WMA Satellite Meeting during the 11th World Congress of Bioethics: Thinking ahead – The future of the Declaration of Helsinki
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ECRIN proposals for amendments to the Declaration of Helsinki: ethics committees, transparency, and choice of comparator

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ECRIN, an infrastructure supporting international cooperation in clinical trials

A pan-European, distributed infrastructure providing coordinated services to ***multinational*** clinical research in Europe:

- access to ***patients*** and to ***expertise*** throughout Europe
- despite the ***fragmentation*** of health, legislative and funding systems
- ***support*** to investigators and sponsors in multinational studies
- to make Europe a single area for clinical research

Suggestions to improve the Declaration of Helsinki

- Ethics Committees
  1 – training of ethics committee members (§15)
  2 – independence of the research ethics committees (§15)

- Transparency
  3 – protocol, raw data, recruitment, incentives (§30)

- Trial design
  4 – methodology based on systematic reviews (§12).
  5 – use of placebo (§32) based on medical grounds
  6 – ethical dimension of non-inferiority and equivalence trials

- Wording
  7 – ‘participants’ instead of ‘subjects’

Ethics Committees: training and independence

1 – training of ethics committee members (§15)

required to ensure credibility and reproducibility of their decisions, a critical issue in multinational trials.

2 – independence of the research ethics committees (§15)

“This committee must be independent of the researcher, the sponsor and any other undue influence”.

challenged when linked to an institution that is also be the initiator or sponsor of a clinical trial.

Transparency

3 – *Authors, editors and publishers all have ethical obligations with regard to the publication of the results of research. Authors have a duty to make publicly available the results of their research on human subjects and are accountable for the completeness and accuracy of their reports. They should adhere to accepted guidelines for ethical reporting. Negative and inconclusive as well as positive results should be published or otherwise made publicly available. Sources of funding, institutional affiliations and conflicts of interest should be declared in the publication… (§30)*

- *20-item registration*
- *Publication of results*
- Registration of full protocol and amendments
- Access to raw, anonymised data Hrynaszkiewicz and Altman *Trials* 2009,10:17
- *optimal use of data (repository ?)*
- *credibility and quality of the trial*
- Recruitment performance Dal Re et al. PLoS Medicine 2011, 8:e1001149
- Incentives

ECRIN Scientific Board: Acceptance criteria

1 - Multicentre trial run in at least two European countries.

2 - Rules for transparency:

- Commitment to register the trial in a public register before inclusion of the first participant, for example on www.clinicaltrials.gov.
- Commitment to publish results irrespective of findings.
- Commitment to make raw anonymised data sets available to the scientific community upon legitimate request to the sponsor or principal investigator once the trial is completed.
- Declaration of conflicts of interest.

3 - Rationale based on up-to-date systematic reviews of clinical data or, where not possible, of preclinical data on the experimental intervention and comparator.

4 - Clinical relevance and/or marked impact on public health.

5 - Suitable overall trial design appropriate to the clinical question, including for example:

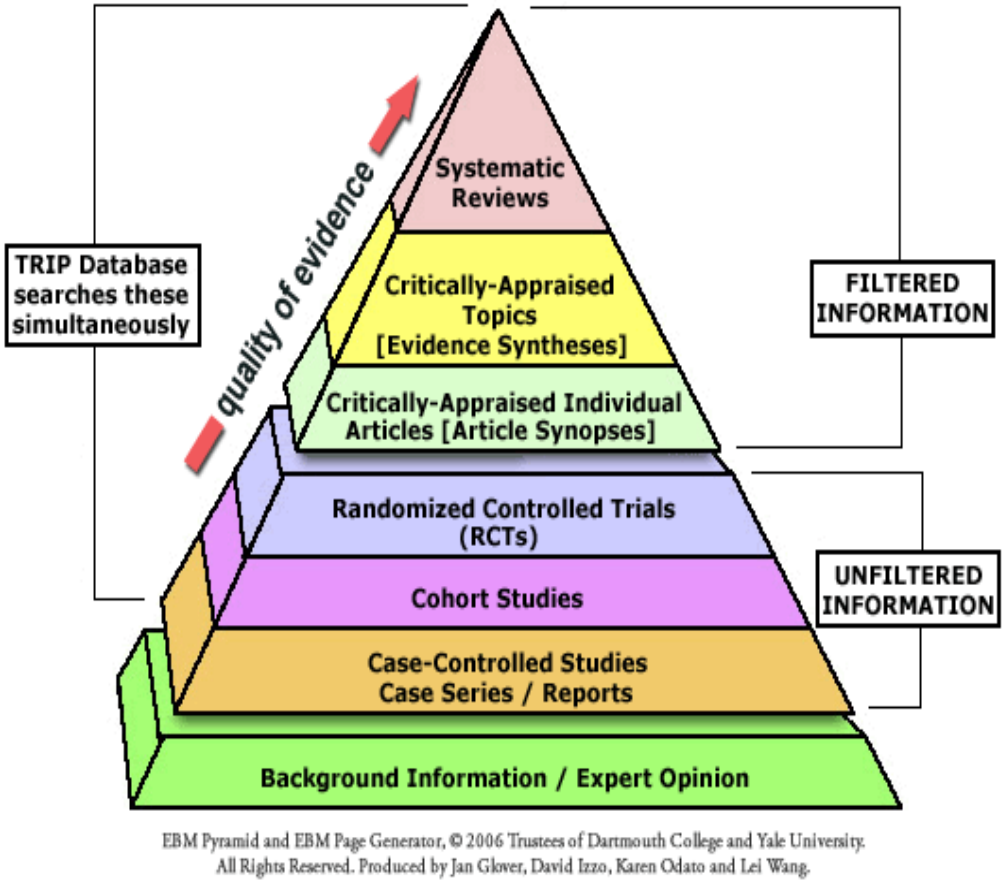
- Selection of an appropriate and justified experimental intervention and comparator.
- Adequate sample size with supporting calculation.
- Relevant patient population (inclusion and exclusion criteria), setting, and duration of treatment and follow up.
- Outcome measures for efficacy and safety with clinically meaningful benefit for the patient.

Design: the clinical relevance should prevail over statistical considerations

Clinical relevance is the goal, statistics is an instrument

4 – methodology based on systematic reviews (§12).

Medical research involving human subjects must conform to generally accepted scientific principles, be based on a thorough knowledge of the scientific literature, other relevant sources of information, and adequate laboratory and, as appropriate, animal experimentation.



Design: the clinical relevance should prevail over statistical considerations

5 – use of placebo (§32) based on medical grounds:
the improper use of placebo harms the participants

Bertelé et al. J Clin Pharmacol. 2012, 68:877-9

The benefits, risks, burdens and effectiveness of a new intervention must be tested against those of the best current proven intervention, except in the following circumstances:

- The use of placebo, or no treatment, is acceptable in studies where no current proven intervention exists; or

- Where for compelling and scientifically sound methodological reasons the use of placebo is necessary to determine the efficacy or safety of an intervention and the patients who receive placebo or no treatment will not be subject to any risk of serious or irreversible harm. Extreme care must be taken to avoid abuse of this option.

