A Taxonomy For The Design, Development And Implementation Of Patient Registries

Eric K Gemmen MA, Senior Director, Quintiles, Inc, Late Phase & Safety Services, Falls Church, VA, USA;
Claudio Faria PharmD, MPH, Associate Director of Clinical Research, University of Massachusetts Medical School, Boston, MA, USA;
ISPOR Taxonomy for Patient Registries Classification, Strategy & Design Working Group
AGENDA

- Objectives
- Background
- Scope and Achievements to-Date
- Design
- Development
- Implementation
BACKGROUND
Patient Registry SIG

Classification, Strategy & Design Working Group

Chair: Chris L. Pashos PhD
Vice President and Executive Director, HERQuLES Abt Bio-Pharma Solutions, Inc.
Goals:

Determine and define:
- a patient registry terminology (common language),
- universal patient registry characteristics and a
- globally harmonized patient registry classification system.

to establish good research practices related to choices of registry strategy and consequent design.
Each term includes:
- brief definition
- broader explanation (in context of registries)
- the associated values & uses
- a discussion of issues or conflicts related to the term.

The issues/conflicts will be the basis of the Working Group’s Good Research Practices papers.
Establishment of 4 Project Teams:

1. Characteristics & Classifications of Patient Registries
2. Design, Development & Implementation
3. Analysis
4. Reporting & Publishing
Classification, Strategy & Design
Working Group

Establishment of 4 Project Teams:

1. Characteristics & Classifications of Patient Registries
2. Design, Development & Implementation
3. Analysis
4. Reporting & Publishing
The Taxonomy Teams’ Methodology

Identification of terms: hand-searched existing sources for terms:

- ISPE, Guidelines for good pharmacoepidemiology practices (GPP)
- CONSORT, ICJME, GRACE Initiative, selected journal requirements for authors
Registry Definition

Prospective observational study of patients with certain shared characteristics (e.g., particular disease, risk factor or exposure) that collects ongoing and supporting data over time on well-defined outcomes of interest for analysis and reporting.

- Is it a ‘study’? Yes.
Focus of Our Taxonomy

Prospective observational study where the primary data elements are collected for the direct purpose of the registry

- Protocol, DMP, SAP yields higher internal validity, quality, completeness

- Not analyses (e.g., studies) of pre-existing data
Team 2: Design, Development & Implementation Members

- **Eric Gemmen MA (Chair)**
  Senior Director, Quintiles Late Phase & Safety Services
- **Yvonne Lis PhD**
  Director, Carter-Lis Associates Limited
- **Gabriel Sandblom MD, PhD**
  Department of Surgery, University Hospital, Lund, Sweden
- **Claudio Faria, PharmD MPH**
  Associate Director of Clinical Research, UMass Medical School
- **Kathryn Starzyck MSc**
  Associate Director of Scientific Affairs, Outcome
- **Murtuza Bharmal PhD**
  Associate Director, Quintiles Late Phase & Safety Services
- **Nancy Dreyer PhD, MPH**
  Outcome
- **Anuprita D Patkar, PhD**
  Associate Director, Health Economics & Reimbursement, ETHICON
- **Donatus Ekwueme PhD**
  Senior Health Economist, U.S. Centers for Disease Control & Prevention
- **Joanna Lis PhD, MBA**
  Manager of Health Economics Department, sanofi-aventis, Warsaw, Poland
- **Maznah Dahlui MD, MPH**
  Department of Social and Preventive Medicine, University of Malaya
Achievements

Identified 25 categories of terms

- **11 in Design including:**
  - research question(s), design characteristics, study population, data elements, data sources, data collection materials & methods, guidelines & standards, registry size and duration, etc.

- **9 in Development section including:**
  - registry purpose, funding and oversight, stakeholders, scope, ethics and privacy, regulatory considerations, etc.

