Opioids for Chronic, Non-Cancer Pain: Science, Policy & Best Practice in a Rapidly Changing Landscape

-DLI Fall Voc Rehab Conference-

Oct 29, 2014

Gary M. Franklin, MD, MPH
Research Professor
Departments of Environmental Health, Neurology, and Health Services
University of Washington

Medical Director
Washington State Department of Labor and Industries

"To write prescriptions is easy,
but to come to an understanding with people is hard."
-- Franz Kafka, “A Country Doctor”

You will not be able to effectively alter epidemic if you don't understand how the epidemic began

- By the late 1990s, at least 20 states passed new laws, regulations, or policies moving from near prohibition of opioids to use without dosing guidance
  - WA law: "No disciplinary action will be taken against a practitioner based solely on the quantity and/or frequency of opioids prescribed." (WAC 246-919-830, 12/1999)
- Laws were based on weak science and good experience with cancer pain: Thus, no ceiling on dose and axiom to use more opioid if tolerance develops

WAC-Washington Administrative Code

Portenoy and Foley
Pain 1986; 25: 171-186

- Retrospective case series chronic, non-cancer pain
- N=38; 19 Rx for at least 4 years
- 2/3 < 20 mg MED/day; 4> 40 mg MED/day
- 24/38 acceptable pain relief
- No gain in social function or employment could be documented

How many chronic pain patients in your state/system are on doses over 100 mg/day?

Limitations of Long-term (>3 Months) Opioid Therapy

- Overall, the evidence for long-term analgesic efficacy is weak
- Putative mechanisms for failed opioid analgesia may be related to rampant tolerance
- The premise that tolerance can always be overcome by dose escalation is now questioned
- 100% of patients on opioids chronically develop dependence
  - More than 60% of patients on opioids for 3 months will still be on opioids 5 years later
  - Jane Ballantyne-"a lost generation"

Ballantyne J. Pain Physician 2007;10:479-91; Martin BC et al. J Gen Intern Med 2011; 26: 1450-57

Evidence of Efficacy of COAT

- Furlan et al 2011 systematic review (2011; Pain Res Manag 16: 337-351)
  - 62 RCTs
    - 51.6% adequately randomized
    - N=11,927 randomized, but only 7807 (65%) finished trials
    - 41/62 RCTs involved at least one author associated with pharmaceutical industry
    - All trials shorter term (<3 months)
    - Enriched enrollment trials underestimated adverse effects
    - Pain improvement moderate (30%) but **function improvement small**
  - Doses used in practice far in excess of those used in RCTs

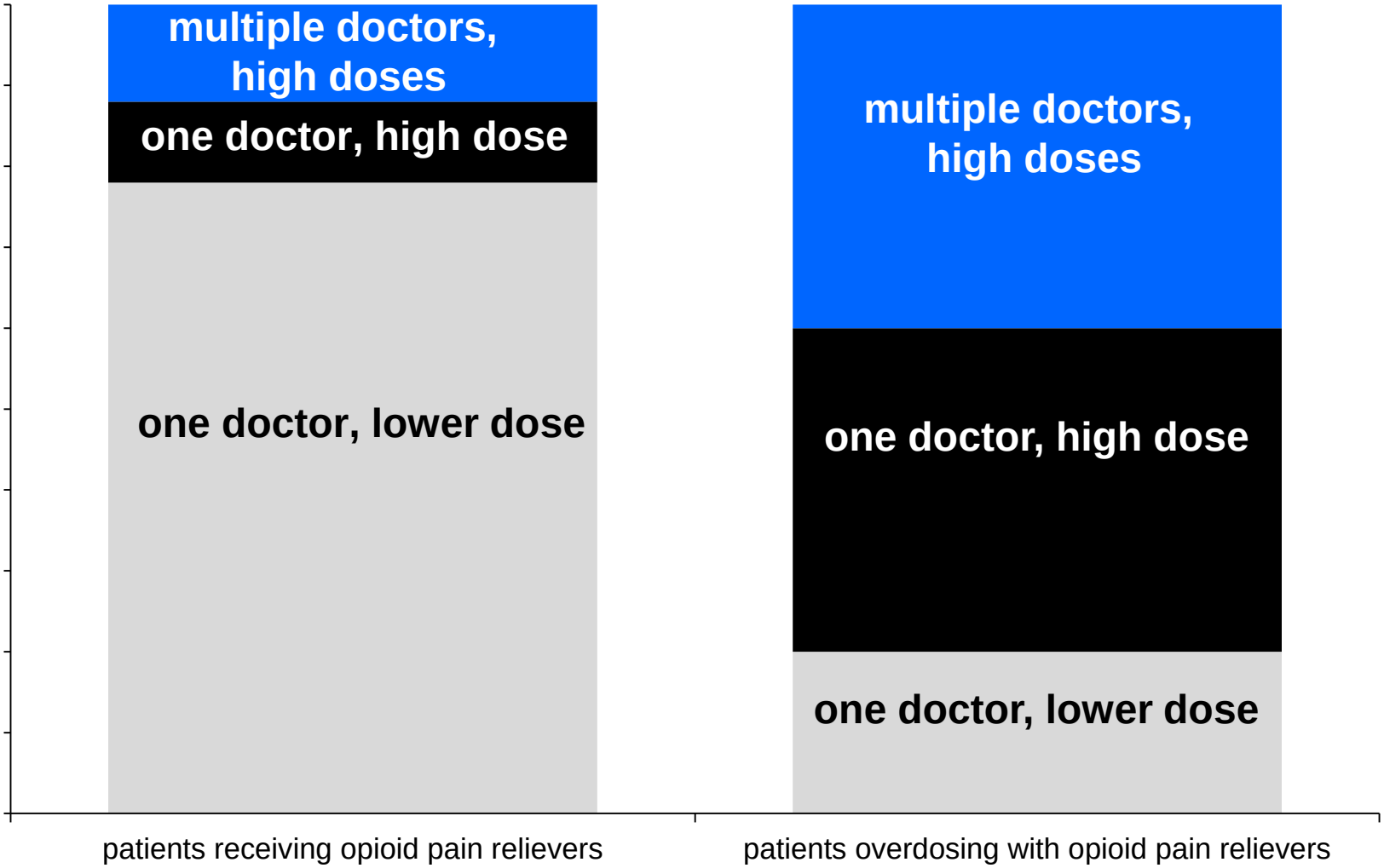
Evidence of effectiveness of COAT

- Noble et al, Cochrane review of longer observational studies (Cochrane Database Syst Rev 2010:CD006605)
  - "The findings of this systematic review suggest that proper management of a type of strong painkiller (opioids) in well-selected patients with no history of substance addiction or abuse can lead to long-term pain relief for some patients with a very small (though not zero) risk of developing addiction, abuse, or other serious side effects. However, the evidence supporting these conclusions is weak, and longer-term studies are needed to identify the patients who are most likely to benefit from treatment."

Evidence of effectiveness of COAT

The Agency for Healthcare Research and Quality's (AHRQ) recent draft report, "The Effectiveness and Risks of Long-term Opioid Treatment of Chronic Pain," which focused on studies of effectiveness measured at > 1 year of COAT use, found **insufficient data on long term effectiveness to reach any conclusion**. (AHRQ 2014).

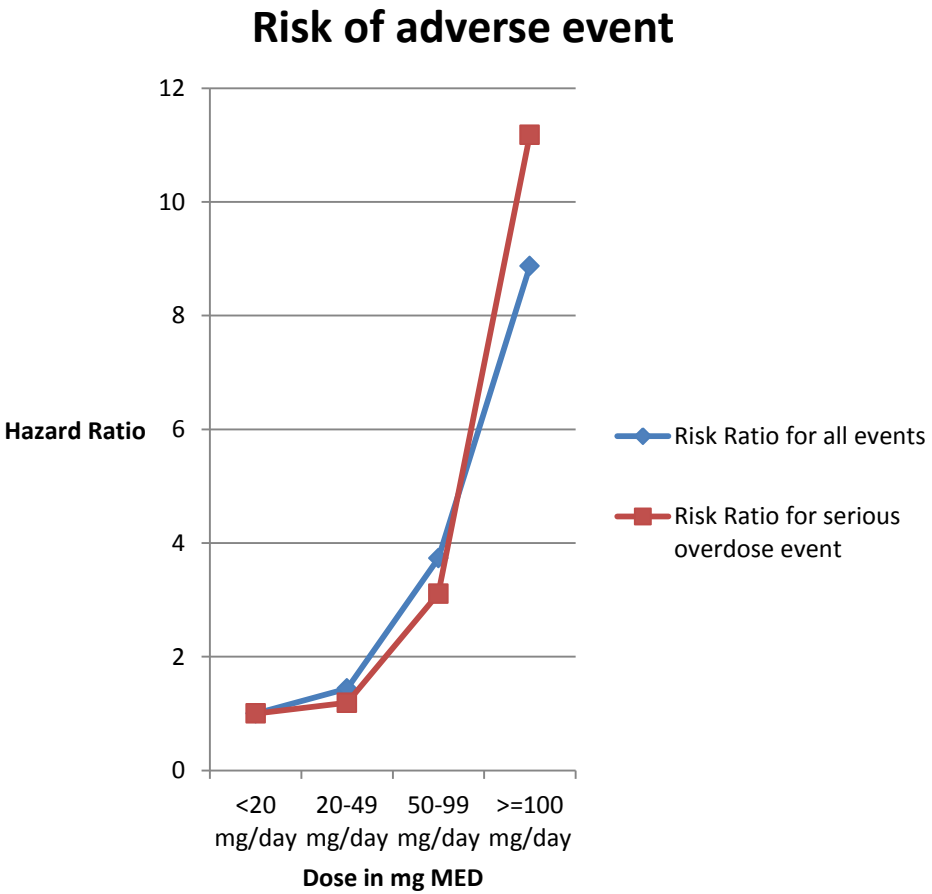
Patients receiving high doses of opioid pain relievers account for disproportionate share of overdoses



CDC Grand Rounds: Prescription Drug Overdoses — a U.S. Epidemic. *MMWR Weekly*. January 13, 2012 / 61(01);10-13

