Good Practice for Patient Registries

AHRQ Annual Meeting

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Speaker: Richard Gliklich, MD,
Principal Investigator, Outcome DEcIDE Center,
President, Outcome
Cambridge, MA

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Premise

Registries can provide unique outcomes information on populations under real-world conditions that are not studied in clinical trials.

- *Reality*
- *Generalizability*
- *Applicability*
- *Availability*

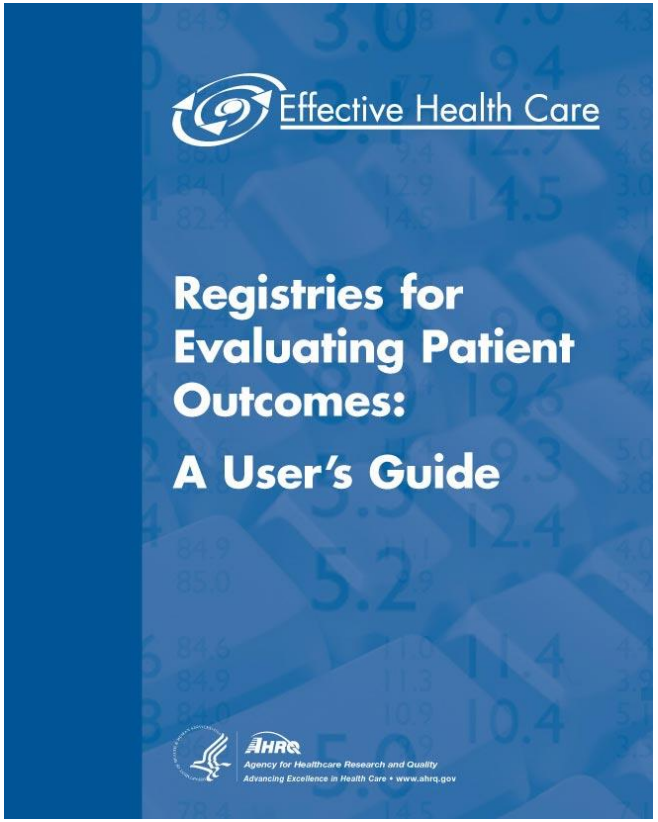
What makes a registry good?

Current guidelines for pharmacoepidemiologic research do not fully address registries

- Experimental Research
  - CONSORT Statement *(JAMA 2001; 285:1987-1991)*
- Observational Research
  - Guidelines for good pharmacoepidemiology practices (Pharmacoepidemiology & Drug Safety 2005:14:589-595)
  - Quality of Reporting of Observational Longitudinal Research (AJE 2005:161:280-288)
  - Guidance for Industry: Good pharmacovigilance practices & pharmacoepi. assessment. DHHS, March 2005
  - Guidance for Industry: Establishing Pregnancy Exposure Registries, DHHS, August 2002.

Registries for Evaluating Patient Outcomes: A User's Guide

- Commissioned by the Agency for Healthcare Research and Quality and the Centers for Medicare and Medicaid Services in the United States
- Purpose: To promote development of high-quality evidence that can be relied on for public and private purposes
- Product: Handbook addresses the creation, operation, analysis, interpretation, reporting and evaluation of registries designed to evaluate patient outcomes



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Registries for Evaluating Patient Outcomes: A User's Guide

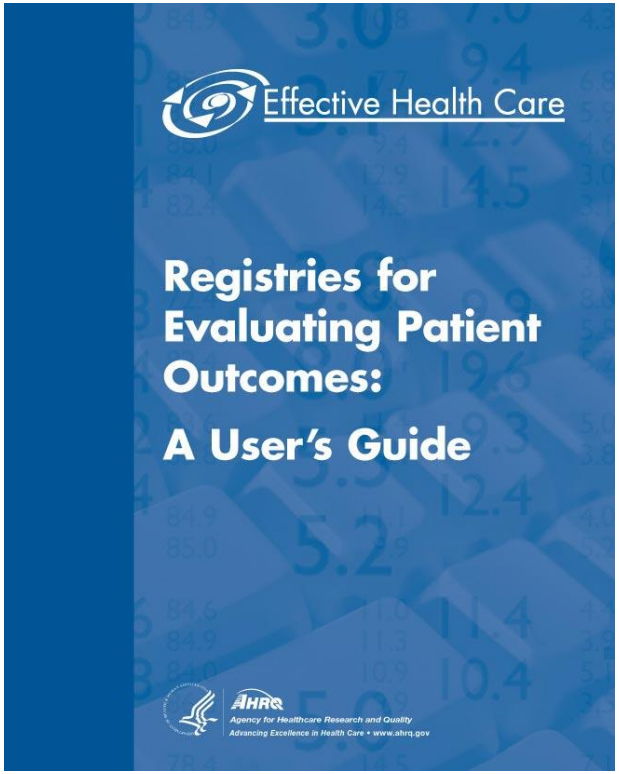
PIs: RE Gliklich, NA Dreyer, Outcome DEcIDE

