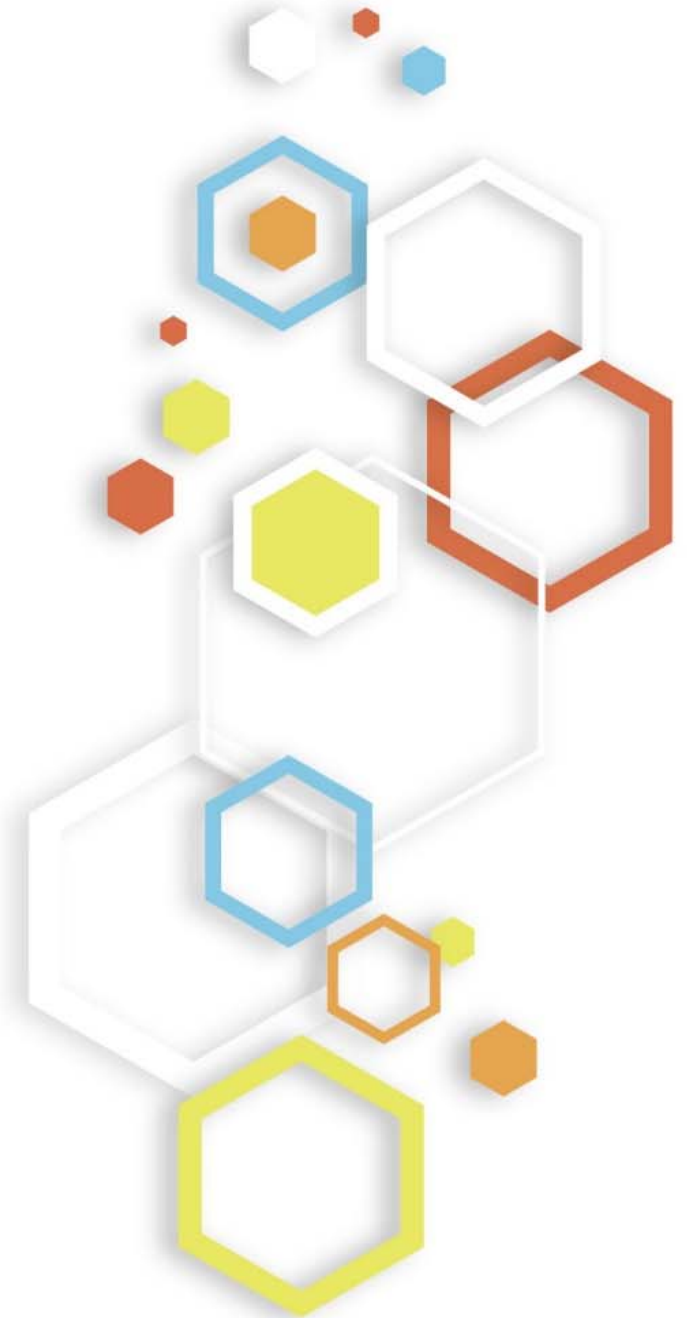


Post-Marketing Safety Monitoring of Self-Reported Symptom- Treatment-Outcome Measurement in Web-based Media Sources

Mark Wolff, Ph.D.
Principal Industry Consultant
Health & Life Sciences Global Practice
SAS Institute



SAS Analytics

Safety Analytics and Signal Detection



Pharmacological Mechanism-Based Safety Prediction - Data Mining Software

Acquisition and Support

Solicitation Number: FDA-SOL-12-1103215

Agency: Department of Health and Human Services

Office: Food and Drug Administration

Location: Office of Acquisitions and Grants Services

Downloaded from jama.bmj.com on August 16, 2012 - Published by group.bmj.com

Research and applications

Identifying primary and recurrent cancers using a SAS-based natural language processing algorithm

Justin A Strauss,¹ Chun R Chao,¹ Marilyn L Kwan,² Syed A Ahmed,³ Joanne E Schottinger,⁴ Virginia P Quinn¹

ABSTRACT

Objective Significant limitations exist in the timely and complete identification of primary and recurrent cancers for clinical and epidemiologic research. A SAS-based coding, extraction, and nomenclature tool (SCENT) was developed to address this problem.

