Assessing the impact of pharmacovigilance: Experience at the US Food and Drug Administration

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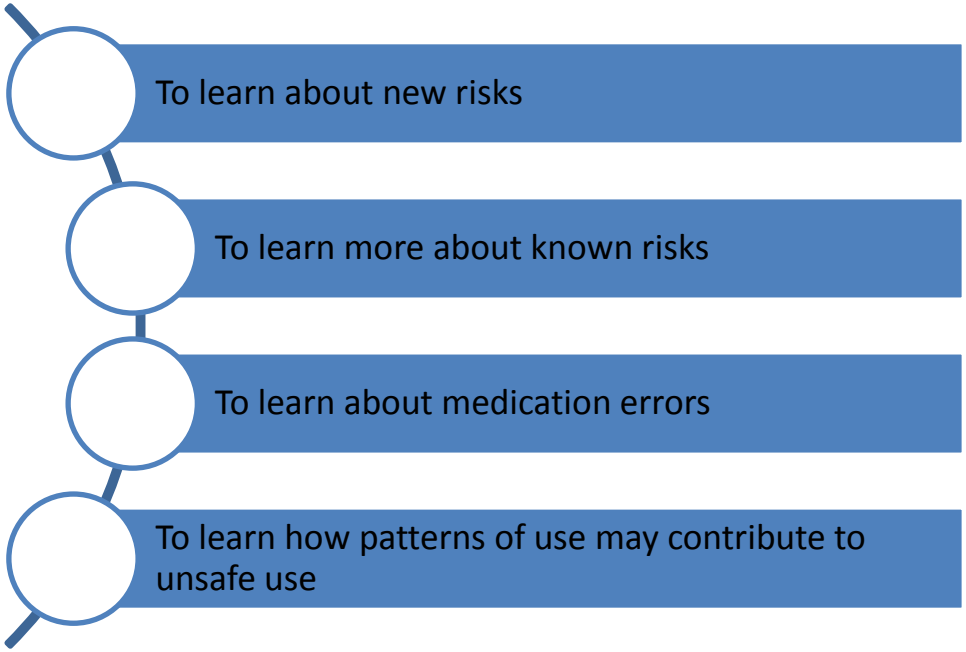
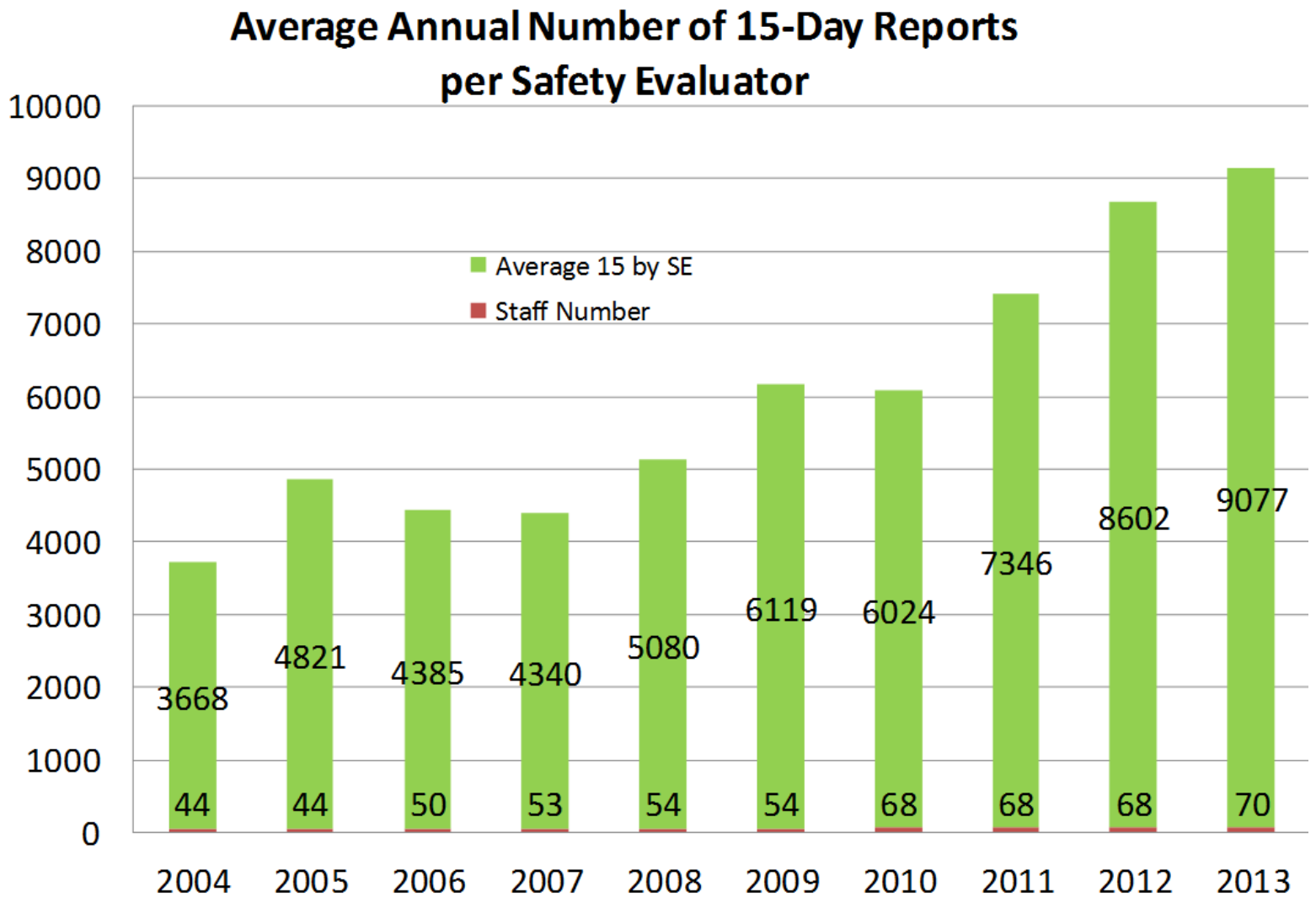
The views expressed in this presentation are those of the presenter and not necessarily those of the US Food and Drug Administration

