

Unintentional Pediatric Exposures to Buprenorphine – Lessons Learned

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Disclosures

- RADARS® System is independently owned and operated by Denver Health & Hospital Authority, a political subdivision of the state of Colorado.
- Funding for the RADARS System comes from data subscriptions, including many manufacturers of prescription opioids and stimulants.
- Specific study discussed today was funded by Reckitt Benckiser Pharmaceuticals.

Root Causes, Clinical Effects, and Outcomes of Unintentional Exposures to Buprenorphine by Young Children[☆]

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Objective To characterize the rates, root causes, and clinical effects of unintentional exposures to buprenorphine sublingual formulations among young children and to determine whether exposure characteristics differ between formulations.

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Retrospective Cross-Sectional Study Design

- Unintentional exposures to buprenorphine-containing products
 - RADARS[®] System Poison Center Program
 - Reckitt Benckiser pharmacovigilance system
- Children age 28 days to <6 years
- Negative binomial regression to estimate average exposure rates
- Root cause, expert panel evaluation of causality and severity of moderate to severe AEs

Table 1: Characteristics of Children Aged 28 Days to < 6 Years with Unintentional Exposures to Buprenorphine

**Key finding: no difference in age distribution between products*

AGE	Total Bup* n=2380	Bup Tablets n=154	Bup/ Naloxone Tablets n=2107	Bup/ Naloxone Film n=118
Not Reported	24 (1.0%)	1 (0.6%)	18 (0.9%)	5 (4.2%)
28 To 364 Days	148 (6.2%)	15 (9.7%)	123 (5.8%)	10 (8.5%)
1 Year To <2 Years	885 (37.2%)	58 (37.7%)	788 (37.4%)	39 (33.1%)
2 Years To <3 Years	888 (37.3%)	61 (39.6%)	787 (37.4%)	40 (33.9%)
3 Years To <4 Years	320 (13.4%)	18 (11.7%)	279 (13.2%)	22 (18.6%)
4 Years To <5 Years	100 (4.2%)	2 (1.3%)	94 (4.5%)	4 (3.4%)
5 Years To <6 Years	36 (1.5%)	0 (0.0%)	35 (1.7%)	1 (0.8%)
Exact Age Not Reported	3 (0.1%)	0 (0.0%)	1 (0.0%)	2 (1.7%)



