GUIDANCE OF EFSA

Guidance on Statistical Reporting[1]

European Food Safety Authority[2, 3]

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ABSTRACT

Statistical analyses are an essential part of risk assessments. Statistical reporting varies considerably amongst the documents that EFSA receives and produces, which can lead to lack of transparency and reproducibility of results. This guidance aims to improve quality, openness and transparency of EFSA's work and information/analyses received by EFSA (including dossiers). It is not intended to provide guidance on which statistical methodology should be applied and how statistical analysis should be performed. A template is proposed, that covers in the broadest possible way, the reporting of relevant aspects of a statistical analysis including: objectives, sources of information (data), study design, data quality, analysis methods, results and interpretation. The guidance and template serve to harmonise and standardise transparent statistical reporting to facilitate reproducibility of the analysis, interpretation and use of the statistical results, and independent peer review.

KEYWORDS

statistical reporting, study design, sampling, guidance, statistics

[1] On request from EFSA, Question No EFSA-Q-2012-00625, approved on 11 November 2014.

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[3] Acknowledgement: EFSA wishes to thank the members of the Working Group on Statistical Reporting: Jean-Louis Bresson, Mikolaj Gralak, Matthias Greiner, Andy Hart, David Makowski, Joe Perry and Hans-Hermann Thulke for the preparatory work on this scientific output and EFSA staff: Davide Arcella, Saghir Bashir, Andreia Carlos, Laura Martino and Luca Pasinato for the support provided to this scientific output.

Suggested citation: European Food Safety Authority, 2014. Guidance on Statistical Reporting. EFSA Journal 2014;12(12):3908, 18 pp., doi:10.2903/j.efsa.2014.3908.

Available online: www.efsa.europa.eu/efsajournal

SUMMARY

EFSA mandated itself to develop a guidance on statistical reporting to improve the quality, openness and transparency of EFSA's work and information/analyses received by EFSA. The guidance aims for harmonisation and standardisation in the reporting of statistical analysis. In view of the nature of the subject, the task was assigned to the Assessment and Methodological Support Unit (formerly Scientific Assessment Support Unit).

The risk assessment process often requires quantitative evaluation of scientific studies from different sources (e.g. dossiers, journal publications, technical reports). The reporting of statistical methodology (including design), analysis and results varies considerably. Lack of transparent and relevant information can lead to delays in the review process whilst additional information is sought from the originating source. If the statistics were consistently reported in a harmonised and standardised way then this would benefit both EFSA and its stakeholders. This approach would be more open and transparent.

This guidance should best guide EFSA panels, Scientific Committee, working groups, units and stakeholders (e.g. applicants) on how to report statistical methodology (including design and conduct), analyses and results (i.e. "explain to the reader what was done") in order to allow independent statistical peer review and reproducibility. The issue of what methodologies should be used for the design, conduct and analysis are outside the scope of this mandate.

The guidance is intended to be general and provide guidelines on the reporting regardless of the type of analysis that was performed. For this reason some aspects that are listed and discussed might not be applicable to a specific study design and/or data analysis.

To facilitate the practical use of the guidance, a template is proposed, that covers in the broadest possible way, the reporting of relevant aspects of a statistical analysis including: objectives, sources of information (data), study design, data quality, analysis methods, results and interpretation. The guidance and template aim to harmonise and standardise statistical reporting in such a way that reproducibility of results and independent peer review is feasible.

The general and specific objectives of the statistical analysis should be stated with scientific background explaining the rationale for the analysis. The sources of information (data) used for the analysis and data quality assurance measures should be reported. These could be pre-existing sources or data specifically collected. The data sources will be dependent on some underlying study design and all measures taken to minimise bias and maximise precision should be detailed. This, together with approaches used to address sample selection, sample size, power, blinding (where relevant) and randomisation (where relevant) should be detailed.

Statistical analysis, including data processing (e.g. transformation of data), details of the methodology (e.g. assumptions, models used) and the software used, have to be documented. Deviations and/or non-compliance issues, planned or unplanned, in relation to the a priori protocol (if any)/statistical plan should be described. The reporting of the results should be consistent with the objectives of the study. Descriptive statistics should be presented for relevant data collected for analysis. The point and interval estimates (e.g. confidence) for all results of the statistical analysis should be presented. A statistical interpretation of results to support the biological/scientific interpretation should be given including a discussion about all relevant uncertainties affecting the statistical analysis and its results.