Materials and methods SCENT employs hierarchical classification rules to identify and extract information from electronic pathology reports. Reports are analyzed and coded using a dictionary of clinical concepts and associated SNOMED codes. To assess the accuracy of SCENT, validation was conducted using manual review

To address ongoing needs for improved identification of cancer diagnoses, a SAS-based coding, extraction, and nomenclature tool (SCENT) was developed at Kaiser Permanente Southern California (KPSC). KPSC is an integrated healthcare organization that provides medical services to a diverse membership of more than 3.5 million people throughout Southern California. Research conducted at KPSC directly impacts practice guidelines and the medical care that patients receive. Each year, approximately 20,000 new cancer cases are diagnosed at KPSC. Given the

FDA Safety Workshop

Adverse Event Data Mining and Signal Detection

THE POWER TO KNOW.

RESEARCH ARTICLE

Predicting Adverse Drug Events Using Network Models

Aurel Cami,^{1,2*} Alana Arnold,¹ Shannon Manz,¹ Ben Reis^{1,2}

Early and accurate identification of adverse drug events (ADEs) is critically important for public health. We have developed a novel approach for predicting ADEs, called predictive pharmacology networks (PPNs). PPNs integrate the network structure formed by known drug-ADE relationships with information on specific drugs and adverse events to predict likely unknown ADEs. Rather than waiting for sufficient post-market evidence to accumulate for a given ADE, this predictive approach relies on leveraging existing, contextual drug safety information, thereby having the potential to identify certain ADEs earlier. We constructed a network representation of drug-ADE associations for 809 drugs and 852 ADEs on the basis of a snapshot of a widely used drug safety database from 2005 and supplemented these data with additional pharmacological information. We trained a logistic regression model to predict unknown drug-ADE associations that were not listed in the 2005 snapshot. We evaluated the model's performance by comparing these predictions with the new drug ADE associations that appeared in a 2010 snapshot of the same drug safety database. The proposed model achieved an AUROC (area under the receiver operating characteristic curve) statistic of 0.87, with a sensitivity of 0.42 given a specificity of 0.95. These findings suggest that predictive network methods can be useful for predicting unknown ADEs.



THE POWER TO KNOW.
Providing software solutions since 1976

INDUSTRIES / LIFE SCIENCES

- Products and Solutions
- Industries
- Careers
- Communications
- Education
- Finance Services
- Government
- Health Care Providers
- Health Insurance
- Insurance
- Life Sciences
- Manufacturing
- Media
- US & UK

Drug Safety

Comprehensively monitor the safety profile of your medications

Regulatory authorities, patients, health care professionals, government officials and the media are increasing their scrutiny of life sciences companies based on continuing, high-profile drug safety issues. Highly publicized safety concerns and market withdrawals of commonly prescribed medications have focused increased attention on the issue of drug safety. Early detection and evaluation of safety concerns reduce the potential impact of a major public relations and liability issue. All therapies carry some risks, but by identifying these risks as early as possible, life sciences companies have the best opportunity to develop and implement an appropriate course of action.

“Consumer are to improve the therapies are about a more analytically of therapy's cost profile.”

Reuter

THE POWER TO KNOW.

David Olajide, PhD
SAS Institute

THE POWER TO KNOW.

THE POWER TO KNOW.

THE POWER TO KNOW.

THE POWER TO KNOW.

THE POWER TO KNOW.

THE POWER TO KNOW.

THE POWER TO KNOW.

THE POWER TO KNOW.

THE POWER TO KNOW.

THE POWER TO KNOW.

THE POWER TO KNOW.

THE POWER TO KNOW.

THE POWER TO KNOW.

THE POWER TO KNOW.

THE POWER TO KNOW.

THE POWER TO KNOW.

THE POWER TO KNOW.

THE POWER TO KNOW.

THE POWER TO KNOW.

THE POWER TO KNOW.

THE POWER TO KNOW.

THE POWER TO KNOW.

EudraVigilance

Signal Detection of Adverse Medical Device Events in the FDA MAUDE Database

Eric Brinsfield, MS
Presenter & Research Collaborator

David Olajide, MSCE, PhD
Author & Primary Research Statistician

SAS Institute Inc.
Cary, NC

Novel Data-Mining Methodologies for Adverse Drug Event Discovery and Analysis

R Harpaz¹, W DuMouchel^{2,3}, NH Shah⁴, D Madigan^{3,5}, P Ryan^{3,6} and C Friedman¹

An important goal of the health system is to identify new adverse drug events (ADEs) in the post-market setting. Mining methods that can transform data into meaningful knowledge to inform patient safety have this purpose. New opportunities have emerged to harness data sources that have not been used in the past. This article provides an overview of recent methodological innovations and data sources for ADE discovery and analysis.

