Supplemental Online Content

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**eFigure 1.** Death Match Algorithm

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**eFigure 3.** Crude Cumulative Incidence of Outcomes by Primary Exposure Status

**eFigure 4.** Crude Cumulative Incidence of Outcomes by Exposure Status Using a Categorical Exposure Definition

**eReferences**

This supplemental material has been provided by the authors to give readers additional information about their work.
eMethods.

Detailed patient inclusion/exclusion

Patients were excluded if they had a history (using all-available data for lookback\(^1,2\)) of opioid overdose or OUD \((n=1,992)\), identified using International Classification of Diseases (ICD) version 9, clinical modification (ICD-9-CM) or ICD-10-CM codes in insurance claims. Exposure status could not be assessed prior to the end of the first 30-day period; therefore, we excluded 869 patients who were not followed for \(\geq 30\) days past the end of the baseline eligibility period. Time-updated five-digit ZIP-code level characteristics were missing for 22 individuals who were excluded from the analytic cohort.

Patients could reenter the analytic cohort after disenrollment, with follow-up time reset to 0, if they reentered the insurance pool and again met eligibility criteria \((n=1,867)\). The statistical approach accounted for repeated measures and variable follow-up duration.

Calculating Daily MME

First, using dose and quantity indicated in the prescription’s National Drug Code and prescription days’ supply recorded in the outpatient pharmaceutical claim record, dose per unit and number of units dispensed were multiplied and then divided by prescription days’ supply, with the resulting milligrams of medication/day then multiplied by an MME conversion factor from CDC conversion tables for each prescription.\(^3\) When overlapping prescriptions of the same ingredient occurred, we assumed that if the start date was \(\leq 7\) days before the end date of the previous prescription, this reflected an early refill and the start date of that prescription was pushed forward to the end date of the previous prescription.\(^4\) Otherwise, the prescriptions were assumed to truly overlap. We allowed for gaps in prescriptions in the baseline period by only requiring \(\geq 90\%\) days at \(\geq 90\) MMEs. Daily MME for each calendar day was then calculated as the sum of MMEs per day across all prescriptions a patient had on that day.

Defining exposure trajectories

During each 30-day period, we compared average dose during the current month to both (1) average dose from the previous month and (2) a 6-month rolling average to classify patients’ prescription trajectories as dose maintained, increased, gradually decreased, rapidly decreased, gradually discontinued, or rapidly discontinued (eTable 2). Specifically, we determined a patient’s average dose in the current month and calculated the change in dose from the previous month as well as the change in dose from a 6-month rolling average and used both of these values to determine dose trajectory. We included the comparison with a 6-month rolling average, in addition to accounting for overlapping prescriptions, in order to minimize the impact of short-term dose variabilities on exposure classification.

We defined gradual dose reduction following CDC guideline recommendations of \(\leq 10\%\) dose reduction per week (\(\leq 34\%\) per month) and anything faster as rapid dose reduction.

Deriving inverse probability weights

We used stabilized IP treatment weights (IPTW) to account for time-dependent confounding.\(^5\) To calculate the IPTW denominator, we used pooled logistic regression to model the probability of experiencing a first rapid dose reduction/discontinuation event during each month of follow-up, given relevant baseline and time-varying confounders. The IPTW denominator included continuous time (restricted cubic spline with 4 knots); all confounders described above; and a one-month lag of other prescriptions, pain (acute or chronic), and surgery. The IPTW numerator was calculated as above, with confounders removed from the model. To account for possible selection bias stemming from potentially informative censoring, we calculated stabilized IP censoring weights (IPCW) in a manner analogous to IPTW, modeling the probability of remaining uncensored given relevant confounders and exposure status. We then multiplied IPCW by IPTW to obtain IPTC-weights.

