Young Child Exposures to Prescription Medication: How Formulation and Packaging Matters

Eric Lavonas, MD, FAACT

Rocky Mountain Poison & Drug Center

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Disclosure

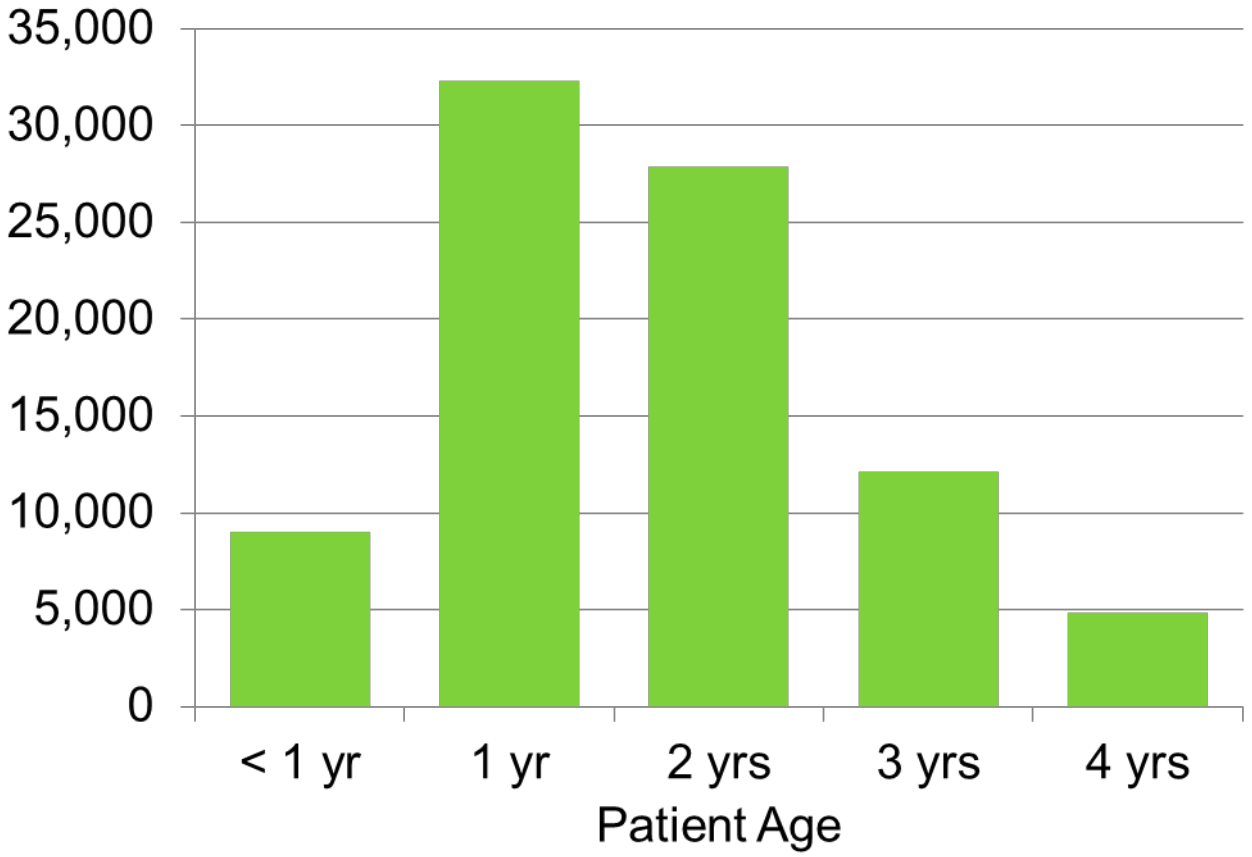
- Research funded by Reckitt-Benckiser Pharmaceuticals
  - Proprietary interest: buprenorphine/naloxone film

Learning Objectives

- Grade the impact of dosage form on frequency and severity of childhood opioid ingestions
- Evaluate the impact of packaging of opioid medications on pediatric exposures

Unintentional Young Child Poisoning

- 67,000 – 86,000 annual ED visits



Ferguson RW, Safe Kids Worldwide, 2013
Franklin RL, *Pediatr* 2008; 122:1244-51; Cohen AL, J Pediar *2008; 152:416-21*.

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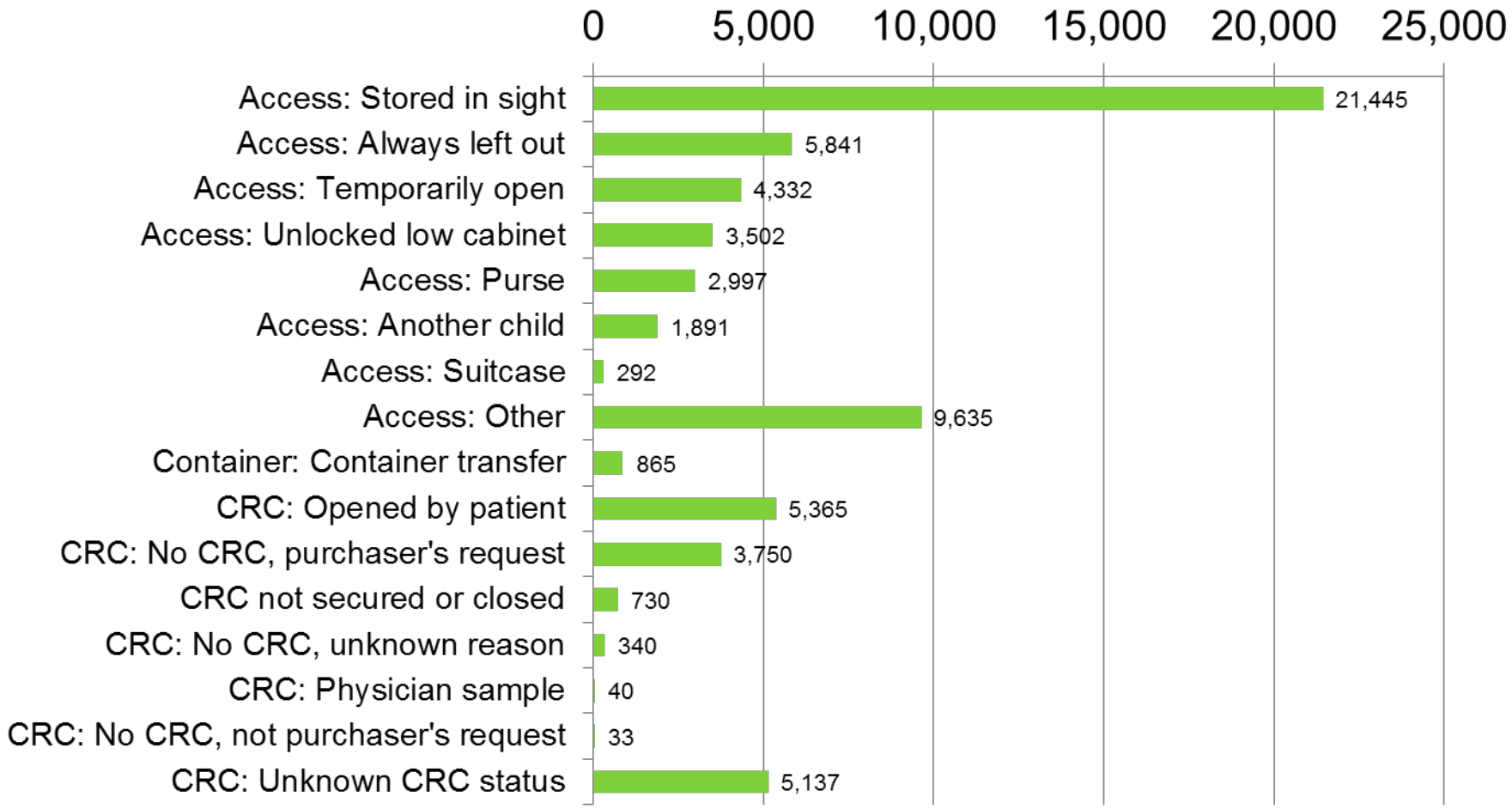
Location and Intended user

