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Use of Real-World Evidence in Pragmatic Clinical Trials to Support Regulatory Decision-Making

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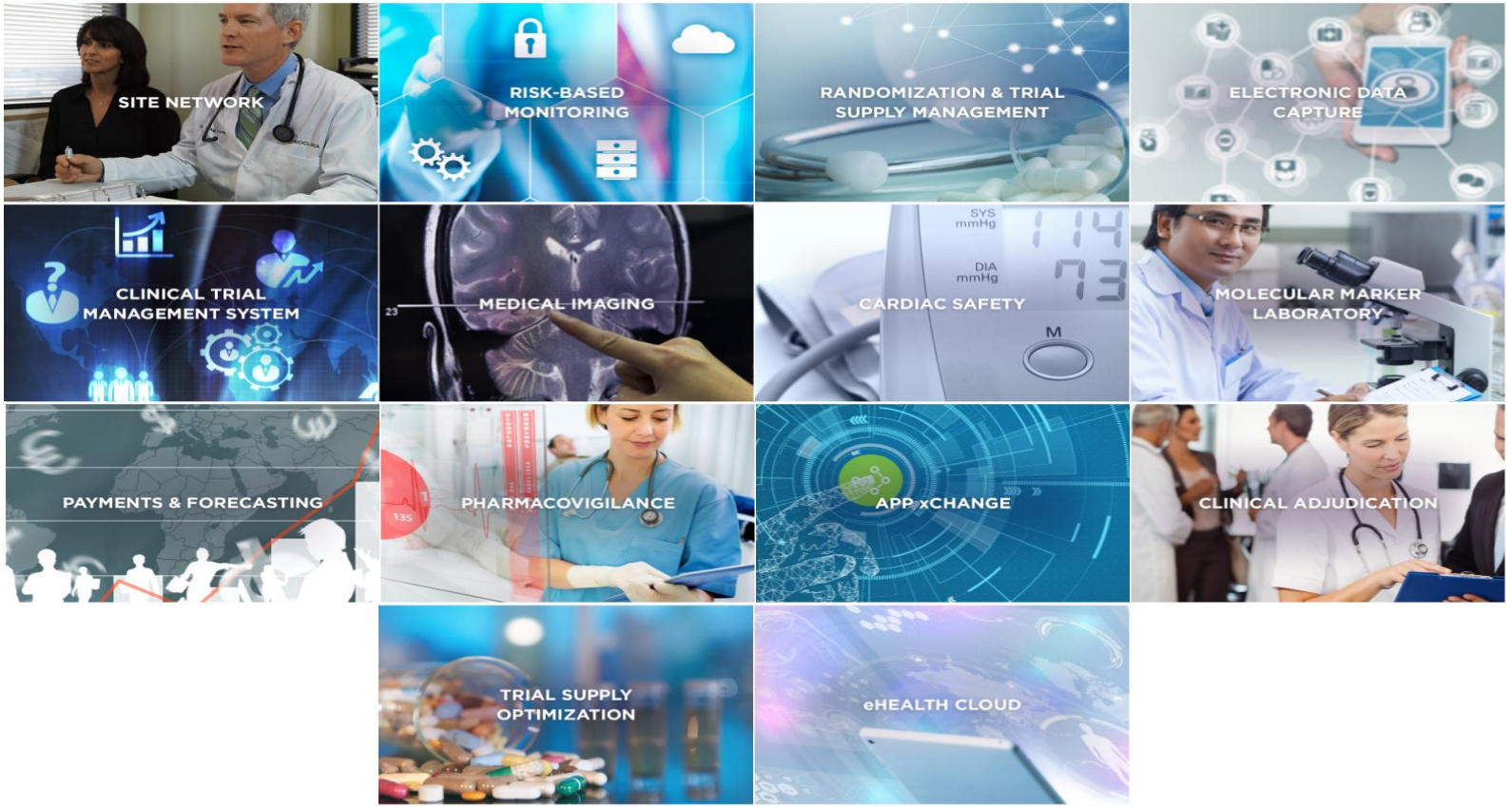
BIOCLINICA: Areas of Expertise



Disclaimer

- The views expressed herein represent those of the presenter and do not necessarily represent the views or practices of Bioclinica Inc. or the views of the general pharmaceutical industry.

Agenda

- ✓ Clinical Trial vs. Health System
- ✓ Comparative effectiveness
- ✓ What regulators think?
- ✓ The first Pragmatic Randomized Controlled Trial (pRCT)
- ✓ pRCTs target partnership-based research
- ✓ Core characteristics of pRCTs
- ✓ When should early pRCTs be considered?
- ✓ A scenario of early initiation of a pRCT
- ✓ Summary

Clinical Trials vs. Health System

Population

"If we want more evidence-based practice, we need more practice-based evidence."

