Twitter-Based Detection of Illegal Online Sale of Prescription Opioid

Tim K. Mackey, PhD, MAS, Janani Kalyanam, PhD, MS, Takeo Katsuki, PhD, and Gert Lanckriet, PhD

Objectives. To deploy a methodology accurately identifying tweets marketing the illegal online sale of controlled substances.

Methods. We first collected tweets from the Twitter public application program interface stream filtered for prescription opioid keywords. We then used unsupervised machine learning (specifically, topic modeling) to identify topics associated with illegal online marketing and sales. Finally, we conducted Web forensic analyses to characterize different types of online vendors. We analyzed 619 937 tweets containing the keywords codeine, Percocet, fentanyl, Vicodin, Oxycontin, oxycodone, and hydrocodone over a 5-month period from June to November 2015.

Results. A total of 1778 tweets (<1%) were identified as marketing the sale of controlled substances online; 90% had imbedded hyperlinks, but only 46 were "live" at the time of the evaluation. Seven distinct URLs linked to Web sites marketing or illegally selling controlled substances online.

Conclusions. Our methodology can identify illegal online sale of prescription opioids from large volumes of tweets. Our results indicate that controlled substances are trafficked online via different strategies and vendors.

Public Health Implications. Our methodology can be used to identify illegal online sellers in criminal violation of the Ryan Haight Online Pharmacy Consumer Protection Act. (*Am J Public Health.* 2017;107:1910–1915. doi:10.2105/AJPH.2017.303994)

See also Bachhuber and Merchant, p. 1858.

In February 2001, an 18-year-old honors student from California died after purchasing Vicodin (hydrocodone/acetaminophen), a commonly abused prescription opioid drug, from a "no prescription" online pharmacy.[1] His name was Ryan Haight, and his untimely death led to passage of the 2008 Ryan Haight Online Pharmacy Consumer Protection Act (RHA; HR 6353), a federal law that amended the Controlled Substances Act (21 USC 801). The RHA was specifically designed to respond to the growing use of the Internet to illegally market and sell controlled substances directly to consumers.[1] More than 15 years later, nonmedical use of prescription medications is a national epidemic, with the US Centers for Disease Control and Prevention reporting that deaths attributable to prescription opioids have more than quadrupled since 1999.[2] This situation has prompted federal and state agencies to both reexamine and revise opioid-related policies and guidance.[2–5]

Policies aimed at curbing prescription opioid abuse have focused on establishing guidelines to prevent inappropriate prescribing, developing abuse deterrents, regulating "pill mills," and preventing drug diversion (such as through state prescription drug monitoring programs).[1,4,6,7] However, the role of the Internet and its continued promotion of prescription opioid abuse remains inadequately addressed despite the passage of the RHA. Specifically, Internet technology is now ubiquitous (e.g., 84% of American adults use the Internet and 65% use a social networking site), fueling the growth of dubious Internet pharmacy Web sites, now estimated in the tens of thousands globally.[8] In a recent report, the National Association of Boards of Pharmacy reviewed more than 11 000 Web sites and found that 96% were not in compliance with state and federal laws or the association's patient safety and pharmacy practice standards (e.g., they did not require valid prescriptions or issued prescriptions via online consultations or questionnaires only), including 13% that dispensed controlled substances.

Previous published studies (including investigative reports by the US Government Accountability Office showing that Oxycontin [oxycodone], Percocet [oxycodone/paracetamol], and Vicodin were successfully purchased from online pharmacies without a prescription) have confirmed the public health and patient safety dangers of illegal online sale of prescription opioids.[9–13] Also, recent studies have established an association between social media technologies and "no-prescription" online pharmacy drug promotion and access.[14–20] Hence, we sought to build on prior research by employing an innovative methodology involving "big data," machine learning, and Web forensic analyses to identify and characterize

ABOUT THE AUTHORS

Tim K. Mackey is with the Department of Anesthesiology and Department of Medicine, University of California, San Diego, and the Global Health Policy Institute, San Diego. Janani Kalyanam is with the Global Health Policy Institute and the Department of Electrical and Computer Engineering, University of California, San Diego. Takeo Katsuki is with the Kavli Institute for Brain and Mind, University of California, San Diego. Gert Lanckriet is with the Department of Electrical and Computer Engineering, University of California, San Diego.