The template also allows for the inclusion of detailed statistical outputs and supplementary study information (e.g. protocol) to encourage a fully open and transparent approach to statistical reporting.

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BACKGROUND AS PROVIDED BY EFSA

EFSA's mission is to support policy makers in their activity by providing and analysing scientific evidence. There are differences in the requirements for statistical reporting in regulatory and research setting. In a research setting, the audience is primarily comprised of peers with scientific expertise in the topic, whereas in a regulatory setting the primary expertise of the audience may be in other areas of science, or outside science (e.g. in policy, economics, law, etc.). Furthermore, in a research setting the focus is on advancing knowledge, including the development and testing of hypotheses, whereas in a regulatory setting the focus is on making decisions between alternative policies or regulatory options. These differences have implications for statistical reporting. In a research setting, it is common to report in detail the methods and assumptions of an analysis, and discuss their validity: the audience may then use their own expertise to interpret critically the implications of the results and any associated uncertainties. In a regulatory setting, detailed description is also important for transparency and peer review, but the regulatory audience will often lack the expertise to interpret for themselves the impact of assumptions and uncertainties on the conclusions. Therefore, in a regulatory setting, it is essential not only to report assumptions and the degree to which they are valid, but also to evaluate and express the impact of this on the interpretation of the results. EFSA's work includes evaluations of submissions from external organisations in relation to regulated products and techniques. In this context, the reports delivered as supporting documents to EFSA frequently lack key information. As a consequence, there is a need to request clarifications, thus increasing the time and the effort needed for the assessment. The availability of clear and detailed recommendations on the reporting should help to shorten the process and minimise disputes.

The risk assessment process often requires quantitative evaluation of scientific studies from different sources (e.g. dossiers, journal publications, technical reports). The reporting of statistical methodology (including design), analysis and results varies considerably. Lack of relevant information can lead to delays in the review process whilst additional information is sought from the originating source. For the statistics were consistently reported in a harmonised and standardised way then this would benefit of both EFSA and its stakeholders, this guidance aims for harmonisation and standardisation through the provision of guidelines on peer review and reproducibility. It is designed to improve the quality, openness and transparency of the work of stakeholders reporting to EFSA and of EFSA's own work in this area. It is aimed at EFSA panels, Scientific Committee, working groups, units and stakeholders.

TERMS OF REFERENCE AS PROVIDED BY EFSA

In view of the above, guidelines should be developed to best guide EFSA panels, Scientific Committee, working groups, units and stakeholders on how to clearly and concisely report statistical methodology (including design and conduct), analyses and results (i.e. "explain to the reader what was done"). The issue of what methodologies should be used for the design, conduct and analysis are outside the scope of this mandate.

The Guidance should be practical and applicable to the different relevant food and feed safety fields, within EFSA's remit including Animal Health and Welfare and Plant Health. In particular, the EFSA Guidance should include:

- How to ensure objective and accurate reporting of statistics
- How to document and present the design, methodology, analysis and results to allow independent peer review
- A glossary of relevant terms.

A draft version of the Guidance should be made available for the Scientific Committee and for public consultation, to ensure all relevant information is taken into account with respect to the reliability and consistency of the methods described in the final document.

For the development of this EFSA Guidance, the SAS Unit[4] should establish a working group of EFSA scientific staff and external experts.

INTRODUCTION TO THE GUIDANCE

This guidance is aimed at covering all areas of EFSA's remit including:

- Food and feed safety, nutrition, animal health and welfare, plant protection and plant health
- Impact of the food chain on the biodiversity of plant and animal habitats
- Environmental risk assessments of genetically modified crops, pesticides, feed additives, and plant pests.

The aim is to improve transparency, support reproducibility and lead to a harmonised and standardised reporting.

The issue of what methodologies should be used for the design, conduct and analysis are outside the scope of this mandate.