No conflicts of interest to disclose

Assessing the Pharmacovigilance System and Its Impact



- Does the current system do this well?
- Is the system efficient?
- Are resources well allocated?
- Does it have a beneficial impact on the public health?


Average Annual Number of 15-Day Reports per Safety Evaluator
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
Average 15 by SE
Staff Number
3668
4821
4385
4340
5080
6119
6024
7346
8602
9077
44
44
50
53
54
54
68
68
68
70
2004
2005
2006
2007
2008
2009
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2011
2012
2013

PHARMACOEPIDEMIOLOGY AND DRUG SAFETY 2013
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ORIGINAL REPORT

Evaluation of FDA safety-related drug label changes in 2010

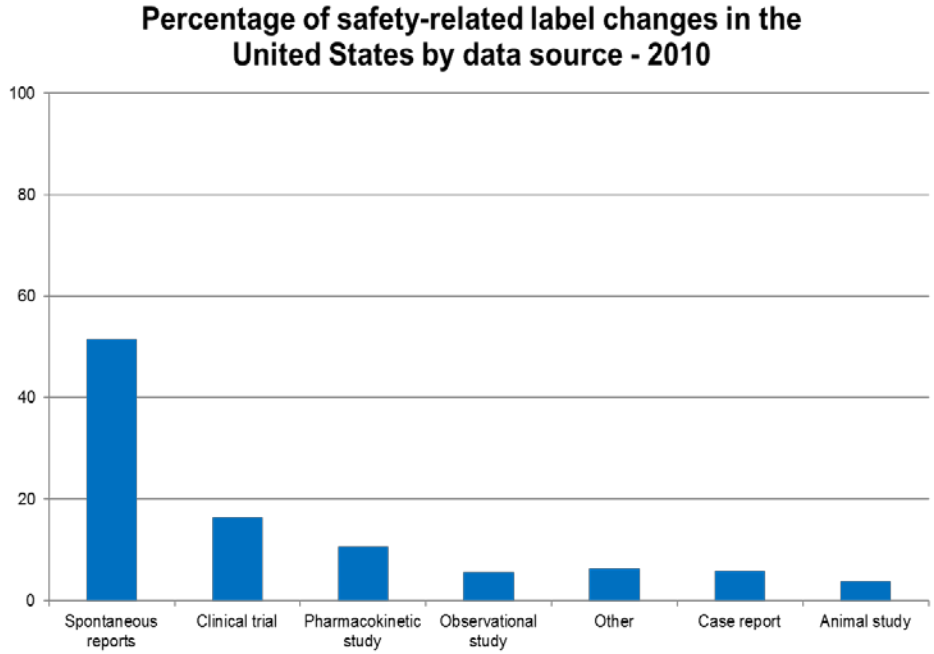
Jean Lester[1,2*], George A. Neyarapally[2], Earlene Lipowski[1], Cheryl Fossum Graham[2], Marni Hall[2] and Gerald Dal Pan[2]