We examined the weights distribution to ensure a mean of one, and truncated weights at the 0.02\(^{nd}\) and 99.98\(^{th}\) percentiles to minimize the influence of extreme weights.\(^5\) Covariate balance was assessed using standardized mean differences. After weighting, covariates were well balanced.
Sensitivity Analyses

First, to address potential issues around cohort selection with regard to baseline variability in opioid dosing, we restricted the analytic cohort to patients determined to have “stable” baseline dosing patterns, defined as a change of ≤30 MME in the 30-day running average between each 30-day period during the 90-day baseline eligibility period and replicated primary analyses in this sub-sample. Second, to address potential outcome misclassification for coprimary outcomes (2) and (3), we restricted nonfatal overdoses to those occurring during an emergency department (ED) or inpatient event in order to assess the potential impact of using all outpatient claims to identify clinically recognized nonfatal opioid overdoses.
**eTable 1. ICD-9-CM and ICD-10-CM Diagnostic Codes Used to Identify Opioid Overdose and Opioid Use Disorder (OUD) in Claims Data**

| ICD-9-CM | ICD-10-CM |
|----------|-----------|
| **Opioid Overdose** | |
| 965.00   | T40.1X1A, T40.1X4A |
| 965.01   | T40.0X1A, T40.0X4A |
| 965.02   | T40.2X1A, T40.2X4A |
| 965.09   | T40.3X1A, T40.3X4A |
| E850.0   | T40.4X1A, T40.4X4A |
| E850.1   | T40.601A, T40.604A |
| E850.2   | T40.691A, T40.694A |
| **Opioid Use Disorder (OUD)** | |
| 304.00   | F11.10 |
| 304.01   | F11.120, F11.121, F11.122, F11.129 |
| 304.02   | F11.14 |
| 304.03   | F11.150, F11.151, F11.159 |
| 304.70   | F11.181, F11.182, F11.188 |
| 304.71   | F11.19 |
| 304.72   | F11.20 |
| 304.73   | F11.220, F11.221, F11.222, F11.229 |
| 305.50   | F11.23 |
| 305.51   | F11.24 |
| 305.52   | F11.250, F11.251, F11.259 |
| 305.53   | F11.281, F11.282, F11.288 |
| 970.10   | F11.29 |
| E9350    | F11.90 |
| E9351    | F11.920, F11.921, F11.922, F11.929 |
| E9352    | F11.93 |
| E9401    | F11.94 |
|          | F11.950, F11.951, F11.959 |
|          | F11.981, F11.982, F11.988 |
|          | F11.99 |
|          | T40.0X1D, T40.0X2D, T40.0X3D, T40.0X4D |
|          | T40.1X1D, T40.1X2D, T40.1X3D, T40.1X4D |
|          | T40.2X1D, T40.2X2D, T40.2X3D, T40.2X4D |
|          | T40.3X1D, T40.3X2D, T40.3X3D, T40.3X4D |
|          | T40.4X1D, T40.4X2D, T40.4X3D, T40.4X4D |
|          | T40.601D, T40.602D, T40.603D, T40.604D |
|          | T40.691D, T40.692D, T40.693D, T40.694D |
|          | T40.0X5A, T40.0X5D |
|          | T40.2X5A, T40.2X5D |
|          | T40.3X5A, T40.3X5D |
|          | T40.4X5A, T40.4X5D |
|          | T40.605A, T40.605D, T40.695A, T40.695D |

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**eTable 2. Algorithm Used to Classify Monthly Prescription Trajectories**

| Dose in previous month | Change in dose from previous month to current month | Change in dose relative to 6-month rolling average | Classification |
|------------------------|-----------------------------------------------|-----------------------------------------------|----------------|
| >60 MME                | >10% increase from last month                   | >10% increase from 6-month rolling average      | Increase       |
|                        | >10% increase from last month                   | <=10% increase from 6-month rolling average     | No change      |
|                        | <=10% increase or decrease from last month      | -                                              | No change      |
|                        | 10.01-34% reduction from last month             | >10% reduction from 6-month rolling average     | Gradual decrease |
|                        | 10.01-34% reduction from last month             | <=10% reduction from 6-month rolling average    | No change      |
|                        | 35-99% reduction                                | >35% reduction from 6-month rolling average     | Rapid decrease |
|                        | 35-99% reduction                                | 10.01-34% decrease from 6-month rolling average | Gradual decrease |
|                        | 35-99% reduction                                | <=10% reduction from 6-month rolling average    | No change      |
|                        | 0 MME                                          |                                                | Rapid stop     |
| 1-60 MME               | >=10 MME increase                               | >=10 MME increase                              | Increase       |
|                        | >=10 MME increase                               | <10 MME increase                               | No change      |
|                        | <10 MME change                                  | -                                              | No change      |
|                        | 10-30 MME reduction but not stopped             | >=10 MME reduction                              | Gradual decrease |
|                        | 10-30 MME reduction but not stopped             | <10 MME reduction                              | No change      |
|                        | 31-59 MME reduction but not stopped             | 31-59 MME reduction                            | Rapid decrease |
|                        | 31-59 MME reduction but not stopped             | 10-30 MME reduction                            | Gradual decrease |
|                        | 31-59 MME reduction but not stopped             | <10 MME reduction                              | No change      |
| 31-60 MME              | 0 MME                                          |                                                | Rapid stop     |
| 1-30 MME               | 0 MME                                          |                                                | Gradual stop   |
### eTable 3. ICD-10 Codes Used to Identify Fatal Opioid Overdose in Linked Death Records