APPLICABILITY OF THIS GUIDANCE

The objective of this document is to provide guidance on how to report statistical analysis in order to allow the evaluation its quality and validity. A template is also proposed aimed at facilitating the implementation of the Guidance.

Some requirements for statistical reporting are specific to particular situations which will be indicated in the guidance and hence will not be applicable to other cases.

In practice, for EFSA, this would mean that all statistical analysis conducted internally, or as part of a grant or procurement should follow this guidance and template. Stakeholders submitting statistical analyses to EFSA (e.g. statistical reports for studies supporting an application) should also follow these guidelines. The absence of any information in the statistical reporting will lead to additional uncertainties (Section 10.2). This guidance does not override any reporting requirements in regulations.

This guidance does not preclude the submission or use of statistical reports which were produced prior to the production of this guidance. However, any limitations in statistical reporting within pre-existing documents may affect evaluation of the quality of the statistical analysis and may have consequences for its interpretation. In some cases, where the recipient of the statistical report considers it necessary, requests for clarification or additional reporting may be made.

Detailed statistical reporting is not required where a narrative summary is given of the results of statistical analysis that is already reported elsewhere and this guidance does not apply in such cases.

OTHER GUIDANCE DOCUMENTS ON RELATED TOPICS

This document aims to provide a concise and practical overview of the general and specific principles relevant to EFSA's work, harmonising them where possible and referring to other existing sources where applicable. There are various initiatives going on in the scientific community aimed at providing guidance on how to improve the quality of reporting, for example the EQUATOR network[5] on reporting of health research and in particular the CONSORT statement (Schulz et al., 2010) and the SAMPL guidelines (Lang et al., 2013). The International Conference on Harmonisation (ICH)

[4] SAS Unit now named AMU Unit
[5] http://www.equator-network.org

Guidelines ICH E3 on "Structure and Contents of Clinical Study Reports" was used as a reference to model the structure of this guidance document (ICH, 1995).

Although there are various initiatives and documents aimed at improving the quality of science, none of them addresses statistical reporting that could be directly applied to the EFSA context. This was the main motivation to provide such a guidance document.

EFSA has published other relevant guidance documents in the areas of transparency in risk assessment (EFSA, 2009), systematic reviews (EFSA, 2010), probabilistic modelling (EFSA PPR Panel, 2012), terminology in risk assessment (EFSA, 2012) and expert knowledge elicitation (EFSA, 2014). EFSA Scientific Committee has published an opinion on statistical significance and biological relevance (EFSA, 2011). All these opinions and guidance documents are of relevance for use in conjunction with this guidance.

The need for transparency in all the steps of risk assessment is emphasized in the general conclusions of EFSA (2009):

- *The scientific outputs must be transparent with regard to the data, methods of analysis and assumptions that are used in the risk assessment process*
- *Transparency is needed in all parts of the risk assessment*
- *To be transparent, a risk assessment should be understandable and reproducible*
- *Where possible, harmonised assessment terminology should be used, preferably based on internationally accepted terminology*
- *There may be differences in risk due to variability among individuals, populations, species or ecosystems. It is important to identify and describe the most influential contributors to variability in risk, preferably by statistical analysis of the underlying data*
- *Any statistical difference must be interpreted in the light of its biological relevance*
- *Although it may be impossible to identify all the uncertainties, each scientific output should describe the types of uncertainties encountered and considered during the different risk assessment steps, and indicate their relative importance and influence on the assessment outcome*
- *Expression of uncertainty and variability in risk estimates may be qualitative or quantitative, but should be quantified to the extent that is scientifically achievable.*

GUIDANCE AND TEMPLATE

The following sections of this document offer guidance on the specific steps that are needed to achieve the principles of transparency summarised above in reporting statistical analysis. This document is presented in a concise form which is intended to serve also as a template for applying the guidance in practice. EFSA encourages the use of the proposed template when this is not the case the same principles apply and the same information should be given.

This guidance intends to support the understanding of "what was done" rather than to be prescriptive about "how it should be done". Authors should take responsibility to be clear of the definitions and provide proper citations for any terms they use. In this context, and given the general nature of this guidance with respect to statistical reporting, EFSA feels that a glossary is not needed.

