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Trials using cohorts: guidance on design, analysis and reporting with real-world examples

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Trials using cohorts: guidance on design, analysis and reporting with real-world examples

- Introduction to Trials within Cohorts
- Hospital based Trials within Cohorts
- Analysis of Trials within Cohorts
- Ethics of Trials within Cohorts

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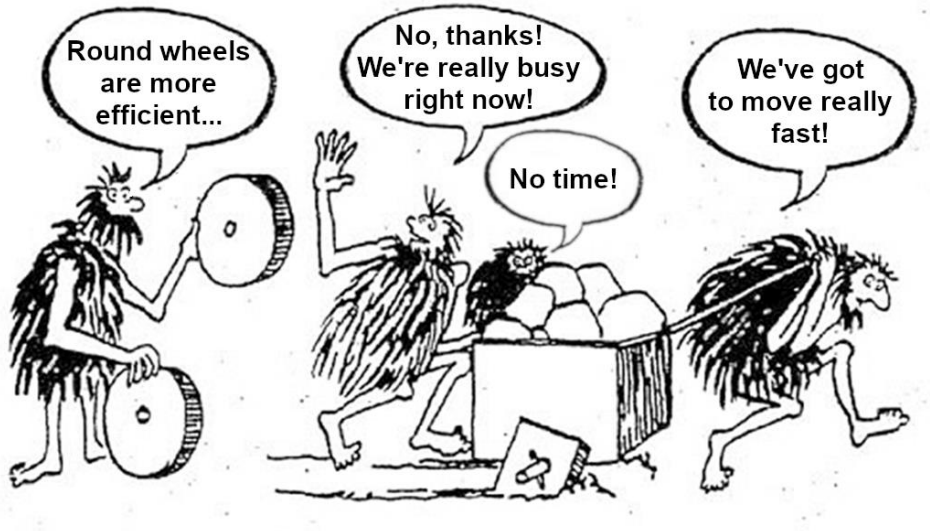
Inefficiency

- There is a lot of it.
- Inefficiency wastes participant goodwill and time, resources
- Practical and ethical issue



Research Methods & Reporting

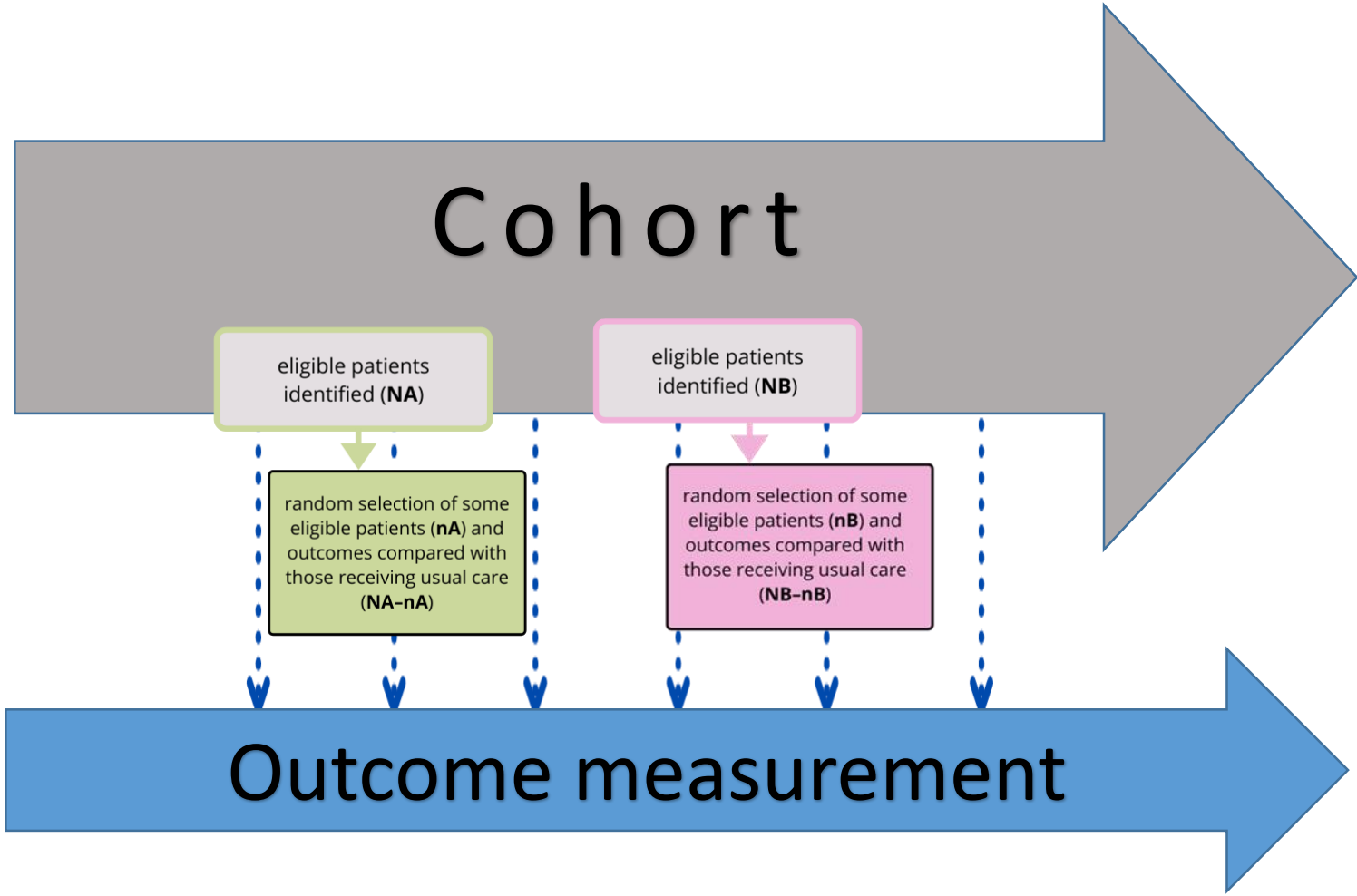
Rethinking pragmatic randomised controlled trials: introducing the "cohort multiple randomised controlled trial" design

