# Evaluation and Treatment of Pain and REMS

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# Disclosure

- Anthony Dekker, DO has presented numerous programs on Chronic Pain Management and Addiction Medicine. The opinions of Dr Dekker are not necessarily the opinions of the VA, the DoD, Indian Health Service or the USPHS. Dr Dekker has no conflicts to report. Dr Dekker is not representing any federal organization. Dr Dekker is a clinical professor at ATSU and George Washington University

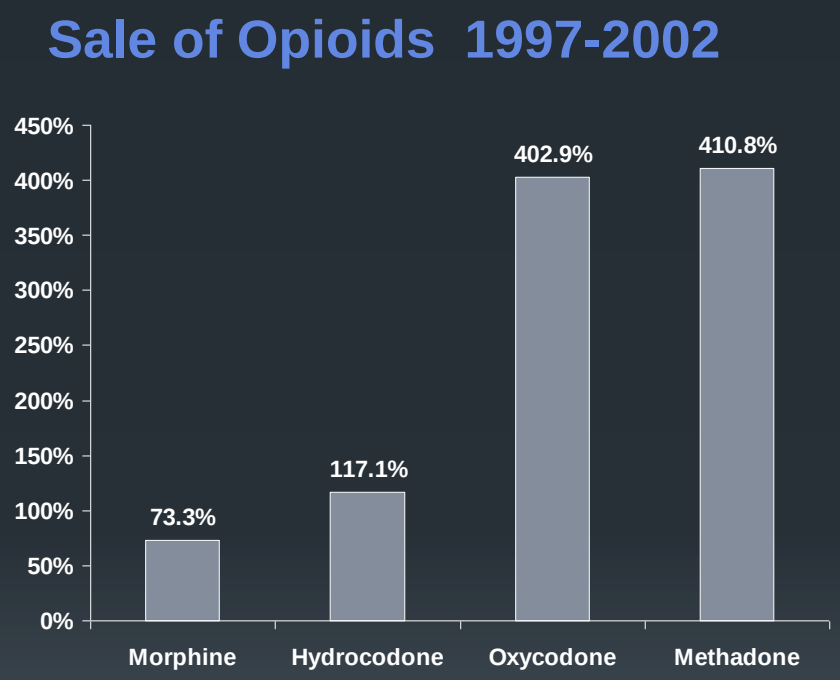
# Pain & Opioids in the US

- Discrepancies in Treatment, *JAMA Pediatr. doi:10.1001/jamapediatrics.2015.1915 Published online September 14, 2015.*
- Rising concerns of complications
- 2016 CDC and HHS Guidelines
- Chronic  Non-Malignant Pain Evaluation and Care evaluations
- Increasing complications from misuse and diversion
- Provider and Pharmacy concerns
- Patient and Community expectations
- DEA investigations
- Patient perceptions of lack of care

# NASPER

## National All Schedules Prescription Electronic Reporting Act

- Signed into law by President Bush August 2005
- Point of care reference to all controlled substances prescribed to a given patient
- MD PMP is to monitor patients and providers
- Treatment tool vs. Law enforcement tool?




Source: 2002 National Survey on Drug Use and Health (NSDUH). Results from the 2002 National Survey on Drug Use and Health: National Findings. Department of Health and Human Services

# Risk Assessment Tools: Examples



| Tool | # of items | Administered |
|---|---|---|
| **Patients considered for long-term opioid therapy:** | | |
| ORT Opioid Risk Tool | 5 | By patient |
| SOAPP® Screener & Opioid Assessment for Patients w/ Pain | 24, 14, & 5 | By patient |
| DIRE Diagnosis, Intractability, Risk, & Efficacy Score | 7 | By clinician |
| **Characterize misuse once opioid treatments begins:** | | |
| PMQ Pain Medication Questionnaire | 26 | By patient |
| COMM Current Opioid Misuse Measure | 17 | By patient |
| PDUQ Prescription Drug Use Questionnaire | 40 | By clinician |
| **Not specific to pain populations:** | | |
| CAGE-AID Cut Down, Annoyed, Guilty, Eye-Opener Tool, Adjusted to Include Drugs | 4 | By clinician |
| RAFFT Relax, Alone, Friends, Family, Trouble | 5 | By patient |
| DAST Drug Abuse Screening Test | 28 | By patient |
| SBIRT Screening, Brief Intervention, & Referral to Treatment* | Varies | By clinician |

# Chronic Non-Malignant Pain (CNMP)

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- Osteoarthritis
- Low back pain and hip pain
- Myofascial pain
- Vaso-Occlusive Disease
- Fibromyalgia
- Headaches (e.g., migraine, tension-type, cluster)
- “Central pain” (e.g., spinal cord injury, CVA, MS)
- Chronic abdominal pain (e.g., chronic pancreatitis, chronic PUD, IBS)
- CRPS, Types I and II
- Phantom limb pain
- Peripheral neuropathy
- Neuralgia (e.g., post-herpetic, trigeminal)

# Treatment Goals



- In malignant pain we treat to goal
- In chronic non malignant pain we treat to function

# Treatment goals in managing CNMP



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- Improve patient functioning
- Identify, eliminate/reduce pain reinforcers
- Increase physical activity
- Decrease or eliminate illegal or complicating drug use

**The goal is NOT pain eradication!**

# CNMP:
## *The clinical challenge*



- Be aware of the “Heart Sink” patient.
- Be aware of the borderline patient
- Remain within your area of expertise.
- Stay grounded in your role.
  - FIRST….Do no harm
  - THEN…..
    - Cure sometimes
    - Comfort always

