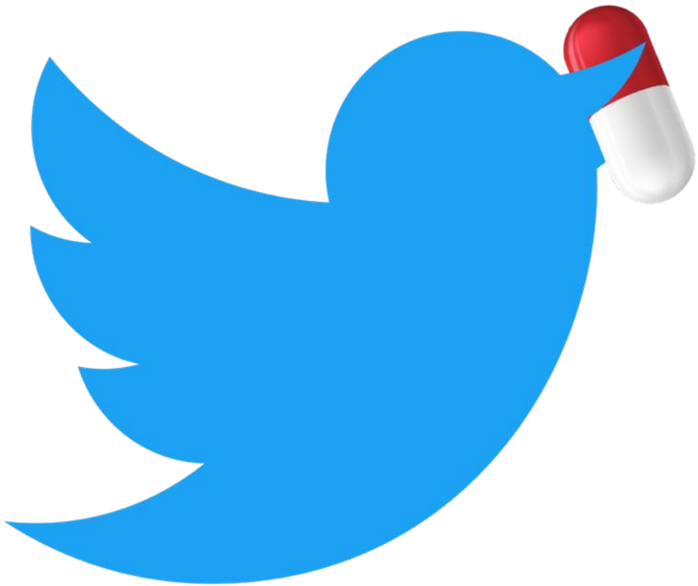
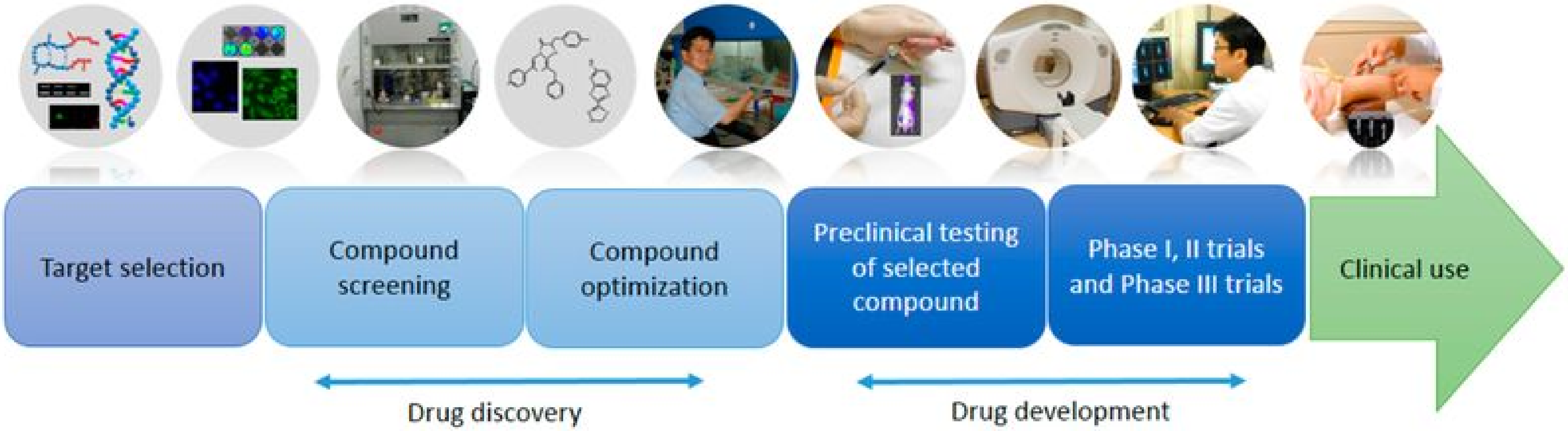
# Pharmacovigilance on Twitter



# Outline

- Motivation: Phases of Clinical Trials
- Short excursion to Twitter
- Pharmacovigilance on Twitter?
  Mining Tweets for Adverse Drug Reactions
- Analysis of Twitter Data for Postmarketing Surveillance in Pharmacovigilance
- Summary

