The Larger Landscape of Pain Management: Seeking Balance

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Current State

- US is experiencing a devastating epidemic of prescription opioid misuse and abuse, including a large number of overdose deaths
- Expert opinion finds that the treatment of pain in the US, particularly chronic pain, is not satisfactory, including an over-reliance on prescription opioids (2011 IOM Report)
- The science and data needed to inform policy implementation is often lacking

How Did We Get Here?

- Opiates have been used by humans since recorded history for medical and non-medical purposes
- In the post-Civil War period, the US experienced an episode of widespread opiate addiction, driven by extensive physician prescribing of morphine injections for pain, and by patent medicines containing laudanum
- Reforms over several decades led to control of this problem and eventually legislative actions to restrict use
- Successive versions of modified opioids (including heroin) introduced with hope of “less addiction”

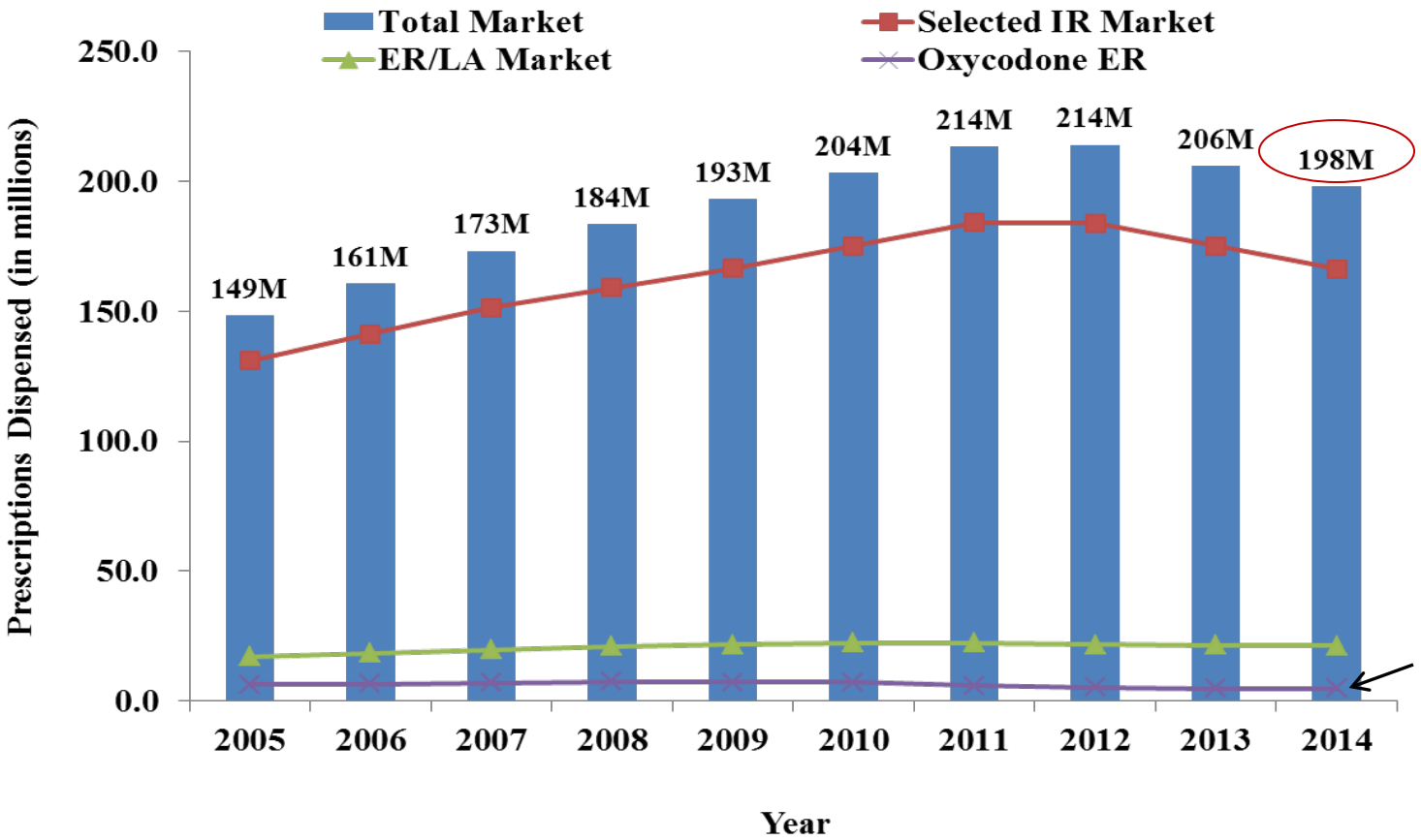
Late 20th Century

- The 19th Century episode, and the heroin epidemic of the 1960's led many prescribers (and patients) to be very wary of opioid use and to fear addiction
- In the 1990's, there was raised awareness of the inadequate treatment of pain and patient group and physician advocacy for improved pain management
- Guidelines for pain management issued by various specialty groups
- It was believed (and taught) that use of opioids for pain treatment would not lead to addiction
- JCAHO issued guidelines that pain be considered the "5th Vital Sign"
- Additional molecules and formulations developed and marketed, including higher-potency ER/LA formulations
- Practitioners responded with ever-increasing prescribing

