

# New Frontiers in Safety Surveillance

John Brownstein, PhD

Associate Professor  
Harvard Medical School

Chief Innovation Officer  
Boston Children's Hospital



@johnbrownstein



# Digital Phenotype



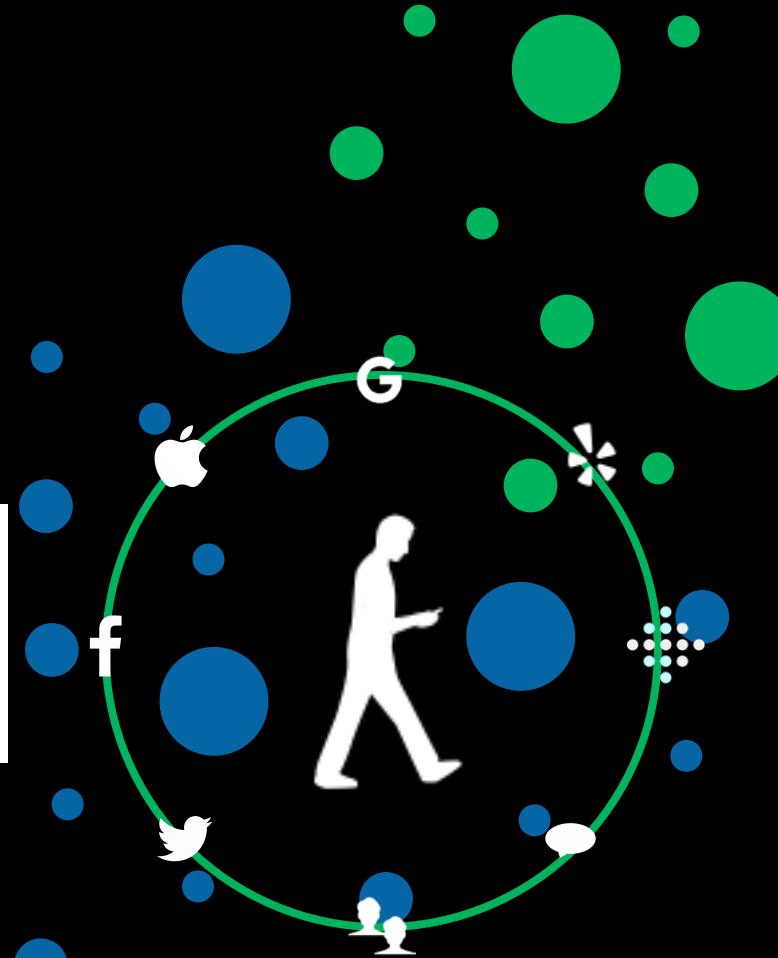
# Digital Phenotype



**IG-CaramelBomBBB** @caramelbombbb  
I need my Ambien back:( I can't sleep to save my life!  
9 months ago Reply Retweet Favorite

**Mac** @rbhaze\_  
Grandma gave me some Percocet for my pain. She came clutch  
10 months ago Reply Retweet Favorite

Drug diversion & abuse







Digital disease detection picks up early signals

Traditional public health monitoring



Distribution of Disease

# Medicine Use

## Negative Reaction

Patients ~~suspect~~ report bad reactions because they ~~don't know they should~~.

Require medical attention

We can amplify their voices by *meeting patients where they are at* and ~~filtering out noise~~.