- **5 in Implementation including:**
  - pre-launch issues, site support, data capture & management, data lock, close-out
Achievements

160+ terms / definitions completed

- 50 terms in Design including:
  observational, non-interventional, naturalistic, active/passive surveillance, historical control, etc.

- 76 terms in Development section including:
  exposure, feasibility, informed consent, IRB/ethics approval, target population, etc.

- 37 terms in Implementation including:
  site identification, regulatory documents, ICF-GCP, database build, clinical research associate, query resolution, loss to follow-up, source document verification (SDV), site close-out, etc.
Challenges

- Scope, i.e., keeping the terms in the taxonomy specific to registries and not simply clinical studies, overall
- The terms ‘registry’ and ‘observational study’ are often used interchangeably, although registries are a subset of observational studies
  - Moreover, the term ‘observational’ may differ in meaning between Europe and the US
    - European definition more strict

\[\text{Observational} \quad \supseteq \quad \text{Purely Naturalistic}\]
Registry Objectives

- Quality of Care
- Safety Monitoring
  - AEs and SAEs
- Clinical Effectiveness
- Adherence and Persistence
- Economic
  - Resource Utilization
  - Direct and Indirect Costs
- Cost Effectiveness
- Treatment Satisfaction

- Final vs. Intermediate Clinical Outcomes

*Mandated vs. Discretionary*
## Registry Objectives

- Scientific
- Commercial
- Clinical
- Clinical Audit

<table>
<thead>
<tr>
<th></th>
<th>Clinical</th>
<th>Clinical Audit</th>
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</thead>
<tbody>
<tr>
<td>Scientific</td>
<td>Safety</td>
<td>Quality Assurance</td>
</tr>
<tr>
<td>Commercial</td>
<td>Effectiveness, Communication with Medical Community</td>
<td>Appropriate Use</td>
</tr>
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</table>
Registry Study Design Characteristics
Prospective Design Possibilities

- Experimental
  - Randomized
    - Placebo Controlled
    - Active Controlled
  - Non-Randomized
    - Non-Controlled
    - Placebo Controlled
    - Active Controlled
    - Historical Controlled
- Observational
  - Naturalistic
  - Interventional*
Prospective Design Possibilities

Observational, Non-interventional or Naturalistic Study:

- No interference with real life care of the patients
- No defined follow-up visits
- Open-label
Prospective Design Possibilities

**Observational, Non-naturalistic Study:**
- Modest interference with real life care of the patients, e.g., defined follow-up visits within Standard of Care
- Laboratory and/or diagnostic tests
Prospective Design Possibilities

Experimental

Observational

Single-arm Cohort: All patients in the same group

Multi-arm Cohort: Patients are split into different groups according to pre-defined criteria, e.g.,
1) Patients initiating treatment
2) Patients remaining on a stable regimen
3) Patients switching treatment
Retrospective Design Possibilities

Retrospective Studies:
- Use historical data
- Can be single-cohort or multi-cohort (see previous definition)

Retrospective Case Control Studies:
- Case refers to person with disease or condition
- Control refers to person without condition
- Frequencies or levels of past exposures in the case group are compared with the control group
- Registry data used to support a case-control study
Observational studies

**Case Control**
- Exposed to risk factor
  - Yes
  - No
- Disease
  - Yes
  - No
- Time

**Cohort**
- Exposed to risk factor
  - Yes
  - No
- Disease
  - Yes
  - No
- Sample of people
  - Yes
  - No
- Time

**Questions**
- Risk Factors
- Incidence
- Risk factors
- Prognosis

**Measures**
- Odds Ratio
- (Est. Relative Risk)
- Incidence
- Relative Risk

Adapted from Fletcher, SW. Principles of Epidemiology. In: Textbook of Internal Medicine, Kelley, WN (Ed), JB Lippincott, Philadelpia 1988.
Other Study Models

- **Ecologic**
  - Population based, rather than individual subject
  - Aggregates patient data at investigational sites, transmitting only a summary of this data for analysis
  - **Avoids privacy issues**
  - **But, loss of variation/power for statistical inference**