BMJ 2010 ; 340 doi: https://doi.org/10.1136/bmj.c1066 (Published 19 March 2010)
Cite this as: *BMJ* 2010;340:c1066

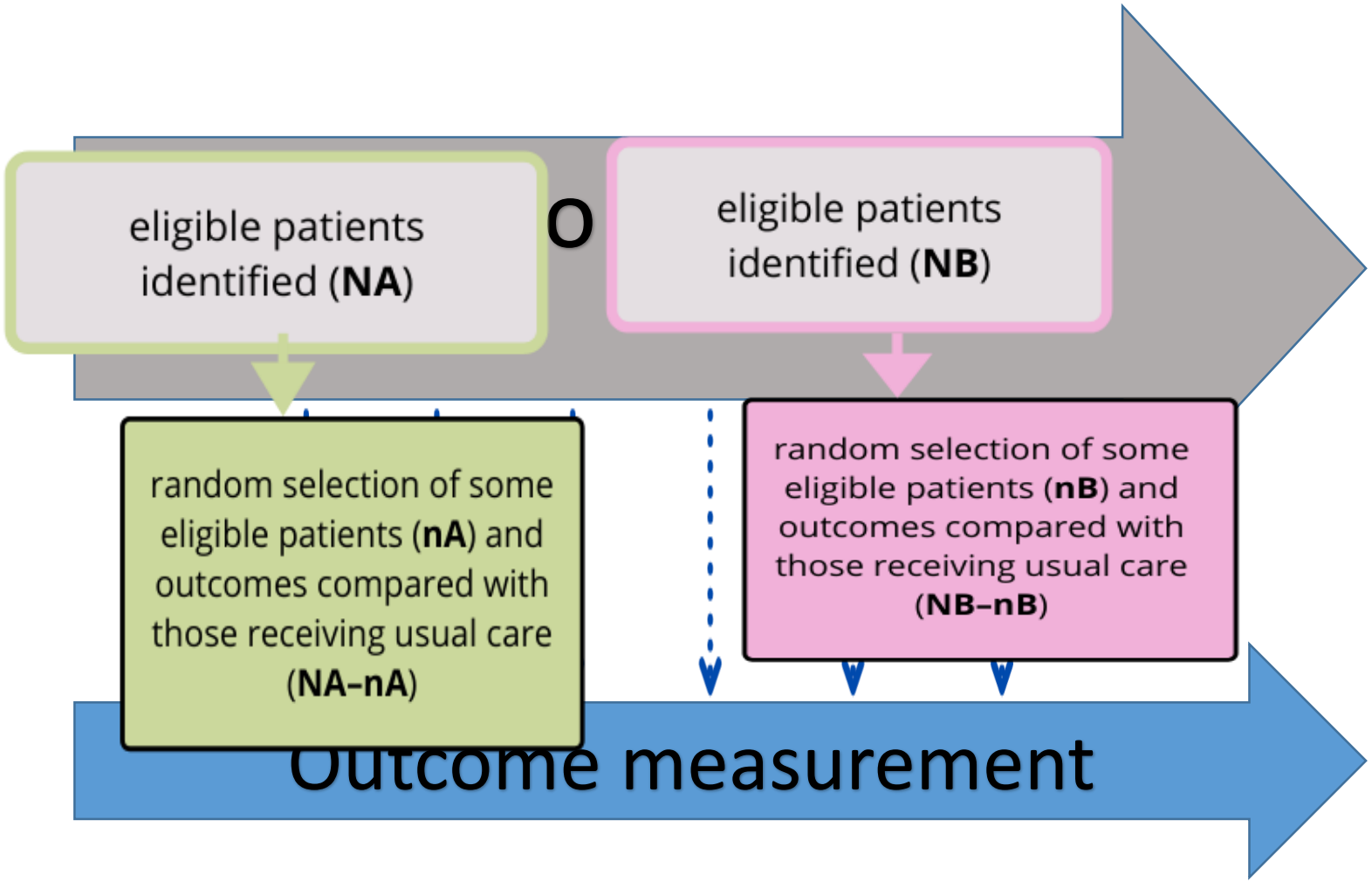
Clare Relton, research fellow [1] [3], *David Torgerson, director of clinical trials unit* [2],
Alicia O'Cathain, professor of health services research [1], *Jon Nicholl, director of the Medical Care Research Unit* [1]

Key features

- Large observational cohort of people with condition of interest
- Regular measurement of 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

We're doing research, testing txs..

Can we use your data for research?

Can we contact you for research purposes e.g. if you are randomly selected?

Do you agree to not be contacted if you are not selected?

