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Internet Surveillance: Content Analysis and Monitoring of Product-specific Internet Prescription Opioid Abuse-related Postings

Stephen F. Butler, PhD, Synne Wing Venuti, MSW,* Christine Benoit, BA,* Richard L. Beaulaurier, PhD,† Brian Houle, MPH,* and Nathaniel Katz, MD, MS*‡§*

Objectives: This study describes the development of a systematic approach to the analysis of Internet chatter as a means of monitoring potentially abusable opioid analgesics.

Methods: Message boards dedicated to drug abuse were selected using specific inclusion criteria. Threaded discussions containing 48,293 posts were captured. A coding system was created to compare content of posts related to 3 opioid analgesics: Kadian, Vicodin, and OxyContin.

Results: The number of posts containing mentions of the target drugs were significantly different [OxyContin (1813) > Vicodin (940) > Kadian (27), $P < 0.001$]. Analyses revealed that these differences were not simply a reflection of the availability of each product (ie, number of prescriptions written). Reliability tests indicated that the content coding system achieved good interrater reliability coefficients (average κ across all categories = 0.76, range = 0.52 to 1.0). Content analysis of a sample of 234 randomly selected posts indicated that the proportion of Internet posts endorsing abuse of Kadian was statistically significantly less than OxyContin (45.5% vs. 68.4%, $P = 0.036$, not adjusted for multiple comparisons).

Discussion: These results suggest that a systematic approach to postmarketing surveillance of Internet chatter related to pharmaceutical products is feasible and yields reliable information about the quantity of discussion of specific products and qualitative information regarding the nature of the discussions. Kadian was associated with fewer Internet mentions than either OxyContin or Vicodin. This investigation stands as a first attempt to establish systematic methods for conducting Internet surveillance.

Key Words: Internet monitoring, opioids, content analysis, aberrant drug behaviors, prescription drug abuse

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From the *Inflexxion, Inc, Newton, MA; ‡Tufts University School of Medicine, Boston; §Analgesic Research, Newton, MA; and †Florida International University, Miami, FL.

Supported by a grant to Inflexxion, Inc from Alpharma, One Executive Drive, Fort Lee, NJ.

Reprints: Stephen F. Butler, PhD, Inflexxion, Inc, Newton, MA 02464 (e-mail: sfbutler@inflexxion.com).

Prescription drug abuse is on the rise in the United States.[1–3] Recently, 30% of individuals identified as illicit drug users reported nonmedical prescription drug use.[4] Nearly half of the prescription drug abuse has been observed in youth and young adults (aged 12 to 25).[4] Use of these drugs by young people has dramatically increased for all categories of pharmaceuticals, most prominently pain relievers (nearly 2 million nonmedical users in 2002).[4]

In response to increasing prescription drug abuse, most notably the increase of OxyContin® (Purdue Pharma L.P., Stamford, CT) abuse in 2000, the Government Accountability Office recommended to the Food and Drug Administration (FDA) "that risk management plans for schedule II controlled substances contain a strategy for monitoring and identifying potential abuse and diversion problems."[2] The Government Accountability Office noted that "Risk management plans were not used at the time OxyContin was approved." Further, "we could not assess the relationship between the increased availability of OxyContin and locations where it is being abused and diverted because the data on abuse and diversion are not reliable, comprehensive, or timely."[2] One key component of effective risk management plans for pharmaceutical companies and policy makers is postmarketing surveillance.[2]

Internet monitoring is currently considered an important source of "leading edge" data that comprise one component of an "early warning" system.[5] The Internet is an ideal medium for prescription drug abusers to communicate with each other. Users share information, termed web-based "chatting,"[6] via chat rooms, bulletin boards, and other forums. Several websites have emerged dealing with recreational, illicit drug use.[7] These sites allow drug users to freely offer ideas, discuss trends and preferences, and offer advice on which drugs provide "the best high," as well as how to extract active ingredients from various formulations or delivery systems.

Recreational drug-related websites offer a glimpse into the world of prescription abusers by allowing observation of abuser-to-abuser (peer-to-peer) communications. One published effort to monitor potentially addictive pharmaceuticals via Internet monitoring tracked discussions of Ultram® (Ortho-McNeil Pharmaceutical, Inc, Raritan, NJ).[8] This study followed Internet discussions of tramadol for 6 months after the drug's

release. Approximately 150 mentions were obtained, about 90% of which suggested that tramadol had limited euphorigenic effects. The study monitored only one substance, without identifiable methods, and for a limited period of time.

There is increasing recognition of Internet monitoring as a potentially informative surveillance tool.[1,5] However, we are not aware of any systematic approach to Internet monitoring of drug abuse. The present study assesses the feasibility of conducting systematic Internet surveillance of potentially addictive pharmaceutical products in online discussion groups. We developed a systematic method for monitoring Internet chatter of 3 pharmaceutical products that we expected to exemplify differences in terms of the amount of Internet "chatter" and the degree to which such chatter would encourage or support abuse of the product.

MATERIALS AND METHODS

Message Board Terminology

Three terms are relevant to Internet discussions of drug abuse (Fig. 1):

- *Mention*: any occasion a word (such as the name of a drug or its synonym) appears.
- *Post*: a single message entered by one user. Thus, a single post (message) may contain one or many specific mentions of a drug.
- *Thread*: a collection of posts on the same subject and displayed in chronologic order; this generally begins with a specific message or question and includes all subsequent responses to that message.