Reported

Verified

# Vernacular-to-Regulatory Translation



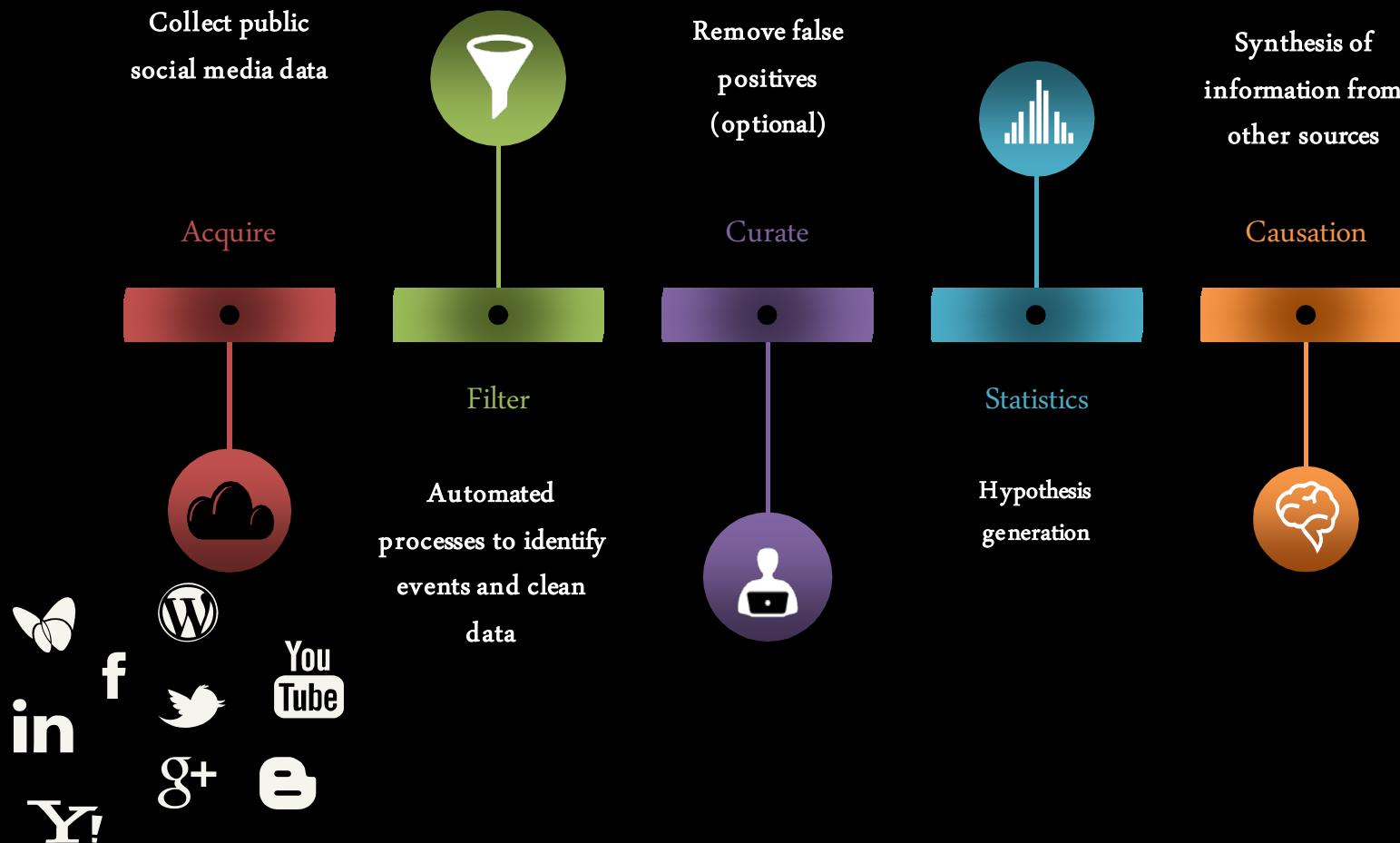


MEDWATCHERSOCIAL



FDA-sponsored social media monitoring platform

# Data Flow for MedWatcher Social



visual snow dont want to eat cross vision lost my appetite  
apetite surpressed googley eyed no appetitey doublevision  
blind appetite is nonexistent blurry vision miss feeling hung  
nnorexic double vision #notevenhungry blindness cant eat  
uldn't see making me eat like a mouse vision change blurry  
st appetite lost their eyesight didn't get hungry seeing doub  
can't eat killed my apetite googly eyed lost teh appetite  
lost apetite crosseyed killed my appetite seeing weird cou  
cross eyed seeing weird colour stomach small changes in vis  
lack of apetite never want to eat seeing weird color never h

# Typos

visual snow dont want to eat  
apetite surpressed googley eyed  
blind appetite is nonexistent  
anorexic double vision #notevenhungry  
uldn't see making me eat like a mouse  
st appetite lost their eyesight  
can't eat killed my apetite googly eyed  
lost apetite crosseyed killed my appetite  
cross eyed seeing weird colour  
lack of apetite never want to eat  
Visual impairment

MedDRA 10047571

Visual impairment  
SNOMED 397540003

cross vision lost my appetite  
blurry vision miss feeling hungry  
blindness cant eat  
vision change blurry  
didn't get hungry seeing double  
lost teh appetite  
seeing weird colour  
small changes in vision  
seeing weird color  
Decreased appetite

MedDRA 10061428

Loss of appetite  
SNOMED 79890006

PROS

CONS

PROS

CONS



Mar 23

**Xanax and Hydrocodone** is like having a **blackout** without the drinking and the hangover

[Expand](#)

[Reply](#) [Retweet](#) [Favorite](#) [More](#)

15

0

37

15

2

0

1

1

44

55

4

5

0

0

0

0

0

4

0

0

1

4

0

0

27

113

1

6

0

0



Mar 23

Xanax and Hydrocodone is like having a **blackout** without the drinking and the hangover

Expand

Reply Retweet Favorite More



All Products »

## Select A Product

Filter by product name

Filters

Posts

Product Stats

View

John

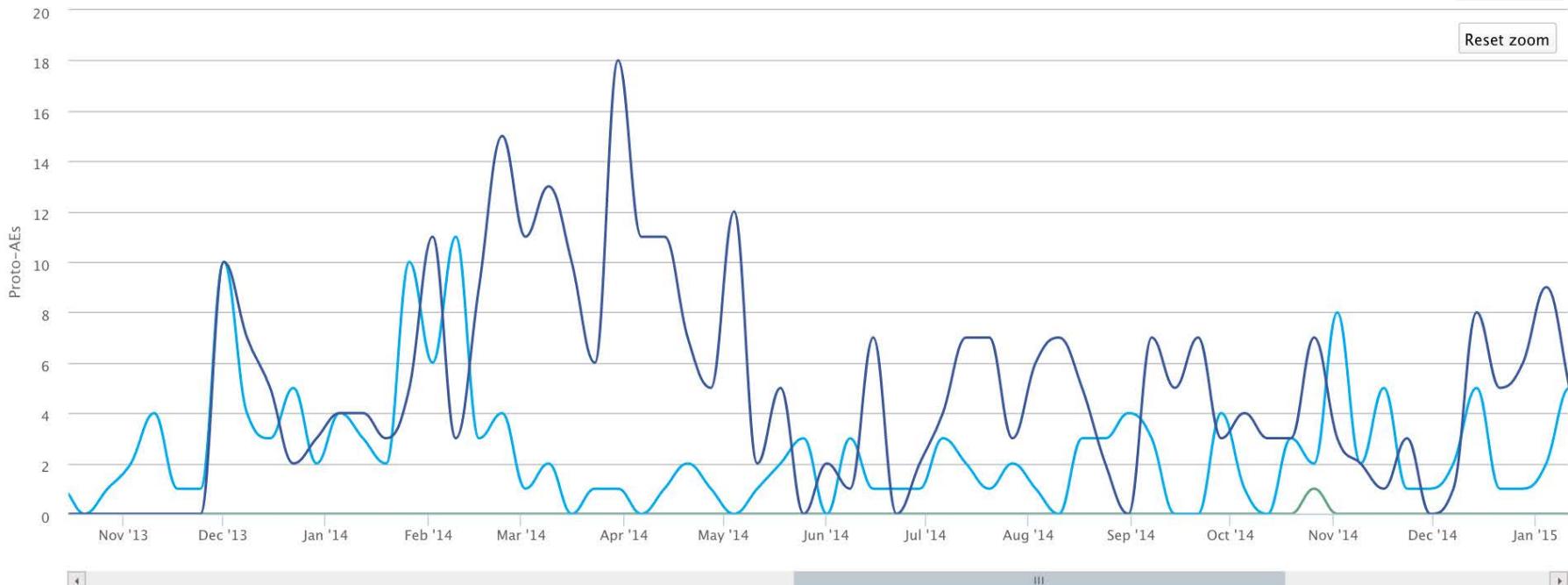


## Proto-AEs

per week

Facebook —  
Twitter —  
Forums —

Reset zoom



**Twitter** ⓘ  
266 Proto-AEs  
5918 Mentions

**Facebook** ⓘ  
375 Proto-AEs  
7747 Mentions

**Forums** ⓘ  
1 Proto-AEs  
3 Mentions

642 Proto-AEs, 13668 Mentions found ([View attrition](#))

— since Jan 1 2012

59,429,028 total posts in DB  
Latest post on Sep 14, 2015 @ 03:13pm

[View System Stats](#)