Location	Intended User	Percent of Cases
Child's home		**68**
	Immediate family	41
	Other live-ins	14
	Visitor	10
	Intended user unknown	3
Someplace else		**32**
	Immediate family	2
	Not immediate family	30
	Intended user unknown	<1

Jacobson BJ, *Am J Pub Health* 1989; 79(7):853-6.

How did it happen?



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NPDS data, unpublished, 2012

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Early Attempts to Reduce Exposures

- Package size restrictions
  - Children's aspirin: 36 tablets (1966, Goddard)
- Education
  - Essex County, Ontario: little effect
- Early experiments in child-resistant packaging
  - Fort Lewis-McCord study (1969, Scherz)
  - Push down and turn

Poisoning Prevention Packaging Act (1970)

- Jurisdiction given to CPSC
- Applies to
  - All controlled drugs (oral formulations)
  - Prescription drugs (specific exceptions)
  - Iron tablets
  - APAP, ibuprofen, aspirin, methyl salicylate
  - Ethylene glycol, methanol
  - Low viscosity hydrocarbons
  - Certain strong acids / bases

Exceptions in PPPA

- Patient or physician request
- Specific listed products
- Intended for non-oral route
- Manufacturer produces 2 package forms
  - “This package for household without young children”

The Test

- 200 children aged 42 – 51 months
  - 5-minute trial → Single visual demonstration → 5-minute trial
  - Pass if ≤20% of children can open the package
- 100 adults aged 50 – 70 years
  - 5-minute trial
  - Pass if ≥ 90% of adults can open and close the package

Immediate impact

- 45% decrease in unintentional poisoning deaths among children aged <5 years
  - Prevented 1.4 deaths/million child-years
  - 24 deaths/year

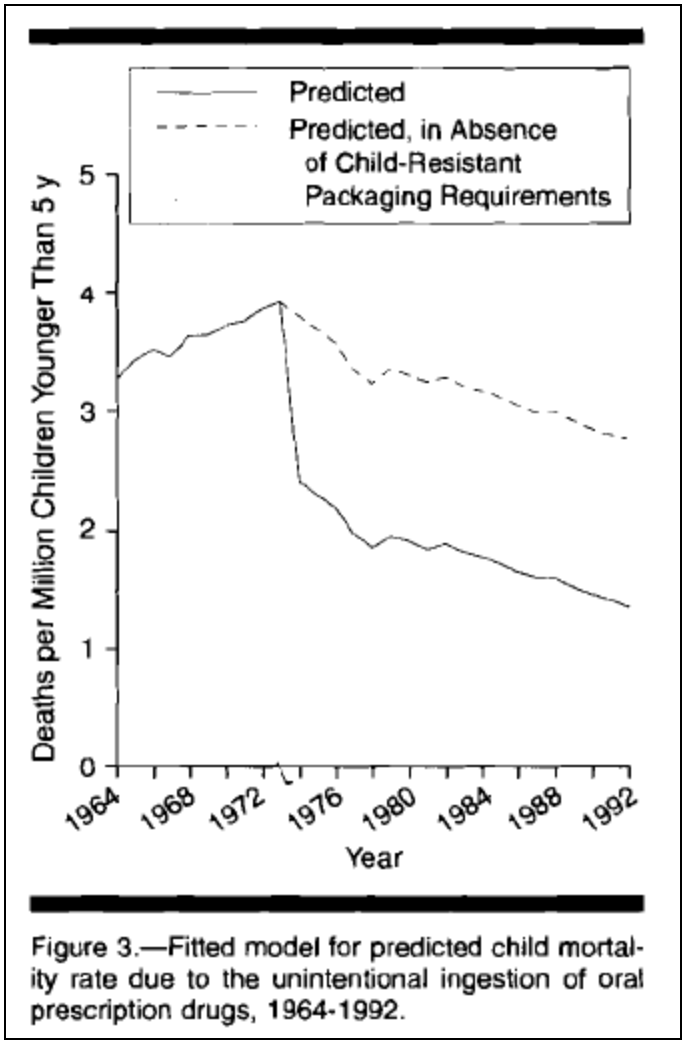
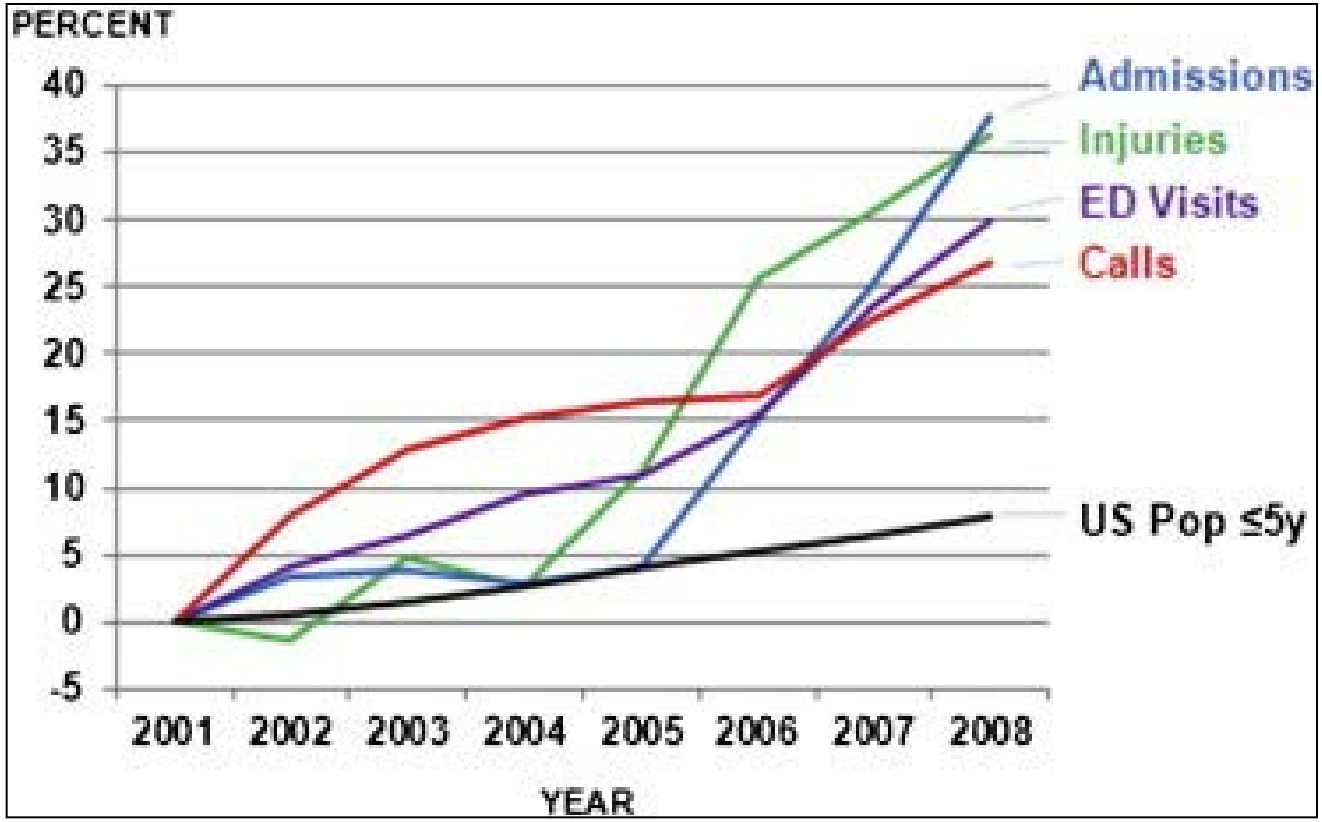