# Non-pharmacologic treatments for CNMP



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- ✓Physical therapy – conditioning, thermal therapies
- ✓Pain Psychology – relaxation / counseling / expectations orientation
- ✓Traditional Indian Medicine
- ✓Massage therapy
- ✓Osteopathic and Chiropractic Manipulative Therapies
- ✓Spinal manipulation
- ✓Acupuncture, with and without stimulation
- ✓TENS units and micro-current therapies
- ✓Nerve ablations and blocks
- ✓Pain management group
- ✓Yoga and meditation

# Non-opioid medications for CNMP

- Acetaminophen
- Non-steroidal anti-inflammatory drugs (NSAIDS)
- Tricyclics
- Anti-depressants/anxiolytics
- Anti-convulsants
- Muscle relaxants
- Topical preparations–e.g. anesthetics, aromatics
- Others (e.g., tramadol)

# Non-opioid medications (cont.)

- **Non-steroidal anti inflammatory drugs (NSAIDS) Inhibit prostaglandin synthesis:**
  - Works on Cyclo-Oxygenase (COX) COX-1 and COX-2
  - ↓ pain-minutes to hours

- **COX-1:**

  Aspirin, Ibuprofen, Naproxen, Ketoprofen, Indomethacin, Diclofenac, Piroxicam, Sulindac

# Non-opioid medications (cont.)

- **COX-2 Inhibitors:**
  - ↓ gastrointestinal effect
  - Normally not present but induced during inflammation
  - Celecoxib (Celebrex®);
  - Rifecoxib (Vioxx®); Valdecoxib (Bextra®) *withdrawn from market due to increased cardiovascular risk*

# Non-opioid medications (cont.)

- **Antidepressants:**
  - ↓ reuptake of serotonin & norepinephrine
  - ↑ sleep
  - Enhance descending pain-modeling paths
  - Tricylics —amitriptyline (Elavil®)—most studied/most SE's and nortriptyline (Pamelor®)
  - SSRIs—not as effective
  - SNRI (venlafaxine,Effexor®;duloxetine,Cymbalta®) preliminary evidence of efficacy in neuropathic pain

# Non-opioid medications (cont.)

- **Antiepileptic drugs:**
  - ↓ neuronal excitability
  - Exact mechanism is unclear
  - Not due to antiepileptic activity
    e.g. phenobarbital is poor analgesic
  - Good for stabbing, shooting, episodic pain from neuropathic pain
  - Gabapentin (Neurontin®)
  - Pregablin (Lyrica®)
  - Carbamazepine (Tegretol®)
  - Topiramate (Topamax®)

# Non-opioid medications (cont.)

- **Other drugs:**
  - **Tramadol (Ultram)**
    - Mixed mu opioid agonist & NE/serotonin reuptake inhibitor
    - Seizure threshold changes
    - NM and TN (now DEA Scheduled)
  - **Corticosteroids**
    - ↓ inflammation, swelling
  - **Baclofen**
    - GABA receptor agonist
    - Used for spasticity

# Indications for opioid therapy

1. Is there a ***clear diagnosis***?
2. Is there ***documentation*** of an adequate work-up?
3. Is there ***impairment of function***?
4. Has non-opioid multimodal therapy ***failed***?
5. Have ***contraindications*** been ruled out?

**Begin opioid therapy:**

Document

Monitor

Avoid poly-pharmacy

# Contraindications to opioid therapy

- Allergy to opioid medications ~ ***relative***
- Current addiction to opioids ~ ***?absolute***
- Past addiction to opioids ~ ***?absolute***
- Current /past addiction, opioids never involved ~ ***relative; absolute?? if cocaine, methamphetamine or other stimulants***
- Severe COPD or OSA~ ***relative***
- ***Concurrent Sedative hypnotics~relative***

# Pain Patient on Opioids + New Provider

## Are chronic opioids appropriate?

### YES!

**Re-document:**
- Diagnosis
- Work-up
- Treatment goal
- Functional status
- Pain P&P

**Monitor Progress:**
- Medication counts
- Function
- Refill flow chart
- Occasional urine toxicology
- Adjust medications
- Watch for scams

### UNSURE

**Physical Dependence vs Addiction:**
- Chemical dependence screening
- Toxicology tests
- Medication counts
- Monitor for scams
- Reassess for appropriateness

**YES!**
- Discontinue opioids
- Instruct patient on withdrawal symptoms
- OBOT Buprenorphine
- Tell patient to go to ER if symptoms emerge

### NO

Educate patient on need to discontinue opioids

**Emergency?**
ie: overdoses
selling meds
altering Rx

**NO!**

Stop or quick taper (document in chart)

