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Max Dose Opioids: How High Can You Go?

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Max Dose Opioids: How High Can You Go?

Maximum Dosing of Opioids: How High Can You Go?

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Learning Objectives

- Describe the rationale for the belief that opioids have no maximum dose
- Describe the data supporting the rationale that high doses of opioids increase toxicity.
- Describe the data supporting the rationale that high doses of opioids do not improve outcomes.
- Identify potential safety concerns with patients taking high doses of opioids



Disclosure Statement of Financial Interest

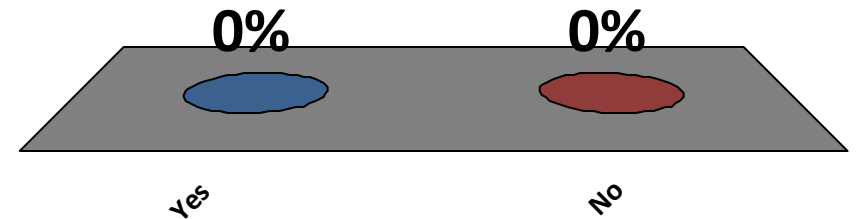
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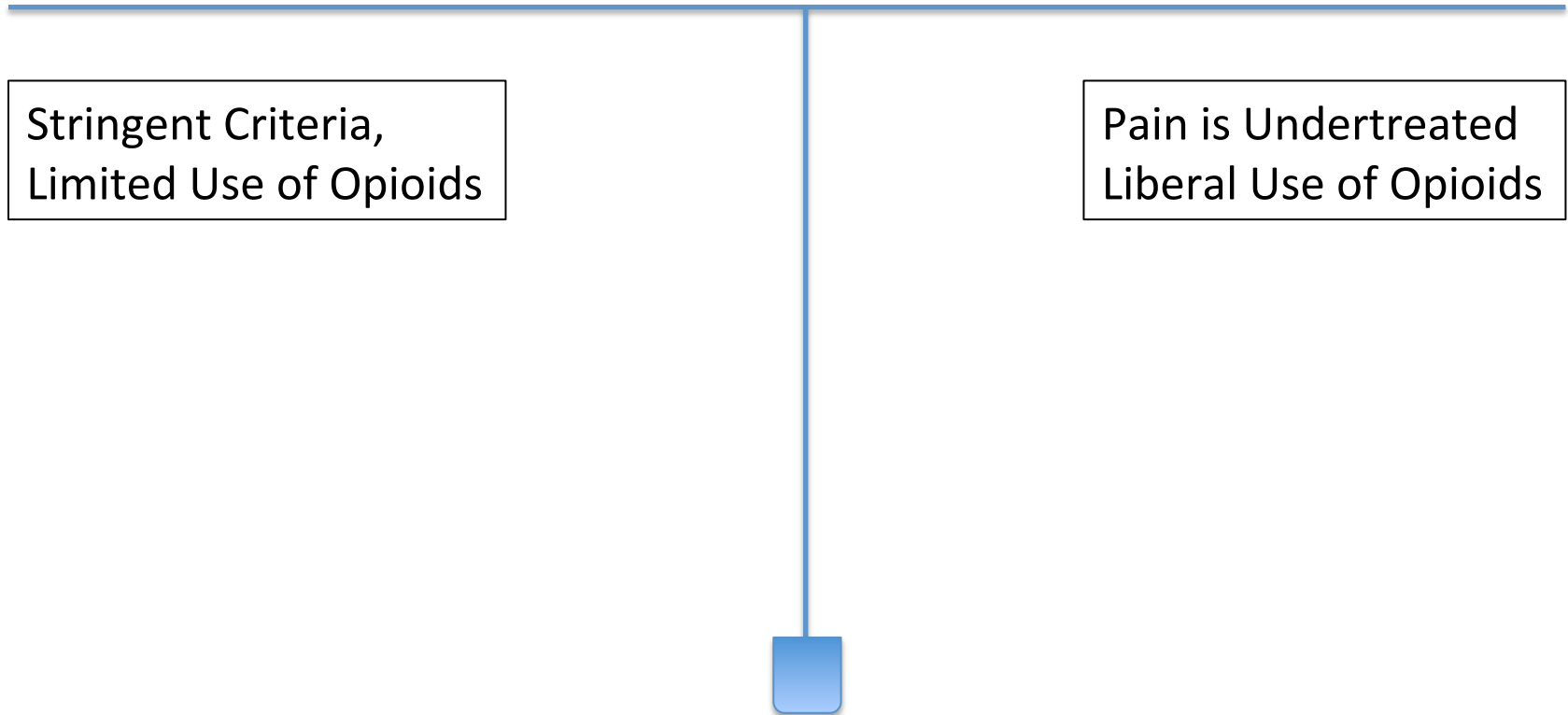
Were you taught in training there is
NO maximum dose of an opioid?