# The journey of a drug



# Clinical Trials

- Phase 0 (optional): Pharmacodynamics and pharmacokinetics in humans
- Phase 1: Screening for safety
- Phase 2: Establishing the efficacy of the drug, usually against a placebo
- Phase 3: Final confirmation of safety and efficacy
- Phase 4: Safety studies during sales

| | Phase 0 | Phase 1 | Phase 2 | Phase 3 |
|---|---|---|---|---|
| subjects: | 10-15 | 20-80 | 50-200 | 200-10 000 |
| time: | weeks | weeks/months | months/years | years |

## Tests for:

- effectiveness
- severe common adverse drug effects

# Adverse drug effects in the US...

... ~2 millions patients

... ~100 000 fatalities

... 4th leading cause of death

# Post-marketing surveillance

One approach of the FDA:

spontaneous reporting system via MedWatch

Problem: sparse data

Solution: the seemingly endless vastness of the internet

# Twitter has...

...over 645 million users

...58 million tweets per day

...80% of users posting tweets about themselves

## Upsides of Twitter

- publicly available
- accessible through API
- 80% of users tweet about themselves
- compact units of text

## Challenges with Twitter

- limited to 280 characters
- Twitter "Slang"
- paucity of relevant data
- frequent misspelling

# Pharmacovigilance on Twitter?
# Mining Tweets for Adverse Drug Reactions 2014

# Phonetic spelling filter

@PsychoIogicaI HA! Not if you’re on # **Seroquil**. EXTREMELY vivid dreams that stay in conscious memory. Very # Freaky ! Any idea why?

@BipolarBlogger did you ever try the **Seriquel** XR??? It has a less sedative effect and has a longer lasting effect

Gone from 50mg to 150mg of **Serequel** last night. Could barely wake up this morning and I feel like my body is made of lead

@AndrewH_Smith Is the Inderal helpful? And yeah, they are short lasting but non addictive. You could try **Seraquel** too but it's pretty strong

# Data acquisition: Target Drugs

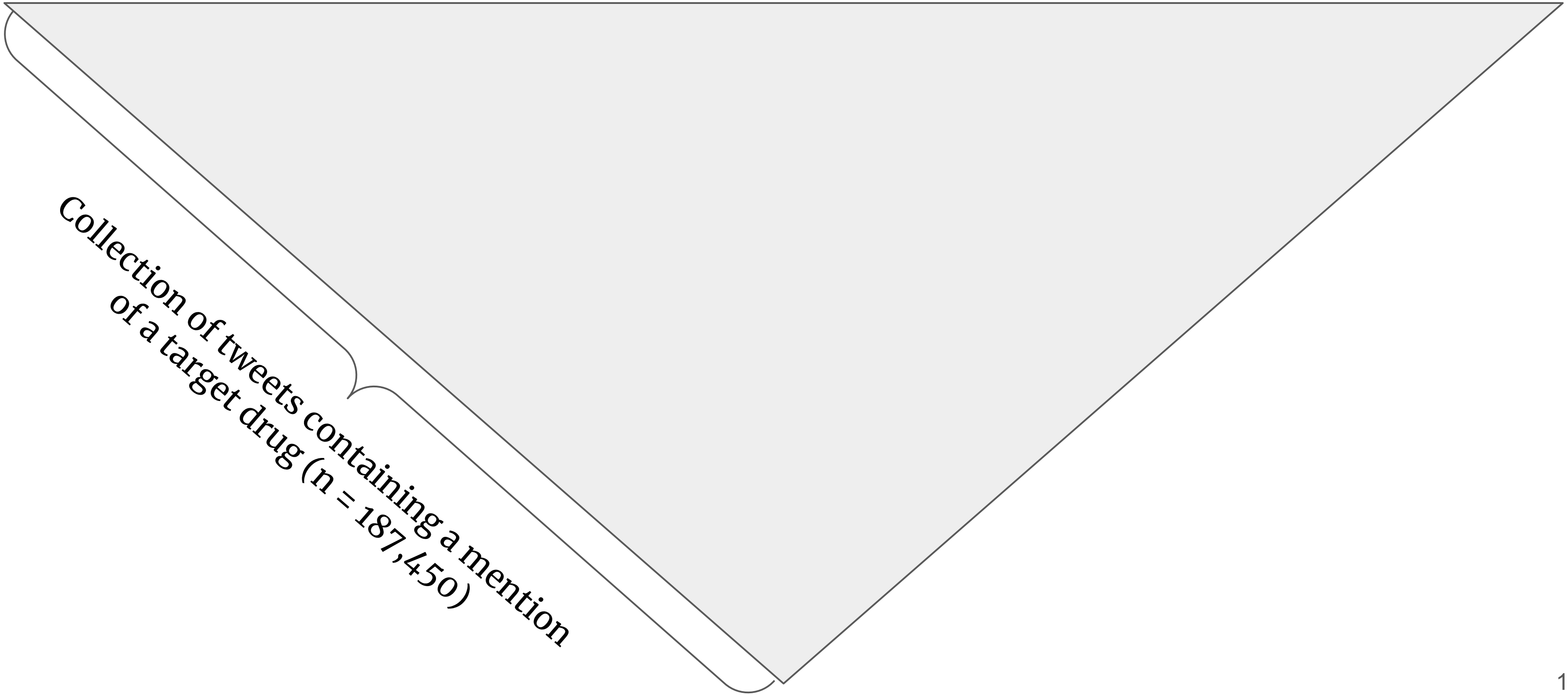
Truth set:

- drugs widely used
- known to have ADR of interest
- recently widespread use of many

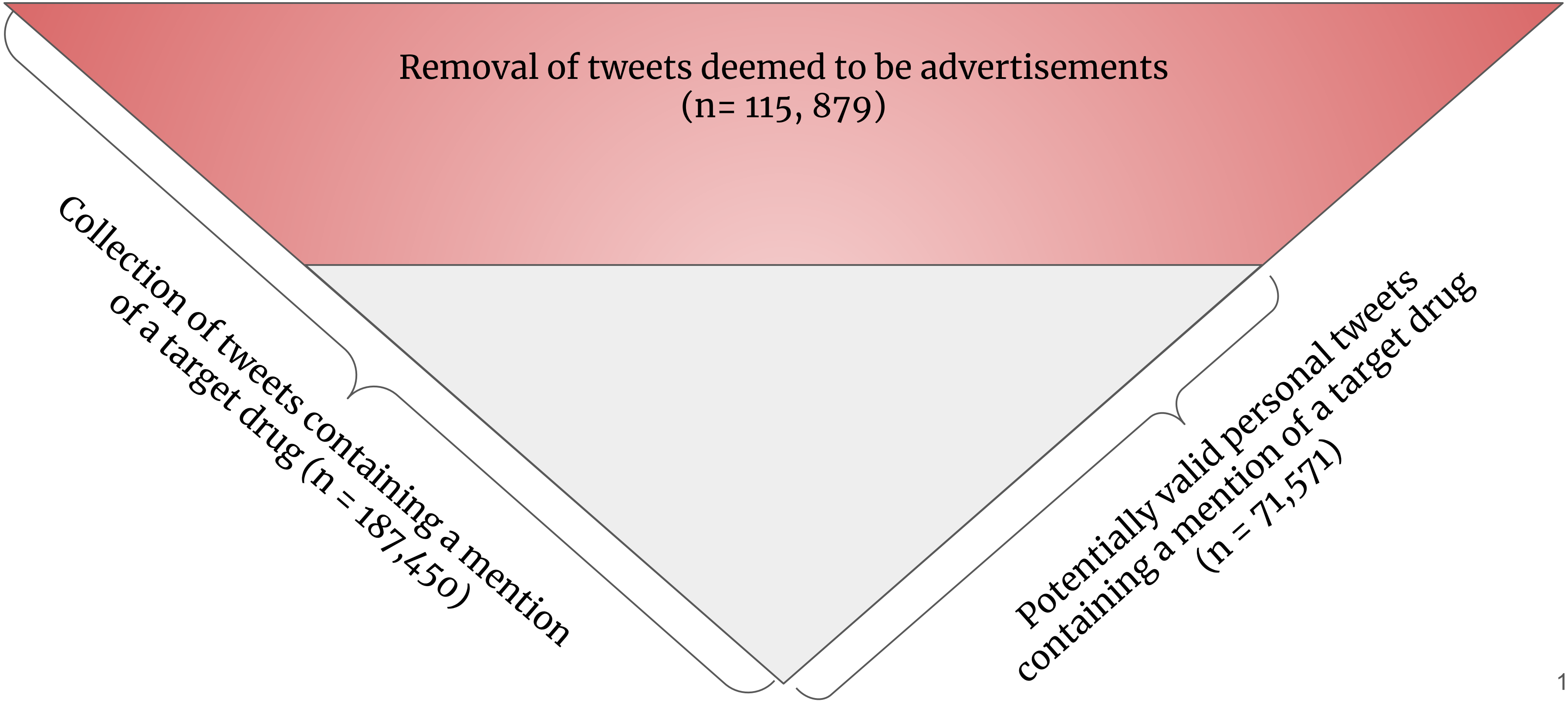
Test set:

- drugs released between 2007-2010
- drugs for central nervous system and mental health conditions
- Treatments for age-related diseases
- Biologics

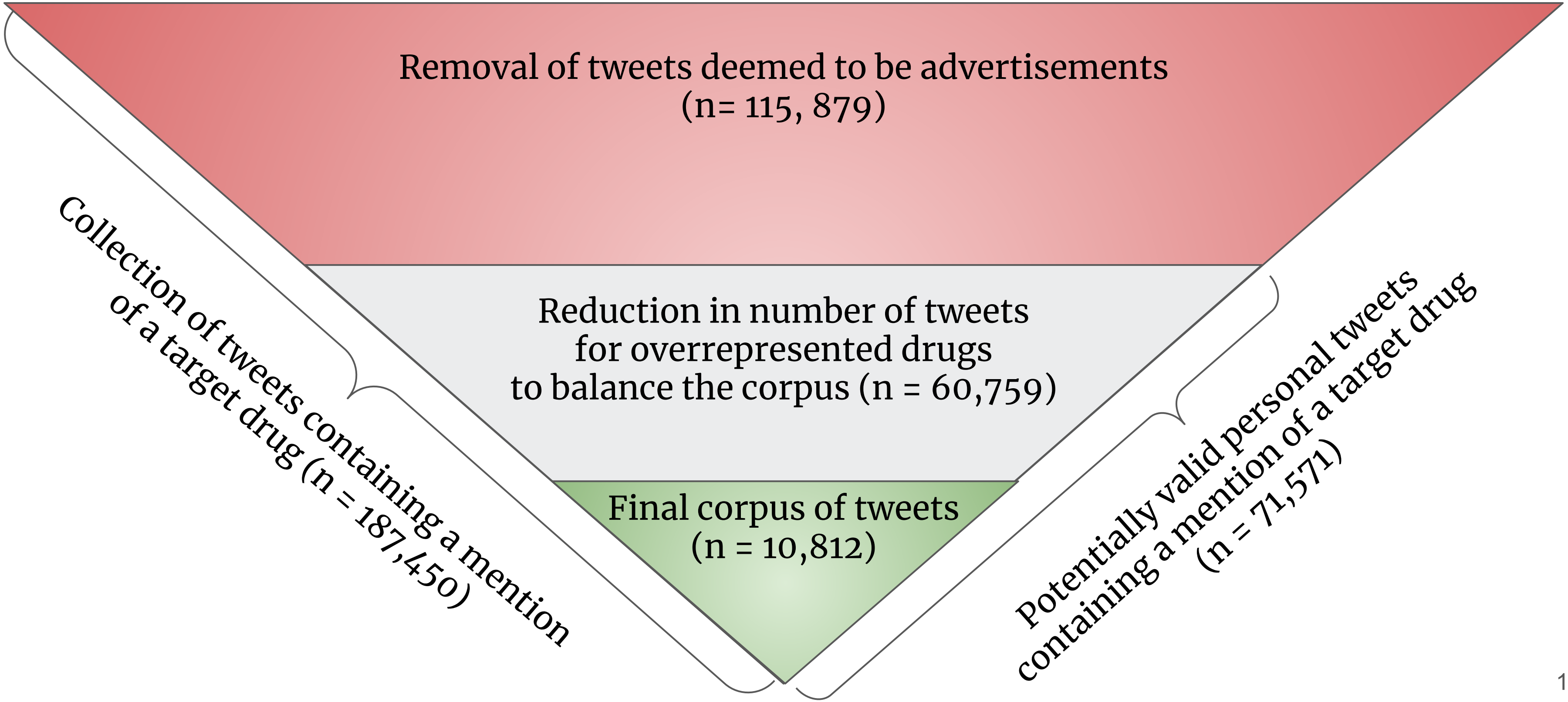
# Obtaining a relevant corpus



# Obtaining a relevant corpus



# Obtaining a relevant corpus



# Annotating

| Sample Comments | Classification | Annotations |
| --- | --- | --- |
| 20s 8th day with #Effexor still experiencing some side effects (drowsiness, sleepiness,GI effects). Moderate improvement in mood #depression | *hasADR* | "drowsiness" - drowsiness: adverse effect, "sleepiness" - sleepiness: adverse effect, "GI effect" – gastro intestinal reaction: adverse effect, "depression" – depression: indication |
| Do not take Cymbalta if you breathe – stolen from Tay | *noADR* | |
| Tomorrow, my second infusion of Tysabri! Good luck for me! #Godblessme #MSLife | *noADR* | "MS" multiple sclerosis: indication |
| Rules of Prozac: 1: You can never sleep, ever again. NEVER EVER 2: No you may NOT switch your brain off. Ever. 3: Exhaustion is your friend. | *hasADR* | "never sleep" – insomnia: adverse effect, "not switch your brain off" – racing thoughts: adverse effect, "exhaustion" – exhaustion: adverse effect |

# Results

| Drug Brand/Generic Name | ADR Mentions Annotated per Drug | Total Number of Tweets in Corpus |
|---|---|---|
| Seroquel/quetiapine | 237 | 1,082 |
| Effexor/venlafaxine | 176 | 461 |
| Vyvanse | 122 | 800 |
| Paxil/paroxetine | 92 | 683 |
| Prozac/fluoxetine | 76 | 1,307 |
| Lamictal/lamotrigine | 73 | 395 |
| Zyprexa/olanzapine | 68 | 377 |
| Humira | 64 | 560 |
| Cymbalta/duloxetine | 63 | 832 |
| Trazodone | 58 | 530 |

