

**“Houston we have a problem!”
The epidemic of non medical use of
prescription opioids**

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Disclosure

- I have participated/consulted in funded (“sponsored”) research by the following “pharmas”
 - Purdue (oxycodone, oxycontin, hydromorphone)
 - Endo (oxymorphone)
- Since very few analgesic drugs have been studied in children, this lecture will include “off label” use of drugs.

Objectives

- Describe a process of discovery and quality improvement in the delivery of medical care that can be used in your own practice
- Describe how we went from the undertreatment of pain to an epidemic of opioid abuse and how this affects your practice
- What are the alternatives?

“The world is full of obvious things which nobody by any chance ever observes.”

Sherlock Holmes -*The Hound of the Baskervilles*
Sir Arthur Conan Doyle



It all started with an observation



An Analysis of 34,218 Pediatric Outpatient Controlled Substance Prescriptions

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Anesthesia and Analgesia. 2016;122(3):807-813

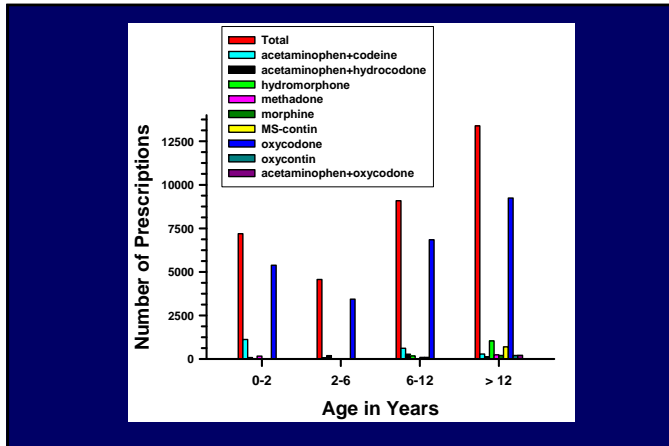
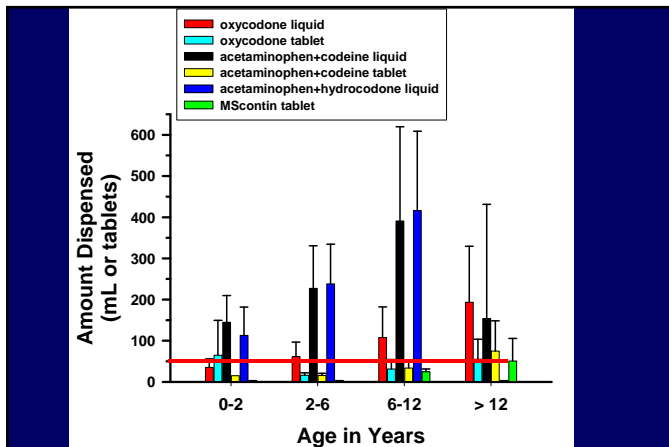


Table 2. Codeine Prescriptions by Year and How Dispensed

Year	Total	Liquid	Tablet
2007	377	306	71
2008	342	280	62
2009	584	497	87
2010	606	545	61
2011	327	289	38
2012	237	210	27
2013	29	22	7
2014	3	2	1



Analysis of Controlled Substance Prescriptions: Summary of Results

Regardless of the opioid prescribed, providers wrote for very large quantities of drug to be dispensed

Another Observation... Which Led to More Questions...

- Research Study Questions:**
- How well is post-op pain managed?
 - How much of the controlled substance prescription remains after 10-14 days at home?
 - Is opioid therapy required at 10-14 days? At 6 months post-discharge?
 - What do parents know about safe disposal of unused opioids?

