

# Risk and Opioid Therapy

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**Chairman**

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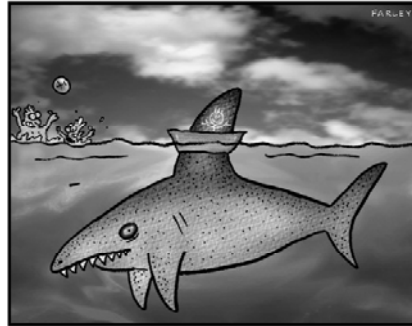


# Opioid Risks

- Issues in chemical dependency: abuse, addiction and diversion
- Special issues in risk management
  - Sleep disordered breathing
  - Methadone overdose deaths

# Opioid Risks

- 2 Basic Rules of Pain Medicine
  - The patient must have more pain than the clinician
  - The clinician must survive



# Base Rates of Addiction/Abuse

- 6-10% Illicit drugs
- 15% Alcohol
- 25% Nicotine
- 33% Have experimented with illicit drugs at least once

(Colliver & Kopstein, 1991; Gfroerer et al, 1992; Regier et al, 1984)

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–It may be initiated with a written agreement, or physician may decide that it is not necessary.

–A month's supply of drug may be given, or it may be wiser to opt for a smaller amount.

–A urine drug screen may or may not be necessary in certain patients.

–Timing of the patient's return to clinic depends on what the risk is.

–If there is a concern about predisposition to addictive disease, a short-acting drug may not be the best choice.

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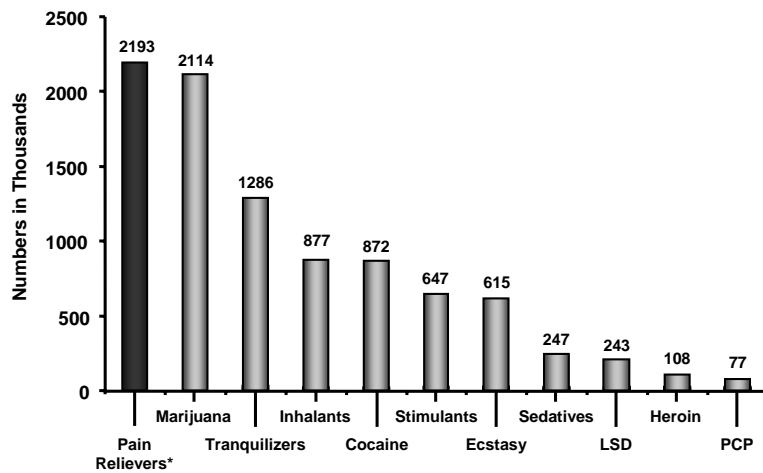
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•This is proactive structuring of therapy.

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Portenoy RK, Payne R, Passik S: Acute and chronic pain. In Lowinson JH, Ruiz P, Millman RB (eds): *Comprehensive Textbook of Substance Abuse*, 4th ed. Baltimore: Williams and Wilkins, 2005, pp. 863-903.

# New Illicit Drug Use in the United States: 2005



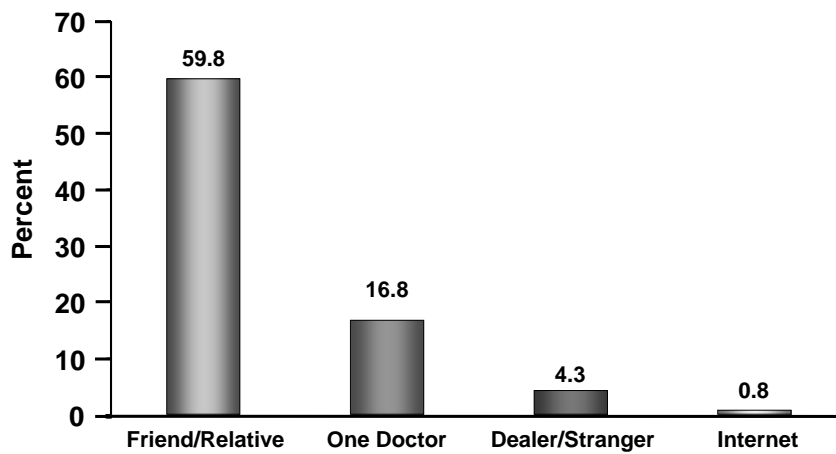
\*526,000 new nonmedical users of OxyContin®.

