Opioid Primer: Managing Chronic Pain Responsibly in the midst of an Epidemic

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Disclosures

- None

Outline

- Historical Background
- The Current Crisis
- Chronic Pain: Risks, Tapers and Best Practices
- Conclusion

Opium Wars

- The Chinese used opium as early as the 7th Century as an aphrodisiac and to preserve vital force (Qi). By 1600 Chinese merchants had learned to mix opium and tobacco → greater demand

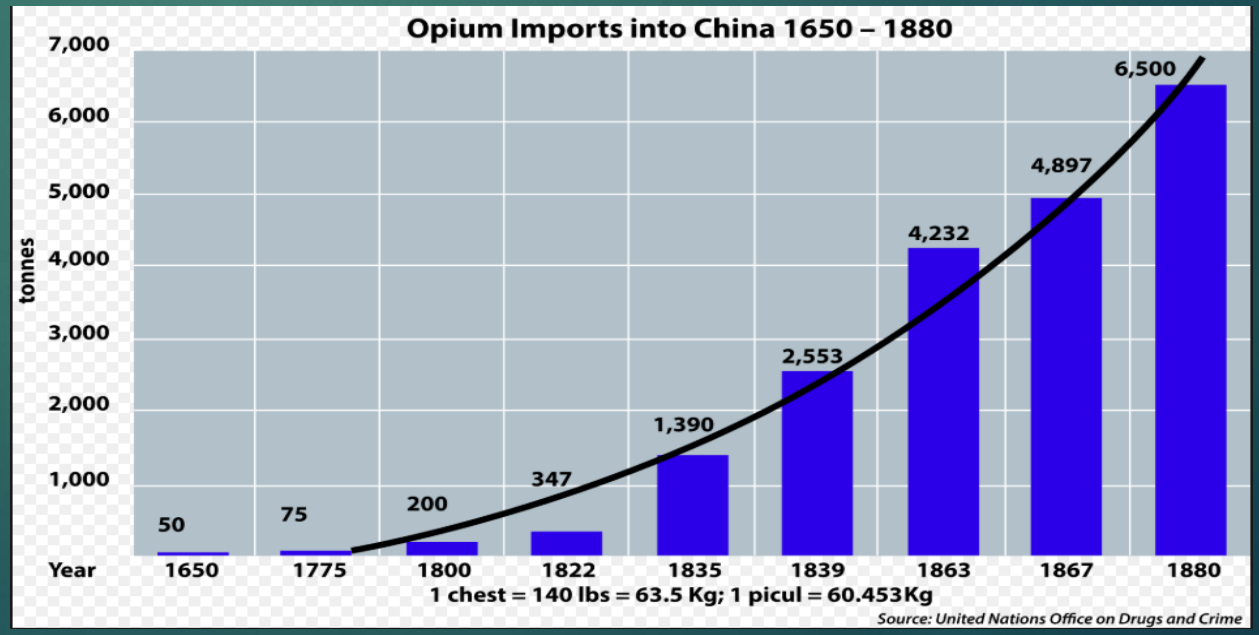
- Chinese Emperor Yongyan tried to ban opium imports in 1799 but could not stop foreign drug shipments into southern ports

- The British East India Company was the most prolific smuggling operation but by 1810 American ships carrying poor quality Turkish opium controlled 10% of the trade and rising.

Warren Delano II 1809-1898

"*Opium has a harm. Opium is a poison, undermining our good customs and morality*"

- Yongyan, Jiaquing Emperor 1810



Opium Wars

- First Opium war lasted from 1839-1842. Treaty of Nanking ceded Hong Kong to Britain and kept Chinese ports open for opium influx
- Britain launched Second Opium War in 1856-1860 which opened additional Chinese ports to opium trade
- France and the US also coerced Chinese into unjust trade agreements to facilitate opium imports: “Century of Humiliation”

"Justice, in my opinion…is with them; and whilst they, the Pagans, the semi-civilized barbarians, have it on their side, we, the enlightened and civilized Christians, are pursuing objects at variance both with justice and with religion...a war more unjust in its origin, a war calculated in its progress to cover this country with a permanent disgrace, I do not know and I have not read of."

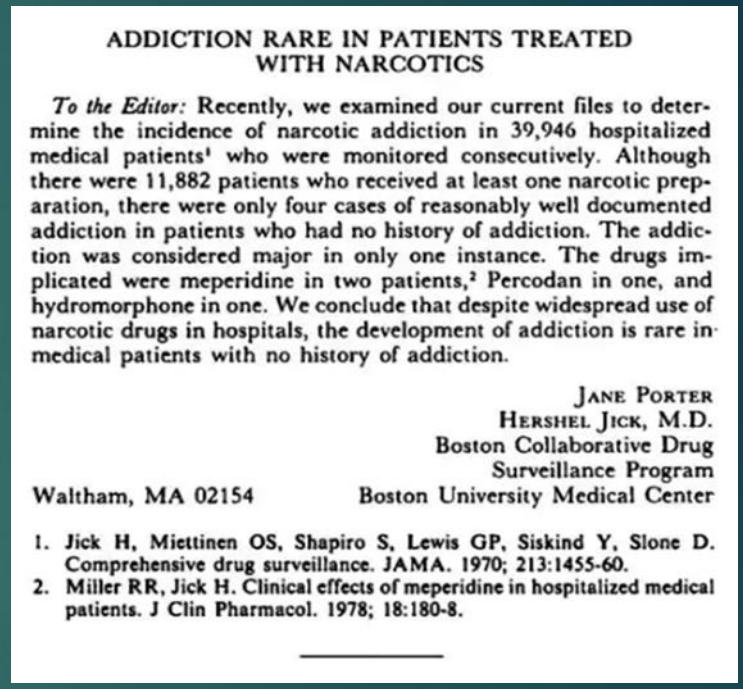
William Gladstone, excerpted from speech to House of Commons 1857

Prelude to a Crisis

- Until the early 1980's, prevailing wisdom was that opioids were not effective or appropriate for the treatment of chronic pain

- 1980: Porter and Jick write a letter to the *NEJM* based on their observation of addiction rates in 11,882 hospitalized patients (3)

- 1986: Portenoy and Russell publish a retrospective study in *Pain* stating "*for non-cancer pain, narcotics can be safely and effectively prescribed…with relatively little risk of producing the maladaptive behaviors which define opioid abuse*." (4)



ADDICTION RARE IN PATIENTS TREATED WITH NARCOTICS

To the Editor: Recently, we examined our current files to determine the incidence of narcotic addiction in 39,946 hospitalized medical patients[1] who were monitored consecutively. Although there were 11,882 patients who received at least one narcotic preparation, there were only four cases of reasonably well documented addiction in patients who had no history of addiction. The addiction was considered major in only one instance. The drugs implicated were meperidine in two patients,[2] Percodan in one, and hydromorphone in one. We conclude that despite widespread use of narcotic drugs in hospitals, the development of addiction is rare in medical patients with no history of addiction.

