PRIVAT: a tool for facilitating peer review of *in vitro* studies

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About me

- Researcher and consultant based at Lancaster University in the UK
- Research Fellow, Evidence-based Toxicology Collaboration at Johns Hopkins Bloomberg School of Public Health
- Editor-in-Chief, *Evidence-Based Toxicology* ; formerly Systematic Reviews Editor, *Environment International*
- Research into systematic review and evidence mapping methods, improving publishing standards for human environmental health research

Declaration of interests

- Personal fees from EBTC to cover my time in working on this project
- Additional personal fees from Elsevier, Taylor & Francis, the Cancer Prevention and Education Society, Yordas Group, University of Central Lancashire, and grants from Lancaster University, which are outside the present work but relate to the development and promotion of systematic review methods in environmental health research, developing tools and guidance to support the improvement of research standards, delivering training, and providing editorial services
- Potential conflicts of interest due to personal relationships with study participants managed via anonymisation process. No other interests that could reasonably be foreseen as compromising the integrity of decision-making in the project.

Bringing together the international toxicology community to facilitate the integration of scientific evidence into regulatory, environmental and public health decision-making

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Pillars of EBTC

An international, member-driven collaboration for improving how we create, use, and publish evidence in toxicology

Raising research standards	Making sense of evidence	Improving access to research	Advocating evidence-based decision-making
Better evidence, less wasted research	Systematic reviews, evidence maps	FAIR data, Open Science, automated SR	Integrating evidence into policy-making

Today's theme: improving peer-review

Today's presentation

- Improving the comprehensiveness and transparency of peer review
- PRIVAT goals, development methodology, and progress
  - Systematic review of in vitro reporting checklists and appraisal tools
  - Delphi process to finalise criteria and tool questions
  - Prototypes for tool design development
  - Next steps
- Lessons learned and general recommendations for study appraisal

Marketing 

- Trying to get you excited as we finalise the manuscripts
- **Subscribe** to EBTC Newsletter for an announcement of publication / follow me on Twitter **@paul_msg**
- **Join** EBTC if you want to be directly involved in more of this sort of thing in future

https://bit.ly/joinEBTC

Improving the comprehensiveness and transparency of peer review

Peer review

- Unreliable mechanism for quality control in publishing: lots of studies get through peer review with important limitations present
- A matter of chance if reviewers cover everything
  - Reviewers will remember to check different things
  - Have different competencies in what they will attend to
  - Different assumptions about what is important
- Not transparent how comprehensive reviews are
- As an editor, hard to know what has been covered and what has been missed. (Area not mentioned because good, or because missed?)

Checklists should help

- Checklists help reviewers cover everything (reminder of all things; explicit guidance on what is important) and show editor what has not been covered (stats again?)
- But peer review also a creative process: each paper different, issues raised different, so no obvious box-checking approach
- So, identify what is important for reviewers of *in vitro* studies to check, and create a tool to help them do this consistently and comprehensively, in a way that allows flexibility

Objective

Create a tool that helps peer-reviewers provide comprehensive comments on in vitro manuscripts, that helps an editor make a well-informed decision about accepting the study

PRIVAT structure

A. 6 domains
B. 27 questions

Feels like a lot, but in practice is fine!

C. Prompt for amount of revision required to address any issues
D. Free text to explain judgement, make suggestions

IV CAT (*In Vitro* Critical Appraisal Tool)

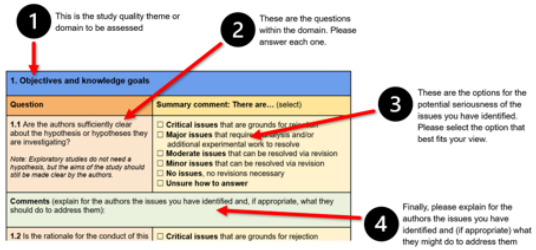
A tool for facilitating comprehensive and transparent peer-review of *in vitro* studies. (Version 1.0)

Instructions for use

IV CAT is a tool to help peer-reviewers provide a structured, comprehensive evaluation of an *in vitro* study manuscript. It is intended to help editors make more consistent, transparent, and informed handling decisions for submissions.

The tool consists of 7 domains. Each domain has a number of questions. For each question, the reviewer is asked to do the following:

- Select a revision recommendation
- Provide comments explaining their recommendation
- If appropriate, advise the authors on how they could improve their manuscript



Submission Metadata	
Reference Number	
Title	
Date of Review	

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Quick Links: General | Objectives | Set-Up | Replicates | Bias | Results | Interpretation | Other | Overall

0. General comments and observations
...vations about the manuscript.

Quick Links: General | Objectives | Set-Up | Replicates | Bias | Results | Interpretation | Other | Overall

1. Objectives and knowledge goals	
Question	**Summary com... ere are...** (select)
1.1 Are the authors sufficiently clear about the hypothesis or hypotheses they are investigating? *Note: Exploratory studies do not need a hypothesis, but the aims of the study should still be made clear by the authors.*	☐ **Critical issue...** grounds for rejection ☐ **Major issues** ...re reanalysis and/or additional exp... work to resolve ☐ **Moderate iss...** ...an be resolved via revision ☐ **Minor issues** ...e resolved via revision ☐ **No issues**, n... necessary ☐ **Unsure how...** ...r
Comments. *Explain for the authors the issues you have... ...nd, if appropriate, what they should do to address them:*	
1.2 Is the rationale for the conduct of this study adequately substantiated?	☐ **Cri...** ...that are grounds for rejection ☐ **M...** ...that require reanalysis and/or ...imental work to resolve ...hat can be resolved via revision ...olved via revision ...ary ☐ **Unsure ho...**
Comments. *Explain for the authors the issues you have i... ...what they should do to address them:*	
1.3 Is there adequate clarity as to whether the study is generating or testing hypotheses?	☐ **Critical issues** thi... ☐ **Major issues** that re... additional experimental... ☐ **Moderate issues** that can... ☐ **Minor issues** that can be res... ☐ **No issues**, no revisions necess... ☐ **Unsure how to answer**
Comments. *Explain for the authors the issues you have identified and, if appropriate, what they should do to address them:*	

