The role of the committee on ethics in research in the assessment of the ethical implications of the use of statistical tests

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Abstract

Brazilian's research ethics has being transformed since the deployments of Platform Brazil, in 2011, and the Resolution CNS 466/12, in 2013. However, the ethical implication of statistical tests uses in quantitative research has been little discussed. While some advocate that the research ethics committees should not be involved with statistical analyzes, others argue the opposite. This paper reviews the role of the ethical implications of the statistical work of research, analyzes the consequences of statistical deviations on the final results of the work and concludes that the committee should take responsibility for the adequacy of the statistical analyzes in research projects. Facing current difficulties regarding establishing an ethic assessment system in research in Brazil, some basic orientation is proposed to statistical analyzes assessment, pointing out a solution to this issue by the so called reproducible research.

Keywords: Research, ethics. Statistics and numerical data. Research. Methods.

Resumo

O papel do comitê de ética em pesquisa na avaliação de testes estatísticos

A ética em pesquisa no Brasil tem passado por transformações desde que se estabeleceu a Plataforma Brasil, em 2011, e a Resolução CNS 466/12, em 2013. No entanto, as implicações éticas do uso de testes estatísticos na pesquisa quantitativa têm sido pouco discutidas. Alguns defendem que os comitês de ética em pesquisa não devem se envolver com análises estatísticas, ao passo que outros advogam o contrário. Por meio de levantamento na literatura, este artigo revisa algumas implicações éticas do uso de testes estatísticos e analisa as consequências de desvios estatísticos sobre os resultados finais dos estudos, defendendo que os comitês devem assumir responsabilidade quanto à adequação das análises estatísticas nos projetos avaliados. Diante das atuais dificuldades de estruturação do sistema de avaliação da ética em pesquisa no Brasil, propõe-se aqui orientações básicas para a avaliação da análise estatística, apontando solução para esse impasse por meio da pesquisa reproduzível.

Palavras-chave: Ética em pesquisa. Estatística e dados numéricos. Pesquisa. Métodos.

Resumen

El papel del comité de ética en investigación en la evaluación de pruebas estadísticas

Brasil ha pasado por transformaciones en el campo de la ética en las investigaciones, desde que fue creada la Plataforma Brasil, en 2011, y la Resolución CNS 466/12, en 2013. Sin embargo, las implicaciones éticas del uso de las pruebas estadísticas en la investigación cuantitativa se han discutido muy poco. Mientras que algunos defienden que los comités de ética en investigación no deben estar involucrados en análisis estadísticos, otros dicen lo contrario. Este artículo examina con el análisis de la literatura, el papel de las implicaciones éticas del uso de pruebas estadísticas y analiza las consecuencias de las desviaciones estadísticas sobre los resultados finales de los estudios y se llega a la conclusión de que los comités deberían asumir la responsabilidad de la adecuación de los análisis estadísticos en los proyectos evaluados. Frente a las dificultades de estructuración del sistema de evaluación de la ética en investigación en Brasil, se propone aquí orientaciones básicas para la evaluación de los análisis estadísticos, destacando una solución para este impase por medio de la investigación reproducible.

Palabras-clave: Ética en investigación. Estadística y dados numéricos. Investigación. Métodos.

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Declara não haver conflitos de interesse.

Research article

This work is the result of the author's reflection, that by working with academic research found different perspectives of the role of the Research Ethics Committee (CEP) in the statistical analysis of the projects submitted to the institutional review. At the literature, while some advocate the idea that this assignment is only of the researcher, others propose that the statistical analyzes relating to the projects should be undertaken by CEP, since the design of the research and the methodology applied originated from statistics [1]. Similarly, both the results and the study's findings derive from statistical findings used for acceptance or rejection of the theoretical proposal and for making decisions that can benefit or not humans.

If the role of statistics in the design of a quantitative project transpires at first glance, it is also clear the relationship between ethics and the research project once in Brazil, as in many other countries, it is considered that a scientific research on human subjects followed appropriate ethical patterns when the project that originated it was evaluated and approved by a competent and independent CEP.

