NEPPC Research Report 20-3 Technical Appendix: "Medication-assisted Treatment for Opioid Use Disorder in Rhode Island: Who Gets Treatment, and Does Treatment Improve Health Outcomes?"

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1. Background on HealthFacts RI

HealthFacts RI is the official name of the All-Payer Claims Database (APCD) for the state of Rhode Island. In any given month the data cover most Rhode Island residents who held medical and/or pharmacy insurance in that month, with the exception of people enrolled in plans that insure fewer than 3,000 Rhode Island residents and, beginning in late 2015, those enrolled in self-insured plans.[1] Dental insurance information is not included. The data set contains limited demographic information (age, gender), information on the medical and pharmacy insurance plans (company name and plan type), the patient's Zip code, detailed information for each specific claim filed in association with health-care services (inpatient and outpatient) received by an individual and prescriptions filled by the individual, and information about the provider including professional credentials and practice address. Instead of names, consistent numerical identifiers are assigned to enrollees and providers in order to link their records over time. Treatments and prescriptions paid for out of pocket, even by individuals carrying insurance, are not recorded in the data, nor are treatments received by uninsured patients. The HealthFacts RI data set we received contains observations dated from April 2011 through May 2019 for health insurance enrollees of all ages in the reporting plans. Some observed individuals have non-Rhode Island Zip codes for all or part of the sample period. This might occur if they work in Rhode Island and are covered by a commercial insurer to a sufficient number of Rhode Island residents, or if they are a child (for example, age 20) on the plan of a Rhode Island resident but live separately from their parents, although children can't be linked to their parents in the data. Alternatively, a non-Rhode Island Zip code could be erroneous. Some individuals have a known pharmacy plan and an "unknown" medical plan. These cases arise when the individual's medical plan is not required to report to HealthFacts RI for any of the reasons just described. Starting in January 2018 the data do not include pharmacy claims for enrollees in Medicare fee-for-service plans, and starting in January 2019 the data do not include medical claims for such enrollees. The

[1] In late 2015 the Supreme Court ruled that self-insured plans could not be mandated to provide claims data to state APCD systems. A self-insured or self-funded plan is a type of coverage offered by some employers where the employer covers the cost of claims as they are accrued rather than paying an insurance premium to an insurance carrier.

missing Medicare fee-for-service data are to be furnished to us at a later date, along with larger updates to the overall database. Using enrollees' Zip codes, we attach information from the American Community Survey indicating the share of households in the Zip code with incomes at or below the federal poverty level in the given year. This information is used to construct an indicator at the person-by-month level of living in a high-poverty Zip code. A high-poverty Zip code is defined as one in which 20 percent or more of the households in that Zip code had income at or below the federal poverty level in the given month (based on the year), and all other Zip codes are deemed "lower-poverty." An individual's Zip code poverty status can change across months if they move across Zip codes or if the same Zip code's poverty status changes.

2. **Repeated Overdose Analysis**

Section VII of the report presents results pertaining to the association between being treated with either buprenorphine or methadone and having a second opioid overdose following an initial, (nonfatal) opioid overdose. This section describes the methods used to generate those results.

To build the sample for the repeated overdose analysis we start by assembling what is termed the *incumbent panel* data set as follows. We retain only observations in which the medical insurance type is not listed as unknown. An individual must have at least 33 retained observations dated from January 2013 through December 2015, must have been at least 19 years of age and residing in Rhode Island as of January 2013, and must not have moved out of state after January 2013 or switched between Medicaid and non-Medicaid insurance plans (in either direction) before January 2017. We exclude a small number of individuals—less than 1 percent of either the unrestricted sample or the incumbent sample—who exhibit inconsistent age changes or gender changes over time. The resulting data set includes all retained observations—regardless of date—for the set of qualifying individuals. The total number of person-by-month observations is more than 36 million, pertaining to over 418,000 unique individuals. The term "incumbent" refers to the fact that members of the panel had health insurance in Rhode Island prior to the Affordable Care Act and Medicaid expansion of 2014.

For the overdose analysis we restrict the sample to members of the incumbent panel who had at least one nonfatal opioid overdose that was treated in either an emergency department or an inpatient hospital setting, and who were observed (at a minimum) in each of the three months immediately following the initial overdose. The resulting *nonfatal opioid overdose sample*

contains 66,392 patient-by-month observations pertaining to 1,755 unique individuals, 412 of whom (just over 23 percent) are observed to have had two or more opioid overdoses. All sample members were at least 18 years of age as of their first overdose.