Signal Detection for Drug Safety - A Project for IMSM 2012

Mark Huff
SAS Institute, Inc.
Health and Life Sciences
100 SAS Campus Drive
Cary, NC

Chia Ying Lee
SAMS
10114 Alexander Drive
Research Triangle Park, NC

Project Description

In 2007 the U.S. Congress passed the Food and Drug Administration Amendments Act which mandated that the FDA develop an automated, electronic safety surveillance system as a means of improving the FDA's ability to protect the public in light of ever increasing drug and device safety concerns. In response to this mandate the FDA created the "Sentinel Initiative". This initiative is based on what the FDA refers to as the emergence of a "Science of Safety" integrating a profound understanding of disease with "new methods of signal detection, data mining, and analysis." The application of advanced and predictive analytics will be critical to the success of this initiative. "Signal Detection" or disproportionality analysis is an important methodology used to predict adverse events associated with specific therapies earlier and with a higher degree of confidence. Although multiple methods of signal detection are presently in use there is great interest on the part of the regulators, the health care community and industry to develop the next generation of signal detection tools. The objectives of the project will be to evaluate current approaches in signal detection tools and to explore and identify potentially novel or more powerful methods.



A Disproportionality Screening Method for Signal Generation with Application to Pooled Clinical Trials and FDA-AERS

David Olajide, PhD
SAS Institute



THE POWER TO KNOW.

Copyright © 2014 SAS Institute Inc. All rights reserved.

SAS® Forum
Switzerland 2014

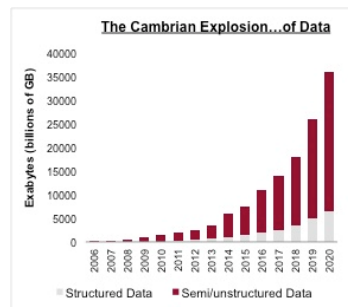
Trends

Unstructured Data and Text Analytics

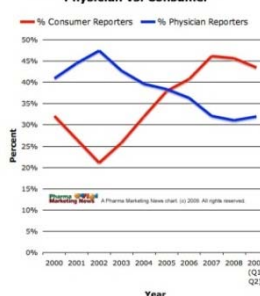
IN FOCUS

Social media gave early warning on Avandia

A NEW REPORT shows that social media gave an early warning on Avandia, a diabetes drug, before the FDA issued a warning. The report, from the Center for Drug Safety and Effectiveness Research, shows that social media was the first to report problems with the drug, which was later found to be linked to heart failure. The report also notes that social media was the first to report problems with the drug, which was later found to be linked to heart failure. The report also notes that social media was the first to report problems with the drug, which was later found to be linked to heart failure.



Percent AERs Where Reporter is Physician vs. Consumer



Pharmacovigilance and the Internet: A Call for Change Aims

The Association of the British Pharmaceutical Industry (ABPI) JUNE 2011

Social Media and Postmarketing Drug Safety

Elizabeth E. Garrard, PharmD, RPh 2012

Design and validation of an automated method to detect known adverse drug reactions in MEDLINE: a contribution from the EU-ADR project.

J Am Med Inform Assoc. NOV 2012

Pharma Challenges: Adverse Event Reporting and Social Media

Stuart L. Friedel and Joseph A. Sena Jr., Davis & Gilbert LLP 2012

The National Science Foundation awards grant University of Virginia to analyze social media and to identify adverse drug reactions

September 2012

Social Media and Postmarketing Drug Safety

The online phenomenon of social media has the potential to advance health literacy, safety, and transparency in the pharmaceutical industry, although potential pitfalls and liabilities have inhibited the industry's participation. In spite of these challenges and fears, the time to join the conversation is now.

Obstacles and Industry Reluctance
Biopharmaceutical manufacturers have been slow to engage with social media, and it is not difficult to understand why. The confines of the old "Web 1.0" world were actually quite well suited to pharma's established communication practices.



