

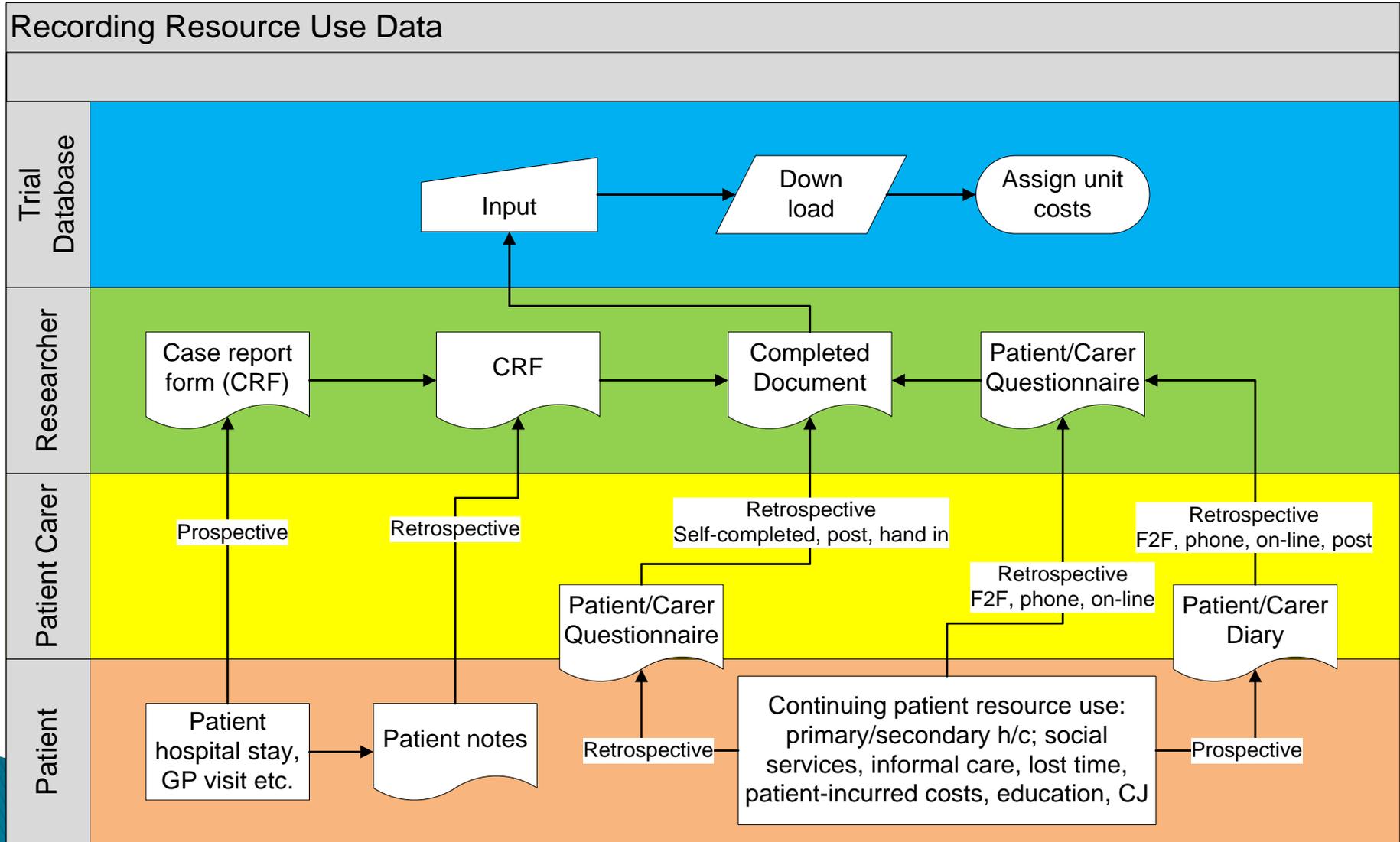
# HEAPs in the context of trial documentation

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# Use of Resource Use Measures (RUMs)



# Definition of a HEAP

- ▶ A document which provides details on the economic analysis to be followed as part of a trial.
- ▶ The final report and any subsequent analysis should follow the main principles outlined in the HEAP.
- ▶ Any deviations from the HEAP should be described and justified in the final report of the trial

