WA Opioid Dosing Guidelines
Centers for Disease Control
1/14/2009

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

Medical Director
Washington State Department of
Labor and Industries

Opioids for Chronic, Non, Cancer Pain

- Most state regulations changed (1998 for WA) from prohibition of use to use without dosing guidance
- Change in policy most likely due to 1) low grade studies (eg, Portenoy) supporting rarity of true addiction, 2) advocacy Re under treatment, 3) disciplinary fatigue

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
- Concluded: “Opioid maintenance therapy can be a safe, salutary and more humane alternative…”

Workers' Comp Guidelines-2000

Principles for Prescribing Oral Opioids

- Single prescribing physician
- Single pharmacy
- Lowest possible dose
- Appearance of misuse of medications
- RTW emphasis
- Track pain and function
- No concomitant use of benzodiazepines or sedative-hypnotics

Workers' Comp Guidelines-2000
Opioid Treatment Agreement

"I understand that this doctor may stop prescribing opioids or change the treatment plan if:

A. I do not show any improvement in pain from opioids or my physical activity has not improved.
B. My behavior is inconsistent with the responsibilities outlined in #1 above.
C. I give, sell or misuse the opioid medications.
D. I develop rapid tolerance or loss of improvement from the treatment

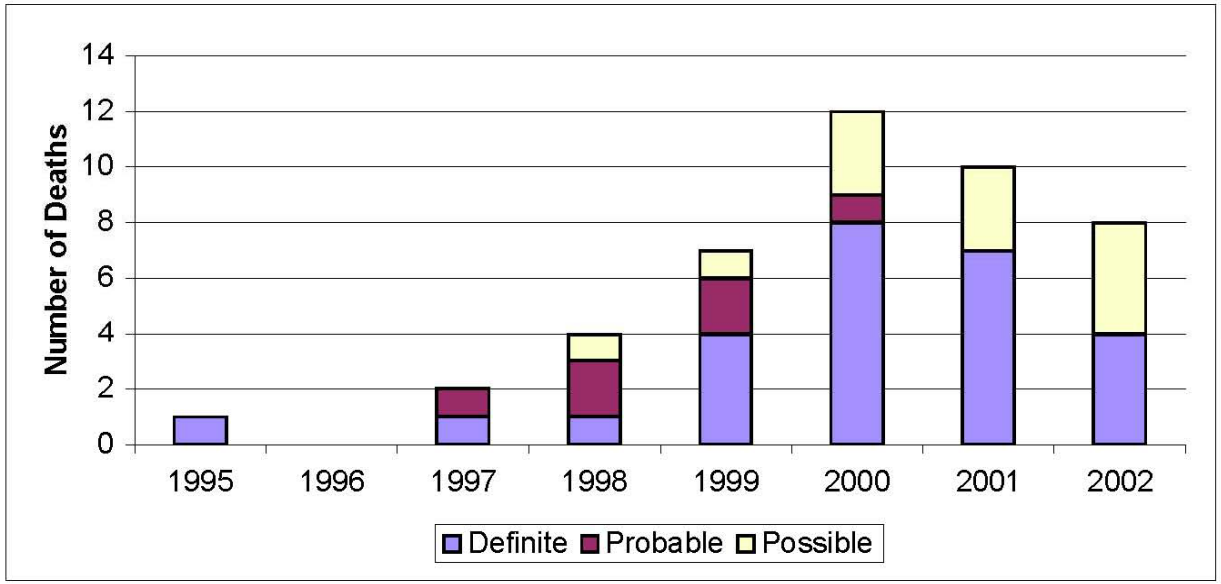
Also includes permission to conduct random urine drug screen

