An Evaluation of Pharmacy Data for Surveillance of Gastrointestinal and Respiratory Outbreaks

Yevgeniy Elbert¹, MS
Shilpa Hakre¹, MPH, DrPH
Howard Burkom², PhD
Julie Pavlin¹, MD, MPH

November 15, 2004

¹Walter Reed Army Institute of Research, Silver Spring, MD
²Johns Hopkins Applied Physics Laboratory, Laurel, MD
1. REPORT DATE
15 NOV 2004

2. REPORT TYPE
N/A

3. DATES COVERED
-

4. TITLE AND SUBTITLE
An Evaluation of Pharmacy Data for Surveillance of Gastrointestinal and Respiratory Outbreaks

5a. CONTRACT NUMBER

5b. GRANT NUMBER

5c. PROGRAM ELEMENT NUMBER

5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

6. AUTHOR(S)

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
Walter Reed Army Institute of Research, Silver Spring, MD

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)

10. SPONSOR/MONITOR’S ACRONYM(S)

11. SPONSOR/MONITOR’S REPORT NUMBER(S)

12. DISTRIBUTION/AVAILABILITY STATEMENT
Approved for public release, distribution unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT

15. SUBJECT TERMS

16. SECURITY CLASSIFICATION OF:

<table>
<thead>
<tr>
<th>a. REPORT</th>
<th>b. ABSTRACT</th>
<th>c. THIS PAGE</th>
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<tbody>
<tr>
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17. LIMITATION OF ABSTRACT
UU

18. NUMBER OF PAGES
40

19a. NAME OF RESPONSIBLE PERSON

Standard Form 298 (Rev. 8-98)
Proscribed by ANSI Std Z39-18
ESSENCE
Electronic Surveillance System for the Early Notification of Community-based Epidemics

• A U.S. Department of Defense (DoD) system
• Designed to detect infectious disease outbreaks
• Serves military active duty members, their beneficiaries, and retirees
• Uses mainly ICD-9-CM codes from outpatient visits
• Delay of 1-4 days from patient visit date to data capture date by ESSENCE
Pharmacy Data Transaction Service (PDTS)

- Developed by the DoD Pharmacoeconomic Center (PEC) program, managed by WebMD
- Data repository for prescriptions filled by beneficiaries of the military health system
- Approx. 61.1 million prescriptions filled annually\(^1\)
  - 82% of prescriptions from MTFs (n=587)
  - 18% from:
    - Tricare Managed Care Support Contractors Network pharmacies (n=50,000)
    - National Mail Order Pharmacy (n=1)
Tricare pharmacy transactions

PDTS

3.2 seconds

Update every 24 hours

ESSENCE
PDTS Fields

• The PDTS formulary and standards maintained through WebMD’s subscription to the American Hospital Formulary Service (AHFS), the National Council for Prescription Drug Programs (NCPDP), and First Data Bank, Inc.

• Medication id fields in PDTS
  - Drug name (Label)
  - Therapeutic class number (GCN)
  - Therapeutic class code (GC3)
  - Other

• Previous study by Scott Eader et al. using ESSENCE data for the DC metropolitan area
  - Significant positive correlation between outpatient visit and PDTS data for GC3 codes identified for Respiratory (RESP) and gastrointestinal (GI) syndromes

• GC3: developed by First Data Bank, Inc.
  3 characters (alpha, numeric, alpha)
  - organ system, pharmacological class, specific therapeutic class, respectively
# PDTS