2000's

- Jan 2001 Congress passed HR 3244 declaring the "Decade of Pain Control and Research"
- In 2000, FDA modified the label of OxyContin® based on reports of abuse and diversion, including boxed warnings and in 2001 initiated a risk management plan
- Opioid prescribing continued to escalate through the decade 2000-2010
- "Pill mills" proliferated in some states, offering prescriptions for cash without even cursory exams

IR and ER/LA Opioid



Nationally estimated number of prescriptions dispensed for selected IR and ER/LA opioid analgesics from U.S. outpatient retail pharmacies

Source: IMS Health, National Prescription Audit ™ Extracted May and August 2015

Unprecedented US Population Exposure to Rx Opioid Drugs

- Research on ethanol has shown that access and availability correlate with behaviors related to abuse and to alcohol-related deaths
- Large majority of prescription opioids involved in abuse were obtained, bought, or stolen from friend or relative; about 20% prescribed by person's single physician
- Most opioid analgesics prescribed by primary care physicians and dentists, not specialists
- Majority of exposure is from IR forms

Use of Opioid Medications in Healthcare Settings

- Hospital use: anesthesia; surgery and post-surgical care; trauma and burn care; palliative care; cancer; terminal illness
- Outpatient surgical, dental and other procedures
- Nursing homes: palliative care, terminal illnesses
- Rehab hospitals
- Hospice care
- Outpatient acute pain—emergency departments, post-surgery, physician's offices, etc.
- Outpatient cancer pain
- Outpatient chronic non-cancer pain—the most controversial area
- Each of the above has legitimate uses for opioids

How to reduce overall population exposure to opioids while retaining appropriate pain management in the various care settings?

Reducing (truly) Inappropriate Prescribing

- No prescriber wants to write a prescription for someone who is abusing the drug. Prescription drug monitoring programs (PDMPs) are intended to alert prescribers and pharmacists about potential “doctor shoppers”
- Florida laws passed in 2010-11 to regulate “pill mills” and implement PDMP’s correlated with significant reduction of predicted opioid overdose deaths in the state

Appropriate Management of Acute Pain in the Outpatient Setting

- Trauma, post-surgery, ruptured disc, etc
- Alternative armamentarium is limited, primarily NSAIDS or acetaminophen
- NSAIDs have well-known serious side effects, may not be appropriate where bleeding is a concern
- Combination hydrocodone/acetaminophen (129M RX in 2012) or oxycodone/acetaminophen most popular
- Major issue is # of tablets/duration of RX
  - Many people don't take/can't tolerate
  - Leads to large excess sitting in medicine cabinets across the country
  - Disposal practices must be improved, but better not to dispense so many to start with

Appropriate Management of Chronic Non-cancer Pain

- Physicians have been urged for 20 years to more aggressively respond to a patient's pain
- But chronic pain is not a single, simple entity
- Most physicians not trained in the currently recommended multimodal approach
- Resources (insurance coverage, other providers) may not be available
- Patient education is time-consuming
- Prescription drug products available and often covered by health insurance

Alternatives to Opioids for Treating Chronic Pain

- Non-pharmacologic interventions such as cognitive behavioral therapy or physical therapy
- NSAIDS or acetaminophen
- Better treatment of underlying disease: joint replacement, disease modifying agents for RA
- Newer pharmacologic therapies

Development of Non-opioid Pain Medications

- Striking that most of the more recently approved medications indicated for chronic pain conditions (e.g., neuropathic pain) were initially developed for a different CNS indication
- Lack of scientific understanding of chronic pain meant that traditional drug discovery methods not likely to yield good candidates
- Current advances should begin to produce a better pipeline for this unmet medical need

FDA Approach to the Current Epidemic of Rx Opioid Abuse

- Prevention of abuse and addiction
  - Prescriber education (ER/LA REMS); updated labels
  - Better data on longer-term use of opioids for pain (required trials)
  - Development of standards for abuse-deterrent formulations
  - Development of alternative pain therapies
  - Improved disposal practices (with Federal and State agencies)
- Prevention of OD deaths: naloxone
- Treatment of Addiction: Medication Assisted Therapy
- Summarized in recent Action Plan

Today's Science Board Discussion

- Many of the current problems relate to historical lack of scientific understanding of pain, of the development of therapies to treat it, and of addiction and its management.
- The following presentations will address the current science in these areas.
- Dr. Throckmorton will then describe FDA policies in the setting of overall Federal actions
- Dr. Hertz will then present additional challenges in drug development
- Dr. Dal Pan will discuss the limitations of current data sources when used to evaluate the effects of interventions

WE ARE EAGER TO HEAR THE SCIENCE BOARD'S THOUGHTS ON ADDITIONAL STEPS FDA MIGHT TAKE TO MITIGATE THE PRESCRIPTION OPIOID EPIDEMIC AND IMPROVE PAIN MANAGEMENT IN THE UNITED STATES