Earliest report of prescription-opioid related deaths

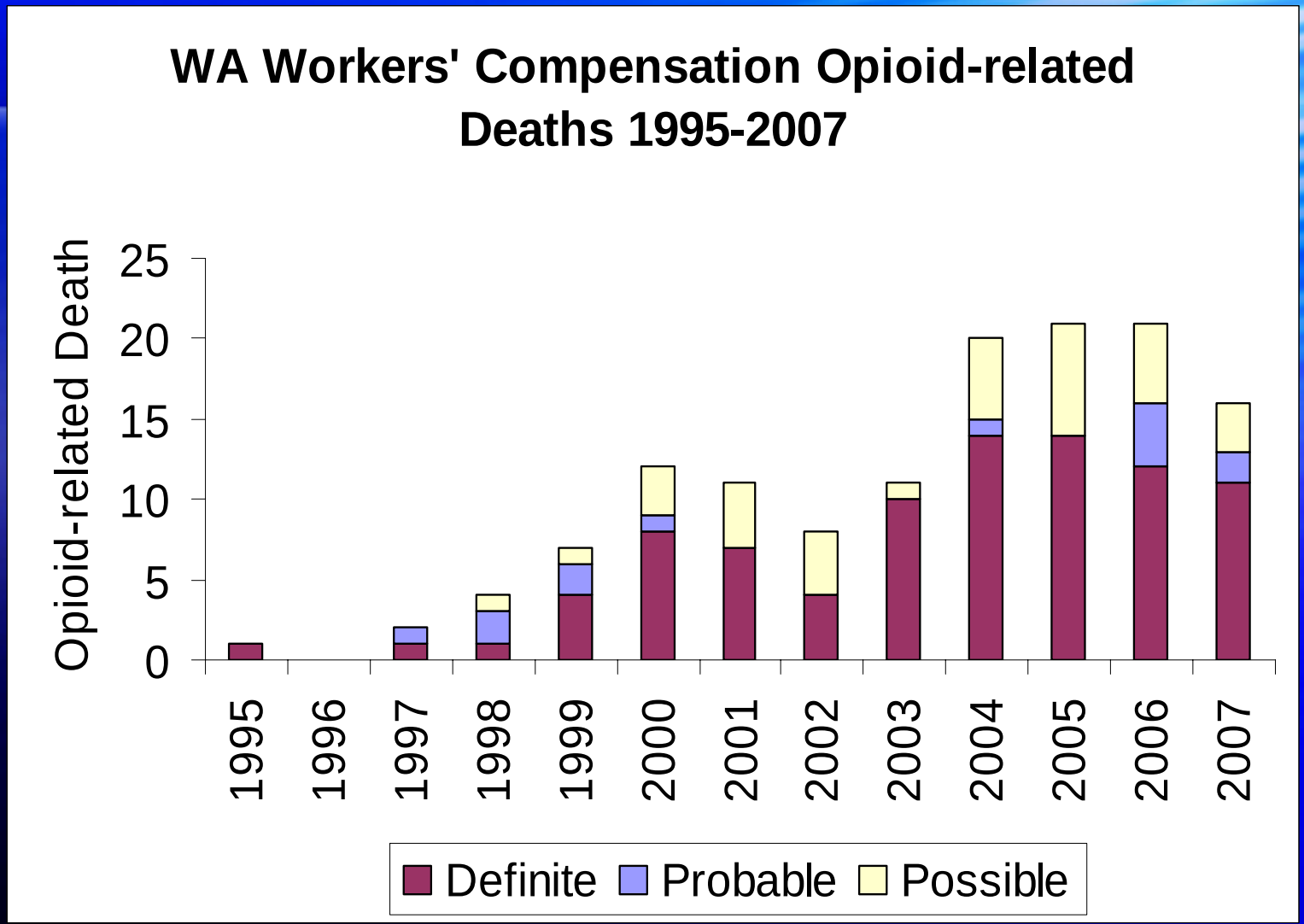
- Office of Diversion Control, US Drug enforcement Administration. Drugs and chemicals of concern: Summary of medical examiner reports on oxycodone-related deaths, 2000-2001. URL: http://www.deadiversion.usdoj.gov/drugs_concern/oxycodone/oxycontin7.htm

Franklin GM, Mai J, Wickizer T, Turner JA, Fulton-Kehoe D, Grant L. Opioid dosing trends and mortality in Washington State workers' compensation, 1996-2002.

Am J Ind Med 48:91-99, 2005.



Washington Workers' Compensation Opioid-related Deaths, 1995-2002


WA Workers' Compensation Opioid-related Deaths 1995-2007
Opioid-related Death
25
20
15
10
5
0
1995
1996
1997
1998
1999
2000
2001
2002
2003
2004
2005
2006
2007
Definite
Probable
Possible

