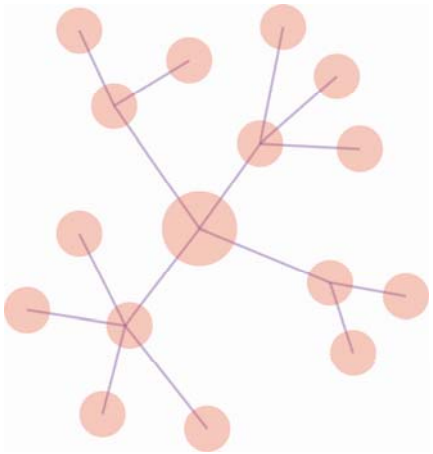
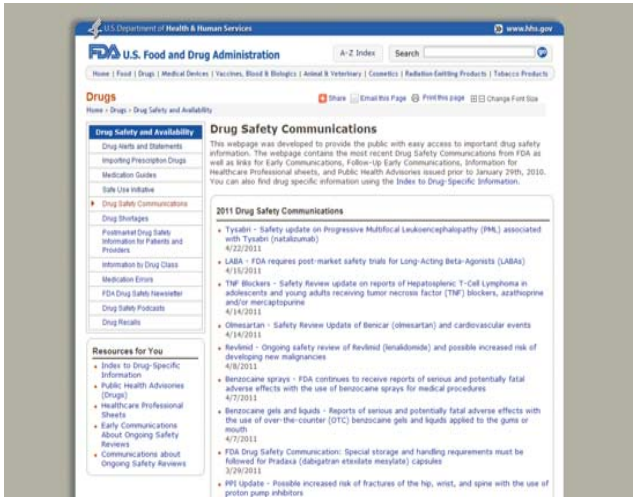


Evaluating Drug Safety Communication Effectiveness

Gregory D. Busse, Ph.D.
Office of Communications
CDER
U.S. FDA

Drug Safety Communications (DSCs)

- Post-market risk communication
  - Potential or actual change to benefit/risk profile of a drug
- Posted on FDA website
  - MedWatch
  - Press Release
  - Podcast



Communication Effectiveness

- Palatability
  - Content
  - Format
  - Accessibility
- Impact
  - Behavior change

Communication Effectiveness

- Multifaceted Construct
- Orientation Specific
  - Social Science
  - Marketing

Marketing Perspective

- Exposure
  - Branding
- Channels
  - What are people reading/watching?
  - How are they getting their information?
    - Twitter
    - Facebook
    - Blogs
    - Instant messaging
    - Emails (friends and family)
- There are open, public discussions in the digital universe about drug safety

Health Information Seeking

- 1/3 of adults in the U.S. currently go online for information on prescription or over-the-counter drugs
  - Pew Internet & American Life Project (2009)

- 41% of people use social media as a healthcare resource
  - National Research Corporation survey of ~23,000 U.S. Residents (Dayton Business Journal, 3/21/11)

twitter Search Have an account? Sign in

FDA_D

Conta

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301.796.34

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Receive the latest drug information from the U.S. Food and Drug Administration. Contact us at 1.888.463.6332 or druginfo@fda.hhs.gov

http://www.fda.gov/Drugs/ResourcesForYou/Consumers/default.htm

Follow

Text follow FDA_Drug_Info to 40404 in the United States

Timeline Favorites Following Followers Lists

FDA_Drug_Info FDA Drug Information
FDA approves Rituxan to treat Wegener's granulomatosis and microscopic polyangiitis. http://1.usa.gov/RituxT
15 hours ago

FDA_Drug_Info FDA Drug Information
As part of the President's Prescription Drug Abuse Action Plan, FDA announces REMS for ER & LA Opiods. http://1.usa.gov/OpREMST
19 Apr

FDA_Drug_Info FDA Drug Information
Drug Safety Podcast: HSTCL reports in patients taking TNF blockers, azothioprine and/or mercaptopurine. http://1.usa.gov/tnfPC
18 Apr

FDA_Drug_Info FDA Drug Information
FDA approves Actemra to treat rare form of juvenile arthritis. http://1.usa.gov/Actemra1
15 Apr

FDA_Drug_Info FDA Drug Information
FDA Drug Safety Communication: FDA requires post-market safety trials for Long-Acting Beta-Agonists (LABAs). http://1.usa.gov/LABAs1
15 Apr

FDA_Drug_Info FDA Drug Information
Communication on lansoprazole delayed-release orally

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About @FDA_Drug_Info

397	11	23,651	1,392
Tweets	Following	Followers	Listed

Following 11

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Done

socialmention*

Blogs Microblogs Bookmarks Comments Events Images News Video Audio Q&A Networks All

TNF Blockers | Search | Advanced Search Preferences

2% strength	1:1 sentiment
29% passion	26% reach

1 hours avg. per mention

last mention 2 hours ago

156 unique authors

17 retweets

Sentiment

positive	14
neutral	225
negative	17

Top Keywords

blockers	213
cancer	109
drugs	81
risk	72
children	69
arthritis	66
reports	50
drug	47
lymphoma	47
patients	46

Top Users

admin	13
mcgeneral	11
fuiszreport	10
luxurygiftsuk	5
LawsuitGuru	4
sweatyblues	3

Mentions about TNF Blockers

Sort By: Date Results: Anytime

Results 1 - 15 of 256 mentions.

Untitled Document

MedscapeRheum: FDA Warns Again of Lymphoma Risk With TNF Blockers in Teens http://bit.ly/fbcwdt

www.facebook.com/profile.php?id=100001577310972&v=wall&story_fbid=156400681089534

2 hours ago - by Mohamed Nabil Salem on facebook

Tumor necrosis factor blocker or inhibitor drugs causes Lymphoma ...

The agency noted, "Although most reported cases of HTSCL occurred in patients treated with a comnination of medicines known to suppress the immune system, includin...

www.greenliveforever.com/healthy-news/journal/tumor-necrosis-factor-blocker-inhibitor-drugs-lymphoma

4 hours ago - by GreenLiveForever.com on google_blog

Serious Fungal Infections with Simponi (golimumab ...

FDA is reminding healthcare professionals about the risk of serious fungal infections with TNF blockers, including Simponi.

arthritisremedy.biz/2011/04/20/serious-fungal-infections-with-simponi-golimumab/

5 hours ago - by ray on google_blog

Experiencing Pain In The Joints Of The Spine? | Ankylosis ...

The three major types of medications include anti-inflammatory drugs such as NSAIDS and COX-2 inhibitors, DMARDS and TNF? blockers (antagonists). In some cases, walk...

www.ankylosisspondylitis.net/experiencing-pain-in-the-joints-of-the-spine-2.html

6 hours ago - by arnasati on google_blog

Arthritis Medications: Different Strokes For Different People

When a person suffers from such a form of arthritis, their immune system generally goes out of whack, and thus TNF blockers may have to be used along with immunosupp...

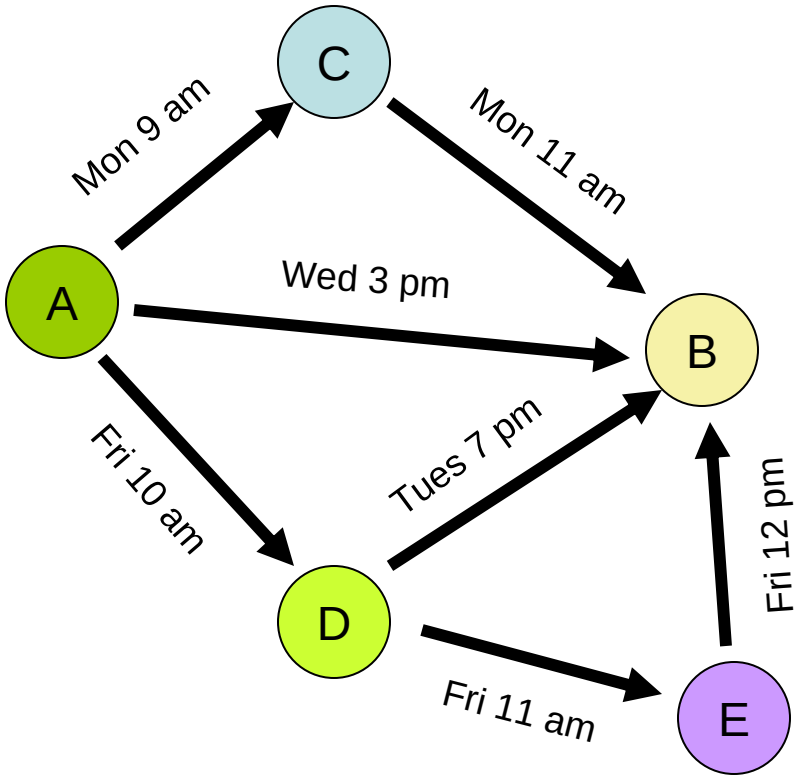
puttingstroke.jestergolf.com/2011/04/20/arthritis-medications-different-strokes-for-different-people/

9 hours ago - by admin on google_blog

CEA-Leti to Implement Multiple EV Group Systems - gooブログはじめ ...