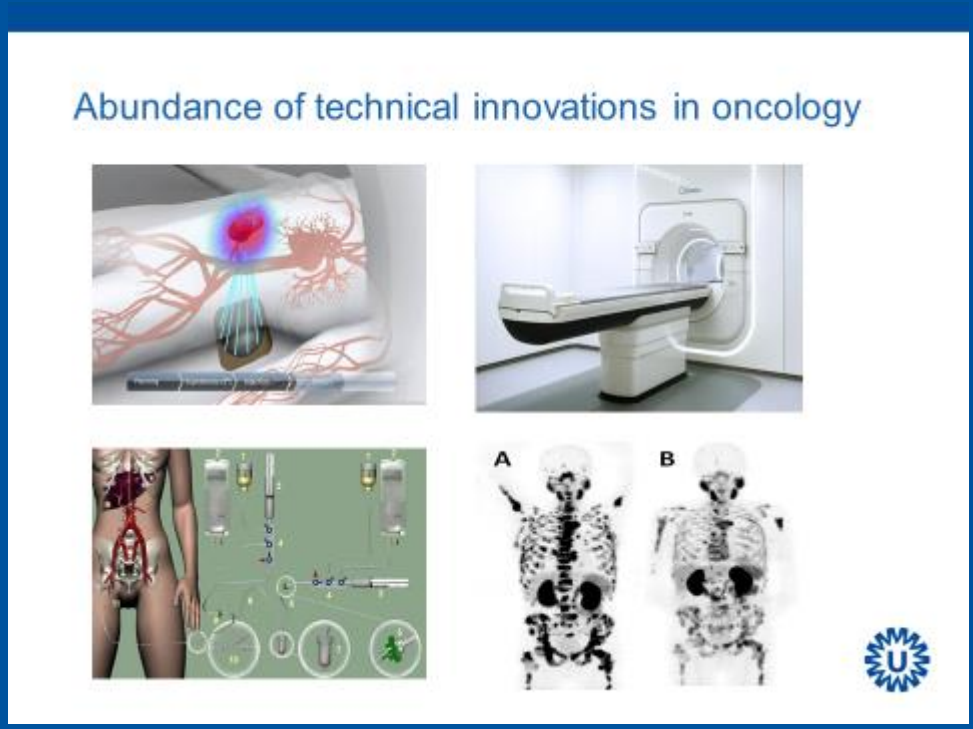
You <u>have been</u> randomly selected

Would you like this?

Broad consent

Specific consent

UMC Utrecht



Helena M Verkooijen
Professor of Evaluation of Image-Guided Interventions
UMC Utrecht, the Netherlands