# Results

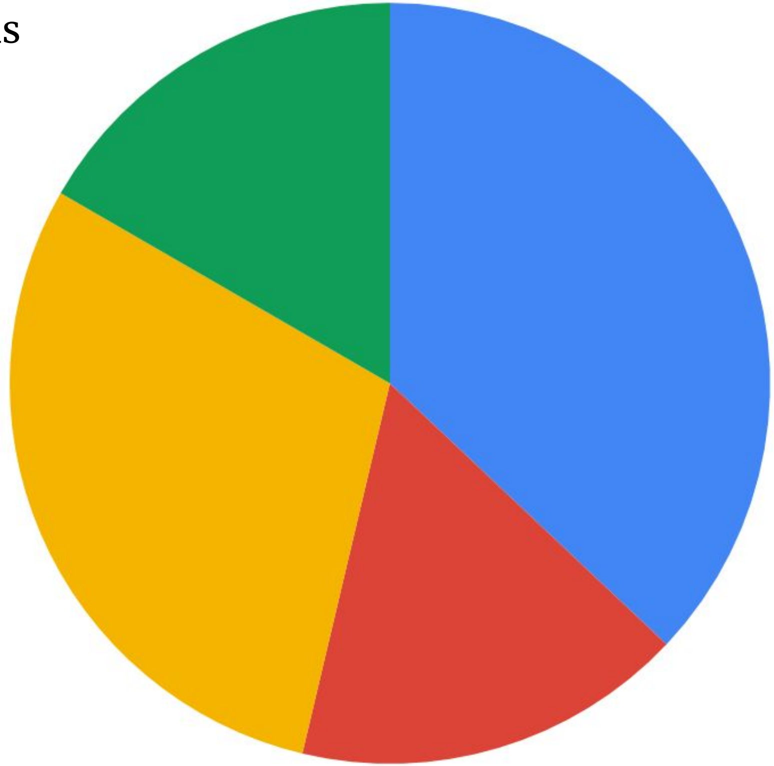
| Drug Brand /Generic Name | Primary Indications | Documented Adverse Effects (no order) | Adverse Effects Found in Tweets (Frequency) |
|---|---|---|---|
| Seroquel/ Quetiapine | Schizophrenia, Bipolar I Disorder: manic episodes, BipolarDisorder | **somnolence**, dry mouth, headache, **dizziness**, asthenia, constipation, fatigue | **somnolence (22.2%)**, abnormal dreams (9.6%), feel like a zombie (8.1%), weight gain (6.6%), restless leg syndrome (6.6%), increased appetite (5.9%), sleep paralysis (2.9%), **dizziness (2.2%)**, psychosis (2.2%), tremors (2.2%) |
