

NOTICE Breast Cancer Study: Social Media Mining for Probable Endocrine Therapy-Induced Adverse Drug Reactions

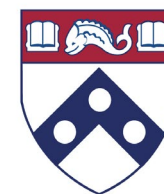
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Matthew K. Breitenstein, Ph.D.

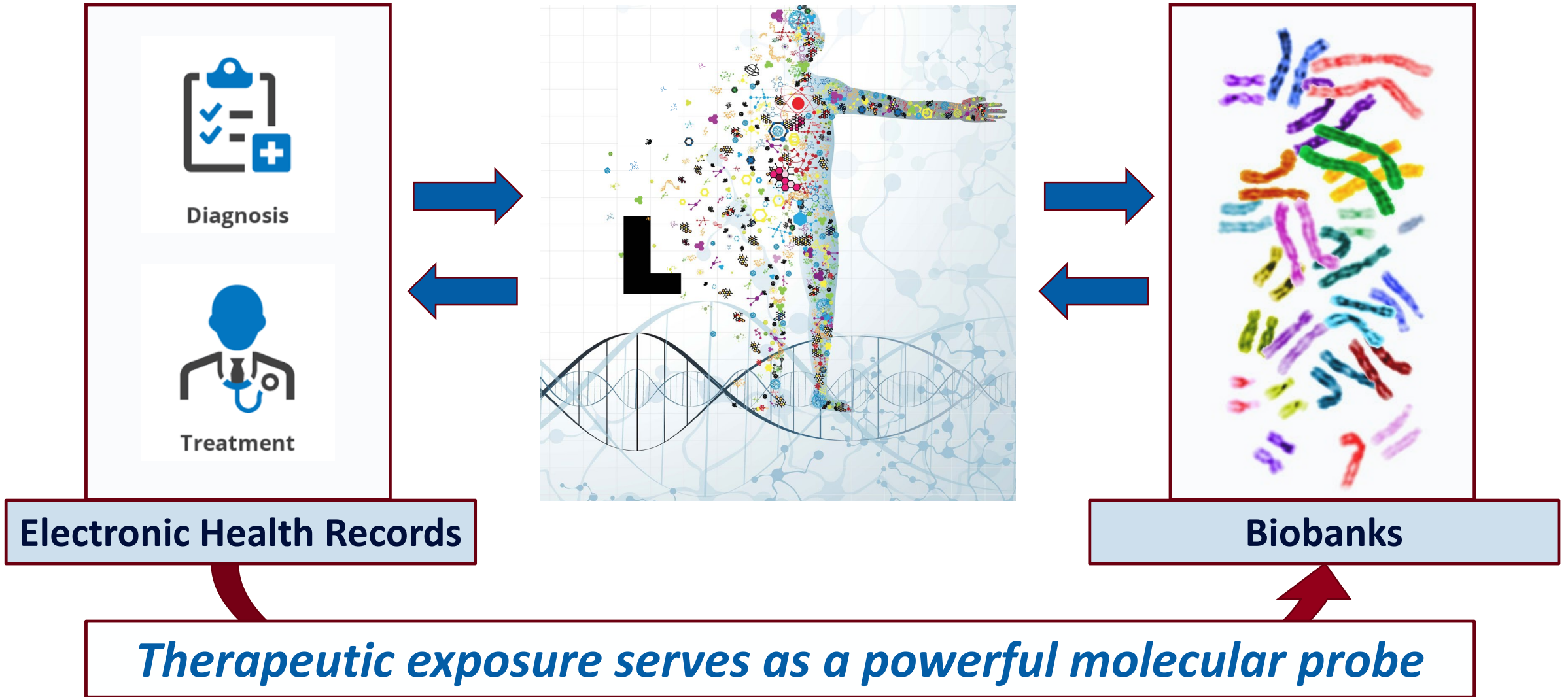
Instructor of Informatics
Perelman School of Medicine
University of Pennsylvania