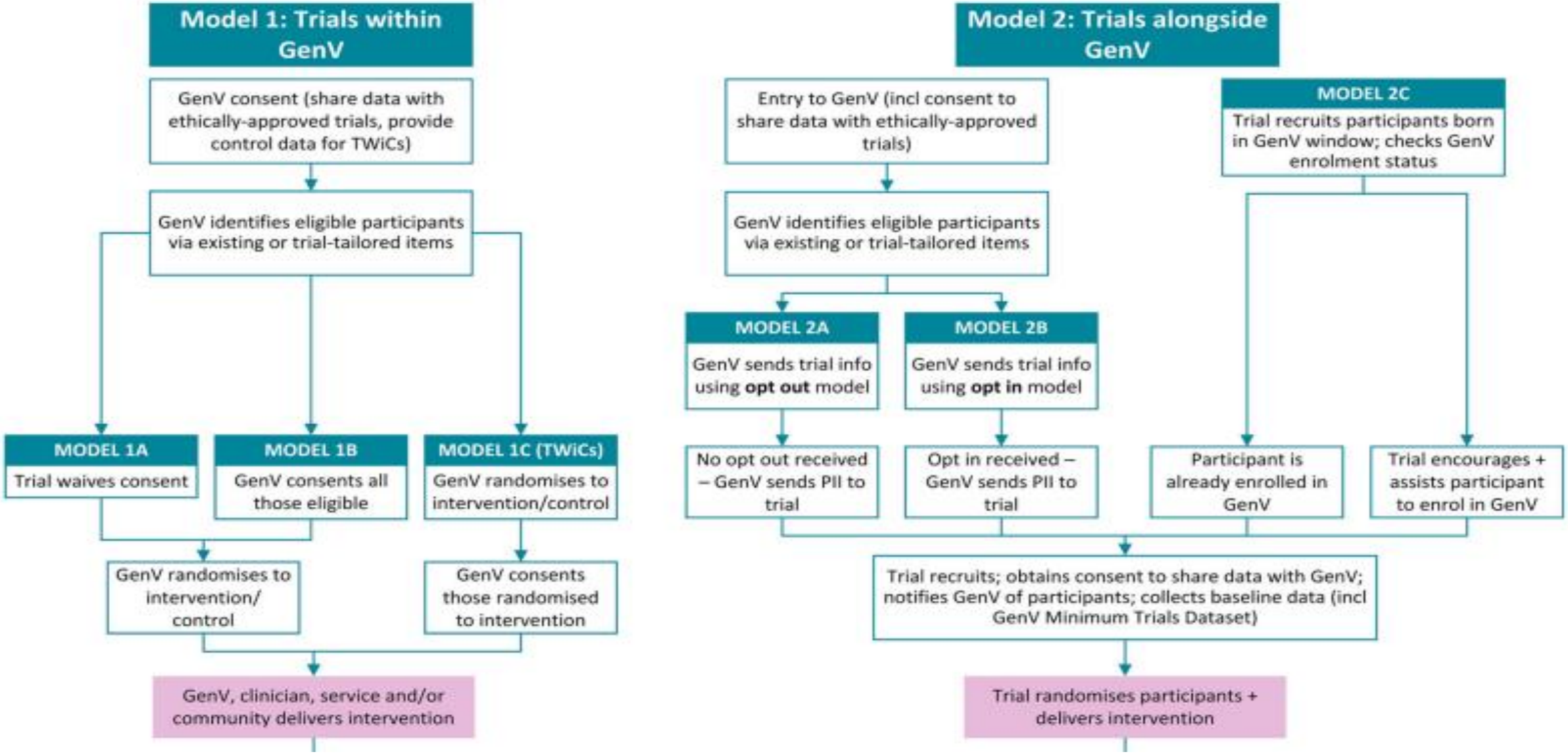
COVIDENCE UK

YOUR DATA, FIGHTING CORONAVIRUS

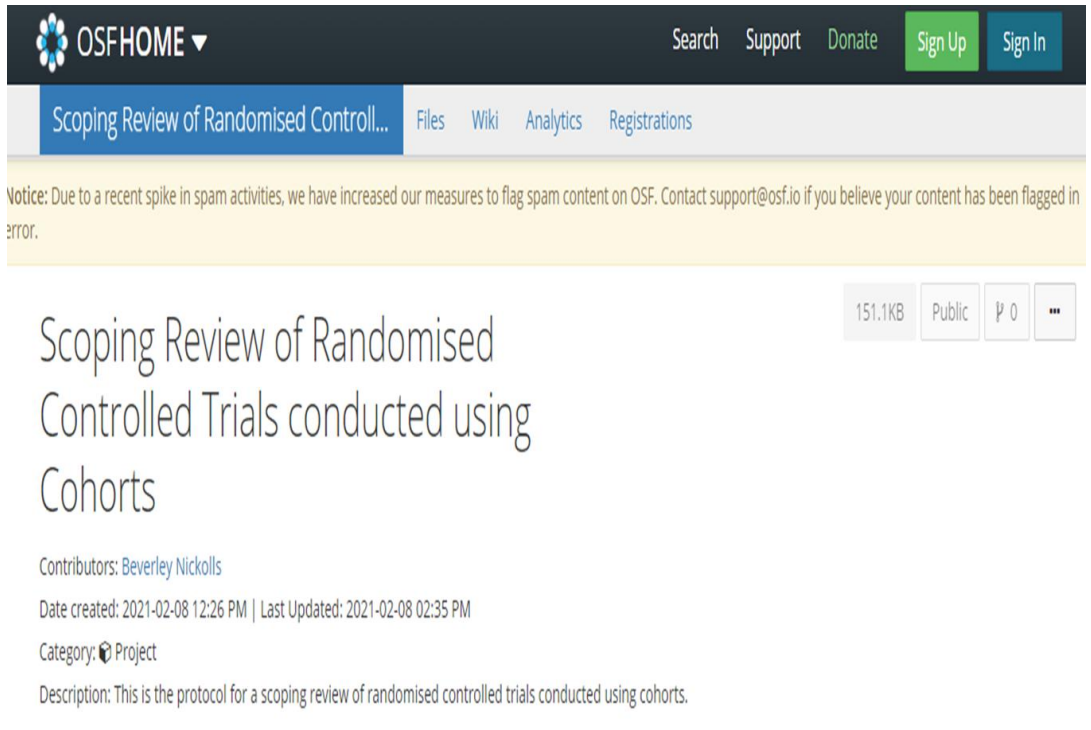
About the COVIDENCE UK Study

The COVIDENCE UK Research Study has been developed in response to the outbreak of coronavirus disease (COVID-19).

Generation Victoria (GenV)



Wake et al. BMC Medical Research Methodology (2020) 20:238



BMC Public Health

BioMed Centr

Study protocol

Open Acce

Treatment of pregnancy-related pelvic girdle and/or low back pain after delivery design of a randomized clinical trial within a comprehensive prognostic cohort study [ISRCTN08477490]

Caroline HG Bastiaenen*[1], Rob A de Bie[1], Pieter MJC Wolters[4], Johan WS Vlaeyen[3], Janneke M Bastiaanssen[1], Aldegonda BA Klabbers[1], Annie Heuts[5], Piet A van den Brandt[1] and Gerard GM Essed[2]

Address: [1]Department of Epidemiology, Maastricht University, P.O.Box 616,6200 MD Maastricht, The Netherlands, [2]Department of Obstetrics and Gynaecology, University Hospital Maastricht, Maastricht, The Netherlands, [3]Department of Medical, Clinical and Experimental Psychology, Maastricht University, The Netherlands, [4]Department of Physiotherapy, Hogeschool Zuyd, Heerlen, The Netherlands and [5]Midwifery practice, Meerssen, The Netherlands

