

Overdose among VA patients receiving opioid therapy for pain: Risk factors and prevention.

Amy S.B. Bohnert, Ph.D.



Affiliations:

VA National Serious Mental Illness Treatment Resource & Evaluation Center
VA Ann Arbor HSR&D Center of Excellence, Center for Clinical Management Research
University of Michigan Medical School, Department of Psychiatry

Acknowledgements

Supported by funding from Veteran Health Administration, Office of Mental Health Operations and VA HSR&D grant CDA-09-204, NIH grant R03 AG042899, and the University of Michigan Department of Psychiatry and Injury Center.

No conflicts of interest to report.



THE BLOG

Featuring fresh takes and real-time analysis from
HuffPost's signature lineup of contributors

The New York Times

The Opinion Pages

ROOM for D



Peter Abaci, M.D.

Chronic pain specialist

GET UPDATES FROM PETE



WORLD U.S. N.Y./REGION BUSINESS TECHNOLOGY SCIENCE HEALTH SPOR

Why Our Approach To Chronic Pain Is Flawed

Opioids Are Rarely the Answer



Andrew Kolodny is president of *Physicians for Responsible Opioid Prescribing* and chairman of the department of psychiatry at Maimonides Medical Center in New York City.

Posted: 08/05/11 09:36 AM ET

UPDATED FEBRUARY 16, 2012, 10:39 AM

epidemic of overdose deaths and addiction

Pain-Topics.org News/Research UPDATE

Sunday, January 1, 2012

What's Really Driving Opioid-Related

THE BLOG

Featuring fresh takes and real-time analysis from
HuffPost's signature lineup of contributors

HOT ON THE BLOG

Sen. Bernie
Hilary Rosen

Login with Facebook to see what your friends are reading



Radley Balko

Senior Writer and Investigative
Reporter, The Huffington Post

GET UPDATES FROM RADLEY BALKO



3k

Painkiller Access Debated as Patients Suffer

Posted: 03/09/2012 6:01 pm

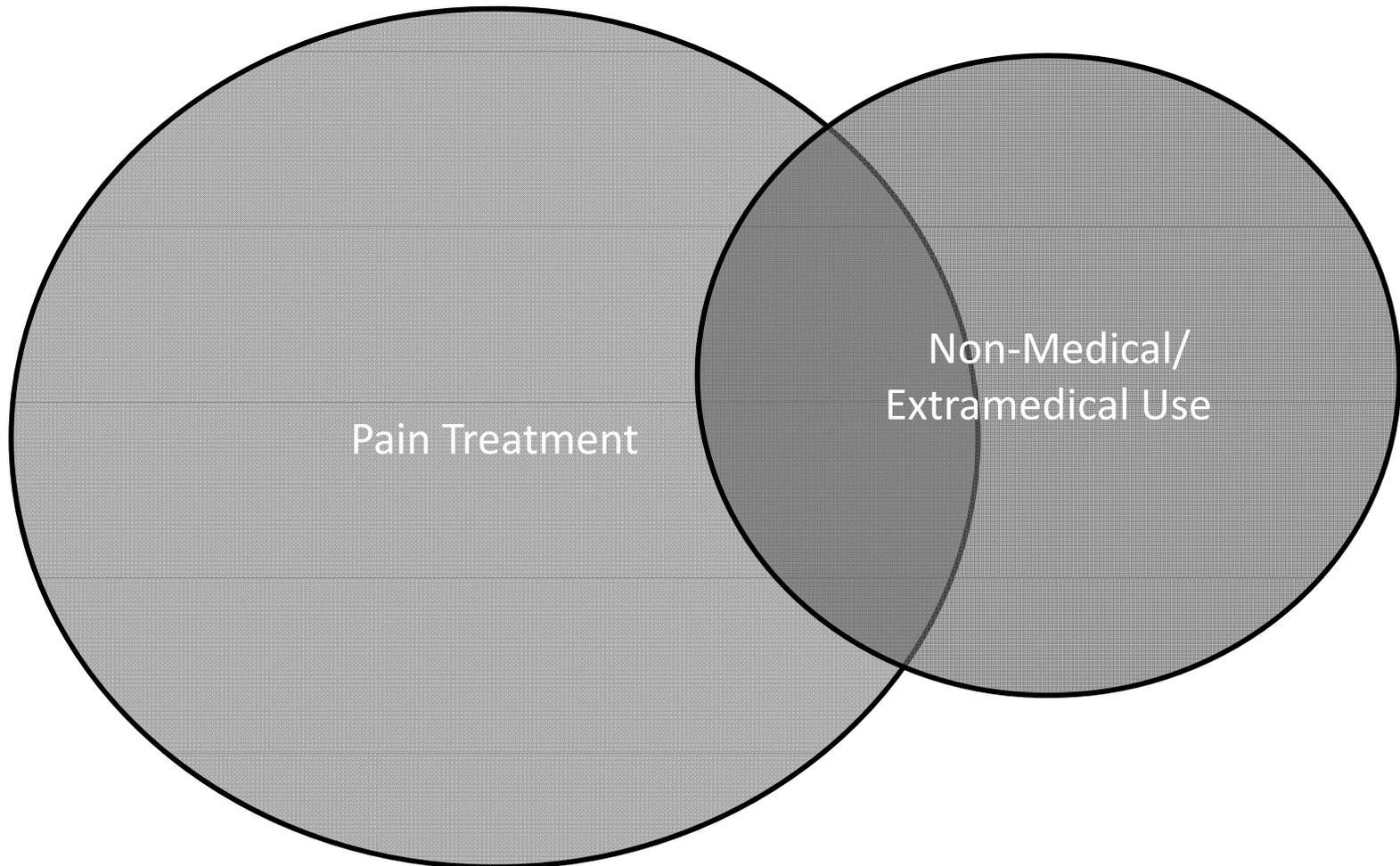
Outline

Objective: To describe strategies for reducing risk of opioid overdose for VA patients with pain.

1. Research on trends and risk factors
2. Potential settings for intervention
3. Prevention strategies, quality of evidence

Use of Prescription Opioids in the U.S.

Prescription Opioids: pain medications that contain opioids (naturally occurring or synthetic) and require a prescription in the U.S., including codeine, percocet, fentanyl etc.