Research Study Questions:

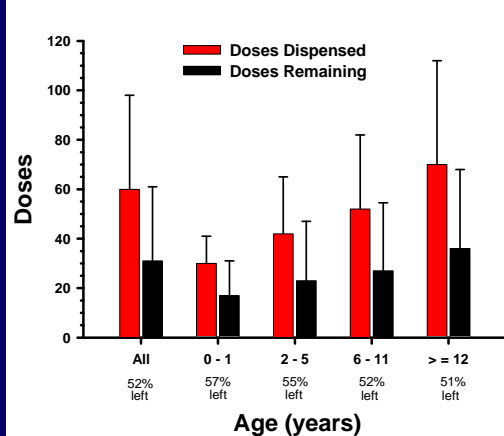
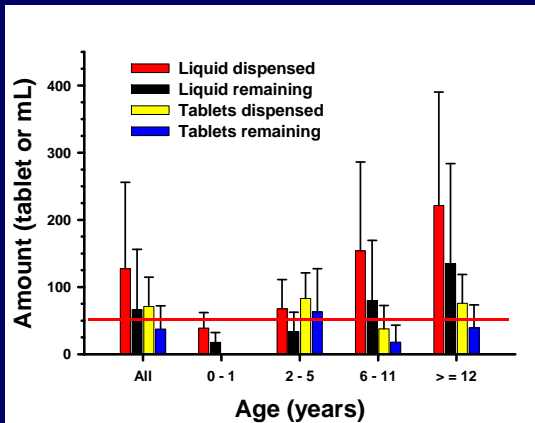
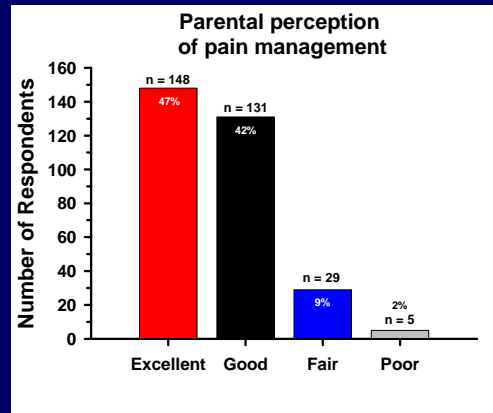
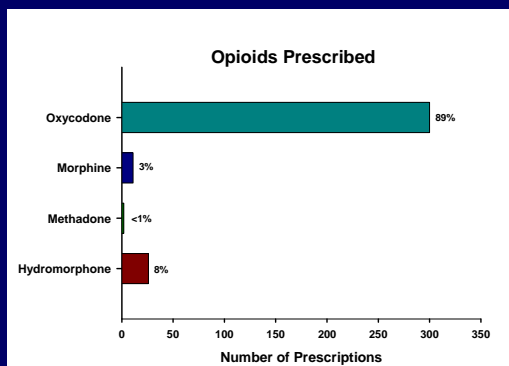
- Were they given instructions on how to dispose of leftover meds?
- Who informed them (physician, nurse, pharmacist)?
- Did they disposed of unused meds?
- Are there at-risk individuals in the home? (Adolescents and risk of NMUPO; young children and risk of accidental ingestion.)