- **Consider multiple simple studies**
  - e.g., Screening for ACE inhibitor tolerability
    - If pass, enter CHF registry that includes ACE inhibitors in one or more arms
    - If fail, enter CHF registry that does not include an ACE inhibitor arm (i.e., make use of screen failures)
Registry Development Attributes
Registry Stakeholders

- **Primary**
  - responsible for creating and funding the registry or those who require the data or who will use the data to inform decision making, e.g.,
    - manufacturers, health care service providers, payers, policy makers, regulatory authorities, academia.

- **Secondary**
  - will benefit from knowledge of the data or would be impacted by the results but who are not instrumental in establishing the registry, e.g.,
    - regulators, reimbursement committees, HTA organizations, treating physicians and their patients, professional or patient societies.

*Registries usually have multiple stakeholders; Building consensus is critical*
Use of Registry Data for Regulatory and Payer Requirements

Do regulatory authorities use registry data for procedure or product approval?
- Yes, but only for conditional approval, i.e., post-approval safety
  - CASES-PMS (Stents), NCGS – Used for conditional FDA approval
    - Needed to be more representative of physicians treating patients
    - Needed to be generalizable to physicians without stenting experience
    - Test training program

- What conditions are placed on the registry for its data to meet the standards expected by regulatory agencies and payers?
  - Registry has identical inclusion/exclusion criteria to that of the registration trial
    - MACE rate <= to that of Phase III trial
  - e.g., Providers must submit data for registry as condition of coverage
Funding and Oversight

- Budget
- Governance
  - Steering Committee
- Data Ownership
- Access Rights

Should be decided prior to start of registry
Ethics and Privacy

- Respect for persons
- Beneficence
- Justice
- CIOMS (WHO)
- ICH-GCP
- Conflicts of interest
- Common Rule
- FDA Regulations
- Research participants
- Informed Consent
- Informed Consent waiver
- IRB/Ethics Committee
- Data Privacy Committee
- De-identified Information
- Privacy Rule/ HIPAA
- Belmont Report
Ethics and Privacy (cont.)

- Personal IDs removed from any study files that are accessible to non-study personnel in accord with applicable laws and regulations.

- Study files should be encrypted and stripped of personal IDs, and code keys stored separate from study files.

- All personnel with access to data containing personal IDs will sign a pledge to maintain the confidentiality of study subjects, and will maintain an ability to verify the origin and integrity of data sets from which personal identifiers will have been removed.

-- from ISPE, GPP
Registry Scope

- Size
  - Patients/Participants
  - Sites
    - Representative?
- Setting or Context
  - One or multiple?
- Normal vs. Standard of Care
- Study Population vs. Target Population
- Inclusion Criteria
  - Note on ‘Naturalistic’
- Geographic Location
- Duration of Observation
  - Episode of care to Lifetime
  - FPI to LPO
- Core Dataset – variables required to achieve primary objectives
- Feasibility
Registry Participants

As registries are observational studies and not investigational trials, the observational unit is generally considered to be the ‘patient’ or the ‘participant’ rather than a ‘subject’.

- Patients/participants are not subjected to any treatment or intervention on account of the study
Operational Considerations

- Timelines
- SOPs
- Monitoring
- Quality Assurance
- Reporting Requirements
- Scientific Advisory Panel
- Pilot
- Closure
Regulations/ Guidelines/ Good Research Practices

- ICH-GCP
- EFPIA Code
- EMEA Clinical Trial Directive
- DHHS Guidance for Industry:
  - Good PV Practices & Pharmacoepidemiologic Assessment (March 2005)
  - Establishing Pregnancy Exposure Registries (August 2002)
- Guidelines for Evaluating Public Health Surveillance Systems
- Quality of reporting of observational longitudinal research
- Registries for Evaluating Patient Outcomes (AHRQ; April 2007)
Interventional or Non-Interventional