Collaborative effort

- Outcome Sciences DEcIDE center
- Duke University EPC
- CMS Coverage and Analysis Group
- 39 contributors from industry, academia, health plans, physician societies, U.S. government, NICE
- 35 invited peer reviewers and public comment, including OCR, OHRP, IOM among others

Example driven: ~23 case studies illustrating specific challenges and solutions

Available on-line and in print at http://effectivehealthcare.ahrq.gov



Gliklich RE, Dreyer NA, eds.
Registries for Evaluating Patient Outcomes: A User's Guide.
Prepared by Outcome DEcIDE Center
AHRQ Publication No. 07-EHC001-1. Rockville, MD:
Agency for Healthcare Research and Quality. April 2007

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What is a Patient Registry?

A patient registry:

- Is an organized system that uses observational study methods to collect uniform data (clinical and other)
- Evaluates specified outcomes for a population defined by a particular disease, condition, or exposure, and that
- Serves a predetermined scientific, clinical, or policy purpose

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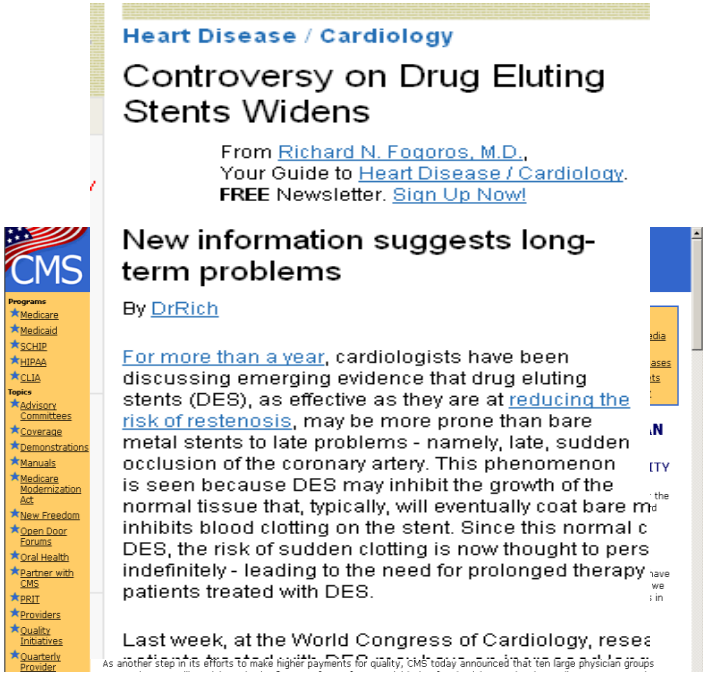
Key Characteristics of Registries

- Data are collected in a naturalistic manner
- Registry is designed to fulfill specific purposes, and these purposes are defined in advance of collecting and analyzing the data
- Registry captures data elements with specific and consistent data definitions
- Data are collected in a uniform manner for every patient.
- Data collected derive from and are reflective of the clinical status of the patient (by history, examination, laboratory test, or patient reported)
- At least one element of registry data collection is active, meaning that some data are collected specifically for the purpose of the registry

Typical Goals of Patient Registries

- Track natural history of a disease process
- Measure or monitor safety and harm
- Evaluate clinical, comparative or cost effectiveness
- Measure and/or improve quality of care



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Taxonomy of Registries: Product

