Recommendation for the use of the MDAR (Materials, Design, Analysis, Reporting) framework and checklist for the reporting of experimental studies in the life sciences

Versions:

25 April 2019	Draft	Draft by Veronique Kiermer, following RIGHT[1] checklist
24 May 2019	Final draft	Including revisions by Sowmya Swaminathan, Debbie Sweet, Valda Vinson, Malcolm Macleod, Veronique Kiermer - elements highlighted in orange will be addressed in the next version.
22 Sept 2019	v2	Including description of the pilot (VK, SS, VV)
18 Oct 2019	v2.1	Correction of MIBBI / FAIRsharing references
31 May 2020	V3 draft	Working draft to incorporate feedback from expert consultation
20 July 2020	V4 draft	Incorporated consensus response to feedback from expert consultation and testing - for working group review
12 Oct 2020	V5 draft	Accepted modifications reviewed by the Working Group as part of v4. Introduced edits for consistency with Commentary language in preparation for release. Added sections on Review, Fuding, Declaration and Management of interests and other information to conform with RIGHT guideline.
22 Nov 2020	V5 final	

Executive summary: The MDAR Framework is an information framework established as a minimum set of requirements generically applicable to reporting studies in the life sciences. The purpose of this framework is to increase reporting transparency, taking into account the current reporting practices and the direction of improvements that are necessary to improve reproducibility. This recommendation (the Elaboration Document) documents the definition of the MDAR Framework and its associated optional implementation tool, the MDAR checklist. It also sets out expectations for MDAR signatories, highlights possible uses of the framework and provides explanation and context for all elements that compose the MDAR reporting framework.

Abbreviations and acronyms:

MDAR	Materials Design Analysis Reporting - used it in reference to the information framework herein described
DOI	Digital Object Identifier
EQUATOR	http://www.equator-network.org/

[1] Adapted from the RIGHT checklist http://www.right-statement.org/right-statement/checklist

ARRIVE	Animal Research: Reporting of in vivo Experiments; https://www.nc3rs.org.uk/arrive-guidelines
FAIR	Findable Accessible Interoperable Reusable
FAIRsharing	https://fairsharing.org/standards

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I. BACKGROUND

Problem statement

In life sciences research, reproducibility of published results is impaired when core information about research materials, study design, experimental design, data and analysis are not available or are inadequately reported. Inconsistent reporting may lead to incorrect interpretation of results and prevent replicability, which in turn may waste research resources and erode trust in the scientific findings.

Aims

The MDAR information framework has been designed as a recommendation for minimum reporting requirements to improve transparency and reproducibility. In addition to a minimum set of requirements, it provides a matching set of best practices representing the direction in which the minimum requirement may evolve over time.

The original statement of task that guided the working group is available[2]. The MDAR information framework is not comprehensive and does not attempt to supersede any existing reporting standards in practice within research communities. It is a generalist framework intended to be broadly applicable to

[2] Chambers, Karen, Andy Collings, Chris Graf, Veronique Kiermer, David T. Mellor, Malcolm Macleod, Sowmya Swaminathan, et al. 2019. "Towards Minimum Reporting Standards for Life Scientists." MetaArXiv. April 30. doi:10.31222/osf.io/9sm4x

research in the life sciences and is meant to be compatible with, and enhanced by, existing specialist standards (e.g., standards and guidelines maintained at EQUATOR Network[3], FAIRsharing[4] and ARRIVE[5]).

The MDAR information framework is expressed in three related documents:

> **The MDAR Framework** describes the information covered by MDAR, organized in a two-dimensional, expandable table. The rows define the reporting objects that are covered by MDAR (according to the sequence Materials, Design, Analysis, Reporting) and the columns list two sets of reporting requirements -- the minimum reporting requirements and desirable elements of reporting which are considered best practice but may not be required at this time. The table is expected to evolve over time, through additions of reporting elements and through elements considered best practice being adopted as requirements.
>
> **The MDAR Checklist** represents the minimum information requirements, and also includes proposed wording for the more aspirational requests included as 'best practice'. The checklist may be adopted as an author-facing tool, to facilitate the provision of all the minimum information; as a journal-facing tool, to facilitate the confirmation that all the minimum information has been provided; and might be used by third parties, to measure progress towards transparency and reproducibility.
>
> The present **MDAR Elaboration Document** follows the guidance set in the RIGHT statement to provide transparent description of the genesis of the MDAR Framework and clarify its content to support implementation.

The three MDAR documents, alongside supplementary documentation, will be hosted on the Open Science Framework by the Center for Open Science, which will act as custodian and ensure the preservation of these documents as community resources. [INSERT RECOMMENDATION OF CITATION AND DOI OF THE FRAMEWORK, CHECKLIST AND SUPPLEMENTARY MATERIAL]

Target populations

The MDAR information framework is designed for researchers reporting studies in the life sciences, principally in the biological, biomedical and preclinical research areas.

The MDAR documents and tools are designed for journals and other publication platforms wishing to increase their reporting transparency standards and become MDAR signatories.

We acknowledge that the framework is likely to be more useful for certain disciplines than others, as it was derived with a focus on laboratory based basic research. We also acknowledge that discipline-specific guidance and norms exist that have not been incorporated in the minimum

[3] http://www.equator-network.org/
[4] https://fairsharing.org/standards
[5] https://www.nc3rs.org.uk/arrive-guidelines

requirements. Where they exist, community-endorsed discipline-specific reporting guidelines should be considered best practice.