Observational
  Non-Interventional – by U.S. definition
  (may be) Interventional – by EU Clinical Trials Directive
  PROs, Diagnostics (labs), Procedures
  implications for ethics, privacy

As there are no generally accepted criteria for determining when additional diagnostic and monitoring procedures should be considered as an intervention, this remains an issue that has to be decided on an individual basis.
Normal Care vs. Standard of Care

Normal Care

- Health care delivery as it is exercised by the average professional in a particular healthcare environment.
  - Normal care, sometimes referred to as “real-world care”, is the result of a study being observational—and, in particular, naturalistic—in design. Patients are observed without undue interference by protocol demands.

Most guidelines address ‘standard of care’:

Standard of care

- International, national or local treatment guideline/protocol, which specifies the most appropriate treatment
  - Not all treatment guidelines or protocols are evidence based.
  - Patients receiving standard of care do not constitute all patients receiving normal care.
  - Normal or real-world care includes some treatments that may not be considered standard of care.
Standard of Care vs. Normal Care

Standard of Care

Certain Labs

Normal Care

Off-label use
Registry Implementation
Where Design Meets Execution

Optimize Registry
Design to Meet Objectives

Operational Realities / Practicality
Continuum of Degree of “Real-Worldliness”
Data Collection Materials and Methods

- CRFs
- Solicited reporting
- Spontaneous reporting
- Measurement precision
  - Weight scales; laboratory normal vs. abnormal ranges
  - Random error vs. Systematic error
Site Support

- Site identification
- Site start-up
- Regulatory Documents
- Site initiation and Training
- Investigator Meetings
- Patient Recruitment
  - Tools
  - Screening/Enrollment Logs
- Helpdesk
- CRA
- Clinical Monitoring
- Study Performance Measures
- Site Motivation Tools
- Site Reimbursement
- Patient Honoraria
- Patient Retention
- Loss to Follow-up
- SDV
The demands of many observational studies and registries require moving research into the community practice environment of private physicians and group practices that have little to no prior experience in clinical research.

Centralized support of these sites can play a large role in their motivation, compliance with data collection and ability to meet enrollment targets.
Site Identification and Recruitment

- Physicians
- Hospitals

- Access existing mailing lists/electronic databases to
  - profile the providers treating the patients necessary for the registry
  - Understand the profile of the target population

- Gauge site interest in participating in registry (feasibility)
  - Clearly state the purpose and objectives of the registry,
  - how the data will be used,
  - and assurances of the protection of identities of individual institutions, providers and patients
  - From this population, invite a composition of sites who...
    1. ...collectively represent a sample of providers representative
      - Geography, specialty, practice setting, patient volume, training, EDC
    2. ...you project will, collectively, recruit and enroll a sample representative of the target population
Site Start-up

- Regulatory Documents
  - CV, Medical License
- Contracts
- Site Initiation and Training
Patient Recruitment and Retention

- **Tools**
  - Web sites / patient on-line communities
  - Newsletters
  - Physician referral

- **Screening / Enrollment Logs**

- **Physician involvement**
  - Steering Committee clinical membership

- **Incentives**
  - Sites
  - Patients

- When does retention compromise validity of outcomes?
  - e.g., adherence, persistence

- **Incentives**
Site Support and Retention

- Helpdesk
- Clinical Monitoring
- CRA
- Study Performance Measures / Reports
- Site Motivation Tools
  - Branding
  - Consistent Data Reports
  - Publication Opportunities
    - Hypothesis/Standard Form
- Site Reimbursement
  - Commensurate with effort involved
Investigator and Prescriber

Data Focus

Investigator

Clinical Research Associate

Medical Sales Liaison

Research Coordinator

Nurse Educator

Prescriber

Relationship Focus
Monitoring Spectrum

- Blend of onsite and remote monitoring
- Sample-based and/or ‘for-cause’ SDV
- Experienced AND Community Sites
- Real world data

- Onsite Monitoring
- 100% SDV
- Experienced Sites
Data Capture and Management

- Data Capture
  - EDC vs. Paper
  - ePRO
- Database Build
- Edit check specifications
- Edit checks
- Data Protection
- Query Resolution
  - DCFs
- Data Cleaning
  - Primary Variables
  - Missing/Error Rates
Data Capture and Management

- Security of the data should be maintained at all times. Access should be limited to authorized individuals.