A. Yes

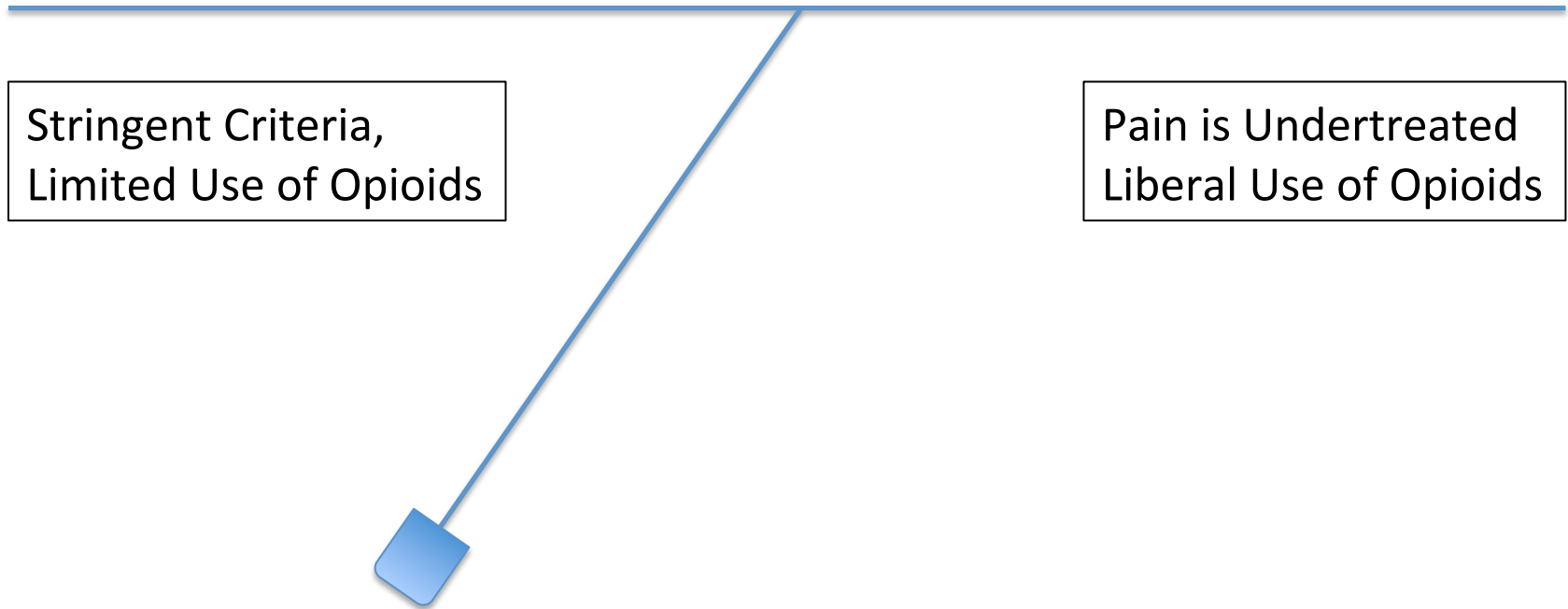
B. No



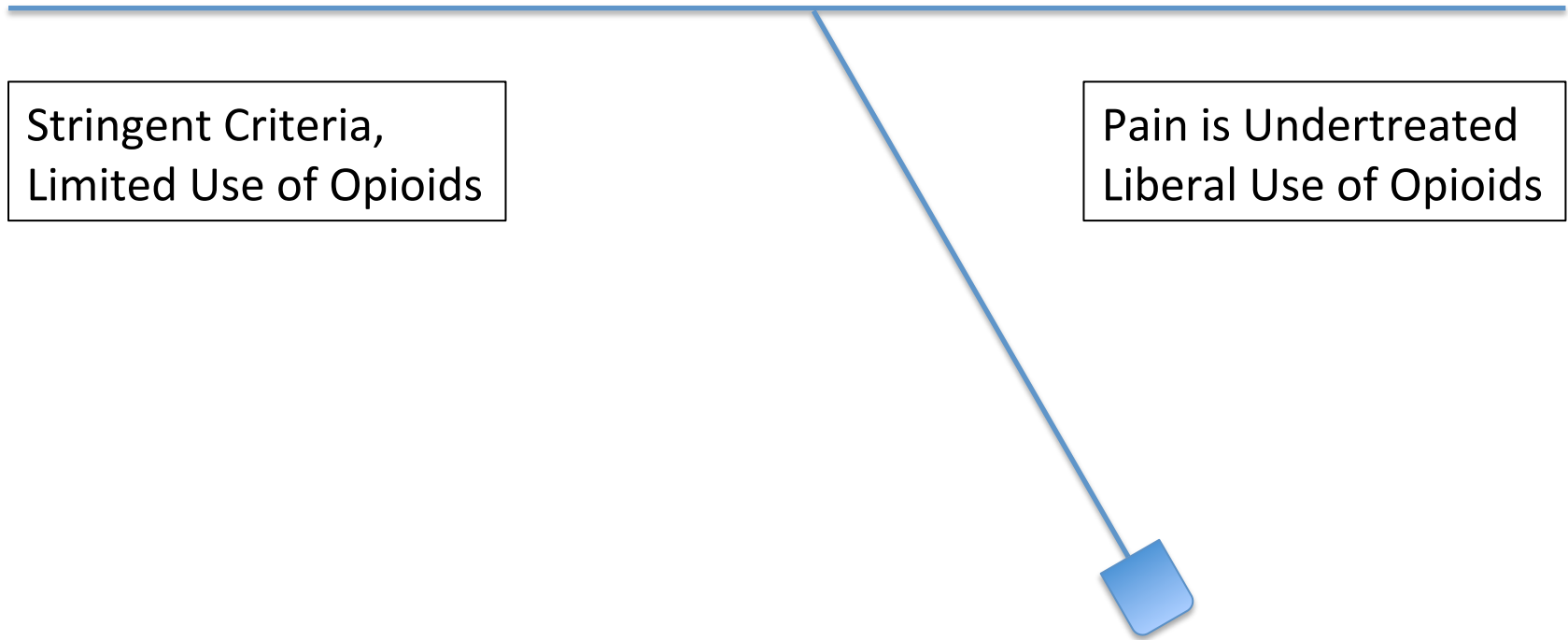
The Opioid Pendulum



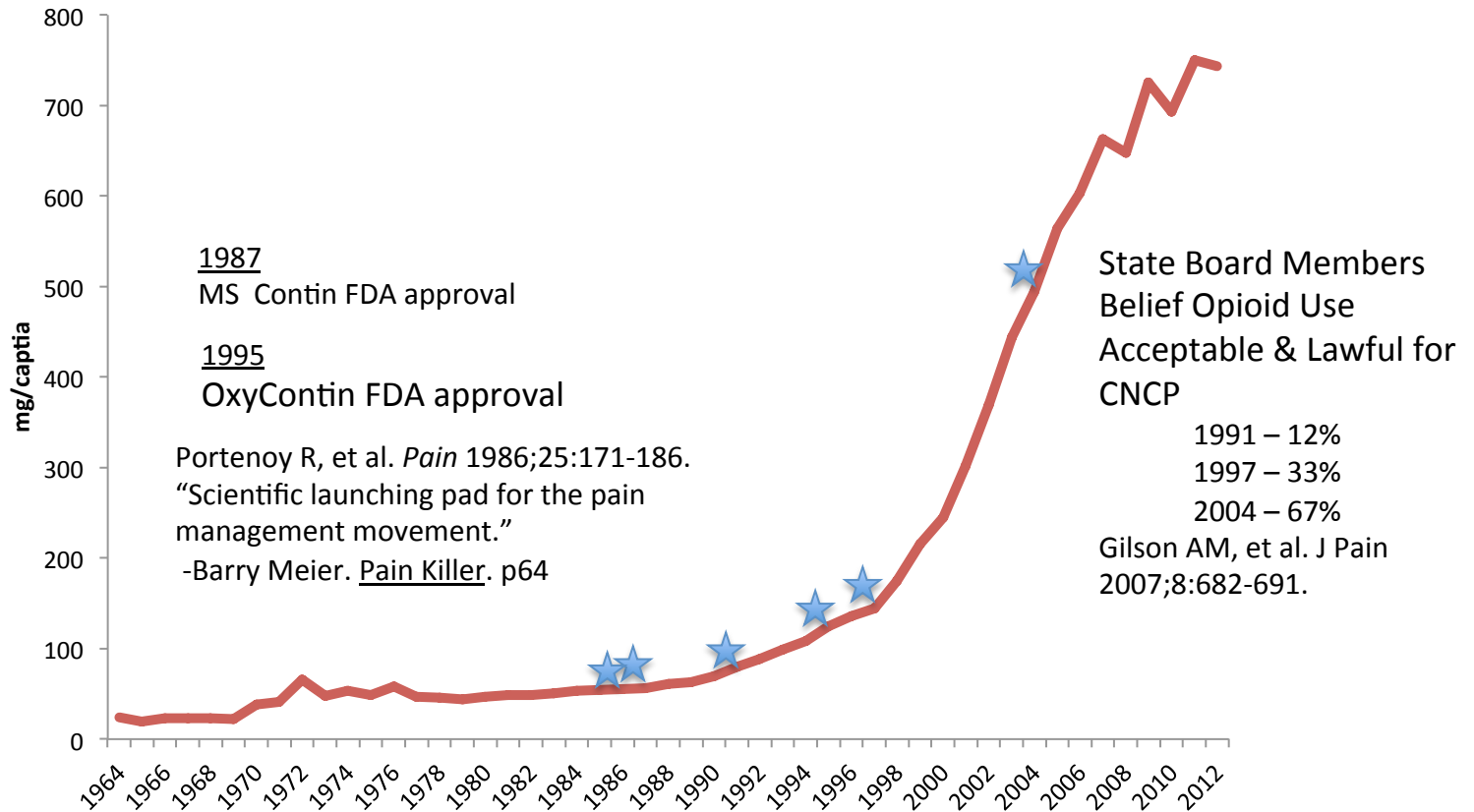
The Opioid Pendulum



The Opioid Pendulum



US Opioid Consumption (MED)