| Effexor/ venlafaxine | Major Depressive Disorder (MDD) | **nausea**, **headache**, somnolence, dry mouth, dizziness | withdrawal syndrome (21.3%), insomnia (11.1%), **headache (4.3%)**, malaise (4.3%), abnormal dreams (4.3%), **nausea (3.4%)**, shaking (3.4%), fatigue (3.4%) |

# Results

| IAA Type | Precision | Recall | F-measure |
|---|---|---|---|
| Span | 0.8099 | 0.9802 | 0.8869 |
| Concept ID | 0.7278 | 0.9688 | 0.8311 |
| Binary Classification | 0.8155 | 0.8829 | 0.8448 |

# Error Analysis

FP Error Analysis



Indication AS ADR
40%

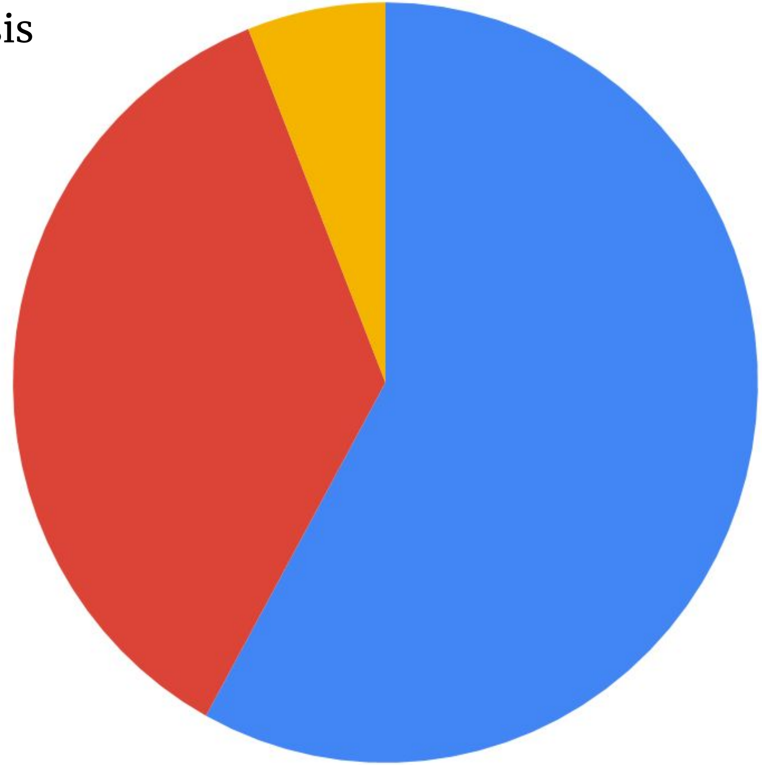
Not a 1st Person Experience
18%

Consumer not Discussing ADR
32%

Other
18%

# Error Analysis

FN Error Analysis



Colloquial/Descriptive Language
58%

No Direct Match in Lexicon
36%

Other
6%

# Discussion

Assessment:

- for Top 10 drugs atl. one ADR found
- often frequencies similar
- many FP due to the nature of tweets
- many FN due to the nature of tweets

Improvement suggestions:

- association rules instead of dictionary
- Machine Learning, f.e. CRFs may prove effective
- more training data needed

# Conclusion

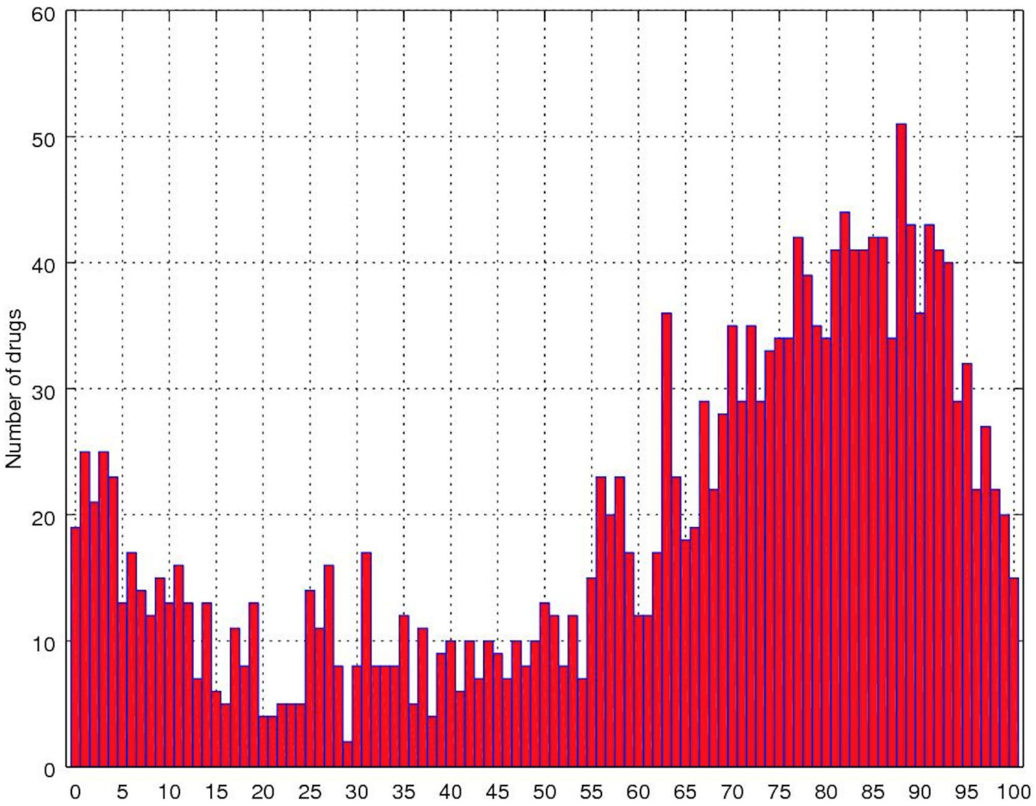
- Twitter is rich of ADR information
- Difficult to extract with dictionary approach
- Imbalanced data

# Analysis of Twitter Data for Postmarketing Surveillance in Pharmacovigilance 2016

# Addressing the challenges

- corpus of 125,669 tweets, with an average of 62.87 tweets collected for each drug
- language model trained on a subset of 300 randomly selected tweets
- sentiment analysis trained on a subset of 300 randomly selected different tweets
- annotated on positive, neutral and negative
- also included emoticons and associations between words to conclude mood

# Tweets per Drug



# Top 3 Sentiment Analysis Tools
## for polarity

**Emoticons:**
Given lists of positive and neutral emotions, if a text contains an emoticon it is assigned the polarity of the first one, else a text is deemed neutral

**Panas-t:**
Provides association strengths between words and eleven moods including surprise, fear, guilt, joviality, attentiveness, fear, etc.