OR

10-week structured taper

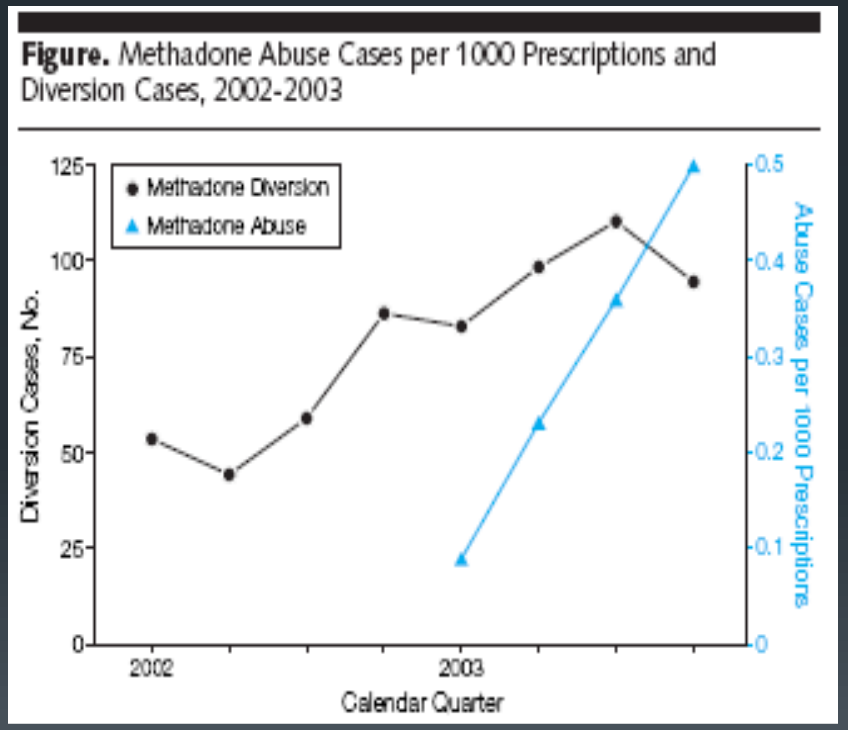
OR

Discontinue opioids at end of structured taper

# FDA Methadone Warning

**FDA ALERT [11/2006]: Death, Narcotic Overdose, and Serious Cardiac Arrhythmias**

**FDA has reviewed reports of death and life-threatening side effects such as slowed or stopped breathing, and dangerous changes in heart beat in patients receiving methadone. These serious side effects may occur because methadone may build up in the body to a toxic level if it is taken too often, if the amount taken is too high, or if it is taken with certain other medicines or supplements. Methadone has specific toxic effects on the heart (QT prolongation and Torsades de Pointes). Physicians prescribing methadone should be familiar with methadone's toxicities and unique pharmacologic properties. Methadone's elimination half-life (8-59 hours) is longer than its duration of analgesic action (4-8 hours). Methadone doses for pain should be carefully selected and slowly titrated to analgesic effect even in patients who are opioid-tolerant. Physicians should closely monitor patients when converting them from other opioids and changing the methadone dose, and thoroughly instruct patients how to take methadone. Healthcare professionals should tell patients to take no more methadone than has been prescribed without first talking to their physician.**



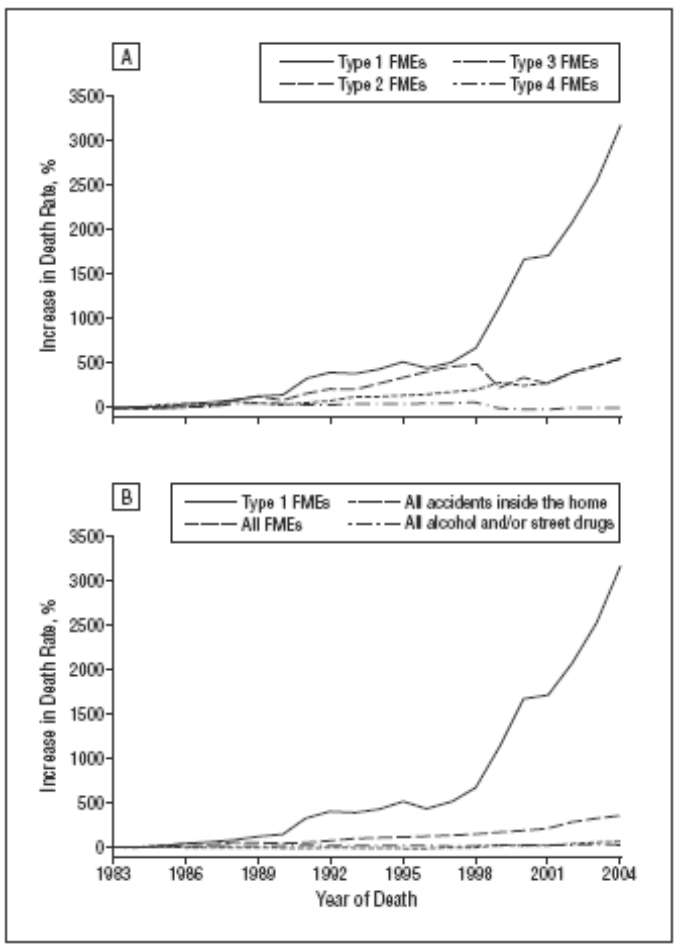



**Figure 2.** Trends in the US fatal medication error (FME) death rate by type of circumstance in which the FME occurs (A) and for various comparison groups (B) (January 1, 1983–December 31, 2004).

## Upper Graph Fig 2a

- Type 1 *(Home with "EtOH/Street")* has increased by **3196%**
  - **Steep and accelerating rate (p<0.001)**
- Type 2 *(Home without EtOH/Street)* and Type 3 *(Non-Home with EtOH/Street)* increased 564% and 555%, respectively
- Type 4 *(Non-Home without "EtOH/Street")* only increased 5%