# System Performance

57M



Posts mentioning  
medical products

380k



Manually classified to  
identify AEs

68%



Precision

-

Positive predictive  
value

88%

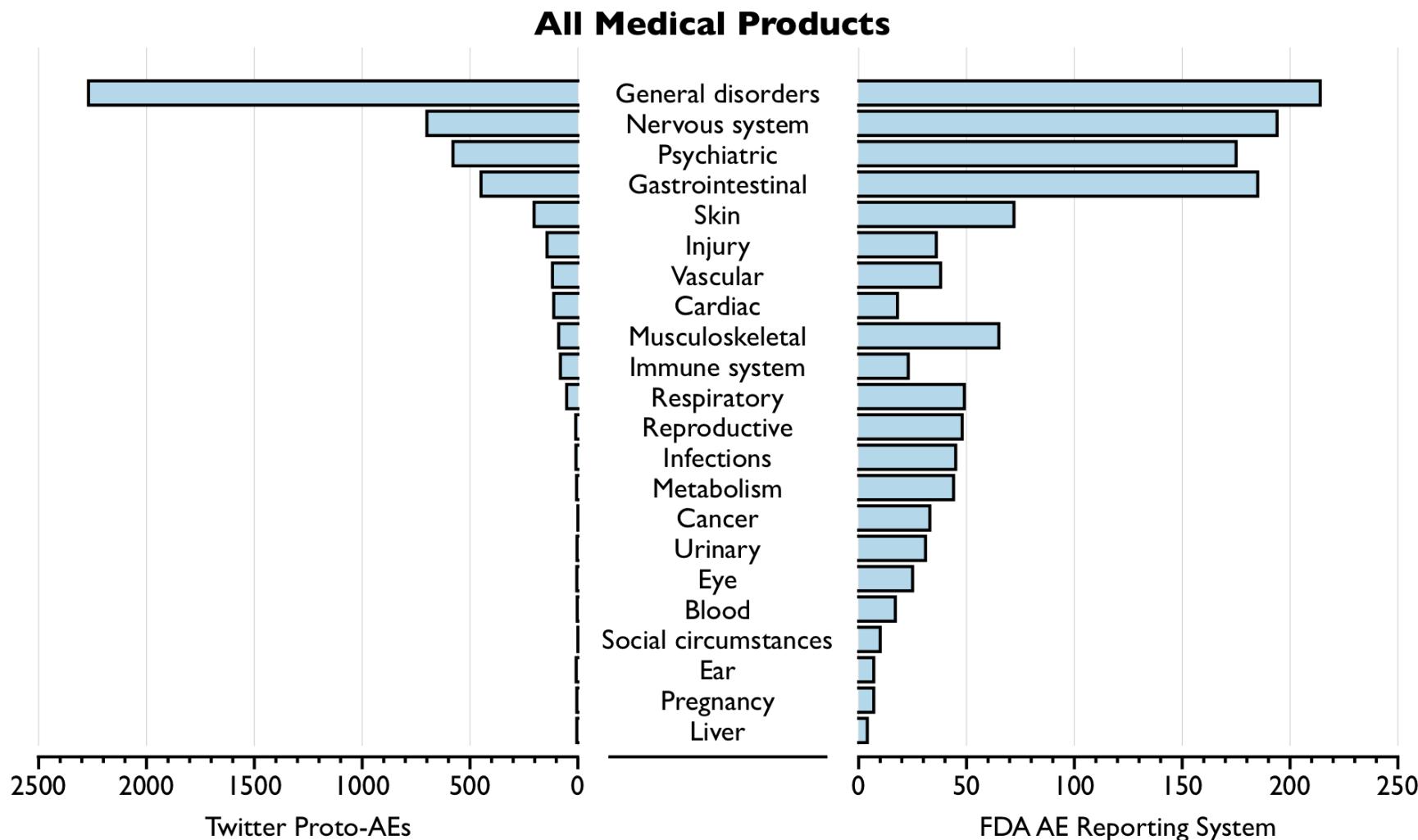


Recall

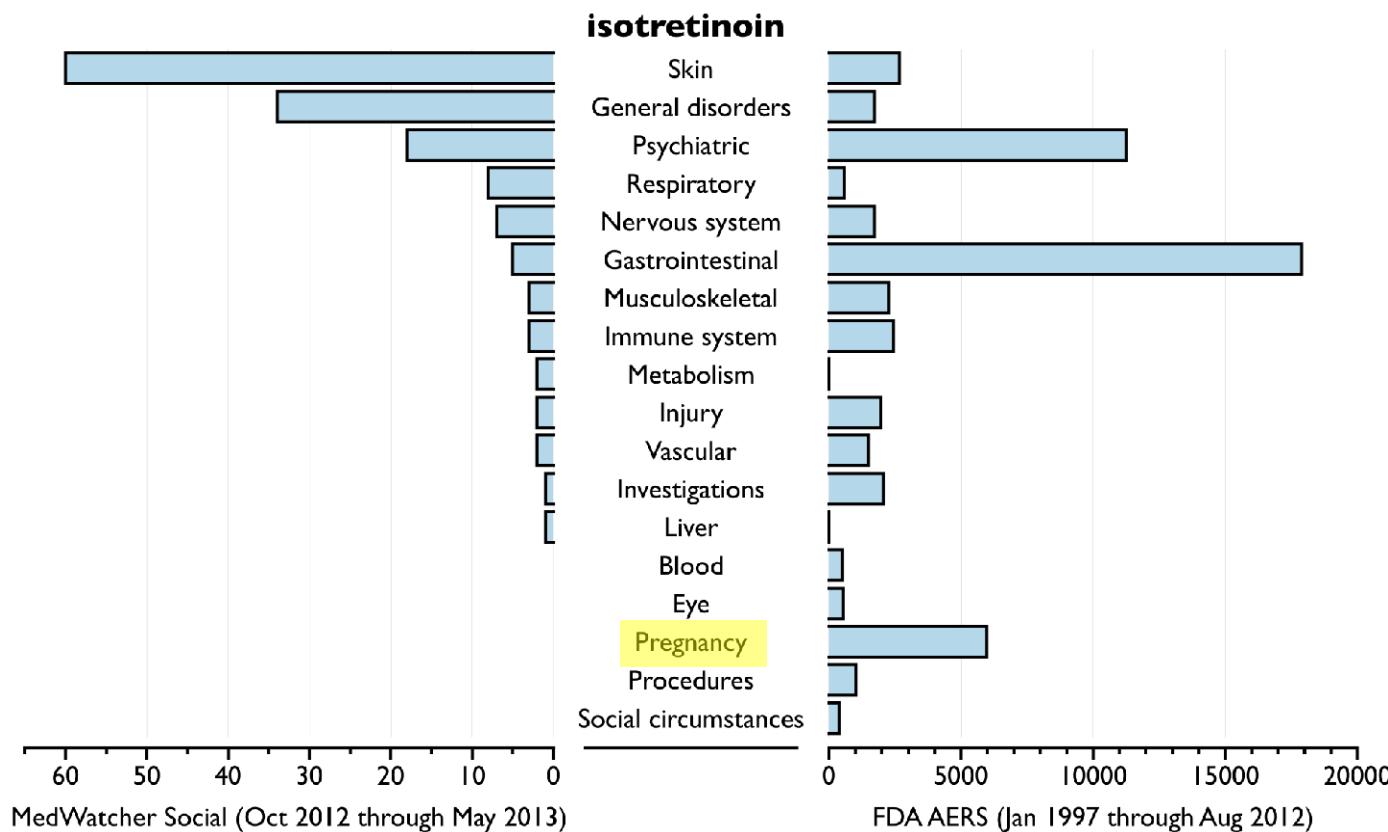
-

Sensitivity

# Overall Association



# Isotretinoin (Accutane) for Acne



- Accutane + tanning isn't a good combination. My lips are SO chapped. #accutaneprobz
- this hair loss is seriouly scaring me im going to stop accutane right now bye
- My liver is keeping me up again. :( I'm probably going to be babying it for the rest of my life after accutane gave me hepatitis. No fun.
- having to put vaseline on your eyelids because they are so dry and hurt so bad <<<< #accutane #accutaneprobz

# KNOWN FREQUENCY ADVERSE EVENTS

## Medicine Guide

Preferred terms appearing in social media and not appearing



**10** VERY COMMON  
decreased blood sugar levels, diarrhoea, nausea

**100** COMMON  
bronchitis, constipation, abdominal distension, faster heart rate, feeling dizzy, flatulence, gastritis, gastro-oesophageal reflux, headaches, indigestion, inflammation of nose/throat, injection site problems, loss of appetite, antibodies to Victoza, skin rash, stomach pain, tiredness, toothache, vomiting

**1k** UNCOMMON  
dehydration, malaise, itching, kidney problems, urticaria

**10k** RARE / VERY RARE  
anaphylaxis, angioedema, GI problems; pancreatitis, hypersensitivity

## SOURCE

emc+ Medicine Guide, Jan 16, 2015, Datapharm  
[medicines.org.uk](http://medicines.org.uk)

## Original Research Article

# Digital Drug Safety Surveillance: Monitoring Pharmaceutical Products in Twitter

Clark C. Freifeld<sup>1, 2</sup>, John S. Brownstein<sup>2, 3, 4</sup>, Christopher M. Menone<sup>5</sup>, Wenjie Bao<sup>5</sup>, Ross Filice<sup>6</sup>,  
Taha Kass-Hout<sup>7</sup> and Nabarun Dasgupta<sup>5, 8, 9</sup> 

- (1) Department of Biomedical Engineering, Boston University, Boston, USA
- (2) Children's Hospital Informatics Program, Boston Children's Hospital, Boston, USA
- (3) Department of Pediatrics, Harvard Medical School, Boston, USA
- (4) Center for Biomedical Informatics, Harvard Medical School, Boston, USA
- (5) Epidemico, Inc., Boston, USA
- (6) Georgetown University Medical Center, Washington, DC, USA
- (7) US Food and Drug Administration (FDA), Silver Spring, USA
- (8) University of North Carolina at Chapel Hill, Chapel Hill, 27599, USA
- (9) 266 Newbury Street, 2nd Floor, Boston, MA 02116, USA

IN THEIR OWN WORDS

---

“@user I just restarted taking victoza which made me so sick to my stomach till my body got used to it.

Twitter, May 3, 2014

Aside from the nausea (worse today) and occasional bouts of hypoglycemia (better today), four days on Victoza and down 5.3 lbs! Amazing!