Thus, a single thread contains a number of posts. Within a thread, any given post may mention one (or more) of the target products, may make several mentions of any single target product, or may contain no mentions of the target drugs whatever. Indeed, the bulk of the posts within a given thread address other drugs (illegal or pharmaceutical drugs), or may deal with virtually any other topic (eg, political discussions, movies, relationship issues, and so on).

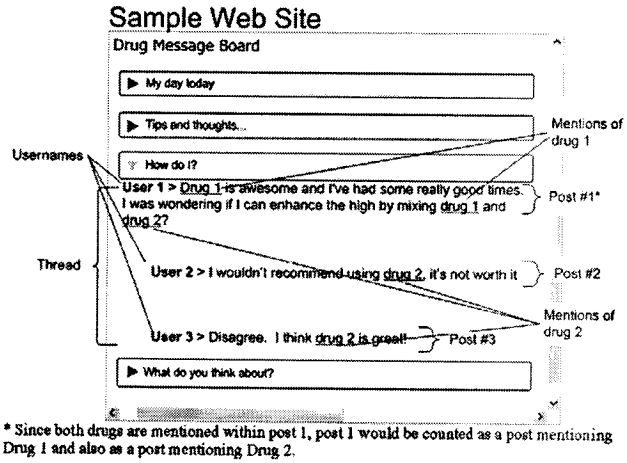

FIGURE 1. Visual representation of relationship between mention, post, and thread on a sample message board.

Collection of Internet Data

Target Drug Selection

The field is increasingly concerned with the measuring of differences in abuse liability between specific opioid preparations, extending beyond the compound.[9] Thus, a major focus of this feasibility test was to determine the extent to which product-specific data could be collected and evaluated from Internet. Toward this end, we selected 3 opioid products for comparison on the basis of the results from a previous study in which a scale was created for measuring opioid attractiveness for abuse of specific products, called the Opioid Attractiveness Scale.[10] The scale, completed by individuals with a history of opioid abuse, determined that OxyContin® (For clarity when referring to groups of drugs we will use the generic name only. When referring to specific brands, we use the trade name.) was highly attractive, Vicodin® (Abbott Laboratories, North Chicago, IL) moderately attractive, and Kadian® (Alpharma Branded Products Division, Piscataway, NJ) relatively unattractive for abuse (Table 1 for product descriptions).

Website Selection

Inclusion criteria for websites were: the site had a message board; promoted free discussion of psychoactive drug use; was open to the public; was privately funded; was moderated by volunteers; and was in English. Sampling websites is a complex issue for which there is as yet no clear methodology.[11] Because this was a feasibility test, we did not attempt to create an exhaustive pool of eligible sites. Rather, we applied the inclusion criteria to a convenience sample of sites known to us from previous research studies. Three message boards [referred to here as Site A, Site B, and Site C (Inflexxion does not disclose the names of websites from which posts are

TABLE 1. Product Descriptions for Each of the Selected Target Drugs

	Kadian®	OxyContin®	Vicodin®
Manufacturer	Alpharma Branded Product Division	Purdue Pharma L.P.	Abbott Laboratories
Product description	Identical polymer coated sustained-release pellets of morphine sulfate contained in capsule form for oral administration	A controlled-release formulation of oxycodone hydrochloride in tablet form for oral administration	Hydrocodone bitartrate and acetaminophen is supplied in tablet form for oral administration

harvested. Such disclosure could influence future research efforts. Interested researchers should contact the first author for more information)] were selected for analysis based upon meeting our inclusion criteria.

Capturing of Internet Data

Threads from the 3 message boards were harvested if the thread contained at least one mention of any of the target drugs. A researcher entered each site and performed keyword searches (each website has a search engine for searching threads) using the keywords, OxyContin®, Vicodin®, and Kadian® (kadien, was also used, as this is a common misspelling). All discussion threads from a 6-month period, February to July 2005, that contained at least 1 keyword were copied into a word processing document. That document was then formatted to be compatible with Atlas.ti (version 5.0.66), a flexible and popular content analysis software program.[12] This data capturing methodology was conducted for one target drug per website at a time and entered into a database by month, drug, and website.

Development of Coding Schema, Codebook, and Coding Form

Our approach followed standard methods of content analysis.[13] An "expert coder" member of the team served as the expert on opioid message boards. Initial drafts of the coding system, codebook, and coding form were developed with input from all research team members. The expert coder worked with 2 graduate-level trainee coders to further develop and refine the content analysis system. Development of the coding schema was an iterative process involving a series of efforts to code a small sample of posts from outside the target sample (to be rated later), revise the coding schema and rules, and code further sample material until acceptable reliability was achieved.[13] On the basis of this work, a codebook and coding form were finalized for use by the coders during the formal reliability test and final coding task.

Formal Reliability Test

The formal reliability test followed recommendations of Neuendorf.[13] A formal reliability sample was constructed from a separate pool of Internet posts related to the 3 target drugs from the message boards (ie, made up of posts that were outside of the time period during which Internet chatter was systematically monitored). All 3 coders independently rated the same material. Messages were selected following maximum variation sampling techniques.[14] All messages included at least some mention of the target products, and some messages were selected because they contained ambiguous or otherwise difficult to code messages as identified by the expert coder. The formal reliability test for categorical decisions included which of the 3 target drugs were discussed in the post; and, for each drug discussed within a post, which were abuse-related; which were not abuse-related; which had an abuse endorsing tone; which had an abuse discouraging tone; and which were coded as "both endorsing abuse and discouraging abuse."