# Definition of a HEAP SOP

- ▶ Procedure for the development and utilisation of a HEAP for Clinical Research. The SOP does not address the use of specific health economics procedures or methods, but rather outlines all important details of the design and conduct of the clinical research and the principle features of its proposed economic analysis, to avoid post-hoc decisions that may affect the credibility and interpretation of the economic analysis

# HEAPs Survey (initial work)

- ▶ Electronic survey targeting registered UK CTUs (<http://www.ukcrc-ctu.org.uk/>)
- ▶ Order of contact, HEs, statisticians, directors
- ▶ Study participants recruited by e-mail
- ▶ Asked questions along lines:
  - Do you have a HE Team embedded in your CTU?
  - Do the RCTs run by your CTU have HEAPs?
  - Do you have a HEAP SOP?
  - Who is the intended audience for your HEAPs?
  - How often does your CTU write HEAPs for trials?

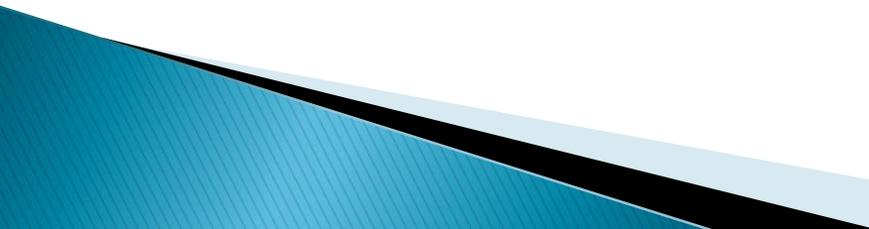
# HEAPs Delphi Consensus Survey

- ▶ A list of potential items for inclusion was developed by examining existing HEAPs
- ▶ Delphi survey was conducted among professional health economists.
- ▶ Consisted of 2 rounds with rating and re-rating
- ▶ Consensus criteria for inclusion in the final list were predefined as  $>70\%$  of participants rating an item 7–9
- ▶ A final item selection meeting was held to scrutinize the results and adjudicate on items lacking consensus.

# Results

- ▶ 62 participants completed round 1 of the survey (initial list included 72 potential items)
- ▶ 72 items carried forward to round 2, and no new items were added.
- ▶ 48 round 1 respondents (77.4%) completed round 2 with consensus on 53 items.
- ▶ At final meeting, the expert panel (n = 9) agreed that 58 items should be included in the essential list, moved 9 items to an optional list, and dropped 5 items.

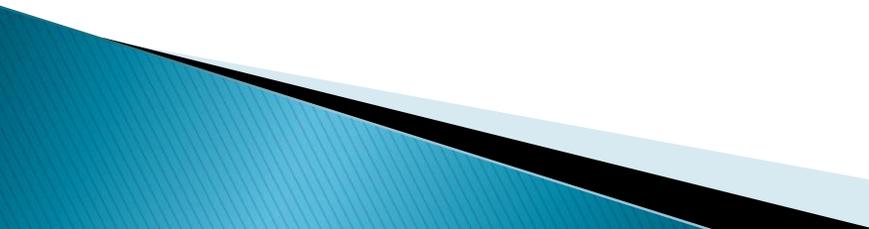
# Conclusions from Study

- ▶ Previous inconsistency towards HEAPs
  - ▶ The HEAP list captures all the most important items & is considered a manageable size; these essential items form a template HEAP that will provide guidance for economic evaluations in RCTs.
  - ▶ Follow on Systematic Review to explore to what extent these essential items were captured in existing protocols and HEAPs
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# Systematic Review

- ▶ Conducted on HE Trials
- ▶ Search terms and their derivatives included “economic evaluation” “cost effectiveness” “plan” “protocol” and “randomised controlled trial”.
- ▶ Cochrane, Embase & Medline databases searched
- ▶ In excess of 6,000 references collected
- ▶ Duplicate, title, abstract and full text screening whittled down to 44 papers referencing some form of HEAP