Facebook, December 9, 2014

# Typical Proto-AEs

# & Patient Benefits

Anyone else having issues with **plugger jamming** on their **flex pen** of victoza?  
The only difference I see is the new needles . I had to stick myself 4 times today to get almost a full dose. Frustration. Doesn't seem related to where I am into pen, first dose, midway , last. **Third pen this has happened on in a row**

Facebook, December 9, 2014

# Product Quality Issues

## IN THEIR OWN WORDS

---

I have 2 boxes of victoza  
insulin pens if interested  
inbox for more information

Facebook, February 3, 2015

Please, if anybody is on  
Victoza for diabetes or insulin  
resistance < i ordered too  
much stock and it is non  
returnable being a fridge item  
> please pop in at [redacted]  
pharmacy .....will organise a  
good price to compensate for  
my blunder.

Facebook, February 27, 2015

# Diversion & Re-Sale

IN THEIR OWN WORDS

---

Just bought 4 Victoza pens  
from my pharmacy (CVS).  
\$800 out of pocket. Uggg. :(

Facebook, February 6, 2015

# Product Pricing

Had my first injection of Victoza. So if it doesn't kill me from one of side effects my sugar should stabilize. One side effect is puzzling. "For type 2 Diabetics only. Not intended for type 1 diabetics". I'm the poster child for type 1 Diabetics.

Facebook, February 6, 2015

# Off-label Use

# Engaging users directly

Dragonnncaaaaaaaaaat~  
@drgncat

Follow

Also my kidneys have been swollen ever since I've been on Viibryd.. but its also been super hot out..

Reply Retweet Favorite More

4:37 PM - 24 Jun 13

MedWatcher @medWatcher

@drgncat -- noticed you're having an issue with Viibryd. @medWatcher invites you to notify the @US\_FDA: tinyurl.com/ldclek3

Details Reply Retweet Favorite More

14 Aug

[Contact](#)

# MEDWATCHER

Make drugs, devices + vaccines safer

Track and report side effects of drugs, vaccines and medical devices.

[Report a Side Effect Now](#)[Log In](#)

Not registered? [Sign Up](#) - It's free!

[Log In](#)[Forgot password](#)[f | Log In with Facebook](#)

Boston Children's Hospital



Back

## Product Info

## \* Product

Continuous Ventilator



Include a Photo

Medical Countermeasure



What other medications or medical products were you using at the time of this side effect?

Antibiotics, via iv line.

Why were you using this device?

Pt suffering from severe pneumonia.

Continue

News



Watch List



Search



Report



Settings

Product InfoEvent Info

## \* Date of Event

May 27, 2014

## \* What happened?

Please describe your experience in as much detail as you can, including any other ongoing illness, allergies, relevant birth defect or other medical conditions. Provide any available lab data.

Oxygen pressure sensor was alarming, but oxygen pressure was within normal range.