| Underlying Cause | Contributing Cause |
|------------------|--------------------|
| X40              | T40.0              |
| X41              | T40.1              |
| X42              | T40.2              |
| X43              | T40.3              |
| X44              | T40.4              |
| X60              | T40.6              |
| X61              |                    |
| X62              |                    |
| X63              |                    |
| X64              |                    |
| X85              |                    |
| Y10              |                    |
| Y11              |                    |
| Y12              |                    |
| Y13              |                    |
| Y14              |                    |

*The death must have a both an underlying cause code and contributing cause code.*
eTable 4. R Packages Used in Analyses

| Package   | Version |
|-----------|---------|
| broom     | 0.5.5   |
| cobalt    | 4.1.0   |
| cowplot   | 1.0.0   |
| dplyr     | 0.8.5   |
| forcats   | 0.5.1   |
| ggplot2   | 3.3.0   |
| ggpubr    | 0.2.5   |
| ggsci     | 2.9     |
| ggstance  | 0.3.5   |
| glue      | 1.4.1   |
| haven     | 2.2.0   |
| here      | 0.1     |
| Hmisc     | 4.4-0   |
| knitr     | 1.29    |
| lattice   | 0.20-38 |
| lubridate | 1.7.10  |
| magrittr  | 1.5     |
| MASS      | 7.3-54  |
| nnet      | 7.3-12  |
| rlang     | 0.4.11  |
| rms       | 5.1-4   |
| stringr   | 1.4.0   |
| survival  | 3.2-13  |
| survminer | 0.4.6   |
| tableone  | 0.11.1  |
| tibble    | 2.1.3   |
| tidyr     | 1.0.2   |
### eTable 5. IPTCW Risk Differences (95% CI) for the Association Between Rapid Tapering or Discontinuation of Opioid Treatment and Outcomes at Multiple Points of Follow-up

|                | Fatal opioid overdose | Nonfatal opioid overdose | Fatal or nonfatal overdose | OUD            |
|----------------|-----------------------|--------------------------|---------------------------|----------------|
| 3 months       | 0.10% (-0.06, 0.27)   | 0.15% (-0.09, 0.38)      | 0.25% (-0.04, 0.54)       | 0.20% (-0.65, 1.06) |
| 6 months       | 0.12% (-0.06, 0.30)   | 0.05% (-0.20, 0.30)      | 0.17% (-0.14, 0.48)       | 0.20% (-0.79, 1.20) |
| 1 year         | 0.13% (-0.09, 0.35)   | 0.18% (-0.13, 0.49)      | 0.33% (-0.04, 0.71)       | 0.53% (-0.65, 1.71) |
| 2 years        | 0.14% (-0.12, 0.40)   | 0.40% (0.00, 0.79)       | 0.58% (0.11, 1.04)        | 0.47% (-1.08, 2.03) |
| 4 years        | 0.38% (-0.01, 0.77)   | 1.04% (0.50, 1.57)       | 1.44% (0.78, 2.09)        | 2.62% (0.21, 5.04) |

Abbreviations: IPTCW – inverse probability of treatment and censoring-weighted; OUD – opioid use disorder; HDLTOT – high-dose long-term opioid therapy

