CRIME LAB
ORANGE COUNTY, CALIFORNIA

Opioids: Use, Abuse and Cause of Death

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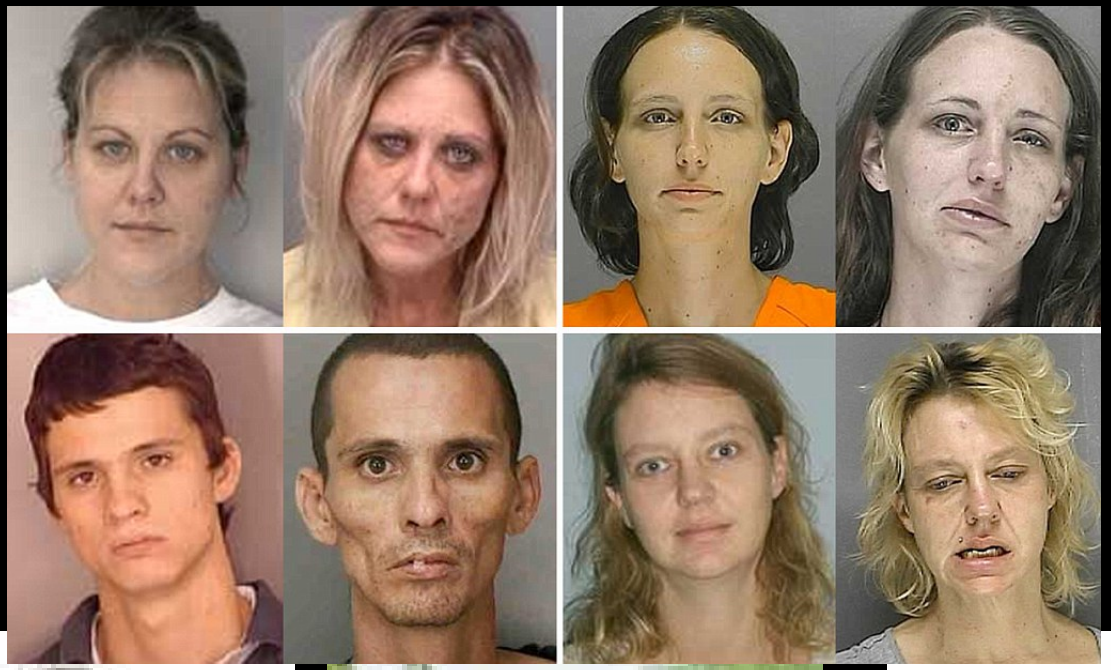
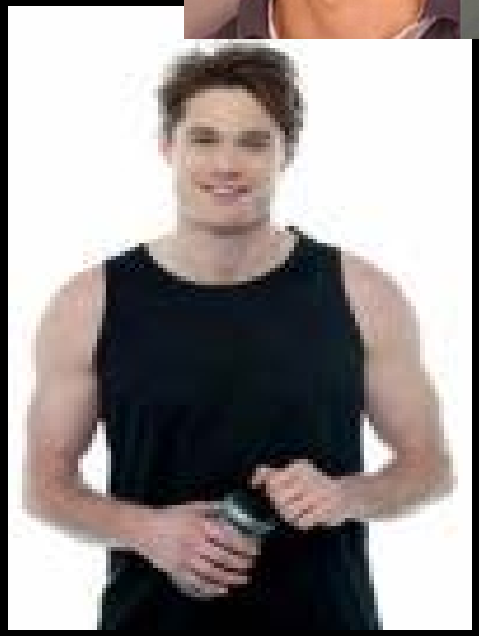
Opioids

- Opioid: Any psychoactive chemical that resembles morphine or other opiates in its pharmacological effects.





Opioid Use

- Opioid prescriptions have increased substantially in the last 20 years, due to consensus in the medical community that non-cancer pain should be treated.

Product	Prescriptions
Morphine	up 59%
Oxycodone	up 23%
Hydromorphone	up 19%
Fentanyl	up 1168%

Throm. Managing chronic pain: an analysis of the use of opioids. Pharmacy Times (online) July 1, 2005.

Opioid Abuse

- DEA reports a 400% increase between 1998 and 2008 in substance abuse treatment admissions from prescription pain medications.
- ER visits for “non-medical use” of painkillers have doubled over the past 5 years.
  - Defined as: higher than recommended dose, taking a drug prescribed to another, drug-facilitated sexual assault, misuse/abuse.
  - Oxycodone, hydrocodone, methadone most common

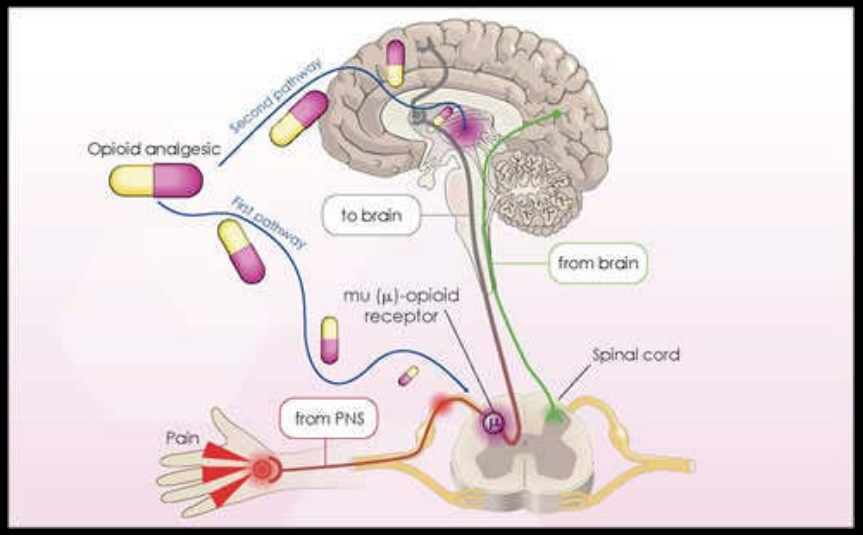
MedPage Today, ABC News June 20, 2010

Top 100 Drugs

- #22 - Suboxone (buprenorphine)
- #25- OxyContin (oxycodone)

