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To the Editor: The quality and reliability of much animal research is in question. Research which is unreliable or of low quality represents an unacceptable waste of animals and research resources. In the US alone, the cost of irreproducible research has been estimated at \$28 billion annually, and issues with research design and reporting are estimated to account for half of that waste¹. To address these issues, the NC3Rs developed the ARRIVE guidelines to improve the reporting of *in vivo* research.^{2,3} We now present the Experimental Design Assistant (EDA; <https://eda.nc3rs.org.uk>), a freely accessible web-based tool, which was launched to help researchers improve the design, conduct, analysis and reporting of animal experiments.

The system includes a computer-aided design tool through which the user develops a diagram that embodies the experimental plan. The diagram offers a new standard notation for describing experiments, where methodological details and analysis plans are explicit (Figure 1). This facilitates communication between collaborators, funding bodies, ethical review committees, journal editors and peer reviewers; it also allows detailed record-keeping, and might serve as an *ex ante* registered protocol.⁴

The structure of EDA diagrams is based on a series of relationships between the different components of the experiment. This allows the use of computer-based logical reasoning to provide feedback and advice on the experimental plans. The feedback helps researchers improve their experimental design, for instance by highlighting missing information or problems with internal consistency. It also provides assistance with identifying and characterising the independent variables and outcome measures to be included in the analysis. Advice about common nuisance variables,

which threaten the internal validity of many animal experiments, is also provided, along with practical suggestions to account for such variables in the randomisation and the data analysis. The feedback does not restrict researchers to using a particular design type, but promotes a better understanding of the implications of common design pitfalls so that researchers can make informed decisions. The feedback also suggests methods of statistical analysis that are appropriate for a given design, along with advice on any data requirements (“assumptions”) for a given test, and possible data transformations.

Other features of the EDA include support for randomisation, blinding and power calculations, procedures which are still underused in animal research ⁵. Based on the diagram, the system generates a randomisation sequence for the study, taking into account any blocking factors. The sequence can be sent directly to a third party nominated by the investigator, thus allowing the investigator to remain unaware of the animals’ group allocation until the data have been collected and analysed. Animal experiments are often too small to yield meaningful results ⁶; the EDA’s power calculation tool – along with extensive guidance on how to choose the appropriate calculation and identify the parameters required – will help researchers determine optimal sample sizes for each experiment.

In conclusion, the EDA is a new resource to help improve the quality of animal research. It can help researchers design robust and reliable experiments in two ways. Firstly, it ensures that the experimental plans are explicit and transparent, thus allowing detailed scrutiny before and after data are collected. Secondly, it encourages improvements by providing researchers with critical feedback, targeted information and access to randomisation and power analysis tools. We will continue to incorporate user input in planned future developments to ensure that the EDA evolves in line with the needs of the research community

References

- 1 Freedman, L. P., Cockburn, I. M. & Simcoe, T. S. The economics of reproducibility in preclinical research. *PLoS Biol* **13**, e1002165, doi:10.1371/journal.pbio.1002165 (2015).
- 2 Cressey, D. Surge in support for animal-research guidelines. *Nature* (2016). <http://www.nature.com/news/surge-in-support-for-animal-research-guidelines-1.19274>.
- 3 Kilkenny, C., Browne, W. J., Cuthill, I. C., Emerson, M. & Altman, D. G. Improving bioscience research reporting: the ARRIVE guidelines for reporting animal research. *PLoS Biol* **8**, e1000412, doi:10.1371/journal.pbio.1000412 (2010).
- 4 Nosek, B. A., Ebersole, C. R., DeHaven, A. C. & Mellor, D. T. The Preregistration Revolution. *Preprint*, doi:10.17605/OSF.IO/2DXU5 (2017).
- 5 Macleod, M. R. *et al.* Risk of bias in reports of in vivo research: A focus for improvement. *PLoS Biol* **13**, e1002273, doi:10.1371/journal.pbio.1002273 (2015).
- 6 Button, K. S. *et al.* Power failure: why small sample size undermines the reliability of neuroscience. *Nat Rev Neurosci* **14**, 365-376, doi:10.1038/nrn3475 (2013).