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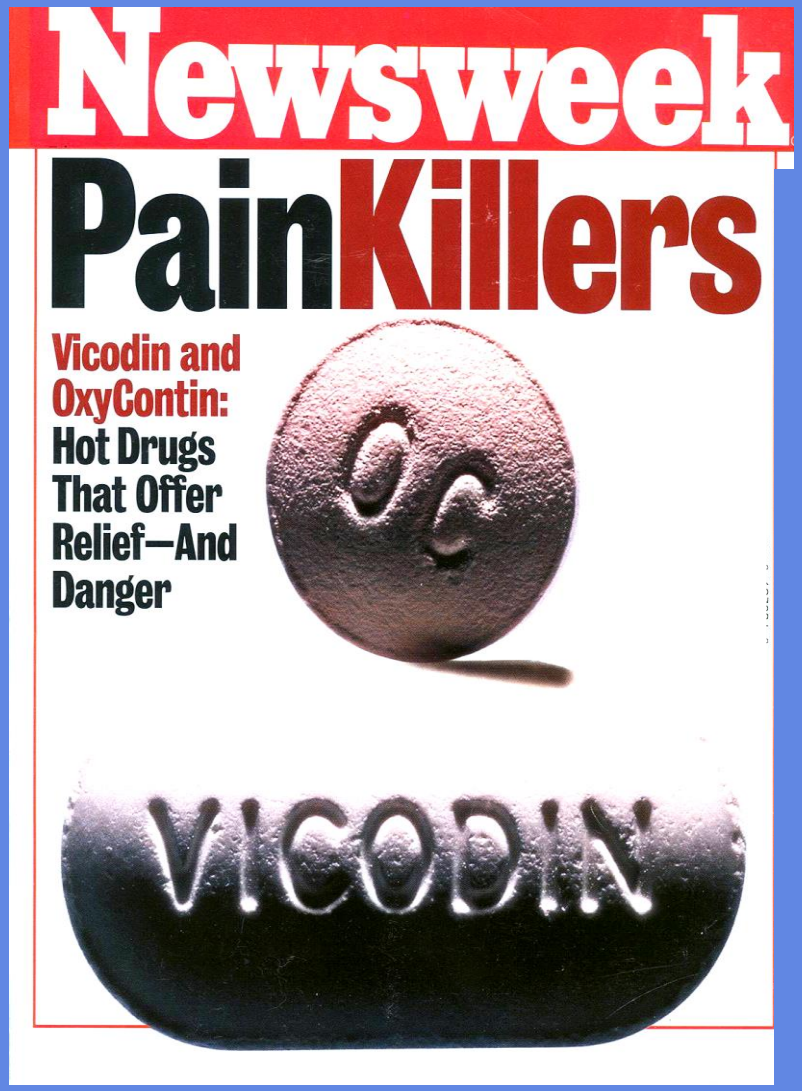
## Lower Graph Fig 2b

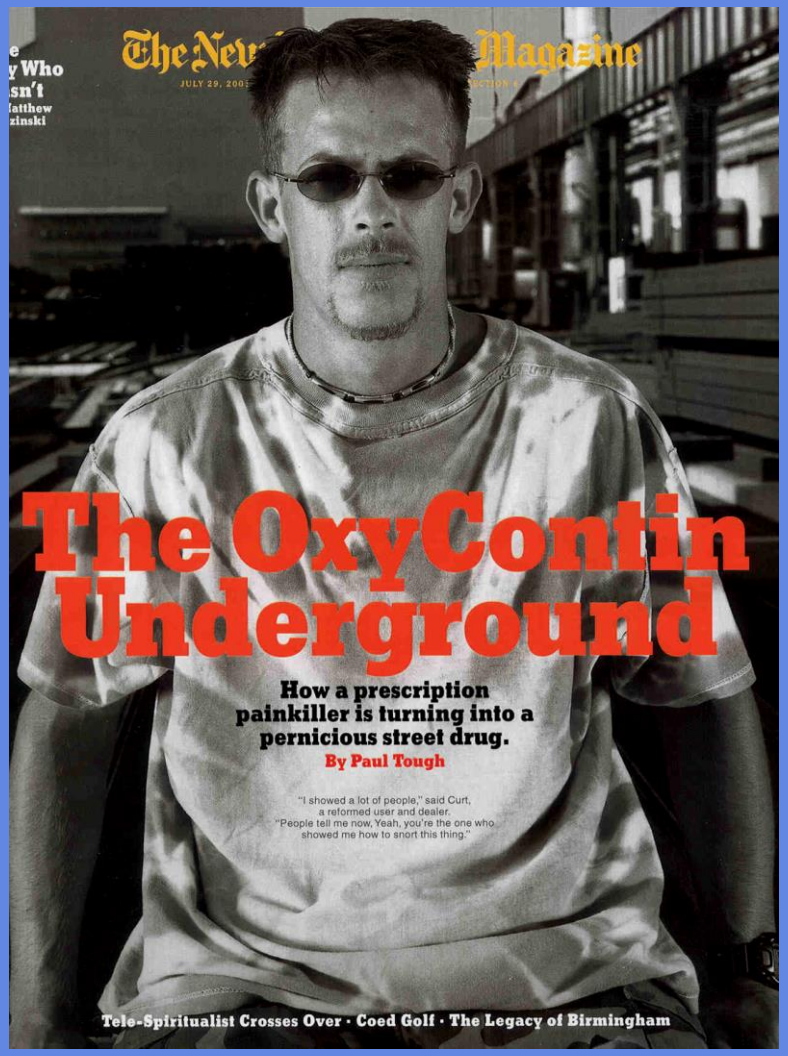
- Type 1 has three components:
  - Fatal Medication Errors
  - Occurring at home
  - In conjunction with EtOH/Street drugs
- The 3 components graphed separately show slight increase
- Component combined (Type 1) shows steep increase by **3196%**

Phillips DP et al. Arch Intern Med. 2008;168(14):1561-66.

- In a study of teenagers who had used drugs illicitly, 6 opioids accounted for 68% of the drugs used, 79% of major outcomes, and 100% of the deaths.

- Zosel A, Bartelson BB, Bailey E, Lowenstein S, Dart R. Characterization of adolescent prescription drug abuse and misuse using the Researched Abuse Diversion and Addiction-related Surveillance (RADARS®) System. *J AmAcad Child Adolesc Psychiatry*. 2013;52(2):196-204.e2. doi:10.1016/j.jaac .2012.11.014.