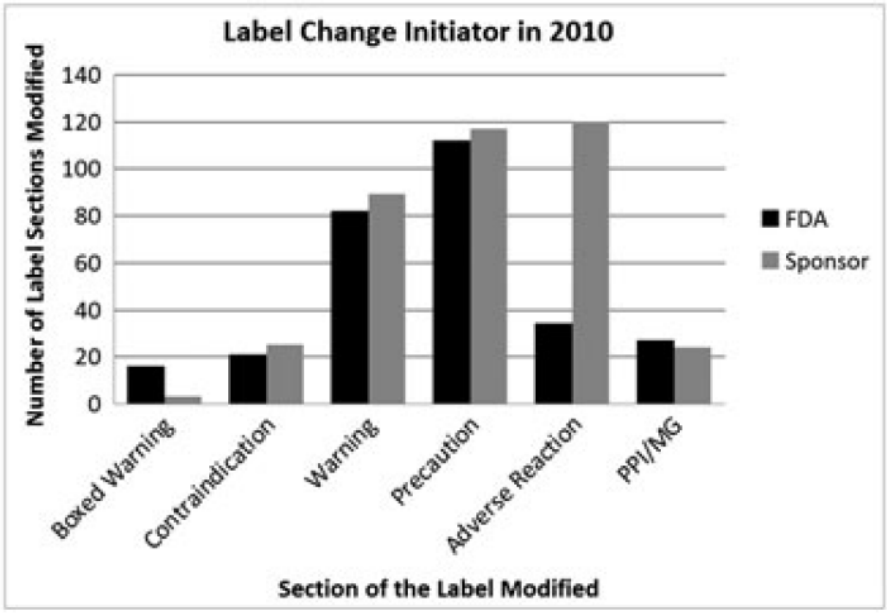
[1] *University of Florida College of Pharmacy, Department of Pharmaceutical Outcomes and Policy 1225 Center Drive, HPNP 3334, Gainesville, FL 32611, USA*
[2] *Food and Drug Administration, Center for Drug Evaluation and Research, 10903 New Hampshire Avenue, Silver Spring, MD 20993, USA*

- Review of all safety-related labeling changes in 2010
- Examined each source of data contributing to the labeling change
- Reviewed who initiated the change – FDA or sponsor