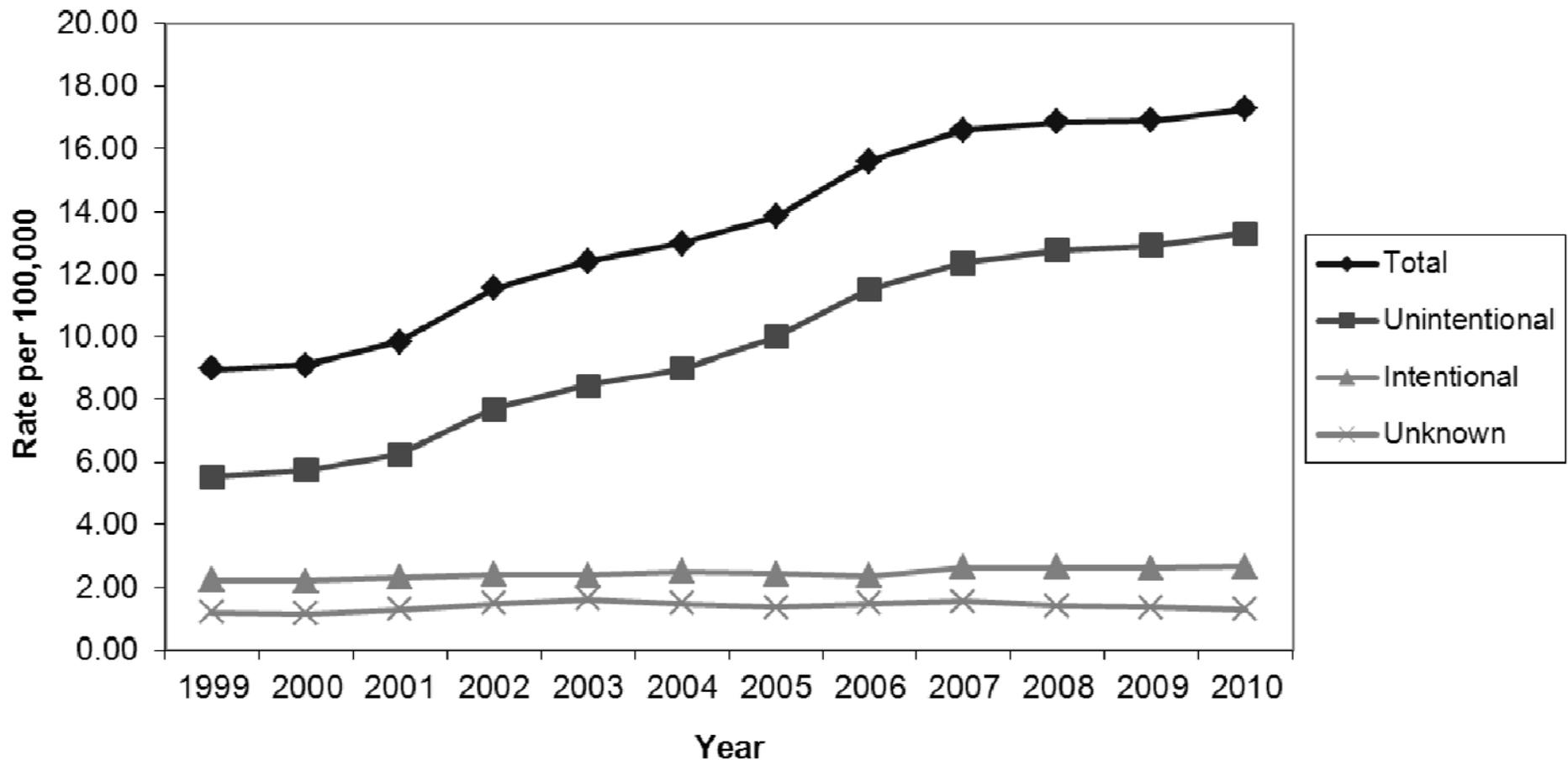


1. Overdose Epidemiology

- Trends Over Time
- Risk Factors

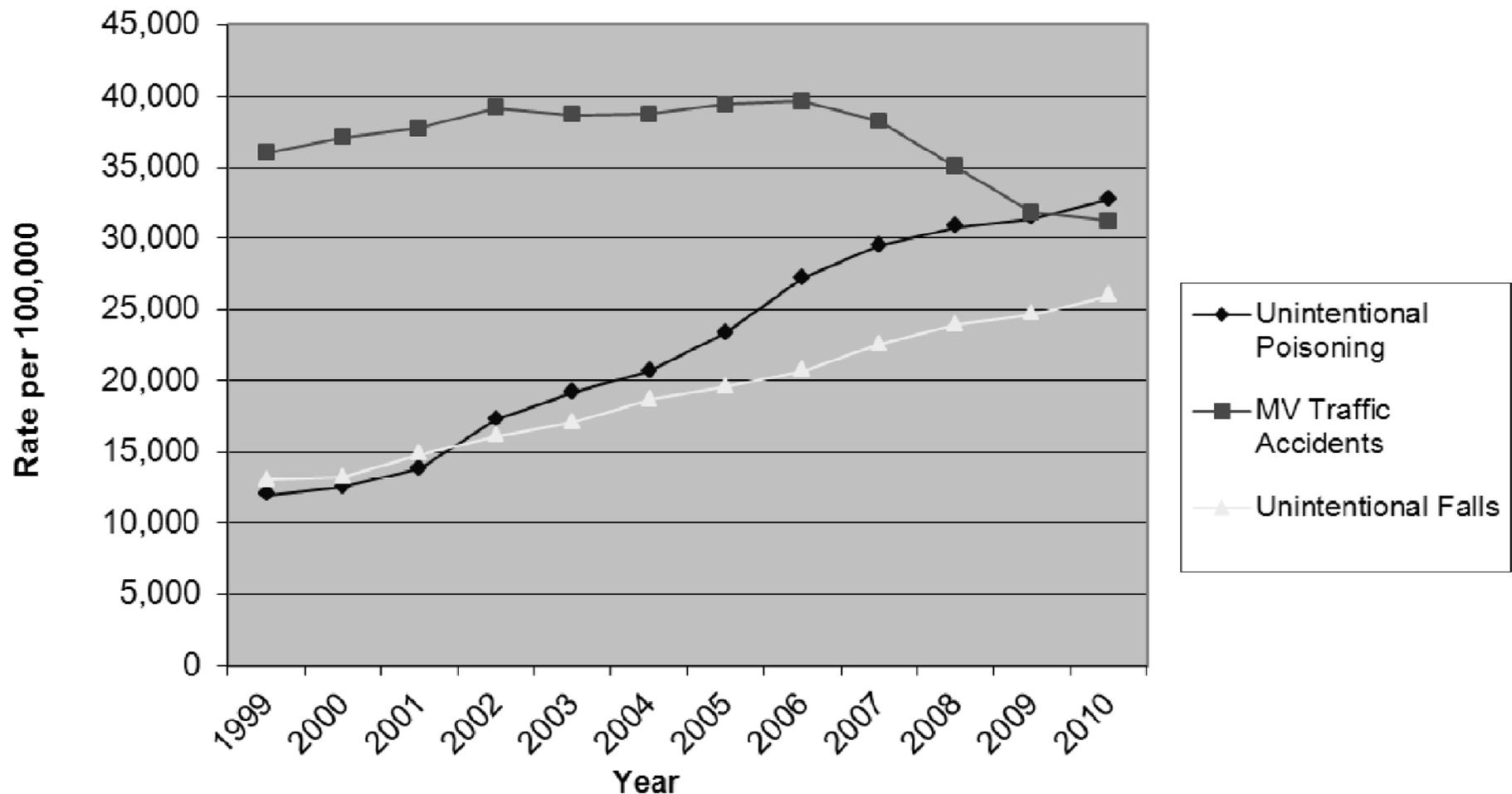
Poisoning/Overdose Mortality Rate in the U.S.

