Annual Scientific Day

Pragmatic clinical trials/Études en Conditions Réelles

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Outline of the studio

- Introduction to pragmatic/real world trials
  - Their pros and cons
- Presentation of SMARTER trial:
  - Physician step prescription and monitoring to improve ARTERial health (SMARTER): A randomized controlled trial in patients with type 2 diabetes and hypertension (Dasgupta K et al, 2017, *Diabetes Obes Metab)*
- Application of **PRECIS-2** (**PR**agmatic **E**xplanatory **C**ontinuum **I**ndicator **S**ummary) tool to SMARTER trial

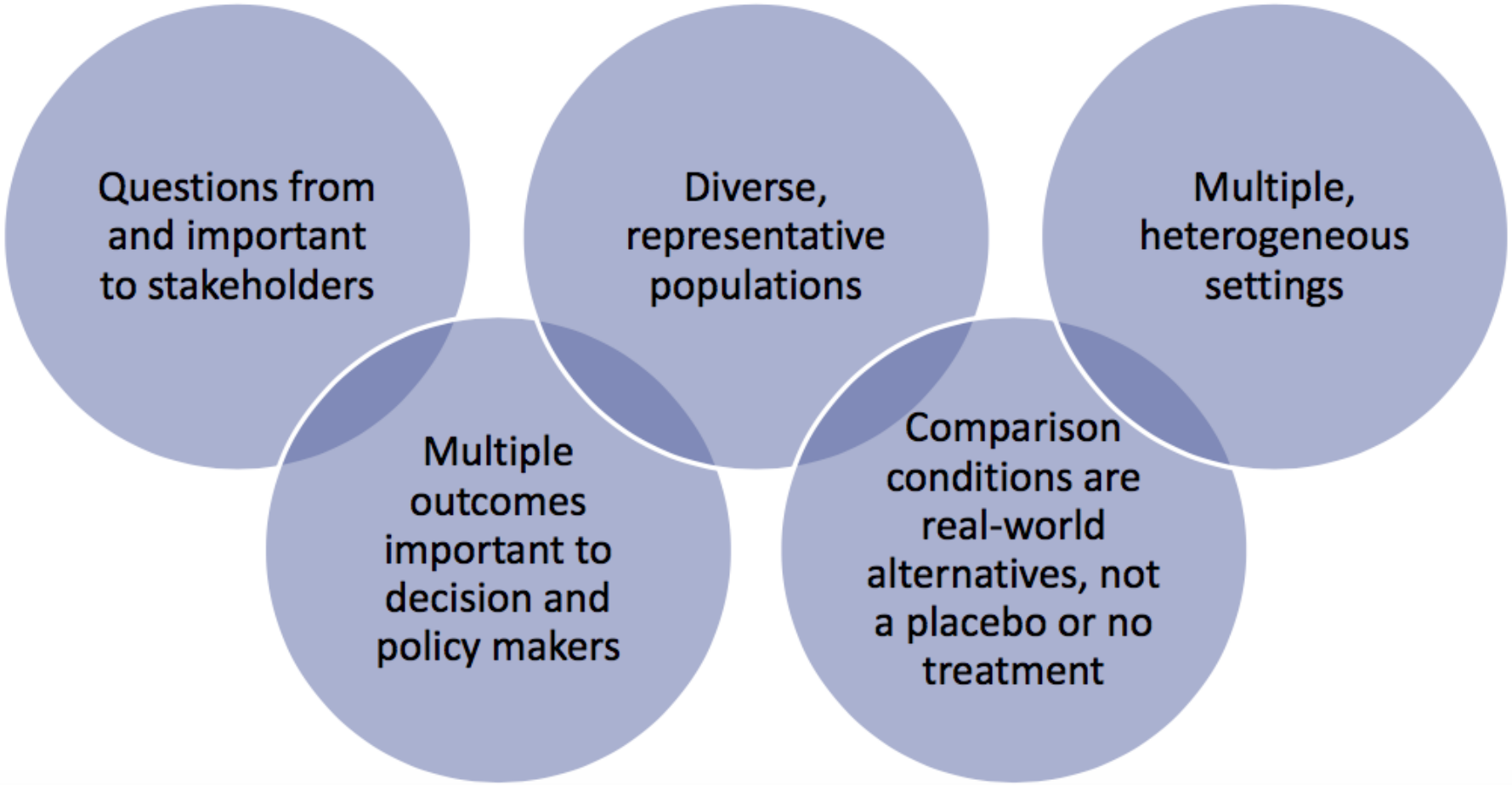
Introduction

- Traditional clinical randomized controlled trials (RCTs), which are the building blocks of evidence-based medicine and clinical practice guidelines, are:
- often expensive (150 million for large CVD trials)
- often not relevant to clinical practice
- slow in generating wide-scale change in practice (only 14% of research findings will have led to widespread changes in care .. And it takes on average 17 years to happen)