SAMHSA. *Results From the 2005 National Survey on Drug Use and Health*. DHHS Publication No. SMA 06-4194, 2006.

NSDUH 2005 Results Survey. The category “Pain Relievers” included:

1. Darvocet, Darvon, or Tylenol with codeine
  2. Percocet, Percodan, or Tylox
  3. Vicodin, Lortab, or Lorcet/Lorcet Plus
  4. Codeine
  5. Demerol
  6. Dilaudid
  7. Fioricet
  8. Fiorinal
  9. Hydrocodone
  10. Methadone
  11. Morphine
  12. OxyContin
  13. Phanaphen with Codeine
  14. Propoxyphene
  15. SK-65
  16. Stadol
  17. Talacen
  18. Talwin
- 
19. Talwin NX
  20. Tramadol
  21. Ultram

## Pain Relievers Obtained for Nonmedical Use: Sources Reported by Users\*



\*Source of drugs for the most recent nonmedical use of pain relievers reported by persons aged 12 or older in the United States 2005.

SAMHSA. *Results From the 2005 National Survey on Drug Use and Health*. DHHS Publication No. SMA 06-4194, 2006.

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## Clinical Approach to Risk: Monitoring Aberrant Drug-taking Behaviors

- Probably more predictive

- Selling prescription drugs
- Prescription forgery
- Stealing or borrowing another patient's drugs
- Injecting oral formulation
- Obtaining prescription drugs from non-medical sources
- Concurrent abuse of related illicit drugs
- Multiple unsanctioned dose escalations
- Recurrent prescription losses

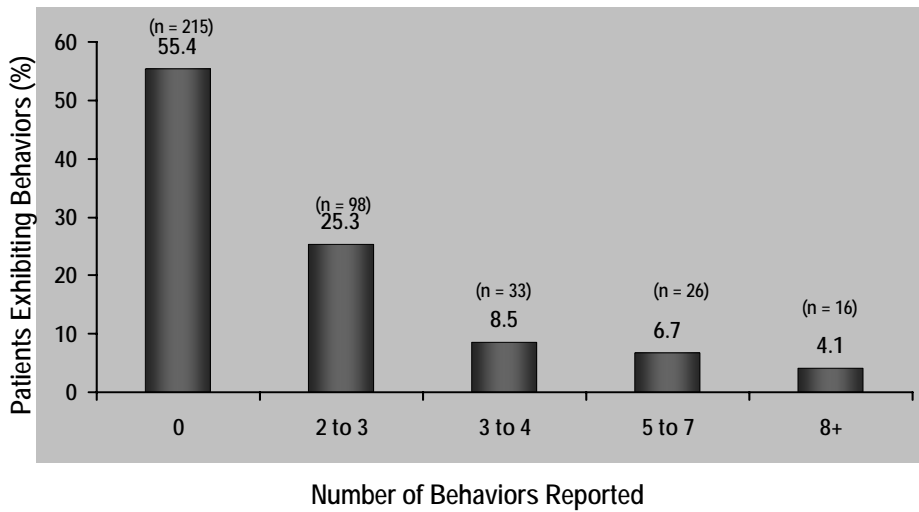
Passik and Portenoy, 1998.