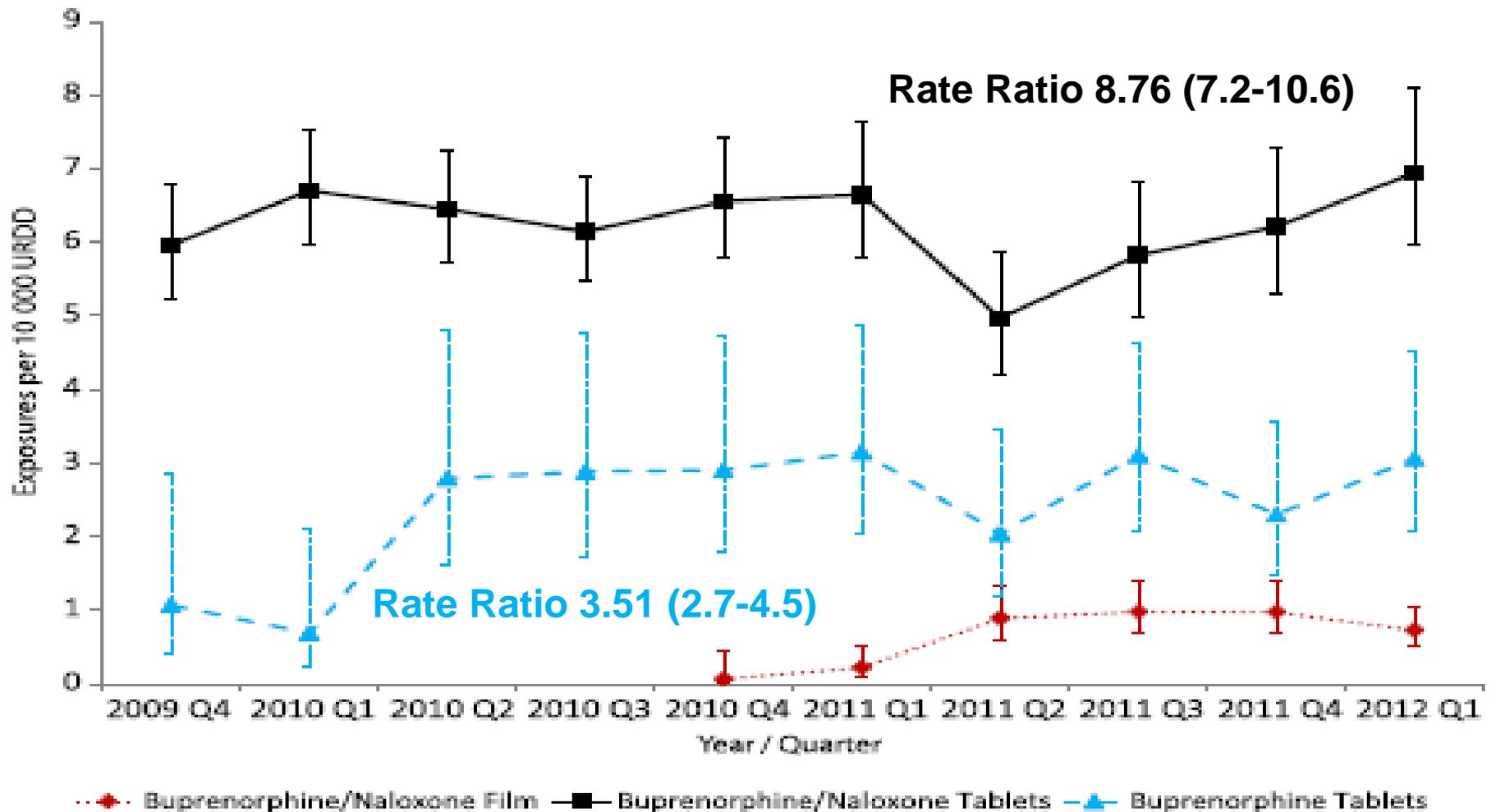


Figure 2. Rates of unintentional exposure to buprenorphine among children aged 28 days to less than 6 years, adjusted for drug availability.

Table III. Identified root causes of unintentional exposure to buprenorphine among children aged 28 days to less than 6 years*

Type	Detail	Total buprenorphine [†] n = 2380	Buprenorphine tablets n = 154	Buprenorphine naloxone tablets n = 2107	Buprenorphine naloxone film n = 118
Access/storage	Stored in sight, not secure, left out	415 (17.4%)	27 (17.5%)	371 (17.6%)	16 (13.6%)
	Accessed from bag (purse, diaper bag, luggage, etc)	110 (4.6%)	5 (3.2%)	101 (4.8%)	4 (3.4%)
	Drug stored in package other than original packaging (tissue, plastic wrap, foil, cup, etc)	75 (3.2%)	4 (2.6%)	66 (3.1%)	5 (4.2%)
Behavioral	Cutting medication	(0.0%)	(0.0%)	(0.0%)	(0.0%)
	Developmental	(0.0%)	(0.0%)	(0.0%)	(0.0%)
	Diversion	(0.0%)	(0.0%)	(0.0%)	(0.0%)
Intended recipient	Mistaken for other child	(0.0%)	(0.0%)	(0.0%)	(0.0%)
	Other risk factors	(0.0%)	(0.0%)	(0.0%)	(0.0%)
	Other risk factors	(0.0%)	(0.0%)	(0.0%)	(0.0%)
Special needs	Supervised caregiver	(0.0%)	(0.0%)	(0.0%)	(0.0%)
	Family member (other than grandparent)	23 (1.0%)	0 (0.0%)	23 (1.1%)	0 (0.0%)
	Babysitter	21 (0.9%)	1 (0.6%)	17 (0.8%)	3 (2.5%)
Visiting another home/away from home/outside of home/homeless	Friend of parent	8 (0.3%)	1 (0.6%)	6 (0.3%)	1 (0.8%)
	Supervised by mom's boyfriend/fiancé	3 (0.1%)	0 (0.0%)	2 (0.1%)	1 (0.8%)
	Visiting a friend/neighbor/mother's boyfriend/house sitting	18 (0.8%)	0 (0.0%)	16 (0.8%)	2 (1.7%)
Visiting another home/away from home/outside of home/homeless	Visiting a relative	9 (0.4%)	0 (0.0%)	9 (0.4%)	0 (0.0%)
	Away from home-other (staying in a hotel, on vacation, at church camp/retreat)	5 (0.2%)	0 (0.0%)	5 (0.2%)	0 (0.0%)
	Exposed while outdoors	3 (0.1%)	0 (0.0%)	3 (0.1%)	0 (0.0%)
	Living in homeless shelter/recovery home	3 (0.1%)	0 (0.0%)	2 (0.1%)	1 (0.8%)

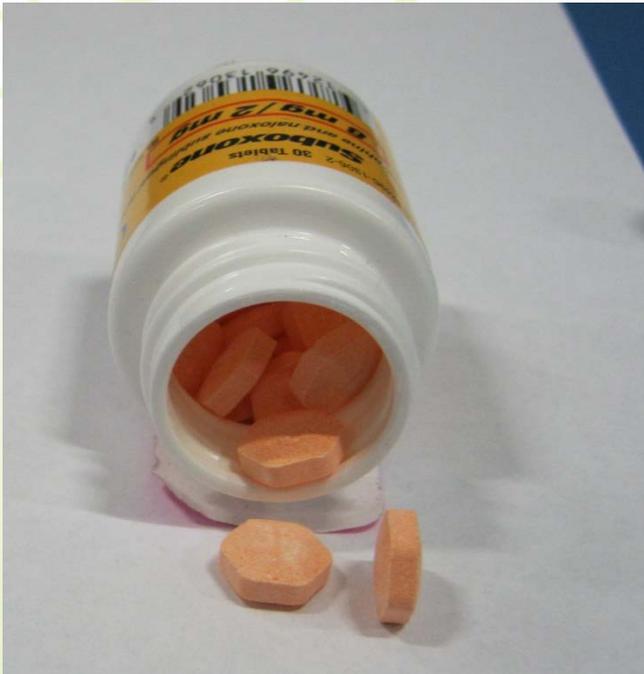
Key Findings of Root Cause Evaluation Pertinent to PROTECT:

- Access/storage
 - Taken out of original package – why?
 - Cutting/altering dose (prescribing behavior and/or patient-driven dosing?)
 - Stigma associated with medication?
- Packaging
 - Unit dose AND child resistant?

*An individual case may have multiple root causes.
[†]Includes data for buprenorphine formulation unspecified (n = 1).

Buprenorphine Packaging

- **Tablets:** typically in bottle with child-resistant closure



Buprenorphine Packaging

- **Film:** unit dose packaging with child-resistant foil pouch



Buprenorphine Packaging



Buprenorphine Packaging

- **NEW Tablet:** unit dose packaging with child-resistant foil blister pack

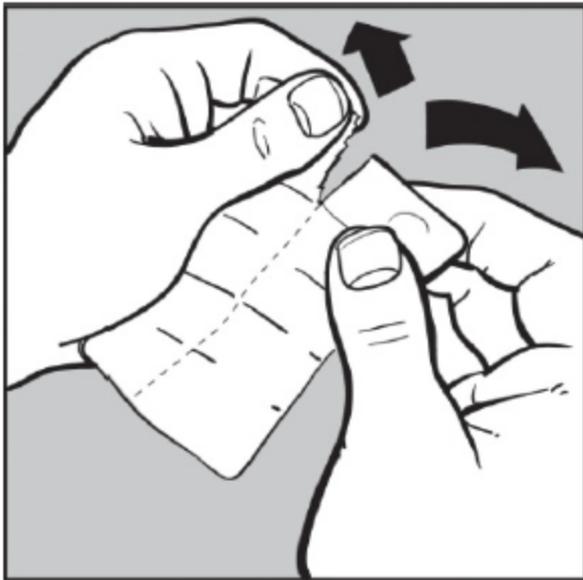


Figure A

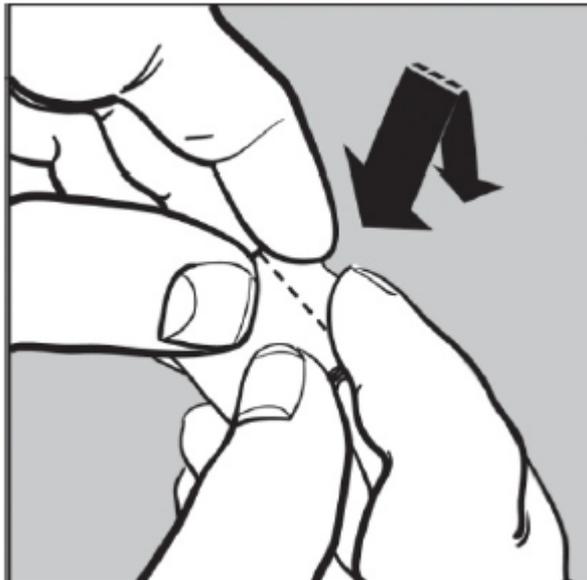


Figure B

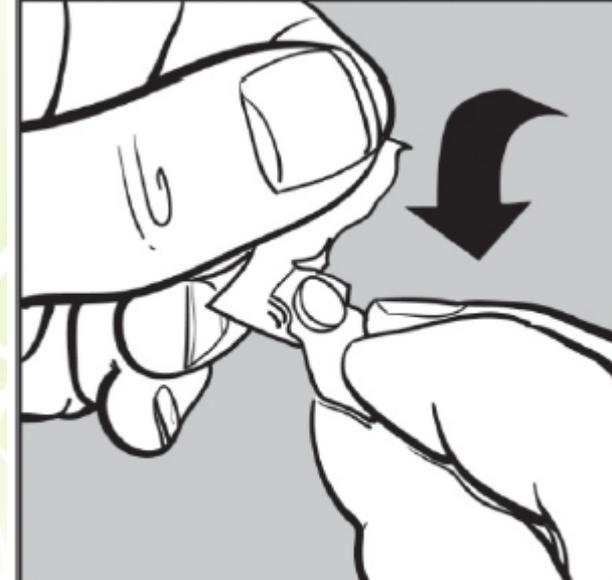


Figure C

Summary

- Toxicity of pediatric exposure is of concern with all opioids and measures to protect these children are imperative in new drug development.
- Access/storage of buprenorphine is the leading contributing factor to pediatric exposures, not a new problem.
- The role of self-management of dosing and alteration of original product, problem specific to patient population, therapeutic indication, drug or drug class?