Correspondence should be sent to Timothy Ken Mackey, PhD, MAS, Global Health Policy Institute, 8950 Villa La Jolla Drive, Suite A203, San Diego, CA 92037 (e-mail: tmackey@ucsd.edu). Reprints can be ordered at http://www.ajph.org by clicking the "Reprints" link.

This article was accepted July 7, 2017.

doi: 10.2105/AJPH.2017.303994

social media use by online pharmacies in their efforts to promote the illegal sale of prescription opioid drugs.

METHODS

We used a 3-step process (involving, as noted, cloud-based computing, machine learning, and Web content analyses) to identify and characterize illicit online vendors marketing the online sale of controlled substances via the popular microblogging site Twitter (which currently has 328 million active users as of the first quarter of 2017). With respect to data collection, we used the cloud-based Amazon Web Services to collect tweets through the Twitter public streaming application program interface (API).

Data Collection

In our first step, we used Amazon Web Services EC2 t2.micro virtual instances preconfigured with RStudio to collect large volumes of tweets filtered for prescription opioid keywords from the Twitter public streaming API, as detailed in a separate published study.[15] We used this strategy to maximize data collection and generate a corpus of tweets more generalizable to the full Twitter "firehose."[15] Our keywords consisted of a combination of international nonproprietary names and brand names of commonly abused prescription opioids (earlier studies had shown that these keywords are commonly used by online pharmacies for promotion purposes).[14,15] Our final list of keywords comprised codeine, fentanyl, hydrocodone, oxycodone, Oxycontin, Percocet, and Vicodin. Tweets were collected over a 6-month period from June to November 2015.

Data Coding

The second step involved the use of a machine learning protocol to isolate word groupings associated with tweets that mentioned marketing and purported sale of prescription opioid drugs. In coding and characterizing large volumes of Twitter data (in the hundreds of thousands), the application of machine learning is a critical strategy to achieve scale and complete analyses in a reasonable time frame (relative to manual annotation by human coders).[21,22] Specifically, unsupervised methods such as topic models have proven to be useful in obtaining a summary of the underlying themes present in large text corpora. We used a model called the Biterm Topic Model (BTM), which is designed to detect themes and patterns in the corpora of short texts (such as tweets). We had previously used this model to examine prescription drug abuse behavior and trends.[14,15]

The BTM first detected a preconfigured number of themes from the filtered data set of tweets containing the study prescription opioid keywords. This process produced a set of themes (or word groupings) that were then coded, via human annotation, to manually identify those clearly associated with prescription opioid marketing, distribution, or sale. For example, themes with a combination of words including "[prescription opioid drug name]," "buy," "cheap," "price," and "discount" (all identified as being used by online pharmacies) were identified and extracted for further analysis.[8,14,23] Themes containing words that were irrelevant (e.g., mentions of news reports, individual substance abuse behavior, or drug safety warnings from the Food and Drug Administration) were discarded along with their associated tweets and were not included in subsequent analyses. Tim K. Mackey and Janani Kalyanam coded the themes and achieved high intercoder reliabilities for the BTM word grouping inclusion criteria ($k = 0.98$).

Importantly, this methodology allowed us to use an unassisted machine learning algorithm to filter out hundreds of thousands of tweets unrelated to the study's objective and isolate tweets that specifically mentioned the marketing and sale of prescription opioid drugs (i.e., "signal" data). We then reviewed and characterized these tweets in our forensic examination.

Forensic Examination

In the third step, we performed content analyses by analyzing tweets from signal data. We focused our forensic Web analyses on tweets that included hyperlinks to external Web pages given our aim of identifying tweets actively promoting the online marketing and sale of prescription opioids directly to consumers (note that Twitter is not specifically an e-commerce platform but can include tweets that promote and link to external Web pages offering products for direct sale).