In some cases, details of statistical analysis are reported in the main body of an opinion, report or application. In other cases, detailed reporting is provided in an Annex or other supporting document. The following guidance applies equally to both cases (except for Sections 1 and 2, see below). Where the guidance requires more detail than is practical in the main body of a document, part or all of the information could be provided in an Annex or supporting materials.

1. Title page

Where the statistical analysis is subject of a separate document, the title page should contain the following information:

- Statistical Report Title (covering key information)
- Pre-registration of study, if applicable
- If the report is in an Annex give a reference to the main document it is annexed to
- Abstract and keywords, if applicable
- Name of sponsor (and bodies that fund or commission the analysis)
- Relevant identification number(s) (e.g. protocol, mandate and question numbers)
- Name and affiliation of person or persons responsible for producing and signing off the report
- Date and version of report.

Where the statistical analysis is reported as part of a larger document (e.g. a Panel Opinion), the title page should follow the usual conventions for the type of document in question.

2. Summary

The summary is intended to provide a concise description of the key elements of the objectives, design, methods and analysis. The key numerical results with quantified uncertainty (e.g. interval estimates) should also be included. It should also include a brief summary of any important additional uncertainties that have not been quantified (see Section 10.2). Where the statistical analysis is part of a larger document (e.g. a panel opinion, dossiers), it is recommended that if key numerical results are identified, these should be included as part of the overall summary of the document.

3. Reporting of objectives and scope

3.1. Background

The scientific background should be presented in order to help the reader understand the rationale for performing the statistical analysis and what gaps in the current knowledge are intended to be addressed.

3.2. General objectives

The general objective of the statistical analysis should be described in a narrative form.

The regulatory setting might play a role in determining the objectives of the analysis and indicating constraints and priorities. If this is the case those elements should be mentioned.

3.3. Specific objectives

The specific objectives of the analysis have to be elaborated in both a formal and narrative way. It should be stated whether they are:

- To explore and describe the data at hand in order to generate new hypotheses (exploratory analysis (see ICH E9 (1998) for definition))
- To estimate a predefined quantity (e.g. estimation of exposure, benchmark doses, prevalence)
- To confirm predefined hypotheses (confirmatory analysis (see ICH E9 (1998) for definition))
- Some other specified purpose.

Predefined hypotheses have to be stated formally, including the endpoints/outcomes to be considered, the significance level and the a priori power of the test. For estimation, the interval estimate to be used should be specified and justified (e.g. confidence or credible interval, level of probability, whether one- or two-sided). It should be reported whether the existence of a difference or the evaluation of the equivalence or non-inferiority is to be assessed, as well as the size of the difference/range of equivalence considered biologically relevant (EFSA, 2010).

The target population has to be specified in order to allow for the generalisation of the results. If subgroups of the population have been specifically addressed by the analysis, they should be described along with the rationale for their choice. Characteristics of the subjects that constitute the population should be identified (e.g. gender, age, ethnicity, species/category/varieties, geographical location, temporal frame).

4. Reporting sources of information

This section should describe any data source or sources that were used (e.g. existing data and/or databases, experimental studies, literature review).

The rationale for the use of a specific source generating the data for the statistical analysis should be reported, including the procedural and/or experimental conditions under which the data were assembled/collected and that could limit the scope of the analysis.

If multiple data sets are used then it should be reported how they were combined. For example, to estimate prevalence, the number of cases could be extracted from an animal register and total population size from trade data.

4.1. Existing sources of data

All the information needed to retrieve the data from the original sources should be documented (e.g., websites, date of download/receipt).

If existing databases were used, the related metadata should also be provided (or referred to in case published somewhere) including:

- Nature of the data (e.g. administrative data, primary data)
- Institution in charge of data management
- Methodology used to collect data (e.g. statistical unit, reference population, study design, sampling strategy, nomenclature, measurement unit)
- Date/period of data collection
- Confidentiality issues (if applicable).

Unpublished data should be included in the report. If not, full description of the data and a justification of why the data could not be attached should be given (see section 12).