Check all outcomes that you attribute to this event.



Non-serious



Other serious



Hospitalization



Disability/permanent damage



Birth defect



Life-threatening



Death



News



Watch List



Search



Report



Settings



# Instagram

**4.27** @checkit0utgirl

my mom got some OxyContin pills. ya boy boutta be faded

**Noemi** ❤ @noemi\_boo18

@ChinooChino lol they use to be morphine and now she sells vicorine something like that

**Mac** @rbhaze\_

Grandma gave me some Percocet for my pain. She came clutch

**MJ Caan** @mjcaan

Oh yeah. You stole all that morphine for nothing. #Helix



crackphotoz Look what I get!!!!!! At least one good thing came out of this!!!! Oh daym! Like I'm going to get so much bank selling this shit! #oxycodone #money #bank #godblesslamar 12h



Instagram



pharmacypimpin

pharmacypimpin

[T|M|L] 7d

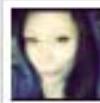
Normal



19 1

#benzo, #norcos, #actavis, #hitech, #percocet, #oxycontin, #hydrocodone, #oxycodone, #xanax, #hydromorphone, #promethazine, #morphinesulfate, #blues, #valium, #opana, #oc80, #morphine, #dilaudid, #fentanyl, #oc, #vcut, #m30, #oxymorphone, #methadone, #a215, #k9, #mbox, #opiates, #op,

@3hunv, @dem6n6l6gy187, @808\_mafia, @idontknowwhattdowithmyhands,



pandauhh  
Ynattirb Radec

[T | M | L] 1w  
X-Pro II



12 0

↪ #benzo, #goodshit, #shittinonem,  
#hydrocodone, #pharmacy, #pills, #1mg, #10,  
#hydros, #eat, #xanax, #opiate, #allsmiles,  
#footballs, #yum, #xan, #silly,

▼ @goaskkatttt, @ninny3g, @tinsley402,  
@yoshelove,

## See what others paid

e.g. dilaudid california

Search

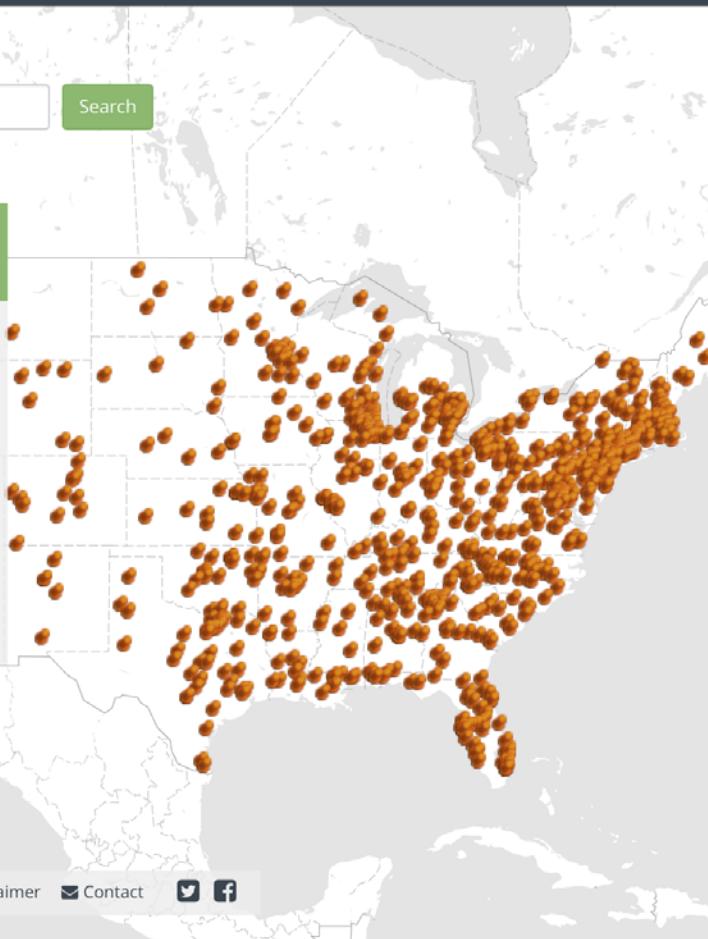
**\$** Did you get a good deal?  
Submissions are anonymous

