Adverse Event Reporting Related to Antiretroviral Agents at FDA

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FDA's Adverse Event Reporting System (AERS) Database

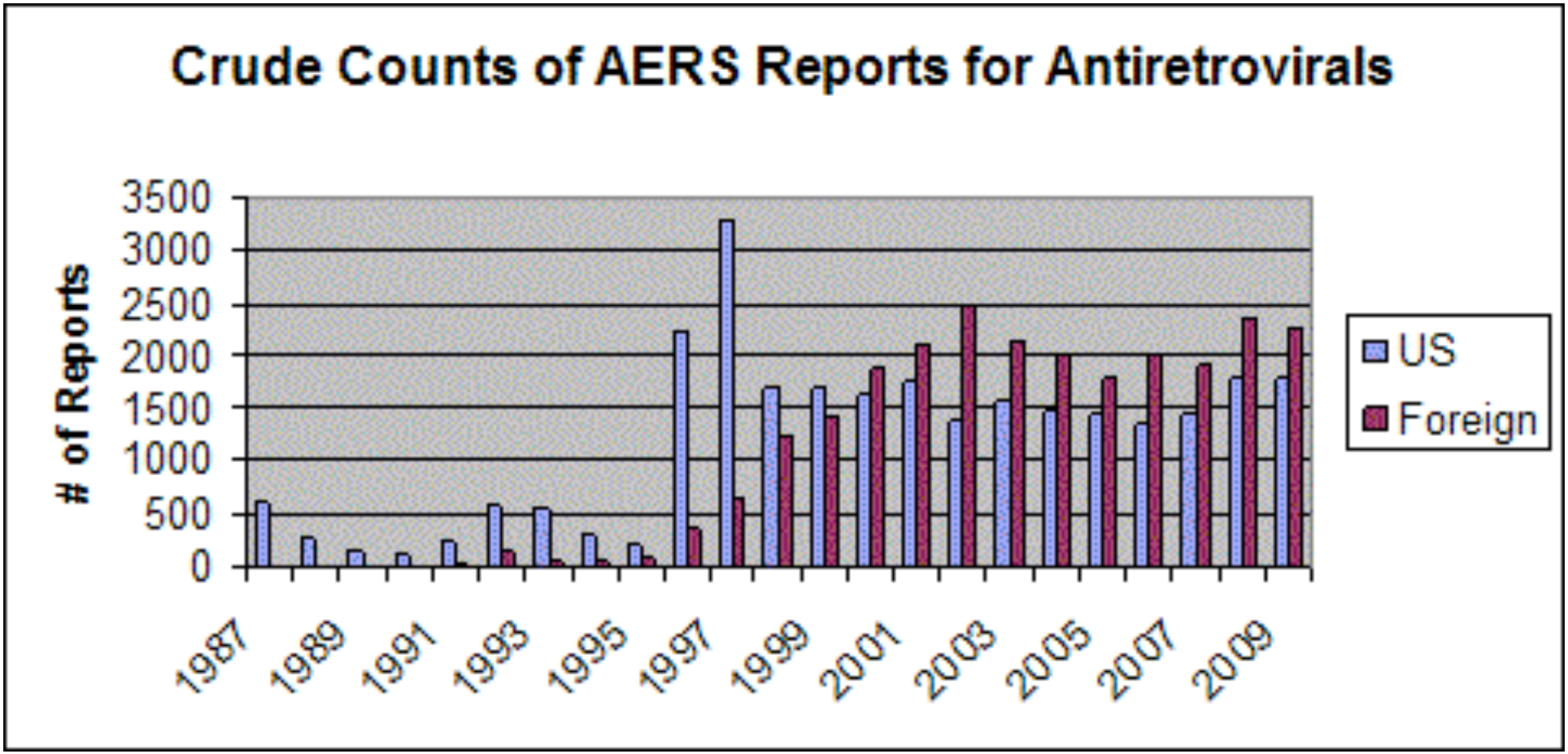
- Adverse event reports from 1969
- Current system dates to 1997
  - New system in procurement
- Contains over 5 million records
- Report source:
  - 95% from industry
  - 5% directly from public ("direct report" via MedWatch program)
- Additional Information at http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Surveillance/AdverseDrugEffects/default.htm