Introduction

- In the 1960s Schwarz and Llellouch proposed a distinction between explanatory trials, which confirm a physiological or clinical hypothesis, and pragmatic trials, which inform a clinical or policy decision by providing evidence for adoption of the intervention into real-world clinical practice
- Pragmatic clinical trials seek to determine the **effectiveness** of an intervention in a real-world setting to inform clinical decision making (Roland and Torgerson, 1998)
- Pragmatic trials evaluate interventions that can be **plausibly** rolled out in clinical practice and that the outcomes used to assess effectiveness are valid and easily understood by a range of users, including clinicians, patients, and decision makers

Core characteristics of pragmatic clinical trials



Key differences between traditional (RCT) and pragmatic trials (PCT)

	A traditional RCT tests a hypothesis under ideal conditions	A PCT compares treatments under everyday clinical conditions
GOALS	To determine causes and effects of treatment	To improve practice and inform clinical & policy decisions
DESIGN	Tests the intervention against placebo using rigid study protocols & minimal variation	Tests two or more real-world treatments using flexible protocols & local customization
PARTICIPANTS	Highly defined & carefully selected	More representative because eligibility criteria are less strict
MEASURES	Require data collection outside routine clinical care	Brief and designed so data can be easily collected in clinical settings
RESULTS	Rarely relevant to everyday practice	Useful in everyday practice, especially clinical decision making

DIABETES, OBESITY AND METABOLISM
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WILEY

ORIGINAL ARTICLE

Physician step prescription and monitoring to improve ARTERial health (SMARTER): A randomized controlled trial in patients with type 2 diabetes and hypertension

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Clinical Trials.gov identifier: NCT01475201

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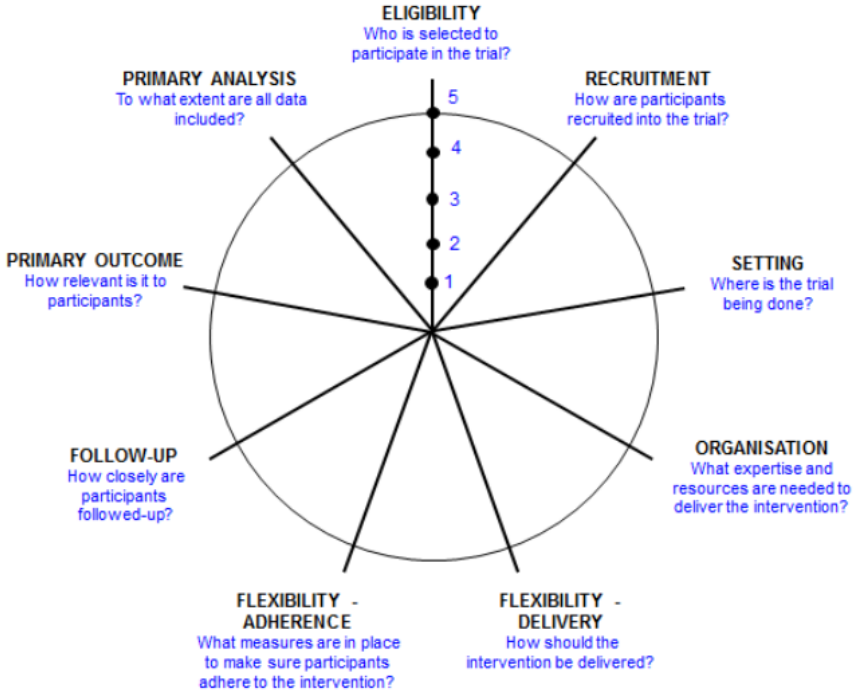
PRECIS-2 tool

- **PRECIS** – **PR**agmatic **E**xplanatory **C**ontinuum **I**ndicator **S**ummary – is a tool to assess clinical trials in terms of the pragmatic/explanatory continuum: https://www.precis-2.org



Eligibility

- **Eligibility** –to what extent are the participants in the trial similar to those who would receive this intervention if it was part of usual care?

For example, score 5 for very pragmatic criteria essentially identical to those in usual care; score 1 for a very explanatory approach with lots of exclusions (e.g. those who don't comply, respond to treatment, or are not at high risk for primary outcome, are children or elderly), or uses many selection tests not used in usual care.

