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Value of Conducting Feasibility Studies in Observational Research

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Presented at: SCOPE Summit for Clinical Ops Executives

The power of **knowledge.**
The value of **understanding.**

Key Topics

- Why Conduct an Observational Study?
- Why Conduct a Feasibility Study?
- Operationalizing a Feasibility Study and Case Studies
- Take-Away Messages
- Questions

Overview

Why Conduct an Observational Study?

- To understand the natural history of a disease
- To explore the intersection between RCTs and clinical exposure post approval
- To understand treatment patterns; stakeholder behaviors; and clinical, economic, and patient outcomes in real-world settings
- Observational studies are designed to be as close to the real world as possible, but recognizing limitations

Why Conduct an Observational Study?

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Real-world data sources

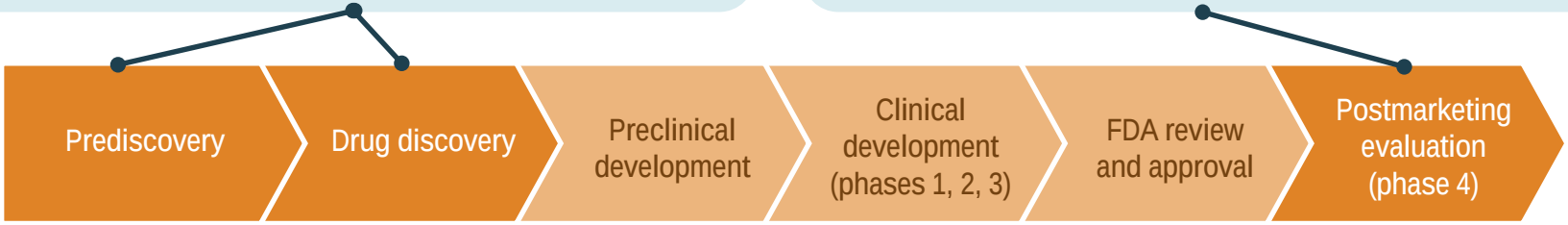
- Claims data
- EMRs/EHRs
- Prospective observational data
- Patient pathways
- Surveillance
- Mortality database
- Primary and secondary care data
- Administrative data
- Disease and device registries
- Pharmacy data
- Cost studies
- Mobile devices
- Consumer data
- Social media

Real-world evidence
Identifying unmet needs

- Natural history
- Comorbidities
- Burden of illness
- Incidence and prevalence
- Disease mechanisms
- Clinical practice patterns

Real-world evidence
Informing clinical and policy decisions

- Usage patterns
- Outcome predictors
- Benefit/risk in subgroups
- Pharmacovigilance
- Population-level impact
- New indications



Why Conduct a Feasibility Study Prior to the Implementation of a Large Observational Study?

- Two areas of focus:
  - Design Feasibility
  - Operational Feasibility

Why Conduct a Feasibility Study Prior to the Implementation of a Large Study?

- Taking the time for and providing resources to feasibility studies provides critical insight into the most time-efficient and cost-effective approach to meeting observational research objectives---”Better, Faster, Cheaper”

Why Conduct a Feasibility Study Prior to the Implementation of a Large Study?

Do sponsors no longer believe recruitment estimates? The CRO 'dilemma'

By Flora Southey
20-Dec-2017 - Last updated on 20-Dec-2017 at 12:42 GMT

A lack of confidence in trial recruitment estimates can cause a "dilemma" for sites bidding for clinical studies, says expert Philipp Bardorrek.

Why Conduct a Feasibility Study Prior to the Implementation of a Large Study?

Editorial

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Journal of Comparative Effectiveness Research

Developing an integrated strategy for evidence generation

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"A new approach will always have a perceived element of risk, and there are aspects of an integrated approach to evidence generation that may be of concern to those accustomed to the 'traditional' industry development model."

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Keywords: evidence generation • evidence planning • health technology assessment • market access • real-world data • real-world evidence • regulatory

It is common for pharmaceutical companies to consider evidence generation as the responsibility of individual departments (e.g., clinical development, medical affairs and health economics and outcomes research). This typically means that evidence is generated in a sequential fashion; for example, waiting for regulatory approval before initiating an outcomes-based study. This is a relatively risk-averse strategy that has served the industry well in generating evidence to satisfy regulatory and reimbursement decisions, and until recently, there has been little need to improve it.

An integrated approach to evidence planning that involves the bringing together of randomized clinical trial (RCT)- and real-world evidence (RWE)-based approaches across all departments offers an innovative operating model. It benefits industry by generating the RWE required to meet the increasing demands of decision makers,

Why Conduct a Feasibility Study?