Figure 3.—Fitted model for predicted child mortality rate due to the unintentional ingestion of oral prescription drugs, 1964-1992.

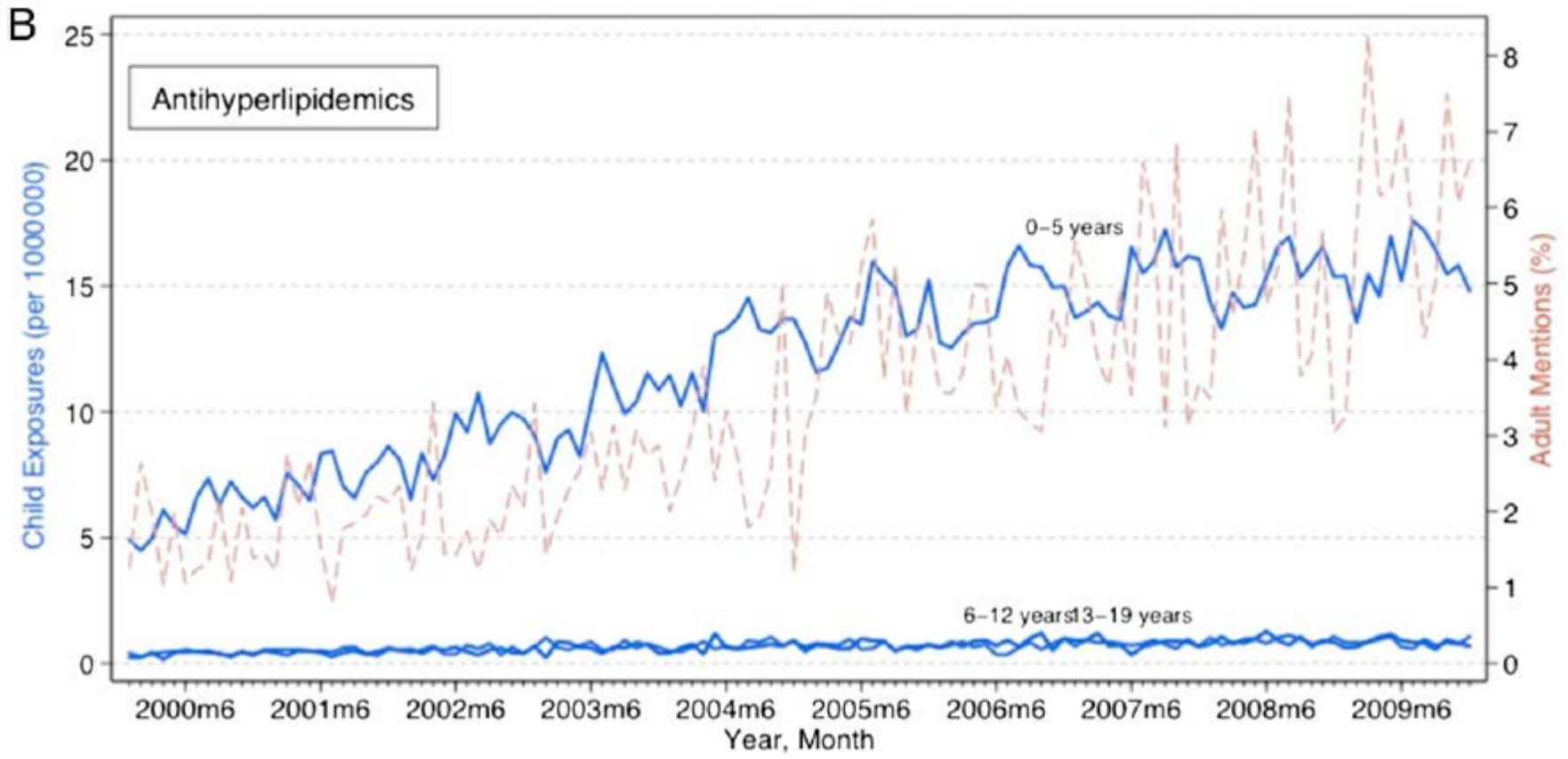
Rodgers G. *JAMA* 1996; 275:1661-5.

Young Child Poisoning Rates are Increasing



Bond GR, *J Pediatr* 2012; 160:265-70.

Young Child Poisoning Rates are Increasing



Burkhardt LC. *Pediatr* 2013; *ePub*.