- ❑ Very explanatory (1)
- ❑ Rather explanatory
- ❑ Equally pragmatic/explanatory
- ❑ Rather pragmatic
- ❑ Very pragmatic (5)

Recruitment

- **Recruitment** - how much extra effort is made to recruit participants over and above what that would be used in the usual care setting to engage with patients?

For example, score 5 for very pragmatic recruitment through usual appointments or clinic; score 1 for a very explanatory approach with targeted invitation letters, advertising in newspapers, radio plus incentives and other routes that would not be used in usual care.

- ❑ Very explanatory (1)
- ❑ Rather explanatory
- ❑ Equally pragmatic/explanatory
- ❑ Rather pragmatic
- ❑ Very pragmatic (5)

Setting

- **Setting** – how different is the setting of the trial and the usual care setting?

For example, score 5 for a very pragmatic choice using identical settings to usual care; score 1, for a very explanatory approach with only a single centre, or only specialised trial or academic centres.

- ❑ Very explanatory (1)
- ❑ Rather explanatory
- ❑ Equally pragmatic/explanatory
- ❑ Rather pragmatic
- ❑ Very pragmatic (5)

Organisation

- **Organisation** – how different are the resources, provider expertise and the organisation of care delivery in the intervention arm of the trial and those available in usual care?

For example, score 5 for a very pragmatic choice that uses identical organisation to usual care; score 1 for a very explanatory approach if the trial increases staff levels, gives additional training, require more than usual experience or certification and increase resources.

- ❑ Very explanatory (1)
- ❑ Rather explanatory
- ❑ Equally pragmatic/explanatory
- ❑ Rather pragmatic
- ❑ Very pragmatic (5)

Flexibility (delivery)

- **Flexibility (delivery)** – how different is the flexibility in how the intervention is delivered and the flexibility likely in usual care?

For example, score 5 for a very pragmatic choice with identical flexibility to usual care; score 1 for a very explanatory approach if there is a strict protocol, monitoring and measures to improve compliance, with specific advice on allowed co-interventions and complications.

- ❑ Very explanatory (1)
- ❑ Rather explanatory
- ❑ Equally pragmatic/explanatory
- ❑ Rather pragmatic
- ❑ Very pragmatic (5)

Flexibility (adherence)

- **Flexibility (adherence)** - how different is the flexibility in how participants must adhere to the intervention and the flexibility likely in usual care?

For example, score 5 for a very pragmatic choice involving no more than usual encouragement to adhere to the intervention; score 1 for a very explanatory approach that involves exclusion based on adherence, and measures to improve adherence if found wanting.

- ❑ Very explanatory (1)
- ❑ Rather explanatory
- ❑ Equally pragmatic/explanatory
- ❑ Rather pragmatic
- ❑ Very pragmatic (5)

Follow-up

- **Follow-up** - how different is the intensity of measurement and follow-up of participants in the trial and the likely follow-up in usual care?

For example, score 5 for a very pragmatic approach with no more than usual follow up; score 1 for a very explanatory approach with more frequent, longer visits, unscheduled visits triggered by primary outcome event or intervening event, and more extensive data collection.

- ❑ Very explanatory (1)
- ❑ Rather explanatory
- ❑ Equally pragmatic/explanatory
- ❑ Rather pragmatic
- ❑ Very pragmatic (5)

Primary outcome

- **Primary outcome** – to what extent is the trial's primary outcome relevant to participants?

For example, score 5 for a very pragmatic choice where the outcome is of obvious importance to participants; score 1 for a very explanatory approach using a surrogate, physiological outcome, central adjudication or use assessment expertise that is not available in usual care, or the outcome is measured at an earlier time than in usual care.

- ❑ Very explanatory (1)
- ❑ Rather explanatory
- ❑ Equally pragmatic/explanatory
- ❑ Rather pragmatic
- ❑ Very pragmatic (5)

Primary analysis

- **Primary analysis** – to what extent are all data included in the analysis of the primary outcome?

For example, score 5 for a very pragmatic approach using intention to treat with all available data; score 1 for a very explanatory analysis that excludes ineligible post-randomisation participants, includes only completers or those following the treatment protocol.

- ❑ Very explanatory (1)
- ❑ Rather explanatory
- ❑ Equally pragmatic/explanatory
- ❑ Rather pragmatic
- ❑ Very pragmatic (5)

PRECIS-2 wheel for SMARTER