Newsweek
PainKillers
Vicodin and OxyContin: Hot Drugs That Offer Relief—And Danger
VICODIN


The New Magazine
The OxyContin Underground
How a prescription painkiller is turning into a pernicious street drug.
By Paul Tough
"I showed a lot of people," said Curt, a reformed user and dealer. "People tell me now, Yeah, you're the one who showed me how to snort this thing."
Tele-Spiritualist Crosses Over · Coed Golf · The Legacy of Birmingham

# Landscape of Drug* Abuse among Teens



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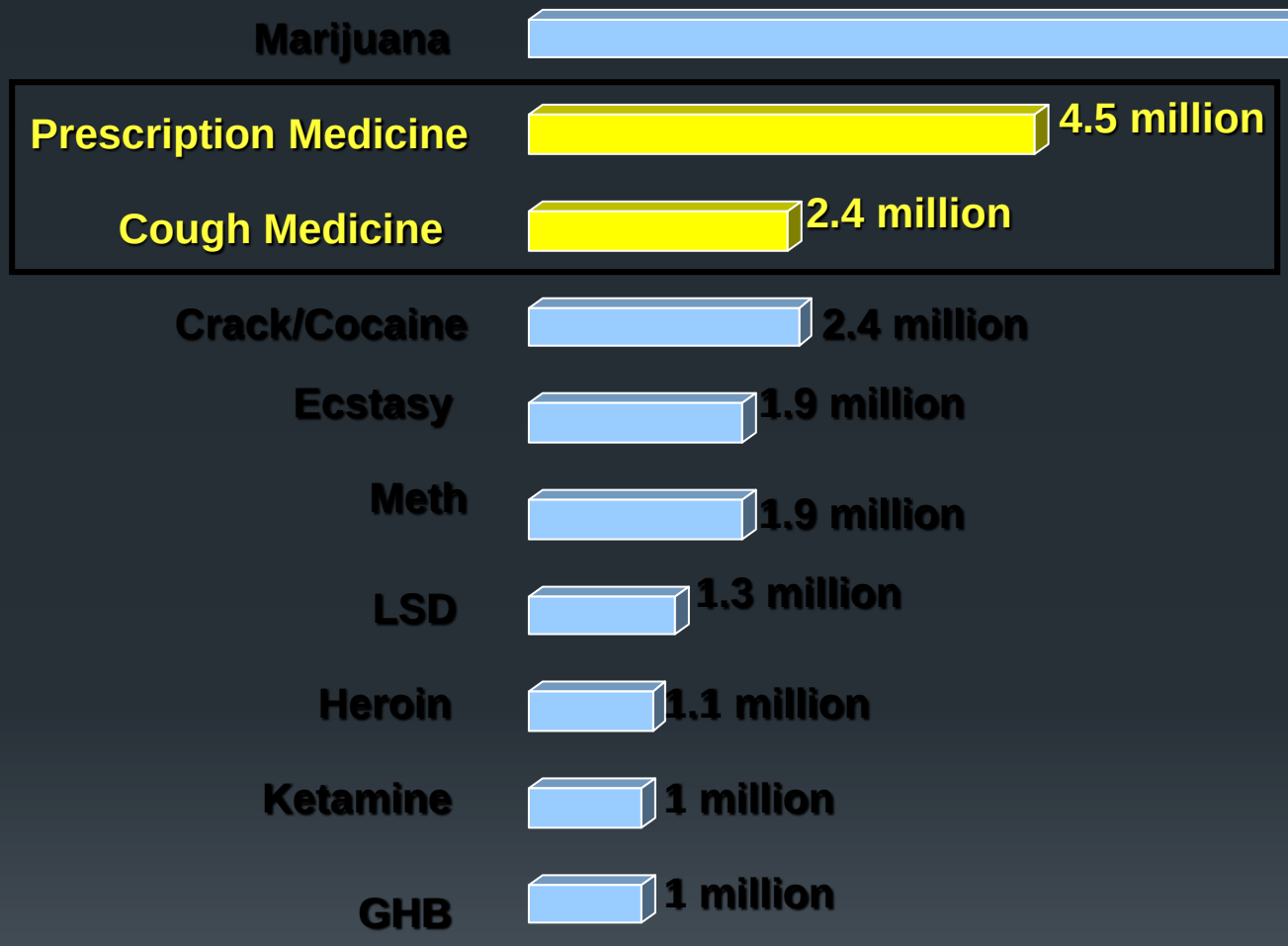
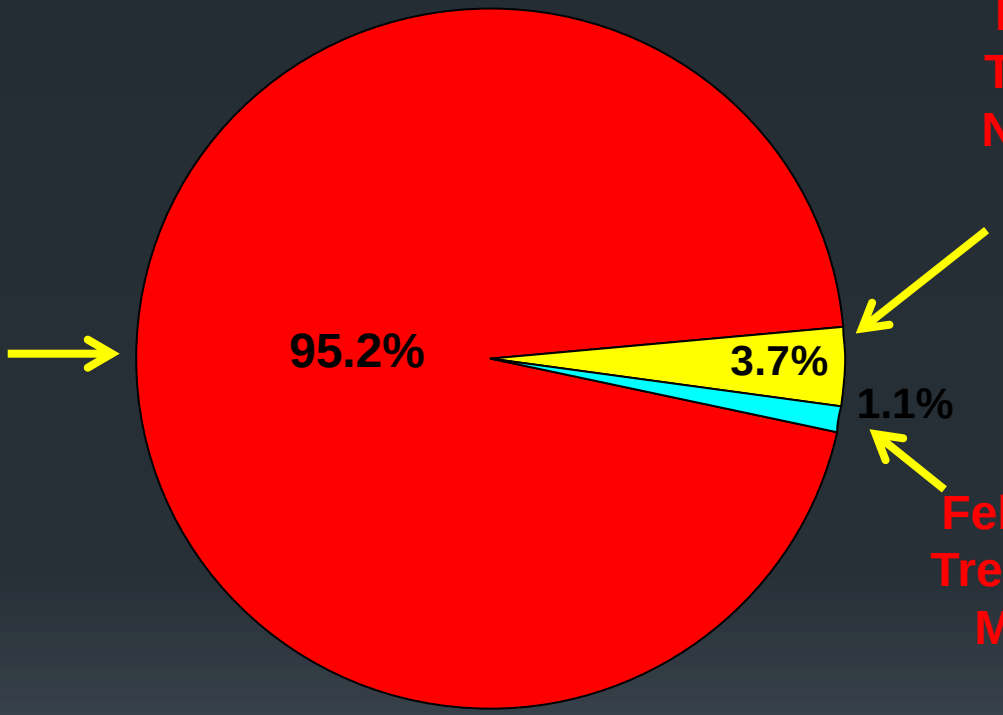



