# Measuring the Impact of Pharmacovigilance Practice on Patient Well-Being

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Pfizer WORLDWIDE RESEARCH & DEVELOPMENT

# Measurement strategies: process, outcomes, value


**Product**

Effectiveness of REMS and RMMs

**System**

Safety signals, label updates, resources

**Innovation**

Data sources, analytics, speed

# Measurement strategies: process, outcomes, value


**Patient Safety**

Effectiveness of REMS a[illegible] RMMs

**Syst[illegible]em**

Safety sig[illegible]als, label updates, [illegible]sources

**Innov[illegible]ation**

Data s[illegible]urces, analytics, speed

# FDA and EMA require similar elements for REMS and aRMM evaluations

US REMS and EU-RMP Strategies

Understanding of risks and safe use
Adherence to labeling / SPC
Effect of risk mitigation on AE rates

# Varenicline US REMS

PHARMACOEPIDEMIOLOGY AND DRUG SAFETY 2013; 22: 705–715
Published online 24 January 2013 in Wiley Online Library (wileyonlinelibrary.com) DOI: 10.1002/pds.3400

ORIGINAL REPORT

The effectiveness of varenicline medication guide for conveying safety inf †

Cheryl Enger[1]*

[1]Epidemiology, O
[2]Epidemiology, W
[3]Division of Pharm

SCOPE

Strengthening Collaborations for Operating Pharmacovigilance in Europe
Work Package 6 – Risk Communication

John D. Seeger[1,3]

ool, Boston, MA, USA

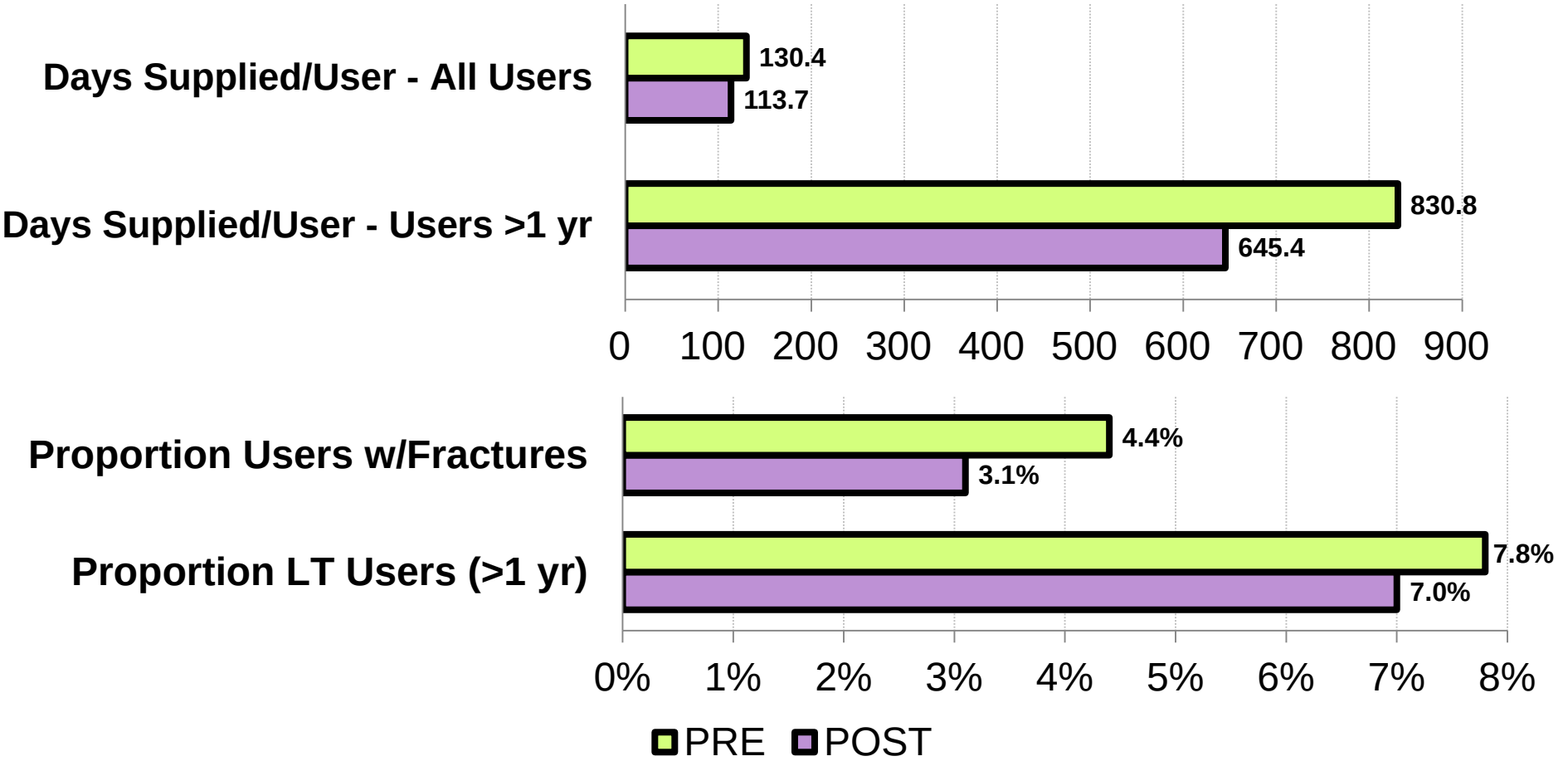
Commentary on "The Effectiveness of Varenicline Medication Guide for Conveying Safety Information to Patients: a REMS Assessment Survey" by Enger *et al.*

