Opioids and Chronic Pain

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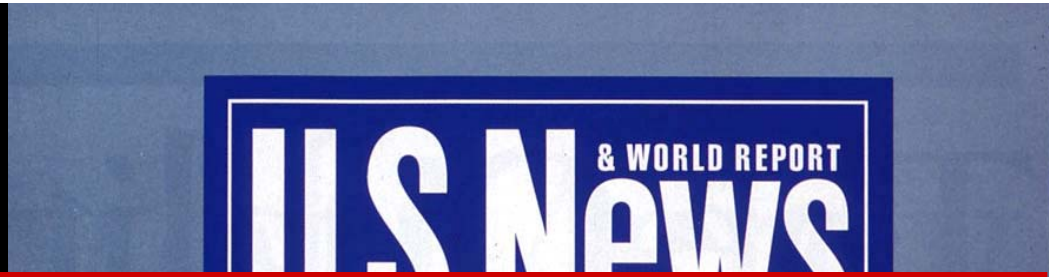
Good and **Bad News…**

- The **Bad News** – This morning I changed my slides…

- The **Good News** – This is a much better presentation.

The Problem…



Opioids = Pain Relief

More Opioids = More Pain Relief

Opioid Efficacy in Chronic Pain

- Most literature surveys & uncontrolled case series
- RCTs are short duration <4 months with small sample sizes <300 pts
- Mostly pharmaceutical company sponsored
- Pain relief modest
- Limited or no functional improvement

Balantyne JC, Mao J. NEJM 2003
Kalso E et al. Pain 2004
Eisenberg E et al. JAMA. 2005
Furlan AD et al. CMAJ 2006
Martell BA et al. Ann Intern Med 2007

# Issues Preventing Opioid Prescribing
n=111

Potential for patients to become addicted	**89%**
Potential for patients to sell or divert	**75%**
Opioid side effects	**53%**
Regulatory/law enforcement monitoring	**40%**
Hassle and time required to track/refill	**28%**

Upshur CC et al. J Gen Intern Med 2006

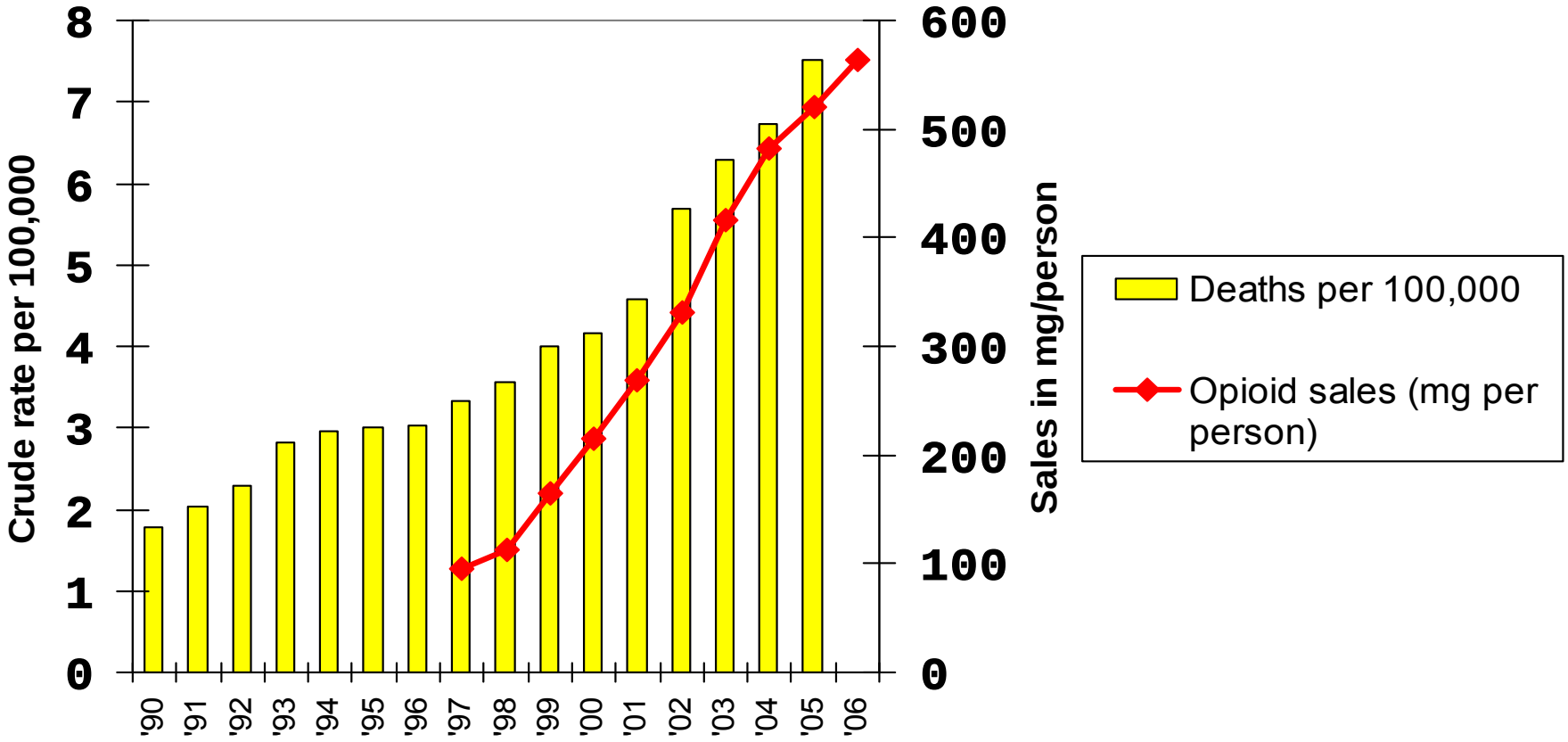
What is the Addiction Risk?

