

Risk Minimization in a Distributed Data Network:

An IMEDS Evaluation Pilot Assessment of the 2010 Class Label Change for Proton Pump Inhibitors

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Abstract #7 [1151]

Aug 26, 2016

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Disclaimers

- The study was fully funded by Pfizer Inc through the IMEDS program of the Reagan-Udall Foundation for the FDA
- Rachel E. Sobel is an employee and shareholder of Pfizer, Inc which manufactures one or more PPIs in this study
- The views expressed in this presentation do not necessarily reflect those of Pfizer, the FDA, or the data partners
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IMEDS Program Overview

A public-private partnership within the Reagan-Udall Foundation designed to build upon the significant progress made on research methodology by FDA's Sentinel Initiative, including its Mini-Sentinel pilot, and the Observational Medical Outcomes Partnership (OMOP).

IMEDS-Methods

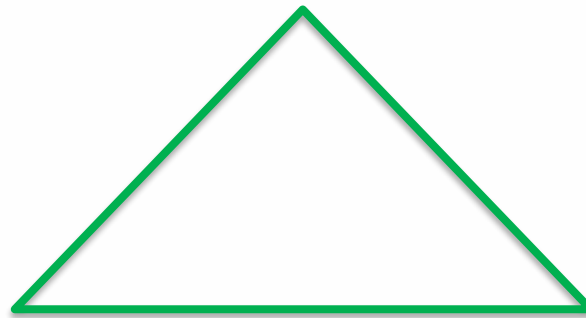
Facilitate methods research aimed at monitoring safety of marketed medical products.

1

IMEDS-Education

Train scientists in how to conduct methods research using electronic healthcare data.

3



IMEDS-Evaluation

Pathway for non-FDA stakeholders to conduct medical product safety evaluations using the same infrastructure as Sentinel.

2

Background and Objectives

Background:

- Evaluation of risk minimization (RM) actions is emerging area of regulatory science
- FDA recently published on the effectiveness of a class-wide label change for long-acting beta agonists (LABAs) using Sentinel¹
- FDA implemented a class-wide label change in May of 2010 for proton pump inhibitors (PPIs) regarding the risk of fracture²

Objectives:

- 1. Develop policies and procedures for IMEDS**
- 2. Test case:** *Using Sentinel rapid analysis tools, to evaluate the impact of the 2010 class-wide PPI label change which:*
 - warned of a potential increase risk of bone fracture,
 - recommended using PPIs for the lowest dose and shortest duration, and
 - recommended managing bone status for those at risk for osteoporosis (OP)

1. Butler et al, *J Allergy Clin Immunol*, 2016

2. <http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm213321.htm>



Methods (1/2)

- **Study Design:** Retrospective Cohort, divided into 2 periods:
 - PRE label change (1Jan07-31May10)
 - POST label change (1Jun10-30Apr15)
 - **Cohort** consisted of:
 - Adults aged ≥ 18 yr prescribed PPIs
 - Incident (no PPI claim in ≥ 183 d) and prevalent users evaluated separately
 - Excluded fracture risk factors: Osteogenesis imperfecta, primary hyperparathyroidism, oral corticosteroids, cancer (non-melanoma), chemo/radiation, aromatase inhibitors, alcoholism, alcoholic cirrhosis (< 183 d), trauma (< 90 d)
 - **Exposure** defined as:
 - 8 PPIs¹ noted in the FDA label change communication
 - Identified via NDC codes in outpatient pharmacy claims
 - Gaps ≤ 14 d allowed
1. esomeprazole, dexlansoprazole, omeprazole, omeprazole+sodium bicarbonate, lansoprazole, pantoprazole, rabeprazole, naproxen+esomeprazole magnesium



Methods (2/2)