Coding of Analysis Sample

Sampling

Using a random number generator, a random sample was selected from the entire pool of harvested Internet posts within the timeframe of the study. The goal was to sample about 100 posts related to each drug. Although the original sampling goal was the same for Kadian®, only 22 posts containing a mention of Kadian® were found in the entire pool of harvested posts. Therefore, all 22 Kadian® posts were included in the final coding sample. Random selection of the other 2 drugs, OxyContin® and Vicodin®, was constrained so that an equal number of mentions per site, per month (6 posts per site, per month, per product) were included.

Procedures

The 2 trained coders and the expert independently coded the analysis sample. Reliability of the coders was reassessed on the final sample. To demonstrate that the levels of reliability achieved during the reliability training were maintained before conducting analyses of the coded data, both coders coded the entire sample.[13] Interrater reliability was calculated on the entire sample for the categorical codes, using the κ statistic. Note that before calculating percentages for analysis, messages coded as "both" were also coded as "endorsing abuse" and "discouraging abuse."

Analysis of the Message Database

The entire database containing all harvested posts across the months of data collection from all websites was formatted for entry into Atlas.ti, the content analysis software. Using Atlas.ti, we reviewed all the words included in the universe of posts, which allowed us to identify variant spellings and misspellings (eg, vicadin, kadien, oyxcontin). Using the Office of National Drug Control Policy website[15] and other sources, we also identified street names for each of the target drugs (eg, Vikes, Oxycotton). The software was programmed to capture these misspellings and street names and add them to the count. Thus, the analyses return the raw count of all occurrences of any mention of the target products. The program also permits a count of the individual posts that contain any mention of any of the target products, their synonyms, or misspellings. Therefore, it was possible to capture the total number of mentions (any time the product or synonym was mentioned) and the number of posts containing at least one mention of a product name. McNemar test of proportions drawn from the same sample were used to compare the target drugs. Finally, the software was programmed to identify the poster's unique, registered username, which allowed a count of the number of unique individuals contributing to a given product's discussion. The resulting data from these analyses were: total number of posts by product, total number of mentions by product, total number of posts

containing at least one mention of each product, total number of unique authors, and the number of unique authors of posts referencing any of the 3 target products.

Availability of Target Drugs

To determine the extent to which any differences in Internet chatter obtained simply reflected differences in availability of the 3 drugs, we examined the Internet data with respect to its relationship to availability of the product. Availability of each target drug was operationalized as the number of prescriptions written (or the number of pills dispensed) during the study period. These data were drawn from marketing data provided by the NDC Health Pharmaceutical Audit Suite (PHAST) data repository. For the months from February 2005 to July 2005, these data included prescriptions and pill counts for OxyContin®, Vicodin®, and Kadian®. Only the data for the brand name of each product were examined because of difficulties making comparisons among drugs for which generic drugs exist (ie, Vicodin) and drugs for which equivalent generics either do not exist (ie, Kadian) or for which a generic has only recently been introduced (ie, OxyContin). For the brand Vicodin®, 4 categories were summed, Vicodin®, Vicodin ES®, Vicodin HP®, and Vicodin Tuss®. For OxyContin® and Kadian®, only the numbers associated with these brand names were used. To test the limits of this method, we elected to examine how the findings would change if we added all hydrocodone prescriptions to the Vicodin® prescriptions. This reflects the possibility that those who post to these websites are using the term "Vicodin" to refer to any hydrocodone product.

Analysis of Website Differences

A series of analyses were conducted to assess differences between the websites in regard to various dependent variables. Mentions, posts, and percentage of posts devoted to the target products were all analyzed for significant differences between sites.

Statistical Analyses

Categorical comparisons were made using χ^2 for independent samples and McNemar tests to compare proportions taken from a shared sample. Continuous data were analyzed using *t* tests and analyses of variance as appropriate. SPSS version 13 was used for analyses.

Human Subjects

Data analyzed for this study were of archives of online discussions that were posted by individuals whose assumption is that any viewer of the forum will be able to read their posting. Kraut et al[16] have persuasively argued that individuals who post in online communication forums that have unrestricted membership "have no reasonable expectation of privacy, and researchers and Institutional Review Boards should be able to treat online communication in them as public behavior." Data collected for this study were text messages posted for public viewing from the forums, which is readily available to any observer directly from the forums.

RESULTS

Collection of Internet Data

Threads were selected which contained at least one mention of the target drugs. A large number of posts (a total of 48,293 individual posts) were harvested over the 6-month monitoring period because all posts from a thread were captured, including many with no reference to the target drugs. Thus, within the 48,293 posts, there were 1813 posts containing at least one mention of OxyContin®, 940 posts containing at least one mention of Vicodin®, and 27 posts containing at least one mention of Kadian® (posts are not mutually exclusive, therefore, a post containing mentions of both OxyContin® and Kadian® would be counted as 1 OxyContin® post and 1 Kadian® post). There were 3897 mentions of OxyContin® or its street names (including misspellings), 1264 mentions of Vicodin® or its street names/misspellings, and 31 mentions of Kadian® or its street names/misspellings.