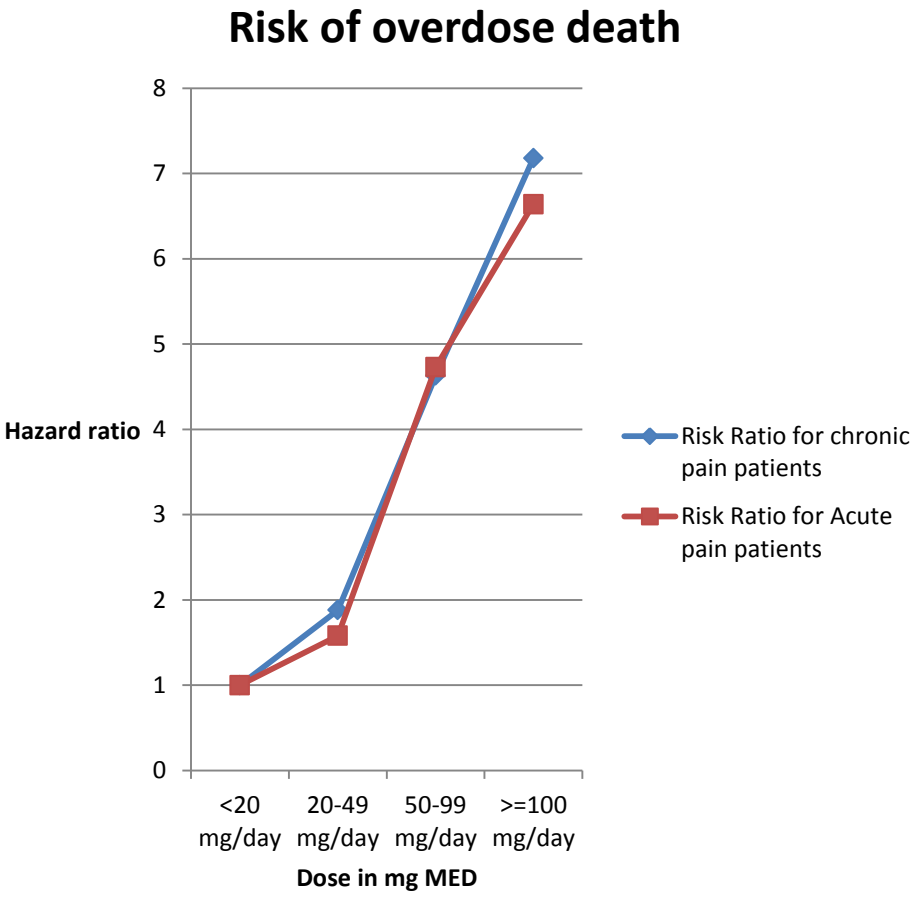
Dunn 2010 - Opioid Prescriptions for chronic pain and Overdose: A cohort study: *Ann Intern Med. 2010; 152(2): 85-92*

- Risk of overdose event in patients (N=9940) prescribed opioids for non cancer pain at GHC
- f/u – 42 months
- **Hazard Ratio (risk)** for overdose death = **8.87** when on **≥100mg/d.**
- **Risk ratio = 3.73** when on **50 to <100mg/d.**



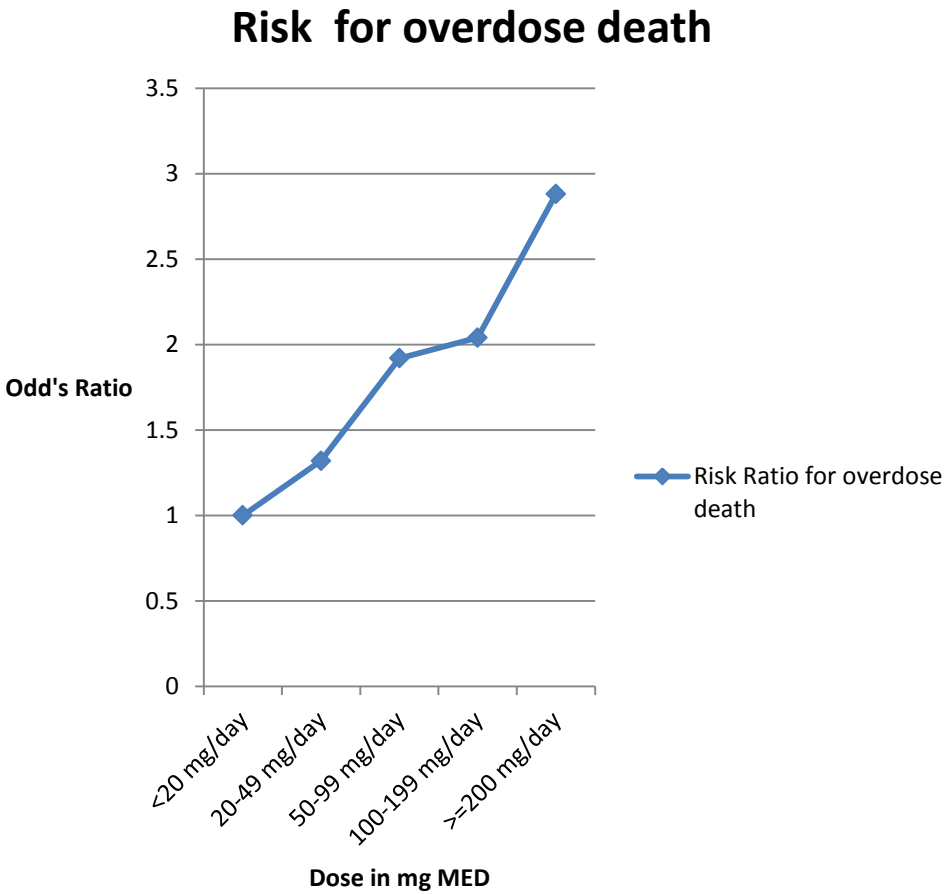
Bohnert 2011- Association between opioid prescribing patterns and opioid overdose related deaths – *JAMA. 2011; 305 (13): 1315-1321*

- Risk of overdose death in a large national sample data (N= 155434)
- f/u – 5 years
- **For ≥100 MED/day**: **chronic pain: HR=7.18** (95% CI, 4.85-10.65) and **acute pain: HR=6.64**(95% CI, 3.31-13.31).
- **For 50-99 MED/day**: **chronic pain: HR=4.63** (95% CI, 3.18-6.74) and **acute pain: HR=4.73** (95% CI, 2.55-8.79).



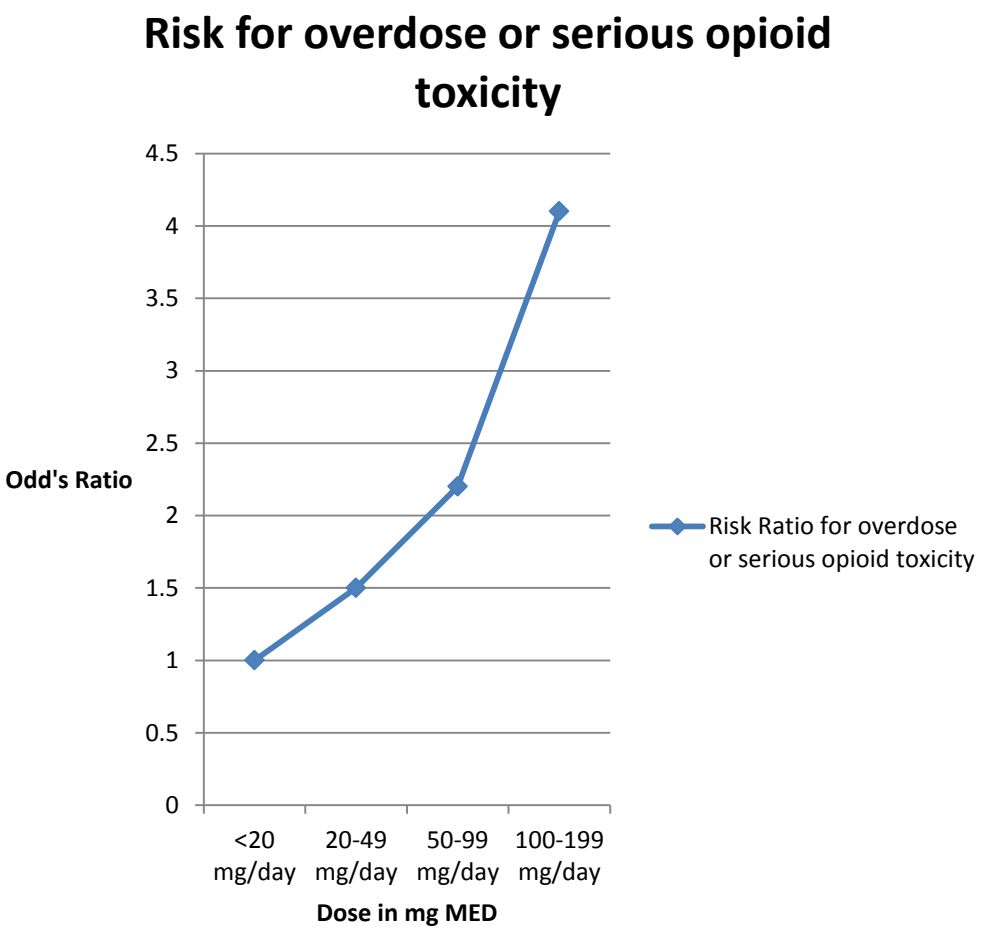
Gomes 2011- Opioid dose and drug related mortality in patients with nonmalignant pain – *Arch Intern Med. 2011; 171 (7); 686-691*

- Risk of overdose death (N = 2212)
- f/u – 113 months
- Risk of overdose death, for **200mg MED or more: OR** (95% CI) **= 2.88** (1.79-4.63)
- **100 to 199mg MED: OR** (95% CI) **= 2.04** (1.28-3.24)
- **50-99 MED: OR** (95% CI) **= 1.92** (1.30-2.85)