Opioid overdoses are identified in the medical claims data based on a set of ICD-9 and ICD-10 diagnostic codes.[2] Although the records do not indicate explicitly whether an overdose was fatal, we can infer that an overdose was nonfatal if the same individual has medical or pharmacy claims or enrollment records after the overdose event. In cases when a second overdose occurs, it cannot be determined from the data whether the second overdose was fatal, and we do not require that the individual be observed in the data subsequent to a second overdose. For an overdose to count as a second overdose it must occur in a calendar month later than the initial overdose and must occur at least two days later than the first overdose. For example, overdoses occurring on March 31 and April 1 of the same year are treated as the same event, but overdoses occurring on March 31 and April 2 are treated as separate events. In most of the analysis the overdose date is given as a month rather than a specific date.

To estimate the association between recent treatment with either methadone or buprenorphine and the risk of repeated overdose, we employ Cox proportional hazard models. This approach estimates the instantaneous risk (or "hazard") of having a second overdose as a function of the elapsed time (in months) after the first overdose and individual risk factors that may be fixed within a person or changing over time. The model assumes that a given fixed factor—such as having ever received medication-assisted treatment (MAT)—multiplies a baseline hazard function by a constant value for any amount of elapsed time, called analysis time. In turn, the baseline hazard function is estimated nonparametrically as the risk of repeated overdose at a given analysis time and setting all explanatory factors at their designated baseline values. The specific baseline values employed in our analysis are described below. Assuming all explanatory factors are fixed over time for an individual, the instantaneous hazard function, $h_i(.)$, at analysis time *t* and for a fixed vector of individual characteristics, $\boldsymbol{X_i}$, can be written as follows:

$$h_i(t|\boldsymbol{X_i}) = h_0(t)exp\{\boldsymbol{X_i'\beta}\}. \qquad (1)$$

[2] The complete set of ICD-9 and ICD-10 codes used to identify opioid overdoses can be obtained upon request from the authors.

In the above equation $h_0(t)$ stands for the baseline hazard function, *exp* stands for the natural exponential function, and $\boldsymbol{\beta}$ is the parameter vector to be estimated. The model is readily extended to allow for explanatory factors that vary over time for an individual. See Cleves, Gould, and Marchenko (2016).

The validity of the proportional hazard assumption can be tested, and the model can be adjusted ("stratified") to account for factors that don't satisfy the assumption. Diagnostic tests indicate that all but two of the factors of interest—gender and opioid use disorder (OUD) diagnosis group—satisfy the proportional hazard assumption. Accordingly, all models are stratified along those factors, which means that separate baseline hazard functions are estimated for each combination of OUD diagnosis (none, use or abuse, dependence) and gender (male, female). The influence of these factors on the repeated overdose risk is revealed by examining the differences between the groups' baseline hazard functions, holding all else constant.

A tie-breaking method is needed for when two "failures" or repeated overdoses for different individuals occur at the same time. We have simultaneous failures in our data set because we discretize the overdose dates to the month. As is recommended in such cases, we use the exact partial likelihood method of tie breaking. However, in the software package used to generate results, using this method means that we can't also obtain standard errors that are robust to misspecification. As a robustness check we run alternative versions of the models using the Breslow tie-breaking method, which is compatible with obtaining robust standard errors. Results are not meaningfully different under those alternative specifications.

The explanatory factor of interest is the number of months out of the three months immediately preceding the overdose in which the individual either received methadone maintenance treatment or filled a prescription for buprenorphine. For those who ever receive MAT, this variable can change over time, ranging from a minimum of zero to a maximum of three; for those who never receive MAT, the value is always zero. Because the recent MAT variable does not vary across observations for panel members who never receive MAT, we also run models that exclude all those who never receive MAT. Results are qualitatively robust.

Other variables in the model include a set of indicators of diagnosis and treatment patterns: ever receiving MAT; ever being diagnosed with alcohol use disorder, a substance use disorder other than opioid use disorder, hepatitis C, any mental illness, depression, or anxiety; ever filling a

high-dose opioid drug prescription (other than medications to treat OUD); ever filling both an opioid prescription and a benzodiazepine prescription in the same month; and ever receiving behavioral therapy. As noted above, gender and level of OUD diagnosis are taken into account through stratification. A high-dose opioid prescription is defined as one involving a morphine milligram equivalent dose of 90 or greater.[3]

In addition to the time-invariant characteristics just described, the model also includes indicators of filling a high-dose opioid prescription in the current month, filling both an opioid and a benzodiazepine prescription in the current month (regardless of dosages), and the number of months out of the preceding three months in which the individual received behavioral therapy. The model also includes indicators of having Medicaid insurance (as opposed to a non-Medicaid plan such as Medicare or commercial insurance), of entering the HealthFacts RI sample in 2012 as opposed to 2011, and of the patient's age range as of their first overdose. The model also includes controls for the fiscal year in which a given observation occurred, to control for secular trends in the risks of repeated overdose not captured by other variables. The fiscal year indicators generally do not have significant effects on outcomes and are suppressed from all tables.