The New Digital Age

- Information Flow
  - Public dialogue flows across time and space
    - A message is born
    - Travels to the next person
    - Forms a network
    - Direct and indirect communication



Adapted from Kossinets et al., 2008

The New Digital Age

- Contagiousness
  - Properties inherent to the message
    - Long, uninteresting, irrelevant
    - Creative and insightful
  - Properties inherent to the source
    - Authoritative and trustworthy
    - Controversial
  - Properties inherent to the receiver
    - Busy or stressed
    - Sick or in fear?
  - Opportunity for engagement
    - Talking with someone, as opposed to talking at someone

Dynamics of Information Flow

- Iribarren and Moro, 2009
  - Information flow is a product of a basic reproductive function (R_0)
  - R_0 = the average number of secondary cases generated by each informed individual
    - $R_0 < 1$ = propagation dies quickly
    - $R_0 > 1$ = propagation continues

The New Digital Age

- “Influencers” or “Connectors” of Conversation
  - Have great sway over or provide an abundance information to large groups of people
    - CNN
    - Blogs
    - You?

- Increase the likelihood that a message will be adopted/passed on

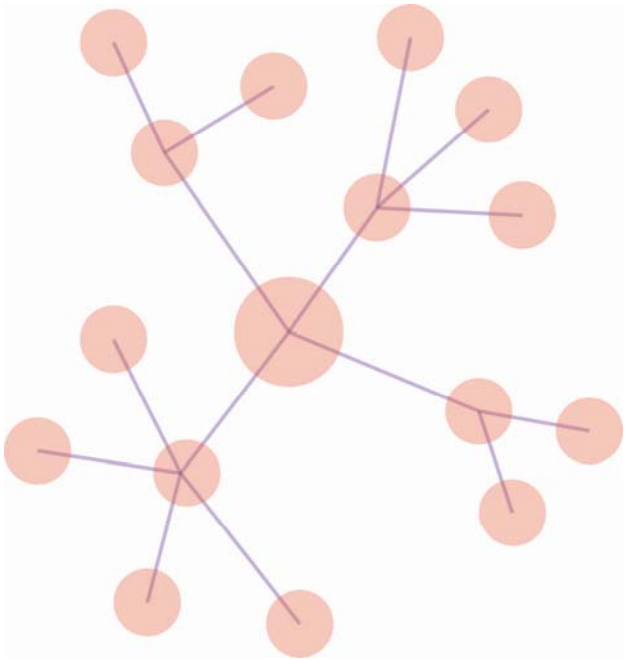
Twitter Influence

- Cha et al., 2010
- Evaluated influence (getting someone to do something) in Twitter
  - 2 billion follower links among 54 million users
  - Indegree (number of followers)
    - Popularity
  - ReTweets
    - Content value
  - Mentions
    - Name value of a user

- ReTweets and Mentions more indicative of influence than indegree
  - Million follower fallacy

Information Flow

- Why it’s important
  - Who is our audience?
    - Small
      - Select patient group
    - Broad
      - The U.S. Public



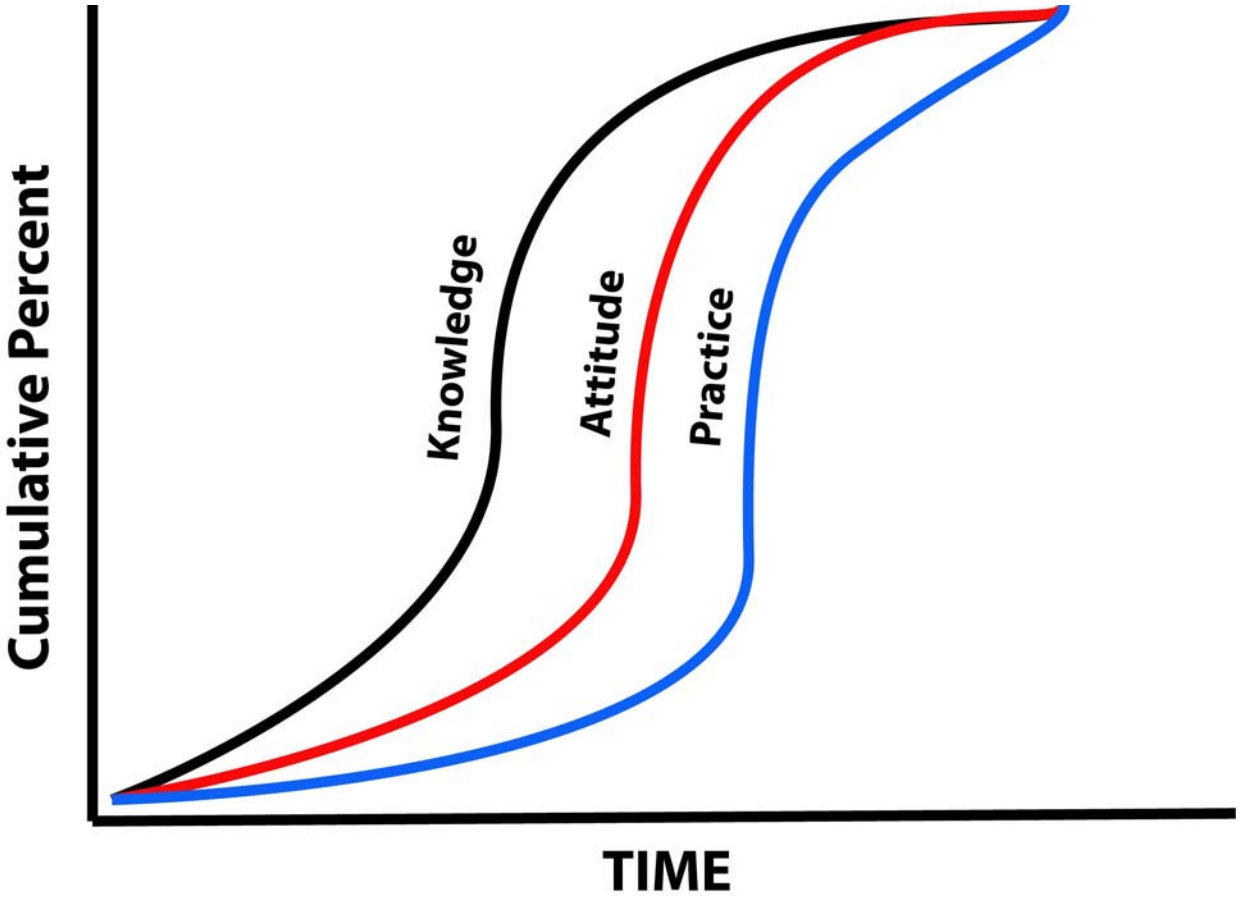
Information Flow

- Accuracy
  - Work hard on getting the message just right
    - As a message moves, there may be message drift
    - Telephone game

Information Flow

- Behavior Change
  - Many messages carry actions that should occur in response to the message
    - Belief perseverance
      - Heuristic or algorithm highly accessible in memory
      - Hard to change, but can the more a message gets repeated

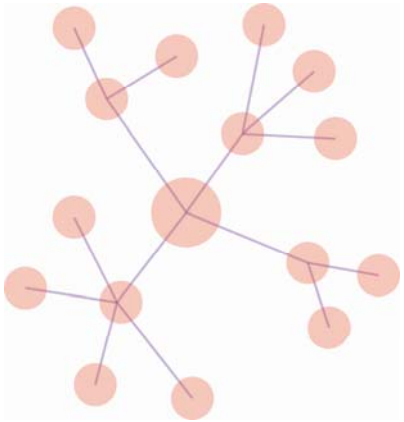
Diffusion of INNOVATION



Adopted from Valente and Fosados, 2006

Broad Goals of this Research

- Measure
  - Message diffusion, dissemination, and duration
  - Message integrity
  - Market penetration



- Build a predictive model
  - Factors that affect the 3D's
    - Cardiac Issue?
    - Significant Adverse event?

- Identify nodes of "influence" or "connectors"

- Increase the marketing effectiveness of our risk communication program

24 Randomly Selected DSCs

• Multaq	14-Jan-11
• Acetaminophen	13-Jan-11
• rHGH	22-Dec-10
• Anzemet	17-Dec-10
• Propoxyphene	19-Nov-10
• Invirase	21-Oct-10
• Biphosphonates	12-Oct-10
• Meridia	8-Oct-10
• Actos	17-Sep-10
• Valcyte	15-Sep-10
• GBCA	9-Sep-10
• Stalevo	20-Aug-10
• Lamictal	12-Aug-10
• Nimodipine	2-Aug-10
• Evamist	29-Jul-10
• Qualaquin	8-Jul-10
• LABAs	2-Jun-10
• Xenical/Alli	26-May-10
• PPIs	25-May-10
• GnRH Agonists	3-May-10
• Zocor	19-Mar-10
• Oral Biphosphonates	10-Mar-10
• Invirase	23-Feb-10
• Maalox	17-Feb-10