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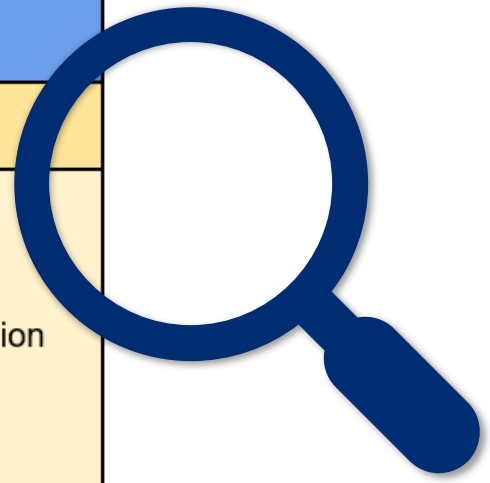
Quick Links: General | Objectives | Set-Up | Replicates | Bias | Results | Interpretation | Other | Overall

2. Experimental set-up	
Question	**Summary comment: There are...** (select)
2.1 Is the experimental set-up suitable for delivering the research objectives?	☐ **Critical issues** that are grounds for rejection ☐ **Major issues** that require reanalysis and/or additional experimental work to resolve ☐ **Moderate issues** that can be resolved via revision ☐ **Minor issues** that can be resolved via revision ☐ **No issues**, no revisions necessary ☐ **Unsure how to answer**
Comments. *Explain for the authors the issues you have identified and, if appropriate, what they should do to address them:*	
2.2 Does the experimental set-up adequately translate to the target situation it is intended to model, e.g. target organism, biological processes, exposure, etc.?	☐ **Critical issues** that are grounds for rejection ☐ **Major issues** that require reanalysis and/or additional experimental work to resolve ☐ **Moderate issues** that can be resolved via revision ☐ **Minor issues** that can be resolved via revision ☐ **No issues**, no revisions necessary ☐ **Unsure how to answer**
Comments (explain for the authors the issues you have identified and, if appropriate, what they should do to address them):	

Quick Links: General | Objectives | Set-Up | Replicates | Bias | Results | Interpretation | Other | Overall

3. Power and replicates	
Question	**Summary comment: There are...** (select)
3.1 Is the experimental unit (the unit that could be randomised, e.g. plate, well, colony, donor, etc.) correctly identified?	☐ **Critical issues** that are grounds for rejection ☐ **Major issues** that require reanalysis and/or additional experimental work to resolve ☐ **Moderate issues** that can be resolved via revision ☐ **Minor issues** that can be resolved via revision ☐ **No issues**, no revisions necessary ☐ **Unsure how to answer**
Comments. *Explain for the authors the issues you have identified and, if appropriate, what they should do to address them:*	
3.2 Is there a sufficient number of	☐ **Critical issues** that are grounds for rejection

1. Objectives and knowledge goals	
Question	**Summary comment: There are…** (select)
1.1 Are the authors sufficiently clear about the hypothesis or hypotheses they are investigating? *Note: Exploratory studies do not need a hypothesis, but the aims of the study should still be made clear by the authors.*	☐ **Critical issues** that are grounds for rejection ☐ **Major issues** that require reanalysis and/or additional experimental work to resolve ☐ **Moderate issues** that can be resolved via revision ☐ **Minor issues** that can be resolved via revision ☐ **No issues**, no revisions necessary ☐ **Unsure how to answer**
Comments (explain for the authors the issues you have identified and, if appropriate, what they should do to address them):	
1.2 Is the rationale for the conduct of this	☐ **Critical issues** that are grounds for rejection



1 Study quality theme for assessment

1. Objectives and knowledge goals	
Question	**Summary comment: There are…** (select)
1.1 Are the authors sufficiently clear about the hypothesis or hypotheses they are investigating? *Note: Exploratory studies do not need a hypothesis, but the aims of the study should still be made clear by the authors.*	☐ **Critical issues** that are grounds for rejection ☐ **Major issues** that require reanalysis and/or additional experimental work to resolve ☐ **Moderate issues** that can be resolved via revision ☐ **Minor issues** that can be resolved via revision ☐ **No issues**, no revisions necessary ☐ **Unsure how to answer**
Comments (explain for the authors the issues you have identified and, if appropriate, what they should do to address them):	
1.2 Is the rationale for the conduct of this	☐ **Critical issues** that are grounds for rejection

2 Questions within the domain. Answer each one

1. Objectives and knowledge goals

Question	Summary comment: There are… (select)
1.1 Are the authors sufficiently clear about the hypothesis or hypotheses they are investigating? *Note: Exploratory studies do not need a hypothesis, but the aims of the study should still be made clear by the authors.*	☐ **Critical issues** that are grounds for rejection ☐ **Major issues** that require reanalysis and/or additional experimental work to resolve ☐ **Moderate issues** that can be resolved via revision ☐ **Minor issues** that can be resolved via revision ☐ **No issues**, no revisions necessary ☐ **Unsure how to answer**
Comments (explain for the authors the issues you have identified and, if appropriate, what they should do to address them):	
1.2 Is the rationale for the conduct of this	☐ **Critical issues** that are grounds for rejection