# What we didn't want

- ▶ Protocols with reference to economic analysis but without providing any HEAP details
  - ▶ Papers whose title suggests a HEAP, but the paper does not provide much HEAP detail with respect to the essential items
  - ▶ Methodological papers
  - ▶ Standalone cost effectiveness analysis or models
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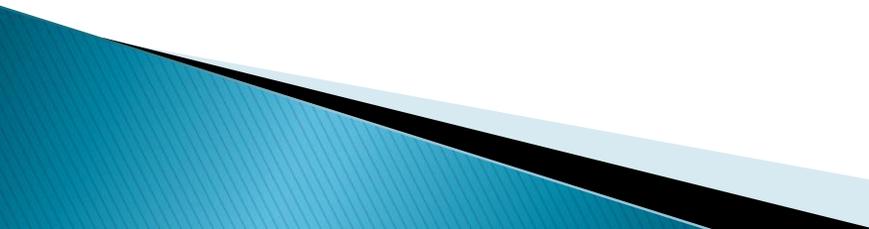
# What we wanted

- ▶ HEAP or dedicated stand-alone economic analysis plan separate from main protocol
  - ▶ Protocols with enhanced economic content similar to the essential items
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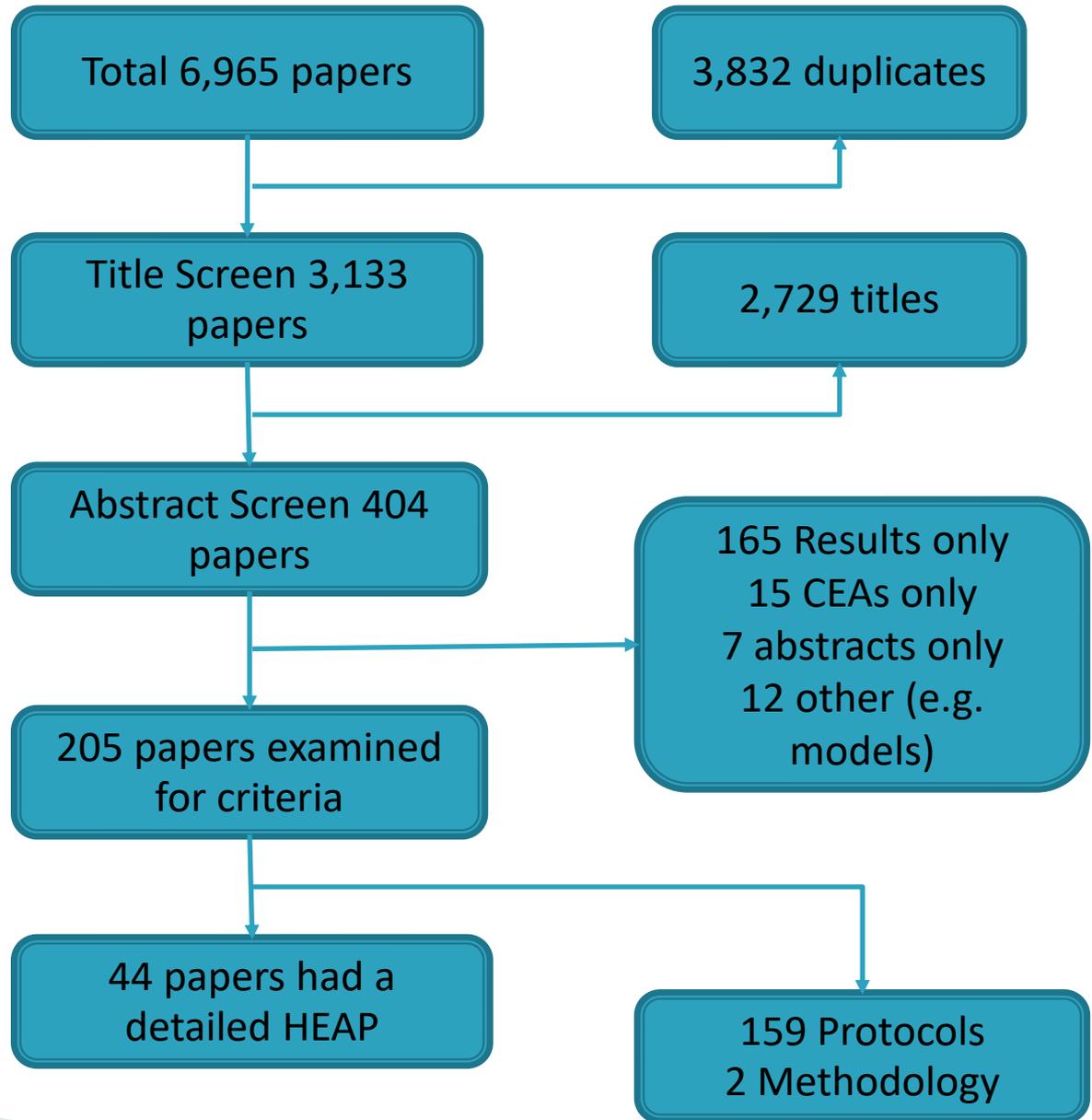
# Essential Items