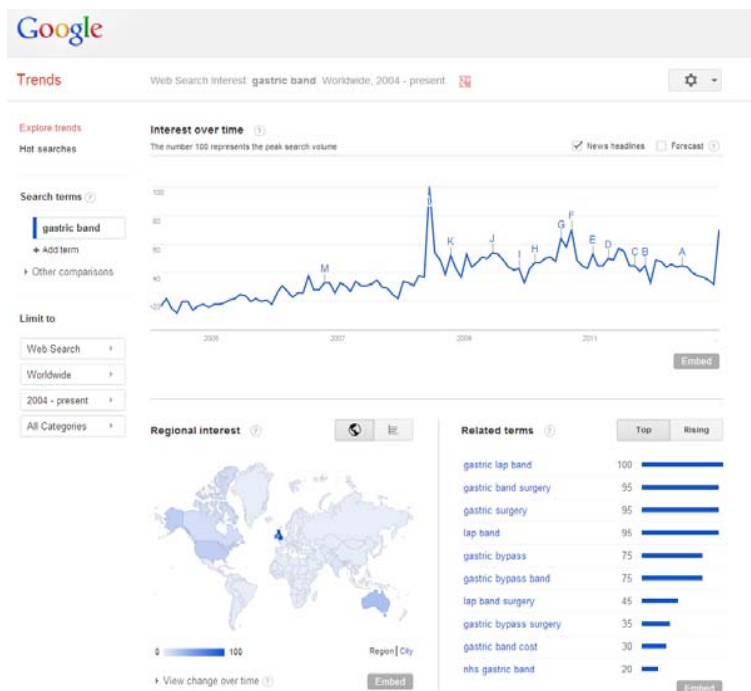
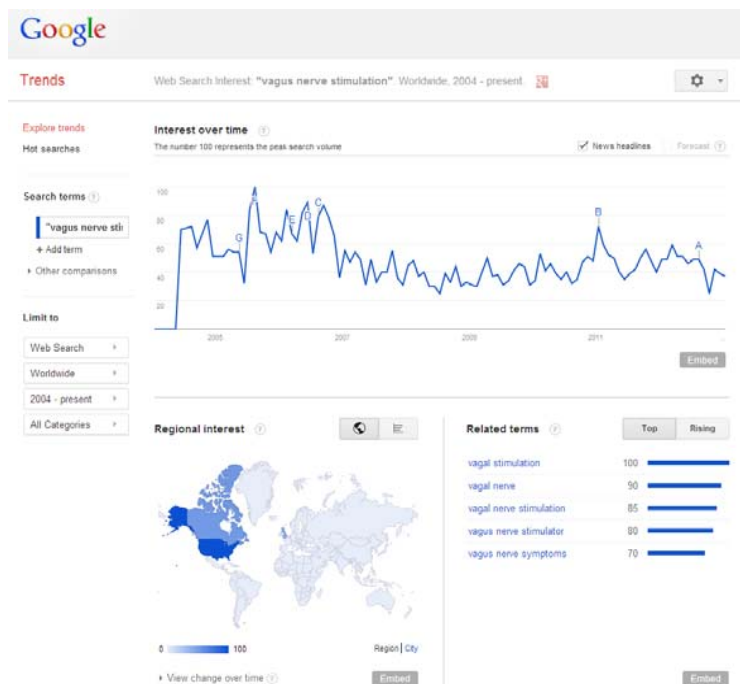
THE POWER TO KNOW.

Copyright © 2014 SAS Institute Inc. All rights reserved.

SAS® Forum Switzerland 2014

Google Trend

This is NOT what SAS is Doing



Draft Guidance

Post marketing Safety Reporting for Human Drug and Biological Products Including Vaccines

FDA's March 2001 draft guidance for industry entitled Post marketing Safety Reporting for Human Drug and Biological Products Including Vaccines

- *Adverse experience information that is submitted via the Internet to an entity with post marketing reporting obligations under 310.305, 314.80, and 600.80 should be reported to FDA if there is knowledge of the four basic elements for submission of an individual case safety report, namely:*

An identifiable patient

An identifiable reporter

A suspect drug or biological product

An adverse experience or fatal outcome suspected to be due to the suspect drug or biological product

- Draft guidance states that those entities should review any Internet sites *sponsored by them* for **adverse experience information**, but are **not responsible for reviewing any Internet sites that they do not sponsor; however, if they become aware of an adverse experience on an Internet site that they do not sponsor, they should review the adverse experience and determine if it should be reported to FDA.**



United States Food and Drug Administration

Project Description

FDA is responsible for communicating about the risks and benefits inherent in all the products it regulates.

- The rise of social media on the Internet, including especially user-generated content such as blogs, forums, message boards, wikis and podcasts, has created new opportunities to interface with the public with respect to emerging hazard situations involving FDA-regulated products.
- The increasing presence of social media promises new capabilities to monitor the effectiveness of FDA's ongoing risk communication efforts. FDA is in need of both historical and "real-time" monitoring and analyses of a representative sample of social media web sites.

The objective of this requirement is to provide FDA with the resources needed to use social media to inform and evaluate FDA risk communications. Specifically, the objective is to provide FDA with:

- Analyses of social media that provide baselines on consumer sentiment prior to FDA communication and that depict changes in social media buzz following FDA communications
- In-house capability for social media monitoring; and surveillance through social media listening for early detection of adverse events and food-borne illness.
- The scope of work includes social media buzz reports, a social media dashboard, and quarterly surveillance reports related to specific product classes.