\* Name of drug

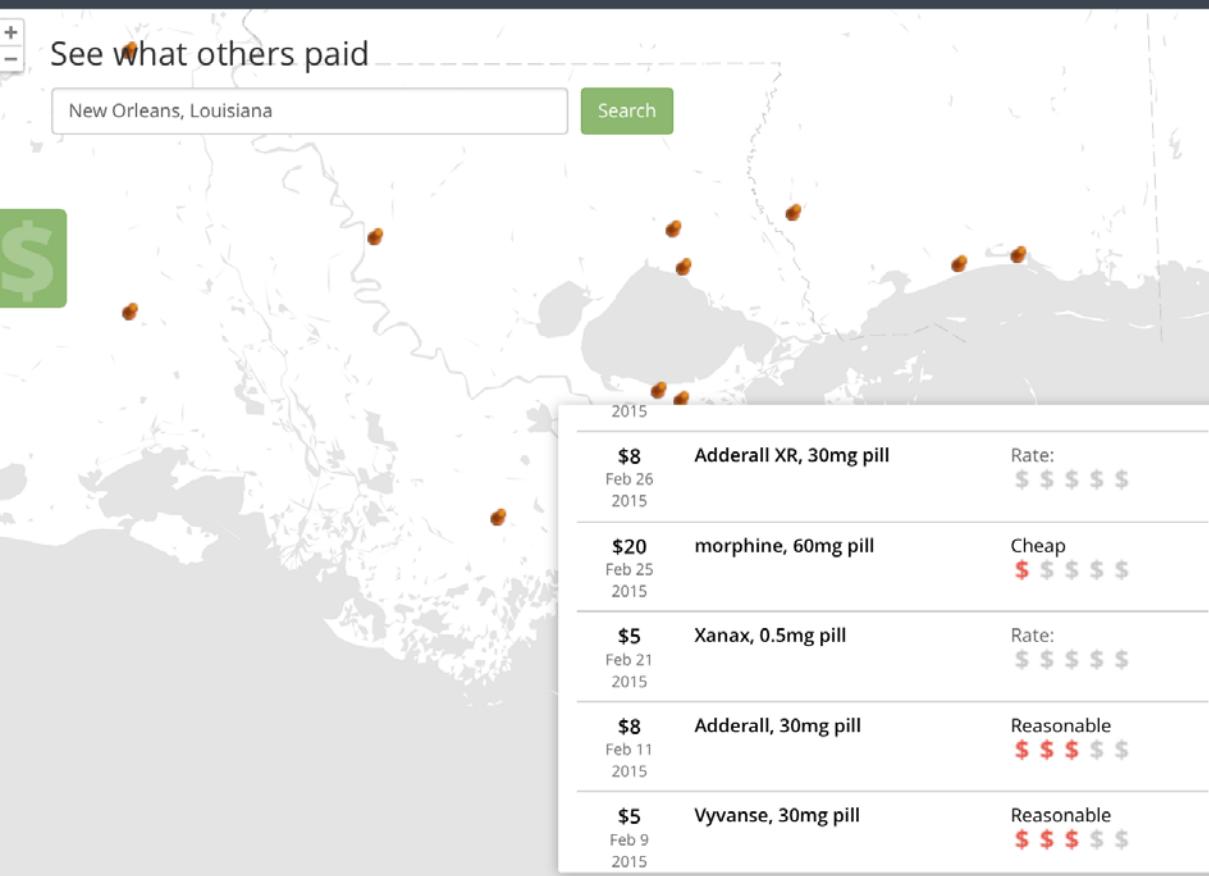
\* Formulation

Please choose a drug to see formulation options

Continue



\$15	Xanax, 2mg pill Texas	Rate: \$\$\$\$\$
\$1	hydrocodone (generic Vicodin), 5mg pill Illinois	Rate: \$\$\$\$\$
\$25	Dilaudid, 4mg pill Georgia	Rate: \$\$\$\$\$
\$10	OxyContin (new OP, hard to crush), 40mg pill Albuquerque, New Mexico	Rate: \$\$\$\$\$
\$4	Adderall, 10mg pill Erie, Pennsylvania	Rate: \$\$\$\$\$
\$5	Vyvanse, 40mg pill Russellville, Arkansas	Rate: \$\$\$\$\$
\$3	Klonopin, 1mg pill St Louis, Missouri	Rate: \$\$\$\$\$
\$8	Adderall XR, 20mg pill Philadelphia, Pennsylvania	Rate: \$\$\$\$\$
\$10	Adderall, 30mg pill Houston, Texas	Reasonable \$\$\$\$\$
\$4	Percocet, 10/650mg pill Swainsboro, Georgia	Rate: \$\$\$\$\$



