

Appendix 1. International Classification of Diseases, Tenth Revision (ICD-10) codes used to identify overdose and suicide mortality

Overdose- and Suicide- Related mortality	ICD-10 Codes
Overdose-related mortality	<p>X40-X45, X60-X65, X85, Y10-Y15, Y45</p> <p><i>Additional codes related to opioid poisoning mortality:</i> T400X1, T40X2, T400X3, T400X4, T400X5, T401X1-T401X4, T402X1-T402X5, T403X1-T403X5, T404X1-T404X5, T40601-T40605, T40691-T40695</p> <p><i>Additional codes related to sedative poisoning mortality:</i> T410X1-T410X5, T411X1-T411X5, T41201-T41205, T41291-T41295, T413X1-T413X5, T414X1-T414X5, T423X1-T423X5, T426X1-T426X5, T428X1-T428X5, T433X1-T433X5, T434X1-T434X5, T43501-T43505, T43591-T43595, T424X1-T424X5, T43591-T43595, T4151, T4152, T4153, T4544, T4155</p> <p><i>Additional codes related to acetaminophen poisoning mortality:</i> T391X-T395X, T398X, T399X</p> <p><i>Additional codes related to other drug poisoning mortality:</i> T507X1-T507X5, T407X1-T407X5, T408X1-T408X5, T44901-T44905, T44991-T44995, T507X1-T507X5</p>
Suicide-related mortality	<p>X7, X60-X84, U03, Y87, T360X2-T360X5, T361X2-T361X5, T362X2-T362X5, T363X2-T363X5, T364X2-T364X5, T365X2-T365X5, T366X2-T366X5, T367X2-T367X5, T368X2-T368X5, T3692-T3698, T1491, R45851, T407-T409, T4-T6, T70, T712</p>

Appendix 2. Heuristic summary of data assembly method

Identified all veterans who received an opioid prescription in Fiscal Year 2013 (FY 2013- October 1, 2012 to September 30, 2013)

Data collection and analysis sample definition:

1. Non time-varying covariates calculated based on patient medical record data from FY2013 (e.g., age, mental health diagnoses)
2. Looked backward in time (5 years) from the last date of opioid prescription in FY 2013 to find the start date of opioid therapy and calculate the duration of opioid treatment episode that was classified into four categories:
 ≤30 days, 31-90 days, 91-400 days, and >400 days
3. Left censored all opioid episode data before FY 2013
4. Outcomes observed from the first date of opioid prescription receipt in FY 2013 to the end of FY 2014:
 - a. Date of opioid cessation (modelled as a time-varying parameter)
 - b. Date of overdose and/or suicide (outcome of interest)
5. Right censor patients at the time of death or the end of observation, whichever comes first

Survival analysis with time of opioid cessation as a time-varying parameter and testing its interaction with duration of opioid treatment:

1. Parameter estimates of overdose/suicide mortality at the time of opioid cessation by opioid treatment duration category
2. Adjusted hazards ratio estimates for overdose/suicide with opioid cessation among the 4 opioid treatment duration categories

Lifetable analyses: Actual observed overdose/suicide mortality rates were calculated every 25 days and displayed in following ways:

- a. After opioid cessation for all patients with opioid cessation
- b. After the start of opioids for all patients who initiated an opioid episode in FY 2013
- c. After opioid cessation for all patients with opioid cessation categorized by the duration of opioid treatment episode

Long-acting	.51	.10	1.67	1.37-2.03	.34	.12	1.40	1.10 to 1.79
Short-acting	.15	.07	1.16	1.01-1.34	.15	.08	1.16	.99 to 1.37
Log maximum daily morphine mg equivalents	.40	.04	1.50	1.40-1.61	.29	.05	1.33	1.22 to 1.45

*Hazard ratios and associated 95% confidence intervals are not estimated for these variables given that these are interaction models. To better understand the interactions, for overdose mortality, the estimated hazard ratios for patients with opioid cessation (with all other covariates at their reference) were 1.39 (≤ 30 days), 2.41 (31-90 days), 3.25 (91-400 days), and 5.65 (>400 days) and for suicide mortality, the estimated hazard ratios for patients with opioid cessation (with all other covariates at their reference) were 2.02 (≤ 30 days), 3.43 (31-90 days), 4.78 (91-400 days), and 7.99 (>400 days).