Poisoning Mortality, by Intent, US Adults age 15+

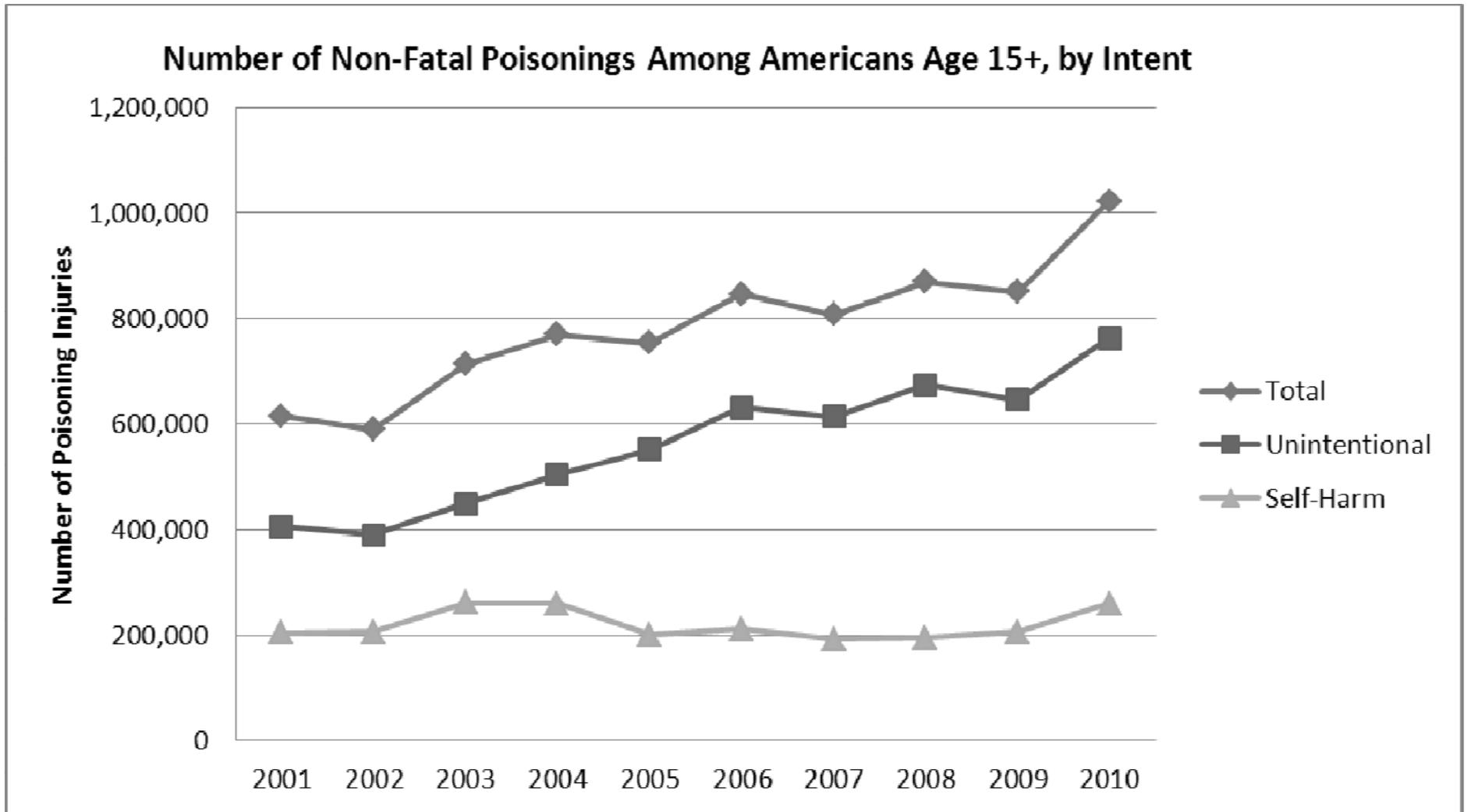


Comparison to Other Major Unintentional Injury Causes of Death

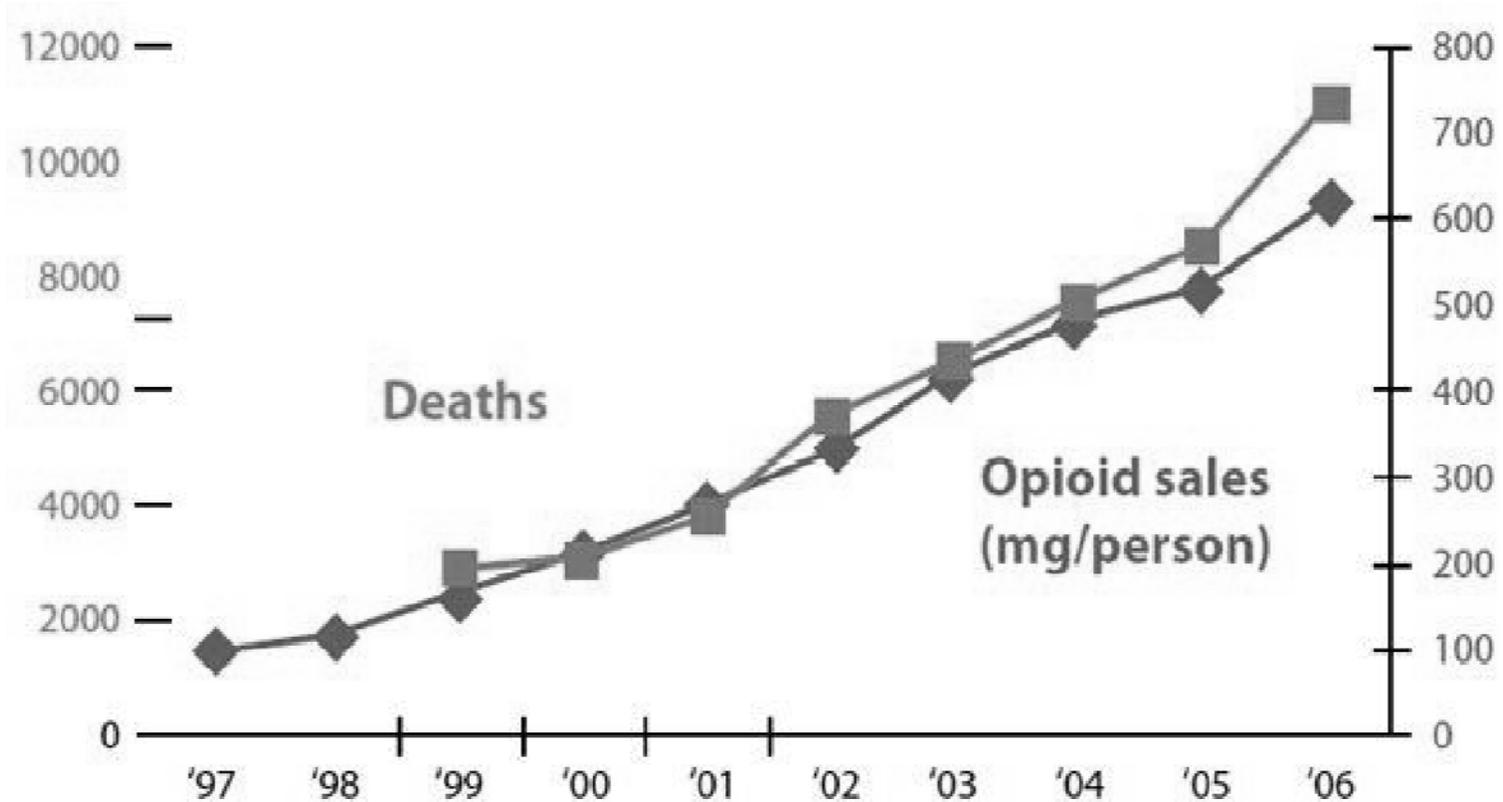
Number of Unintentional Deaths by Selected Injury Causes among adults age 18+ in the US



Non-Fatal Poisoning/Overdose in the U.S.



Opioid Analgesics: Sales and Overdoses



Medscape

Source: Medscape/CDC

Overdose Rates are Elevated Among VA Patients

Gender/ Age Group	U.S. 2005		V.H.A. FY2005		Standardized Mortality Ratio ^b	95% Confidence Interval