WA Workers' Compensation

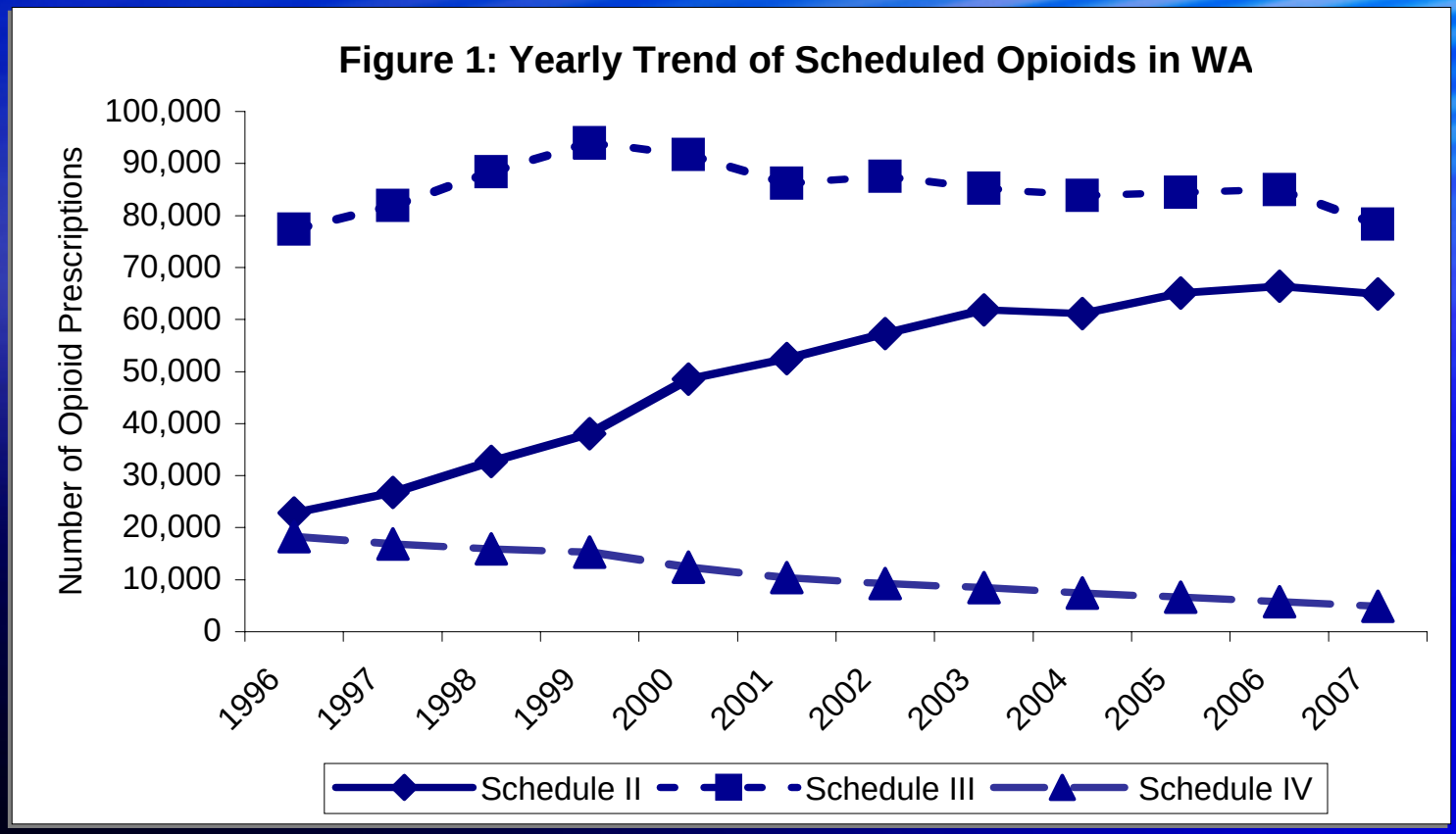