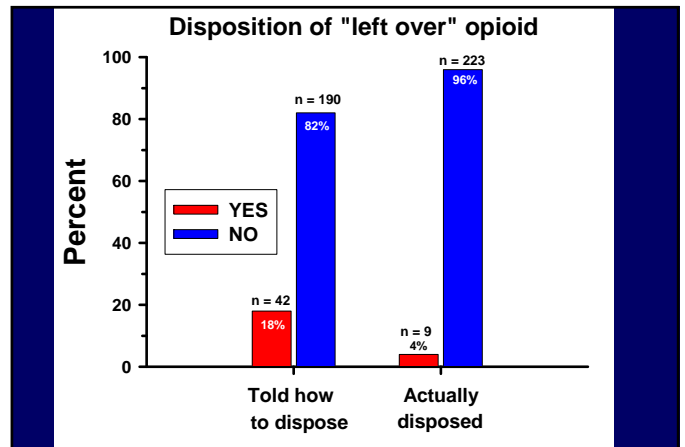
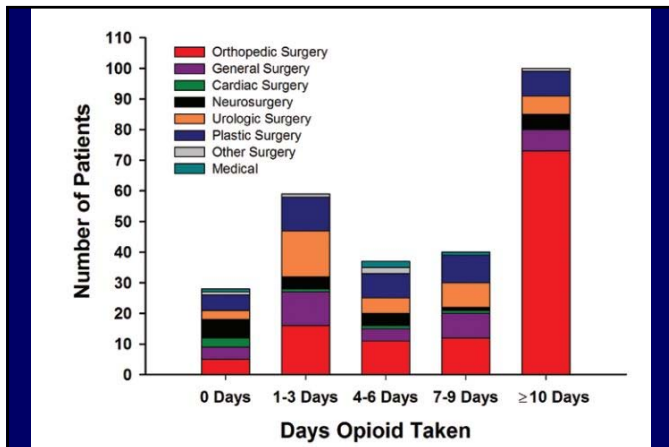
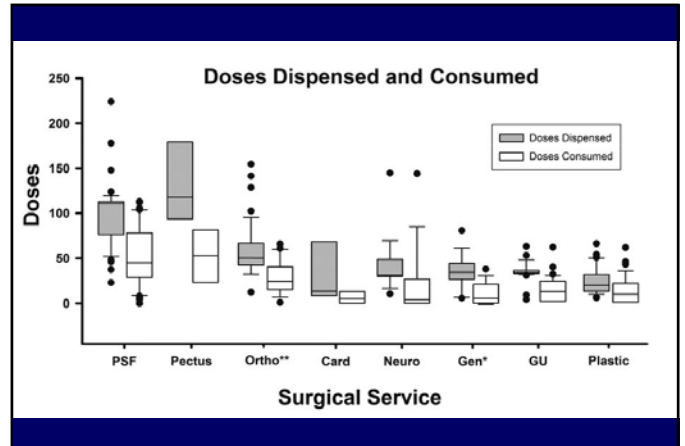
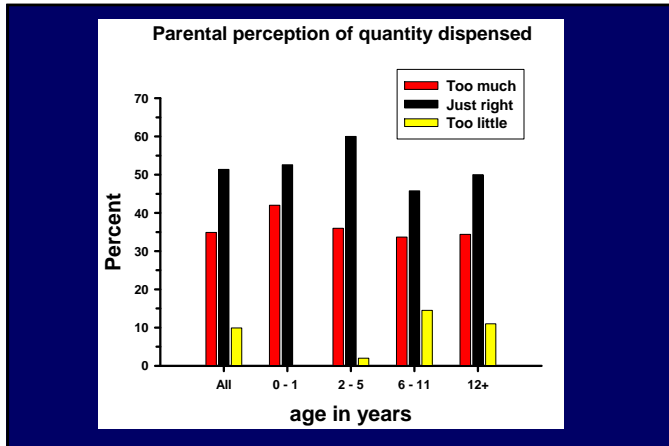


Opioid Prescribing for the Treatment of Acute Pain in Children on Hospital Discharge

Constance L. Monitto, MD,* Aaron Hsu, MHS,* Shuna Gao, BA,* Paul T. Vozzo, BA,* Paul S. Park, BS,* Deborah Roter, DrPh,† Gayane Yenokyan, MD, MPH, PhD,‡ Elizabeth D. White, RN, Deepa Kattail, MD, MHS,* Amy E. Edgeworth, RN, MSN, CRNP,* Kelly J. Vasquez, RN, MSN, CPNP* Sara E. Atwater, RN, MSN, CPNP,* Joanne E. Shay, MD, MBA,* Jessica A. George, MD, MEd,* Barbara A. Vickers, MD, MPH,* Sabine Kost-Byerly, MD,* Benjamin H. Lee, MD, MPH,* and Myron Yaster, MD*