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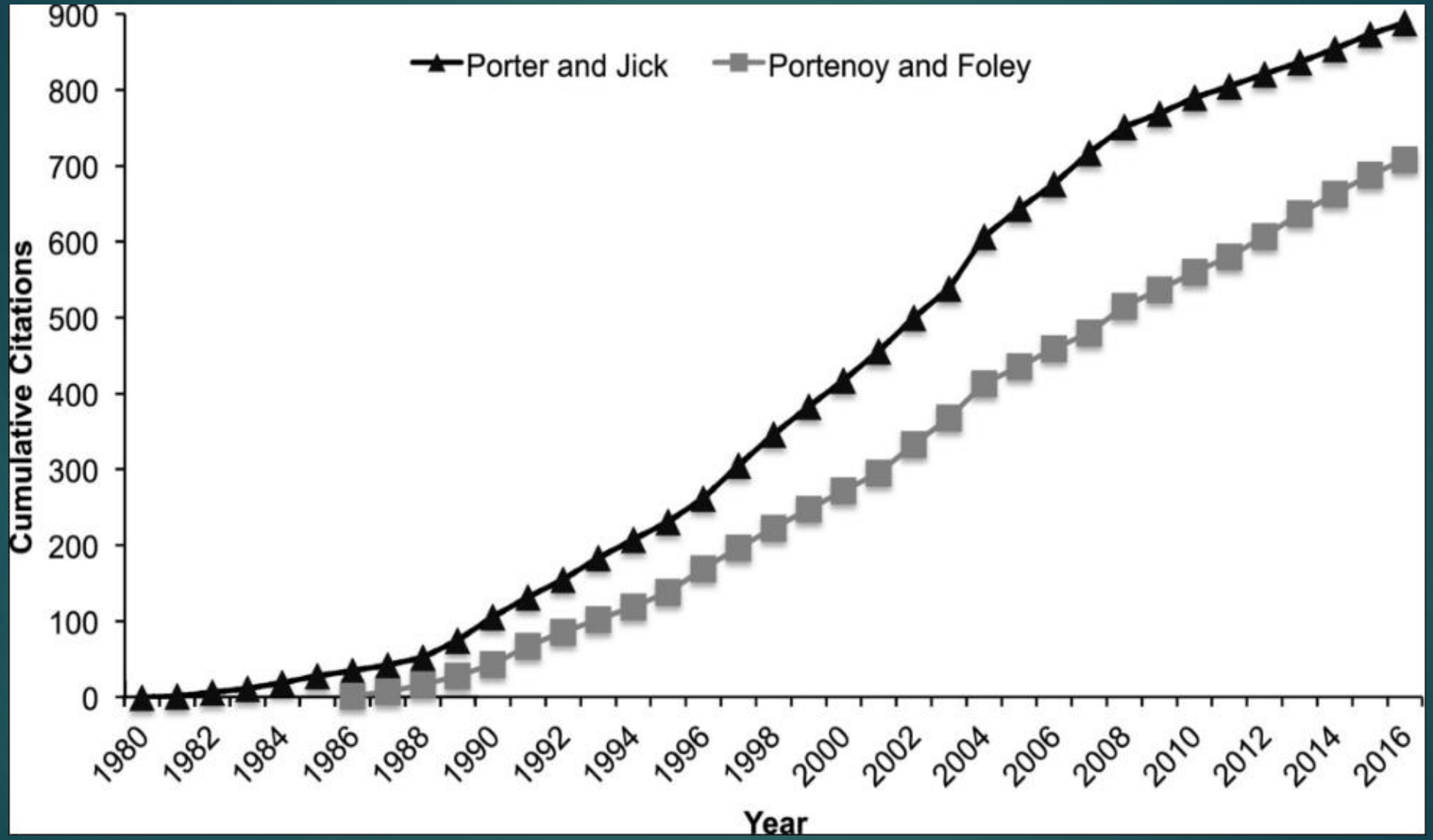
1. Jick H, Miettinen OS, Shapiro S, Lewis GP, Siskind Y, Slone D. Comprehensive drug surveillance. JAMA. 1970; 213:1455-60.
2. Miller RR, Jick H. Clinical effects of meperidine in hospitalized medical patients. J Clin Pharmacol. 1978; 18:180-8.



https://www.drugandalcoholdependence.com

Prelude to a Crisis

- 1987-1995: MS Contin, Duragesic and Oxycontin FDA approved
- **1999-2000: VA officially introduces concept of pain as the "fifth vital sign." JCAHO requires pain to be treated and assessed**
- **2004: FSMB guidelines suggest Physicians can be sanctioned for providing "inadequate" pain control**
- 2006: CMS demands that hospitals perform a patient satisfaction survey which includes three questions on assessment and treatment of pain

The Current Crisis

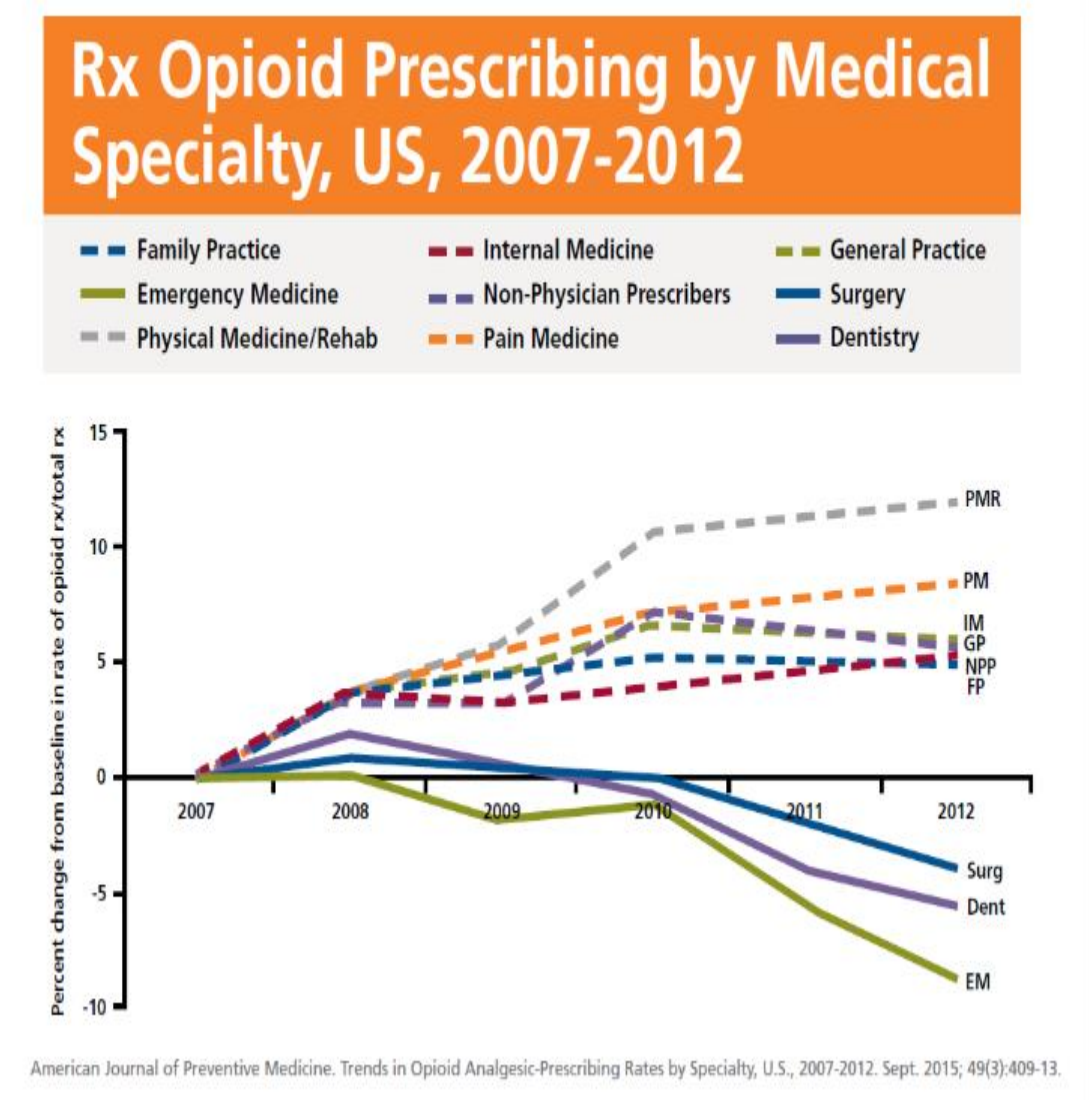
- In 2014 the US (4.3% of world population) used 65% of all the world's opioids. **Per capita, 430% higher than Europe and 1500% higher than the rest of the world**