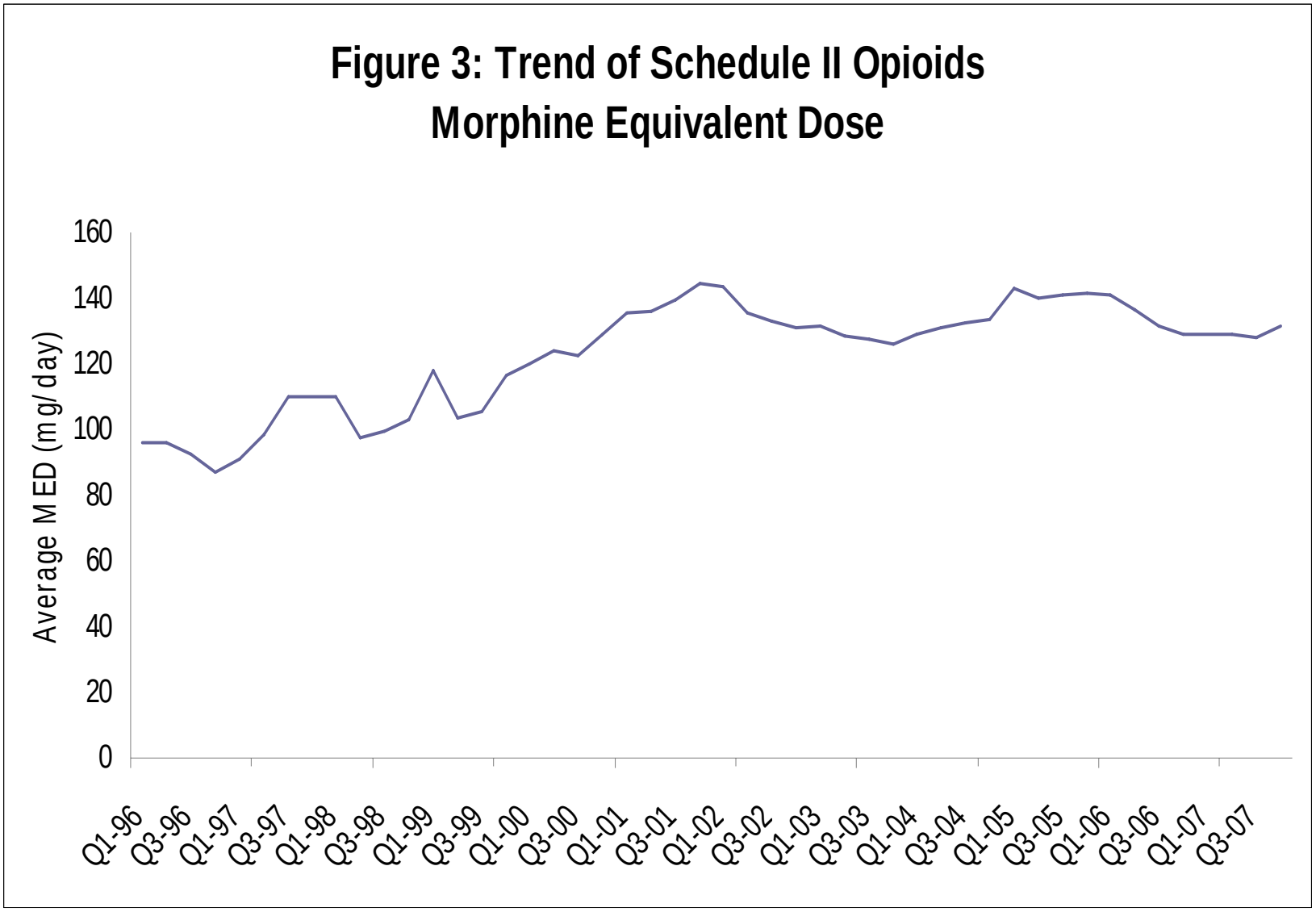
