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Short communication

"I just wanted to tell you that loperamide WILL WORK": A web-based study of extra-medical use of loperamide

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ABSTRACT

Aims: Many websites provide a means for individuals to share their experiences and knowledge about different drugs. Such User-Generated Content (UGC) can be a rich data source to study emerging drug use practices and trends. This study examined UGC on extra-medical use of loperamide among illicit opioid users.
Methods: A website that allows for the free discussion of illicit drugs and is accessible for public viewing was selected for analysis. Web-forum posts were retrieved using web crawlers and retained in a local text database. The database was queried to extract posts with a mention of loperamide and relevant brand/slang terms. Over 1290 posts were identified. A random sample of 258 posts was coded using NVivo to identify intent, dosage, and side-effects of loperamide use.
Results: There has been an increase in discussions related to loperamide's use by non-medical opioid users, especially in 2010–2011 Loperamide was primarily discussed as a remedy to alleviate a broad range of opioid withdrawal symptoms, and was sometimes referred to as "poor man's" methadone. Typical doses ranged 70–100 mg per day, much higher than an indicated daily dose of 16 mg.
Conclusions: This study suggests that loperamide is being used extra-medically to self-treat opioid withdrawal symptoms. There is a growing demand among people who are opioid dependent for drugs to control withdrawal symptoms, and loperamide appears to fit that role. The study also highlights the potential of the Web as a "leading edge" data source in identifying emerging drug use practices.
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1. Introduction

To design effective prevention and policy measures, the substance abuse field requires timely and reliable information on new and emerging drug trends. Although existing epidemiological data systems, such as the National Survey on Drug Use and Health (NSDUH), the Community Epidemiology Work Group (CEWG), and the Drug Abuse Warning Network (DAWN), provide critically important data about drug abuse trends, they lag in time. Additional methods are needed to expand access to hard-to-reach populations and to enhance early identification of emerging trends.

There is an enormous amount of information available online about illicit drugs (Bogenschutz, 2000; Halpern and Pope, 2001; Boyer et al., 2001; Wax, 2002; Deluca et al., 2007; Nielsen and Barratt, 2009), and the World Wide Web has been identified as one of the "leading edge" data sources for detecting patterns and changes in drug trends, and as a useful tool for reaching hidden populations (Griffiths et al., 2000; Schifano et al., 2006; Butler et al., 2007, 2008; Murguia et al., 2007; Mounteney et al., 2010; Miller and Sonderlund, 2010). Many Web 2.0 empowered social platforms, including Web forums, provide a means for individuals to freely share their experiences, and post questions, comments, and opinions about different drugs. Such user-generated content (UGC) can be used as a very rich source of unsolicited, unfiltered and anonymous self-disclosures of drug use behaviors from hard-to-reach populations of illicit drug users (Boyer et al., 2001, 2005, 2007b; Boyer, 2004; Falck et al., 2004; Miller and Sonderlund, 2010; Lange et al., 2010). Prior studies have utilized such sources to explore a variety of topics within the drug abuse field. For example, by monitoring user discussions on a website that also facilitates online purchases of pharmaceutical opioids, Boyer et al. identified striking increases in the use of kratom to modulate opioid withdrawal symptoms (Boyer et al., 2007a). UGC has been also used to monitor the non-medical use of tramadol (Cicero et al., 1999), explore user

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Table 1
Content analysis of loperamide mentions in web-based posts ($N = 258$).

Intentions and reported efficacy of loperamide use	Number	Percent	Coder reliability	
			Percent agreement	Cohen's Kappa
Self-treatment of withdrawal symptoms	177	69%	95%	0.88
Positive views (79%)			90%	0.81
Negative or ambivalent views (21%)			89%	0.70
Use to get high or control pain (potential to cross blood–brain barrier)	65	25%	96%	0.86
Positive views (31%)			88%	0.54
Negative or ambivalent views (69%)			91%	0.78
Use to potentiate other opioids	7	27%	Low numbers to compute	
Use as indicated	6	23%	Low numbers to compute	
Other or undetermined	30	12%	Low numbers to compute	

endorsement of the illicit use of acetaminophen and hydrocodone, oxycodone and morphine sulfate ER (Butler et al., 2007), examine tampering methods for selected pharmaceutical products (Cone, 2006), and assess the effects of recreational use of salvia divinorum (Lange et al., 2010). Although there is a growing recognition that the web provides unprecedented opportunities for research across a wide range of topics within the drug abuse field, web-based studies and especially those that rely on UGC remain under-utilized (Miller and Sonderlund, 2010).

