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

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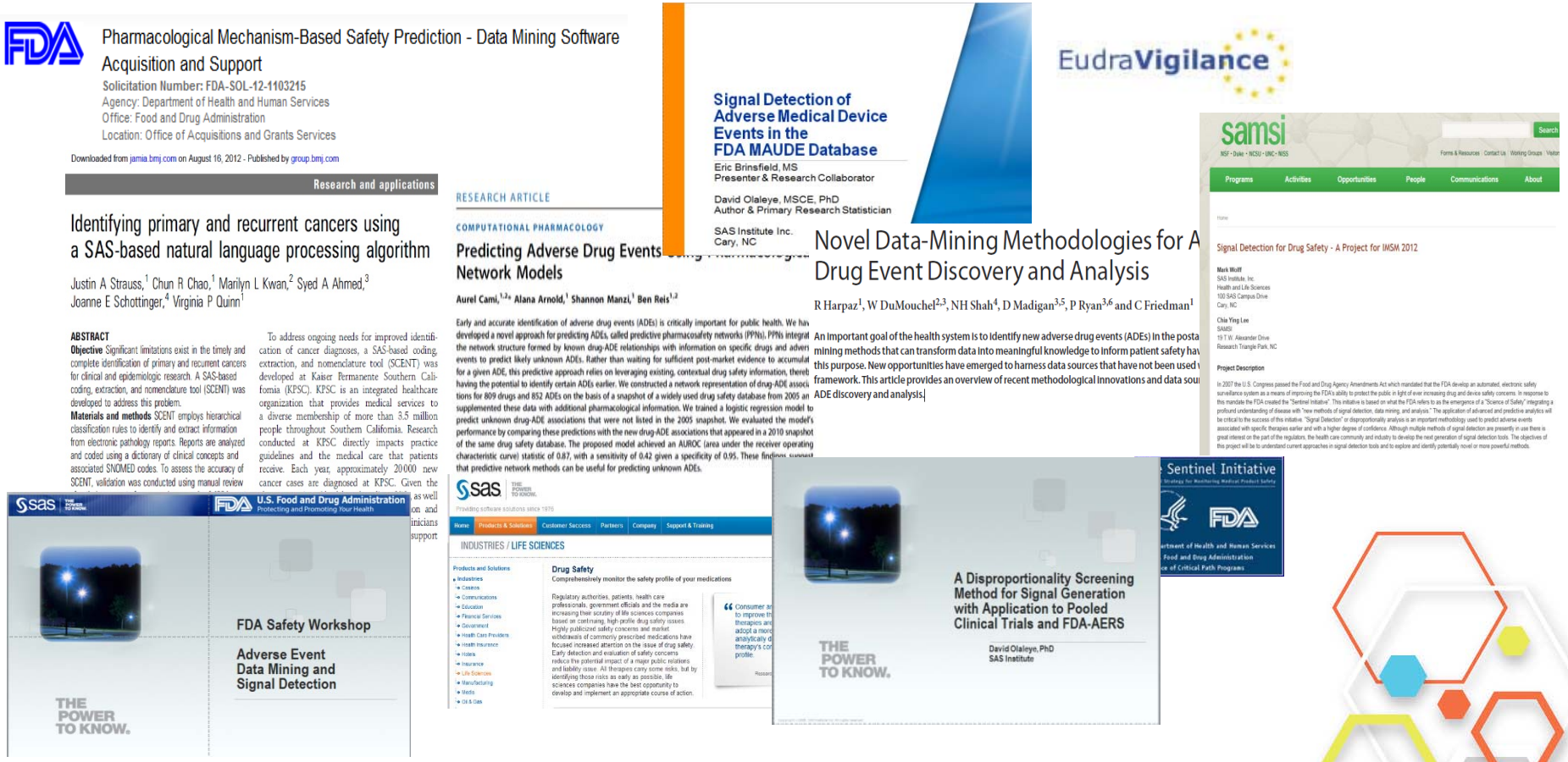
SAS Institute

sas THE POWER TO KNOW.