- Probably less predictive

- Aggressive complaining about need for higher doses
- Drug hoarding during periods of reduced symptoms
- Requesting specific drugs
- Acquisition of similar drugs from other medical sources
- Unsanctioned dose escalation 1–2 times
- Unapproved use of the drug to treat another symptom
- Reporting psychic effects not intended by the clinician

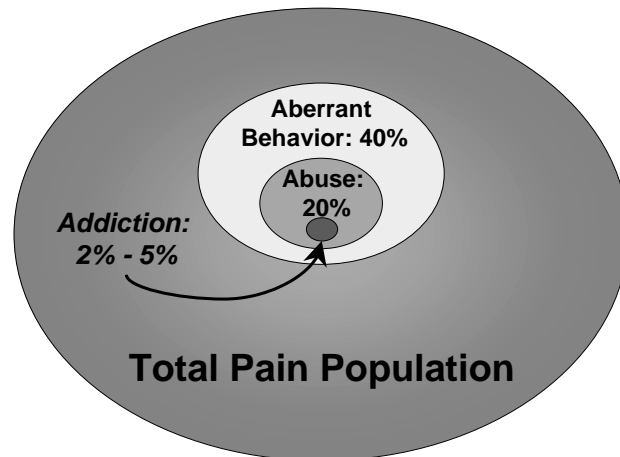


# Aberrant Behaviors (n = 388)



(Passik, Kirsh et al, 2005)

# Risk of Aberrant Behaviors



Webster LR, Webster RM. *Pain Med.* 2005;6:432-442.

This slide shows the relationship and frequency of aberrant behavior, abuse and addiction in a pain practice. In this study 40% of the patients displayed one or more aberrant behaviors within one year. 20% of the patients met a diagnosis of abuse while less than 5% met a diagnosis for opioid addiction. Other reports suggest similar rates of aberrant behavior and abuse in pain practices. This slide also shows that all addicts are abusers and will display aberrant behavior but not all aberrant behavior is abuse and not all abuse is necessarily addiction.

Webster LR, Webster RM. Predicting aberrant behaviors in opioid-treated patients: preliminary validation of the opioid risk tool. *Pain Med*; publication pending.

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# Management of Risk Is a “Package Deal”

- Understanding laws and regulations
- Screening & risk stratification: “Universal Precautions”
- Compliance monitoring commensurate with risk status
- Education about drug storage & sharing
- Role of abuse-deterrent formulations

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# Risk: Laws and Regulation

- Federal: Controlled Substances Act
  - Criminal statute
  - Prescribing is legal if it is consistent with
    - usual professional practice
    - Legitimate medical purpose
  - Compliance determined by documentation of therapeutic relationship, clinical formulation that warrants treatment, assessment and reassessment of outcomes,
  - Must document prescriptions

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## Risk: Laws and Regulation

- Federal: Controlled Substances Act
  - Mainly concerned with diversion
    - Do not prescribe if there is a significant risk that diversion is occurring

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## Risk: Laws and Regulation

- State: varied agencies and regulations
  - State criminal statutes: concerned with diversion
    - Role of prescription monitoring programs
  - State civil laws/regulations
    - Medical practice laws (the Medical Board) are concerned with physician practice

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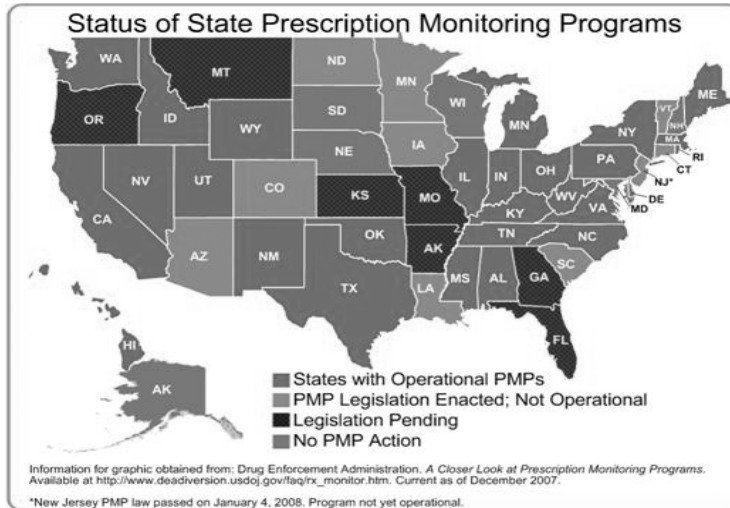
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# Risk: Laws and Regulation