This study builds on interdisciplinary collaboration between researchers at the Center for Interventions, Treatment, and Addictions Research (CITAR), and the Ohio Center of Excellence in Knowledge-enabled Computing (Kno.e.sis). In 2011, the centers initiated an exploratory study to develop automated data collection and analysis tools to process web-based data on knowledge, attitudes, and behaviors related to the illicit use of buprenorphine and other pharmaceutical opioids.

In the process of developing techniques to automate the coding and analysis of web forum data on buprenorphine, we identified extensive web-based discussions about the extra-medical use of loperamide, a piperidine derivative that acts on opioid receptors in the intestine. It is approved by the U.S. Food and Drug Administration for the control of diarrhea symptoms. Because of its general inability to cross the blood–brain barrier, loperamide is considered to have no abuse potential and is therefore available without a prescription (Ericsson and Johnson, 1990). To date, little is known about the extra-medical use of loperamide among illicit opioid users. This content analysis study was designed to examine intentions of loperamide use as reflected in web-based discussions as well as dosage and side effects.

2. Methods

A website that allows for the free discussion of illicit drugs and is accessible for public viewing was selected for the study. Although the larger project included additional websites, this exploratory study of loperamide use was limited to a website that focused primarily on illicit opioid use, as opposed to other websites that focused on other types of drugs or were broader in scope. The selected website limits the number of active memberships at any given time period, but it has had over 2500 unique members since its inception in 2004. The web-forum posts were retrieved using web crawlers and retained in a local text corpus. All unique user names were anonymized. The corpus was queried to extract posts mentioning loperamide and relevant brand/slang terms, i.e., entity spotting. The application of computer science techniques allowed for the automation and rapid retrieval of relevant web-posts.

Over 1290 posts, covering a time period between 2005 and 2011, were identified and entered into an NVivo data base for manual coding. Because postings on the selected website are made anonymously and intended for public viewing, the University's Institutional Review Board determined the study to be exempt from the human subjects review.

A random sample of 258 (20%) posts was selected for content analysis. The study used the Complementary Explorative Data Analysis framework, which integrates qualitative and quantitative methods in content analysis of media communications (Sudweeks and Simoff, 1999). First, using a qualitative approach and preliminary "open" coding of a subset of posts, a coding scheme was developed. Next, the 258 posts were coded to identify the intent of loperamide use, information on reported dosage, and side-effects. Qualitative and quantitative approaches were used to make sense of the coded data and to discover temporal patterns of identified codes and themes.

Two formal reliability sub-samples were used. The first sub-sample included 129 randomly selected posts, representing 50% of the total sample. It was used to assess the coding of the broad themes related to user's intentions regarding their loperamide use. The second sub-sample included 75 posts and was used to assess coding reliability related to user opinions about effectiveness of loperamide in controlling withdrawal or producing euphoric effects. The second sub-sample was purposefully selected to ensure that a sufficient number of key characteristics were included in the reliability check. For example, since the incidence of posts indicating positive opinions about loperamide's potential to cross blood-brain barrier was relatively low, the randomly selected reliability subsample may have contained an insufficient number of such posts for a coder reliability assessment. After reviewing, clarifying and pre-testing coding rules, the reliability sub-samples were then independently coded by three coders (the first and second authors and a student research assistant). SPSS was used to calculate: (1) percentage agreement; and (2) Cohen's kappa, which takes into account chance correction when calculating inter-coder agreement. Kappa of 0.40–0.75 indicates acceptable and above 0.75 indicates excellent agreement (Neuendorf, 2009).

Table 2
Quotes on extra-medical use of loperamide from web-based posts.

Use to self-treat withdrawal symptoms:

"Back in the day when I would run out of pills early, I would take 8–10 lopermide tabs and get some pretty good relief from withdrawal."

"If you take a shitload of lope [loperamide] like 10–20 pills at once in withdrawal, you'll get relief from some of the physical symptoms. I'm not sure exactly how it works, but it's definitely more than just relieving the GI [gastro-intestinal] symptoms. I'm guessing if you just bombard your blood with it, some of it has to make it through? Not sure."

