Precompetitive Use of Algorithms to Predict Adverse Events

Sean Khozin, MD, MPH

Acting Associate Director, Oncology Center of Excellence
Director, Information Exchange and Data Transformation (INFORMED)
Food and Drug Administration

@FDAOncology
@SeanKhozin

The information in this presentation does not necessarily represent the view of the FDA

Disclosures: None

U.S. FOOD & DRUG ADMINISTRATION

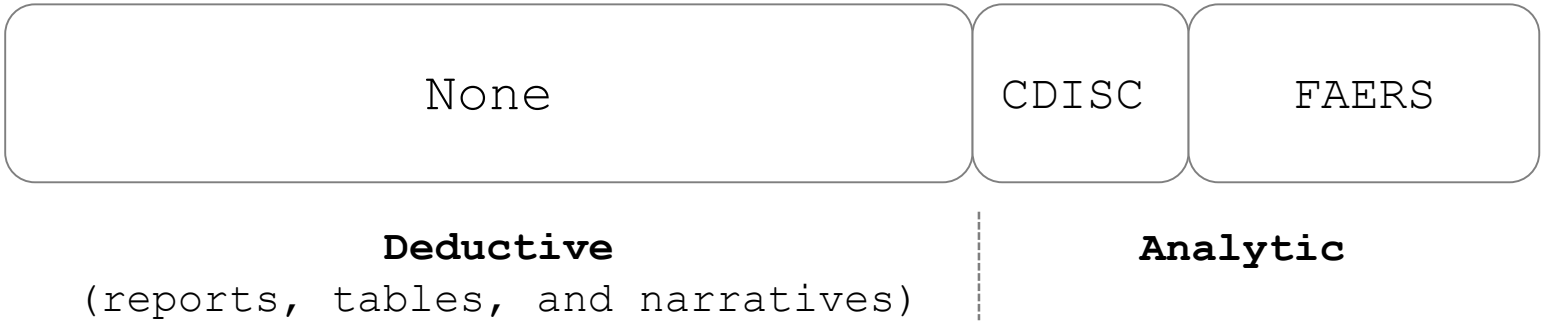
Precompetitive Use of Algorithms to Predict Adverse Events

A great idea!

But…

Safety signal detection at the FDA (and beyond)