- Prescription Monitoring Programs



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# Risk: Laws and Regulation

- State: varied agencies and regulations
  - Approach to compliance:
    - Same strategy as compliance with the Controlled Substances Act
    - Consultation when prescribing “out of the box”
    - Consultation when the patient is complex

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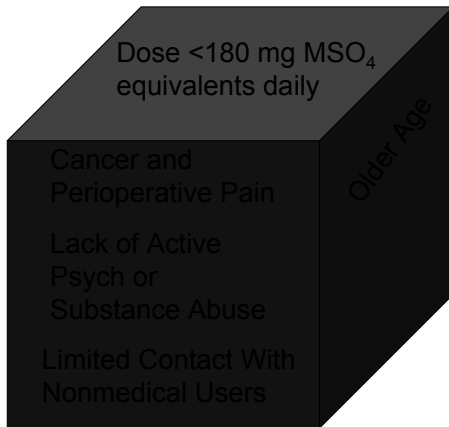
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# Opioid Prescribing: In and Out of the Box



Pain Syndrome in Which Opioid Use Controversial

Dose >180 mg MSO<sub>4</sub> equivalents daily

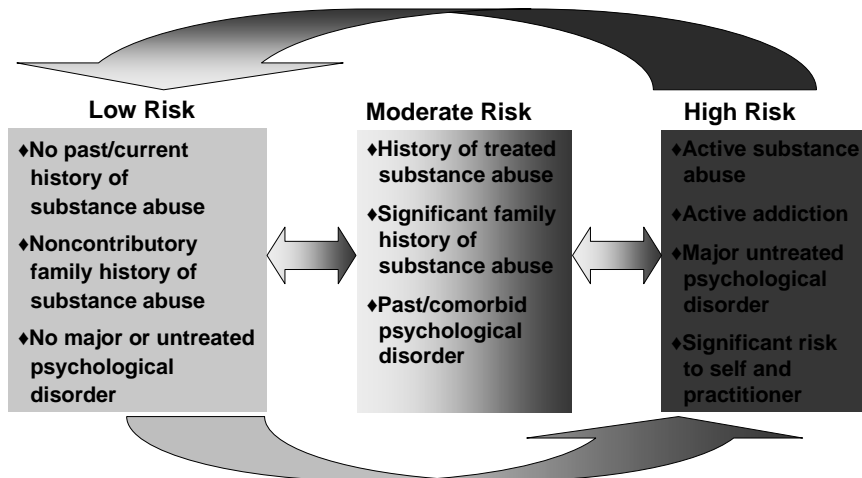
Active Psych or Substance Abuse

Contact With Nonmedical Users

Younger Age

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# Stratify Risk



Gourlay DL, et al. *Pain Med.* 2005;6:107-112.

As mentioned previously, physicians must have a triage scheme for estimating the risk for patient management and referral. This strategy developed by Gourlay et al stratifies patients into 3 treatment groups:

- Group I represents the majority of patients who will present to the primary care office with chronic pain; they have no personal or family history of substance abuse, no major or untreated psychological disorder, and are therefore quite suitable for treatment by the primary care physician
- Patients in Group II should be comanaged by a primary care physician and a specialist because of their history of treated substance abuse, significant family history of substance abuse, and/or past or comorbid psychological disorder; these patients are not actively addicted, but they are at higher risk for addiction
- Patients in Group III are the most difficult to manage because of their active substance abuse and/or addiction; they may also have a major untreated psychological disorder and pose a significant risk to themselves and the healthcare practitioner