FIGURE 1

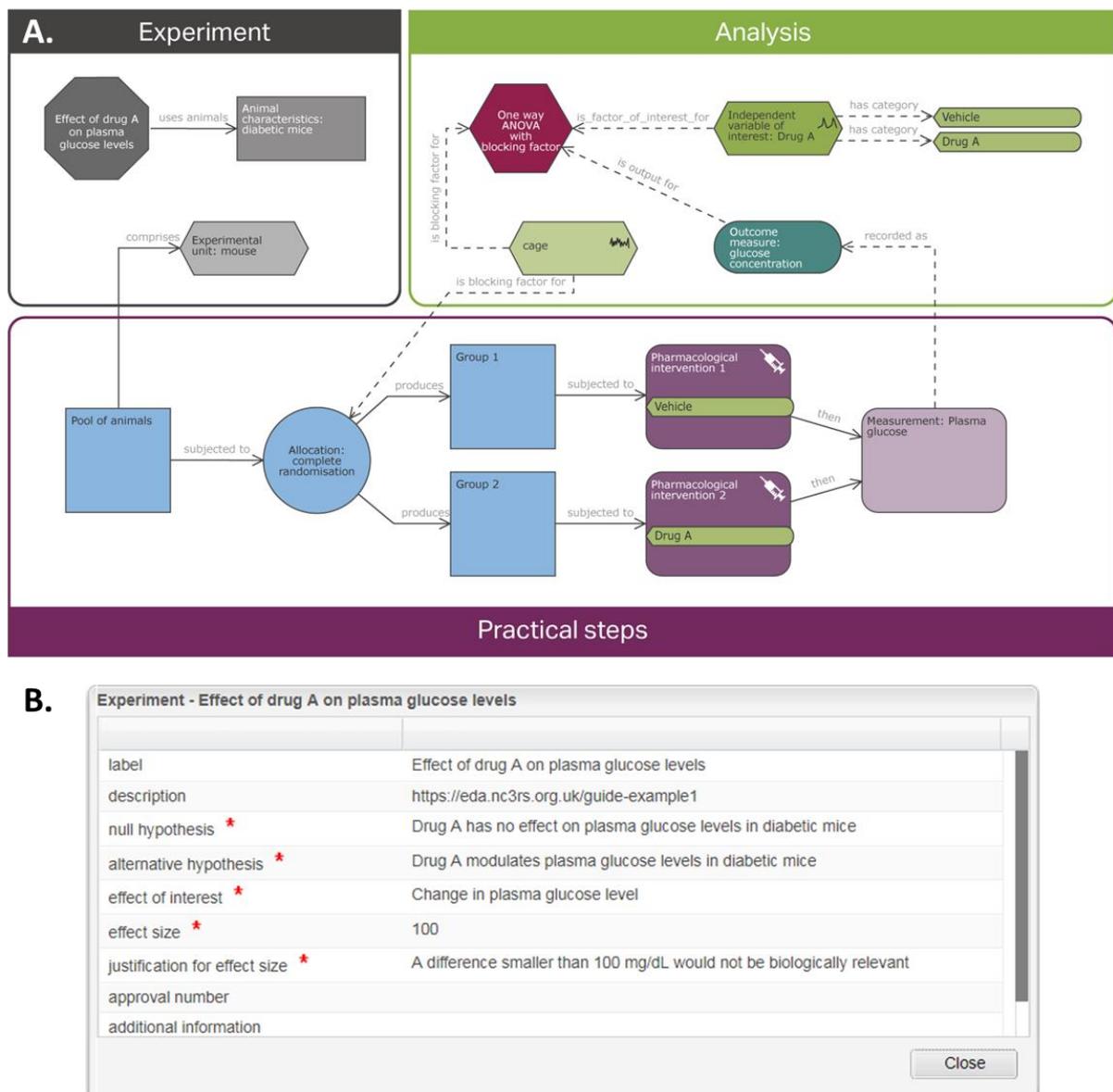


Figure 1. Example of an EDA diagram.

(A) EDA diagram representing a two-group comparison in which each cage of mice will contain both treatments. Diagrams are composed of nodes and links to represent an entire experimental plan. The grey nodes contain high level information about the experiment, such as the null and alternative hypotheses, the effect of interest, the experimental unit and the animal characteristics. The blue and purple nodes represent the practical steps carried out in the laboratory such as the allocation to groups, the group sizes and role in the experiment, the treatments and the measurements taken. The green and pink nodes represent the analysis, the outcome measures and the independent variables of interest and nuisance variables (e.g. blocking factors). (B) Properties of the experiment node. Each node contains distinct properties where details related to a specific step of the experiment are captured.