*Excludes ETOH

NSDUH, 2006

# Past Year Perceived Need for and Effort Made to Receive Specialty Treatment among Persons Aged 12 or Older Needing But Not Receiving Treatment for Illicit Drug or Alcohol Use: 2008






**20.8 Million Needing But Not Receiving Treatment for Illicit Drug or Alcohol Use**

(233,000)

Source: NSDUH 2008

# "Pharming Culture"



- ✓Today's teens are more likely to have abused Rx and OTC drugs than most illicit drugs
- ✓Every day 2,500 teens 12-17 *try* a painkiller for the 1st time

MTF, 2006

# Concerning Trends



- **Adolescents 12-13**
- **Teen Females**
- **Young Adults 18-24**

# Top Reasons for Rx & OTC Drug Misuse

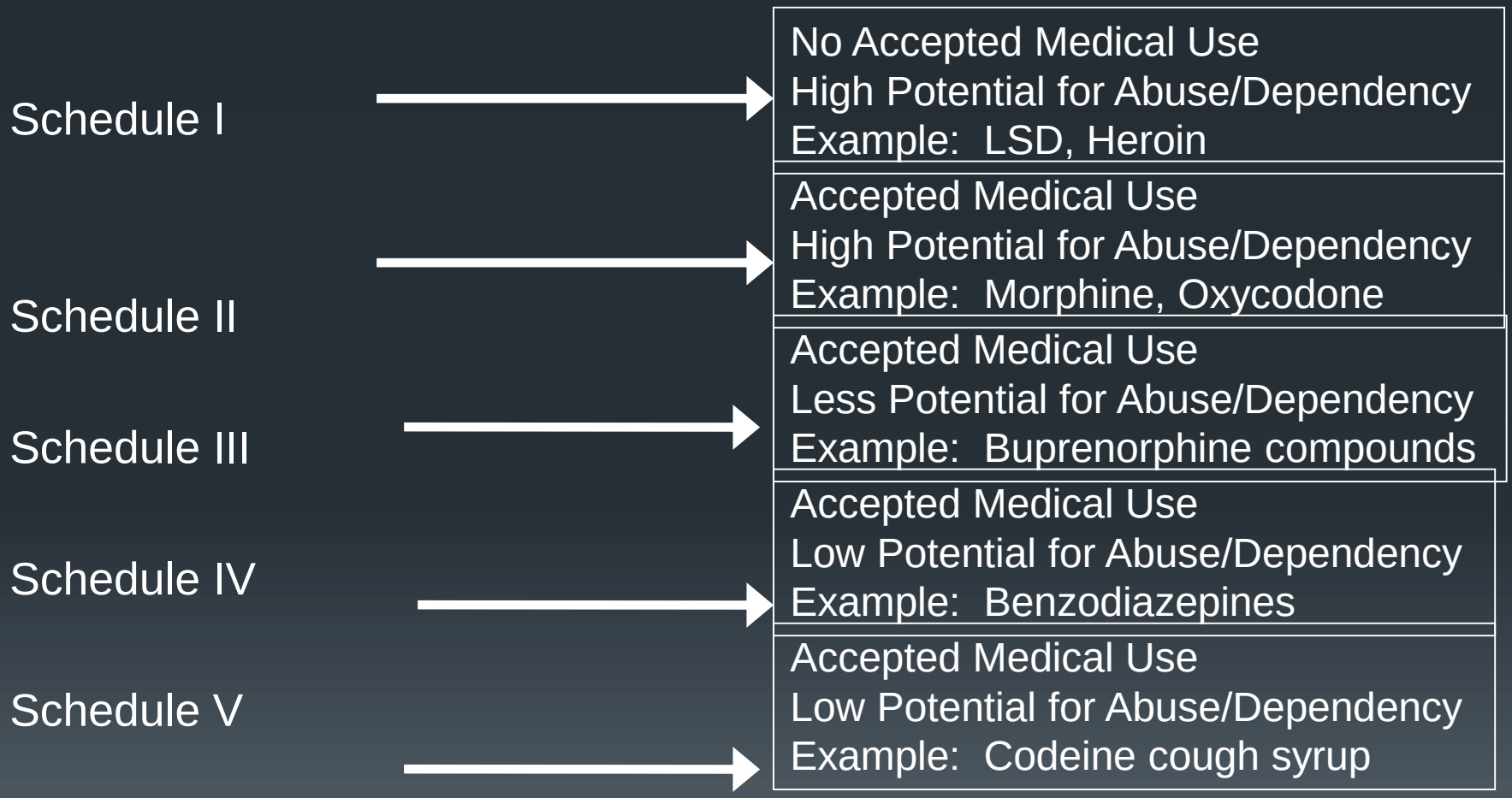


- ✓**Social with friends**
- ✓**Legal - Widely Available**
- ✓**Easily Accessible**
- ✓**Affordable: Low Cost/Free**
- ✓**Safe - Prescribed**
- ✓**Non-addictive: Medicine**