SAS Analytics

Safety Analytics and Signal Detection

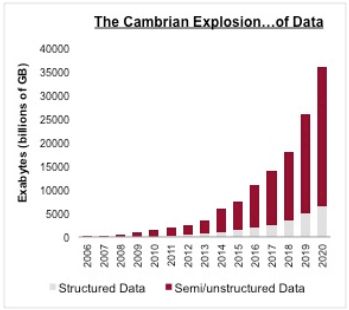


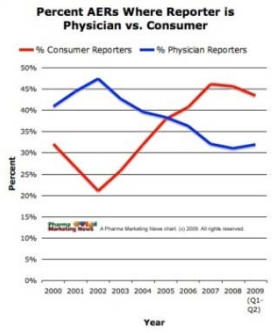
Trends

Unstructured Data and Text Analytics


IN FOCUS

Social media gave early warning on Avandia






Social Media and Postmarketing Drug Safety

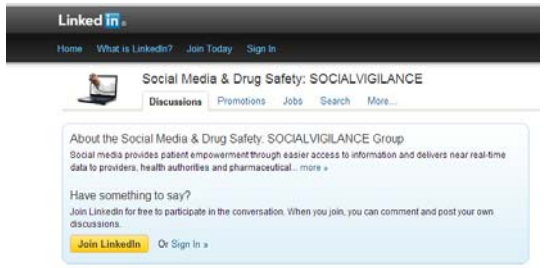
This article explores the use of social media by the pharmaceutical industry and examines how this technology can promote drug safety transparency and health literacy.

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.

In the first generation of the World Wide Web, the vast majority of websites were noninteractive environments in which users were limited to the passive viewing of information provided to them. The advent of Web 2.0 brought about the modern norm of sites allowing users to interact with other users and contribute openly to site content. All the buzz today surrounds social media, which refers to online forums and technologies that let users share opinions, insights, and experiences, create their own content and media, and have conversations about topics of common interest.

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 communications practices.



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

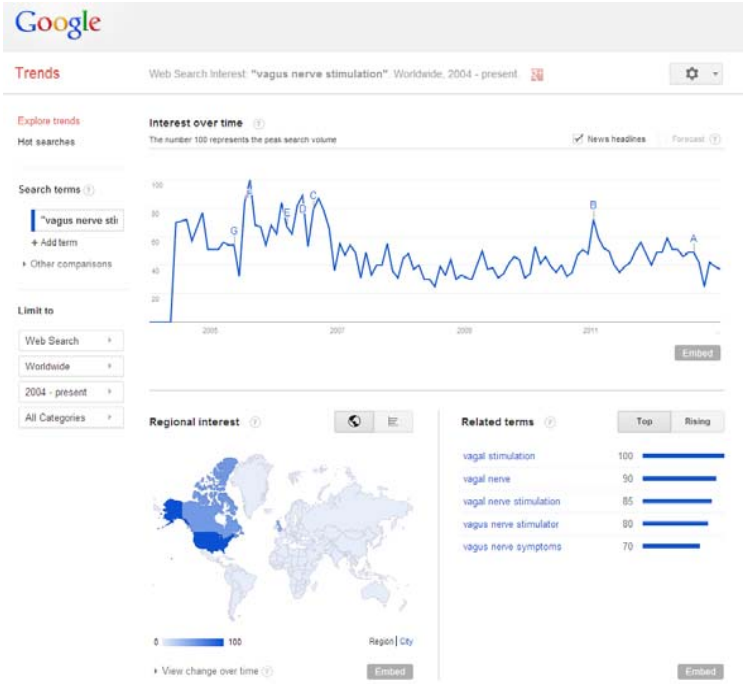
Design and validation of an automated method to detect known adverse drug reactions in MEDLINE: a contribution from the EU-ADR project.
J Am Med Inform Assoc. NOV 2012

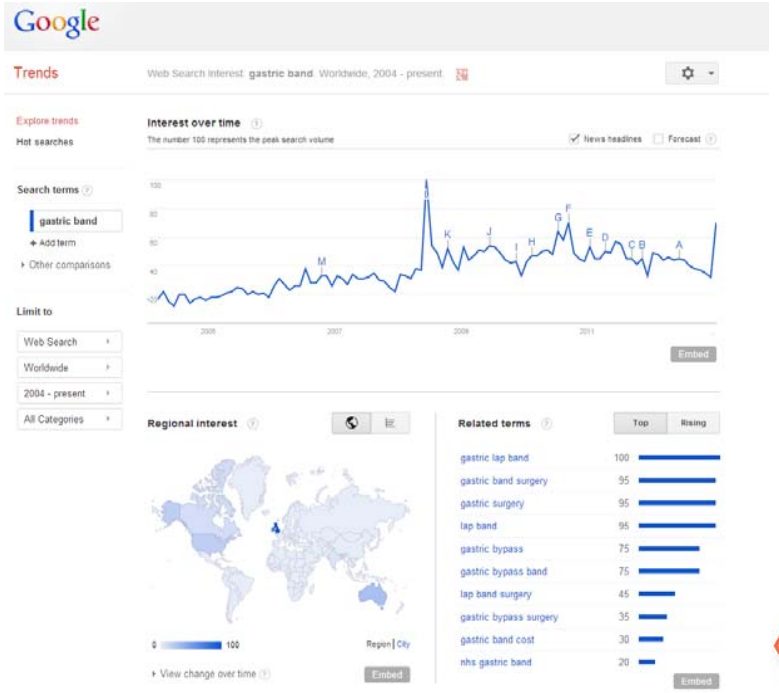
Pharma Challenges: Adverse Event Reporting and Social Media
Stuart L. Friedel and Joseph A. Sena Jr., Davis & Gilbert LLP
2012

