Quality control in cardiovascular research: a difficult task

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The paper by Pasini and Steffenino draws the attention upon an important topic: quality control of cardiovascular research in scientific publications. The issue should be split into two different aspects: multicenter clinical trials and "independent" research, either basic or pathophysiological or clinical.

Multicenter clinical trial is expensive research, which is, almost invariably, financially supported by the industry. An inherent problem with this kind of research is that only working hypotheses that are of interest for the companies will be tested. The company by which the trial is paid for has a legitimate interest to sell its products and, of course, is not willing to support research whose goals fall outside its marketing strategy. Evidence-based medicine relies heavily on such trials: it has taught many physicians that "common clinical sense" not always leads to treatments that are beneficial for patients. This is an important achievement and is not to be underscored. However, this process shifts the steering wheel of research from the hands of "independent" investigators to those of the industry, which *per se* is not "independent" (in that it does not pursue scientific results in themselves). We do not mean by this that results are manipulated to support conclusions in the industry's interests: this is probably never the case, as research is usually monitored by competent investigators who do not work on the industry's payroll. However, research projects are designed to stay within the industry's strategic plans, and the issue is not the research being made but the research that never goes through this process. We could probably explain our point better with an example. There have been numerous large trials on various drugs in heart failure. Several of them have shown a decrease in mortality, sometimes very large. One could come to the conclusion that, by adding up different categories of effective drugs in the same patients, mortality would be nil or negative; in fact, a few patients should even resuscitate! This is clearly a joke, but is also the clinical reality: we do add up several different drugs in patients with heart failure, only we have no evidence to support our decisions. It is true that trials test one drug at a time, but "on top" of conventional therapy. However, in these study designs only the test drug is controlled, while dosage and the "mix" of other drugs can vary. As a consequence, results only apply to the test drug and not to the combination of drugs actually used. A couple of small trials testing in a controlled way more drugs simultaneously have been performed, but clearly the industry will not spend a lot of money by testing a combination of drugs, some of which might belong to competitors.

"Independent" research is also exposed to the risk of poor quality. This may stem from inadequate study design, inappropriate methodology, erroneous data analysis, and wrong conclusion. This is usually taken care of in the peer review process. Other problems include data doctoring, inadvertent or fraudulent omission of information that might mar data interpretation. Causes of fraud in science can be numerous; often it stems from the pressure to publish manuscript in an effort to obtain developments in own career. Pasini and Steffenino acknowledge this problem, but correctly track down to competition among researchers the improvement in Italian research in cardiology.

From what outlined above, the need for quality control in cardiovascular research is evident. Pasini and Steffenino suggest

that an Agency be appointed in charge with such task. We have doubts about such solution, especially concerning effectiveness and fairness. Multicenter trials are often performed in different countries: which Agency should then be in charge? The one in the coordinating country or all of them? What if their guidelines differ? Most importantly, why should the companies or the individual researchers choose to undergo an outside quality control process? As for fairness, Pasini and Steffenino suggest that the Agency could be structured in keeping with the ISO 9000 organization. There are inherent differences, though: companies submit their products to ISO 9000 where they are evaluated by independent third parties. This is the critical issue: scientific research, whether supported or not by the industry, is performed by clinical or basic researchers; the Agency's composition would be the same. Given the acknowledged "pressure to publish", even the best meaning Agency made of peers would not be above the suspicion of a conflict of interests. Pasini and Steffenino indicate six tasks for this Agency: it should a) issue guidelines, b) publish standards, c) assess adherence to standards, d) provide advice to researchers, e) keep a record of research projects and ongoing trials claiming compliance with published guidelines, and f) provide rules and assistance in the assessment and management of cases of suspected misconduct. We believe that every kind of support from the Agency should be welcome; we do not believe, in contrast, that the Agency should act as some sort of scientific police: the assessment of adherence to standards (point c) is difficult to achieve, could cause aggravation to researchers (additional paperwork, to say one), and, above all, introduces control on research *while* it is being done. Scientific fraud should be prosecuted and made public by everybody who has information about. An *ad hoc* designed agency is something else. We consider these aspects a little frightening: in 1938 Bertolt Brecht made his Galileo say: "*Cities are small, and so are heads, full of superstition and plague"*. Nowadays cities are no longer small, but heads still are: would the Agency let Galileo do his work?