

## Preclinical Confirmatory Studies and Systematic Reviews

### Glossary

| Term                     | Definition   | Reference   |
|--------------------------|--|---|
| Accessibility of results | The degree to which results are accessible e.g. for other researchers, see also Open Access and Open Data  | -   |
| Bias                     | Systematic error in an estimate (e.g., variance, effect size) caused by violations of assumptions, inadequacies in the design, conduct, or analysis of an experiment.  | <a href="https://catalogofbias.org/">https://catalogofbias.org/</a>   |
| Blinding                 | Procedure to prevent performance bias. Will ensure that experimenters are unaware of the intervention condition during outcome assessment and analysis                 | <a href="https://catalogofbias.org/biases/performance-bias/">https://catalogofbias.org/biases/performance-bias/</a>                                 |
| Comparator               | Comparator group acts as a control with an effective intervention (as opposed to a placebo group). Allows comparison of effect sizes between two effective treatments. | Active comparator arm:<br><a href="https://clinicaltrials.gov/ct2/about-studies/glossary">https://clinicaltrials.gov/ct2/about-studies/glossary</a> |

| Term  | Definition  | Reference   |
|---|---|---|
| <b>Confirmatory preclinical study</b>       | Experimental studies to scrutinize preclinical findings through replication of results alongside investigations into boundary conditions and robustness through conduct of additional (control) conditions and multi center studies. See also Exploratory preclinical study | <a href="https://doi.org/10.1371/journal.pbio.1001863">https://doi.org/10.1371/journal.pbio.1001863</a> |
| <b>Construct Validity</b>                   | Extent to which a measured outcome is representative of the phenomenon studied  | <a href="https://doi.org/10.1371/journal.pmed.1001489">doi: 10.1371/journal.pmed.1001489</a>            |
| <b>Control (negative, positive control)</b> | A baseline comparison group that receives no or placebo treatment (negative) or an effective comparison treatment (positive; see comparator).   | -   |
| <b>Data management</b>                      | Protocol describing data storage, data sharing, data preservation, and data description   | <a href="http://www.dcc.ac.uk/webfm_send/1279">http://www.dcc.ac.uk/webfm_send/1279</a>                 |
| <b>Data security</b>                        | Models to ensure management of threats to data privacy, storage, longevity  | -   |

| Term                     | Definition   | Reference   |
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| Data sharing             | Making data accessible and reusable for others to different degrees by providing direct links to repositories or describing procedures through which data can be obtained. | -   |
| Data synthesis strategy  | Strategy to combine data from various sources into one estimate of an effect (e.g., strategy for a meta-analysis)  | -   |
| Design of a study        | The setup of a study, specifically what interventions take place, what measurements are taken, what procedures are implemented to reduce bias                              | <a href="https://www.nc3rs.org.uk/experimental-design-assistant-eda">https://www.nc3rs.org.uk/experimental-design-assistant-eda</a>   |
| Dissemination of results | The way results are communicated and shared with peers and a broader public. See also Open Access  | <a href="http://ec.europa.eu/research/participants/docs/h2020-funding-guide/grants/grant-management/dissemination-of-results_en.htm">http://ec.europa.eu/research/participants/docs/h2020-funding-guide/grants/grant-management/dissemination-of-results_en.htm</a> |
| Effect size              | Quantitative measure that estimates the magnitude of differences between groups, or relationships between variables.   | <a href="https://doi.org/10.4300/JGME-D-12-00156.1">https://doi.org/10.4300/JGME-D-12-00156.1</a>   |

| Term                          | Definition   | Reference   |
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| Efficacy of the intervention  | Outcome measure of the effect of interest. See also Effect Size.   | -   |
| Experimental unit             | Biological entity subjected to an intervention independently of all other units, such that it is possible to assign any two experimental units to different treatment groups.  | <a href="https://eda.nc3rs.org.uk/experimental-design-unit">https://eda.nc3rs.org.uk/experimental-design-unit</a>                                   |
| Exploratory preclinical study | Studies that search for novel biological associations and phenomena in preclinical settings often employing less rigorous experimental designs, low sample sizes. Further, many analyses are conducted to generate hypotheses. To avoid false positive results, discovered effects need to be confirmed in further preclinical studies | <a href="https://doi.org/10.1371/journal.pbio.1001863">https://doi.org/10.1371/journal.pbio.1001863</a>   |
| Ecological validity           | Extent to which results provide a correct basis for generalisations to other contexts of the same population.  | Paragraph 2.6:<br><a href="https://learningstatisticswithr.com/book/studydesign.html">https://learningstatisticswithr.com/book/studydesign.html</a> |
| External Validity             | Extent to which results provide a correct basis for generalisations to other populations or specifically in preclinical research to humans.  | Paragraph 2.6:<br><a href="https://learningstatisticswithr.com/book/studydesign.html">https://learningstatisticswithr.com/book/studydesign.html</a> |