Commonly filled medications, 2003

<table>
<thead>
<tr>
<th>GC3</th>
<th>DESCRIPTION</th>
<th>COUNT</th>
<th>PERCENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>S2B</td>
<td>NSAIDS, CYCLOOXYGENASE INHIBITOR - TYPE</td>
<td>5603369</td>
<td>6.34</td>
</tr>
<tr>
<td>H3A</td>
<td>ANALGESICS,NARCOTICS</td>
<td>4256802</td>
<td>4.81</td>
</tr>
<tr>
<td>M4E</td>
<td>LIPOTROPICS</td>
<td>4049267</td>
<td>4.58</td>
</tr>
<tr>
<td>Z2A</td>
<td>ANTIHISTAMINES</td>
<td>3812841</td>
<td>4.34</td>
</tr>
<tr>
<td>D4K</td>
<td>GASTRIC ACID SECRETION REDUCERS</td>
<td>3395463</td>
<td>3.84</td>
</tr>
<tr>
<td>A4D</td>
<td>HYPOTENSIVES, ACE INHIBITORS</td>
<td>2659102</td>
<td>3.01</td>
</tr>
<tr>
<td>J7C</td>
<td>BETA-ADRENERGIC BLOCKING AGENTS</td>
<td>2373543</td>
<td>2.68</td>
</tr>
<tr>
<td>H2S</td>
<td>SELECTIVE SEROTONIN REUPTAKE INHIBITOR (SSRIS)</td>
<td>2230604</td>
<td>2.52</td>
</tr>
<tr>
<td>W1A</td>
<td>PENICILLINS</td>
<td>2039720</td>
<td>2.31</td>
</tr>
<tr>
<td>A9A</td>
<td>CALCIUM CHANNEL BLOCKING AGENTS</td>
<td>1966936</td>
<td>2.22</td>
</tr>
<tr>
<td>P3A</td>
<td>THYROID HORMONES</td>
<td>1700412</td>
<td>1.92</td>
</tr>
<tr>
<td>B3J</td>
<td>EXPECTORANTS</td>
<td>1654859</td>
<td>1.87</td>
</tr>
<tr>
<td>J5D</td>
<td>BETA-ADRENERGIC AGENTS</td>
<td>1557748</td>
<td>1.76</td>
</tr>
<tr>
<td>Q7P</td>
<td>NASAL ANTI-INFLAMMATORY STEROIDS</td>
<td>1420677</td>
<td>1.61</td>
</tr>
<tr>
<td>H2F</td>
<td>ANTI-ANXIETY DRUGS</td>
<td>1311393</td>
<td>1.48</td>
</tr>
<tr>
<td>H4B</td>
<td>ANTICONVULSANTS</td>
<td>1299466</td>
<td>1.47</td>
</tr>
<tr>
<td>P5A</td>
<td>GLUCOCORTICOIDs</td>
<td>1265605</td>
<td>1.43</td>
</tr>
<tr>
<td>R1F</td>
<td>THIAZIDE AND RELATED DIURETICS</td>
<td>1247417</td>
<td>1.41</td>
</tr>
<tr>
<td>W1D</td>
<td>MACROLIDES</td>
<td>1242950</td>
<td>1.41</td>
</tr>
<tr>
<td>A4F</td>
<td>HYPOTENSIVES, ANGIOTENSIN RECEPTOR ANTAGONIST</td>
<td>1223731</td>
<td>1.38</td>
</tr>
</tbody>
</table>

- **Painkillers**
- **Cholestrol reducers**
- **Allergy relievers**
STUDY OBJECTIVES

1) Determine medications commonly prescribed for GI and RESP syndromes during outbreaks

2) Examine trends in daily counts of medications filled for GI, RESP, Asthma visits during outbreaks

3) Conduct retrospective surveillance on drug groups that correlated with GI and RESP outpatient visits during outbreaks
METHODS

• List compiled of known GI and RESP outbreaks

• Commonly prescribed non-refill medications identified for each outbreak
  – By linking ambulatory and pharmacy data by date of visit/prescription written and unique encrypted identifiers common to both data sets

• Trends in medications filled and GI/Resp visits investigated during outbreaks
  – Moving 7-day averages of daily counts
### RESULTS

**Outbreaks**

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>No. of Outbreaks</th>
<th>Viral</th>
<th>Bacterial</th>
<th>Unknown</th>
</tr>
</thead>
<tbody>
<tr>
<td>GI</td>
<td>21</td>
<td>13</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>RESP</td>
<td>7</td>
<td>2</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>28</strong></td>
<td><strong>15</strong></td>
<td><strong>6</strong></td>
<td><strong>7</strong></td>
</tr>
</tbody>
</table>
GI Outbreaks
35 C company members ill
- Nausea
- Diarrhea
- Fever
- Headache

