



THEMATIC SERIES

How to write a scientific paper—Writing the methods section

Como escrever um artigo científico – Estruturação e redacção da secção de métodos

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Introduction

The methods section is the most important part of a scientific paper because it provides the essential information that allows the reader to judge the validity of the results and conclusions of the study reported. Therefore, in this section the authors should provide a clear and precise description of how the study was performed and the rationale for the methodological choices and characteristics of the study design. This section should be written in a clear and concise manner, but should always present enough information so that: (1) the study could be replicated by other researchers, in order to evaluate the reproducibility of results (it should not be a step-by-step tutorial but should be a systematic and complete description of what was done), and (2) the readers are able to judge the validity of results and conclusions presented. This will typically be the first section to be written in a paper (although many times the last to be finalized after corrections and reviews of authors and reviewers), mainly because it should be already thought of and written as a part of the research protocol/proposal, prepared at the initial phase of the research work, and because it sets the stage for the results and conclusions presented in a paper. From

a journalistic point of view this section should answer questions like ‘‘who’’, ‘‘what’’, ‘‘where’’, ‘‘when’’, ‘‘why’’ and ‘‘how’’; and should do it having into account the difficult balance between completeness (sufficient details to allow replication and validity verification) and brevity (the impossibility of describing every technical detail and the need to strictly follow the guidelines/instructions for authors provided by journals and recommendations regarding word count limits). In this article, we describe and discuss some general recommendations that should help preparing the methods section of our manuscripts; and we propose a general structure and recommended content for this section. Because this section is so intimately related to the foundations of science, the scientific method and the study design, we begin by reviewing some general concepts and principles and then follow with the presentation of a proposal for its structure and content.

Basics of the scientific method and study design

Although many authors and schools of thought have different definitions and understandings regarding this matter, it is fair and generally consensual to say that science is a systematic endeavor aiming at the acquisition, development and updating of knowledge; and knowledge could be defined as a set of models that aim to describe, understand, explain,

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control and eventually modify the real world.^{1–4} The practice of science, generically named scientific research, aims to define questions and find answers that may contribute to the building of knowledge using the so called scientific method. The scientific method, particularly in the natural sciences, mainly relies on the empirical observation of the world, as objective and unbiased as possible, and the adequate use of processes as deduction, induction^{1–3} and abduction,⁴ in order to generate and test hypothesis and subsequently models that allow us to describe, explain and modify the real world. In general, scientific research questions look for the estimation of population parameters or the confirmation or discovery of relationships, eventually of a causal nature, among objects (physical matter, processes, interventions or concepts). In a quantitative research paradigm the objects are regarded as variables that researchers may measure and/or control, and a variable is simply defined as a characteristic that may vary among the subjects or units of observation under study. When estimating parameters or assessing relationships, that quantitatively translate the answer to the research question, researchers are interested in minimizing random errors and systematic errors. Random errors are associated with usual sources of variability, generally measurement and sampling variability, that may affect the estimation^{5,6}; and they directly affect the precision of the parameter estimates presented. Systematic errors or bias are associated with phenomena that may affect the validity of the estimation and conclusions.^{5–9} Validity simply refers to the ability that a method or a study has to measure or estimate what it really intends to measure or estimate. Thus, validity refers to the credibility of the study design and results and the degree to which these results can be applied to the general population of interest.^{5,6} Internal validity refers to the credibility of the study itself and is determined by the degree to which study conclusions correctly depict the truth in the study.^{5,6} External validity refers to whether the results of a study can be generalized to a larger population of interest.^{5,6}

Random errors are controlled or dealt with mainly by an adequate choice of measurement methods and instruments, an adequate choice of sampling methods and sample size and an adequate use of statistical methods for data analysis and presentation.⁵

Systematic errors or bias are the main target when selecting a study design and defining the methodological characteristics of the study. The methods and strategies to control and minimize systematic errors are the main factors affecting the validity of the study results and conclusions.^{5,7–11} There are many different sources of systematic errors that should be considered when designing, implementing and reporting a research study and many authors have presented different proposals for their definition and systematization.^{9–11} It is classical though, particularly in the field of clinical or epidemiological research, to classify systematic errors or bias in three main categories^{5,6,9}: selection bias, information bias and confounding.