Opioid Effects

- Pain relief (analgesia)
- Euphoria
- Sedation
- Respiratory depression
- Constipation
- Itching
- Constricted pupils



3 Opioid Receptors

- Three major receptor subtypes
  - Mu (μ)
    - mu_1 analgesia
    - mu_2 respiratory depression
  - Kappa (κ)
  - Delta (δ)

Table 2. Summary of opioid pharmacological effects

Opioid receptor	Pharmacological effect
μ (mu)	Analgesia — Supraspinal Respiratory depression Miosis Euphoria Decreased gastrointestinal activity Drowsiness Nausea, vomiting Changes in body temperature Mental clouding Tolerance Increased addiction potential
κ (kappa)	Analgesia — Spinal Diuresis Sedation Dysphoria Mild repiratory depression Miosis Reduced addiction potential
δ (delta)	Analgesia Dysphoria Delusions Hallucinations

Common short-acting opioids

Drug	Example	Dose	Duration
Codeine	Tylenol with Codeine	300 mg/tablet, 1-2 tablets every 4-6 hours	3-4 hours
Hydrocodone	Vicodin, Lortab	5 mg/tablet, 1-2 tablets every 4-6 hours	3-4 hours
Oxycodone	Percocet	20 mg/tablet, every 4 hours	3-4 hours
Meperidine (Pethidine)	Demerol	50-100 mg/tablet or 25-100 mg/mL solutions, every 3-4 hours	2-4 hours
Tramadol*	Ultram, Ultracet	50 mg/tablet, 1-2 tablets every 4-6 hours	3-4 hours

Common long-acting opioids

Drug	Example	Dose	Duration
Oxycodone	OxyContin	10-80 mg every 12 hours	8-12 hours
Morphine	MS Contin	15-200 mg every 8-12 hours	8-12 hours
Methadone	Dolophine	5-100 mg every 8-12 hours	8-12 hours or more
Buprenorphine	Subutex, Suboxone	0.2-0.4 mg every 6-8 hours 2-32 mg daily	8-12 hours at low doses 24-72 hours at high doses
Fentanyl	Duragesic patch	25-200 mcg/hour, every 2-3 days	48-72 hours

Morphine Equivalents

Drug	Opioid Dose (mg)
Morphine (IM,IV,SC)	10.0
Morphine (PO)	60
Methadone (IM,SC)	10
Methadone (PO)	20
Codeine (IM)	130
Codeine (PO)	200
Oxycodone (IM)	12.8
Heroin (IV, SC)	5.0
Fentanyl (IV)	0.1

A Review of the Effects of Opioids on Psychomotor and Cognitive Functioning Zacny, Exp and Clin Psychopharm, 3(4)432-466, 1995.

Adjunct agents for pain

- Anticonvulsants: Neurontin, Lyrica
- Benzodiazepines and muscle relaxants: Valium, Soma
- Local anesthetics: LidoDerm patch
- Serotonin and norepinephrine re-uptake modulators (SSRI): Effexor, Prozac
- Tricyclic antidepressants: Elavil
- Over-the-counter: NSAIDs, Aspirin, Tylenol

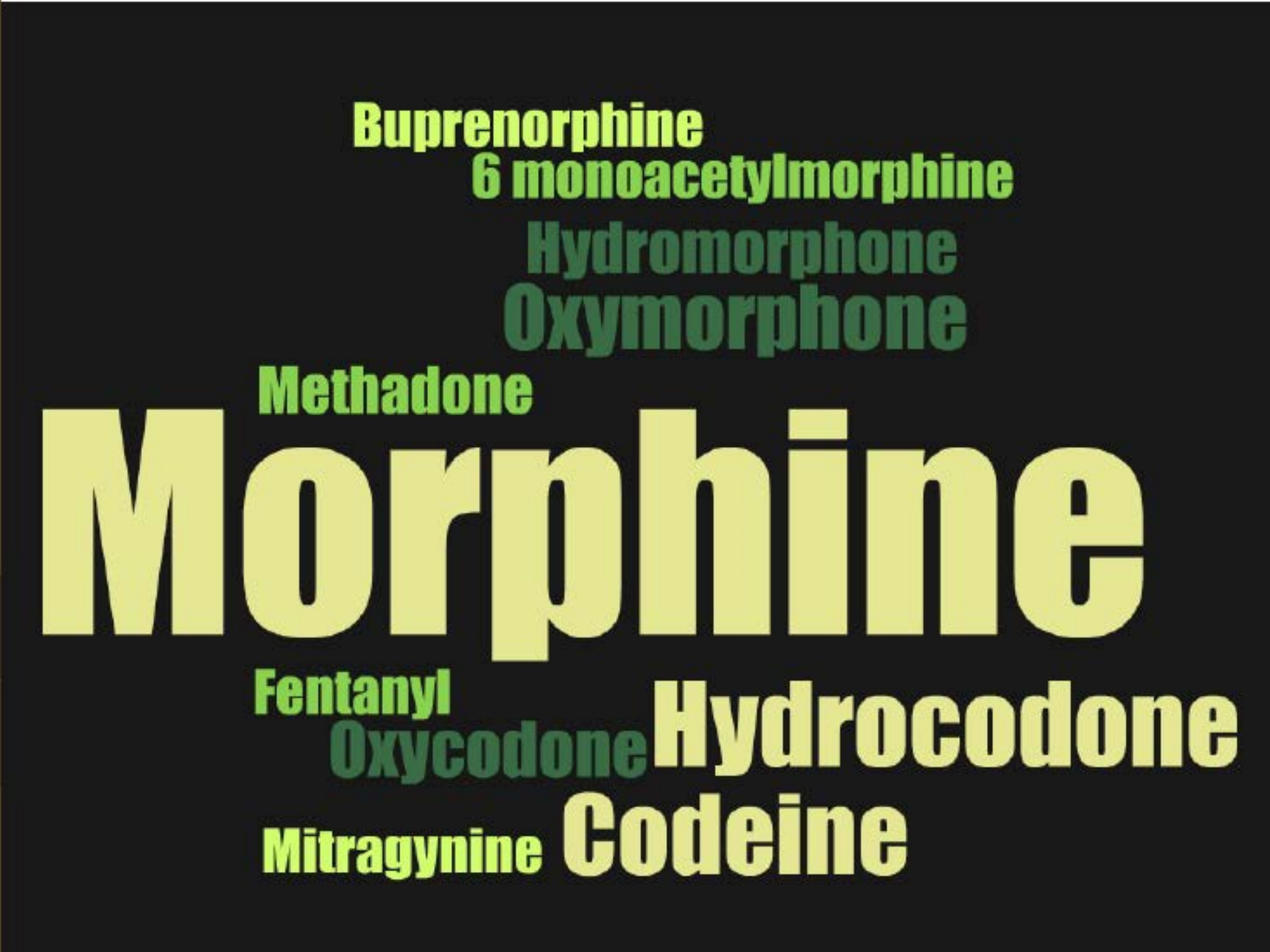
A typical medicine list for a chronic back pain patient