### eTable 6. Unweighted and IPTC-Weighted Hazard Ratios (HR) for Outcomes Comparing Patients Exposed to Rapid Tapering or Discontinuation vs Patients Who Had Their Dosage Maintained or Gradually Tapered or Discontinued

|                | Unweighted HR\(^a\) (95% CI) | Weighted HR\(^a\) (95% CI) |
|----------------|------------------------------|-----------------------------|
| **Fatal opioid overdose** |                              |                             |
| 0 – 12 months of follow-up | 1.59 (0.68 - 3.70)            | 1.79 (0.69, 4.69)           |
| 13 – 48 months of follow-up | 1.39 (0.65 - 2.99)             | 1.55 (0.68, 3.56)           |
| **Nonfatal opioid overdose** |                              |                             |
| 0 – 12 months of follow-up | 1.60 (1.03 - 2.49)            | 1.26 (0.80, 2.00)           |
| 13 – 48 months of follow-up | 1.85 (1.22 - 2.82)             | 2.01 (1.30, 3.12)           |
| **Fatal or nonfatal overdose** |                              |                             |
| 0 – 12 months of follow-up | 1.67 (1.12 - 2.47)             | 1.43 (0.94, 2.18)           |
| 13 – 48 months of follow-up | 1.81 (1.24 - 2.64)             | 1.95 (1.31, 2.90)           |
| **Opioid use disorder** |                              |                             |
| 0 – 12 months of follow-up | 1.08 (0.96 - 1.21)             | 1.07 (0.94, 1.21)           |
| 13 – 24 months of follow-up | 1.02 (0.88 - 1.19)             | 1.01 (0.85, 1.19)           |
| 25 – 48 months of follow-up | 1.25 (1.04 - 1.51)             | 1.28 (1.01, 1.63)           |

\(^a\) referent level is maintained dose, increased dose, or gradually decreased/discontinued dose

Abbreviations: IPTCW – inverse probability of treatment and censoring-weighted; OUD – opioid use disorder; HDLTOT – high-dose long-term opioid therapy
**eTable 7.** Unweighted and IPTC-Weighted Hazard Ratios (HR) for Outcomes Comparing Patients Exposed to Rapid Reduction or Discontinuation or Exposed to Gradual Reduction or Discontinuation vs Patients Who Had Their Dosage Maintained or Gradually Tapered or Discontinued

|                               | Unweighted HR (95% CI) | Weighted HR (95% CI) |
|-------------------------------|------------------------|----------------------|
|                               | Gradual reduction or discontinuation<sup>a</sup> | Rapid reduction or discontinuation<sup>a</sup> |
| **Fatal opioid overdose**     |                        |                      |
| 0 – 12 months of follow-up    | 1.02 (0.32 - 3.24)     | 1.60 (0.63 - 4.05)   |
| 13 – 48 months of follow-up   | 1.08 (0.29 - 3.97)     | 1.46 (0.51 - 4.12)   |
| **Nonfatal opioid overdose**  |                        |                      |
| 0 – 12 months of follow-up    | 1.38 (0.78 - 2.46)     | 1.75 (1.10 - 2.79)   |
| 13 – 48 months of follow-up   | 1.70 (0.78 - 3.69)     | 2.55 (1.31 - 4.96)   |
| **Fatal or nonfatal overdose**|                        |                      |
| 0 – 12 months of follow-up    | 1.26 (0.74 - 2.15)     | 1.78 (1.17 - 2.70)   |
| 13 – 48 months of follow-up   | 1.78 (0.88 - 3.57)     | 2.57 (1.41 - 4.69)   |
| **Opioid use disorder**       |                        |                      |
| 0 – 12 months of follow-up    | 1.07 (0.92 - 1.24)     | 1.09 (0.97 - 1.24)   |
| 13 – 24 months of follow-up   | 1.11 (0.92 - 1.34)     | 1.14 (0.97 - 1.33)   |
| 25 - 48 months of follow-up   | 1.73 (0.91 - 3.32)     | 2.00 (1.11 - 3.59)   |