Data assets

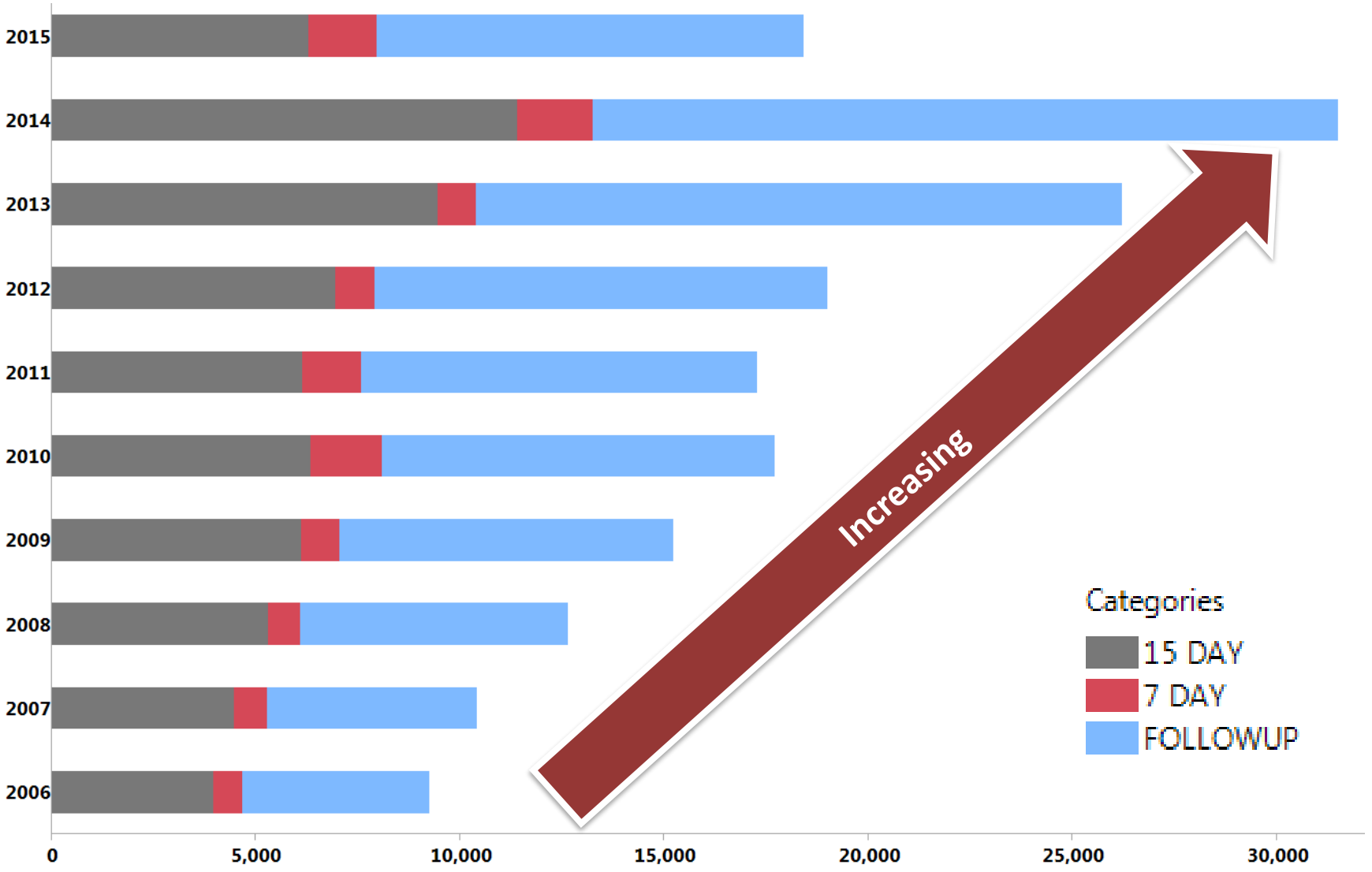


How many "Post Its" does it take: FDA Oncology Premarket reports (commercial sponsors) 1/1/2006 to 6/29/2015

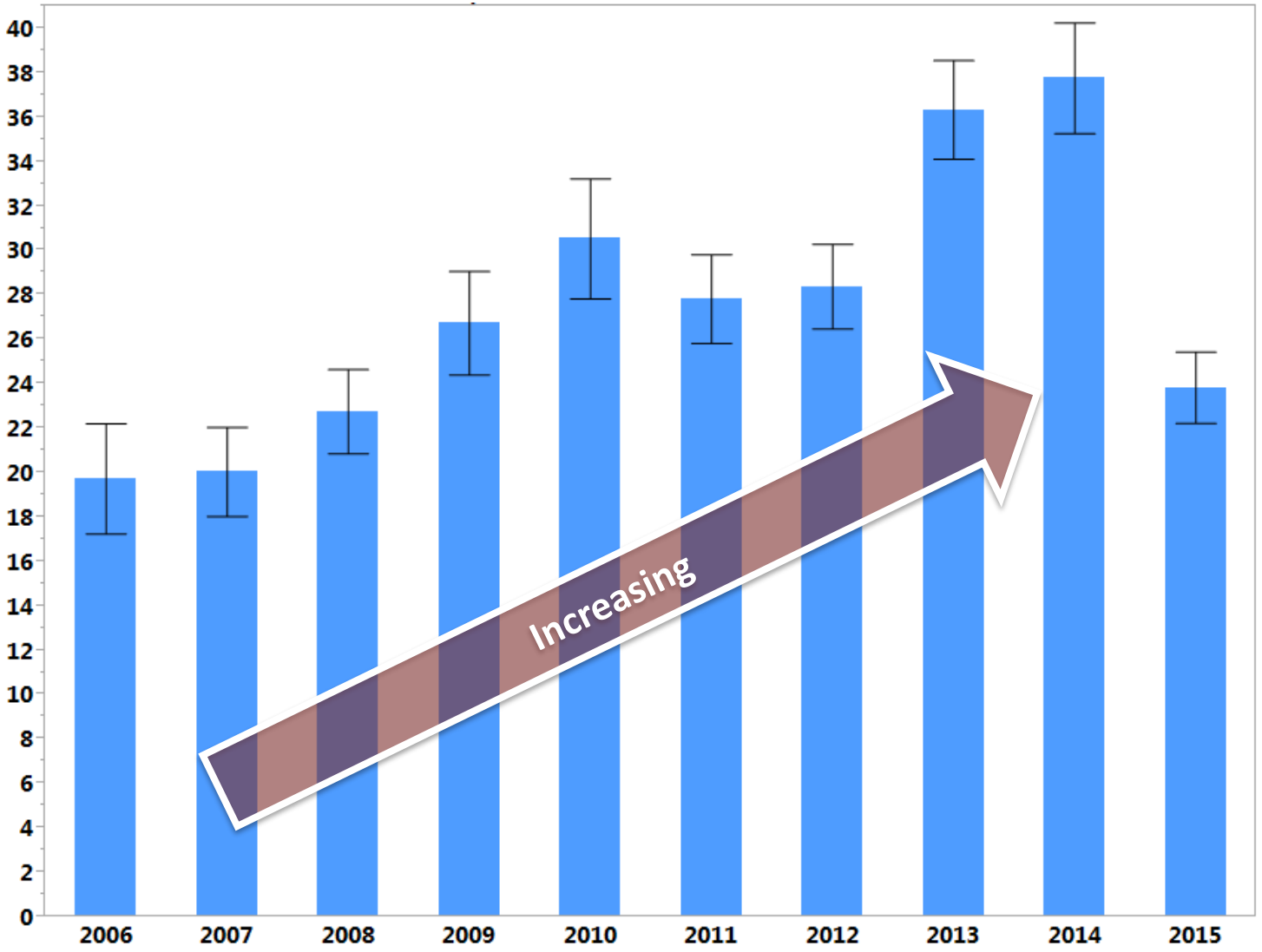
		# safety reports			
Division	**# INDs**	**15-day**	**7-day**	**f/u**	**Total**
DHP	473	18,243	3,326	27,547	49,116
DOP1	651	22,327	4,300	32,539	59,166
DOP2	669	25,723	4,266	39,327	69,316
Total	**1,793**	66,293	11,892	99,413	**177,598**