- Published rates of abuse and/or addiction in chronic pain populations are 3-19%
- Known risk factors for addiction to any substance are good predictors for problematic prescription opioid use
  - Past cocaine use, h/o alcohol or cannabis use
  - Lifetime history of substance use disorder
  - Family history of substance abuse, a history of legal problems and drug and alcohol abuse
  - Tobacco dependence
  - History of severe depression or anxiety

Akbik H et al. JPSM 2006
Ives T et al. BMC Health Services Research 2006
Liebschutz JM et al. J of Pain 2010
Michna E el al. JPSM 2004
Reid MC et al JGIM 2002

Unintentional Opioid Overdoses & Annual Prescription Opioid Sales

1990 - 2006



Source: Paulozzi, CDC, Congressional testimony, 2007 National Vital Statistics System

What is the Overdose Risk?

- Risk of fatal overdose seems directly related to the maximum prescribed daily opioid
  - Doses (morphine equivalents) 50-99 mg/d had a 3.7-fold increase in overdose risk
  - Doses ≥100 mg/d had an 8.9-fold increase in overdose risk with a 1.8% annual overdose rate
- Doses > 120 mg/d had 2x the risk of substance-related health services utilization encounters (withdrawal, intoxication, overdoses)

Dunn KM et al. Ann Intern Med 2010
Braden JB et al. Arch Intern Med 2010
Bohnert ASB et al. JAMA 2011

Case

A 42 year old man with chronic hip pain on disability presents requesting “oxys”. His hip pain began 2 years ago after a hip fracture complicated by postoperative joint infections. He was recently “cleared” by his orthopedist. He complains of inadequate pain relief and intolerances to a variety of nonopioids and nonpharmacotherapies.

- **Is his pain real and/or is he “drug seeking”?**
- **Should you prescribe opioid analgesics?**
- **If so, how will you know if the opioids are helpful or harmful?**

Is his **chronic** pain real?

- There are no “pain meters” & vital signs are not reliable
- Pain is subjective to the patient & to the examiner
- It is difficult to distinguish **inappropriate** drug-seeking from **appropriate** pain relief-seeking
- **There is no way on the first visit(s) to know for certain if the patient’s pain is real or not**

Is he **addicted** ("drug-seeking")?

