Meandering journey towards routine trial adaptation: survey results on barriers to use of adaptive designs in confirmatory trials

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Outline

- ❑ Motivation and contextual definition of an adaptive design
- ❑ Rationale for the investigation
- ❑ Addressing research questions
- ❑ Results
- ❑ Some recommendations and conclusions
- ❑ Acknowledgements and references

Motivation

- Disappointing ‘success’ rate of new treatments in phase 3 (Dent et al, 2011; Kaplan et al, 2015)
- Questionable assumptions on design parameters (Vickers, 2003; Charles et al, 2009; Clark et al, 2013)
- Obsession with 2-arm trials

➢ Efficiency, value for money in research, and ethical implications?

Contextual definition of an Adaptive Design

- Use accumulating outcome data
- Modify ‘aspects’ of the design
- Preserves scientific validity and trial integrity
- ‘Adaptation by design’

➢Sounds a brilliant concept, BUT … !

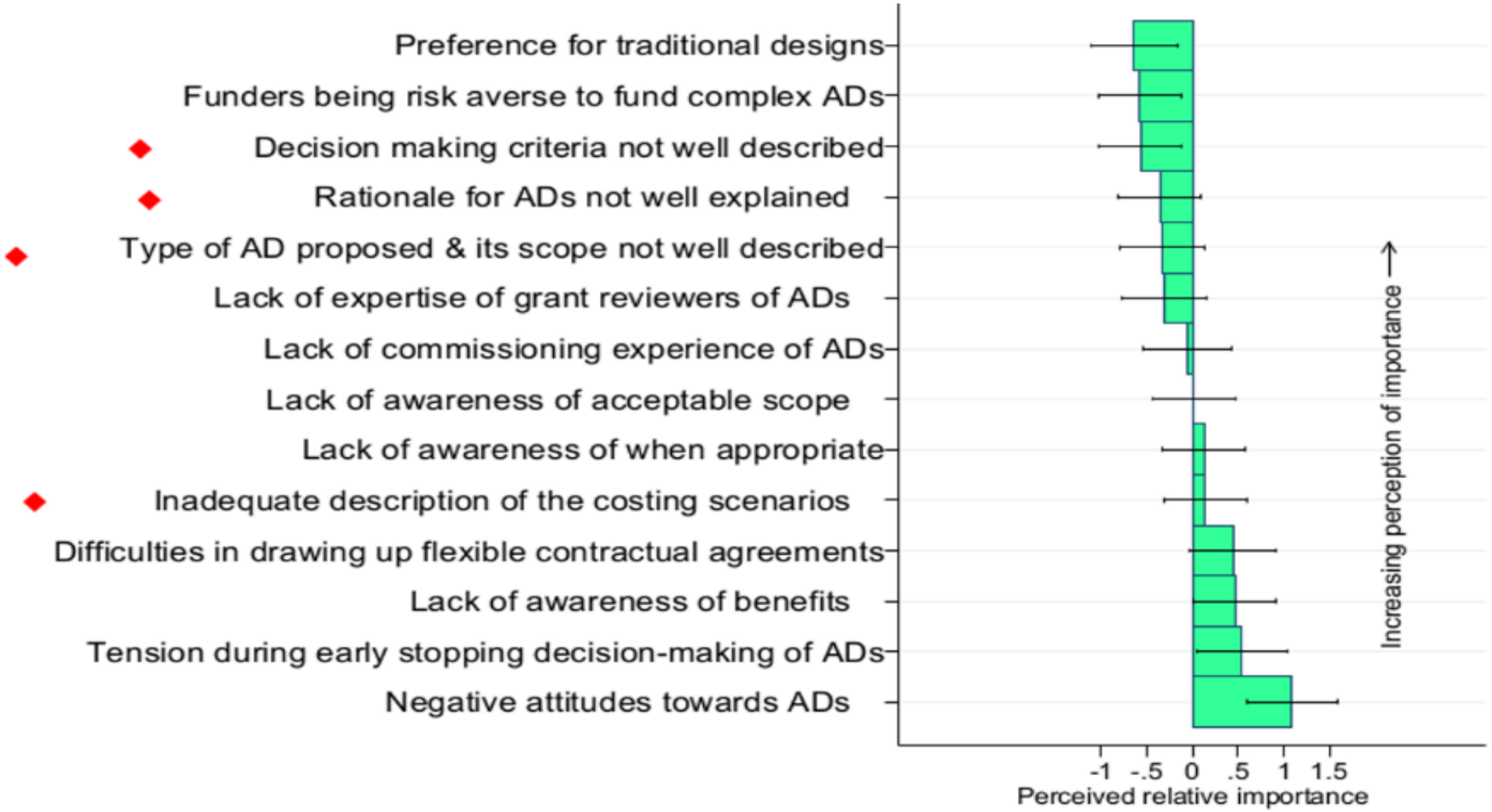
Rationale for the investigation

- Why adaptive designs are underused?
- Understanding obstacles among key stakeholders is paramount
- Limitations of previous related research (Quinlan et al,2010; Kairalla et al,2012; Jaki,2013; Morgan et al,2014)
  - Perceptions of public funders
  - Focus of early phase trials
  - Pharmaceutical industry
  - Setting