May include all or a subset of patients exposed to a drug, device or biologic

Device registries

- Implantable cardioverter defibrillators (ICD)
- Stents
- Orthopedic devices

Pharmaceutical product registries

- Cox 2 inhibitors
- Thalidomide

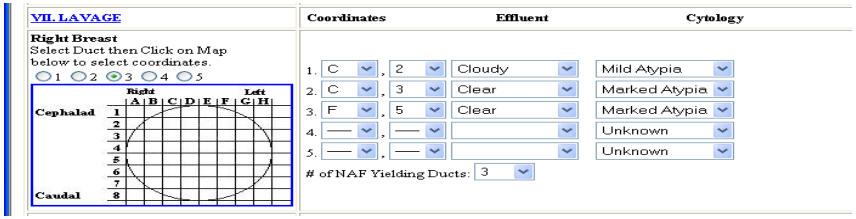
Patient Initials	Patient SSN	Pharmacy	Physician	Status	Next Test Due Date	Outcomes
AAA	111223333	Walgreen's	Epps, Susie	Weekly	08/12/2004	08/05/2004
FJW	111111111	Brooks	Epps, Susie	Monthly	08/28/2004	08/21/2004
RDC	111111112	Brooks	Epps, Susie	Weekly	08/10/2004	08/03/2004
LNT	222222221	Walgreens	Epps, Susie	Q2M	08/26/2004	08/23/2004

Pregnancy registries

- Exposed population = mother *and* fetus

Taxonomy of Registries: Service

Targeting a health care service, procedure or clinical encounter



Procedure registries

- Primary coronary intervention
- Normal pressure hydrocephalus registry
- Society Thoracic Surgeons (STS) database

Clinical service (and quality measurement) registries

- Hospitalization registries
- P4P

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Taxonomy of Registries: Disease/Event

Patients enrolled share a common disease or event experience, regardless of treatment or other exposures

Acute diseases or events

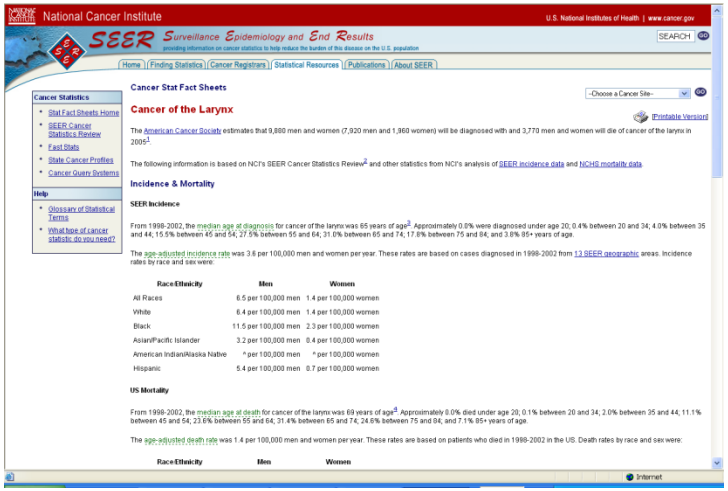
- National Registry Myocardial Infarction (NRMI)
- Organ transplant registries

Chronic diseases

- ESRD registry
- Heart failure registry
- Cancer registries (SEER)

