

Spontaneous Adverse Drug Reaction Report Data and Their Potential for Safety Knowledge Discovery

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Goals of the Presentation



⇒ Discuss adverse event (AE) report data in the context of data mining use cases

- What are the constraints and limiting factors in algorithmic manipulation of AE data stores
- How can those constraints be best overcome?
- Is there a future for AE report data in pharmacovigilance



The NEW ENGLAND JOURNAL of MEDICINE

“..represents the weakest form of epidemiologic evidence”

Perspective
OCTOBER 26, 2006

Protecting the Health of the Public — Institute of Medicine Recommendations on Drug Safety

Bruce M. Psaty, M.D., Ph.D., and Sheila P. Burke, M.P.A., R.N.

The principal challenge for drug safety surveillance efforts is data quality

➔ ***“The fundamental problem inside the FDA is the quality of information on which the FDA can base its evaluations.”***

***Opening Pandora’s Pillbox:
Using Modern Information
Tools To Improve Drug Safety***
Scot Gottlieb, MD
Health Affairs, Volume 24, Number 4
July/August 2005
Pp 938-948

The current AERS system is FDA's principal post-marketing monitoring tool.... This current monitoring system, by itself, is not adequate for a successful, state-of-the-art drug safety program.

Office of Management
Budget Formulation and Presentation
FY 2007
Food and Drug Administration
<http://www.fda.gov/oc/oms/ofm/budget/2007/TOC.htm>



FDA AER System was never intended or designed to support “data mining”, hypothesis generation, or knowledge discovery

- ➔ **Data quality issues**
- ➔ **Process issues**



⇒ Ambiguity

- Data definitions
- “Regulatory Semantic”
 - *Serious rash vs. non-Serious breast cancer*
 - *“Expected vs. Unexpected*
 - *“Walks like a duck but....”*
 - *Diagnostic test ordered confirms a diagnosis but symptoms do not.*

⇒ Consistency

- Narrative Structure

⇒ Concept representation

- Coding system granularity
- Qualifiers and modifiers
- Differing coding systems over time
 - *MedDRA does not be ANSI criteria for a “standard” vocabulary or terminology*



➔ True capture (reporting) rate of events

➔ Time dependent biases

- Pharmacokinetic differences
- Product labeling
- Market Influences,
- Regulatory (Formulary) Issues
- Product lifecycle
- Stimulated reporting (event date vs. report date)
 - *Customer support services*
 - *Publicity*
 - *Litigation*

➔ Nature of the event (Effort after Meaning)

- Reporter Biases

- ➔ Reporting Rates
- ➔ “Relative Risk” with sensitivity analysis based on presumed capture rate
- ➔ Proportional Reporting Ratios