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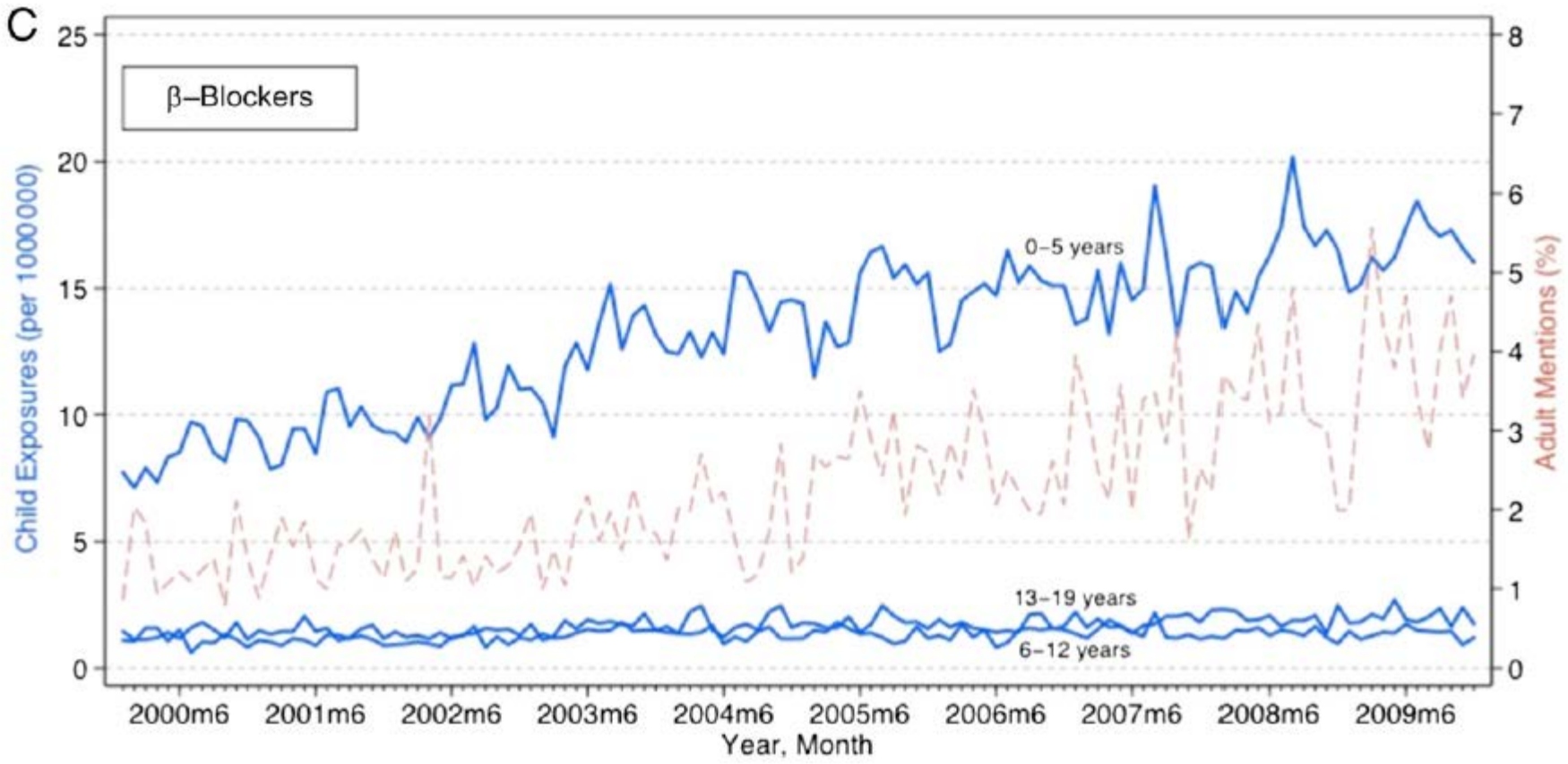

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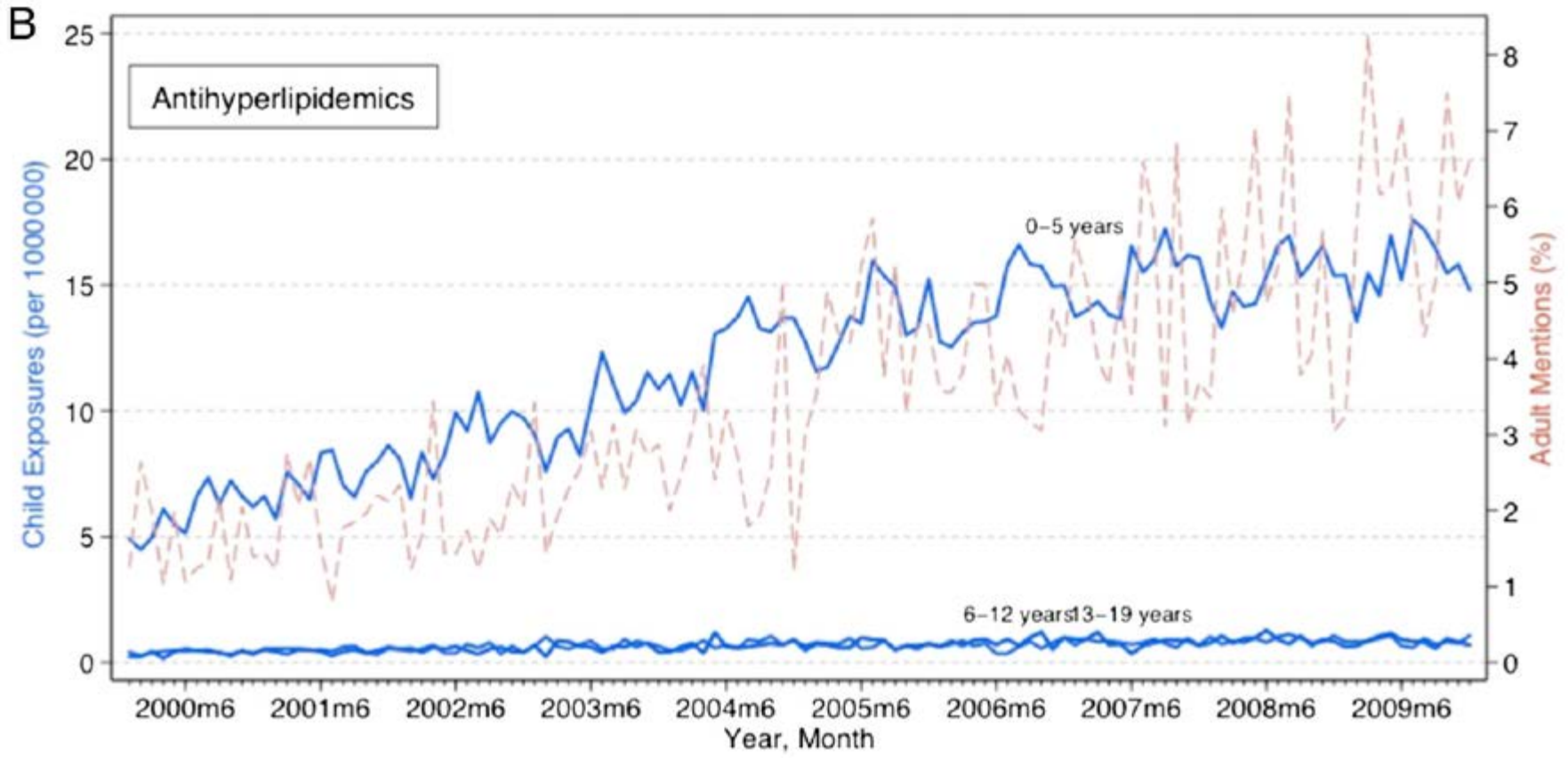
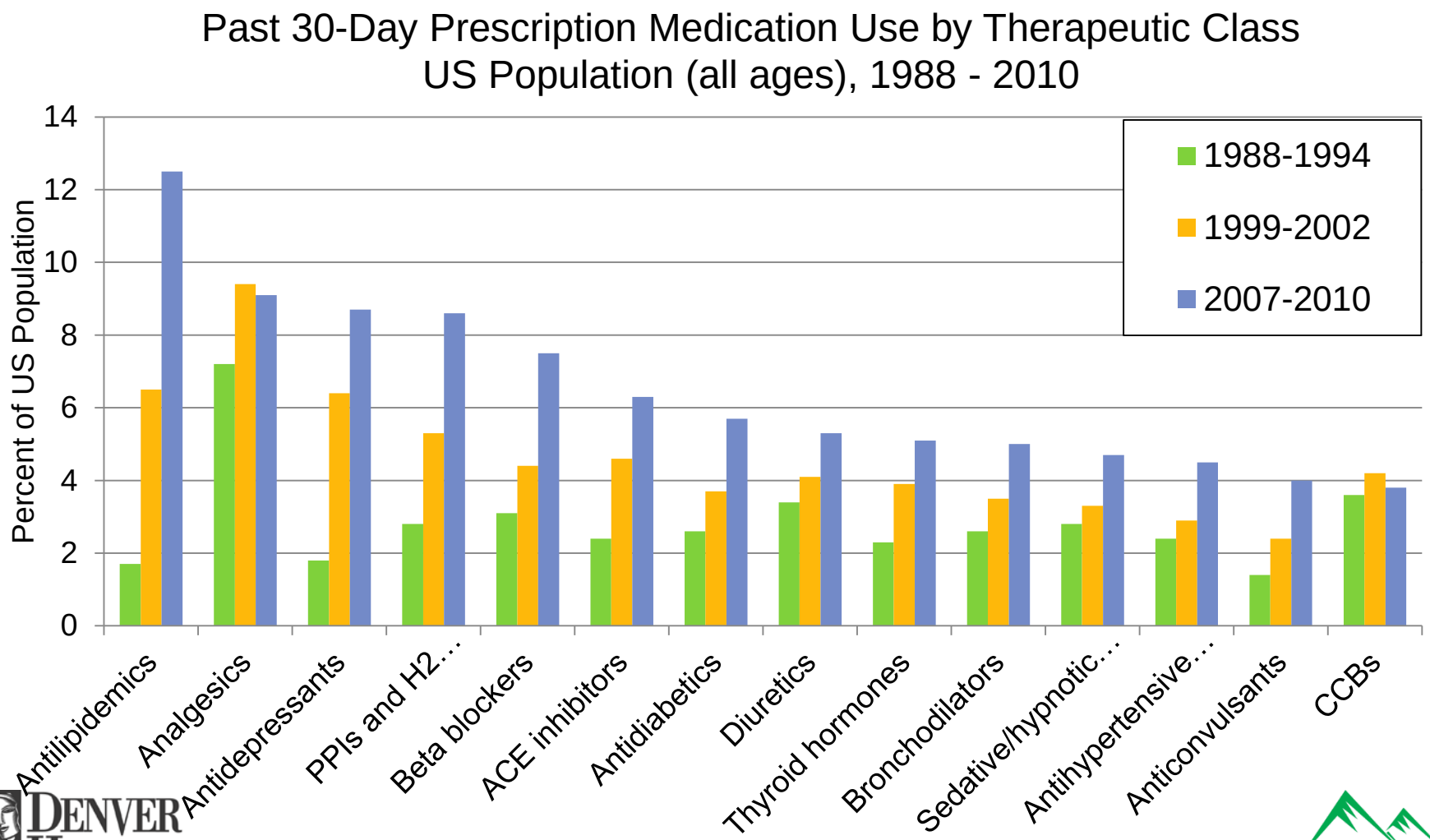
Young Child Poisoning Rates are Increasing