CI=Confidence Interval; FY=Fiscal Year

Appendix 4. Full life table data for deaths from overdose or suicide over time (in 25-day intervals) while on opioids—for patients who initiated opioids in FY2013—and after stopping treatment with opioids

25-Day Interval	Overdose/ Suicide Deaths	Number Censored	Sample Size	Conditional Probability of Overdose/ Suicide Death	Conditional Probability Standard Error	Overdose/Suicide Deaths per 100,000 Patients
Patients Who Initiated Opioids in FY2013 (After Initiation)						
1-25	88	39437	933199.5	0.000094	0.000010	9.4
26-50	59	40928	892929	0.000066	0.000009	6.6
51-75	42	33854	855479	0.000049	0.000008	4.9
76-100	32	33507	821756.5	0.000039	0.000007	3.9
101-125	23	31240	789351	0.000029	0.000006	2.9
126-150	35	30658	758379	0.000046	0.000008	4.6
151-175	24	27919	729055.5	0.000033	0.000007	3.3
176-200	29	28661	700741.5	0.000041	0.000008	4.1
201-225	24	27567	672598.5	0.000036	0.000007	3.6
226-250	17	24233	646674.5	0.000026	0.000006	2.6
251-275	29	23793	622644.5	0.000047	0.000009	4.7
276-300	9	20660	600389	0.000015	0.000005	1.5
301-325	12	21320	579390	0.000021	0.000006	2.1
326-350	8	20271	558582.5	0.000014	0.000005	1.4
351-375	14	28029	534424.5	0.000026	0.000007	2.6
376-400	4	43787	498502.5	0.000008	0.000004	0.8
401-425	12	41789	455710.5	0.000026	0.000008	2.6
426-450	5	44753	412427.5	0.000012	0.000005	1.2
451-475	7	37344	371374	0.000019	0.000007	1.9
476-500	13	40948	332221	0.000039	0.000011	3.9
501-525	3	37263	293102.5	0.000010	0.000006	1.0
526-550	5	37141	255897.5	0.000020	0.000009	2.0
551-575	8	36126	219259	0.000036	0.000013	3.6
576-600	7	32760	184808	0.000038	0.000014	3.8
601-625	2	36323	150259.5	0.000013	0.000009	1.3
626-650	0	27131	118530.5	0	0	0
651-675	3	36202	86864	0.000035	0.000020	3.5
676-700	0	28668	54426	0	0	0
701-725	1	31469	24357.5	0.000041	0.000041	4.1
726-750	0	8622	4311	0	0	0
751-775	0	0	0	0	0	0
Patients Who Stopped Treatment with Opioids (After Stopping)						
1-25	344	50325	774505.5	0.000444	0.000024	44.4
26-50	174	50971	723513.5	0.000240	0.000018	24.0