	Accidental Poisonings	Crude Rate per 100,000 person-years	Accidental Poisonings	Crude Rate per 100,000 person-years		
Males	15,679	14.51	960	20.62	1.98	1.85, 2.10
18-29 yrs	3,390	13.45	28	21.86	1.62	1.02, 2.23
30-64 yrs	11,826	17.53	841	36.81	2.10	1.96, 2.24
65+ yrs	463	3.01	91	4.06	1.35	1.07, 1.63
Females	7,647	6.68	53	11.82	1.61	1.18, 2.04
18-29 yrs	1,024	4.28	1	1.70	n/a	n/a
30-64 yrs	6,155	8.91	50	15.34	1.72	1.24, 2.20
65+ yrs	468	2.19	2	3.14	n/a	n/a
Total	23,326	10.49	1,013	19.85	1.96	1.83, 2.08

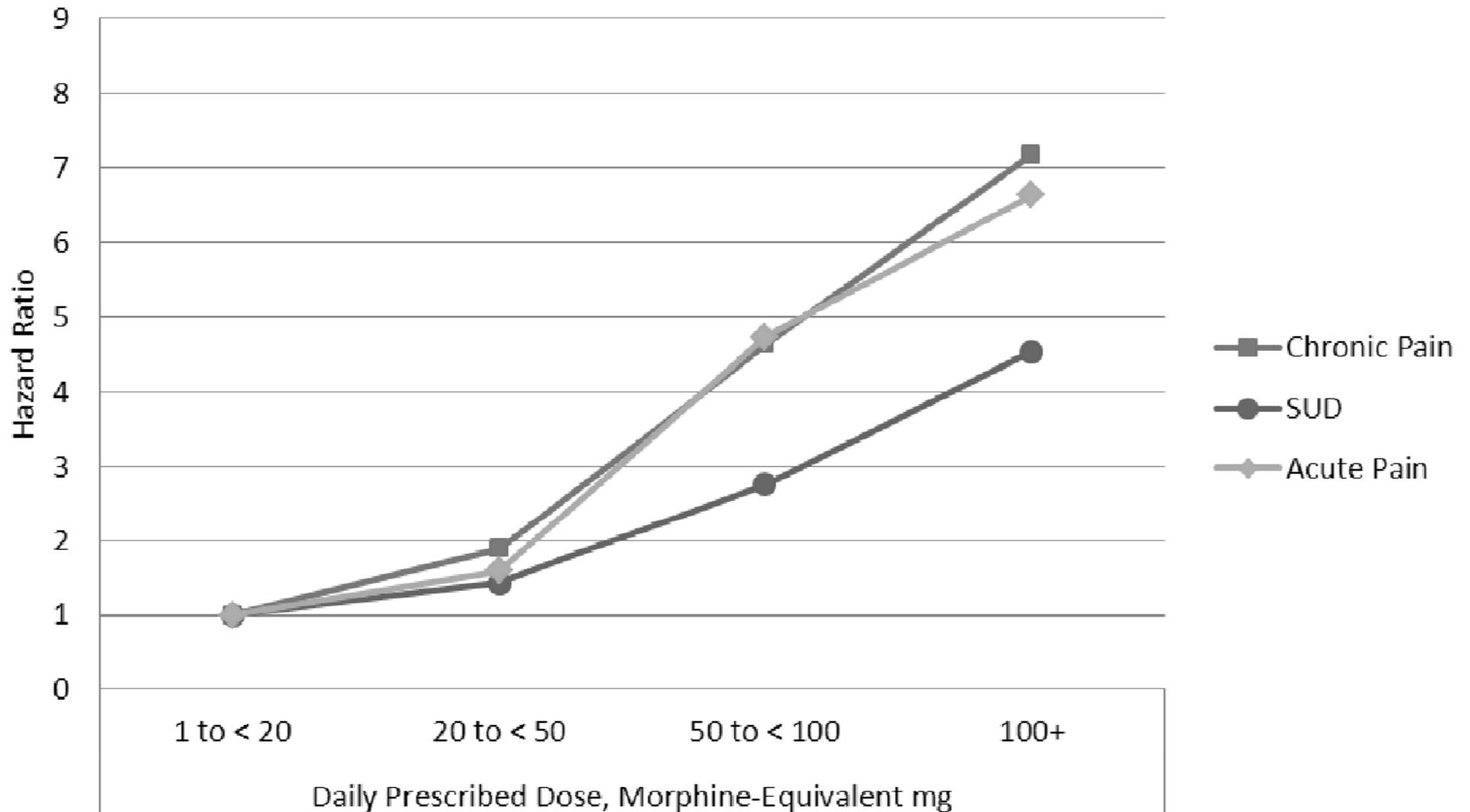
From Bohnert, Ilgen, Galea, et al., 2011 *Med Care*