473 Sponsors

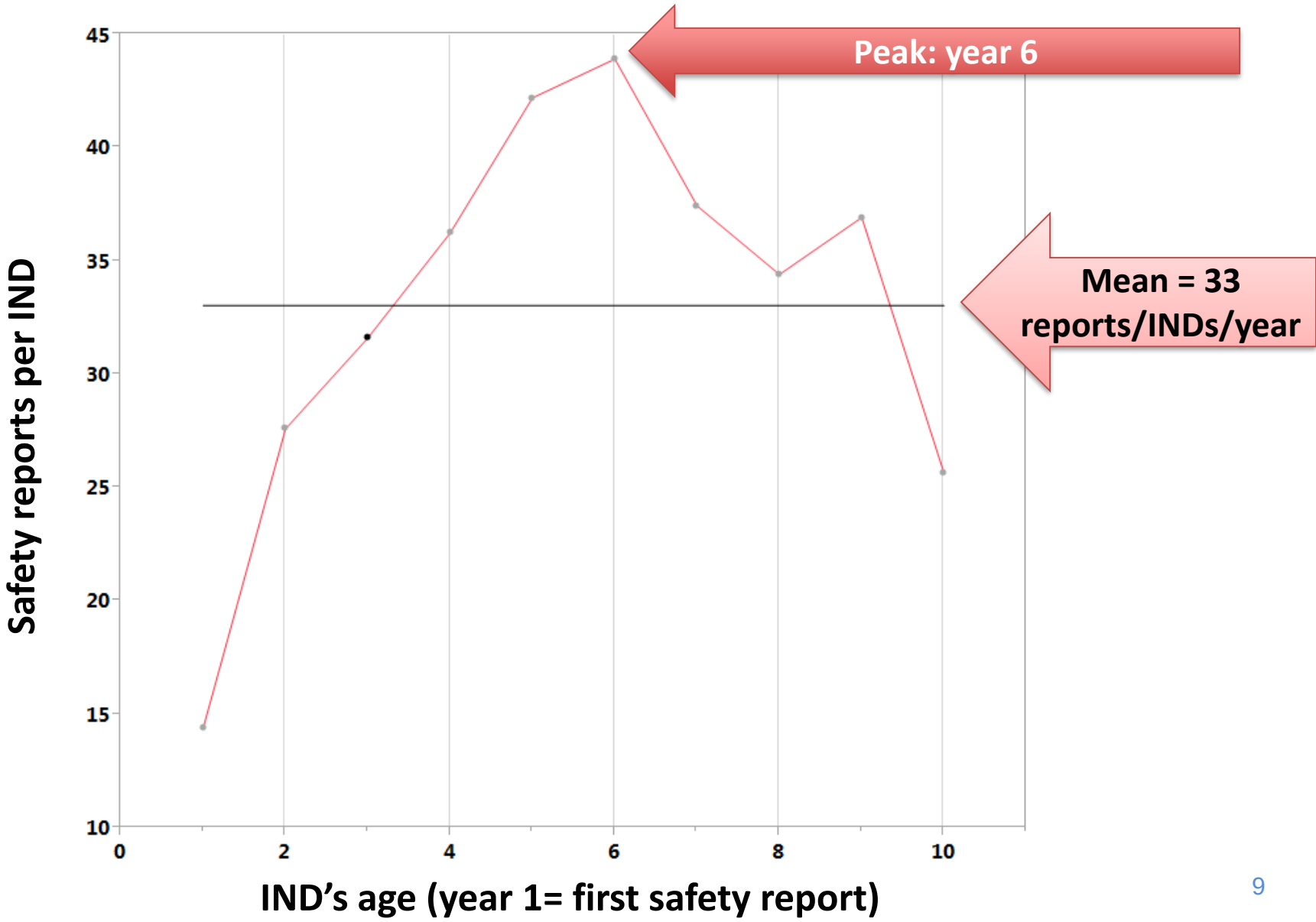
Number of safety reports per year



Average number of safety reports/IND



Safety reports/IND over IND's lifespan



CCR Perspectives in Regulatory Science and Policy

Clinical Cancer Research

The Majority of Expedited Investigational New Drug Safety Reports Are Uninformative

