Trials within Cohorts

4 examples from UK research of the innovative 'cohort multiple RCT' design

Clare Relton & Ellie Holding: Yorkshire Health Study

ScHARR at the University of Sheffield

Peter Bower: CLASSIC.

NIHR School for Primary Care Research, University of Manchester

Sally Barber : Born in Bradford

Bradford Teaching Hospitals NHS Foundation Trust

Lesley Brown: CARE 75+

Bradford Teaching Hospitals NHS Foundation Trust

Why we started

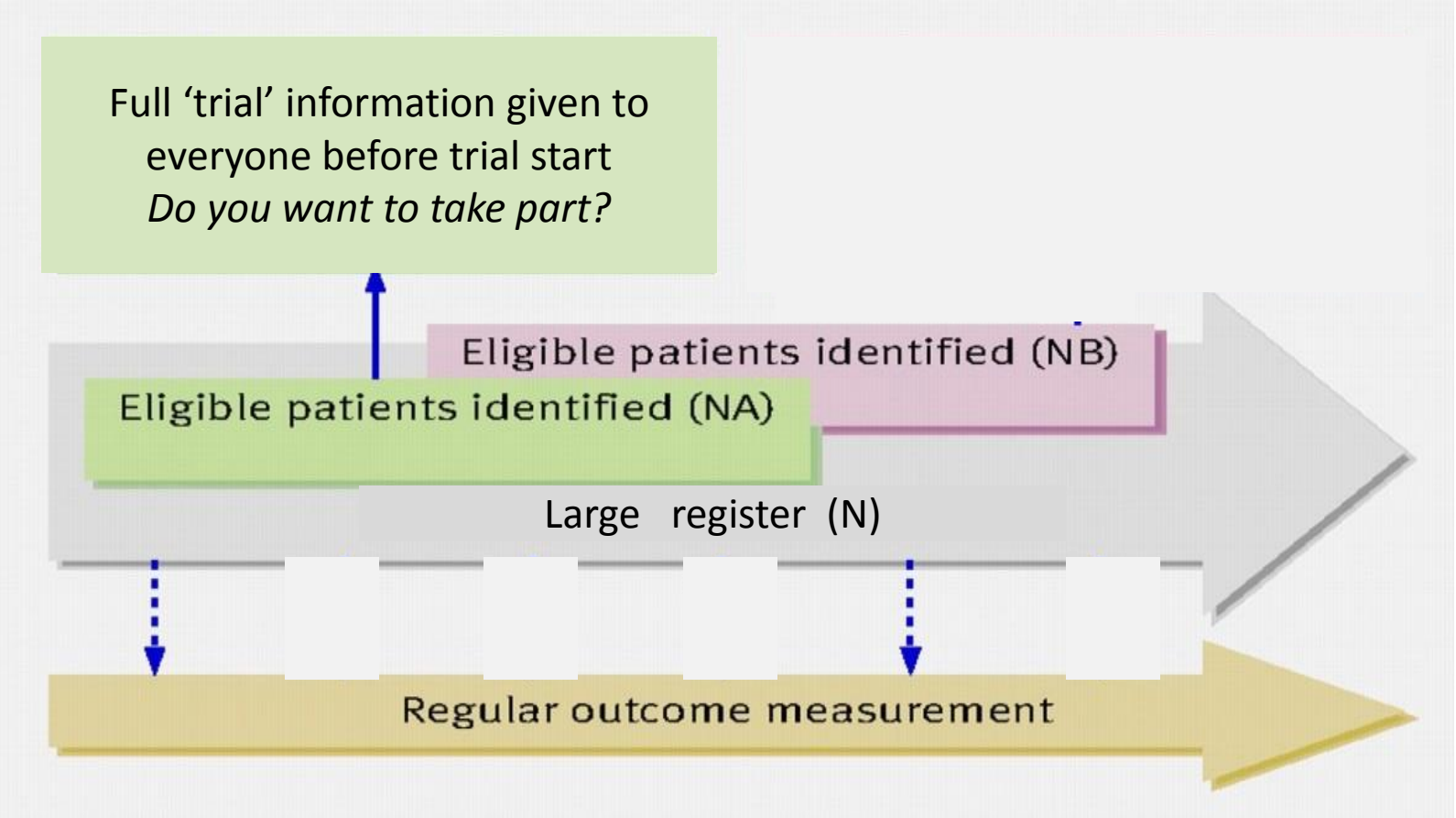
- Pragmatic randomised controlled trials (RCTs)
  - Compare the ‘trial’ intervention to usual care
  - Help inform routine practice
  - Recruit one ‘population’ per trial – disbanded at trial end
  - ‘Full’ information to all participants
- Shortcomings
  - Recruitment
  - Ethics
  - Patient preferences
  - Treatment comparisons