Burkhardt LC. *Pediatr* 2013; *ePub*.

Image Credit: http://statenislandpolitics.wordpress.com/2013/08/07/a-nation-of-pill-takers/.

Medication Use is Increasing

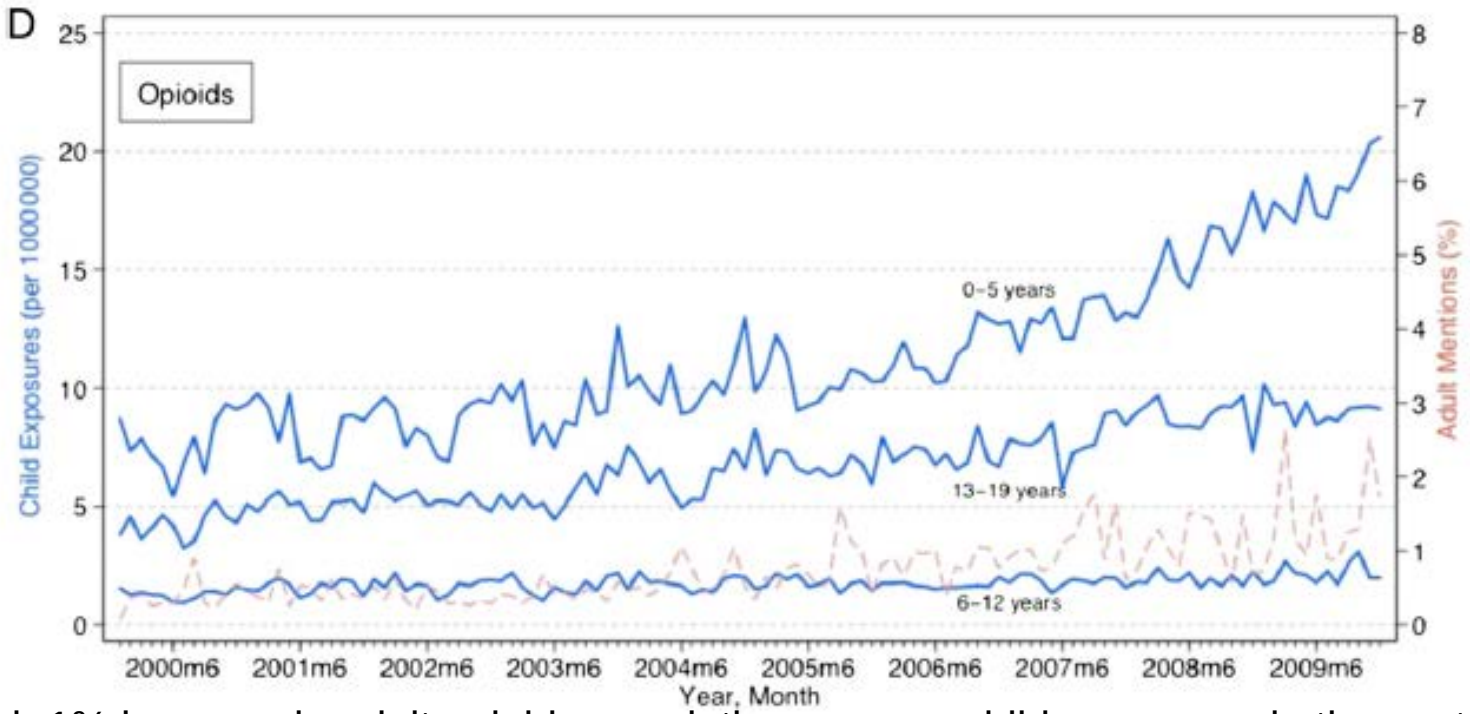


Data Source: http://www.cdc.gov/nchs/hus/contents2012.htm#092.