1987
MS Contin FDA approval

1995
OxyContin FDA approval

Portenoy R, et al. *Pain* 1986;25:171-186.
"Scientific launching pad for the pain management movement."
-Barry Meier. Pain Killer. p64

State Board Members
Belief Opioid Use
Acceptable & Lawful for
CNCP

1991 – 12%

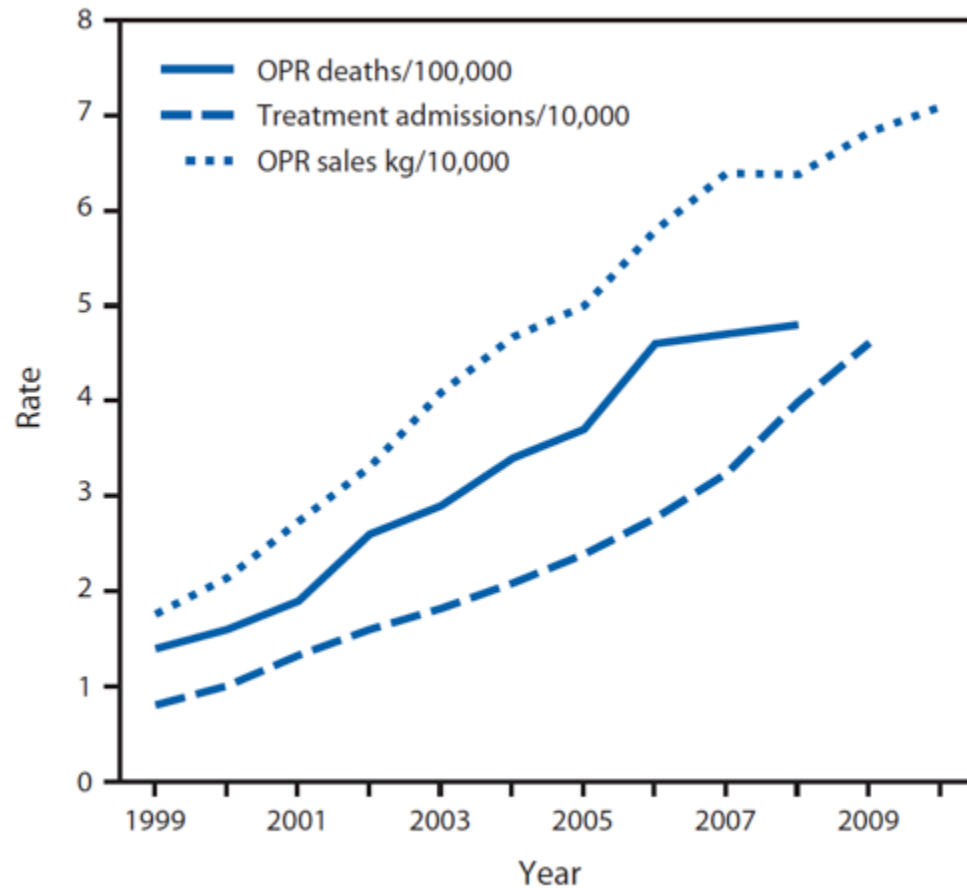
1997 – 33%

2004 – 67%

Gilson AM, et al. *J Pain*
2007;8:682-691.



FIGURE 2. Rates* of opioid pain reliever (OPR) overdose death, OPR treatment admissions, and kilograms of OPR sold — United States, 1999–2010



* Age-adjusted rates per 100,000 population for OPR deaths, crude rates per 10,000 population for OPR abuse treatment admissions, and crude rates per 10,000 population for kilograms of OPR sold.