First, we reviewed each hyperlink to determine whether it was still "live" (i.e., whether there was a valid URL linked to an active Web page). We then discarded tweets with "dead" hyperlinks (i.e., URLs linked to inactive Web pages or broken hyperlinks). Second, we assessed the type of Web site associated with the hyperlink to determine whether it engaged in marketing of prescription opioid products or direct sale of prescription opioid drugs to consumers. For Web sites categorized as marketing prescription opioid drugs, we then examined Web page hyperlinks to determine whether any of them redirected to a site selling prescription opioid drugs.

For all Web sites categorized as selling prescription opioid drugs (via either a hyperlink directly embedded in a tweet or a hyperlink in an associated Web page), we then used 2 external databases to determine the site's legal classification and domain registration information. In assessing legal classifications, we used the Internet security monitoring company LegitScript LLC, which categorizes Internet pharmacy Web sites as "rogue" (vendors engaging in illegal, unsafe, or misleading activity), "unapproved" (vendors with regulatory compliance risks, such as those operating legally in one jurisdiction but not in others), "unverified" (vendors not subject to LegitScript review or monitoring), or "legitimate" (vendors adhering to LegitScript criteria).[15,24] In determining site domain registration information, we used a WHOIS lookup Web tool to identify a Web site's Internet Protocol (IP) address location and registry information.

Characteristics such as legal status and Web site domain name registration are important to identify given that, per US federal law and the RHA, the online sale or foreign importation of controlled substances is illegal and could constitute a federal criminal offense.

RESULTS

We collected and analyzed 619 937 tweets containing our selected prescription opioid drug keywords. Using the BTM machine learning protocol, we identified and annotated 1778 (0.003%) tweets as "signal" data containing content associated with illicit online drug sales (the percentage of relevant tweets ranged from 0% to 95%; Table 1). These results indicate that the absolute volume of tweets related to illegal promotion and sale of prescription opioid drugs is relatively small in comparison with Twitter communications related to other news, education, and behavioral aspects of prescription opioid drug abuse. For example, in our prior analysis of a larger prescription opioid data set, we detected several million tweets related to behavioral and risk trends via the BTM, including high volumes of polydrug abuse discussions.[14] A visual summary of our methods and main findings is provided in Figure 1.

In our examination of the signal data, we detected 1608 tweets with embedded hyperlinks; however, only 46 of these hyperlinks (consisting of 7 distinct URLs) were still "live" at the time of our June 2016 content analysis. An in-depth analysis of the 7 distinct URLs uncovered the presence of (1) 3 "rogue" online pharmacies; (2) 1 online pharmacy that could not be verified through LegitScript but directly sold controlled substances without a prescription; (3) 2 online pharmacies using blogs, social media, user forums, and affiliate marketing to sell prescription opioids; and (4) 1 online classified advertisement involving sale of controlled substances. Twitter accounts tweeting this content consisted of 3 primary categories: rogue online pharmacy Twitter accounts, user accounts used to retweet online pharmacy advertisements, and user accounts that retweeted but had no noticeable link to an online pharmacy.

A visual summary of our forensic analyses is provided in the Figures A and B (available as a supplement to the online version of this article at http://www.ajph.org), and a depiction of geographical IP addresses and Web site registrant addresses is provided in an interactive online Google map (see https://drive.google.com/open?id=13qnaNCAKlVJVOezTUObv3Szto1Q&usp=sharing).

Illicit Online Pharmacies

The first category involved tweets containing live hyperlinks to illicit online pharmacies classified as rogue (Figure A). One of the most active marketers was a rogue online pharmacy (example A in Figure A) marketing its services as an "online pharmacy shop" and "overseas online pharmacy" (with a Canadian IP location and a registrant address in Italy). The site exhibited the typical characteristics of an illegal online pharmacy, including the sale of prescription drugs from multiple categories, overseas delivery (with international money transfers directed to Pakistan), and sale without a valid prescription.[8,25] Importantly, the site's "pain relievers" product category advertised the direct sale of a host of controlled substances such as Percocet, Oxycontin, hydrocodone, Codogesic (codeine), and Vicodin.