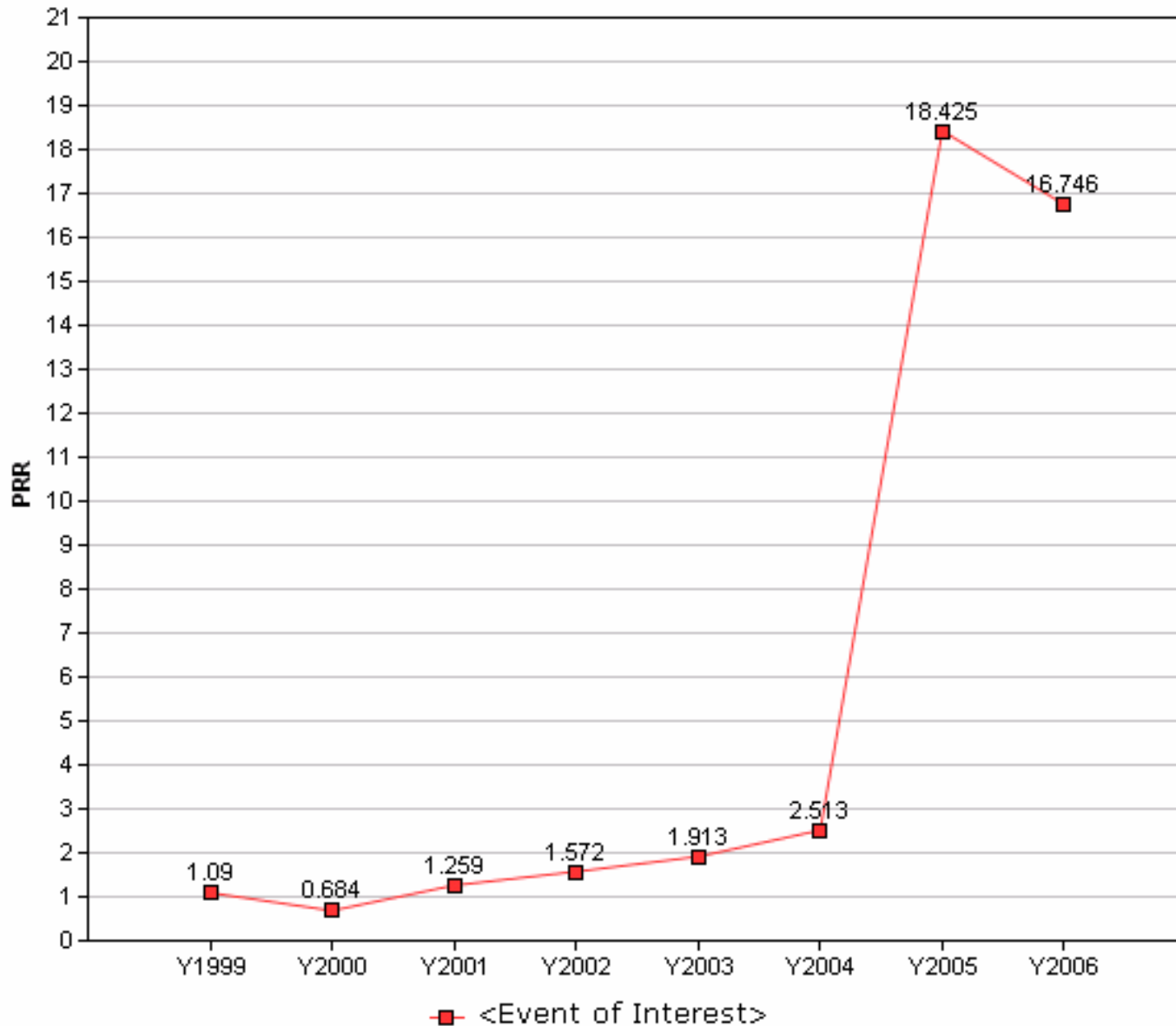
➔ Assumptions

- Product or Products have same likelihood of having an AE reported
- Coding rules are consistent
 - *Standard “case definitions”*
- Data rules are adhered to similarly