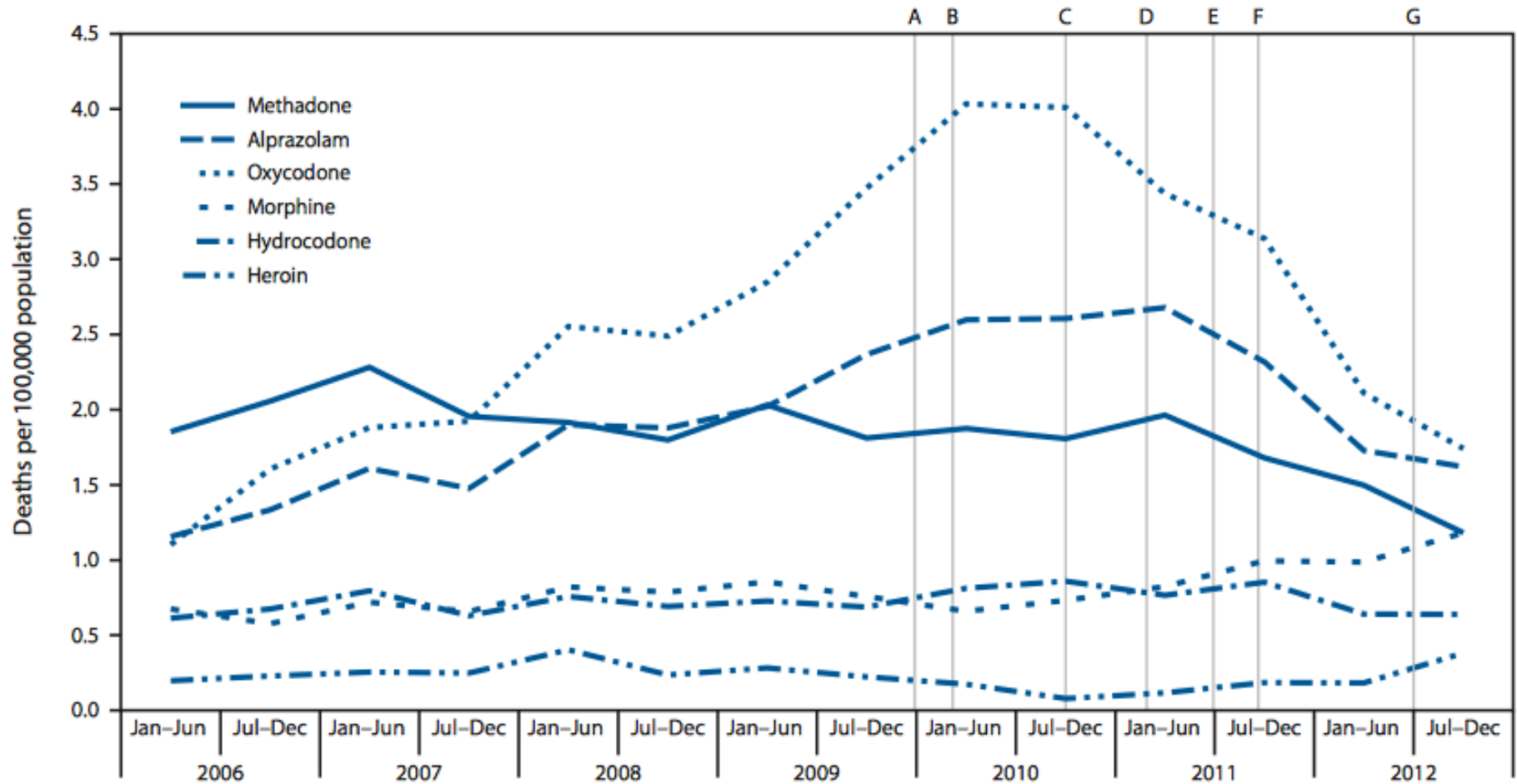


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Opioid Use (and Misuse) Too Prevalent.

States (FL) crack down



A. January 4, 2010. Pain clinics must register.

B. February, 2010. Operation Pill Nation: U.S. Drug Enforcement Agency and state and local law enforcement begin investigation of pain clinics.

C. October 1, 2010. Pain clinic regulation expanded.

D. February 23, 2011. Operation Pill Nation: joint law enforcement raids begin.

E. July 1, 2011. Physician dispensing prohibited and statewide regional strike forces activated.

F. September 1, 2011. Mandatory reporting to prescription drug monitoring program begins.

G. July 1, 2012. Wholesale distributor regulations expanded.

Pendulum Swinging Back?

Bronx Survey (N = 33)

Total pharmacies called	50
Total responding	33 (100%)
No Class II narcotic analgesics	17 (52%)
Oxycodone/ASA/APAP only	12 (36%)

New York City Survey (N = 94)

Total pharmacies called	112
Total responding	94 (100%)
No Class II narcotic analgesics	27 (29%)
Oxycodone/ASA/APAP only	24 (25%)
Class II Narcotic Analgesics:	
Levorphanol	19 (20%)
Hydromorphone	14 (15%)
Oral morphine	3 (3%)
Methadone	2 (2%)

- FL pain patients struggling to find pharmacies with opioids in stock
- “They just don’t have the medications because they run out [of] their allocation within the first week.”
 - Chris Young, chronic pain sufferer
- “I turn away sometimes 20 people a day.”
 - Bill Napier, pharmacist
 - Owner, Panama Pharmacy



Guideline Recommendations

- VA/DoD
 - Consider referral for doses exceeding 200mg/day MED
- Washington state
 - Doses should not exceed 120mg MED without patient demonstrating functional improvement or referral
- Canada
 - 200mg/day MED = “watchful dose” (Canadian guidelines)
- American Pain Society/American Academy of Pain Medicine
 - 200mg/day MED (“high” dose) warrants reassessment/monitoring
- CDC Opioid prescribing guidelines (draft)
 - Caution above 50 mg/day; avoid > 90 mg/day



How High Can You Go?



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Opioid Tolerance

- *In theory*, opioid doses can be continually titrated upwards
- Tolerance develops to most opioid-mediated effects
 - NOT constipation



ON THE
EFFECTS
OF LARGE DOSES OF OPIUM
IN A CASE OF
DIABETES MELLITUS;

BY MR. WM. MONEY,

HOUSE-SURGEON OF THE GENERAL INFIRMARY AT NORTHAMPTON.

COMMUNICATED BY

MR. BRODIE.

Read July 19, 1814.



High dose opium (1814)

- Patient presented with polydipsia, polyuria, and “pain in the region of his kidneys.”
- Admitted to Northampton Infirmary in January 1814
 - “was cupped in the back and bled in the arm”
 - No apparent effect other than “the removal of the pain in the loins.”
- Feb. 10th began taking 1 grain of opium Q HS
 - By Mar. 1st was taking 24 grains of opium daily
 - “very little inconvenience was felt from these large doses of opium so long continued.”



Early Hospice Data (St. Christopher's, London)

- Descriptive cohort study of 500 patients with advanced malignant disease
- Pain treated Q 4 hours
 - Diamorphine 2.5 mg (initial dose) ← Heroin!
 - Cocaine HCl 10mg
 - Ethyl alcohol 95% 2.5mL
 - Syrup (66% sucrose in water) 5 mL
 - Chloroform water QS to 20mL
- Results
 - “no single optimal or maximum effective dose”
 - “tolerance not a practical problem”
 - “psychological dependence does not occur”
 - Physical dependence manageable
 - Long term use (> 2 weeks) associated with higher doses ($p < 0.001$)



Early Hospice Approach (Royal Victoria Hospital, Montreal)

- Utilized Brompton mixture
 - Morphine instead of diamorphine
 - Dosing
 - Starting dose of 2.5 to 5mg q 4 hours ATC
 - Dose titration q 48 to 72 hours
 - 2.5, 5, 10, 15, 20, 30, 40, 60, 90, 120
 - 120mg q 4 hours = 720mg/day
- No systematic reporting of efficacy or toxicity
- Adverse effects described
 - Sedation (transient)
 - Nausea/vomiting (phenothiazine coadministration)
 - Constipation
 - Tolerance-dependence
 - Dose increases felt to be secondary to clinical deterioration



Pharmacokinetic Study of 200mg Morphine CR Tablet

- Methods: Crossover study (n = 25)
 - Advanced malignancy
 - Stable on **400mg/day** PO morphine
 - Randomized to 100mg or 200mg CR tablet
- Results
 - Dosing ranged from 400 to 2000 mg/day
 - PK parameters similar
 - Pain control (VAS) similar
 - “No unpredictable adverse effects occurred..”
 - 73% reported sedation; 41% reported N/V
 - “..rate of reporting of volunteered side effects was low.”



Cancer Pain Data: Morphine

- Cochrane review (n = 4,241, 62 studies)
 - “Morphine is an effective analgesic for cancer pain.”
 - Visual analog scale (VAS) most commonly used outcome
 - Average daily dose: 100 – 250mg (range: 25 – 2000mg)
 - “...but the randomized trial literature is small given the importance of this medication.”
 - No measurement of function
 - Adverse events
 - GI toxicity most commonly reported
 - No mention of concerns of respiratory depression or overdose



Cancer Pain Data: Oxycodone

- Cochrane review (n = 1,390, 17 studies)
 - Similar pain relief to morphine, other opioids (VAS)
 - Average daily dose (reported in 9/17 studies)
 - 21 MED (Imanaka 2013)
 - 60 MED (Parris 1998)
 - 69 MED (Mercadante 2010)
 - **135 MED (Bruera 1998)**
 - **135 MED (Gabrail 2004)**
 - **150 MED (Mucci-LoRusso 1998)**
 - **150 MED (Salzman 1999)**
 - **180 MED (Hagenn 1997)**
 - **180 MED (Heiskanen 1997)**
 - No measurement of function
 - Toxicity similar to morphine, other opioids
 - No safety signals



But those were all *Cancer Pain* studies...