Objective

SAS Text Analytics and Device Safety Monitoring

Preform automated text analysis of publicly available Social Media and Unstructured Data sources from the web Related to the “Vagus Nerve Stimulator” and “Essure” device.

Collect, Processes and Analyze text/unstructured data/documents

- Identify documents that;
 - Refer specifically to the device of interest device
 - Contain terms identified as “Adverse Events” (AE)
 - AE terms consistent with the product label
 - AE terms not on the product label
 - Terms that identify other drugs, substances or devices
 - Cross reference results with PubMed and MAUDE
 - Perform document author “Veracity/Integrity analysis

Establish a BASELINE of web based information, cross-referenced by scientific literature and safety databases
In order to develop an enhanced device safety monitoring program.



Recently Published Research

Drug Safety

Digital Drug Safety Surveillance: Monitoring Pharmaceutical Products in Twitter

Published online: 29 April 2014



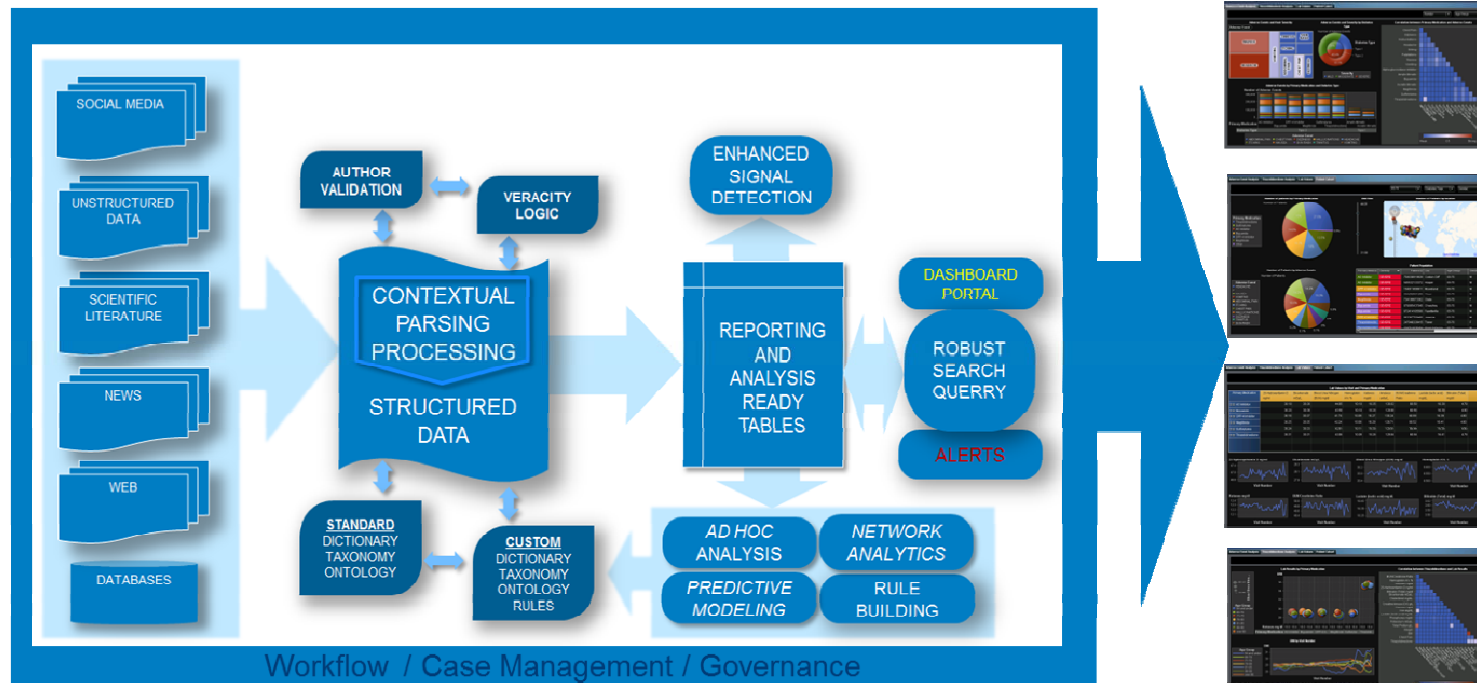
"The resulting dataset contained a high volume of irrelevant information, but provided a useful starting point."

"We did not seek to verify each individual report as truthful, but rather to identify overall associations between Twitter and official spontaneous report data as a preliminary proof of concept."