However, even though it appears evident the relationship of the research project on ethics and statistics, a survey conducted in October 2013, in Medline, recorded only 26 articles whose title contains the words "statistics" and "ethics", eight of them from the same author, Douglas G Altman [2-9], produced in 1980 and 1981. These articles address the data collection, analysis, research designs, sample size, interpretation of results, presentation of results, misuse of statistics, quality of articles published in medical journals. Among the other 18 articles [10-27] linking the two themes that database, only six were published from 2000 [22-27]. The small number of published articles, however, does not mean that ethics and statistical have dissociated, however indicates the need to review the current extent of this relationship.

One explanation for the diminished frequency of works that include both aspects of the quantitative research projects may relate to the fact that the ethical issues discussed by Altman find themselves incorporated as biase to the research. In the paper entitled "Basic of medical studies," Abhaya Indrayan [28] points this by listing 36 biases and forms to avoid them, which were introduced to the research method. Of these methods, we highlight some of the main aspects that are supposed to be present in the relationship between ethics and statistics in science. Thus, it is expected:

- from science the generalization, that is, that knowledge is credible in similar populations; that the results are reproducible, and that it is possible to reduce the uncertainty degree of predictions;
- that the research project is a complete document that explains *a priori* the scientific method applied in the research and how it will be operationalized, and thus that the project constitutes a script to be strictly followed from beginning to end;
- the statistical analysis is faithful to the hypothesis test or the objectives described in the project, so that the data is not consciously or unconsciously directed for a particular result;
- that the written work resulting from the research has respectability and credibility, that is, the reader must assume that everything was done correctly, according to the limits of science and that the application of knowledge resulted from the study will benefit or at least will not harm humans. It is only ethical to conduct scientific well formatted experiments with the scientific method [8].

In addition to these general aspects, in Brazil the medical research must also follow the rules and guidelines of CEP/Conep system. As it is well known, the ethical regulation of research in Brazil is approved by the National Health Council (CNS), a collegiate body attached to the Ministry of Health. Through the CNS, the National Commission for Ethics in Research (Conep) and the local CEPs throughout the country, implement the recommendations and assumptions regulated by the CNS Resolution 466/12 [29] and its relateds.

Due to the implementation of resolution, it is expected from CEPs the ethics protection both of research participants and the population that will use the knowledge derived from the study. Such ethical protection is guided, among other things, by respect for the autonomy of the participant, the beneficence and non-maleficence study regarding the health and the participant's physical integrity, as well by justice in the distribution of burdens and benefits in individual and collective dimensions. The protection extends also to the assessment of the exposure to unnecessary risks and the productive use of resources, as these are finite and sometimes scarce.

To address all these ethical aspects, the results of studies must to be scientifically correct. A scientifically correct result does not imply no error, but the error only justified when inherent to the limitation of the scientific method, never a result from deliberate omission or negligence. Therefore, it is expected that CEP acts as guarantor of respectability and credibility of research and therefore as a protective body of research participants, failing to approve

projects that do not respond to the questions of scientific research. We believe this justifies the statistical analysis of the projects submitted to evaluation by CEP, as we shall demonstrate.

Assumptions for statistical tests

Statistics is a science component connected to research models that, in health, are encompassed by epidemiology. Either in the area of descriptive epidemiology, which deals with occurrences of diseases or health problems, or within the analytical epidemiology, which relates to the associations and causal relationships, there will be a study design that forwards the results to be statistically analyzed. The delineation can be classified in observational (cross-sectional, cohort or case-control) or interventionist (clinical trials). It is important to consider that the flawed delineation and the negligent application of a quantitative research, specifically in health, can cause serious damage to individuals and society. For a didactic and brief revision of different research designs, please read the article of Hochman, Nahas, Oliveira Filho and Ferreira, research designs [30].

Before debateing the relevance of the analysis by CEP of the application of statistical parameters of the researches submitted to the institutional assessment, it is necessary to clarify the context in which the statistic is inserted. As the dictionary definition, statistics is the science of collecting, presenting and analyzing numerical data [31]. Statistical analysis operates on the theory of probability and is used in projects of quantitative research based on sample variables. Variables are sets of measurements of the phenomena under study. The possibility of extending the information gathered in the studies derives from the characteristics of the sample, which should mirror the aspect of reality that is intended to portray.

A research project conceptualizes the document describing objectively, through the scientific method, the research question and how this question will be answered. Research projects consist on the exposure of the problem in screen, objectives, method and results. Some types of project also add discussion and final considerations, or conclusion, as appropriate. In a quantitative researches, which attempt to describe some aspect of measurable natural phenomena, can also formulate a hypothesis and, through statistical tests, produce evidence that support or contradict it.