Opioids

- "One pill can kill"
  - Especially: high potency, LA/ER formulations
- Utilization increasing in adults and children
  - Young child & adolescent exposures increasing in turn

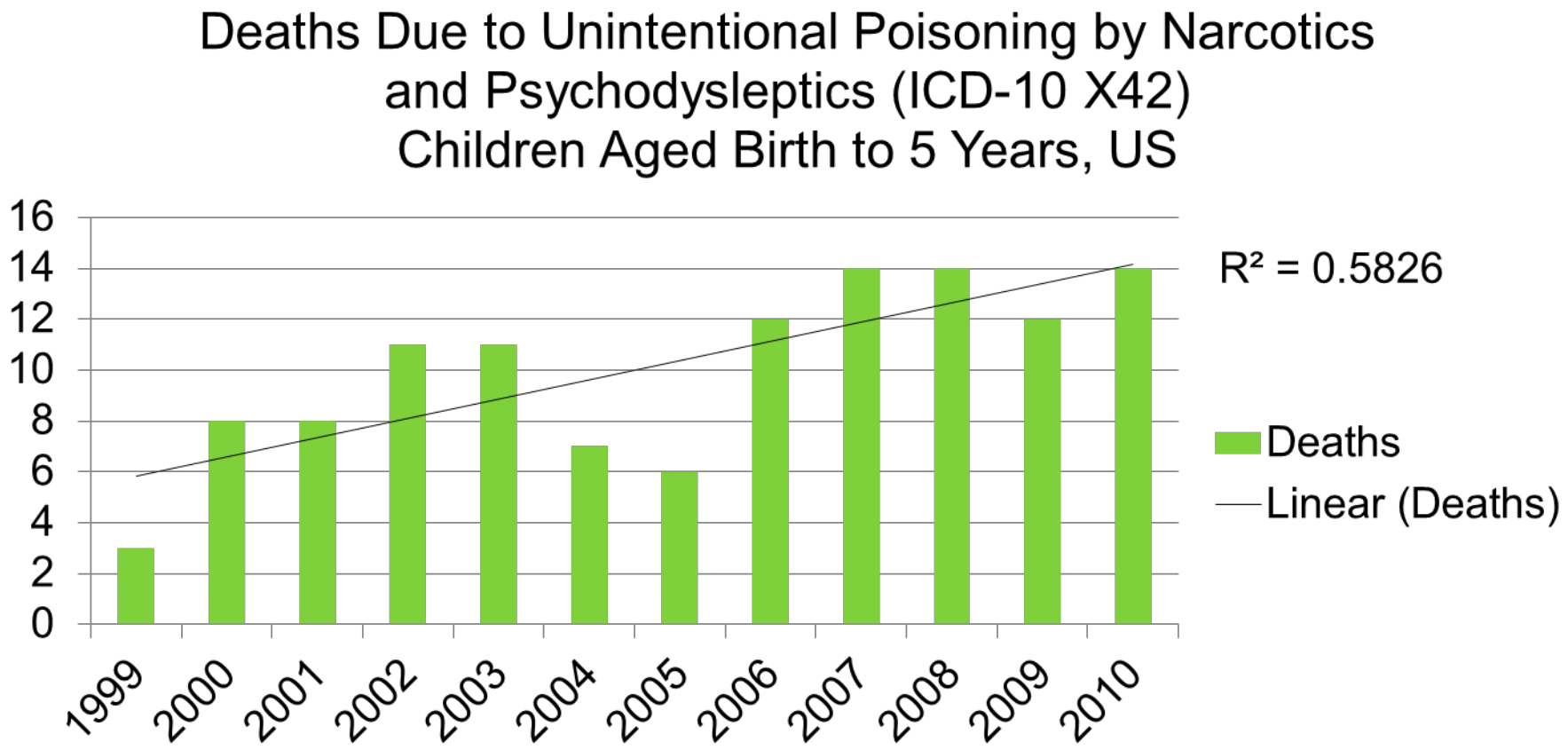
Young Child Exposures to Opioids More Than Doubled Since 2000



For each 1% increase in adult opioid prescriptions, young child exposures in the next 1 – 6 months increase 1.53% (CI: 1.13 – 1.88%).

Burkhardt LC. *Pediatr* 2013; *ePub*.

Young Child Deaths are Increasing



Data Source: CDC WONDER.

Young Child Exposures Match Prescribing; Outcomes Match Typical Dose/Potency

Opioid	Cases	Major Outcome or Death n (%)
Hydrocodone	6,003	8 (0.3)
Oxycodone	2,036	14 (1.1)
Morphine	419	5 (1.9)
Methadone	415	16 (5.7)
Buprenophine	176	5 (4.0)
Fentanyl	123	3 (3.8)
Hydromorphone	68	0 (0.0)

Exposure cases in the RADARS System Poison Center Program, 2003Q1 – 2006Q2
Patient age birth to < 6 yo (N = 9,240)
Spearman' ρ for interaction between cases and URDD by 3-digit ZIP code: 0.67

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Bailey JE, *Ann Emerg Med* 2009; 53(4):419-24..

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Buprenorphine

- High potency partial μ-opioid agonist
- Office-based treatment of opioid dependence
- Mandatory provider training
- Mandatory patient education

Buprenorphine

- 3 sublingual formulations
  - Buprenorphine tablets
  - Buprenorphine/naloxone tablets
  - Buprenorphine/naloxone film

Image Credits: http://becauseilive.hubpages.com/hub/Drug_Addiction_Treatment__Suboxone__Subutex
http://janaburson.wordpress.com/2012/08/21/taper-off-suboxone-using-the-films/

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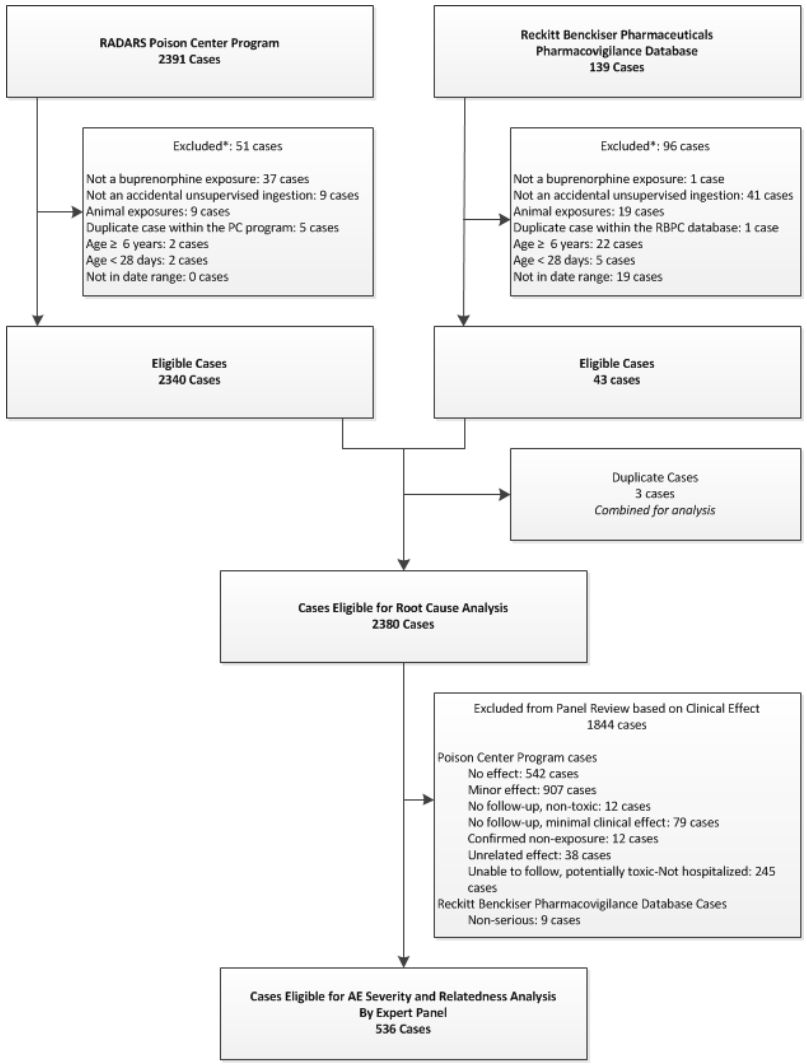
Pediatric Root Cause Study