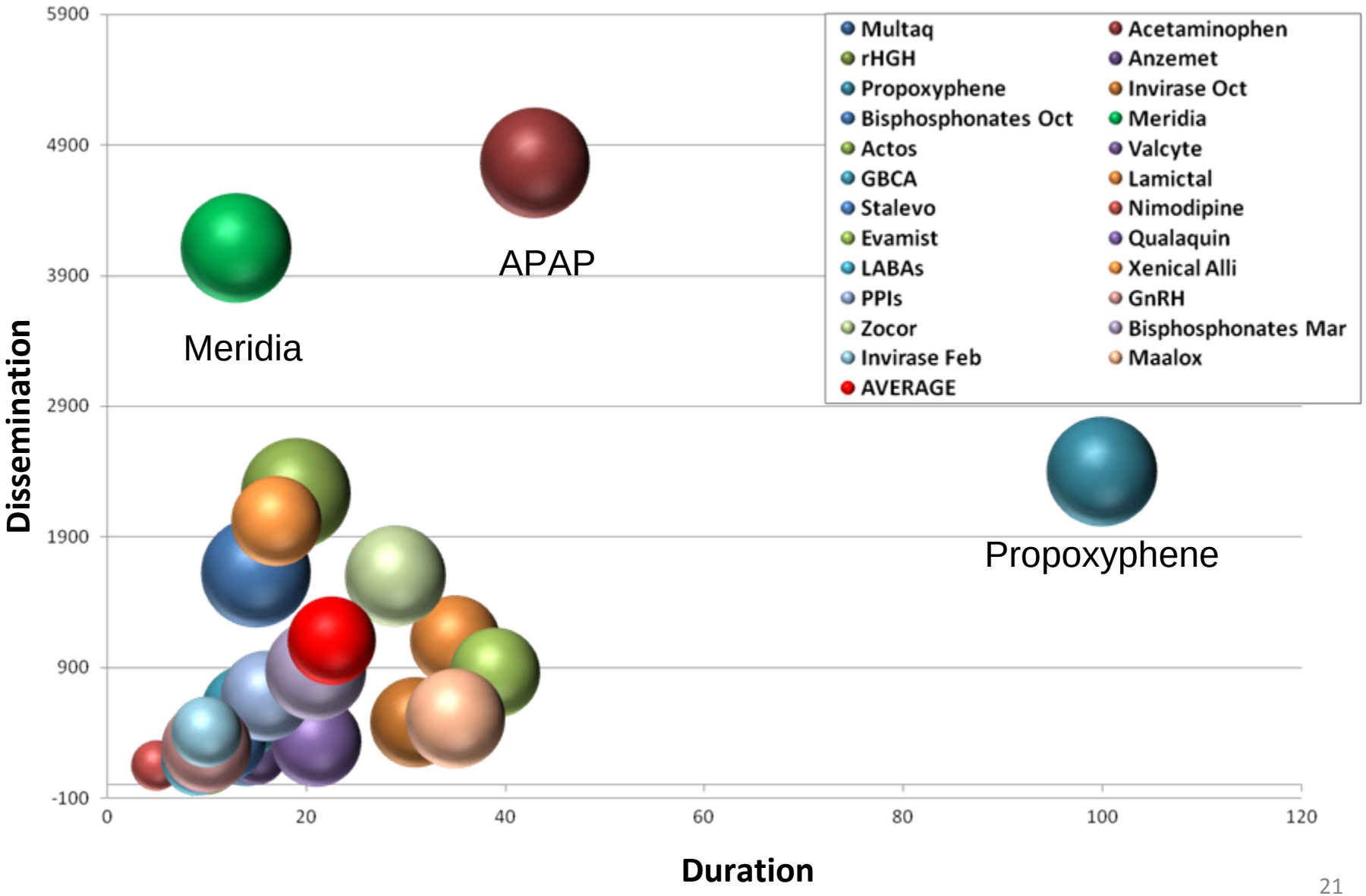
DSC issues ranged in topic and intent, including new warnings, prescribing restrictions, early communications, market withdrawals, etc.

Measuring DSC Behavior
Defining the Three D's

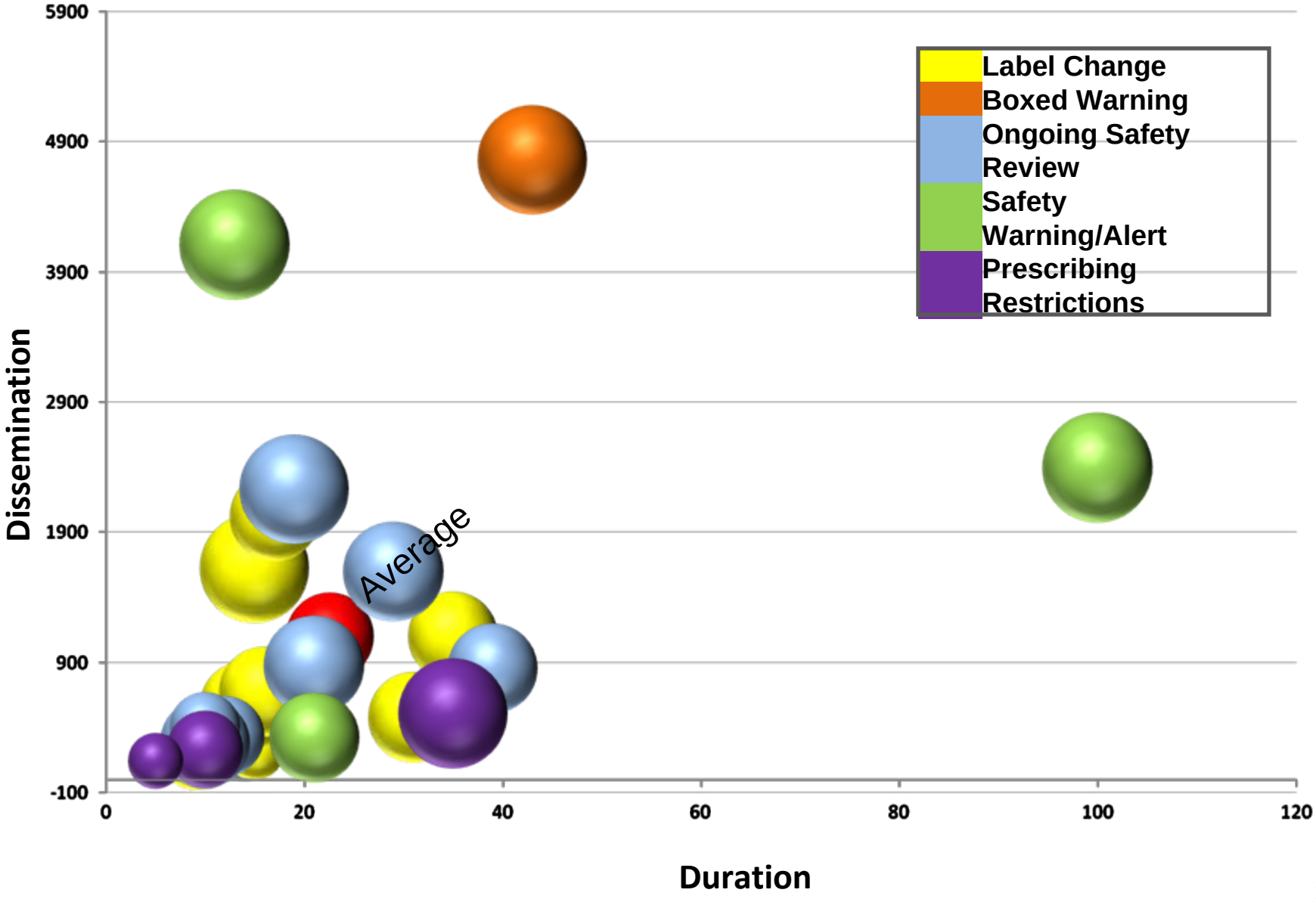
Focused on 3 key indicators of DSC behavior after release:

1. **Dissemination** – *How the message spreads online*
   - The "height" of the DSC behavior
     - Calculated as total posts per day
     - Aggregate: total posts in days 0-13 after release
2. **Diffusion** – *Degree to which the message spreads*
   - The "depth" or "width" of DSC behavior
     - Diversity of posting media type and posting engagement (finite number; 11)
     - Aggregate: # of media types where DSC appeared in days 0-13
3. **Duration** – *Length of time the message receives notable online activity*
   - The "length" of DSC behavior
     - Number of days topic generates posts after launch
     - Aggregate: # of days before daily post activity returns to pre-release average
     - Pre-launch average is defined by the average daily posts in 2 weeks prior