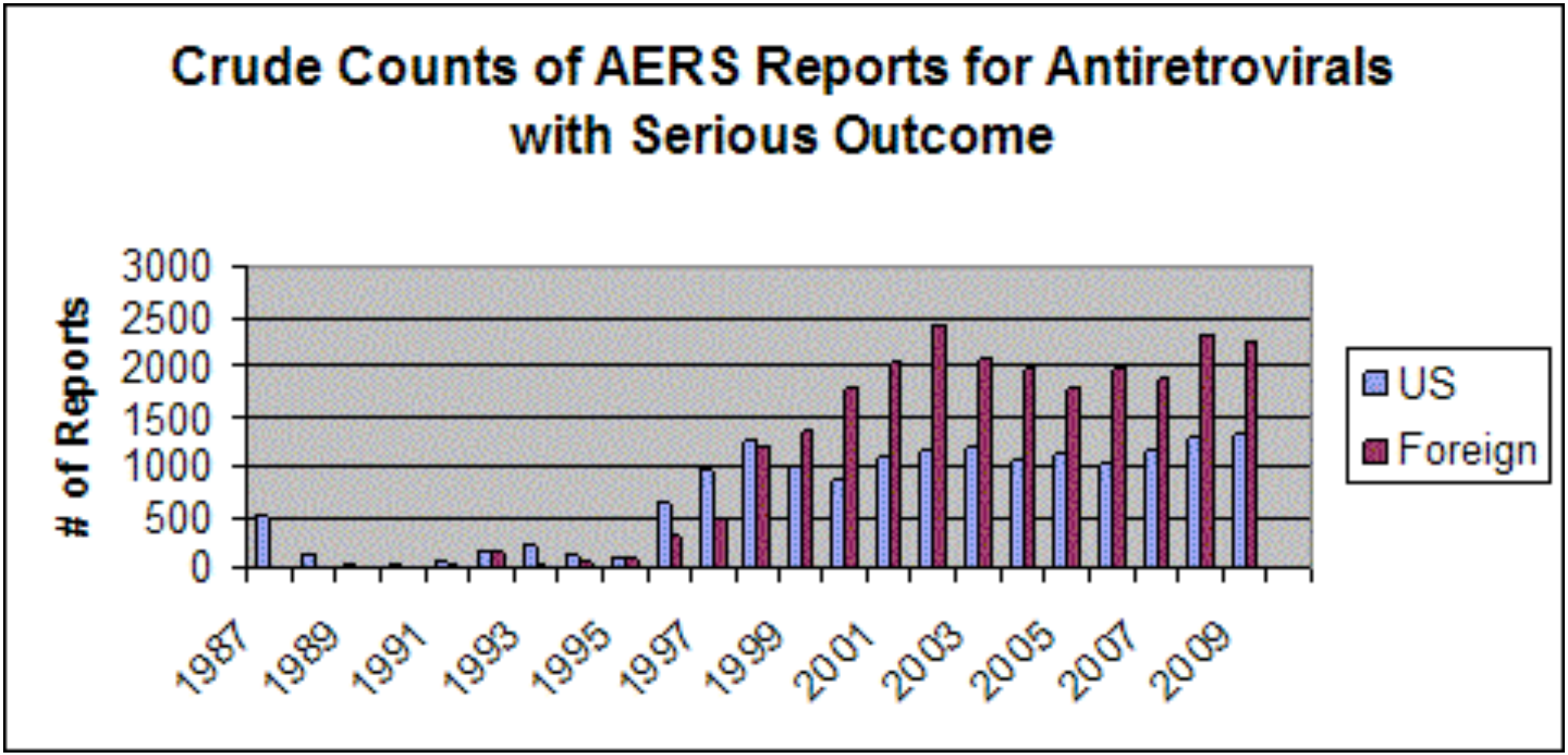
Challenges in Analyzing Spontaneous Adverse Event Reports

- The extent of reporting is not known, but is estimated to be less than 10% of adverse drug reactions
- The quality of reports is often suboptimal, and thus not always suitable for thorough medical evaluation
  - Most of the useful information is in the narrative section, which is a free text field, and thus has highly variable quality

