Points of view

Quality assurance in cardiovascular medical publications

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Italian cardiological research is steadily growing and the majority of clinical centers is involved in local or multicenter research protocols. Genuine enthusiasm for research fostered by the national professional bodies, increasing competition among cardiologists for purposes of career and rising pressure by the manufacturing industry contribute to this growth. Technological progress has also rendered the management, statistical analysis and transfer of large amounts of data easy. As a result, Italian research produces an increasing number of scientific papers and a very large number of abstracts are presented at major and minor congresses.

The intellectual honesty of publications is of concern both with regard to all medical publications in general and to cardiological papers. This issue has recently been addressed by the Swiss Academy of Medical Sciences[1]. In view of the perceived need for a national body evaluating possible research misconduct, the Committee for Publication Ethics (COPE) was founded in 1997 in Great Britain[2]: COPE is a voluntary body providing a discussion forum and advice for scientific editors. Although primarily involved in the detection and evaluation of cases of suspected scientific misconduct, COPE has developed and issued guidelines for good publication practice including design, ethical approval and data analysis of scientific trials in medicine. Similar initiatives have been taken in the United States[3] and in Denmark where the Danish Committee on Medical Dishonesty has been set up by the Ministry of Science[4]. A recent international survey of biostatisticians[5] came to the conclusion that: "fraud is not a negligible phenomenon in medical research, and increased awareness of the forms in which it is expressed seems appropriate".

Publication of wrong, false or misleading scientific data is not only morally bad: it may do patients real harm, misguide further trials and cause waste of time and money. Quality and honesty in medical research publication is the primary interest of everyone: the scientific community, the industries who support and promote research and – above all – the patients. Attention to the issue of quality as a component of ethics in clinical research has recently been recalled in a major American medical journal[6].

Quality in medical research is probably a very complex issue and its definition is beyond the scope of this paper. One basic component of quality, however, seems to be unquestionable and rather straightforward, i.e. the accuracy in the production, collection, handling and analysis of data. "Procedural" quality may be a workable definition for this. Moral integrity and intellectual honesty in medical publications should not be viewed separately from procedural quality in medical research. In fact, lack of either is prejudicial to genuine research, and both are often concomitantly absent – since one who has followed inaccurate procedures is not likely to declare it.

Large multicenter trials are generally performed with the help of clinical research organizations. In these trials procedural quality and honesty are generally guaranteed by close monitoring of the investigating centers, source verification and data management by professionals not involved in data collection.

Many important papers, however, report the results of single or multicenter "independent" studies conducted without the help of clinical research organizations. This kind of spontaneous research, although in general particularly productive, may be more exposed to the risk of poor procedural quality or incomplete honesty. It should therefore be encouraged and helped to seek and achieve a stronger credit. In fact, editors, referees and readers of scientific papers, even when they are attentive to possible errors, have no choice but to assume that authors have carefully, properly and honestly performed and reported their experiments. In the past, famous institutions and investigators with apparently good track record were not immune from similar problems.

Some helpful suggestions for the assessment and improvement of procedural quality in medical research may be offered by quality assurance systems. The need for quality assurance and certification has been recognized in the manufacturing industries as well as in the medical profession. Several standards for quality assurance have been proposed. The most popular and worldwide used are the ISO 9000 guidelines. They basically require that the procedures followed to obtain a given "product" be formalized in writing, be traceable and that the results of the original experimental records be available for review. The aim of such a quality system is to curb non-conformity to procedural standards; certification is provided, and periodically checked by specific, independent, third accreditation bodies.

Although direct application of the ISO model to medical research is probably inappropriate and overly bureaucratic, some basic concepts of quality assurance systems can be usefully applied to medical scientific activities. Quality assurance in this setting should cover the proper use of 1) adequate and certified facilities and equipment, 2) patient information policies, and 3) data storage, verification, transfer and analysis procedures. Adhesion to transparent policies for authorship and coauthorship, conflicts of interest, and redundant publication should also be included in a quality assurance program.

Such quality assurance procedures are currently followed by large independent research bodies in the field of cardiology in Italy, like the "Mario Negri" Institute and the ANMCO Research Center, and should be applied also in spontaneous research projects which, due to financial restrictions and limited technical means, do not involve independent, certified clinical research organizations.