Rare diseases

- Lysosomal storage disorders
- Cystic fibrosis
- Hemophilia



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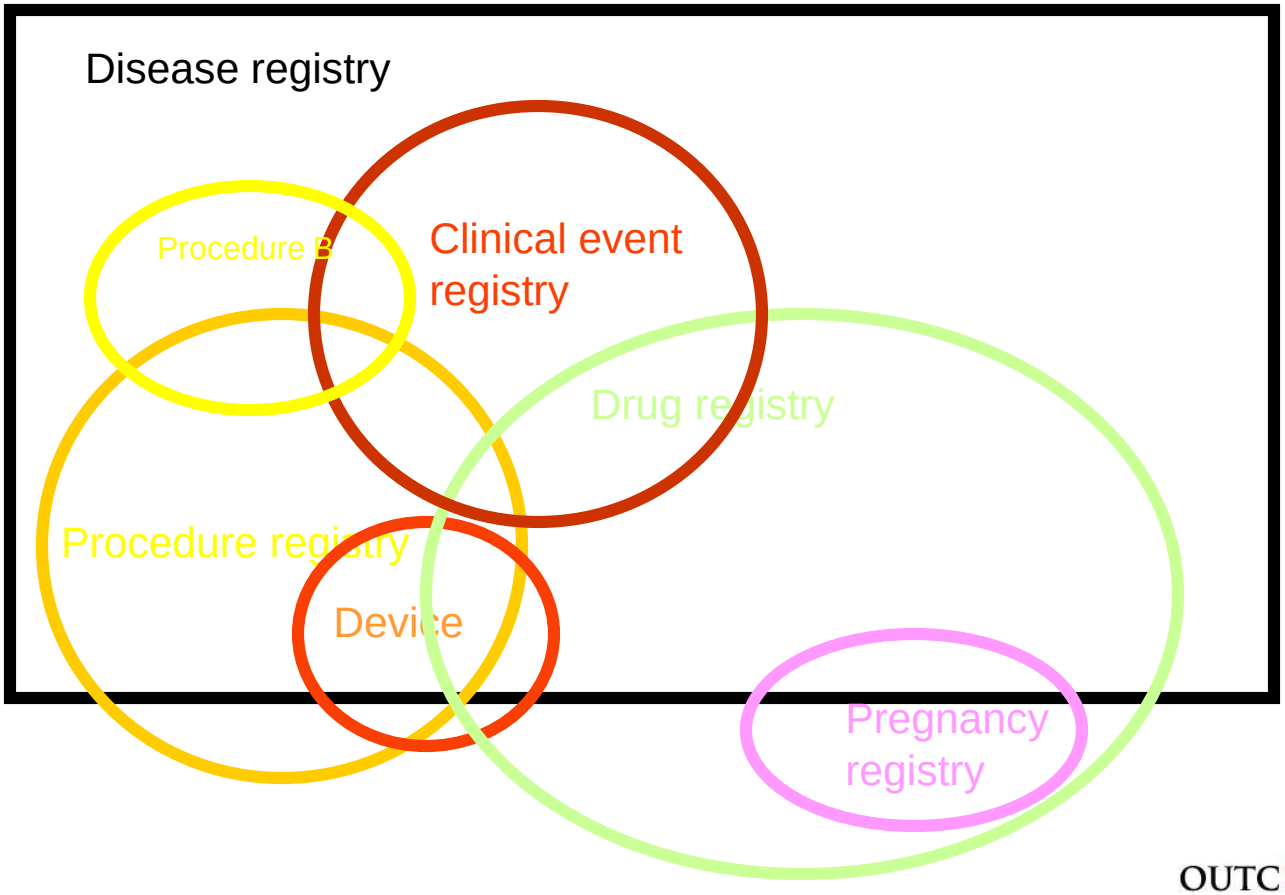
Registry types and perspective



Sections of Handbook

- Creating a Registry
  - Planning
  - Design
  - Data Elements
  - Other Data Sources
  - Ethical and Legal Issues
- Operating Registries
- Evaluating Registries

Planning

- State the purpose
- Identify stakeholders
- Establish governance
- Define scope of registry
- Define target population
- Assess feasibility
- Secure funding

Design

- Design registry with respect to its major purposes
  - Different levels of rigor are necessary for different types of registries
  - The specific clinical questions of interest will guide definitions of study subjects, exposures, and outcome measures
- Choose a study design
- Select data sources, populations, comparison groups
- Determine whether sampling is needed
- Identify possible sources of bias (systematic error) and address them to the extent that is practical and achievable

Data Elements

- Select based on importance and relationship to the primary outcome
- Consider data collection burden and incremental costs for collection
- Whenever possible, use established standards and common data definitions or validated instruments
- Weigh pros/cons of using patient identifiers
- Use pilot testing to assess feasibility and burden as well as reliability, validity, and potential for missing data

Data Sources

- Registries can include data from many sources
- Primary data are collected for direct purposes of the registry
- Secondary data were originally collected for other purposes
  - Medical records
  - Institutional or organizational databases
  - Administrative and claims data
  - Death and birth records
  - Census databases
  - Existing registry databases
- When selecting data sources, consider cost, timeliness, structure, availability and quality

Ethics, data ownership, and privacy

- Review ethical and data privacy requirements early in planning phase to ensure compliance
  - Common Rule
  - HIPAA
  - Local requirements
- "The research purpose of a registry, the status of its developer, and the extent to which registry data are individually identifiable largely determine applicable regulatory requirements."
- Also important: registry transparency, oversight/governance and data ownership