**SANN:**
A dictionary-based rule-based sentiment classifier using the MPQA polarity lexicon

# Results

| | Emoticons | Panas-t | SANN | Majority vote: (all 18) |
|---|---|---|---|---|
| F1-measure | 0.941 | 0.929 | 0.920 | 0.665 |
| Accuracy | 0.936 | 0.932 | 0.932 | 0.576 |

# Top 4 Sentiment Analysis Tools
## for effect

**EmoticonsDS:**
Uses a large sentiment-scored word list based on the co-occurrence of each token with emoticons in a corpus of over 1.5 billion messages

**SenticNet:**
A semantic and affective resource for concept-level sentiment analysis, modelling the polarities of common-sense concepts and relations between them

**SentiWordNet:**
Lexical SA tool based on WordNet using polarity scores associated with WordNet synsets

# The 4th Top Sentiment Analysis Tools

## for effect

**AFINN:**
Twitter based sentiment lexicon providing emotion ratings for words

# Results

| | Emoticon sDS | SenticNet | SentiWord Net | AFINN | Majority vote: (all 18) |
|---|---|---|---|---|---|
| F1-measure | **0.638** | 0.621 | 0.616 | 0.615 | 0.627 |
| Accuracy | 0.592 | 0.595 | 0.592 | 0.597 | **0.604** |

# Tested Classifiers
## for Mention of Effect

**Multinomial Naive Bayes**

**Support Vector Machine**

**Logistic Regression**

...with 10-fold cross-validation

# Results

| | Both classes | | | +ME class | | | −ME class | | |
|---|---|---|---|---|---|---|---|---|---|
| Classifier | Recall | Prec | F1 | Recall | Prec | F1 | Recall | Prec | F1 |
| Multinomial NB | 0.847 | 0.852 | 0.849 | 0.848 | 0.981 | 0.909 | 0.961 | 0.688 | 0.794 |
| Logistic Regression | 0.85 | 0.851 | 0.850 | **0.855** | 0.984 | **0.914** | 0.969 | 0.689 | 0.799 |
| SVM | **0.855** | **0.892** | **0.873** | 0.8 | **1.0** | 0.887 | **1.0** | **0.71** | **0.823** |

# Conclusion

- sentiment analysis for polarity promising
- data distribution still a problem
- SVMs seem to work really good

# Summary

- Twitter is rich of medical information
- promising methods in polarity and effect detection
- Twitter lingo still a problem
- also data distribution and imbalanced data

**References:**


Pharmacovigilance on Twitter?
Mining Tweets for Adverse Drug Reactions
Karen O'Connor1, Pranoti Pimpalkhute1, Azadeh Nikfarjam, MS1, Rachel Ginn1, Karen L Smith, PhD2, Graciela Gonzalez, PhD1
1Arizona State University, Tempe, AZ; 2Regis University, Denver, CO

Phonetic Spelling Filter for Keyword Selection in Drug Mention Mining from Social Media
Pranoti Pimpalkhute, MS,1 Apurv Patki, MS,1 Azadeh Nikfarjam, Phd,2 and Graciela Gonzalez, Phd2

Analysis of Twitter Data for Postmarketing Surveillance in Pharmacovigilance
Julie Pain and Jessie Levacher and Adam Quinquenel

**Picture of Drug Discovery** (Slide 3):
Drug Discovery by Molecular Imaging and Monitoring Therapy Response in Lymphoma
Senthilkumar Kalimuthu, Ju Hye Jeong, Ji Min Oh and Byeong-Cheol Ahn

# Phase 1

- assesses maximum tolerated dose and toxicity
- concerne: safety, pharmacodynamics and pharmacokinetics
- 20-80 subjects
- lasts weeks/months