

Evaluating Estimand Implementation in Clinical Trials in the UK and beyond

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Background

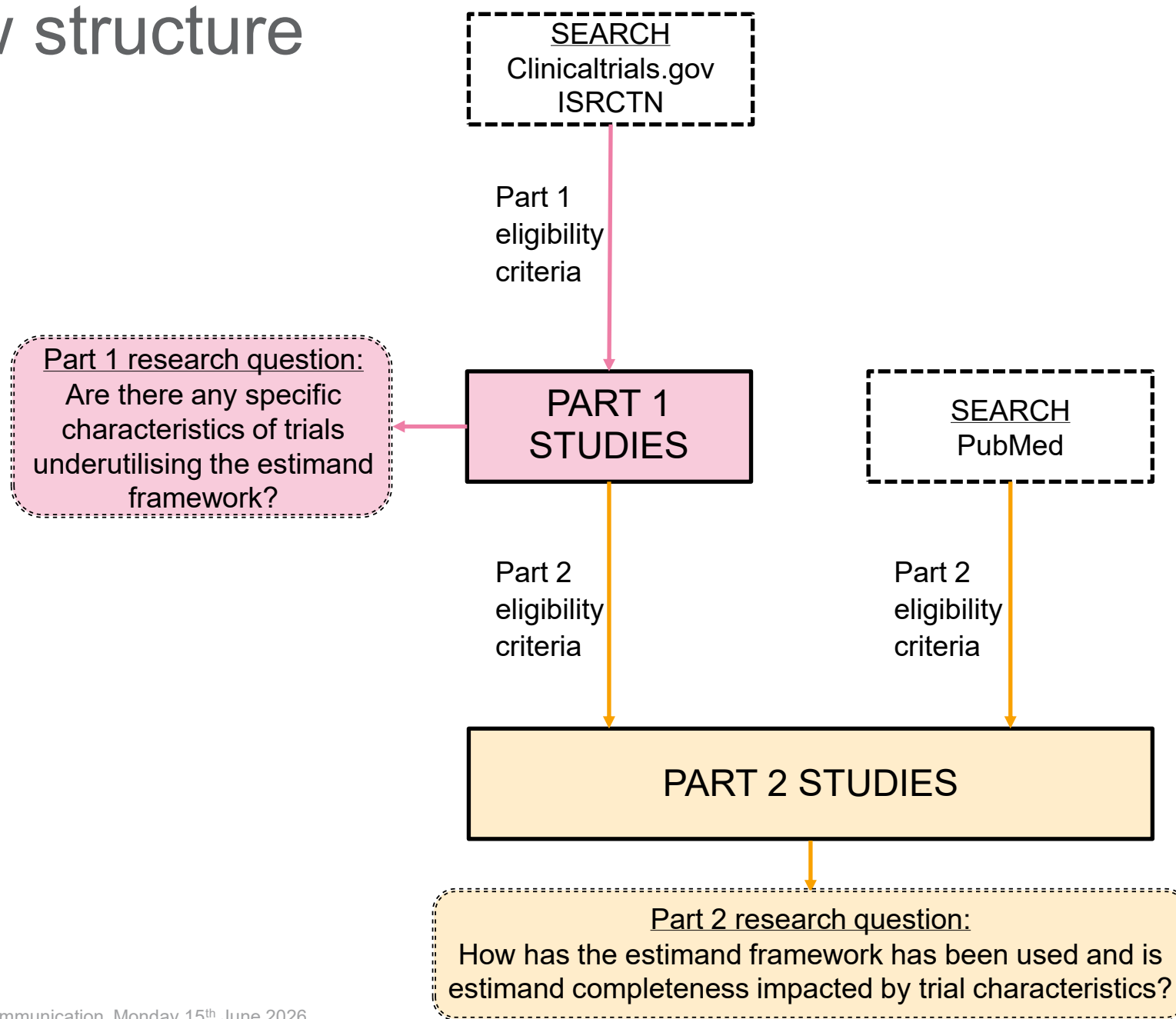
- Estimands aim to clarify the precise questions addressed by clinical trials.
- Three reviews had been published exploring estimand use in clinical trials to the end of 2020, all finding shortfalls in estimand use(1, 2, 3).
- There has been little work exploring why estimands are not used in the development and reporting of all clinical trials, and the barriers to their wider adoption.

1. Kahan BC, Morris TP, White IR, Carpenter J, Cro S. Estimands in published protocols of randomised trials: urgent improvement needed. *Trials*. 2021;22(1):686.
2. Cro S, Kahan BC, Rehal S, Chis Ster A, Carpenter JR, White IR, et al. Evaluating how clear the questions being investigated in randomised trials are: systematic review of estimands. *BMJ*. 2022;378:e070146.
3. Clark TP, Wicentowski RH, Cro S, Sydes MR, Kahan BC. Are estimands being correctly used? A review of UK research protocols. *Trials*. 2025;26(1):310.



