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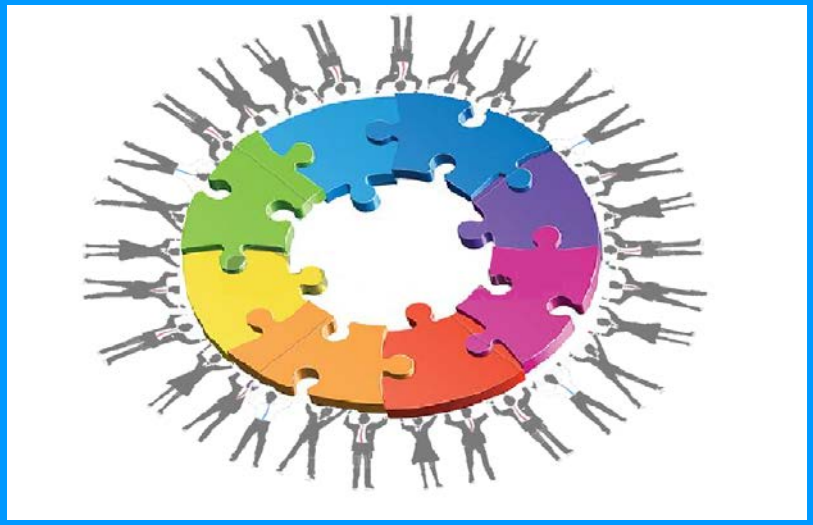
‘Trials within Cohorts’ (TwiCs) Symposium



10-11th November 2014

Manson Lecture Theatre

London School of Hygiene & Tropical Medicine

Supported by Yorkshire & Humber & North Thames CLAHRCs

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What are TwiCs?

Clare Relton

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Outline

- Problems with standard designs
- Rethinking…..
- The ‘cmRCT’ design
- Key features

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Standard pragmatic trials

- Problems
  - poor recruitment rates
  - unrepresentative recruited population
  - lack of long term outcomes
  - patient & clinician treatment experiences altered
  - informed consent barrier to recruitment

…. poor generalisability

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Rethinking….

- Origins
  - Our experiences
  - Increased efficiency
  - Increased generalisability
  - Ethical approach
  - Zelen (Single Randomised Consent Design)

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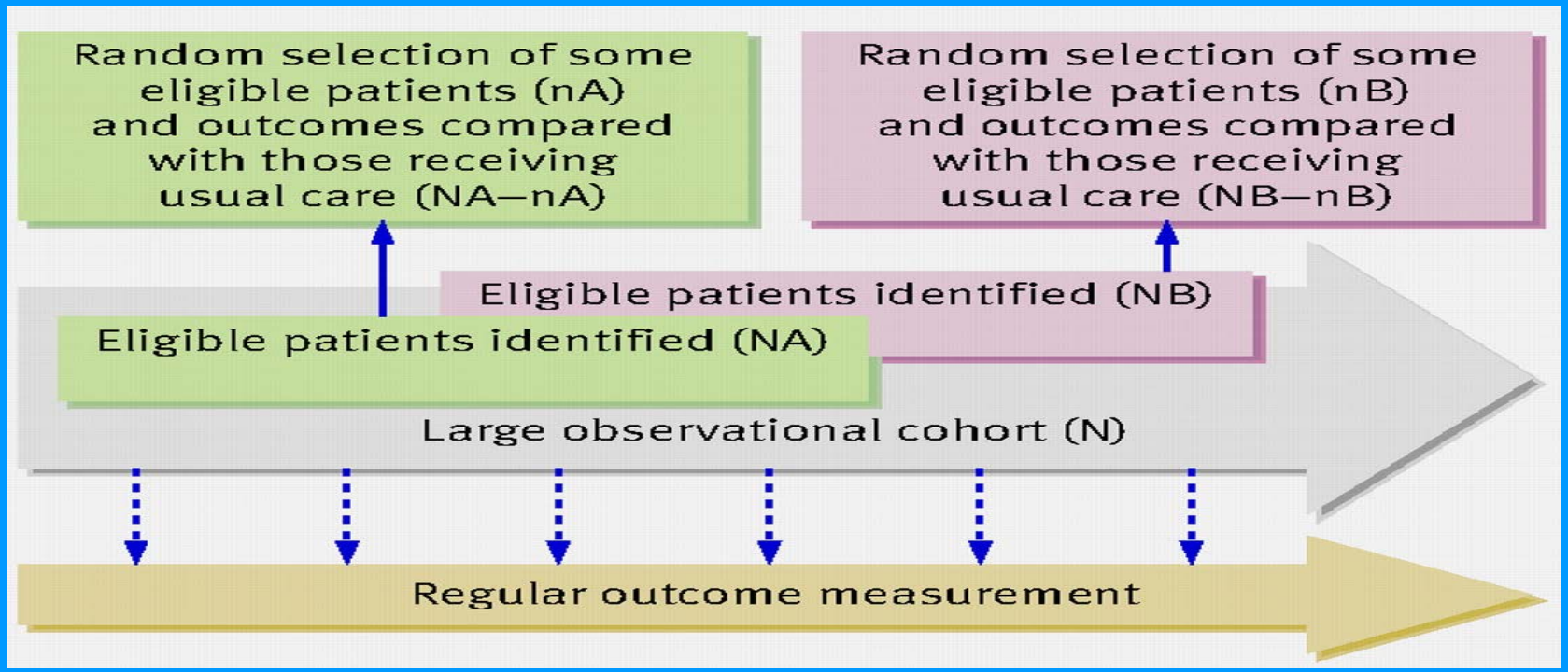
‘Cohort multiple RCT’ design



