Opioids and Risk Management

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Conflict of Interest Disclosure

I have no conflicts and nothing to disclose

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Objectives

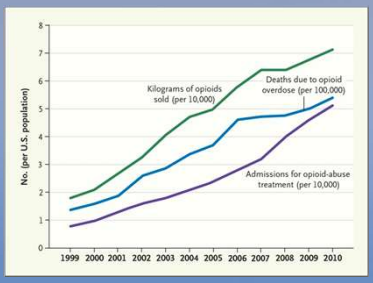
- Describe the current issues with opioid prescribing in the US
- Apply fundamental concepts of opioid pain management
- Implement effective monitoring for patients on opioid therapy
- Employ strategies to mitigate opioid prescribing risk
- Describe the role of state PDMP databases
- Describe the role of Naloxone in opioid prescribing
- Utilize abuse deterrent opioid agents
- Recognize and use the different types of toxicology screens
- Implement strategies to mitigate risk of opioid misuse

What Are We Up Against?

- 2017: 68% of 70,200 drug overdose deaths due to opioids (~48,000)[1]
- 2017: opioid overdose deaths 6x higher than in 1999[1]
- 2017: 11.5 million Americans age >12 misused a prescription pain reliever (hydrocodone, oxycodone, codeine – most common)[3]
- 2019: 4.3 million people used a prescribed opioid for a non-medical reason in the past month
- 2016: Most common source of pain relievers:
  1. "friend or relative" (53%)
  2. "physician's prescription" (35%)[4]

1. https://www.cdc.gov/drugoverdose/epidemic/index.html Accessed July 2019
2. https://www.cdc.gov/drugoverdose/data/overview.html Accessed July 2019
2. See https://www.cdc.gov/nchs/data/factsheets/factsheet_drug_poisoning.pdf. Accessed July 2018.
2. Substance Abuse and Mental Health Services Administration. (2017). *Key substance use and mental health indicators in the United States: Results from the 2016 National Survey on Drug Use and Health* (HHS Publication No. SMA 17-5044, NSDUH Series H-52). Rockville, MD: Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration.
3. Ibid.

What Are We Up Against?



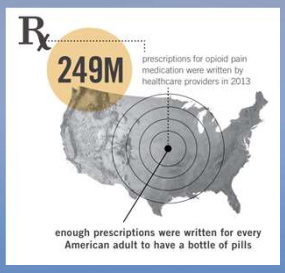
1999 – 2017: opioid prescriptions and opioid related deaths quadrupled

1. Volkow ND et al. Medication-Assisted Therapies — Tackling the Opioid-Overdose Epidemic. N Engl J Med 2014; 370:2063-2066
2. https://www.cdc.gov/drugoverdose/data/overview.html Accessed July 2019

What Are We Up Against?

https://www.cdc.gov/drugoverdose/pdf/Publications_At-A-Glance-a.pdf Accessed July 2019

What Are We Up Against?



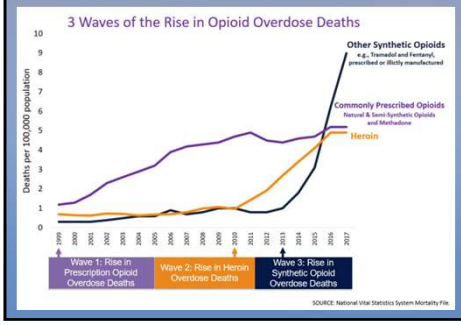
https://www.cdc.gov/drugoverdose/epidemic/Confidence_in_A_Climate.pdf Accessed July 2019

What Are We Up Against?

- Only 30% of medical schools require instruction on opioid prescribing[1]
- Trainees receive <1 hour of dedicated training on analgesics[2]
- Only half of primary care physicians surveyed feel only "somewhat comfortable" managing pain[2]
- Veterinary schools mandate an average of 87 hours to dedicated pain curriculum compared to 16 hours spread across multiple courses at medical schools[3]

1. Morley- Forster et al J Pain Res 2013
2. Institute of Medicine 2011
3. Watt-Watson et al Pain Res Manage 2009

Where Are We Now?



Wave 1: increased prescribing of opioids, deaths mostly prescription related (1999-2009)

Wave 2: rapid increase in deaths from heroin (2010-2013)

Wave 3: rapid increase in deaths from synthetic opioids, mostly fentanyl (2013 – present)

Where Do We Go From Here?