End-users and settings

By signing up to the MDAR Framework, the journal signatories express their support for transparent reporting principles outlined by the MDAR Framework, and commit to taking steps to incorporate the MDAR guidelines into their journal practices. The Framework includes minimum information that is deemed necessary to ensure adequate reporting of specific objects as well as best practice requirements that the MDAR Framework identifies as aspirational based on current community readiness. Each signatory may choose to limit their request for information to the minimum requirements or to extend it to include more information, based on their own specialty and the readiness of their community.

The MDAR framework is agnostic to the means of implementation chosen by the signatory. For example, journals may choose to collect information from authors using the MDAR checklist or through other means. While adoption of the MDAR checklist is not a requirement for MDAR signatories, it is a practical tool for implementers seeking to integrate a ready-to-use instrument in their workflows. Others may choose different means to implement the MDAR framework and may opt to supplement the checklist with additional information requests.

However, we strongly recommend that signatories seek to harmonize, wherever possible, the language of author-facing requests to that presented in the checklist. Consistent language will reinforce norms and simplify compliance for authors who interface with multiple implementers, including journals and funders.

Authors who wish to increase the reporting transparency of their manuscripts, grant application and grant reporting may use the checklist as a tool to verify their outputs before submission, and can even use it to guide study design.

Guideline development groups

MDAR steering group:

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MDAR tester group:
The checklist has been tested in the context of journal submission workflows by 13 journals from 10 publishers:
Science (AAAS), Scientific Reports (Springer Nature), BMC Microbiology (Springer Nature), PLOS Biology (PLOS), eLIFE (eLIFE), EMBO journals (EMBO Press), PNAS (NAS Press), Ecology & Evolution (Wiley), Microbiology Open (Wiley), Epigenetics (Taylor & Francis), Molecular Cancer Therapeutics (AACR), PeerJ, F1000R.
The journals followed a joint protocol for this pilot [link to protocol] -- see 'Development process below'.

Evidence
Baseline reference material
STAR methods (Cell Press): https://www.cell.com/cell/abstract/S0092-8674(16)31072-8
Nature Research checklists: https://www.nature.com/authors/policies/checklist_old.pdf (2013)
https://www.nature.com/documents/nr-reporting-summary-flat.pdf (2017)
eLife checklist:https://elife-cdn.s3.amazonaws.com/xpub/guides/transparent_reporting.pdf
EMBO checklist: http://emboj.embopress.org/authorguide#transparentprocess
PLOS policies: https://journals.plos.org/plosone/s/best-practices-in-research-reporting
Equator Network guidelines: http://www.equator-network.org/
ARRIVE checklist: https://www.nc3rs.org.uk/arrive-guidelines
TOP guidelines: https://cos.io/top/ and https://science.sciencemag.org/content/348/6242/1422.full
MIBBI: https://doi.org/10.1038/nbt.1411
FAIRsharing: https://www.nature.com/articles/s41587-019-0080-8

Studies of reporting status and intervention and consensus study reports
Macleod et al., "Risk of Bias in Reports of In Vivo Research: A Focus for Improvement"PLOS Biology, 2015, https://doi.org/10.1371/journal.pbio.1002273

The NPQIP Collaborative Group, T.N.C., 2019. "Did a change in Nature journals' editorial policy for life sciences research improve reporting?" BMJ Open Sci. 3, e000035. https://doi.org/10.1136/bmjos-2017-000035

Hair, Kaitlyn, Malcolm R. Macleod, Emily S. Sena, Emily S. Sena, Kaitlyn Hair, Malcolm R. Macleod, David Howells, et al. 2019. "A Randomised Controlled Trial of an Intervention to Improve Compliance with the ARRIVE Guidelines (IICARus)." *Research Integrity and Peer Review* 4 (1): 12. https://doi.org/10.1186/s41073-019-0069-3. And Preprint bioRxiv, https://doi.org/10.1101/370874

Han et al., "A Checklist Is Associated with Increased Quality of Reporting Preclinical Biomedical Research", PLOS ONE 2017, https://doi.org/10.1371%2Fjournal.pone.0183591

Landis, Story C., Susan G. Amara, Khusru Asadullah, Chris P. Austin, Robi Blumenstein, Eileen W. Bradley, Ronald G. Crystal, et al. 2012. "A Call for Transparent Reporting to Optimize the Predictive Value of Preclinical Research." *Nature* 490 (October): 187.

National Academies of Sciences, Engineering, and Medicine. 2018. *Open Science by Design: Realizing a Vision for 21st Century Research*. Washington, DC: The National Academies Press. https://doi.org/10.17226/25116.

National Academies of Sciences, Engineering, and Medicine. 2019. *Reproducibility and Replicability in Science*. Washington, DC: The National Academies Press. https://doi.org/10.17226/25303.

Development process

Document development:

The Working Group group, composed of journal editors and reproducibility researchers, drew from their collective experience at journals implementing a range of different approaches to enhance reporting quality and transparency, and on studies characterizing the efficacy of such interventions (referenced above as baseline reference material.)