- Lortab (hydrocodone) 4-8 per day *for breakthrough pain*
- OxyContin (oxycodone) 40 mg twice a day *for long-acting pain relief*
- Flexeril (cyclobenzaprine) *for muscle spasm*
- Neurontin (gabapentin) *for neuropathic pain*
- Effexor (venlafaxine) *for depression, anxiety and neuropathic pain*
- Xanax (alprazolam) *for anxiety*
- Ambien (zolpidem) *for insomnia*

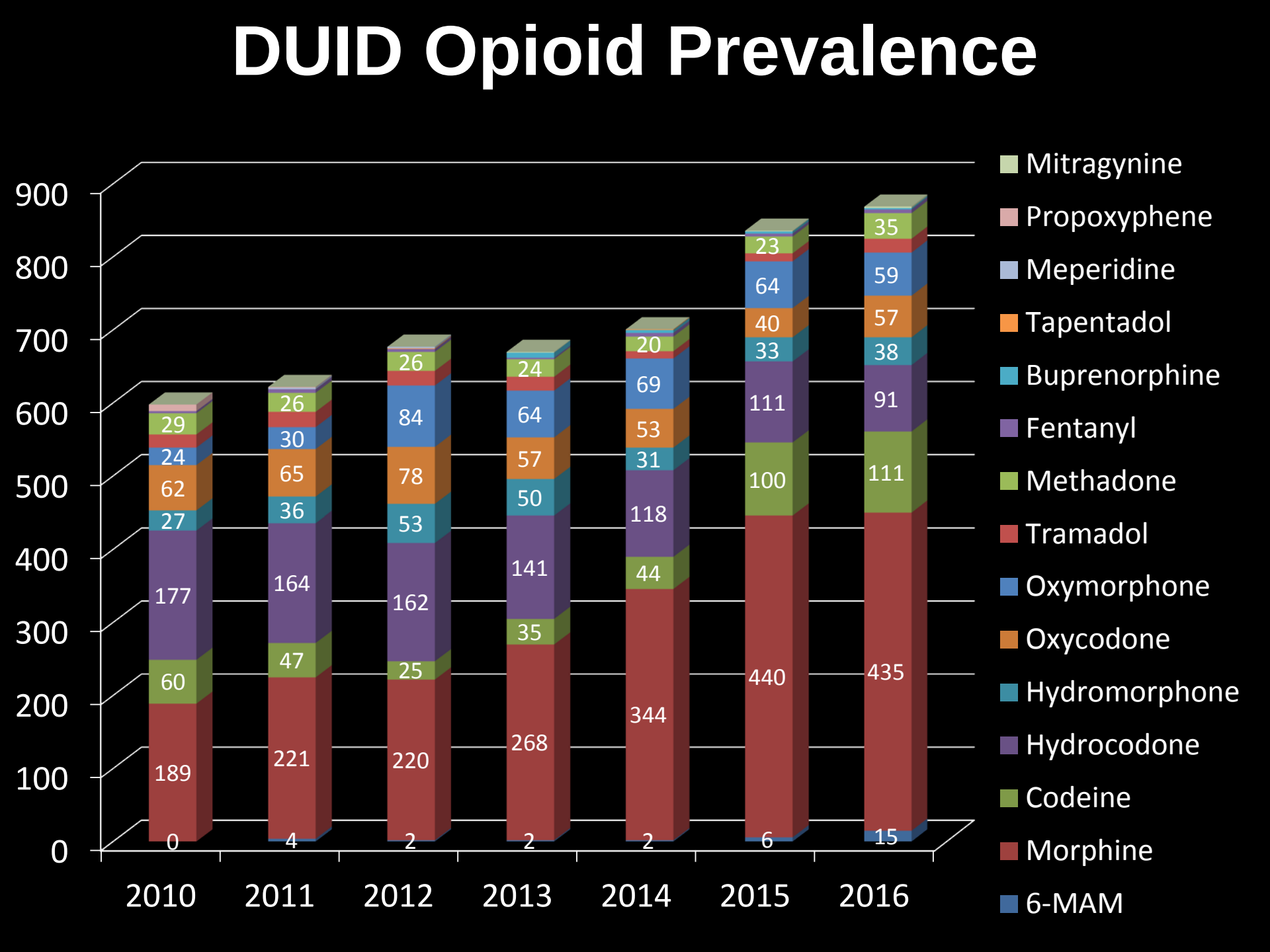
Opioid routes of administration

- *Medicinal administration*
  - Oral
    - Immediate-release
    - Controlled-release
  - Intramuscular (IM)
  - Intravenous (IV)
  - Epidural
  - Rectal

