Opioid use for chronic nonmalignant pain in children and adolescents

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June 12, 2015

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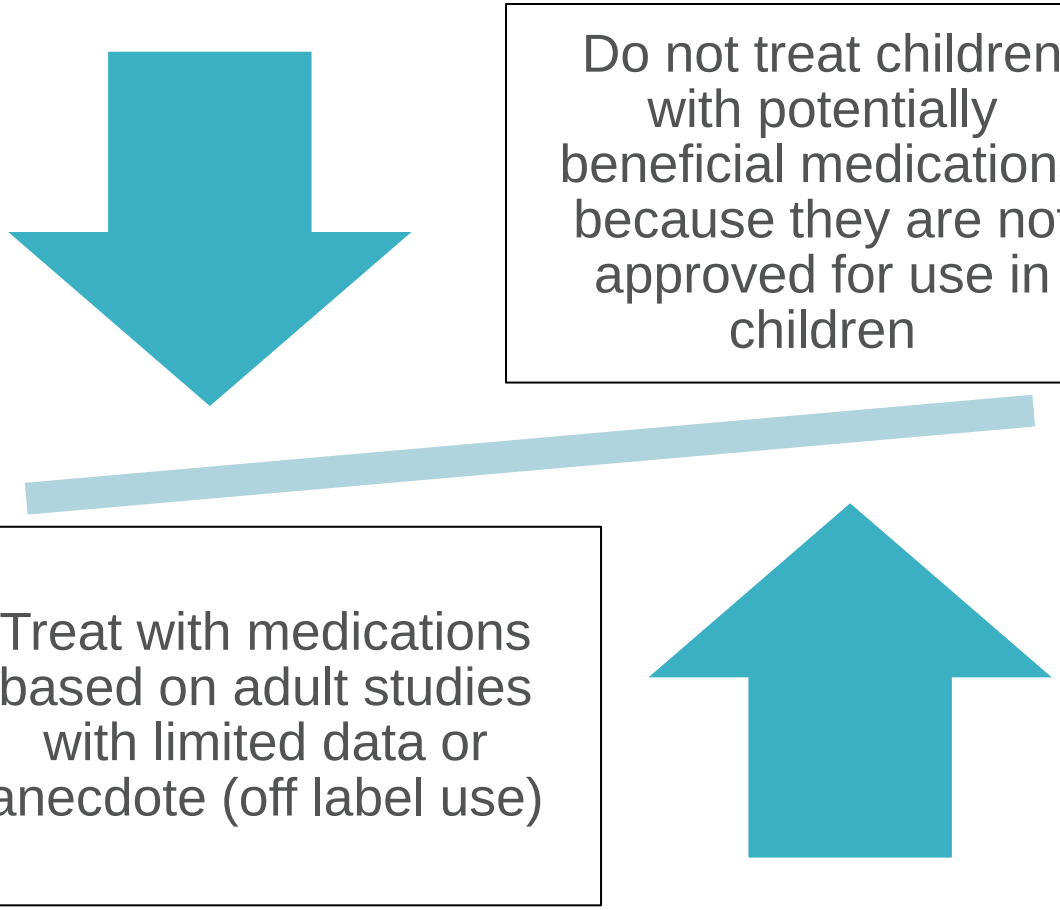
Disclosures

- Special Government Employee, United States Food and Drug Administration, Anesthetic and Analgesic Drug Products Advisory Committee
- Chair, Pediatric Research Network for Pain (PRN-Pain)
- Consultation to
  - Pfizer