Results of Coding Schema Development Process

The coding schema development process resulted in the final instructions (including coding schema, codebook, and coding form). The final coding process is as follows. First, the coder reads and familiarizes him/herself with the coding categories. Next, the coder reads a post thoroughly. The coder then identifies which target drug/s are discussed in the post. Next, the coder then has to determine if a post is clearly abuse-related (a message clearly discusses using a drug in a manner other than how it was intended and for recreational use) or not clearly abuse-related (the information presented in the post does not allow a coder to determine that the discussion is about using a drug in ways other than for its intended use; note the initial definitions of these 2 main categories were slightly modified). If the mention is not clearly abuse-related, the coder marks the scoring sheet as such and then moves on to the next target drug mentioned. If there were no other target drugs mentioned, the coder then moves to the next post.

Once a mention was determined to be clearly abuse-related, the next task is to code that mention as either "Endorses abuse" (endorses or promotes using the drug in any way other than how it is prescribed), "Discourages abuse" (expresses a barrier to recreational use such as being too dangerous, too expensive, too strong, too hard to get, etc.), or "Both" (posts that contain both endorsing and discouraging messages related to the specific target drug; note the initial definitions of each of these subcategories were slightly modified). The coder repeats this process for each target drug mentioned in a post before moving on to the next post.

TABLE 2. Reliability Test Results for Categorical Ratings*

Coder Pair	OxyContin in Post	Vicodin in Post	Kadian in Post	Abuse-related	Not Abuse-related	Encourages Abuse	Discourages Abuse	Average
Reliability results for formal reliability sample								
Expert and coder 1	0.98	0.98	1	0.57	0.60	0.55	0.62	0.76
Expert and coder 2	0.98	1	1	0.50	0.51	0.62	0.69	0.76
Coder 1 and coder 2	0.97	0.98	1	0.48	0.57	0.60	0.70	0.76
Average	0.98	0.99	1	0.52	0.56	0.59	0.67	0.76
Reliability results for analysis sample								
Coder 1 and coder 2	0.98	1	1	0.76	0.76	0.69	0.74	0.85

*All values are κ statistics. Note that values below 0.40 are considered poor agreement, 0.40 to 0.75 are considered fair to good agreement, and above 0.75 reflects excellent agreement.[15–17]

Formal Reliability Test

Table 2 presents κ coefficients achieved during the formal reliability test for categorical decisions. These κ's (Table 2) were in the acceptable ranges outlined by Cicchetti and Banerjee et al.[17–19] No κ's fell below 0.40, and the average κ's were all above this minimum.

Coding of Content Analysis Sample

Two hundred thirty-four individual posts containing at least one verbatim mention of any of the 3 target drugs (the target 300 unique posts was not achieved due to the low number of Kadian® posts available) were randomly selected from the total of 48,293 individual posts. The randomization process produced 99 posts containing at least one mention of the brand product (or synonyms) for OxyContin-related, 113 for Vicodin-related, and the 22 Kadian-related posts. Of the 234 posts, 195 (83%) mentioned one of the target drugs, 36 (15%) mentioned 2 of the drugs, and 3 (1%) mentioned all 3 products. Within the 234 posts, there were 276 unique verbatim mentions of individual drugs, including 136 unique mentions of OxyContin® (49%), 118 mentions of Vicodin® (43%), and 22 of Kadian® (8%).

Reliability

Interrater reliability (calculated on the entire sample for the categorical codes and the continuous rating), including κ statistics comparing the 2 coders are presented in Table 2 for coding analysis sample. The reliability statistics are all within the acceptable range.[18]

Content Analysis

Table 3 presents comparisons of the target drugs for the coding categories. Because some posts contained discussions of more than one drug, there were a total of 276 coded drugs in the 234 posts. Among posts mentioning OxyContin®, 80.1% were abuse-related. Of the abuse-related OxyContin® posts, 68.4% were coded as endorsing abuse, 39.7% were coded as discouraging abuse. For Vicodin®, the percentages were: abuse-related posts were 78.8%, with 57.6% of abuse-related posts coded as endorsing abuse and 46.6% as discouraging. Finally, 68.2% of Kadian® posts were coded as abuse-related,

TABLE 3. Coding of Target Drugs Within Posts and Comparisons

	Codes* for all Drugs	Codes for OxyContin	Codes for Vicodin	Codes for Kadian†			
	N = 276 (%)	N = 136 (%)	N = 118 (%)	N = 22 (%)	OxyContin vs. Vicodin	OxyContin vs. Kadian	Vicodin vs. Kadian
Abuse-related	78.6	80.1	78.8	68.2	$\chi^2 = 0.1$, $df = 1$, $P = 0.793$	$\chi^2 = 1.6$, $df = 1$, $P = 0.205$	$\chi^2 = 1.2$, $df = 1$, $P = 0.276$
Not Abuse-related	21.0	19.9	21.2	27.3	$\chi^2 = 0.1$, $df = 1$, $P = 0.793$	$\chi^2 = 0.6$, $df = 1$, $P = 0.427$	$\chi^2 = 0.4$, $df = 1$, $P = 0.528$
Encourages abuse	62.0	68.4	57.6	45.5	$\chi^2 = 3.1$, $df = 1$, $P = 0.076$	$\chi^2 = 4.4$, $df = 1$, $P = 0.036$	$\chi^2 = 1.1$, $df = 1$, $P = 0.291$
Discourages abuse	43.1	39.7	46.6	45.5	$\chi^2 = 1.2$, $df = 1$, $P = 0.268$	$\chi^2 = 0.3$, $df = 1$, $P = 0.610$	$\chi^2 = 0.01$, $df = 1$, $P = 0.921$

*This count is number of codes assigned to the posts. A given post will be coded for OxyContin, if it contains at least one mention of OxyContin, and will be coded for Vicodin, if it also contains a mention of Vicodin. Thus, there were an average of 1.2 codes assigned to the 234 posts in the sample.