Gerald J. Dal Pan*

*US Food and Drug Administration, Silver Spring, MD, USA*

# Impact of a 2010 label change for PPIs

## PPI Use Patterns and Incident Fractures in Sentinel (IMEDS)*




**Results similar for prevalent users (data not shown)**

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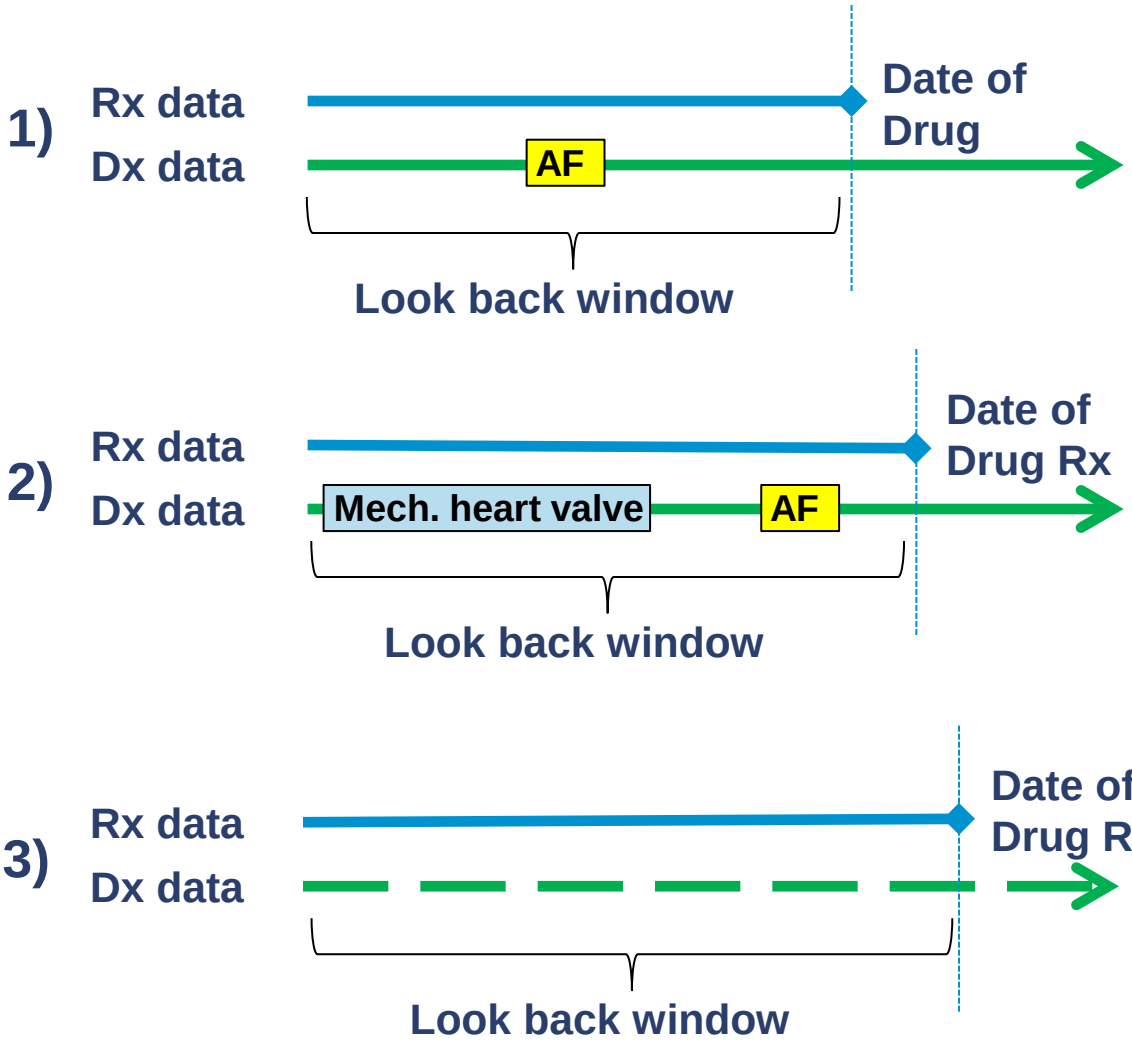
REAGAN - UDALL FOUNDATION FOR THE Food and Drug Administration



