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

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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
# Location and Intended user

<table>
<thead>
<tr>
<th>Location</th>
<th>Intended User</th>
<th>Percent of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Child’s home</td>
<td>Immediate family</td>
<td>68</td>
</tr>
<tr>
<td></td>
<td>Other live-ins</td>
<td>41</td>
</tr>
<tr>
<td></td>
<td>Visitor</td>
<td>14</td>
</tr>
<tr>
<td></td>
<td>Intended user unknown</td>
<td>10</td>
</tr>
<tr>
<td>Someplace else</td>
<td>Intended user unknown</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Immediate family</td>
<td>32</td>
</tr>
<tr>
<td></td>
<td>Not immediate family</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Intended user unknown</td>
<td>30</td>
</tr>
</tbody>
</table>

### How did it happen?

<table>
<thead>
<tr>
<th>Description</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Access: Stored in sight</td>
<td>21,445</td>
</tr>
<tr>
<td>Access: Always left out</td>
<td>5,841</td>
</tr>
<tr>
<td>Access: Temporarily open</td>
<td>4,332</td>
</tr>
<tr>
<td>Access: Unlocked low cabinet</td>
<td>3,502</td>
</tr>
<tr>
<td>Access: Purse</td>
<td>2,997</td>
</tr>
<tr>
<td>Access: Another child</td>
<td>1,891</td>
</tr>
<tr>
<td>Access: Suitcase</td>
<td>292</td>
</tr>
<tr>
<td>Access: Other</td>
<td></td>
</tr>
<tr>
<td>Container: Container transfer</td>
<td>865</td>
</tr>
<tr>
<td>CRC: Opened by patient</td>
<td>5,365</td>
</tr>
<tr>
<td>CRC: No CRC, purchaser's request</td>
<td>3,750</td>
</tr>
<tr>
<td>CRC not secured or closed</td>
<td>730</td>
</tr>
<tr>
<td>CRC: No CRC, unknown reason</td>
<td>340</td>
</tr>
<tr>
<td>CRC: Physician sample</td>
<td>40</td>
</tr>
<tr>
<td>CRC: No CRC, not purchaser's request</td>
<td>33</td>
</tr>
<tr>
<td>CRC: Unknown CRC status</td>
<td>5,137</td>
</tr>
</tbody>
</table>

NPDS data, unpublished, 2012
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

Young Child Poisoning Rates are Increasing

Young Child Poisoning Rates are Increasing

![Graph showing increasing child poisoning rates](image-url)
Young Child Poisoning Rates are Increasing
Young Child Poisoning Rates are Increasing

Burkhardt LC. *Pediatr* 2013; ePub.
Medication Use is Increasing

Past 30-Day Prescription Medication Use by Therapeutic Class
US Population (all ages), 1988 - 2010

Percent of US Population

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%).

Young Child Deaths are Increasing

Deaths Due to Unintentional Poisoning by Narcotics and Psychodysleptics (ICD-10 X42) Children Aged Birth to 5 Years, US

R² = 0.5826

Data Source: CDC WONDER.
Young Child Exposures Match Prescribing; Outcomes Match Typical Dose/Potency

<table>
<thead>
<tr>
<th>Opioid</th>
<th>Cases</th>
<th>Major Outcome or Death n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydrocodone</td>
<td>6,003</td>
<td>8 (0.3)</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>2,036</td>
<td>14 (1.1)</td>
</tr>
<tr>
<td>Morphine</td>
<td>419</td>
<td>5 (1.9)</td>
</tr>
<tr>
<td>Methadone</td>
<td>415</td>
<td>16 (5.7)</td>
</tr>
<tr>
<td>Buprenorphine</td>
<td>176</td>
<td>5 (4.0)</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>123</td>
<td>3 (3.8)</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>68</td>
<td>0 (0.0)</td>
</tr>
</tbody>
</table>

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
Buprenorphine

• High potency partial $\mu$-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
Pediatric Root Cause Study

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

![Diagram of Pediatric Root Cause Study]

*Some cases had more than one reason for exclusion*
Film Exposure Rates are Less than Tablet Exposure Rates

## Most Common Root Causes

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

No Relationship Found Between Formulation and Severity

### Table V. Maximum AE severity in cases undergoing focused review

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

*Includes data for buprenorphine formulation unspecified (n = 1).
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
Put your medicines **up and away** and out of sight

More than **60,000** young children end up in emergency departments every year because they got into medicines while their parent or caregiver was not looking.

**Share your place!**
Post a photo of where you store medicines on Twitter, Instagram or Facebook.

Click here to find out how.

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

- www.safekids.org/medsafety
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
Novel Approaches

- Hand-held PCA
Thank You

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