†The Kadian percentages for abuse-related and not abuse-related do not add to 100%, because 1 post was identified as Kadian-related but its content was determined to be uncodable for the remaining categories.

with 45.5% coded as endorsing abuse and an equal percentage 45.5% as not endorsing abuse. For all but one code, OxyContin®, Vicodin®, and Kadian® were not significantly different from each other. The exception was the 45.5% of morphine-related (Kadian® posts coded as endorsing abuse was significantly less than the 68.4% for OxyContin® ($P = 0.036$)]. The significance of this difference must be considered preliminary because this comparison would not have been significant if the P value had been adjusted for multiple comparisons.

Comparisons of Codes by Website

Table 4 presents a breakdown of the various content analysis codes by website. Significant differences in the discussions of the 3 products were observed primarily with respect to Kadian®, with significantly more discussion of Kadian® on Site A than on Sites B and C. The other 2 products were discussed at about the level on all 3 websites. In general, there was a trend for more discouraging posts and more ambivalent (both endorsing and discouraging) discussions on Sites B and C.

Analysis of the Entire Message Database

What follows is a series of analyses on the basis of the entire set of harvested Internet posts collected over a 6-month period from the 3 websites. Within the total 48,293 separate posts, there were 3897 mentions of OxyContin® or its street names (including misspellings), 1264 mentions of Vicodin® or its street names/misspellings, and 31 mentions of Kadian® or its street names/misspellings. McNemar test of proportions drawn from the same sample revealed differences between the number of mentions of OxyContin® and Kadian® was highly significant ($\chi^2 = 3864$, $df = 1$, $P < 0.001$), as was the difference between Vicodin® and Kadian® ($\chi^2 = 1231$, $df = 1$, $P < 0.001$), whereas OxyContin® and Vicodin® were also different from each other ($\chi^2 = 1231$, $df = 1$, $P < 0.001$). These data suggest that the raw number of times OxyContin® is mentioned is significantly greater than the number of times Vicodin® is mentioned, and both are mentioned significantly more often than Kadian®.

Figure 2 presents the number of mentions of the 3 target products for all websites over the 6 months. There is a certain amount of fluctuation of mentions, especially of OxyContin®, however, the relative position of the lines (ie, which lines are above or below the other lines) remains consistent.

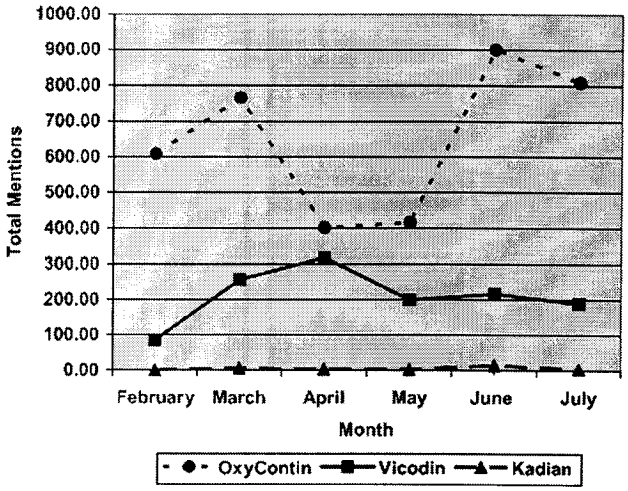

FIGURE 2. Total mentions of target drugs by month, during calendar year 2005.

Analysis of the number of posts containing at least one mention of a target drug revealed that there were messages from individual posts in which the target product was mentioned multiple times. There were 1813 posts containing at least one mention of OxyContin® (an average of 2.1 mentions per post), 940 posts containing at least one mention of Vicodin® (an average of 1.3 mentions per post), and 27 posts over the 6 months containing a reference to Kadian® (an average of 1.1 mentions per post; note that searching for misspellings of Kadian resulted in 5 additional posts identified as Kadian-related). The proportion of OxyContin® posts to all posts harvested was greater than the proportion of Kadian® ($\chi^2 = 1784$, $df = 1$, $P < 0.001$) and Vicodin posts ($\chi^2 = 871$, $df = 1$, $P < 0.001$), and the proportion of Vicodin® posts was greater than Kadian® ($\chi^2 = 911$, $df = 1$, $P < 0.001$).