Safety Analytics

Contextual Parsing



SAS

Analytic Approach to Veracity and Data Integrity

RULES

Known Patterns events
Rules and thresholds based on known behaviors
 Biological/Clinical Plausibility
 Product label
 IP Address/URL
 Author ID

ANOMALY DETECTION

Unknown Patterns and Behaviors
Algorithms used to unusual patterns
 Multivariate outlier/inlier detection
 Constant findings
 Clustering/association analysis
 Distribution analysis

PREDICTIVE MODELS

Complex Patterns
Identify patterns which describe inaccurate information
 Apply unsupervised/supervised learning techniques
 Like patterns of comments and content
 Author verification
 Higher level concept disambiguation

NETWORK ANALYTICS

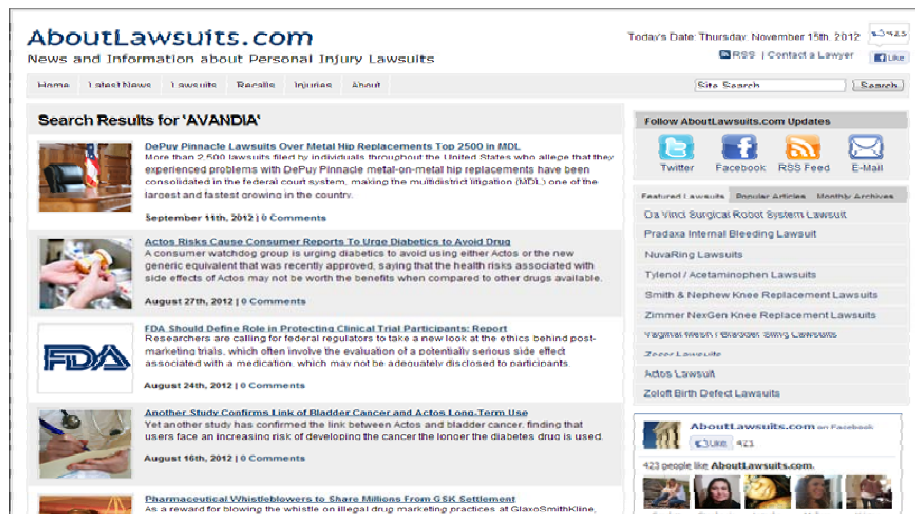
Associative Linking
Discovery through automated link analysis
 Collusive networks
 Understand complex multivariate relationships over time
 Use vectors and momentum of events/behavior as predictor
 Link authors to malicious content

Proactively apply combinations of all approaches at entity and network levels



Case Study

Avandia



My mother had a heart attack in 2008 she had been on avandia for about 2 or 3 years and was still on it when she had her heart attack it was not until after she had her heart attack that the doctor took her off of avandia. She had never had heart problems before she was put on Avandia. After her heart attack her heart was so weak the doctor's thought they were going to have to put a defibrillator in her chest because Avandia has weakened her heart and she has suffered numerous bouts of congestive heart failure. She is 74 now and to think she went all her life not having heart problems and now because of avandia she has to suffer in her old age going back and forth to doctors and not knowing if she will wake up in the mornings. I to suffer and worry about my mother everyday I am afraid I will lose her to another heart attack. I just wish this drug had never existed.

After having a heart attack at 46 years of age had stints put in 5 1/2 years ago when I got out of the hospital my primary doctor put me on pill called avandia every 6 months I would get my blood work done and it was always the same high cholesterol and other things I always felt weird I exercise ate wright but I never felt good no energy short of breath so after 5/12 years of taking avandia my doctor told me to stop taking avandia I felt good again then I had another heart attack because of taking avandia I now have permanent heart heart damage I wish my doctor would have listen to me for all those times I complained now I will suffer for the rest of my life not knowing how long I have to live