- Feasibility studies help to
  - Evaluate appropriate study design (e.g., database vs prospective observational study)
  - Estimate the cost and time necessary to complete the study
  - Confirm requirements for institutional review board (IRB), ethics committees, heath authority notifications/reviews and data privacy laws
  - Ascertain the level of interest among potential principal investigators (PIs) and if needed information is available
  - Determine optimal content of data collection instruments, as well as time commitment to complete them
  - Estimate the number of eligible patients available and the number of sites needed to collect the targeted data from the targeted number of patients

Systematic Approach to Study Design

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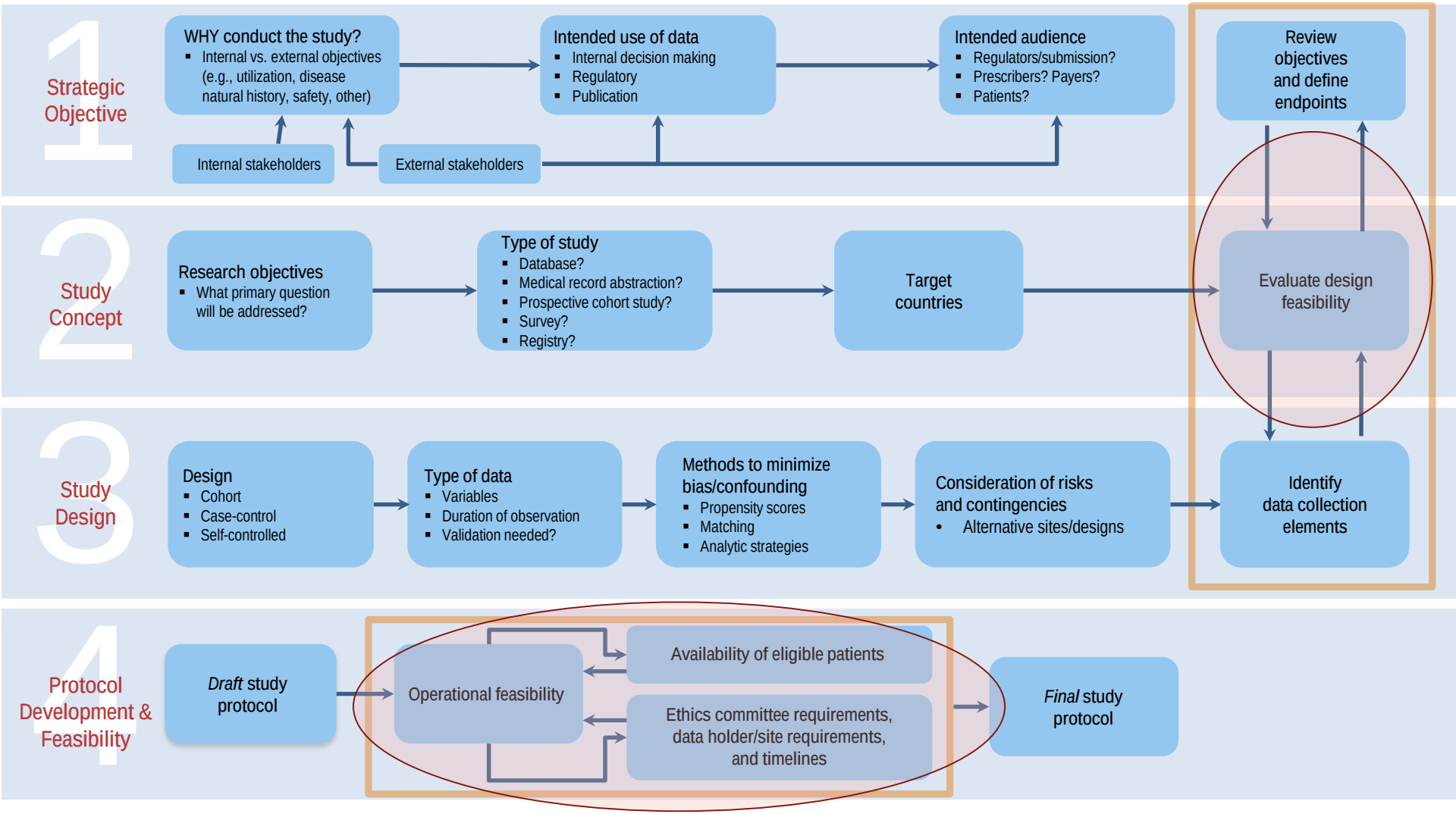

Where Does Feasibility Fit Into the Research Planning Process?

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Study Conceptualization

- Strategic Purpose
- Research Questions
- Endpoints of Interest

Feasibility

- Literature review to determine what has been done previously in this or related areas
- Outreach to key opinion leaders to vet the study concept and gather initial input (and who can provide clinical guidance throughout study implementation)
- Exposures and outcomes of interest
- Covariates and potential confounders
- Choice of comparator(s)

Where Does Feasibility Fit Into the Research Planning Process?

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Protocol Development

- Data Sources
- Methods
- Sample Size
- Variables of Interest

Feasibility

- Evaluation of data sources
- Determination of existing measures
  - Existing measures to be used, availability in the languages required, and existing validation or potential to validate outcome or exposure
- Cognitive testing of new measures
  - Ensure comprehension and that response option scales function as intended

Where Does Feasibility Fit Into the Research Planning Process?