<sup>a</sup>Referent level is maintained dose or increased dose

Abbreviations: IPTCW – inverse probability of treatment and censoring–weighted; OUD – opioid use disorder; HDLTOT – high-dose long-term opioid therapy
**eTable 8.** Outcome Frequency Overall and by Exposure Status Among a Subsample of 12 364 Patients Determined to Have Stable Baseline Dosing

| Outcome                        | Events | Person-months of follow-up\(^b\) | Events | Person-months of follow-up | Events | Person-months of follow-up |
|--------------------------------|--------|----------------------------------|--------|---------------------------|--------|---------------------------|
| **Fatal opioid overdose**      |        |                                  |        |                           |        |                           |
| Overall                        | 26     | 270,645                          | 14     | 149,836                   | 12     | 120,808                   |
| 0 – 12 months of follow-up    | 14     | 118,464                          | 9      | 89,619                    | 5      | 28,845                    |
| 13 – 48 months of follow-up   | 12     | 152,180                          | 5      | 60,217                    | 7      | 91,963                    |
| **Nonfatal opioid overdose**  |        |                                  |        |                           |        |                           |
| Overall                        | 88     | 269,371                          | 39     | 149,611                   | 49     | 119,759                   |
| 0 – 12 months of follow-up    | 41     | 118,256                          | 30     | 89,528                    | 11     | 28,728                    |
| 13 – 48 months of follow-up   | 47     | 151,114                          | 9      | 60,083                    | 38     | 91,031                    |
| **Fatal or nonfatal overdose\(^a\)** | 113    | 269,371                          | 52     | 149,611                   | 61     | 119,759                   |
| 0 – 12 months of follow-up    | 54     | 118,256                          | 38     | 89,528                    | 16     | 28,728                    |
| 13 – 48 months of follow-up   | 59     | 151,114                          | 14     | 60,083                    | 45     | 91,031                    |
| **Opioid use disorder**       |        |                                  |        |                           |        |                           |
| Overall                        | 1501   | 248,404                          | 912    | 143,295                   | 589    | 105,109                   |
| 0 – 12 months of follow-up    | 816    | 114,139                          | 620    | 87,317                    | 196    | 26,821                    |
| 13 – 24 months of follow-up   | 394    | 65,542                           | 195    | 32,811                    | 199    | 32,730                    |
| 25 – 48 months of follow-up   | 291    | 68,723                           | 97     | 23,165                    | 194    | 45,557                    |

Abbreviations: HDLTOT – high-dose long-term opioid therapy
\(^a\)Some individuals had both a nonfatal and then a fatal overdose, explaining why the number of combined events is less than the number of fatal overdoses plus the number of nonfatal overdoses.
\(^b\)Person-months of follow-up differ across each outcome analysis because an individual may have experienced a nonfatal outcome (e.g., OUD or nonfatal opioid overdose) prior to a fatal overdose. Therefore, that individual would contribute fewer person-months to the analysis with the nonfatal outcome than to the fatal opioid overdose outcome analysis.
**eTable 9.** IPTCW Risk Differences (95% CI) for the Association Between Rapid Tapering or Discontinuation of Opioid Treatment and Outcomes Among a Subsample of 12 364 Patients Determined to Have Stable Baseline Dosing at Multiple Points of Follow-up

| Time (years) | Fatal opioid overdose | Nonfatal opioid overdose | Fatal or nonfatal overdose | OUD |
|-------------|-----------------------|--------------------------|----------------------------|-----|
| 3 months    | 0.10% (-0.07, 0.27)   | -0.02% (-0.19, 0.14)     | 0.08% (-0.16, 0.31)       | 0.28% (-0.80, 1.37) |
| 6 months    | 0.09% (-0.08, 0.26)   | -0.07% (-0.27, 0.12)     | 0.02% (-0.24, 0.28)       | 0.44% (-0.89, 1.77) |
| 1 year      | 0.06% (-0.18, 0.30)   | 0.03% (-0.28, 0.34)      | 0.11% (-0.29, 0.50)       | 0.68% (-0.89, 2.25) |
| 2 years     | 0.00% (-0.27, 0.26)   | 0.46% (0.03, 0.88)       | 0.47% (-0.03, 0.96)       | 1.00% (-1.01, 3.01) |
| 4 years     | 0.19 (-0.30, 0.67)    | 0.91% (0.32, 1.50)       | 1.11% (0.35, 1.87)        | 2.13% (-0.77, 5.03) |

Abbreviations: IPTCW – inverse probability of treatment and censoring-weighted; OUD – opioid use disorder; HDLTOT – high-dose long-term opioid therapy