Alternative approach

- **Trials within Cohorts (TwiCs)**
  - embed one or more randomised controlled trials (RCTs) within a cohort or register
  - http://www.twics.global/

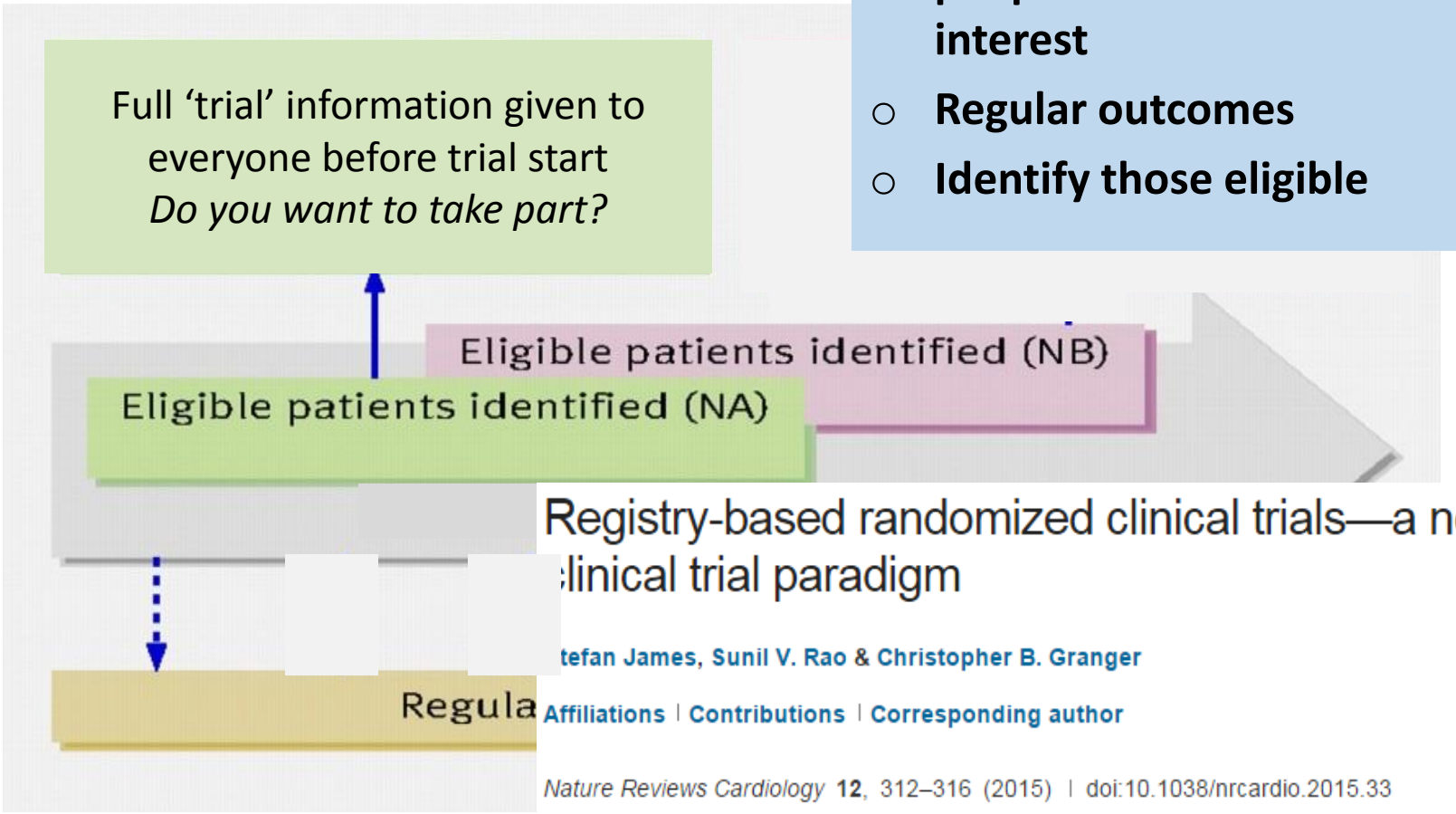
- Different TwiCs design approaches
  - Randomised *registry* RCT design
  - *cohort* multiple RCT design