The Working Group collected reporting elements relevant to the scope of this framework and prioritized items in 3 tiers of importance. The guiding principles were to keep a generalist stance, limiting the focus on a small number of items most likely to be relevant in the largest number of studies, or known to be important for study reproducibility.

The Working Group rationalized the organization of reporting elements in a two-dimensional, expandable table defined along the following axes:

- Reporting objects, categorized according to the logic of the scientific process:
    - Materials: focus on biological reagents and unique specimens
    - Design: focus on study design, experimental design, statistics and methodologies
    - Analysis: focus on data, code and analysis
    - Reporting: focused on adherence to discipline-specific standards of particular importance.
- Reporting level, categorized by increasing precision and detail, broadly along the following directions:
    - Whether access to the item is provided;
    - Unique identification, with an unambiguous pointer to external information where relevant;
    - Minimum characterization of the item;
    - Best practice characterization of the item.

Through discussion and voting, the Working Group determined which reporting objects to include in the table and what minimum level of reporting, ranging from accessibility to specific characterization, is appropriate for each object. Consensus was achieved on most items, if no consensus could be reached, voting was used to determine the outcome by simple majority.

A checklist was derived to request information corresponding to the minimum set. The group iterated the language of the checklist based on discussion and consultation with other checklists developers, and other domain experts, and based on feedback from pilot participants (see below). The checklist is meant to assist in operationalizing the framework but is not an obligatory step for implementation of the framework; MDAR does not prescribe a specific implementation mode for integrating into workflows.

Evaluation via pilot

The checklist was tested via a pilot in which 13 journals participated (see MDAR tester group above). The objectives of the pilot were to assess:

- **Author experience using the checklist:** each participating journal asked authors to fill out the checklist for their submitted manuscript. Authors were then sent a brief survey to evaluate their experience and their perception of how helpful the checklist was. Journals could elect to ask authors at any stage in the process for manuscripts undergoing evaluation (submission, revision, etc). The pilot target was to have 20 author-completed checklists per journal.
- **Editors/journals staff experience using the checklist:** Members of the editorial team from each participating journal were asked to complete the checklist for 20 manuscripts currently undergoing evaluation (at any stage of the process). There was no requirement for a particular editorial role in those scoring manuscripts, as indeed the exercise was deemed to be most useful if there were a range of experiences amongst scorers, to reflect the expertise of those who would be using the checklist once adopted as editorial practice. Due to time constraints on the pilot, there was no requirement that the manuscripts be the same as those evaluated by authors. All members of the editorial teams who participated in the evaluation were asked to fill out a short survey about their experience with the checklist and their perception of its helpfulness.
- **Inter-assessor agreement on all elements of the checklist:** . We recognize that different journals will elect to use the checklist in different ways, but one important feature of each component of the checklist will be the extent to which individuals agree on whether a manuscript is or is not compliant with that item. This is important because low agreement may reflect poor wording or a complexity in the underlying attribute being assessed which warrants more detailed elaboration and guidance. For instance, in the NPQIP study agreement between assessors for the item “Is the variance similar (difference less than 2 fold) between the groups that are being statistically compared” was only 50%. As one component of the evaluation of the checklist we therefore asked journals participating in the evaluation to have 2 members of their editorial team independently assess at least 10 submitted manuscripts against the checklist.

It is important to note that the aim of the pilot study was to capture feedback on quality and ease of use, evaluating the response to the checklist in terms of perception of helpfulness, from the point of view of two key audiences (authors and editors), and in terms of the quality of wording and definition of

attributes being measured. This pilot did not attempt to evaluate whether the checklist improved reporting, which will need to be done over a longer time frame.

The study used a systematic review training platform (learn.syrf.org.uk) for the editor evaluation, which allows each publisher to set up their own project, retaining the confidentiality of their manuscripts, yet use the same checklist, and have the summary data for scores, and agreement between scorers, available to the Edinburgh team for analysis. For authors evaluation, authors were sent a checklist as a locked word document format.

The pilot ran between June 2019 and August 2019. The study protocol can be found on OSF [https://doi.org/10.17605/osf.io/2k3va] Results were presented at the National Academies workshop " Enhancing Scientific Reproducibility through Transparent Reporting" on 25-26 Sept 2019 in Washington DC[6]. [Presentation slides, scoring data, and inter-assessor agreement datacan be found on OSF as supplemental material[7] to the statement of task[8]

Stakeholder feedback

A group of 42 external stakeholders with experience in using and developing checklists, or particular interest in improving the reporting of research, have been contacted and invited to provide feedback on the approach and material. Participants at the National Academies workshop on 25-26 September, 2019, were also invited to submit further feedback.

Their feedback was reviewed by the Working Group and compared with the feedback previously received from the pilot. The Working Group took a consensus based approach to determine which feedback to integrate into the MDAR materials (Framework, Checklist and Elaboration Document.)

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[6] National Academies of Sciences, Engineering, and Medicine. 2020. Enhancing Scientific Reproducibility in Biomedical Research Through Transparent Reporting: Proceedings of a Workshop. Washington, DC: The National Academies Press. https://doi.org/10.17226/25627.

[7] osf.io/2k3va/

[8] Chambers, Karen, Andy Collings, Chris Graf, Veronique Kiermer, David T. Mellor, Malcolm Macleod, Sowmya Swaminathan, et al. 2019. "Towards Minimum Reporting Standards for Life Scientists." MetaArXiv. April 30. doi:10.31222/osf.io/9sm4x.