- Controls, such as document encryption, should be used to ensure the authenticity, integrity, and confidentiality of electronic records when transmitted over open systems (e.g., the internet).

- Adequate back up of the data should be maintained throughout the course of the study.

- From ISPE GPP
Close Out

- Site Close-out
- Data Transfer
- Record Retention
- Database Archiving
Archiving

1. Study protocol and all approved modifications;
2. Final study report;
3. All source data and, where feasible, any biologic specimens.
4. Copies of electronic versions of analytic data sets and programs
4. SOPs followed
5. Copies of signed informed consents
6. Copies of signed IRB approvals
7. Copies of training documents
# Essential Characteristics of a Registry

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observational</td>
<td>• Real world assessment</td>
</tr>
<tr>
<td>Non-interventional</td>
<td>• No protocol-defined treatment/management, allocation of patients and patient visits  &lt;br&gt;• Limited risk; ethics review/consent is required, however focus is on protection of personal health information</td>
</tr>
<tr>
<td>Data Collection</td>
<td>• Dictated by patient and patient experience  &lt;br&gt;(i.e., heterogeneous and missing data)  &lt;br&gt;• Need to define key assessments and outcomes of interest</td>
</tr>
<tr>
<td>Outcomes Evaluation</td>
<td>• Baseline assessment critical  &lt;br&gt;• Longer-term observation period  &lt;br&gt;• Hypothesis-generating versus hypothesis-testing</td>
</tr>
</tbody>
</table>
### Key Differences versus other Study Designs

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Registry (versus Traditional RCT)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Treatment</td>
<td>Evaluate care in real-world setting; No treatment assignment</td>
</tr>
<tr>
<td>2 Time period/Duration</td>
<td>Long-term outcomes collected</td>
</tr>
<tr>
<td>3 Patients</td>
<td>‘Typical’ patients seen in community setting; Limited inclusion/exclusion criteria; Can involve large numbers of patients;</td>
</tr>
<tr>
<td>4 Methods</td>
<td>Do not require comparator/placebo; Open-label; No defined/mandated interventions; No random allocation of patients (generally)</td>
</tr>
</tbody>
</table>
### Key Differences versus Other Study Designs II

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Registry versus Traditional RCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 Statistical Analysis and Data Collection</td>
<td>Hypothesis generating; no sample size calculation; focus on ‘generalizability’ Heterogeneous patients</td>
</tr>
<tr>
<td>6 Patient Consent &amp; Ethics Review</td>
<td>Focus on handling of personal health information and not risk</td>
</tr>
<tr>
<td>7 Safety</td>
<td>Voluntary reporting of adverse events Unsolicited (vs. solicited) adverse event collection</td>
</tr>
</tbody>
</table>
# Registry Classification I