- **Outcomes:**

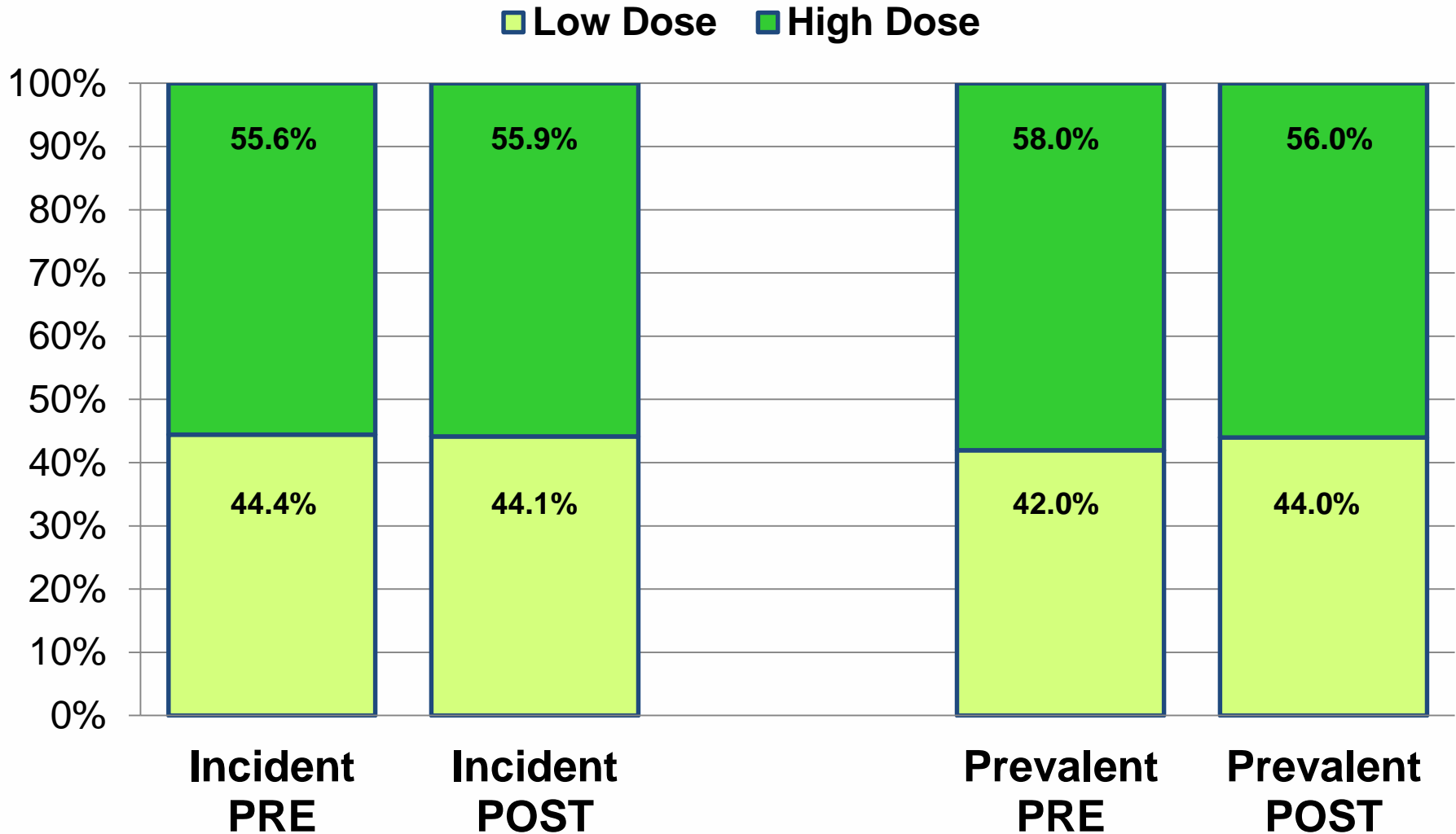
- Number of PPI users overall
- Mean duration of PPI use
- Proportions of PPI use ≥ 1 yr
- Proportions of PPI use at low/high doses
- Proportions of PPI users with incident fractures
- Proportions of PPI users with OP screening or interventions (eg., DEXA scans, OP medications/New OP Dx, Calcium/Vit D use)

- **Analysis:**

- Used select publicly-available Sentinel tools and programs (Level 1 Modular Programs)
- Nine Sentinel data partners participated
- Descriptive analyses only (consistent with typical FDA use)
 - rates and proportions stratified by age, sex, and year



Results – Proportion of Low vs. High Dose Use



Results – Incident Osteoporosis Interventions

Incident PPI Users

	PRE LABEL CHANGE 1Jan07-31May10 n = 1,488,869		POST LABEL CHANGE 1Jun10-30Apr15 n = 2,224,420	
	<i>All Users</i>	<i>Long Term Users</i>	<i>All Users</i>	<i>Long Term Users</i>
Anti-OP Medication or OP Diagnosis	1.65%	8.65%	1.25%	6.14%
Bone Density Screening	2.98%	16.00%	2.45%	12.19%
Calcium/Vit D Supplementation	0.16%	0.53%	0.07%	0.17%

Results similar for prevalent users (data not shown)