The hypothesis is the proposal of the researcher to solve the problem of research. The hypothesis test is the search for probabilistic evidence leading to accept or reject the hypothesis. For the probabilistic analysis of all these elements, the authors conclude on the explicit goals. Thus, statistics is a critical analytical instrument in quantitative scientific papers. The misuse of statistics, which produces erroneous results, disables the scientific work; it can therefore be characterized as an ethical issue [4].

As the statistical tests are mathematical developed formulas to calculate the probability of occurrence of certain phenomena in different circumstances, there is always a model and theory involved in the statistical results. When the studies are descriptive, statistics infers population parameters. Although the analytical studies are models destined to test hypotheses that, in health, are usually assessed by parameters related to the vital statistics such as demographics, birth rate, incidence of disease and mortality in the population or subgroup.

To explain the selection criteria of these parameters, we can think of the voting intention analysis, applied during elections, to foresee the candidate with the most probability of votes. To try, in fact, to infer the result, it requires - necessarily - a probabilistic sample [7], that is, a set of people who portrays the main characteristics of population, incorporating variables of sex, age, educational, economic, as well as those concerning other cultural aspects and associated to living conditions.

To better understand how you define a probability sample, it is necessary to know the idea of randomness. A random sample is obtained by applying one of the sampling techniques, whether simple random, stratified, cluster or systematic. In quantitative researches, the so-called convenience samples do not respond to the question of the research in a scientifically correct manner and do not produce reliable results; therefore, in the absence of the model, no statistics is applied to the proposed objective.

To perform statistical tests, the research objectives must be known. The objectives are clarifications on what the researcher wants to do. The primary objectives are generalized statements, while the secondary objectives are specific declarations. If the work has hypotheses, they should be described in a testable form. By testable form comprehends the way in which the hypothesis may be falsified. When the research contains a hypothesis testing, the statistical analysis will be directed to accept or reject the hypothesis and to identify variables that somehow interfere in the studied relation. If there is no hypothesis, the statistical analysis will be conducted in accordance with the clarifications of goals.

In analytical studies, hypotheses and objectives of any research are translated into variables, which represent the connections of theoretical dimension to mathematics. In other words, they are the numbers obtained by measurements or countings that will be used for statistical formulas. When one wants to know the lifetime of a person, the scale and the measuring unit are chosen. For an adult, the most frequently used measurement unit are the years. If it is necessary a greater precision, months, weeks or days are chosen. But when it comes to the birth of a child, it is preferable to choose minutes or hours. In the first month of life, it is preferable the counting to be in days. Thus, the variable will be, sometimes measured in years, sometimes in months, sometimes in weeks ... The statistical tests use variables and are created in accordance with the scale of measures, from which the parametric or nonparametric tests originate.

Statistics employs measurements or countings, which require precision. Undefined terms must be objectified so they can be measured (for example, profile or quality works must be translated into measurament). It seems that everyone understands what means nutritional status or quality of life. However, when compared, it is seen that the measurement instruments are different and, therefore, do not measure the same dimensions. For science, communication is essential and hence the ambiguity must be removed, especially in the case of statistical models that operate by generalization.

Compound variables are generally conceptual and obtained from questionnaires. The concepts should be well established and recognized by the scientific community. Thus, for example, it is relevant that a research on quality of life make use of the World Health Organization's questionnaire of quality of life, abbreviated WHOQOL [32], since it is already been defined, tested, validated for the Portuguese language and globally accepted. A new measuring instrument must go through validation process before being applied.

A hypothesis test must have a dependent variable and one or more independent variables, or explanatory. For example: we want to test the hypothesis that smoking causes lung cancer. It seems there is a sense in the smoking-cancer relationship. The independent variable is smoking and the dependent - result of smoking - is cancer. You can test more than one independent variable, such as asbestos and smoking, which enhance its effects, and others more.

However, to ensure the reproducibility of the study - essential feature of any scientific project - it is necessary to indicate in advance the variables that will be analyzed and establish the theoretical relationship of these variables with the systematic literature review presented in the introduction of ths present work. The violation of this item directs the analysis for the mistakes of randomness. In jobs involving relationships between variables, there will always be hypothesis testing. Considering the alpha error of 5% (or p = 0.05), in every 20 tests we expect a random false-positive association. This error, of "crossing data", can be obtained with the combinatorial analyzis of 7 variables, resulting in 21 combinations.