*Sobel RE et al. *PDS* 25(S1): S6. Results generated in pilot of Sponsor access to Sentinel tools and data system (RUF IMEDS)

# Do physicians adhere to the apixiban SPC?

## A drug utilization study linking prescription & diagnostic data streams



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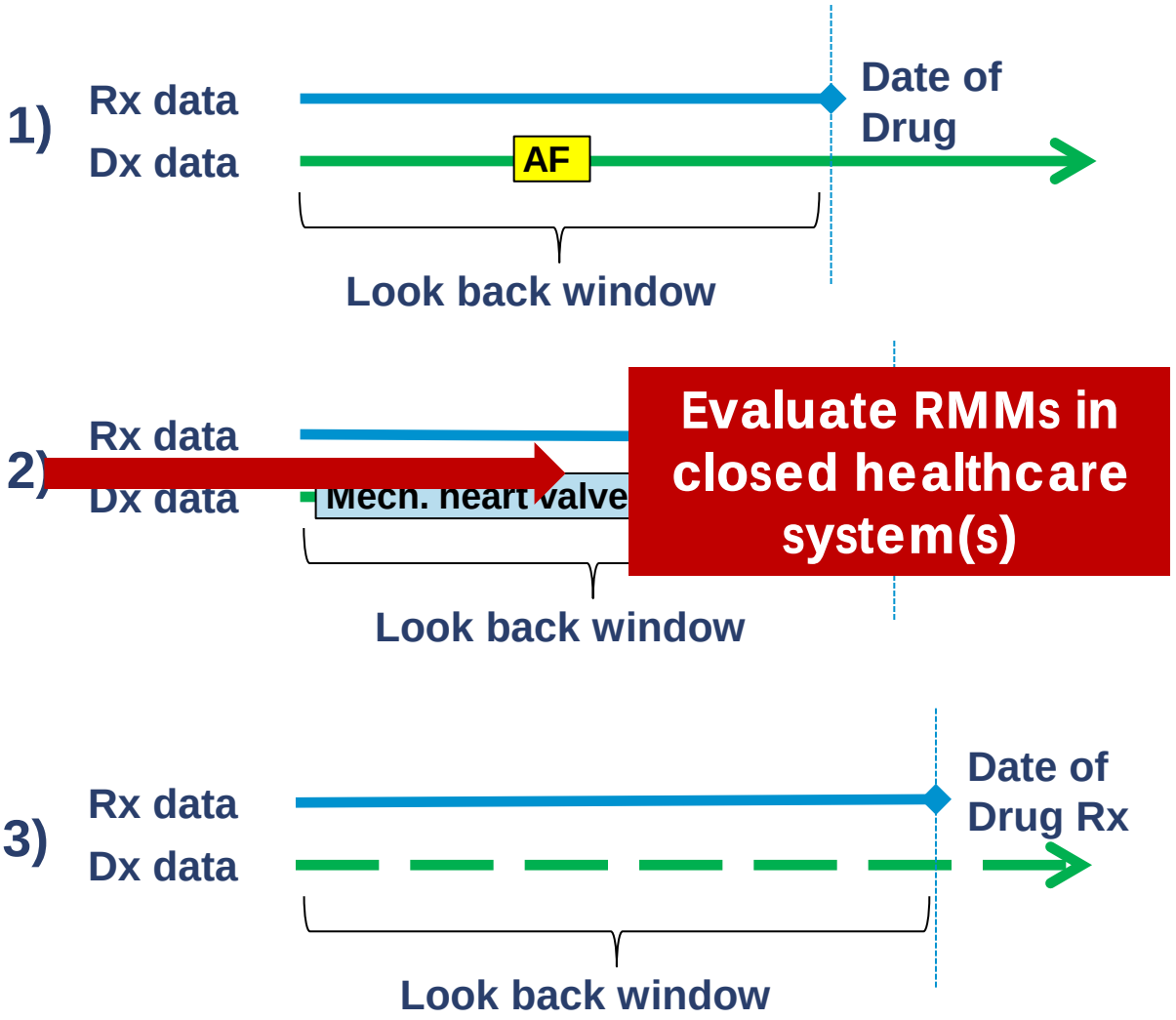





http://www.encepp.eu/encepp/viewResource.htm?id=14474

# EU legislation impact on Industry PV system
## More complex and resource intensive

Table 4: Areas of pharmacovigilance with biggest impact from new legislation

| PhV areas that saw biggest impact of new legislation: | % of respondents | n |
|---|---|---|
| Pharmacovigilance system master file | 74% | 19 |
| New PBRER format | 74% | 19 |
| Risk-management plans | 63% | 19 |
| Reporting of non-serious ADRs | 32% | 19 |
| Article 57 requirements | 26% | 19 |
| PRAC | | |