Cancer Pain

- Assumed to be terminal
- Neuropathy a common toxicity of chemotherapy
- Generally prone to infection
- Pain localized to tumor locale or diffuse as disease progresses

Noncancer pain

- Long term life expectancy?
- Fibromyalgia & neuropathy common
- Competent immune system?
- Pain stabilizes



“the scientific launching pad for the
pain movement.”*

Pain, 25 (1986) 171–186
Elsevier

171

PAI 00878

Chronic Use of Opioid Analgesics in Non-Malignant Pain: Report of 38 Cases

Russell K. Portenoy and Kathleen M. Foley

*Pain Service, Department of Neurology, Memorial Sloan-Kettering Cancer Center, and Department of
Neurology, Cornell University Medical College, New York, NY 10021 (U.S.A.)*

(Received 10 June 1985, accepted 28 October 1985)



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*Barry Meier in *Pain Killer*, p. 64

Case Series Demographics (n = 38)

Diagnosis*	n
Back pain	14
Facial, abdominal pelvic or extremity pain	9
Other	15

*All non-malignant pain

Duration (years)	n
< 2	7
2 – 3	10
4 – 5	6
> 6	15

Opioid	n
Oxycodone	12
Methadone	7
Levorphanol	5
Methadone/oxy	3
Propoxyphene	2
Meperidine	2
Others	7

Dose (mg, MED)	n
< 30	11
30 – 60	14
61 – 90	0
91 – 120	2
121 – 150	2
151 – 180	1
> 180	3
Unknown	5

6 (15.7%) received > 120 mg MED



Case Series Results (n = 38)

- Efficacy
 - “comfort enhanced” in 24 of 38 (63%)
 - “adequate” pain relief (29%); “partial” pain relief (34%)
- Toxicity
 - “no episodes of clinically significant adverse effects”
 - e.g. acute overdose, respiratory depression, excessive sedation, myoclonus
 - 2 episodes of abuse
 - 1 patient with history of psychosis
 - 1 patient with history of oxycodone abuse



Portenoy & Foley Conclusion

“..a remarkably positive response in this population.

Nonetheless, few patients had dramatic improvement in employment status or family relationships...

Furthermore, psychological distress...was neither markedly ameliorated nor exacerbated.

These data suggest opioid maintenance therapy can provide acceptable, though often incomplete, analgesia for a significant group of refractory patients, but is no panacea for the profound impairment commonly occurring in this population.”



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Take Home Points

- No apparent increased risk in the 15% on high-dose opioids (> 120 MED)
 - Reasonable safety results, especially considering 50% took opioids 4+ years
- Potential endpoints for future study
 - Employment status improvement
 - Relationship status improvement
 - Psychological distress



Non-cancer Pain Data

- n = 4,893; 26 studies (1 RCT)
- Efficacy
 - “...weak evidence suggests that patients who are able to continue opioids long-term experience clinically significant pain relief.
 - “Whether quality of life or functioning improves is inconclusive.”
- Toxicity:
 - 23% discontinued oral opioids due to adverse events



The 1 RCT for CNCP

- Randomized, open-label, parallel group
 - Transdermal fentanyl vs. PO morphine SR
 - 13-month duration
- Patients
 - Chronic low back pain (n = 680) in need of strong opioid (investigator determined)
 - Exclusion criteria
 - Regular strong opioid use within 4 weeks of entry
 - History of alcohol or substance abuse
 - Mean age: 54 years; 61% female



	Transdermal Fentanyl (n = 338)	SR Morphine (n = 342)
Starting dose	25 mcg/hr	60 mg/day
Final dose, mean (range)	57 mcg/hr (12.5 – 250)	140 mg/day (6 – 780)
VAS endpoint scores	56.0	55.8
No loss of work (<u>n = 131</u>)*		
baseline	35%	49%
endpoint	59%	67%
QOL, physical health (SF-36)		
baseline	25.8	25.7
endpoint	30.8	30.5
QOL, mental health (SF-36)		
baseline	41.2	43.0
endpoint	41.1	44.2
Constipation	52%	65%

*Due to 70% non-working subjects at baseline (e.g. retired, disabled)
p < 0.05

Zero cases of death or addiction.



Comments on Allan, et al.

- Average opioid dose > 120 mg MED “max” dose recommended by some
 - Does NOT account for breakthrough IR opioids used by 50% (dosing not provided in manuscript)
 - No data break down on very high dose subjects
 - Highest dose 780 mg MED
- Both groups experienced improvement in physical QOL
 - Numerically, increased ability to work
 - Likely underpowered
- No difference in mental health QOL
- No serious toxicity over 13 months of opioid use



Summary

- Patients with and without cancer tolerate high doses of opioids (in clinical trial settings)
 - Little to no evidence for risk of overdose or respiratory depression
- No apparent ceiling effect on opioids
 - Wide range of dosing, including some very high doses
- Endpoints, and trial design limit generalizability of efficacy



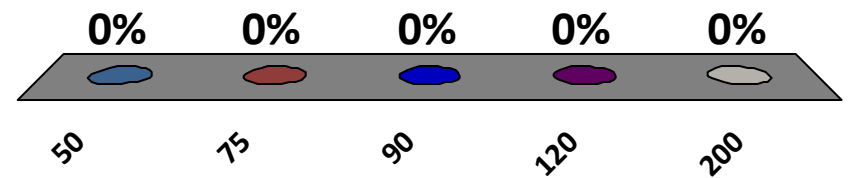
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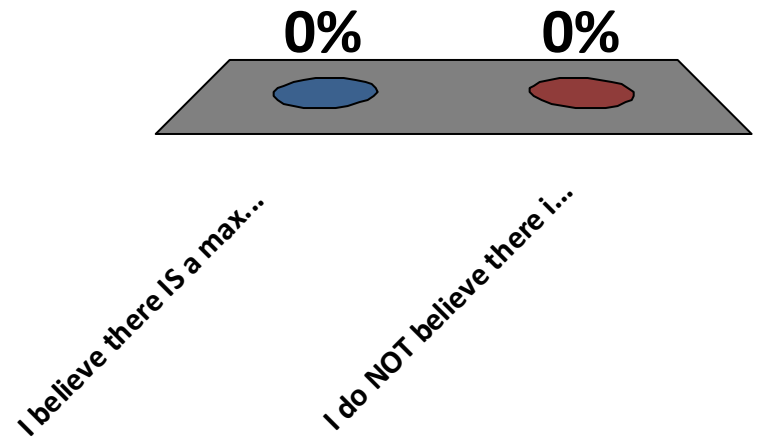
Which of the following morphine milligram equivalent (MME) doses is the maximum you feel comfortable prescribing on a regular basis for chronic pain?

- A. 50
- B. 75
- C. 90
- D. 120
- E. 200



Which of the following best describes your position?

- A. I believe there **IS** a maximum opioid dose that should not be exceeded in the treatment of chronic nonmalignant pain.
- B. I do **NOT** believe there is a maximum opioid dose in the treatment of chronic nonmalignant pain.