II. RECOMMENDATIONS

Information requirements: rationale
This section is adapted from an elaboration document that accompanied the original Nature checklist (Nature, 2013 and 2017).

The MDAR information framework is by definition not comprehensive. The selection of information items to include in the framework has been based on the estimated frequency with which items are poorly reported and/or the impact that poor reporting, even if infrequent, will have on accurate interpretation and reproducibility. In deciding what to include, the Steering Group weighed reported evidence alongside their experience and their understanding of the research community's readiness to provide the required information.

For example, the Working Group considered that some items that are not relevant across all the life sciences are sufficiently common and their reporting sufficiently problematic when inadequate that they needed to be included in the framework. Other items were not included even if their adequate reporting would undoubtedly contribute to reproducibility and reporting quality when it was deemed that they were the purview of specialized fields only, or that a reporting requirement would, at this point in time, create an undue burden on the research community and journals.

Information requirements: clarification

1. MATERIALS & SUBJECTS

1.1. General requirement:
For all Materials and Research Subjects, the following applies.

Requirements:
The MDAR Framework requires a dedicated "Materials Availability Statement" providing transparent disclosure about availability of newly created materials including details on how material can be accessed and describing any restrictions on access.

Replication may require the exact same materials to be used. All experimental models used in the study must be listed and described unambiguously: animals, human subjects, plants, microbe strains, cell lines, primary cell cultures. All unique chemical and biological materials, including commercially and non-commercially obtained materials, newly created materials and unique specimens, should be made available for replication purposes, unless there are restrictions to availability, which should be specified.

Best practice: Where possible, the MDAR Framework recommends deposition of newly created resource materials in community-recognized repositories.

Unambiguous description:
The inherent complexity and variability of biological materials is often the cause of replication challenges. It is critical to unambiguously refer to biological reagents that have been used in the study.

For a subset of biological reagents, the use of RRIDs (Research Resource Identifiers) is recommended. These are persistent unique identifiers for referencing a research resource[9]. RRIDs use established community identifiers where they exist, and can be referenced and obtained for new resources at scicrunch.org where instructions for citation are also provided.

In addition to the above requirements and best practice applying to all materials used in a study, specific recommendations apply to the following categories of materials and subjects (1.2 to 1.6). Not all descriptors will be relevant in all cases, but the best practice recommendations are provided as a guide and resource; specialist communities have norms that relevant journals will apply as policies. In addition other specific guidelines exist or are in development for other types of materials (e.g., small molecules, proteins). Where such community-endorsed guidelines exist they constitute best practice.

1.2. Antibodies:
Requirements: For commercial reagents, the description must include supplier name, catalog number and RRID if available.

Best practice: The inherent variability of antibodies has been cited as the cause of many reproducibility challenges[10][11], and it is essential that antibodies be identified unambiguously. Variability has been demonstrated at the level of the batch number. Batch/clone number should be included. At the time of this writing, RRIDs do not consistently include the batch number and so RRIDs are useful but insufficient for referencing antibodies. For newly generated antibodies, source and validation should be described. Antibodies should have been profiled to determine their sensitivity, specificity and range of reactivity in the assay being considered. Citing validation data in the specific assays and species is best practice.

1.3. Nucleic acid constructs
Requirements: Unambiguous description of DNA and RNA constructs must be provided to allow reuse. Short novel sequences, including primers and probes, should be included or deposited in a public repository.

Best practice: Plasmids, DNA and RNA constructs should be deposited in a repository such as Addgene that also conducts quality control and distribution.

1.4. ***Cell materials:***

Cell materials	Unambiguous identification requirements	Best practice

[9] https://scicrunch.org/resources
[10] https://www.nature.com/news/reproducibility-crisis-blame-it-on-the-antibodies-1.17586
[11] https://doi.org/10.1038/nmeth.3995

Cell lines	Species, strain, accession number in repository or supplier name, catalog number, clone number, or RRID.	- RRID, or lot/batch number. - Confirm cell lines are not on ICLAC list (see below), - Timing and details of latest authentication testing and mycoplasma contamination testing. - Description of culture history (passage number), - Sex of origin (where relevant). - Genetic modification status (where relevant).
Primary cultures	Species, strain, sex of origin, genetic modification status.	

Best practice: The use of cross-contaminated or misidentified cell lines continues to impact the reliability of conclusions in the biomedical literature[12],[13],[14],[15]. The International Cell Line Authentication Committee (ICLAC) maintains a register of misidentified cell lines[16]. To curb inadvertent use of these flawed reagents, researchers should check their cell lines stocks against the list of commonly misidentified cell lines maintained by the International Cell Line Authentication Committee (ICLAC; http://iclac.org/databases/cross-contaminations/). The list has been integrated into the Cellosaurus cell line knowledge resource (https://web.expasy.org/cellosaurus/) and is also available through the NCBI BioSample database (http://www.ncbi.nlm.nih.gov/biosample/). Best practice requires that cell lines from the ICLAC Register of Misidentified Cell Lines are not used and that all other cell lines are routinely authenticated.