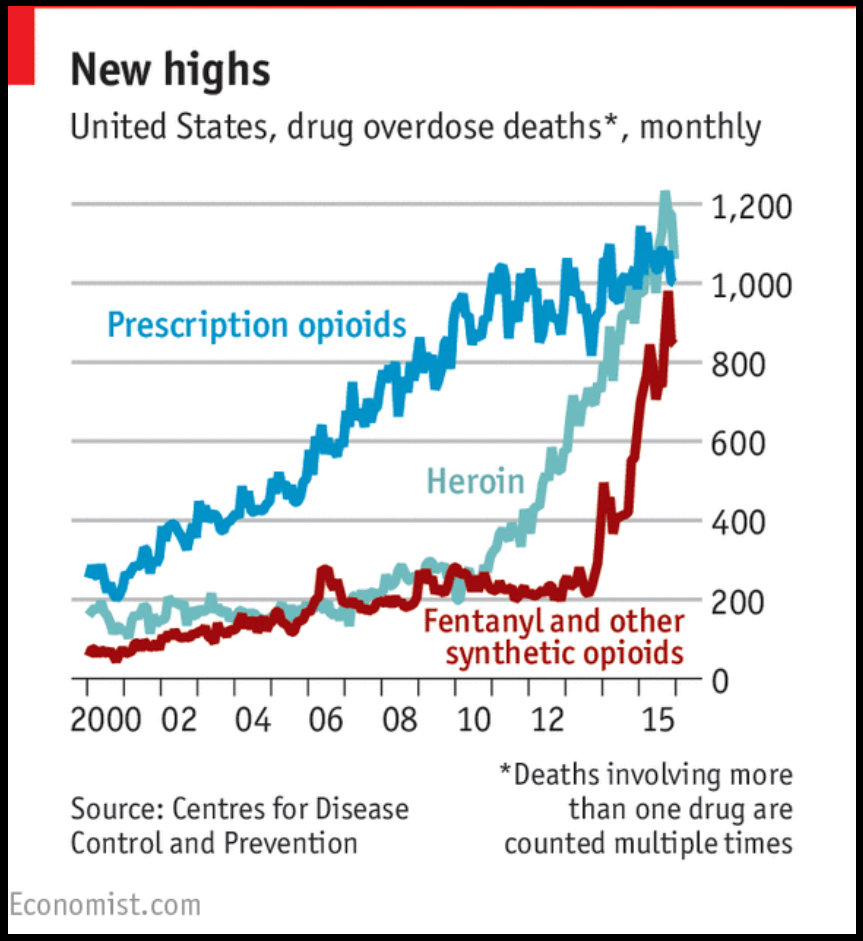
- *Recreational use*
  - Smoking
  - Subcutaneous (skin-popping)
  - Intravenous (IV) (mainlining)
  - Inhalation


Buprenorphine
6 monoacetylmorphine
Hydromorphone
Oxymorphone
Methadone
Morphine
Fentanyl
Oxycodone
Hydrocodone
Mitragynine
Codeine

DUID Opioid Prevalence



Opioid Abuse



- 26% increase in CT
- 35% increase in DE
- 39% increase in ME
- 62% increase in MD

Opioid Abuse

DRUG OVERDOSES

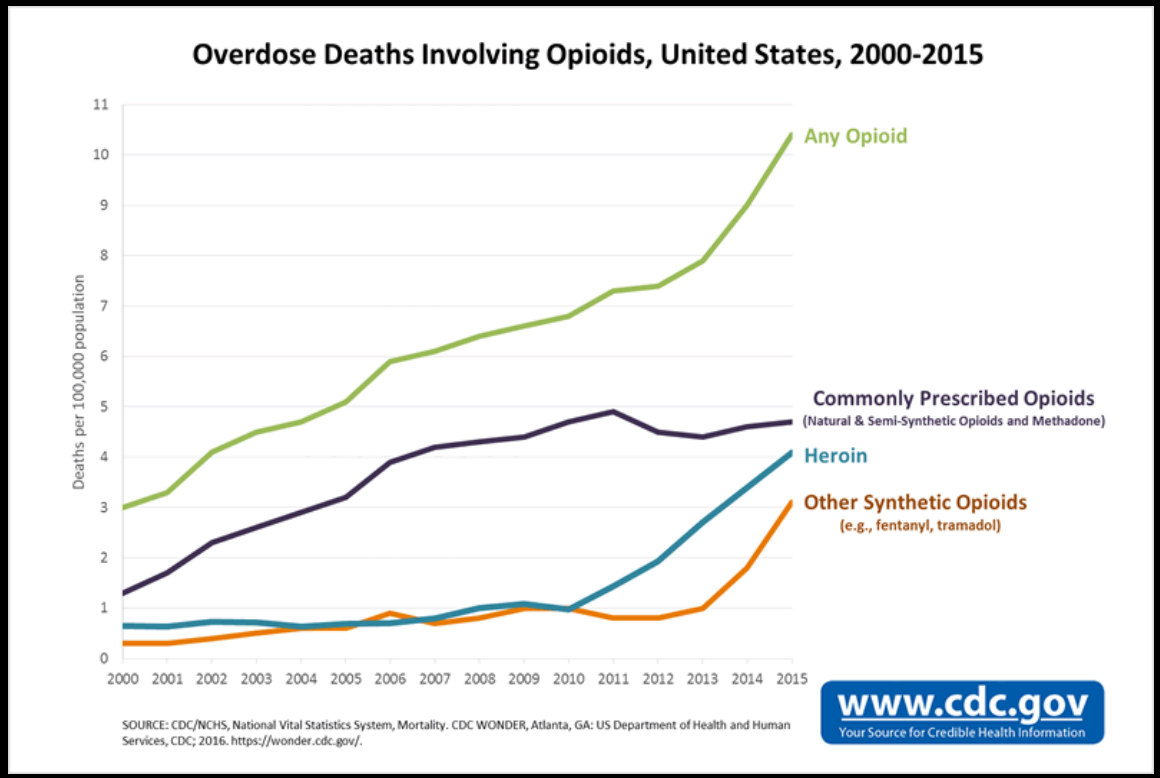
KILL MORE

THAN CARS, GUNS, AND FALLING.