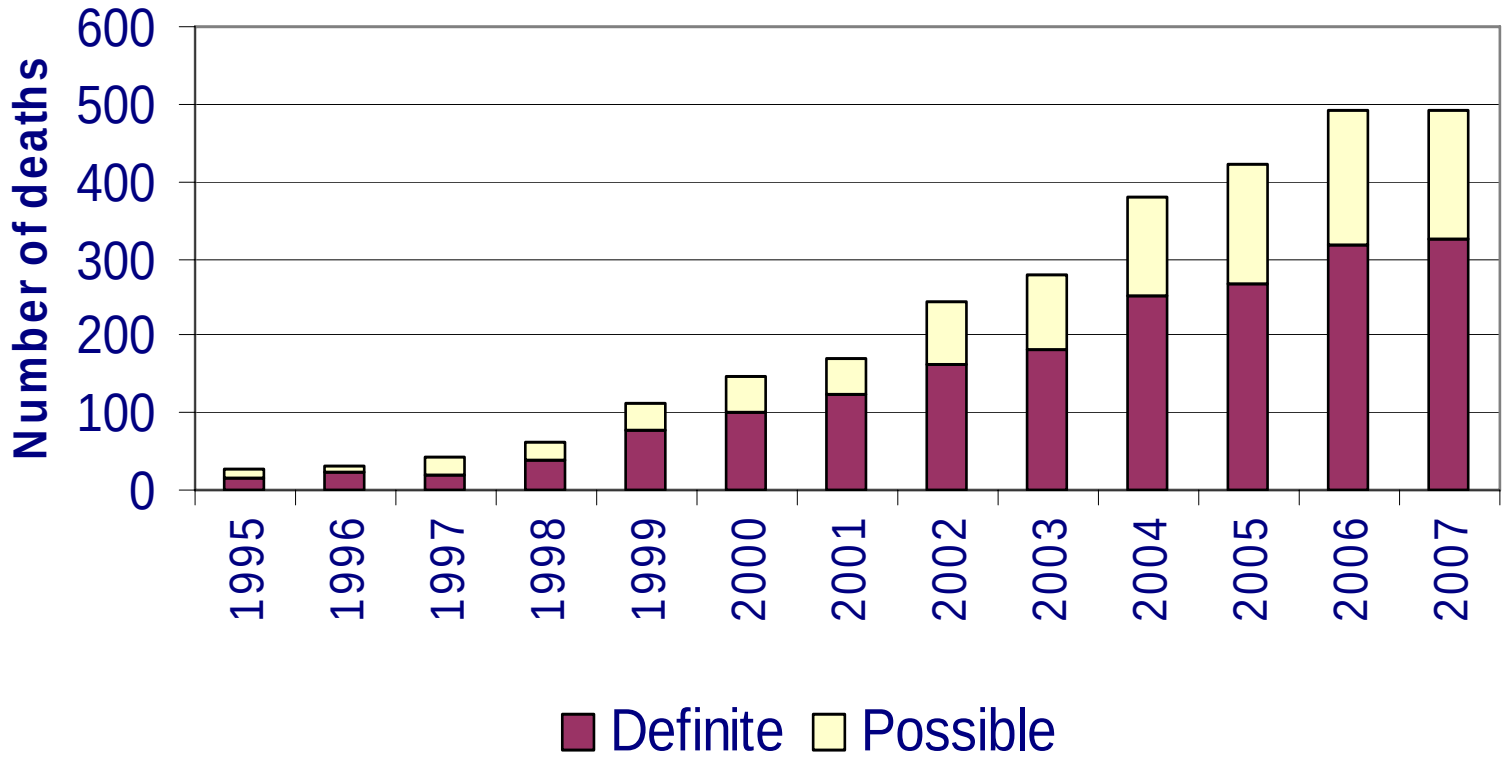