DEPARTMENT of
BI STATISTICS
EPIDEMIOLOGY &
INFORMATICS



Perelman
School of Medicine
UNIVERSITY of PENNSYLVANIA

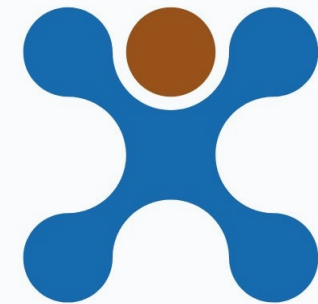
Translational Informatics



Precision Medicine Insights Ecosystem

1. i-mAB – biomarker enrichment pipeline
2. eENUMERATE – deep learning interpretation
3. PharmacoQTL – pathway extrapolation
4. **NOTICE** – pharmacovigilance

Novel approaches for Observing
Therapy-Induced Concurrent Events



Breitenstein Laboratory
translational informatics & cancer precision medicine

Background

- Extended adjuvant endocrine therapy is highly effective in breast cancer recurrence prevention
 - 3-10 years
 - Unknown long-term side effects
 - Patients commonly terminate therapy early
- Two classes of endocrine therapy
 - Aromatase inhibitors (**AIs**)
 - exemestane, letrozole, anastrozole
 - Reduce concentration of circulating estrogens via allosteric regulation of the aromatase enzyme, whereas
 - Selective estrogen receptor modulators (SERMs)
 - tamoxifen, raloxifene, and toremifene
 - Limit response to circulating estrogen via antagonist competition with estrogen receptor in the breast
 - Potential for previously unknown/unappreciated mechanistic difference

NOTICE Data Perspectives

- Patient utilization:
 - **Twitter social media**
 - Reddit
- Local healthcare prescription/diagnosis:
 - Electronic health records
 - Data warehouse
 - Unstructured clinical notes
- National utilization:
 - Private insurance claims
 - SEER-Medicare

Preliminary data

| Endocrine Therapy | (n) RA cases/patients | HR* (95% CI) | P-value |
|----------------------|-----------------------|---------------------|---------|
| No endocrine therapy | 6/4,071 | 1.00 (reference) | |
| SERMs only | 5/2,537 | 1.20 (0.36 – 3.95) | 0.77 |
| Als only | 5/712 | 6.37 (1.77 – 22.92) | 0.005 |
| SERMs then Als | 3/1,875 | 0.91 (0.21 – 3.86) | 0.90 |
| AI then SERMs | 0/49 | --- | --- |

*Adjusted for age, smoking status and use of chemotherapy

Preliminary data



Patient #1
@Patient1



Sorry, just catching up. Letrozole was horrible for me. Only took for 30 days due to SE's. Switched to Exemestane. Little better except for awful bone pain. Took allergy med - Claritin which helped bone pain. Until your scan, try the Claritin, see if it helps. You never know.

← ↻ 3 ★ 7 ...

__:__ PM - __ Jan 2018 · ...



Patient #2
@Patient2



I was fine & obliviously happily living my life until the new Dr told me I was beating the odds. I didn't even know that the lump that came back after 17 years was I operable st 4 Breast cancer. Still the Anastrozole seems to be doing ok unless this bloody pain in my back is C

← ↻ ★ ...

__:__ AM - __ Nov 2017 · ...



Patient #3
@Patient3



So I'm having a hugely bad reaction to Tamoxifen - I phoned the hospital this afternoon and they told me to stop taking it and they'll call me back tomorrow with a suggested course of action (I've already unsuccessfully...

[facebook.com/patient3/posts/n ...](https://facebook.com/patient3/posts/n...)

← ... ↻ ... ★

__:__ AM - __ Apr 2018 · ...



Patient #4
@Patient4



I had to stop taking AIs because of depression & fatigue. Just started on tamoxifen.