CONSORT
TRANSPARENT REPORTING of TRIALS

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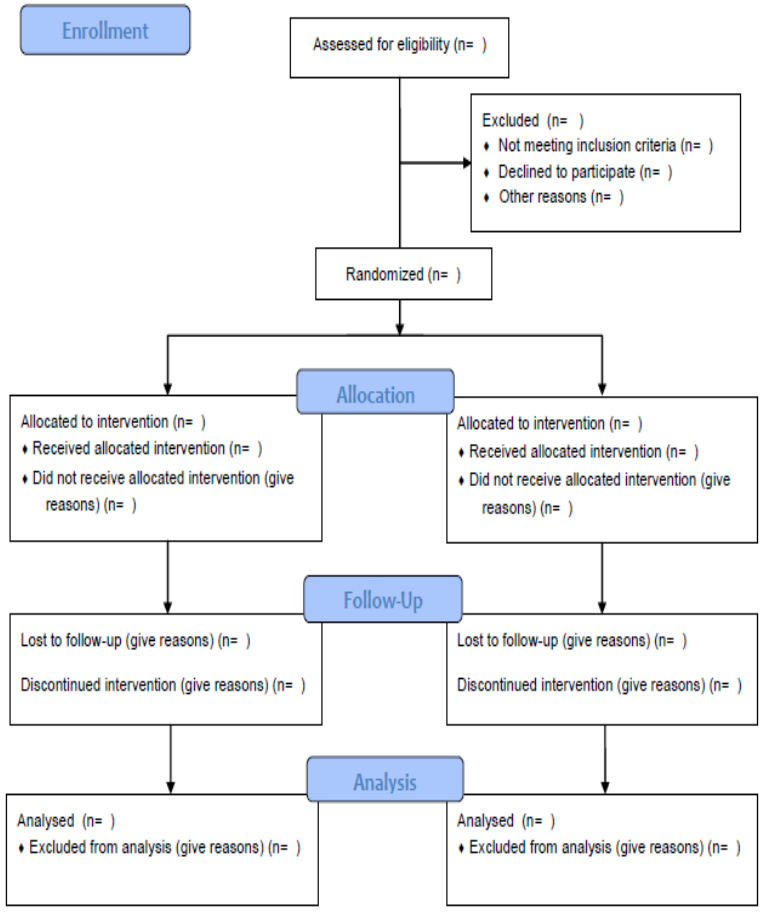
CONSORT 2010 Flow Diagram



Where do participants come from?

How is information collected?

How do we report these trials/ studies?

Research Methods & Reporting

CONSORT extension for the reporting of randomised controlled trials conducted using cohorts and routinely collected data (CONSORT-ROUTINE): checklist with explanation and elaboration

BMJ 2021 ; 373 doi: https://doi.org/10.1136/bmj.n857 (Published 29 April 2021)
Cite this as: *BMJ* 2021;373:n857

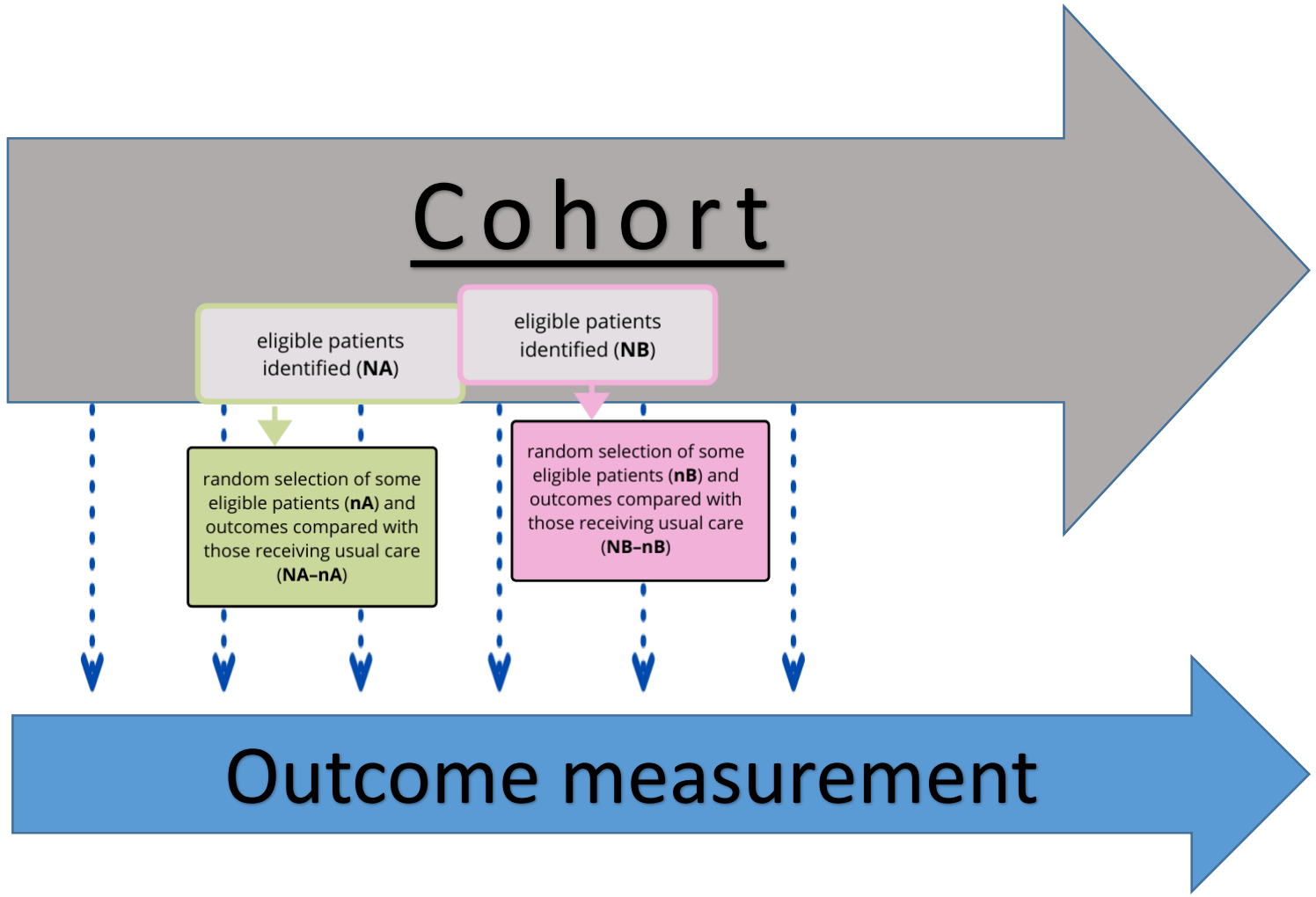
Linda Kwakkenbos, lecturer [1], Mahrukh Imran, research coordinator [2], Stephen J McCall, assistant professor [3] [4], Kimberly A McCord, doctoral student [5], Ole Fröbert, professor [6], Lars G Hemkens, senior scientist [5] [7] [8], Merrick Zwarenstein, professor [9] [10], Clare Relton, senior lecturer [11], Danielle B Rice, doctoral student [2] [12], Sinéad M Langan, professor [13], Eric I Benchimol, professor [10] [14] [15], Lehana Thabane, professor [16], Marion K Campbell, professor [17], Margaret Sampson, manager of library services [18], David Erlinge, professor [19], Helena M Verkooijen, professor [20] [21], David Moher, senior scientist [22], Isabelle Boutron, professor [23] [24], Philippe Ravaud, professor [23] [24], Jon Nicholl, professor [25], Rudolf Uher, professor [26], Maureen Sauvé, vice president for advocacy and public relations [27] [28], John Fletcher, associate editor [29], David Torgerson, professor [30], Chris Gale, reader [31], Edmund Juszczak, professor [3] [32], Brett D Thombs, professor [2] [33]