Randomised registry trials



Randomised registry trials

- **Large register/ cohort of people with condition of interest**
- **Regular outcomes**
- **Identify those eligible**



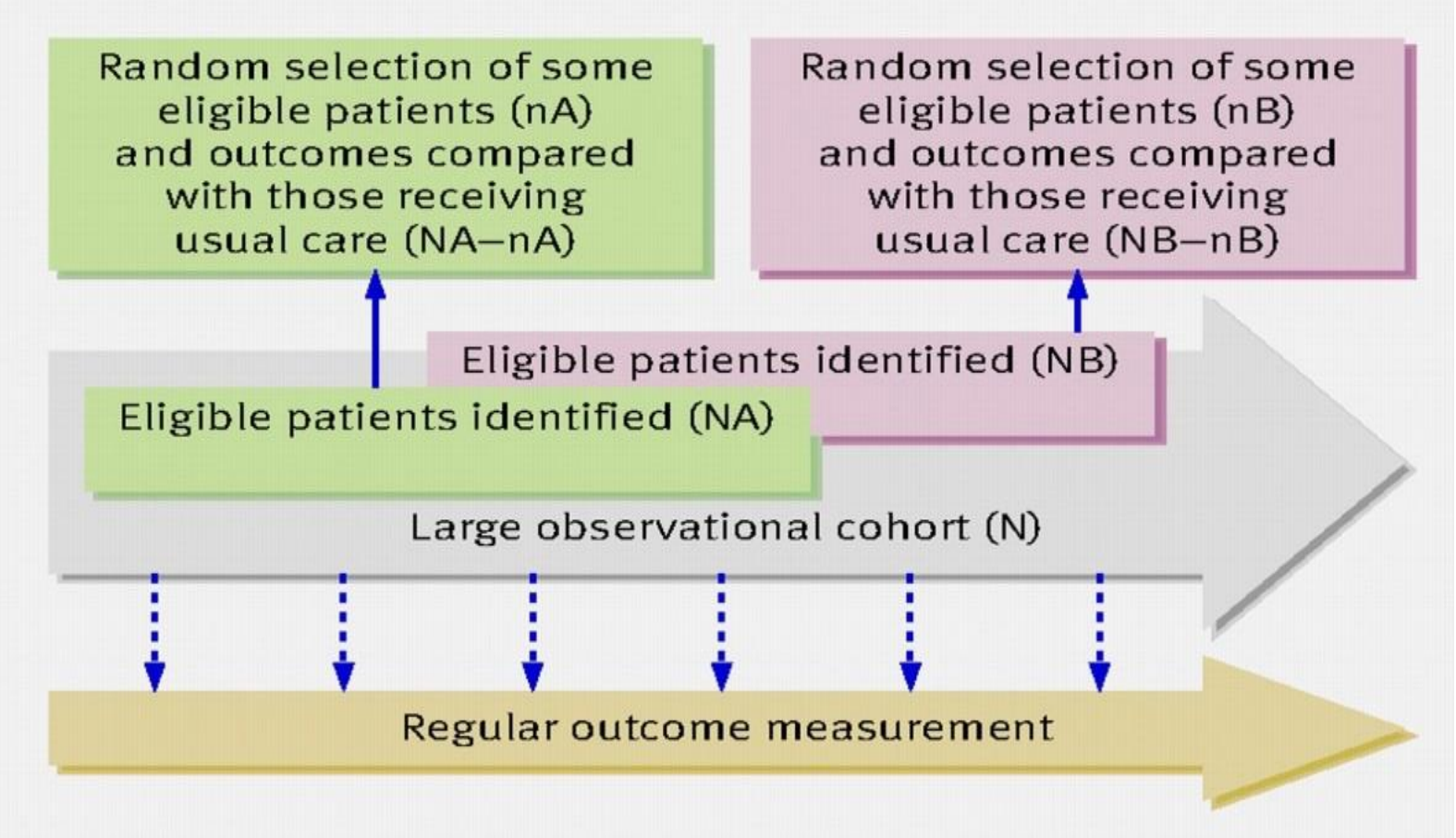
Registry-based randomized clinical trials—a new
linical trial paradigm