Scoping review of trials opened to recruitment or published between 2021 - 2024

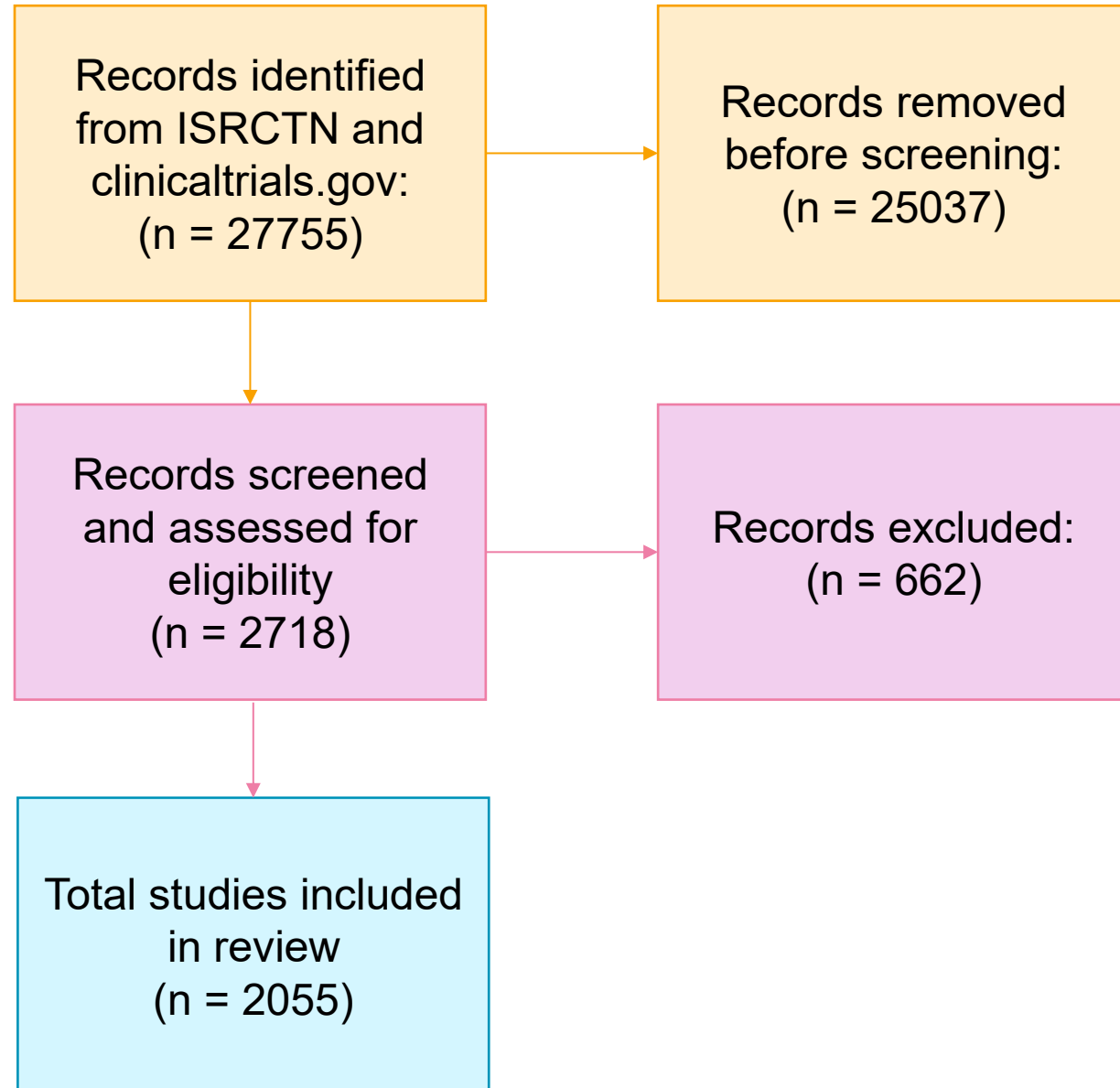
Scoping review structure



Part 1

Research question:

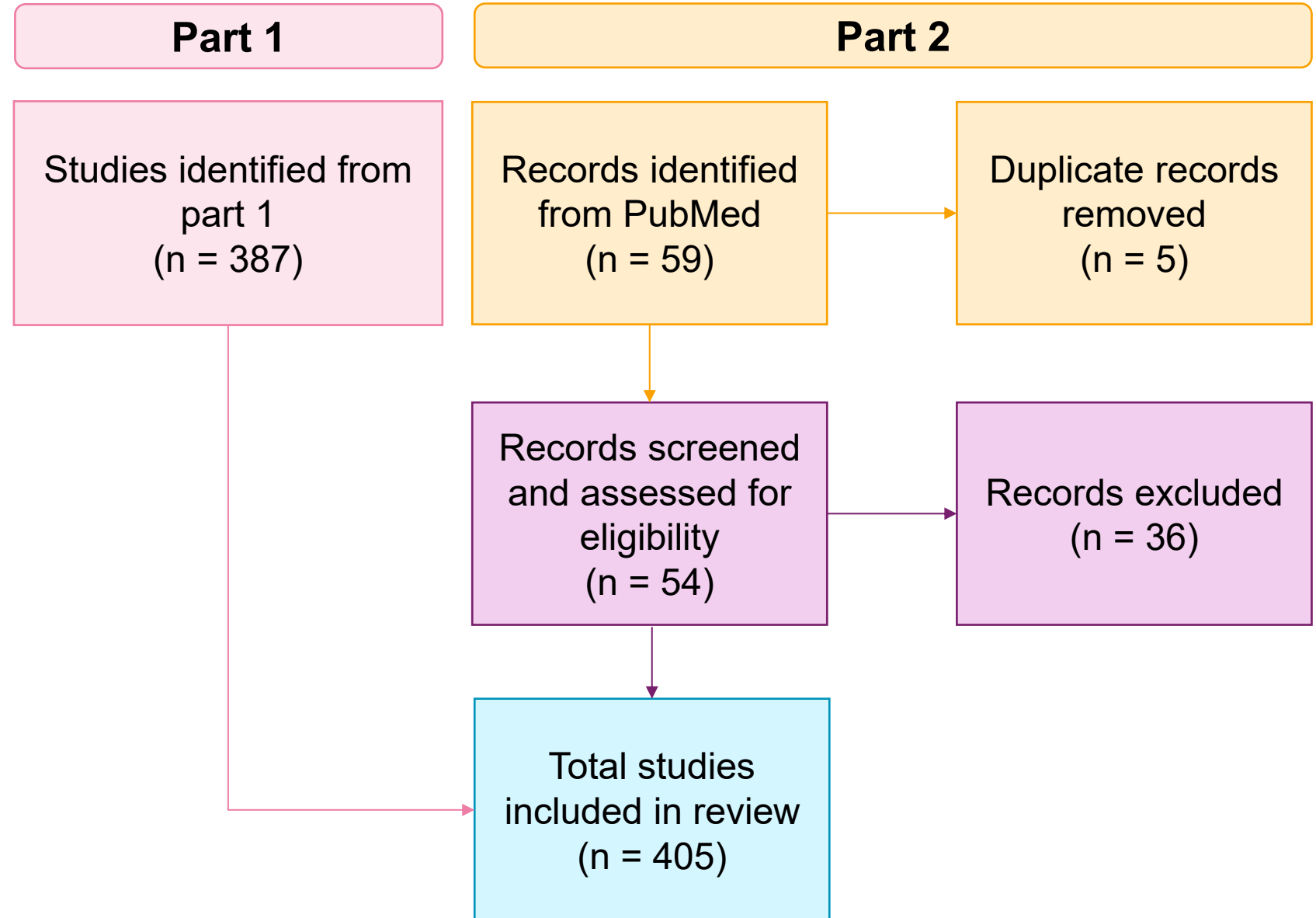
- To ascertain the **extent of estimand use** in clinical trials according to their protocol and/or SAP between 2021 and 2024, and whether specific types of trials underutilise the framework.



Part 2

Research question:

- To explore **how the estimand framework has been used** in clinical trials opened to recruitment or published between 2021 and 2024, and assess whether estimand completeness is impacted by trial characteristics.