Registry Developer or Purpose of Registry	Extent An Individual May Be Identified from Health Information			Waiver of Authorization, Documentation of Consent, or Consent Process
	1. De-identified health information**	2. Health information excludes direct identifiers	3. Health information includes direct identifiers	
1A. Federal or State Public Health Agency: Registry for *public health practice within agency's legal authority* **not** *involving research*	No requirements.	The Privacy Rule permits use or disclosure to a public health authority for public health activities. The Common Rule is not applicable.	The Privacy Rule permits use or disclosure to a public health authority for public health activities. The Common Rule is not applicable.	Waivers are not applicable.
1B. Federal or State Public Health Agency: Registry as agency *research project*	No requirements, unless identifiable health information is disclosed to the registry developer to create the de-identified data, in which case the Privacy Rule requires a business associate agreement with the data source. If the Common Rule applies*, it permits an IRB grant of exemption from review, unless a re-identification code is used.	Privacy Rule permits use or disclosure of limited data set provided the data source and registry developer enter into a data use agreement. If information containing direct identifiers is disclosed to the registry developer to create the limited data set, the Privacy Rule requires a business associate agreement with the data source. If the Common Rule applies*, it permits an IRB grant of exemption, unless a re-identification code used.	Privacy Rule permits use or disclosure with a patient authorization or a waiver of authorization. If the Common Rule applies*, IRB review and documented consent are required, unless an IRB grants a waiver of documentation or waiver for the consent process.	Privacy Board or IRB approval of a waiver of authorization depends on satisfaction of specific regulatory criteria. If the Common Rule applies*, IRB approval of a waiver of consent documentation or process depends on satisfaction of specific regulatory criteria.
2. Registry produces evidence in support of labeling for a *FDA regulated product.*	No requirements.	Privacy Rule permits use or disclosure to a person responsible for an FDA-regulated product.	Privacy Rule permits use or disclosure to a person responsible for an FDA-regulated product FDA regulations, and Common Rule if applicable*, require IRB review, a documented consent process, and protection of confidentiality of research data.	Waivers are not applicable.

Sections

Creating a Registry

Operating Registries

- Recruitment and management of providers and patients
- Data collection and quality assurance
- Adverse event collection and management
- Data analysis and interpretation

Evaluating Registries

Patient and Provider Recruitment & Management

- Recruitment occurs at many levels
  - Facilities (hospital, practice, pharmacy)
  - Providers
  - Patients
- Motivation for participation at each level differs
  - Relevance, importance, scientific credibility, risks, burdens, incentives
- Goals for recruitment, retention and follow-up should be explicit and deviations continuously evaluated for risk of introducing bias

Data Collection & Quality Assurance

Data collection

- Includes collecting, cleaning, storing, monitoring and reporting registry data
- Broad range of data collection procedures and systems available

Critical factors in data quality

- Data element structure and definition, training of personnel, how data problems are handled