Procedural conditions should be reported e.g. inclusion/exclusion criteria as applied to select sub-sets of the existing data. For example criteria based on:

- Relevance for the specific issue (e.g. exposure assessment of (sub)populations, geographical regions, materials or test organisms used)
- Specific requirements for the purpose of the analysis (e.g. coverage of endpoints, sensitivity, specificity, appropriate statistical treatment of data, representativeness of data)
- Study design (e.g. robustness of statistical design, potential bias).

4.2. Direct data collection

If the study included collecting data that was subsequently analysed, the method of data collection should be documented as part of the planned study design (see section 5).

5. Reporting of study design

This section addresses the key features of the design that should be covered. However, some of the sub-sections may not be applicable to particular study designs/situations and in those cases the section should remain with the text "Not applicable". The rationale for the study design should be documented and a protocol (or any *a priori* plan) attached (see Section 12.1). In cases where a design element (e.g. blinding), that should be present for a particular study design, is missing then its omission should be justified.

5.1. Study Design

The following overarching items should be documented:

- The type of design of the experiment/study/survey (e.g. factorial, cohort, case-control, cross-sectional, longitudinal, stratified, clustered)
- The interventions by treatment level and administration route (if applicable)
- The primary and secondary endpoints along with auxiliary and confounding factors (if applicable) and their expected biological, chemical and/or physical relevant effect (if applicable)
- The setting (e.g. location, dates)
- The eligibility criteria (if applicable)
- The timescale (e.g. acute vs. chronic exposure) with the duration of treatment and follow-up (if applicable)
- Spatial scale and environmental conditions (if applicable)
- The persons involved in each phase of the implementation process including providers, data collectors and outcome adjudicators
- Methods of data collection (e.g. interview, medical examination, etc.) (if applicable)
- For cohort studies, the follow-up process should be reported, providing information related to matching criteria and number of individuals exposed and non-exposed

- For case-control studies, the choices of cases and controls should be reported and justified, and in the case of matching, the criteria and number of controls per case should be presented
- Stopping rules (if applicable)
- Ethical approval (if applicable, in case it is not requested).

In addition, specific detailed elements of the design should be given, and these are listed in the subsequent sections.

The elements to be considered to develop a protocol for a systematic review are listed in the EFSA Guidance on Systematic Review (EFSA, 2010; Section 3.1) and for the reporting of a systematic review these same elements should be included.

5.1.1. Randomisation and blinding

In case of randomisation and/or blinding, the reporting should cover:

- The method to generate the random allocation sequence
- The type of randomisation (e.g. central, dynamic)
- Level at which the randomisation was applied (see Section 5.2.1)
- The mechanism to implement the random allocation sequence
- Blocking/clustering and/or stratification (see Section 5.2.3)
- Methods to conceal intervention sequence
- Methods used for blinding
- The persons involved in each phase of the implementation process including their access to the randomisation list, with dates
- Access to the randomisation list (if applicable) should be reported with respect to the date of access, the accessing person, and reason (e.g. emergency code breaking).

5.2. Sampling

The sampling strategy should be reported, including the definition of the sampling unit, the sample size required to meet the objectives and the sampling design used to get the sample from the target population.

5.2.1. Experimental and sampling units

The definition of the experimental unit should be provided. For example, in an experimental setting with two rats per cage it should to be specified whether the treatment(s) were randomised at the level of the cage or the individual rat.

The definition of the sampling unit should be provided. If two-stage sampling is practiced, e.g., in surveys of farmed animal populations, the sampling units at all levels should be described.

It should also be stated which unit, sampling or experimental, was considered for each statistical analysis.

5.2.2. Sample size

The rationale of the sample size adopted, together with any *a priori* calculation on which it was based, should be reported in terms of:

- The biologically relevant effect or expected estimate
- The precision of measurements (e.g. limit of quantification, if applicable)
- The level of confidence (if applicable) and whether one or two-sided
- The power of the study or the desired precision of survey estimates (if applicable)
- Requirement of EFSA and/or other regulatory Authorities
- The multiplicity of endpoints measured (if applicable).

Methods and results of sample size/power calculation used should be described.