Partnership Attitude Tracking Survey (PAT): Released in April 2006 by The Partnership for a Drug-Free America

# Schedules of Substances

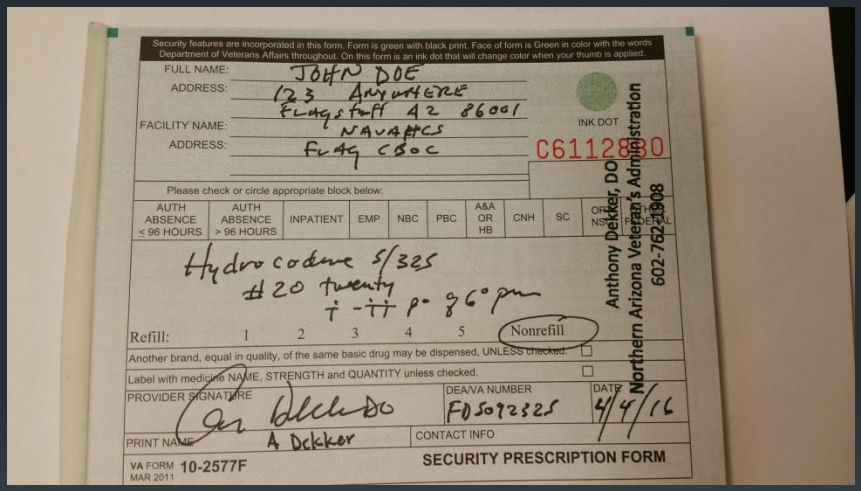




# Prescription Requirements

In order to be legal, a prescription must:

- Be issued by a registered practitioner
- For a legitimate medical purpose
- In the usual course of professional practice




**21 CFR §1306.04(a)**

# Prescription Requirements



- DEA does not define nor regulate medical practice standards. State Medical Boards do.
- There are no federal limits on the quantity of controlled substances that may be prescribed. Be careful.
- Corresponding responsibility for proper prescribing & dispensing rests with the pharmacist who fills the prescription.

# Medical issues in opioid prescribing

- Potential benefits
  - Analgesia
  - Function
  - Quality of life
  - Lower costs
- Potential risks
  - Toxicity
  - Functional impairment
  - Physical dependence
  - Addiction
  - Hyperalgesia
  - Overdose

# Review of opioid efficacy (cont.)





- **In long-term studies**:
  - Usually observational – non randomized / poorly controlled
  - Treatment durations ≤ 6 years.
  - Patients usually attain satisfactory analgesia with moderate non-escalating doses (≤ 195 mg now reduced to 100mg morphine/d), often accompanied by an improvement in function, with minimal risk of addiction.
- The question of whether benefits can be maintained over years rather than months remains unanswered.
  - Ballantyne JC: Southern Med J 2006; 99(11):1245-1255

# Conclusions as to opioid efficacy

- Opioids are an essential treatment for some patients with CNMP.
  - They are rarely sufficient
  - They almost never provide total lasting relief
  - They ultimately fail for many
  - They pose some hazards to patients and society
- It is not possible to accurately predict who will be helped – but those with contraindications are at high risk

# Desirable patient characteristics:

- No substance abuse disorder
- Reliable
- History of good medical compliance
- Willing to do their part to recover
- Recognizes that opioids are only a partial solution
- Good support (no substance abusers in the home)

# If prescribing opioids:

- Establish treatment goals, such as:
  - Functional improvement
    - Work
    - Play
    - Socialization
  - Affective normalization
  - Pain ***reduction*** (versus pain ***relief***)

# Formulate a treatment plan:

- Goals
  - Function
    - What should the person do anatomically?
  - Quality of life
  - Pain
  - Affect?
- Opioids or not
- Other treatment components

# Practical suggestions:



- Have realistic expectations
- Treat the entire patient, holistic care
- Select appropriate patients
  - Screen for contraindications!
  - ***Be comfortable screening for Substance Use***
  - If pain does not result primarily from activity in the nociceptive system, it will not be eliminated by
    - Opioids / Spinal fusion / Epidural steroid injections / Antidepressants / NSAIDs

# Conclusions as to opioid efficacy

- A trial (1-2 mo±) generally is safe
- (IF contraindications are ruled out)
- People who expect to take opioids and lie around the house while they get well, won't.
  - Push functional restoration, exercises
  - Lifestyle changes and weight loss
  - Make increased drugs contingent on increased activity

# Kratom

- Illegal in Thailand
- Mu receptor agonist and a stimulant
- Currently legal in the US
- Over 50% of the toxicology of a major lab screening patients with addictions were positive.  Only two labs testing as of January 2013.


eXperience
KRATOM
Black Label

# Mitragyna Speciosa

- Used in:
  - Malaysia
  - Thailand
  - Indonesia
- Local names:
  - Ithang
  - Biak Biak
  - Ketum
  - Kakuam

# Kratom Pharmacology

- Mitragynine
- Structurally similar to some hallucinogens
- No hallucinogenic activity or effects
- Acts on opioid receptors

# Kratom & Opioid Treatment

- Currently used for heroin and methadone dependence in some countries
  - New Zealand
  - Thailand
- Used in detox to manage withdrawal symptoms from opioids