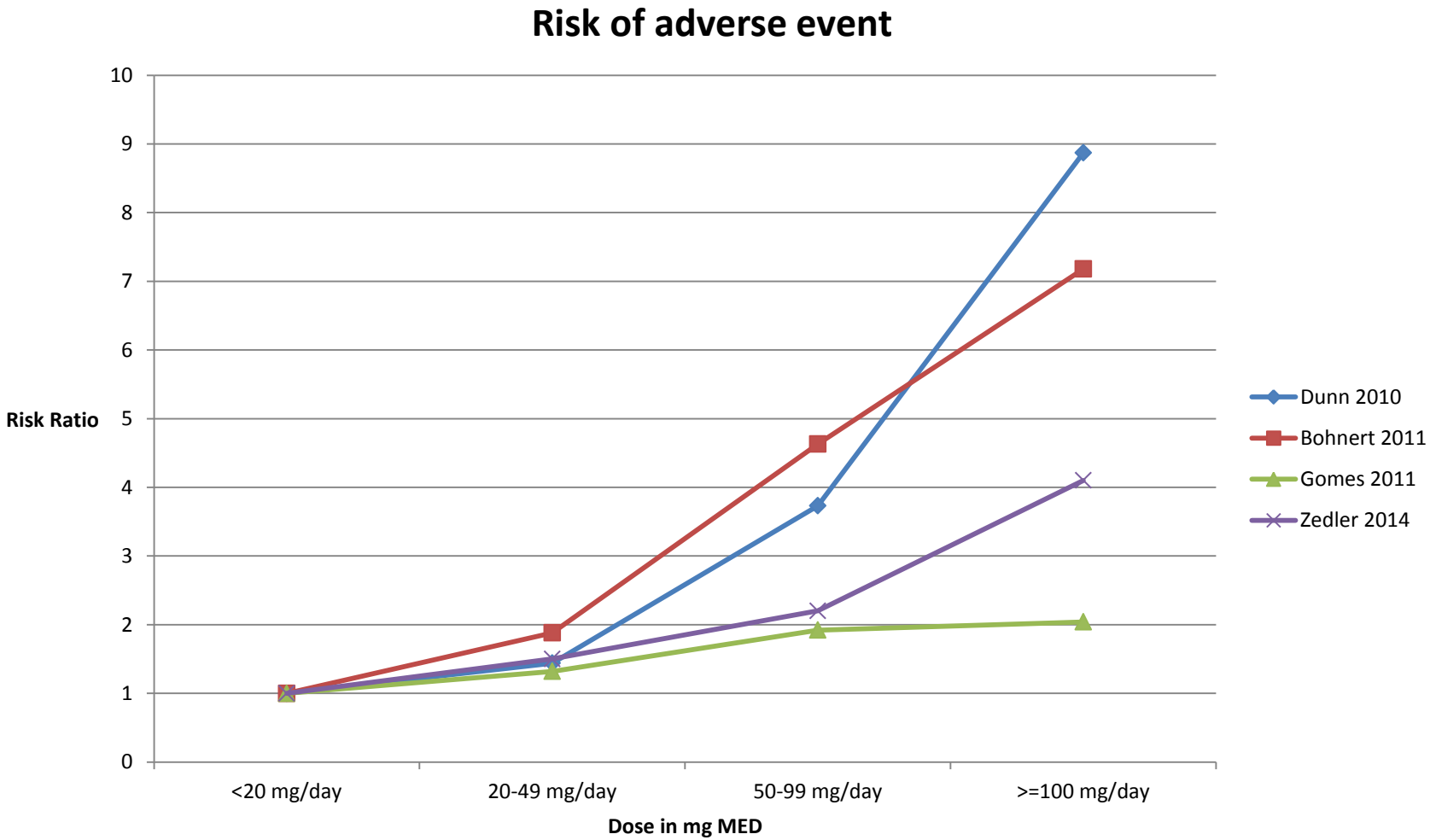


Zedler 2014-Risk factors for serious prescription opioid related toxicity or overdose among veterans health administration patients – *Pain Med (2014)*

- Risk of opioid related toxicity or overdose among VA patients (N= 8987)
- f/u – 2 years
- For **100 mg MED: OR = 4.1**, 95% CI, 2.6–6.5
- **50-99 mg MED**: **OR = 2.2**, 95% CI, 1.5–3.2
- **20-49 mg MED**: **OR = 1.5**, 95% CI, 1.1– 1.9
- **History of opioid dependence OR = 3.9**, 95% CI, 2.6–5.8



Risk – 4 studies



Early opioids and disability in WA WC. Spine 2008; 33: 199-204

- Population-based, prospective cohort
- N=1843 workers with acute low back injury and at least 4 days lost time
- Baseline interview within 18 days(median)
- 14% on disability at one year
- **Receipt of opioids for > 7 days, at least 2 Rxs, or > 150 mg MED doubled risk of 1 year disability, after adjustment for pain, function, injury severity**

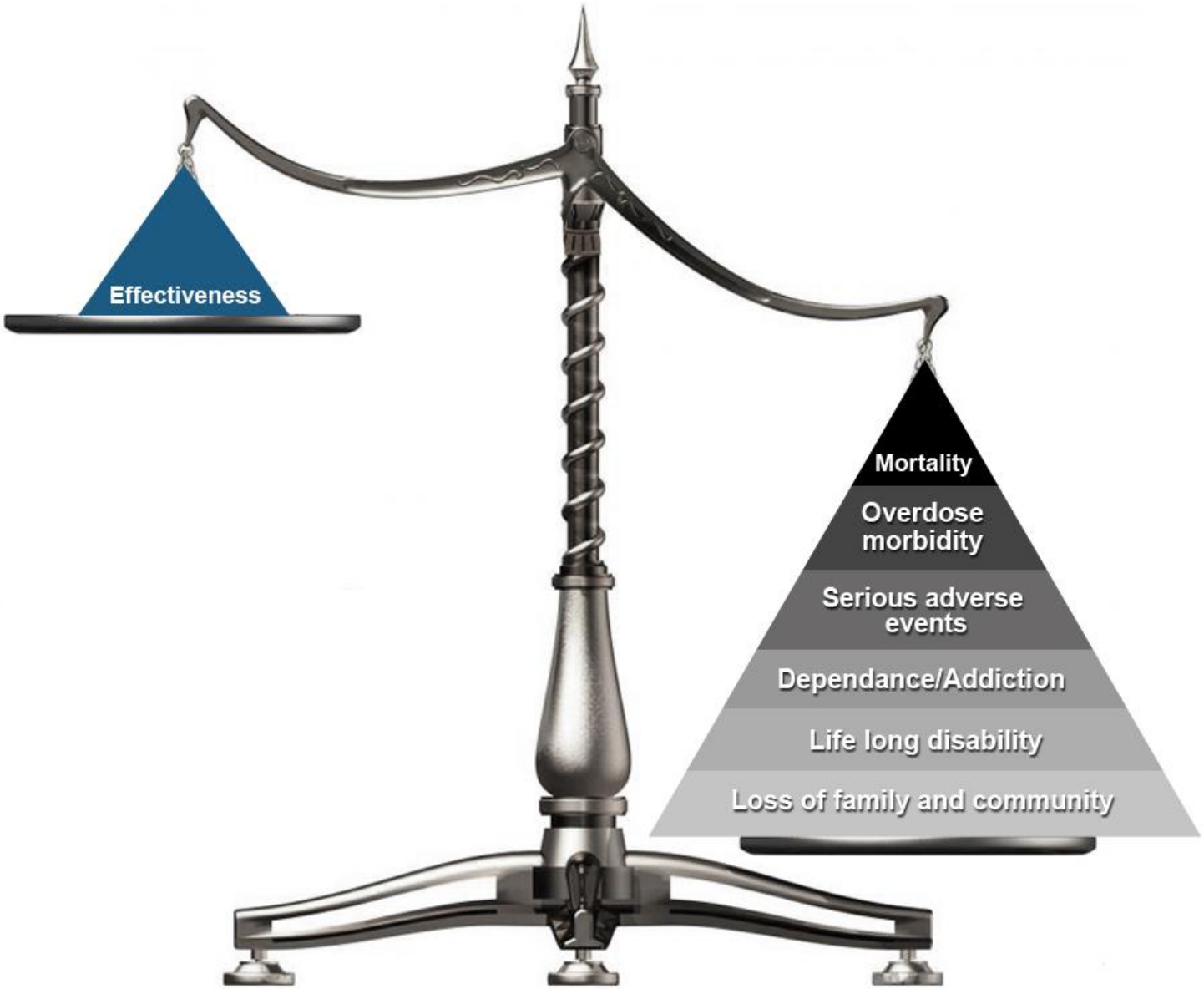
Incidence rate of Opioid Use Disorders after Initiation of Rx opioids*

	Incidence Rate	Adjusted OR(95% CI)
No opioids	0.004%	1.0
Acute, low dose	0.12%	3.31 (2.54-4.31)
med dose	0.12%	3.04 (2.30-4.01)
high dose	0.12%	2.68 (1.45-4.98)
Chronic, low dose	0.72%	17.63 (12.33-25.20)
med dose	1.28%	35.19 (24.75-50.02)
high dose	6.1%	171.95(105.97-279.00)

Chronic->/=90 days; low dose-1-36 mg; med dose-36-120 mg; high dose->120 mg

Edlund et al, Clin J Pain 2014; 30: 557-564

Risk/Benefit of Opioids for Chronic Non-Cancer Pain



AMDG opioid dosing guideline 2007

- 120 mg/day MED as a “yellow-flag” threshold was a consensus best guess among our clinical experts
- The threshold was linked to improvement in pain and function
- Now in state regulation

Washington Agency Medical Directors' Opioid Dosing Guidelines

- **Developed with clinical academic pain experts in 2006-released online April 2007**
- **Part I – If patient has not had clear improvement in pain AND function at 120 mg MED (morphine equivalent dose) , "take a deep breath"**
  - If needed, get one-time pain management consultation (certified in pain, neurology, or psychiatry)
- **Part II – Guidance for patients already on very high doses >120 mg MED**

AMDG agency medical directors' group

www.agencymeddirectors.wa.gov

Guidance for Primary Care Providers on Safe and Effective Use of Opioids for Chronic Non-cancer Pain

- **Establish an opioid treatment agreement**
- **Screen for**
  - Prior or current substance abuse
  - Depression
- **Use random urine drug screening judiciously**
  - Shows patient is taking prescribed drugs
  - Identifies non-prescribed drugs
- **Do not use concomitant sedative-hypnotics**
- **Track pain and function to recognize tolerance**
- **Seek help if dose reaches 120 mg MED, and pain and function have not substantially improved**
- **Use PDMP initially and for monitoring**

http://www.agencymeddirectors.wa.gov/opioiddosing.asp
MED, Morphine equivalent dose

Open-source Tools Added June 2010 Update of AMDG Opioid Dosing Guideline

- Opioid Risk Tool: Screen for past and current substance abuse
- CAGE-AID screen for alcohol or drug abuse
- Patient Health Questionnaire-9 screen for depression
- 2-question tool for tracking pain and function
- Advice on urine drug testing