5.2.3. Sample selection strategy

A description of the sampling design should be provided as well as the rationale supporting the choice (e.g. in the survey context: a clustered sample could be adopted instead of a stratified sample; in the experimental setting: a blocking design may be adopted instead of a completely randomized design, etc.).

If the sample selection is not based on a random selection scheme that appropriately reflects the investigation of the study objective, a justification should be provided. Relevant differences between the general population/target population and the selected sample should be reported including any issues related to the representativeness of the data.

It should be mentioned whether any auxiliary information was used in order to improve the efficiency of the sampling design (e.g. stratification variables) or to reflect the aggregation of sampling units (clustering). If an informed choice in terms of resource allocation has been made to optimise the sample size of primary (e.g. herds) and secondary sampling units (e.g. animals per herd), the rationale and supporting evidence should be described.

Any sub-sampling (e.g. where there are five animals per cage and only one is selected for necropsy/blood sampling) should be documented including if such selection is random.

Any known or plausible deviation from independence among the sampling units should be described. For example, if individual animals come from the same litter or if individuals are repeatedly sampled over time.

Specific sampling designs, such as for example pooled samples, should be described in sufficient detail to allow a critical review.

6. Reporting data quality

This section addresses the reporting of the elements of data collection and pre-processing that could influence data quality. However, some of the sections may not be applicable to particular study designs/situations and in those cases the section should remain with the text “Not applicable”. If no quality control or quality assurance procedures were used then this should be stated with justification. The details of the procedures used should be provided in Section 12.8.

6.1. Data collection quality assurance

All the actions put in place in order to minimise bias and maximise precision at the level of data collection should be described including:

- Training of data collectors (if applicable)
- Pilot test of the questionnaire (if applicable)
- If missing data were imputed, then the methods used and actions taken to ensure that bias was not introduced and that variance was not compromised should be described
- Description of methods which have been adopted to minimise the amount of missing data
- Methodology used to edit data (e.g. macro or micro-editing, list of checks applied to identify mistakes)
- Methodology used to prevent measurement errors.

Any pre-processing activities performed on the extracted data that could affect results such as computation of standard errors on the basis of confidence intervals and/or transformation of measurement unit (e.g. from mmol to mg) should be documented. For systematic reviews, it should be also stated which criteria were used to assess the methodological quality of individual studies and how the quality appraisal was used in weighting the evidence.

7. Reporting the methods of analysis

When analysing confirmatory studies, the a priori definition of the methods for analysis may be critical to the interpretation of results. For such analyses, therefore, reporting should describe and justify the initial pre-defined plan for processing and analysis of data and any additions, deviations or adjustments made during the course of the analysis.

For exploratory studies, it is sufficient to describe the analysis as it was conducted. This should include a full description of the methods used for the final analysis, i.e., the analysis that generated the results as presented. If the final analysis was preceded by a series of significantly different analyses, it is recommended to provide an overview of those and explain the rationale that led to the choice of the final analysis.

When an estimate is the output of the analysis, the report should describe and justify the initial pre-defined plan for processing and analysis of data and any additions, deviations or adjustments made during the course of the analysis, following the same principle expressed before for confirmatory studies.

7.1. Data processing

This section is intended to cover the processing of data prior to the analysis and therefore it excludes issues covered in section 7.2, 9.1.1, 9.1.2 and 9.1.3.

All methods used for processing of data should be reported and justified, where alternative approaches could be considered. This includes:

- Transformations (e.g. the use of logarithms and the base of the logarithms should be made explicit) and the rationale for it
- Processing for the creation of descriptive summaries or graphs (e.g. calculation of averages or percentages, pooling of different subsets of data, selection of bin intervals for histograms)

- Methods used for selection and/or weighting of data (including, in the case of systematic reviews, appraisal of the methodological quality of studies)

- Any other methods used for processing data.

7.2. Statistical analysis

Most analyses involve some form of explicit or implicit statistical modelling. The following should be included when reporting the methods used:

- The unit, sampling or experimental, that was considered for each statistical analysis

  - Any hierarchical structure of the data and any lack of independence (if applicable).