Risk Factors Among Pain Patients

- Opioid Dose (prescribed or amount filled)

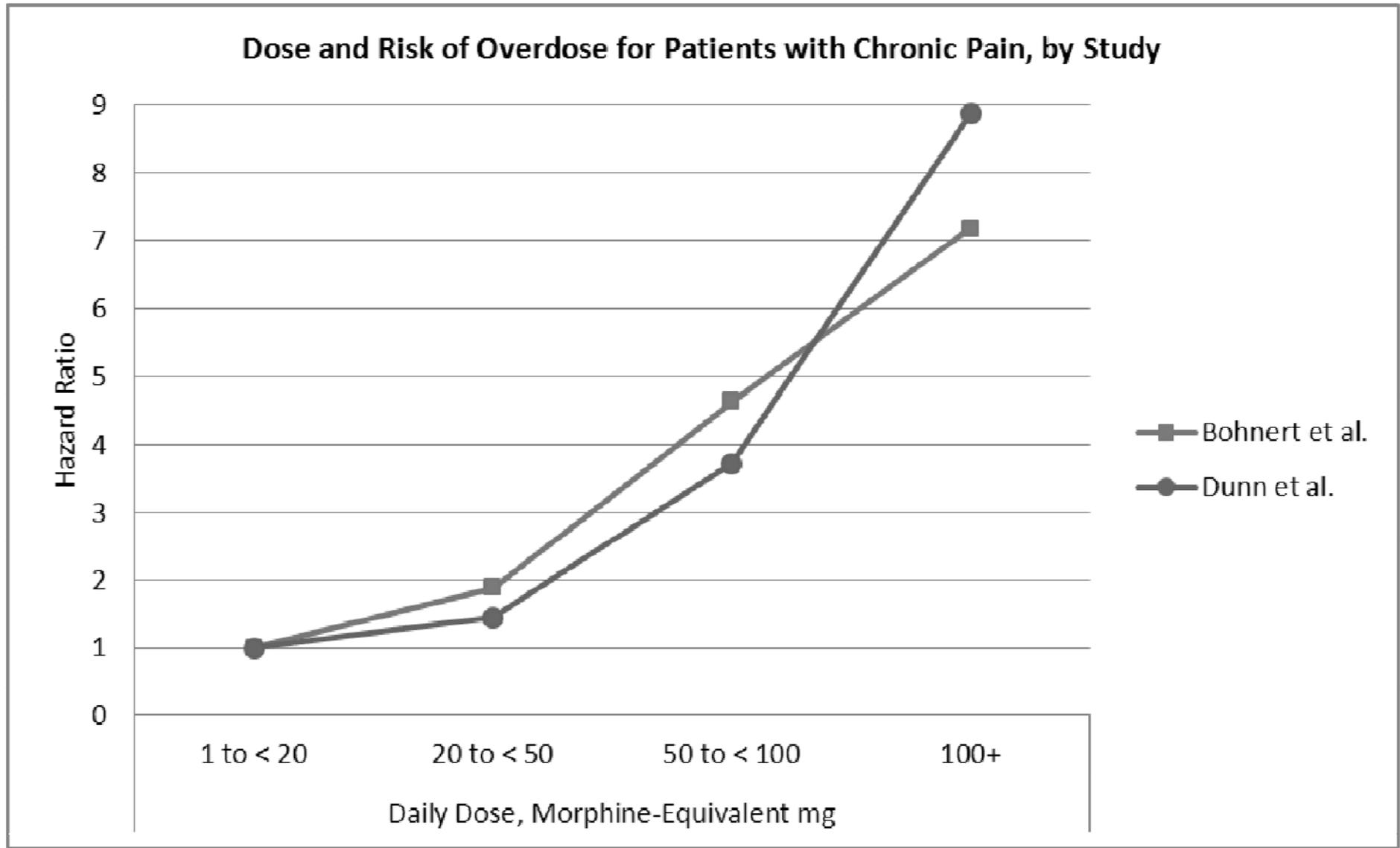
Risk of Opioid Overdose Among VA Patients, Prescribed Opioid Dose