"Loperamide alone is enough to keep me well without being miserable, If I megadose."

"But I just wanted to tell you that loperamide WILL WORK. I take 105 mg of methadone per day, and recently have been running out early due to a renewed interest in IVing [intravenous use] that shit. 200 mg of lope (100 pills) will make me almost 100 [%] again. It brings the sickness down to the level of, say, a minor flu. Sleep returns, restlessness dissipates. Sometimes a mild 'opiation' is felt."

"So you just stick with it. Don't go and score big with your next paycheck. Overcome the need to make everything numb. Learn to live with normality for a while. It'll all seem worthwhile soon enough. Go for a walk. Get out of the house. Go grab some loperamide from the store, the desperate junky's methadone."

Use to get high:

Post A: "F. . . taking diarrhea medicine to get high! If it was possible to get high off lmodium it would be illegal like all the other good drugs. C'mon guys just go buy some real drugs and stop wasting your time. It ain't gonna work."

Reply to post A: "Man, don't be so negative. Are you going through WD [withdrawals]? Just because it's legal doesn't mean there's no potential. . . It doesn't hurt to try. . .."

Side-effects:

"I used to sing the praises of loperamide. . ..and still do, as a short term stand-by until you can score. Long term maintenance. . . it really wears you out, starts to feel "toxic" though I doubt it actually is toxic. . . After a few days I would get severely dehydrated because it makes me lose all thirst . . . my stomach feels like I took a strong stimulant, eating is basically impossible, constipation is surprisingly not bad but still there. . ."

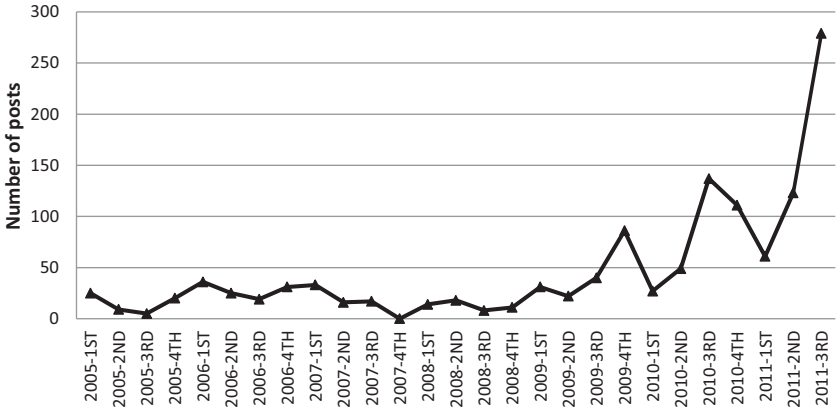

Fig. 1. Number of posts with loperamide mentions over time.

3. Results

The first post on loperamide use appeared in 2005, soon after the inception of the website in 2004. In 2010–2011, there was a notable increase in discussions related to loperamide (Fig. 1). Almost 70% of posts discussed loperamide as a remedy to self-treat opioid withdrawal symptoms. About 25% of the sample posts discussed issues related to loperamide's potential to cross blood–brain barrier to produce euphoric or analgesic effects. The remaining posts included a few mentions of its use as indicated, i.e., controlling diarrhea or its purported efficacy in potentiating the effects of other opioids (Table 1). The coder reliability assessment indicated acceptable to excellent agreement in relation to identifying the intent and effectiveness of loperamide use (Table 1).

Loperamide's use to "get high" was more commonly discussed in "theoretical" terms (Table 2). The majority of such posts expressed skeptical or ambivalent views regarding its potential to produce euphoria or analgesia (Table 1). In contrast, the majority of withdrawal-related mentions of loperamide were classified as endorsing its efficacy to control a broad range of withdrawal symptoms (Table 2). Only 20% expressed negative or ambivalent views regarding its effectiveness (Table 1). The majority reported using "megadoses" of loperamide, averaging 70 mg per day, and in some cases ranging from 100 mg to 200 mg per day (50–100 2 mg pills). These doses are significantly higher than an indicated dose of 16 mg per day (Table 2).