OPIOID DOSE CALCULATOR

Opioid (oral or transdermal)	Mg per day	Morphine equivalents
codeine		0
fentanyl transdermal (in mcg/hr)		0
hydrocodone	20	20
hydromorphone		0
methadone		
up to 20mg per day		
21 to 40mg per day		
41 to 60mg per day	50	500
>60mg per day		0
morphine		0
oxycodone		0
oxymorphone		0
TOTAL daily morphine equivalent dose (MED) =		520

http://www.agencymeddirectors.wa.gov/opioiddosing.asp#DC

Available as mobile app:
http://www.agencymeddirectors.wa.gov/opioiddosing.asp

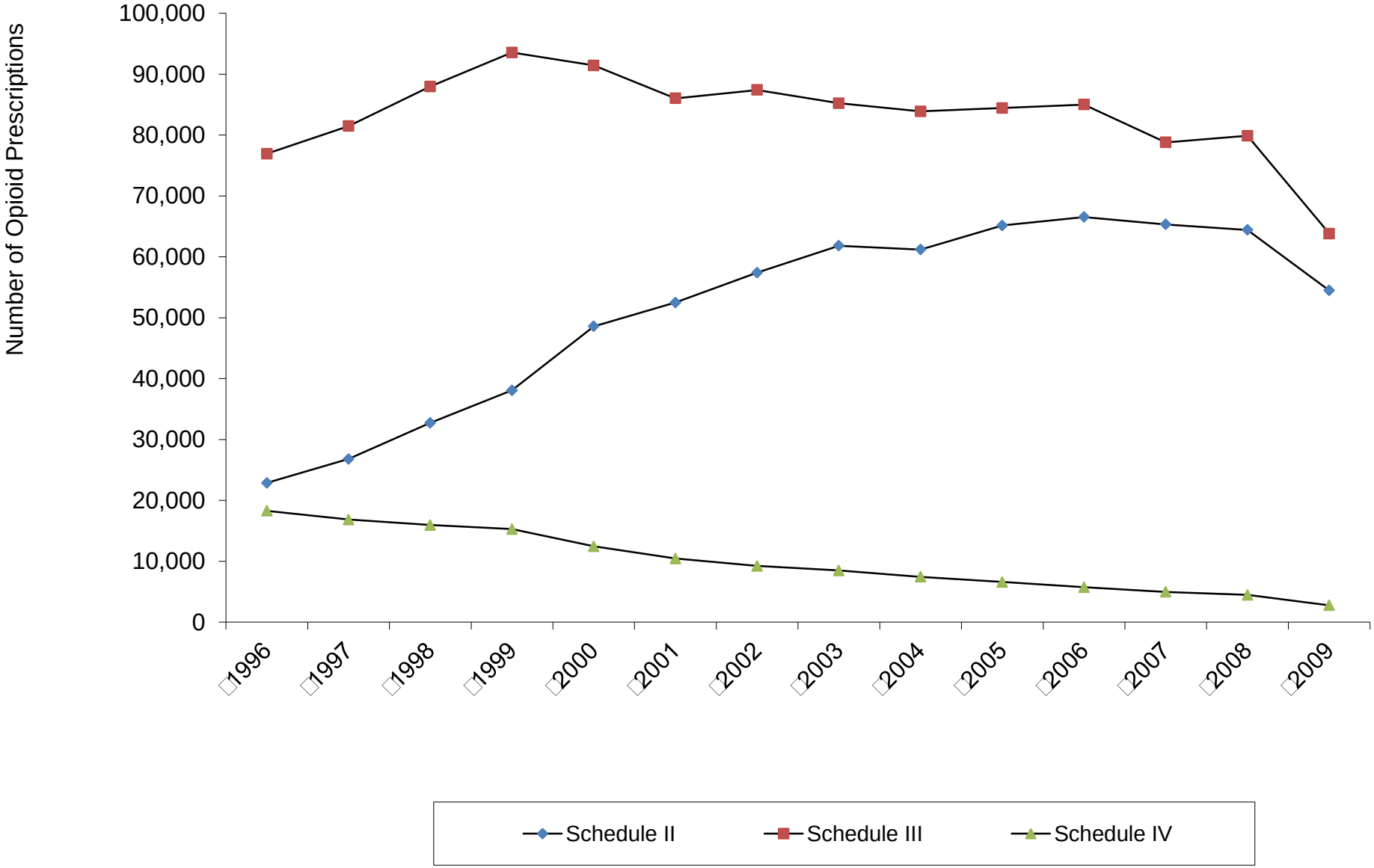
Dosing policies since 2007

- 2009: CDC recommends 120 mg/day MED threshold
- 2010: ESHB 2876-Directs DOH Boards and Commissions to establish dosing guidance and best practices
- 2012: CT workers comp-90 mg/day MED
- 2013: OH State medical Board-2013-80 mg/day MED
- American College of Occupational and Environmental Medicine-50 mg/day MED
- CA work comp 80-120 mg/day MED*
- Update WA AMDG opioid guideline by June, 2015
- Bree Collaborative to consider adopting AMDG guideline in 2015

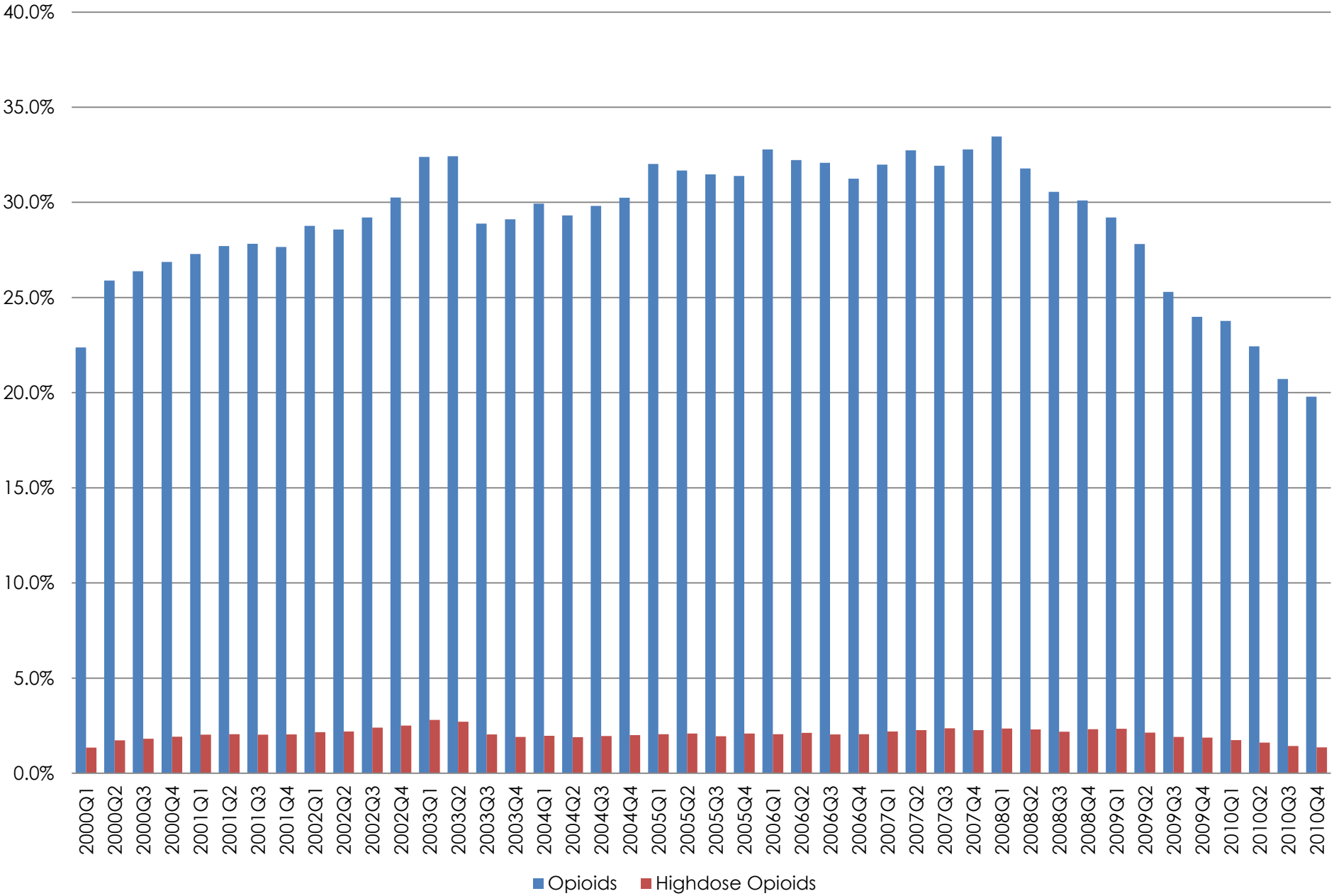
*Not final

Yearly Trend of Scheduled Opioids

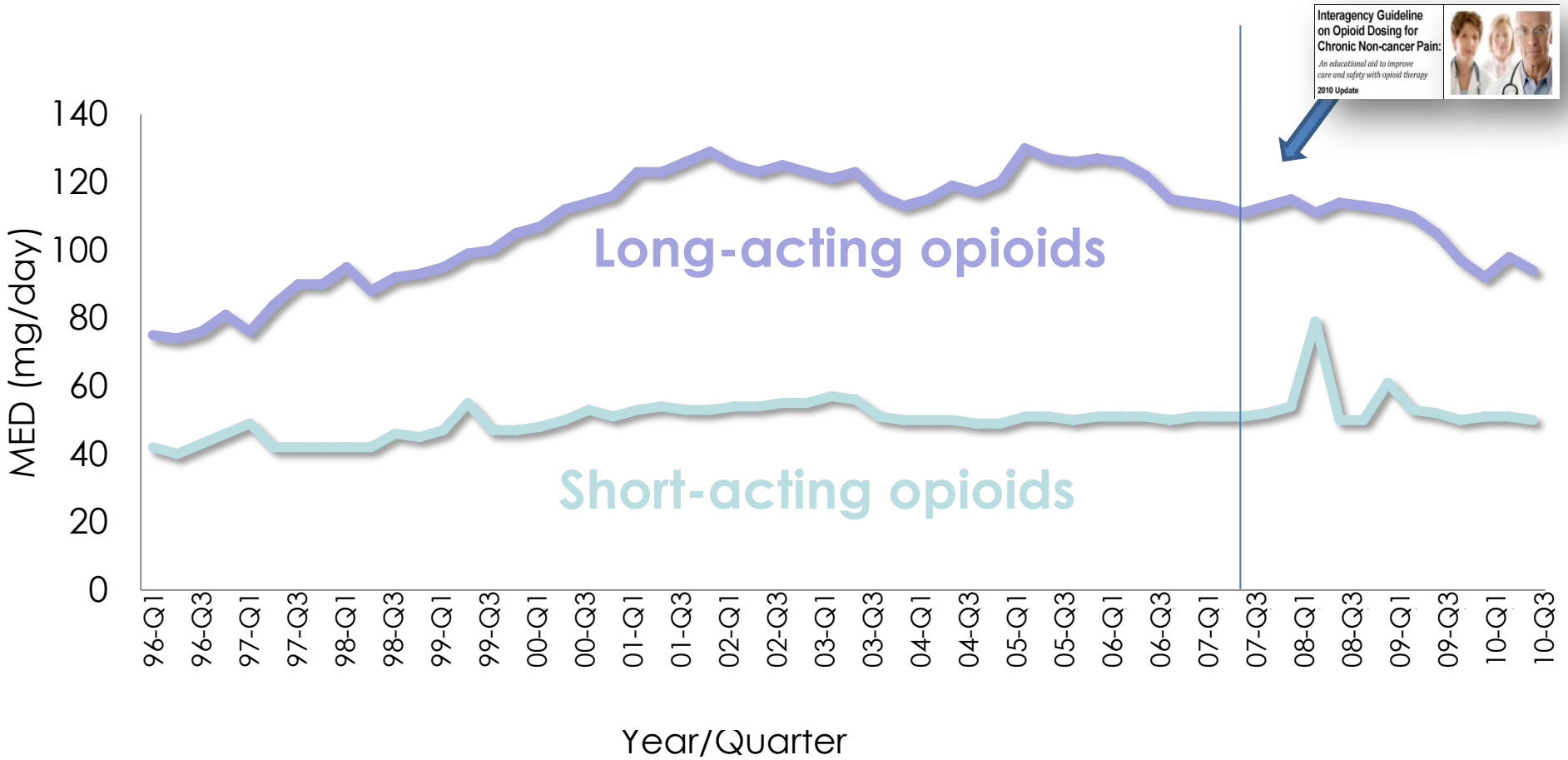
(Franklin et al, Am J Ind Med 2012; 55: 325-31)