Green, LW. *American Journal of Public Health*, 2006.

Clinical Trial

- ✓ Specific patient population meeting the inclusion and exclusion criteria

Health System

- ✓ Differing age groups (paediatrics, elderly)
- ✓ Race, ethnicity, gender variances
- ✓ Unstudied comorbid conditions
- ✓ Differing concomitant drugs (including OTC)
- ✓ Lifestyle variances including smoking, dietary habits
- ✓ Differences in disease severity
- ✓ Varying levels of compliance

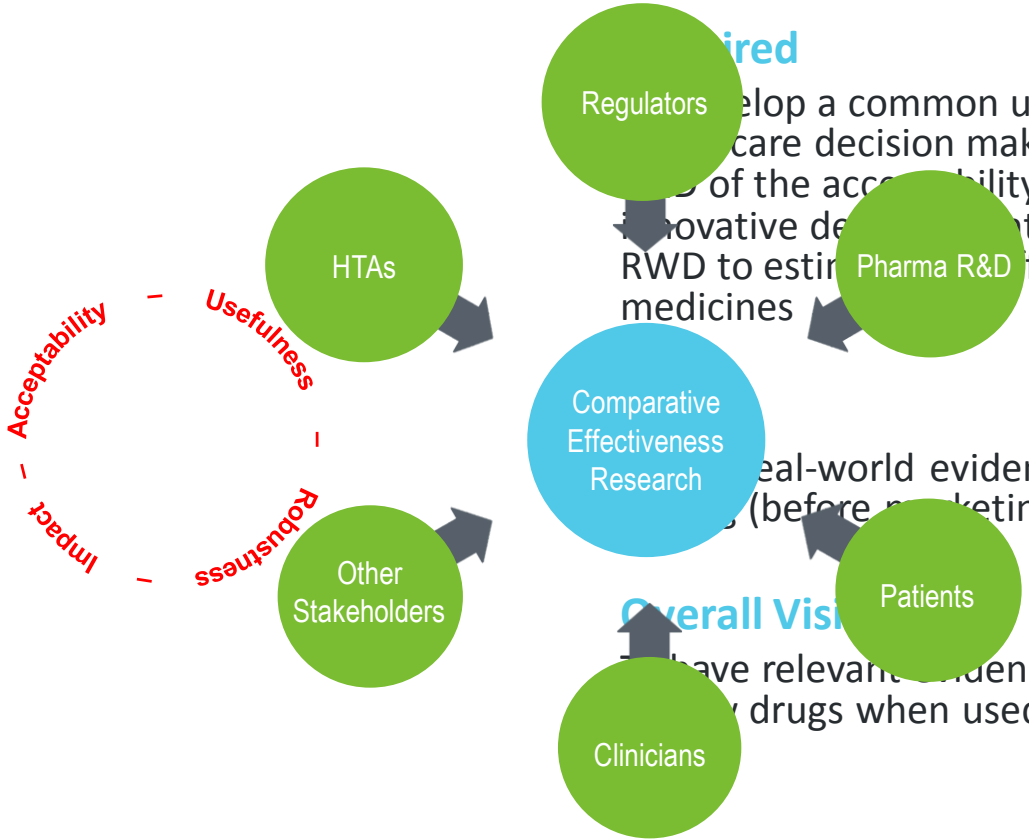
Efficacy ⟷ **EVIDENCE GAP** ⟷ Effectiveness

Clinical Trial vs. Health System

	Clinical Trial	Health System
Population		
Studies/Sources	✓ Randomized Clinical Trials	Real-World Data (RWD) ✓ Observational Studies ✓ Healthcare Databases ✓ Registries ✓ Administrative and Healthcare Claims ✓ Pragmatic Trials
Outcomes	✓ Efficacy, safety	✓ Effectiveness, patient reported outcomes (PRO), resource use

Efficacy — **EVIDENCE GAP** — Effectiveness

Comparative Effectiveness Research: It benefits all



ired

elop a common understanding amongst care decision makers and pharmaceutical of the acc bility and usefulness of ovative de t programmes which use RWD to estir fectiveness of new medicines

eal-world evidence (RWE) in an early (before keting authorisation)

erall Visi

ave relevant idence to assess effectiveness drugs when used in standard practice

What Regulators Think?