Results – Incident Osteoporosis Interventions

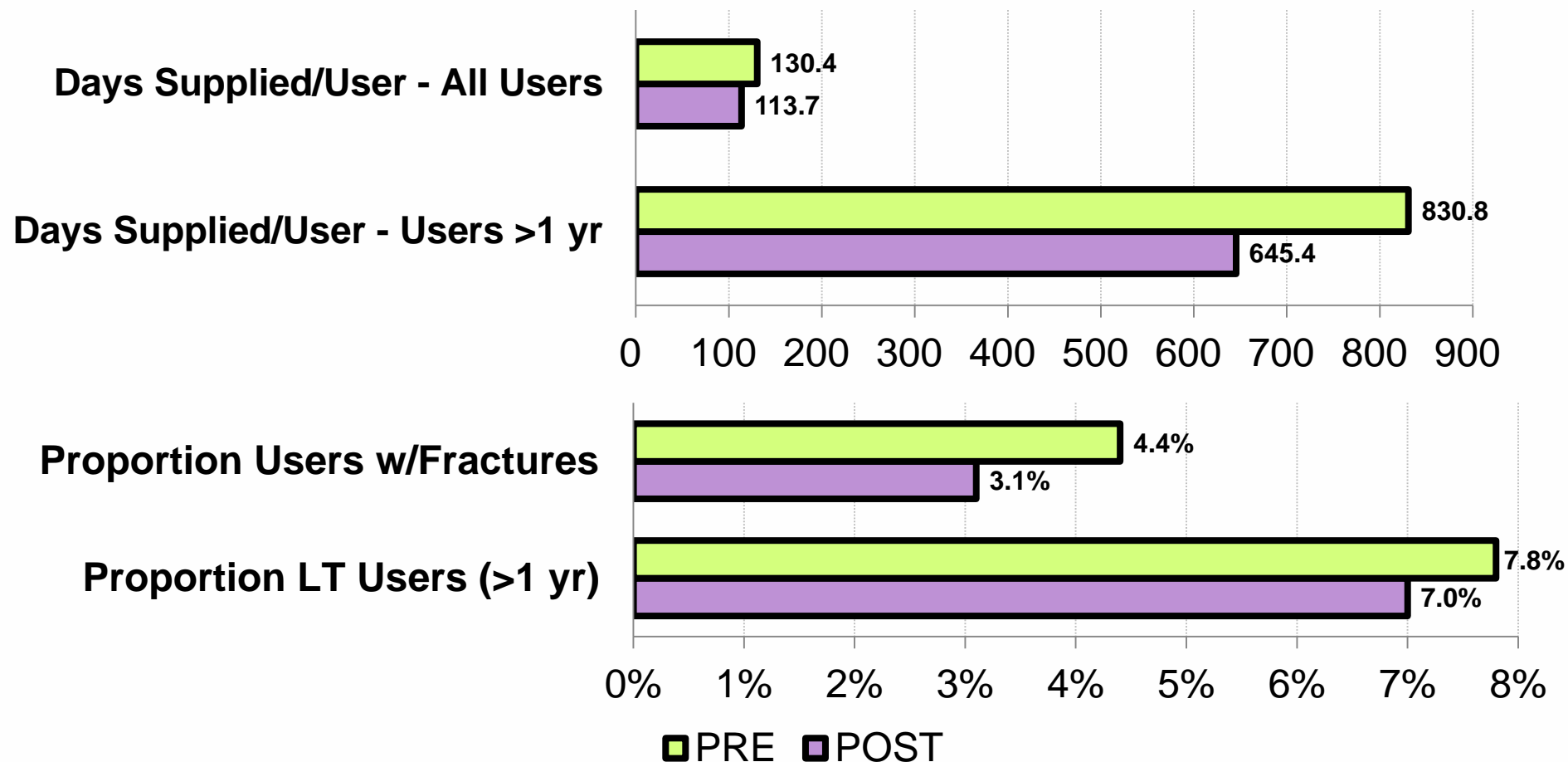
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Results similar for prevalent users (data not shown)