- The US used 97% of the world's hydrocodone in 2014 and ranked #1 in oxycodone prescriptions

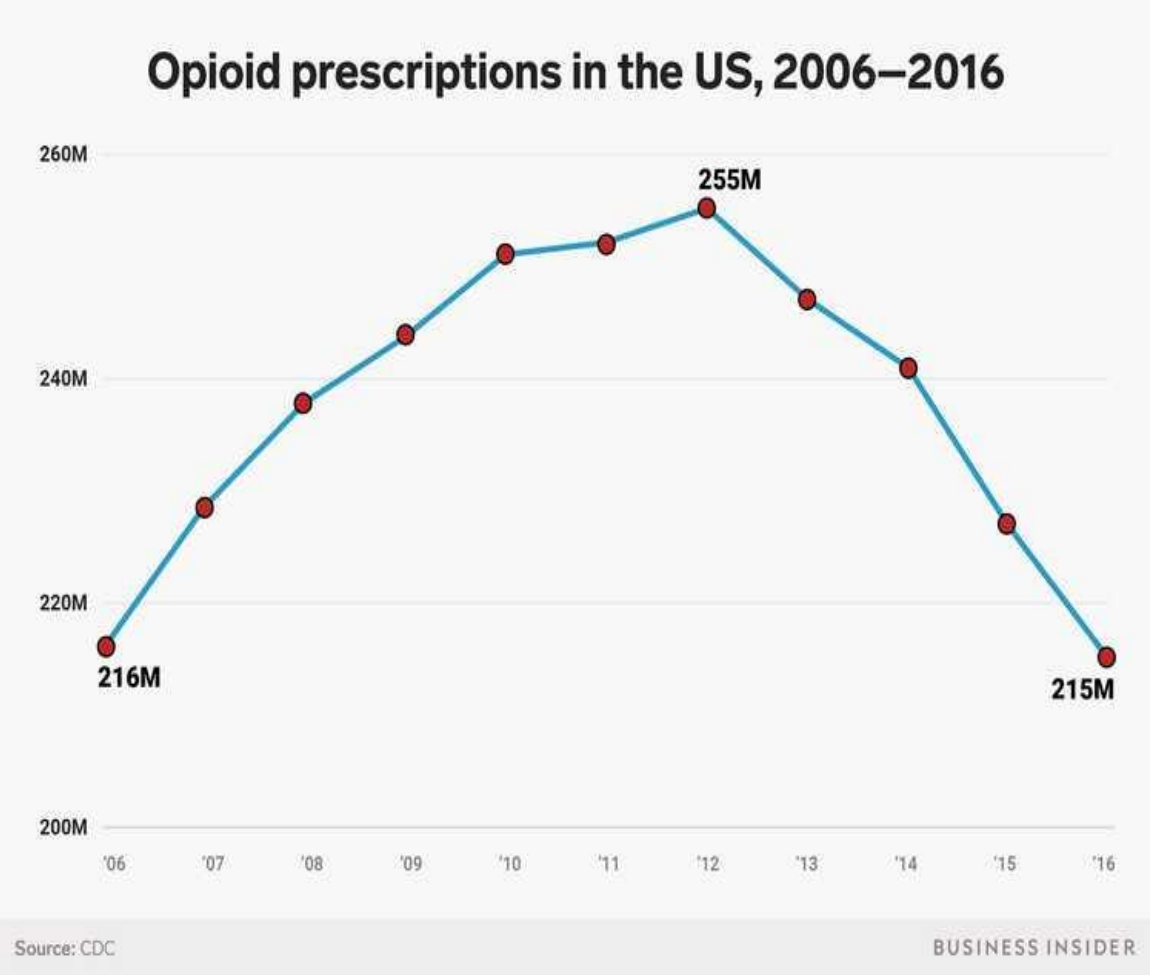
- **Between 2000-2014, US had a 200% increase in prescription drug overdose deaths** (6)

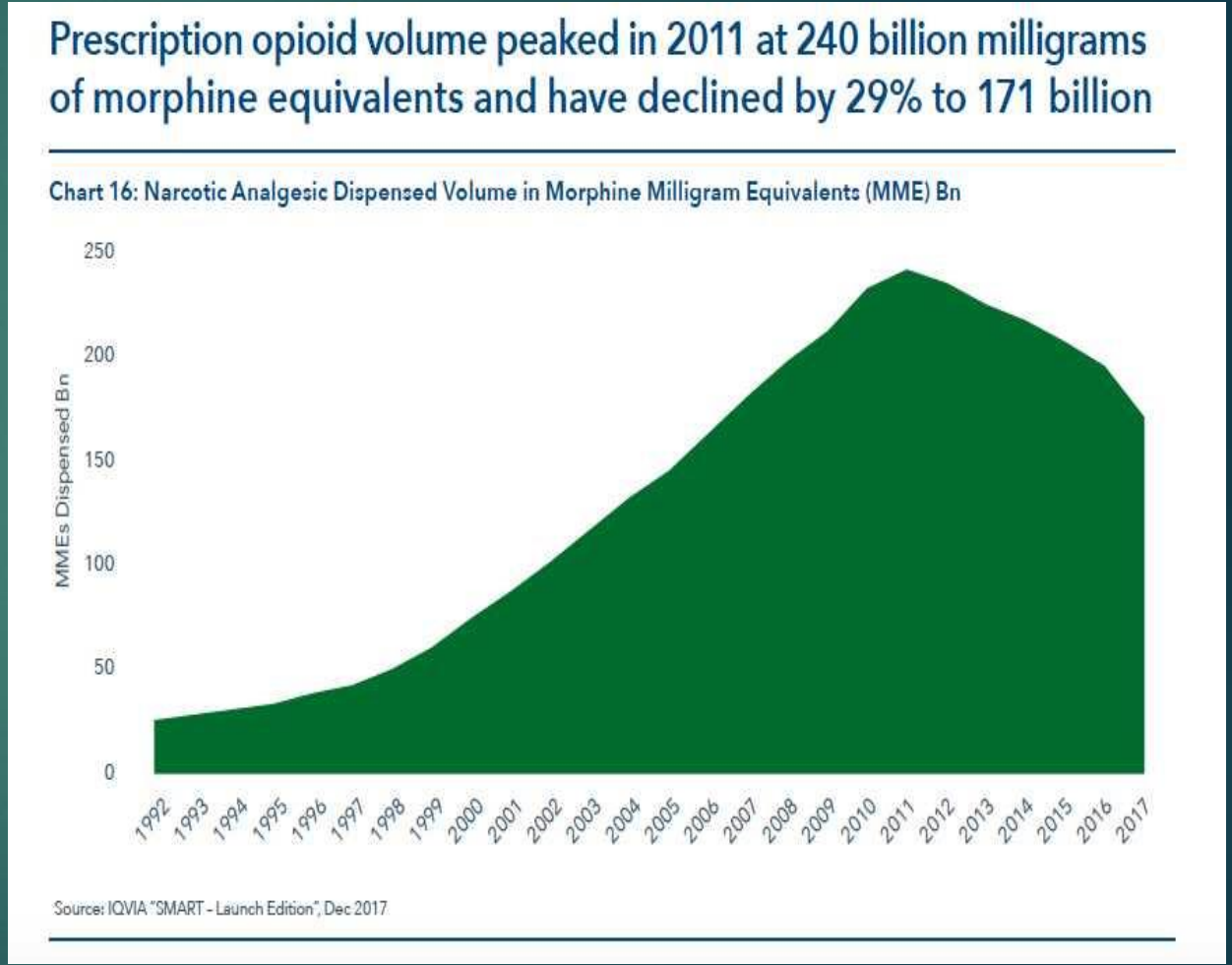
- President declares opioid crisis a public health emergency in October 2017; nearly $500M in grants awarded by HHS