- Improve Opioid Prescribing
- Prevent Opioid Use Disorder
- Treat Opioid Use Disorder
- Reverse Overdose

Improving Opioid Prescribing

1. Opioids are not first-line therapy

Adjuvant Therapies

Improving Opioid Prescribing

2. Establish realistic goals for pain and function

Improving Opioid Prescribing

3. Discuss risks and benefits of opioid therapies

Improving Opioid Prescribing

4. Avoid long-acting agents in opioid naïve patients

Opioid Tolerant vs Naïve

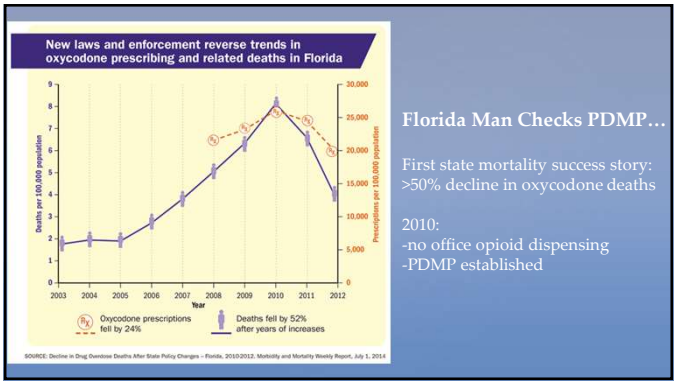
- **Opioid tolerant patients:**
  - *Morphine 60mg PO daily*
  - Fentanyl patch 25mcg/hr
  - Oxycodone 30mg PO daily
  - Hydromorphone 8mg PO daily

Improving Opioid Prescribing

5. Use the lowest effective dose

Improving Opioid Prescribing

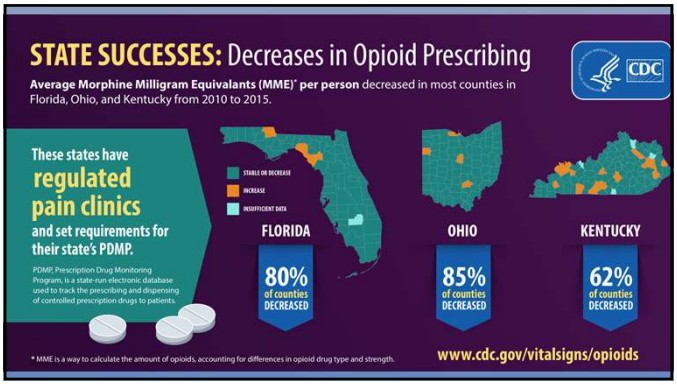
6. Review multistate PDMP databases



Florida Man Checks PDMP…

First state mortality success story:
>50% decline in oxycodone deaths

2010:
-no office opioid dispensing
-PDMP established



Improving Opioid Prescribing

7. Prescribe short durations for acute pain

Improving Opioid Prescribing

8. Evaluate risks/benefits frequently

Improving Opioid Prescribing

9. Use urine drug testing

Improving Opioid Prescribing

10. Avoid concurrent opioid and benzodiazepine prescribing

Improving Opioid Prescribing

11. Offer treatment for opioid use disorder

Improving Opioid Prescribing

Who here can prescribe naloxone?

Improving Opioid Prescribing

Who here can prescribe buprenorphine?

Improving Opioid Prescribing

Who here can prescribe methadone?

Naloxone and Good Samaritan Laws

- Naloxone is NOT a controlled substance
- Naloxone has NO abuse potential

Naloxone and Good Samaritan Laws

- **Third-Party Prescribing**: prescribing to a person who will not be the recipient of the drug ☑
- **Prescription via Standing Order**: prescription without a direct patient-prescriber relationship ☑

Naloxone and Good Samaritan Laws

- **July 15th 2017**: All 50 states + DC pass laws to improve naloxone layperson access
- **December 31st 2018**: 46 states + DC pass an overdose Good Samaritan law shielding from arrest or prosecution when an overdose is reported