Figure 3: Trend of Schedule II Opioids
Morphine Equivalent Dose



Prescription Opiate Deaths
Washington State, 1995-2007



Hospitalizations for Prescription Opiate Overdose, WA 1987-2007

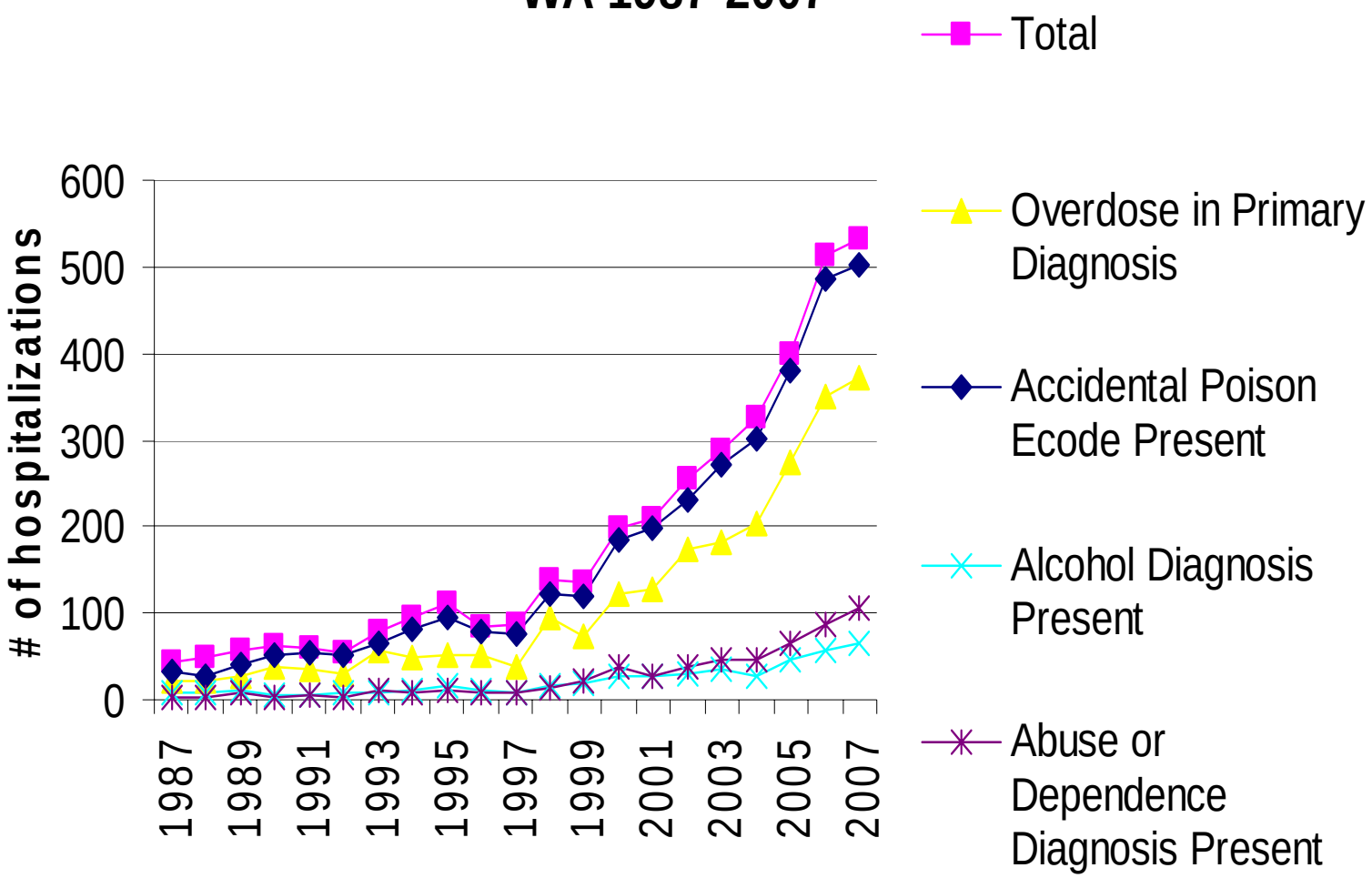


Table 4. Most Frequent Suspect Drugs in Death and Serious Nonfatal Outcomes, 1998-2005

Drug Name	Rank/Deaths	Drug Class
Death outcome		
Oxycodone	1/5548	Opioid analgesic
Fentanyl	2/3545	Opioid analgesic
Clozapine	3/3277	Antipsychotic
Morphine	4/1616	Opioid analgesic
Acetaminophen	5/1393	Analgesic
Methadone	6/1258	Opioid analgesic
Infliximab	7/1228	DMARD
Interferon beta	8/1178	Immunomodulator
Risperidone	9/1093	Antipsychotic
Etanercept	10/1034	DMARD
Paclitaxel	11/1033	Antineoplastic
Acetaminophen-hydrocodone	12/1032	Combination analgesic
Olanzapine	13/1005	Antipsychotic
Rofecoxib	14/932	NSAID
Paroxetine	15/850	Antidepressant

Moore, et al. Serious Adverse Drug Events Reported to the Food and Drug Administration, 1998-2005 - Arch Intern Med. 2007;167(16):1752-1759

What's Causing the Deaths?
My Opinion

- Dramatically increasing avg daily doses not proven to be associated with improved outcomes, and are most likely related to increased tolerance
- Tolerance for euphoric effects likely precedes tolerance for respiratory depression

Central sleep apnea and ataxic breathing related to chronic opioid use

- Walker et al.J Clin Sleep Med 2007; 3:455-61
  - Retrospective cohort
  - N=60 on chronic opioids matched to N=60 not on opioids by age, sex and BMI
  - Dose response between opioid MED and apnea/hypopnea, obstructive apnea, hypopnea, and central apnea indices
  - 92% prevalence of ataxic or irregular breathing during NREM sleep at >/= 200 mg MED

Newly submitted study

- 9000 enrollees large pre-paid health plan on opioids at least 3 months
- Dramatic increase (24 fold) in risk of combined morbidity/mortality at 100 mg/day MED

What's causing the deaths?
A CDC opinion

"It has been difficult to determine the extent to which increases in opioid-related deaths have been due to specific prescribing practices, improper taking of the medication by patients, diversion of the drug from the patient to someone else, or other means".

Fingerhut, CDC, 2008

http://www.cdc.gov/nchs/products/pubs/pubd/hestats/poisoning/poisoning.htm (updated 3/6/2008)

Purdue Opinion-May 9, 2007 Letter Re: AMDG Opioid Dosing Guidelines

" More often accidental deaths involving opioid analgesics are due to abuse or misuse of opioids and not due to the therapeutic use of opioids for chronic pain."

New York Times, May 10, 2007

Narcotic Maker Guilty of Deceit Over Marketing

"Pleaded guilty …to criminal charges…"

"Purdue Pharma agreed to pay $600 million in fines.."

"…misled doctors and patients when it claimed the drug was less likely to be abused than traditional narcotics."