The Current Crisis

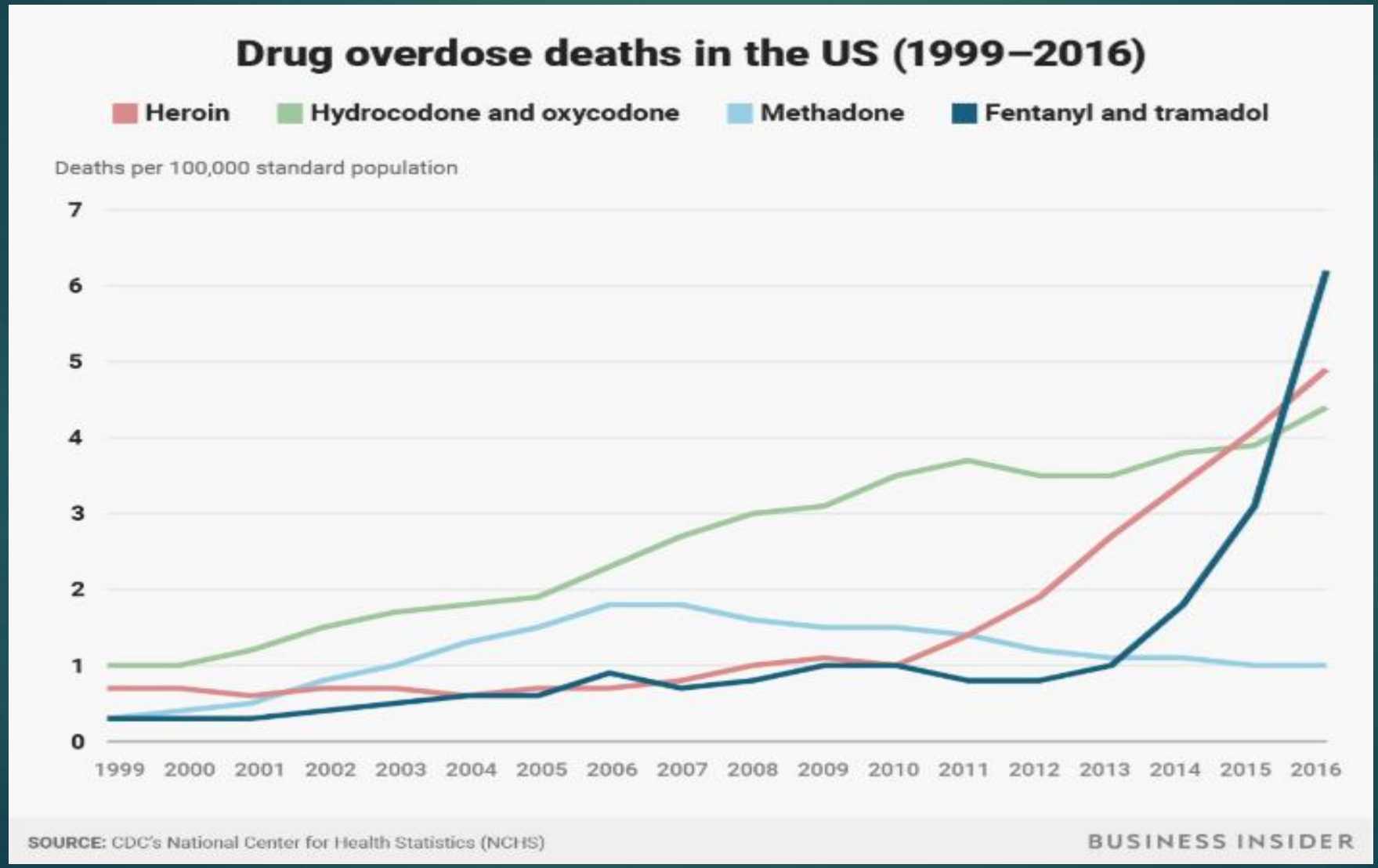


The Current Crisis: Volumes are Down





The Current Crisis: Deaths are Up



Opioids: Misuse and Abuse

- CDC estimates that 80% of heroin users start with prescription opioids (10)
- Adults who take prescription opioids have ***misuse*** rates between 13%-30% (20)
- **Nearly ¼ of chronic pain patients on opioids meet diagnostic criteria for ETOH use disorder** (23)
- Meltzer's 2012 study documented 23% rate of prescription opioid misuse/abuse in a primary care cohort; **85% had aberrant drug or substance use** (24)

Opioids: Pick your Poison

Likeability and abuse liability of commonly prescribed opioids.

Wightman R[1], Perrone J, Portelli I, Nelson L.

Intravenous oxycodone, hydrocodone, and morphine in recreational opioid users: abuse potential and relative potencies.

Stoops WW[1], Hatton KW, Lofwall MR, Nuzzo PA, Walsh SL.

- Oxycodone and hydromorphone have consistently higher rates of misuse/abuse while multiple studies showed no difference between morphine and hydrocodone (16)

- **Oxycodone has higher "likability," potency and diversion risk compared with hydrocodone or morphine** (17)

- Up to 40% of recreational abusers will crush PO formulations; **addition of acetaminophen makes nasal/IV route very unpleasant and acts as a deterrent** (17)

Opioids: Fraud and Diversion

Crooked Michigan Doctor Sentenced

Played Key Role in Drug Distribution and Health Care Fraud Conspiracies

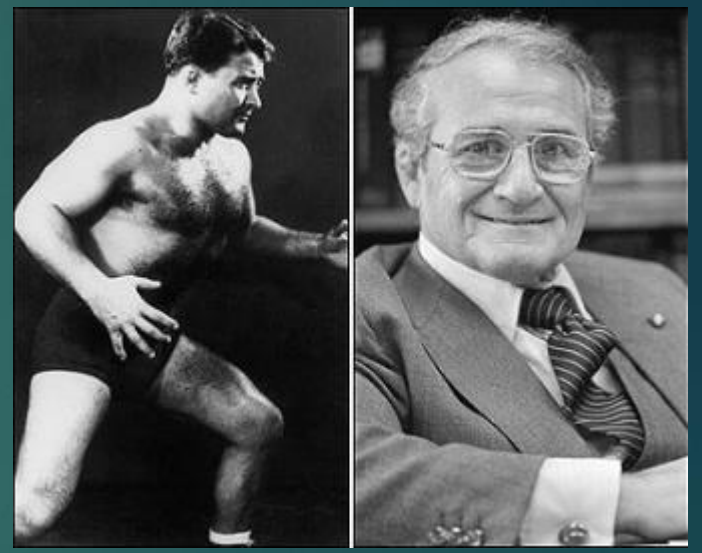
Generally, here's how the scheme worked:

- Two individuals associated with ACS would go out and recruit patients—vulnerable Medicare recipients who were struggling on fixed incomes—to visit Moret at ACS and receive a cursory exam or sometimes no exam at all.
- Moret would then write them medically unnecessary prescriptions for controlled substances.
- The patients would go out and fill those prescriptions, and then turn the medications over to the ACS recruiter in exchange for money.

