

# Clinical relevance assessment of animal preclinical research (RAA) tool: Development and explanation



## BACKGROUND

**Only a small proportion of preclinical research, performed in animal models prior to clinical trials in humans, translates into clinical benefit in humans.** Possible reasons for the lack of translation of the results observed in preclinical research into human clinical benefit include the design, conduct, and reporting of preclinical studies. **There is currently no formal domain-based assessment of the clinical relevance of preclinical research.**

**To address this issue, we have developed a tool for the assessment of the clinical relevance of preclinical studies,** with the intention of assessing the likelihood that therapeutic preclinical findings can be translated into improvement in the management of human diseases.

## METHODS

We first searched the EQUATOR network for guidelines that describe the design, conduct, and reporting of preclinical research. We then searched the references of these guidelines to identify further relevant publications and developed a set of domains and signalling questions. Finally, we conducted a modified Delphi-consensus to refine and develop the tool. **Delphi panel members included specialists in evidence-based (preclinical) medicine specialists, methodologists, preclinical animal researchers, a veterinarian, and clinical researchers.** A total of 20 Delphi-panel members completed the first round and 17 members from 5 countries completed all three rounds.

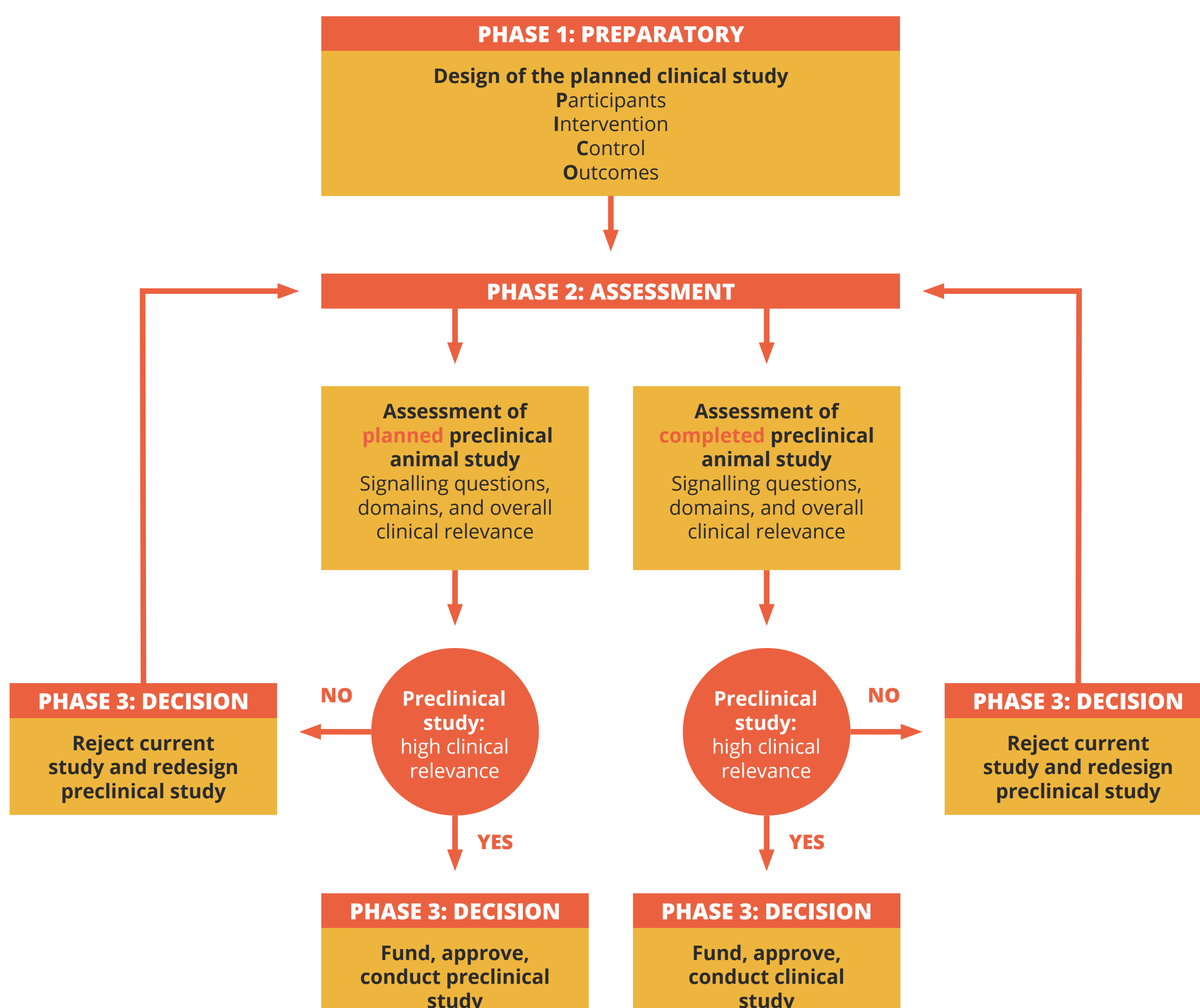
## RESULTS

**This tool has eight domains as shown in the table below:**

DOMAIN	CLASSIFICATION
<b>Domain 1</b> Clinical translatability of results to human disease or condition (construct validity)	Low concern • Moderate Concern • High Concern
<b>Domain 2</b> Experimental design and analysis	Low concern • Moderate Concern • High Concern
<b>Domain 3</b> Bias (internal validity)	Low concern • Moderate Concern • High Concern
<b>Domain 4</b> Reproducibility of results in a range of clinically relevant conditions (external validity)	Low concern • Moderate Concern • High Concern
<b>Domain 5</b> Reproducibility and replicability of methods and results in the same model	Low concern • Moderate Concern • High Concern
<b>Domain 6</b> Implications of the study findings (study conclusions)	Low concern • Moderate Concern • High Concern
<b>Domain 7</b> Research integrity	Low concern • Moderate Concern • High Concern
<b>Domain 8</b> Research transparency	Low concern • Moderate Concern • High Concern
<b>OVERALL CLASSIFICATION</b>	High clinical relevance • Uncertain clinical relevance

## USING THE TOOL

With a total of 28 signalling questions, **this tool provides a framework for researchers, journal editors, grant funders, and regulatory authorities to assess the potential clinical relevance of preclinical animal research.**



## CONCLUSION

We have developed a tool to assess the clinical relevance of preclinical studies and the likelihood of whether or not therapeutic preclinical findings can be translated into improvement in the management of human diseases.