The Controversy

- For over 20 years, opioid therapy for chronic pain has been controversial
- What can we agree on?
 - Chronic pain has substantial negative effect and patients need and deserve compassionate care based on evidence-based medicine
 - Increase in prescribing of opioids has led to increase in diversion, addiction, and fatal overdoses



The Patient

- 48-year-old female with non-malignant chronic pain resulting from failed back surgery s/p motor vehicle accident 6 years ago
- Treated with non-opioid analgesics and non-pharmacologic interventions with little success; when unable to work she was considered a suitable candidate for opioid treatment of chronic pain
- She reported good response to opioid therapy and had improvement of function at 1 year
 - Pain score was reduced from 9/10 to 6/10 and she was able to return to work
 - Treatment at that time was oxycodone ER 20 mg every 12 hours.



The Patient

- After 2 years of opioid therapy, her mother developed Alzheimer's disease and the patient became her caregiver
- Pain relief was not as good as it used to be and she requested a dose increase of the oxycodone
- Over the next 4 years, she requested dose increases on a regular basis because her pain and functioning continued to worsen
- Current medication is oxycodone ER 80 mg every 8 hours (____morphine equivalent dose)
- She is house bound, mother has died, can't get out of bed in the morning, nothing is working
- What do you do?



Describe the data supporting the rationale that high doses of opioids do not improve outcomes



Effectiveness of Long-Term Opioid Therapy

- Long-lasting benefits for patients are NOT supported by strong evidence
- Controlled trials lasting 1-6 months suggest moderate analgesia compared with placebo
 - No long-term studies have determined if efficacy is maintained
 - Most studies completed have industry support and evidence of bias



Effectiveness of Long-Term Opioid Therapy

- Studies of long-term opioid therapy versus other treatments are few; limited advantages for opioids
- American Pain Society/American Academy of Pain Medicine 2009 evaluation of evidence
 - 21 out of 25 recommendations based on low-quality evidence
- Quality evidence other treatments are equivalent or superior to opioids in chronic pain

Chou R, Ballantyne JC, Fanciullo GJ, et al. Research gaps on use of opioids for chronic noncancer pain: findings from a review of the evidence for an American Pain Society and American Academy of Pain Medicine clinical practice guideline. *J Pain*. 2009; 10:147–159.

Hegmann KT, Weiss MS, Bowden K, et al. ACOEM practice guidelines: opioids for treatment of acute, subacute, chronic, and postoperative pain. *J Occup Environ Med*. 2014 Dec;56(12):e143-59.



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Effectiveness of Long-Term Opioid Therapy

- No trials document improved objective functional outcomes; more than 100 trials document many adverse effects
- Survey of primary care patients with chronic pain treated with opioids state they continue to have moderate to severe pain and functioning is poor

Hegmann KT, Weiss MS, Bowden K, et al. ACOEM practice guidelines: opioids for treatment of acute, subacute, chronic, and postoperative pain. *J Occup Environ Med.* 2014 Dec;56(12):e143-59.

Sullivan MD, Von Korff M, Banta-Green C, et al. Problems and concerns of patients receiving chronic opioid therapy for chronic noncancer pain. *Pain.* 2010; 119:345-353.



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Effectiveness of Long-Term Opioid Therapy

- 2015 evaluation of effectiveness and harm of long-term opioids for chronic pain through published randomized trials and observational studies
 - NO study of opioid therapy vs. no opioids evaluated long-term (> 1 year) outcomes related to pain, function, quality of life, abuse or addiction
 - Good and fair-quality observational studies suggest increased risk for overdose, myocardial infarction, fractures, substance abuse, sexual dysfunction
 - For some harms, higher doses = increased risk



Unproven efficacy, neglected safety?

- Study evaluated hypotheses
 - There is no strong evidence-based foundation for the conclusion that long-term opioid treatment of chronic nonmalignant pain is effective
 - Main problem associated with the safety of such treatment has been neglected - *assessment of the risk of addiction*
- Scientometric analysis of the articles representing clinical research
 - Quality of presented evidence (type of study)
 - Duration of the treatment phase
 - Sufficiency of representation of addiction was assessed by counting the number of articles published



Unproven efficacy, neglected safety?

- Results

- No randomized controlled trial with opioid treatment lasting greater than 3 months was found
- All studies with a duration of opioid treatment greater than 6 months (n = 16) were conducted without a proper control group
- Profound differences in the number of addiction articles related specifically to chronic nonmalignant pain patients and to opioid addiction in general
- Inadequate number of chronic pain-related publications were observed

- Conclusion

- No strong evidence-based foundation for the conclusion that long-term opioid treatment of chronic nonmalignant pain is effective
- Little data evaluating addiction from opioid treatment of chronic nonmalignant pain are available



Consequences of High Dose Opioids

- Chronic opioid therapy is associated with the development of tolerance to analgesic effects
- Opioid therapy may also paradoxically induce abnormal pain sensitivity, including hyperalgesia and allodynia
- Increasing opioid doses may not improve function and pain control



Describe the data supporting the rationale that high doses of opioids increase toxicity



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Risks of Higher Doses

- Dunn et al. estimated the rates of opioid overdose and the association with an average prescribed daily opioid dose among patients receiving medically prescribed, long-term opioid therapy in an HMO setting
- Cox proportional hazards models were used to estimate overdose risk as a function of average daily opioid dose (morphine equivalents) received at the time of overdose.
- 9940 persons who received 3 or more opioid prescriptions within 90 days for chronic noncancer pain between 1997 and 2005



Risks of Higher Doses

- Average daily opioid dose over the previous 90 days obtained from automated pharmacy data. Primary outcomes--nonfatal and fatal overdoses--were identified through diagnostic codes from inpatient and outpatient care and death certificates
- 51 opioid-related overdoses were identified, including 6 deaths
 - Patients receiving 1 to 20 mg/d of opioids (0.2% annual overdose rate),
 - Patients receiving 50 to 99 mg/d had a 3.7-fold increase in overdose risk (95% CI, 1.5 to 9.5) and a 0.7% annual overdose rate
 - Patients receiving 100 mg/d or more had an 8.9-fold increase in overdose risk (CI, 4.0 to 19.7) and a 1.8% annual overdose rate.
- Conclusion
 - Patients receiving higher doses of prescribed opioids are at increased risk for overdose, which underscores the need for close supervision of these patients



Association of Maximum Dose with Risk of Death

- Examination of the association of maximum prescribed daily opioid dose and dosing schedule (“as needed,” regularly scheduled, or both) with risk of opioid overdose death among patients with cancer, chronic pain, acute pain, and substance use disorders
- Case-cohort study; Veterans Health Administration, 2004-2008
- All unintentional prescription opioid overdose decedents (n = 750) and a random sample of patients (n = 154,684) among those individuals who used medical services in 2004 or 2005 and received opioid therapy for pain
- Measure associations of opioid regimens (dose and schedule) with death by unintentional prescription opioid overdose in subgroups