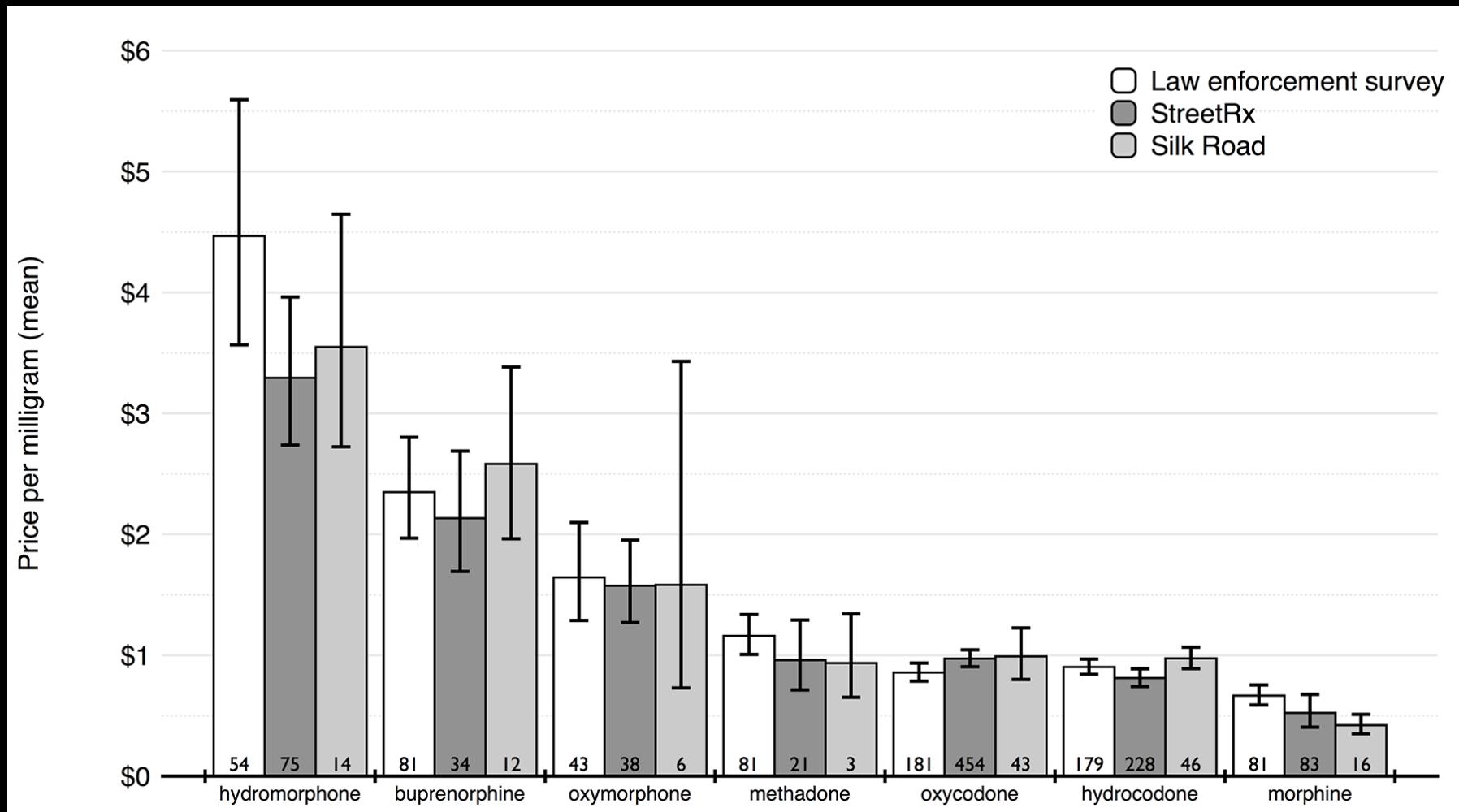
Prices for Any — New Orleans

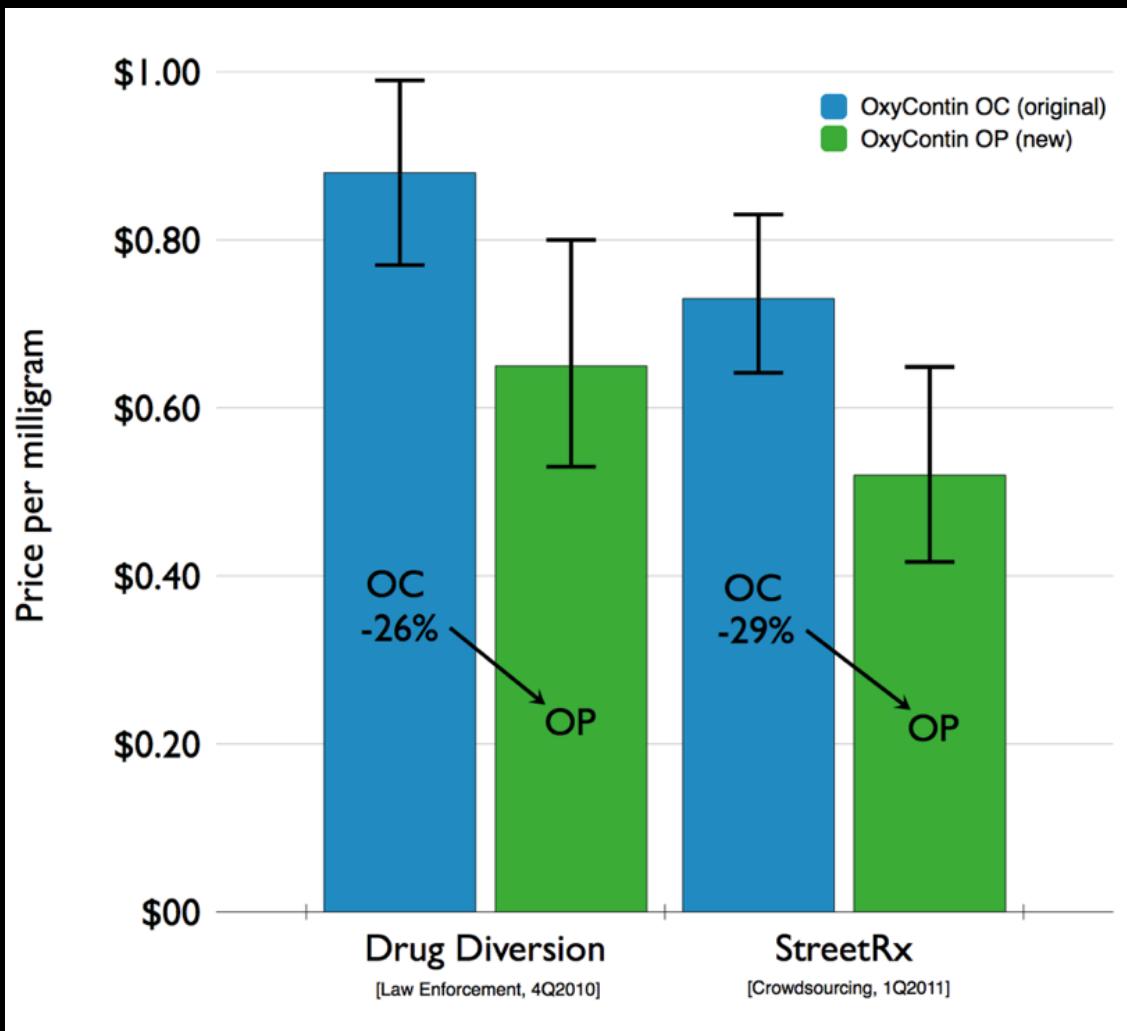
Include products with the same active ingredient

\$0.53	Fioricet (WITHOUT codeine), pill	Rate: \$\$\$\$\$
Mar 3 2015	Louisiana	
\$20	Norco hydrocodone, 7.5/325mg pill	Overpriced \$\$\$\$\$
Mar 3 2015	Louisiana	
\$10	Adderall, 30mg pill	Not Bad \$\$\$\$\$
Mar 3 2015	Laurel, Mississippi	
\$10	Norco hydrocodone, 10/325mg pill	Overpriced \$\$\$\$\$
Mar 2 2015	Baton Rouge, Louisiana	
\$2	Apo-Oxycodone CR (imprinted APO OCD), 80mg pill	Overpriced \$\$\$\$\$
Mar 1 2015	Baton Rouge, Louisiana	
\$5	Adderall XR, 30mg pill	Cheap \$\$\$\$\$
Feb 28 2015	Covington, Louisiana	
\$3	clonazepam, 1mg pill	Rate: \$\$\$\$\$
Feb 28 2015	Houma, Louisiana	
\$10	Xanax, 2mg pill	Overpriced \$\$\$\$\$
Feb 28 2015	Louisiana	
\$10	methadone, 10mg pill	Overpriced \$\$\$\$\$
Feb 28 2015	Baton Rouge, Louisiana	

Drug	n	Crowdsourced Data from StreetRx	Predicted Relative Potency	Clinical Equianalgesic Potency <sup>b</sup>
		Mean, US\$ (95% CI)	(95% CI) <sup>a</sup>	Milligrams
Hydromorphone	75	3.29 (2.74-3.96)	6.3 (5.8-6.8)	4
Oxymorphone	38	1.57 (1.27-1.95)	3.0 (2.9-3.2)	3
Methadone	21	0.96 (0.71-1.29)	1.8 (1.8-1.9)	1.5
Oxycodone	454	0.97 (0.90-1.04)	1.9 (1.5-2.2)	2
Hydrocodone	228	0.81 (0.74-0.89)	1.5 (1.3-1.8)	1
Morphine	83	0.52 (0.40-0.68)	1.0	1
Tramadol	21	0.05 (0.03-0.07)	0.1 (0.07-0.13)	0.3