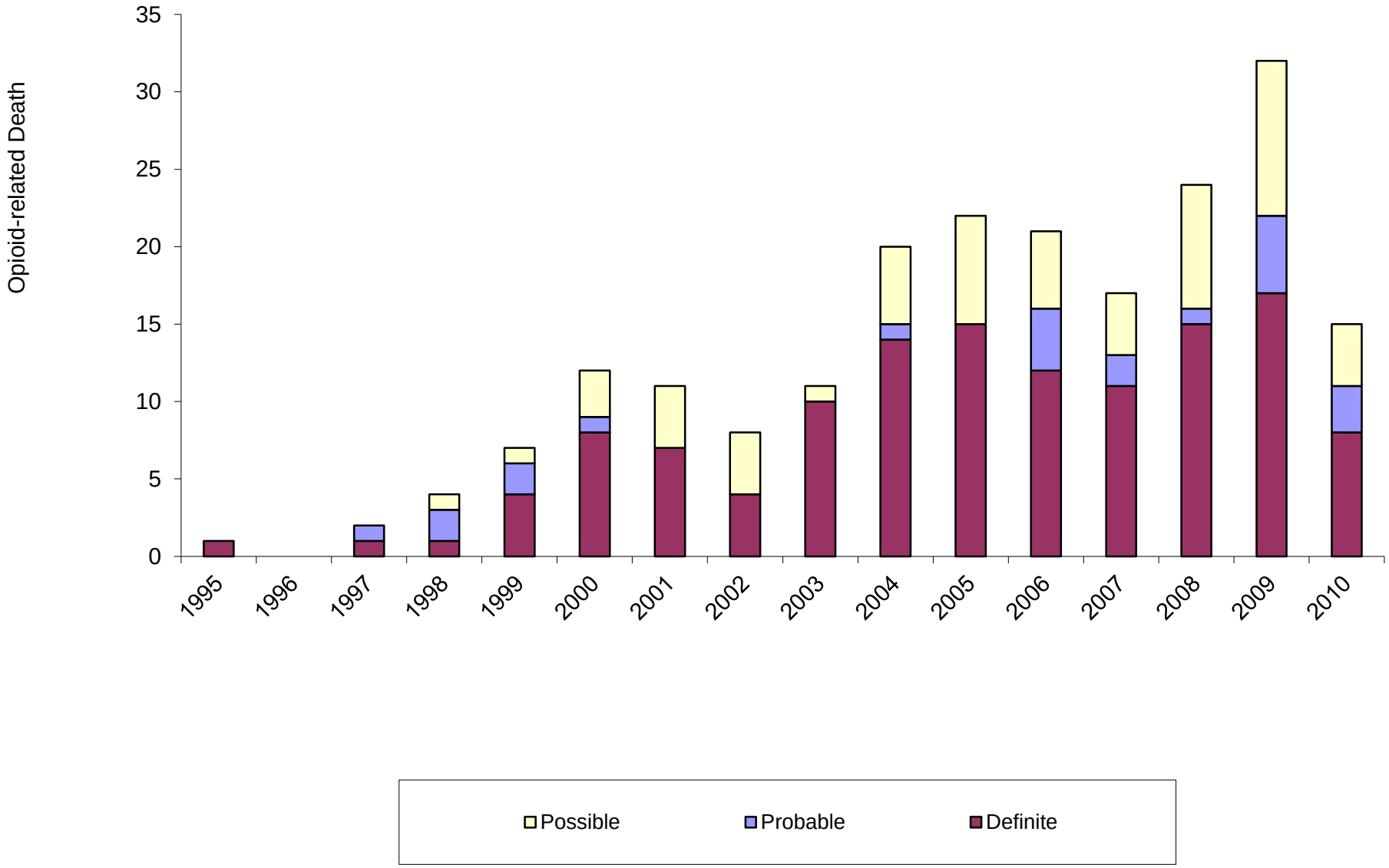
Percent of Timeloss Claimants on Opioids
2000 - 2010



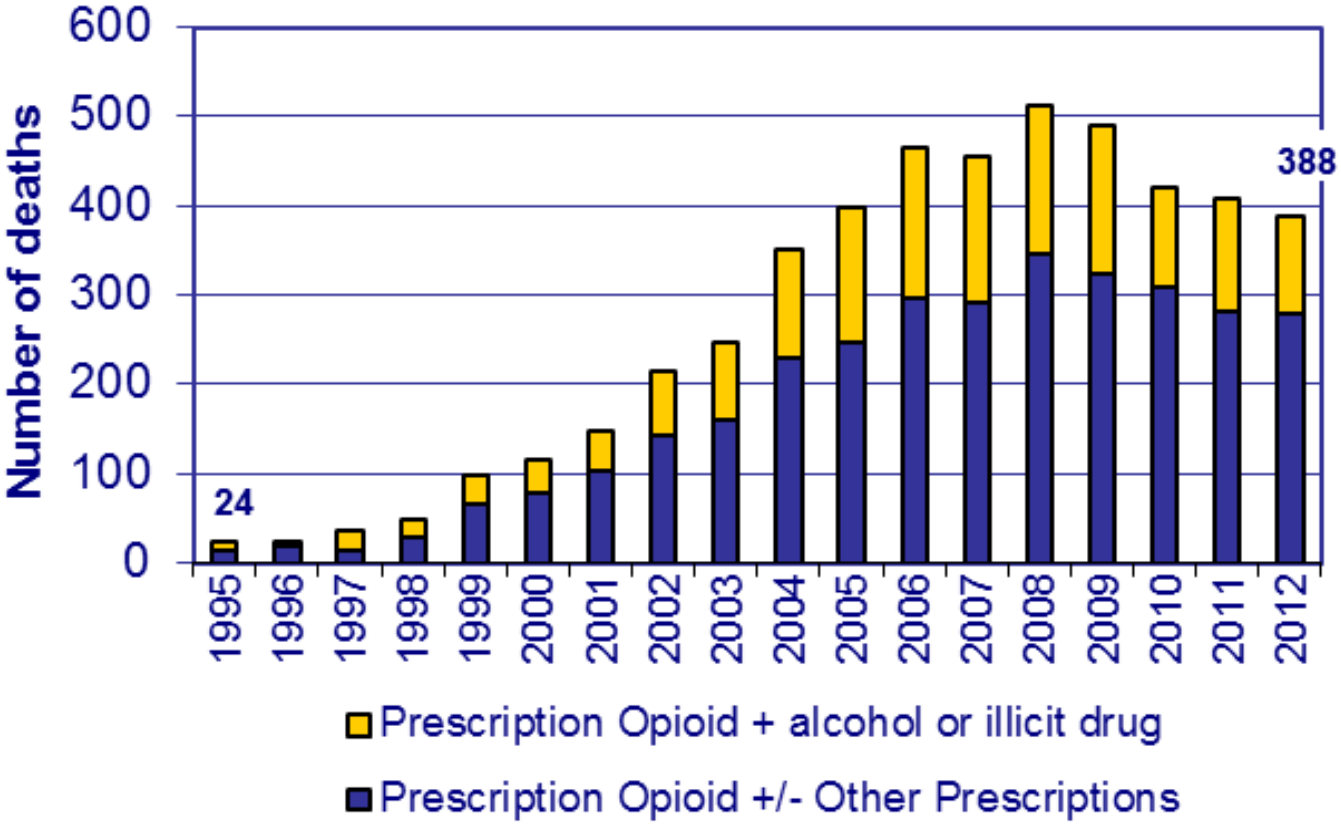
Average Daily Dosage for Opioids, Washington Workers' Compensation, 1996–2010



WA Workers' Compensation Opioid-related Deaths 1995-2010

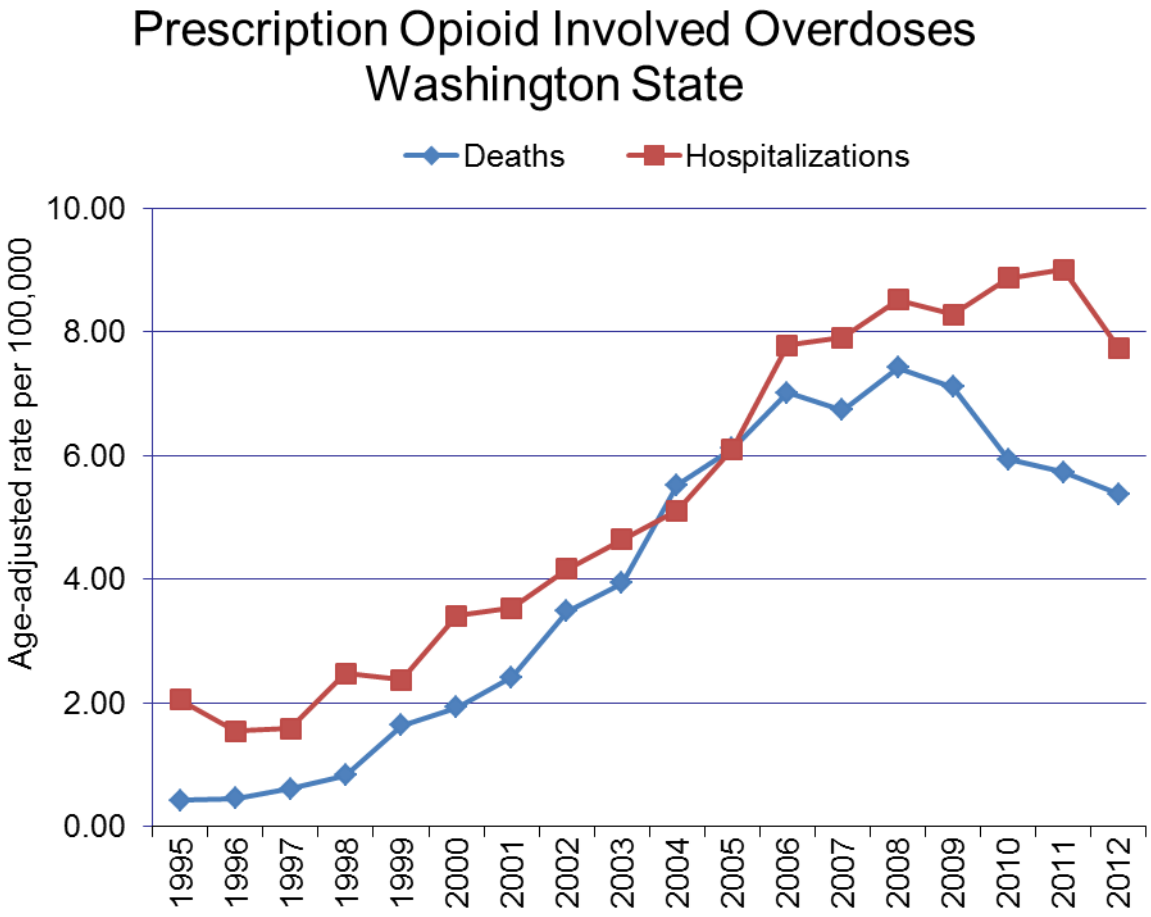


Unintentional Prescription Opioid Overdose Deaths
Washington 1995-2012
-27% sustained decline-