Naloxone and Good Samaritan Laws

		Most recent change	Immunity: Prescribers			Immunity: Dispensers			Immunity: Lay administrators		Lay distribution & possession		Prescribing Permitted	
			Civil	Criminal	Disciplinary	Civil	Criminal	Disciplinary	Civil	Criminal	Lay distribution	Pres. w/o Rx	3rd Party	Standing order
CT	Conn. Gen. Stat. Ann. § 17a-714a; Conn. Gen. Stat. Ann. §§ 20-633c, d	Oct. 1, 2017	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	-	-	Yes	Yes[24]
MA	Mass. Gen. Laws Ann. ch. 94C, §§ 19(d); 19B; 19B1/2; 34A Mass. Gen. Laws Ann. ch. 112 § 12FF	Aug 9, 2018;	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	-	Yes	Yes	Yes
ME	Me. Rev. Stat. Ann. tit. 22, § 2353	Aug 1, 2018	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	-	Yes	Yes
NH	N.H. Rev. Stat. Ann. § 318-B:15	June 2, 2015	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	-	Yes	Yes
RI	31-2-9 R.I. Code R. §§ 5.1-5.8; R.I. Gen. Laws Ann. § 21-28.9-1 -5	July 2, 2016	-	-	Yes	-	-	Yes	Yes	Yes	Yes[21]	Yes	Yes	Yes
VT	Vt. Stat. Ann. tit. 18, § 4240; Vt. Stat. Ann. tit. 26, § 2080	May 28, 2015	Yes	Yes	-	Yes	Yes	-	Yes	Yes	Yes[166]	Yes[27]	Yes	Yes

Improving Opioid Prescribing

How did you choose this pain regimen?

Opioid Pharmacology

- Pharmacology
- Formulations
- Metabolism
- Peak Effect
- Duration of Action
- End Dose Failure
- Time to Steady State
- Incomplete Cross Tolerance
- Adverse Effects

Opioid Pharmacology

- Receptors
  - mu (μ), kappa (κ), delta (δ)
- Mechanism of Action
  - primarily bind μ receptor
  - inhibit pre-synaptic Ca^{2+} influx
  - promote post-synaptic K^{+} efflux
  - prevent release of glutamate, substance P which leads to hyperpolarized post-synaptic membrane

Opioid Metabolism

Table 3. Guidelines for Opioids in Kidney and Liver Disease:

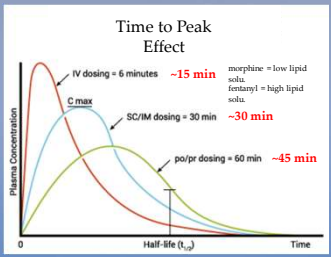
	Kidney Disease		Liver Disease	
	Renal Failure	Dialysis	Stable Cirrhosis	Severe Disease
Morphine	Do not use	Do not use Not dialyzed	Caution ↓ dose ↓ frequency *	Do Not Use
Oxycodone	Caution ↓ dose ↓ frequency*	Caution	Caution ↓ dose ↓ frequency*	Caution ↓ dose ↓ frequency*
Hydromorphone	Preferred ↓ dose ↓ frequency*	Preferred Not dialyzed, but minimal toxicity	Caution ↓ dose ↓ frequency*	Caution ↓ dose ↓ frequency*
Fentanyl	Preferred	Preferred Not dialyzed, but minimal toxicity	Preferred	Preferred
Codeine	Do not use	Do not use	Do not use	Do not use
Methadone	Preferred – with consultation only	Preferred – with consultation only. Not dialyzed, but minimal toxicity	Preferred – with consultation only	Preferred – with consultation only

* ↓ dose means reduce dose by 25-50%
↓ frequency means reduce standing orders for short-acting opioids from Q4H to Q6H

[1]Avoid sustained-release oral opioids and fentanyl patches in kidney disease. Note that even the "safest opioids are not dialyzable.

[2]Consult with an experienced clinician before initiating or adjusting the dose of methadone.

Peak Effect



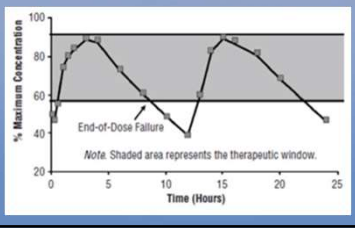
Peak Effect = Maximum Plasma Concentration

Duration of Action

- Most oral and IV opioids: ~**4 hours**
- Methadone: 6-8 hours
- Fentanyl patch: 48-72 hours
- Buprenorphine patch: 7 days

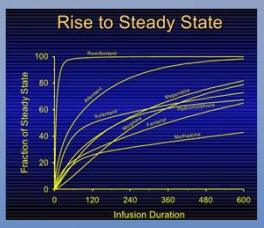
End of Dose Failure

Pain at the end of a dose interval before duration of action is complete (i.e. pain at <4 hours)



Steady State

- **Steady State:** dynamic equilibrium between intake and elimination – 4-5 half lives
- Generally ok to increase short-acting opioid dose up to 100% per day



Incomplete Cross Tolerance

Increased sensitivity to an opioid when rotated to new opioid

- **Well controlled pain**: decrease new opioid dose by 50%
- **Acute pain**: do not decrease dose