"The recruiters, who often personally transported the patients to and from the clinic and their pharmacies, would then sell the drugs on the streets, where they had a lot more value—more than $15 million in total," Kramer explained.

Chronic Pain: Antecedents

- Early pain pioneers like John Bonica viewed pain as a complex psychological and environmental disorder rarely amenable to a biomedical “fix”



- Bonica pioneered Multidisciplinary treatment programs (MTP) which demanded patient investment: 15-25 hours per week per patient for 3-5 weeks (38)
- A 2015 Cochrane review showed that MTP’s were more effective than “usual care” in reducing pain and disability for chronic low back pain sufferers (39)
- CPT codes in the mid-late 1980’s shifted towards procedures and fee for service. **MTP programs declined from ~ 2000 in 1988 to < 80 in 2005** (40)

Chronic Pain: Do Opioids work?

The effectiveness and risks of long-term opioid therapy for chronic pain: a systematic review for a National Institutes of Health Pathways to Prevention Workshop.

Chou R, Turner JA, Devine EB, Hansen RN, Sullivan SD, Blazina I, Dana T, Bougatsos C, Deyo RA.

- Chou's 2015 study in Annals examined a diverse selection of RCT's and observational studies in Cochrane database and Medline where opioids were prescribed for > 3 months

- **No study evaluated the long term (> 1 year) effectiveness of opioid vs. non opioid treatments** (41)

- Good quality studies demonstrated opioid risk esp. with higher dose: fractures, abuse, overdose risk, sexual dysfunction

- **Insufficient evidence to support opioids for chronic pain. Dose reduction lowers risk**

Chronic Pain: Do Opioids work?

Sex and Age Differences in Global Pain Status Among Patients Using Opioids Long Term for Chronic Noncancer Pain.

LeResche L[1,2], Saunders K[2], Dublin S[2], Thielke S[3], Merrill JO[4], Shortreed SM[2], Campbell C[5], Von Korff MR[2].

- LaResche et al. surveyed > 2000 patients ages 21-80 on chronic long term opioids
- They examined whether opioids improved pain intensity, mood and function (employment). These patients had a “favorable” global pain status
- **Only 15% of females and 26% of males on long term COT had a favorable status**. Young and middle aged women underperformed men (42)
- Majority of patients with “unfavorable” status- depressed/unemployed/in pain– still **self rated** opioids as “extremely helpful.”
- **Study concluded that long term COT did not improve pain and function for vast majority of patients**

Chronic Pain: Do Opioids work?

Effect of Opioid vs Nonopioid Medications on Pain-Related Function in Patients With Chronic Back Pain or Hip or Knee Osteoarthritis Pain: The SPACE Randomized Clinical Trial.

Krebs EE[1,2], Gravely A[1], Nugent S[1], Jensen AC[1], DeRonne B[1], Goldsmith ES[1,3], Kroenke K[4,5,6], Bair MJ[4,5,6], Noorbaloochi S[1,2].

- Krebs et al. SPACE Trial randomized 240 VAMC patients with chronic knee, hip and LBP into an opioid and non-opioid treatment arm
- Both arms had a built in 3 step treatment escalation over 12 months
- Primary endpoint: pain related function (BPI). Secondary endpoint: pain intensity
- **No significant difference in pain related function between groups**
- **Non opioid arm had significantly lower pain intensity**
- **Opioid group had significantly higher adverse medication effects and higher dropout**

Chronic Pain: Known Risks

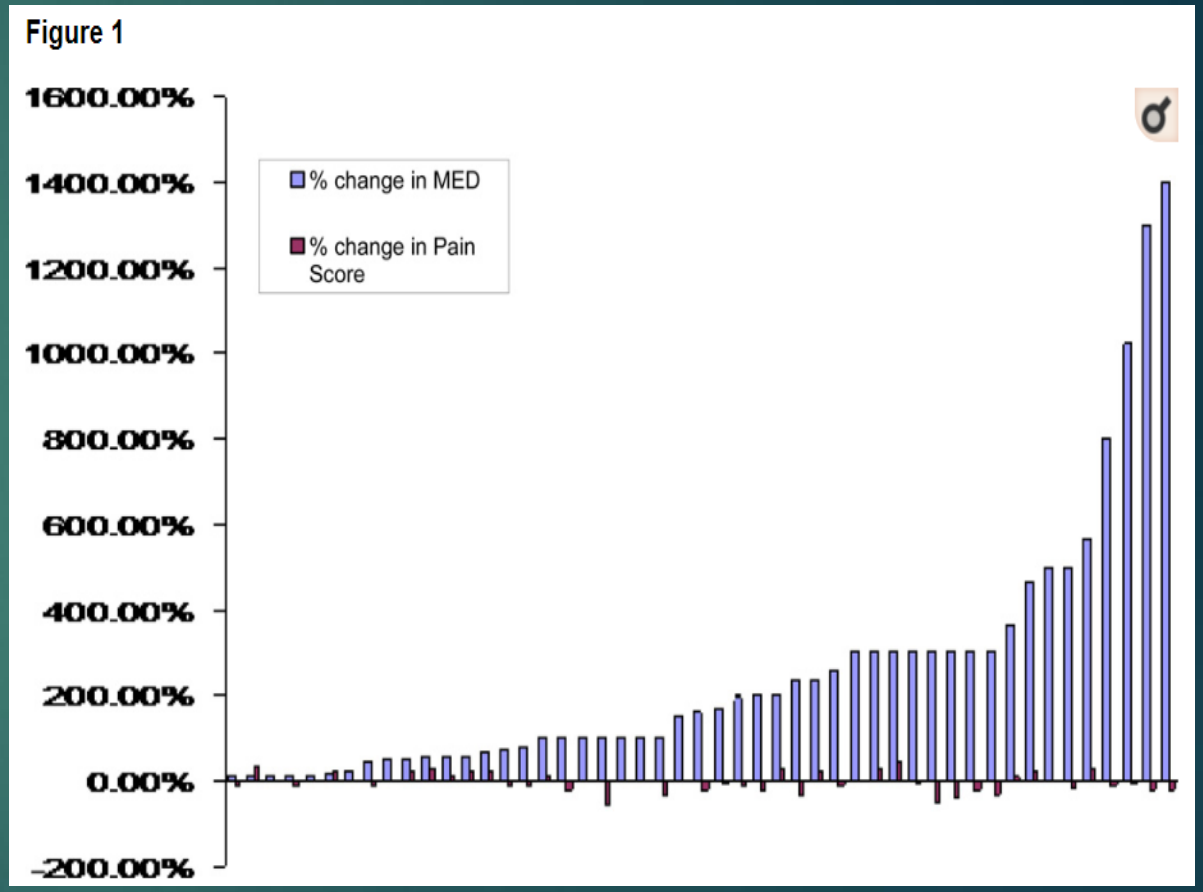
- In the primary care setting abuse rates range from 0.8-8%, **dependence rates are has high as 26% and misuse/diversion, aberrant UDS nearly 40**% (41)
- Long term opioid therapy increases elderly fall risk and fractures, causes constipation and lowers libido and sex hormones (41, 44)
- Long term COT worsens clinical depression and **independently increases suicide risk** probably because of behavioral disinhibition with higher opioid dose (46)
- Opioid doses > 20 MED are associated with increased risk of road accidents (41)

Chronic Pain: High dose = Low Pain?