DSC Behavior: Case Plots



DSC Behavior: By DSC Type

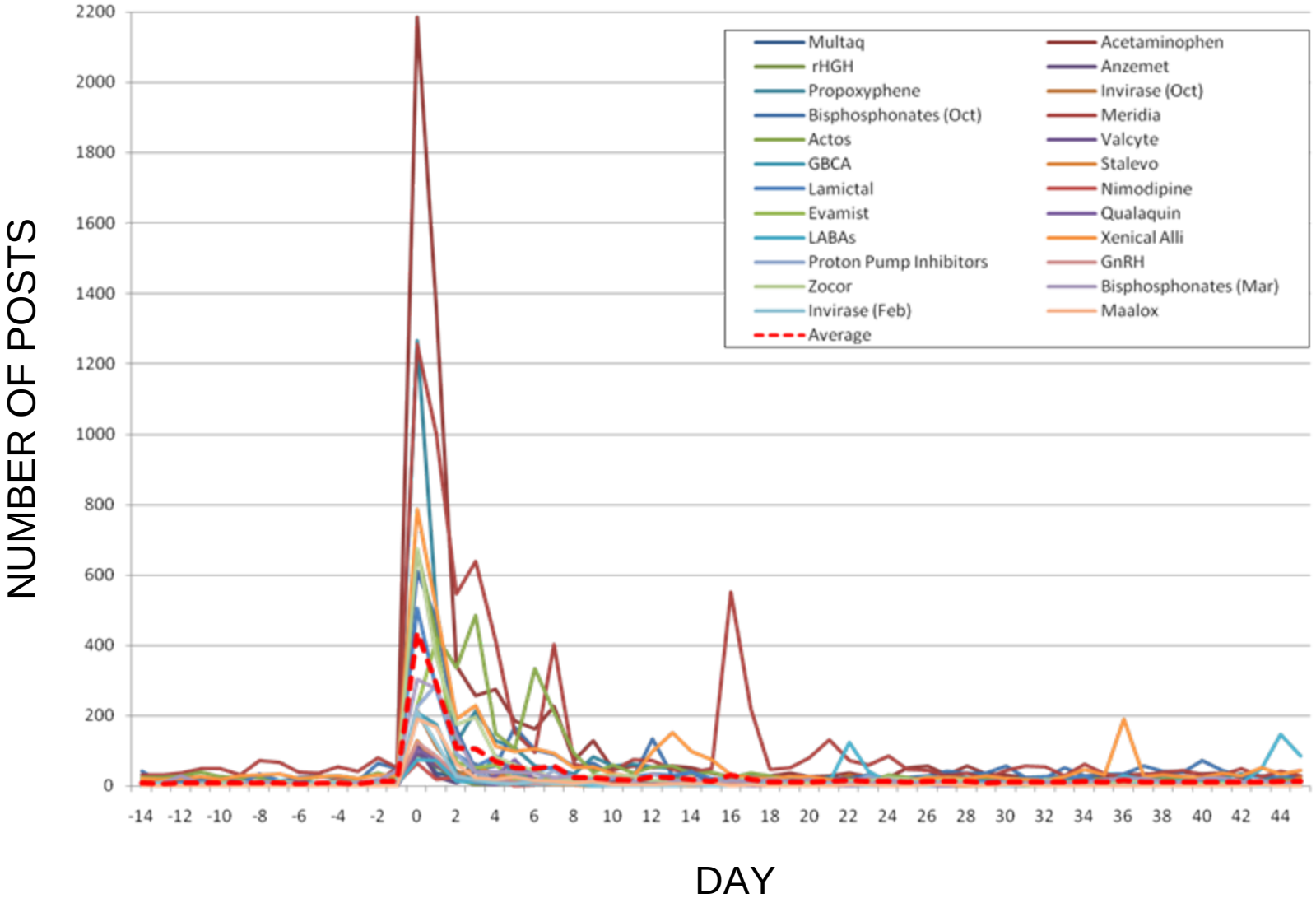


Interesting Findings

- 3Ds strong predictors of each other
  - Diffusion & Dissemination → Duration ($p = .04$)
  - Duration & Diffusion → Dissemination ($p = .001$)
  - Duration & Dissemination → Diffusion ($p = .000$)
  - Suggests a higher order construct (Behavior)
    - Must conduct factor analysis

- Caveat: We are still early in our analysis

Dissemination



Highest Performing DSCs

The following DSCs ranked top in the main indicators of dissemination (7 days):

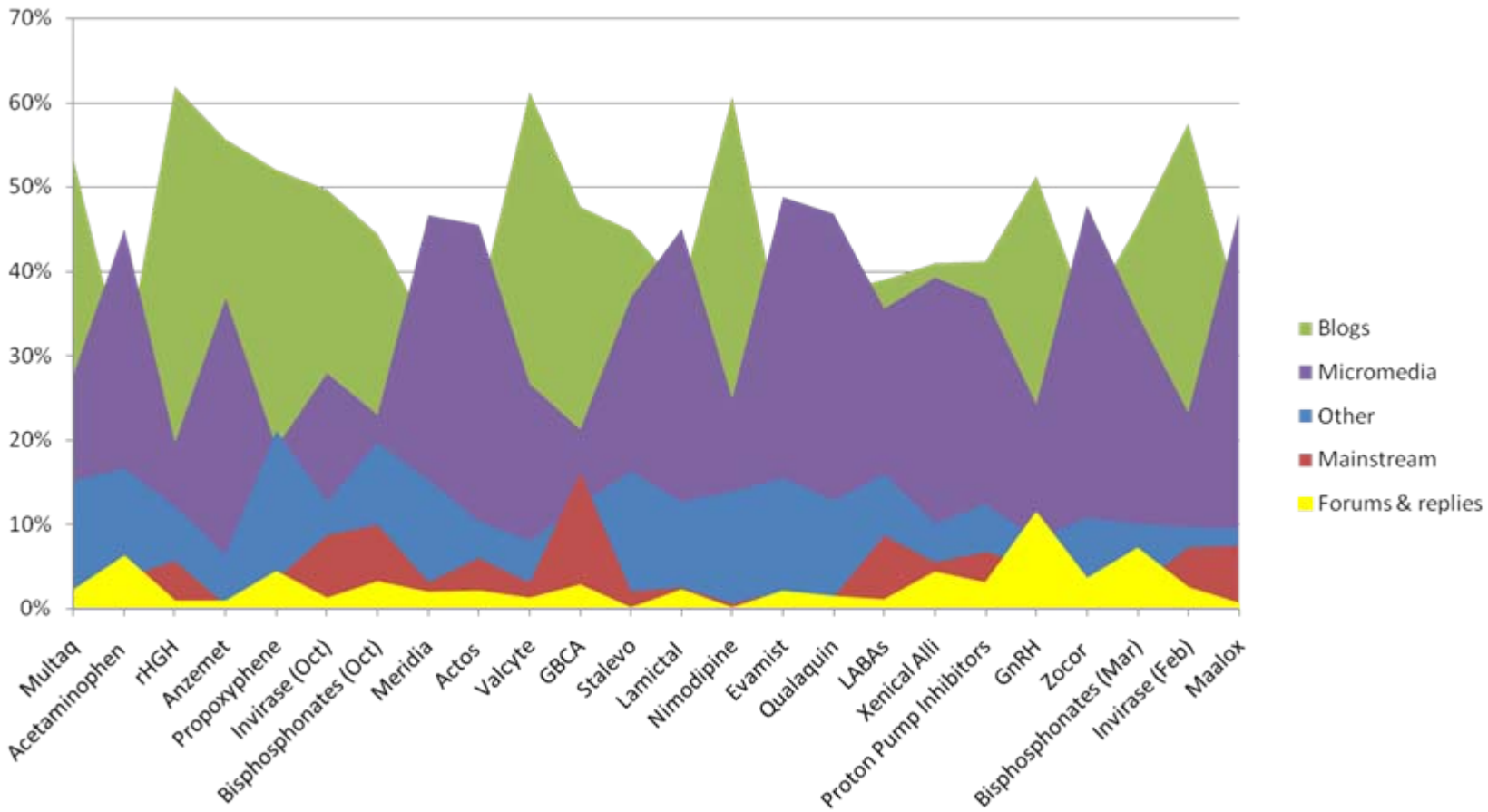
	Dissemination		
Rank	**Total Posts**	**Total Posts/Day**	**# of Peaks in week 1**
1	Acetaminophen	Acetaminophen	Multaq
2	Meridia	Meridia, Actos (tied)	Anzemet
3	Actos		Actos
4	Propoxyphene	Propoxyphene	Nimodipine
5	Xenical/Alli	Xenical/Alli	Xenical/Alli

Lowest Performing DSCs

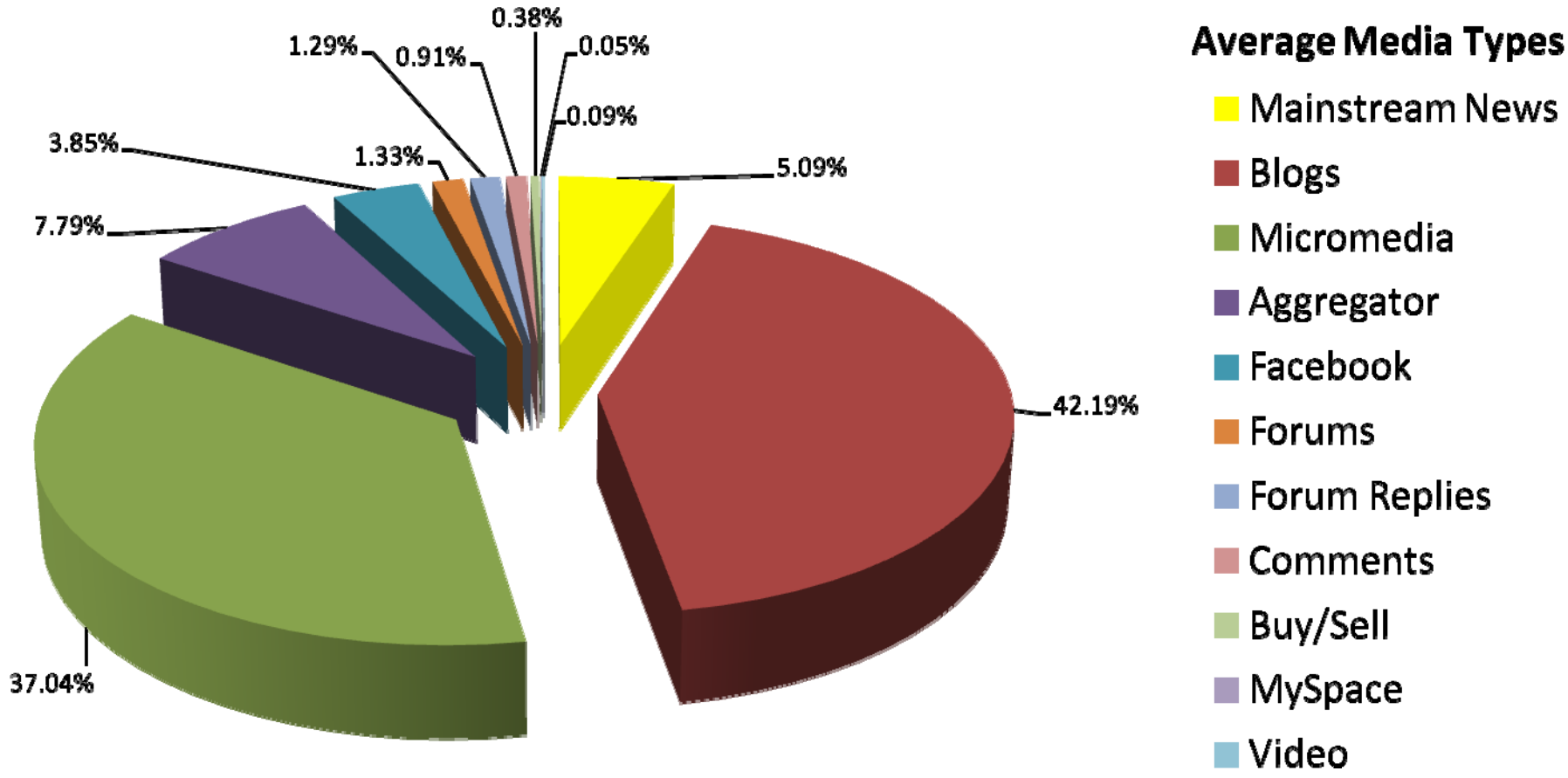
The following DSCs ranked in the bottom 5 for dissemination indicators:

	Dissemination		
Rank	**Total Posts**	**Total Posts/Day**	**# of Peaks in week 1**
24	Nimodipine	Nimodipine	Invirase (Feb)
23	LABAs	rHGH, LABAs (tied)	Bisphosphonates (Mar)
22	rHGH		PPIs
21	Anzemet	Anzemet	LABAs
20	Valcyte	Valcyte	Maalox

Diffusion : Post Media Type (% Share of Total Posts)



Diffusion: Average Media Breakdown



Diffusion: Top Media Influencers (week following DSC release)

FDA was a go-to resource for one of the highest and lowest scorers within our 3D framework

Media Type	Acetaminophen	Meridia	Nimodipine	Propoxyphene
Twitter Top 2	@BreakingNews (MSNBC), (2,041,434 followers)	@CNNbrk (3,519,670 followers)	@theheartorg (2,119 followers)	@ElNuevoDia (31,996 followers)
	@nprnews (386,084 followers)	@rolandsmartin (CNN), (33,347 followers)	@PatientSafety01 (1,590 followers)	@FDA_Drug_Info (13,943)
@FDA_Drug_Info Followers	16,218 followers	11,397 followers	No followers detected	13,943 followers
Blogs Top 2	HealthCentral.com (Karen Lee Richards, co-founder of National Fibromyalgia Assn.)	ConceptsNews.com		
	Forum.opiophile.org	Blogs.wsj.com	Drugs.com	Staho.com
Mainstream Top 2	News.yahoo.com	CNN.com	NewsInferno.com	Reuters.com
	Online.wsj.com (Wall Street Journal)	WashingtonPost.com	No mainstream news	ABCNews.com

FDA Twitter Influence

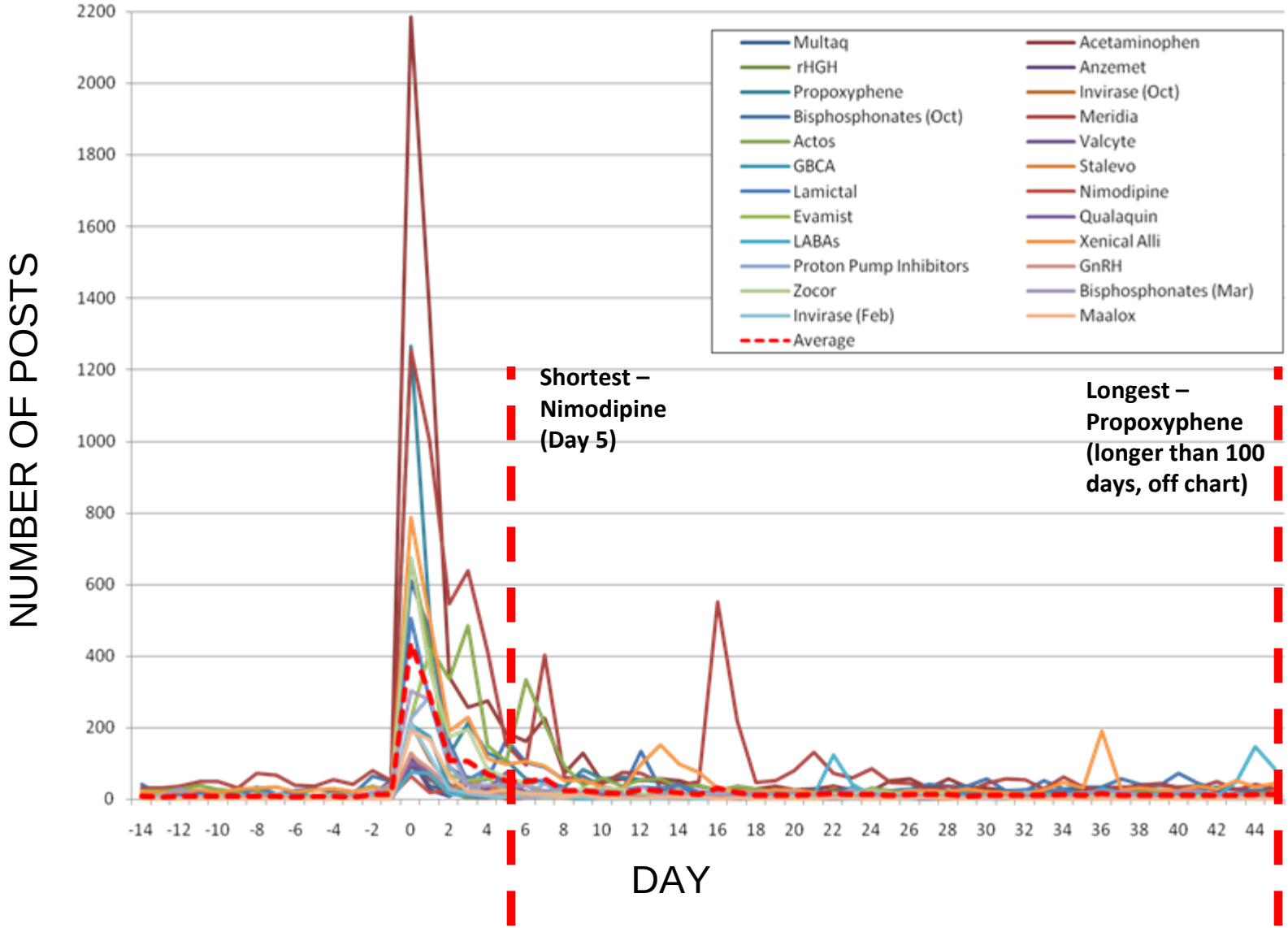
Engagement Metrics (Week-of)	Multaq	Acetaminophen	rHGH	Anzemet
ReTweets	0	0	0	0
FDA.gov	24	120	27	33
@FDA_Drug_Info	3	22	2	2
Engagement (Comment Count)	31	31	31	18

Engagement Metrics (Week-of)	Propoxyphene	Bisphosphonates (Oct)	Meridia	Valcyte
ReTweets	0	80	289	20
FDA.gov	72	88	103	45
@FDA_Drug_Info	16	44	58	21
Engagement (Comment Count)	1,770	19	1,226	10

Engagement Metrics (Week-of)	GBCA	Nimodipine	Qualaquin	LABAs
ReTweets	26	20	21	5
FDA.gov	41	24	18	9
@FDA_Drug_Info	26	19	10	6
Engagement (Comment Count)	444	5	28	7

Engagement Metrics (Week-of)	Xenical/Alli	GnRH Agonists	Zocor	Bisphosphonates (Mar)
ReTweets	141	11	83	32
FDA.gov	45	19	45	34
@FDA_Drug_Info	12	11	22	13
Engagement (Comment Count)	402	29	331	684

Duration


NUMBER OF POSTS
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
-14 -12 -10 -8 -6 -4 -2 0 2 4 6 8 10 12 14 16 18 20 22 24 26 28 30 32 34 36 38 40 42 44
DAY
Multaq
rHGH
Propoxyphene
Bisphosphonates (Oct)
Actos
GBCA
Lamictal
Evamist
LABAs
Proton Pump Inhibitors
Zocor
Invirase (Feb)
Average
Acetaminophen
Anzemet
Invirase (Oct)
Meridia
Valcyte
Stalevo
Nimodipine
Qualaquin
Xenical Alli
GnRH
Bisphosphonates (Mar)
Maalox
Shortest – Nimodipine (Day 5)
Longest – Propoxyphene (longer than 100 days, off chart)

Major Themes Thus Far

- Major dissemination occurs within 1 week
  - Pattern Predictability
  - Variability in the dissemination cascade
    - Targeted message (nimodipine; small reach)
    - Popular drug (APAP; broad reach)
- DSCs also vary on supplemental material attached to the announcement
  - PR; Podcast; Consumer Update, QA