Quality assurance

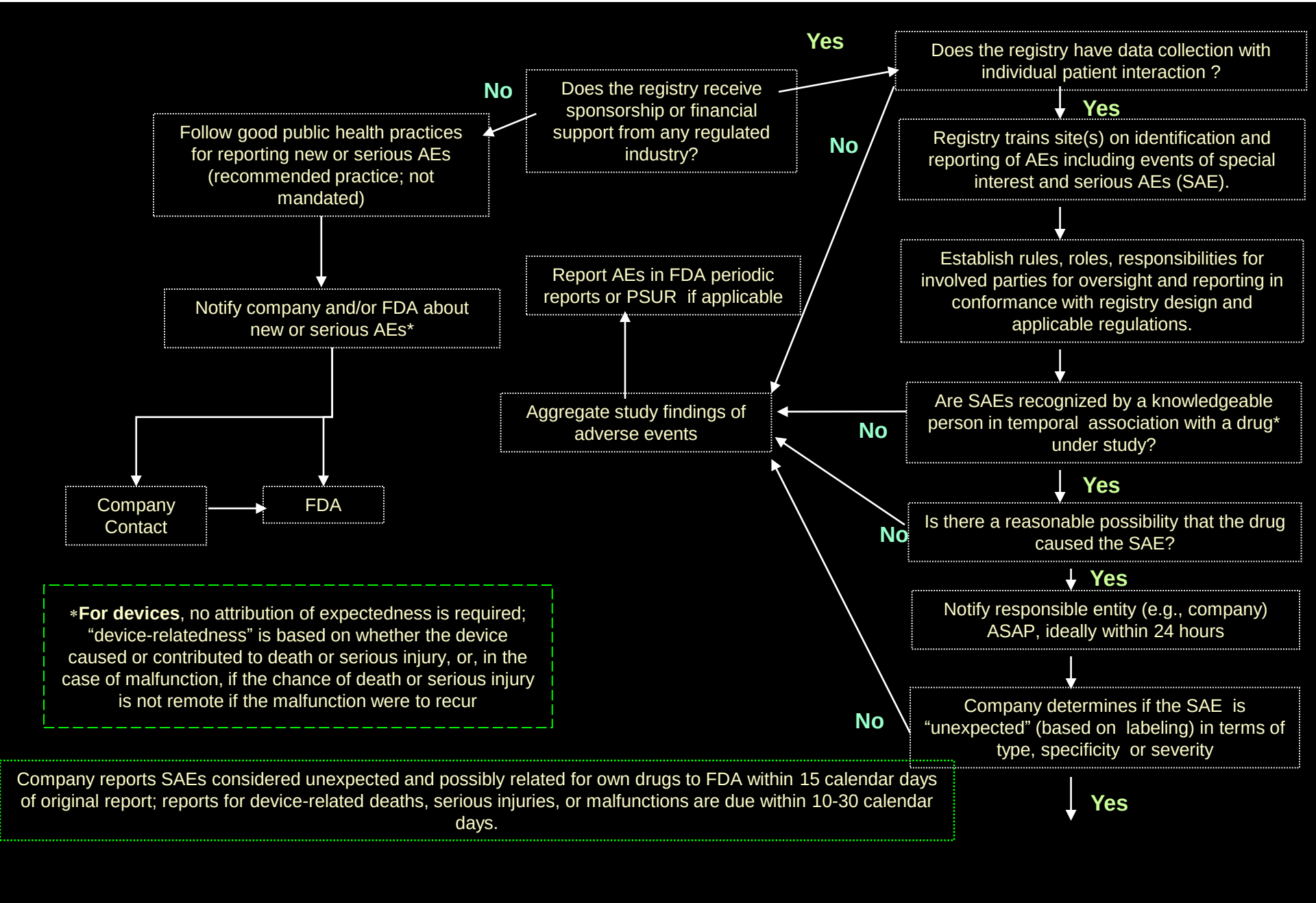
- Define requirements at registry creation
- Risk-based approach
  - Most important or likely sources of error or potential lapses in procedures that may impact quality in the context of intended purpose

Adverse Event Detection, Processing, & Reporting

- Important for any registry, especially with direct patient and/or physician contact
- Collection of spontaneously reported or solicited safety information
  - Protocol-defined procedures strongly recommended
  - Investigators and site staff appropriately trained
- Processing, coding and managing of AE data
- Reporting and regulatory requirements

Best Practices for Adverse Event Reporting to FDA in Registries of Post-Marketed Products

Gliklich R, Dreyer N, eds. Registries for Evaluating Patient Outcomes: A User's Guide. AHRQ Pub. 07-EHC001-01 2007.



Analysis and Interpretation

Analysis

- **Importance of a statistical analysis plan**
  - Analytic plans and statistical techniques for primary and secondary objectives
- **Report on characteristics of the patient population, exposures of interest and endpoints**

Interpretation

- **Who was studied?**
  - Is the actual population representative of the target population?
- **How were the data collected, edited and verified?**
  - Completeness of data collection and data quality
  - How were missing data handled and reported
- **How were the analyses performed?**

Case Examples

23 case examples are included to illustrate practical challenges and how they were addressed. E.g.,

- **NRMI** – "*Creating a Registry to Fulfill Multiple Purposes and Using a Publications Committee to Review Data Requests*"
- **GWTG-Stroke** – "*Using Performance Measures to Develop a Data Set*"
- **BPH** – "*Developing and Validating a Patient-Administered Questionnaire*"
- **GWTG** – "*Using Recognition Programs to Recruit Sites*"
- **OPTIMIZE-HF** – "*Using Registry Tools to Recruit Sites*"
- **ESCF** – "*Using Registry Data to Evaluate Outcomes by Practice*"

How do you know what makes a registry “good enough”?