The National Science Foundation awards grant University of Virginia to analyze social media and to identify adverse drug reactions
September 2012

Google Trend

This is NOT what SAS is Doing





Draft Guidence

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

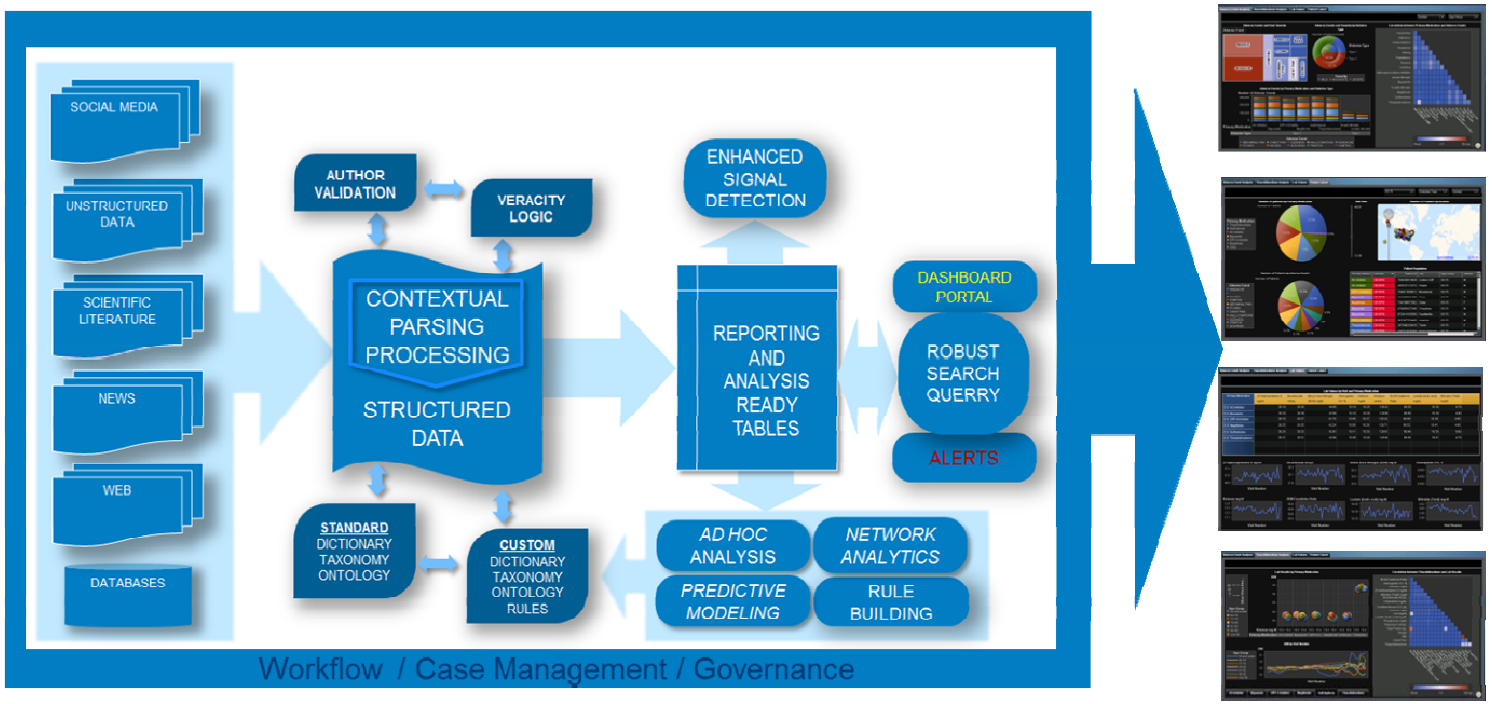
Published online: 29 April 2014

"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



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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