tefan James, Sunil V. Rao & Christopher B. Granger

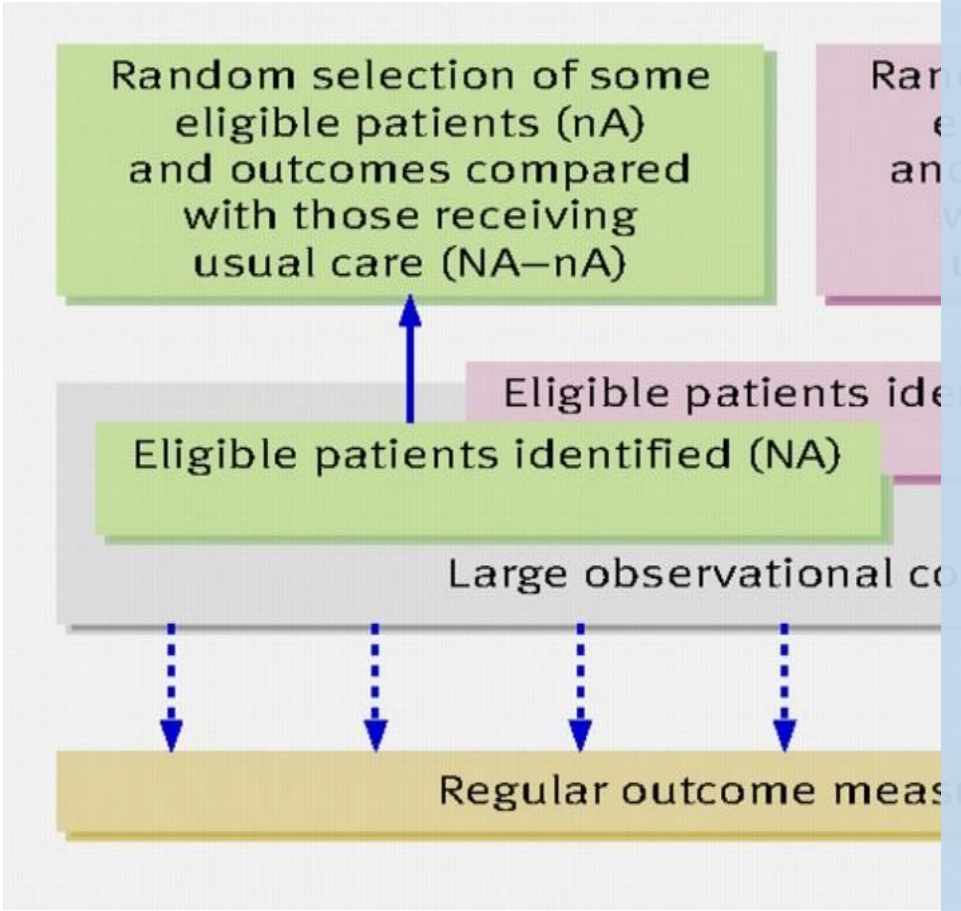
Affiliations | Contributions | Corresponding author

Nature Reviews Cardiology **12**, 312–316 (2015) | doi:10.1038/nrcardio.2015.33
Published online 17 March 2015

‘Cohort multiple RCT’ (cmRCT)



‘Cohort multiple RCT’ (cmRCT)



- **Large observational cohort of people with condition of interest**
- **Regular outcomes**
- **Capacity for multiple trials**
- **For each trial**
  - **Identify those eligible**
  - **Random selection for trial intervention**
  - **Comparison of outcomes with those eligible but not randomly selected**
  - **Patient centred informed consent**

4 UK examples of the ‘cohort multiple RCT’ design

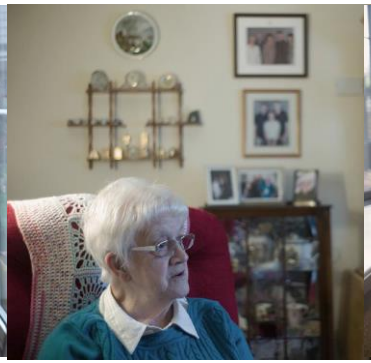
1. Community Ageing Research 75+ (CARE)
2. Yorkshire Health Study (YHS)
3. Comprehensive Longitudinal Assessment of Salford Integrated Care (CLASSIC)
4. Born in Bradford Better Start (BIBBS)