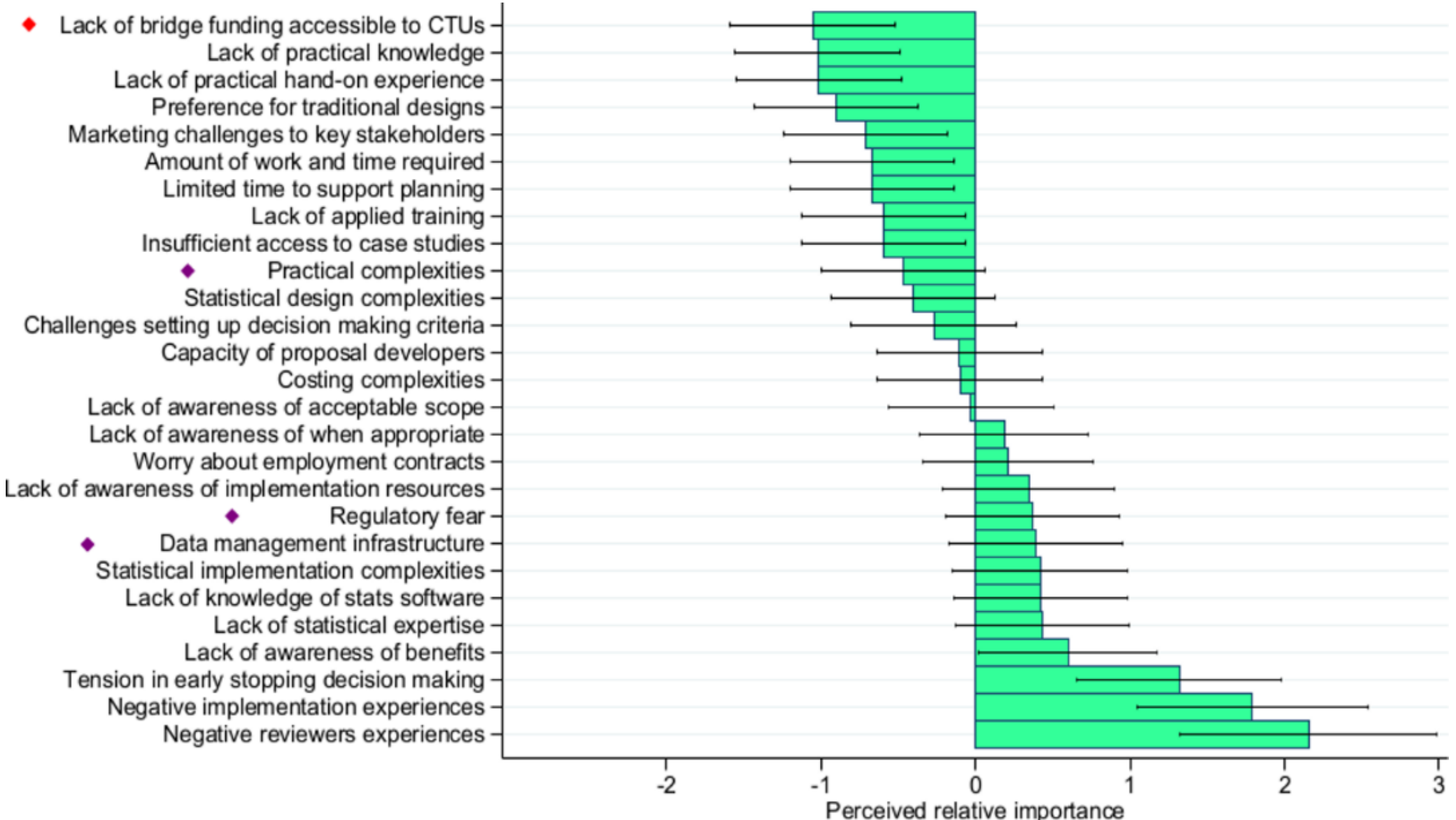
Addressing the research question

- Cross-disciplinary, cross-sector interviews of key stakeholders (Dimairo et al, 2015)
- Follow-up parallel online surveys:
  a) Registered UK CTUs (Directors/Designated Senior Statisticians)
     - 30/55 (55 %)
  b) Public Funders (Boards and advisory panel members and chairs)
     - 86/212 (41 %)
  c) Private Sector
     - 17/25 (68 %)

Results(1): Perceptions of UK public funders



Results (2): Perceptions of UK CTUs



Results(3): Some concerns raised

- Robustness in decisions-making
- Credibility/acceptability to change practice
- Fear of introducing operational bias
- Impact on secondary important objectives
- Fear of early stopping for efficacy

Some recommendations

- Small design development grants
- Implementation support accessible to CTUs (MRC AD Working Group efforts)
- More focus on translational applied training
- Encourage more accessible publication of ‘successful’ and ‘unsuccessful’ case studies
- Learning about opportunities and pitfalls: retrospectively designed case studies
- Outreach awareness targeting boards and advisory panel members of funding bodies
- Adequate communication of adaptive designs aspects (proposals and publications)
- Adaptive designs consensus guidance document tailored for the public sector

Conclusions and limitations

- Still multifaceted individual and organisational obstacles requiring addressing
- Most barriers are linked to the lack of practical knowledge
- Average response rates and sample representativeness
  - Findings may provide a conservative picture on some of the barriers and concerns

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