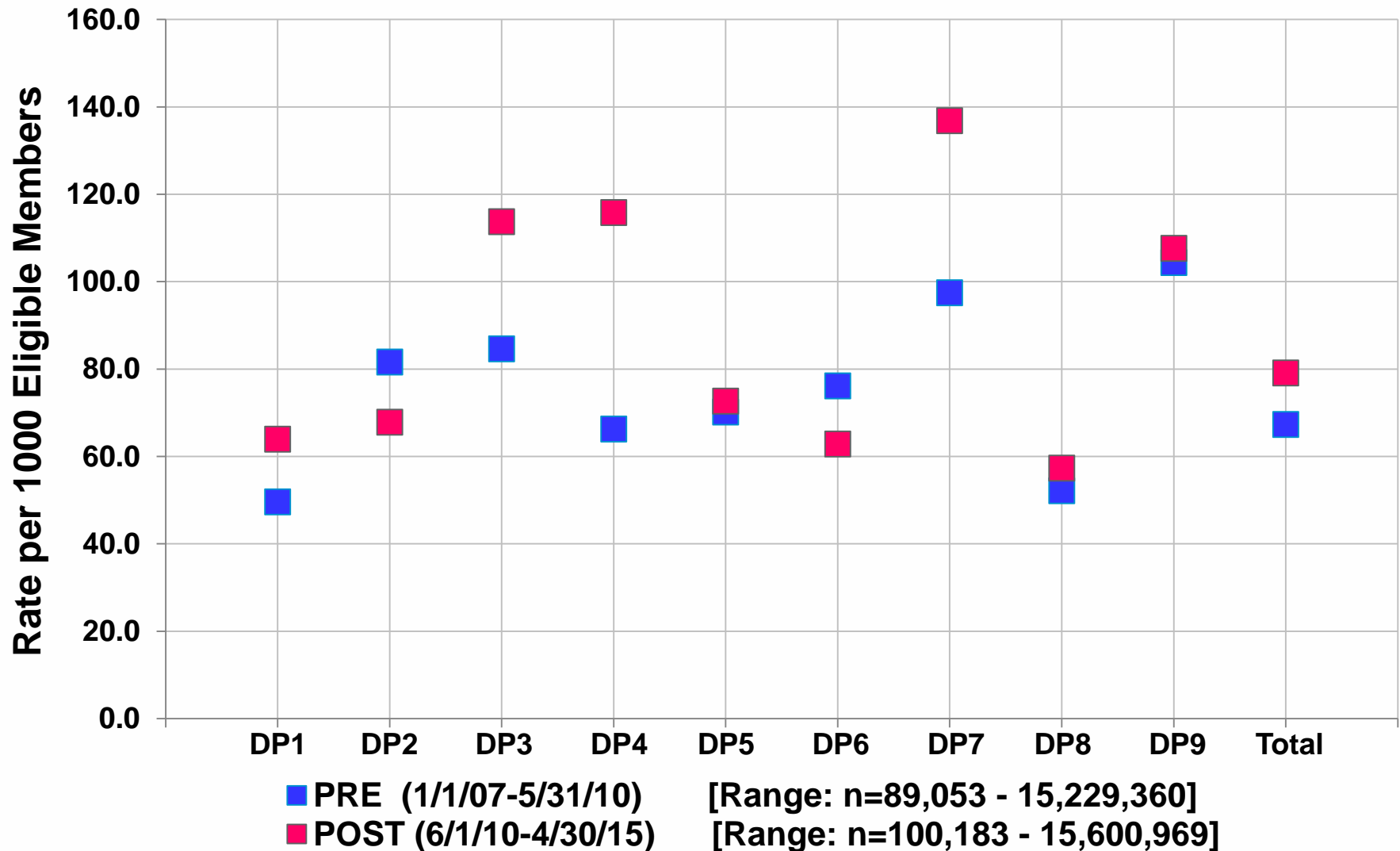


Results – PPI Use Patterns and Incident Fractures



Results similar for prevalent users (data not shown)

Data Partner Variation: Prevalent PPI Users per 1000 Eligible Members



Discussion and Conclusions

- Data suggest that the length of PPI therapy, number of long term users, and fracture outcomes were reduced after the label change
 - OP management generally *decreased* after the label change (unexpected)
- Demonstrated ability to use select Sentinel tools to characterize the utilization patterns and outcomes possibly associated with RM actions at a population level
- Limitations include lack of confounding control, simple descriptive analysis techniques, and several outcomes were defined only by diagnosis or medication code
 - Alternative explanations for observations may exist, e.g., changes in populations, individual plan formulary/reimbursement status, or other secular trends
- The results show the potential value of a large distributed data network in assessing RM effectiveness

We thank the participating data partners Group Health, Harvard Pilgrim, Healthcore, HealthPartners, Humana, Marshfield, Meyers Primary Care, Optum, and Vanderbilt for their contributions, expertise, and data provision for this pilot, but wish to emphasise that the conclusions are not necessarily those of the data partners themselves

Thank You and Questions

- Related Abstract:
 - *Poster Session C: Safety & Effectiveness - GU & Hormones* on Sunday, 8/28/2016 from 8:00 AM - 1:45 PM.
 - **564 Oral Contraceptives and VTE across the Sentinel data network – An IMEDS Evaluation pilot assessment [915].** Bate A, Sobel RE, Marshall J, Daniel G, McCall T, Reynolds RF, Brown J.



Backups

Results – Incident PPI Users

	PRE Label Change 1Jan07-31May10	POST Label Change 1Jun10-30Apr15
Initial Member Count	82,311,554	102,031,732
Valid Medical &/or Drug Coverage	53,064,740	59,978,100
Age ≥18 yr	41,310,331	49,226,165
Incident PPI use	3,246,214	4,201,716
≥183d Continuous Enrollment	1,858,342	2,813,021
No exclusion criteria	1,488,869	2,224,420