"The most useful source of knowledge will come from randomization in the context of clinical practice." – [illegible]liff, former FDA Commissioner

Pragmatic Randomized Controlled Trial (pRCT)

A study comparing several health
randomised, diverse population r
practice, and measuring a broad

To ensure generalisability, pragm
the patients to whom the treatm
possible.

For instance, inclusion criteria wo
comorbidity, concomitant medica
etc.); the follow-up would not be
interventional and allowing for tr

Pre-licence pRCT: An example

The Salford Lung Studies investigate real-world effectiveness of a novel once-daily investigational treatment (LABA/ICS in the form of a vilanterol/fluticasone furoate Dry Powder Inhaler) compared with the existing therapies for COPD and asthma.

After randomisation, both patient groups received care as usual by their own GP, community pharmacist, practice nurses, etc, in order to allow for 'usual', real-world conditions.

http://www.salfordlungstudy.co.uk/

*The results presented here are general comments on PCTs and not a reflection on any outcomes or characteristics of the Salford Lung Study

pRCTs: Partnership-based research built to improve care

- Pragmatic clinical trials are designed to **improve practice & policy**
- They take place in settings **where everyday care happens**, such as community clinics, hospitals, and health systems
- **Collaborating providers and organizations are integral partners** and gain practical evidence on how to improve patient health and satisfaction
- **Pragmatic partnerships engage at multiple levels –** including patients, practitioners, health systems and communities

Core Characteristics of Pragmatic Trials

Questions from and important to stakeholders

Diverse, representative populations

Multiple, heterogeneous settings

Multiple outcomes important to decision and policy makers

Comparison conditions are real-world alternatives, not a placebo or no treatment

When should early pRCTs be considered?

OBJECTIVE: Identify which effectiveness questions would be regarded by stakeholders as particularly suited to be addressed by early pRCTs

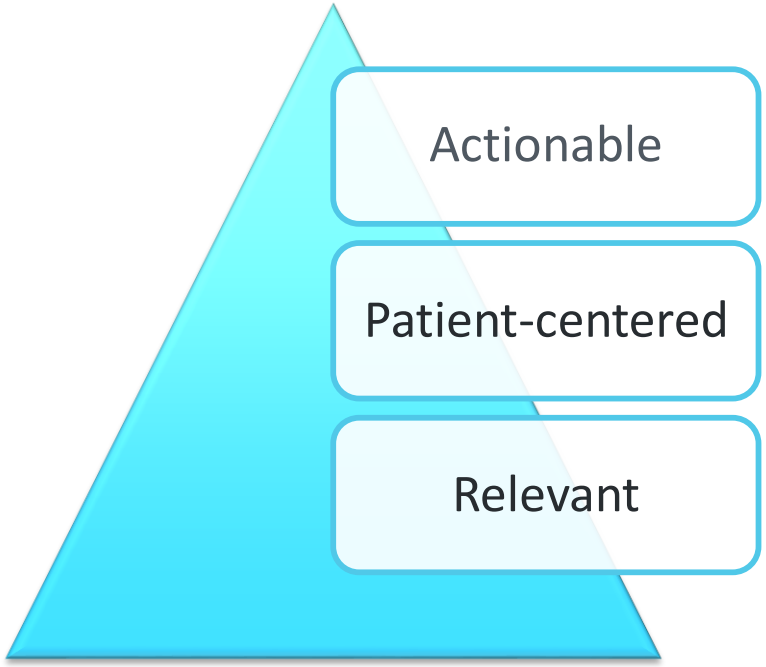
- pRCTs have a role in situations when RCTs can't answer the question of effectiveness; in particular when **efficacy is not predicted to match effectiveness**
- pRCTs could **allow enrolment of a greater number of patients** than RCTs , including those who may otherwise be excluded from conventional RCTs
- Ability to capture effectiveness of drugs when **comparators are used in a manner in the real-world that can't be replicated in RCTs**, for instance when a medicine is used off-label
- When **wide variability in usual** care makes it hard to define a single comparator
- pRCTs were generally thought of as **longer-term trials** since they can be **more adaptive**
- And...

Scenario: Exceptional efficacy in phase I/II trials

- ✓ Strict adherence to study protocol; patients assessed during trial-prescribed visits
- ✓ Homogeneous patient population
- ✓ Does not provide real-world data

- ✓ Flexible adherence to study protocol; patients assessed during routine care
- ✓ Heterogeneous patient population
- ✓ Provides real-world data

Summary



Designed around application to practice, with an emphasis on successful implementation.

Research questions and goals are strongly aligned with patient-centered research and care.

Transparent reporting of results that are focused on issues and data that are relevant for making decisions and taking action.

Thank you!