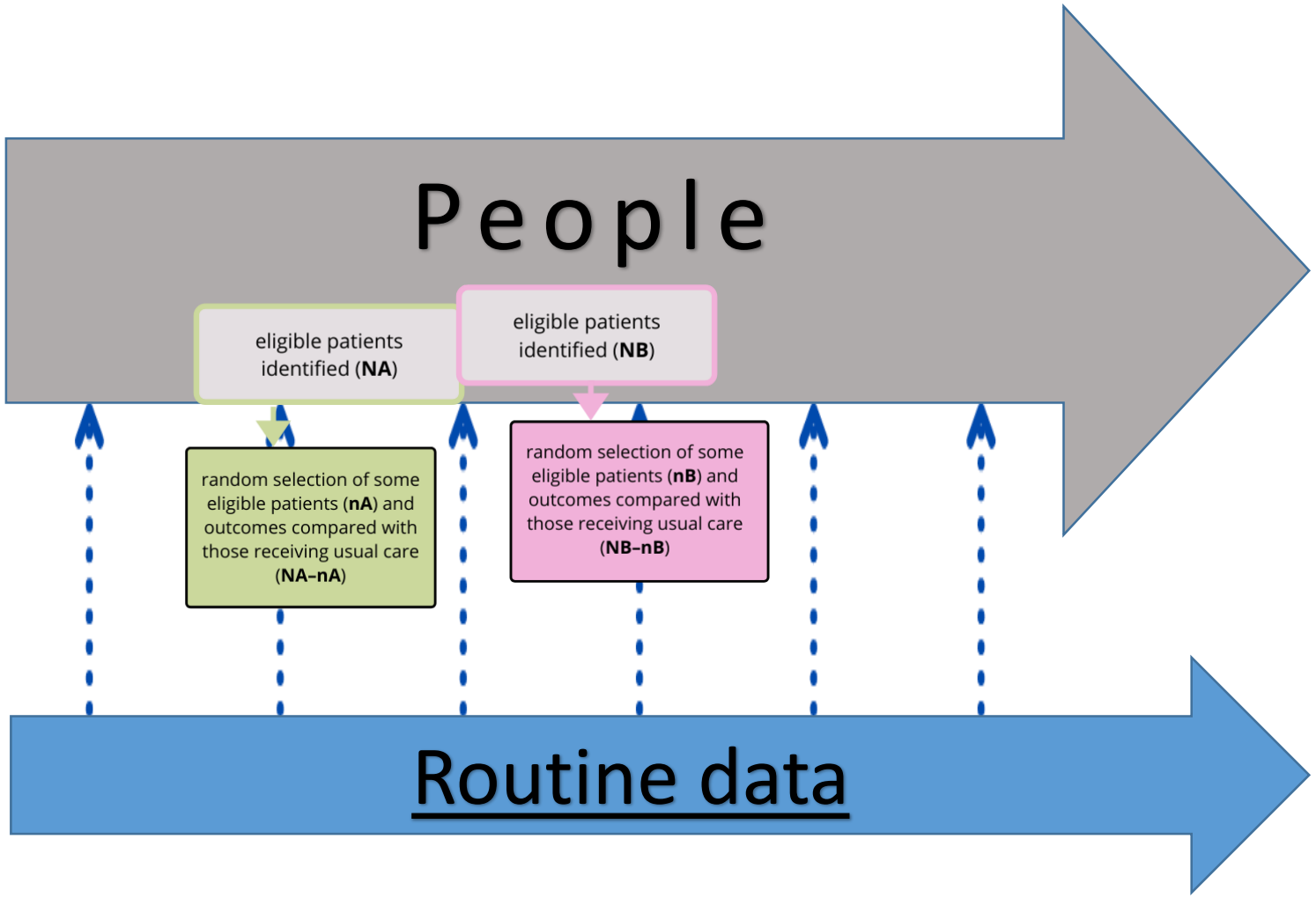
CONSORT-ROUTINE

Cohort – a group of individuals collected for the purpose of conducting research

Routine data - collected for purposes other than research or without specific *a priori* research questions developed