← 1 ↻ ... ★

__:__ PM - __ Jul 2017 · ...

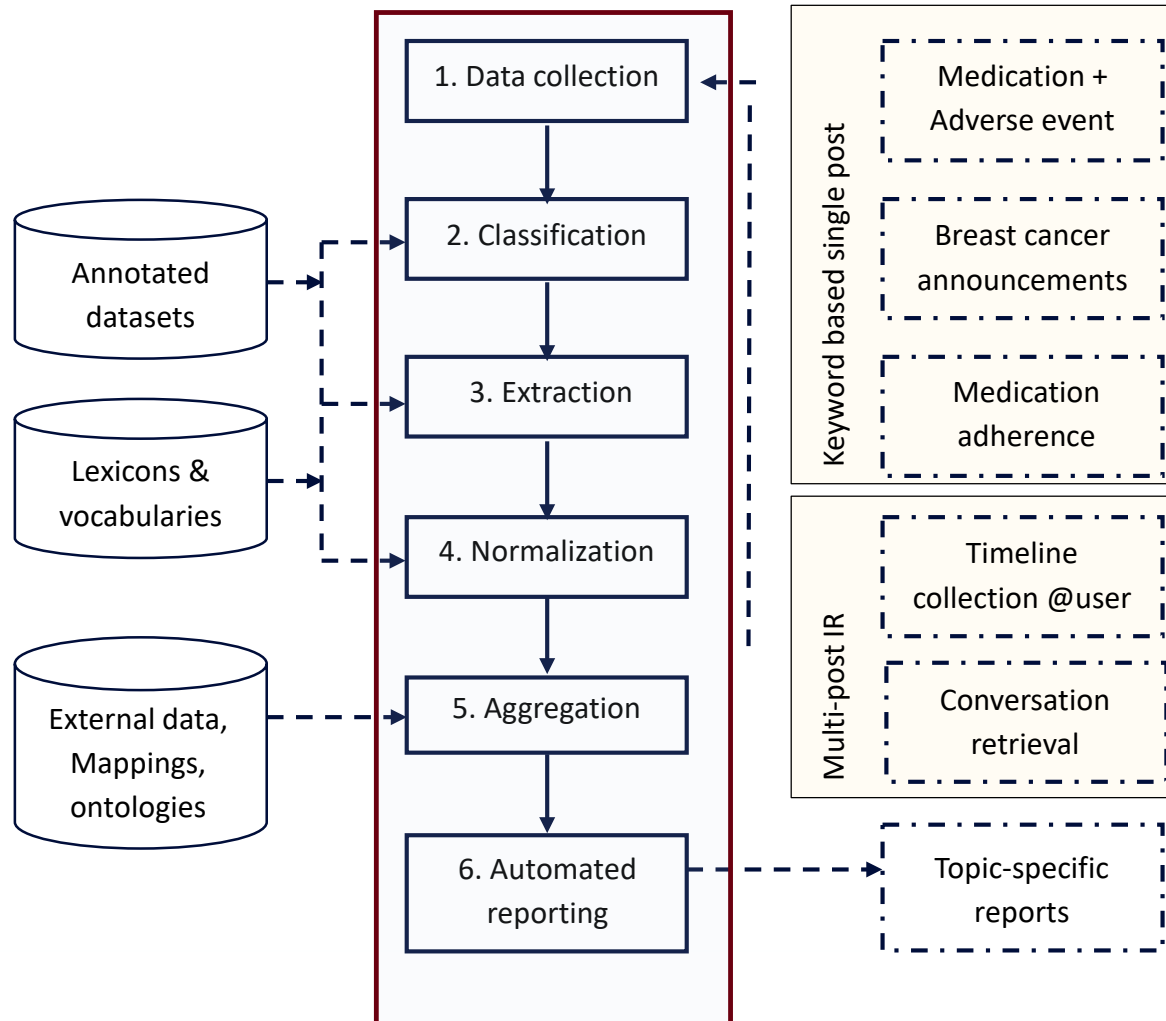
Phenomena of interest

- Extended adjuvant endocrine therapy utilization for breast cancer recurrence prevention
 - **Aromatase inhibitors:**
 - Individual agent utilization
 - Potential adverse events
 - Adherence
 - Patient stopping and starting
 - Early termination of treatment
 - Agent switching

Research Ethics

- Infrastructure IRB
 - Pre-study surveillance
 - Twitter API
- Study IRB
 - Data capture
 - Data storage
 - Patient contact (this study does not propose re-contacting patients)
 - Exclusion of vulnerable populations
 - Supplementary healthcare data perspectives
- **Publicly posted patient data is treated as HIPAA protected data as soon as it is captured**