Relton, Torgerson, O’Cathain & Nicholl. BMJ 2010;340:c1066

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❖ Cohort

- ❖Recruit observational cohort of patients
- ❖Regular outcome measurement for whole cohort
- ❖Facility for multiple trials
- ❖Time and cost efficiencies
  - ❖unequal randomisation

- New or ready made?
- Narrow (disease specific) vs broad (population based)

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❖ For each RCT

- ❖Eligible patients identified, from which some are randomly selected to be offered the intervention
- ❖Outcomes of randomly selected patients compared to not randomly selected.

Randomisation

- Random allocation ‘done’ to all?
- Random selection of some?

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❖ ‘Patient centred’ Informed consent (IC)

- ❖ IC relevant to ‘patient’ identity & experience
- ❖ Imagine….
- ❖ Patients are not told
  - ❖ about treatments that they are not then offered
  - ❖ that their treatment will be chosen ‘at random’

- ❖ People enter trials primarily to obtain direct or indirect benefit
- ❖ Effective communication – intelligible & relevant

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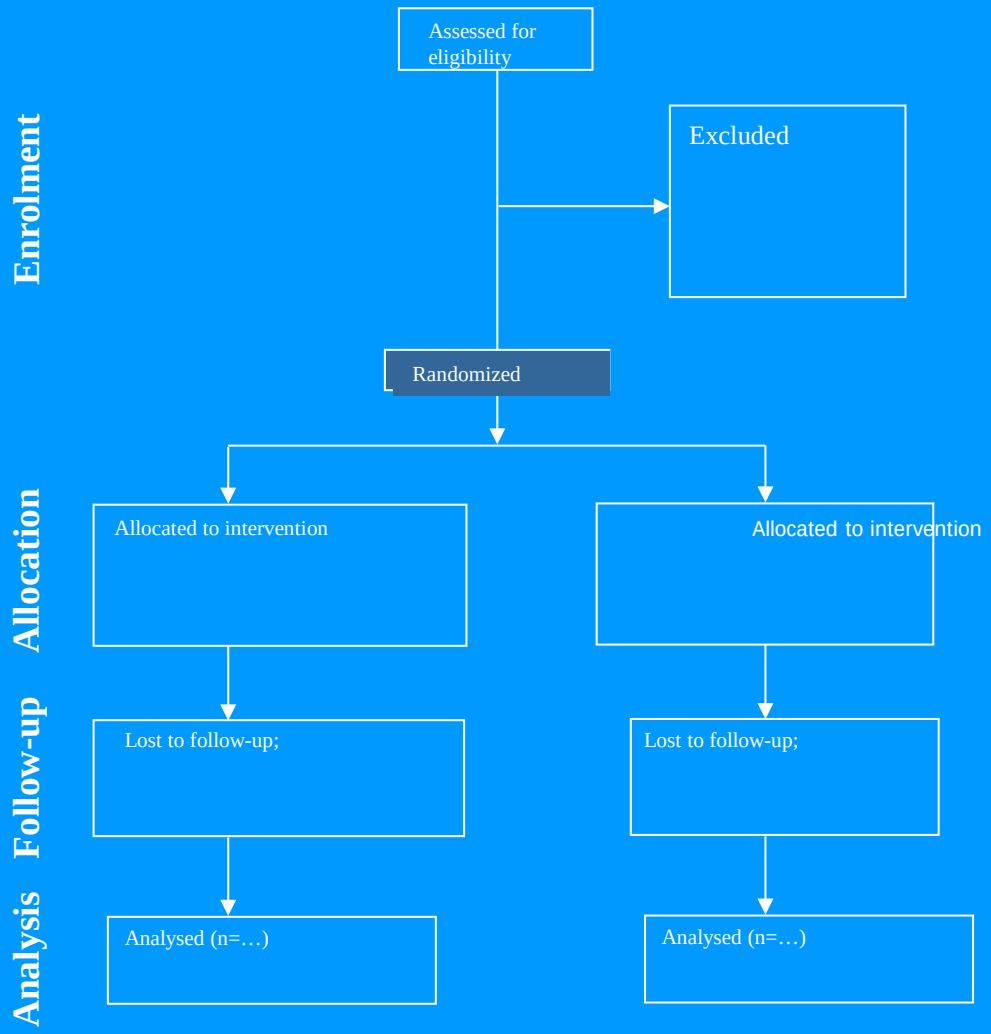
RQ: Does chocolate improve memory & concentration?