- Physical dependence
  - *Biological adaptation*
  - Signs and symptoms of withdrawal (e.g., pain) if opioid is abruptly stopped

- Addiction (3 **C**'s)
  - *Behavioral maladaptation*
  - Loss of **C**ontrol
  - **C**ompulsive use
  - **C**ontinued use despite harm

} **Aberrant Medication Taking Behaviors** *(Pattern & Severity)*

- Opioid Dependence (DSM IV)
  - *Behavioral maladaptation+/- Biological*

Aberrant Medication Taking Behaviors

The Spectrum of Severity

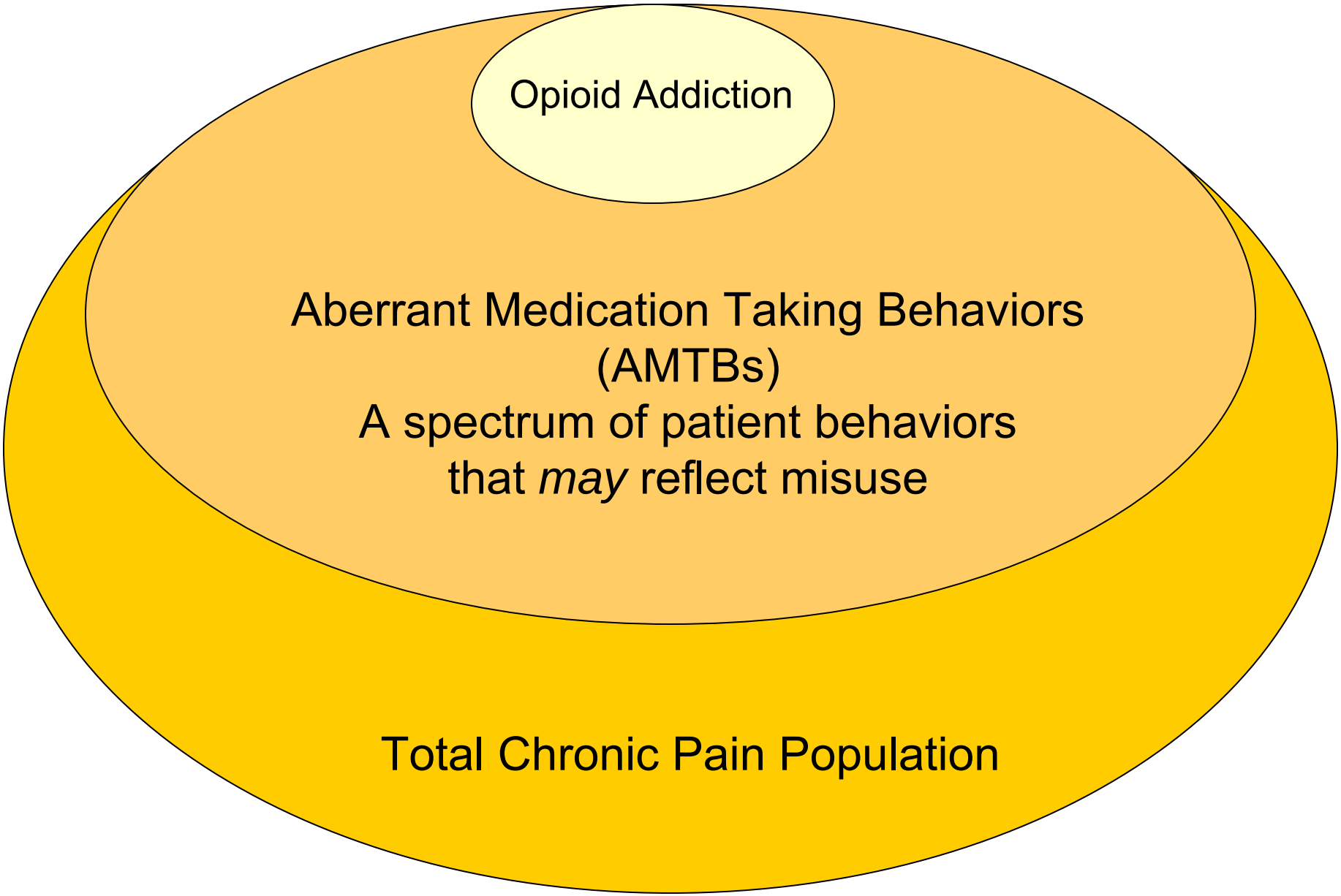
- Requests for increase opioid dose
- Requests for specific opioid by name, “brand name only”
- Non-adherence w/ other recommended therapies (e.g., PT)
- Running out early (i.e., unsanctioned dose escalation)
- Resistance to change therapy despite AE (e.g. over-sedation)
- Deterioration in function at home and work
- Non-adherence w/ monitoring (e.g. pill counts, urine drug tests)
- Multiple “lost” or “stolen” opioid prescriptions
- Illegal activities – forging scripts, selling opioid prescription