51-75	114	37647	679030.5	0.000168	0.000016	16.8
76-100	90	32587	643799.5	0.000140	0.000015	14.0
101-125	79	28793	613019.5	0.000129	0.000014	12.9
126-150	83	25452	585818	0.000142	0.000016	14.2
151-175	66	25255	560381.5	0.000118	0.000014	11.8
176-200	57	22147	536614.5	0.000106	0.000014	10.6
201-225	53	22158	514405	0.000103	0.000014	10.3
226-250	40	19671	493437.5	0.000081	0.000013	8.1
251-275	43	19232	473946	0.000091	0.000014	9.1
276-300	37	18971	454801.5	0.000081	0.000013	8.1
301-325	32	18978	435790	0.000073	0.000013	7.3
326-350	23	22722	414908	0.000055	0.000012	5.5
351-375	24	29883	388582.5	0.000062	0.000013	6.2
376-400	27	33875	356679.5	0.000076	0.000015	7.6
401-425	32	31115	324157.5	0.000099	0.000017	9.9
426-450	12	31039	293048.5	0.000041	0.000012	4.1
451-475	14	30090	262472	0.000053	0.000014	5.3
476-500	15	29133	232846.5	0.000064	0.000017	6.4
501-525	10	29487	203521.5	0.000049	0.000016	4.9
526-550	5	27212	175162	0.000029	0.000013	2.9
551-575	9	27563	147769.5	0.000061	0.000020	6.1
576-600	9	25903	121027.5	0.000074	0.000025	7.4
601-625	4	24313	95910.5	0.000042	0.000021	4.2
626-650	3	23556	71972	0.000042	0.000024	4.2
651-675	2	23383	48499.5	0.000041	0.000029	4.1
676-700	2	23575	25018.5	0.000080	0.000057	8.0
701-725	3	12762	6848	0.000438	0.000253	43.8
726-750	0	456	236	0	0	0
751-775	0	2	7	0	0	0
776-800	0	0	6	0	0	0
801-825	0	0	6	0	0	0
826-850	0	1	5.5	0	0	0
851-875	0	1	4.5	0	0	0
876-900	0	0	4	0	0	0
901-925	0	0	4	0	0	0
926-950	0	0	4	0	0	0
951-975	0	0	4	0	0	0
976-1000	0	1	3.5	0	0	0
1001-1025	0	1	2.5	0	0	0
1026-1050	0	0	2	0	0	0
1051-1075	0	1	1.5	0	0	0

1076-1100	0	0	1	0	0	0
1101-1125	0	0	1	0	0	0
1126-1150	0	0	1	0	0	0
1151-1175	0	0	1	0	0	0
1176-1200	0	1	0.5	0	0	0
1201-1225	0	0	0	0	0	0

Appendix 5. Full life table data for deaths from overdose or suicide over time (in 25-day intervals) by duration on opioids among those who stopped treatment with opioids

25-Day Interval	Overdose/ Suicide Deaths	Number Censored	Sample Size	Conditional Probability of Overdose/ Suicide Death	Conditional Probability Standard Error	Overdose/Suicide Deaths per 100,000 Patients
Patients Who Stopped Treatment with Opioids (≤30 days Duration on Opioids)						
1-25	78	15574	392898	0.000199	0.000022	19.9
26-50	59	15215	377425.5	0.000156	0.00002	15.6
51-75	40	12657	363430.5	0.00011	0.000017	11.0
76-100	31	11747	351188.5	0.000088	0.000016	8.8
101-125	33	10985	339791.5	0.000097	0.000017	9.7
126-150	34	10025	329253.5	0.000103	0.000018	10.3
151-175	29	9919	319247.5	0.000091	0.000017	9.1
176-200	28	8801	309858.5	0.00009	0.000017	9.0
201-225	25	8402	301229	0.000083	0.000017	8.3
226-250	17	7009	293498.5	0.000058	0.000014	5.8
251-275	14	6428	286763	0.000049	0.000013	4.9
276-300	18	6255	280407.5	0.000064	0.000015	6.4
301-325	17	5887	274318.5	0.000062	0.000015	6.2
326-350	9	8761	266977.5	0.000034	0.000011	3.4
351-375	11	17425	253875.5	0.000043	0.000013	4.3
376-400	12	21191	234556.5	0.000051	0.000015	5.1
401-425	19	20070	213914	0.000089	0.00002	8.9
426-450	4	19866	193927	0.000021	0.00001	2.1
451-475	7	19601	174189.5	0.00004	0.000015	4.0
476-500	10	18914	154925	0.000065	0.00002	6.5
501-525	8	19018	135949	0.000059	0.000021	5.9
526-550	3	17881	117491.5	0.000026	0.000015	2.6
551-575	4	17746	99675	0.00004	0.00002	4.0
576-600	7	17015	82290.5	0.000085	0.000032	8.5
601-625	2	15872	65840	0.00003	0.000021	3.0
626-650	3	15296	50254	0.00006	0.000034	6.0
651-675	0	15824	34691	0	0	0
676-700	0	15871	18843.5	0	0	0
701-725	3	10509	5653.5	0.000531	0.000306	53.1
726-750	0	392	200	0	0	0
751-775	0	0	4	0	0	0
776-800	0	0	4	0	0	0
801-825	0	0	4	0	0	0
826-850	0	1	3.5	0	0	0

