Some Interesting Patterns in the Adverse Event Reporting System of the Food and Drug Administration

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Research Objective

- To analyse the AERS database of FDA in search of interesting patterns
  - Any interesting pattern might be of use to FDA and/or Professionals in the domain
  - The findings might pave ways for new directions in pharmacovigilance
- Data miners might not have the necessary domain knowledge for interpreting any observed patterns even though they might be good at finding such patterns
Outline of Presentation

• AERS Database of FDA
• Data preprocessing
• Approach to find interesting patterns
• Some patterns found
• Concluding remarks
FDA AERS Data Repository

- FDA AERS Data repository
  - Adverse event reporting system (AERS)
  - Quarter-wise Data in multiple Tables
  - This study considered only 13 Quarter data (2004 Q1-2007 Q1)
Who reports adverse events?

- **MD**: Physicians
- **PH**: Pharmacists
- **OT**: Other health professionals
- **LW**: Lawyers
- **CN**: Consumers
Categories of adverse events

- DE: Death
- LT: Life threatening
- HO: Hospitalization
- DS: Disability
- CA: Congenital anomaly
- RI: Required intervention to prevent impairment
- OT: Other
Importing AERS data into Oracle Database

• Why oracle database
  – Difficulty of inference from AERS data (collection of tables only)
  – Need for data cleaning
  – Need for a database system for executing queries of research interest
  – Need to handle large volume of data
  – Incremental addition of future/past data
Why mine 50 most frequently reported drugs in FDA AERS?

- Total distinct ISR in 13 qtr = 1009535
- Sum of distinct ISR count of top 50 drugs = 799543
- Most frequent: VIOXX
  - 70452 distinct ISR
- Second most frequent: ASPIRIN
  - 49634 distinct ISR
- Third most frequent: LIPITOR
  - 26750
Top 50 drugs in AERS

<table>
<thead>
<tr>
<th>Name</th>
<th># ISR</th>
<th>Name</th>
<th># ISR</th>
<th>Name</th>
<th># ISR</th>
<th>Name</th>
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ISR Counts for Top 50 AERS Drugs
Qtr-wise ISR Counts for Top 50 AERS Drugs

- ISR counts in the Table and Graph are for 13 quarters combined
- For temporal pattern discovery data against smaller time scale will provide more insight
- FDA AERS provides quarterly reports
- Quarter-wise data for individual drugs can be extracted from the reports
# ISR Count of each drug by QTR

<table>
<thead>
<tr>
<th>Year/Qtr</th>
<th>QTR Index</th>
<th>VIOXX</th>
<th>ASPIRIN</th>
<th>LIPITOR</th>
<th>AVONEX</th>
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ISR count for each drug by QTR

![Graph showing ISR count for each drug by QTR]
Mining objectives?

- Exploring existence of interesting pattern among AERS reports for different drugs
- Finding the patterns
- Modeling the patterns for predictive purposes
Discovery of temporal reporting pattern among drugs

- Clustering for temporal patterns
- Clustering algorithms and parameters
  - K-means with Euclidean distance
  - Number of clusters varied from 2 to 10
  - See the clustering table
## K-Means clusters of 50 drugs

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</table>
An Interesting Cluster

• Always only VIOXX and ASPIRIN form a separate cluster
  – VIOXX got withdrawn after 2004
  – ASPIRIN is in use for long time
  – As number of clusters changed from 2 to 10, always the formation of a separate cluster with VIOXX and ASPIRIN shows a very strong affinity of these two AERS data
  – Closer look needed?
Probing Deeper

• Do ASPIRIN and VIOXX show any interesting similarity with respect to specific adverse effects (such as Death, Hospitalization etc) as well?

• Do ASPIRIN and VIOXX show any interesting similarity with respect to the occupation of the reporter (Doctor, Pharmacists etc) as well?
Adverse Event Classification of Aspirin (quarterly)
Adverse Effect Classification of VIOXX (quarterly)
Adverse Effect Comparison of VIOXX and ASPIRIN

DEATH AND LIFE THREATENING

Number of ISR

QTR

DE_VIOXX
DE_ASPIRIN
LT_VIOXX
LT_ASPIRIN
Adverse Effect Comparison of VIOXX and ASPIRIN (contd...)

HOSPITALIZATION, DISABILITY, AND OTHERS*

Number of ISR

QTR

1 2 3 4 5 6 7 8 9 10 11 12 13

HO_VIOXX
HO_ASPIRIN
DS_VIOXX
DS_ASPIRIN
OT_VIOXX
OT_ASPIRIN
Occupation-wise Classification of Adverse Effect of Aspirin (quarterly)

ASPIRIN

Number of ISR

QTR

MD
PH
OT
LW
CN
Occupation-wise Classification of Adverse Effect of VIOXX (quarterly)
Occupation-wise Comparison of AERS Reports of VIOXX and Aspirin

![Graph showing occupation-wise comparison of AERS reports for VIOXX and Aspirin.](image)
Occupation-wise Comparison of AERS Reports of VIOXX and Aspirin (contd…)

![Graph showing occupation-wise comparison of AERS reports for VIOXX and Aspirin](image)
Concluding Remarks

• Why AER patterns for ASPIRIN and VIOXX exhibited a high degree of similarity?
• Did the awareness of the adverse effect of VIOXX influence the consumption of ASPIRIN?
• Did the media attention of VIOXX have any influence on the reporting of ASPIRIN related adverse events?
• Were the contributions of the lawyers in the reporting patterns for VIOXX a little unusual?
• Would the timing and impact of VIOXX related awareness and actions have remained the same in the absence of reporting by lawyers?
• Are the detailed reporting patterns important to FDA and other concerned professionals in the domain of public health and pharmacovigilance
Thank You!

Questions?