1. Selection bias refers to systematic errors associated with the selection of study participants or units of observation.^{5,6,12}

2. Information bias refers to systematic errors associated with the measurement or classification of study variables (typically classified into three main groups: dependent variables – outcome or response variables; independent variables – predictive, exposure or intervention variables and confounding variables – confounders or extraneous factors) and the methods and instruments used for that purpose.^{5,6}
3. Confounding refers to a phenomenon where certain variables (confounding variables) that are associated simultaneously with the outcome and predictors under study interfere with the valid estimation of the true predictor's effect on the outcome.^{5–8} Confounding is, of course, of particular importance in causal research. Sadly, the real world is much more complex than we would like, so simple, unambiguous, direct relationships between objects can be difficult to ascertain. Thus, in causal research, the validity of a study is judged by the degree to which its outcomes can be attributed to manipulation of independent variables and not to the effects of confounding variables. It is important to emphasize that confounding variables are hardly ever fully controlled; and in many instances the influence of those variables is not fully appreciated by researchers. Therefore, the study design must be defined so as to control as many extraneous factors as possible, so that any potential cause-and-effect relationship between two objects can be judged validly.

The study design is the overall plan for addressing the aims or purpose of the study and answering the research questions or testing the study hypotheses.⁵ It generally defines the way researchers should look at the world, when seeking empirical evidence regarding the research question, in order to avoid fallacies and systematic errors usually associated with the unstructured or unscientific empirical observation of the world. The selection of a research design should be driven first by the research purpose (questions) and second by feasibility issues. Questions to consider when selecting a study design include⁵:

1. How much do we know about the topic under study?
2. Will there be an intervention? Will all subjects get it? Do we control who gets the intervention? Is it feasible to randomly assign subjects to the intervention?
3. How often and when will data be collected from subjects?
4. How can factors that may potentially interfere in the relationship between predictors and outcomes be minimized or controlled?

The answer to these questions comprises the justification for the study design selected and should be always succinctly explained. The different study designs and methodological characteristics will affect the validity of the study results. Thus, although a more thorough description of the various types of study designs is beyond the focus of this article, it is very important that researchers know the basics regarding study design and that researchers adequately describe it.⁵

In conclusion, the choice of the most appropriate study design and the adequate planning and implementation of the research methods are the foundations of good research work; and their main purpose is exactly to minimize random

and systematic errors that may affect the answer to the research question. Thus, the methods section in a paper should essentially report in a concise but complete manner how well random and systematic errors were considered and controlled by researchers, so that the validity and precision of the estimates that quantitatively translate the answer to the research question may be judged by the readers.

Structure and content of the methods section

In most journals the "Methods" section is designated as "Materials and Methods" or "Participants and Methods" emphasizing the two main areas that should be addressed. First, "Materials" refers to what was observed (e.g.: humans, animals, tissues, cells, etc.) and the interventions (e.g.: drugs, devices, etc.) and instruments (e.g.: measurement technologies) used in the study. Second, "Methods" refers to how subjects or objects were selected, manipulated or observed to answer the research question, how measurements were performed and how the data were analyzed.^{13–15}

The writing of the Methods section should be clear and orderly to avoid confusion and ambiguity. The methods section should ideally be structured in a set of subsections describing its main content.^{13–15} A possible structure is proposed along this paper including the following subsections^{13–15}:

1. Study design;
2. Selection of participants – selection criteria and selection methods;
3. Data collection – variables, methods and instruments and
4. Data analysis.

Each one of these subsections could have additional sub-headings as appropriate. It should be stressed that the proposal that follows is deemed to be broad and general in scope, and should always be completed with some other specific indications in the context of the particular type of study it is important (1) to look at many other examples of methods sections in articles with similar scopes and aims as ours and (2) to use some of the many reporting guidelines that are available for the most common study types^{16,17} (e.g.: CONSORT for clinical trials¹⁸; STROBE for observational studies¹⁹; STARD for diagnostic research²⁰; PRISMA for systematic reviews and meta-analysis²¹; etc.).