Using the individuals' screen name as a personal identifier, we were able to examine the contribution of unique authors. In general, discussions of drugs seemed to reflect the contributions of a reasonably large number of individuals relative to the size of the discussion. For

TABLE 4. Comparisons of the Codes by Website

Website	Proportion of Drugs in Posts			Codes for all Posts Combined				
	OxyContin in Post (%)	Vicodin in Post	Kadian in Post	Abuse-related	Not Abuse-related	Encourages Abuse	Discourages Abuse	Both Encourages and Discourages
Site A	46.7	37.4	15.9*	74.8	24.3	58.9	26.2‡	9.3†
Site B	46.5	50.0	3.5*	86.0	14.0	67.4	52.3‡	30.2†
Site C	55.4	42.2	2.4*	75.9	24.1	60.2	55.4‡	30.1†

*$\chi^2 = 15.0$, $df = 2$, $P = 0.001$ (Site A > Site B and Site C).
†$\chi^2 = 20.6$, $df = 2$, $P < 0.001$ (Site A < Site B and Site C).
‡$\chi^2 = 16.5$, $df = 2$, $P < 0.001$ (Site A < Site B and Site C).

instance, the largest number of posts was about OxyContin®, and an average of 53% of posts (965/1813) was the result of unique contributors. For Vicodin®, the proportion was greater; an average of 68% posts (653/940) was by unique contributors. Finally, 78% of the posts (21/27) that addressed Kadian® resulted from a unique contributor. Although it is certainly possible for a single individual to have more than one screen name, it is at this point unclear the extent to which this is a serious source of error.

Role of Availability of Target Drugs

There is no agreement as to the most useful denominator for adjusting raw counts of abuse-related data with respect to pharmaceutical products.[20] Availability is often operationalized as prescriptions written or pills dispensed. Figure 3 presents the total mentions for each product adjusted by prescriptions written by month. The picture revealed is somewhat different than the raw totals presented above in Figure 2. Despite the greater numbers of OxyContin® raw mentions, these values are divided by the larger number of prescriptions written for OxyContin® each month.

Comparing these rates reveals that the rates of Kadian® mentions and posts to prescriptions are significantly lower than the rates for OxyContin® (for mentions $\chi^2 = 297.7$, $df = 1$, $P < 0.001$; for posts $\chi^2 = 115.1$, $df = 1$, $P < 0.001$) and Vicodin® (for mentions $\chi^2 = 477.2$, $df = 1$, $P < 0.001$; for posts $\chi^2 = 346.3$, $df = 1$, $P < 0.001$). However, OxyContin® achieved lower rates than Vicodin® (for mentions $\chi^2 = 174.3$, $df = 1$, $P < 0.001$; for posts $\chi^2 = 532.2$, $df = 1$, $P < 0.001$).

Another way to present these data is to calculate the average 6-month rate for target drug posts per 100,000 prescriptions written. For OxyContin®, there were 69.1 posts per 100,000 prescriptions written [95% confidence interval (CI) = 64.8-73.5], for Vicodin®, 169.5 posts per 100,000 prescriptions (95% CI = 158.7-181.1), whereas there were 11.2 Kadian® posts per 100,000 prescriptions (95% CI = 7.4-16.4). Thus, OxyContin® posts were 6.2 times more frequent per 100,000 prescriptions than Kadian® posts, whereas Vicodin® posts were 15.1 times more frequent per 100,000 prescriptions than Kadian® posts. Vicodin® posts were 2.5 times more frequent per 100,000 prescriptions than OxyContin® posts. (Data were available for pill quantity dispensed. However, the proportions of prescriptions and pill counts were almost identical among the 3 target drugs, making separate analyses uninformative.)

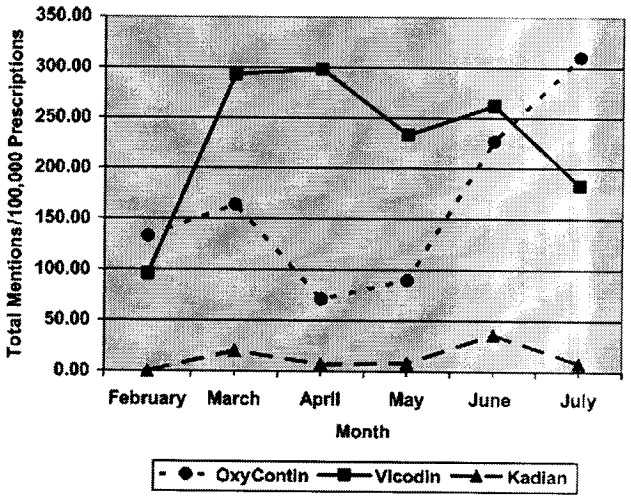

FIGURE 3. Total mentions of target drugs by month per 100,000 prescriptions, during calendar year 2005.

It is important to emphasize that these conclusions are dependent upon the choice of denominator. A case in point is our choice to compare brand name discussions on the Internet to branded prescription data. At the time of data collection, Kadian® and OxyContin® had no direct generic. However, Vicodin® does have generic versions and it is possible that people may use the term "Vicodin" to refer to any hydrocodone product. To examine the impact of changing the denominator, we recalculated the tests using all hydrocodone products at all dosages as the denominator. Inclusion of all hydrocodone products increased the number of prescriptions 88.5 times the number of Vicodin-only prescriptions. This large increase in denominator changed the proportion of Vicodin-related posts from the highest ratio to the lowest ratio. The rates of Vicodin dropped from 169.5 posts per 100,000 Vicodin-only prescriptions to a mere 1.9 posts per 100,000 Vicodin plus all hydrocodone prescriptions (95% CI = 1.8-2.0). Thus, the ratio of Vicodin® posts to Vicodin® plus all hydrocodone prescriptions was significantly less than rates of OxyContin® posts to OxyContin® prescriptions ($\chi^2 = 21{,}061.1$, $df = 1$, $P < 0.001$) and Kadian® posts to Kadian® prescriptions ($\chi^2 = 105.5$, $df = 1$, $P < 0.001$). It should be noted, however, that the generic term "hydrocodone" was not included in the search of related posts. This means that posts mentioning only "hydrocodone" or synonym would not have been identified, likely undercounting the number of relevant posts. Nevertheless, the enormous increase in the denominator due to generic prescriptions raises issues about the meaning of brand versus generic names to those who abuse substances, and comparability of rates of Internet chatter related to brand versus generic medications.