- For estimation, precise specification of the parameter to be estimated and the estimator chosen to estimate it (e.g. ratio estimator, post-stratified estimator)

- For exploratory or confirmatory studies, specification of the hypotheses tested

- Choice and motivation of probability levels to be used for interval estimation and hypothesis testing (if not already specified in the analysis objectives as described in Section 3.3)

- Description and justification of any methods used to handle multiplicity in hypothesis testing or interval estimation (if applicable)

- Handling of missing, imputed or censored data, including rationale and implications

- Identification and handling of outliers (if applicable)

- Brief description of alternative models considered, rationale for selection of the chosen model, and justification of its suitability to address the objectives of the analysis

- For Bayesian models, a description and justification of the prior distributions along with the sources of information and how they have been derived in case of informative priors

- Complete specification and justification of the chosen model, such that it can be reproduced by others, including:

  - Data selected for use in the model

  - List of model parameters, covariates and response variables

  - Model equations, formulas

  - Treatments factors, blocking factors (if applicable)

  - Fixed effects versus random effects (if applicable)

  - Specification and justification of the assumptions, including those regarding distributions and dependencies (including absence of dependency). For generalized linear models, the choice of error distributions and link functions. Handling of missing or censored data within the model and any assumptions implied by this.

- Identification and justification of any relevant data points that are excluded from the model (e.g. outliers)

- Description and justification of methods used for any weighting of data within the model
- Specification of the parameter estimation methodology (e.g. Restricted Maximum Likelihood, Bayesian, Markov Chain Monte Carlo, Integrated Nested Laplace Approximation)
- Description of methods used for producing any model diagnostics
- Description and justification of methods (if not standard practice) used for testing model assumptions
- For Bayesian models, a sensitivity analysis for describing the impact of alternative priors (if applicable) on the posterior distribution
- Description and justification of methods used for additional analysis of the model, e.g. subgroup analysis and meta-regression (Liberati et al., 2009)
- Description and justification of any other methods used for validating and/or verifying the model or assessing its robustness or performance e.g. sensitivity analysis.

7.3. Software

Where the analysis has been conducted with any software package it should be identified in the report (including version and operating system). If additional details are needed to enable reproduction of the analysis, these should be provided.

Where the analysis has been conducted with a purpose-built computer program, this should be described in the report and the validation of the software be documented.

All programs, log and outputs for the final analysis (i.e. the results and analysis reported) should be made available on request for review in electronic format. Tables, graphs and listings should allow identification of program that created them with the date and time (e.g. timestamping).

8. Deviation from the protocol and/or analysis plan

Major deviations and/or non-compliance issues, planned or unplanned, in relation to the a priori protocol (if any)/statistical plan should be reported and reasons given in this section. The intention is to understand how analysis, representativeness and generalisability are impacted.

9. Reporting the Results

Descriptive statistics and the results of analyses (including a quantification of precision) should be presented. Whenever any transformation is applied to the data (e.g. log, percent change) then results should be presented for the transformed values along with the results in the original measurement units when it facilitates the interpretation. The reasons for missing data should be reported and summarised.

9.1. Summary of inputs variables

A summary of inputs variables, for example, demographic variables or design variables should be reported as described in Section 9.2.

9.2. Objectives and endpoints/ outcomes

The results should be presented in a structured way, for example, for each objective by their respective endpoints and outcomes.

9.2.1. Descriptive statistics

Descriptive statistics should be presented for relevant data considered in an analysis in a manner that is suitable for interpretation (e.g. by treatments groups, species type). A combination of tables and graphs should be used to communicate the key features of the data. Where this results in a large volume of material, tables and graphs in the main report could be restricted to those variables most critical to the analysis, with others being placed in annexes or accompanying documents (Section 11).

Quantitative summary statistics (including graphical method) presented will depend on the type of variable and should include the following:

- Categorical and ordinal variables:
  - Percentage(s)/proportion(s) presented with both the numerator and the denominator(s)
  - Total and number of missing observations.
- Continuous variables:
  - Total and number of missing observations
  - Median, minimum and maximum values
  - Characteristic percentiles (e.g. lower and upper quartiles, 95%)
  - Means and standard deviations.