Another identified rogue online pharmacy (located in Pakistan, with a US IP) marketed itself as the "World Most Trusted Health Care Online Mall" (example B in Figure A). The hyperlinks sent prospective consumers to its Web page offering the sale of codeine phosphate (a narcotic analgesic), and the site also advertised the sale of other prescription painkillers. The third online pharmacy characterized itself as a "Canadian Drugstore" (example C in Figure A), but its WHOIS information indicated an IP address in the United States and a registrant address in Pakistan. Although this site was categorized as rogue, we were unable to detect sale of controlled substances; however, other prescription drugs were sold without the need for a valid prescription.

A second category included a link to an online pharmacy (located in Pakistan, with a German IP) that was not listed in the LegitScript database (example D in Figure A) but offered the sale of several therapeutic classes of prescription drugs (including sleeping pills, antibiotics, injectable steroids, and growth hormones), a live customer service chat, discreet packaging, and sale without a prescription. The site included more than 30 different products in its "analgesics/pain relievers" category, including Percocet. The site also advertised the sale of other dangerous and powerful controlled substances such as morphine, Valium (diazepam), and ketamine.

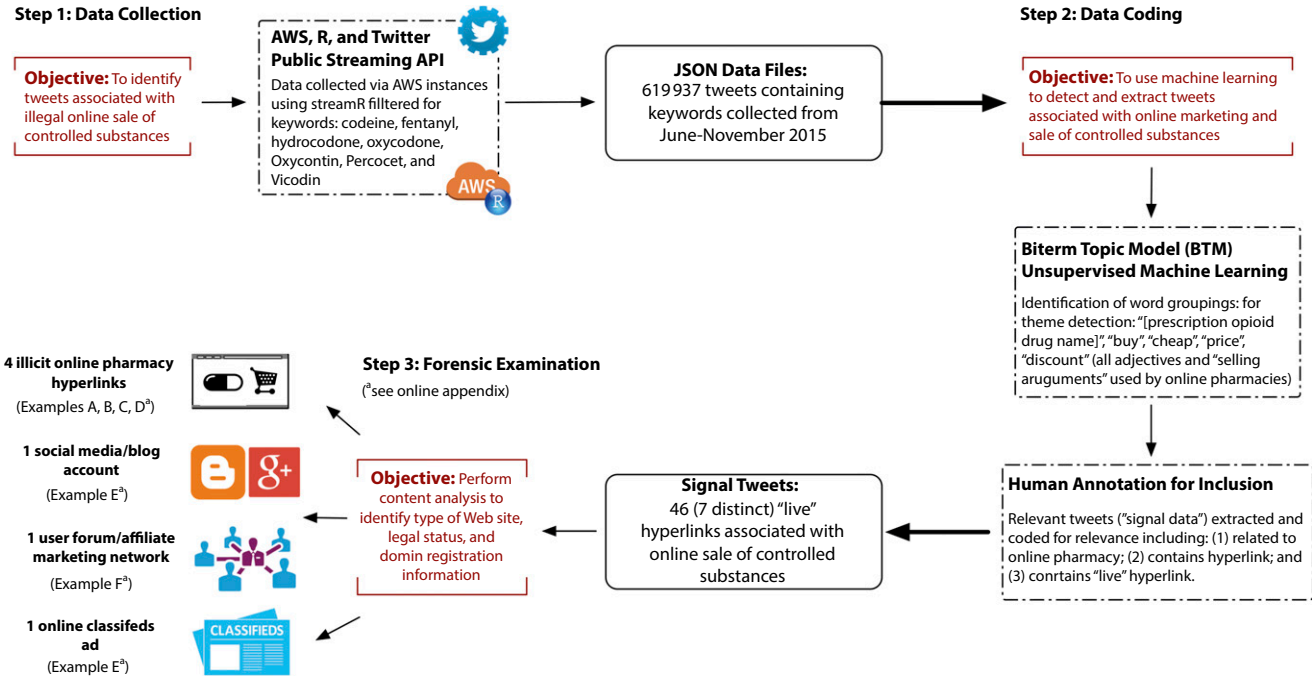
Blogs, Social Media, User Forums, and Affiliate Marketing