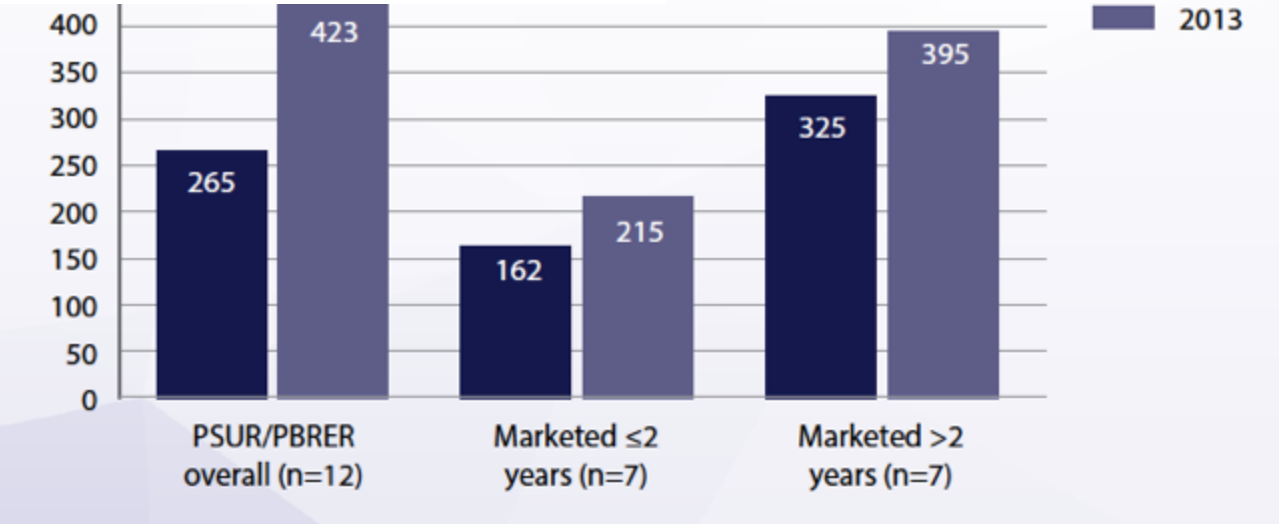
*PRAC: Pharmacovigilan*

The Cost-Effectiveness of Periodic Safety Update Reports for Biologicals in Europe

urs)

JC Bouvy[1,2], HC Ebbers[1], H Schellekens[3,4] and MA Koopmanschap[2]

