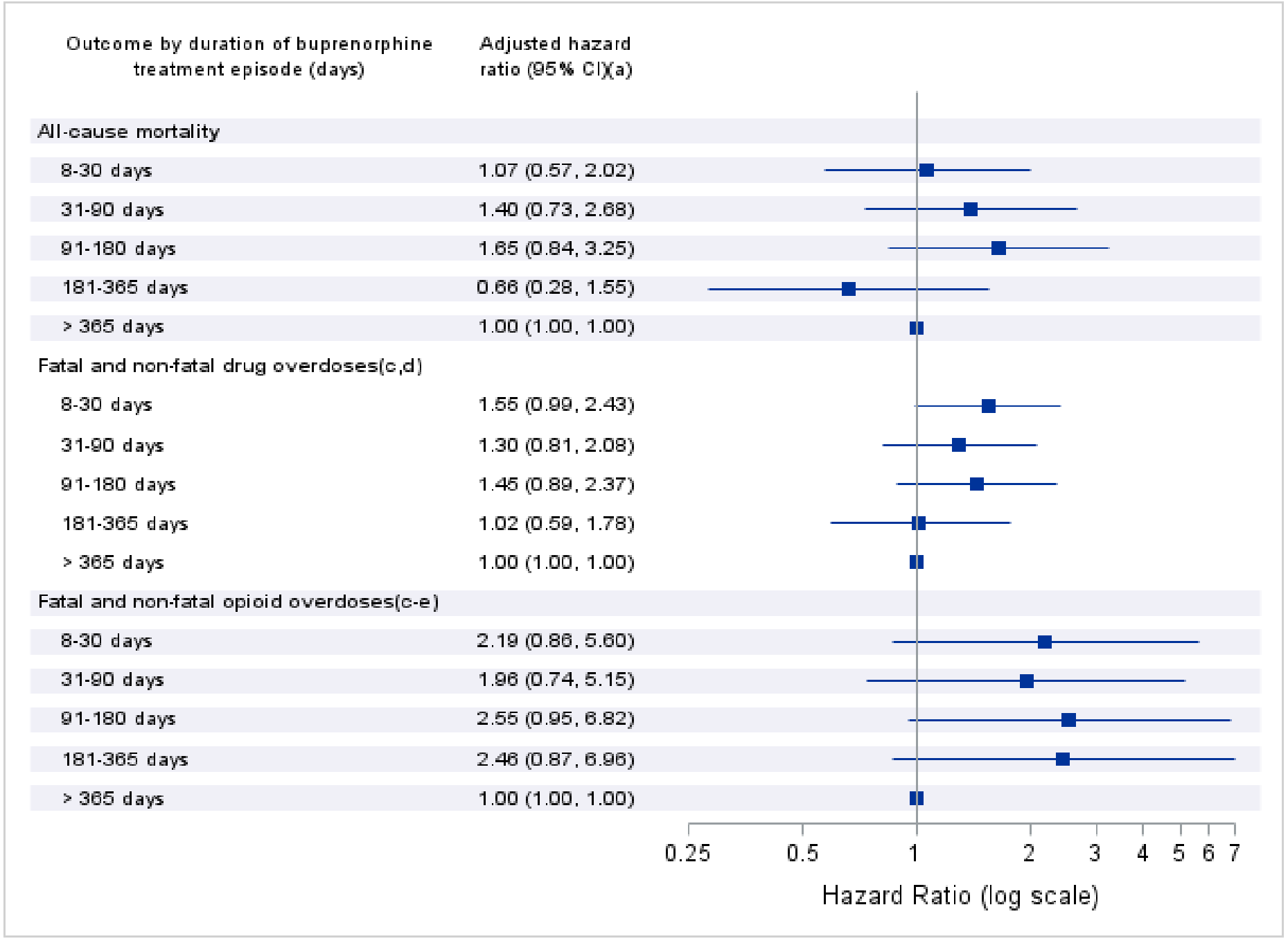
*Overdose fatalities available from 4 of 8 sites

Model contrasts for fatal and nonfatal opioid overdose

Contrasts	Hazard ratio (95% CI)
8-30 vs. 31-90 days	1.14 (0.69, 1.87)
8-30 vs. 91-180 days	0.71 (0.42, 1.21)
8-30 vs. 181-365 days	1.76 (0.75, 4.16)
31-90 vs. 91-180 days	0.63 (0.35, 1.14)
31-90 vs. 181-365 days	1.55 (0.63, 3.82)
91-180 vs. 181-365 days	2.47 (0.99, 6.14)