851-875	0	0	3	0	0	0
876-900	0	0	3	0	0	0
901-925	0	0	3	0	0	0
926-950	0	0	3	0	0	0
951-975	0	0	3	0	0	0
976-1000	0	1	2.5	0	0	0
1001-1025	0	1	1.5	0	0	0
1026-1050	0	0	1	0	0	0
1051-1075	0	1	0.5	0	0	0
1076-1100	0	0	0	0	0	0
Patients Who Stopped Treatment with Opioids (31-90 Days Duration on Opioids)						
1-25	29	5154	72116	0.000402	0.000075	40.2
26-50	26	4831	67094.5	0.000388	0.000076	38.8
51-75	10	3480	62913	0.000159	0.00005	15.9
76-100	13	3032	59647	0.000218	0.00006	21.8
101-125	11	2704	56766	0.000194	0.000058	19.4
126-150	8	2298	54254	0.000147	0.000052	14.7
151-175	4	2232	51981	0.000077	0.000038	7.7
176-200	5	1770	49976	0.0001	0.000045	10.0
201-225	4	1660	48256	0.000083	0.000041	8.3
226-250	5	1486	46679	0.000107	0.000048	10.7
251-275	8	1480	45191	0.000177	0.000063	17.7
276-300	6	1826	43530	0.000138	0.000056	13.8
301-325	1	2524	41349	0.000024	0.000024	2.4
326-350	2	3332	38420	0.000052	0.000037	5.2
351-375	1	3081	35211.5	0.000028	0.000028	2.8
376-400	3	3253	32043.5	0.000094	0.000054	9.4
401-425	3	2778	29025	0.000103	0.00006	10.3
426-450	3	2919	26173.5	0.000115	0.000066	11.5
451-475	3	2809	23306.5	0.000129	0.000074	12.9
476-500	0	2614	20592	0	0	0
501-525	0	2722	17924	0	0	0
526-550	1	2558	15284	0.000065	0.000065	6.5
551-575	1	2536	12736	0.000079	0.000079	7.9
576-600	0	2187	10373.5	0	0	0
601-625	1	2218	8171	0.000122	0.000122	12.2
626-650	0	2192	5965	0	0	0
651-675	0	2091	3823.5	0	0	0
676-700	0	2022	1767	0	0	0
701-725	0	733	389.5	0	0	0
726-750	0	21	12.5	0	0	0

751-775	0	1	1.5	0	0	0
776-800	0	0	1	0	0	0
801-825	0	0	1	0	0	0
826-850	0	0	1	0	0	0
851-875	0	0	1	0	0	0
876-900	0	0	1	0	0	0
901-925	0	0	1	0	0	0
926-950	0	0	1	0	0	0
951-975	0	0	1	0	0	0
976-1000	0	0	1	0	0	0
1001-1025	0	0	1	0	0	0
1026-1050	0	0	1	0	0	0
1051-1075	0	0	1	0	0	0
1076-1100	0	0	1	0	0	0
1101-1125	0	0	1	0	0	0
1126-1150	0	0	1	0	0	0
1151-1175	0	0	1	0	0	0
1176-1200	0	1	0.5	0	0	0
1201-1225	0	0	0	0	0	0
Patients Who Stopped Treatment with Opioids (91-400 Days Duration on Opioids)						
1-25	107	13422	184729	0.000579	0.000056	57.9
26-50	47	15122	170350	0.000276	0.00004	27.6
51-75	38	11131	157176.5	0.000242	0.000039	24.2
76-100	23	9557	146794.5	0.000157	0.000033	15.7
101-125	22	8206	137890	0.00016	0.000034	16.0
126-150	20	7173	130178.5	0.000154	0.000034	15.4
151-175	18	7299	122922.5	0.000146	0.000035	14.6
176-200	13	6565	115972.5	0.000112	0.000031	11.2
201-225	9	7267	109043.5	0.000083	0.000028	8.3
226-250	8	6865	101968.5	0.000078	0.000028	7.8
251-275	10	7102	94977	0.000105	0.000033	10.5
276-300	6	7033	87899.5	0.000068	0.000028	6.8
301-325	6	6867	80943.5	0.000074	0.00003	7.4
326-350	9	7067	73970.5	0.000122	0.000041	12.2
351-375	6	6187	67334.5	0.000089	0.000036	8.9
376-400	8	6266	61102	0.000131	0.000046	13.1
401-425	5	5553	55184.5	0.000091	0.000041	9.1
426-450	1	5540	49633	0.00002	0.00002	2.0
451-475	3	5154	44285	0.000068	0.000039	6.8
476-500	3	5049	39180.5	0.000077	0.000044	7.7
501-525	2	5199	34053.5	0.000059	0.000042	5.9