Falling	28,360 deaths
Guns	32,351 deaths
Traffic accidents	33,692 deaths
Drug overdoses	41,340 deaths

(16,917 from opioid pain medicine)

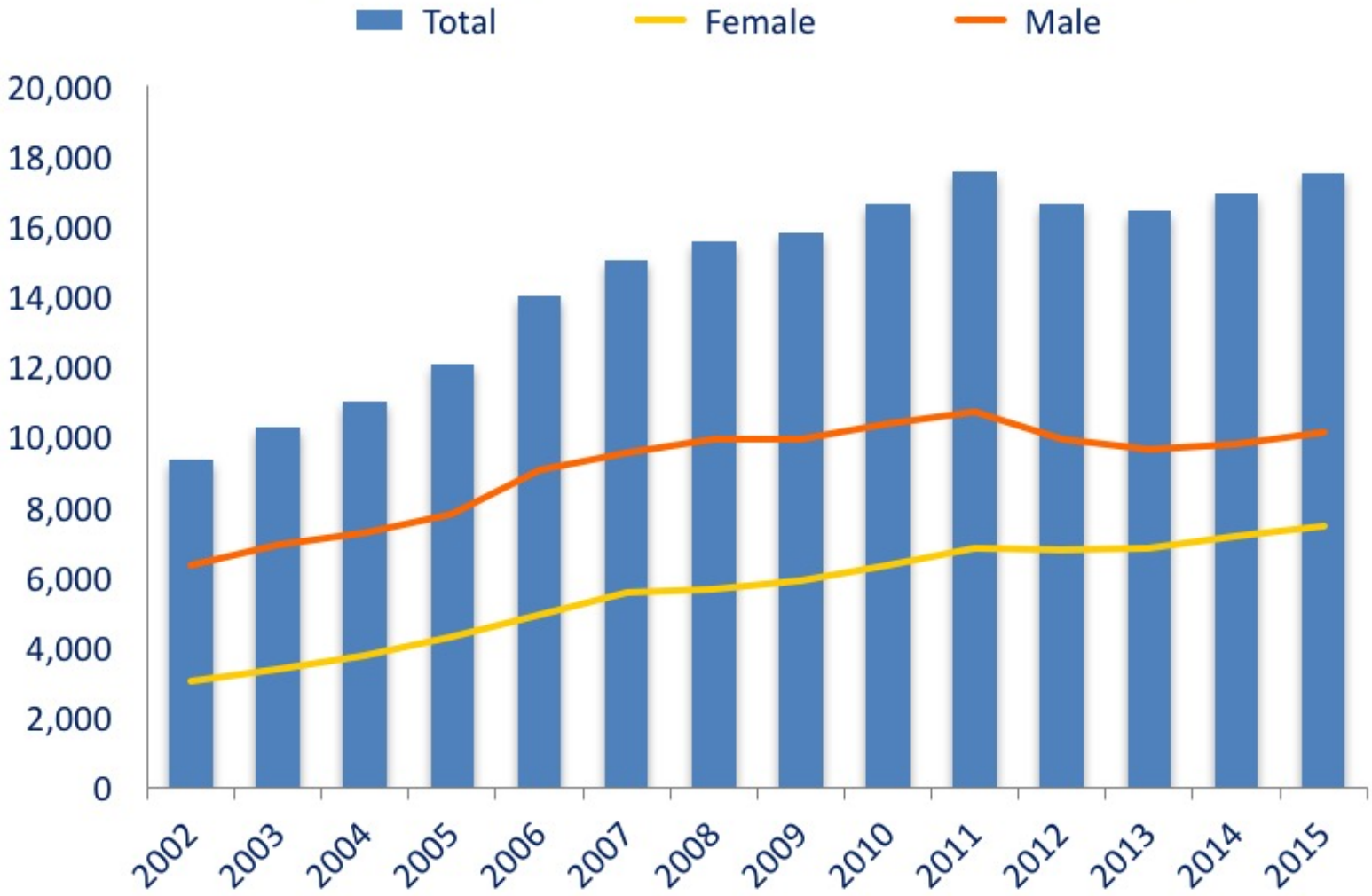
Source: CDC Wide-ranging OnLine Data for Epidemiologic Research (WONDER) on Mortality: http://wonder.cdc.gov/mortsql.html (2011)



National Institute on Drug Abuse

National Overdose Deaths

Number of Deaths Involving Prescription Opioid Pain Relievers (excluding non-methadone synthetics)