Source: Lester et al. Pharmacoepidemiol Drug Safety 2013 Mar;22(3):302-5

Safety Labeling Changes





Source: Lester et al. Pharmacoepidemiol Drug Safety 2013 Mar;22(3):302-5

Understanding What Product a Patient Actual Took in an Adverse Event Report

ARTICLES

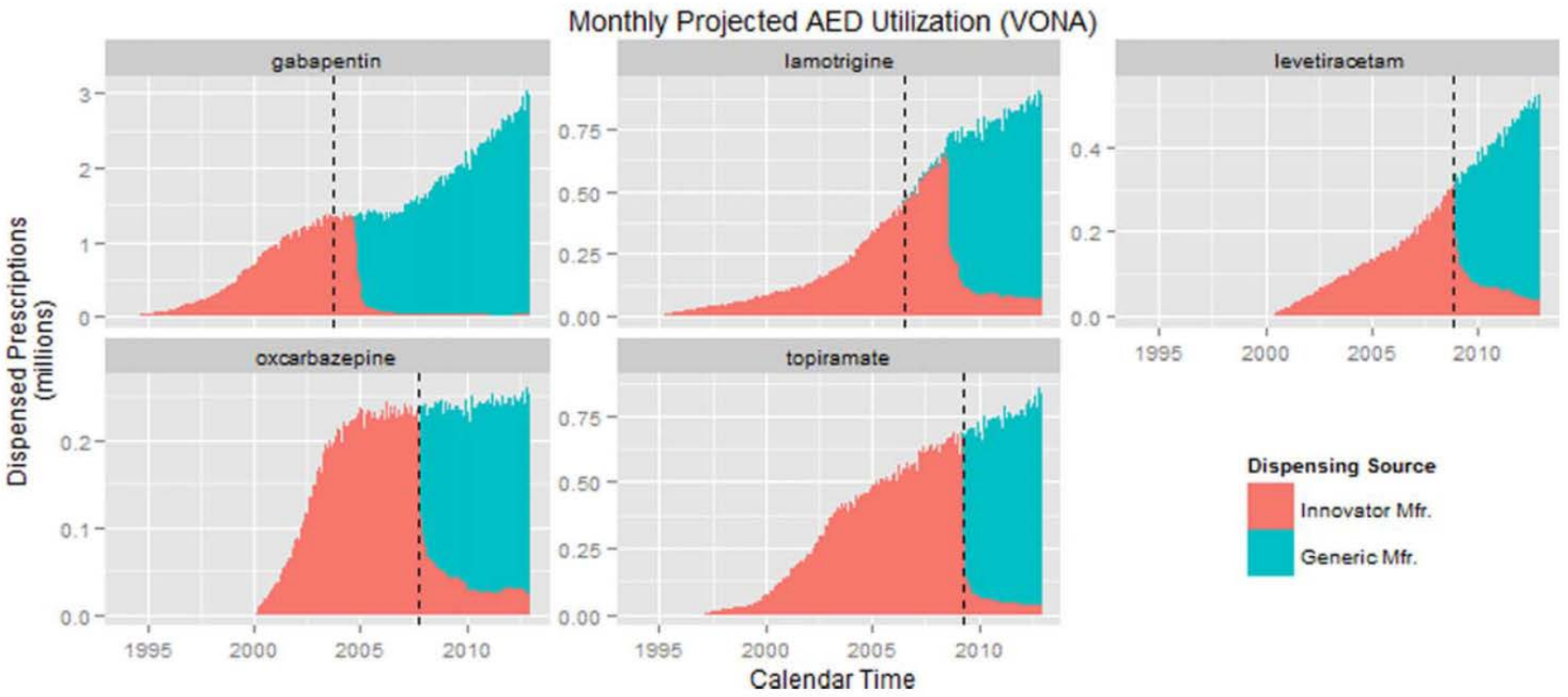
Patterns in Spontaneous Adverse Event Reporting Among Branded and Generic Antiepileptic Drugs

J Bohn[1,2,3], C Kortepeter[3], M Muñoz[3], K Simms[3], S Montenegro[3] and G Dal Pan[3]

- Five anti-epileptic drugs before and after generic introduction
- Measured drug utilization over time
- Measured adverse event report source over time
- Manually reviewed 2500 reports to determine which product the patient actually took