1.4. Laboratory animals and model organisms:

Experimental animals	Unambiguous identification requirements	Best practice
Laboratory animals or model organisms	Species, strain, sex, age, genetic modification status Accession number in repository or supplier name, catalog number, clone number, or RRID.	See ARRIVE guidelines See GMOD project guidelines[17]
Animal observed in or captured from	Species, sex and age where possible	

[12] https://doi.org/10.1371/journal.pone.0186281
[13] https://journals.plos.org/plosbiology/article?id=10.1371/journal.pbio.2001438
[14] https://onlinelibrary.wiley.com/doi/full/10.1002/ijc.25242
[15] https://elifesciences.org/articles/41676
[16] https://iclac.org/databases/cross-contaminations/
[17] http://gmod.org/wiki/Main_Page

the field		

Best practice: The Animal Research: Reporting In Vivo Experiment (ARRIVE)[18] guidelines initially developed in 2010[19] and revised in 2019[20],[21] provide a comprehensive framework to improve reporting of research using animals. MDAR refers readers to the ARRIVE guidelines and recommends their use where relevant.

Communities working with model organisms have established standard recommendations for the description of strains and clones to help tracking reagents and curation of datasets for reuse. They may include guidelines about formal species designation, gene identifiers, phenotypes controlled vocabularies. Adoption of these guidelines is recommended as best community practice.

1.5. Plants and microbes:

Requirements: For plants, provide species and strain, ecotype and cultivar where relevant, unique accession number if available, and source (including location for collected wild specimen.) For microbes, provide species and strains, unique accession number if available, and source.

Best practice: for relevant studies, describe the biosafety conditions and containment used.

1.6. Human research participants:

Requirements: All research involving human participants must have the appropriate ethics approval (see section 2 below). Patients have a right to privacy and informed consent must be obtained before release of any potentially identifying or sensitive information[22]. All efforts should be made to protect patient privacy and anonymity. Identifying information should not be included in the manuscript unless the information is crucial and the individual has provided explicit written consent.

Where it does not compromise privacy, and where possible, provide description of relevant demographic variables of the population studied, such as age, sex, gender or ethnicity. Describe the methods used to assign these variables. Ensure correct use of the appropriate population qualifiers, avoiding the use of terminology that might stigmatize participants.

See also Ethics section 2.5.1.

[18] https://www.nc3rs.org.uk/arrive-guidelines

[19] https://journals.plos.org/plosbiology/article?id=10.1371/journal.pbio.1000412

[20] Percie du Sert N, Hurst V, Ahluwalia A, Alam S, Avey MT, Baker M, et al. (2020) The ARRIVE guidelines 2.0: Updated guidelines for reporting animal research. PLoS Biol 18(7): e3000410. https://doi.org/10.1371/journal.pbio.3000410

[21] Percie du Sert N, Ahluwalia A, Alam S, Avey MT, Baker M, Browne WJ, et al. (2020) Reporting animal research: Explanation and elaboration for the ARRIVE guidelines 2.0. PLoS Biol 18(7): e3000411. https://doi.org/10.1371/journal.pbio.3000411

[22] http://www.icmje.org/recommendations/browse/roles-and-responsibilities/protection-of-research-participants.html

Best practices: More information and best practice about patient privacy, anonymity, and informed consent can be found in the International Committee of Medical Journal Editors (ICMJE) Privacy and Confidentiality guidelines. MDAR recommends adherence to ICMJE best practices. Recommendations about case reports are provided by CARE

Where relevant, other information such as inclusion criteria and other information about the participants should be included, alongside specification of whether characteristics are self-declared or assigned, and the methodology of assignment.

2. DESIGN

2.1. Study protocol

Requirements: While clinical trials (as defined by WHO[23]) are not formally part of the scope of this recommendation, MDAR refers authors to the International Committee of Medical Journal Editors (ICMJE) recommendations when clinical information is included. ICMJE requires clinical trials registration in one of the publicly-accessible registries approved by the WHO or ICMJE before enrollment of participants has begun. The trial registration number or DOI must be reported or cited in the manuscript.

Best practice: For most other studies, it is best practice to provide a statement indicating whether key aspects of the study design (including the research question, key design features, and analysis plan) was prepared and registered before data collection began. If yes, provide a reference (DOI) to the pre-registration.

2.2. Laboratory protocols

Best practice: Publishing protocols providing detailed step-by-step description of experimental procedures are actively encouraged to enhance reproducibility and supplement summary information in Methods sections. If such protocols are available, DOI or other citations should be included in the manuscript.

2.3. Study experimental design information related to statistical analysis

Requirements: For *in vivo* animal studies, the authors must indicate how the following elements of experimental design have been done, or indicate that they were not carried out[24],[25] :

- ***Sample size determination:*** When confirming an effect of known size, it is considered best practice to estimate before conducting the experiments what sample size is needed to ensure statistical power of detection. Studies with low power have lower chances of detecting a true effect and low power also reduces the likelihood that a statistically significant result reflects a true effect. Low power leads to overestimation of effect size and low reproducibility of results[26].

[23] https://www.who.int/ictrp/faq/en/#faq1
[24] https://www.nature.com/articles/nature11556
[25] https://www.nc3rs.org.uk/arrive-guidelines
[26] Button, Katherine S., John P. A. Ioannidis, Claire Mokrysz, Brian A. Nosek, Jonathan Flint, Emma S. J. Robinson, and Marcus R. Munafò. 2013. "Power Failure: Why Small Sample Size Undermines the Reliability of Neuroscience." Nature Reviews Neuroscience 14 (5): 365–76. https://doi.org/10.1038/nrn3475.