We suggest that a national body or agency should be created for quality assurance in cardiology research with the aim of promoting procedural quality and ensuring intellectual honesty in cardiological publications. For this purpose the agency should: a) issue guidelines for researchers (e.g., about keeping adequate records available for inspection, proof of review board approval, signed patient consent forms, traceable source documentation of data, a permanent copy of the final database, details of the statistical work-up), b) publish standards (e.g., about certifications of the laboratory performing biochemical determinations, maximum time and physical conditions allowed for storage of biochemical samples, double check of biochemical determinations, random sample verification of database consistency before analysis), c) assess adherence to standards, d) provide advice to researchers, clinical and research institutions and publishers, and last but not least e) provide rules and assistance in the assessment and management of cases of suspected misconduct.

The agency should in no way interfere with prospective authors in the choice of the subject and methods of their investigation, with local ethical committees and institutional review boards in the approval of the studies being proposed, or with editorial boards in evaluating papers for publication. The request for certification is voluntary. Authors who wish to receive certification of their paper by the agency will be requested to comply, and to declare their compliance, with the norms issued by the agency about scientific production. Authors will authorize the agency to verify data collection and management, according to a codified audit procedure whilst ensuring full respect of all rights regarding confidentiality and intellectual property. Their paper will be assigned a registration number by the agency. This will represent a sort of recognized "mark" pertaining to procedural quality. This "quality mark" should be welcomed by everybody in the scientific community, including the same authors, and by all those who will have to judge the paper in their own interest and also to safeguard that of others. Of course, this certification will not mean that the methods used were appropriate for the purposes of the research, nor that the conclusions being drawn are correct or scientifically important: this evaluation is, and will remain, up to peer reviewers, journal editors, journal readers, and the scientific community at large. Certification by the agency will not even exclude that mistakes or even fraud may be present in the paper. However, the authors' explicit statement of compliance with a body of written rules, and the acceptance of possible data and procedure audit (for instance, on a random basis) by the agency, will certainly reduce errors and discourage misconduct. The knowledge that in case of suspected fraud, pre-defined assessment procedures are followed and that pre-specified, immediate and severe measures are taken if fraud is documented will also certainly act as a deterrent against deliberate misconduct. Criteria for the definition of suspected fraud should be clearly stated, but should basically include failure by authors to provide, upon request by the agency during a random-based audit, documentation of results as specified by the agency standards.

There may be understandable reluctance to the creation of such a national agency. First, as pointed out by Smith[7], everybody likes to think that local bodies, such as hospitals or research institutions, can keep their houses in order and that they can comply with the highest ma-

terial, scientific and moral standards of research. Research, however, is not the primary mission of most clinical centers of cardiology, and the local bodies may not, and most often do not, have enough experience to deal with all these aspects and – as far as the specific problem of misconduct is concerned – are not prepared to face the tremendous conflict of interest which is inherent to the exposure of one of their staff involved in a suspected or proven case.

Second, one may wonder why an experienced and successful investigator should accept to justify his/her way of conducting research. Experience and success are not necessarily a proof of procedural quality and honesty of the work being done. Obtaining certification is certainly straightforward for "good" researchers who would anyhow spontaneously comply with the agency's rules, and who would have no reason to fear possible audit. Those researchers would probably be pleased that the procedural quality of their work is certified. Some, or many, might not stand this challenge without improving their way of conducting research.

Third, the agency, with its unusual authority in the verification of documents and procedures, may be perceived by someone as a body resembling "scientific police". It is not more of a police than any other independent accreditation agency in charge of quality assurance certification. The concept of possible inspection and verification in this field is as basic as it is in all other instances where adherence to rules by everybody is to be assumed – at least when investigators searching for a new discovery consider that the issue of confidentiality is no longer a concern.

Last, but not least, it may be questioned how, and by whom, should the competence of the agency members be established and, by the same token, how bias should be avoided. Although this issue is open to discussion, the agency should probably include a managing board (a limited number of senior members with experience in the management of research and who have been active scientists themselves in the recent past) which is designated by the professional associations of cardiologists. In addition, a variable number of consultants (successful, active investigators in the various fields of cardiology research) should be chosen by the managing board for the evaluation and assessment of single items and for the formulation and updating of standards. Agency board members and consultants should be changed on a regular basis. Possible conflicts of interests should be disclosed by all those who wish to cooperate with the agency, just as peer reviewers of medical journals are expected to do when they are requested to evaluate a paper submitted for publication in a journal.

Basic and clinical cardiological research is very widespread, vital and fertile in Italy just as in many other developed countries, and there is no reason to believe that, unlike Great Britain or Denmark where this issue has been addressed, the quality and honesty of independent research in our country should not be viewed with careful interest. Difficult as it may seem, a national initiative for the promotion of procedural quality and intellectual honesty in cardiology research seems to be both adequate and timely.

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