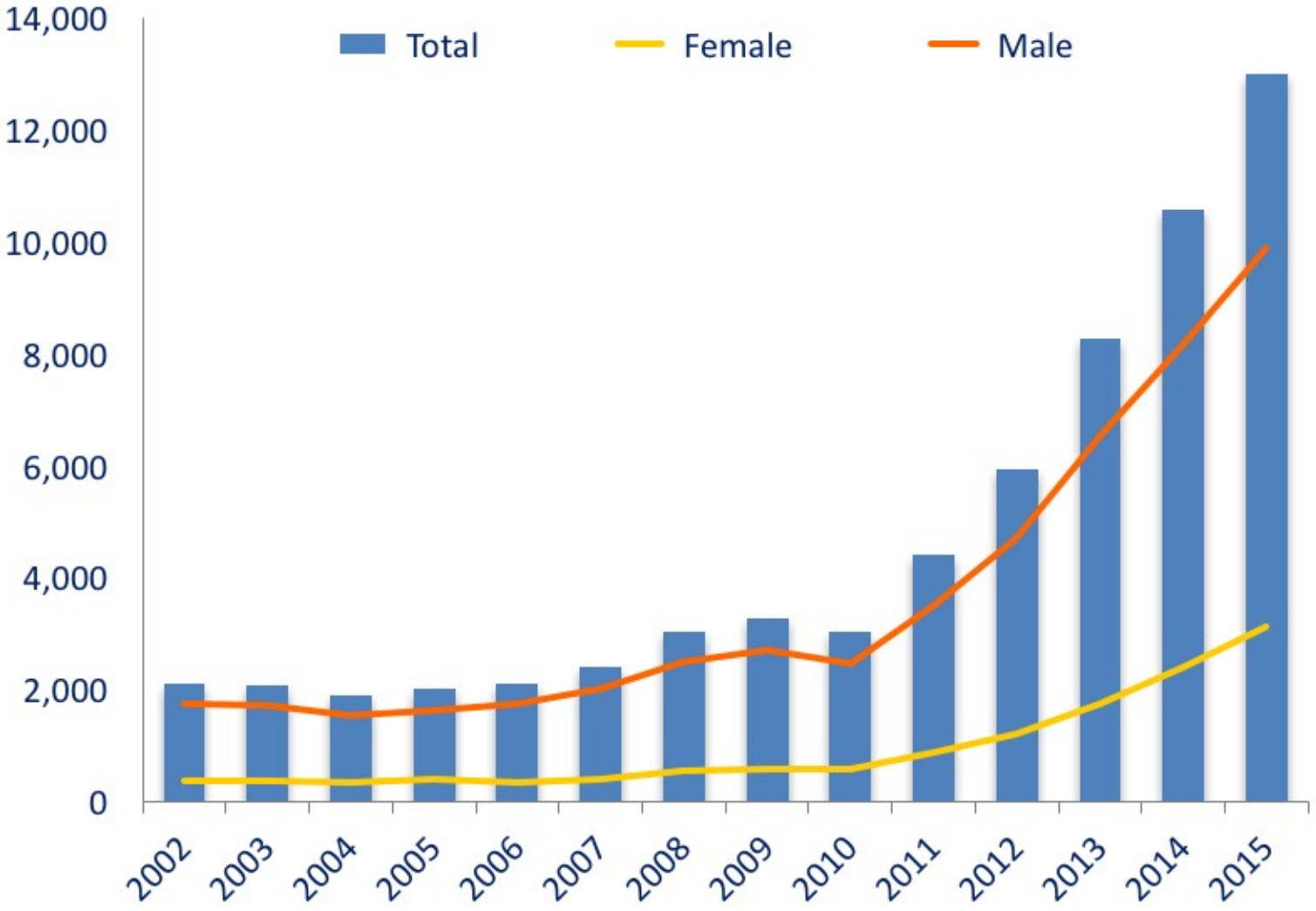


Source: National Center for Health Statistics, CDC Wonder

National Institute on Drug Abuse

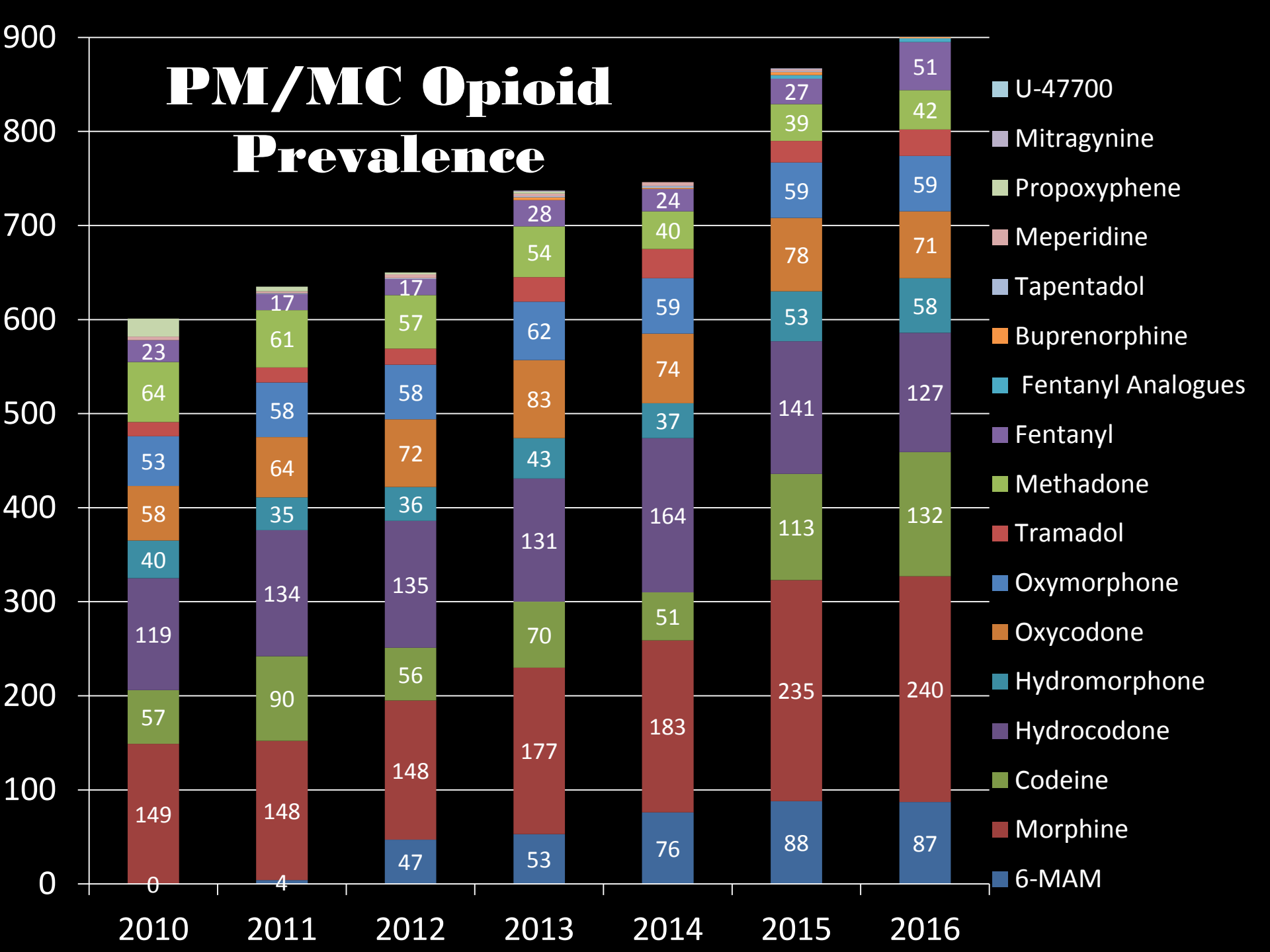
National Overdose Deaths

Number of Deaths Involving Heroin



Source: National Center for Health Statistics, CDC Wonder

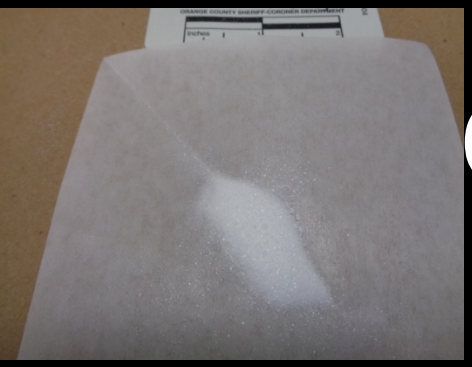

54
199


PM/MC Opioid Prevalence
900
800
700
600
500
400
300
200
100
0
2010
2011
2012
2013
2014
2015
2016
0
149
57
119
40
53
58
64
23
4
148
90
134
35
64
58
61
17
47
148
56
135
36
72
58
57
17
53
177
70
131
43
83
62
54
28
76
183
51
164
37
74
59
40
24
88
235
113
141
53
78
59
39
27
87
240
132
127
58
71
59
42
51
U-47700
Mitragynine
Propoxyphene
Meperidine
Tapentadol
Buprenorphine
Fentanyl Analogues
Fentanyl
Methadone
Tramadol
Oxymorphone
Oxycodone
Hydromorphone
Hydrocodone
Codeine
Morphine
6-MAM

Fentanyl & Analogs

Why Fentanyl?

- Fentanyl and analogues are the most potent opioids available.
- Approximately 50-100 times more potent than morphine and 30-50 times more potent than heroin