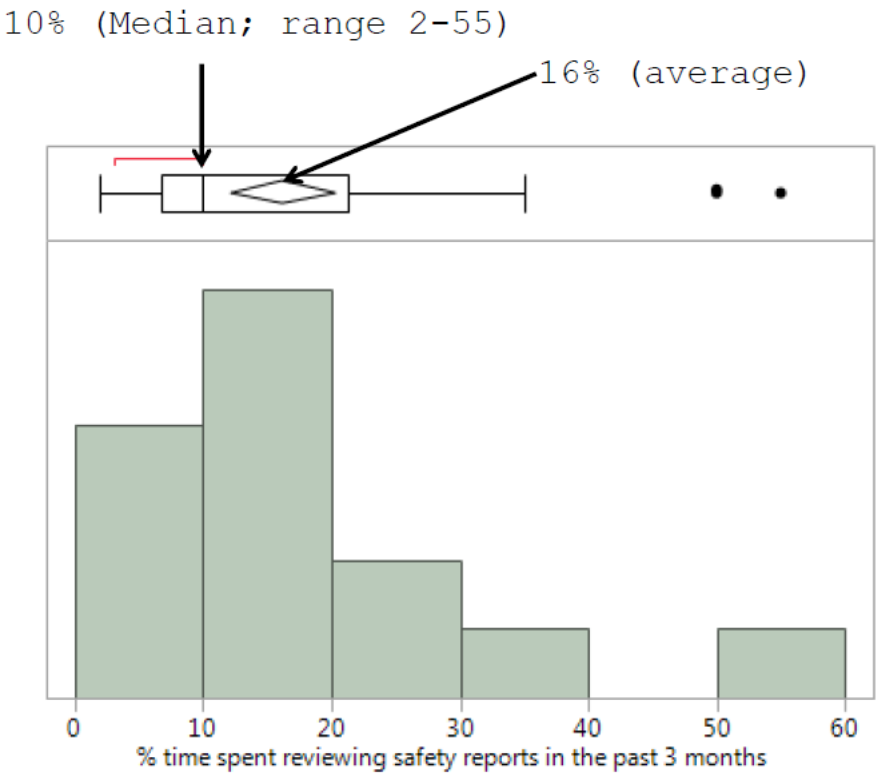
Jonathan P. Jarow, Sandra Casak, Meredith Chuk, Lori A. Ehrlich, and Sean Khozin

Abstract

Sponsors of human drug and biologic products subject to an investigational new drug (IND) application are required to distribute expedited safety reports of serious and unexpected suspected adverse reactions to participating investigators and the FDA to assure the protection of human subjects participating in clinical trials. On September 29, 2010, the FDA issued a final rule amending its regulations governing expedited IND safety reporting requirements that revised the definitions used for reporting and clarified when to submit relevant and useful information to reduce the number of uninformative reports distributed by sponsors. From January 1, 2006, to December 31, 2014, the FDA's Office of Hematology and Oncology Products received an average of 17,686 expedited safety reports per year. An analysis of FDA submissions by commercial sponsors covering this time period suggested a slight increase in the number of expedited safety reports per IND per year after publication of the final rule. An audit of 160 randomly selected expedited safety reports submitted to the FDA's Office of Hematology and Oncology Products in 2015 revealed that only 22 (14%) were informative. The submission of uninformative expedited safety reports by commercial sponsors of INDs continues to be a significant problem that can compromise detection of valid safety signals.
Clin Cancer Res; 22(9); 1–3.

FDA INFORMED: Exploratory survey of medical officers at the office of hematology and oncology products

April 2016



Based on 44 responses to the following question:

On average, what percent of your time in the last 3 months has been spent reviewing expedited premarket 15- and 7-day safety reports?