As a final note, the last 3 months in Figure 3 show a sharp increase in the proportion of OxyContin® mentions and posts relative to prescriptions figures. This reflects a drastic (54%) monthly decline in OxyContin® prescriptions written from April's prescription figures to July. However, there was no corresponding decline in Internet chatter regarding OxyContin®.

Analysis of Website Differences

Analyses of the websites revealed somewhat different patterns of discussion among the various websites. Site A contained much more absolute discussion of the target drugs than the other 2 sites. There was a significant difference between the websites in the number of total

posts dealing with the target drugs [$F_{(2,15)} = 38.4$, $P < 0.001$]. Site A's mean over the 6 months was 340.8 (SD = 106.6, 95% CI = 228.9-452.8) messages per month, which was significantly different from Site B's mean of 80.0 (SD = 27.3, 95% CI = 51.4-108.6) and Site C's mean of 41.2 (SD = 18.1, 95% CI = 22.1-60.2). Sites B and C were not different from each other.

The websites also differed in terms of overall site activity related to the target drugs. Analysis of posts dedicated to at least one of the 3 target drugs as a proportion of all harvested posts at each site revealed a significant difference among the sites [$F_{(2,15)} = 34.1$, $P < 0.001$]. In this analysis, Site B had the highest average percentage of posts dedicated to the target drugs with a mean over the 6 months of 0.15 (ie, 15% of all posts containing discussion of the target drugs; SD = 0.03, 95% CI = 0.11-0.19) which was significantly greater than Site A at 0.05 (5%; SD = 0.02, 95% CI = 0.03-0.06) and Site C's mean of 0.06 (6%; SD = 0.01, 95% CI = 0.05-0.07). Sites A and C were not different from each other.

DISCUSSION

This study presents an initial feasibility test of systematic methods for tracking Internet chatter of specific, potentially abusable pharmaceutical products. To our knowledge, this study represents the first attempt to apply systematic methods for collecting, sampling, and analyzing relevant Internet message posts. The ultimate goal of this work is to develop methods that will allow ongoing, continuous monitoring of Internet chatter of specific pharmaceutical products, as one component of multipronged prescription drug abuse-surveillance.

The systematic components of this study are inclusion criteria for the message boards monitored, systematic sampling of posts, creation of a reliable content analysis system designed to educe what is being said about the abuse potential of particular products, and using pharmaceutical marketing data to adjust for drug availability. This study supports the notion that these methods represent a feasible methodology for obtaining data that can potentially differentiate the level of chatter on the Internet vis-à-vis different analgesic products. However, as the discussion on denominators shows, the meaning of the different levels of chatter may be different depending on the denominator chosen to calculate rates. Which denominator proves to be most informative about societal drug abuse remains a question for future research.[20]

This system was applied to message board posts that discussed 3 drugs: Kadian®, OxyContin®, and Vicodin®. The content analysis procedure revealed a significant difference (uncorrected for multiple tests) between the percentage of OxyContin® and Kadian® posts coded as "endorsing abuse." Examination of the database of more than 48,000 posts revealed significant differences between the drugs regarding how often a product was mentioned, how many posts contained at least one mention of a product, and how these posts were related to availability. Kadian® had significantly fewer mentions and posts than either OxyContin® or Vicodin®, and OxyContin® had more than Vicodin®. Finally, it was shown that availability alone might not account for Internet chatter levels.

Internet monitoring has become part of comprehensive postmarketing surveillance.[1,5] There are several aspects of these message boards that raise the possibility that they may be important in the spread of interest in a particular pharmaceutical. For example, it is generally believed that most (over 50%) of those who visit online forums are "lurkers," individuals who frequently read message boards, but do not post messages.[21] Thus, the amount of discussion and what is said about a particular substance or product on these message boards may not only represent the views and interests of those who post messages, but may also influence the attitudes and interests of the lurkers. Although this is an untested hypothesis, current thinking on the dissemination of products and social trends generally supports this assumption. In Gladwell's explanation of how social "epidemics" spread, mavens are individuals who become aware of emerging social trends early, learn about the topic, and are effective in passing along the information.[22] In their field of interest, mavens are instrumental in moving an emerging social trend to the "tipping point," where it becomes an "epidemic." Regarding prescription drug abuse, one might hypothesize that the amount of chatter should correlate with a desire to use a particular substance. Although those who post on message boards may not be representative of ordinary consumers,[23] they may be important catalysts influencing the dissemination of social trends throughout their social group. Therefore, Internet monitoring may be useful in detecting emerging trends resulting from mavens posting information that is rapidly disseminated to lurkers and other potential abusers.

