Facilitating healthcare decisions by assessing the certainty in the evidence from preclinical animal studies.

Hooijmans, CR[1], de Vries, RBM[1], ***Ritskes-Hoitinga, J[1]***, Rovers, MM[1], Leeflang, MM[2], IntHout, J[1], Wever, KE[1], Hooft, L[3], de Beer, H[4], Kuijpers, T[5], Macleod, MR[6], Sena, ES[6], ter Riet, G[7], Morgan, RL[8], Thayer, KA[9], Rooney, AA[9], Guyatt, GA[8], Schünemann, HJ[8], Langendam, MW*[2] , on behalf of the GRADE Working Group

[1] Systematic Review Centre for Laboratory animal Experimentation (SYRCLE), Department of Health Evidence, Radboud University Medical Center, Nijmegen, The Netherlands
[2] Department of Clinical Epidemiology, Biostatistics and Bioinformatics, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands
[3] Cochrane Netherlands, University Medical Center, Utrecht, The Netherlands.
[4] Guide2Guidance, The Netherlands
[5] Dutch College of General Practitioners, Utrecht, The Netherlands
[6] Center for Clinical Brain Sciences, University of Edinburgh, United Kingdom
[7] Department of General Practice, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands
[8] Department of Health Research Methods, Evidence, and Impact, McMaster University, Hamilton, ON Canada; Department of Medicine, McMaster University, Hamilton, Canada
[9] Division of the National Toxicology Program, National Institute of Environmental Health Sciences, National Institutes of Health, Department of Health and Human Services, USA

Background

Laboratory animal studies are used in a wide range of human health related research areas, such as basic biomedical research, drug research, experimental surgery and environmental health. The results of such studies are currently used to inform decisions regarding clinical research in humans, for example the decision to proceed to clinical trials. If the research question relates to potential harms with no expectation of benefit (e.g., toxicology), studies in experimental animals may provide the only relevant data and directly inform clinical management decisions.

Objectives, Methods, Results

Systematic reviews and meta-analyses are important tools to provide robust and informative evidence summaries of these animal studies. Rating how certain we are about the evidence could provide important information about the probability of translational success of findings in experimental animal studies to clinical practice and probably improve it. Evidence summaries and ratings of evidential certainty could also be used (1) to support selection of interventions with best therapeutic potential to be tested in clinical trials, (2) to justify a regulatory decision limiting human exposure (to drug or toxin), or to (3) support decisions on the utility of further animal experiments.

Conclusions

The Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) approach is the most widely used framework to rate the certainty in the evidence and strength of health care recommendations. We will present how the GRADE approach can be used to rate the certainty in the evidence of preclinical animal studies in the context of therapeutic interventions.

Further Reading

Hooijmans et al. 2018 http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0187271