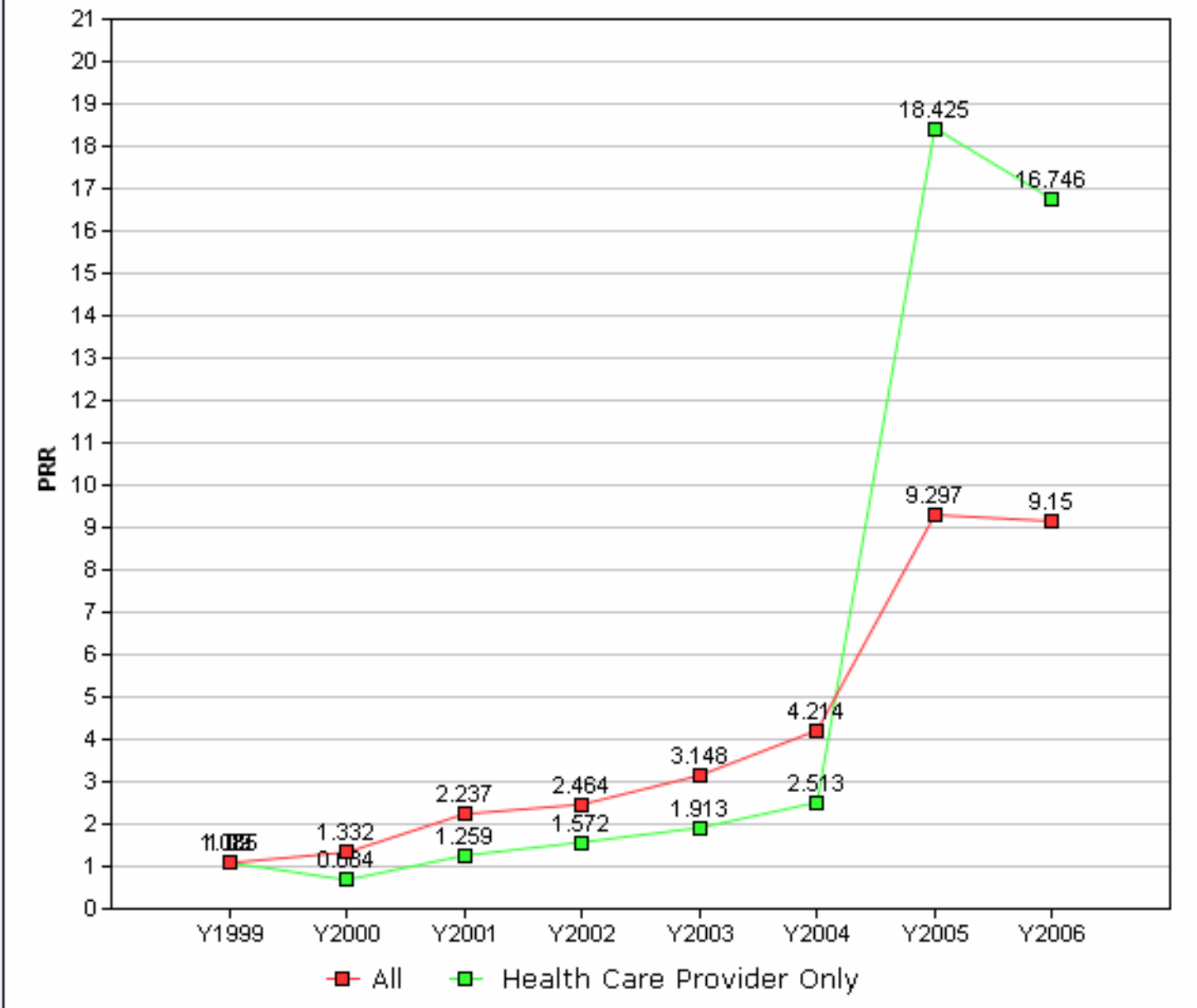
➔ Needed information

- Background rate for the “population”
- Exposed population denominator data

Workshop - Annual

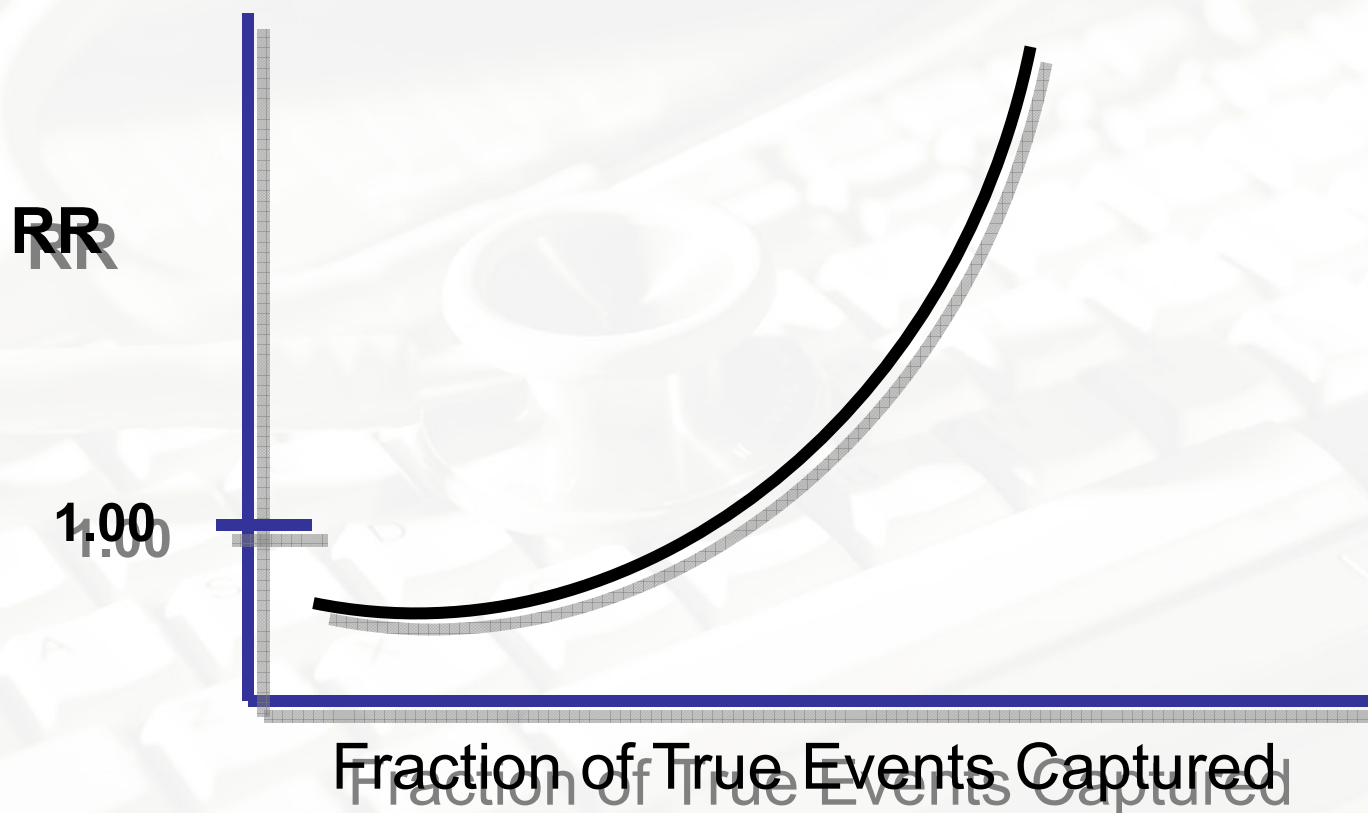


Workshop - Annual



Sensitivity Analysis: RR vs. Percent of Capture

Relative Risk vs. Fraction of Event Capture



Path Forward for Spontaneous AE Data



- ⇒ **Unburden the reporter**
- ⇒ **Simplicity**
- ⇒ **Data Standards**
 - HL7 ICSR Standard
 - SNOMED CT
 - Abandon the regulatory semantic
- ⇒ **Standard Structure to AE Narrative (XML based standard)**
- ⇒ **Harness data mining for structured and unstructured data (Text mining, NLP)**
- ⇒ **Uniform data definitions and data practices**

A Metadata Model for Pharmacovigilance System