Association of Maximum Dose with Risk of Death

- Frequency of fatal overdose over the study period among individuals treated with opioids was estimated to be 0.04%
- Risk of overdose death directly related to the maximum prescribed daily dose
- Adjusted hazard ratios (HRs) associated with a maximum prescribed dose of 100 mg/d or more, compared with the dose category 1 mg/d - 20 mg/d
 - Among those with substance use disorders, adjusted HR = 4.54
 - Among those with chronic pain, adjusted HR = 7.18
 - Among those with acute pain, adjusted HR = 6.64
 - Among those with cancer, adjusted HR = 11.99
 - Receiving both as-needed and regularly scheduled doses was not associated with overdose risk after adjustment.
- Among patients receiving opioid prescriptions for pain, higher opioid doses were associated with increased risk of opioid overdose death



Impact of High-dose Opioid Analgesics on Overdose Mortality

- Prospective observational cohort in North Carolina with one year follow-up
 - Quantification of dose-dependent overdose mortality using prescription monitoring program
 - Examination of the contributions of benzodiazepines and extended release opioid formulations to mortality
- Residential population of North Carolina (n = 9,560,234), with 2,182,374 opioid analgesic patients
- Exposure was dispensed prescriptions of solid oral and transdermal opioid analgesics; person-years calculated using intent-to-treat principles
- Outcome was overdose deaths involving opioid analgesics in a primary or additive role. Poisson models were created, implemented using generalized estimating equations.



Impact of High-dose Opioid Analgesics on Overdose Mortality

- Results
 - Opioid analgesics were dispensed to 22.8% of residents
 - Among licensed clinicians, 89.6% prescribed opioid analgesics, and 40.0% prescribed ER formulations
 - 629 overdose deaths, half of which had an opioid analgesic prescription active on the day of death
 - Of 2,182,374 patients prescribed opioids, 478 overdose deaths were reported (0.022% per year)
 - Mortality rates increased gradually across the range of average daily MED

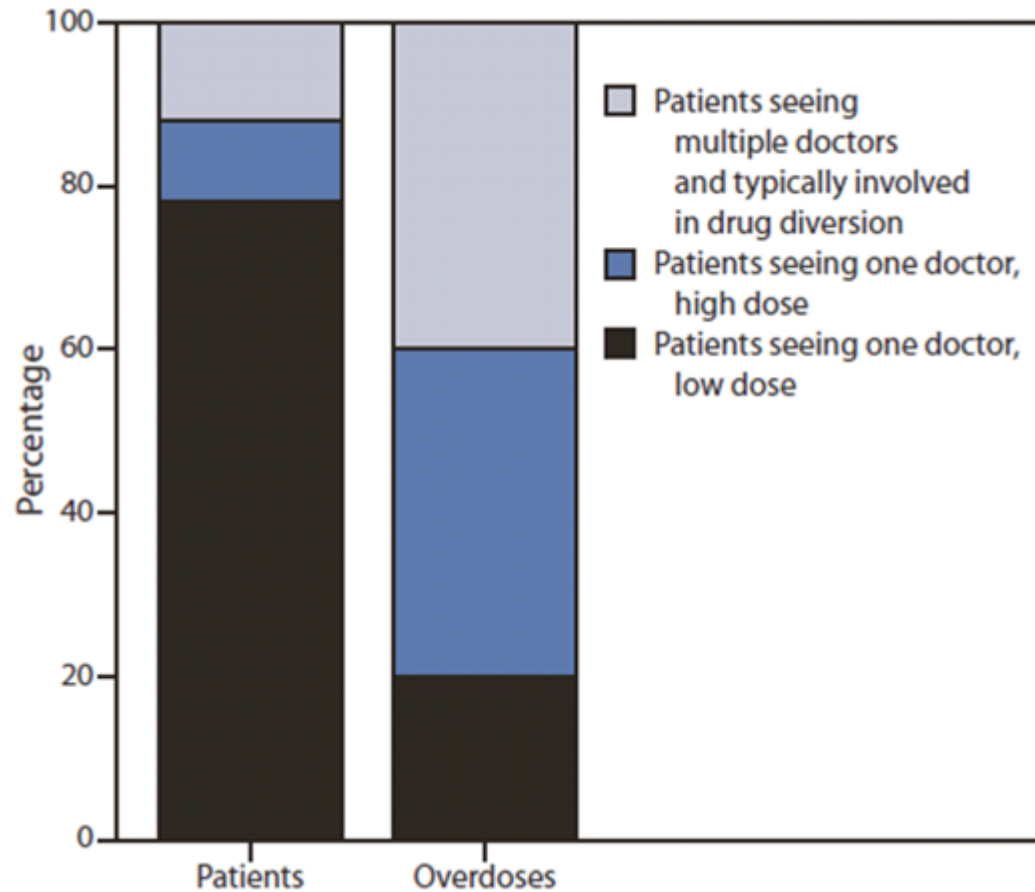


Impact of High-dose Opioid Analgesics on Overdose Mortality

- Results
 - 80.0% of opioid analgesic patients also received benzodiazepines
 - Rates of overdose death among those co-dispensed benzodiazepines and opioid analgesics were ten times higher (7.0 per 10,000 person-years, 95 percent CI: 6.3, 7.8) than opioid analgesics alone (0.7 per 10,000 person years, 95 percent CI: 0.6, 0.9).
- Conclusions
 - Dose-dependent opioid overdose risk among patients increased gradually and did not show evidence of a distinct risk threshold
 - Urgent need for guidance about combined classes of medicines to facilitate a better balance between pain relief and overdose risk



Patients Prescribed Opioids



<http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6101a3.htm>

Dunn KM, Saunders KW, Rutter CM, et al. Opioid prescriptions for chronic pain and overdose. *Ann Intern Med* 2010;152:85–92.
Bohnert AS, Valenstein M, Bair MJ, et al. Association between opioid prescribing patterns and opioid overdose-related deaths. *JAMA* 2011;305:1315–21.



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Identify potential safety concerns with patients taking high doses of opioids



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Safety Concerns

- Overdose and death (co-prescribe naloxone)
- Addiction
- Co-prescribing with other CNS depressants
- Accidents
- Fractures, osteoporosis
- Sexual dysfunction, hypogonadism
- Dysphoria, depression
- Immunologic effects