Major Themes Thus Far

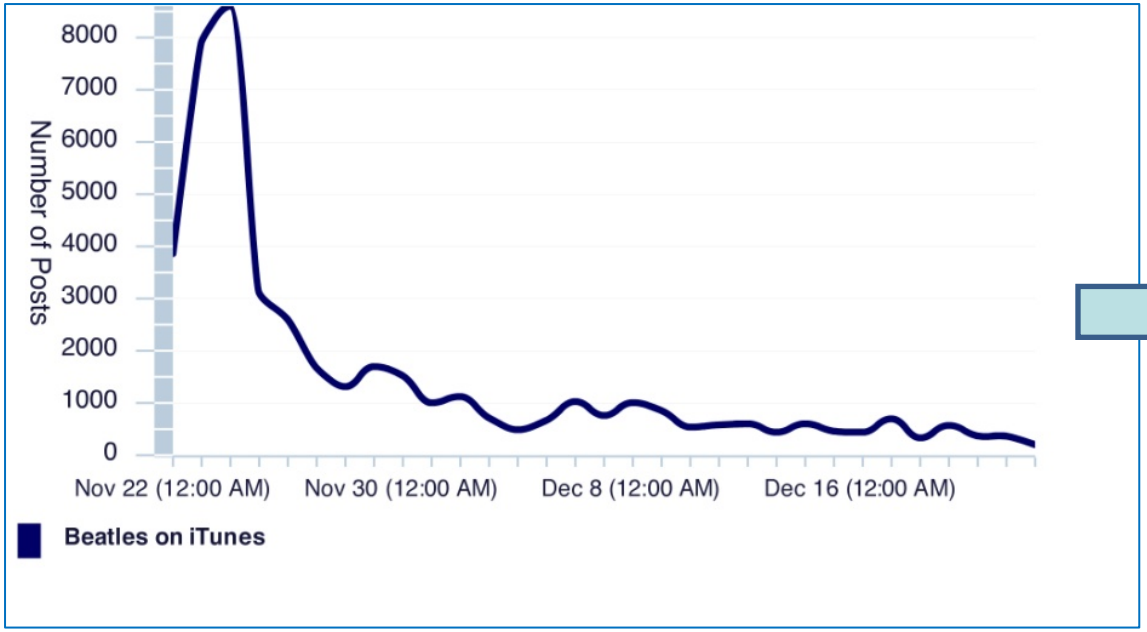
- Blogs and micromedia make up the lion share of activity
  - Does one tweet equate to one mainstream news story?
    - Variable weighting
    - Needs further analysis

Discussion

- Multipurpose DSCs
  - Informative
    - We are looking at a safety signal, but too early to recommend changes in prescribing or use
    - We have changed the way HCPs and PTs should view the risks and benefits of the drug
  - Persuasive
    - HCPs and PTs should be using the drug differently
- Should we be develop different dissemination/diffusion strategies for risk communication based on the intent of the message?
  - Broadcast versus viral propagation?

Broadcast Propogation

Beatles arrive on iTunes



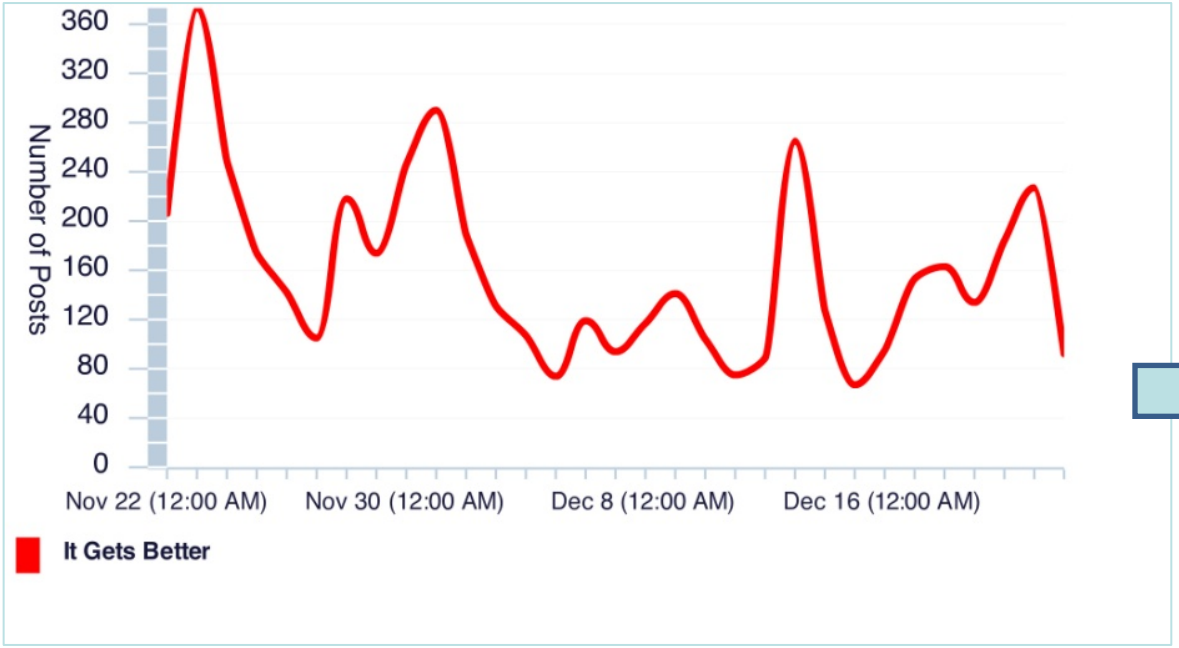
Website Release & Paid Ads

Traditional & Online News Outlets

Micro-blog broadcast

Viral Diffusion

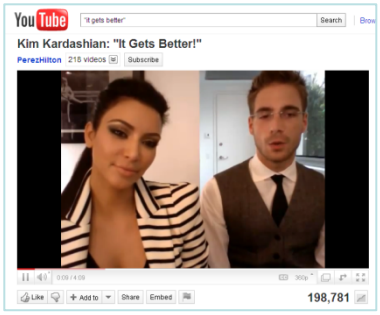
It Gets Better Project



User Generated Content

Social Platforms

Celebrity Endorsement



Discussion

- The role of “influence” or “connectors” in risk communication
  - Informational vs. persuasive

- How does “influence” or presence of “connectors” contribute to risk communication?
- What is the value of identifying/leveraging “influencers” or “connectors” of risk issues and information flow?
- What is the value of increasing FDA influence or its ability to be a connector?

Where have we been and where are we going?

- External Audit (Retrospective)
  - The echoes of conversation
    - Build methodology, expect large error
- Internal Audit
  - Build predictive constructs
- External Audit
  - Real-time analysis
    - Refine model, reduce error
- Forecasting
- Application to risk communication development and distribution

Acknowledgements

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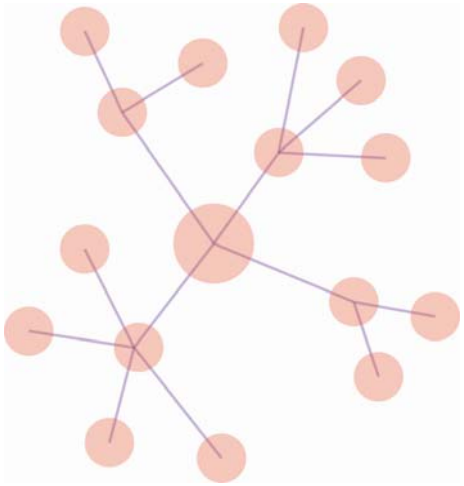
Jordan Black
Mike Greenberg, MD
Doug Bell



Thanks, Questions?

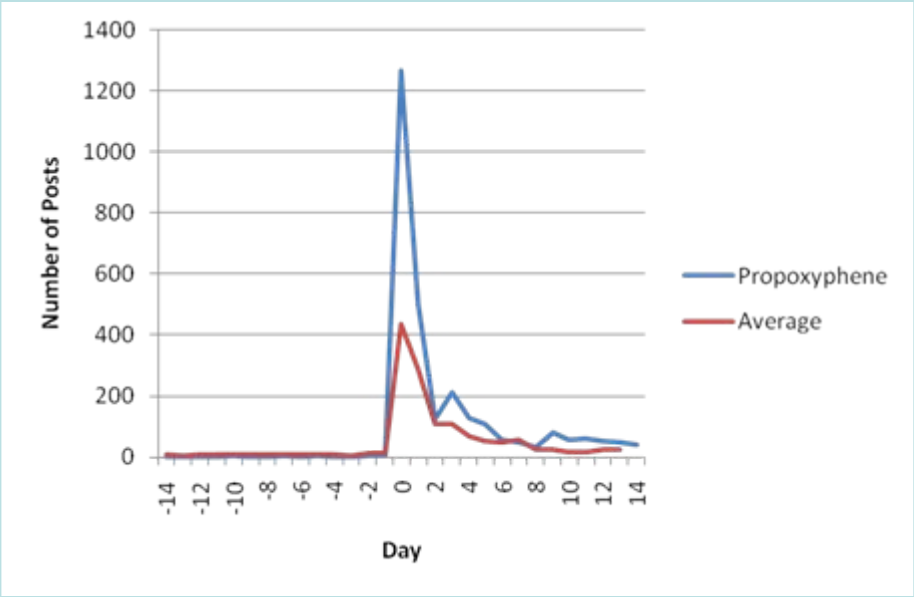
Selected References

1. The Social Life of Health Information: Americans' pursuit of health takes place within a widening network of both online and offline sources. Washington, D.C.: Pew Internet & American Life Project, 2009. (Accessed November 8, 2010 at http://www.pewinternet.org/~/media//Files/Reports/2009/PIP_Health_2009.pdf).
2. Brittany Hart. Patients flock to Facebook for health care needs | Dayton Business Journal. 2011. (Accessed April 25, 2011 at http://www.bizjournals.com/dayton/news/2011/03/18/patients-flock-to-facebook-for-health.html)
3. Valente TW, Fosados R. Diffusion of Innovation and Network Segmentation: The Part Played by People in Promoting Health. Sexually Transmitted Diseases, 2006; 33(7): S23-S31.
4. Cha M et al. Measuring User Influence in Twitter: The Million Follower Fallacy. Proceedings of the Fourth International AAAI Conference on Weblogs and Social Media, 2010.
5. Iribarren JL, Moro E. Impact of Human Activity Patterns on the Dynamics of Information Diffusion. Physical Review Letters, 2009; 103: 038702-1 - 038702-4.
6. Kossinets G et al. The Structure of Information Pathways in a Social Communication Network. Knowledge Discovery and Data Mining – KDD, 2008; 435 – 443.