<http://www.aboutlawsuits.com/avandia-lawsuit-settlement-reached-in-cases-10153>

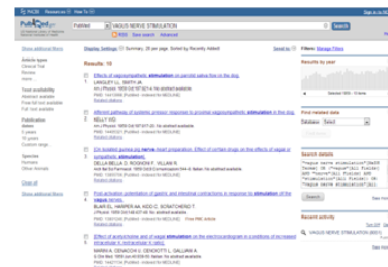


DATA

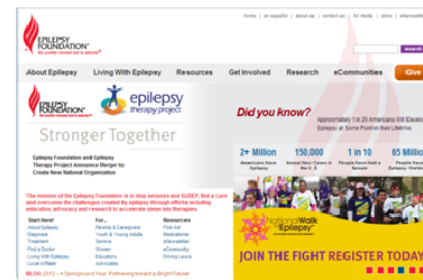
On Line Data Sources



Healthyplace.com



ncbi.nlm.nih.gov/pubmed/



Epilepsyfoundation.org



Epilepsy.com



http://www.accessdata.fda.gov



Vnsmessaggeboard.com

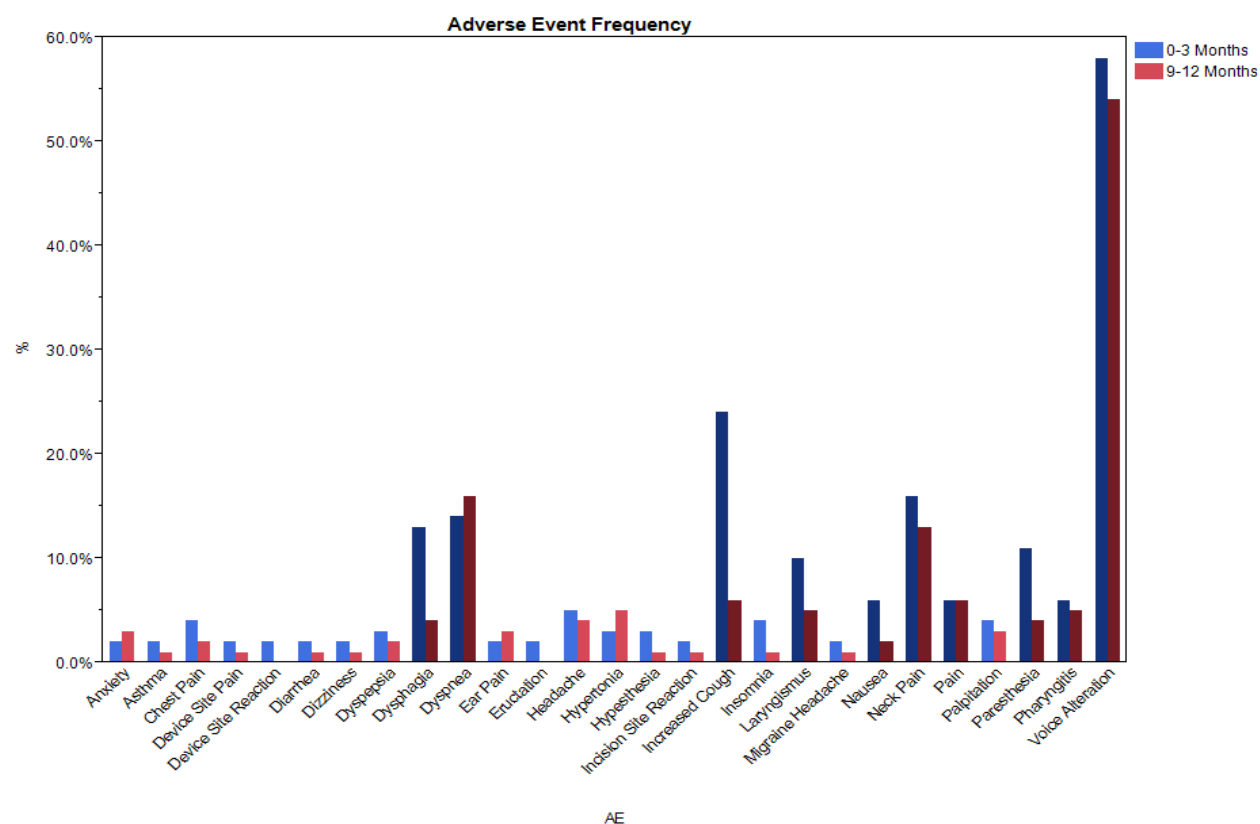


VNS Device

Label Data



AE	0-3 Months	9-12 Months
Voice Alteration	58%	54%
Increased Cough	24%	6%
Neck Pain	16%	13%
Dyspnea	14%	16%
Dysphagia	13%	4%
Paresthesia	11%	4%
Laryngismus	10%	5%
Nausea	6%	2%
Pain	6%	6%
Pharyngitis	6%	5%
Headache	5%	4%
Chest Pain	4%	2%
Insomnia	4%	1%
Palpitation	4%	3%
Dyspepsia	3%	2%
Hypertonia	3%	5%
Hypesthesia	3%	1%
Device Site Reaction	2%	0%
Dizziness	2%	1%
Anxiety	2%	3%
Asthma	2%	1%
Device Site Pain	2%	1%
Diarrhea	2%	1%
Ear Pain	2%	3%
Eructation	2%	0%
Incision Site Reaction	2%	1%
Migraine Headache	2%	1%



