

Supplementary Online Content

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eTable 1. Multivariable Cox Proportional Hazards Regression Models of Death by Opioid Overdose Among Patients

eTable 2. Multivariable Cox Proportional Hazards Regression Models of Death by Opioid Overdose Among Patients, Stratified by SUD Status

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

eTable 1: Multivariable Cox proportional hazards regression models^a of death by opioid overdose among patients

Treatment and Patient Characteristics ^a	Risk of Opioid Overdose Death within Specific Subgroups			
	Subgroup 1: Chronic Pain HR (95% CI)	Subgroup 2: Cancer HR (95% CI)	Subgroup 3: Acute Pain HR (95% CI)	Subgroup 4: SUD ^b HR (95% CI)
<i>Daily Opioid Dose</i> ^c	1.96 (1.74, 2.21)	2.42 (1.76, 3.34)	1.97 (1.58, 2.46)	1.69 (1.38, 2.07)
<i>Opioid Fill Type</i>				
Regularly Scheduled Only	1.00	1.00	1.00	1.00
PRN only	1.10 (0.84, 1.42)	2.71 (1.28, 5.72)	0.92 (0.58, 1.47)	0.95 (0.63, 1.44)
Simultaneous PRN and Regularly Scheduled	1.32 (0.98, 1.77)	1.84 (0.84, 4.04)	1.11 (0.67, 1.84)	1.24 (0.74, 2.08)
<i>Pain-Related Diagnoses</i>				
Cancer	0.99 (0.72, 1.36)	--	0.66 (0.35, 1.23)	1.03 (0.63, 1.69)
Chronic Bodily Pains	0.69 (0.35, 1.33)	1.52 (0.74, 3.13)	0.56 (0.33, 0.93)	0.74 (0.46, 1.20)
Headache	1.02 (0.74, 1.41)	0.72 (0.29, 1.79)	1.17 (0.69, 1.97)	0.77 (0.44, 1.35)
Neuropathy	0.64 (0.38, 1.07)	0.21 (0.03, 1.56)	0.83 (0.39, 1.76)	0.43 (0.15, 1.18)
Injuries and Acute Pain	1.37 (1.08, 1.74)	0.94 (0.50, 1.77)	--	1.24 (0.86, 1.79)
<i>Other Diagnoses</i>				
Substance Use Disorders	2.53 (1.99, 3.22)	3.09 (1.73, 5.53)	2.25 (1.53, 3.31)	--
Other Psychiatric Disorders	1.87 (1.47, 2.38)	1.68 (0.94, 3.00)	1.78 (1.19, 2.66)	1.73 (1.10, 2.71)
COPD, CVD, and Sleep Apnea	0.63 (0.50, 0.80)	0.73 (0.38, 1.42)	0.76 (0.50, 1.16)	1.01 (0.66, 1.54)
<i>Demographics</i>				
Male	1.42 (0.90, 2.24)	1.58 (0.44, 5.62)	2.80 (0.98, 7.98)	1.19 (0.50, 2.84)
Age (Reference: 18-29)				
30-39	0.56 (0.27, 1.16)	0.90 (0.10, 8.26)	0.50 (0.18, 1.41)	0.33 (0.11, 1.01)
40-49	0.94 (0.49, 1.79)	0.35 (0.04, 3.14)	0.68 (0.28, 1.63)	0.32 (0.12, 0.83)
50-59	0.43 (0.22, 0.83)	0.23 (0.03, 2.03)	0.37 (0.15, 0.91)	0.16 (0.06, 0.44)
60-69	0.18 (0.08, 0.39)	0.06 (0.01, 0.68)	0.11 (0.03, 0.42)	0.06 (0.02, 0.25)
70+	0.06 (0.02, 0.18)	--	0.12 (0.03, 0.52)	--
Race (Reference: White)				
Black	0.37 (0.24, 0.59)	0.77 (0.32, 1.84)	0.53 (0.27, 1.04)	0.34 (0.17, 0.65)
Other/Missing	1.00 (0.69, 1.44)	0.71 (0.21, 2.36)	1.20 (0.63, 2.29)	0.63 (0.28, 1.40)
Hispanic Ethnicity	0.85 (0.46, 1.57)	2.59 (0.84, 7.98)	0.88 (0.31, 2.46)	0.49 (0.15, 1.59)

^a All variables entered simultaneously into one model for each subgroup

^b Substance Use Disorders

^c Four category variable of dose (1 - < 20, 20 - < 50, 50 - < 100, or 100+ mg/day) treated as a continuous variable.

eTable 2: Multivariable Cox proportional hazards regression models^a of death by opioid overdose among patients, stratified by SUD^b status

<i>Opioid Treatment Characteristics^a</i>	Risk of Opioid Overdose Death within Specific Subgroups, Stratified by SUD^b status					
	Chronic Pain + SUD	Chronic Pain + no SUD	Cancer + SUD	Cancer + no SUD	Acute Pain + SUD	Acute Pain + no SUD
	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)
<i>Opioid Fill Type</i>						
Regularly Scheduled Only	1.00	1.00	1.00	1.00	1.00	1.00
PRN only	0.88 (0.56, 1.39)	1.23 (0.89, 1.70)	2.40 (0.77, 7.50)	2.95 (1.14, 7.63)	0.75 (0.36, 1.59)	1.04 (0.57, 1.90)
Simultaneous PRN and Regularly Scheduled	1.31 (0.75, 2.28)	1.36 (0.96, 1.92)	1.18 (0.36, 3.89)	2.34 (0.84, 6.56)	1.07 (0.42, 2.72)	1.20 (0.66, 2.17)
<i>Maximum Prescribed Daily Opioid Dose</i>						
1 to < 20 mg/d	1.00	1.00	1.00	1.00	1.00	1.00
20 to < 50 mg/d	1.52 (0.86, 2.67)	2.17 (1.38, 3.41)	3.08 (0.60, 15.70)	1.27 (0.40, 4.03)	1.08 (0.47, 2.49)	2.39 (1.00, 5.68)
50 to < 100 mg/d	2.33 (1.20, 4.53)	6.54 (4.10, 10.42)	7.25 (1.25, 41.98)	5.90 (1.85, 18.85)	2.57 (0.96, 6.90)	8.32 (3.51, 19.72)
100+ mg/d	4.03 (2.05, 7.95)	9.89 (6.07, 16.11)	15.08 (2.50, 90.78)	10.69 (3.23, 35.38)	2.37 (0.78, 7.23)	14.46 (5.65, 36.95)

^a Adjusted for same covariates shown in eTable 1, with simultaneous entry of all variables

^b Substance Use Disorders