CLINICAL PHARMACOLOGY & THERAPEUTICS | VOLUME 93 NUMBER 5 | MAY 2013

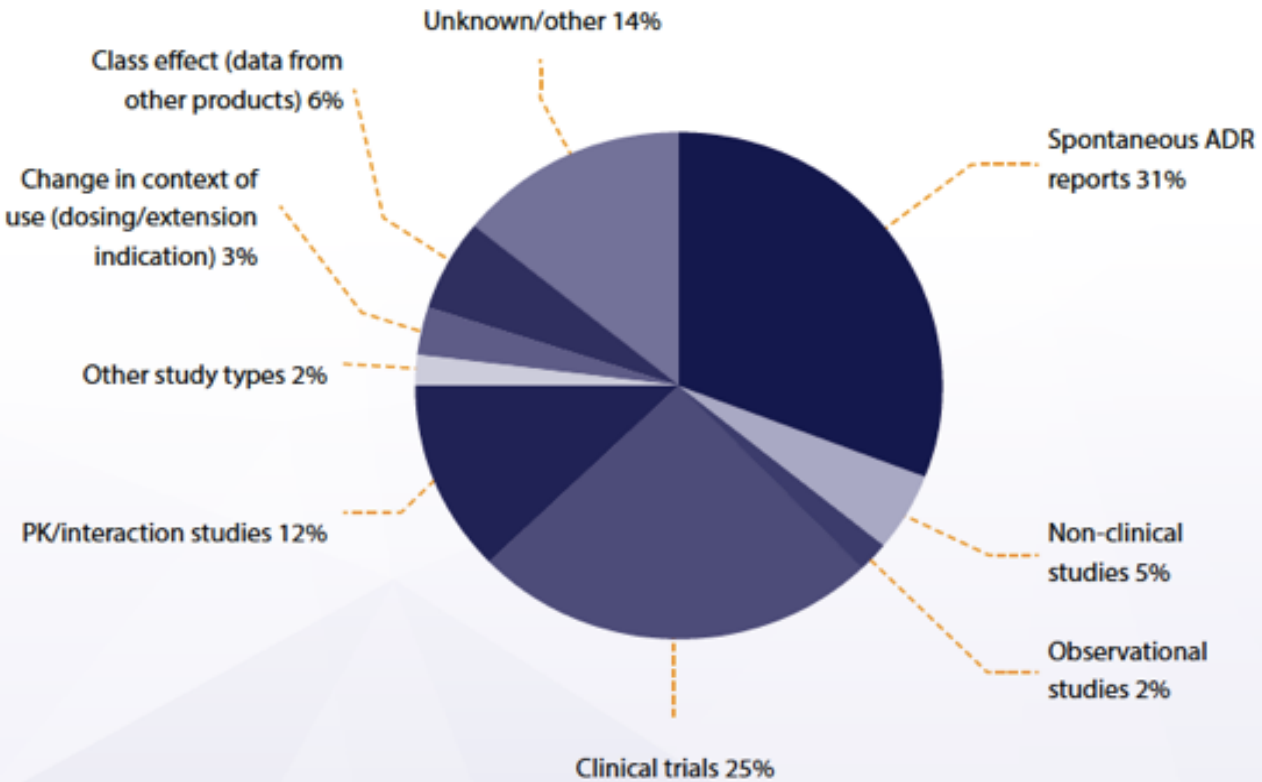





Escher report, 2014: pp. 60, 62

# EU legislation impact on Industry PV system
## Source of safety information for label change

Figure 2: Sources of safety variations for all NASs approved in 2007 (n=334)




*Observational studies include database studies and registries. Paediatric trials are included in the clinical trials, Paediatric PK studies are included under PK/interaction studies. Percentage of requested PASSs resulting in an SmPC change: 4% (13 SmPC changes in total). Study types: four observational studies, four PK/interaction studies, five interventional studies.*



Escher report, 2014: p. 67

# Measuring the Value of Innovation in PV
## Big data and advanced analytics



**Digital data streams everywhere**

**Hope for better *and* faster insights**

# Hypothesis-free signal detection in EHR data

Alternative or complement to spontaneous reports?

Drug Saf (2015) 38:1201–1210
DOI 10.1007/s40264-015-0341-5

ORIGINAL RESEARCH ARTICLE

## Useful Interplay Between Spontaneous ADR Reports and Electronic Healthcare Records in Signal Detection

Alexandra C. Pacurariu[1,2] · Sabine M. Straus[1,2] · Gianluca Trifirò[1,3] · Martijn J. Schuemie[1] · Rosa Gini[4] · Ron Herings[5] · Giampiero Mazzaglia[6] · Gino Picelli[7] · Lorenza Scotti[8] · Lars Pedersen[9] · Peter Arlett[10] · Johan van der Lei[1] · Miriam C. Sturkenboom[1] · Preciosa M. Coloma[1]