If no sample size calculation was performed, the authors should report why they think the sample size is adequate to measure their effect size.
For animal studies, authors must explain how the sample size was decided and provide details of any a priori sample size calculation (or report that no a priori estimation was done). When performing an interim evaluation of the results, investigators should use statistical methods that take into account multiple evaluations of the data. For all experiments, the sample size (n) must be reported as an exact number (not a range).

- ***Randomization:*** Whether samples are randomly assigned to experimental groups, to processing order, or to positions in a multiwell device may influence experimental outcome. Ideally, data should be collected randomly or the samples appropriately blocked. Randomization helps minimize potential confounding factors such as the order of treatments and measurements, or animal/cage location. A statement of whether randomization was used must be provided. If used, the statement should describe the randomization methods.
- ***Blinding:*** Whenever possible, the investigator should be unaware of the sample group allocation during the experiment and when assessing its outcome to prevent unconscious bias. Although blinding is not always possible, a statement describing the level of blinding must be provided (even if simply to state that blinding was not possible), describing who was aware of the group allocation at the different stages of the experiment (allocation, conduct of the experiment, outcome assessment and data analysis).
- ***Inclusion/exclusion criteria:*** Investigators should define the criteria for identifying and dealing with outliers before running the experiments to prevent confirmatory bias[27]. When reporting the results, they must explain any discrepancy between sample size at the beginning and end of each analysis due to attrition or exclusion. (See 3.1 below).

More information about description of statistics is required and recommended under section 3 (Analysis - Statistics.)

2.4. Sample definition and replicates

Requirements:

Number of times the experiment was replicated in the laboratory: when describing the results of an experiment, state how many times the experiment was independently performed in the laboratory.

Define whether data describe technical or biological replicates: for each reported experiment, define how many replicates were performed and whether they are biological (derived from different experimental units or subjects) or technical (multiple contemporary measurements from the same experimental unit or subject) replicates.

Best practice:

[27] Wagenmakers, Eric-Jan, Ruud Wetzels, Denny Borsboom, Han L. J. van der Maas, and Rogier A. Kievit. 2012. "An Agenda for Purely Confirmatory Research." Perspectives on Psychological Science 7 (6): 632–38. https://doi.org/10.1177/1745691612463078.

Samples must be unambiguously described including a clear definition of the unit of study. In studies using model organisms, cell lines, primary cell cultures, plants or microbes, the unit of study is the smallest object that could be randomly and independently assigned to an intervention.

The **groups** being compared, including control groups should be clearly defined. If no control group has been used, the rationale for this should be stated.

It is often unclear whether **replicates** represent biological or technical replicates. In reporting their results, authors should provide enough details about the sample collection to distinguish between independent data points and technical replicates. Depending on the experimental design, technical replicates will reflect the variation of the assay and/or sample preparation by assaying a sample from the same source multiple times. Biological replicates are intended to reflect the biological variability and require processing samples from different sources. Experimental design should be taken into account to define biological replicates – for example, they may require animals from different litters.

2.5. Ethics

2.5.1. Studies involving human participants

Requirements: All research involving human participants must have been approved by the authors' Institutional Review Board (IRB) or by equivalent ethics committee(s). The manuscript must report the authority granting approval and reference number for the regulatory approval.

The World Medical Association (WMA) Declaration of Helsinki provides a framework of ethical principles for medical research involving human participants, including research on identifiable human material and data.

Approval by an adequate ethics committee is intended to ensure that subjects have been properly instructed and have indicated that they consent to participate by signing the appropriate informed consent paperwork.

See also description requirements in section 1.6.

2.5.2. Studies involving experimental animals

Studies involving animals must be conducted according to internationally-accepted standards.

Requirements: Authors must obtain prior approval from their Institutional Review Board or relevant authority. The name of the authority reviewing and granting regulatory approval, as well as a reference number for that regulatory approval must be provided.

Best practice: Additional requirements may apply for certain types of experiments and for specific species for example non-human primates[28].

[28] https://acmedsci.ac.uk/policy/policy-projects/use-of-non-human-primates-in-research

2.5.3. Studies involving specimen and field samples.
Requirements: Authors must disclose that they hold relevant permits for the work, including the full name of the authority that approved the study; if none were required, authors should explain why.

Best practice: In case of field samples collection, best practice calls for disclosing whether the land accessed is privately owned or protected, and whether any protected species were sampled (with full detail of animal husbandry and care/welfare where relevant).

2.6. Dual Use Research of Concern (DURC)
Requirements: Authors must disclose whether their study is subject to consideration as dual use research of concern, and if it is, the manuscript must report the authority granting approval and reference number for the regulatory approval.

Best practice: When study material that can be harmful outside the laboratory context, the manuscript should describe appropriate biosafety and containment procedures.