A third category included illicit online pharmacies that used Internet marketing strategies (Figure B). One rogue online pharmacy (located in Pakistan, with a Canadian IP) used the popular blogging platform blogspot.com (example E in Figure B) to post advertisements for Valium, Percocet, and other controlled substances without a prescription. The blog post included a hyperlink to the online pharmacy site and was advertised as "a safe website." It also used fake quality seals purporting that

TABLE 1—Summary of Twitter Analysis: Online Pharmacies Promoting Illegal Sale of Prescription Opioid Drugs, 2015

Drug Name	Total Tweets, No.	Most Correlated Tweets, No.	Relevant Tweets, %	Tweets With Links (Provided Tweet Is Relevant), %	Live Links, %	Distinct Links, No.
Codeine	431 625	874	48	68	3.1	2
Percocet	75 215	410	69	99	0.3	1
Fentanyl[a]	28 711	. . .	. . .	. . .	. . .	. . .
Vicodin	28 610	286	95	100	1.4	2
Oxycontin	27 734	465	59	99	2.9	2
Oxycodone	18 061	336	82	99	2.6	1
Hydrocodone	9 981	282	93	87	10.0	3

[a]We were not able to detect tweets correlated with illicit online pharmacy marketing through our Biterm Topic Model approach to content coding data.



Note. AWS = Amazon Web Services; API = application programming interface; JSON = JavaScript Object Notation.
[a]See Figures A and B, available as supplements to the online version of this article at http://www.ajph.org, for examples A–F.

FIGURE 1—Summary of Methodology and Main Findings: Study of Online Pharmacies Promoting Illegal Sale of Prescription Opioid Drugs, 2015

the site was a "best choice," a common marketing tactic for illicit online pharmacies.[8,25] In addition, the blog post embedded a link to the site's Google+ social media page and allowed users to tweet or favorite (via Facebook) the post promoting access to controlled substances.

A second tweet linked to a thread on a user forum associated with Indian music and advertising the sale of hydrocodone (example F in Figure B). The thread's advertisement redirected users to an affiliate marketing Web page (i.e., an online advertiser that collects fees for redirecting user traffic to e-commerce sites) that listed 10 additional hyperlinks, all advertising the sale of hydrocodone or other controlled substances "without prescription." Hyperlinks redirected users to 9 Web sites (7 rogue online pharmacies and 2 online pharmacies selling controlled substances without a prescription [but not listed in the LegitScript database]) and an additional affiliate marketer. Registrant addresses included Latvia, India, and the United States, with some registrant addresses protected by Web privacy services located in Russia and the Netherlands that anonymized registration information.

Other Online Sources

In addition, our Twitter surveillance detected an individual user advertising the "street" sale of controlled substances via an online classifieds Web site in the Hills District of Sydney, Australia (example G). The post advertised the sale of numerous controlled substances with no prescription required, express delivery, discreet packaging, and even door-to-door delivery services. Also, the site offered discounts for bulk purchases and directed prospective customers to submit an order via e-mail.

DISCUSSION

Our results indicate that a small percentage (< 1%) of tweets collected for a set of common prescription opioid analgesic product keywords were associated with online marketing or direct-to-consumer sale of controlled substances. Even though these tweets numbered only in the thousands, each tweet represents a potential patient safety hazard and substance abuse risk given that all of the Web sites associated with the tweets were categorized as "rogue" or were clearly involved in "no-prescription" sale of controlled substances, a direct violation of the RHA. Thus, it appears that Twitter represents a viable modality for criminal actors to engage in the illegal marketing and sale of prescription controlled substances online, despite laws in the United States and other countries specifically prohibiting these practices.[1,26,27]

Our study's methodology can also be adapted for other approaches aimed at detecting small volumes of Twitter discussions that may be associated with criminal health-related activities. This form of "anomaly detection" when mining large volumes of unstructured social media data is made possible through advances in machine learning such as the BTM. The targeted data generated from our "big data" strategy could also serve as an important digital tool for stakeholders (such as law enforcement personnel, drug regulators, and substance abuse researchers) actively engaged in the

fight against illegal online distribution and sale of controlled substances.