The baseline value for most variables in the model is zero—this applies to all binary (yes/no or 1/0) indicators that can take on the value zero. The baseline insurance category is non-Medicaid, the baseline age range as of the first overdose is ages 18 through 30, the baseline fiscal year is 2012, and the baseline sample entry year is 2011.

Table 1 in the main report describes the sample means of the dependent and independent variables used in the model, considering the entire sample combined and then separating those with a single observed overdose from those with two or more observed overdose events. These characteristics draw on all of an individual's observations, including those dated prior to the first overdose.

Table A1 shows the estimated coefficients, expressed as hazard ratios, from four different specifications of the stratified proportional hazard model described above. A hazard ratio that is greater than 1.0 means that the factor is associated with an increased risk of having a repeated

[3] The complete set of ICD-9 and ICD-10 codes used to identify the conditions and treatments listed in this paragraph, as well as the list of drug codes used to identify opioids and benzodiazepines, can be obtained upon request from the authors.

overdose relative to the baseline risk, as of any given number of months after the first overdose. The regression results indicate that the instantaneous risk of having a second overdose (at a given number of months after the first overdose) decreases with the number of MAT treatments in the preceding three months, controlling for all of the additional factors listed above. However, as shown in column 1, when we do not control for whether the patient ever receives MAT, this association is weak due to confounding with the unobserved risk factors that drive selection into receiving MAT.

Unobserved shocks to health status could confound the association between recent MAT and overdose risk. For example, someone who experiences a life setback might be less capable of showing up to the methadone clinic or filling their buprenorphine prescription and, also due to the setback, might be more likely to resume abusing opioids at levels that pose a higher risk of overdose. As shown in column 4, we offer some control for such unobserved shocks by conducting a placebo test of whether overdose risk responds to MAT in the upcoming three months and/or to behavioral therapy in the upcoming three months, either of which might also be indicative of current life circumstances or health status. Results indicate that, if anything, the negative association between recent MAT is even stronger when including future MAT and behavioral treatments, whereas the association between either of those controls and overdose risk is null.

As additional robustness checks we estimate similar models (a) on more restricted and less restricted samples, (b) in which we require a minimum of six months of follow-up time instead of just three months, (c) using the Breslow tie-breaking method with robust standard errors, and (d) on just the set of individuals who ever received MAT. In all cases we observe a statistically significant negative association between the number of recent MAT treatments and the risk of having a second overdose. These results can be obtained by the authors upon request.

3. Estimating Associations between Enrollee Characteristics and Treatment with Buprenorphine or Methadone

In Section VIII of the paper we describe results of multivariable probit regression analysis that identifies factors associated with higher or lower chances of being treated with either methadone or buprenorphine. The analysis is restricted to the set of patients in the incumbent panel described above who have ever been diagnosed with opioid dependence, applying some

additional sample restrictions. In particular, prior to imposing the incumbent panel restrictions and selecting those who have at least one observation with a diagnosis of opioid dependence, we exclude observations in which the individual's age was less than 18 and observations in which the medical insurance payer was United Healthcare.

The analysis draws on all of a patient's retained observations to determine outcomes and explanatory factors. The outcome of interest is defined as being treated with methadone (or, separately, buprenorphine) in at least three separate calendar months. For a month to count as a methadone month, the patient must have at least one claim in the month that includes the procedure code for methadone maintenance treatment (H0020); additional methadone claims in the same month for the same patient do not count. For a month to count as a buprenorphine month, the pharmacy claims data must indicate that the patient filled at least one buprenorphine prescription in that month or had an "open prescription" in that month. An open prescription is one that should not yet have run out as of the given date, based on when it was filled and the days' supply given in the claim. We exclude denied claims and claims involving buprenorphine formulations used to treat any condition other than opioid use disorder (OUD). The complete list of national drug codes for the allowed forms of buprenorphine can be obtained from the authors upon request.