The hypothesis exists to be tested, and it is imperative to remember that the data can never be molded to confirm it. Data exploration to find significant *p* that fit the hypotheses is a path that should not be accepted. Not explaining the variables that guided the statistical analysis is like taking a proficiency test with a shooter who does not have in advance the defined targets. Imagine three shots towards a white wall, without any track target. After identifying the wall sites affected by the projectiles, targets would be drawn around them, concluding that the shots were well-aimed.

Following the same logic, the researcher must specify *a priori* errors accepted in his study. The alpha error is related to the probability of reaching a false-positive explanation and depends on a theoretical decision of the researcher. The beta error although determines the size of the sample, and it is important to establish for not making the work inconclusive, whether for a small sample that would expose participants, or for an excessive sample size, that woul produce unnecessary data [6]. To calculate the sample size, the researcher must have clearly defined the questioning of the research and, in the case of the multivariate analysis, the number of variables that will be worked in the analyzes.

In the statistical analysis of medical researches, other factors other than these are important, such as randomization, the use of placebo and blinding. The balance (*equipoise*) [33], obtained by randomization, is an ethical issue of evaluation for CEP, treated in the CNS Resolution 466/12, item III-2, paragraph f:

... if there is necessity for random distribution of survey participants in experimental and control groups, ensure that a priori it is not able to establish the advantages of a procedure over another, through a literature review, observational methods or methods that do not involve humans. The item III-3, paragraph b, is about the placebo: have fully jus-

tified, when appropriate, the use of placebo in terms of non-maleficence and of methodological requirement, being that the benefits, risks, difficulties and effectiveness of a new therapeutic method must be tested by comparing it with the best proven prophylactic, diagnostic and therapeutic current methods. It does not exclude the use of placebo or any treatment in studies where there are no proven methods of prevention, diagnosis or treatment [29].

So having the assumptions of the research is critical for the onset of the statistical tests applications and if these assumptions are not met, the statistical analysis will not apply or be reliable.

Statistical fragility producing incorrect results

The statistical analysis may achieve different results, depending on the used data analysis. To decide between a parametric test and a nonparametric test in a given analysis of small sample, it is necessary to verify the assumption of normal distribution in the population. The evidence that the population distribution is normal leads to the choice for a parametric testing, and if not normal, for the non-parametric test.

In general, it is possible to affirm that when the values and graphics are not conclusive, statistical tests are of great value. In this case, there may be mentioned at least six possible test - Anderson-Darling; Cramer-von Mises; Lilliefors (Kolmogorov-Smirnov); Pearson; Shapiro-Wilk; Shapiro-Francia [34] - allowing the professional the choice of a test that best fits the situation. It should be noted that these choices are open gaps for tendentiousness. As this example, others could be cited.

The treatment of losses and of extreme values may affect the results. An example within health researches are the random losses and losses for refusal of continuing the research, which should not be treated equally. The loss for refusal constitutes a separate group that requires investigation. In small samples, the extreme values can influence the results, especially in regression testing. In hypothesis testing, it is up to the professional justifies if these values will be erased or if nonparametric methods will be used. The treatment of losses and extreme values associated with the statistical method used, which depends on personal decisions that can only be evaluated with the final results.

Choosing the appropriate test for each type of verification and sample also contributes to mistakes. Such misunderstandings may arise from the failure to check the assumptions of the sample [4], for example, random, normal distribution of the population, equal variance, analysis of residuals. They may be related to the use of inadequate sliding scale, treating an ordinal variable as if it were nominal or discrete variable as if it was the reason, or even with the variety of resultants in the screen. In the latter case, for example, it is common that the application of a chi-square test produces the same screen of Pearson's test, Yates' correction and Fisher's test [2]. Each of these results fit in a special situation [35]. From this it follows that the exploration of data towards significant p that fit the hypotheses is a path that should not be accepted.

Finally, among the statistical fragility able to produce incorrect results, it is important to mention the area expertise and the statistician's degree of experience. The statistics, whose the principles are wide, covers various techniques and practicing areas. Thus, for example, a statistical quality control applied to industry uses different tests from those used in clinical trials, besides requiring different professional skills. Therefore, to analyze research projects in health, it is not enough to be statistically trained in mathematics only; but it is also necessary to expand the training towards health area.