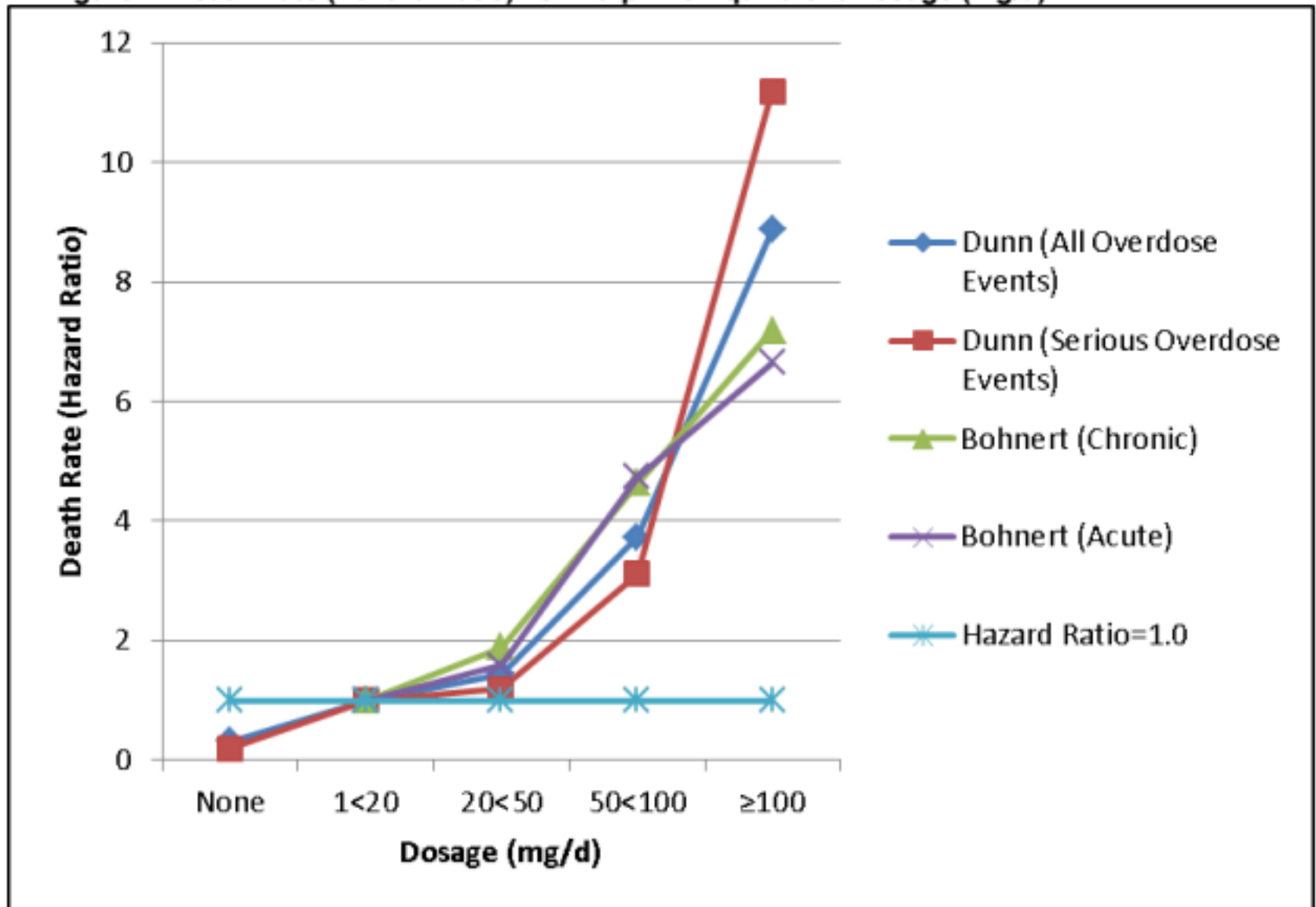


Cytochrome P450 Defects – A Cause of High Doses?

- CYP-3A4, CYP-2D6 and CYP-2C9 defects
- 20 to 30% of pain patients likely have a genetic opioid metabolic defect (GOMD)
- Some opioids are “pro” drugs that must be converted to a metabolite to be effective (i.e., hydrocodone, codeine, tramadol and, to a lesser extent, oxycodone)
- Some opioids, including tapentadol and oxymorphone, mostly bypass the CYP450 system and are metabolized by glucoronidation
- Practitioner can screen patients for a possible GOMD by asking simple questions; routine laboratory screening not recommended



Figure 2. Death Rate (Hazard Ratio) vs. Morphine Equivalent Dosage (mg/d)*



Adapted from Dunn 2010 and Bohnert 2011.

*Statistical significance present for acute and chronic pain at and above 50 mg per day of oral morphine equivalent dose.

Where is Tennessee?

- IMS Health's National Prescription Audit, 2012
- Prescribing rates per 100 persons

State	Opioid Pain Relievers; Rank	Long-acting or extended release; Rank	High dose opioids; Rank	Benzodiazepines; Rank
TENNESSEE	142.8 / 2 nd	18.2 / 5 th	8.7 / 2 nd	61.4 / 3 rd
VIRGINIA	77.5 / 29 th	9.9 / 36 th	4.7 / 21 st	33.5 / 31 st



Exit Plan - Tapering

Indication	Taper method
<ul style="list-style-type: none"> • Medication adverse effects indicate risks are greater than benefit, or • Comorbidities increase risk of complication, or • Morphine equivalent dose exceeds recommended threshold. 	10% per week
<ul style="list-style-type: none"> • Function and pain are not improved, or • Tolerance has developed with long-term opioid prescription, or • Comorbidities increase risk of complication. 	10% every 2–4 weeks
<ul style="list-style-type: none"> • Urine drug screen is consistent with substance abuse concerns, or • Patient's behavior suggests possible misuse or diversion of medication. Such behaviors might include: <ul style="list-style-type: none"> ○ Selling prescription drugs ○ Forging prescriptions ○ Stealing or borrowing drugs ○ Frequently losing prescriptions ○ Aggressive demand for opioids ○ Injecting oral/topical opioids ○ Unsanctioned use of opioids ○ Unsanctioned dose escalation ○ Concurrent use of illicit drugs ○ Getting opioids from multiple prescribers ○ Recurring emergency department visits for chronic pain management 	<p>Rapid discontinuation: 15–33% per day over 3–7 days</p> <p>and/or</p> <p>Refer patient for chemical dependency or addiction counseling. (See Referral Criteria.)</p> <p>https://www.ghc.org/all-sites/guidelines/chronicOpioid.pdf</p>

Conclusions

- Adverse events and death associated with opioid analgesic use have increased substantially over the past 20 years
- MED recommendations are decreasing in new guidelines to 70 MED or below – Tennessee remains at 120 MED
- Risk of opioid-related adverse events increases with dose
- Doses greater than 50 mg MED daily show elevated risk, and little evidence of benefit
- Highest risk appears to be in those on more than 200 mg MED daily
- All patients on chronic opioids should be stratified by risk



Conclusions

- Having an exit strategy is a must
- Implement a structured stepwise program to reduce dose in patients on high dose
- Tapering to lower doses, opioid rotation, or change to buprenorphine are options
- Safety and effectiveness of opioid therapy for chronic non-cancer pain should be routinely evaluated by the prescriber
- Universal precautions should be used in every patient, every time when prescribing opioids for chronic pain
- **CO-PRESCRIBE NALOXONE!**



Next Friday afternoon...

- 53-year-old female with non-malignant chronic pain resulting from failed back surgery s/p motor vehicle accident 8 years ago presents to establish care after her PCP retired
- Oxycodone ER 60 mg Q 12 hours (2 tabs remaining)
- Hydrocodone 5/325 (14 tabs remaining from a 3 month old prescription s/p dental work)
- Clonazepam, sertraline, HCTZ
- Function
 - Improved with dose reduction from 240 mg/day oxycodone over last 6 months
 - Returned to work



What change would you make to this patient's opioid regimen in addition to co-prescribing naloxone?

- A. No new Rx until reviewing medical records from retired PCP
- B. Continue oxycodone ER 60 mg Q 12
- C. Decrease oxycodone ER to 40 mg Q 12
- D. Change to morphine SR 60 mg Q 8 hours
- E. Change to methadone 5 mg Q 6 hours