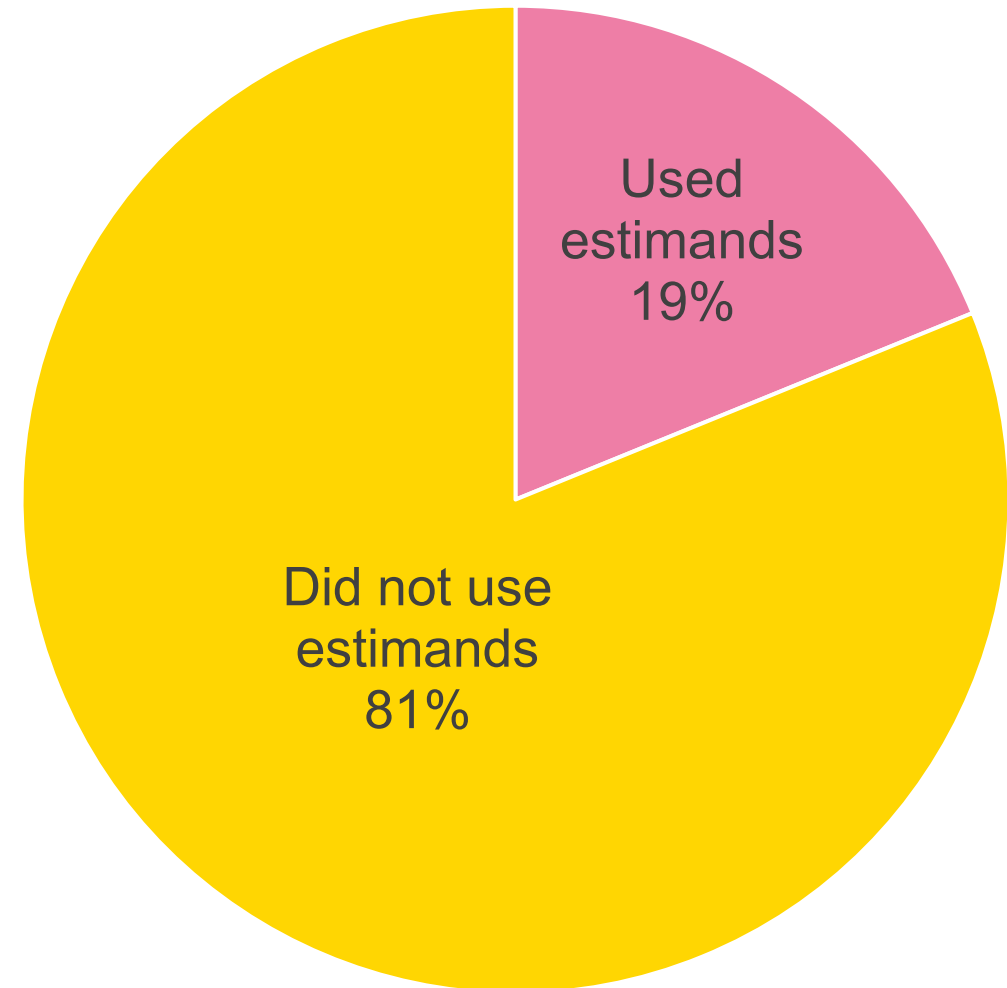


Part 1 results – extent of estimand use

387 of 2055 studies used estimands

Factors significantly influencing estimand use:

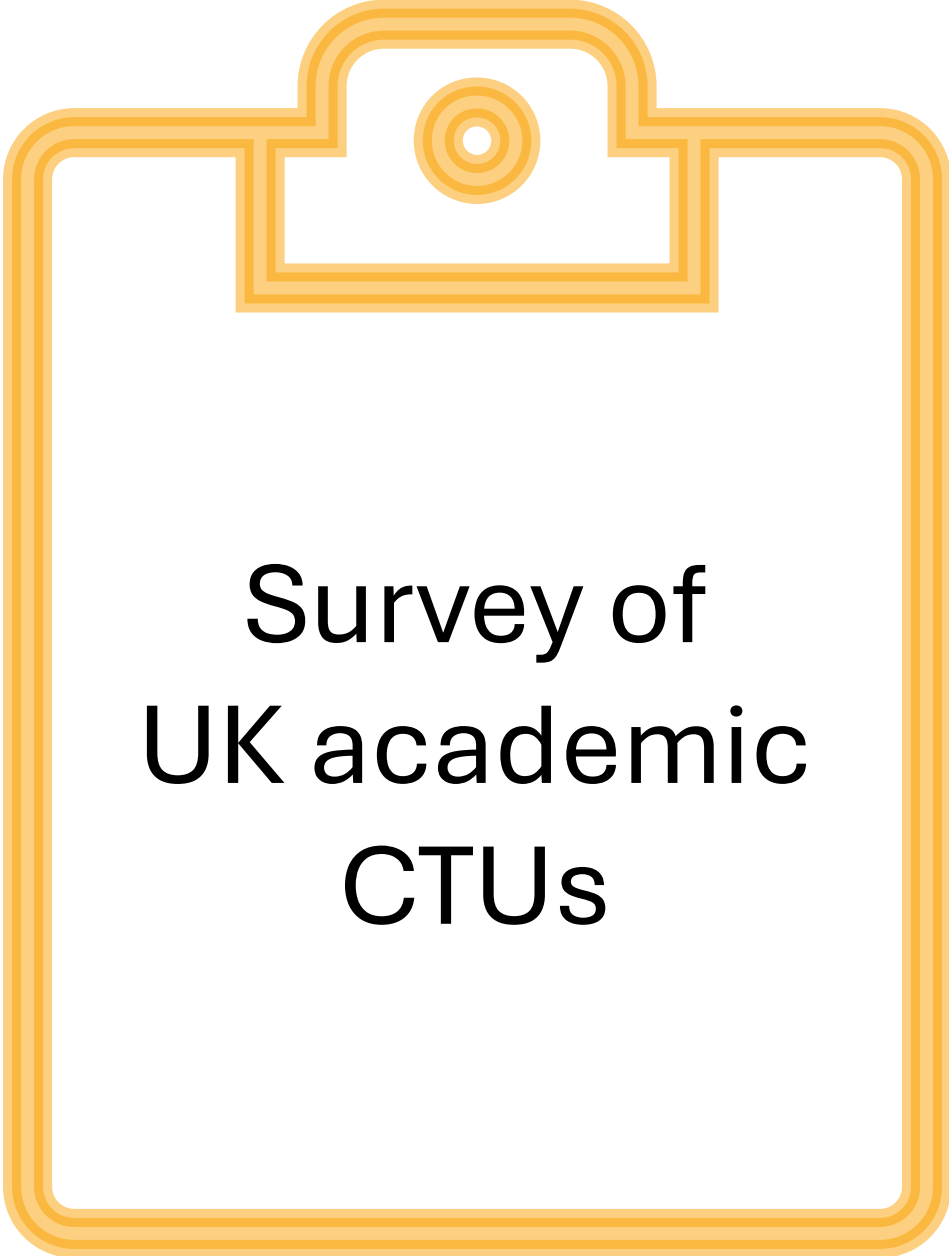
- Industry funder
- Non-cancer trial
- Running in multiple countries
- Randomised trial
- Later phase



Part 2 results – how estimands have been used

- Estimands were more frequently outlined in the SAP than the protocol.
- When estimands were specified in the SAP, they were more often fully detailed.
- Estimands were more likely to be fully described in industry funded trials than non-industry.

Estimand element	Percentage of studies including estimand element by:	
	Overall	
	• Overall	
	• Industry funded (n=371)	
	• Non-industry funded (n=29)	
Intercurrent event strategies (described)	97%	(97%, 86%)
Endpoint	93%	(94%, 82%)
Population	91%	(94%, 50%)
Summary measure	86%	(86%, 82%)
Treatment conditions	80%	(82%, 68%)
Intercurrent event strategies (named)	73%	(73%, 68%)



Survey of UK academic CTUs

Survey background

AIM: To assess the current use of estimands in UK academic clinical trials, and barriers to their implementation.

Survey circulated via the UKCRC CTU network

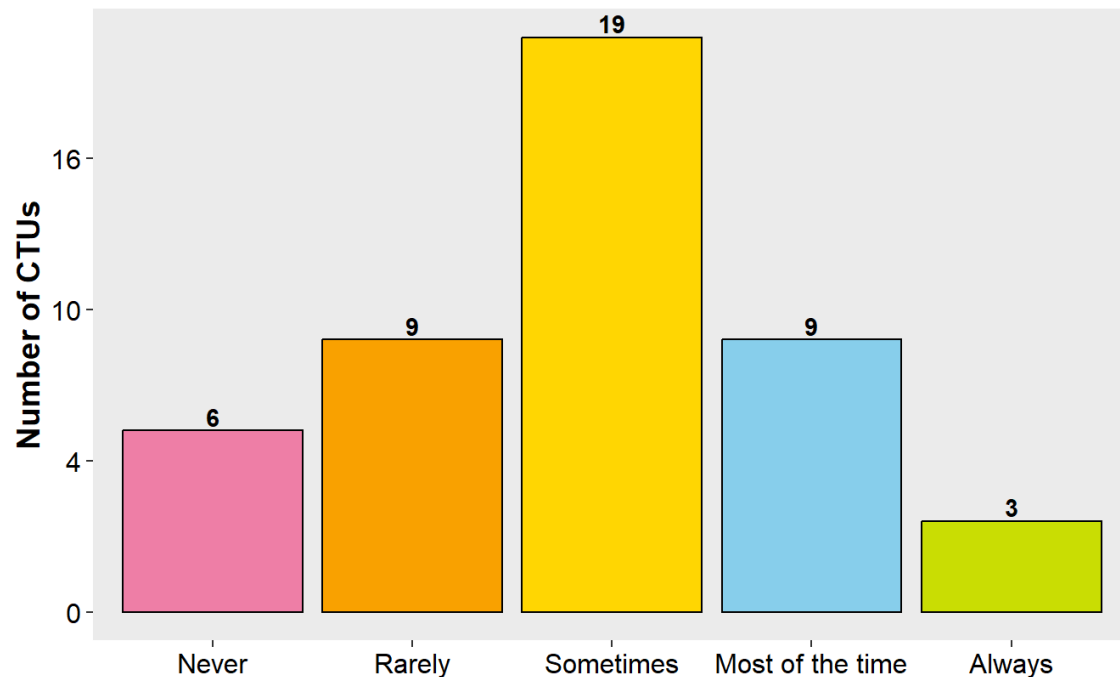
Initial non-responders contacted individually, via known contacts where possible