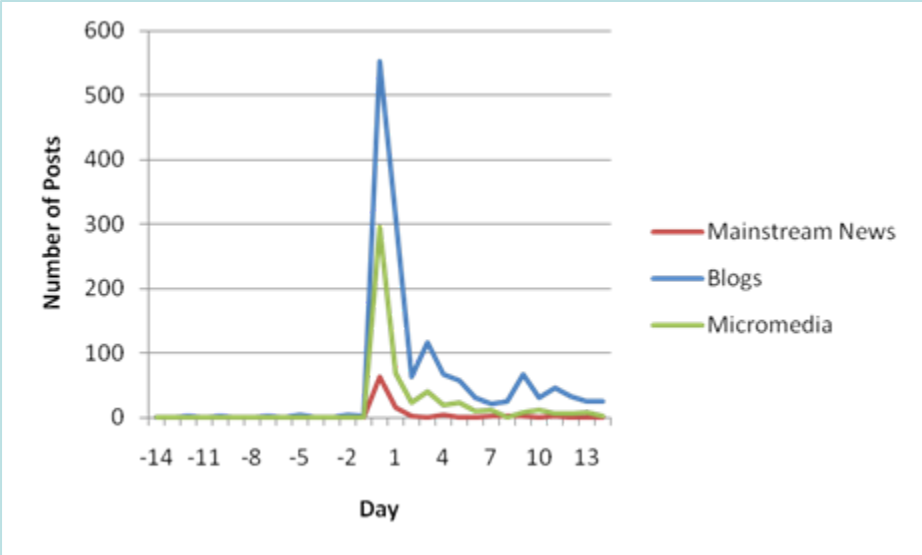
Additional Case Studies

Feature DSC: Propoxyphene

Dissemination and Duration



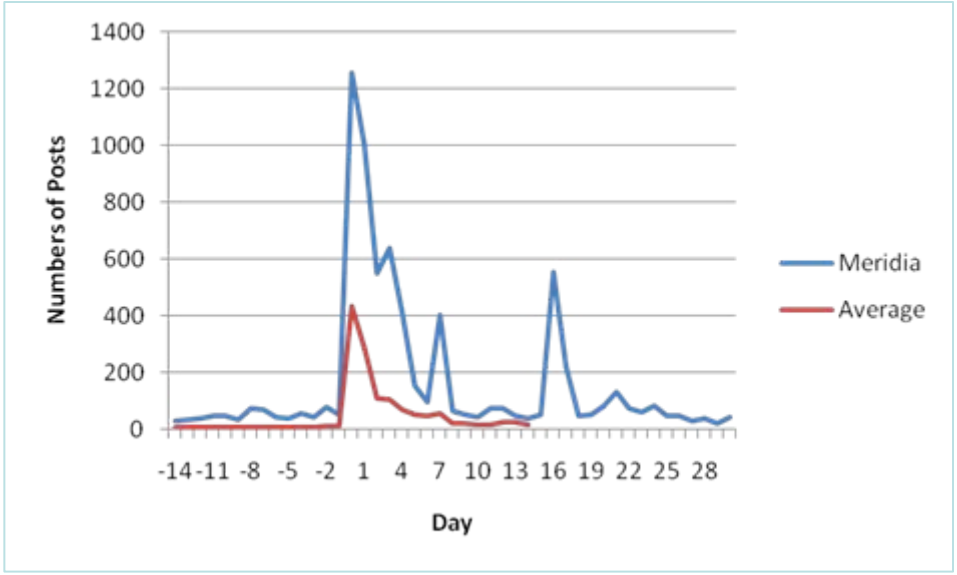
Diffusion



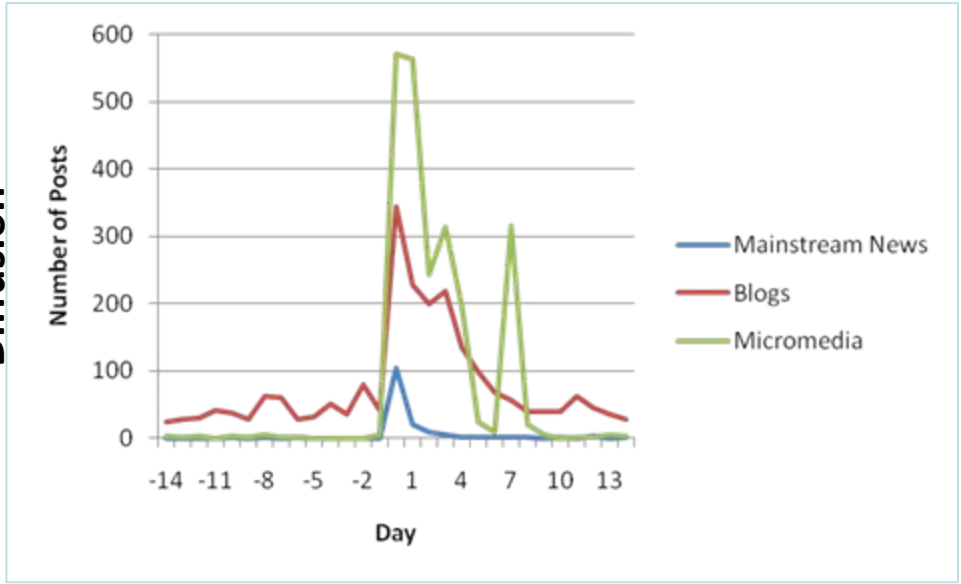
- Dissemination
  - High Unique Source Count
  - Relatively low Unique Source %
    - Suggests posters are generally high-volume posters
  - Greatest magnitude of dissemination highly localized to Day 0
- Duration
  - Longest in duration at 100+ days
- Diffusion
  - Greatest disproportion of blog activity versus other channels (553 blog posts on Day 0; avg for Day 0=127)