The writing of Methods section should be direct, precise and in the past tense. Complex sentence structures should be avoided, as well as descriptions of unimportant aspects or too much details. In general the description of procedures and measurements should be organized chronologically; and, in each subsection, content should be organized from the most to the least important.^{13–15}

Study design

Typically the Methods section begins with a general paragraph describing the study design and the main methodological characteristics of the study, establishing the setting

for the description of participants selection and data collection. In the context of clinical and epidemiological research, the classical classifications and characteristics most frequently considered when describing and systematizing the study design are^{5,6}:

1. The definition of the descriptive vs. analytical nature of the study. Descriptive studies aim to describe population parameters or associations (hypothesis generating studies) and analytical studies try to answer causal questions (hypothesis testing studies).
2. Reporting the comparative vs. non-comparative nature of the study (is there a group comparison?).
3. Reporting the interventional vs. non-interventional nature of the study (is there an intervention to be evaluated?).
4. Reporting the existence of control over the interventions or factors under study and the existence of randomization. These two criteria allow the classification of studies into three main groups: experimental, quasi-experimental and observational studies. In experimental studies the researchers have direct control over the interventions or factors under study and allocate them to the subjects using a random process – randomization (e.g.: randomized controlled trials). In quasi-experimental studies researchers control the interventions or factors under study but they do not implement randomization procedures (e.g.: non-randomized clinical trials). In observational studies researchers are unable to directly control the interventions or factors under study and do not implement randomization procedures (e.g.: cohort studies, case–control studies, etc.).
5. Reporting the type of randomization procedures when those are implemented (e.g.: parallel groups vs. cross-over, balanced vs. unbalanced groups, complete vs. incomplete designs, factorial designs, etc.).
6. Reporting, in observational studies, if the participant selection was based on the predictor variables (cohort studies) or the outcomes (case–control studies) under assessment.
7. Reporting the cross-sectional vs. longitudinal nature of the study (having into account the existence of an assumed or factual follow-up period).
8. Reporting the prospective vs. retrospective nature of the study (having into account the point in time where the predictors are measured in relation to the outcomes or the point in time where recruitment of participants starts).

The different study designs and methodological characteristics will affect the validity of the study results. Thus, although a more thorough description of the various types of study designs is beyond the focus of this article, it is very important that researchers know the basics regarding study design and are able to adequately describe it.^{5,6}

Ethical considerations

A clear presentation of the ethical considerations is mandatory in all animal or human studies. Although it may not

be a subsection by itself, as an alternative it could be a part of the subsection "Selection of participants", this presentation is important and should take into account the international guidelines on good clinical and research practices.^{22–25} In general, references regarding the informed consent obtained on human subjects and the approval of the research protocol by an ethical committee or an institutional review board should be presented. In Portugal, submission of the research protocol to the national data protection agency (Comissão Nacional de Protecção de Dados – CNPD) could also be necessary.²⁶ In the case of experimental studies on human subjects (clinical trials) the approval by a national ethical committee is legally mandatory.²⁷ If the study raises any additional specific ethical concern this should be adequately described (e.g.: studies on especially vulnerable subgroups).²⁸ Although not directly linked with the ethical considerations, it is important to stress that for experimental studies on human subjects (clinical trials) authors should give an appropriate reference to the registration of the study protocol on a clinical trials registration database.²⁹ Most journals today only accept for publication clinical trials previously registered.

Selection of participants – selection criteria and selection methods

The participants selected for inclusion in a study and the methods of selection will ultimately determine the limits that are placed on the generalizations that can be made regarding the study results. Judging the external validity of a study (i.e.: assessing to whom the study results may be applied) requires a comprehensive description of the selection criteria and selection methods and descriptive data regarding the study sample be provided.⁵

This subsection could begin with a brief presentation of the study setting, in order to contextualize the study presented. This should include the setting, location(s) and relevant dates of the study, indicating, for example, periods of recruitment, exposures or interventions, follow-up and data collection.

After presentation of the study setting, there are three major topics that should be addressed in this subsection⁵:

1. Specification criteria (selection criteria),
2. Methods for selection of participants (sampling) and
3. Recruitment process.

First, a full and thorough description of the criteria for selection of participants – inclusion and exclusion criteria – should be presented and its rationale explained.⁵ Authors should clearly indicate the target population and the accessible population in the study.

A general description of the characteristics of participants is also important and could also be added, but this is a matter of discussion because many authors and journals believe this should be a part of the results section. For human subjects it is important to describe general demographic and clinical characteristics. For animal subjects it is important to adequately describe the species, weight, strain, sex, age and eventually details regarding special characteristics or living conditions.

In studies involving animal models or mechanical models, a detailed description must be provided regarding the preparations made prior to beginning the experimental protocol. In addition, all aspects of animal or tissue preparation required prior to initiation of the research protocol must be described in detail. With any animal preparation or mechanical model there must be enough detail provided so that the reader can duplicate it or evaluate its relevance.