Collectively, the illegal online pharmacies assessed here used a variety of digital marketing strategies to promote their questionable products and services. The catalyst for online promotion began with Twitter and then expanded to the use of blogs, other social media platforms, user forums, fake "quality" seals, and even local online classified advertisements. These results indicate that online pharmacies may engage in multichannel digital marketing campaigns to reach consumers, including leveraging social media, as these communication forms are subject to lower standards of regulation and oversight than are Web search engines (e.g., in 2011, Google settled with the US Department of Justice for $500 million in connection with knowingly advertising no-prescription online pharmacies that sold Oxycontin and Ritalin [methylphenidate] and has since taken corrective action).[8,28]

In addition, we discovered through our Web forensic analyses that the majority of sites had non-US registrant addresses, with many linked to Pakistan. This is alarming given news reports that have identified Pakistan as both a source and an exporter of fake, counterfeit, and falsified medications, including via online sales.[29] Recently there have been at least 2 separate criminal convictions of Pakistani nationals arrested for distribution of illicit controlled substances to Internet consumers.[30,31] One of these indictments involved a Pakistani national who allegedly used Internet Web site ads and filled orders for other Internet pharmacy sites to illegally import, distribute, and sell prescription drugs sourced from Pakistan, India, and China (including unapproved versions of the controlled substances phentermine, diazepam, alprazolam, and lorazepam).[30] Hence, in addition to the risk of dependence, abuse, overdose, and possible death, our analysis indicates that these Pakistan-affiliated sites may present a separate safety risk of exposing the public to fake versions of medications.[32–34]

Limitations

There are limitations regarding the generalizability of our study results. For example, we did not begin the process of content coding data for illicit online pharmacy themes and hyperlinks until approximately 8 months after we completed Twitter data collection. This was primarily attributable to our efforts to first examine prescription drug abuse behavior as detailed in our previously published study using the BTM.[14] This delay probably resulted in a higher percentage of signal data with "dead" hyperlinks, suggesting that our methodology is most effective when used with real-time data as opposed to retrospective data.

Also, we did not examine non–English-language tweets (75 619 non-English tweets, accounting for approximately 11% of our entire prefiltered data set, were collected but discarded in our preanalysis data cleaning process). In addition, hyperlinks that redirected to live Web sites were reviewed for content at a specific point in time after tweets had been collected. Hence, it is possible that the content provided on the online pharmacies we reviewed changed between the time of data collection and the content analysis process. We addressed this limitation by reviewing active Web page links (at the time of our content analysis) and links to pages cached in Google search engine results. We did not detect any noticeable differences when both live and cached pages were available and compared.

Also, registrant addresses collected during forensic analyses are of dubious validity. In some cases, the registrant address fields did not match valid geographic locations or involved mismatching data (e.g., a listed address in Pennsylvania but a listed zip code in Arizona). Finally, because of the illegal nature of the transactions identified, we could not purchase controlled substances and test them for authenticity and potency. The practice of buying prescription drugs for a fictional patient and making payments to an illicit online pharmacy raises serious ethical and legal challenges and is generally considered illegal by the US Drug Enforcement Agency (DEA).

Public Health Implications

We have described an innovative methodology for filtering large volumes of Twitter content to specifically isolate tweets promoting the illegal online sale of controlled substances, an activity contributing to the current national prescription drug abuse epidemic. The methodology also has the potential to be used for surveillance and detection of other health-related illegal online activities, including the promotion and online sale of illicit and synthetic drugs.[35] As evidenced by our findings, extremely questionable vendors are advertising highly addictive controlled substances and selling them directly to consumers via Twitter without the necessary oversight of a clinician, regulatory agency, or state public health or law enforcement agency. At the time of the completion of our study, the "rogue" Web sites we identified remained active online, continuing to place the public at risk.

Crucially, the unregulated online sale of controlled substances to US consumers is a direct violation of federal law under the RHA. Hence, our methodology can be useful in surveillance efforts, with violating Web sites reported directly to the DEA and the Food and Drug Administration for additional enforcement action (including through the Food and Drug Administration's BeSafeRx Web site, the DEA's reporting form for suspicious online pharmacies, and the requirement that US-based Internet service providers remove illegal content or issue cease and desist letters).