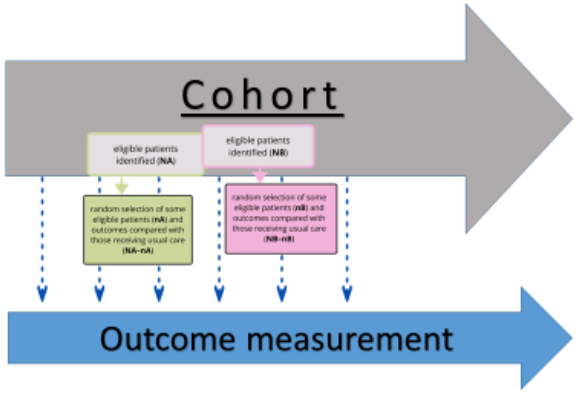
- Electronic Health Record
- Registry
- Administrative Database e.g. government, private health insurance database, or a social care or education database

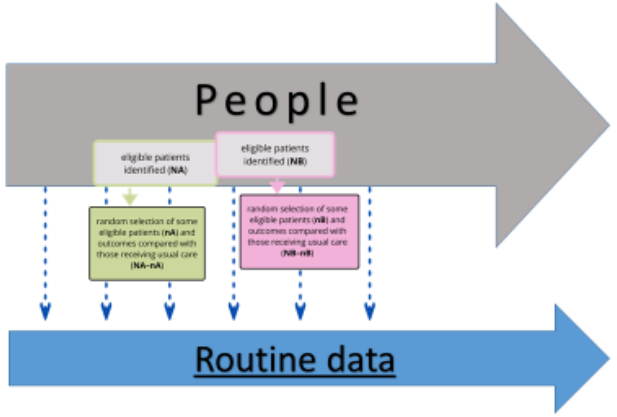

Cohort
eligible patients identified (NA)
eligible patients identified (NB)
random selection of some eligible patients (nA) and outcomes compared with those receiving usual care (NA–nA)
random selection of some eligible patients (nB) and outcomes compared with those receiving usual care (NB–nB)
Outcome measurement


People
eligible patients identified (NA)
eligible patients identified (NB)
random selection of some eligible patients (nA) and outcomes compared with those receiving usual care (NA–nA)
random selection of some eligible patients (nB) and outcomes compared with those receiving usual care (NB–nB)
Routine data

Uses of cohorts or routine data

- to identify eligible participants
- to collect/determine outcomes
- to implement an intervention
- or for a combination of these purposes





CONSORT-ROUTINE

BCS70
1970 British Cohort Study

Cohort – a group of individuals collected for the purpose of conducting research

NHS Digital

CPRD

Personal details	Name	Address	Sex	Date of Birth	NHS number
Cancer diagnosis	Type of cancer	Date diagnosed	How diagnosed		
Cancer treatment	Type of treatment	Date of treatment	Where treated		
Outcomes	Date of death	Cause of death			

GOV.UK

Routine care – data collected for purposes other than research or without specific *a priori* research questions developed

- Electronic Health Record
- Registry
- Administrative Database e.g. government, private health insurance database, or a social care or education database

Trials use cohort and/or routine data sources to

- identify eligible participants
- automate randomisation
- deliver an intervention
- collect data, including assessing outcomes

Cohorts and routinely collected databases can vary in the way they represent complete, random, or convenience samples.

Characteristics of the cohort or database can influence all aspects of the research

Terminology

Some trials might use a cohort or routinely collected data to either identify and recruit participants or collect outcome data

Others might do both

- cohort embedded trial
- cohort-nested trial
- cohort multiple RCT (cmRCT) design
- Trial-within-a-cohort
- Trials within Cohorts (TwiCs)

Informed Consent

- Can be applied at different levels and in different ways compared with conventional trial designs.
- Consent might be sought and obtained to use the cohort or routinely collected database and for the trial
- Consent that is typical in conventional trials might not be done because of features of the integrated cohort or database and trial design.

Analysis

- Access information on participants not enrolled in the trial
- Differences in characteristics
- Assessment of acceptability of intervention
- Assess representativeness of the participants in the trial
- Assess the generalisability of the results

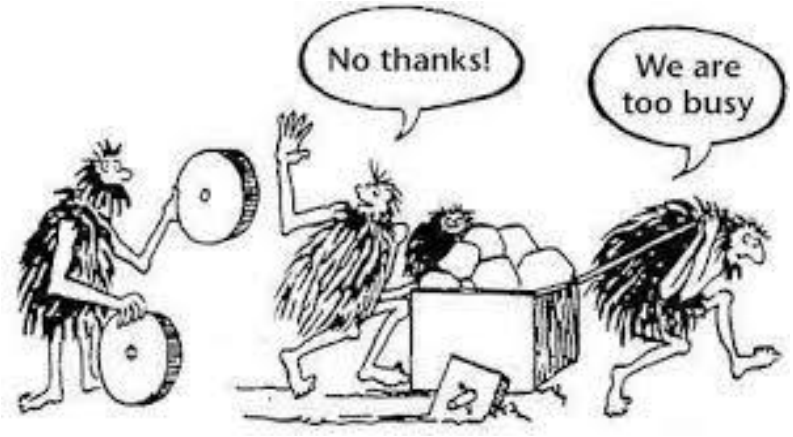
Table 1. Baseline Characteristics of the Patients According to Randomization Status and Treatment Group.*

Characteristic	Patients Who Underwent Randomization		Patients Who Did Not Undergo Randomization	
	Thrombus Aspiration (N=3621)	PCI Only (N=3623)	Thrombus Aspiration (N=1162)	PCI Only (N=3535)
Age — yr†	66.5±11.5	65.9±11.7	66.8±13.5	69.4±12.5
Male sex — no. (%)	2721 (75.1)	2703 (74.6)	829 (71.3)	2360 (66.8)