Second, the methods for selection of participants should be carefully explained. This should include an account of how the subjects were identified and how they were sampled from the target population under study (sampling methods).⁵ When selecting subjects from a target population, probabilistic sampling methods (random samples) are preferred because they more appropriately guarantee representativeness of the sample. When reporting probabilistic sampling methods authors should describe the sampling frame, the instruments used for the random selection process and, if appropriate, the use of complex sampling methods with stratification or clustering and weighting procedures. Although probabilistic methods are preferred, for practical reasons, non-probabilistic sampling methods (non-random samples) are much more common (e.g.: consecutive samples, convenience samples, systematic samples, etc.). Although non-random sampling methods do not guarantee the representativeness of the sample, they do not necessarily prevent us from validly answering the research question. It should be stressed that non-probabilistic sampling methods are in many instances appropriate. For example, most of randomized clinical trials do not select participants through a random sampling process, and they still are able to appropriately answer the causal question regarding efficacy of therapeutic interventions, relying on the random allocation of alternative interventions (randomization), even when the participants selection is crucial point is to be able to generate comparable study groups and make fair comparisons (equipose) between groups and, at least in this case, representativeness of the sample, although also important, is regarded as secondary.

The third topic to be addressed in the "Selection of participants" subsection is the recruitment process.⁵ Authors should describe in detail how recruitment was undertaken and particularly how effective it was. They should present a complete account of the subjects selected from the sampling frame, those that accepted and those that refused to participate, ideally with a summary of reasons for refusal and a brief characterization of the subjects refusing to participate. Methods implemented to reduce refusal rate should also be described.

In addition to the three main topics described above, in comparative studies it is also important to describe some particular methods of group allocation and/or participant selection that aim to improve their comparability. In experimental studies (randomized controlled trials) a thorough account of randomization procedures should be presented including¹⁸: methods used to generate the random allocation sequence, details on any restrictions to randomization (stratification or blocking), methods for allocation concealment and implementation details of the randomization process. In this type of studies this is often an independent subsection of the methods section. In observational

studies (e.g.: cohort studies, case–control studies, etc.) authors should describe and give details regarding the implementation of methods such as stratification and matching, whenever those are used.¹⁹

Finally, in longitudinal studies a full description should be presented of the follow-up procedures implemented, often as a separate subsection. This should include a description of the completeness and quality of participants follow-up (number and reasons for losses of follow-up, drop-outs, drop-ins, etc.) and, in comparative studies, methods implemented to guarantee equality of follow-up conditions, for example, blinding of researchers or healthcare professionals responsible for the follow-up and the adequate control of co-interventions.⁵

Data collection – variables, methods and instruments

The next step in the methods section is to describe the data collection process, including the variables measured and the methods and instruments used for their measurement. In a quantitative research paradigm the adequate and unbiased empirical observation and measurement of variables is the cornerstone of the scientific method; thus this subsection deserves careful and thorough consideration.

Variables are observable objects that are measured, manipulated, or controlled in a study. Variables can be concrete concepts, such as height, weight, and blood pressure, or abstract concepts, such as stress, coping or quality-of-life. Variables should be operationally defined by indicating how the variable will be observed and measured in the study. Abstract variables (constructs), such as quality-of-life or stress, should be defined both conceptually and operationally. The conceptual definition explains the theoretical meaning of the variable, while the operational definition specifies how it will be measured. For example, when measuring quality-of-life, researchers could present a brief conceptual definition of the construct, but should always add details regarding its operational definition, by indicating the model and instrument applied to measure quality-of-life, for example, by using the SF-36 health questionnaire.

In general, the variables in a study could be classified in one of four major groups²:

1. Predictor (independent, exposure or intervention) variables,
2. Outcome (dependent) variables,
3. Confounding (extraneous) variables or
4. Interaction (effect modifier) variables.

