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CHALLENGES FOR PRAGMATIC TRIALS IN EUROPE



Regulatory-Payer Mismatch in Standards, Methods, Purposes

- Push in past years to harmonize regulatory approval standards between US, Europe, Japan
 - Regulatory standards primarily based on expectation of explanatory trials -- safety and **efficacy**
- Payment decision-makers interested in range of outcomes relevant to end users in clinical settings – **effectiveness**
- Outcomes of interest to payers often considered achievable with modeling and observational methods
- Payers and some HTA bodies more likely than regulators to accept observational evidence
 - In Europe, national single-payer health systems dominate; observational often default for assessing effectiveness



Lack of Agreement between HTA/Payment Decision-Makers

- Lack of agreement on which outcomes are best
 - Quality of life? (Which aspects?)
 - Workplace productivity?
- Lack of agreement on types of evidence to accept
 - Which metrics to use? Which instruments?
 - What threshold of clinical benefit?
 - What balance between internal and external validity?
- Examples
 - Alzheimer disease, mini-mental status exam vs. delay in institutionalization
 - Metrics for psoriasis



Infrastructure Challenges

- PCTs often call for large study population
 - Often seek to use networks of community medical practices for “real-world” patients and settings
 - Must coordinate participation/recruitment across national boundaries
 - Potential complications include ethics review
- Cost of PCTs (large trials, long-term endpoints)
 - Observational less costly, but requires general population use of new technology in clinical practice
 - Preferable to harmonize regulatory/payer standards for earlier use of PCTs



Making Pragmatic Trials “Practical”

PCTs Central to CER

- CER is defined as research designed to inform a decision
- PCTs can be defined as trials designed to inform a decision

Who Has an Interest in How it's Done?

- Payers/HTA Bodies
- Regulators
- Methodologists
- Researchers/Industry
- Clinicians, Patients

Consulting stakeholders for method choice, assessment of feasibility, prioritization of CER will clarify stakeholder goals and requirements; facilitate practicality of PCTs; foster greater opportunities for implementation



Example Approach to International Facilitation of PCTs

- Greenpark Collaborative: international Initiative
- Objectives
 - Pilot study to determine the feasibility of developing technology-specific guidance documents for the life sciences industry with recommendations for the design of clinical studies that address the information needs of payers and HTA bodies
 - To develop a draft guidance for Alzheimer's disease as a case study to evaluate feasibility
 - To consider the possible design of a global initiative to support additional guidances