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Protocol Development

- Data Sources
- Methods
- Sample Size
- Variables of Interest

Feasibility

- Qualitative interviews with prospective PIs:
  - Availability of target population
  - Unique challenges to recruitment
  - Availability of the most relevant data through the planned data sources
  - Operational challenges
- Country selection
  - Willingness to support the study locally
  - Ethics requirements and timing
  - Cultural considerations

Where Does Feasibility Fit Into the Research Planning Process?

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Protocol Feasibility

- Availability of Patients
- Site Interest
- Contracting, Fees
- Ethics
- Timelines

Feasibility

- Site feasibility questionnaire sent to prospective sites along with protocol synopsis:
  - Site interest and resources to conduct the study
  - Enrollment targets
  - Obstacles to enrollment
  - Contracting requirements (including fees, templates)
  - IRB/ethics approvals

A Systematic Approach to Study Design…

results in a well-conceptualized, realistic study approach

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Study Planning

- Coordinated multidisciplinary review
- Confer with sponsor and other stakeholders to ensure understanding of objectives
- Initial feasibility

Feasibility

Recommend initial feasibility to evaluate the following:

- Availability of data and/or target population
- Eligibility criteria
- Sample size
- Timelines

Optimal Methodology

- Multisite prospective observational study
- Survey
- Medical record abstraction (MRA)
- Literature review
- Meta-analysis
- Retrospective database analysis
- Hybrid design

Case Studies

Operationalizing a Feasibility Study: Case Study 1

- Study Design:
  - Characterize the burden of illness of non–small cell lung cancer (NSCLC) in 3 European Union (EU) countries
  - Conduct medical record abstraction and prospective patient survey

Goal and approach of feasibility assessment

  - Determine key variables to be collected as part of the study via literature review
  - Assemble advisory board
  - Recruit 2 investigators/sites in each country to participate in in-depth telephone interviews and conduct a 1-hour telephone interview to discuss feasibility assessment and study logistics
  - Contact prospective sites to request participation in the feasibility assessment
  - Create web-based feasibility questionnaire

Operationalizing a Feasibility Study: Case Study 1

- What did we learn?
  - Approach to treatment of NSCLC varies greatly from country to country (complex MRA case report forms [CRFs])
  - Total number of sites necessary to realize sample size
  - Contracting variations
  - Opt-out process in France

Operationalizing a Feasibility Study: Case Study 2

- Study Design
  - Prospective patient survey in oncology in the United States

Approach to feasibility

- Determine key variables to be collected as part of the study
- Contact prospective sites to request participation in the feasibility assessment

Operationalizing a Feasibility Study: Case Study 2

- Patient Population
  - Patient volume
  - Ability to enroll
- Site Categorization
  - Type of center (e.g., hospital-based clinic, office-based)
  - Types of health care providers
  - Number of health care providers

Operationalizing a Feasibility Study: Case Study 2

- Study Logistics
  - Time frame for study
  - Ethics review process
  - Contracting process
  - Staff availability
  - Administrative logistics

Operationalizing a Feasibility Study: Case Study 3

- Study Design
  - PASS study in a neurological indication involving a patient and physician survey to evaluate educational materials
- Goal and approach of feasibility assessment
  - Recruit clinical experts and site staff in each country to participate in in-depth interviews
    - Review the patient and physician survey forms
    - Ask the physicians if all information requested in the survey form is easily available and if the physicians have any suggestions on how to improve the forms
    - Determine by consulting experts and site staff the feasibility of collecting patient-reported data
    - Request feedback on the logistical considerations of meeting the protocol requirements

Operationalizing a Feasibility Study: Case Study 3

- What did we learn?
  - Patients live in a variety of settings; some unanticipated by the client and varied by country
  - Patients had a wide range of cognitive deficits ranging from mild to severe and assent vs consent requirements would need to be carefully considered
  - Only CGRO data would be reliable
  - Significant changes made to the design
  - Client was able to successfully propose these changes to the regulatory agency prior to the start of data collection

Take-Away Messages

- Observational studies are increasingly important to pharmaceutical companies as they are required to demonstrate real-world clinical, patient-centered, and economic value of their assets
- Feasibility studies support decision making on the final study design and provide critical inputs into determining the cost and time necessary to conduct observational research
- Crucial takeaway: Plan, Plan, and PLAN, early and strategically, apply best practices, and test processes prior to operationalization

Thank You! Any Questions?

Please visit our website for more information: www.rtihs.org

For technical inquiries, please contact:

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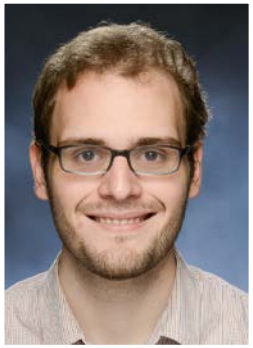

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