- Food and water samples from the FTX tested
  - 5/13 samples tested positive for *Campylobacter jejuni*
Top 5 ICD-9 codes used during a C. jejuni outbreak

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>558.9</td>
<td>Gastroenteritis, noninfect NEC</td>
</tr>
<tr>
<td>787.91</td>
<td>Diarrhea NOS</td>
</tr>
<tr>
<td>008.8</td>
<td>Enteritis, viral NOS</td>
</tr>
<tr>
<td>535.00</td>
<td>Gastritis, acute w/o hemorrhage</td>
</tr>
<tr>
<td>535.50</td>
<td>Gastritis NOS w/o hemorrhage</td>
</tr>
</tbody>
</table>

Top 5 prescriptions written during C. jejuni outbreak

<table>
<thead>
<tr>
<th>Category</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antidiarrheals</td>
<td>25</td>
</tr>
<tr>
<td>Analgesics/antipyretics</td>
<td>16</td>
</tr>
<tr>
<td>Quinolones</td>
<td>16</td>
</tr>
<tr>
<td>Antiemetic/antivertigo agents</td>
<td>14</td>
</tr>
<tr>
<td>Expectorants</td>
<td>10</td>
</tr>
</tbody>
</table>
RESULTS

*Campylobacter jejuni* Outbreak

7-day moving averages

<table>
<thead>
<tr>
<th>Date</th>
<th>GI Syndrome Visits</th>
<th>Medications Filled</th>
</tr>
</thead>
<tbody>
<tr>
<td>10/1/2002</td>
<td>30</td>
<td>Antiemetics</td>
</tr>
<tr>
<td>10/15/2002</td>
<td>25</td>
<td>Antidiarrheals</td>
</tr>
<tr>
<td>10/29/2002</td>
<td>20</td>
<td>Quinolones</td>
</tr>
<tr>
<td>11/12/2002</td>
<td>15</td>
<td>Antihistamines</td>
</tr>
<tr>
<td>11/26/2002</td>
<td>10</td>
<td>GI visits</td>
</tr>
<tr>
<td>12/10/2002</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>12/24/2002</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>
**Top 5 ICD-9 codes used during a Salmonella outbreak**

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>535.00</td>
<td>Gastritis, acute w/o hemorrhage</td>
<td></td>
</tr>
<tr>
<td>005.89</td>
<td>Poisoning, food, bacterial NEC</td>
<td></td>
</tr>
<tr>
<td>787.91</td>
<td>Diarrhea NOS</td>
<td></td>
</tr>
<tr>
<td>558.9</td>
<td>Gastroenteritis, noninfct NEC</td>
<td></td>
</tr>
<tr>
<td>005.9</td>
<td>Poisoning, food NOS</td>
<td></td>
</tr>
</tbody>
</table>

**Top 5 prescriptions during the Salmonella outbreak**

<table>
<thead>
<tr>
<th>Category</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antidiarrheals</td>
<td></td>
</tr>
<tr>
<td>NSAID</td>
<td></td>
</tr>
<tr>
<td>Analgesics/antipyretics</td>
<td></td>
</tr>
<tr>
<td>Quinolones</td>
<td></td>
</tr>
<tr>
<td>Antihistamines</td>
<td></td>
</tr>
</tbody>
</table>
RESULTS

Salmonella Outbreak
7-day moving averages

Analgesics/antipyretics: Acetaminophen, Tylenol, etc.
Antidiarrheals: Loperamide, Imodium, Pepto-bismol, etc.
Antihistamines: Includes Phenergan, Promethazine (antiemetics)
Quinolones: Ciprofloxacin, Levaquin, etc.
RESULTS
GI OUTBREAK 3

• At a U.S. Air Force training base in Texas$^3$
  – Norovirus outbreak
  – In all 464 trainees affected
  – Lasted 7 days
  – 7/7 stool samples tested positive for Norovirus
Top 5 prescriptions written during a Norovirus outbreak