In this sense, the statistician is defined as the person who performs statistical analysis of a project. We will then have occasional statisticians, who know the basics of the area, but rarely analyze data, and experienced statisticians, trained by specialized courses in epidemiology and statistics, and who are dedicated to the study and application of statistics in healthcare. The statistical packages commercially available for computers allow people with little experience analyze statistical data. It is only necessary a spreadsheet with data that computers will produce results.

An analysis conducted without a deep understanding of the statistical foundations is concerning. Curran-Everett, Taylor and Kafadar [36] criticize the statistical approach in undergraduate and medical schools that emphasize methods and neglect basics teaching of the area. In the article "Fundamental concepts in statistics: elucidation and illustration", authors review the foundations of statistics and approach to topics such as estimates of uncertainty about population parameters, statistical and scientific significance, and limitations of statistics. Written in an objective and synthetic form, it is recommended to those who want to review or better understand the meaning of statistical formulas and their applications.

Ethical aspects

The CNS Resolution 466/12, item III-2, warns: *Research in any area of knowledge involving human subjects must conform to the following requirements: a) be appropriate to the scientific principles that justify it and with concrete possibilities of answering uncertainties* [29]. It is in this ethical assumption that the rigor of the scientific method and statistical analysis will be supported.

The hypothesis tests carry with them a complex development process that does not admit error. The test of the null hypothesis must result in one of two antagonistic words: accept or reject. These words indicate that a theory is opposed to another, and that only one of them is the scientific truth accepted at the time. However, when the sample size is small, the test does not indicate a precise result, that is, it does not reject, but also is not able to accept, which makes it impossible to conclude. This adverse situation can be avoided with proper calculation of the sample size *a priori*.

However, if the sample size can not be determined, it is not ethical to perform the work, once it would imply submitting human beings to unnecessary risks. And it is precisely because of this concern that CEP analysis must indeed be rigid in order to verify that all ethical and regulatory requirements are being met by a given research. This is because CEP is the ethical co-responsible for the research, and any not identified failure in the study relapses on the committee, either by being unable to identify methodological inconsistencies in a study, whether to approve a job that is not able to answer the research question .

By approving a project, CEP declares to the researcher and to the scientific community the work compliance with standards that define what is ethically permissible in studies conducted in the country. Thus, the committee assumes the responsibility of having nurtured so that only the inevitable mistakes happen, making sure that every effort was made for the target population not be damaged.

In Brazil, the CNS Resolution 466/12, in its item III-3 determines that *researches should use appropriate methods to answer the studied questions, specifying them, whether being a qualitative, quantitative or quail-quantitative research* [29]. In addition to classify the types of research, the standard gives CEP the responsibility to identify the appropriate method to answer the question that guides the study. In this context, it is essential to delegate to CEP the task of analyzing the research design, especially considering the statistical parameters, as is the basic analytical tool of quantitative research.

There are research projects that ambiguously describe the statistical analysis. Here's an example. Quantitative variables will be tested using parametric tests or, if not applicable, non-parametric tests. Chi-square tests will be used for qualitative variables. The expected alpha error is 5%. The statistical program will be the SPSS 20.0. Its description says nothing important. It is as if the researcher was asking CEP for a non completed but signed check, so that later the values were completed with the product available.

Hereafter, we exemplify the objective statistical description, assuming the hypothesis test on smoking as a risk factor for lung cancer. An objective statistical description would be something similar to: *lung cancer will be the dependent variable and smoking, the independent variable. Chi-square test will be used to test the independency of data. The relationship between smoking, and having cancer because of smoking, and not have cancer will be made by odds ratio*. As the research is designed it emerges the need of adjustmenting other variables: *the adjustments will be made through logistic regression with the variables alcoholism, exposure to asbestos and gender*. In this case, the variables included in the analysis were cited in the secondary objectives. The objectivity of statistical analysis demonstrates how the researcher is situated in the event he is researching. The choice of variables resulted from a detailed study of literature and the results were included in the study because they are part of a theory developed by the researcher.

Let's illustrate the subjective statistical description of the statistical tests with the same variables from the previous example, but with addition of others that could be an interesting result. Now the statistitian will use lung cancer as the dependent variable and will make bivariate analyzes of all other variables as independent variables. From the results, it will formulate the hypothesis, once variables resulting in $p < 0.05$ will become a risk factor. In this example, the variables were listed with the expectation that some results in $p < 0.05$.