1. Objectives and knowledge goals	
Question	**Summary comment: There are…** (select)
1.1 Are the authors sufficiently clear about the hypothesis or hypotheses they are investigating? *Note: Exploratory studies do not need a hypothesis, but the aims of the study should still be made clear by the authors.*	☐ **Critical issues** that are grounds for rejection ☐ **Major issues** that require reanalysis and/or additional experimental work to resolve ☐ **Moderate issues** that can be resolved via revision ☐ **Minor issues** that can be resolved via revision ☐ **No issues**, no revisions necessary ☐ **Unsure how to answer**
Comments (explain for the authors the issues you have identified and, if appropriate, what they should do to address them):	
1.2 Is the rationale for the conduct of this	☐ **Critical issues** that are grounds for rejection

3 Options for seriousness of issues identified

1. Objectives and knowledge goals	
Question	**Summary comment: There are…** (select)
1.1 Are the authors sufficiently clear about the hypothesis or hypotheses they are investigating? *Note: Exploratory studies do not need a hypothesis, but the aims of the study should still be made clear by the authors.*	☐ **Critical issues** that are grounds for rejection ☐ **Major issues** that require reanalysis and/or additional experimental work to resolve ☐ **Moderate issues** that can be resolved via revision ☐ **Minor issues** that can be resolved via revision ☐ **No issues**, no revisions necessary ☐ **Unsure how to answer**
Comments (explain for the authors the issues you have identified and, if appropriate, what they should do to address them):	
1.2 Is the rationale for the conduct of this	☐ **Critical issues** that are grounds for rejection

Explain judgements and what authors can do to address them

1 Study quality theme for assessment

2 Questions within the domain. Answer each one

3 Options for seriousness of issues identified

4 Explain judgements and what authors can do to address them

1. Objectives and knowledge goals	
Question	**Summary comment: There are…** (select)
1.1 Are the authors sufficiently clear about the hypothesis or hypotheses they are investigating? *Note: Exploratory studies do not need a hypothesis, but the aims of the study should still be made clear by the authors.*	☐ **Critical issues** that are grounds for rejection ☐ **Major issues** that require analysis and/or additional experimental work to resolve ☐ **Moderate issues** that can be resolved via revision ☐ **Minor issues** that can be resolved via revision ☐ **No issues**, no revisions necessary ☐ **Unsure how to answer**
Comments (explain for the authors the issues you have identified and, if appropriate, what they should do to address them):	
1.2 Is the rationale for the conduct of this	☐ **Critical issues** that are grounds for rejection

PRIVAT domains

Objectives and knowledge goals

- Hypotheses
- Rationale
- Exploratory

Experimental set-up

- Suitability
- Applicability

Power and replicates

- Experimental units
- Sufficient power
- Sufficient replicates

Safeguards against systematic error (bias)

- Authentication
- Measurement
- Baseline characteristics
- Blinding
- Complete data

Interpretation of results

- Limitations
- Over/understatement
- Contextualisation

Generation and reporting of results

- Protocol adherence
- Data normalisation, cleansing
- Statistical methods
- Selectivity
- Raw data and code

Other issues relevant to publication

- Declaration of interests
- Summary sections
- Reproducibility
- Ethical clearance

IV CAT development methodology

Avoid common trap

- ICEMAN developers found 29 tools for assessing effect modifiers
- None had done all of
  - Systematic survey of prior methods guidance
  - Formal development by expert panel
  - Extensive pretesting
  - Manageably small number of key items
  - Overall rating reflecting a continuum
  - Fillable forms to facilitate use
- We also did not want to create just yet another tool!

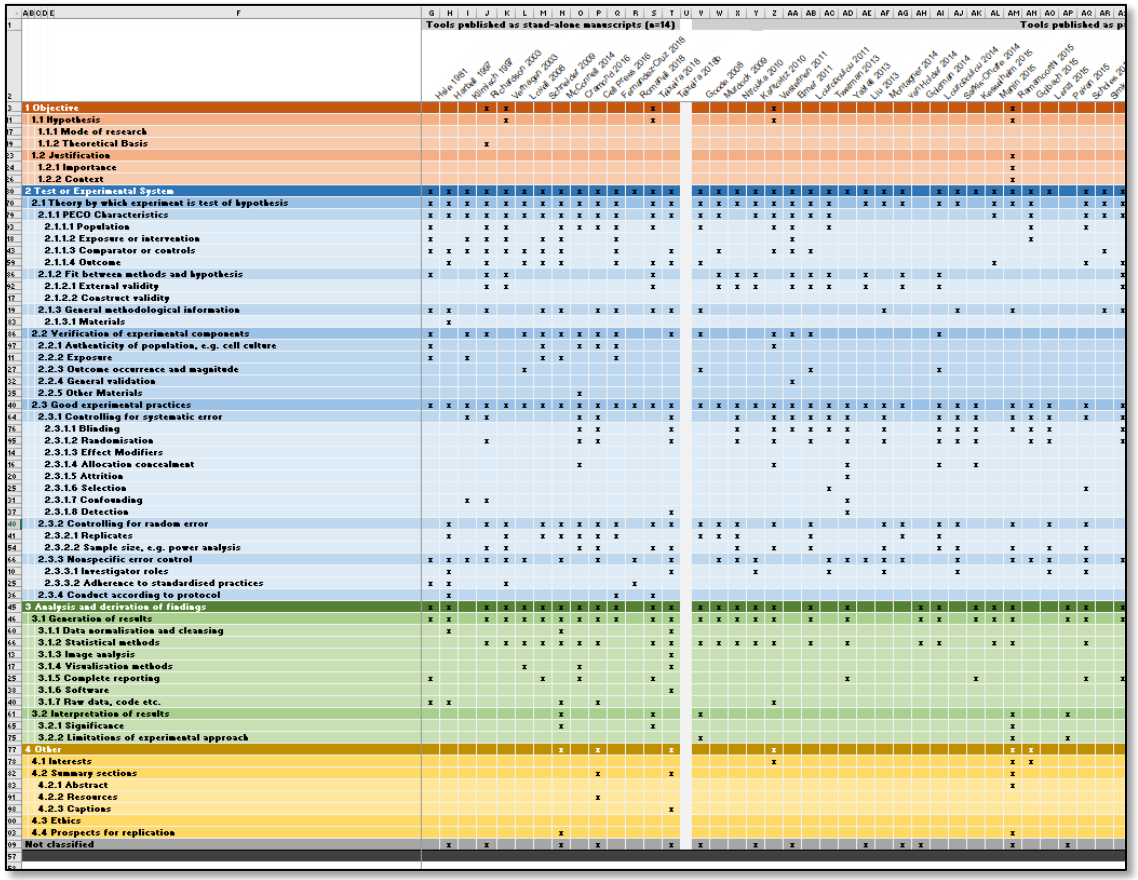
https://pubmed.ncbi.nlm.nih.gov/32778601/