Ballantyne:Pain Physician; 2007; 10:479-91

- “Overall, the evidence supporting long-term analgesic efficacy is weak”
- “The putative mechanisms for failed opioid analgesia may be related to (rampant) tolerance or opioid-induced hyperalgesia”
- “The premise that tolerance can always be overcome by dose escalation is now questioned.”

Ballantyne, cont'd
Re: longer term clinical trials

- Good results from case series, but..
- "A review of the open-label follow-up studies (from RCTs), however, has shown that 56% of patients abandon the treatment because of lack of efficacy or side-effects."
- Many trials use 'enrichment"-select out non-responders pre-trial

Ballantyne: Re: effect on function and QOL

- "Epidemiological studies are less positive, and report failure of opioids to improve QOL in chronic pain patients."
- Eriksen, J Pain 2006: 125: 172-179
  - "…it is remarkable that opioid treatment of long-term/chronic non-cancer pain does not seem to fulfill any of the key outcome opioid treatment goals: pain relief, improved quality of life and improved functional capacity."

Ballantyne, Re: Addiction

- No clear case definition-true incidence unknown (addiction>craving)
- “After a decade or more of acceptance that therapeutic opioid use was unlikely to result in addiction (5%)…A systematic review published in 1992 (Fishbain et al, Clin J Pain 1992; 8: 77-85) reporting addiction rates of up to 18.9 % failed to penetrate…educational materials…”

Agency Medical Director's Opioid Dosing Guideline

- http://www-dev.agencymeddirectors.wa.gov/opioiddosing.asp#CME
- http://www-dev.agencymeddirectors.wa.gov

AMDG Opioid Dosing Guideline

- Developed during 2006 by 15 clinical pain specialists in collaboration with the AMDG
- It is an **Educational Pilot**
- We will conduct formal evaluation of impact during Spring-Summer, 2008
- Plan to reconvene clinical group Fall,2008 to review evaluation and plan next steps

Opioid Dosing Guideline

- **Part I-** If patient has not had clear improvement in pain AND function at 120 mg MED, “take a deep breath”
  - if needed, get one time pain management consultation (certified in pain, Neuro, Physiatry)
- **Part II-** guidance for patients already on very high doses above 120 mg MED

Other Important Considerations

- May want to use urine tox screen
- Are there other important comorbid issues-eg, past history substance abuse, **current smoking**

Innovations

- Opioid dosing calculator for MED
- 2 HRs free online CME (Category I)
- Educational pilot, not a new standard or regulation