The set of predictive factors is the same for either outcome and consists of the following: the patient's sex, the year of the patient's first observation in the database, the patient's age group as of the first observation, having Medicaid insurance as opposed to non-Medicaid insurance,[4] living in a high-poverty Zip code,[5] and indicators of having a diagnosis (ever) of alcohol use disorder, substance use disorder (not including alcohol or opioids), depression, anxiety, mental illness (not including OUD), hepatitis C, and opioid overdose, respectively. We analyze treatment with methadone separately from treatment with buprenorphine because these two outcomes differ in terms of how each is associated with the predictive factors. As a result of

[4] Age group and Medicaid insurance status are based on the patient's earliest observation in the database. The sample excludes individuals who switched to a Medicaid plan from a non-Medicaid plan or vice versa before December 2016. Therefore, someone on Medicaid as of their first observation is likely to have been on Medicaid in most if not all of their subsequent observations, and similarly for those initially not on Medicaid.
[5] Using the American Community Survey, we define a Zip code as "high poverty" in a given year if 20 percent or more of households had income at or below the federal poverty level in the given year. As each patient is observed in multiple periods and may move across Zip codes over time, a given patient is said to reside in a high-poverty Zip code if they lived in such a Zip code in more than half of their observations.

those different associations, a model that tries to predict the outcome of receiving at least one of the two medications fits the data relatively poorly. The probit model for either binary outcome, denoted *Y*, can be expressed as follows:

$$P(Y_i = 1|\boldsymbol{X_i}) = \Phi(\boldsymbol{X_i'\beta}). \qquad (2)$$

In the equation above, $\boldsymbol{X_i}$ is a vector of explanatory factors (fixed over time for the individual and including the constant 1), $\boldsymbol{\beta}$ is the parameter vector to be estimated, and Φ(.) stands for the cumulative normal distribution function.

Table 2 in the main report shows the sample means of the outcomes and the predictive factors over the regression sample (in column 2), along with sample means for the larger patient panel (column 1). Table A2 shows the estimated coefficients from the probit models. All standard errors were estimated using the robust option. Results of logit models using the same variables are very similar both quantitatively and qualitatively. However, postestimation analysis indicates that the probit models offer a better fit with the data and better predictive power.

For robustness we estimated similar models (a) using a sample that imposed fewer restrictions for inclusion, and (b) in which the dependent variables are defined as having at least one month on methadone and one month on buprenorphine, respectively, rather than at least three months on either medication. Results are qualitatively very similar to those described above.

References

Cleves, M., W. G. Gould, and J. Marchenko. 2016. *An Introduction to Survival Analysis Using Stata*. Revised third edition. College Station, Texas: Stata Press.

Table A1: Associations between Selected Characteristics and Time to Second Overdose
Nonfatal Opioid Overdose Sample

	(1) Repeated OD	(2) Repeated OD	(3) Repeated OD	(4) Repeated OD
Number of Past 3 Months with MAT	0.921*	0.831***	0.839***	0.785***
	(0.042)	(0.040)	(0.041)	(0.054)
Number of Past 3 Months with Behavioral Therapy	1.007	0.990	0.979	0.972
	(0.065)	(0.067)	(0.067)	(0.081)
Fills High-dose Opioid Rx in Current Month	0.883	1.044	1.073	1.072
	(0.197)	(0.244)	(0.255)	(0.255)
Fills Both Opioid and Benzodiazepine Rx in Current Month	1.084	1.222	1.393*	1.403*
	(0.192)	(0.226)	(0.263)	(0.265)
Receives MAT (Ever)		2.097***	1.763***	1.710***
		(0.290)	(0.252)	(0.248)
Behavioral Therapy (Ever)		1.244*	1.010	1.000
		(0.151)	(0.132)	(0.131)
Fills High-dose Opioid Rx (Ever)		1.024	1.096	1.101
		(0.120)	(0.132)	(0.133)
Fills Both Opioid and Benzodiazepine Rx Same Month (Ever)		0.859	0.931	0.930
		(0.098)	(0.110)	(0.110)
Alcohol Use Disorder Diagnosis (Ever)			1.587***	1.594***
			(0.195)	(0.196)
Anxiety Diagnosis (Ever)			1.172	1.167
			(0.270)	(0.269)
Depression Diagnosis (Ever)			0.801	0.804
			(0.170)	(0.171)
Other Mental Illness Diagnosis (Ever)			1.500	1.498
			(0.462)	(0.461)
Other Substance Abuse Disorder Diagnosis (Ever)			1.366	1.364
			(0.397)	(0.397)
Hepatitis C Diagnosis (Ever)			1.506***	1.505***
			(0.164)	(0.163)
Medicaid			0.982	0.980
			(0.113)	(0.113)
First Overdose Age 31–42			0.738**	0.735**
			(0.109)	(0.108)
First Overdose Age 43–52			0.615***	0.613***
			(0.096)	(0.095)
First Overdose Age 53–90			0.648***	0.647***
			(0.104)	(0.104)
Enters Sample 2012 (vs. 2011)			1.375*	1.377*
			(0.231)	(0.231)
Number of Next 3 Months with MAT				1.093
				(0.071)
Number Next 3 Months with Behavioral Therapy				1.011
				(0.082)
Fiscal Year Indicators	Yes	Yes	Yes	Yes
Total Individuals in Sample	1755	1755	1755	1755
Individuals with Two or More Overdoses	412	412	412	412
Observations (Person-by-Month)	66392	66392	66392	66392