Out of the 50 UKCRC CTUs, 46 responded

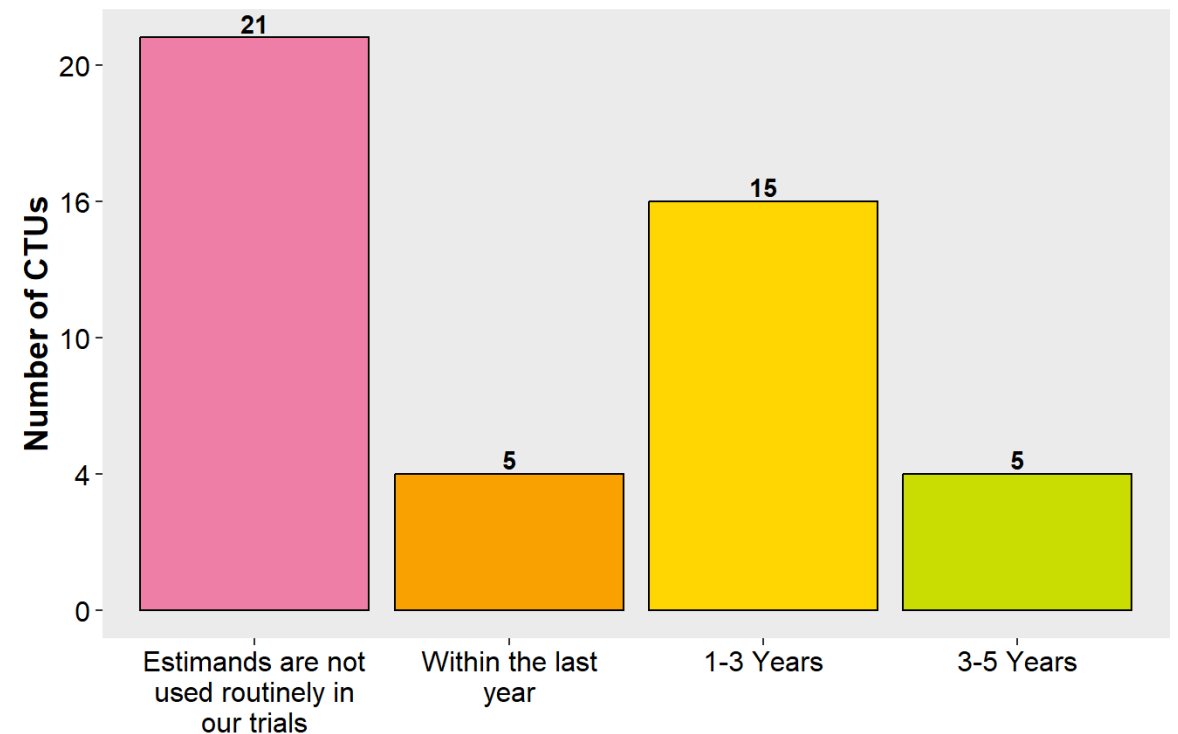
Survey – use of estimands

- 87% of CTUs answering the survey used estimands in the last three years.
- 54% included them in standard operating procedures and guidance.

Thinking about the last 3 years, how often has the estimand framework been used when new trials are being developed?