Four steps

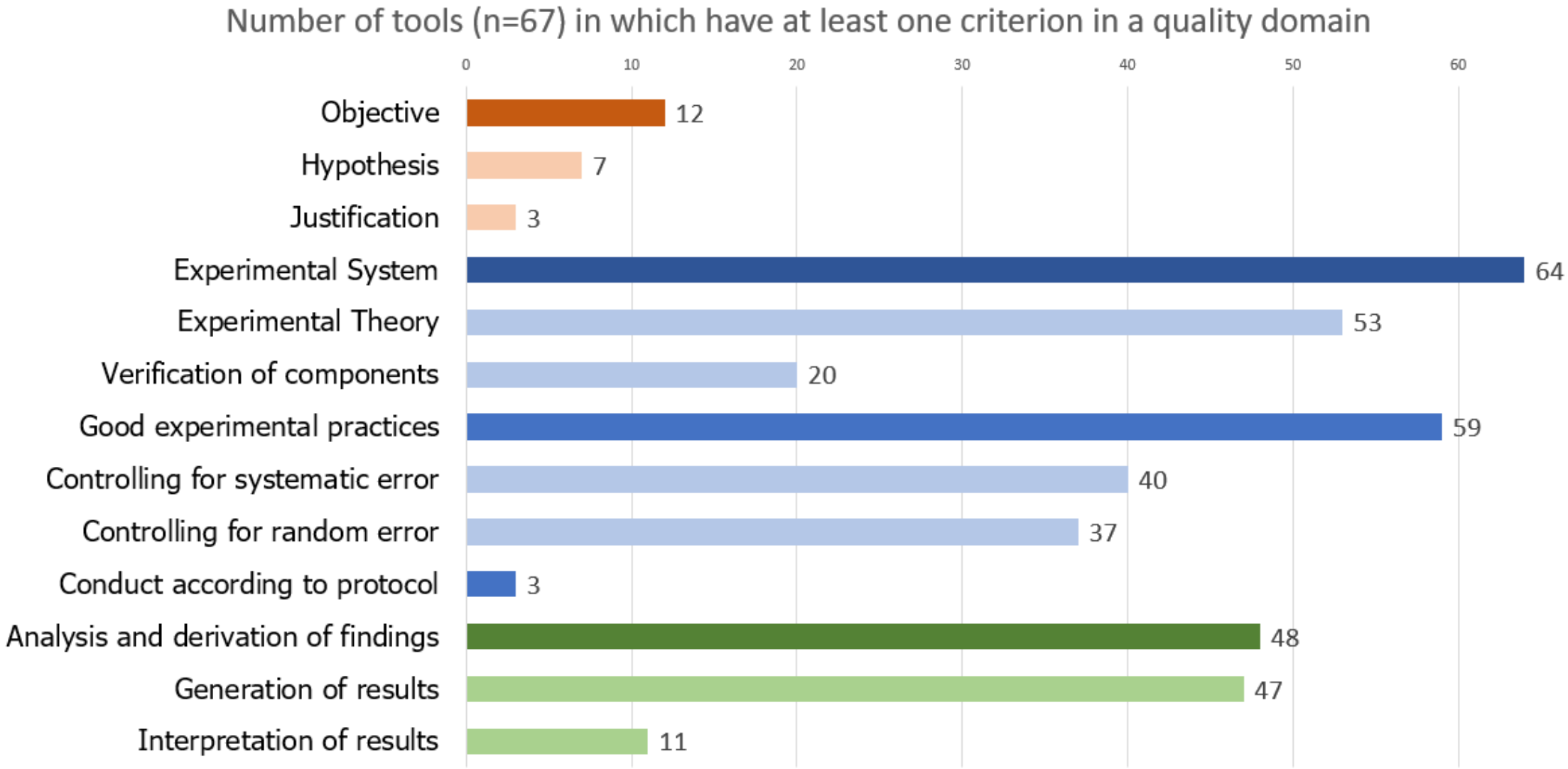
1. Systematic review of in vitro appraisal tools
2. 2-stage Delphi process to determine evaluation criteria
3. 1-stage prototype testing round
4. Workshop to determine the format of the tool