In case of a systematic review any potential sources of heterogeneity should be described at least in a narrative form. If a quantitative heterogeneity analysis is performed, its results should be included in the report.

9.2.2. Results of statistical analysis

The reporting of the main results should be consistent with the objectives of the study as discussed in Sections 3.2 and 3.3. The point and interval estimates (e.g. confidence) for all results from the statistical analysis should be presented. Where the analysis provides distributions for estimators they should be described (e.g. Bayesian method, bootstraps).

9.2.2.1. Results of supporting analysis

Supporting analysis should be reported in a consistent manner to the main statistical analysis, making the intention of the analysis clear, for example:

- Model diagnostics
- Missing data methods (if applicable)
- Testing model assumptions
- Model building including intermediate model results (if applicable)
- Model validation
- Assessing robustness or performance (i.e. sensitivity analysis)
- Additional analysis of the model, e.g. subgroup analysis and meta-regression

- For confirmatory analysis, whether such analysis was post-hoc.

9.2.3. Graphical summaries

Graphs should be designed carefully to allow objective assessment and the following points should be taken into consideration:

- The image should not be distorted (e.g. use appropriate scales for axes)
- Keep colour coding consistent across graphs
- Use high quality graphs with fonts that are readable
- Do not use superfluous three-dimensional graphics (e.g. shadows) in bar, line and pie charts.

Data used for a graph should be available in Tables or Listing in the body of the report or in Sections 11.1 and 11.3.

10. Reporting the interpretation of the results

10.1. Reporting results and their interpretation

The reporting should cover all the results of the analysis regardless of whether they were statistically significant or not. The interpretation of the results should be consistent with the objective and the design of the analyses. The biological relevance should be discussed in parallel with the statistical significance (EFSA, 2011). The conclusions should reflect the outcomes of the statistical analyses performed and their biological interpretation.

In the case of a narrative summary of different results performed without a meta-analysis, the methodological quality of the different sources of evidence should be taken into account and described.

10.2. Reporting uncertainty

Each scientific output should describe the types of uncertainties encountered and considered during the different assessment steps, and indicate their relative importance and influence on the assessment outcome (EFSA, 2009). In the context of a statistical analysis, this should start with the presentation of the measures of uncertainty generated by the analysis, e.g. interval estimates, coefficient of variation, etc. In addition, all other elements introducing uncertainty should be described, including:

- Assumptions made in the analysis (e.g. model choice, distributional assumption), and the extent to which they are valid and their potential impact on the results
- Direction and potential magnitude of potential biases, including deviations from the design
- Degree of generalizability and applicability to the target population (also referred to as external validity)
- Level of heterogeneity in outcomes
- Any other choices (e.g., prior distributions).

11. Detailed statistical outputs

The essential/important results should be presented in summary form in the body of the report. Detailed and supporting results should be presented in this section and cross referenced in the text.

11.1. Tables

This section should present tabulated summary results. The tabulations can include both summary/descriptive statistics and outputs from statistical modelling.

11.2. Graphs

This section should present graphical summary results for which there should also be a table presented in the Section 11.1.

11.3. Listings

This section should present listings of individual data that is referenced in the report. Also see Section 12.5) for details about providing the electronic version of the data.

12. Supplementary study information

Key study information and documents, with signature and dates, should be attached to this section as described in by the sections below. If documents listed are not available then it should be stated why.

12.1. Protocol and protocol amendments

12.2. Sample information (data) collection form

12.3. Statistical analysis plan and amendments

12.4. Randomisation list

12.5. Raw data

The raw data should be provided in electronic format or a link to a database in case they are publicly available in order to allow the replication of the analysis. Raw data should be accompanied by a data dictionary containing the description of the variables and the metadata needed to properly analyse them. The details and structure of the electronics files should be presented in this section.

12.6. Publications based on the study and/or analysis

12.7. Unpublished references

12.8. Quality assurance procedures

Measures taken to ensure the quality of the data, analysis and reporting should be reported in this section. These can include data/information versioning, QC of the programmes used for analysis and processing, versioning of the outputs and the QC measures to ensure any results presented in the body of the report. All measures taken to minimise bias should also be presented here. If QC measures are not taken then this situation should be justified.

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