## Reference

Gourlay DL, Heit HA, Almahrezi A. Universal precautions in pain medicine: a rational approach to the treatment of chronic pain. *Pain Med.* 2005;6:107-112. [p. 111]

# Risk Assessment and Structuring Therapy

- ❑ Measures for screening for addiction risk
  - CAGE AIDD
  - Opioid Risk Tool (Emerging Solutions in Pain)
  - SOAPP (see [painedu.org](http://painedu.org))
  - Many others
- ❑ Psychiatric interview assessment of risk
  - Chemical
  - Psychiatric
  - Social/Familial
  - Genetic
  - Spiritual

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# ORT Validation

Mark each box that applies

	Female	Male	
1. Family history of substance abuse			• Exhibits high degree of sensitivity and specificity
- Alcohol	<input type="checkbox"/> 1	<input type="checkbox"/> 3	
- Illegal drugs	<input type="checkbox"/> 2	<input type="checkbox"/> 3	
- Prescribing drugs	<input type="checkbox"/> 4	<input type="checkbox"/> 4	
2. Personal history of substance abuse			• 94% of low-risk patients did not display an aberrant behavior
- Alcohol	<input type="checkbox"/> 3	<input type="checkbox"/> 3	
- Illegal drugs	<input type="checkbox"/> 4	<input type="checkbox"/> 4	
- Prescribing drugs	<input type="checkbox"/> 5	<input type="checkbox"/> 5	
3. Age (mark box if 16-45 years)	<input type="checkbox"/> 1	<input type="checkbox"/> 1	
4. History of preadolescent sexual abuse	<input type="checkbox"/> 3	<input type="checkbox"/> 0	• 91% of high-risk patients did display an aberrant behavior
5. Psychological disease			
- ADD, OCD, bipolar, schizophrenia	<input type="checkbox"/> 2	<input type="checkbox"/> 2	
- Depression	<input type="checkbox"/> 1	<input type="checkbox"/> 1	

N = 185

ORT = opioid risk tool; ADD = attention deficit disorder; OCD = obsessive-compulsive disorder  
 Webster LR, Webster RM. *Pain Med.* 2005;6:432-442.

# Risk Assessment and Structuring Therapy

- Initial strategy (“structure”) for prescribing
  - Must consider “proactive strategies” to reduce risk for misuse/abuse and enhance monitoring
  - Reassess frequently and adjust structure when appropriate

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# Structuring Therapy: Role of Urine Drug Screening

- Low threshold for urine drug screening

Urine Toxicology	Aberrant Behaviors		Total
	Yes	No	
Positive	10 (8%)	26 (21%)	36 (29%)
Negative	17 (14%)	69 (57%)	86 (71%)
Total	27 (22%)	95 (78%)	122

Katz N, Fanciullo GJ. *Clin J Pain.* 2002;18:S76-S82.

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# Formulations and Risk

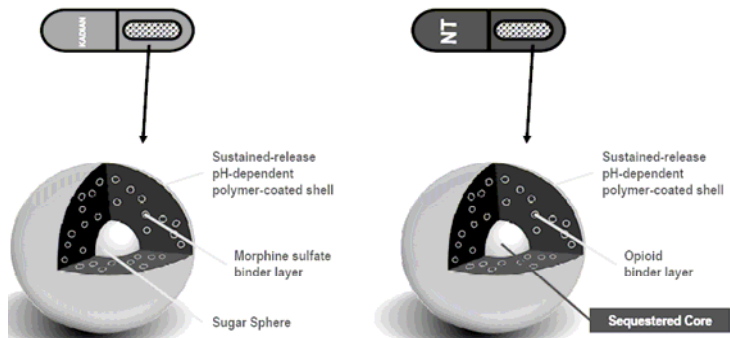
- Risk of abuse may vary with drug and formulation
    - Higher concern: Short-acting drugs, including the rapid onset fentanyl drugs for breakthrough pain
    - Higher concern: Oxycodone, hydromorphone, hydrocodone
    - Lower concern: Long-acting drugs, particularly transdermal fentanyl and methadone
    - Emergence of abuse deterrent formulations
-