Content Categorization

Categories (from MeSH Taxonomy)

All MeSH Categories

Analytical, Diagnostic and Therapeutic Techniques and Equipment Category

Therapeutics

Electric Stimulation Therapy

Vagus Nerve Stimulation

All MeSH Categories

Analytical, Diagnostic and Therapeutic Techniques and Equipment Category

Therapeutics

Physical Therapy Modalities

Electric Stimulation Therapy

Vagus Nerve Stimulation

I have been dealing with epilepsy for years now, many of which have included uncontrollable seizures and have been accompanied by symptoms including impaired vision, dizziness, and difficulty breathing. Since I have started using the **vagal nerve stimulator**, I have found these symptoms to have subsided. Though I have since experienced minor palpitations, such occurrences have been rare. I believe the worst is over. Based upon my experiences with the **VNS** device, I would recommend it to others as a possible solution.



SAS

Entity Extraction

DISEASE = epilepsy

SYMPTOM = impaired vision;
dizziness; difficulty breathing

DEVICE = vagal nerve
stimulator

SIDE-EFFECT = palpitations;
difficulty sleeping

I have been dealing with **epilepsy** for years now, many of which have included uncontrollable seizures and have been accompanied by symptoms including **impaired vision**, **dizziness**, and **difficulty breathing**. Since I have started using the **vagal nerve stimulator**, I have found these symptoms to have subsided. Though I have since experienced minor **palpitations**, such occurrences have been rare. I believe the worst is over. Based upon my experiences with the **VNS** device, I would recommend it to others as a possible solution.



SAS

Sentiment Analysis

NEGATIVE (impaired)

NEGATIVE (difficulty)

NEUTRAL (the worst is over)

POSITIVE (I would recommend)

POSITIVE (a possible solution)

I have been dealing with epilepsy for years now, many of which have included uncontrollable seizures and have been accompanied by symptoms including *impaired* vision, dizziness, and *difficulty* breathing. Since I have started using the vagal nerve stimulator, I have found these symptoms to have subsided. Though I have since experienced minor palpitations, such occurrences have been rare. I believe *the worst is over*. Based upon my experiences with the VNS device, *I would recommend* it to others as *a possible solution*.



Corpus

Web Site Data

SOURCE	#
epilepsy	5,353
epilepsyfoundation	8,653
healthyplace	13,115
healthyplace	11,272
pubmed/medline	2,180
MAUDE	17,152
TOTAL	57,726

- **24,998 DOCUMENTS WERE PROCESSED**
- **4243 AUTHORS**
- **SEVEN YEAR SPAN**
- **FOUR WEBSITES**
- **15,621 AE IDENTIFIED (AS PER VNS LABEL AES)**

Documents were selected when "Vagal Nerve Stimulation" or ESSURE or an appropriate a synonym was present

Expanded stemming of key terms and synonyms as well as custom mapping can be preformed

- Results include any of the PTs that exist in the MeSH 2013 release
- Only PTs that occurred 1 or more times have been included
- PTs are not limited to VNS professional drug label
- The results due not discriminate between a disease versus an adverse event, cause, symptom, etc.



VNS

Author Validation

Documents	27178
Authors	4243
No Author	1722
No Date	151
Date Range	2004 to 2012

dennis100	5971	22%
Birdbomb	942	3.5%
Holly Gray	537	2.0%
Dispatch	494	
labrat	305	

290 authors	>10
103 authors	>25
32 authors	>50
11 authors	>100

82 authors posted in 2 sources
2 authors posted in 3 sources
No one posted in all 4

Author Dennis100

This directory is	: Negative
Number of articles	: 6922
Number of positive articles	: 103
Number of negative articles	: 6590
Number of neutral articles	: 116
Positive percent	: 1.49%



SAS IP

Draft US Patent Applications

Semantic Field Normalization/Contextualization for Self-Reported Symptom-Treatment-Outcome Measurement in Web-based Media Sources

Barry deVille, Mark Wolff, *Michael Wallis*,

Adaptation of “Semantic Nets” to Establish Veracity of Symptom-Treatment Outcome Reports in Health Related Web Interactions

Barry deVille, Mark Wolff, *Michael Wallis*, *James Cox*, *Zheng Zhao*



SAS® Forum Switzerland 2014

make connections • share ideas • be inspired

Mark Wolff, Ph.D.

Principal Industry Consultant

Health & Life Sciences Global Practice

SAS Institute

(919) 280-3872

mark.wolff@sas.com



Copyright © 2014, SAS Institute Inc. All rights reserved.