Bradford Teaching Hospitals NHS
NHS Foundation Trust

UNIVERSITY OF LEEDS

1. The Community Ageing Research 75+ (CARE 75+) study

≥ 75 years, community dwelling older people with well characterised frailty recruited from GP practices across Bradford and Leeds

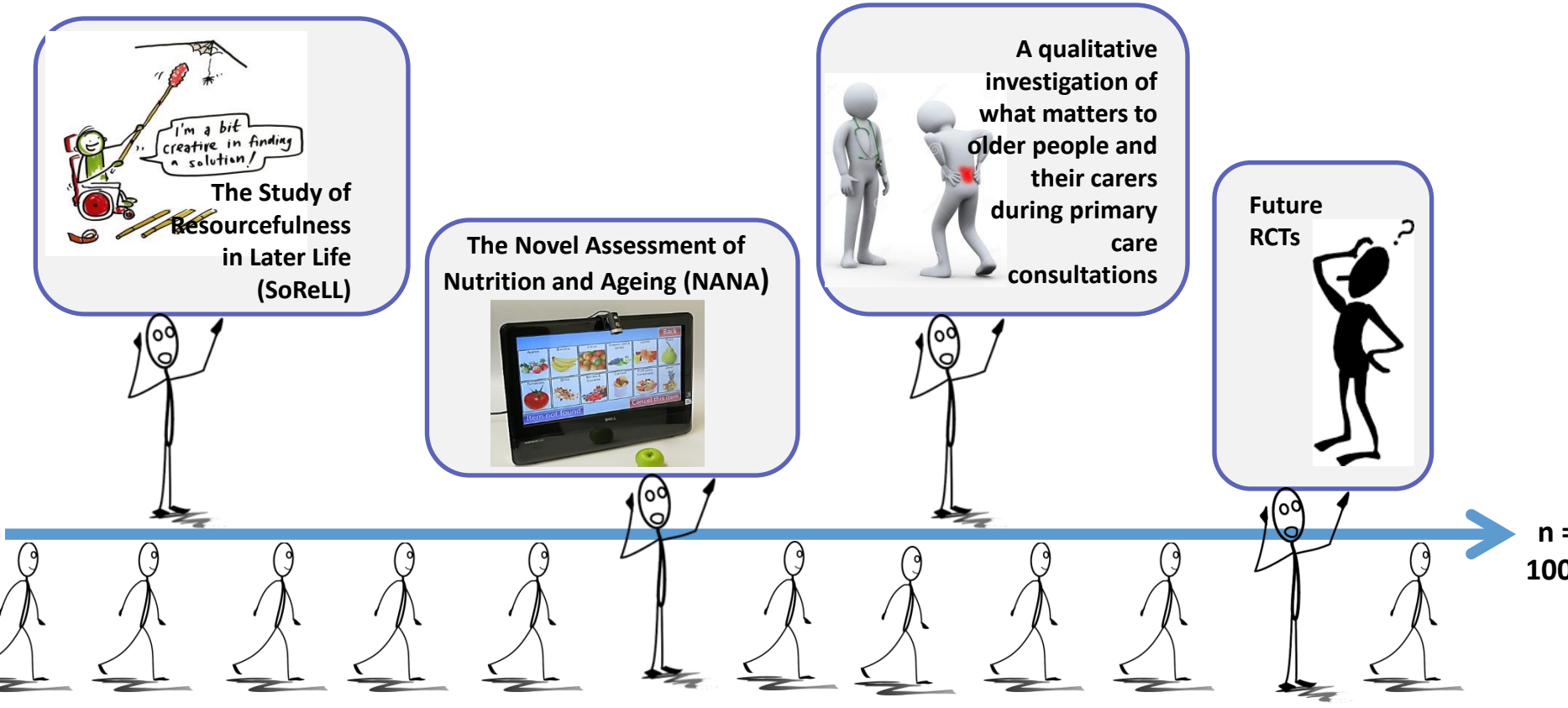



The research was funded by the CLAHRC Yorkshire and Humber. The views expressed are the views of the authors and not necessarily those of the NHS, the NIHR or the Department of Health