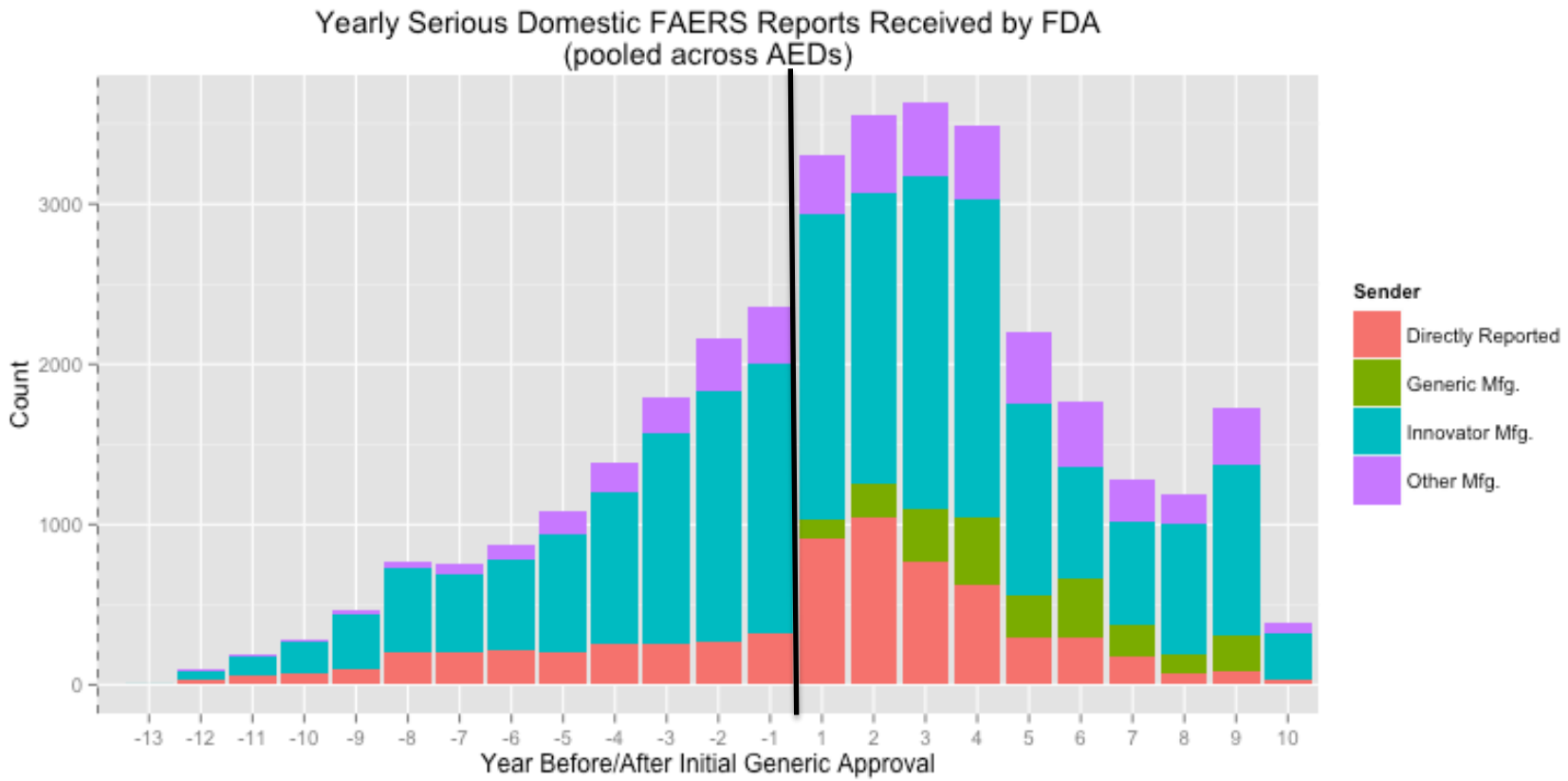
Source: Based on Bohn et al. Clin Pharmacol Ther 2015;97: 508-17/

Drug Utilization



Source: Based on Bohn et al. Clin Pharmacol Ther 2015;97: 508-17/

Source of AED Reports



Source: Based on Bohn et al. Clin Pharmacol Ther 2015;97: 508-17/

Results of Manual Review

Table 3: Summary of Product-Identifying Information in a Subset of FAERS Reports for 5 AEDs Stratified by Product of Interest

	Gabapentin	Lamotrigine	Levetiracetam	Oxcarbazepine	Topiramate	All
n	497	499	499	500	500	2495
Name Used to Describe Product (%)						
Both Brand and Generic	272 (54.7)	269 (53.9)	225 (45.1)	168 (33.6)	71 (14.2)	1005 (40.3)
Brand	45 (9.1)	40 (8.0)	94 (18.8)	71 (14.2)	79 (15.8)	329 (13.2)
Generic	139 (28.0)	168 (33.7)	120 (24.0)	167 (33.4)	298 (59.6)	892 (35.8)
None	41 (8.2)	22 (4.4)	60 (12.0)	94 (18.8)	52 (10.4)	269 (10.8)
General Terms Used to Describe Product (%)						
Brand	1 (0.2)	2 (0.4)	1 (0.2)	2 (0.4)	2 (0.4)	8 (0.3)
Generic	25 (5.0)	62 (12.4)	102 (20.4)	83 (16.6)	80 (16.0)	352 (14.1)
None	471 (94.8)	435 (87.2)	396 (79.4)	415 (83.0)	418 (83.6)	2135 (85.6)
Manufacturer Mentioned (Narrative) (%)						
Innovator	8 (1.6)	2 (0.4)	4 (0.8)	3 (0.6)	0 (0.0)	17 (0.7)
Generic	15 (3.0)	7 (1.4)	16 (3.2)	18 (3.6)	17 (3.4)	73 (2.9)
None	474 (95.4)	490 (98.2)	479 (96.0)	479 (95.8)	483 (96.6)	2405 (96.4)
Manufacturer Provided (FAERS Fields) (%)						
Innovator	134 (27.0)	273 (54.7)	14 (2.8)	111 (22.2)	11 (2.2)	543 (21.8)
Generic	27 (5.4)	27 (5.4)	59 (11.8)	71 (14.2)	80 (16.0)	264 (10.6)
None	336 (67.6)	199 (39.9)	426 (85.4)	318 (63.6)	409 (81.8)	1688 (67.7)
Manufacturer Switch Mentioned (%)	20 (4.0)	49 (9.8)	69 (13.8)	51 (10.2)	55 (11.0)	244 (9.8)
Most Likely Product Type (%)						
Innovator	9 (1.8)	3 (0.6)	3 (0.6)	4 (0.8)	2 (0.4)	21 (0.8)
Generic	35 (7.0)	65 (13.0)	109 (21.8)	89 (17.8)	89 (17.8)	387 (15.5)
Undetermined	453 (91.1)	431 (86.4)	387 (77.6)	407 (81.4)	409 (81.8)	2087 (83.6)

