

Reports of investigations using quantitative methods in the clinical setting: a call for papers

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The understanding of the reasons for human suffering and the identification of effective means to mitigate it had two major developments in the history of civilization. Aristotle, Hippocrates and other Greek philosophers were the leaders of the first revolution, when they started to explain natural phenomena through the use of logic and observation, leaving aside metaphysical grounds, and creating the philosophical basis of the scientific method.

After a long period of recrudescence of religious explanations for the facts of life, the Renaissance experienced the second major revolution in the development of the scientific method. Rather than returning to the Greek philosophers, the thinkers of this new era started to challenge them. Descartes, Bacon and others proposed that the use of quantitative methods could better explain natural phenomena than the scholastic interpretation of reality. At the beginning of the 16th century, the natural philosophy of Aristotle was still taught in Jesuit and other colleges, saying, for example, that things are divided into those which could move by an intrinsic power and into those which would depend on an extrinsic power. Surprisingly, stones were classified as a special case of the first condition, since they had a dormant intrinsic power, which would need activation such as elevation from the ground. The theory of gravity proposed by Newton is certainly a better explanation for the fall of stones, and may be recognized as a major example of the transformation of the scientific method that occurred at that time.

In the field of biology and medicine, the move from qualitative to quantitative explanations for natural phenomena led to the development of physiology, pathology, pharmacology and other sciences, which modified profoundly the understanding of the causes, consequences, and methods of prevention and treatment of diseases.

On the clinical scene, however, the qualitative method for

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- Clinical investigation
- Quantitative methods
- Clinical epidemiology

the description of phenomena prevailed for centuries after Descartes and is still in use today. A look at traditional medical textbooks shows that the description of most diseases and their forms of treatment are mostly based on similarity between clinical presentation and the result of treatment. This is particularly critical in the evaluation of treatments, since the observation of their usefulness in patients was mainly based on comparison before and after intervention (case series), or on comparison with historical therapies. A remarkable example of such understanding was the ligation of mammary arteries as a therapy for refractory angina pectoris. This practice was enthusiastically accepted by some American surgeons in the nineteen fifties. They believed that blood from the mammary arteries would be diverted to the coronary circulation through collateral channels proximal to the site of ligation. The use of a clinical trial to identify the real effect of this procedure with the determination of the placebo effect is one of the first examples of the application of quantitative methods to the clinical setting, controlling for several confounders (1). Cobb and collaborators (1) randomized 17 patients with severe angina pectoris to internal mammary ligation or to a sham surgical procedure. The physicians who evaluated the patient's postoperative experience were not informed about the surgery that had been actually performed in the operating room. The results showed that the number of nitroglycerin tablets used was reduced by 42% in those whose internal mammary arteries were not ligated and by 34% in those whose internal mammary arteries were ligated. In each group, five patients reported a significant improvement after their surgery. This trial is a historical example of the use of quantitative methods in the clinical setting, and it certainly prevented the use of an ineffective therapy in many patients. Some physicians and researchers did not learn with this experience, however. A surgery of transmyocar-

dial laser revascularization has been used to relieve angina despite the absence of an effect on hard endpoints - myocardial infarction, death - in trials with no control for the placebo effect (sham procedure) (2).

The randomized clinical trial celebrated its 50th birthday a few years ago (3), and has been progressively recognized as the main tool to identify the utility of treatments. The application of this experimental design, together with observational studies, to the clinical scenario may be recognized as the third revolution in the evaluation and practice of medicine. It did not come to prevail over old knowledge and methods, but to improve them. Independently of the heading - clinical epidemiology, evidence-based medicine, clinical pharmacology, clinical investigation, or others - the application of quantitative methods to the investigation of cause, diagnosis, prognosis and treatment of diseases should be recognized as a major contribution to the development of medical sciences. The evaluation of performance of screening methods and of the effectiveness of therapies, and the consequent characterization of their cost/effectiveness are progressively being incorporated into medical practice and certainly will contribute to its precision.

The Brazilian Journal of Medical and Biological Research, the leading Brazilian Journal in the field of medical and biological sciences, has been mostly devoted to the publication of results arising from basic science investigations. Even the Clinical Investigation section traditionally presents the results of investigation of mechanisms and markers of disease in studies frequently conducted on patients or volunteers. Studies evaluating the performance of screening tests, clinical trials, and studies of risk of diseases using epidemiological models are sporadically seen in the Journal. Researchers from these areas frequently have difficulties in publishing the results of their investigations, moving to specialty journals with lower impact, epidemiological journals or journals

from developed countries, where they sometimes face hard requirements as authors from the developing world.

In this issue of the Journal (see pages 1441-1446), Moreira Jr. and co-workers present an example of the new clinical investigation paradigm. The authors evaluated the observance of the standards to be followed in clinical trials in papers published in four major journals, focusing on subgroup analysis. They observed that only 41% of the papers that reported subgroup analysis identified if the studies were planned *a priori* or were *post hoc* analyses. Among other pitfalls, most trials did not test for interaction before looking at effects on subgroups. This study clearly shows that it is not sufficient to employ clinical trials in the evaluation of the usefulness of therapies, but that such studies

need to be correctly conducted, interpreted and reported. We do not know if the authors have tried to publish their findings in a major international journal, but we may suppose that they could have problems in doing so, since a major journal would hardly publish a heavy criticism of its own work.

Reports such as the contribution by Moreira and associates, original investigations in the field of applied clinical investigation, and meta-analysis and reviews of these investigations will be welcome in the Brazilian Journal. Together with the traditional areas of our Journal, the Clinical Investigation section may extend its expertise to this field, and could provide a privileged space for international reporting of clinical investigations.

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