

Unintentional Pediatric Exposures to Buprenorphine – Lessons Learned

Jody L. Green, PhD, CCRP

*Director of Research Administration,
Rocky Mountain Poison and Drug Center*

*Assistant Professor, School of Nursing (Research),
Vanderbilt University Medical Center*

19 September 2013



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[☆]

Eric J. Lavonas, MD^{1,2}, William Banner, MD, PhD^{3,4}, Pamela Bradt, MD, MPH⁵, Becki Bucher-Bartelson, PhD¹, Kimberly R. Brown, BS¹, Pradeep Rajan, ScD⁶, Lenn Murrelle, MSPH, PhD⁶, Richard C. Dart, MD, PhD^{1,2}, and Jody L. Green, PhD¹

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.

Lavonas, E.J., Banner, W., Bradt, P., Bucher-Bartelson, B., Brown, K.R., Rajan, P., Murrelle, L., Dart, R.C., Green, J.L., 2013. Root Causes, Clinical Effects, and Outcomes of Unintentional Exposures to Buprenorphine by Young Children. The Journal of pediatrics. Aug 22. pii: S0022-3476(13)00817-2. doi: 10.1016/j.jpeds.2013.06.058.

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%)



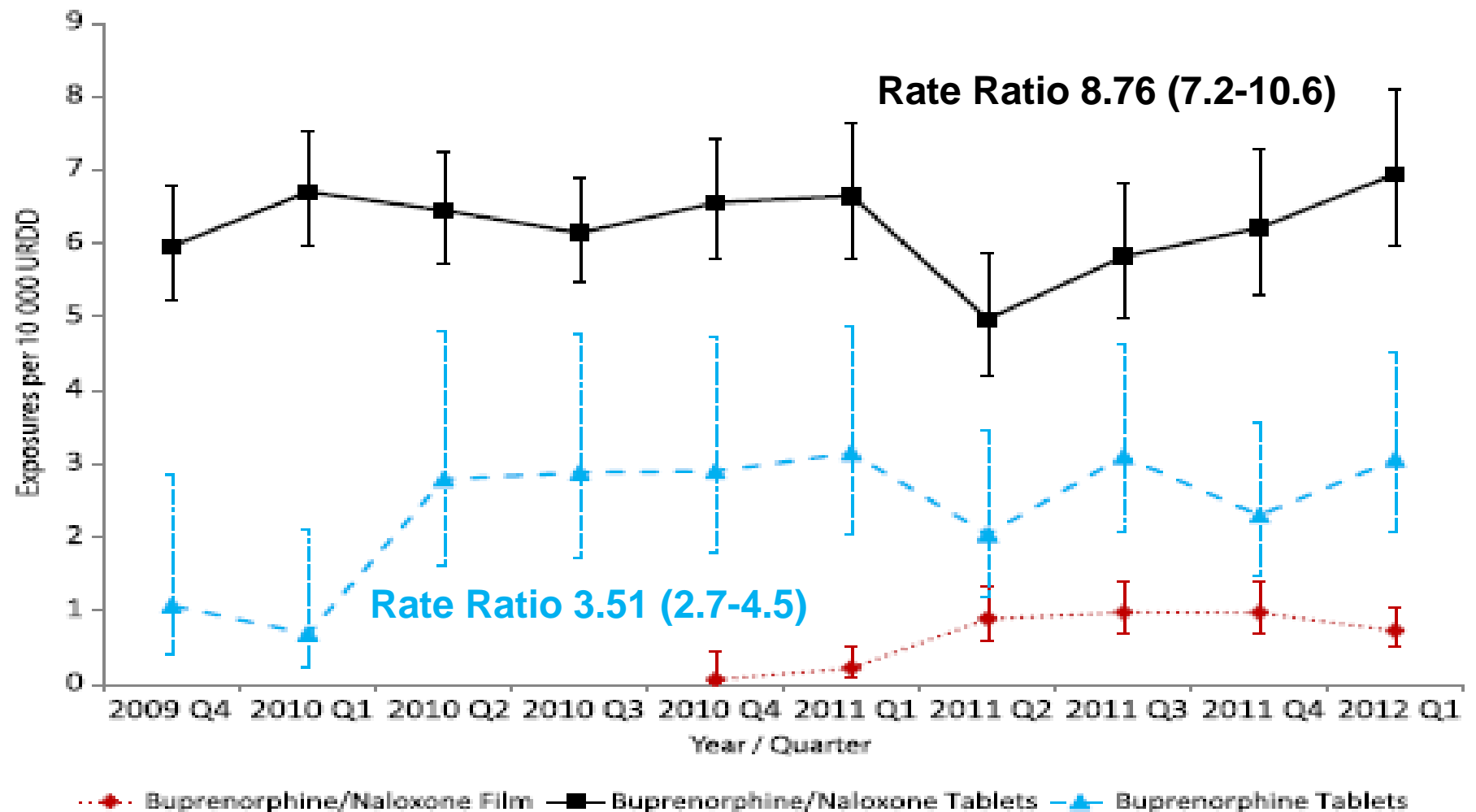


Figure 2. Rates of unintentional exposure to buprenorphine among children aged 28 days to less than 6 years, adjusted for drug availability.