Systematic review of *in vitro* tools

- 67 tools
- 998 total criteria after splitting compound questions
- 676 unique criteria
- 63 assessment categories

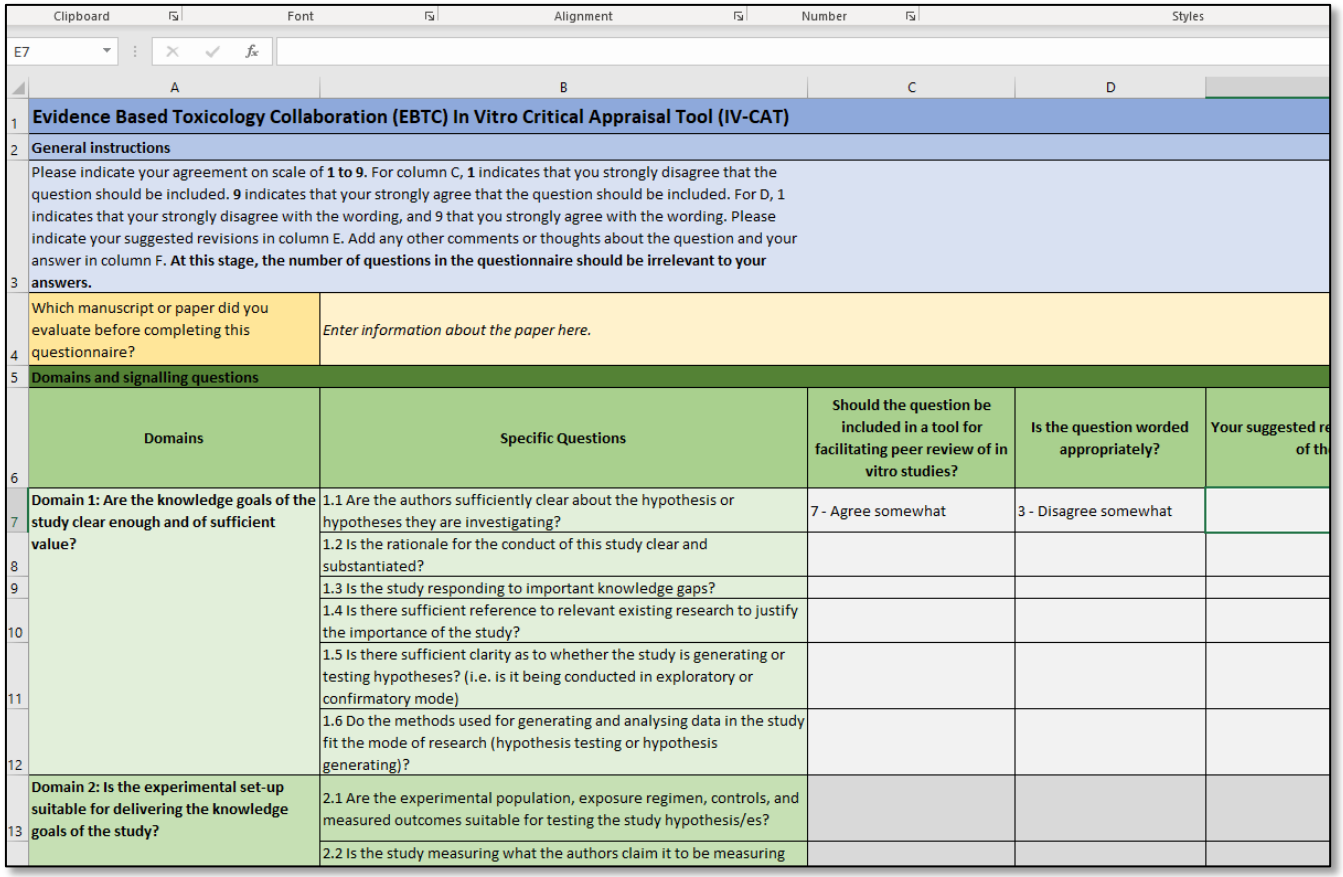


Domain coverage by tools



Delphi process

- Created straw man tool
- Two rounds of Delphi (discovery, elimination, refinement)
- 15 panellists, selected for diversity, unknown to investigators