The alpha error favors that the raise in the number of analyzed variables increases the probability that some will result in the expected p. This study does not have the power to conclude on risk factor, once it is nothing more than a descriptive study, and the utmost production would be a hypothesis that will need another specific study to test it. In this

model, named "cross-checking", the researcher will have freedom to choose the variables that he judges more interesting to develop the article to be submitted in the publication, which represents the bias of statistics. Thus, if the text is approved, any result will have the ethical approval of CEP. The production of Haas [37] explores more deeply this topic.

CEP has limitations that make it impossible to analyze data. Thus, there is no way to identify whether the analyzes were assessed according to the conditions of the test and if the choice was adequate. But CEP has power to judge the appropriateness of the research project planning and verify, in the end, if what was run corresponded to planned. Studies of May [1], in 1975 and Altman [9], in 1981, show the importance of the structure of the research project for ethics, defending the presence of experienced statisticians in CEP.

May bases himself on the principle that the primary protection guarantee of research subjects against unnecessary risks and abuse happens in the revision, before the research begins. Thus, the approval of the research project depends on the approval of the statistical description. In 1994, thirteen years after the publication of Altman's work [9], it was found that the lack of statistical judgment of the research was still going on in England.

In the same year, the very Altman [38], in an editorial published in the British Medical Journal entitled "The scandal of poor medical research", returned to approach the subject. However, only 10 years later, in 2004, the statisticist was included in the regulation for the composition of research ethics committees in the UK by the National Research Ethics Service (NRES) [39,40].

On the other hand, in Brazil, the CNS Resolution 466/12 seems to address the statistical analysis in paragraph 9 of section X-3: *once the project is approved, the CEP, or Conep, in the event that acts as CEP or in the exercise of its original jurisdiction, becomes co-responsible with regard to the ethical aspects of research* [29]. It infers from this text that CEP should gather sufficient arguments to justify the approval of research projects and, therefore, their responsibility equals the researcher with respect to statistical analysis cited in the project. It follows the logical conclusion that CEP's failure to gather arguments to defend the research project implies in the failure of not approving the project. However, it is authorized the operation of committees that have no statistical advisers, which may impair a proper evaluation and approval of the research project.

On the other hand, as the activity of the participants of CEP is voluntary, it could hardly get all committees to rely on experienced statisticians to evaluate all research projects, even considering the multidisciplinary nature expected in its composition. The difficulty of relying on statisticians in CEP, as well as the possible overload of work of these professionals, once they are the better able to analyze key aspects of a myriad of projects, shows that the discussion of the proposal must be deepened in order to find viable solutions for the whole CEP/Conep system.

Given this difficulty and the failure to establish specific standards for the statistical analysis of research projects from CNS Resolution 466/12 [29], there are committees that end up evaluating with more or less severity studies with statistical tests, which opens the possibility, for example, of research agencies and researchers refer clinical trials to the more flexible CEP. Considering these contingency problems, it could be useful to establish scripts for analysis of the statistical aspects of projects submitted to ethical evaluation. Thus, in order to reduce differences between the CEPs as to criteria assessments, a script with basic guidelines on the items required for the analysis of statistics in quantitative research projects, as described in Table 1.

Table 1. Basic items necessary for statistical analysis in research projects

1. Knowledge gap - what science does not know
2. Work proposition - what the study proposes to know
3. Verification of the conditions for the application of statistical tests *a. Goals – listing of the studing proposition* *b. Hypothesis testing - situation in which the researcher proposes a solution to a research problem* *c. Design* *d. Delimitation of the sample (inclusion and exclusion)* *e. Sampling and / or randomizing* *f. Controls* *g. Blinding* *h. Placebo*
4. Explanation of alpha error
5. Explanation of beta error
6. Demonstrative calculation of sample size
7. Variables that will compose the hypothesis test. Dependent variable and independent variables

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8. Possible statistical tests for hypothesis testing
9. Descriptive variables related to the objectives and the proposed statistical tests
10. Statistical criterion to finish (in the case of clinical trials in which the differences are so considerable, that continuing the experiment at the expense of a group is no longer ethical)

Furthermore, regarding the ethical responsibility of CEP, is important to consider that, as the Conep, the committees are bodies whose power emanates directly from the CNS, the highest forum of social control of health. Therefore, the ethical responsibility of the CEP and Conep in the assessment of research protocols goes beyond the normative dimension, putting on the ethical character that moves the democratic spirit, modeler of the Federal Constitution.