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 or Developmental	Cutting medication				(1.7%)
	Diversion				(0.0%)
	Intended re				(0.0%)
Mistaken for	Other child				(0.0%)
	Other risk fa				(0.0%)
					(0.0%)
Special need	Supervised caregiver				(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 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:

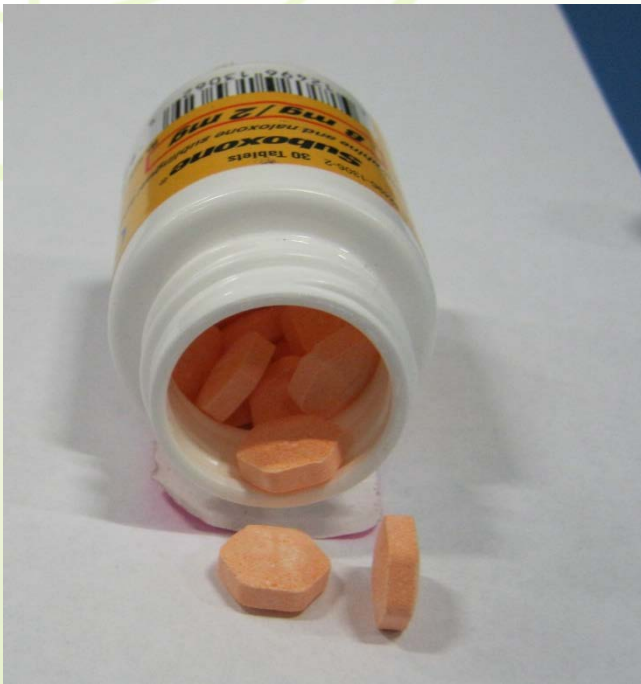
- Access/storage
 - Taken out of original package – why?
 - Cutting/altering dose (prescribing behavior and/or patient-driven dosing?)
 - Stigma associated with medication?
- Packaging
 - Unit dose AND child resistant?

*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

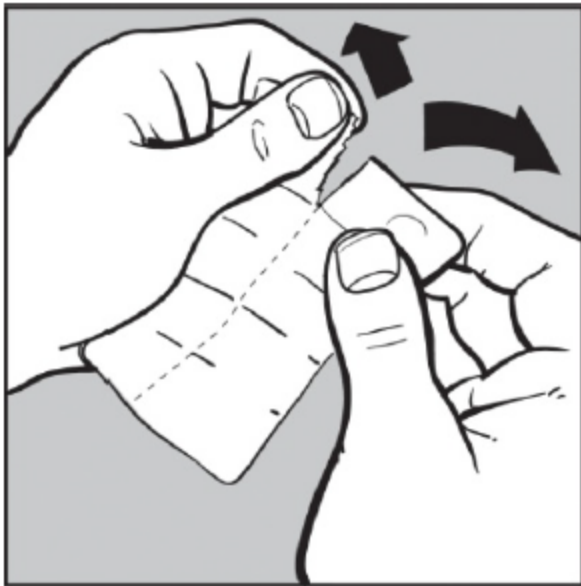


Figure A

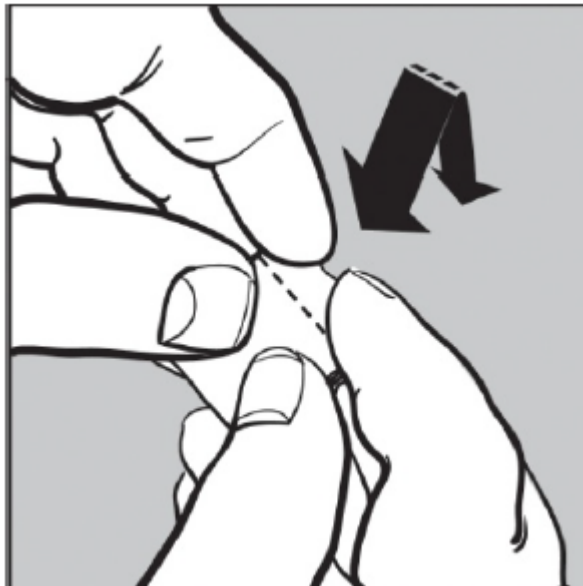


Figure B

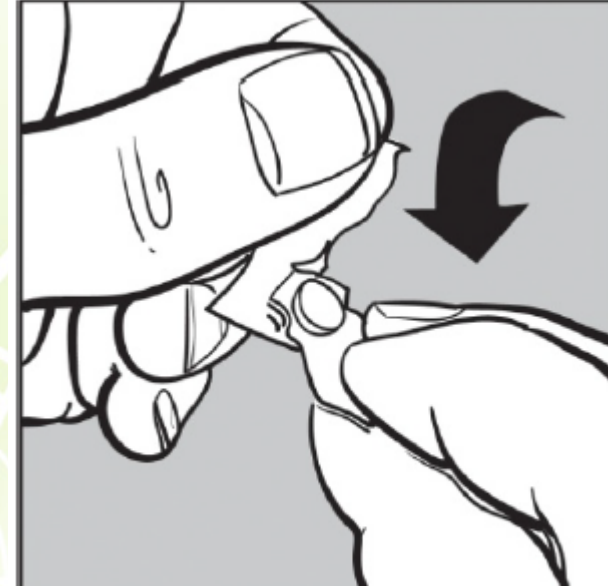


Figure C

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?