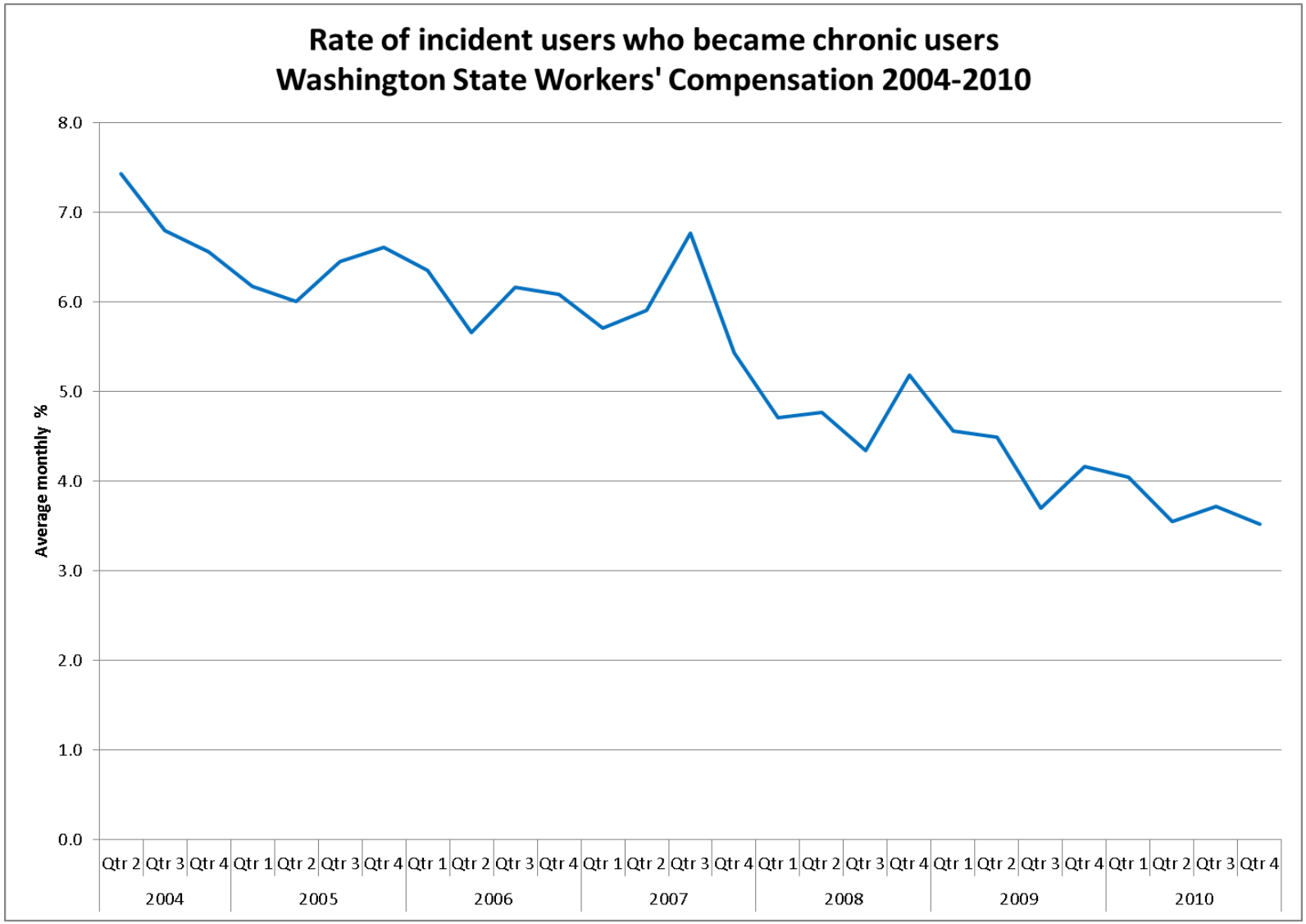


* Tramadol only deaths included in 2009, but not in prior years.

Source: Washington State Department of Health, Death Certificates


Prescription Opioid Involved Overdoses
Washington State
Deaths
Hospitalizations
Age-adjusted rate per 100,000
10.00
8.00
6.00
4.00
2.00
0.00
1995
1996
1997
1998
1999
2000
2001
2002
2003
2004
2005
2006
2007
2008
2009
2010
2011
2012

New study-submitted-Garg et al, 2013

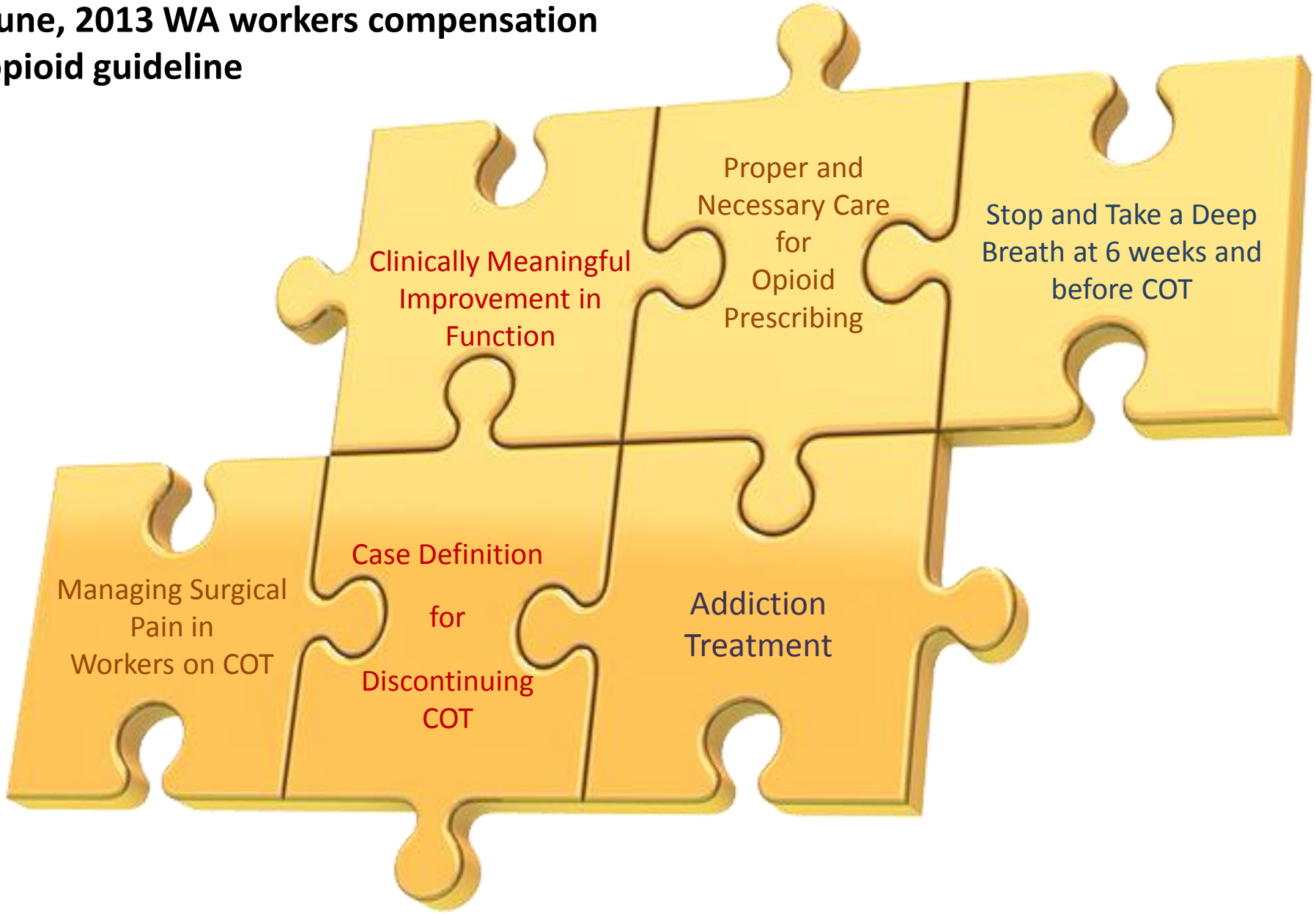


New primary care survey in WA*

- Most providers (72%) reported concern about opioid overdose, addiction, dependence, or diversion. Only 25% indicated concern about regulatory scrutiny.
- Prescribing providers in WA reported ongoing concerns regarding opioid use for CNCP, but those affiliated with a health care organization with opioid prescribing guidelines and access to pain consultation were less likely to report being concerned about opioid-related problems or to have discontinued prescribing opioids.