- Antidiarrheals
- Antihistamines

Top 5 ICD-9 codes used during a Norovirus outbreak

- Gastroenteritis, noninfect NEC
- Enteritis presumed infect origin
- Diarrhea NOS
- Nausea with vomiting
- Vomiting alone
RESULTS

Norovirus Outbreak
7-day moving averages

Graph showing the increase in GI Syndrome Visits during the norovirus outbreak, with peaks around 3/4/2004. The graph also indicates a rise in medications filled, particularly antidiarrheals and antihistamines, during the outbreak period.
RESP
Outbreaks
RESULTS
RESP OUTBREAK 1

• At the Marine Corps Recruit Depot in San Diego\(^3\)
  – Largest Group A Streptococcus outbreak since 1968
  – 160 recruits admitted for pneumonia (radiographically confirmed)
  – November 1 – December 20
  – Sputum, blood and throat cultures
    • Group A Streptococcus isolated
Top 5 ICD-9 codes used during a Streptococcus A outbreak

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>465.9</td>
<td>Infct up rsprt mt sites, acute NOS</td>
<td>30</td>
</tr>
<tr>
<td>786.05</td>
<td>Pneumonia, organism NOS</td>
<td>20</td>
</tr>
<tr>
<td>462</td>
<td>Pharyngitis, acute</td>
<td>15</td>
</tr>
<tr>
<td>786.2</td>
<td>Shortness of breath</td>
<td>10</td>
</tr>
<tr>
<td>0</td>
<td>Cough</td>
<td>5</td>
</tr>
</tbody>
</table>

Top 5 prescriptions written during a Streptococcus A outbreak

<table>
<thead>
<tr>
<th>Description</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zinc replacement</td>
<td>15</td>
</tr>
<tr>
<td>Macrolides</td>
<td>15</td>
</tr>
<tr>
<td>Sympathomimetic agents</td>
<td>15</td>
</tr>
<tr>
<td>Expectorants</td>
<td>20</td>
</tr>
<tr>
<td>Analgesics/antipyretics</td>
<td>20</td>
</tr>
</tbody>
</table>
RESULTS

Streptococcus A Outbreak
7-day moving averages

<table>
<thead>
<tr>
<th>Date</th>
<th>Medications Filled</th>
</tr>
</thead>
<tbody>
<tr>
<td>10/15/2002</td>
<td></td>
</tr>
<tr>
<td>10/30/2002</td>
<td></td>
</tr>
<tr>
<td>11/14/2002</td>
<td></td>
</tr>
<tr>
<td>11/29/2002</td>
<td></td>
</tr>
<tr>
<td>12/14/2002</td>
<td></td>
</tr>
<tr>
<td>12/29/2002</td>
<td></td>
</tr>
</tbody>
</table>

- **Expectorants**: Robitussin, Guaifenesin, etc.
- **Zinc replacement**: Cepacol Cold Care, etc.
- **Sympathomimetic agents**: Sudafed, etc.
- **Analgesics/antipyretics**: Acetaminophen, Tylenol, etc.
RESULTS
RESP OUTBREAK 2

• Influenza in an Advanced Individual Training population in VA in November, 2003
  – Approx. 187 cases total
  – Oct. 31st – Nov. 7th
  – Rapid flu tests positive; 5 CDC viral cultures Flu A positive, subtyped Korea-like or Fujian-like viruses
Top 5 ICD-9 codes used during an influenza outbreak

- Pharyngitis, acute (462)
- Bronchitis NOS (490)
- Cough (786.2)
- Bronchitis, acute (466.0)
- Infct up rsprt mlt sites, acute NOS (465.9)

Top 5 prescriptions written during an influenza outbreak

- NSAIDS
- Beta-adrenergic agents
- Cough and/or cold preparations
- Analgesics/antipyretics
- Expectorants