The most commonly discussed side effects of loperamide use were constipation, dehydration, and other types of gastrointestinal discomforts (Table 2). Some people also reported mild withdrawal symptoms from using loperamide for an extended period of time.

4. Conclusions

The study contains several limitations that are inherent to many web-based studies, such as a lack of demographic indictors, inconsistently available geographic information, drug use characteristics, and an inability to validate self-reported data. Further, it is difficult to determine the representativeness of the sample and the generalizability of study findings. Difficulty in obtaining a representative sample of illicit drug users is a universal problem in research with hidden and hard-to-reach populations such as illicit drug users (Carlson et al., 1994; Sloboda, 2005). Prior research has suggested that web forum participants may represent trend-setters, a group that is difficult to identify and recruit in community-based research (Butler et al., 2007; Boyer et al., 2007b) but very important to capture for identification of new developments in drug abuse epidemiology. Despite these limitations, this web-based study is among the first to describe patterns of extra-medical drug use of loperamide and self-treatment behaviors among illicit opioid users.

Web-based discussions about loperamide's use to self-treat withdrawal symptoms are significant in the context of research indicating rising rates of opioid dependence disorder but a general lack of participation in treatment programs among opioid users (McCabe et al., 2008). Our study adds new knowledge to the scant literature on self-care behaviors among opioid users (Boyer et al., 2007a; Monte et al., 2009; Daniulaityte et al., 2012) and suggests there is a growing demand among opioid users for accessible and affordable remedies to assist in their self-treatment efforts.

Most interestingly, the increase in loperamide-related discussions in the fall of 2010 coincides with the introduction of reformulated, tamper-resistant oxycodone tablets (Cicero et al., 2012). Although it is difficult to determine a clear relationship between these two events, prior studies have shown that introduction of tamper-resistant products contributed to the decreases of non-medical use of oxycodone, but was associated with increases in non-medical use of other opioids, including heroin (Cicero et al., 2012; DeVeaugh-Geiss et al., 2012; Coplan et al., 2012).

Although loperamide is a safe drug when used appropriately (Ericsson and Johnson, 1990; Fletcher et al., 1995; Litovitz et al., 1997), dangerous side effects, including respiratory depression and paralytic ileus, have been reported among young children (Friedli and Haenggeli, 1980; Marcovitch, 1980; Minton and Smith, 1987; Minton and Henry, 1990; Ahmad, 1992). Loperamide's toxicity has been linked to a high number of pediatric deaths in the developing countries where malnutrition is common, illiteracy rates are high, and access to appropriate medical supervision is poor (Bhutta and Tahir, 1990; Gussin, 1990; Minton and Henry, 1990; Bhutta and Balchin, 1996). Patterns of extra-medical use of loperamide (i.e., high dosage and prolonged use), as reflected in web-based discussions, warrant further attention as they might relate to adverse health consequences.

We recognize that our data are preliminary and our study population is selective. Nonetheless, these findings identify drug use behaviors that have not been reported in prior studies. The study highlights the importance of the web-based data for their "sensitivity" to new and emerging drug use practices. However, because of this "sensitivity," web-based data is also subject to "Type 1 error" of incorrectly identifying or overgeneralizing information on emerging drug use trends (Mounteney et al., 2010). Validity and generalizability of web-based findings can be improved by increasing the scope of web-based monitoring (a greater number and diversity of web-based sources), and by integrating multiple data collection methods, including survey research with community recruited samples (Mounteney et al., 2010; Griffiths et al., 2000). Although this study is largely based on manual coding, the

on-going development of our larger project will aim to incorporate leading-edge information processing techniques to facilitate automatic or semi-automatic knowledge discovery. These techniques will contribute to increased validity and generalizability by allowing effective processing of large amounts of web-based data.

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Contributors

R. Daniulaityte, A. Sheth, R. Falck, R. Carlson, and D. Cameron designed the study. D. Cameron, S. Perera, L. Chen, and A. Sheth developed Web crawlers and extracted information from web sites. R. Daniulaityte performed manual coding and analysis of selected posts, reviewed literature and wrote the first draft of the paper. R. Carlson contributed to coder reliability assessment. All authors reviewed, commented, and edited the manuscript. All authors contributed to and have approved the final manuscript.

Conflict of interest

All authors declare that there are no conflicts of interest.

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