<table>
<thead>
<tr>
<th>Registry Type</th>
<th>Design</th>
<th>Measurement</th>
<th>Application/Use</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Simple Cohort</strong> &lt;br&gt; Epidemiologists &lt;br&gt; Public Health &lt;br&gt; Clinicians</td>
<td>• Prospective  &lt;br&gt; • Non-interventional  &lt;br&gt; • Sample-based  &lt;br&gt; • Collection of information in population that share common exposure (i.e., pregnancy registry)</td>
<td>• Clinical outcomes i.e., morbidity, mortality</td>
<td>• Pregnancy registry  &lt;br&gt; • Determine association/correlation between exposure and outcome</td>
</tr>
<tr>
<td><strong>Outcomes</strong> &lt;br&gt; Epidemiologists &lt;br&gt; Policy makers &lt;br&gt; Governments &lt;br&gt; Public Health &lt;br&gt; Academia</td>
<td>• Prospective  &lt;br&gt; • Non-interventional  &lt;br&gt; • Population-based  &lt;br&gt; • Collection of information in population</td>
<td>• Clinical outcomes i.e., morbidity, mortality</td>
<td>• Understand natural history of patient cohort that share common characteristic i.e., social science research, population-based research, epidemiological research  &lt;br&gt; • Examples: mortality, literacy, access to medical care, etc.</td>
</tr>
<tr>
<td><strong>Safety Surveillance</strong> &lt;br&gt; Manufacturers &lt;br&gt; Regulators &lt;br&gt; Clinicians</td>
<td>• Prospective  &lt;br&gt; • Non-interventional  &lt;br&gt; • Sample-based  &lt;br&gt; • Collection of information in patients receiving common intervention</td>
<td>Adverse Events  &lt;br&gt; • Unexpected AEs  &lt;br&gt; • SAEs</td>
<td>• Support product registration  &lt;br&gt; • Conduct post-marketing surveillance (‘real world setting’)  &lt;br&gt; • Identify ‘signals’</td>
</tr>
</tbody>
</table>
## Registry Classification II

<table>
<thead>
<tr>
<th>Registry Type</th>
<th>Design</th>
<th>Measurement</th>
<th>Application/ Use</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Risk Management</strong>&lt;br&gt;Regulators Manufacturers</td>
<td>• Prospective&lt;br&gt;• Interventional&lt;br&gt;• Population-based&lt;br&gt;• Use one or more tools to meet goal(s)&lt;br&gt;• May collect info beyond FDA-approved labelling</td>
<td>• Clinical outcomes as compared to clinical studies&lt;br&gt;• Safety information and adverse events compared to clinical studies&lt;br&gt;• Compliance with prescribed management and prescribing protocols&lt;br&gt;• Impact of tools on ensuring compliance an outcomes</td>
<td>• Mandated by regulators to meet specific goals and objectives in minimizing known risks while preserving benefits&lt;br&gt;• Assessing product’s risk-benefit balance&lt;br&gt;• Developing and evaluating tools to minimize risks while preserving benefits&lt;br&gt;• Making adjustments to risk management tools to further improve risk-benefit balance</td>
</tr>
<tr>
<td><strong>Disease</strong>&lt;br&gt;Regulators Manufacturers</td>
<td>• Prospective&lt;br&gt;• Non-interventional&lt;br&gt;• Population-based&lt;br&gt;• Collects information in cohort of patients with common disease</td>
<td>• Drug utilization and safety&lt;br&gt;• Outcomes – morbidity and mortality&lt;br&gt;• Resource utilization&lt;br&gt;• Clinical management</td>
<td>• Understand natural history of disease&lt;br&gt;• Identify, compare and evaluate management patterns&lt;br&gt;• Identify ‘signals’ relating to safety, effectiveness and outcomes&lt;br&gt;• Quantify burden of illness, QoL&lt;br&gt;• May be iterative in establishing and benchmarking best practices&lt;br&gt;• Assess screening, identification and monitoring practices&lt;br&gt;• Cost-effectiveness</td>
</tr>
</tbody>
</table>
### Registry Classification III

