National Electronic Injury Surveillance System – Cooperative Adverse Drug Event Surveillance Project (NEISS-CADES)

Pediatric Safety Surveillance Workshop
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Division of Healthcare Quality Promotion
“The findings and conclusions in this presentation are those of the author and do not necessarily represent the official position of the Centers for Disease Control and Prevention”
Overview

1. Introduction

2. Design & data collection

3. Analytic characteristics & examples

4. Summary
1. Introduction:

An Injury-based Approach
William Sutton
Gentleman, Innovator, &... Bank Robber

1901 - 1980

http://www.fbi.gov/libref/historic/famcases/sutton/sutton.htm
“Slick Willie” Sutton
Gentleman, Innovator, &… Bank Robber

“Why do you rob banks?”
“Because, that’s where the money is.”

1901 - 1980

http://www.fbi.gov/libref/historic/famcases/sutton/sutton.htm
“Slick Willie” Sutton
Gentleman, Innovator, &… Bank Robber

“Why do you rob banks?”
“Because, that’s where the money is.”

• Not *is there* money in banks?
• Which bank has the *most $*?

http://www.fbi.gov/libref/historic/famcases/sutton/sutton.htm
“Where the highest costs are incurred, therein lies the highest potential for over-all cost reduction”
Sutton’s Law & Drug Safety

“Where the highest costs are incurred, therein lies the highest potential for over-all cost reduction”

“Where the highest number of ADEs occur, therein lies the highest potential for over-all harm reduction”
ADVERSE DRUG EVENTS

The Magnitude of Health Risk Is Uncertain Because of Limited Incidence Data
2. Design and Data Collection

National Electronic Injury Surveillance System – Cooperative Adverse Drug Event Surveillance (NEISS-CADES)
NEISS-CADES:
Began in 2004

- U.S. Consumer Product Safety Commission (CPSC):
  - Administers the National Electronic Injury Surveillance System (NEISS) to monitor consumer product injuries

- CDC, with FDA expertise and support, enhanced to:
  - Identify and record injuries from drugs (ADEs)
  - Cooperative Adverse Drug Event Surveillance (NEISS-CADES)
Injury from the use of a drug:
- ED visit
- Treating physician explicitly attributed
- To a drug*
- Intended for therapeutic use

Drugs include: Rx, OTC, supplements, vaccines
NEISS-CADES: Population Representative

- Stratified probability sample of 24-hour EDs
  - 63 hospitals
  - 4 strata by hospital size / 1 stratum for pediatric
- Cases weighted by inverse probability of selection
NEISS-CADES: Data Collection

- Ongoing public health surveillance based on chart abstraction
Identifying ADE Cases

1. Look in Diagnosis Section of chart:
   Do diagnoses include key words?
   - Allergic reaction
   - Adverse effect
   - Side-effect (s/e)
   - Secondary to (2° to, due to, related to)
   - Ingestion (poisoning)
   - Toxicity (overdose, supra-therapeutic level)
   - Medication error

   Or suspicious symptoms?
   - Angioedema (face/lip/throat swelling)
   - Anaphylaxis (severe allergy)
   - Rash (urticaria, dermatitis)
   - Bleeding (GI Bleed, hematemesis, epistaxis, hypocoaguability, high INR/PT)
   - Hypoglycemia (low blood sugar)

2. Is a Drug involved?
   Drugs include: prescription meds, over-the-counter meds, vaccines, vitamins, & dietary supplements.

3. Is there evidence of:
   - Suicide attempt?
   - Intentional overdose?
   - Abuse / Recreational use?

4. Fill out ADE Screen:
   - Record ED chart DIAGNOSIS word for word
   - Record drug name(s)
   - If available, record dose, route, frequency, and duration
   - Record reason for visit, testing, and treatments
   - Record any other information (e.g., discharge instructions or medication error information)

START

STOP

Do not report ADE

NO

YES

STOP

Do not report ADE

NO

YES

NO

FINISH
### Drug data
- Name of implicated medication(s)
- Dose, frequency, duration, route
- Concomitant drugs

### Patient demographics

### Testing and treatments in ED

### Physician diagnoses

### Patient disposition

### Narrative description of event

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**NEISS Case Adverse Drug Event**

Did an adverse drug event occur? Adverse Drug events:
- Include side-effects, allergic reactions and medication errors.
- Include accidental ingestions in children and unintended overdoses with high levels of medication in adults.
- Do NOT report drug abuse, 'recreational' drug use, self-harm or cases due to alcohol or illegal drugs.

Drugs include: Prescription Medications, Over-the-Counter Medications, Medicants, Medicated Creams/Ointments, Vaccinations/Immunizations, Vitamins, and Herbal/Nutritional Supplements.