***Franklin et al, 2013, J Am Board Fam Med (in press)**

June, 2013 WA workers compensation opioid guideline



Opioid Use in Workers' Compensation

(continue)

- Measuring the Impact of Opioid Use
  - Beyond acute phase, effective use should result in clinically meaningful improvement in function (CMIF)
  - CMIF is an improvement in function of at least 30% compared to start of treatment or in response to a dose change
  - Evaluation of clinically meaningful improvement should occur at 3 critical phases (acute, subacute and during COT)

Continuing to prescribe opioids in the absence of CMIF or after the development of a severe adverse outcome is not proper and necessary care. In addition, the use of escalating doses to the point of developing opioid use disorder is not proper and

Opioid Prescribing Precautions

- Opioid Use with Co-morbid Substance Use or Mental Health Disorders
  - Patients with these disorders are more likely to:
    - Receive COT
    - Receive potent opioids, higher doses & concurrent sedative-hypnotics
    - Have complications from opioids (e.g. misuse, abuse or overdose)

- Be cautious when prescribing COT for workers with co-morbid mental health disorder
- Workers with current substance use disorder (excluding nicotine) should not receive COT
- Those with a history of opioid use disorder should only receive COT under exceptional circumstances

Opioid Prescribing Precautions

(continue)

- Drugs and Drug Combinations to Avoid
  - Do not use long-acting or extended-release opioids for acute pain or post-op pain
  - Combining opioids with benzodiazepines, sedative-hypnotics or barbiturates is not recommended
  - Use caution when prescribing methadone for pain

Due to methadone's nonlinear pharmacokinetics, unpredictable clearance and multiple drug-drug interactions, providers should use extreme caution when prescribing this drug for pain

Prescribing Opioids for a Work-related Injury or Occupational Disease

- Opioids in the Acute Phase (0-6 weeks after injury or surgery)
  - Use of opioids as initial treatment for back sprain or other strains is not supported, but if prescribed, should be limited to short-term

- Opioid use should result in improvements in pain and function of at least 30% or to pain interference of ≤ 4
- Providers should check PMP and administer screening tools per AMDG Guideline before prescribing opioids
- L&I will not pay for opioids beyond 6 weeks in absence of CMIF

Prescribing Opioids for a Work-related Injury or Occupational Disease (continue)

- Opioids in the Subacute Phase (between 6 and 12 weeks)
  - Opioid use beyond the acute phase is rarely indicated if injury is a sprain or strain
  - Provider must perform the following best practices
    - Screen for opioid risk (ORT, SOAPP-R, DIRE or CAGE-AID)
    - Screen for depression to identify potential impact to treatment
    - Administer baseline urine drug test (UDT)

- Access PMP to ensure controlled substance history is consistent
- Document clinically meaningful improvement in function and pain with acute use

Prescribing Opioids for a Work-related Injury or Occupational Disease (continue)

- Opioids in the Chronic Phase (beyond 12 weeks)
  - Provider must document CMIF with opioid use, failure of alternatives, signed treatment agreement, time-limited treatment plan, specialist consultation as needed and no contraindication or evidence of having serious adverse outcomes
  - Continued coverage will depend on sustained CMIF and pain interference score ≤ 4 with stable dosing along with other criteria

Because COT is associated with substantial risk of harm, opioid prescribing or dose increases that do not result in CMIF is considered not proper and necessary

Prescribing Opioids for a Work-related Injury or Occupational Disease (continue)

- Opioids for Catastrophic Injuries
  - Injuries in which significant recovery of physical function is not expected (e.g. severe burns, crush or spinal cord injury)
  - Provider must document the following:
    - A current signed treatment agreement
    - Stable opioid dose at or below 120mg/d MED
    - Consultation with pain specialist if dose > 120mg/d MED before further dose escalation
    - No relative contraindication to opioid use
    - No aberrant behavior identified by PMP or UDT

Managing Surgical Pain in Workers on COT

- Workers on COT who are undergoing surgery are more likely to have difficulty with post-op pain control
- Before Surgery - Surgeon and AP should:

  - Have a coordinated treatment plan for managing surgical pain
  - Obtain a pre-op anesthesia consult
  - Access the PMP and review worker's controlled substance history to get accurate information on opioid dose
  - Prepare the worker for surgery by setting appropriate expectations for pain management
  - Consider an opioid taper, but not required
  - Avoid dose escalation before surgery
  - Avoid prescribing new benzodiazepines or sedatives
  - Consider a consult with pain specialist for workers on high dose opioids

Managing Surgical Pain in Workers on COT

(continue)

- Day of Surgery – Anesthesiologist should:
  - Use anti-inflammatories, acetaminophen or both
  - Continue pre-op opioids to decrease risk of withdrawal and use regional blocks, if appropriate
  - Consider other non-opioid adjuvants (e.g. gabapentin, ketamine or lidocaine) for opioid sparing effects

Managing Surgical Pain in Workers on COT (continue)

- After Surgery – Surgeon (Hospitalist) and AP should:
  - Continue pre-op opioids with extra analgesia via PCA while hospitalized
  - Use care when transitioning from PCA to oral opioids. Do not perform "straight" conversion from IV to oral and expect more time to stabilize pain control
  - Discharge on same pre-op opioid regimen and supplement with *only short-acting* opioids. Do not prescribe long-acting or extended-release for post-op pain
  - Avoid new sedatives and benzodiazepines
  - Taper total opioids to pre-op dose or lower by 6 weeks

Discontinuing COT

- In most cases, it's best to taper opioids off completely
- Case definition for when to discontinue:
  - Worker or AP request OR
  - Worker maintained on opioids for at least 3 months and no sustained CMIF OR
  - Worker's risk from continued treatment outweighs benefit OR
  - Worker has experienced a severe adverse outcome or overdose event OR
  - Evidence of aberrant behavior OR
  - Use of opioids is not incompliance with DOH pain management rules, L&I's rules, AMDG Guideline or this Supplement

Discontinuing COT

(continue)

Due to lack of high quality evidence of safety and comparative efficacy, ultra rapid detoxification, using antagonist drugs with or without sedation, will not be covered.

- Step 1 – Discontinuing in the Uncomplicated Worker
  - A gradual taper of 10% per week by AP
  - Adjuvant agents (e.g. clonidine) and psychological support (e.g. cognitive behavioral therapy) to assist the taper

Discontinuing COT

(continue)

- Step 2 – Discontinuing in the Complicated Worker
  - Failed Step 1
  - High risk for failure due to high dose
  - Concurrent benzodiazepine use
  - Co-morbid substance use or mental health disorder
  - Consultation with pain specialist, SIMP provider or addiction specialist
  - Inpatient detox followed by SIMP
  - Adjuvant agents (e.g. clonidine) and psychological support (e.g. cognitive behavioral therapy) to assist the taper

Additional Services

- L&I may authorize up to 6 months of addiction treatment when:
  - Worker has failed Step 1 and 2 AND
  - Opioid use disorder (DSM-V) is diagnosed and identified as barrier to recovery AND
  - Documentation of how treatment will improve work capacity and/or the ability to progress in vocational retraining AND
  - A time-limited treatment plan
- Treatment options for opioid use disorder
  - Medication assisted (e.g. buprenorphine, methadone or naltrexone)
  - Drug-free treatment
  - Residential treatment

Concrete steps to take

- Collaboration among State agencies at the highest levels
- Reverse permissive laws
- Set dosing and best practice Guidelines/Rules opioid use for acute, subacute and chronic, non-cancer pain
- Establish metrics for tracking progress; Track deaths and overdose ED visits and hospitalizations; Track high MED and prescribers
- Implement an effective Prescription Monitoring Program;
- Encourage/incent use of best practices (web-based MED calculator, use of state PMPs)
- DO NOT pay for office dispensed opioids
- ID high prescribers and offer assistance (eg, (academic detailing, free CME,ECHO)
- Incent community-based Rx alternatives (activity coaching and graded exercise early, opioid taper/multidisciplinary Rx later)

New state policies

Connecticut WC policy-7/1/2012

90 mg/day MED

MaineCare (Medicaid)-4/1/2012

Total 45 day maximum for non-cancer pain

New Mexico-Medical commission Rule 16.10.14-2012

A health care practitioner shall, before prescribing, ordering, administering or dispensing a controlled substance listed in schedule II, III or IV, obtain a patient PMP report for the preceding twelve (12) months

CA-several bills moving through-funding, mandatory use of CURES

OH-New state Medical Board guidelines with 80 mg/day MED "yellow flag" threshhold-Oct, 2013; URL: http://www.med.ohio.gov/webhost/ooat.html; new statute requires mandatory reporting of neonatal abstinence syndrome

Opioid Poisonings in WA Medicaid

- < 50% have chronic opioid use (> 90 days supply)
- 75% of opioid poisonings occurred in cases with prescribed doses < 120 mg MED
- About 45% have sedative-hypnotics in prior month
- 45% have another medication poisoning diagnosis on the same day
- 10-15% have an alcohol diagnosis on the same day
- Most cases have additional opioid prescriptions after poisoning
- Over 60% of methadone poisonings occurred in cases that did not have a prescription for methadone in the prior year

Fulton-Kehoe et al. Draft

Concrete steps to take

- Collaboration among State agencies at the highest levels
- Reverse permissive laws
- Set dosing and best practice Guidelines/Rules opioid use for acute, subacute and chronic, non-cancer pain
- Establish metrics for tracking progress; Track deaths and overdose ED visits and hospitalizations; Track high MED and prescribers
- Implement an effective Prescription Monitoring Program;
- Encourage/incent use of best practices (web-based MED calculator, use of state PMPs)
- DO NOT pay for office dispensed opioids
- ID high prescribers and offer assistance (eg, (academic detailing, free CME,ECHO)
- Incent community-based Rx alternatives (activity coaching and graded exercise early, opioid taper/multidisciplinary Rx later)

The State of US Health, 1990-2010
Burden of Diseases, Injuries, and Risk Factors
JAMA 2013; 310: 591-608