**Key Points**

Overall, a spontaneous reporting system (SRS) is better suited to detection of signals than an electronic health record (EHR)-based system, especially for certain types of reactions (rare events and those with a high drug-attributable risk).

Use of EHRs might be justifiable in some situations where SRSs perform poorly (e.g. outcomes with a high background incidence), provided that the additional costs can be taken into account.

SRSs and EHR-based signal detection systems can be complementary, the additional value of one to the other varying across events, as a function of the background incidence of the event.

ry

Months relative to first prescription

No influential outliers



Cederholm S et al. *Drug Safety* 38(1), 87-100, 201; Hauben M et al. PDS 25(S1): S441, 2016; Hauben M et al. *Drug Safety* 39 (10), 1015, 2015

# Does NLP-derived data improve safety information from structured EHR data?

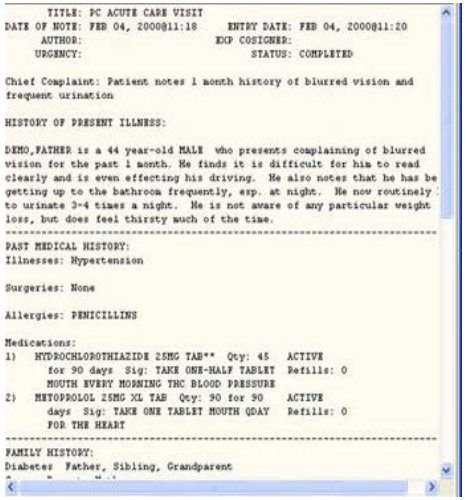
## NLP in Electronic Medical Record (EMR) Systems

### Structured ("Coded")

| | Gender (M/F) | Age | Weight (lbs.) | Height (in.) | Smoking (1=No, 2=Yes) | Race |
|---|---|---|---|---|---|---|
| Patient #1 | M | 59 | 175 | 69 | 1 | White |
| Patient #2 | F | 67 | 140 | 62 | 2 | Black |
| Patient #3 | F | 73 | 155 | 59 | 1 | Asian |
| . | . | . | . | . | . | . |
| . | . | . | . | . | . | . |
| . | . | . | . | . | . | . |
| . | . | . | . | . | . | . |
| . | . | . | . | . | . | . |
| Patient #75 | M | 48 | 90 | 72 | 1 | White |