CLUB 15
KRATOM
XL
15 CAPSULES
ULTRA ENHANCED KRATOM

# Kratom

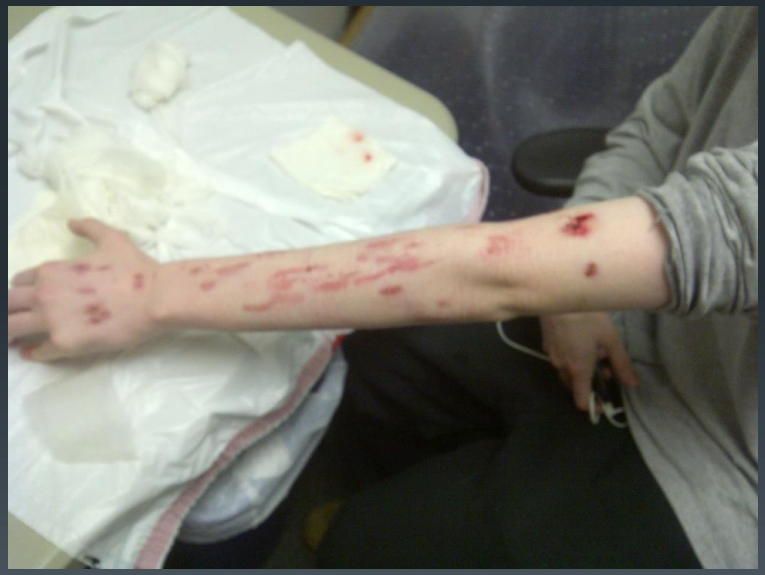
- Seems to be a stimulant in lower doses
  - Mitragynine
- Seems to be sedative in higher doses
  - 7 hydroxymitragynine
- Often produces a mixed effect
- Onset 5 t o 10 minutes
- Duration several hours

# Kratom Side Effects

- Short term (immediate)
  - Dry mouth
  - Increased or decrease urination
  - Loss of appetite
  - Nausea and/or vomiting
- Side effects
  - Anorexia/weight loss
  - Depression
  - Addiction

# Krokodil

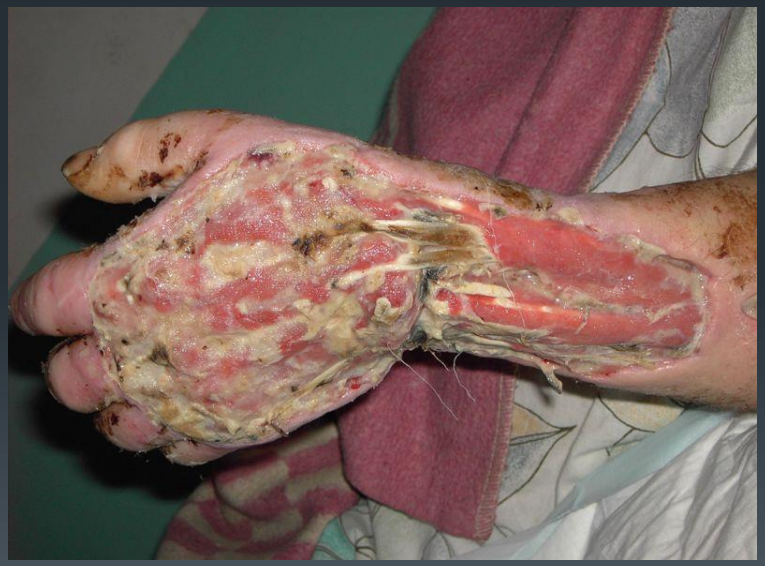
- desomorphine that is home-cooked from codeine using toxic household products including paint thinner, gasoline, red phosphorus and iodine. When injected it is supposedly 8-10 times more potent than heroin, faster-acting, but shorter-lasting.

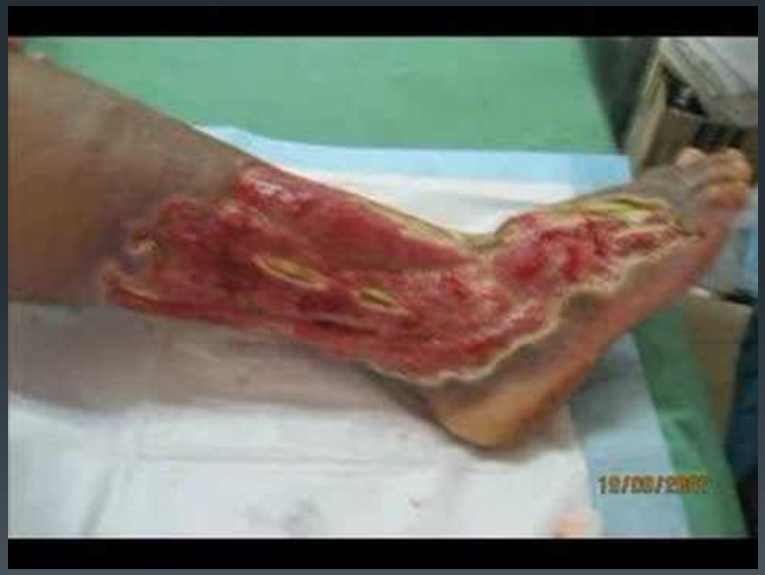


# Krokodil

- Vasculitis
- Necrosis
- Infection with resistance
- Analgesia

# Vasculitis, Ischemia, numb





# Acetyl fentanyl

- Schedule I
- Russian Mafia
- Enhanced mu receptor affinity
- Enhancement for heroin when cut

- Philadelphia and Pittsburgh had over 50 deaths in 2013
- DEA believes that 10% of all heroin deaths are related to illegal fentanyl

# IDU for several medications