Social Media Mining Pipeline



- Modular pipeline
- Vertical components (middle column) can be customized, replaced or improved dynamically
 - Each component defines interfaces and links to common data models for inputs and outputs
 - May be used in isolation or sequentially

Results

- Corpus of 1,266 aromatase inhibitor tweets
 - Ascertained over a 90-day period
 - Original tweets
 - Initial tuning dramatically reduced noise
- Individual agent utilization*:
 - Anastrozole **19.6%** (85/434)
 - Letrozole **28.7%** (198/690)
 - Exemestane **21.8%** (31/142)

**describes first person intake or possible intake*

Results

Informative Tweet Contents:

- Demographic
- Disease stage
- Treatment initiation/cessation
- Adherence decisions
- Agent switching
- Therapeutic efficacy
- Therapeutic duration details

Probable ADRs observed:

1. Musculoskeletal pain
2. Joint swelling
3. Mental/behavioral health exacerbation


Early Cessation

- I'm facing this now: on a 1-mo (so far) hiatus from anastrozole as per MO due to some nasty SEs. We're also doing rule-outs of other potential causes. #bcsm
- This is me. I was ready to give up a sport a love. Had convinced myself I was too old [redacted] because the back pain had become intolerable. I took a break from Arimidex and what a difference. It's been 3 months.
- Stopped tamoxifen just short of the five years due to [redacted]. Tried arimidex, too many brutal side effects. Going rogue.

Agent Switching

- My leg swelled and felt warm. I was on anastrozole. Now on Letrozole.
- Thanks for this post. I couldn't tolerate Anastrozole. Made my joints so stiff & painful. Felt like an old woman. My oncologist swapped me onto Tamoxifen even though I'm post menopause. This is much better for me - some sweats but joints are fine. I'm [redacted medical history] so marginal benefits

Anastrozole

- Looking for #BreastCancer people who are taking or have taken anastrozole (arimidex) ... after about 9 weeks of use I am experiencing severe joint pain and swelling of the ankles and feet. Anybody else go through this? Any suggestions on how to manage it? Thank you! 
- Many examples of individual agent utilization

Other signals

- Detailed oncology history
 - Location
 - Stage
 - Grade
 - BRCA status
 - Laterality
- Family medical history
- Mental health status
- Additional medication usage
- Off-label usage
 - Male weight lifting
 - Gender affirming treatment

Potential Limitations

- Patient reliability
 - Not limited by physician-mediated reporting mechanisms (FAERS)
 - Accuracy of history
 - Hyperbole
- Incomplete profile
- Selection bias
- Prevalence
- Patient linkage to local healthcare data

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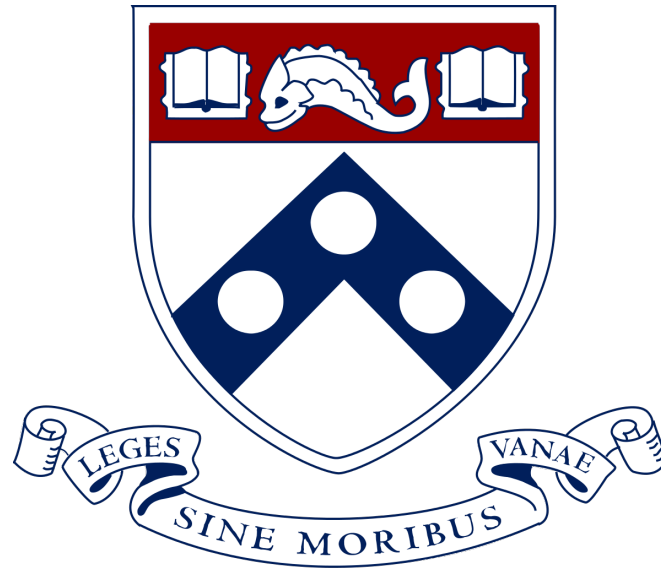


Thank you!

Matthew K. Breitenstein, PhD

mkbreitenstein@gmail.com

@MKBreit



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