Demographics. diagnoses, procedures, Rx, lab orders &/or results, billing, operations data

### Unstructured ("Free Text")



TITLE: PC ACUTE CARE VISIT
DATE OF NOTE: FEB 04, 2000@11:18 ENTRY DATE: FEB 04, 2000@11:20
AUTHOR: EXP COSIGNER:
URGENCY: STATUS: COMPLETED

Chief Complaint: Patient notes 1 month history of blurred vision and frequent urination

HISTORY OF PRESENT ILLNESS:

DEMO,FATHER is a 44 year-old MALE who presents complaining of blurred vision for the past 1 month. He finds it is difficult for him to read clearly and is even effecting his driving. He also notes that he has be getting up to the bathroom frequently, esp. at night. He now routinely to urinate 3-4 times a night. He is not aware of any particular weight loss, but does feel thirsty much of the time.

PAST MEDICAL HISTORY:
Illnesses: Hypertension

Surgeries: None

Allergies: PENICILLINS

Medications:
1) HYDROCHLOROTHIAZIDE 25MG TAB** Qty: 45 ACTIVE
for 90 days Sig: TAKE ONE-HALF TABLET Refills: 0
MOUTH EVERY MORNING THC BLOOD PRESSURE
2) METOPROLOL 25MG XL TAB Qty: 90 for 90 ACTIVE
days Sig: TAKE ONE TABLET MOUTH QDAY Refills: 0
FOR THE HEART

FAMILY HISTORY:
Diabetes Father, Sibling, Grandparent

HISTORY OF PRESENT ILLNESS:

DEMO,FATHER is a 44 year-old MALE who presents complaining of blurred vision for the past 1 month. He finds it is difficult for him to read clearly and is even effecting his driving. He also notes that he has be



For an applied example (acute liver injury) see Walker A *et al*.. *Int J Medical Informatics* 86: 62-70, 2016; Zhou X et al.. *PDS* 23(S1): S397, 2016

# Social big data – does it contribute to PV?

**Digital Social Media**

PHARMACOEPIDEMIOLOGY AND DRUG SAFETY (2016)
Published online in Wiley Online Library (wileyonlinelibrary.com) **DOI**: 10.1002/pds.4090

ORIGINAL REPORT

## Can social media data lead to earlier detection of drug-related adverse events?

Mei Sheng Duh[1]*, Pierre Cremieux[1], Marc Van Audenrode[2], Francis Vekeman[2], Paul Karner[1], Haimin Zhang[2] and Paul Greenberg[1]

[1]*Analysis Group, Inc., Boston, MA, USA*
[2]*Groupe d'analyse, Ltée, Montréal, QC, Canada*

# Social big data – does it contribute to PV?

**Digital Soc**


PHARMACOEPIDEMIOLOGY
Published online in Wiley Onli

Can social medi erse
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Mei Sheng Duh[1]*, Pierre g[2] and
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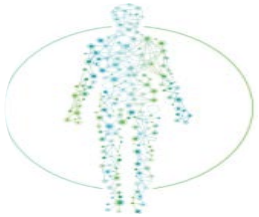
# However beautiful the strategy, you should occasionally look at the results*

Creates the foundation for an adaptable, learning PV system based on rigorous outcomes assessment

Provides a transparent framework for evaluating the performance of system-wide PV strategies

Helps us identify when and why people behave in unexpected and risky ways



Optimizes the benefit-risk profile of medicines for patient well-being



*R. Langworth, *More Quotations Churchill Never Said* (2009)

# Concluding thoughts…refine, replace, retire lest the beautiful strategy to nowhere

- Assess real world outcomes of regulatory actions to identify opportunities for improvement
- Create a learning system to measure how the value of these actions change over time
- Re-allocate effort if these actions do not achieve the objective of public health and patient well-being