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Information

'we don't know which treatment is best'

'will you take part in research?'

'you will be given x or nothing'

'this will be decided by chance'

Information

'You have (not) been selected to try X'

People/patients approached

Assessed for eligibility

Excluded

Enrolment

Randomized

Allocation

Allocated to intervention

Allocated to intervention

Follow-up

Lost to follow-up;

Lost to follow-up;

Analysis

Analysed (n=…)

Analysed (n=…)

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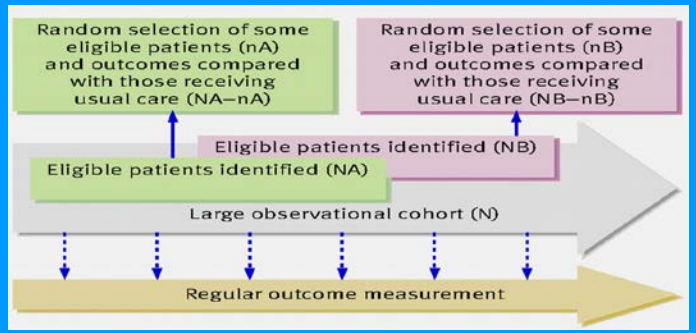
‘cmRCT’ design

❖ Key features

- ❖ Cohort - multiple trials facility
- ❖ Random selection of some
- ❖ Px relevant information and consent



• Benefits

- Recruitment: improved quantity and representativeness
- Long term outcomes as standard
- Ongoing information on natural history of the condition and TAU
- Increased comparability between each trial conducted within the cohort
- Increased efficiency (time and cost), particularly for expensive or high risk interventions

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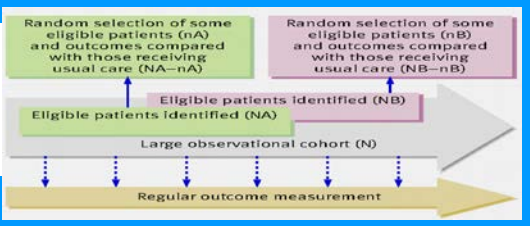
We thought that

Most suited to……

- Open trials with 'treatment as usual' as comparator
- RQs with easily measured & collected outcomes
- Conditions where many clinical trials will be conducted
- Chronic conditions
- Highly desired treatments or expensive treatments

Least suited to……..

- Closed trial designs with masking or placebo arms
- RQs with hard to measure and hard to collect outcomes
- Acute or short term conditions



What are TwiCs?

Approach to pragmatic RCT (BMJ 2010) which rethinks:

- The nature of trial infrastructures
- How trial populations are identified
- The concept of randomisation
- The timing and content of the information provided to 'trial' populations

In an attempt to create a system for producing efficient, effective and ethical pragmatic trials (to provide robust information to aid routine healthcare decision making).

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- Key publications


Contents lists available at SciVerse ScienceDirect

Contemporary Clinical Trials

journal homepage: www.elsevier.com/locate/conclintrial

A pilot 'cohort multiple randomised controlled trial' of treatment by a homeopath for women with menopausal hot flushes

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RESEARCH METHODS & REPORTING

Rethinking pragmatic randomised controlled trials: introducing the "cohort multiple randomised controlled trial" design

Clare Relton,[1,3] David Torgerson,[2] Alicia O'Cathain,[1] Jon Nicholl[1]

- Meetings (University of Sheffield workshop 2012, Prostate Cancer RCT Consensus Group 2013, Utrecht Medical Centre symposium 2013)

- Used and adapted in UK, Canada, Netherlands

- Renamed - TwiCs

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What's next?