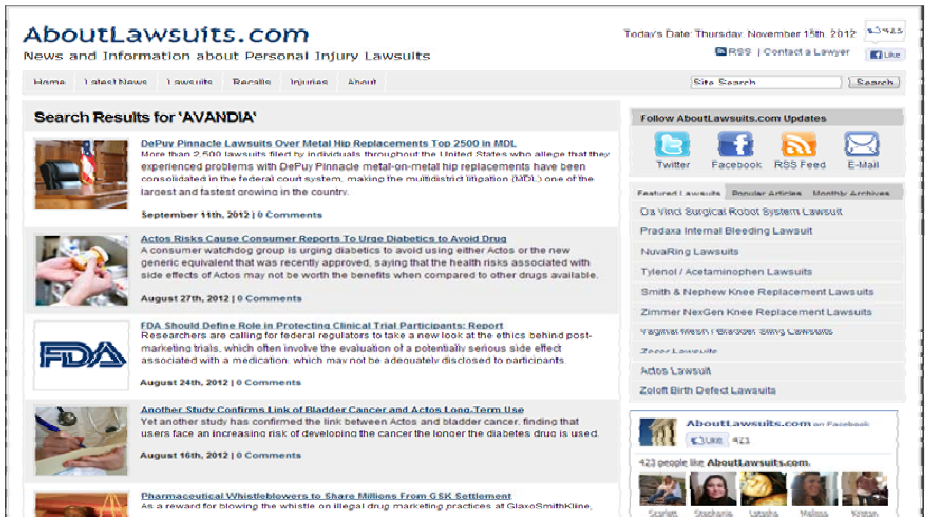
PREDICTIVE MODELS
Complex Patterns
Identify patterns which describe inaccurate information
- Apply unsupervised/supervised learning techniques
- Like patterns of comments and content
- Author verification
- Higher level concept disambiguation

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 defibulator in her chest because Avandia has weakend her heart and she has suffered numerous bouts of conjestive 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 attact 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 pll called avandia every 6 months I would get my blood work done and it was always the same high colestro and other things I always felt wierd I exersize ate wright but I never felt good no energy short of breath so after 5/12 years of takeing avandia my doctor told me to stop takeing avandia I felt good again then I had another heart attact becouse of takeing 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