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Limitations

- Setting: only ED visits
  - No inpatient follow-up or mortality

- Underestimates
  - Relies on caregiver recognition, physician documentation, and accurate abstraction
  - High PPV, lower sensitivity

- Selection biases
  - Acute onset ADEs
  - ADEs which can be diagnosed in ED
3. Analytic Characteristics & Examples

*Known Harms ➔ ED visits*
### Analytic Characteristics

**Sensitivity and +PV**

#### Gold Standard Independent Chart Review

<table>
<thead>
<tr>
<th></th>
<th>Case +</th>
<th>Case -</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case +</td>
<td>25</td>
<td>4</td>
</tr>
<tr>
<td>Case -</td>
<td>43</td>
<td>4,489</td>
</tr>
</tbody>
</table>

33% Weighted Sensitivity

92% Weighted +PV

*NEISS-CADES Coder*

*MMWR 2005;54:380-3*
## Analytic Characteristics

### Data Quality: Completeness

<table>
<thead>
<tr>
<th>Patient Characteristic</th>
<th>% Complete (N=10,383)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>100%</td>
</tr>
<tr>
<td>Sex</td>
<td>100%</td>
</tr>
<tr>
<td>Disposition</td>
<td>100%</td>
</tr>
<tr>
<td>Diagnosis in medical record</td>
<td>99%</td>
</tr>
<tr>
<td>Treatment in medical record</td>
<td>91%</td>
</tr>
<tr>
<td>Testing in medical record</td>
<td>84%</td>
</tr>
<tr>
<td>Race/Ethnicity</td>
<td>76%</td>
</tr>
</tbody>
</table>

## Analytic Characteristics

### Data Quality: Completeness

<table>
<thead>
<tr>
<th>Drug Characteristic</th>
<th>% Complete (N=10,383)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Name of Drug</td>
<td>97%</td>
</tr>
<tr>
<td>Route of administration</td>
<td>82%</td>
</tr>
<tr>
<td>Dosage</td>
<td>37%</td>
</tr>
<tr>
<td>Frequency</td>
<td>43%</td>
</tr>
<tr>
<td>Duration of use</td>
<td>41%</td>
</tr>
</tbody>
</table>

## Analytic Characteristics

### Data Quality: Validity

<table>
<thead>
<tr>
<th>Data Field</th>
<th>Data Element Sensitivity (Coder-Gold Standard Agreement)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient age &amp; sex</td>
<td>100%</td>
</tr>
<tr>
<td>Names of drugs involved</td>
<td>93%</td>
</tr>
<tr>
<td>Primary diagnoses</td>
<td>93%</td>
</tr>
<tr>
<td>Primary drug dose</td>
<td>80%</td>
</tr>
<tr>
<td>Indicated treatments</td>
<td>80%</td>
</tr>
<tr>
<td>Primary drug frequency</td>
<td>68%</td>
</tr>
<tr>
<td>Diagnostic tests ordered</td>
<td>61%</td>
</tr>
<tr>
<td>Primary drug duration</td>
<td>56%</td>
</tr>
<tr>
<td>Other drugs taken</td>
<td>52%</td>
</tr>
<tr>
<td>Primary drug route</td>
<td>40%</td>
</tr>
</tbody>
</table>

## Analytic Characteristics

### Timeliness

<table>
<thead>
<tr>
<th>Event</th>
<th>% Complete (N=10,383)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADE reported within 7 days</td>
<td>67</td>
</tr>
<tr>
<td>ADE reported within 30 days</td>
<td>93</td>
</tr>
</tbody>
</table>

### ED Visit → Analytic Dataset

- Duration: 9 – 21 months
- (e.g., Calendar year 2009 ready September 2010)

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Estimated Annual Impact of Ambulatory Adverse Drug Events in Children ≤18 years

- Deaths: ?
- Hospitalizations: 15,000 (0.2 per 1,000)
- Emergency visits: 160,000 (2.0 per 1,000)

No. of ED Visits for Adverse Drug Events, 2004-2005

Rates of ED Visits for Adverse Drug Events, 2004-2005

Unintentional Overdoses Cause Most ED Visits in Children <5 Years Old

<table>
<thead>
<tr>
<th>Type</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unintentional Overdoses</td>
<td>58%</td>
</tr>
<tr>
<td>Allergic Reactions</td>
<td>28%</td>
</tr>
<tr>
<td>Side Effects</td>
<td>5%</td>
</tr>
<tr>
<td>Vaccine Reactions</td>
<td>8%</td>
</tr>
<tr>
<td>Secondary Effects</td>
<td>1%</td>
</tr>
</tbody>
</table>

Medicines Cause More ED Visits For Overdoses Than All Other Consumer Products Combined