When describing the variables in a study the authors do not need to give a full and complete description of all variables measured, however the main predictors and all outcome variables should be described with sufficient detail as to allow replication and assessment of the quality of the measurement or classification. For these variables a full account of their conceptual definition, operational definition, classification or diagnostic criteria applied (if appropriate), methods of measurement, instruments used and a brief description of the evidence regarding their

validity and reproducibility should be presented. This detailed presentation should be extended to any other variable of particular importance for the study or with uncommon measurement procedures or instruments.⁵

For those variables where it is deemed necessary, the description of the measurement methods and instruments should include the manufacturer and model, calibration procedures, evidence regarding the validity and reproducibility of instruments and how measurements were made. The instruments used to measure variables must be reliable and valid. Validity is the extent to which an instrument measures what it reports to measure. Reliability refers to the consistency with which an instrument measures a study variable. Internal consistency (e.g.: Cronbach's alpha), test–retest reliability, and inter-rater reliability are examples of methods used to assess the reliability of an instrument, particularly in the context of abstract concepts (constructs) measurement. These psychometric or clinimetric properties of instruments determine the overall study validity. It is important to select and describe instruments that have established reliability and validity in the population that the investigator plans to study (e.g.: older adults or children) and use instruments that are properly translated, adapted and validated for the study population. Although not formally prohibited, the use of instruments that were not previously submitted to an adequate translation, adaptation and validation process impose important limitations to the credibility and validity of the study results and its use should be always indicated.

Finally, particular methods to control bias associated with the measurement or classification of study variables should be described. For example, implementation of blinding procedures for participants and for researchers collecting data (especially outcomes measurement) should be indicated and explained.

Data analysis

In the last part of the methods section authors should describe with sufficient detail the statistical methods used for the study data analysis, including descriptive statistics and methods for statistical inference.⁵ This presentation should have a close link to the aims of the study and should precisely establish what will be presented in the results section.

This subsection should include an initial general sentence regarding the descriptive statistics used, having into account the main types of variables analyzed (e.g.: means or medians, standard deviations or quantile ranges, absolute frequencies and proportions, etc.). Next, a brief description of inferential methods used should follow, including the indication of confidence intervals calculated, an account of the statistical hypothesis tests applied and the indication of any uni- or multi-variable regression or modeling procedures employed. A special note should be added regarding the use of precision intervals as the best method to express the precision of parameter estimates presented in a study. Their presentation is increasingly deemed essential and they are more informative than the classical *p*-values of hypothesis testing.

Some additional aspects regarding the statistical analysis should be addressed whenever it is deemed necessary, taking into account the main study aims:

1. Describing the specifics regarding methods used to account for confounding in observational studies (e.g.: multi-variable regression methods for effect measures adjustment, propensity scores,³⁰ causality modeling using directed acyclic graphs and structural models,^{31–33} etc.).
2. Describing methods to examine subgroups, interactions and effect modification in experimental and observational studies.³⁴
3. Describing any interim analysis, stopping rules and adjustments that may be used, particularly in experimental studies.¹⁸
4. Describing any particular adjustments made taking into account the sampling methods and weighting procedures used.
5. Describing methods used to account for missing data.
6. Describing methods used for sensitivity analysis.

Also important in this section is to describe the estimates and explanation of methods for the sample size and power determination.⁵ The determination of the sample size before the beginning of the study is crucial to ensure the appropriate power of hypothesis testing and the precision of parameter estimates. In many instances, particularly in observational studies, a formal sample size calculation is not possible for practical reasons (for example, the study sample is assembled retrospectively or is already fixed before the beginning of the study). Even in these situations it is advisable to present results of a formal power analysis, in order to give an indication of the power of hypothesis tests and the magnitude of differences that researchers are able to detect in those settings. Some authors prefer to incorporate the paragraph regarding sample size determination as a part of the "Selection of participants" subsection.

Finally, an indication of the level of type I errors (alpha level) assumed in all statistical hypothesis testing (usually, a 5% alpha level is assumed) and an indication of the statistical software package used for analysis (with a reference) should be presented in this subsection.

Conclusion

The methods section is the most important part of a scientific paper because it provides the crucial information that allows the reader to judge the validity of the results and conclusions of the study reported. Therefore, in this section, the authors should provide a clear and precise description of how the study was performed and the rationale for the methodological choices and characteristics of the study design. A clear and precise account of how a study was performed, and the rationale for specific study methods are the crucial aspects of scientific writing. A proposal for the structure and content of the methods has been presented and explored giving a general guidance for the writing and assessment of the quality of this section and of the study reported. We hope that somehow this paper may comprise a useful tool for authors, reviewers and readers of scientific

papers, and in particular those of the *Portuguese Journal of Pulmonology (Revista Portuguesa de Pneumologia)*.

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