RESULTS

RESP Outbreak 2
RESULTS

Influenza Outbreak
7-day moving averages

Date
Medications filled
Visits


OUTBREAK

RespVisits
Expectorants
Analgesic/antipyretic
Antitusssives
RESULTS

**GI group**

1. Antiemetics
2. Antidiarrheals
3. Antihistamines
4. Analgesics/antipyretics
5. Antispasmodics
6. Antacids
7. Quinolones
8. Intestinal adsorbents and protectives
9. Penicillins
10. Absorbable sulfonamides

**RESP group**

1. Expectorants
2. Cough and/or cold preparations
3. Analgesics/antipyretics
4. Antitussives, non-narcotic
5. Sympathomimetic agents
6. NSAIDS
7. Macrolides
8. Quinolones
9. Zinc replacement
10. Penicillins
STUDY OBJECTIVES

1) Determine medications commonly prescribed for GI and Respiratory (RESP) syndromes

2) Examine trends in daily counts of medications for GI, RESP, Asthma visits during outbreaks

3) Conduct retrospective surveillance on GI and RESP syndrome drug groups and GI and RESP outpatient visits at installations where outbreaks occurred
METHODS

• Retrospective surveillance conducted on pharmacy and outpatient visit data for approx. 1 year prior to and including the outbreak timeframe
  – Regression/Exponential Weighted Moving Average (EWMA) detection algorithms run on daily total GI/RESP visits, daily total PDTS syndrome groups and each GC3 group → output of p-values
  – P-values from individual larger count GC3 groups (>1 prescription in 3 days) were combined using Fisher and Edgington combination p-value methods
    • More information on combination p-value methods → Dr. Howard Burkom’s talk at 2:00 p.m.
  – Detections with approximately 1 per 6 weeks false alert rate were identified graphically
Salmonella Outbreak
(12/9/02 to 12/18/02)
C. jejuni Outbreak
(11/16/02 – 11/18/02)
Norovirus Outbreak$^3$
(02/17/04 to 02/24/04)
Influenza Outbreak
(11/1/03 to 11/18/03)
Group A Streptococcus Outbreak
12/08/02 to 12/12/02

Outpatient Visits
ESSENCE VISITS
EDGINGTON Rx
FISHER Rx
ESSENCE Rx
Outbreak

Alerted earliest
CONCLUSIONS

• Use of the GC3 classification system in military pharmacy data can increase sensitivity without significantly affecting the false alert rate.
  – A limitation: Certain medications were found in more than one GC3 group. If these don’t contribute to an outbreak, the signal is weakened.

• Outbreaks were characterized by increases in certain GC3 groups and combinations of GC3 groups but these varied by outbreak type.

• Syndromic drug groups were formed using medications more commonly used during outbreaks, increasing the overall sensitivity of the system.
CONCLUSIONS

• The ESSENCE outpatient visit detector, the gold standard, alerted for all 6 outbreaks.

• The ESSENCE pharmacy detector performed well and alerted for 5/6 outbreaks.

• The two p-value combination methods have distinct advantages. The Fisher method alerted for 5/6 outbreaks and was more sensitive to individual GC3 increases. Whereas, the Edgington method alerted for 3/6 outbreaks but was more responsive to consensus and in 2 outbreaks alerted earlier.

• Combination methods are more sensitive and specific if low count gc3 streams are accumulated or dropped.
FUTURE RESEARCH

• Investigate performance of algorithms for other outbreaks

• Investigate performance of detectors for a GC3 group switch, i.e., ignore product groups that don’t meet a certain minimum count

• Continue to investigate product groups that give more signal and less noise

• Prospective surveillance using ESSENCE pharmacy and combination method detectors
REFERENCES


ACKNOWLEDGEMENTS

CPT Jeffrey K. Brown, USAMRID, Fort Detrick, MD

LCDR Scott Thornton, NEPMU-6, Pearl Harbor, HI

MAJ Samuel Jang, CHPPM, Aberdeen Proving Grounds, MD

Asha Riegodedios, MPH, NEHC, Bethesda, MD
THANK YOU FOR YOUR ATTENTION