Information Exchange and Data Transformation (INFORMED)

A holistic approach to regulatory science

Launch of FDA's New Digital Health Incubator

… **to support the integration of data analytics into regulatory decision making**, we're taking another new step with the creation of an internal data science incubator called the Information Exchange and Data Transformation; or INFORMED

Remarks by Scott Gottlieb, M.D.
Commissioner of Food and Drugs
Academy Health's 2018 Health Datapalooza
Washington, DC
April 26, 2018

https://www.fda.gov/NewsEvents/Speeches/ucm605697.htm

Information Exchange and Data Transformation (INFORMED)

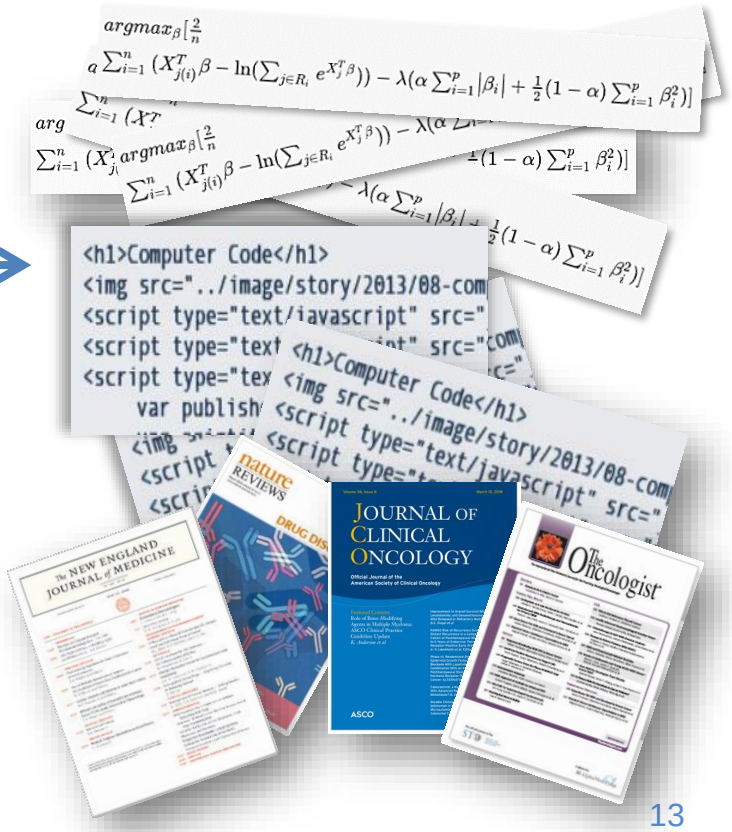
Input

- CDISC
- Electronic health records
- Digital premarket safety
- Biometrics
- Apps

Collaborative partnerships

National Cancer Institute · Project Data Sphere · flatiron · IBM Watson · Stanford University · MIT · Harvard · ASCO CancerLinQ (Learning Intelligence Network for Quality) · Johns Hopkins University

Output



Creating new data assets

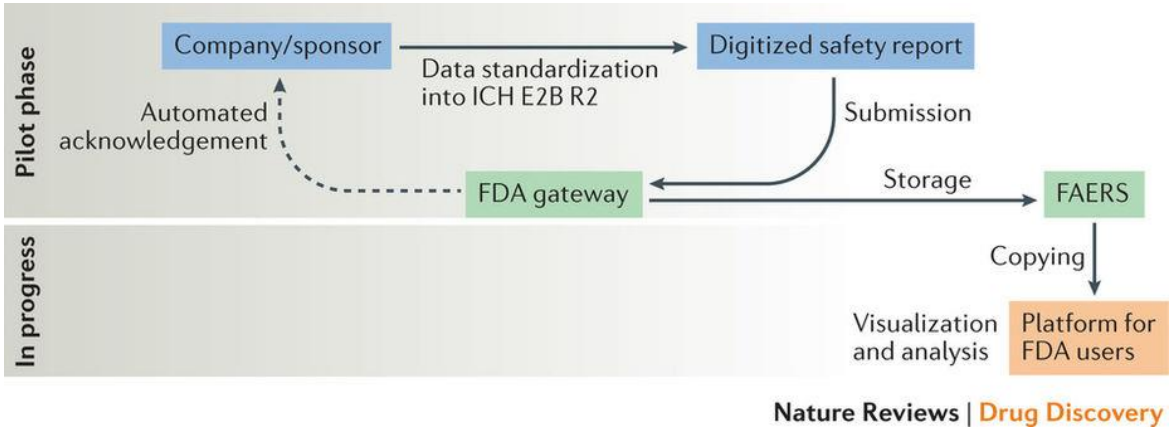
IND 7 & 15 day

nature REVIEWS DRUG DISCOVERY

Biobusiness Briefs

Regulatory watch: Evaluating the potential for digital submission of expedited premarket safety reports to the FDA

Sean Khozin, Meredith Chuk, Tamy Kim, Suranjan De, Sanjay Sahoo, Geoffrey Kim & Richard Pazdur