| Term                                    | Definition  | Reference   |
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| Extraction of data from primary studies | Process of extracting the relevant information to a synthesis from individual studies (e.g., an effect size to be included in a meta-analysis)            | -   |
| FAIR criteria                           | Acronym for data sharing standards: Findable, Accessible, Interoperable, Reusable.  | <a href="http://www.nature.com/articles/d41586-019-01720-7">http://www.nature.com/articles/d41586-019-01720-7</a> |
| False positive                          | Statistically significant result obtained by chance when the effect being investigated does not exist.  | <a href="https://doi.org/10.1038/nmeth.2738">https://doi.org/10.1038/nmeth.2738</a>                               |
| False negative                          | Statistically non-significant result obtained when the effect being investigated genuinely exists.  | <a href="https://doi.org/10.1038/nmeth.2738">https://doi.org/10.1038/nmeth.2738</a>                               |
| Feasibility                             | Likelihood that an experiment can be conducted under the given constraints (number of experimental units available, laboratory equipment, time, personal) |   |

| Term                                    | Definition   | Reference   |
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| Independent variable of interest        | Factor that a researcher manipulates within a controlled environment in order to test its impact on the outcome measured. Also known as: predictor variable, factor of interest.   | Paragraph 2.4:<br><a href="https://learningstatisticswithr.com/book/studydesign.html">https://learningstatisticswithr.com/book/studydesign.html</a>   |
| Internal Validity                       | Refers to the rigour of the study design and statistical analysis to isolate cause and effect, and attribute the effect observed to manipulation of the independent variable of interest. In an experiment with high internal validity, sources of bias and chance observations are minimised. See Bias, Randomisation, and Blinding | Paragraph 2.6:<br><a href="https://learningstatisticswithr.com/book/studydesign.html">https://learningstatisticswithr.com/book/studydesign.html</a>   |
| Long-term safeguarding of research data | Preservation of data over long time scales (at least 10 years). See also data security, data management  | <a href="https://www.dfg.de/foerderung/antrag_gueltig_gremien/antragstellende/nachnutzung_forschungsdaten/index.html">https://www.dfg.de/foerderung/antrag_gueltig_gremien/antragstellende/nachnutzung_forschungsdaten/index.html</a> |
| Metadata                                | Data about experimental, datasets outlining content, timestamp, authors, explanation of variables.   | <a href="https://doi.org/10.1038/sdata.2016.18">https://doi.org/10.1038/sdata.2016.18</a>   |
| Methods against bias                    | Procedures to reduce bias in a study like randomisation and blinding but also improved statistical methods   | -   |

| Term                                 | Definition  | Reference   |
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| Multicenter study                    | Procedure where multiple labs collect data for the same study design to investigate variability between labs to estimate generalisability of results                                      | <a href="https://journals.plos.org/plosbiology/article?id=10.1371/journal.pbio.2003693">https://journals.plos.org/plosbiology/article?id=10.1371/journal.pbio.2003693</a>                               |
| Nuisance variable                    | Sources of variability or conditions that could potentially bias results. Also known as: confounding factor, confounding variable   | Paragraph 2.7:<br><a href="https://learningstatisticswithr.com/book/studydesign.html">https://learningstatisticswithr.com/book/studydesign.html</a>   |
| Null Hypothesis Significance Testing | NHST is a method of statistical inference to assess the probability that the observed data (or more extreme) will occur given a null hypothesis of no effect of our variable of interest. | <a href="https://www.nature.com/articles/nmeth.2698">https://www.nature.com/articles/nmeth.2698</a>   |
| Open access                          | Freely available research articles for anyone, no subscription needed.  | <a href="https://doi.org/10.12688/f1000research.8460.3">https://doi.org/10.12688/f1000research.8460.3</a>   |
| Open data                            | Freely available and reusable data, without barriers see FAIR criteria  | <a href="https://book.fosteropenscience.eu/en/02OpenScienceBasics/02OpenResearchDataAndMaterials.html">https://book.fosteropenscience.eu/en/02OpenScienceBasics/02OpenResearchDataAndMaterials.html</a> |