CLAHRC Yorkshire and Humber

Funded & supported by NIHR

CARE 75+ supporting sub-studies



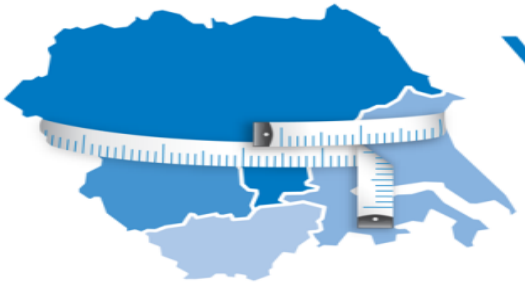
CARE 75+ cohort

Advantages and challenges of the cmRCT with an older population

- Participants gained confidence in research process being part of CARE75+.
- Detailed profile of participants in the cohort
- Researchers specifically target recruitment of those with specific characteristics, for example those with frailty.
- Extensive range of assessments at multiple time-points in the cohort, to accommodate future studies.
- Some participants expressed confusion re their involvement (CARE 75+ and/or sub-studies).

- PI - Dr Andrew Clegg: Andrew.Clegg@bthft.nhs.uk
- CARE75+ manager: Anne.Heaven@bthft.nhs.uk
- CLAHRC frailty theme manager: lesley.Brown@bthft.nhs.uk

2.



Yorkshire Health Study

Your health, your research

- Why we started
  - To address the needs outlined in the Foresight, 'Healthy Weight, Healthy Lives' report
  - Obesity - Risk factor - Long term conditions
  - Observe trends over time
  - Facilitate evaluation of interventions
  - Funded by NIHR CLAHRC for South Yorkshire & CLAHRC Yorkshire & Humber

Yorkshire Health Study

Your health, your research

- What we did
  - Regional long term observational population based study of adults (16-85yrs)
  - 2 stage recruitment via 43 GPs, 155,000 questionnaires sent
  - Self reported information
    - Personal characteristics (age, gender, ethnicity, height, weight, waist size, education, occupation, postcode)
    - Health (status, life satisfaction, long term conditions)
    - Health related behaviours (tobacco, alcohol, (un)healthy foods, exercise)
    - Health care resource usage
  - Consent to follow up (contact, data linkage) and 'tailored disclosure' for controls in TAU trials

Yorkshire Health Study

Your health, your research

- Currently have
  - 2 waves of data collection from a well phenotyped cohort
  - A regional recruitment platform providing quick and efficient identification and recruitment to studies
    - 2 RCTs (with TAU as comparators) (one using the 'cohort multiple RCT' design)
    - 1 data linkage study (Bowel Cancer Screening Programme)
    - 11 observational studies (surveys/ interviews/ case control)
    - 11+ secondary data analyses

3. CLASSIC

- Why we started
  - Planned to use a cohort to assess effects of ‘large scale integrated car’ programme
  - Provided opportunity for embedded study of a component of the programme (telephone health coaching)
  - Design assessed the ‘population health’ benefits of an intervention, not a selected subsample
  - Interested to explore the innovation!

CLASSIC

- What we did
  - Recruited a large (n=4377) cohort of older people
  - Selected a sample within the cohort meeting criteria for telephone health coaching
    - Multiple long-term conditions
    - ‘Patient activation’ level 2 or 3
  - Offered a randomly selected subsample the coaching, on the basis of eligibility NOT perceived need or enthusiasm

CLASSIC

- Currently in follow up

- Positives
  - Innovative
  - Patient centred recruitment
  - Assess value of intervention in eligible population

- Negatives
  - Research logistics
  - Relatively low uptake of intervention
  - Complexities over power and analysis

3. Born in Bradford Better Start (BiBBs)

Big Lottery: £49 million over 10 years

Bradford Trident: Community led partnership

Pregnant mums, and 0-3 years

- Bowling and Barkerend, Bradford Moor, Little Horton

Evidenced based interventions for key outcomes:

- Nutrition & obesity, language & communication, socio-emotional well-being

What we are doing

LOTTERY FUNDED

Better Start BRADFORD
INVESTING IN THE FUTURES OF OUR CHILDREN

BORN IN BRADFORD'S BETTER START

BORNINBRADFORD

How we are doing it

BIBBS cohort

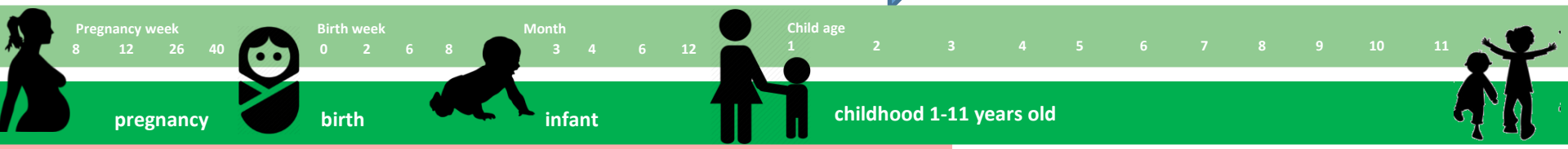
- Fidelity and implementation
- Effectiveness evaluation

Outcome data (routinely collected)

Consent and pregnancy baseline data

Participation data

Better Start Bradford Interventions



Women/Children in BSB area but not in cohort

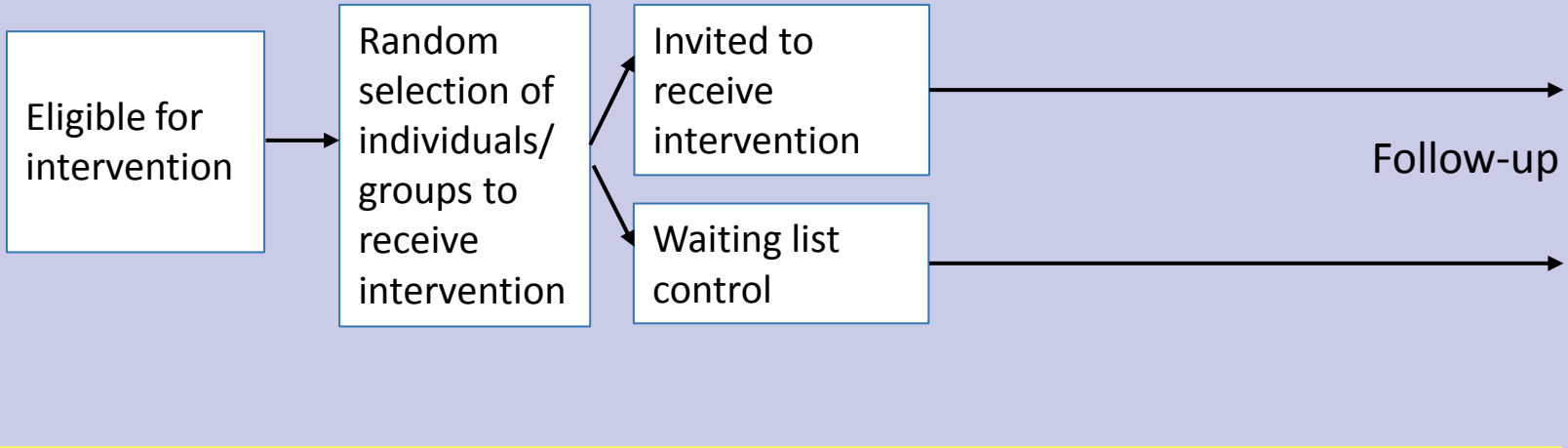
- Fidelity and implementation

How we are doing it

Trials within Cohorts (TwiCs)

BIBBS cohort

- Randomised controlled trial



Progress to date: Study designs for TWICs currently being worked up

>300 women have been recruited into BIBBS cohort

5 BSB are being delivered and evaluated

What did we learn?

Advantages

- Well characterised profile of participants
- Easy identification and targeting of those with specific characteristics
- Participants gained confidence in research process by being part of cohorts.
- Simple conversations (with no ethical challenges) when offering the intervention being trialled

Challenges

- Research logistics & long term funding
- Participants sometimes confused re their involvement
- Complexities over power and analysis

Future research

- Is the 'tailored' disclosure of information ethical?
- How best to address the analysis issues?
- Is it more efficient than the standard approach to trial design?
- If yes, how/ where should they be used and funded?

Trials within Cohorts

Thank you to all the funders of all studies including the Big Lottery, NIHR HTA programme, NIHR CLAHRC South Yorkshire and NIHR CLAHRC Yorkshire & Humber

Views and opinions are those of the authors and do not necessarily reflect those of the NHS, NIHR, NETSCC, HS&DR or DoH

For more information see www.twics.global