Dual use research of concern is research intended with legitimate purposes but defined by the US National Security Advisory Board for Biosecurity as any "life sciences research that, based on current understanding, can be reasonably anticipated to provide knowledge, information, products, or technologies that could be directly misapplied to pose a significant threat with broad potential consequences to public health and safety, agricultural crops and other plants, animals, the environment, materiel, or national security."[29]

Many journals have a formal policy for evaluating risks associated with the publication of dual use research[30],[31]. The widespread view is that openness in science helps to alert society to potential threats and to defend against them, and accordingly only very rarely (if at all) are the risks anticipated to be perceived as outweighing the benefits of publishing a paper that has otherwise been deemed appropriate for publication. Nevertheless, through formal policy and processes journals can help evaluate and deal with the risk associated with such research, including deciding against publication if the risk is too high. In relevant fields, journals should have policies and processes reflecting these considerations.

3. ANALYSIS

3.1. Attrition
Requirements: Authors must state if any sample or data point is omitted from the analysis, and explain whether the exclusion was due to attrition or intentional. In case of intentional exclusion, authors must provide a justification.

[29] https://osp.od.nih.gov/biotechnology/dual-use-research-of-concern/
[30] https://science.sciencemag.org/content/299/5610/1149.long
[31] https://www.nature.com/authors/policies/biosecurity.html

3.2. Statistics

Requirements: Authors must describe the statistical tests used during the analysis and justify their choices, including for example whether the data meet the assumptions of the tests

Best practice: The following summary reflects best practices that are often inadequately reported, rather than a comprehensive recommendation. Authors are encouraged to review this summary and attendant references, and to report details in their submissions. Journals apply their own policies on requiring some of these elements.

Assumptions: Many statistical tests require that the data be approximately normally distributed; when using these tests, authors should explain how they tested their data for normality, which may be difficult if sample sizes are small. If the distribution is not normal, mean and standard deviation calculations are not appropriate.
Authors should specify whether the tests are one-sided or two-sided. They should also estimate the variation within each experimental group and ensure that the variance is similar for groups that are being statistically compared.

Multiple comparisons: When making multiple statistical comparisons on a single data set, authors should explain how they adjusted the alpha level to avoid an inflated Type I error rate, or they should select statistical tests appropriate for multiple groups (such as ANOVA rather than a series of t-tests).

Central estimates and distribution: Statistical measures, such as 'center' (mean, median) and error bars (standard duration, standard error of the mean), used to describe a dataset must be stated. When P values are used, the P value for each test must be reported regardless of overall significance. We note that the American Statistical Association in a 2016 statement[32] clarifying the proper use and interpretation of P values highlighted that scientific conclusions should not be based on whether a p-value passes a given threshold. For best practices we refer authors to the 2016 statement and to the collection of articles published in the American Statistician in 2019[33].

Small sample sizes: When the sample size is small, authors should use tests appropriate to small samples or justify their use of large-sample tests. Mean and standard deviation are not appropriate with small sample sizes, and bar graphs are often misleading. Plotting independent data points is usually more informative and where possible independent data points must be shown. When technical replicates are reported, error and significance measures reflect the experimental variability, not the variability of the biological process; it is misleading not to state this clearly.

3.2. Data availability

Requirements: Journals apply their own policy about the level of data sharing required as a condition to publication. As a minimum, MDAR Framework requires that a dedicated "data availability statement" is

[32] https://amstat.tandfonline.com/doi/abs/10.1080/00031305.2016.1154108#.XMXMTiJKh0w
[33] https://www.nature.com/articles/d41586-019-00874-8

recommended, including persistent identifiers and other modes of access to the datasets when possible, and licensing information where available.

- The authors indicate whether newly created datasets are available, including specific protocols for access or restriction on access.
- If data are publicly available, a persistent identifier (accession number in repository, or DOI) or where relevant, a URL must be provided in the article at publication.
- When publicly available data are reused, a persistent identifier (accession number in repository, or DOI or citation) should be provided.

Best practice:

- The MDAR framework recommends adoption of FAIR Data Principles[34]
- A formal citation should be included in the reference list when a publicly available dataset is re-used, to provide due credit and attribution to data generators. Citations to previous articles and direct citations to datasets are encouraged[35]. The MDAR framework encourages adoption of data citation per recommendations by Cousijn et al.[36]

Resources:
Recommendations of repositories for different types of data are maintained by several publishers and organizations:

- PLOS: http://journals.plos.org/plosbiology/s/data-availability#loc-recommended-repositories
- SpringerNature: http://www.springernature.com/gp/group/data-policy/repositories
- EMBO Press: http://emboj.embopress.org/authorguide#datadeposition
- Elsevier:https://www.elsevier.com/authors/author-services/research-data/data-base-linking/supported-data-repositories
- COPDESS: https://copdessdirectory.osf.io

3.3. Code availability

Requirements: Journals apply their own policy about the level of code sharing required as a condition to publication. As a minimum, MDAR Frameworks requires a decideated "code availability statement" that provides transparent disclosure about the availability of newly generated custom computer code (or the software or mathematical algorithm). For all such newly generated code that is essential for replicating the main findings of the study, the authors indicate whether the code or software or algorithm is available. If code is publicly available, a persistent identifier (accession number in repository, or DOI, or citation) or where relevant, a URL must be provided in the article at publication.

For the purpose of reproducibility, best practice recommends that a version of the code verified to be executable be referenced in the article.