LACK OF CORRELATION BETWEEN OPIOID DOSE ADJUSTMENT AND PAIN SCORE CHANGE IN A GROUP OF CHRONIC PAIN PATIENTS

Lucy Chen, Trang Vo, Lindsey Seefeld, Charlene Malarick, Mary Houghton, Shihab Ahmed, Yi Zhang, Abigail Cohen, Cynthia Retamozo, Kristen St. Hilaire, Vivian Zhang, and Jianren Mao

- Chen studied the effect of increased opioid dose on numeric pain scores of 109 patients at MGH followed for 704 days
- **Dramatically increased opioid doses did not reduce reported pain levels** (55)
- In some cases, **reduced opioid dose improved pain score** = ?Opioid induced hyperalgesia



Chronic Pain: High Dose = High Risk

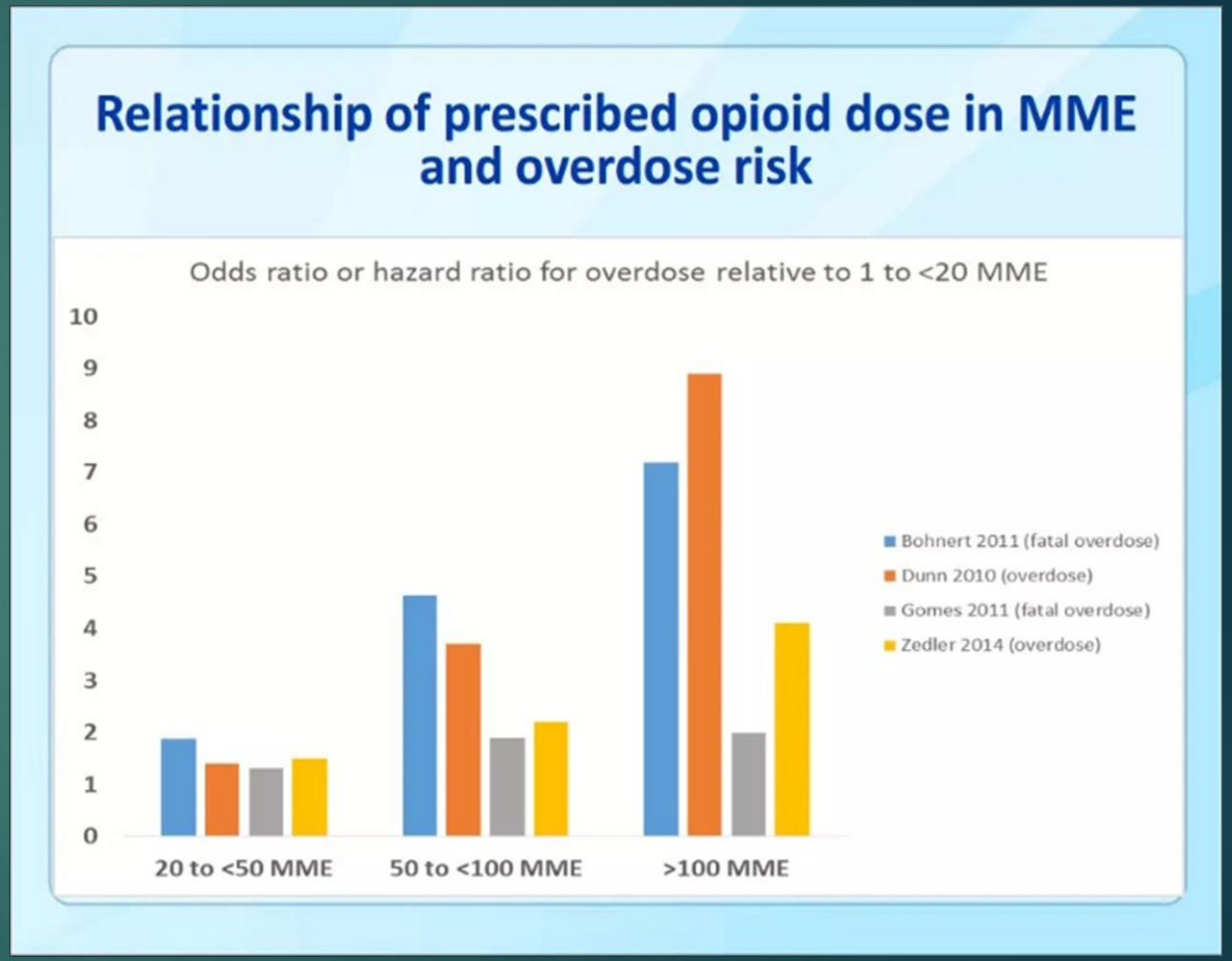
Association between opioid prescribing patterns and opioid overdose-related deaths.

Bohnert AS[1], Valenstein M, Bair MJ, Ganoczy D, McCarthy JF, Ilgen MA, Blow FC.

- Bohnert's 2011 observational study in JAMA examined common variables found in 1136 OD deaths among 155,000 VA patients on long term COT between FY 2004-2008
- Study concluded that risk of OD death increased significantly when MED > 50 (45)
- **Patients at highest risk: middle aged white males with chronic or acute pain, substance use disorders and psychiatric illness and comorbidities such as OSA, COPD** (45)
- Study found a large number of OD deaths in patients prescribed 0 MED (in VA system) suggesting doctor shopping and **diversion/saving and hoarding of pills causative** (45)

Chronic Pain: 90 MED threshold?

- **Lower MED dose decreases OD risk and does not worsen pain**
- The 2016 CDC guidelines somewhat arbitrarily chose > 120 MED as an initial “cutoff.” **Now 90 MED is the suggested threshold**
- 2015 Cochrane review showed RR of fatal OD increased 9X when MED > 100
- Conclusion: **Risk but no Reward when MED > 90** so reducing dose is prudent (48)



Source: Face Facts

Opioids and Benzos: Risky Business

Benzodiazepine prescribing patterns and deaths from drug overdose among US veterans receiving opioid analgesics: case-cohort study.

Park TW[1], Saitz R[2], Ganoczy D[3], Ilgen MA[4], Bohnert AS[4].

- Park's 2015 study published in *BMJ* examined OD deaths in 2400 veterans prescribed COT from 2004-2009
- **Concurrent benzodiazepine usage increased OD risk by a factor of 3.86** (49)
- **Risk of OD with combination therapy increased linearly with prescribed opioid dose** (49)
- Hernandez's 2018 study in JAMA showed **benzo and opioid use increases OD risk 5 X in first 90 days** among 71,000 MEDICARE part D recipients (50)

Short vs. Long acting Opioids

Short-Acting Opioids Are Associated with Comparable Analgesia to Long-Acting Opioids in Patients with Chronic Osteoarthritis with a Reduced Opioid Equivalence Dosing.

Ghodke A[1], Barquero S[2,3], Chelminski PR[1,2], Ives TJ[1,2].