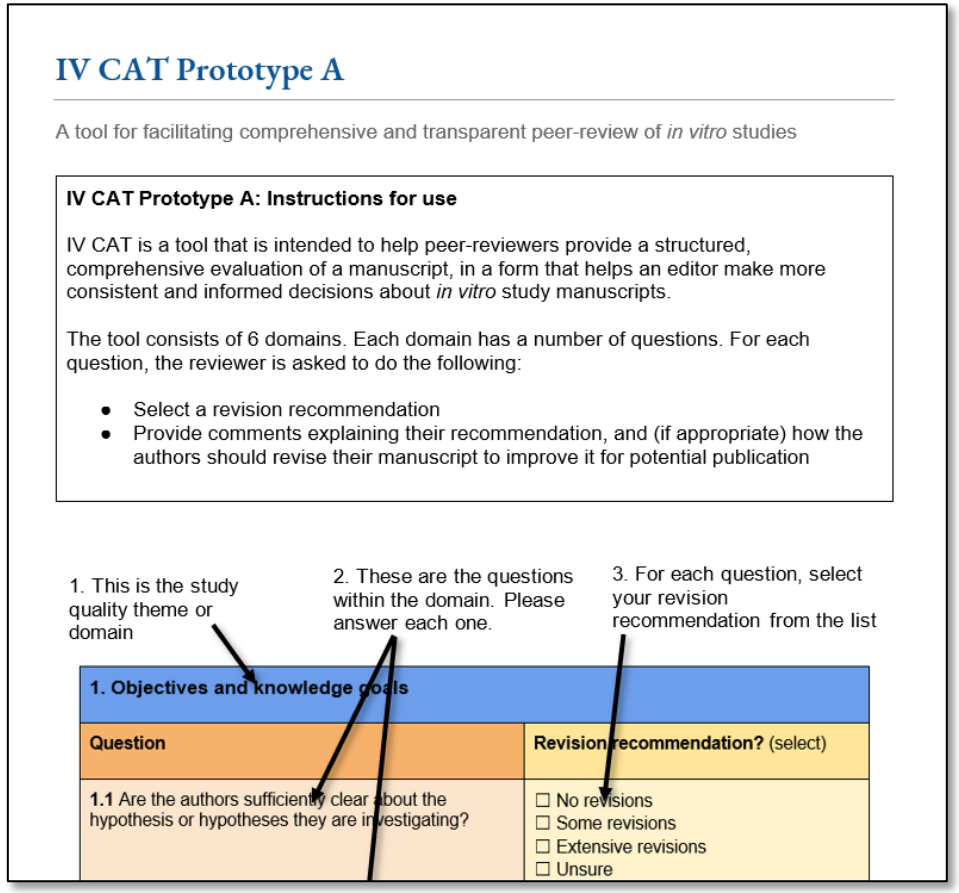
Clipboard | Font | Alignment | Number | Styles

E7

	A	B	C	D
1	**Evidence Based Toxicology Collaboration (EBTC) In Vitro Critical Appraisal Tool (IV-CAT)**			
2	**General instructions**			
3	Please indicate your agreement on scale of **1 to 9**. For column C, **1** indicates that you strongly disagree that the question should be included. **9** indicates that your strongly agree that the question should be included. For D, 1 indicates that your strongly disagree with the wording, and 9 that you strongly agree with the wording. Please indicate your suggested revisions in column E. Add any other comments or thoughts about the question and your answer in column F. **At this stage, the number of questions in the questionnaire should be irrelevant to your answers.**			
4	Which manuscript or paper did you evaluate before completing this questionnaire?	*Enter information about the paper here.*		
5	**Domains and signalling questions**			
6	**Domains**	**Specific Questions**	**Should the question be included in a tool for facilitating peer review of in vitro studies?**	**Is the question worded appropriately?**
7	**Domain 1: Are the knowledge goals of the study clear enough and of sufficient value?**	1.1 Are the authors sufficiently clear about the hypothesis or hypotheses they are investigating?	7 - Agree somewhat	3 - Disagree somewhat
8		1.2 Is the rationale for the conduct of this study clear and substantiated?		
9		1.3 Is the study responding to important knowledge gaps?		
10		1.4 Is there sufficient reference to relevant existing research to justify the importance of the study?		
11		1.5 Is there sufficient clarity as to whether the study is generating or testing hypotheses? (i.e. is it being conducted in exploratory or confirmatory mode)		
12		1.6 Do the methods used for generating and analysing data in the study fit the mode of research (hypothesis testing or hypothesis generating)?		
13	**Domain 2: Is the experimental set-up suitable for delivering the knowledge goals of the study?**	2.1 Are the experimental population, exposure regimen, controls, and measured outcomes suitable for testing the study hypothesis/es?		
		2.2 Is the study measuring what the authors claim it to be measuring		

Prototypes and workshop

- Compared two prototypes designed in response to Delphi
- Participants tested prototypes on published in vitro studies



IV CAT Prototype A

A tool for facilitating comprehensive and transparent peer-review of *in vitro* studies

IV CAT Prototype A: Instructions for use

IV CAT is a tool that is intended to help peer-reviewers provide a structured, comprehensive evaluation of a manuscript, in a form that helps an editor make more consistent and informed decisions about *in vitro* study manuscripts.

The tool consists of 6 domains. Each domain has a number of questions. For each question, the reviewer is asked to do the following:

- Select a revision recommendation
- Provide comments explaining their recommendation, and (if appropriate) how the authors should revise their manuscript to improve it for potential publication

1. This is the study quality theme or domain
2. These are the questions within the domain. Please answer each one.
3. For each question, select your revision recommendation from the list

1. Objectives and knowledge gaps	
Question	**Revision recommendation?** (select)
1.1 Are the authors sufficiently clear about the hypothesis or hypotheses they are investigating?	☐ No revisions ☐ Some revisions ☐ Extensive revisions ☐ Unsure

Reviewed manuscripts

- 2 published papers provided for participants to evaluate
- One paper consistently rejected by participants
- Most reviewers recommended major revisions to both papers
- Need larger test sample, but seems use of the tool would make a difference to peer review and editor decisions if used

Questions for participants

Usability

Please rate each of the following statements *

	Disagree strongly	Disagree somewhat	Neither agree nor disagree	Agree somewhat	Agree strongly
The tool is intuitive to use	○	○	○	○	○
The tool is well structured	○	○	○	○	○
The tool is an appropriate length	○	○	○	○	○
The tool took an appropriate amount of time to complete	○	○	○	○	○
The revision recommendation options are appropriate	○	○	○	○	○

Improve your peer review?