There are several important study limitations. Although Internet message boards used for analysis were selected according to prespecified inclusion criteria, they were not randomly sampled from a known pool of eligible websites. A sampling bias may exist in the differences between the norms, trends, and visitors on these websites versus others. Sampling websites on the Internet is notoriously difficult and was beyond the scope of this study. Aside from its enormous size (Google searches over 4 billion websites), many sites have little or no traffic.[11] Rather than attempting to develop a sample that can generalize to the entire Internet, this study focused on the feasibility of systematically monitoring Internet discussions that may relate meaningfully to real-world diversion and abuse. It is unclear how the potential sampling bias will influence the detected quantity and content of chatter vis-à-vis a given abusable prescription product. The message boards included in this study are different from each other regarding the amount and tone of discussion devoted to potentially abusable pharmaceutical products. These different patterns may reflect the larger missions of Sites A and C, which extend beyond drug use to other cultural phenomena (eg, movies, politics, pop culture). Site B is specifically about illicit drug use, which may account for the larger proportion of

posts devoted to the target drugs. Further research is needed to examine how message boards differ and what characteristics are relevant to monitoring sites for societal trends in abuse.

Another limitation is the unresolved question of whether contributors to Internet discussions are somehow representative of the larger population of recreational drug users. Although addressing this question was beyond the scope of this study, we and others who monitor the Internet to evaluate trends hypothesize that such message boards may serve as an "early warning system" of possible trends in drug use.[5] We had reason to believe that Kadian® would be of less interest to recreational abusers than the other products on the basis of the results of attractiveness for abuse studies and informal discussions with clinicians who treat opioid abuse. Results of the Internet chatter seem to be consistent with this view of "reality." However, the present study did not directly address this critical issue. Further research is needed to analyze this question, possibly by comparing Internet chatter with indicators of use/abuse prevalence such as government-collected data [eg, Drug Abuse Warning Network (DAWN) data], interviews with key informants, data collected at clinical sites, or other appropriate comparisons. Nor are we able to address the ultimate promise of Internet monitoring, namely anticipating popular trends and, in combination with other sources, confirming a signal.[1,5,24] In this sense, the magnitude of posts about a drug and their positive or negative valence, may not only be an indicator of current abuse trends, but also impact use by others (lurkers and those they talk with) who may seek out and perhaps prefer a particular drug.

Analyses of product availability used prescription (or pill count) marketing data as the denominator. We felt it was logical to use brand names only for the primary analysis to compare the target drugs. It is unknown how those who post on message boards differentiate brand names from generic. The name "Vicodin" may be used to describe any hydrocodone formulation. An exploratory analysis using total hydrocodone prescriptions resulted in changes in the relative position of "Vicodin" to the other 2 drugs with respect to its availability-adjusted rate of Internet chatter. Generic versions of extended-release OxyContin® have recently become available. Kadian® has no generic available, although generic versions of other extended-release morphine products are available. The impact of including or excluding generics may affect the conclusions drawn with respect to availability-adjusted rates of Internet mentions.

Examining chatter as a proportion of product availability raised other issues. The level of Internet chatter around Kadian® is virtually at a floor. Yet, the OxyContin® and Vicodin® marketing data had much greater prescription figures than Kadian®, and the ratio of Internet mentions/posts over total prescriptions may appear large for a product with few prescriptions. Virtually any level of Kadian® chatter might appear comparable to OxyContin® or Vicodin® chatter when the denominator is prescriptions written (or pills dispensed). When all hydrocodone prescriptions are included with Vicodin® prescriptions, the low level of Kadian® chatter yielded a significantly greater ratio of posts per 100,000 prescriptions than Vicodin®. At what near-0 level of Internet chatter would one consider the chatter of a potentially abusable pharmaceutical to be, in fact, "nearly zero?"

The converse was true for Vicodin®. When total hydrocodone prescriptions were used as the denominator, the Vicodin® ratio was lower than Kadian®, whereas the absolute amount of Internet posts about Vicodin® was nearly 35 times that of Kadian®. Thus, there may be availability (ie, prescription) figures that are so large that interpreting rates based on such figures reduces, rather than enhances, interpretability. The nature of the relationship between availability of a product and the associated Internet chatter is an empirical question that needs to be addressed. The present findings suggest that the level of chatter associated with the target drugs is not directly discernable from the availability data alone.

Further studies are needed to contextualize these preliminary study findings as well as to explore the nature and scope of other potential influences on Internet drug abuse chatter. For instance, it is largely unclear whether the extent and direction of media coverage influence on drug abuse discussions on the Internet. Additionally, future studies should compare Internet chatter regarding a variety of pharmaceutical products with abuse rates of these drugs detected by other data sources, such as data from emergency departments, poison control centers, substance abuse admissions, and arrests. Such comparisons would be important to more fully elucidate the relationship between Internet chatter and levels of drug abuse in the community.

This study represents a systematic approach to Internet monitoring that was determined to be feasible and to yield interesting and potentially important findings about the level of Internet chatter of the target products and the tone of messages that are posted about the target drugs. This study supports the feasibility of using Internet chatter for postmarketing surveillance; however, further research is needed to clarify the relationship between surveillance data and real-world abuse. This study also supports the growing awareness that prescription opioid products are not alike in their abuse potential, and that product-specific monitoring is necessary to generate an accurate picture of prescription drug abuse, and target risk management interventions. Providing reliable and timely Internet data to health, law enforcement, and community leaders may enable them to respond promptly and effectively to limit the potential damage when pharmaceutical agents become significant public health problems.

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