Our methodology can also help ensure that the RHA is better implemented, monitored, and enforced in a constantly evolving digital environment in which social media use is becoming ubiquitous in a broad range of Internet-using populations, including young people susceptible to substance abuse.[1] Improved RHA monitoring and enforcement could better protect the Ryan Haights of the present and future from the dangers of "digital" substance abuse and addiction to prescription painkillers. AJPH

CONTRIBUTORS

T. K. Mackey and J. Kalyanam conducted the data analyses and wrote the initial draft of the article. T. K. Mackey and T. Katsuki collected the data for the study. T. K. Mackey, J. Kalyanam, and G. Lanckriet designed the study. All of the authors contributed to the formulation, drafting, and completion of the article.

ACKNOWLEDGMENTS

Tim K. Mackey and Takeo Katsuki received funding for the data collection phase of this project from the Alliance for Safe Online Pharmacies (ASOP), a social

welfare organization addressing the issue of illicit online pharmacies. We greatly acknowledge this support.

Note. Tim K. Mackey is a noncompensated member of the ASOP academic advisory panel, and (as noted) both Mackey and Takeo Katsuki received funding for this study from ASOP through a pilot research grant exploring online prescription drug abuse risks. The funder had no role or input in the study.

HUMAN PARTICIPANT PROTECTION

No protocol approval was needed for this study because publicly available data were used.

REFERENCES

1. Mackey TK, Liang BA, Strathdee SA. Digital social media, youth, and nonmedical use of prescription drugs: the need for reform. *J Med Internet Res*. 2013;15(7):e143.

2. Centers for Disease Control and Prevention. Understanding the epidemic. Available at: https://www.cdc.gov/drugoverdose/epidemic/index.html. Accessed August 6, 2017.

3. Volkow ND, McLellan AT. Opioid abuse in chronic pain—misconceptions and mitigation strategies. *N Engl J Med*. 2016;374(13):1253–1263.

4. Frieden TR, Houry D. Reducing the risks of relief—the CDC opioid-prescribing guideline. *N Engl J Med*. 2016;374(16):1501–1504.

5. Meldrum ML. The ongoing opioid prescription epidemic: historical context. *Am J Public Health*. 2016;106(8):1365–1366.

6. Kattan JA, Tuazon E, Paone D, et al. Public health detailing—a successful strategy to promote judicious opioid analgesic prescribing. *Am J Public Health*. 2016;106(8):1430–1438.

7. Kennedy-Hendricks A, Richey M, McGinty EE, Stuart EA, Barry CL, Webster DW. Opioid overdose deaths and Florida's crackdown on pill mills. *Am J Public Health*. 2016;106(2):291–297.

8. Mackey TK, Nayyar G. Digital danger: a review of the global public health, patient safety and cybersecurity threats posed by illicit online pharmacies. *Br Med Bull*. 2016;118(1):110–126.

9. Bachhuber MA, Cunningham CO. Availability of buprenorphine on the Internet for purchase without a prescription. *Drug Alcohol Depend*. 2012;130(1–3):238–240.

10. Boyer EW, Wines JD. Impact of Internet pharmacy regulation on opioid analgesic availability. *J Stud Alcohol Drugs*. 2008;69(5):703–708.

11. Forman RF. Availability of opioids on the Internet. *JAMA*. 2003;290(7):889.

12. Forman RF, Woody GE, McLellan T, Lynch KG. The availability of Web sites offering to sell opioid medications without prescriptions. *Am J Psychiatry*. 2006;163(7):1233–1238.

13. US Government Accountability Office. Internet pharmacies: federal agencies and states face challenges combating rogue sites. Available at: http://www.gao.gov/assets/660/655751.pdf. Accessed August 6, 2017.

14. Kalyanam J, Katsuki T, Lanckriet G, Mackey TK. Exploring trends of nonmedical use of prescription drugs and polydrug abuse in the Twittersphere using unsupervised machine learning. *Addict Behav*. 2017;65:289–295.

15. Katsuki T, Mackey TK, Cuomo R. Establishing a link between prescription drug abuse and illicit online pharmacies: analysis of Twitter data. *J Med Internet Res*. 2015;17(12):e280.