Anesthesia and Analgesia. 2017;125: 2013-22





Storage and Disposal of Morphine at the End of Treatment

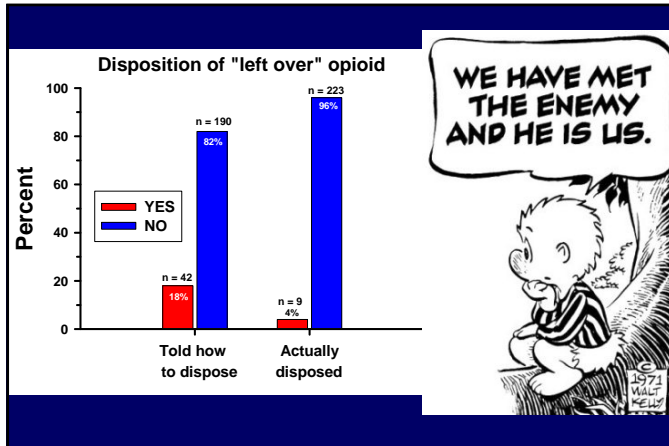
Storage, n (%)	
Room	
Kitchen	115 (65)
Bathroom	27 (15)
Parent's bedroom	18 (10)
Child's bedroom	9 (5)
Other	8 (5)
Open or closed space	
Open	76 (44)
Closed	96 (56)
Disposal of morphine at the end of treatment, n (%)	
Return to pharmacy	93 (55)
Throw away	45 (27)
Keep at home	16 (9)
Do not know	16 (9)

Abou-Karam M, et al. Parental Report of Morphine Use at Home after Pediatric Surgery. J Pediatr 2015; 167: 599-604

NMUPO and Adolescents

- 27% mistakenly believe that misusing and abusing prescription drugs is safer than using street drugs.
- 33 % say they believe "it's okay to use prescription drugs that were not prescribed to me to deal with an injury, illness or physical pain."

2012 Partnership Attitude Tracking Study (PATS)-MetLife Foundation



Opioids, Pain, and Surgery

- 51 million Americans undergo surgery/year
- For moderate to severe pain, opioids remain the gold standard for pain management

If the only tool you have is a hammer, **you tend to see every problem as a nail**
 Abraham Maslow

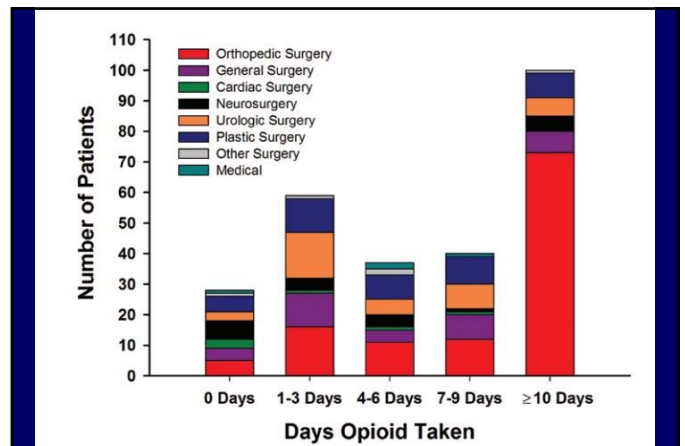
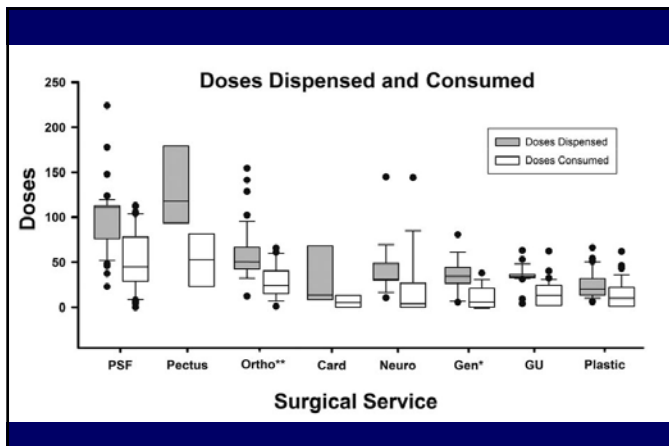
"Duh!"

- 80% of patients receive opioids after surgery
- > 80% receive either oxycodone or hydrocodone
- Surgical patients routinely receive the opioids most commonly implicated in overdose deaths

Haven't we seen this before?

Pain is the 5th vital sign

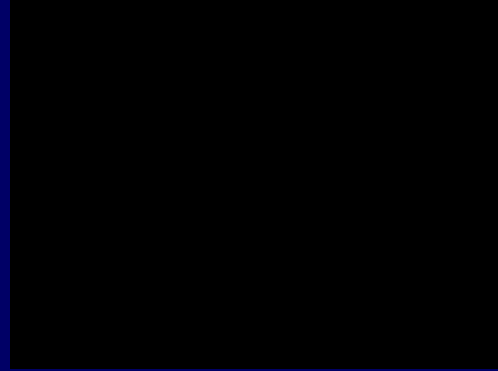
Opioidphobia



We need DATA!