Design: the clinical relevance should prevail over statistical considerations

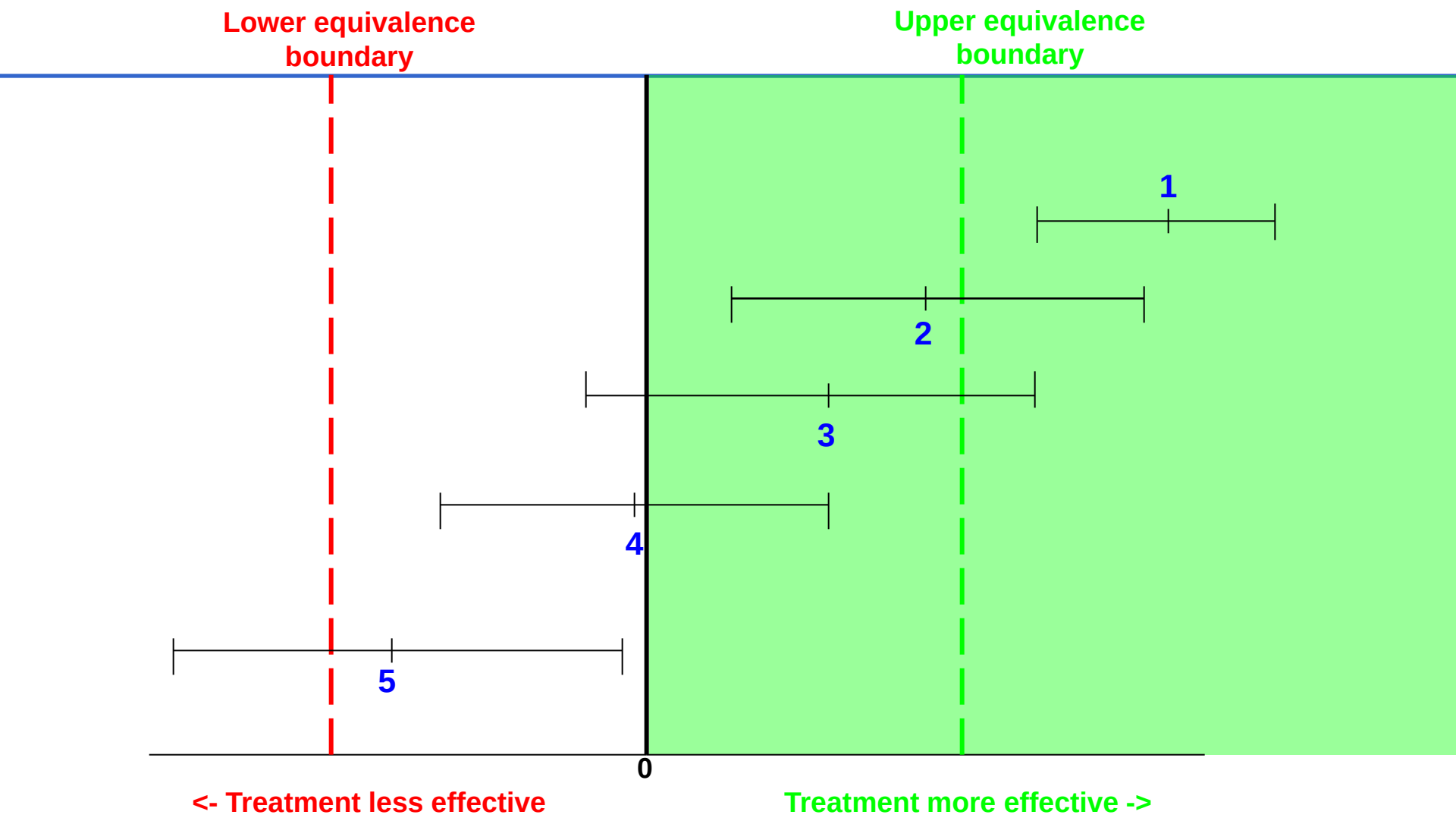
6 – ethical dimension of non-inferiority and equivalence trials:

Garattini & Bertelé, Lancet 2007, 370:1875-7

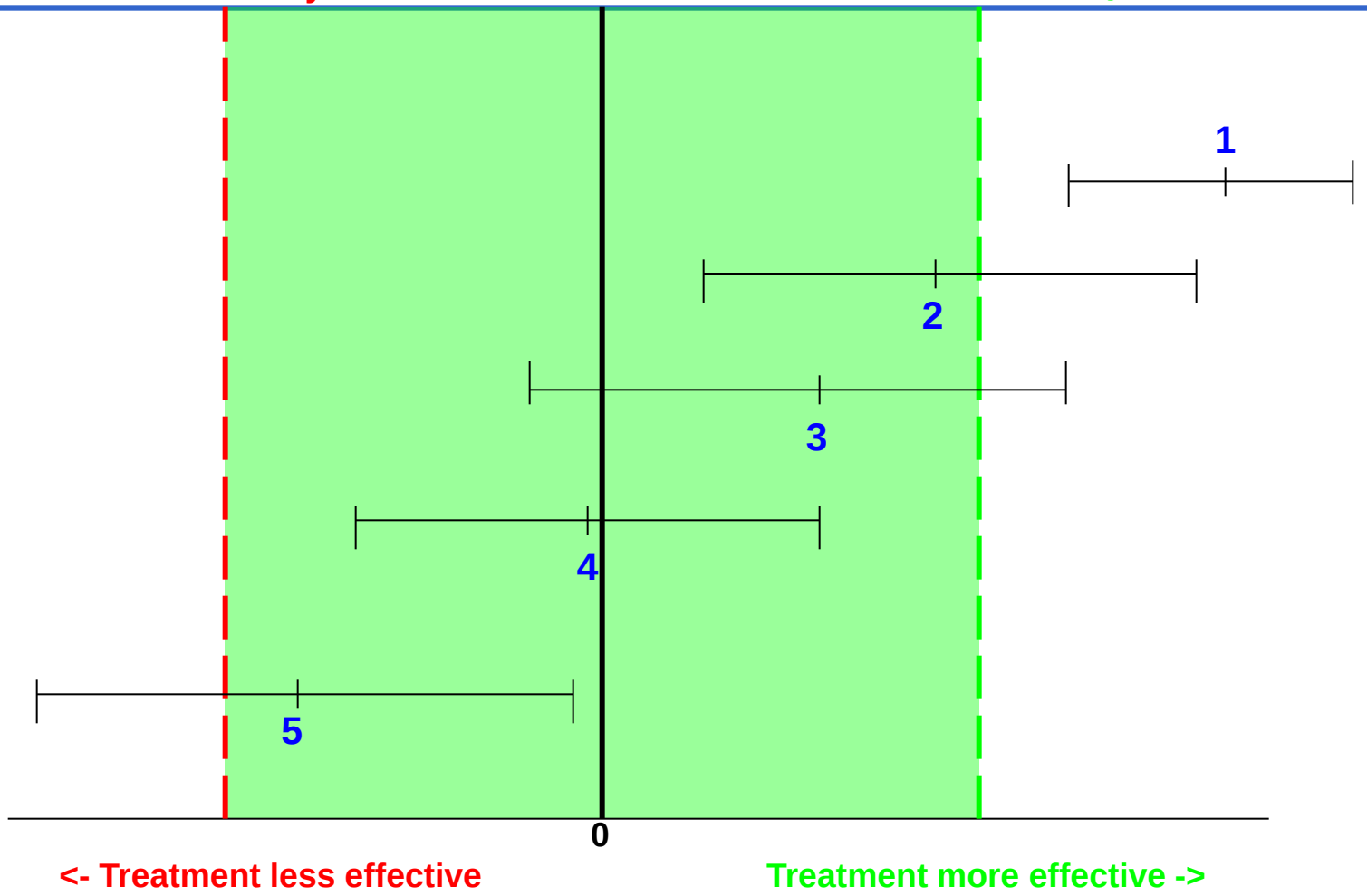
participants take risks without expected benefits