Aberrant Medication Taking Behaviors

Differential Diagnosis

- Inadequate analgesia – “Pseudoaddiction”
  - Disease progression
  - Withdrawal mediated pain
  - Opioid-induced hyperalgesia
- Addiction
- Opioid analgesic tolerance??
- Self-medication of psychiatric and physical symptoms other than pain
- Criminal intent - diversion

Weissman DE, Haddox JD. 1989
Evers GC. 1997
Chang C et al 2007


Opioid Addiction
Aberrant Medication Taking Behaviors
(AMTBs)
A spectrum of patient behaviors
that *may* reflect misuse
Total Chronic Pain Population

When Are Opioids Indicated?

- Pain is moderate to severe
- Pain has significant impact on function and on quality of life
- Non-opioid pharmacotherapy has been tried and failed
- **Patient agreeable to…**
  - **take opioid as prescribed (e.g. no dose escalation)**
  - **close monitoring (e.g. pill counts, urine drug testing)**

Variability Opioid Response

Mu Receptor

- G protein-coupled receptor family, signal via second messenger (cAMP)
- >100 polymorphisms in the human MOR gene
- Mu receptor subtypes
  - Not all patients respond to same opioid in same way
  - Not all pain responds to same opioid in the same way
  - Incomplete cross-tolerance between opioids

Opioid Safety

- Allergies are rare
- Side effects are common
  - Nausea, **sedation**, constipation
  - Urinary retention, sweating
- Organ toxicities are rare
  - Hypothalamic-pituitary-gonadal axis - ↑prolactin, ↓ LH, FSH, testosterone, estrogen, progesterone
- Overdose especially when combined w/ other sedatives

Opioid Choice

- Duration and onset of action
  - "Rate hypothesis" - fast on, fast off – most rewarding – addicting
  - Short-acting opioids increase risk of opioid-withdrawal mediated pain
- Patient's prior experience
  - *Mu* polymorphisms – differences in opioid responsiveness
- **Currently there are NO abuse resistant opioids or opioid formulations!!**

Key Principles

- Maintain a risk (harm) – benefit framework
- Judge the treatment NOT the patient

Assessing Benefit

PEG (Pain, Enjoyment, General activity) scale (0-10)

What number best describes your Pain on average in the past week? *(No pain - Pain as bad as you can imagine)*

What number best describes how, during the past week,

- **pain has interfered with your Enjoyment of life?** *(Does not interfere-Completely interferes)*
- **pain has interfered with your General activity?** *(Does not interfere – Completely interferes)*

Krebs EE, et al. J Gen Intern Med. 2009

Assessing Risk/Harm

"Universal Precautions"

- Risk assessment
- Agreements/contracts/informed consent
- Monitor for aberrant medication taking behavior
- Monitor for adherence, addiction and diversion
  - Urine drug testing
  - Pill counts
  - Prescription monitoring program data
- Initially small quantities & frequent visits
- Establish a refill & cross coverage system