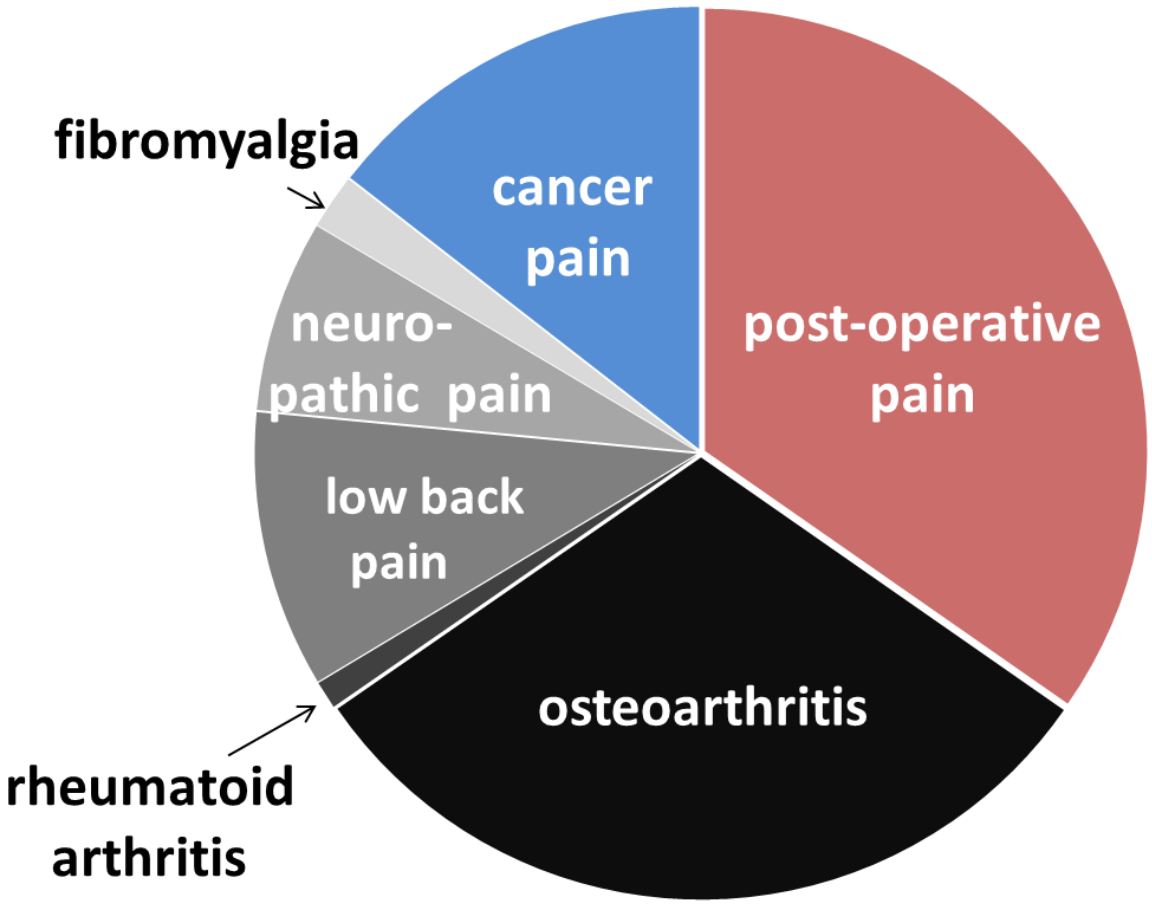
- Years lived with disability 2010
  - Low back pain 3.18 million YLD
  - Major depressive disorder 3.05 million YLD
  - Other MSK disorders 2.6 million YLD
  - Neck pain 2.13 YLD
  - Anxiety disorders 1.86 million YLD

  - Diabetes (#8) 1.16 million YLD
  - Alzheimers (#17) .83 million YLD
  - Stroke (#23) .63 million YLD

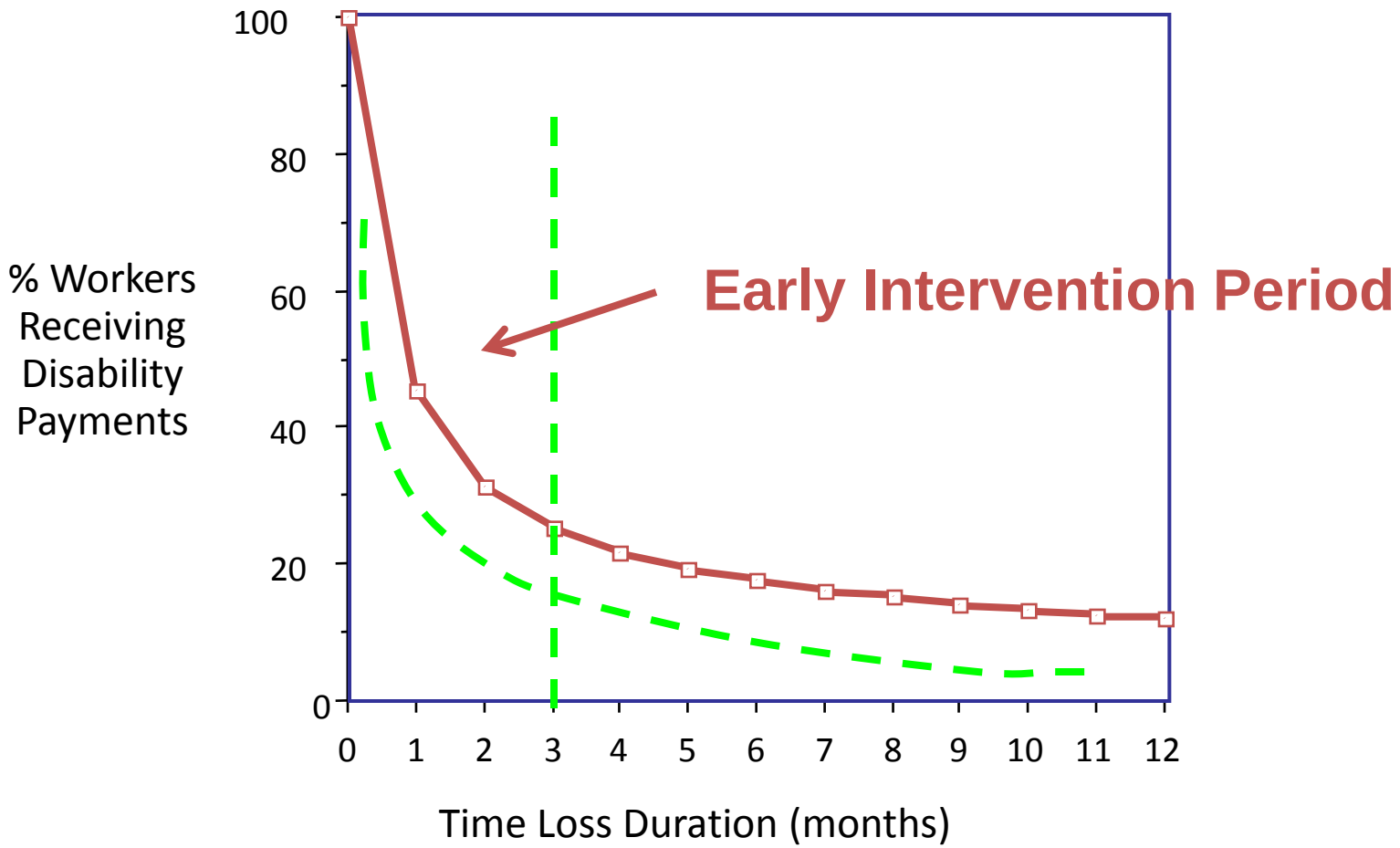
Half of United States opioids market is treatment for chronic, non-cancer pain

U.S. opioids market revenues for 7 leading indications, 2010

Source: GBI Research. Opioids Market to 2017. June 2011



Changes in Disability Status among Injured Workers in WA State



Adapted from Cheadle et al. Am J Public Health 1994; 84:190–196.

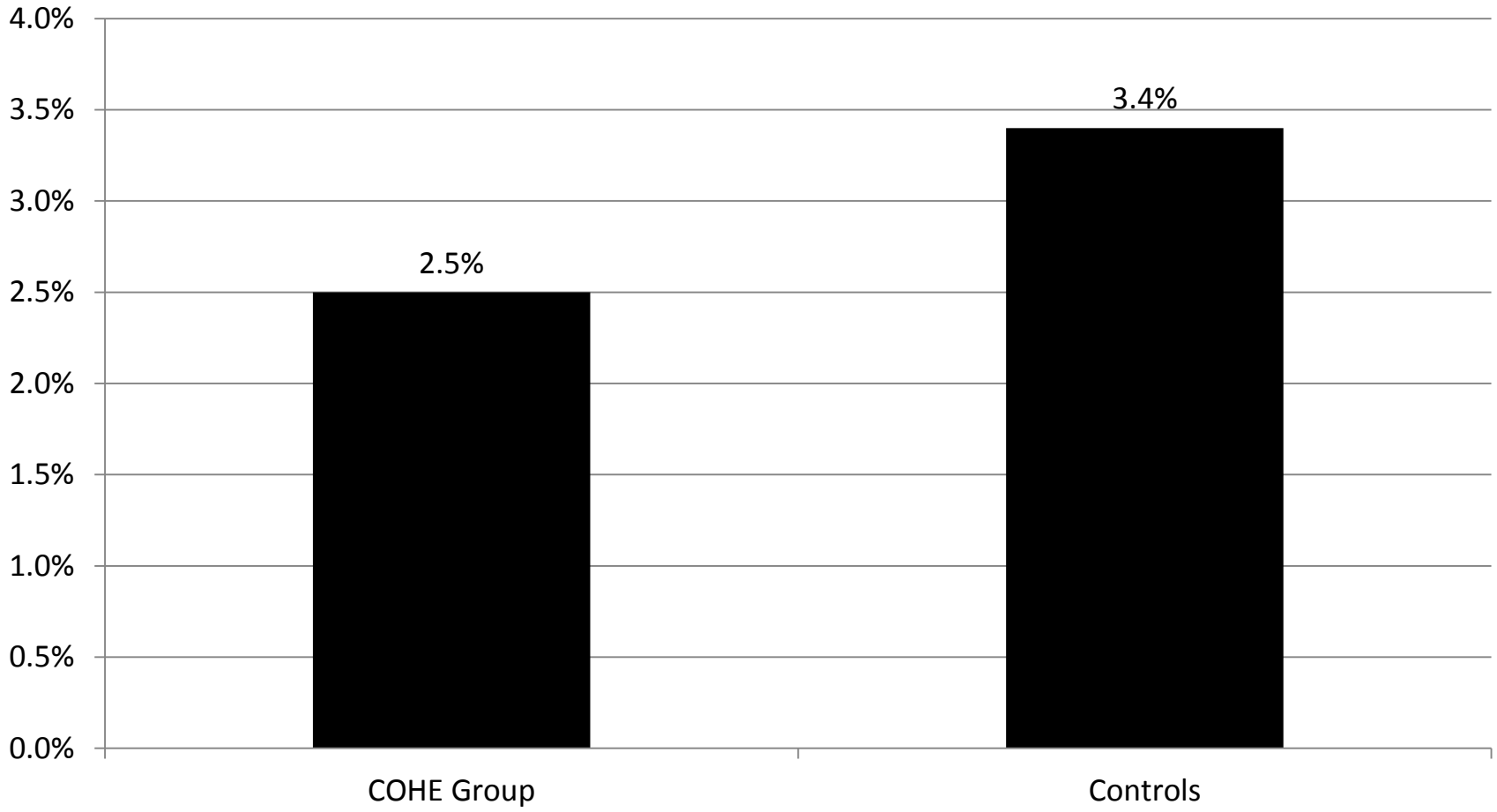
Franklin et al, AJIM, 2014 (in press)

Workers' Compensation: Poor Quality Health Care and the Growing Disability

Problem in the United States

- ❑Opioids
- ❑Lumbar fusion
- ❑Thoracic outlet syndrome
- ❑Bad docs

Receipt of SSDI for Compensable Claims: 8 Years Follow Up Post Injury, 2002 – 2010 (n=24,741)



THANK YOU!

For electronic copies of this presentation, please e-mail Laura Black

ljl2@uw.edu

For questions or feedback, please e-mail Gary Franklin

meddir@u.washington.edu