- explicitly mentioned in the informed consent sheet

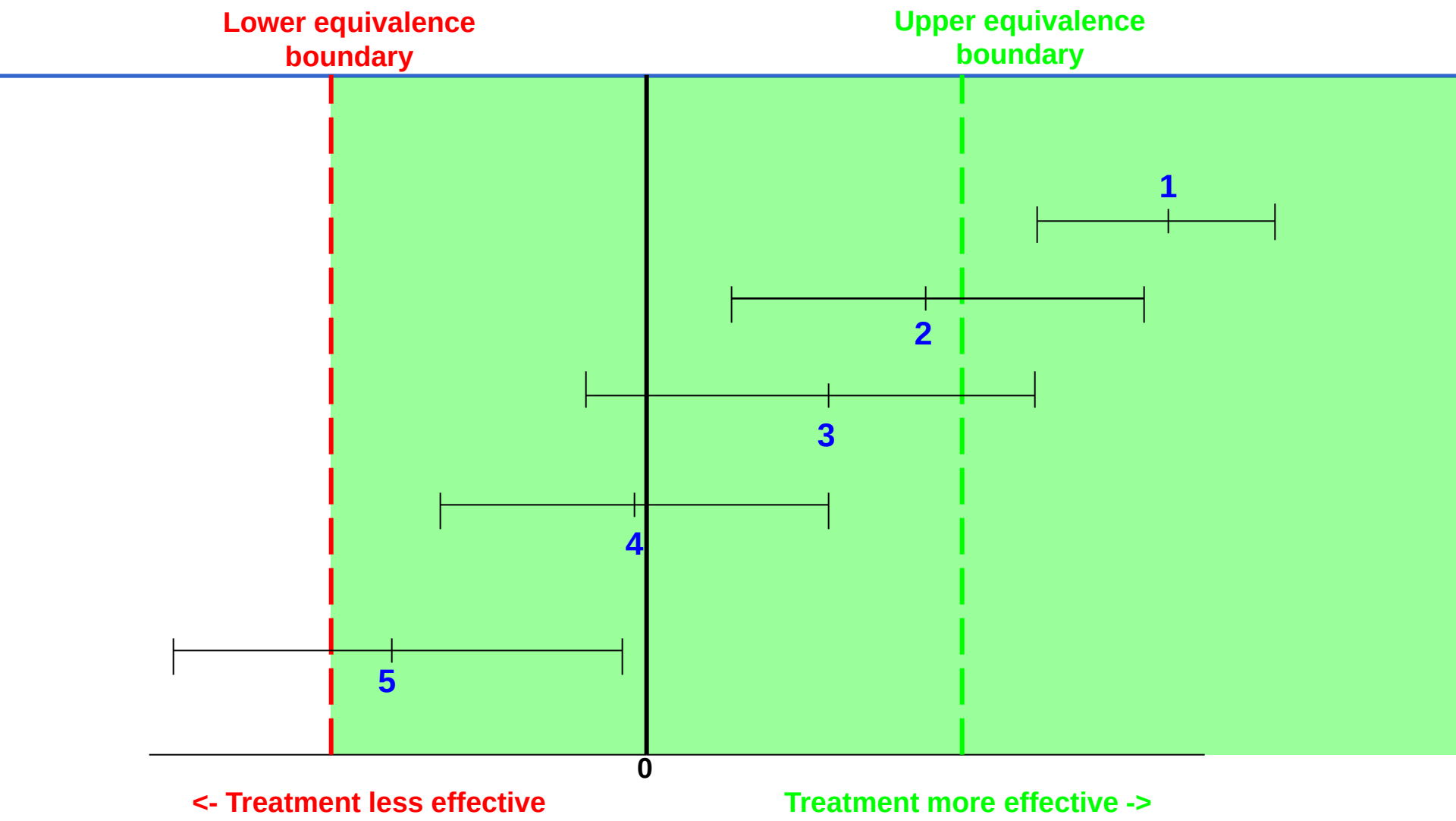
Superiority



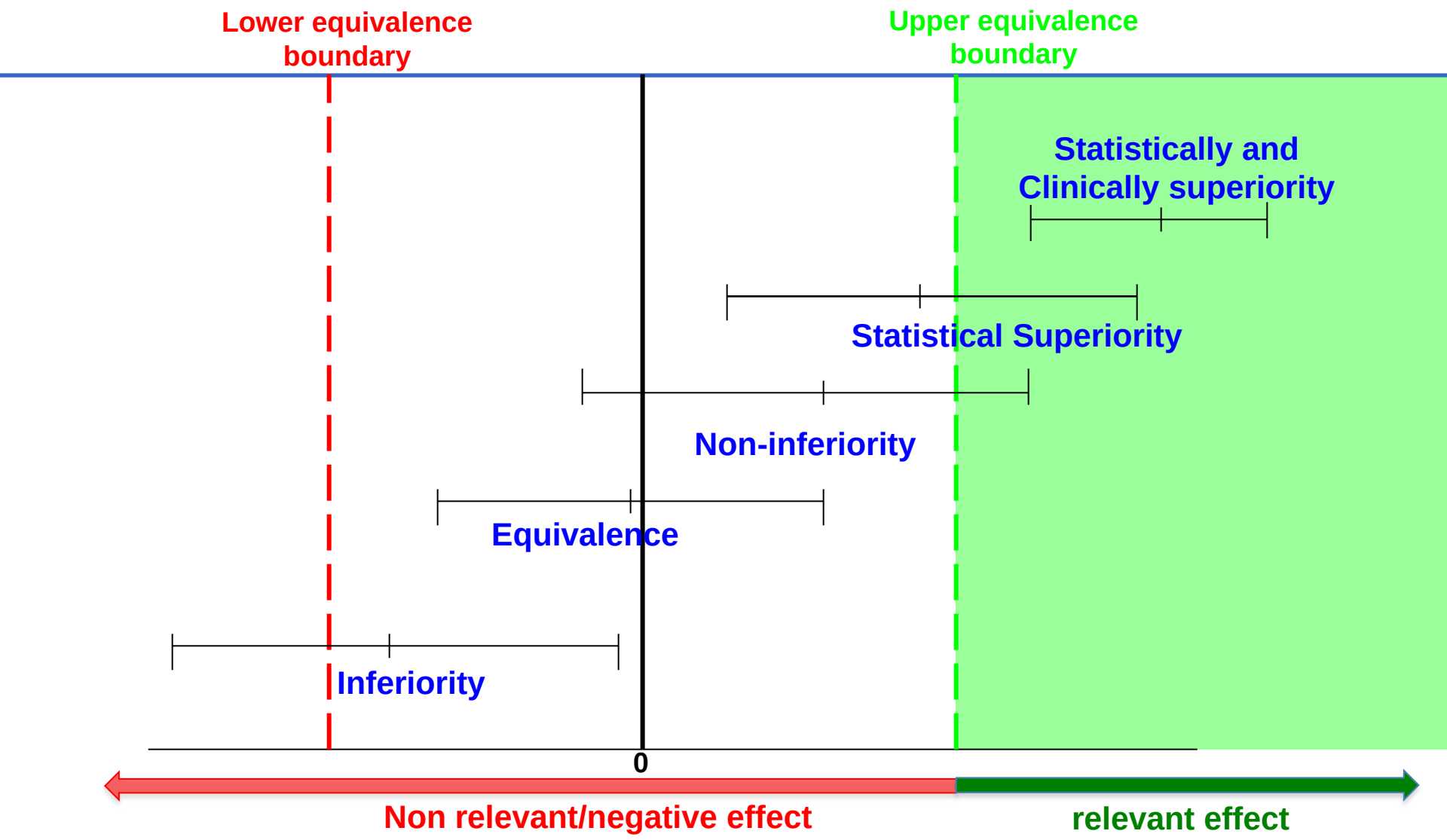
Equivalence



Non-Inferiority



Statistically and Clinically Superiority



Wording

7 – ‘participants’ instead of ‘subjects’ or ‘cases’

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Thank you !