# Formulations and Risk

- Remoxy™
    - SR oxycodone formula in viscous gel base
    - Deters dose dumping: as gelatin capsule dissolves, SR oxycodone released via GI tract
    - Difficult to crush, break, freeze, heat, dissolve
      - Cannot inject viscous gel-cap base
      - Resists crushing & dissolution in alcohol, water, acidic beverages
-

# Formulations and Risk

- EMBEDA™
  - Phase III double-blind, randomized, placebo-controlled, 12-wk, multicenter trial
  - >500 OA (hip/knee) pts moderate-severe pain
  - Primary endpoint: significant pain relief ( $P < .05$ )

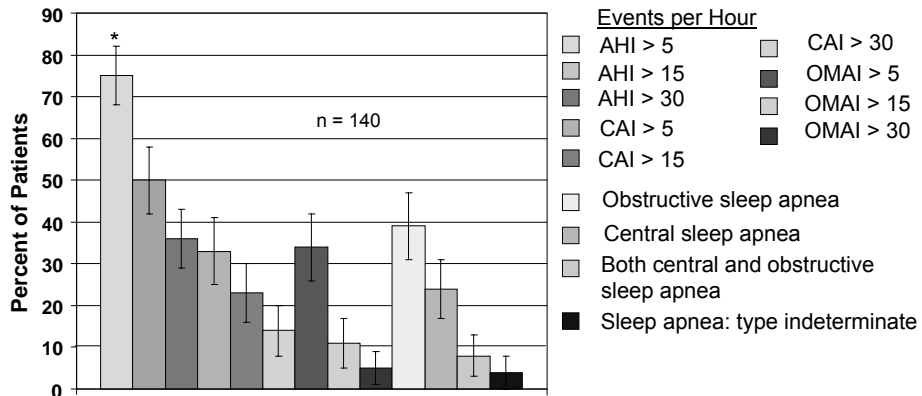


## Special Issue in Risk: Sleep-Disordered Breathing

- Limited data but high risk potential
- Consider routine use of strategies to mitigate risk



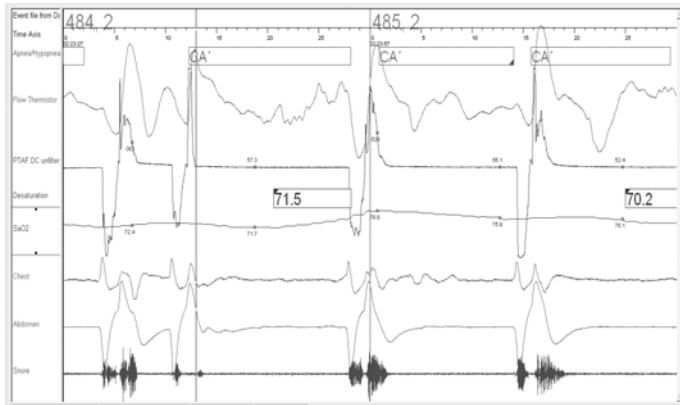
# Sleep Disorders and Opioids



\*Bars indicate hi/lo of 95% CI; AHI = apnea-hypopnea index; CAI = central apnea index; OMAI = obstructive and mixed apnea index

Webster LR, et al. Sleep-disordered breathing and chronic opioid therapy. *Pain Med*, 2009

# Sleep Disorders and Opioids



## 1-Minute Panel of 42-year-old Chronic Nonmalignant Pain Patient

*Opioid Dose is transdermal fentanyl 50 mcg, sustained-released oxycodone 40 mg TID, oxycodone 5 mg not to exceed 8/day*

