

TABLE 1/BASELINE DESCRIPTIVE OPIOID-RELATED VARIABLES

Time Period for Baseline Opioid Variables (BL_avg_daily, BL_avg_above90) = 180 days prior to Cohort Randomization

Episode start = Date of patient's cohort randomization – 180 days

Episode end = Date of patient's cohort randomization OR

If there is a date that patient discontinued enrollment in Kaiser Permanente (KP) [i.e., DATE_DEPART is not null] and DATE_DEPART < Date of patient's cluster randomization, then Episode end = Episode start – DATE_DEPART

Procedure:

- 1) Identify all opioid dispensings in the episode of interest. *NOTE: As described above, if DATE_DEPART < Cohort randomization date, then "Episode of interest" = DATE_DEPART – Episode start. (I.e., Episode duration will equal 180 days for majority of people, but for 6 subjects episode duration is <180 days due to disenrollment; their episode duration equals the exact # of days they were enrolled out of the pre-study period.)
- 2) Of #1, identify all opioid dispenses in the episode with a days supply that would cross over into the patient's study enrollment period, i.e., past the cohort randomization date or, if patient left KP prior to cohort randomization date (DATE_DEPART < Cohort Randomization date), then past the patient's DATE_DEPART). These are 'Final Dispensings'; the remaining dispensings in the episode are 'Within Episode Dispensings'. *NOTE: A patient may have more than one Final Dispensing.
- 3) Identify all opioid dispensings prior to the episode start date that have a days supply that would have crossed over into the start of the episode. These are 'Prior Dispensings' *NOTE: a patient may have more than one Prior Dispensing.
- 4) Calculate the Total Morphine Milligram Equivalents (MME) for each opioid dispensing from #2 and #3 (i.e., final, within episode, and prior). We preferentially used the CDC Recommendations for conversion,¹ supplemented with other sources for missing products.²⁻⁴
- 5) For each Final Dispensing, calculate the days between patient's final dispense date and their cohort randomization date or, if applicable, their DATE_DEPART; this is the 'Final Days Supply' and represents the portion of the Final Dispenses day supply that should accrue to the episode. Multiply the Final Dispensing's Total MME by (Final Days Supply/days supply); this is 'Final Morphine Equivalents' and represents the portion of the Final Dispensing's morphine equivalents that should accrue to the episode.
- 6) For each Prior Dispensing, calculate the days between the beginning of the episode and the dispense date; this is the 'Pre-Episode Days'. Subtract this Pre-Episode Days from the Prior Dispensing days supply; this is the 'Stockpile Days Supply' and represents the opioid days they came into the episode with. Multiply the Prior Dispensing's Total Morphine Equivalents by (Stockpile Days Supply/days supply); this is 'Stockpile Morphine Equivalents' and represents the portion of the prior dispensing's morphine equivalents that should accrue to the episode.

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- 7) For each patient, sum the morphine equivalents from a) Within Episode Dispensings morphine equivalents (from #4), b) each Final Morphine Equivalents, and c) Stockpile Morphine Equivalents; this summation is the patient's "**Episode Morphine Equivalents**"
- 8) For each patient, sum the days supply from a) Within Episode Dispensing days supply, b) Final Days Supply, and c) Stockpile Days Supply; this is the "**Episode Days Supply**." *NOTE: If a patient has two or more prescriptions with supply that would cover the same calendar days, avoid double counting those overlapping calendar days.
- 9) Calculate **Average Daily Morphine Milligram Equivalents Dose (BL_avg_daily)** as Episode Morphine Equivalents/Episode Duration

OPIOID-RELATED VARIABLES FOR OUTCOME ANALYSES

90-Day Time Periods for Developing Quarterly Variables (Qavg_daily)

*NOTE: Cohort Randomization Date = Day 1

1. Baseline = Q0 = Day -90 to day -1
2. "3 months" = Q1 = Day 1 to day 90
3. "6 months" = Q2 = Day 91 to day 180
4. "9 months" = Q3 = Day 181 to day 270
5. "12 months" = Q4 = Day 271 to day 360

After allowing for any gaps in enrollment <95 days, in order to calculate **Average Daily Morphine Milligram Equivalents Dose** for a 90-day time period, **subject must have at least 68 days of observation within the 90-day period. If <68 days, then period is missing.**

If subject has 68-90 days of observation within a time period, then "Episode Duration" = # of days of observation (DATE_DEPART- Episode start).

To calculate Winsorized quarterly variables (W_Qavg_daily): Calculate percentiles and Winsorize at the 99th percentile, setting any average daily dose that is above the 99th percentile to the value of the 99th percentile.

360-Day Time Period for Developing 1-Year Follow-Up Variable (W_YR_avg_daily)

- Time period = Cohort randomization + 360 days
- After allowing for any gaps in enrollment <95 days, in order to calculate **Average Daily Morphine Milligram Equivalents Dose** for the year-long time period, **subject must have at least 270 days of observation within the 360-day period. If <270 days, then period is missing.**
- If subject has 270-360 days of observation within a time period, then "Episode Duration" = # of days of observation (DATE_DEPART- Episode start).
- Average of all datapoints across the entire year, with a minimum of 270 days (75%) before computing the average, then Winsorize at the 99th percentile.

References

1. National Center for Injury Prevention and Control. CDC compilation of benzodiazepines, muscle relaxants, stimulants, zolpidem, and opioid analgesics with oral morphine milligram equivalent

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- conversion factors, 2017 version. Atlanta, GA: Centers for Disease Control and Prevention; 2017. Available at <https://www.cdc.gov/drugoverdose/resources/data.html>.
2. Deyo RA, Smith DH, Johnson ES, et al. Opioids for back pain patients: primary care prescribing patterns and use of services. *J Am Board Fam Med*. 2011;24(6):717-727.
 3. Von Korff M, Saunders K, Thomas RG, et al. De facto long-term opioid therapy for noncancer pain. *Clin J Pain*. 2008;24(6):521-527.
 4. Prescription Drug Monitoring Program - Training and Technical Assistance Center. Calculating Daily Morphine Milligram Equivalents: Technical Assistance Guide No. 01-13. 2013. Accessed 03/10/2017, Waltham, MA.