- ▶ Administration (12 items)
  - ▶ Trial introduction and background (7 items)
  - ▶ Economic overview (6 items)
  - ▶ Data collection and management (7 items)
  - ▶ Data analysis (14 items)
  - ▶ Modelling (9 items)
  - ▶ Reporting (2 items)
  - ▶ Appendices (1 item)
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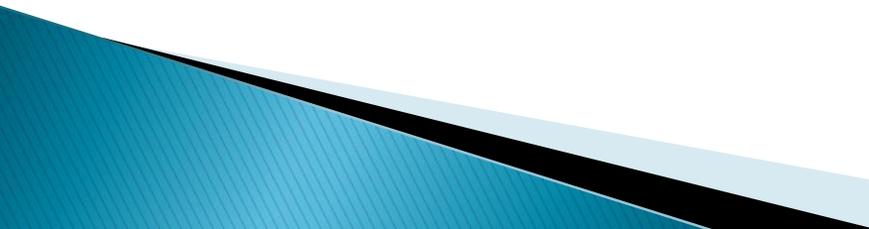
# Some particularly important areas

- ▶ Admin: Funding, Trial No, Roles & Responsibilities
  - ▶ Overview, Aims & Objective, SIPOC, exclusion & inclusion
  - ▶ Resource use measured
  - ▶ Unit costs
  - ▶ Cost analysis (how they go about putting together resource use and unit costs)
  - ▶ Outcomes (QALYs, infections avoided etc)
  - ▶ Incremental analysis
  - ▶ Uncertainty Analysis
  - ▶ Sensitivity Analysis
  - ▶ Dealing with missing data
  - ▶ Reporting guidelines (e.g. CHEERS)
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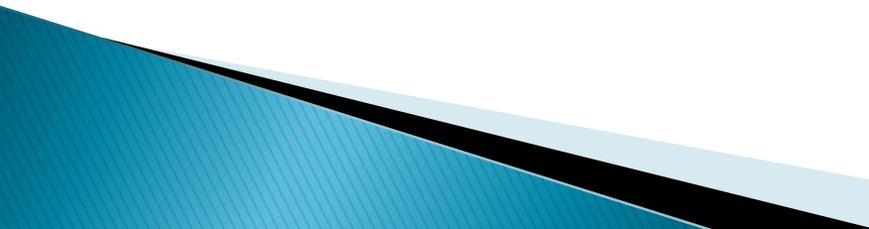
# PRISMA Diagram