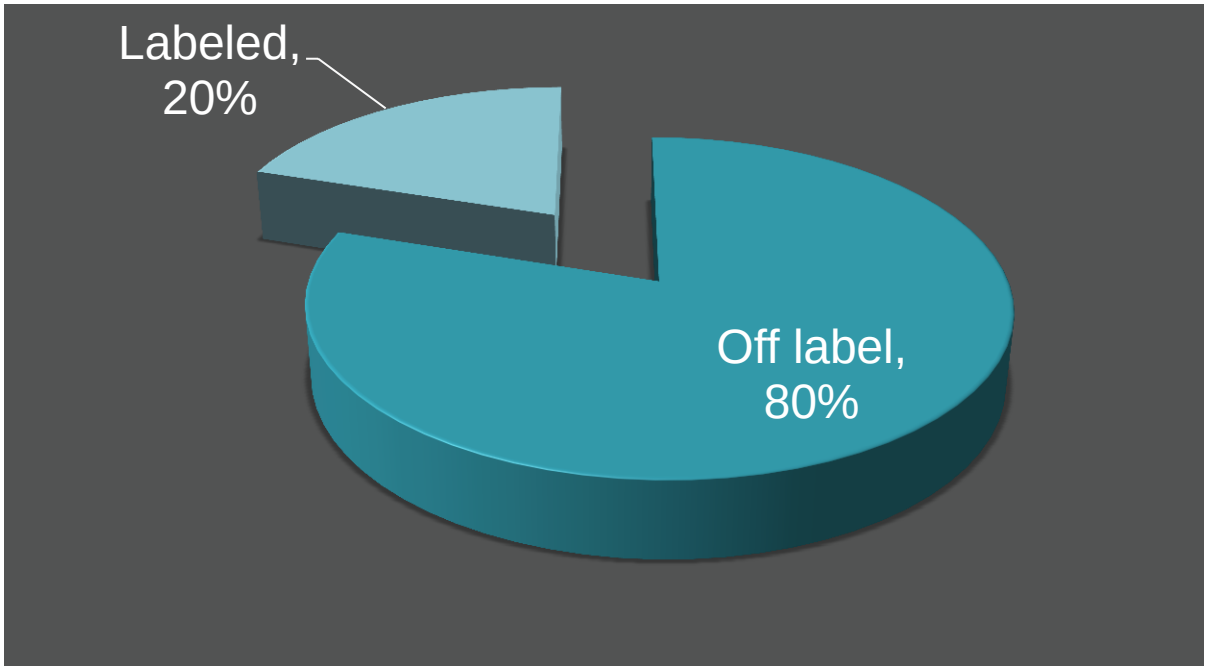
Outline

- With very rare exception, opioids have not been labeled for use in individuals less than 18 years of age
- Persistent, recurrent, and chronic pain in infants, children, and adolescents are often qualitatively different than chronic pain problems in adults
- Children are not little adults BUT adults are big children

Pediatric drug development: Choices for pediatricians



Medications used in pediatrics labeled for indications in children



Drug labeling for children

- Limited or no data on safety
  - Pharmacokinetics (PK)
  - Pharmacodynamics (PD)
  - Serious adverse events (SAE)
- Limited or no efficacy data
- Limited or no data on long-term use
- Limited or no data on long-term sequelae

FDA: CDER

- 1994: survey data to establish sufficiency for pediatric use and labeling
- 1997: FDAMA (FDA Modernization Act): pediatric studies lead to patent extension
- 1998: Pediatric Rule (challenged in 2000, enjoined by the Court in 2002)
- 2002: Best Pharmaceuticals for Children Act (BPCA)
- 2003: Pediatric Research Equity Act (PREA) replaced Pediatric Rule
- 2007: FDAAA (FDA Amendments Act): reauthorization of BPCA and PREA
- 2012: FDASIA (FDA Safety and Innovation Act)
  - Makes BPCA and PREA permanent
  - Pediatric development plans submitted earlier during drug development

FDA: CDER

FDAMA, BPCA, PREA impact
(through April 30, 2015)

- 522 new pediatric trials
- Pediatric information in product labeling in >160 drugs
- http://www.accessdata.fda.gov/scripts/sda/sdNavigation.cfm?sd=labelingdatabase

Analgesics with pediatric indications

Note: for the 0 to 6 month age group, there are 0

Acetaminophen, Aspirin, NSAIDs

- APAP (≥2 y)
- ASA
- Ibuprofen (≥ 6 m)

Opioids (non-combinaiton products)

- Fentanyl transdermal (≥2 y)
- Buprenorphine injection
- Fentanyl citrate injection
- ~~Meperidine~~

Extrapolation

- Expert consensus: the effectiveness of opioids may be extrapolated from studies on adults and older children down to those 2 years of age and older
- Lacking sufficient data on drug metabolism, dose response, and toxicity

Chronic pain and development

- Acute pain problems in pediatrics have many characteristics in common with adult presentations
- Persistent, recurrent, and chronic pain in infants, children, and adolescents are often qualitatively different than chronic pain problems in adults
- It is a corollary that treatment approaches may vary accordingly

Chronic pain in pediatrics

- Common pediatric chronic pain
  - Headache
  - Abdominal pain
  - Musculoskeletal pain
- Common adult chronic pain
  - Neuropathic
  - Related to aging and degeneration
- Opioid use not indicated
  - Rare exceptions when pain has clearer nociceptive origin and defined endpoint

Children are not little adults, but adults are big children

- Adults with chronic pain often recall having had difficulties in their earlier years
- Prospective longitudinal or cross-sequential studies show contiguity or continuity between pediatric and adult chronic pain
  - Abdominal pain
  - Headaches
  - Back pain

Clinical recommendations

- Prescribe opioids for acute pain in infants and children only if knowledgeable in pediatric medicine, developmental elements of pain systems, and differences in pharmacokinetics and pharmacodynamics in young children

- Avoid opioids in the vast majority of chronic non-malignant pain problems in children and adolescents, as evidence shows no indication

- Opioids are indicated for a small number of persistent painful conditions, including those with *clear pathophysiology* and when an endpoint to usage may be defined

Clinical recommendations

- Opioids may be indicated for some chronic pain conditions in children and adolescents, when there is *clear pathophysiology,* and no definable endpoint
- Utilize safety guardrails when prescribing opioids to younger patients
  - Limiting total dispensed
  - Educating parents about dosing, administration, storage and disposal (minimizing risks of diversion or accidental ingestion)
  - Adolescents should undergo screening for risk of substance abuse
- Consult or refer to a pediatric pain specialist when chronic pain problems in children and adolescents are complicated or persistent