Outcome by duration of final buprenorphine treatment episode(a)
Adjusted Hazard Ratio (95% CI)
All-cause mortality
8-30 days
1.25 (0.68, 2.31)
31-90 days
1.59 (0.85, 2.98)
91-180 days
1.93 (1.00, 3.71)
181-365 days
0.79 (0.35, 1.82)
> 365 days
1.00 (1.00, 1.00)
Fatal and non-fatal drug overdoses(b)
8-30 days
1.39 (0.89, 2.16)
31-90 days
1.30 (0.82, 2.07)
91-180 days
1.48 (0.91, 2.42)
181-365 days
0.74 (0.41, 1.36)
> 365 days
1.00 (1.00, 1.00)
Fatal and non-fatal opioid overdoses(b,c)
8-30 days
2.10 (0.82, 5.34)
31-90 days
1.85 (0.70, 4.87)
91-180 days
2.94 (1.11, 7.79)
181-365 days
1.19 (0.37, 3.88)
> 365 days
1.00 (1.00, 1.00)
0.33
0.5
1
2
3
4
5
6
7
Hazard Ratio (log scale)

All treatment episodes



Limitations

- Death data limited in some systems
  - In-hospital deaths
  - Lacking cause-of-death
  - In state only
- All-cause mortality lacks specificity and may not be the ideal outcome
- Pre-fentanyl in some regions – if it impacts retention and mortality
- Do not know what patient factors or provider/program factors led to discontinuation
- Practice patterns may have changed since study period, fewer barriers
- Selection bias
- Uncertain how patients were tapered or stopped

Summary

1. Of individuals who stopped buprenorphine treatment, a majority stopped before 90 days of treatment
2. Greatest risk for all-cause mortality was among those that stopped treatment between 91 and 180 days
3. Greatest risk for fatal and nonfatal overdose was also among those that stopped treatment between 91 and 180 days
4. Staying on treatment longer than 365 days was associated with the lowest risk for overdose compared to shorter treatment lengths (not statistically significant)

Clinical implications: first consider strategies to maximize retention

- Greater medication dose and supply at initiation
- Lower threshold services: reduced monitoring and easier access via telehealth
- Manage of co-occurring use disorders and depression
- Longer-acting buprenorphine formulations
- Manage risk of insurance discontinuity and clinician/program change
- Consider support of clinical pharmacists/team-based care
- Digital supports
- *Follow CTN-100: Optimizing Retention, Duration, and Discontinuation Strategies for Opioid Use Disorder Pharmacotherapy trial*

Shulman M, et al., Contemp Clin Trials 2025; Shulman, et al., Contemp Clin Trials 2024; Nguyen et al., JAMA Psych 2026

Assess patient needs and intentions at the start of treatment and periodically

- Is there anything we can do to improve your experience with the medication?
- Do you have any goals about how long you would like to be taking medications?
- If so,
  - Why?
  - When?
  - How long do you anticipate it might take?
  - Can we discuss alternatives?

Current ASAM and SAMHSA Guidelines

No limit on the time people with an opioid use disorder remain on treatment

- Make patients aware of the risks
- Discuss treatment alternatives
- Discuss naloxone to prevent fatal overdose
- Taper slowly
- Monitor closely
- Remain in treatment past discontinuation

The ASAM National Practice Guideline for the Treatment of Opioid Use Disorder – 2020 Focused Update

TIP 63: Medications for Opioid Use Disorder - Full Document | SAMHSA Publications and Digital Products

IF patient plans to taper or stop: provide education, counseling, and support

- No clear optimal period after which you can safely discontinue buprenorphine treatment
- Risk of overdose could be fatal, esp. given changes in drug supply

BUT

- If you have decided to taper, let's work together on a plan to align with your treatment goals
- Realistic timeline and expectations
- Schedule appointments for during after discontinuation

Hayes CJ et al., Addiction 2026

IF patient plans to taper or stop: consider clinical strategies to support tapering

- Prescribe or provide naloxone
- Avoid dose variability and abrupt discontinuation
- ***Consider***
  - Smaller increments of dose reduction as absolute dose decreases
  - Change in formulation (ER buprenorphine, film for low doses)
  - Longer taper
  - Withdrawal management
  - Low threshold to increase/re-start

Colver et al, Subst Use Addctn J 2026; Horowitz MA et al. Ther Adv Psychopharmacol, 2025; Glanz et al., JAMA Netw Open 2019

Thank you and questions/comments

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