- Overall central apnea index: 185 events per hour
  - Sleep duration: 7½ hours
  - Respiratory rate: four breaths per minute
  - $V_t$  : 200 to 300 ml
- $V_t$  = tidal volume

# How to Minimize Sleep Apnea Risk

- Order sleep studies on “at risk” patients
  - ↑BMI, ↑ opioid dose, ↑ age (middle-aged)
  - Methadone, benzodiazepines
- Provide appropriate therapeutic interventions
- Restudy with major dose changes
- Decrease dose with poor treatment compliance

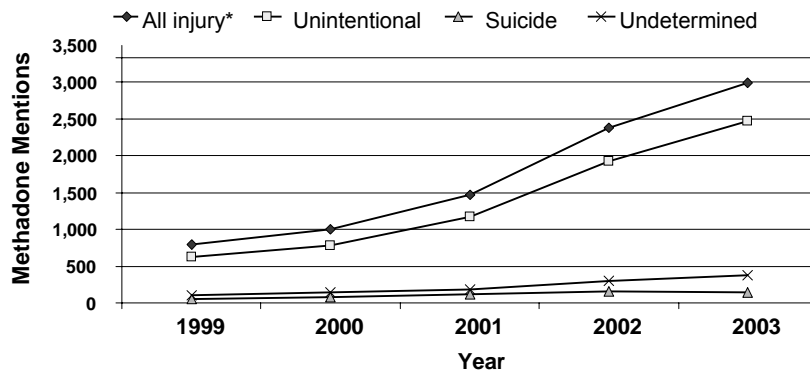
BMI = body mass index



## Special Issue in Risk: Methadone Risk

- Unique pharmacology requires knowledge and skills for prescribing
- Risk related to pharmacokinetics and QTc effects

# Injury Deaths with Mention of Methadone by Intent of Injury: US, 1999-2003



\*Includes intent categories homicide and legal intervention

Minino AM, et al. Deaths: Injuries, 2002. NVSR 54:10. NCHS. 2006. Accessed April 19, 2007 at: [http://www.cdc.gov/nchs/data/nvsr/nvsr54/nvsr54\\_10.pdf](http://www.cdc.gov/nchs/data/nvsr/nvsr54/nvsr54_10.pdf).

Anderson RN, et al. Deaths: Injuries, 2001. NVSR 52:21. NCHS. 2004. Accessed April 19, 2007 at: [http://www.cdc.gov/nchs/data/nvsr/nvsr52/nvsr52\\_21acc.pdf](http://www.cdc.gov/nchs/data/nvsr/nvsr52/nvsr52_21acc.pdf). Accessed April 19, 2007.

# Suggested Guidelines to Initiate Methadone for Pain

Total Daily Morphine	Starting Methadone Dose	
	Healthy adult < 70 years	Adult w/ chronic illness or > 70 years
Opioid naïve	5 mg tid	2.5 mg bid
60 mg – 100 mg	5 mg tid	5 mg bid
> 100 mg	5 mg qid	5 mg bid

Webster LR. Methadone-Related Deaths. *J. of Opioid Mgmt.* October 2005.

In a paper to be published this month in *Journal of Opioid Management* I suggested a very conservative approach to initiating methadone therapy. This is far more conservative than many of my colleagues would recommend. Certainly some patients are able to tolerate a much more rapid conversion or titration. Nevertheless given the reports of deaths associated with methadone, these starting guidelines should help clinicians ensure patient safety and give methadone pain therapy a greater chance of success. Safety must come first. Most aggressive pain control may follow once the mechanisms behind the increase in methadone-related deaths are further understood.

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## Conclusion

- Best practice in opioid therapy requires knowledge of risks
  - Best practice in opioid therapy requires use of strategies to minimize risk of abuse/addiction/diversion, and risk of adverse drug effects
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