**eTable 10.** Unweighted and IPTC-Weighted Hazard Ratios (HR) for Outcomes Comparing Patients Exposed to Rapid Tapering or Discontinuation vs Patients Who Had Their Dosage Maintained or Increased or Gradually Tapered or Discontinued Among a Subsample of 12 364 Patients Determined to Have Stable Baseline Dosing

| Outcome                          | Unweighted HR* (95% CI) | Weighted HR* (95% CI) |
|----------------------------------|-------------------------|-----------------------|
| **Fatal opioid overdose**        |                         |                       |
| 0 – 12 months of follow-up       | 1.34 (0.38 -4.77)       | 1.14 (0.31 -4.14)     |
| 13 – 48 months of follow-up      | 0.98 (0.34 -2.78)       | 0.98 (0.31 -3.10)     |
| **Nonfatal opioid overdose**     |                         |                       |
| 0 – 12 months of follow-up       | 1.18 (0.58 -2.41)       | 1.13 (0.55 -2.32)     |
| 13 – 48 months of follow-up      | 2.96 (1.43 -6.13)       | 3.16 (1.49 -6.73)     |
| **Fatal or nonfatal overdose**   |                         |                       |
| 0 – 12 months of follow-up       | 1.27 (0.68 -2.37)       | 1.17 (0.62 -2.20)     |
| 13 – 48 months of follow-up      | 2.26 (1.25 -4.07)       | 2.28 (1.22 -4.28)     |
| **Opioid use disorder**          |                         |                       |
| 0 – 12 months of follow-up       | 1.09 (0.92 -1.29)       | 1.09 (0.91 -1.30)     |
| 13 – 24 months of follow-up      | 1.06 (0.87 -1.29)       | 1.06 (0.86 -1.32)     |
| 25 – 48 months of follow-up      | 1.03 (0.81 -1.32)       | 1.14 (0.86 -1.50)     |

*Referent level is maintained dose, increased dose, or gradually decreased/discontinued dose

Abbreviations: IPTCW – inverse probability of treatment and censoring-weighted; OUD – opioid use disorder; HDLTOT – high-dose long-term opioid therapy

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### eTable 11. Outcome Frequency Overall and by Exposure Status, Considering Only Nonfatal Opioid Overdoses Occurring During an Emergency Department or Inpatient Event

| Outcome                          | Overall Events | Person-months of follow-up | Maintained, increased, or gradually reduced/discontinued Events | Person-months of follow-up | Rapidly reduced or discontinued Events | Person-months of follow-up |
|----------------------------------|----------------|---------------------------|-----------------------------------------------------------------|---------------------------|----------------------------------------|---------------------------|
| Nonfatal opioid overdose         | 206            | 472,752                   | 89                                                              | 244,135                   | 117                                    | 228,617                   |
| 0 – 12 months of follow-up       | 95             | 204,947                   | 62                                                              | 148,189                   | 33                                     | 56,758                    |
| 13 – 48 months of follow-up      | 111            | 267,804                   | 27                                                              | 95,945                    | 84                                     | 171,859                   |
| Fatal or nonfatal overdose      | 259            | 472,752                   | 111                                                             | 244,135                   | 148                                    | 228,617                   |
| 0 – 12 months of follow-up       | 122            | 204,947                   | 77                                                              | 148,189                   | 45                                     | 56,758                    |
| 13 – 48 months of follow-up      | 137            | 267,804                   | 34                                                              | 95,945                    | 103                                    | 171,859                   |

Abbreviations: HDLTOT – high-dose long-term opioid therapy

*aSome individuals had both a nonfatal and then a fatal overdose, explaining why the number of combined events is less than the number of fatal overdoses plus the number of nonfatal overdoses.

*bPerson-months of follow-up differ across each outcome analysis because an individual may have experienced a nonfatal outcome (e.g., OUD or nonfatal opioid overdose) prior to a fatal overdose. Therefore, that individual would contribute fewer person-months to the analysis with the nonfatal outcome than to the fatal opioid overdose outcome analysis.
### eTable 12. IPTCW Risk Differences (95% CI) for the Association Between Rapid Tapering or Discontinuation of Opioid Treatment and Overdose Outcomes, Considering Only Nonfatal Opioid Overdoses Occurring During an Emergency Department or Inpatient Event

|            | Nonfatal opioid overdose | Fatal or nonfatal overdose |
|------------|--------------------------|----------------------------|
| 3 months   | 0.15% (-0.09, 0.38)      | 0.25% (-0.04, 0.53)       |
| 6 months   | 0.04% (-0.21, 0.29)      | 0.16% (-0.15, 0.46)       |
| 1 year     | 0.16% (-0.14, 0.46)      | 0.31% (-0.06, 0.68)       |
| 2 years    | 0.36% (-0.03 - 0.75)     | 0.54% (0.08, 1.00)        |
| 4 years    | 1.03% (0.51, 1.55)       | 1.43% (0.79, 2.07)        |