- Can cause respiratory depression sufficient enough to cause the user to stop breathing



Chemistry & Pharmacology

FENTANYL

- Synthetic μ-opioid receptor with high lipid solubility
- Rapid onset, short duration
  - Action is immediate with intravenous use
  - Peak effect 5-15 minutes
  - Duration is only 1-2 hours
- Crosses blood brain barrier
- Doses as small as 0.25 mg can be fatal
- Readily absorbed through the skin
- Dependence develops in a few days

ACETYL FENTANYL

- Synthetic μ-opioid receptor with high lipid solubility
- Rapid onset, short duration
  - Action is immediate with intravenous use
  - Peak effects slightly longer than fentanyl
  - Duration is only 1-2 hours
- Crosses blood brain barrier
- Doses as small as 1 mg can be fatal
- Readily absorbed through the skin
- Dependence develops in a few days

Powder, Tar, Liquid, Patch, and Pill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36 01


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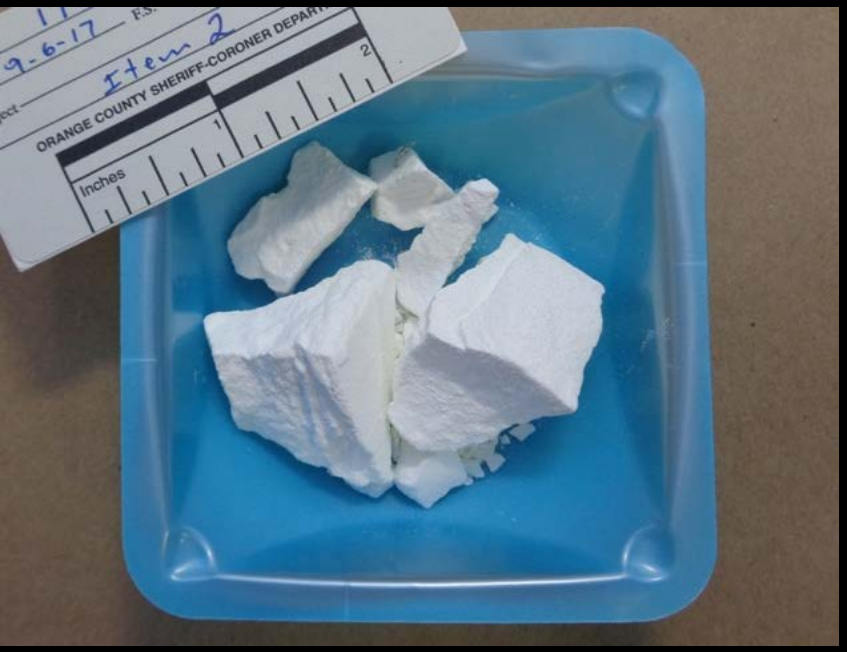
1
2
WATSON
353