FSMB Guidelines 2004 www.fsmb.org
Gourlay DL, Heit HA. Pain Medicine 2005
Chou R et al. J Pain 2009

Opioid Risk Assessment: **SOAPP® - SF**

Screener & Opioid Assessment for Patients with Pain

Evaluate for relative risk for developing problems (e.g. aberrant medication taking behaviors) 86% sensitive, 67% specific

0=Never, 1=Seldom, 2=Sometimes, 3=Often, 4=Very often

1. How often do you have **mood swings**?
2. How often do you **smoke a cigarette** within an hour after you wake up?
3. How often have you taken **medication other than the way it was prescribed**?
4. How often have you used **illegal drugs** (for example, marijuana, cocaine, etc) in the past 5 years?
5. How often, in your lifetime, have you had **legal problems** or been arrested?

≥ 4 is POSITIVE

< 4 is NEGATIVE

Discussing Monitoring with Patients

- Discuss risks of opioid medications
- Assign responsibility to look for early signs of harm
- Discuss agreements, pill counts, drug tests, etc. as ways that you are helping to protect patient from getting harmed by medications
  - Statin - LFT monitoring analogy
- Use consistent approach, but set **level of** monitoring to match risk

Monitoring
Urine Drug Tests

- **Evidence of therapeutic adherence**
- **Evidence of non-use of illicit drugs**

- Know limitations of test and your lab
- Know a toxicologist/clinical pathologist
- Complex patient-physician communication

Gourlay DL, Heit HA, Caplan YH. Urine drug testing in primary care. Dispelling myths and designing strategies monograph (www.familydocs.org/files/UDTmonograph.pdf)

Urine Toxicology Monitoring in Patients on Opioids for Chronic Pain

		BEHAVIOR ISSUES		
		YES	**NO**	**TOTAL**
URINE TOX	**POSITIVE**	10 (8%)	26 (21%)	36 (29%)
	NEGATIVE	17 (14%)	69 (57%)	86 (71%)
	TOTAL	27 (22%)	95 (78%)	122

26/122 (21%) of patients had no aberrant behavioral issues BUT had abnormal drug test

Katz NP et al. Clinical J of Pain 2002

Monitoring

Pill & Patch Counts

- **Confirm medication adherence**
- **Minimize diversion**
- My strategies…
  - 28 day (rather than 30 day) supply
  - If patient “forgets” pills, schedule return visit with in a week

Continuation of Opioids

- You must convince yourself that there is benefit
- Benefit must outweigh observed harms
- If small benefit, consider increasing dose as a **“test”.**
- If no benefit, hence benefit cannot outweigh risks – so STOP opioids. (Ok to taper and reassess.)
- You do not have to prove addiction or diversion – only assess Risk-Benefit ratio

Discussing Lack of Benefit/Increased Risk

- **A demonstration….**

Exit Strategy
Discussing Lack of Benefit

- Stress how much you believe / empathize with patient's pain severity and impact
- Express frustration re: lack of good pill to fix it
- Focus on patient's strengths
- Encourage therapies for "coping with" pain
- Show commitment to continue caring about patient and pain, even without opioids i.e., you are abandoning the treatment, not the patient
- Schedule close follow-ups during and after taper

Exit Strategy
Discussing Possible Addiction

- Give specific and timely feedback why patient's behaviors raise your concern for possible addiction
- Benefits no longer outweighing risks
  - "I cannot responsibly continue prescribing opioids as I feel it would cause you more harm than good."
- Always offer referral to addiction treatment
- Stay 100% in "Benefit/Risk of Med" mindset

Summary

- Opioids can be effective and safe but are imperfect
- Use risk/harm-benefit framework
- Use consistent approach, but set level of monitoring to match risk
- Judge the treatment and not the patient
- If there is benefit in the absence of harm, continue opioids
- If there is no benefit or if there is harm, discontinue opioids

Opioidprescribing.com

- BUSM's new online program, with material from the fall meeting in this series.
- **3 *AMA PRA Category 1 Credits*™** available, plus risk management and opioid education credits