Khozin S, et al. Nature Reviews Drug Discovery (2016)

Creating new data assets

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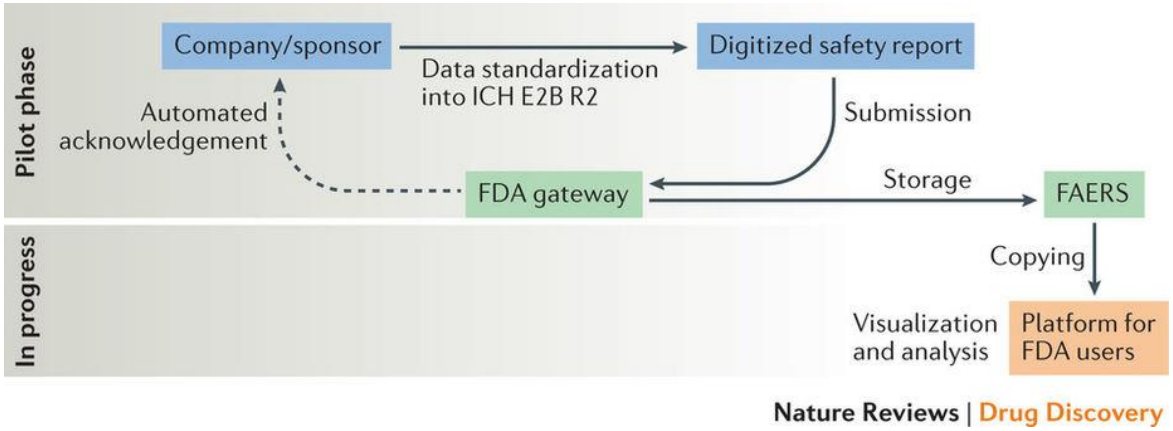

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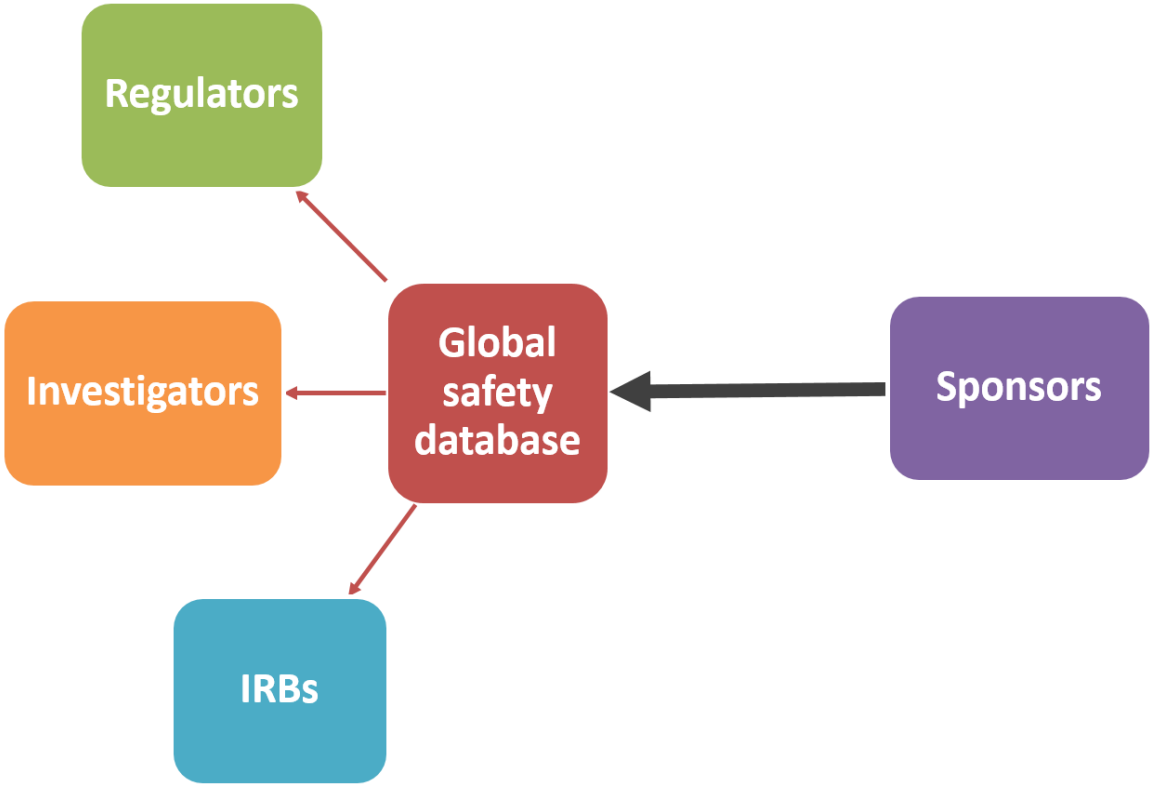
Central global safety data bank