Abbreviations: IPTCW – inverse probability of treatment and censoring-weighted; OUD – opioid use disorder; HDLTOT – high-dose long-term opioid therapy

### eTable 13. Unweighted and IPTC-Weighted Hazard Ratios (HR) for Overdose Outcomes Comparing Patients Exposed to Rapid Tapering or Discontinuation vs Patients Who Had Their Dosage Maintained or Gradually Tapered or Discontinued, Considering Only Nonfatal Opioid Overdoses Occurring During an Emergency Department or Inpatient Event

|                      | Unweighted HR\(^a\) (95% CI) | Weighted HR\(^a\) (95% CI) |
|----------------------|-------------------------------|-----------------------------|
| **Nonfatal opioid overdose** |                               |                             |
| 0 – 12 months of follow-up | 1.55 (0.98 -2.44)            | 1.22 (0.76 -1.95)           |
| 13 –48 months of follow-up | 1.91 (1.24 -2.94)            | 2.10 (1.33 -3.29)           |
| **Fatal or nonfatal overdose** |                              |                             |
| 0 – 12 months of follow-up | 1.63 (1.09 -2.43)            | 1.40 (0.91 -2.16)           |
| 13 – 48 months of follow-up | 1.85 (1.26 -2.72)            | 2.00 (1.33 -3.02)           |

\(^a\)referent level is maintained dose, increased dose, or gradually decreased/discontinued dose

Abbreviations: IPTCW – inverse probability of treatment and censoring-weighted; OUD – opioid use disorder; HDLTOT – high-dose long-term opioid therapy
Figure 1. Death Match Algorithm

1. First name, Last name, Middle name, Gender, DOB
   \[N=12,315 (55.4\%)]

2. First name, Last name, Middle Initial, Gender, DOB
   \[N=97 (0.4\%)]

3. First name, Last name to last name | father’s last name | maiden name, Middle name, Gender, DOB
   \[N=5,003 (22.5\%)]

4. First name to middle name, Last name to last name | father’s last name | maiden name, Gender, DOB
   \[N=2 (0\%)]

5. Fuzzy on First name, Exact on Middle initial, Last name to last name | father’s last name | maiden name, Gender, DOB
   \[N=304 (1.4\%)]

6. Fuzzy on Last name to last name | father’s last name | maiden name; Exact on First name, Middle initial, Gender, DOB
   \[N=531 (2.4\%)]

7. Fuzzy on Last name to last name | father’s last name | maiden name, First name, No middle name; Exact on gender, DOB
   \[N=3,977 (17.9\%)]
**eFigure 2. Timelines of Eligibility and Exposure Ascertainment and Covariate and Outcome Ascertainment**

A. Timelines of Eligibility and Exposure Ascertainment

- 90-day assessment for HDLTOT
- 30-day exposure ascertainment window
- Change in dose since month -1
- Change in dose since month 1
- Change in dose since month t-2

B. Timelines of Covariate and Outcome Ascertainment

- Baseline characteristics
- All available lookback (e.g., depression, cancer)
- 6-month lookback (e.g., pain, surgery)
- Co-medication use (e.g., SSRI)
- Outcome ascertainment in month 2
- Co-medication use (e.g., SSRI)
- Outcome ascertainment in month t-1

Abbreviations: HDLTOT – high-dose long-term opioid therapy; SSRI – selective serotonin reuptake inhibitor

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eFigure 3. Crude Cumulative Incidence of Outcomes by Primary Exposure Status

Abbreviations: OUD – opioid use disorder; HDLTOT – high-dose long-term opioid therapy
eFigure 4. Crude Cumulative Incidence of Outcomes by Exposure Status Using a Categorical Exposure Definition

Abbreviations: OUD – opioid use disorder; HDLTOT – high-dose long-term opioid therapy
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