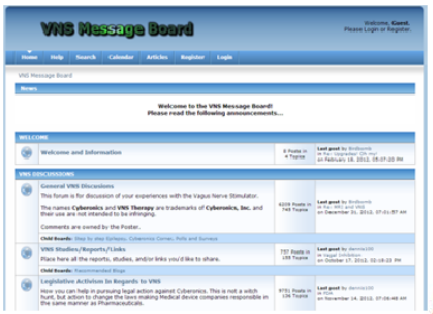
Healthyplace.com

ncbi.nlm.nih.gov/pubmed/

Epilepsyfoundatio.org

Epilepsy.com

http://www.accessdata.fda.gov

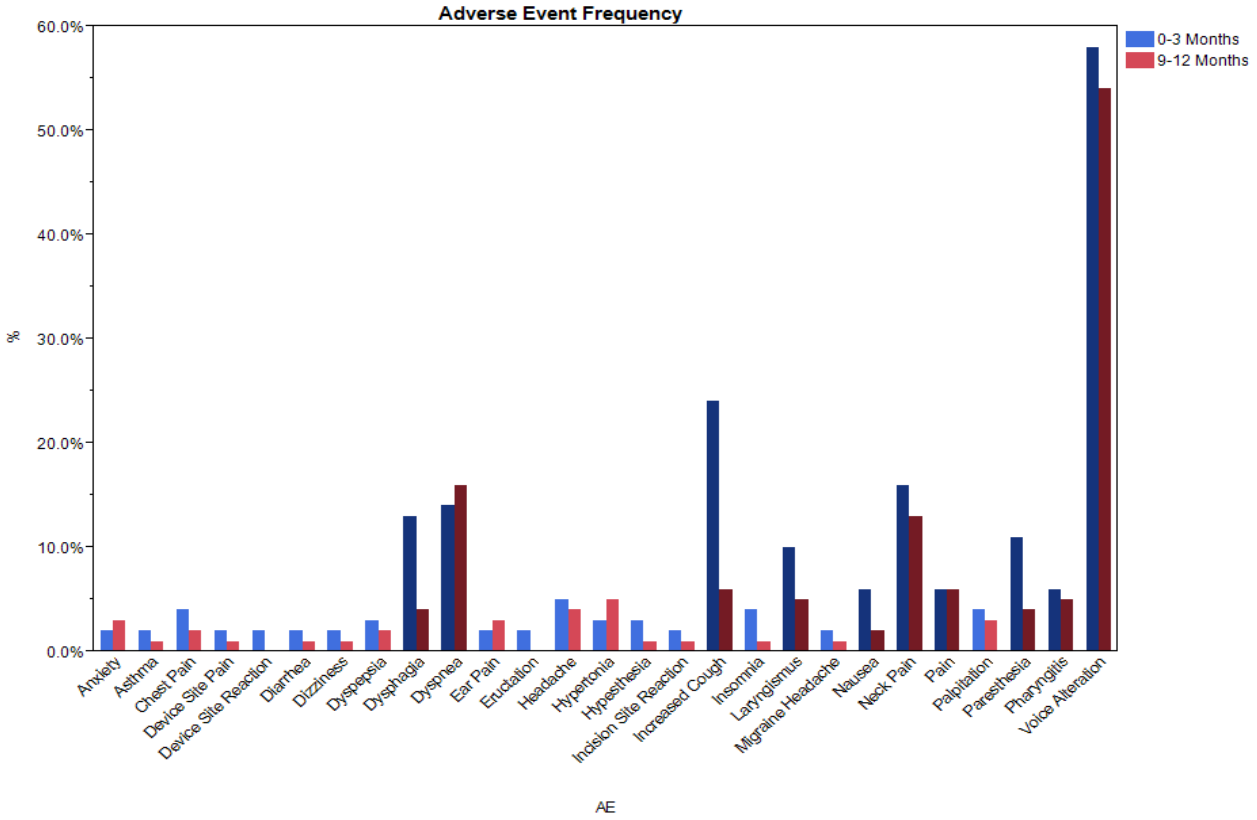


Vnsmessageboard.com

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.

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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.

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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

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

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

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*

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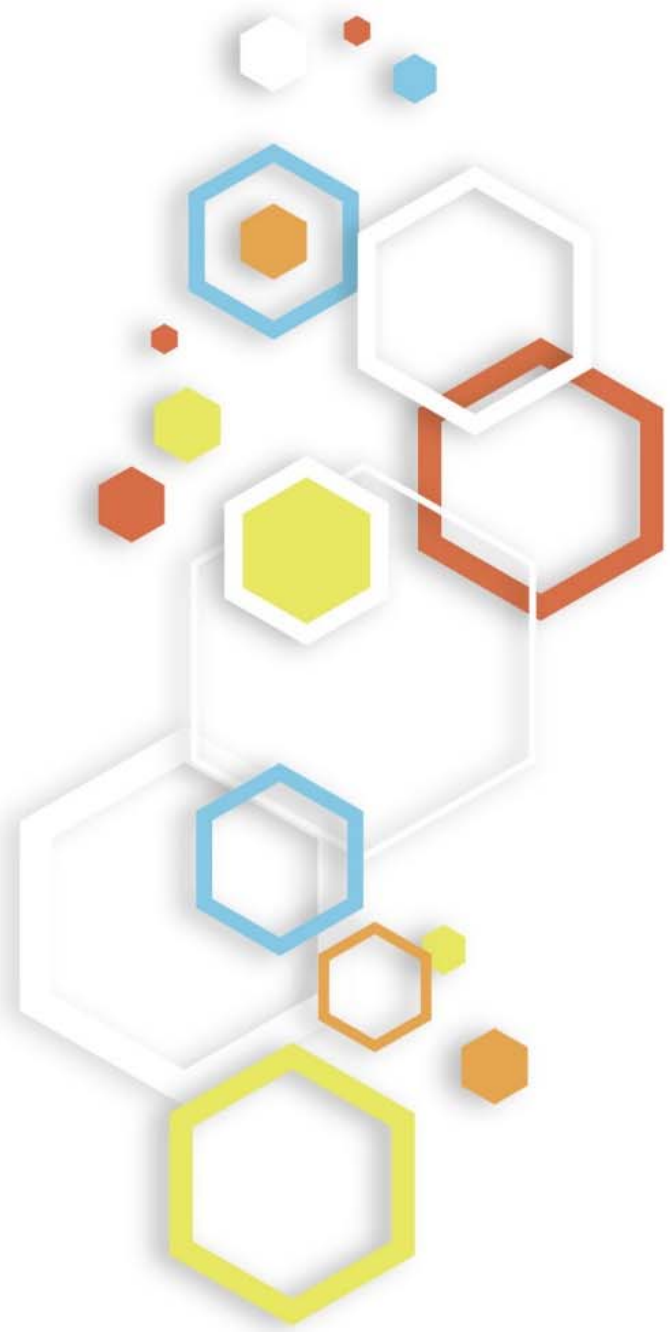

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