OPIOID DOSE CALCULATOR

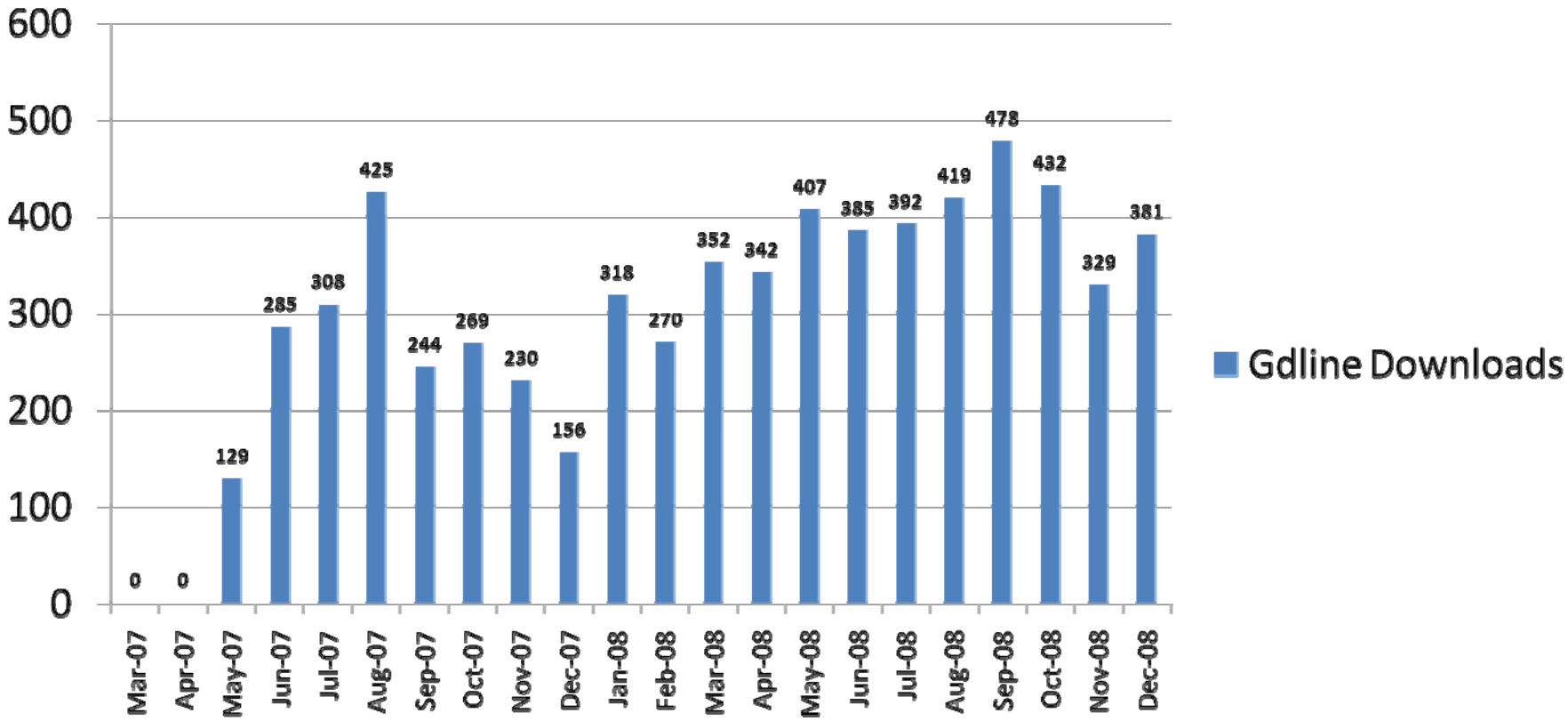
Optional:	Patient name:	
	Today's date:	**October 9, 2007**
Instructions:	Fill in the mg per day* for whichever opioids your patient is taking. The spreadsheet will automatically calculate the total morphine equivalents per day.	
Opioid (oral or transdermal):	**mg per day*:**	**Morphine equivalents:**
codeine		0
fentanyl transdermal (in mcg/hr)		0
hydrocodone		0
hydromorphone		0
methadone		
up to 20mg per day		0
21 to 40mg per day	Since doses at or below 40mg per day are below the threshold for pain management consultation no opioid conversion calculations are necessary for this dosing range (assuming no other opioids are being taken).	
41 to 60mg per day		0
>60mg per day		0
morphine		0
oxycodone		0
oxymorphone		0
TOTAL daily morphine equivalent dose (MED) =		0

* **Note: All doses expressed in mg per day with exception of fentanyl transdermal, which is expressed in mcg per hour**

Opioid Dosing Guideline Evaluation

- Subgroup of expert clinicians will advise evaluation
- Preliminary eval ideas:
  - Degree of diffusion, including geographic distribution of “hits” on website
  - Survey of primary care physicians to determine acceptability and utility of guideline
  - Opioid dosing patterns
  - Deaths

AMDG – Opioid Dosing Guideline



What's next?

- The AMDG opioid dosing guidelines are an educational pilot, not a new standard
- By March, 2009, evaluation of guideline implementation completed
- Reconvene pain expert advisory group

New Guidelines-will they help?

- **Utah**
  - Requested by statute
  - Great tools, eg, screening instruments for past substance abuse
  - No specific recommendation on dose-risk/benefit may be problematic at or above 120-200 mg/day
- **APS/AAPM-in press**
  - Evidence-based guidelines
  - High dose Rx at or above 200 mg/day MED

Must solve access problem

- Only 13 certified (pain) specialists agreed to be “go to” consultants on the AMDG website
- Not a single pain specialist in Spokane willing to see the “120” patients with chronic pain
- Heat on this point (When is a pain doctor a drug pusher? Tina Rosenberg, NYT Sunday Magazine, June 17, 2007)
- Considering advanced training for primary care docs to become qualified to mentor each other
- Have successfully “beta tested” telemedicine consults with pain specialists and primary care MDs

Proposed Prevention Measures-CDC Congressional Testimony-3/11/08

- Get the most out of state prescription drug monitoring programs
- Modify patient behavior with insurance mechanisms
- Screen for drug misuse in EDs
- Provide practice guidelines for primary care
- Make painkillers tamper resistant

Conclusions

- Dramatically increasing doses and deaths occurred rather quickly after law changes
- Guidelines with “best practices” have been around for years with little effect
- Focus on dosing is most likely method to prevent high doses associated with severe morbidity and mortality

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

THANK YOU!

For electronic copies of this presentation, please e-mail

Melinda Fujiwara
vasudha@u.washington.edu

Questions or innovative ideas, please
e-mail Gary Franklin

meddir@u.washington.edu