526-550	0	4506	29199	0	0	0
551-575	1	4896	24498	0.000041	0.000041	4.1
576-600	1	4544	19777	0.000051	0.000051	5.1
601-625	1	4308	15350	0.000065	0.000065	6.5
626-650	0	4112	11139	0	0	0
651-675	1	3838	7164	0.00014	0.00014	14.0
676-700	2	3985	3251.5	0.000615	0.000435	61.5
701-725	0	1222	646	0	0	0
726-750	0	34	18	0	0	0
751-775	0	0	1	0	0	0
776-800	0	0	1	0	0	0
801-825	0	0	1	0	0	0
826-850	0	0	1	0	0	0
851-875	0	1	0.5	0	0	0
876-900	0	0	0	0	0	0
Patients Who Stopped Treatment with Opioids (>400 Days Duration on Opioids)						
1-25	130	16175	124762.5	0.00104	0.000091	104.0
26-50	42	15803	108643.5	0.000387	0.00006	38.7
51-75	26	10379	95510.5	0.000272	0.000053	27.2
76-100	23	8251	86169.5	0.000267	0.000056	26.7
101-125	13	6898	78572	0.000165	0.000046	16.5
126-150	21	5956	72132	0.000291	0.000064	29.1
151-175	15	5805	66230.5	0.000226	0.000058	22.6
176-200	11	5011	60807.5	0.000181	0.000055	18.1
201-225	15	4829	55876.5	0.000268	0.000069	26.8
226-250	10	4311	51291.5	0.000195	0.000062	19.5
251-275	11	4222	47015	0.000234	0.000071	23.4
276-300	7	3857	42964.5	0.000163	0.000062	16.3
301-325	8	3700	39179	0.000204	0.000072	20.4
326-350	3	3562	35540	0.000084	0.000049	8.4
351-375	6	3190	32161	0.000187	0.000076	18.7
376-400	4	3165	28977.5	0.000138	0.000069	13.8
401-425	5	2714	26034	0.000192	0.000086	19.2
426-450	4	2714	23315	0.000172	0.000086	17.2
451-475	1	2526	20691	0.000048	0.000048	4.8
476-500	2	2556	18149	0.00011	0.000078	11.0
501-525	0	2548	15595	0	0	0
526-550	1	2267	13187.5	0.000076	0.000076	7.6
551-575	3	2385	10860.5	0.000276	0.000159	27.6
576-600	1	2157	8586.5	0.000116	0.000116	11.6
601-625	0	1915	6549.5	0	0	0

626-650	0	1956	4614	0	0	0
651-675	1	1630	2821	0.000354	0.000354	35.4
676-700	0	1697	1156.5	0	0	0
701-725	0	298	159	0	0	0
726-750	0	9	5.5	0	0	0
751-775	0	1	0.5	0	0	0
776-800	0	0	0	0	0	0