Central global safety data bank

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JOURNAL OF CLINICAL ONCOLOGY

ASCO SPECIAL ARTICLE

Streamlining Adverse Events Reporting in Oncology: An American Society of Clinical Oncology Research Statement

Laura A. Levit, Raymond P. Perez, David C. Smith, Richard L. Schilsky, Daniel F. Hayes, and Julie M. Vose

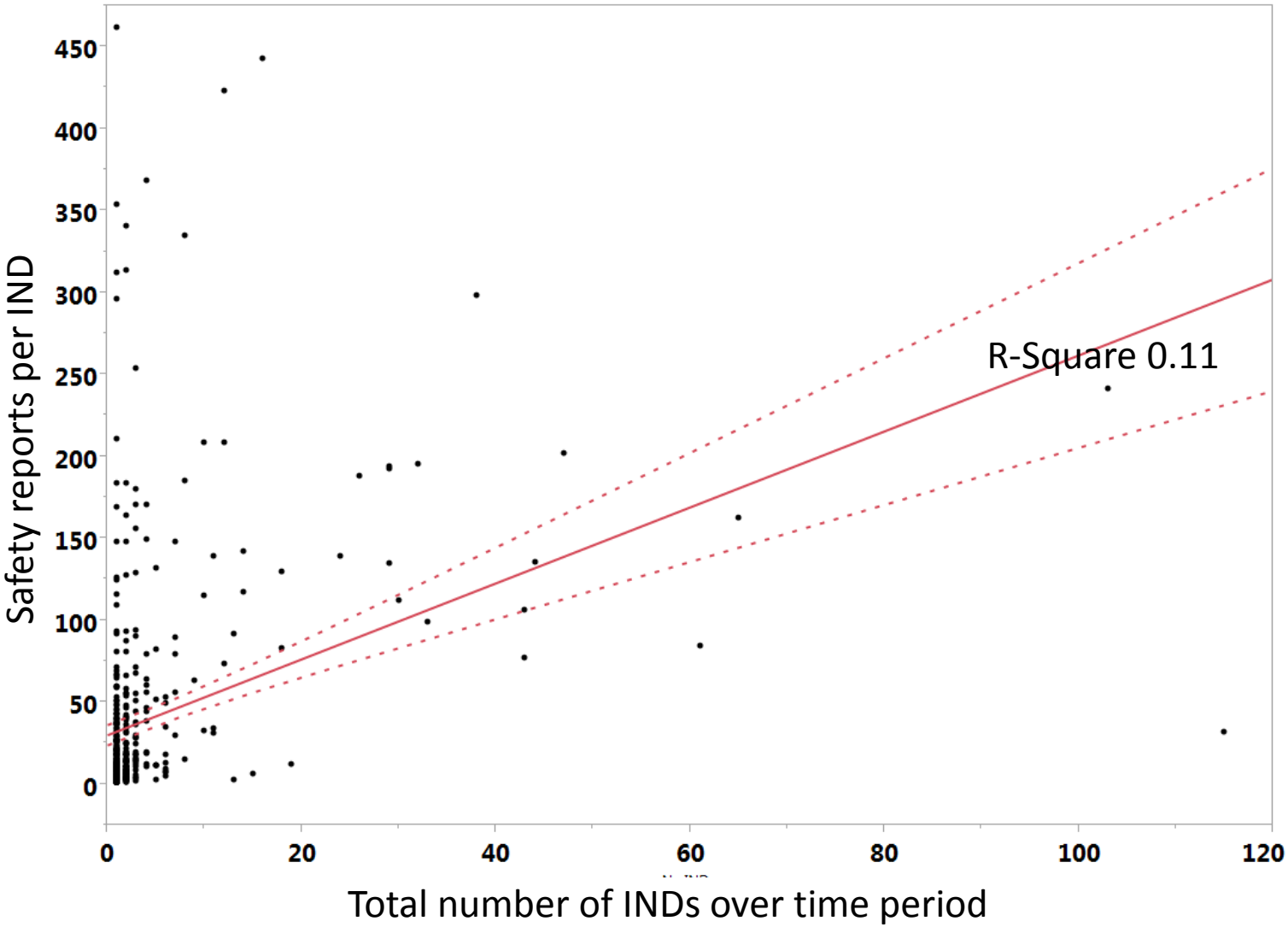
Recommendation 4.a. A neutral third party should develop a central electronic portal for reporting AEs.

A neutral third party, such as a nonprofit organization formed by an industry consortium or a public-private partnership, should create a globally available, central electronic portal that enables users to report and access AE data relevant to all trials in which they participate. This would provide investigators with context to inform clinical judgments regarding attribution of AEs, as well as facilitate regulators, sponsors, and IRBs identification of important safety signals.