Opioid Dose and Risk of Unintentional Overdose Death, by Condition Type



From Bohnert, Valenstein, Bair et al., 2011 *JAMA*

Opioid Dose and Overdose in Chronic Pain Patients



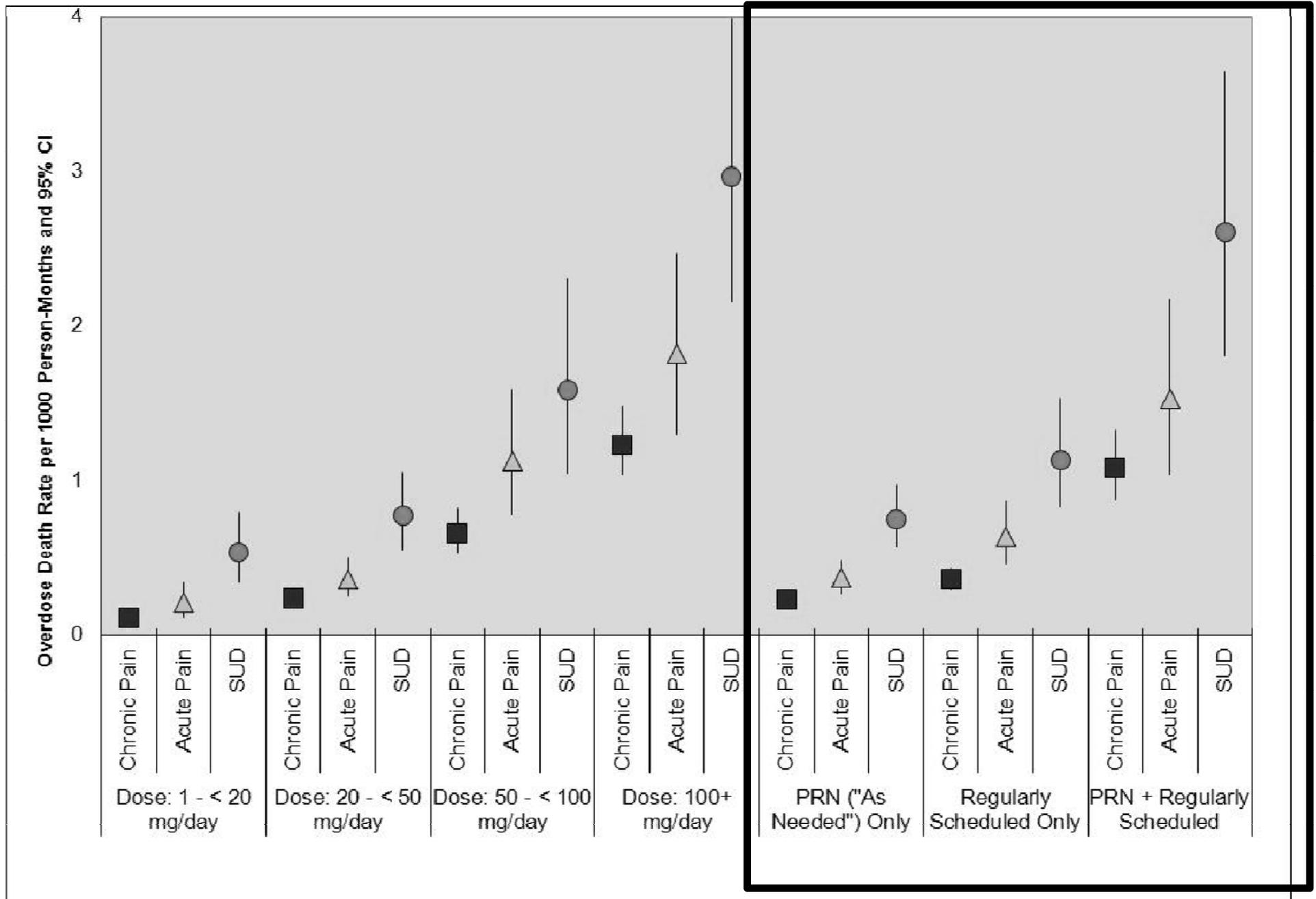
Bohnert et al.: VA Patients (national sample)

Dunn et al.: Group Health Cooperative (Washington state)

Risk Factors Among Pain Patients

- Opioid Dose
- Opioid Schedule (but confounded by dose)

Unadjusted Overdose Rates by Prescribing Characteristics



From Bohnert, Valenstein, Bair et al., 2011 *JAMA*

Risk Factors Among Pain Patients

- Opioid Dose
- Opioid Schedule
- Opioid Type? (limited evidence)

Opioid Type

- Paulozzi et al. *Pain Med* 2012
 - Case-control study of New Mexico drug overdoses

Risk Factors Indicator Variables	Crude OR	(95% CI)
Type of opioid prescribed		
Buprenorphine	21.5	8.3–56.0
Codeine	0.6	0.3–1.0
Fentanyl	7.7	4.8–12.4
Hydrocodone	1.4	1.1–1.7
Hydromorphone	11.8	6.2–22.3
Meperidine	1.1	0.4–3.0
Methadone	13.4	7.8–23.0
Morphine	6.1	4.1–9.0
Oxycodone	3.2	2.5–4.1
Propoxyphene	1.4	0.9–2.0

- Research to date has not accounted for patient selection factors.
 - Note: Krebs et al., 2011 found lower all-cause mortality for methadone than morphine using propensity score adjustment

Risk Factors Among Pain Patients

- Opioid Dose
- Opioid Schedule
- Demographic Characteristics

Demographic Characteristics

Table 1. Characteristics of the Sample of Veterans Health Administration Patients Receiving Opioid Therapy

Characteristic	No. (%)		P Value
	Opioid Overdose Decedents (n = 750)	All Others (n = 154 684)	
Male sex	700 (93.3)	144 304 (93.3)	.96
Age, y			<.001
18-29	31 (4.1)	3995 (2.6)	
30-39	60 (8.0)	8407 (5.4)	
40-49	313 (41.7)	23 888 (15.4)	
50-59	297 (39.6)	50 216 (32.5)	
60-69	38 (5.1)	29 985 (19.4)	
≥70	11 (1.5)	38 183 (24.7)	
Race			<.001
Black	52 (6.9)	25 409 (16.4)	
White	625 (83.3)	110 965 (71.7)	
Other/missing	73 (9.7)	18 310 (11.8)	
Hispanic ethnicity	23 (3.1)	6342 (4.1)	.15

VA patients:
Younger ages
and those of
White race over-
represented in
opioid overdose
deaths

Risk Factors Among Pain Patients

- Opioid Dose
- Opioid Schedule
- Demographic Characteristics
- Pain Diagnosis and Co-morbidity
 - Pain Type
 - Substance use disorders
 - Other mental health conditions

Unadjusted Association of Patient Characteristics with Unintentional Overdose

	Opioid Overdose Decedents, N = 750 n (%)	All Others, N = 154,684 n (%)	p - value
Pain-Related Diagnoses			
Cancer	91 (12.1)	36,712 (23.7)	< 0.001
Chronic Bodily Pain	588 (78.4)	107,158 (69.3)	< 0.001
Headache	90 (12.0)	10,208 (6.6)	< 0.001
Neuropathy	32 (4.3)	8,339 (5.4)	.17
Injuries and Acute Pain	222 (29.6)	29,522 (19.1)	< 0.001
Other Diagnoses			
Substance Use Disorders	296 (39.5)	15,195 (9.8)	< 0.001
Other Psychiatric Disorders	498 (66.4)	51,929 (33.6)	< 0.001
COPD, CVD, and/or Sleep Apnea	467 (62.3)	123,025 (79.5)	< 0.001

Risk Factors Among Pain Patients

- Opioid Dose
- Opioid Schedule
- Demographic Characteristics
- Pain Diagnosis and Co-morbidity
- “Doctor Shopping” and Other Behavioral Factors

“Doctor Shopping”

- Peirce, Smith, Abate, Halverson *Med Care* 2012
 - Case-control study in West Virginia of drug-related deaths
 - Doctor shopping (DS): 3+ doctors prescribe in 6 months
 - Pharmacy shopping (PS): 4+ pharmacies in 6 months

	Odds Ratio	95% CI
No DS, No PS	1.0	--
DS, no PS	2.03	1.60 – 2.57
PS, no DS	3.18	2.25 – 4.48
Both DS and PS	3.60	2.74 – 4.73

Adj. for age, # Rx,
type Rx

- Little research on behavioral factors other than these severe indicators of problematic use

Risk Factors Among Pain Patients

- Opioid Dose
 - Opioid Schedule
 - Opioid Type?
 - Demographic Characteristics
 - Pain Diagnosis and Co-morbidity
 - Behavioral Factors
- Medication
- Patient
-
- A diagram with two large right-facing curly braces. The top brace groups the first three items: Opioid Dose, Opioid Schedule, and Opioid Type?. The bottom brace groups the last three items: Demographic Characteristics, Pain Diagnosis and Co-morbidity, and Behavioral Factors. The word 'Medication' is positioned to the right of the top brace, and the word 'Patient' is positioned to the right of the bottom brace.