<table>
<thead>
<tr>
<th>Registry Type</th>
<th>Design</th>
<th>Measurement</th>
<th>Application/ Use</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Drug and Drug Class</strong></td>
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</tr>
<tr>
<td></td>
<td>• Prospective (some retrospective)</td>
<td>• Safety and effectiveness</td>
<td>• Post-marketing surveillance</td>
</tr>
<tr>
<td></td>
<td>• Sample-based</td>
<td>• Outcomes - morbidity and mortality</td>
<td>• Compare effectiveness to efficacy</td>
</tr>
<tr>
<td></td>
<td>• Collects information on patient cohort receiving common treatment</td>
<td>• Resource utilization</td>
<td>• Study non-approved uses</td>
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<tr>
<td></td>
<td></td>
<td>• Clinical management and add-on therapy</td>
<td>• Identify drug-related ‘signals’</td>
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<td></td>
<td></td>
<td></td>
<td>• Cost effectiveness</td>
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<td></td>
<td></td>
<td></td>
<td>• Willingness to pay</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>• Reimbursement evaluation</td>
</tr>
<tr>
<td><strong>Management</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Prospective/retrospective</td>
<td>• Treatment and management patterns</td>
<td>• Care mapping</td>
</tr>
<tr>
<td></td>
<td>• Collect information on common population</td>
<td>• Resource utilization</td>
<td>• Continuous quality improvement</td>
</tr>
<tr>
<td></td>
<td>• Population/sample-based</td>
<td>• Outcomes</td>
<td>• Resource utilization and costing</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Burden of illness</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Quality of care</td>
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<td></td>
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<td></td>
<td>• Provider performance</td>
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<tr>
<td></td>
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<td>• Health economic evaluation</td>
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<td></td>
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<td>• Reimbursement evaluation</td>
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<tr>
<td><strong>Resource Utilization</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Prospective or retrospective</td>
<td>• Direct costs i.e., medical care, drug use, hospitalization</td>
<td>• Burden of illness</td>
</tr>
<tr>
<td></td>
<td>• Sample-based</td>
<td>• Productivity costs i.e., absenteeism, productivity</td>
<td>• Cost of care</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>• Reimbursement evaluation</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Health economic evaluations</td>
</tr>
</tbody>
</table>

**Sponsors**
- Clinicians
- Manufacturers
- Regulators
- Payers

**Payers**
- Policy makers
- Clinicians
- Health administrators

**Academia**
Method: Survey

Survey Objective 1:

- Determine the relative weight of key factors in physician / investigator decisions to enroll in and continue participating in a patient registry:
  - Publication opportunities
  - Access to aggregate data/reports
  - Importance of scientific purpose
  - Protocol feasibility and probability of success
  - Credibility of scientific steering committee
  - Adequate reimbursement to offset burden
Method: Survey

Survey Objective 2:

- Identify other factors that investigators value related to enrollment/retention
  - e.g., access to international network of peers, quality improvement tools, disease management recommendations, practice & patient management tools, technology, onsite materials, etc.
Team 1: Achievements

- Developed working definition
- Identified common elements and considerations
- Agreement as to what is NOT a registry
- Identified commonly used registry designs and applications
- Set the stage for further discussion/clarification (to follow in subsequent sections)
Effectiveness

- **Registries are:**
  - Observational, longer follow-up, include off-label use
  - Strong external validity, particularly if large sample size

- **Analysis methods**
  - Longitudinal data analysis
  - Cross sectional data analysis
  - Prevalence of events
Effectiveness

- **Missing data**
  - Categories
  - Handling missing data

- **Potential for Bias**
  - Selection, ascertainment, measurement biases
  - Adjust for imbalance
    - Covariate analyses, multilevel analyses,
    - Matching approaches
    - Propensity scoring
Cost-Effectiveness

- Registries well-suited to collect ‘real-world’ data
- Incremental Effectiveness – issues identified
- Disease-related cost over fixed time frame
  - Identify relevant resources to include in cost
  - Treatments, administration, safety and effectiveness
    - E.g. Management of adverse events, long term complications of progressing disease
Cost-Effectiveness

- Dealing with missing data
  - Variable Follow-up - balance long timeframe with need to impute
  - Missing assessments, incomplete information

- Dealing with potential bias - effect on cost
  - Selection bias, ascertainment and measurement bias

- Cultural and country differences