Feature DSC: Meridia

Dissemination and Duration



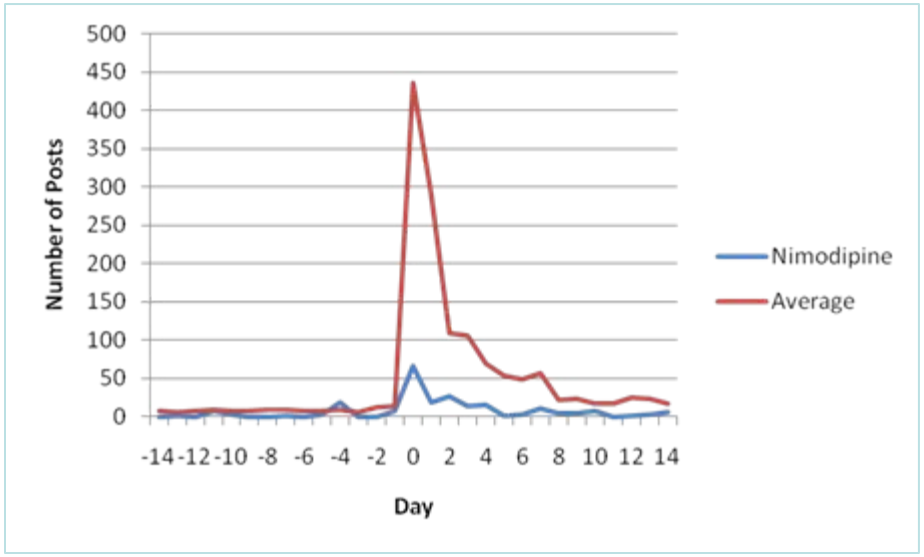
Diffusion



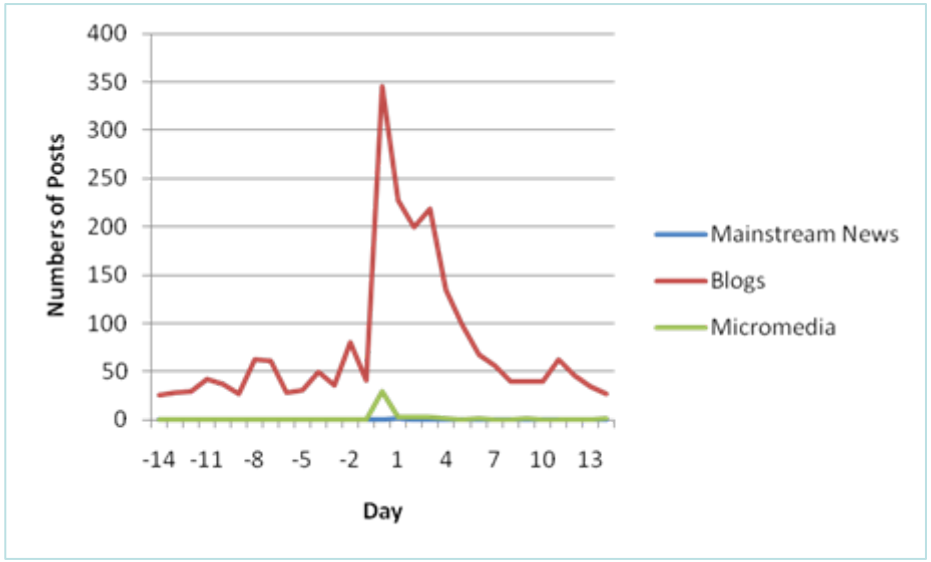
- Dissemination
  - Second-highest Unique Source Count
  - Second-lowest Unique Source %
    - Suggests heavy posting by relatively smaller group of individuals
  - Following return to baseline, experienced peak on Day 16 that abruptly ended (heavy blog activity around FDA news on other obesity drugs)
- Duration
  - Reached baseline at Day 13 but re-entered news later
- Diffusion
  - Wide channel diffusion, first in blogs and aggregators, second highest in micromedia and Facebook

Feature DSC: Nimodipine

Dissemination and Duration



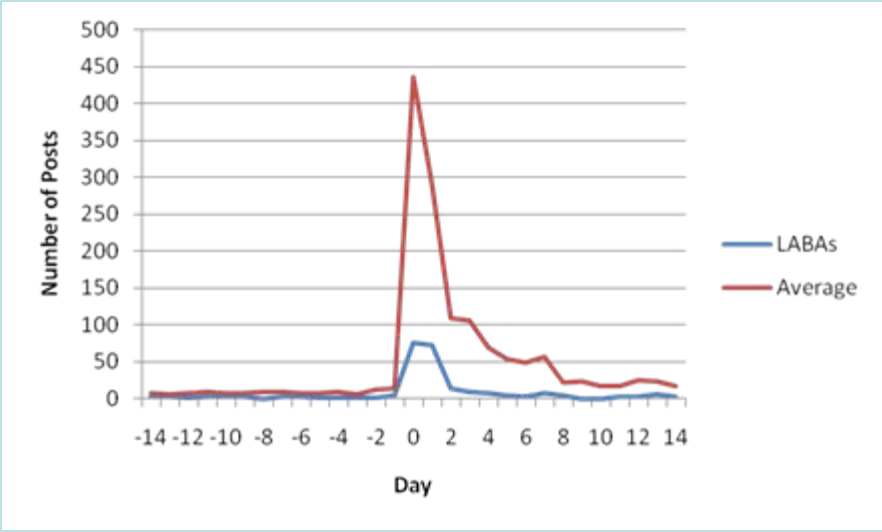
Diffusion



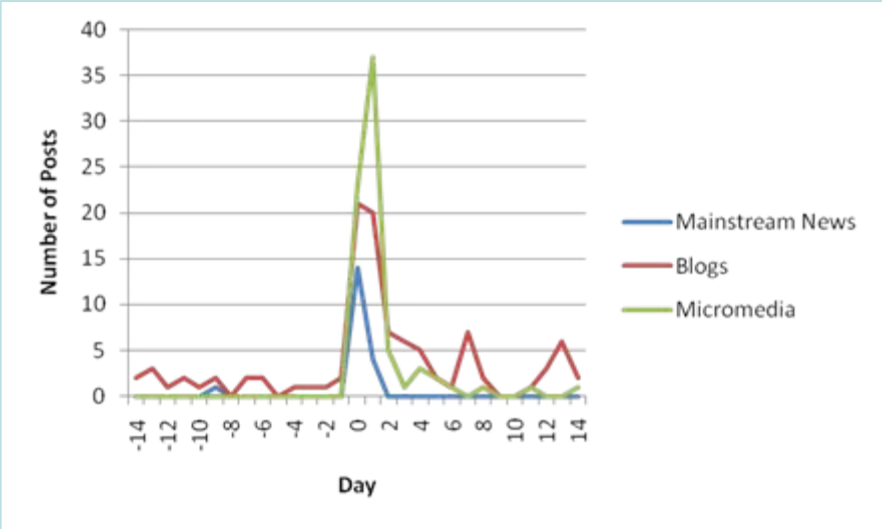
- Dissemination
  - One of just 5 DSCs with 3 peaks within Week 1
  - Last in nearly all dissemination and engagement measures
- Duration
  - Shortest in duration
  - May be attributed to targeted professional critical care audience
- Diffusion
  - Nearly exclusive to blog activity
  - No mainstream news coverage
  - Very low diffusion score

Feature DSC: LABAs

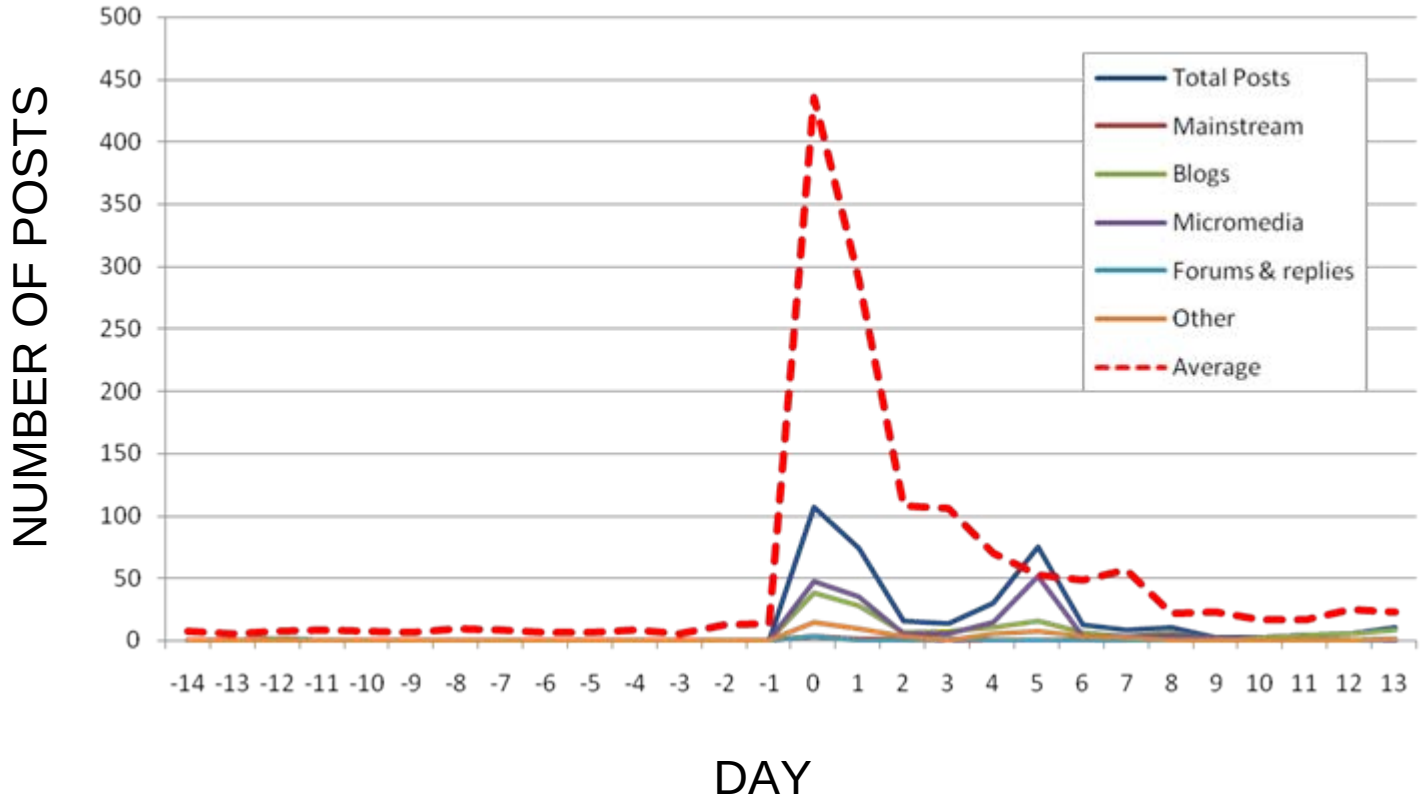
Dissemination and Duration



Diffusion



- Dissemination
  - Second fewest number of posts
  - Third-highest clicks to DSC page on FDA.gov
  - Third-longest time on site
  - Nearly as many FDA visits (5,711) as top-performing Meridia DSC (6,135) and more page views (8,456 versus 7,932)
- Duration
  - Second shortest duration aside from Nimodipine
- Diffusion
  - Broad balance of mainstream news, blogs, micromedia
  - Mainstream news may have contributed to secondary and tertiary peaks

Feature DSC: Qualaquin

- This is the lowest-performing Safety Warning/Alert, coming in much lower than strong performer Propoxyphene and Meridia
- A malaria drug being used off-label for leg cramps