Source: Based on Bohn et al. Clin Pharmacol Ther 2015;97: 508-17/

ARTICLES

Assessment of the Impact of Scheduled Postmarketing Safety Summary Analyses on Regulatory Actions

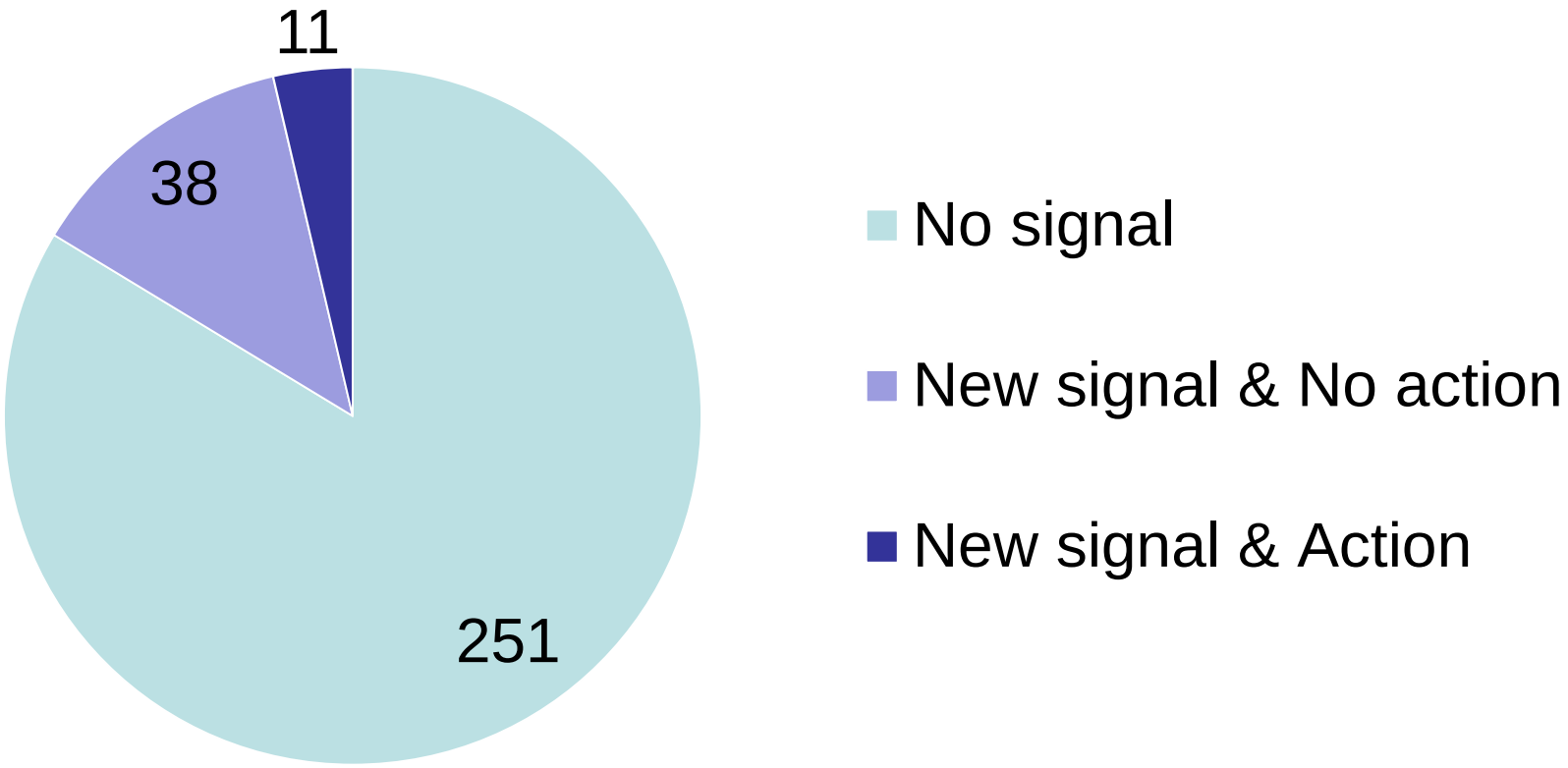
S Sekine[1,2], EE Pinnow[1], E Wu[1], R Kurtzig[1], M Hall[1] and GJ Dal Pan[1]