Overall, if you were to use this tool, how much do you think it would improve the comprehensiveness and consistency of your peer-reviews? *

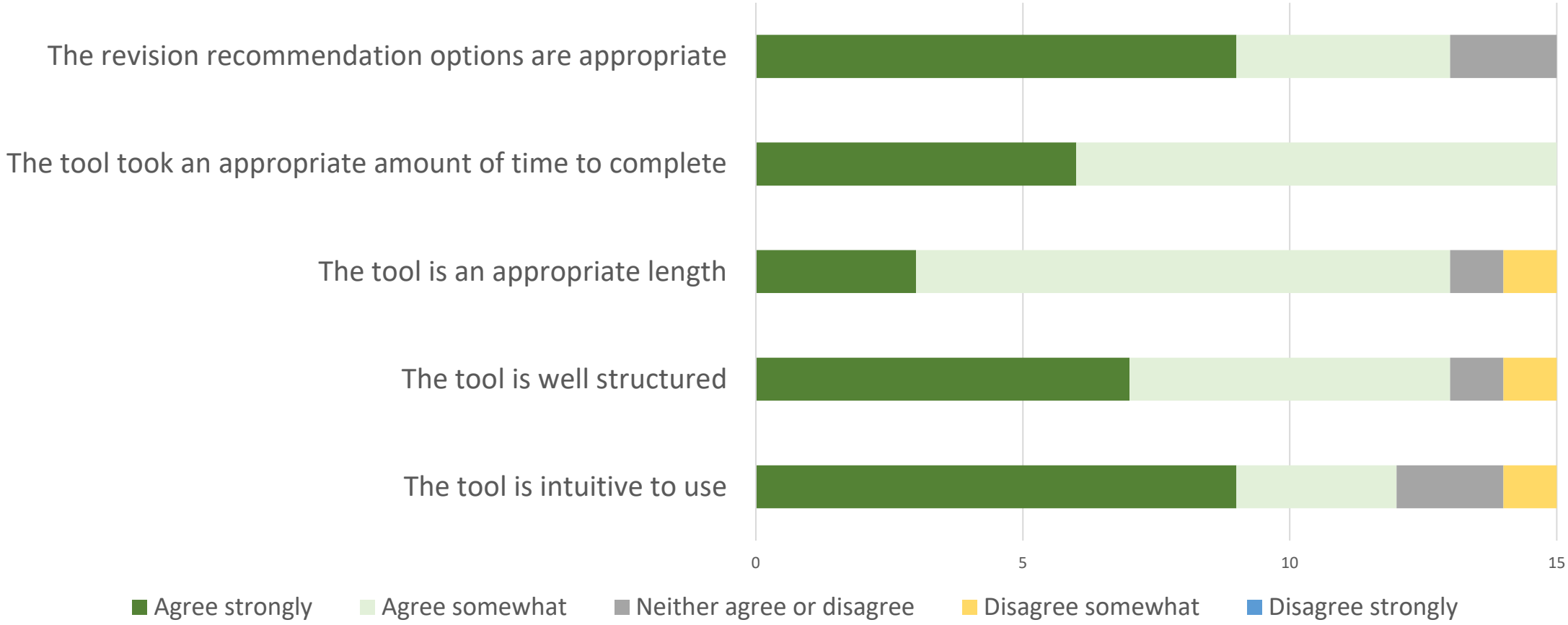
	1	2	3	4	5	
It would make no difference	○	○	○	○	○	It would improve them a lot

Would you use it?

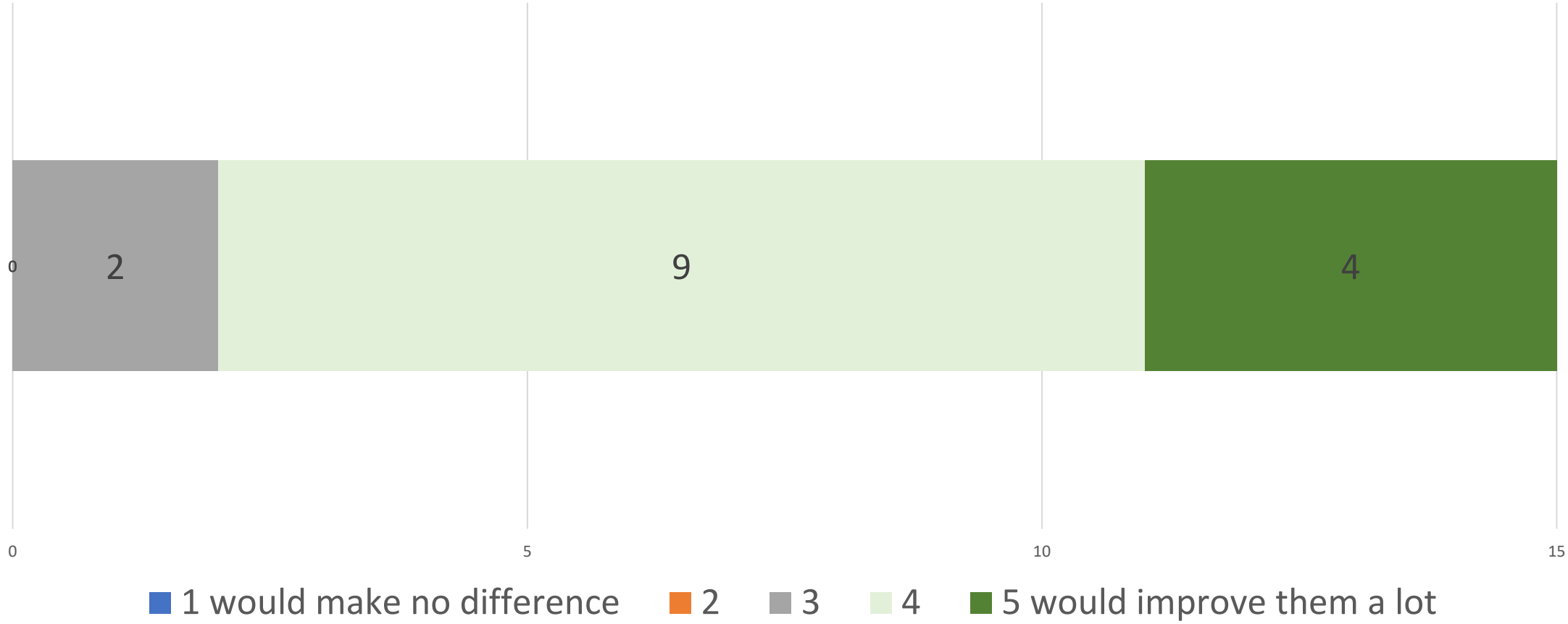
How likely do you think it is, that you would consistently use this tool when reviewing in vitro studies? *