Little research on provider characteristics, clinic setting, health system characteristics

Methodological Limitations of Risk Factor Research

- Cautions of observational healthcare data
- Challenges in studying rare events such as overdose

2. VA Clinic Setting and Overdose

- In progress work
- Retrospective study of types of clinics visited
prescription opioid overdose
- Objective to identify clinical settings where opportunities to intervene with patients at risk for overdose exist

Methods

- Retrospective, descriptive analysis
- Sample: all unintentional opioid overdose decedents, FY04-FY07
 - Last visit was outpatient
 - Contact with VHA in last two years before death
 - N = 985

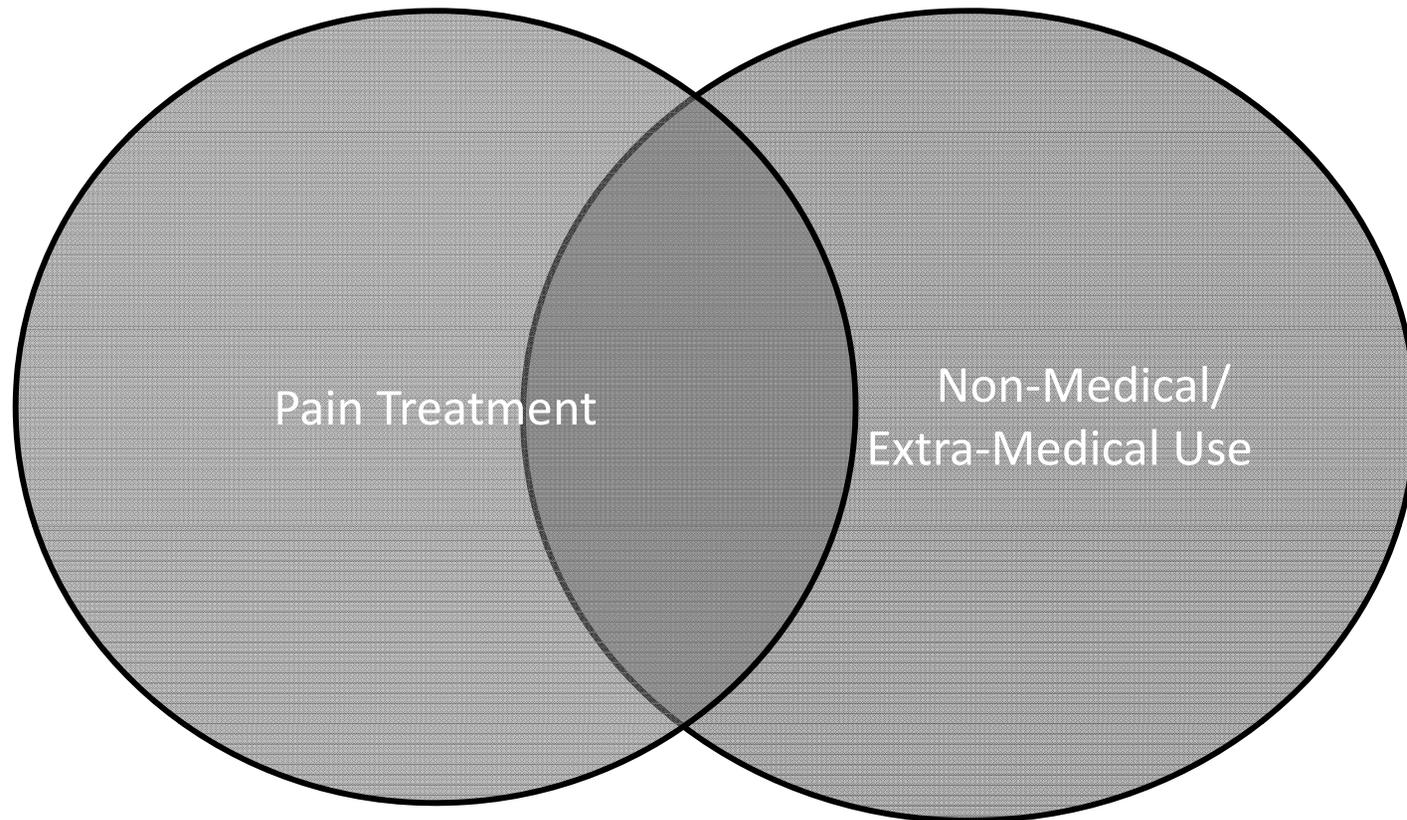
Outpatient Treatment Received Prior to Unintentional Opioid Overdose Death		Total N = 985	
Overall – Any Treatment or Contact		N	(%)
	7 days prior	277	28.1
	30 days prior	557	56.6
	1 year prior	903	91.7
Categories of Treatment	Any Substance Abuse (SA) Treatment		
	7 days prior	16	1.6
	30 days prior	50	5.1
	1 year prior	200	20.3
	Any Mental Health Treatment (no SA)		
	7 days prior	86	8.7
	30 days prior	214	21.7
	1 year prior	538	54.6
	Any Mental Health or SA Treatment		
	7 days prior	98	10.0
	30 days prior	242	24.6
	1 year prior	566	57.5
	Pain Clinic Treatment		
	7 days prior	10	1.0
	30 days prior	23	2.3
	1 year prior	97	9.9
	Primary Care (PC) Treatment		
	7 days prior	96	9.8
	30 days prior	269	27.3
	1 year prior	752	76.4

Implications

- Over half had been seen in the prior 30 days
- Primary care and mental health clinic use was common and interventions in these settings may have a greater impact

3. Overdose Prevention in Pain Treatment Settings

Prevention of Prescription Opioid Overdose in the U.S.



Strategies:

- Patient selection
- Prescription drug monitoring systems
- Prescribing practices
- Patient and caregiver education
- Monitoring

Strategies:

- Diversion reduction
- Universal prevention to reduce initiation
- Harm and use reduction

-Naloxone Distribution?