# Cross-Validation of Black Market Prices





# Dark Web surveillance

Agora Beta

Listings Profile Wallet Orders Forums Info/Help

DRUGS > OPIOIDS > OXYCODONE >

Search

No-FE first Sort Default Show domestic first Choose Go

More: 1 2 3 4 5 6

Name	Price	Vendor	
80MG OXY AGORA OXY DEAL 1 PERSON PER WEEK This is only available to one person a week. 80mg oxycontin sells around \$120 all day. This deal gives you 10x 80mg oxycontin for only \$750 including shipping, after you the same person has ... OXYCODONE 30mg \$35 each!! X 30 PILLS ( MFG by Xanodyne 54 199 IMPRINTS RARE!) OXYCODONE 30mg QUANTITY: 30 PILLS PRICE: \$35 MFG: Xanodyne Pharmaceuticals, Inc. AR 199 IMPRINT (THESE ARE THE OLD ONES FROM A WHILE BACK, NOT SURE HOW WE CAME UP ON THESE BUT ARE STRAIGHT FROM S ... 15mg RoxycodoneOxycodone IR Full escrow on all my opiate products. I have Green A214/Peach 113 Roxycodone/Oxycodone 15mg IR pharmaceutical grade pills. This listing is for 1 Green A214/Peach 113 Roxycodone/Oxycodone 15mg IR ... OxyContin 10mg / 10 Tabs These are Oxycontin 10mg Instant Release pills. They are the "old formula" and can be smoked, snorted, I-Ved or popped. There is a thin white coat that can be washed off so it can be crushed. Thi ... 1 HYDROCODONE 5mg PILL ONLY \$4.99 *****SALE PRICE*****SALE PRICE***** This listing is for 1 5mg Hydrocodone pill. This is a white oblong pill with red dots and imprint of V3 ... 20mg Oxycodone x 50 Oxycodone 20mg 50 pills Oval white pills, OXY on one side, and 20 on the other side (It is not my picture, i just borrowed it. But the pills looks like these in the picture, but mine are oval) Oxycodone 30mg • non-FE listing	2.40874559 BTC 3.91699092 BTC 0.05558643 BTC 0.37057624 BTC 0.01849175 BTC 3.33518621 BTC	From: Australia From: USA From: USA From: USA From: USA From: Canada To: Worldwide	Cocaine_Oxy_Vape_Australia ladywalker opiateconnect zunidog lifecare blow

0 NEW MESSAGES

LOG

Opioids

Buprenorphine (10+)  
Codeine (20+)  
Dihydrocodeine (7)  
Fentanyl (100+)  
Heroin (300+)  
Hydrocodone (10+)  
Hydromorphone (8)  
Morphine (30+)  
Opium (10+)  
**Oxycodone (100+)**  
Other (100+)

Main menu: Chemicals Counterfeits (900+) Data (600+) Drug paraphernalia (200+) Drugs (15100+) Electronics (100+) Forgeries (300+) Info/eBooks (2600+) Jewelry (100+) Services (400+) Tobacco (200+)

# OTHER SOCIAL MEDIA EFFORTS AT FDA

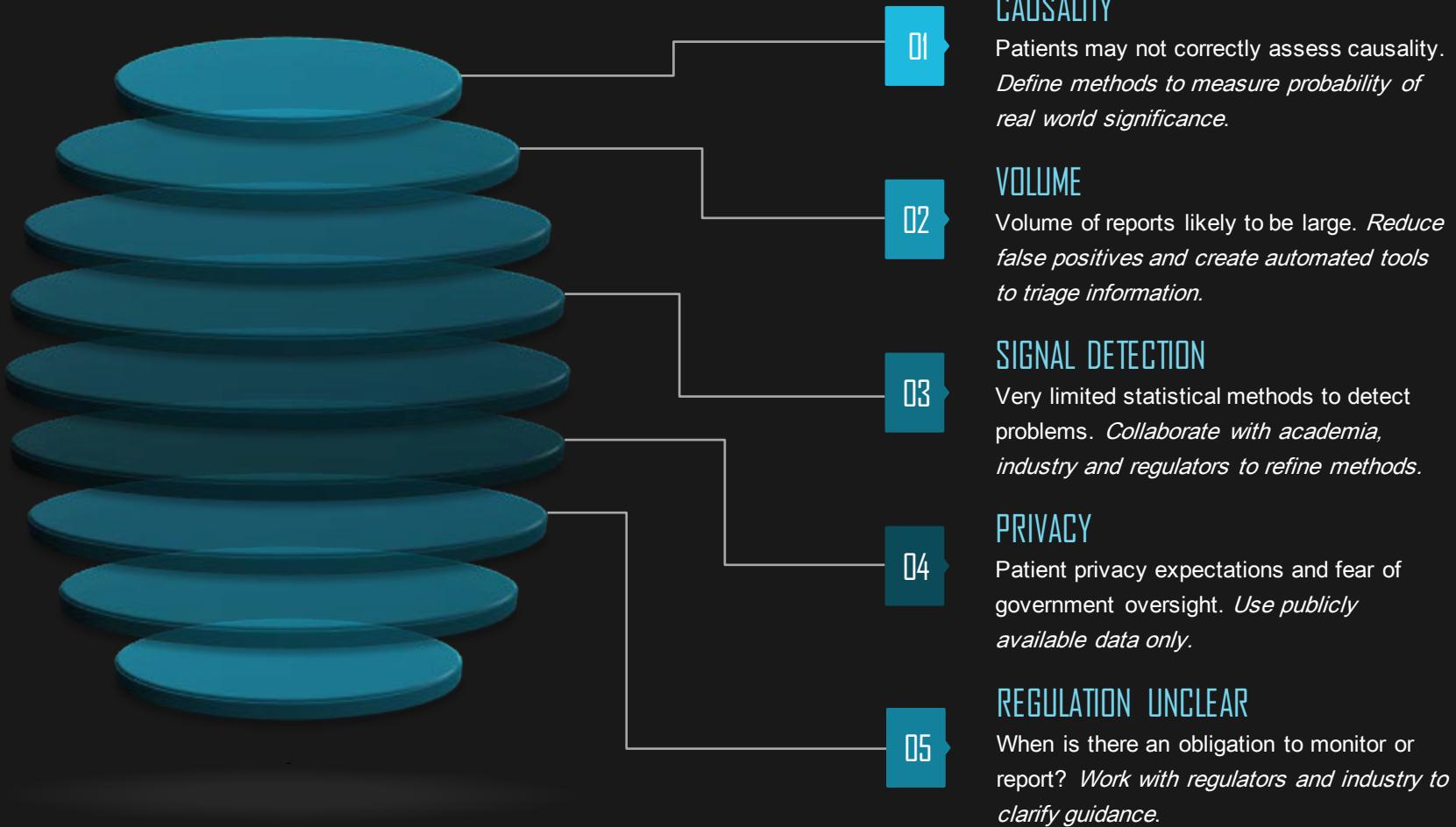
## **Tobacco products**

- FDA Center for Tobacco Products
- Monitoring existing and emerging tobacco products
- Use, outcomes, perceptions, attitudes

## **Supply chain monitoring**

- FDA Office of International Programs
- Monitoring China-to-US supply chain vulnerabilities
- Food, drug, and ingredients

# LIMITATIONS OF SOCIAL MEDIA



# Questions?

[John\\_brownstein@harvard.edu](mailto:John_brownstein@harvard.edu)



[@johnbrownstein](https://twitter.com/johnbrownstein)