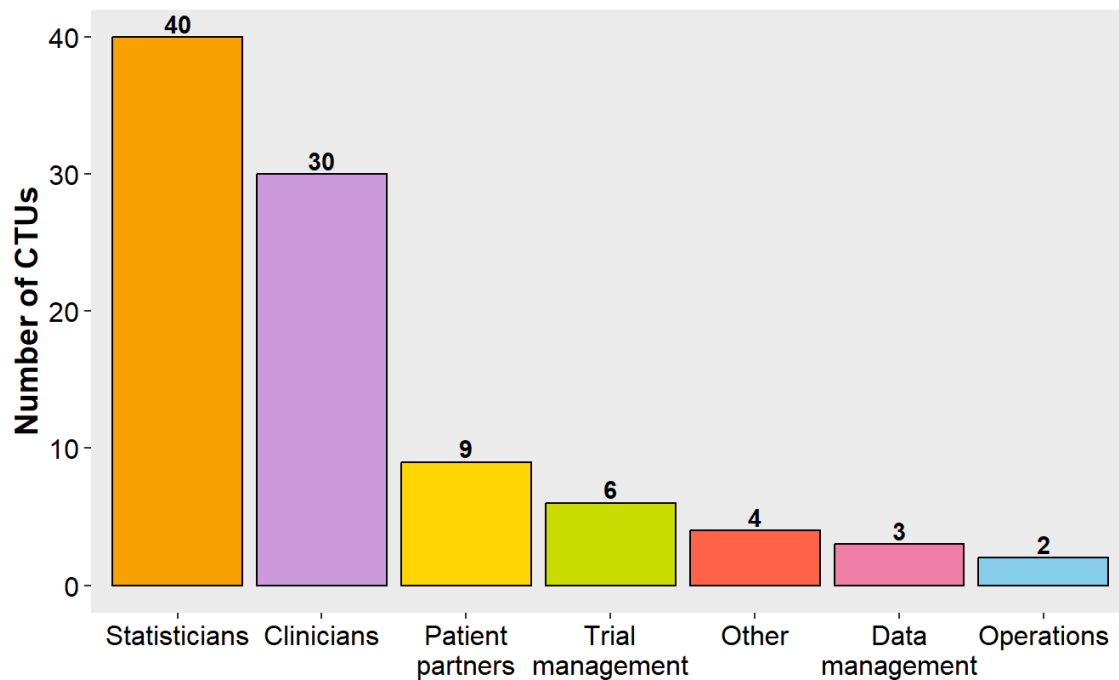
When did your CTU start routinely using estimands in trials?



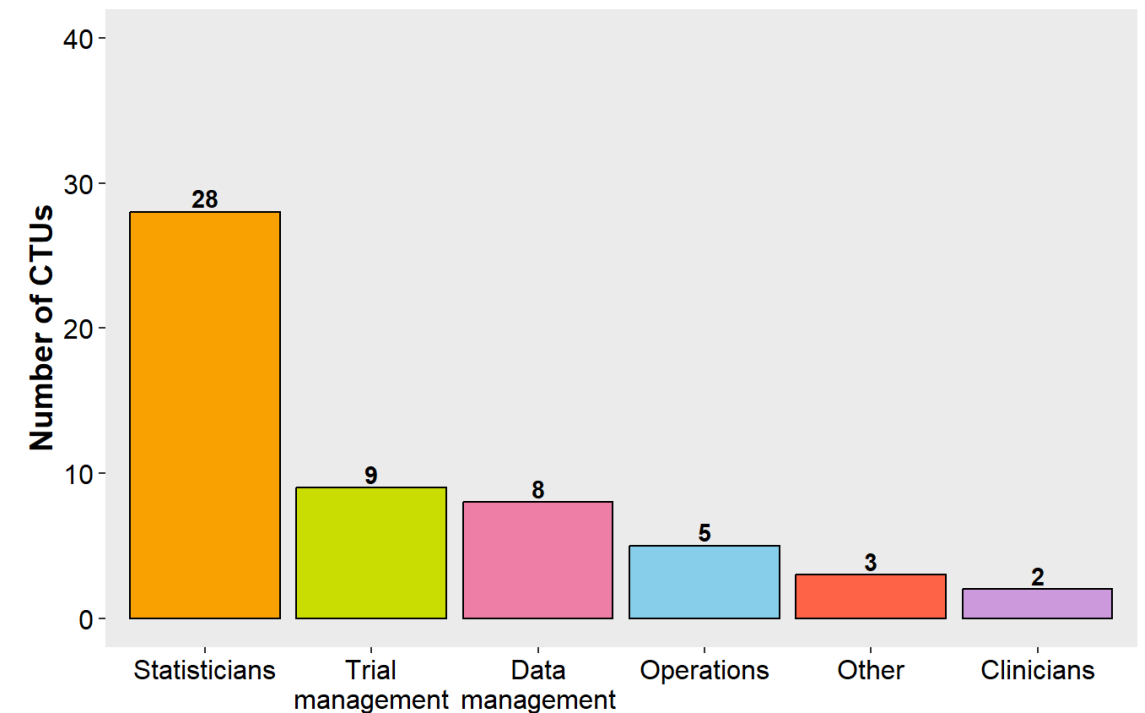
Survey – estimand development

- All CTUs using estimands involved statisticians in their development
- 30 CTUs involved clinicians in estimand development, but only 2 reported clinicians attending training

Who is usually actively involved in the development of estimands for the trials in your unit?