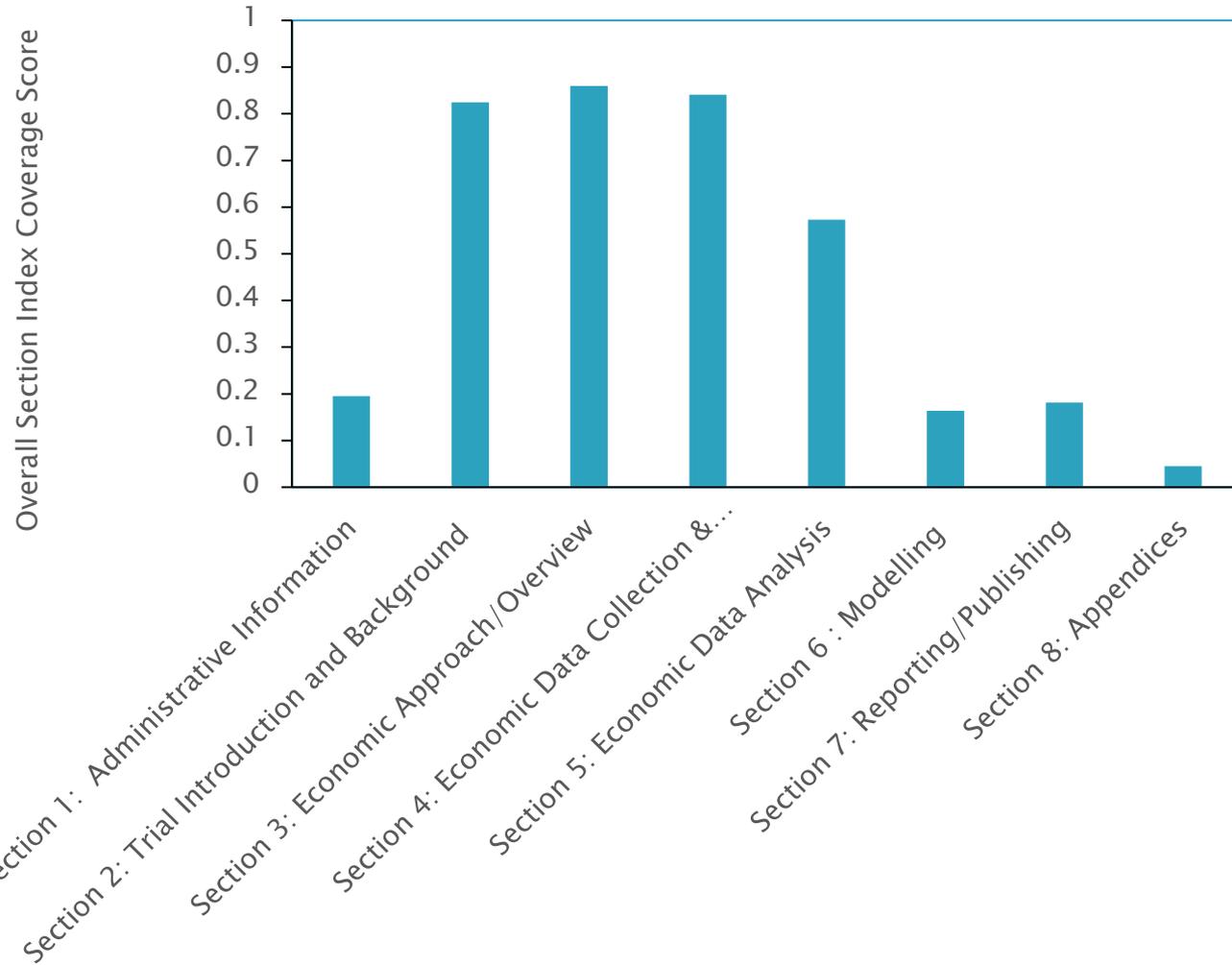
# Scoring

- ▶ All items scored for their appearance using a value of 1 if present and a value of 0 if not
  - ▶ Two people scored all HEAP sections independently (MD, CR) checking against the 67 essential and optional items.
  - ▶ A third reviewer (JT) resolved any lack of consensus.
  - ▶ No weighting was applied to the score. The scores were then totalled and expressed as a proportion of the total possible score,
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# Results

- ▶ Only two studies managed to capture more than 60% of the prerequisite content.
  - ▶ The majority of the studies were conducted in the Netherlands (13/44), followed by the UK (12/44)
  - ▶ 35/44 of the health economics analysis plans were based on multicentre or single-centre RCTs, 6 were cluster RCTs, 2 reported a factorial RCT design and 1 had a non-RCT design.
  - ▶ Mixed perspectives, e.g. societal, healthcare.
  - ▶ Other useful findings not previously considered
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Bar Chart Illustrating Overall Degree of Section Coverage



# Conclusion

- ▶ This review established HEAPs are not widely-published documents.
- ▶ A fuller HEAP comprising the recent more inclusive Delphi study undertaken would allow for a more standardised approach.
- ▶ Other good practices outlined in this study could also be used such as:
  - detailed process flow charts;
  - illustrations of models:
  - tabulations of resource use and the data source

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  - ▶ MRC Hubs for Trial Methodology Research
  - ▶ DIRUM Database
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