- Safety analyses conducted 18 months after approval or after 10,000 patients have used, whichever is later
- In addition to FDA's routine pharmacovigilance activities
- Focus is on identification of risks

- Required by law since 2007
- Summary of safety findings is posted on FDA's website
- Study designed to determine the impact of these scheduled safety summary analyses

Source: Sekine et al. Clin Pharmacol Ther 2016 Feb 8. doi: 10.1002/cpt.346. [Epub ahead of print]

Results of the Scheduled Safety Summary Analyses



Source: Sekine et al. Clin Pharmacol Ther 2016 Feb 8. doi: 10.1002/cpt.346. [Epub ahead of print]

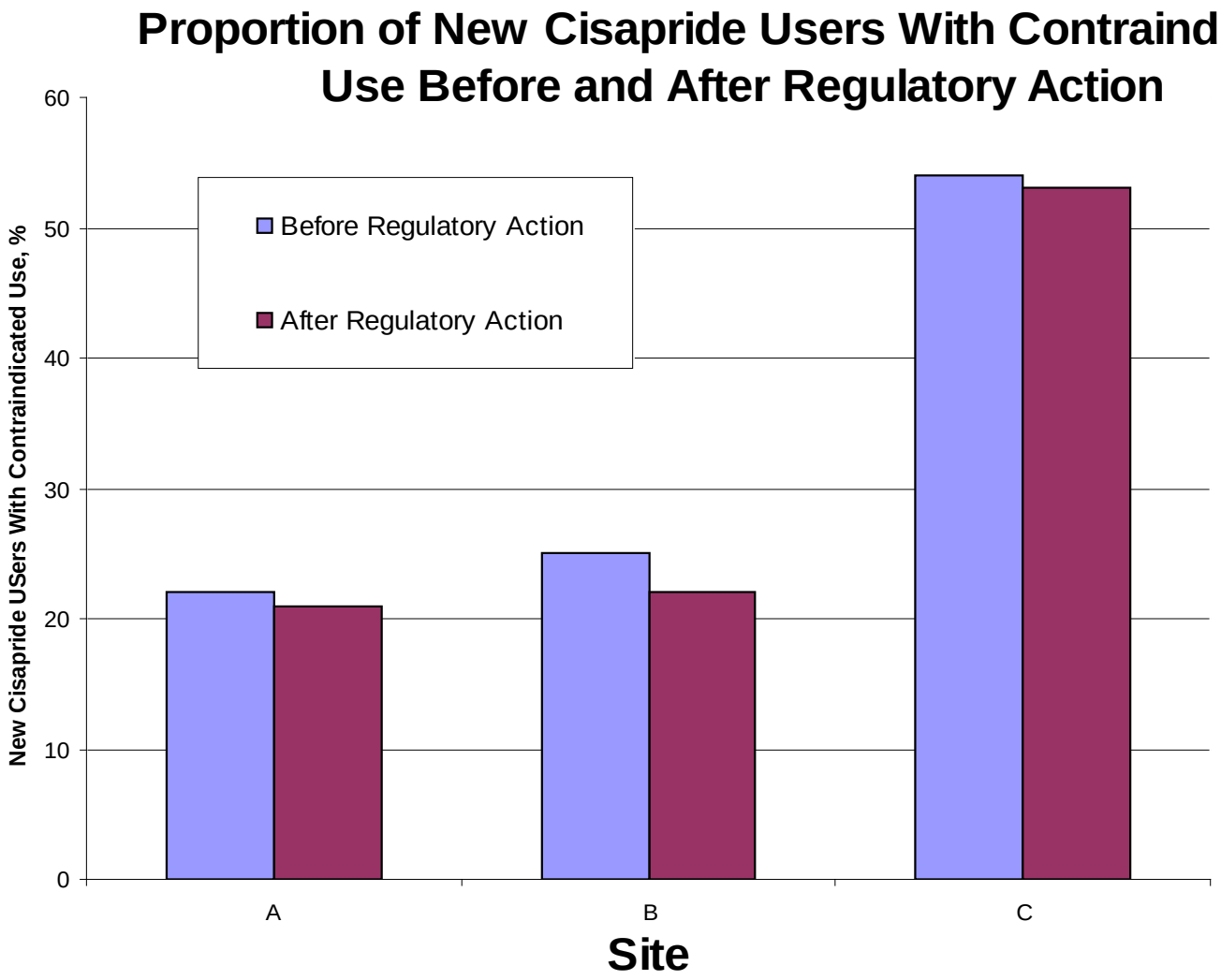
Contribution of Scheduled Safety Summary Analyses to Safety-related Labeling Changes