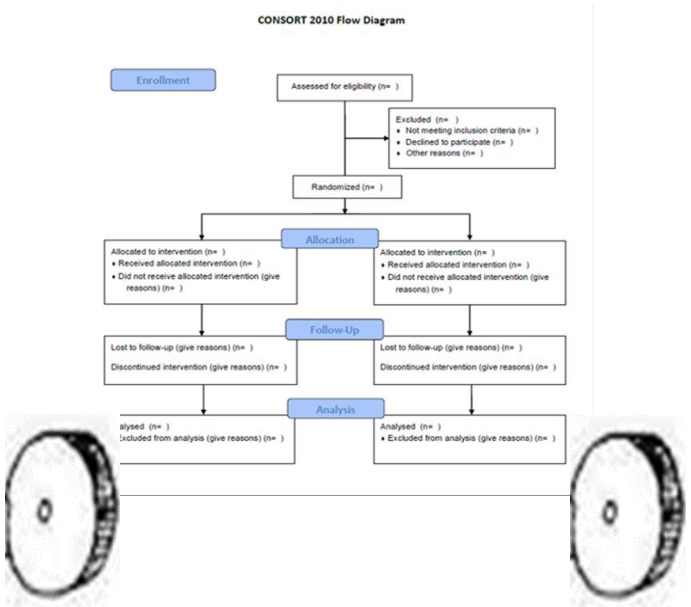
WORLD MEDICAL ASSOCIATION

Final thoughts

"Even the best proven interventions must be evaluated continually through research for their safety, effectiveness, efficiency, accessibility and quality"



CONSORT-ROUTINE



Thank you

Hospital based Trials within Cohorts - Monday 17th May

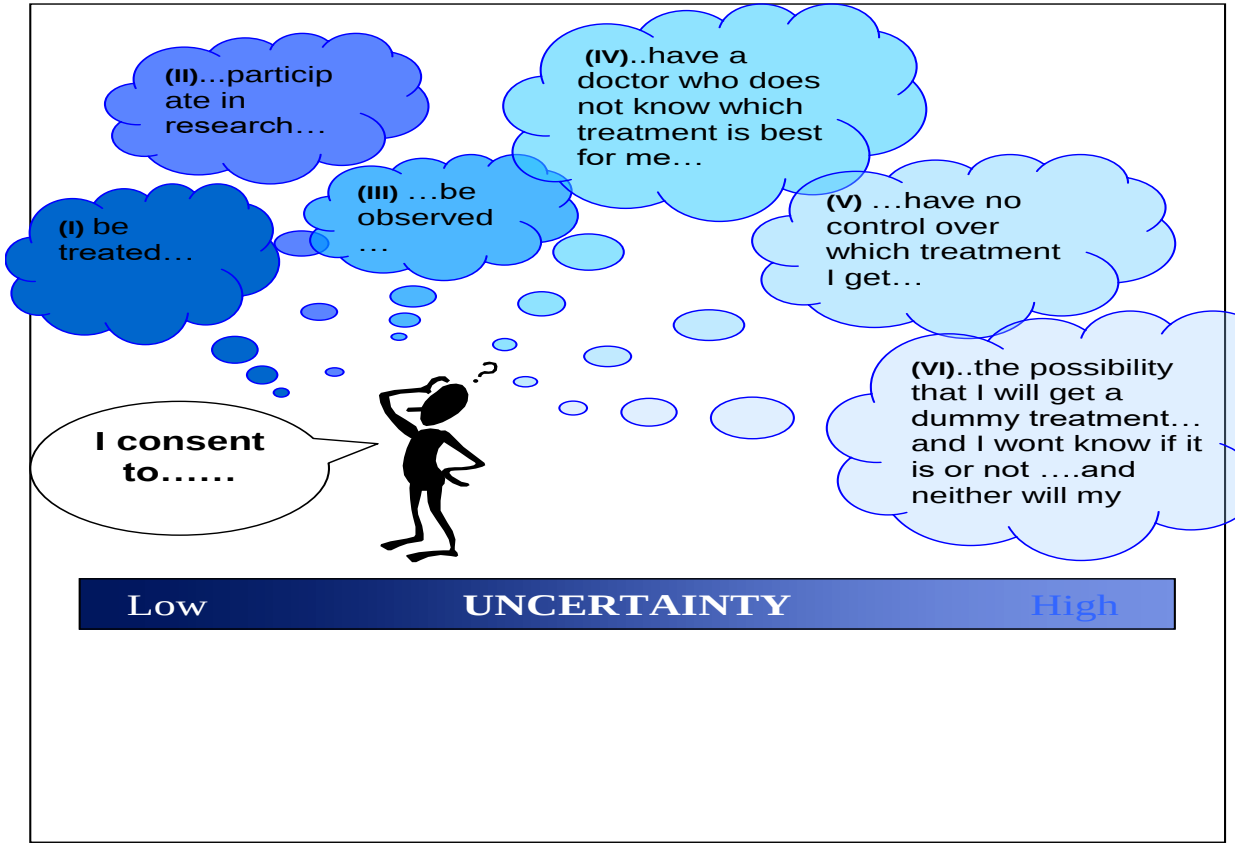
Analysis of Trials within Cohorts - Tuesday 25th May

Ethics of Trials within Cohorts - Thursday 27th May

c.relton@qmul.ac.uk

www.twics.global

Consent to?



- To provide data for research
- To have data linked
- For data to be used in an (intervention?) study
- To be contacted again
- To be *'randomised'*
- To be offered tx
- To receive tx