Source: Authors' calculations using HealthFacts RI.

Notes: The term "overdose" always refers to one that involved opioids. The dependent variable "Repeated OD" is an indicator of having a second opioid overdose a given number of months after an initial (nonfatal) opioid overdose. All coefficients represent hazard ratios using Cox proportional hazard models. Standard errors are given in parentheses. A hazard ratio that is greater than 1.0 means that the factor is associated with an increased risk of having a repeated overdose relative to the baseline risk, as of any given number of months after the first overdose. The baseline hazard function was estimated separately (stratified) by a combination of gender and OUD diagnosis category. The estimation employs the exact partial likelihood method for treating tied second-overdose times across individuals. The sample consists of HealthFacts RI enrollees who had at least one nonfatal opioid overdose between April 2011 and May 2019 and at least three months of consecutive observations immediately following their first overdose. These individuals were selected from a larger sample of enrollees who were observed, at a minimum, in all months from January 2013 through December 2015 (excepting up to three months), who were at least age 19 as of January 2013, and who did not switch between Medicaid and non-Medicaid insurance plans between their first month in the sample and December 2016. The sample further excludes observations with an unknown medical insurance carrier. Medicaid status is as of January 2015. All diagnosis-related variables, such as "Alcohol Use Disorder (Ever)," are defined as having at least one observation (either before or after the first overdose) with the given diagnosis. All sample members were at least 18 years of age at the time of their first overdose. The omitted category for first overdose age is ages 18–30.

Table A2: Probit Models of the Probability of Having at Least 3 Months of Buprenorphine/Methadone Treatment Opioid Dependence Sample within the Restricted Incumbent Panel

	(1) Methadone (At Least 3 Months)	(2) Buprenorphine (At Least 3 Months)
Entry Age 45–64	–0.328***	–0.365***
	(0.037)	(0.032)
Entry Age 65+	–0.845***	–1.013***
	(0.116)	(0.086)
Medicaid	0.700***	0.032
	(0.037)	(0.033)
Female	–0.078**	–0.106***
	(0.036)	(0.030)
Alcohol Use Disorder (Ever)	–0.380***	–0.004
	(0.037)	(0.031)
Opioid Overdose (Ever)	0.335***	0.252***
	(0.055)	(0.049)
Hepatitis C (Ever)	0.959***	0.213***
	(0.041)	(0.038)
Depression (Ever)	0.015	–0.008
	(0.050)	(0.042)
Anxiety (Ever)	–0.067	0.055
	(0.049)	(0.043)
Other Mental Illness (Ever)	0.030	–0.015
	(0.056)	(0.048)
Other Substance Use Disorder (Ever)	0.273***	0.538***
	(0.047)	(0.041)
High-poverty Zip Code	0.112***	–0.180***
	(0.040)	(0.036)
Constant	–1.289***	–0.803***
	(0.062)	(0.053)
Observations	8951	8951

Source: Authors' calculations using HealthFacts RI.

Notes: Robust standard errors in parentheses. The restricted incumbent panel consists of individuals who were observed, at a minimum, in most months (missing as many as three) from January 2013 through December 2015, who were at least age 19 as of January 2013, and who did not switch between Medicaid and non-Medicaid insurance plans between their first month in the sample and December 2016. The panel further excludes observations with United Healthcare insurance, observations with an unknown medical insurance carrier, out-of-state observations, observations with age under 18, and individuals with missing poverty indicators in more than half of their observations. The opioid dependence sample consists of individuals in the restricted incumbent panel who ever received an opioid dependence diagnosis. Entry age is an individual's age as of their first month in the sample. Medicaid status is as of January 2015. All diagnosis-related variables, such as "Alcohol Use Disorder (Ever)," are defined as having at least one observation with the given diagnosis. "High-poverty Zip Code" means that, as of January 2015, the individual resided in a Zip code in which 20 percent or more of households had incomes at or below the federal poverty level.