1 out of every 180 two-year-olds each year
# OTC Medicines Commonly Involved in ED Visits for Overdoses


<table>
<thead>
<tr>
<th>Drug class</th>
<th>Cases</th>
<th></th>
<th>Drug class</th>
<th>Cases</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Unsupervised ingestion</td>
<td></td>
<td></td>
<td>Medication error</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Acetaminophen</td>
<td>289 (10.5)</td>
<td></td>
<td>• Anticonvulsants</td>
<td>29 (10.0)</td>
<td></td>
</tr>
<tr>
<td>• Opioids/benzodiazepines</td>
<td>211 (7.7)</td>
<td></td>
<td>• Cough and cold agents</td>
<td>29 (10.0)</td>
<td></td>
</tr>
<tr>
<td>• Cough and cold agents</td>
<td>202 (7.4)</td>
<td></td>
<td>• Antipsychotics</td>
<td>19 (6.6)</td>
<td></td>
</tr>
<tr>
<td>• NSAIDs</td>
<td>167 (6.1)</td>
<td></td>
<td>• Opioids/benzodiazepines</td>
<td>18 (6.2)</td>
<td></td>
</tr>
<tr>
<td>• Antidepressants</td>
<td>161 (5.9)</td>
<td></td>
<td>• Antidepressants</td>
<td>16 (5.6)</td>
<td></td>
</tr>
<tr>
<td>• Antihistamines</td>
<td>160 (5.8)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Number of Cases and Cumulative Percent of Cough and Cold ADEs, 2004-2005

Adapted from Schaefer MK, et al. *Pediatrics* 2008;121: 783-787
Number of Cases and Cumulative Percent of Cough and Cold ADEs, 2004-2005

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Number of Cases and Cumulative Percent of Cough and Cold ADEs, 2004-2005

Adapted from Schaefer MK, et al. *Pediatrics* 2008;121: 783-787
Underlying Causes of Emergency Visits for Child Overdoses, 2004-2005

PROTECT Partnership

- Preventing Overdoses & Treatment Errors in Children Taskforce

- Federal agencies, manufacturers (OTC), professional organizations, safety experts
  - Innovative safety packaging
  - Standardization of volumetric units for liquid medicines
  - “Up & Away” educational campaign
Packaging Innovation to Prevent Ingestions

Active

Passive
Standardizing Volumetric Dosing Devices and Instruction

Guidance for Industry

Dosage Delivery Devices for OTC Liquid Drug Products

Guideline Volumetric Measures for Dosing of Over-the-Counter Oral Liquid Drug Products for Children ≤ 12 years of Age

1. Introduction

As part of multiple stakeholder efforts to help prevent accidental, unsupervised medication ingestions and overdoses in children, this document suggests ways to improve the consistency and standard format of volumetric measures within the dosing directions on the outer packaging and immediate container label, as well as on the dosing device for OTC oral liquid drug products with dosing directions for children, defined as ≤12 years of age (both covered under the monograph system as well as an approved NDA/ANDA). While research evidence is limited, the recommendations made herein do represent the integration of stakeholder communications and standards, including those from authoritative bodies and professional organizations, as well as knowledge gained from consumer experience and research with OTC medicine products.

http://www.chpa-info.org/scienceregulatory/Voluntary_Codes.aspx
4. Summary

Points to Consider
Regarding the System

1. Age in months for children <2 years
2. No documentation of indication
3. Identifies: admit / transfer / observation
4. Physician-documented AEs & implicated drug
   • Sometimes: dose, schedule, formulation, route
   • Not biologics or devices
5. Concomitant medications collected
6. OTC medications collected
7. Free text must be examined for clinical setting
8. Diagnosis of AE by ED clinician
9. Reporting of AE from ED
10. No data on deaths
11. Collects AEs across age subpopulations
12. Includes 5 pediatric-specialty and 58 general hospital EDs
Does the System?

1. Professional staff that monitors, codes, and standardizes data reported. Validation of data with re-review of charts is not done.

2. Accepts diagnosis indicated by treating clinician

3. No “trigger events” / All reports are physician-diagnosed ADEs

4. Not linked to EMRs

5. Age in months for children <2 years
6. No growth & development data
7. No birth history
8. Codes AEs to MedDRA Preferred Terms (PTs)
9. Unique patient identifiers *may* allow follow-up but only in *extreme* circumstances
10. No cost data per visit
11. No cost data per treatment
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• Sue Johnson

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• Joel Freidman
• Cathleen Irish
Additional Slides
The Public Health Approach

Identify the Problem

Identify Risk & Protective Factors

Design Intervention

Evaluate Impact

- 1 in 180 two-year olds
- Unsupervised ingestions

98,000 ED visits/year for children <=5 years old

Improve child-resistant packaging