Aside from instances of the CEP / Conep system, it is also necessary to consider that the ethical responsibility by studies is shared *a posteriori* by scientific journals, whose reviewers assess the methodological approach of the research reported in scientific articles, submitted for publication. In general, journals adopt strict rules in the analysis of the scientific method of work, since its credibility is directly related to this rigor. So, they play the role of the maintainers of the quality of studies [9].

It should be noted, however, that even though frustrating for the researcher to verify that his project was rejected by scientific journals for methodological failure, the verification of irregularities by CEP, in the design phase, prevents the effects of exposure of participants to the experiment risks since scientific publications can do nothing to protect the research subject. At this stage, the best way to review the experience and statistical rigor seems to be the objectivity of statistical description.

Therefore, the more objective and detailed the description, the more accurate can be the analysis. If there is no descriptive detail, any result is possible. With respect to guarantees to participants, it is preferable CEP to detect methodological errors in the design phase, thus avoiding damage to the subject of research, than to have unpublished work by the magazines based on methodological errors. In this case, in addition to reject the work, it is able to reprove the team that conducted the survey, extending to the evaluators of the CEP/Conep system because, as the item VII-4 of CNS Resolution 466/2012: *The ethical review of project researches involving human subjects must be associated to its scientific analysis* [29].

We must mention the promising idea of reproducible research, developed by Christopher Gandrud in the book Reproducible research with R and RStudio, [41] which may result in a better solution than what proposed in this paper; however, there will be a long way to go until it is accepted by the scientific community. The author compares the publications of current scientific work with advertisements. For him, the research consists in the availability of researchers independent from computing environment, from the code and data that produced the results, so that it is possible to reproduce the work and improve it. Currently, there are tools that make this idea feasible, as the R [42] program, used in large universities and by researchers from around the world along with the RStudio [43], which incorporates features to facilitate the management of R, the LaTeX [44] or Markdown [45] languages, with the package knitr [46], all available for free over the Internet. However, ethical and copyright issues remain to be discussed and standardized before being deployed.

Reproductive researches as the above model would avoid many of the problems discussed in this article, and would be able to identify ethical situations or of statistical trap impossible to be detected without reanalysis. When the statistical analysis is not shown the result becomes a matter of faith, however, being presented becomes a technical issue. As an example of the ethical question of the multiple regression test, we highlight the section 15.5 of the book "Statistics: theory and applications - using Microsoft Excel," Levine, Stephan, Krehbiel and Berenson:

... there is a behavior outside of ethical standards when someone uses the multiple regression analysis and intentionally fails to remove the evaluation variables that have a high collinearity with other independent variables, or intentionally fails to use methods other than the least-squares regression when the conditions necessary for the least-squares regression are seriously violated [47].

The availability of data and code analysis as proposed in reproductive researches would be a breakthrough for science, but would not solve the issue of falsification of raw data. However, the transparency for the scientific community with the publication would be an ethical act of respect for human beings and would decrease the weight that CEP and scientific journals have nowadays, but without eliminating their responsibilities.

Final considerations

Being statistics a research component, it must be acknowledged its relationship with ethics. It is considered ethically appropriate a complete and objective research project, which responds to research issues when approved by a competent ethics committee. The resulting error of an adequate scientific research is only ethically justified when the scientific method was approved *a priori* and executed in its entirety and integrity.

The scientific method applied to quantitative studies in humans using the probability theory by statistics. In these works, the statistic is a vital tool for the application of research in ethics, especially in clinical trials, for its potentiality in damage production. Therefore, there is no way to separate, within the CEP, the ethical analysis of the statistics in quantitative research projects. Incomplete, misleading or ambiguous statistic descriptions do not meet the requirements for approval. It is important, then, that the CEP, as well as the Conep, do not fail to provide proper assessment of the statistical aspects of the studies.

The control instrument of a statistically well-designed research project may be different from that proposed in this work, but supervision and monitoring are necessary and must to be applied. Otherwise, the ethics regulation of research in Brazil will not fully achieve its objective.

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