Patient Selection

- DoD/VA Opioid Guidelines 2010
 - Contraindicated for patients:
 - With severe respiratory instability
 - With acute psychiatric instability/suicide risk
 - Who have a substance use disorder (if not in treatment)
 - On medications with life-limiting interaction potential
 - Who actively divert meds
 - With an allergy, intolerance or lack of positive response to opioids

Prescription Drug Monitoring Programs

- PDMPs: State-level registries of pharmacy records of certain controlled substances; rely on providers to check and alter prescribing behavior if evidence of “doctor shopping”
- Evidence: has not impacted overdose rates in observational evaluation (Paulozzi, Kilbourne, Desai, *Pain Med* 2011)
- Inconsistent implementation has likely limited impact

Prescribing Practices

- Some evidence from observational studies

REDUCE RISK OF OVERDOSE

- NOTE: no research has formally tested the impact of dose limits or compared outcomes among patients randomized to dose



▶ POTENTIAL DOSE-RELATED RISK OF OPIOID DEATHS IN VETERANS 1,2



▶ MEDICATION SAFETY NEWS FROM THE VA NATIONAL PHARMACY BENEFITS MANAGEMENT SERVICES [PBM] AND THE FOOD AND DRUG ADMINISTRATION [FDA]..... 1-2



▶ DRONEDARONE SAFETY CONCERNS 3



VA Center for Medication Safety

○ ISSUE 3 | ○ VOLUME 1 | ○ SEPTEMBER 2011

Medication *safety in seconds*

A MONTHLY PUBLICATION FROM VA MEDSAFE:
VA'S COMPREHENSIVE PHARMACOVIGILANCE CENTER

Helping to achieve safe medication use



POTENTIAL DOSE-RELATED RISK OF OPIOID DEATHS IN VETERANS

A recent VHA case-cohort study evaluated the association of maximum prescribed daily opioid dose with risk of opioid overdose death among veterans in various diagnostic subgroups. Data were obtained from 154,684 patients who used VHA medical services in 2004 or 2005 and received opioid therapy for pain during the 5-year study period (2004–2008) and 750 unintentional prescription opioid overdose decedents. The results showed that maximum prescribed doses of opioids of 100 mg/d or more morphine equivalents were associated with greater than a 4- to 11-fold increased risk of opioid overdose-related deaths depending on the diagnostic subgroup (substance use disorder, chronic pain, acute pain, and cancer) (Table 1).

Overall, fatal overdose was rare, being identified in about 0.04% of individuals treated with opioids during the 5-year study period. The overall

TABLE 1. Risk of Opioid Overdose-Related Deaths

DIAGNOSTIC SUBGROUP	HAZARD RATIO †	95% CI	ARDA
Substance Use Disorders	4.54	2.46-8.37	0.14%
Chronic Pain	7.18	4.85-10.65	0.25%
Acute Pain	6.64	3.31-13.31	0.23%
Cancer	11.99	4.42-32.56	0.45%

ARDA, Absolute risk difference approximation

† Adjusted hazard ratio associated with maximum prescribed daily opioid dose in morphine equivalents of 100mg/d or more relative to the dose category of 1 mg/d to less than 20mg/d

Patient and Caregiver Education

- Strength of Evidence: has not been studied in a randomized controlled trial

Monitoring

Monitoring recommendations from DoD/VA guidelines (2010):

- Assess for adherence and misuse at every visit
- Random urine drug screens
- Evaluate for adverse effects
- Consider on-going evaluation of potential drug-drug interactions

Naloxone Distribution

- Naloxone is used to reverse opioid overdoses, evidence based in medical settings
- Existing community-based programs have distributed naloxone to trained laypersons (needle exchange participants)
 - For examples, see: Seal et al., 2005; Doe-Simkins et al., 2009 (nasal naloxone); Tobin et al., 2008; Markham Piper et al., 2008

Naloxone Distribution in Medical Settings

- Adaptation to pain care setting focused on training caregiver
- Strength of Evidence: feasibility established (Project Lazarus – Albert, Branson, Sanford et al., 2011), no studies of efficacy/effectiveness

Thank you for attending this Webinar!
Questions?

- Contact
 - Amy.Bohnert@va.gov
 - 734-845-3638

References

Albert S, Brason FW, 2nd, Sanford CK, Dasgupta N, Graham J, Lovette B. Project Lazarus: community-based overdose prevention in rural North Carolina. *Pain Med.* Jun 2011;12 Suppl 2:S77-85.

Bohnert AS, Ilgen MA, Galea S, McCarthy JF, Blow FC. Accidental poisoning mortality among patients in the Department of Veterans Affairs Health System. *Med Care.* Apr 2011;49(4):393-396.

Bohnert AS, Valenstein M, Bair MJ, et al. Association between opioid prescribing patterns and opioid overdose-related deaths. *JAMA.* Apr 6 2011;305(13):1315-1321.

Doe-Simkins M, Walley AY, Epstein A, Moyer P. Saved by the nose: bystander-administered intranasal naloxone hydrochloride for opioid overdose. *Am J Public Health.* May 2009;99(5):788-791.

Dunn KM, Saunders KW, Rutter CM, et al. Opioid prescriptions for chronic pain and overdose: a cohort study. *Ann Intern Med.* Jan 19 2010;152(2):85-92.

References

Krebs EE, Becker WC, Zerzan J, Bair MJ, McCoy K, Hui S. Comparative mortality among Department of Veterans Affairs patients prescribed methadone or long-acting morphine for chronic pain. *Pain*. Aug 2011;152(8):1789-1795.

Markham Piper T, Stancliff, S., Rudenstine, S., Sherman, S., Nandi, V., Clear, A., Galea, S. Evaluation of a naloxone distribution and administration program in New York City. *Substance Use and Misuse*. 2008;43(7):858-870.

McLellan AT, Turner B. Prescription opioids, overdose deaths, and physician responsibility. *JAMA*. Dec 10 2008;300(22):2672-2673.

Paulozzi LJ, Kilbourne EM, Desai HA. Prescription drug monitoring programs and death rates from drug overdose. *Pain Med*. May 2011;12(5):747-754.

Paulozzi LJ, Kilbourne EM, Shah NG, et al. A history of being prescribed controlled substances and risk of drug overdose death. *Pain Med*. Jan 2012;13(1):87-95.

Peirce GL, Smith MJ, Abate MA, Halverson J. Doctor and pharmacy shopping for controlled substances. *Med Care*. Jun 2012;50(6):494-500.

References

Seal KH, Thawley R, Gee L, et al. Naloxone distribution and cardiopulmonary resuscitation training for injection drug users to prevent heroin overdose death: a pilot intervention study. *J Urban Health*. Jun 2005;82(2):303-311.

Tobin KE, Sherman SG, Beilenson P, Welsh C, Latkin CA. Evaluation of the Staying Alive programme: Training injection drug users to properly administer naloxone and save lives. *Int J Drug Policy*. Apr 22 2008;20(2):131-136.