- Unintentional exposures
  - Age 28 days to < 6 years
  - Demographics similar to other studies
- Root cause analysis
- Adverse events & outcomes analysis



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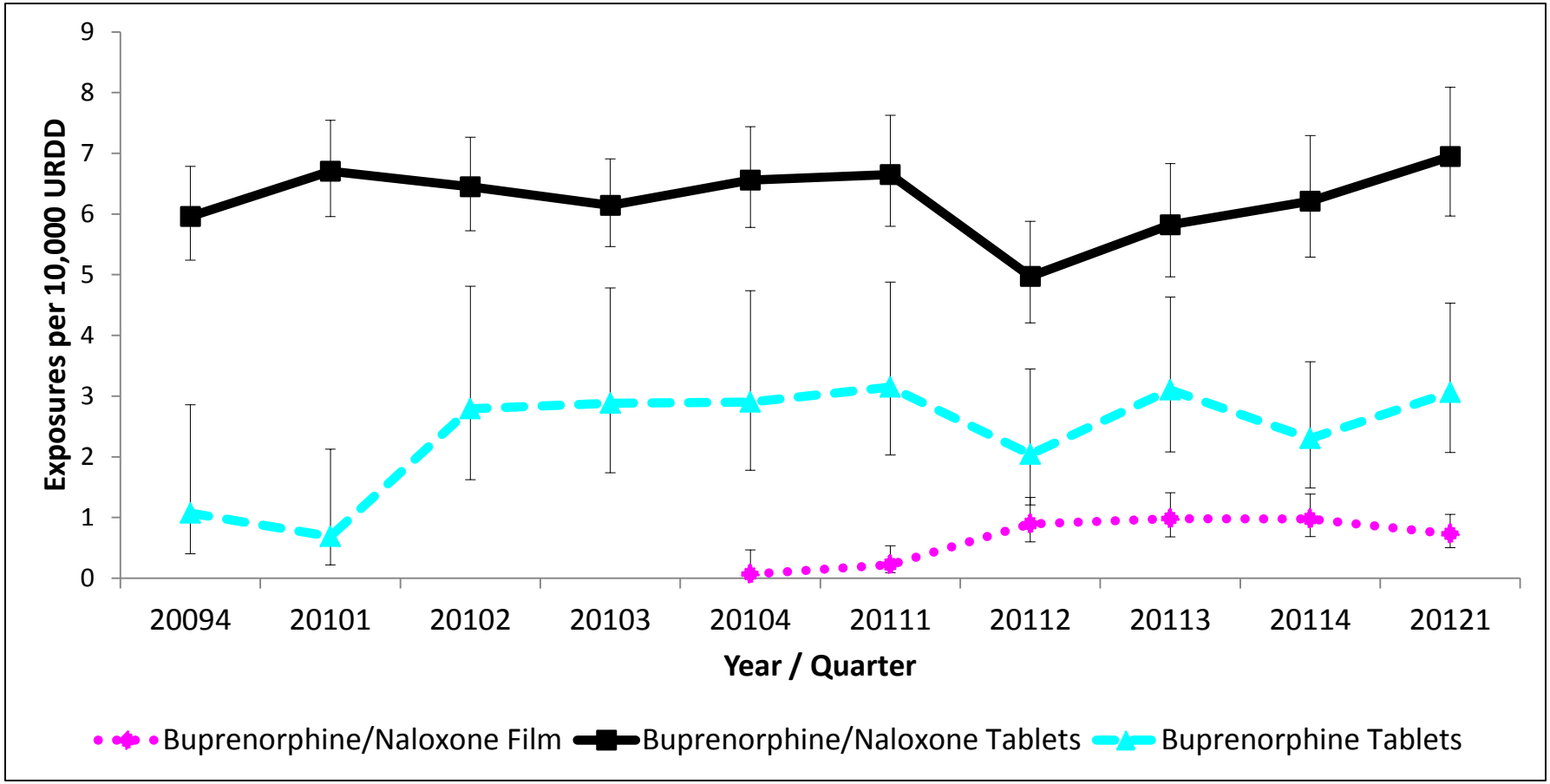
Film Exposure Rates are Less than Tablet Exposure Rates



Lavonas EJ, *J Pediatr* 2013, *ePub.*

Most Common Root Causes

Cause	Number of Cases	% of Cases with At Least 1 Root Cause (n = 1361)	% of All Cases (N = 2380)
Stored in sight	415	30.5	17.4
Not parents' med	374	27.5	15.7
Accessed from bag / purse	110	8.1	4.6
Not original packaging	75	5.5	3.2
Supervision: grandparent	62	4.6	2.6
Patient opened bottle	30	2.2	1.3
Supervision: Other relative	23	1.7	1.0