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[34] Wilkinson, Mark D., Michel Dumontier, IJsbrand Jan Aalbersberg, Gabrielle Appleton, Myles Axton, Arie Baak, Niklas Blomberg, et al. 2016. "The FAIR Guiding Principles for Scientific Data Management and Stewardship." Scientific Data 3 (1): 160018. https://doi.org/10.1038/sdata.2016.18.
[35] https://www.force11.org/datacitationprinciples
[36] https://doi.org/10.1038/sdata.2018.259

4. REPORTING

The MDAR framework is intended as a generic minimum recommendation applicable to reporting studies in the life sciences to increase reporting transparency and reproducibility. It is fully compatible with, and actively recommends the adoption of discipline-specific guidelines that have been established and endorsed through community initiatives.
Journals have their own policy about requiring specific guidelines and recommendations to complement MDAR.
Authors and journals are encouraged to consult guidelines, references are provided below as a resource.

Requirements: Author must report if relevant guidelines have been followed, and whether a checklist accompanies the submission.

Resources:

Study type	Guidelines and recommendations	Examples (non-comprehensive)
Health-related research	ICMJE guidelines: http://www.icmje.org/recommendations/	Clinical trials pre-registration
	EQUATOR Network: http://www.equator-network.org/	Randomized Controlled Trials: CONSORT checklist Meta-analyses: PRISMA checklist Description of biospecimen: BRISQ
Animal research	ARRIVE guidelines: https://www.nc3rs.org.uk/arrive-guidelines	
Minimal information standards for reporting common biosciences methods	FAIRsharing: https://fairsharing.org/standards	Microarray experiments: MIAME Proteomics experiments: MIAPE

III. REVIEW

The three documents -- MDAR Framework, MDAR Checklist, and MDAR Elaboration Document -- were sent to 42 domain experts including individuals who have developed relevant guidelines and checklists, or studied issues related to irreproducibility of published work in the life sciences. And 22 individuals submitted responses including suggestions for improvements and additions.

The pilot study also allowed the Working Group to identify elements of the three documents that required clarification -- through the feedback obtained from pilot participants and the results of the inter-assessor agreement analysis. The feedback from pilot participants also highlighted issues of scope of application and feasibility.

The Working Group reviewed all feedback and reached consensus on which modifications to implement. The consensus reflected attempts to strike a balance between coverage of all identified reporting challenges and feasibility of implementation. Resulted many language clarification as well as some substantive changes including:

- New requirements for nucleic acid constructs – RNA, DNA, plasmids, probes;
- A requirement for registered study protocols to have DOIs or a trial registration number in a recognized database;
- A requirement for sex of origin to be described for primary cell lines, along with strengthened language for misidentified cell lines.

IV. FUNDING, DECLARATION AND MANAGEMENT OF INTERESTS

Funding

The Working Group received no specific funding for this initiative. Their employers supported the initiative by allowing them to volunteer time and expertise.

Declarations

Several members of the Working Group are employed by publishing organizations that may or may not endorse the MDAR Framework. The Working Group strived to include a diversity of publishers in the pilot to ensure that the outcomes would be as broadly applicable as possible.

The Center for Open Science (COS) was chosen by the Working Group to host and ensure stewardship of the project outcomes in the summer of 2020 at the conclusion of the initiative, and based on their experience hosting similar recommendations like the TOP guidelines. COS is a registered non-profit, for information on its support and finances, see https://www.cos.io/about/finances

V. OTHER INFORMATION

Access

The original Statement of Task was published as a preprint, publicized through a series of blog posts by Working Group participants:
Chambers, Karen, Andy Collings, Chris Graf, Veronique Kiermer, David T. Mellor, Malcolm Macleod, Sowmya Swaminathan, et al. 2019. “Towards Minimum Reporting Standards for Life Scientists.” MetaArXiv. April 30. doi:10.31222/osf.io/9sm4x.

A record of key documents and results from the pilot study were added as supplementary material to this Statement of Task:
osf.io/2k3va/

The final documents representing the outcomes of this initiative are released here:
https://doi.org/10.17605/osf.io/2k3va
[UPDATE LINK TO FINAL DOCUMENTS WHEN READY]

Limitations and suggestions for further research

The Working Group employed an iterative process, including a pilot study, to ensure that the MDAR Framework was adapted to the current state of reporting and was useful to users. However, the efficacy of the MDAR Framework to improve reporting quality and to influence research practice was not evaluated during this development process. We suggest that studies of the effectiveness of endorsement, and of strategies to increase author engagement, should be conducted once the Framework has been endorsed by a critical mass of journals.

We have acknowledged above that the Framework is likely to be more useful for certain disciplines than others, as it was derived with a focus on laboratory based basic research. We also acknowledge that discipline-specific guidance and norms exist that have not been incorporated in the minimum requirements. Where they exist, community-endorsed discipline-specific reporting guidelines should be considered best practice. As new discipline-specific reporting guidelines emerge, they should similarly be included in the consideration of best practices.

The MDAR Framework was developed with the view that it should evolve over time to reflect the evolution of reporting practices in the life sciences community. It is our hope that with time the best practices outlined in this document and the Framework will become routine practice and can be incorporated in the minimum requirements.

We recommend that community consultation takes place at regular intervals in the future, ideally every two years, to collect feedback from implementation, review new evidence about effectiveness of the Framework and evolution of reporting practices in general, with the view to update the Framework.