| Term  | Definition  | Reference   |
|---|---|---|
| Outcome measure   | Any variable recorded during a study to assess the effects of a treatment or experimental intervention. Also known as: dependent variable, response variable  | Paragraph 2.4:<br><a href="https://learningstatisticswithr.com/book/studydesign.html">https://learningstatisticswithr.com/book/studydesign.html</a> |
| Statistical Power   | Probability that a significance test detects an effect (i.e. a deviation from the null hypothesis), if an effect exists (i.e. true positive result).  | <a href="https://doi.org/10.1177/0956797616647519">https://doi.org/10.1177/0956797616647519</a>   |
| Pre-registration of the study, pre-registration of study protocol | Formal registration of methods, experimental design, and analysis procedures prior to data-collection   | <a href="https://doi.org/10.1177/1745691618771357">https://doi.org/10.1177/1745691618771357</a>   |
| Registered Report   | Type of article that undergoes a two-stage review. Before data collection reviewers assess the scientific premise and in depth methodology including an analysis plan. Upon acceptance in stage 1, articles are in principle accepted independent of the results. After data collection, reviewers only assess whether experiments were conducted according to the plan from stage 1. | <a href="https://doi.org/10.1016%2Fj.cortex.2012.12.016">https://doi.org/10.1016%2Fj.cortex.2012.12.016</a>   |
| Preprint  | Sharing of a manuscript prior to peer-review mostly on dedicated repositories like BioArxiv.  | <a href="https://www.plos.org/why-preprint">https://www.plos.org/why-preprint</a>   |



| Term                                  | Definition   | Reference   |
|---------------------------------------|--|---|
| Publication bias                      | Studies remain often unpublished when an outcome is contrary to the initial hypothesis. This leads to an overrepresentation of positive findings impeding a meta analytic assessment of the investigated effect. | <a href="https://catalogofbias.org/biases/publication-bias/">https://catalogofbias.org/biases/publication-bias/</a>   |
| Quality management                    | Procedures in a laboratory to increase study quality through standard operating procedures that ensure rigorous experimental design and reduction of measurement errors.   | <a href="https://doi.org/10.15252/embr.201847143">https://doi.org/10.15252/embr.201847143</a>   |
| Quality-assessment of primary studies | Retrospective procedure to evaluate whether studies follow reporting standards and whether they are at a risk of bias.   | <a href="https://handbook-5-1.cochrane.org/chapter_8/table_8_5_at_the_cochrane_collaborations_tool_for_assessing.htm">https://handbook-5-1.cochrane.org/chapter_8/table_8_5_at_the_cochrane_collaborations_tool_for_assessing.htm</a> |
| Randomisation                         | Assignment procedure to control for random variations between experimental units included in a study.  | <a href="https://eda.nc3rs.org.uk/experimental-design-allocation">https://eda.nc3rs.org.uk/experimental-design-allocation</a>   |
| Repository                            | Online database where information like experimental data or analysis code is deposited and archived  | -   |

| Term                      | Definition   | Reference   |
|---------------------------|--|---|
| Rigor                     | The strict application of the scientific method to ensure robust and unbiased experimental design, methodology, analysis, interpretation and reporting of results. This includes full transparency in reporting experimental details so that others may reproduce and extend the findings. | <a href="https://grants.nih.gov/reproducibility/faqs.htm#4828">https://grants.nih.gov/reproducibility/faqs.htm#4828</a>   |
| Sample size               | Number of experimental units per group, also referred to as N number. See also Statistical Power and Sample Size determination   | -   |
| Sample size determination | Procedures to determine how many experimental units to include in a design. Depends on power, effect size, and significance level  | <a href="https://doi.org/10.1038/nmeth.2738">https://doi.org/10.1038/nmeth.2738</a>   |
| Scientific premise        | Rigor of the prior research: strengths and weakness of the data and previously performed work upon which a study is built upon   | <a href="https://nexus.od.nih.gov/all/2016/01/28/scientific-premise-in-nih-grant-applications/">https://nexus.od.nih.gov/all/2016/01/28/scientific-premise-in-nih-grant-applications/</a> |
| Search strategy           | Strategy to search databases for relevant studies, typically done systematically with a pre-specified set of searches and search terms.  | -   |

| Term            | Definition   | Reference   |
|-----------------|--|---|
| Sharing of data | The extent to which data is made available to others, see also Open Data   | -   |
| Study quality   | The assessment of a study's quality with respect to design, measurement, question  | -   |
| Triangulation   | Scientific method for evidence generation through use of different approaches addressing the same underlying question under consideration of specific biases of each approach. | <a href="https://doi.org/10.1038/d41586-018-01023-3">https://doi.org/10.1038/d41586-018-01023-3</a> |