- Type of surgical procedure
- Preoperative patient characteristics
 - Age
 - Gender
 - Race
 - Language
 - Prior opioid or alcohol use/abuse
 - Preoperative medication use (antidepressants, benzodiazepines)

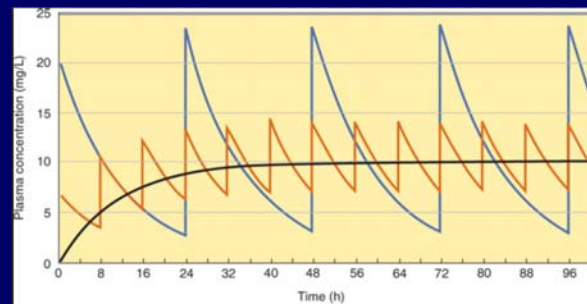
Strategies to limit opioid use after surgery



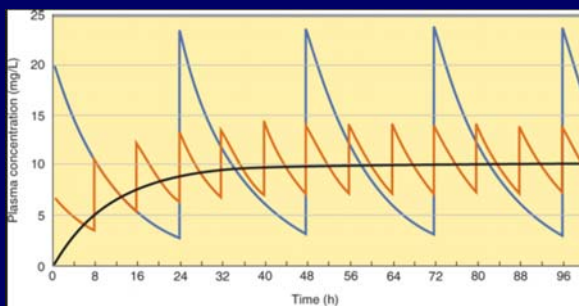
The “Usual Suspects”

- Regional and Neuraxial Anesthesia
- Multimodal analgesia
 - Acetaminophen
 - NSAIDs
 - Gabapentoids
- Non pharmacologic approaches

PK it's not just for exams



Acetaminophen AND Ibuprofen



After Surgery in Germany, I Wanted Vicodin, Not Herbal Tea

By FIROOZEH DUMAS JAN. 27, 2018

- <https://www.nytimes.com/2018/01/27/opinion/sunday/surgery-germany-vicodin.html>



Basic/Translational Development of Forthcoming Opioid- and Nonopioid-Targeted Pain Therapeutics

Knezevic, Nebojsa Nick; Yekkirala, Ajay; Yaksh, Tony L.
*Anesthesia & Analgesia*125(5):1714-1732, November 2017.

Current and Future Targets

- **NMDA Receptor Blockade**
 - Ketamine, Methadone, Dextromethorphan
- **Opioid Receptor**
 - Mu, Kappa, Delta, Neuropeptide nociception
 - Peripherally active agonists
 - Biased ligands
- **Alpha 2 agonists**
 - Clonidine, Tizanidine, Dexmedetomidine

Peripherally restricted opioids

- Reduced side effect profile and minimum abuse and drug seeking behavior
- **Kappa** peripherally restricted agonists are in phase 2 and 3 trials and are effective for acute, chronic, inflammatory and visceral pain as well as pruritus

Biased Ligand Opioids

- Combine a classic mu agonist with a beta arrestin molecule modulating opioid side effects. Specifically reducing:
 - Tolerance
 - Respiratory depression
 - Pruritus
- In phase 2 trials

Cannabinoids

- Cannabinoid receptors (CB1 and CB2) are G protein coupled receptors (like opioids).
- CB1 receptors are in spinal cord **neurons**, particularly dorsal root ganglia
- CB2 are in spinal cord **microglia**
- Psychotropic and abuse potential effects are CB1, analgesia are CB1 and CB2

Cannabinoids

- There is NO postoperative data
- There is A LOT of anecdotal data, particularly for opioid substitution
- There is evidence that it may be effective in neuropathic pain
- We NEED data but there are enormous hurdles in studying a Class 1 drug

Conclusions Future Directions

- Need to identify reasons for overprescribing of these meds and mitigate risk to patient by behavior change and data-driven practices
 - Develop new methods of disposal
- BUT**
- We can't forget the need for humane pain management which for moderate to severe pain almost always requires opioids

A Journey of Discovery



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