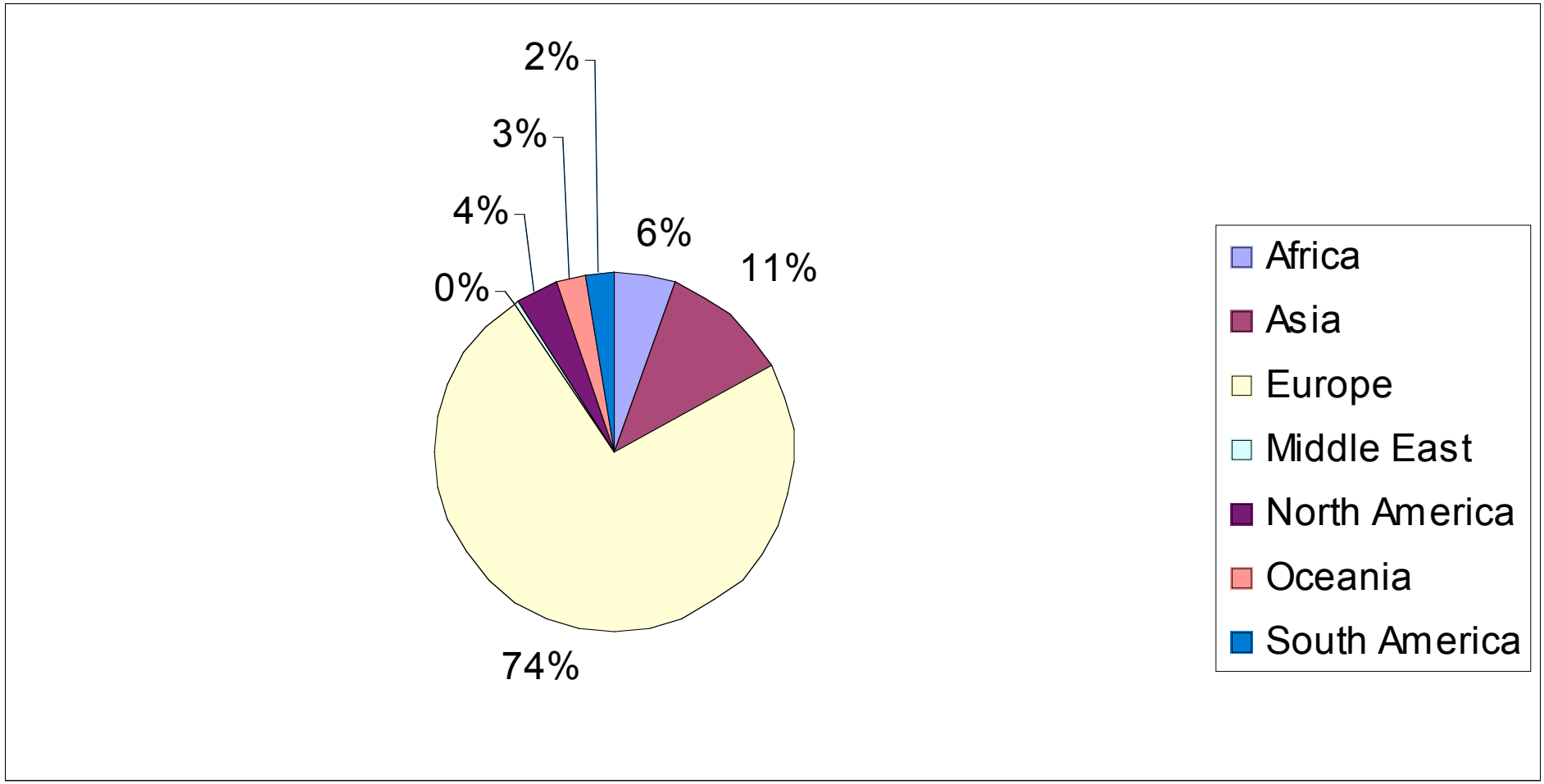
Identifying Signals in Spontaneous Reporting Databases is Challenging

- Ideally, *rates* of adverse drug events could be calculated, but...
  - Numerators (exact number and extent of adverse events) impossible to know
    - Reporting by public not required
  - Denominators (drug exposure) impossible to know
    - Number of prescriptions filled is not an absolute measure of exposure due to non-compliance, misuse, abuse, etc.


Crude Counts of AERS Reports for Antiretrovirals
# of Reports
3500
3000
2500
2000
1500
1000
500
0
1987
1989
1991
1993
1995
1997
1999
2001
2003
2005
2007
2009
US
Foreign


Crude Counts of AERS Reports for Antiretrovirals with Serious Outcome
# of Reports
3000
2500
2000
1500
1000
500
0
1987
1989
1991
1993
1995
1997
1999
2001
2003
2005
2007
2009
US
Foreign

Non-US Antiretroviral Reports in AERS by Region



Sentinel Overview

- As mandated by FDA Amendments Act Section 905- Develop an active electronic safety monitoring system to
  - Strengthen FDA's ability to monitor postmarket performance of medical products
  - Augment, not replace, existing safety monitoring systems
  - Enable FDA to access existing automated healthcare data by partnering with data holders (e.g., insurance companies with large claims databases, owners of electronic health records, others)
- Data remains with data holders behind existing firewalls
- Data holders would run queries—FDA-requested, or other—(or could opt out)
  - Convey results summaries for review
  - According to strict privacy and security safeguards

How does Sentinel augment what we are already doing?

- Safety issues can be identified and evaluated in near real-time
- Sentinel expands the capacity for evaluating safety issues
  - Improved access to subgroups, special populations
  - Improved precision of risk estimates due to expanded number of populations available for study
- Active surveillance can identify an increased risk of common AEs (e.g., MI, fracture) that health care providers may not suspect are related to medical products

Looking Forward

- Mini-Sentinel 1
  - Access private healthcare data environments with varied attributes to conduct analyses
  - Evaluate FDA-prioritized medical product-adverse event pairs
  - Develop and apply epidemiological and statistical methodologies for signal detection signal strengthening, and signal validation
- Mini-Sentinel 2
  - Access Federal Partners (DoD, VA, CMS) healthcare data environments
  - Evaluate FDA-prioritized medical product-adverse event pairs
  - Develop and apply epidemiological and statistical methodologies for signal detection signal strengthening, and signal validation
  - Evaluate interpretability of query findings resulting from a decentralized analytic approach
- Cooperative agreement for neutral institutions and/or organizations to convene surveillance discussions
  - Explore and obtain input on methodological, data development, and technical issues (e.g., development of research designs, tools, and methodologies) from a variety of stakeholders
  - Communicate findings to a broad range of stakeholders

Questions?