- ER/LA opioids do not reduce addiction risk. **Tamper resistant formulations (ER) may reduce risk of recreational use and abuse but pills can be chewed, or the mechanism defeated in >35% of cases** (16)
- Overdose death rates have climbed as patients migrate to IR products, heroin, **or simply overtake ER pills** (18)
- Ghodke's 2017 study in *Pain* showed that **SA opioids provided comparable analgesia with ER/LA formulations at lower MED dose** (51)
- 2015 JAMA study: **2.5 X higher OD risk** with ER/LA vs SA opioids in 319 VA OD deaths; **risk highest at initiation of therapy** (53)

Source: PinsDaddy.com

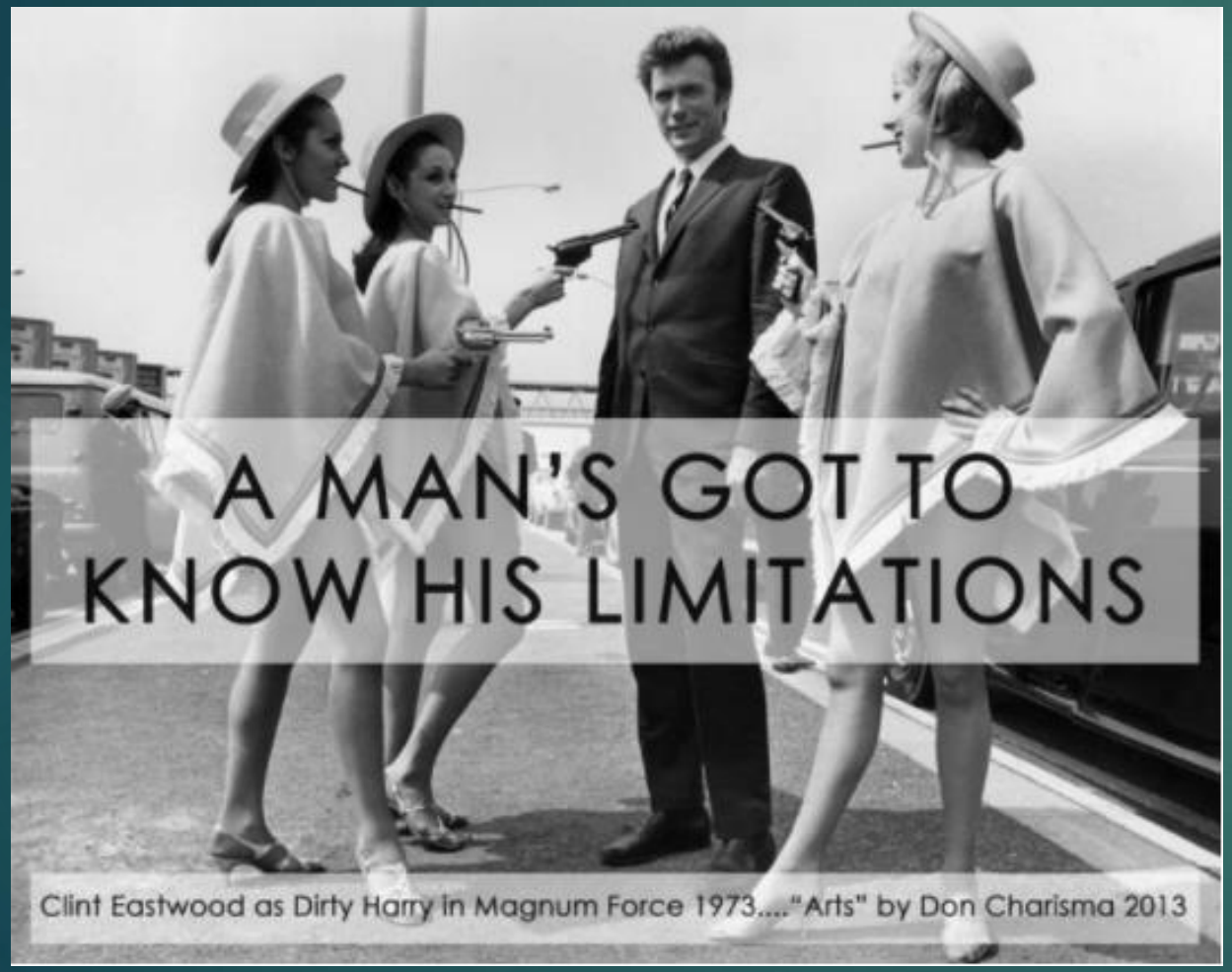
Methadone: The Widowmaker

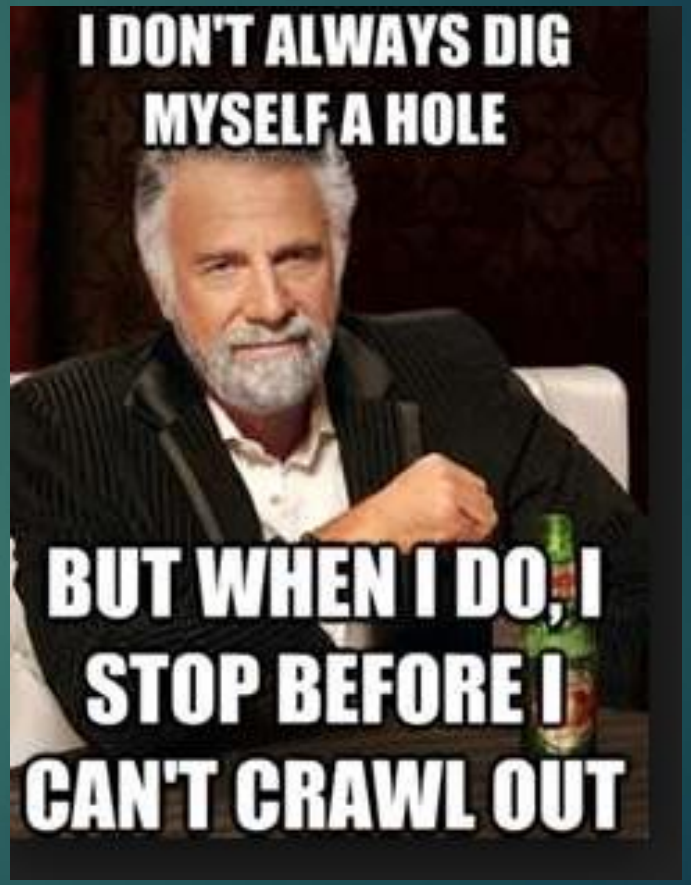
Methadone Prescribing and Overdose and the Association with Medicaid Preferred Drug List Policies - United States, 2007-2014.

Faul M, Bohm M, Alexander C.

- Methadone is a LA opioid formulation used for MAT with an analgesic T ½ of 4-8 hrs
- Methadone prolongs the QT interval and can cause sudden cardiac death as well as delayed respiratory depression
- Methadone's long and variable T ½ (**24 hrs opioid tolerant, 55 hrs opioid naive**) = respiratory and cardio depressant effects persist long after analgesia has worn off
- **In 2014, methadone accounted for 1% of all opioid prescriptions but 23% of opioid deaths** (54)

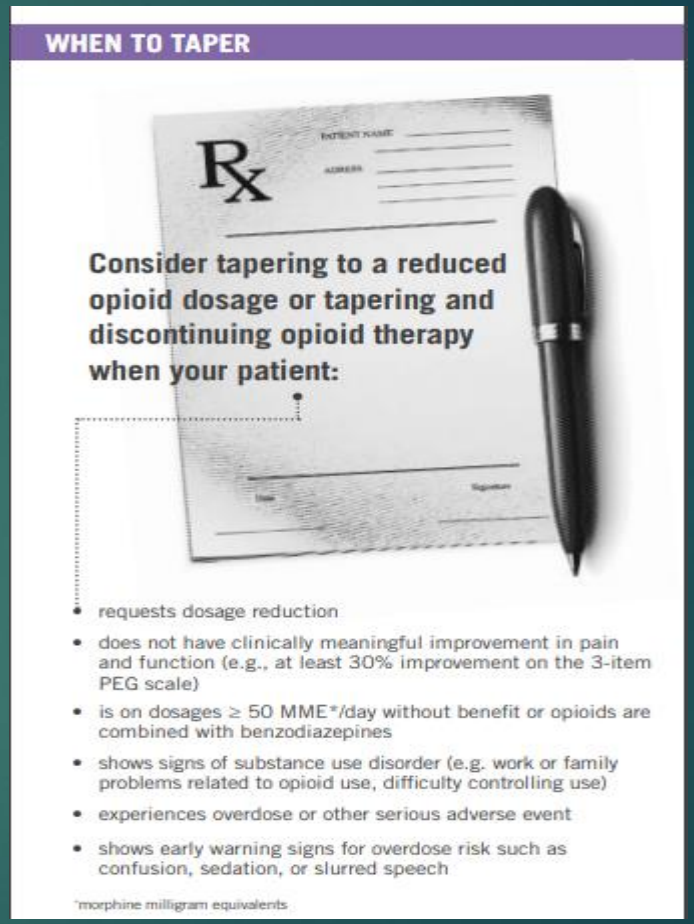
Tapering Opioids





When to Taper

- **When** function does not improve
- **When** patients misuse, abuse, divert medications or take dangerous sedatives
- **When** the risks of opioid therapy outweigh the benefits
- **When** opioid dose exceed CDC recommended guidelines (> 90 MED)