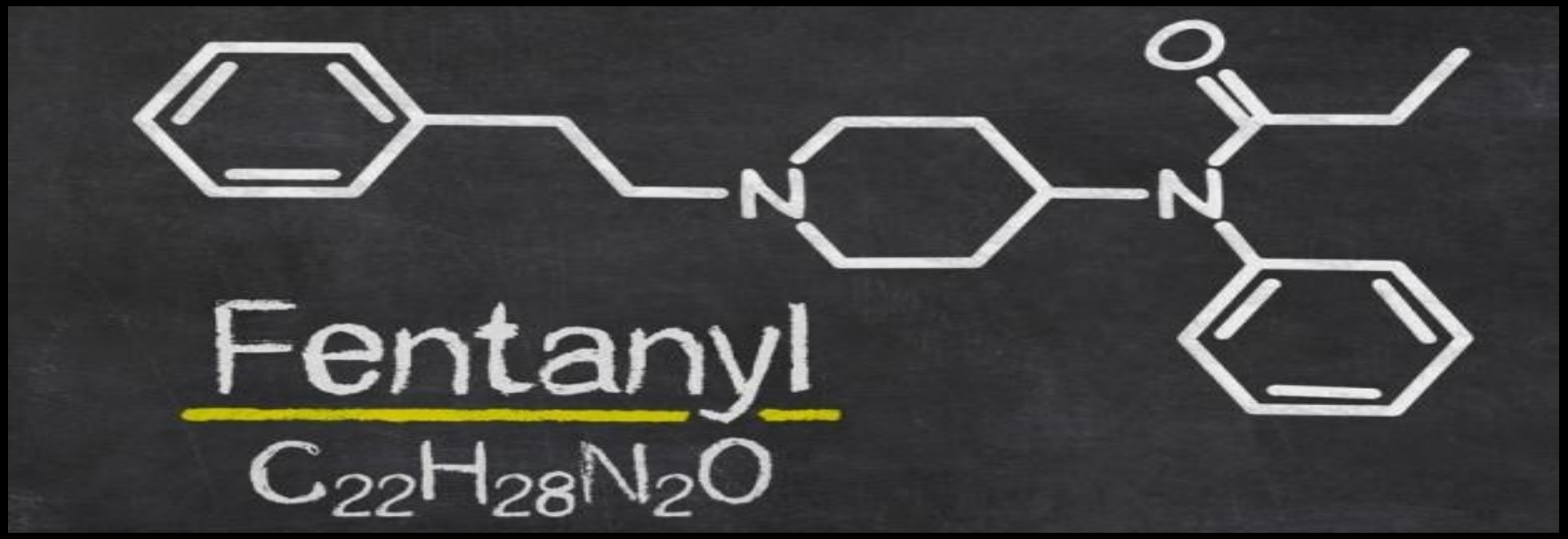

9-6-17
Item 2
ORANGE COUNTY SHERIFF-CORONER DEPART
Inches
1
2


Inches
1
2
P
215


ORANGE CO
Inches
1
2
P
215

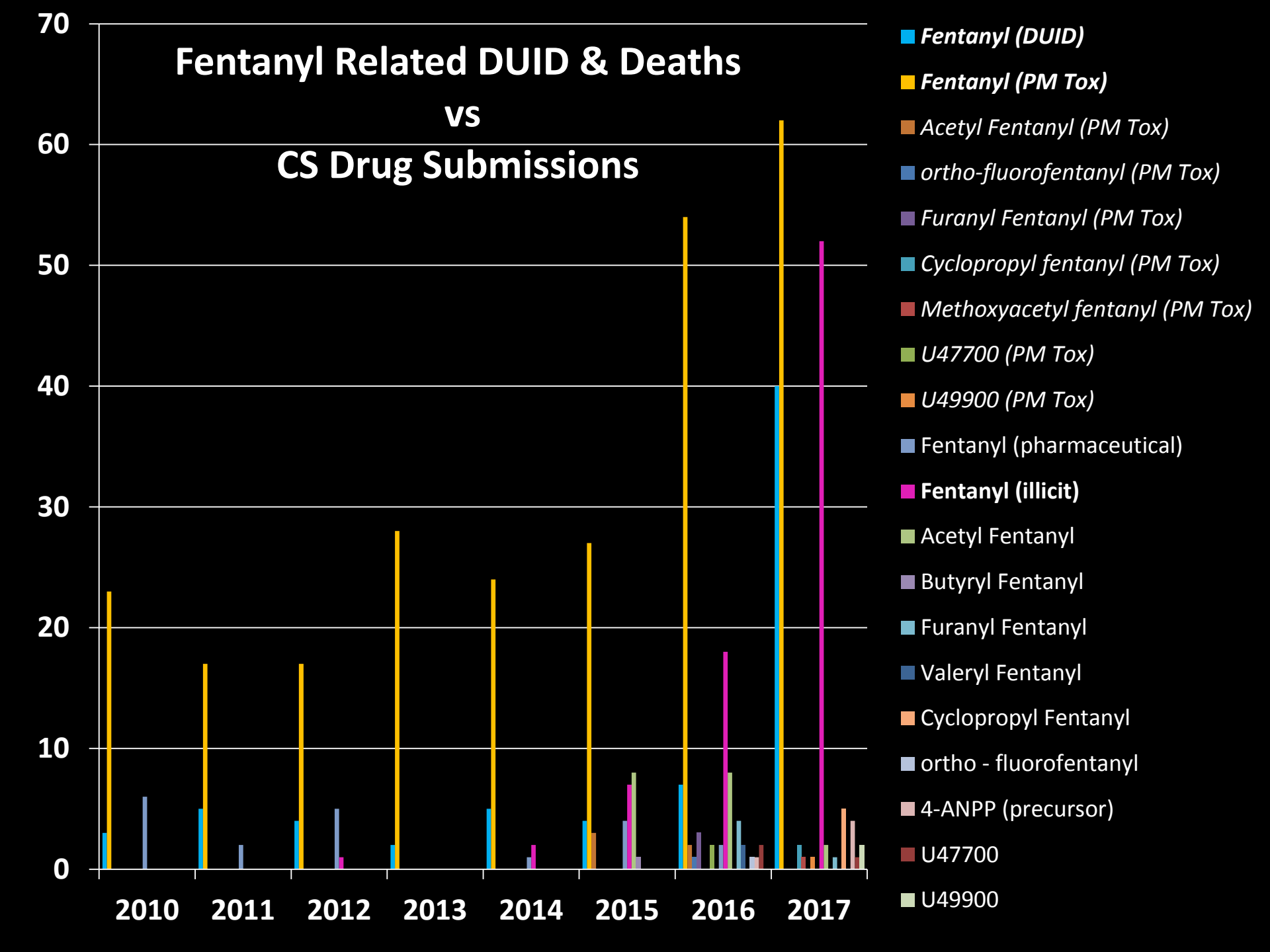
Over 30,000 Counterfeit Pills

9 Analogs Identified



Acetyl
Furanyl
Valeryl
Butryl
U47700
Methoxyacetyl

ortho-Fluoro
Cyclopropyl
U49900
Acryl
Tetrahydrofuran
Carfentanil


Fentanyl Related DUID & Deaths
vs
CS Drug Submissions
70
60
50
40
30
20
10
0
2010
2011
2012
2013
2014
2015
2016
2017
Fentanyl (DUID)
Fentanyl (PM Tox)
Acetyl Fentanyl (PM Tox)
ortho-fluorofentanyl (PM Tox)
Furanyl Fentanyl (PM Tox)
Cyclopropyl fentanyl (PM Tox)
Methoxyacetyl fentanyl (PM Tox)
U47700 (PM Tox)
U49900 (PM Tox)
Fentanyl (pharmaceutical)
Fentanyl (illicit)
Acetyl Fentanyl
Butyryl Fentanyl
Furanyl Fentanyl
Valeryl Fentanyl
Cyclopropyl Fentanyl
ortho - fluorofentanyl
4-ANPP (precursor)
U47700
U49900

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