Thank you

Back up slides

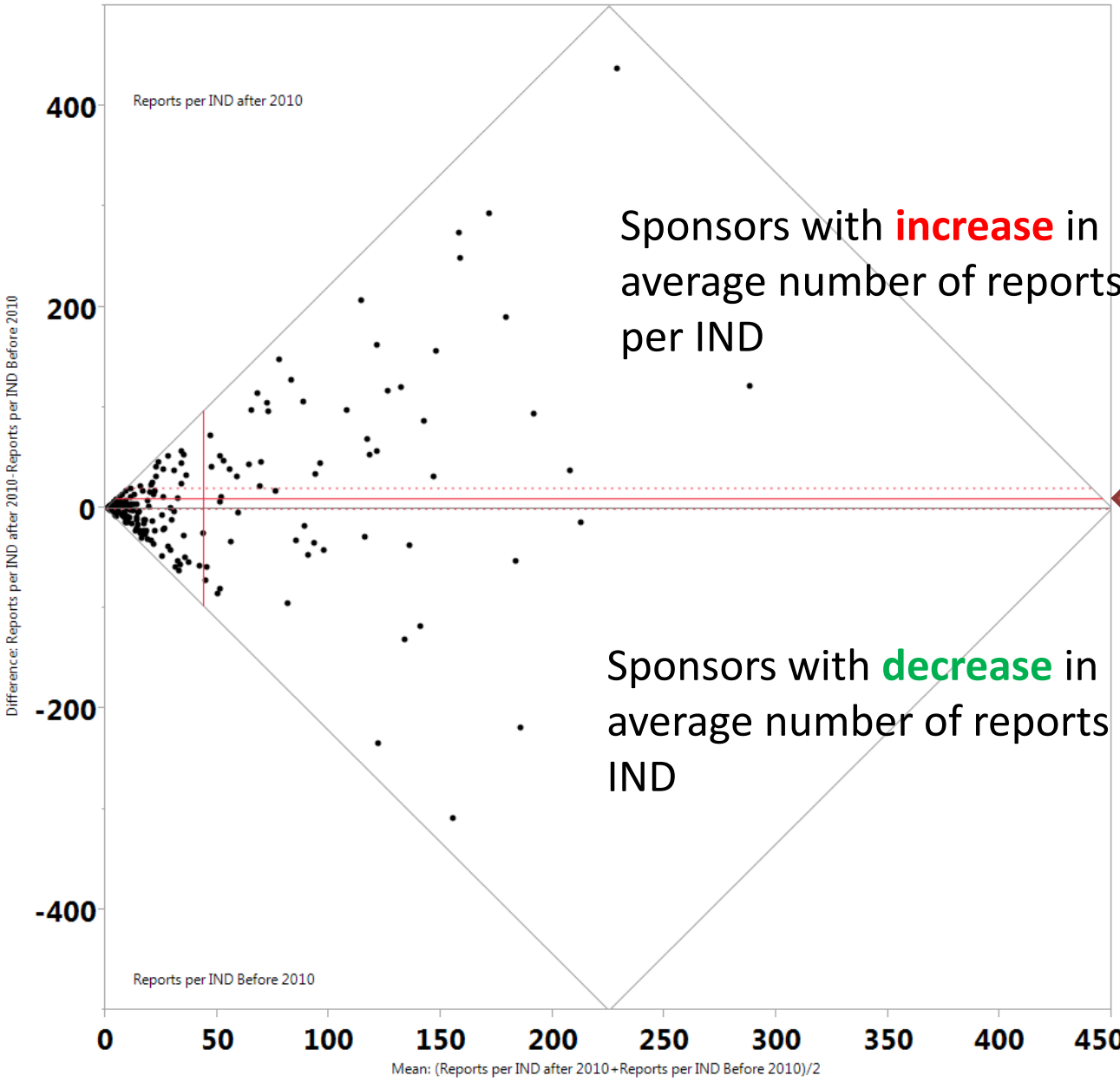
No “economies” of scale



Matched pairs analysis

- Method
  - Reports divided into two groups:
    - Before 2010; after 2010
  - Excluded
    - Year 2010 (intervention) and 2015 (partial)
    - Sponsors with no INDs either before or after 2010
- 198 Sponsors identified

Reports per IND before and after 2010 ruling: Matched pairs analysis



Sponsors with **increase** in average number of reports per IND

Sponsors with **decrease** in average number of reports per IND

Mean #reports/IND:
--Before 2010 = **38.9**
--After 2010 = **48.4**

Mean difference = **9.6** (95% CI 19.9, -0.72)