Source: CDC.gov

How to Taper

- Tapers are not “one size fits all.” Length depends on starting MED
- **Slower taper = more successful taper**
- Dose reductions of 10% per week or 30-60 MED per month usually well tolerated
- **Taper Long acting medications FIRST**
- **Reasons to accelerate taper**: suicidality, co-administration of sedatives, patients on methadone, substance abuse or misuse

OPG
OREGON PAIN GUIDANCE

https://www.oregonpainguidance.org/guideline/tapering

Tapers: Do they actually work…YES

- Opioid induced hyperalgesia (OIH) involves central sensitization and multiple pain receptor systems
- **Can occur after a single bolus or IV opioid infusion**
- Studies show that patients weaned off opioids generally do not experience *worse* pain
- **Many patients have reduced pain and improved mood and function**

Pain Med. 2015 Oct;16(10):1975-81. doi: 10.1111/pme.12812. Epub 2015 Jun 27.

Clinical Implications of Tapering Chronic Opioids in a Veteran Population.

Harden P[1], Ahmed S[1], Ang K[1], Wiedemer N[1].

J Opioid Manag. 2006 Sep-Oct;2(5):277-82.

Significant pain reduction in chronic pain patients after detoxification from high-dose opioids.

Baron MJ[1], McDonald PW.

Pain Med. 2016 Sep;17(9):1676-85. doi: 10.1093/pm/pnv079. Epub 2016 Jan 11.

Opioid Tapering in Fibromyalgia Patients: Experience from an Interdisciplinary Pain Rehabilitation Program.

Cunningham JL[1], Evans MM[2], King SM[2], Gehin JM[2], Loukianova LL[2].

Pain. 2017 Jul;158(7):1380-1394. doi: 10.1097/j.pain.0000000000000907.

Sustained improvements in pain, mood, function and opioid use post interdisciplinary pain rehabilitation in patients weaned from high and low dose chronic opioid therapy.

Huffman KL[1], Rush TE, Fan Y, Sweis GW, Vij B, Covington EC, Scheman J, Mathews M.

Safer Opioid Alternatives

- Buprenorphine products are effective for chronic pain and safer than conventional opioids (56)
- **<u>Buprenorphine has a “ceiling effect” for respiratory depression but not analgesia</u>**
- Butrans is a transdermal patch (5-20 mcg/hr) FDA approved in 2010 and on VCC formulary
- Belbuca is a buprenorphine film placed on the inside of the cheek and dosed 150-900 mcg BID

https://www.buppractice.com

Conclusion

- **There is no level I evidence that chronic opioids relieve pain or improve function in the long term**
- **Reduce chronic pain patients on high dose opioids to < 90 MED over 1-3 months**
- **Be alert for opioid misuse, addiction, and diversion**
- **Today's chronic pain or post-surgical patient is tomorrow's OUD/Overdose**

Chronic Pain: VA BOM regulations

https://www.dhp.virginia.gov/medicine/docs/FAQPrescribingBuprenorphine.pdf

18VAC85-21-60. Evaluation of the chronic pain patient.

Prior to initiating management of chronic pain with a controlled substance containing an opioid, a medical history and physical examination, to include a mental status examination, shall be performed and documented in the medical record

Perform a urine drug screen or serum medication level

Perform a query of the Prescription Monitoring Program as set forth in § 54.1-2522.1 of the Code of Virginia

Assess the patient's history and risk of substance misuse/abuse

Discuss with the patient the known risks and benefits of opioid therapy and the responsibilities of the patient during treatment to include securely storing the drug and properly disposing of any unwanted or unused drugs.

18VAC85-21-70. Treatment of chronic pain with opioids.

Nonpharmacologic and non-opioid treatment for pain shall be given consideration prior to treatment with opioids.

Carefully consider and document in the medical record the reasons to exceed 50 MME/day;

Prior to exceeding 120 MME/day, document in the medical record the reasonable justification for such doses or refer to or consult with a pain management specialist.

Prescribe naloxone for any patient when risk factors of prior overdose, substance abuse/misuse doses more than 120 MME/day, or concomitant benzodiazepine is present

Regularly evaluate for opioid use disorder and initiate specific treatment for opioid use disorder, consult with an appropriate health care provider, or refer the patient for evaluation and treatment if indicated.

18VAC85-21-80. Treatment plan for chronic pain.

Include a treatment plan that states measures to be used to determine progress in treatment, including pain relief and improved physical and psychosocial function, quality of life, and daily activities.

Include further diagnostic evaluations and other treatment modalities or rehabilitation that may be necessary depending on the etiology of the pain and the extent to which the pain is associated with physical and psychosocial impairment.

Document in the medical record the presence or absence of any indicators for medication abuse/misuse, or diversion and shall take appropriate action.

Keep your patients safe by complying with VA Board of Medicine Guidelines 18VAC85-21 10-120

https://www.dhp.virginia.gov/medicine/docs/FAQPrescribingBuprenorphine.pdf

1. **DO** check the VA Rx monitoring database before starting opioids (https://virginia.pmpaware.net/) and at least every 3 months thereafter.
2. **DO** have a written treatment agreement and informed consent with every patient on chronic opioids.
3. **DO** prescribe naloxone to every patient on >120 MME, or patients on <120 MME who also take benzodiazepines or dangerous sedatives https://www.cdc.gov/drugoverdose/prevention/index.
4. **DO** screen for substance abuse and utilize the Opioid Risk Tool when you start patients on chronic opioids https://www.drugabuse.gov/sites/default/files/files/OpioidRiskTool.pdf.
5. **DO** see chronic opioid patients at least every 3 months and document your rationale for continuing opioids. Utilize the PEG screening tool to assess function
6. **DO** consider referral to a pain specialist when patients are on >120 MME.
7. **DO** perform urine drug screening at the first visit, every 3 months in the first year, and every 6 months thereafter when prescribing chronic opioids.
8. **DO** assess patients for substance abuse and opioid use disorders regularly and refer for Addiction treatment https://www.vcuhealth.org/locations/vcu-medical-center/jackson-center-vcu-med-ctr.
9. **DO** taper patients to <120 MME and consider stopping opioids if function doesn't improve http://mytopcare.org/wp-content/uploads/2013/06/PEG-Pain-Screening-Tool1.pdf

1. **DON'T** co-prescribe opioids and benzodiazepines.
2. **DON'T** routinely start patients on chronic opioids without considering alternative treatment options.
3. **DON'T** start patients on long acting or "sustained release" opioids like Oxycontin.
4. **DON'T** prescribe chronic opioids to patients with substance abuse or opioid use disorders.
5. **DON'T** escalate opioid doses >50 MME unless absolutely necessary.
6. **DON'T** prescribe opioids for greater than 7 days when treating acute pain or after a surgical procedure.

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Questions?