Source: Based on Sekine et al. Clin Pharmacol Ther 2016 Feb 8. doi: 10.1002/cpt.346. [Epub ahead of print]

Labeling Changes to Promote Safe Use – The Case of Cisapride

- Cisapride – gastrointestinal promotility agent
- Can cause life-threatening cardiac arrhythmias if
  - Used with certain contraindicated concomitant medications
  - Used in person with certain other diseases
- Regulatory Action – June 1998:
  - Boxed warning contraindicating use in certain patients and with certain concomitant medications
  - Company sent Dear Healthcare Provide Letter to practitioners
- Study: Look at prescribing patterns one year before and one year after regulatory action
- Finding:
  - High prevalence of contraindicated use at three sites
  - No change in prescribing patterns after regulatory action

Labeling Changes to Promote Safe Use – The Case of Cisapride - Results



Adapted from Smalley et al. Contraindicated Use of Cisapride. JAMA 2000;284:3036-3039

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ORIGINAL REPORT

Patient understanding of drug risks: an evaluation of medication guide assessments

Caitlin Knox[1]*, Christian Hampp[2], Mary Willy[2], Almut G. Winterstein[1,3] and Gerald Dal Pan[2]

[1] *Pharmaceutical Outcomes and Policy, College of Pharmacy, University of Florida, Gainesville, FL, USA*
[2] *Office of Surveillance and Epidemiology, Center for Drug Evaluation and Research, U.S. Food and Drug Administration, Silver Spring, MD, USA*
[3] *Epidemiology, College of Public Health and Health Professions and College of Medicine, University of Florida, Gainesville, FL, USA*

- Reviewed patient-knowledge surveys for 66 Medication Guides
- For each Medication Guide survey, an "acceptable knowledge rate" was achieved if 80% or more of survey respondents correctly answered questions about the primary drug risk
- 20 of 66 (30.3%) Medication Guide assessments met 80% threshold

Source: Knox C et al. Pharmacoepidemiol Drug Safety 2015 May;24(5):518-25

Assessing the Impact of Communications

Drug Saf (2015) 38:565–575
DOI 10.1007/s40264-015-0291-y

STUDY DESIGN

Methodological Approaches to Evaluate the Impact of FDA Drug Safety Communications

Aaron S. Kesselheim[1] · Eric G. Campbell[2] · Sebastian Schneeweiss[1] · Paula Rausch[3] · Brian M. Lappin[4] · Esther H. Zhou[5] · John D. Seeger[1] · John S. Brownstein[6] · Steven Woloshin[7] · Lisa M. Schwartz[7] · Timothy Toomey[1] · Gerald J. Dal Pan[8] · Jerry Avorn[1]

Published online: 13 May 2015

- Study the impact of FDA's communication on zolpidem
- Prescribing trends
- Health outcomes

- Direct interview of physicians and patients
- National survey of patients
- Descriptions of risk messages in traditional and social media

Thank you