Which groups attended training on estimands?



“In what ways (if any) do you feel that the estimand framework has helped in trial development, conduct or analysis in your unit?”

Informed and aided conversations with and input from key stakeholders

Helped to refine research questions

Improved consideration of intercurrent events

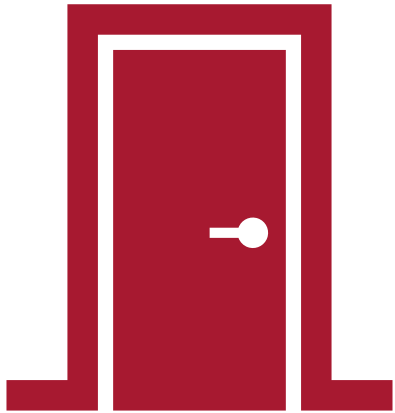
Improved data collection

Improved analysis

Helped development of trial documents

Clearer publications

Barriers and facilitators to estimand use



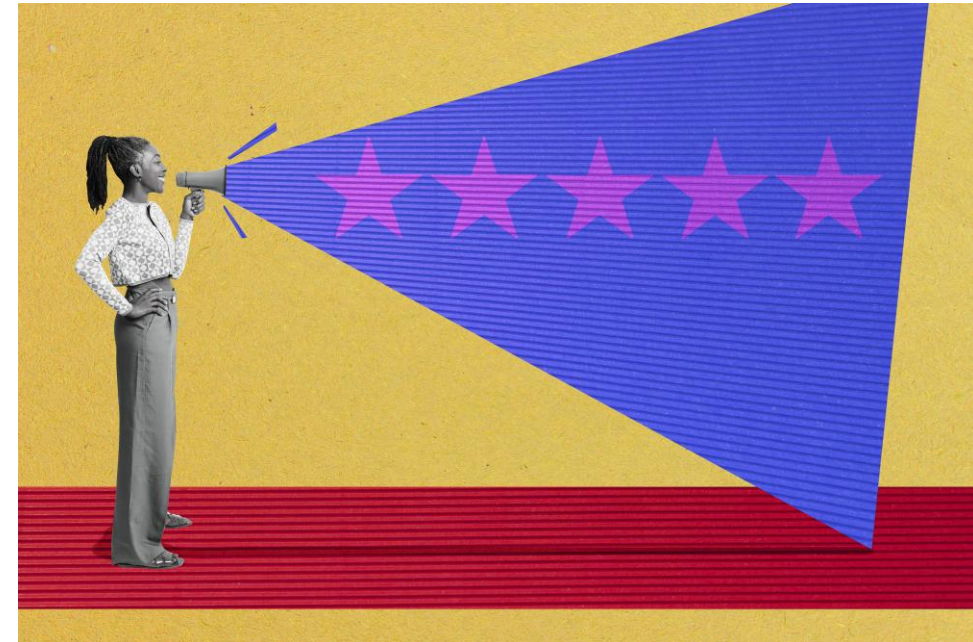
The role of individuals

Varied perspectives on estimands

“Some senior statisticians appear a little reluctant to use the estimand framework.”

Resistance to change

“People's willingness to embrace improvement rather than continuing to do what has always been done because it's easier and quicker.”



Awareness and understanding

Knowledge, experience and confidence

“Lack of experience within the unit and among collaborators.”

Training and guidance availability

“Attending workshops and reading papers [has] helped with the concept but not the practicalities.”



The clinical trials environment

CTU-level factors

“Lack of time to learn properly about estimands and implement them has meant we haven't done it at all.”

Pressure external to the CTU

“Unfortunately, estimands [are] not a requirement for funders and journals at publication stage and therefore Chief Investigators cannot see the value of using them when they are [already] used to report[ing] PICO.”



Types of clinical trial

Specific characteristics of a trial

“Phase I and II trials (which are the majority of trials) benefit less from the use of [the] estimand framework.”



Key factors



Lack of training, guidance and examples



Unfamiliarity and lack of understanding, especially among clinicians



Time constraints

Conclusions and next steps

Conclusions:

- UK academic CTUs use estimands, but not always routinely.
- There is a gap between estimand use and training.
- Barriers to estimand use are complex and interlinked.

Next steps:

- Further exploration of barriers to estimand use and training needs via an ongoing qualitative study targeting diverse stakeholders.
- Developing training materials.



Acknowledgements and questions

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Thank you to all the trials units who responded to the survey.



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