Evaluating Registries

- Quality component analysis
  - Research quality (scientific process)
    - Planning; design; data elements & data sources; ethics, privacy and governance
  - Evidence quality (data/findings)
    - Patients; data elements & data sources; QA; analysis; reporting
- Components classified as
  - Basic Practice (draft names)
  - Future Directions/Potential Enhancement (draft names)

Research Quality: Basic

- PLANNING: A written study plan documents: goals, design, study population, recruitment, data collection, human subject protection, data element, sources, & review/QA. Feasibility is considered at the outset.
- Plans address how data will be evaluated, incl. what comparative information, if any, will be used to support study hypotheses or objectives.
- DESIGN: The size required to detect an effect, should it exist, or achieve a desired level of precision is acknowledged, whether or not met.
- Follow-up time needed to detect events of interest is acknowledged, whether or not feasible to achieve. To the extent feasible, follow-up time is adequate to address the main objective.
- DATA ELEMENTS: Outcomes are clinically meaningful and relevant, i.e., useful to the medical community for decision-making.
- ETHICS, PRIVACY, GOVERNANCE: Registry has received review by required oversight committees
- COMMUNICATION PLAN for results is addressed.

Research Quality: Potential Enhancements

- PLANNING: Formal study protocol with review from key stakeholders prior to finalization. Pilot studies are useful when studying hard to reach populations or when sensitive data are sought.
- DESIGN: Use of concurrent comparators in situations where treatments are evolving rapidly.
- Formal statistical calculations to support sample size, whether or not that size is achievable within practical constraints.
- DATA ELEMENTS & SOURCES: Multiple methods of data collection may be required for some purposes.
- Use validated scales and tests when such tools exist for purpose needed.
- Adapt levels of QA based on observed performance.
- Coding consistent with nationally approved coding systems; standardized data dictionaries, validated assessment tools….
- Publication policies are specified in advance of collecting data.

Evidence Quality: Basic

- PATIENTS: Participants are similar to the target population; attention is paid to minimize selection bias to the extent feasible.
- For safety studies, registry personnel are trained to ask about AEs in a consistent, clear & specific manner, and know how to report.
- DATA ELEMENTS & SOURCES: Data are reasonably complete.
- QA: Reasonable efforts have been expended to assure that appropriate patients have been systematically enrolled and followed in as unbiased a manner as possible; reasonable efforts have been devoted to minimize losses to follow-up. Data are checked using range and consistency checks.
- ANALYSIS: Accepted analytic techniques are used; they may be augmented by new or novel approaches.
- REPORTING: Results are reported for all main objectives; follow-up time is described so readers can assess its impact on conclusions drawn; report clearly states any conclusions drawn and implications of results, as appropriate.

Evidence Quality: Potential Enhancements

- **PATIENTS: External validity is described; for comparative effectiveness and safety, contemporaneous comparison data are collected.**
- **DATA: Results that can be confirmed by an unbiased observer enhance accuracy and reliability (e.g., death, test results, scores from validated measurements for PRO or clinical rating scales).**
- **QA: Potential sources of errors relating to accuracy and falsification are rigorously evaluated and quantified (e.g., through database and site reviews). For studies of safety, effectiveness and comparative effectiveness, a sample of data are compared with patient records.**
- **ANALYSIS: Loss to follow-up is characterized at all stages of study conduct. For safety studies, risks and/or benefits of "exposure" are evaluated quantitatively, *beyond statistical significance*. Sensitivity analyses are used to examine the effect of varying the inclusion/exclusion criteria & other assumptions.**
- **REPORTING: Inferences about causality are based on a variety of factors, including the strength of the association, biases, temporal relation, etc.**

Some Unanswered Questions

- When should a registry end?
- What are the privacy implications of linking multiple data sources into registries?
- How can different registries or other data sources working together, interfacing
- How should a registry be designed specifically for adverse event collection?

Thank You

Contact Information:

Richard Gliklich MD

President

Outcome

201 Broadway

Cambridge, MA 02139

richg@outcome.com

617-621-1600 x530

www.outcome.com

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DEcIDE Center