	1	2	3	4	5	
I would use it rarely, if ever	○	○	○	○	○	I would use it every time

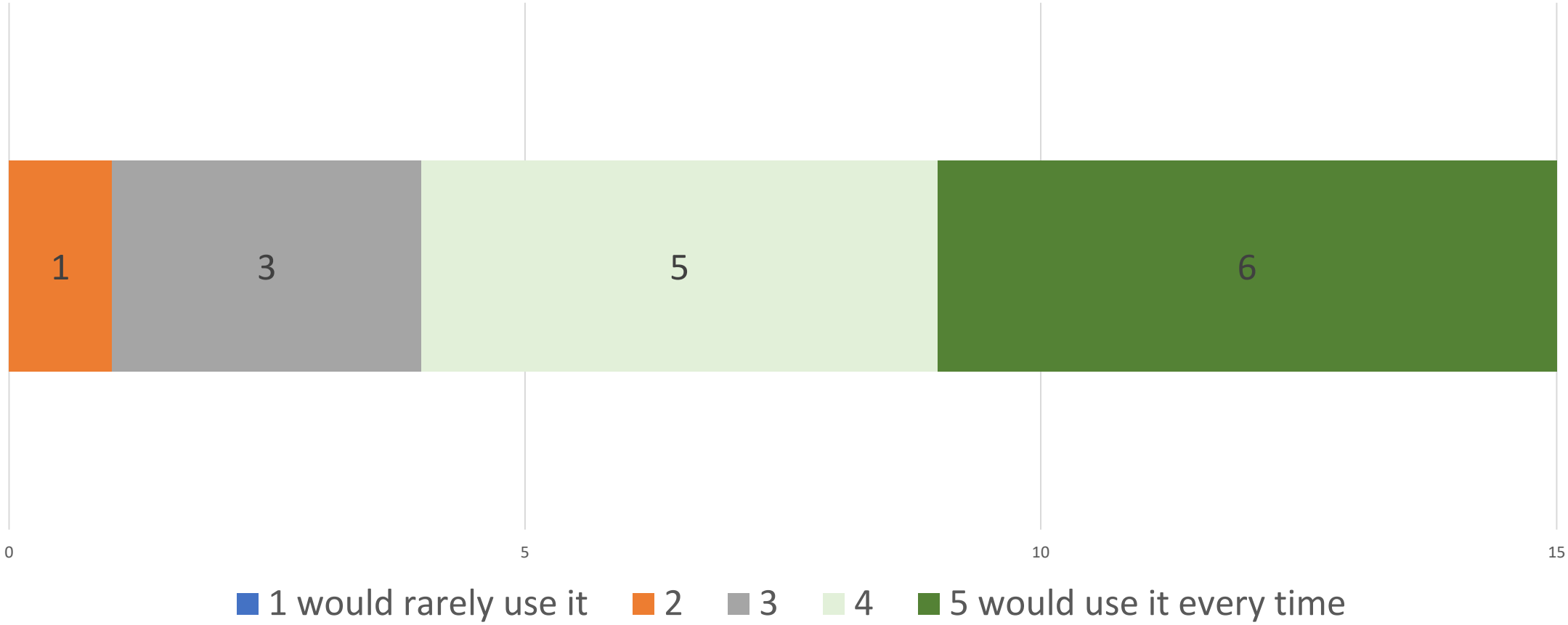
Usability (A)


The revision recommendation options are appropriate
The tool took an appropriate amount of time to complete
The tool is an appropriate length
The tool is well structured
The tool is intuitive to use
0
5
10
15
Agree strongly
Agree somewhat
Neither agree or disagree
Disagree somewhat
Disagree strongly

Improve your peer review? (A)



Would you use it? (A)



Next steps

Lancaster University

ebtc
Evidence-based Toxicology Collaboration

Johns Hopkins
Bloomberg School of Public Health

Radboudumc

Can you help?

- Try it out / user testing
- Training in peer review with tool
- Journal uptake

Improving peer-review?

- Tools are only a (small?) part of it
- Publishing is complex, so is peer-review
- So let's discuss!

Acknowledgements

- Carlijn Hooijmans and Rob de Vries, Radboudumc
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- Rob Wright, Johns Hopkins University
- Stephen Wattam, WAP Consulting Ltd
- ICF: Courtney Lemeris, Jessica Wignall, Caroline Foster, Johanna Rochester, River Williams, Robyn Blain, Kathleen Clark, Jennifer Seed, Alessandria Schumacher

Thank you for listening!

- EBTC operates on a Cochrane-like model, with members running collaborative projects through thematic Working Groups
- Members support each other in conducting high-quality, high-impact projects of strategic value to the EBT community
- To join the collaboration, go to bit.ly/joinEBTC

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