Lavonas EJ, *J Pediatr* 2013, *ePub.*

No Relationship Found Between Formulation and Severity

Table V. Maximum AE severity in cases undergoing focused review

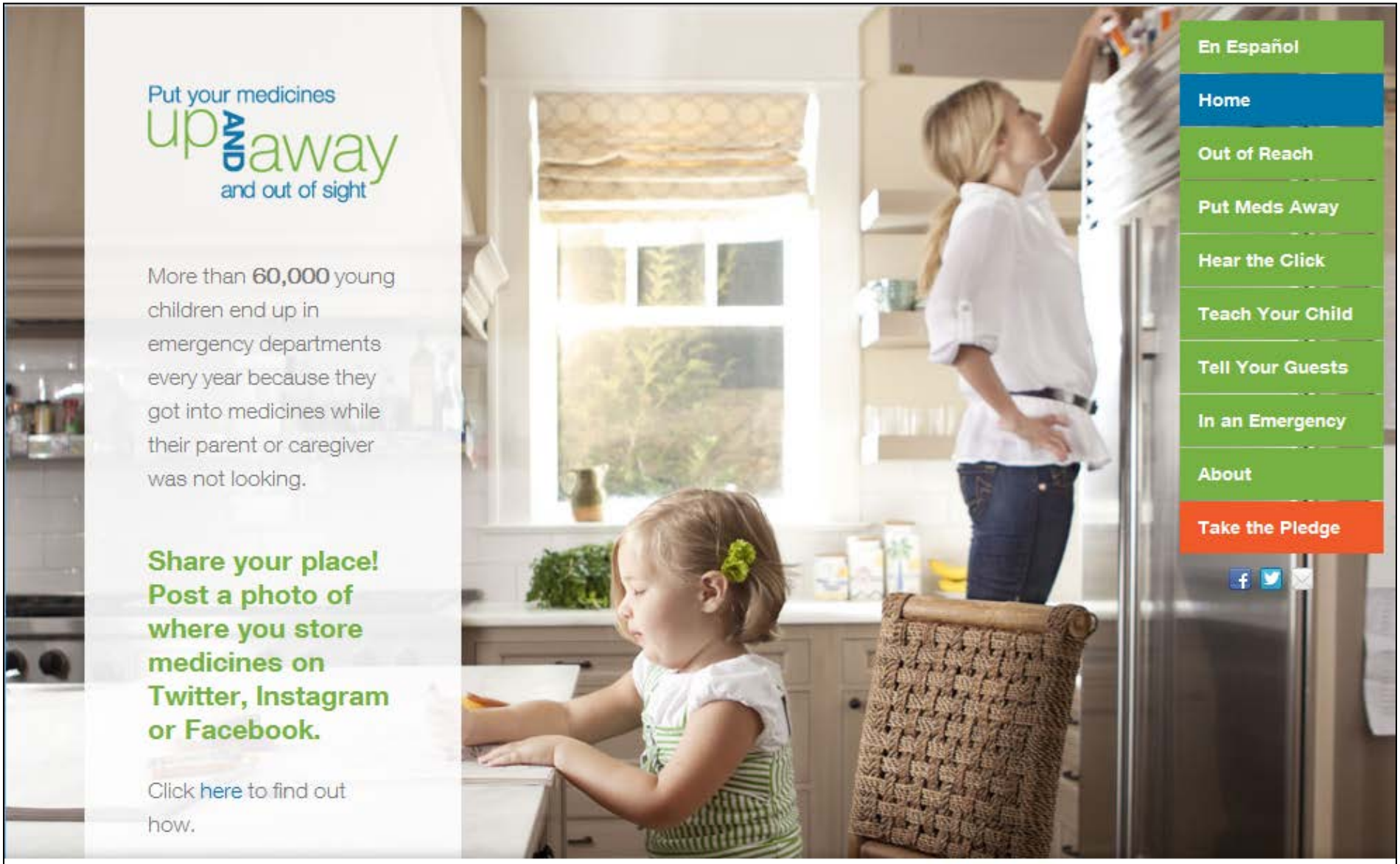
Maximum AE severity	All formulations* n = 536	Buprenorphine tablets n = 38	Buprenorphine/naloxone tablets n = 471	Buprenorphine/naloxone film n = 26
Not applicable or panel excluded	17 (3.2%)	0 (0.0%)	16 (3.4%)	1 (3.8%)
Unable to determine	4 (0.7%)	0 (0.0%)	4 (0.8%)	0 (0.0%)
Grade 1, mild	99 (18.5%)	8 (21.1%)	85 (18.0%)	6 (23.1%)
Grade 2, moderate	180 (33.6%)	9 (23.7%)	161 (34.2%)	10 (38.5%)
Grade 3, severe	190 (35.4%)	14 (36.8%)	167 (35.5%)	9 (34.6%)
Grade 4, life-threatening	42 (7.8%)	6 (15.8%)	36 (7.6%)	0 (0.0%)
Grade 5, death	4 (0.7%)	1 (2.6%)	2 (0.4%)	0 (0.0%)

*Includes data for buprenorphine formulation unspecified (n = 1).

Lavonas EJ, *J Pediatr* 2013, *ePub.*

What Do We Know?

- Opioids are quantitatively different than other drug classes
  - Same basic lessons apply
- Engineering controls work
- Education
  - Works best if messages are clear, consistent, and repeated often
  - Rarely outperforms engineering controls



Up & Away is an initiative of PROTECT in partnership with the **Centers for Disease Control and Prevention** (CDC).

Put your medicines up AND away and out of sight

PROTECT advancing children's medicine safety

Education Initiatives

- http://www.cdc.gov/MedicationSafety/protect/protect_Initiative.html
- www.safekids.org/medsafety

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Engineering Controls

- Unit-of-dose, child-resistant packaging
  - Bonus: Can incorporate “calendaring” features to improve compliance
- Spill- and pour-resistant packaging
  - Bonus: Can reduce dosing errors

Image Credits: http://health.uml.edu/thc/HealthIssues/BirthControlMethodsCPS/Pill1.jpg
http://blogs.mydevstaging.com/blogs/goodyblog/files/2011/05/tylenol-infants-syringe1.jpg

Novel Approaches

- Hand-held PCA

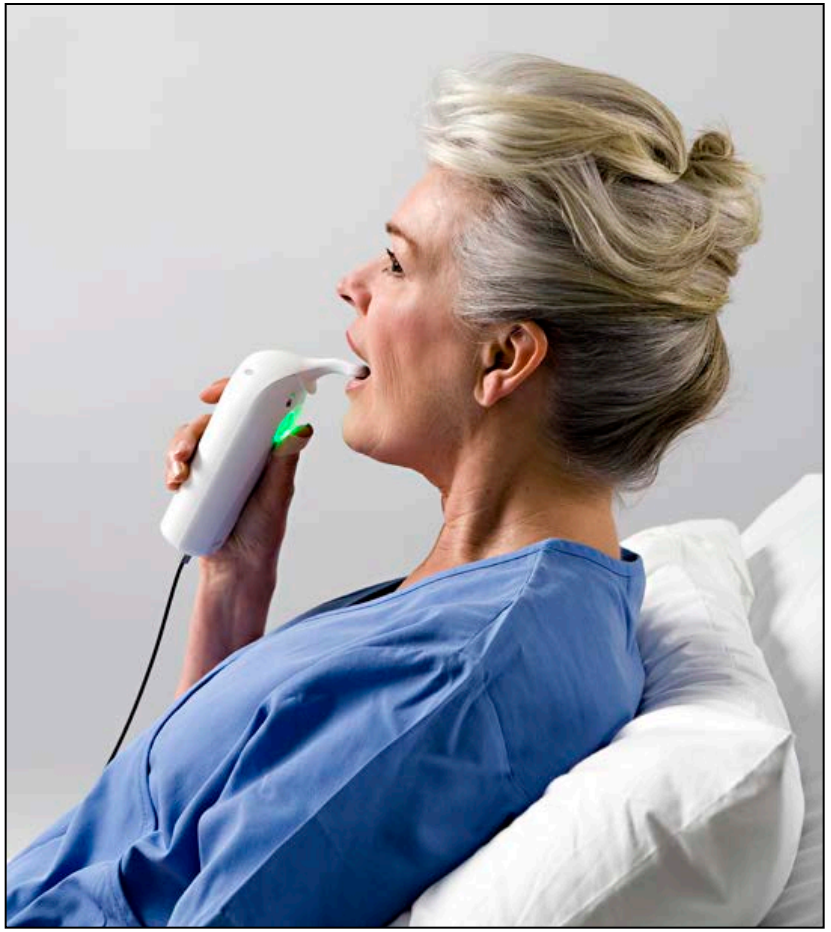

Photo Credit: www.acelrx.com

Thank You

- eric.lavonas@rmpdc.org