16. Hanson CL, Cannon B, Burton S, Giraud-Carrier C. An exploration of social circles and prescription drug abuse through Twitter. *J Med Internet Res*. 2013;15(9):e189.

17. Hanson CL, Burton SH, Giraud-Carrier C, West JH, Barnes MD, Hansen B. Tweaking and tweeting: exploring Twitter for nonmedical use of a psychostimulant drug (Adderall) among college students. *J Med Internet Res*. 2013;15(4):e62.

18. Liang BA, Mackey T. Direct-to-consumer advertising with interactive Internet media: global regulation and public health issues. *JAMA*. 2011;305(8):824–825.

19. Mackey TK. Global reach of direct-to-consumer advertising using social media for illicit online drug sales. *J Med Internet Res*. 2013;15(5):e105.

20. Liang BA, Mackey TK. Prevalence and global health implications of social media in direct-to-consumer drug advertising. *J Med Internet Res*. 2011;13(3):e64.

21. Yoon S, Elhadad N, Bakken S. A practical approach for content mining of tweets. *Am J Prev Med*. 2013;45(1):122–129.

22. Cole-Lewis H, Varghese A, Sanders A, Schwarz M, Pugatch J, Augustson E. Assessing electronic cigarette-related tweets for sentiment and content using supervised machine learning. *J Med Internet Res*. 2015;17(8):e208.

23. Orizio G, Rubinelli S, Schulz PJ, et al. "Save 30% if you buy today": online pharmacies and the enhancement of peripheral thinking in consumers. *Pharmacoepidemiol Drug Saf*. 2010;19(9):970–976.

24. Mackey TK, Aung P, Liang BA. Illicit Internet availability of drugs subject to recall and patient safety consequences. *Int J Clin Pharm*. 2015;37(6):1076–1085.

25. Orizio G, Merla A, Schulz PJ, Gelatti U. Quality of online pharmacies and Websites selling prescription drugs: a systematic review. *J Med Internet Res*. 2011;13(3):e74.

26. Liang BA, Mackey T. Searching for safety: addressing search engine, Website, and provider accountability for illicit online drug sales. *Am J Law Med*. 2009;35(1):125–184.

27. World Health Organization. Safety and security on the Internet: challenges and advances in member states. Available at: http://www.who.int/goe/publications/goe_security_web.pdf. Accessed August 6, 2017.

28. US Department of Justice. Google forfeits $500 million generated by online ads and prescription drug sales by Canadian online pharmacies. Available at: http://www.justice.gov/opa/pr/2011/August/11-dag-1078.html. Accessed August 6, 2017.

29. Somra G. The backstreet labs feeding Pakistan's fake drug trade. Available at: http://www.cnn.com/2015/08/30/asia/pakistan-fake-drugs/index.html. Accessed August 6, 2017.

30. US Immigration and Customs Enforcement. Pakistani man indicted and arrested for selling and distributing new, misbranded, and counterfeit prescription drugs. Available at: https://www.ice.gov/news/releases/pakistani-man-indicted-and-arrested-selling-and-distributing-new-misbranded-and. Accessed August 6, 2017.

31. US Department of Justice. Pakistani national sentenced in international counterfeit drug conspiracy. Available at: https://www.justice.gov/usao-edtx/pr/pakistani-national-sentenced-international-counterfeit-drug-conspiracy. Accessed August 6, 2017.

32. Mackey TK, Liang BA. The global counterfeit drug trade: patient safety and public health risks. *J Pharm Sci*. 2011;100(11):4571–4579.

33. Attaran A, Barry D, Basheer S, et al. How to achieve international action on falsified and substandard medicines. *BMJ*. 2012;345:e7381.

34. Braden JB, Edlund MJ, Sullivan MD. Suicide deaths with opioid poisoning in the United States: 1999–2014. *Am J Public Health*. 2017;107(3):421–426.

35. Tofighi B, Lee JD. Internet highs—seizures after consumption of synthetic cannabinoids purchased online. *J Addict Med*. 2012;6(3):240–241.