“Don’t go for perfection; you will never reach it.”  
Salvador Dali

The commandments of medicine

Ever since the introduction of the Hippocratic oath, if not before, ethics have been fundamental to medical science and physicians who have been taking care of the sick. The first commandment of doctors was to prescribe only regimens for the good of patients according to their ability and judgment, and not to do harm to the one who is already suffering, in short: Primum nil nocere.

The oath continues with the vow not to administer deadly medicine to anyone, if asked, nor counsel such; and similarly not to give a woman a pessary to cause an abortion. Importantly, the oath also requires respect for the patient, i.e., the promise to enter a house only for the good of the sick, guarding against all intentional ill-doing, all seduction and especially the pleasures of love with women or with men, be they free or slaves. Finally, the oath stresses that all the doctor learns about his patients shall be kept secret and never be revealed to anyone anywhere. The Hippocratic oath ends by enjoining doctors to teach their art to the young. Education was an integral part of the medical mission from the very start.

Can we still adhere to this ancient oath? Obviously, since Hippocratic times, medicine has been through several stages of progress and reversal, from empathic consolation of patients to dangerous and often ineffective remedies. By and large, doctors were convinced that whatever they did was in the best interests of their patients. They did not always realize that sometimes their remedies were not only ineffective, but dangerous. Indeed, when Dr. Cralk was called to George Washington’s house on 13 December 1799, because of the former U.S. president’s slight fever, he – in good faith – prescribed bleeding according to the textbook knowledge of the day. When his condition further worsened, he continued to bleed the president until he eventually died. Was he a good doctor? Certainly, according to the state of the art of his time, he did the right thing. In fact he most probably killed his patient with a treatment based on a concept of ancient times – but did so in good faith: nobody, including doctors, is perfect.

An unforeseen fall

One and a half centuries later things got worse: The fact that physicians can intentionally breach the Hippocratic oath became obvious during the Second World War. Indeed, we had to learn and to accept that even highly educated family men who had graduated in the best gymnasium and universities of their country and trained in respected hospitals, were able to perform the most cruel experiments on innocent twins, children and adults [1]. Indeed, as reported by one of the few survivors of the “angel of death”, Josef Mengele (1911–1979), the physician of Auschwitz, waited personally at the ramp of the concentration camp to select twins for his perverted experiments. Twins, he felt, would be the ideal subjects to compare the effects of his interventions with germs, bacteria and other measures unknown until today in genetically identical human organisms. Eva Moses Kor and her twin sisters were enrolled in Mengele’s randomised case-controlled, albeit ruthless experiments and barely survived the sepsis induced by intentionally injected bacteria in one of them (with the other serving as control). The lessons learned from these atrocities are clear: without strict rules, even the most noble intentions of mankind can be abused by a few.

Proper rules

In response to these atrocities, the Nuremberg trials and later the Helsinki declaration, regulations on Good Clinical Practice and Good Manufacturing Practice, among others, set necessary ethical standards of medical research that were increasingly implemented.

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around the world. Thanks to these regulations, clinical science developed within well defined ethical boundaries, leading eventually to evidence-based medicine as practised today. The Federal Drug Administration in the US and now also the European Medical Evaluation Agency in London have contributed to the advent of ever safer and effective drugs by regulating research and development. Indeed, the Contergan scandal made strict measures for drug development necessary to minimise unforeseen effects of novel compounds.

Overall, these regulations have worked amazingly well; thanks to these rules we now have an array of drugs available to effectively and safely treat hypertension, hypercholesterolaemia, infarction and heart failure, among others. Obviously, even the strictest rules could not prevent surprises such as the catastrophic phase 1 study at Northwick Park Hospital with the novel antibody TGN1412, which proved highly effective in immuno disease models in rodents, but nearly killed the volunteers who were involved in the first human tests. Nevertheless, thanks to close collaboration between industry and academia, today’s clinical science and drug development programmes provide useful regulations that ensure proper discovery and effective remedies for the benefit of patients and society at large.

Lifelong learning as a duty

Rules for appropriate research and medical practice, however, are not sufficient to assure optimal care. As outlined by the ESC White Paper published first in the European Heart Journal and the statement of the National Cardiovascular Journals published in the current issue of Cardiovascular Medicine [see page 122], the official organ of the Swiss Society of Cardiology (SSC), physicians have an ethical duty to remain abreast of current knowledge. With the ever increasing diagnostic and therapeutic options and the increasingly shorter half-life of current knowledge, postgraduate education has become a real necessity: only an educated doctor is a good doctor. The CME (Continuing Medical Education) accreditation was introduced for good reasons. Indeed, doctors that do not keep up-to-date with progress in their fields may not only miss opportunities but pose a danger as well. In response to that, most countries have put laws into effect that define the minimal postgraduate training required to maintain a medical license to practice.

How good is the teaching?

Professional medical associations such as the ESC and in this country the SSC continue to support these obligations by providing either congresses, post-graduate courses and/or scientific publications such as the ESC Journal Family [3, 4] and the ESC Textbook of Cardiovascular Medicine [5] among others. In Europe, the costs of continuing medical education (CME) are insufficiently supported by governments and employers. In most European countries there is in fact no support at all, and many universities have little or no funds to support their physicians’ education either. Thus, unrestricted educational grants, travel support and satellite symposia sponsored by industry have become an integral part of postgraduate training. This ensured excellent programmes with speakers and experts from around the world.

In spite of these efforts, medical associations have been increasingly criticised for accepting alternative financial support from industry. Medical education, training and research critically depend on our ability to assess the quality and reliability of any information offered. Indeed, bias of any kind may distort scientific information, and we are exposed to multiple conflicts of interest, be they intellectual, professional, or financial in nature. We love our favourite hypothesis, we depend on our favourite tool and we may be seduced by invitations, honoraria and gifts. No doubt: our judgement is influenced by many factors – not just the industry that is mainly held responsible for it – and it is essential that we are aware of it.

A necessary partnership

As outlined in the ESC White Paper, intensive collaboration between basic and clinical researchers from academic institutions on the one hand, with engineers and scientists from the research divisions of device and pharmaceutical companies on the other, is essential for innovation and optimal care. Without it, new diagnostic tools and better treatments could never be developed. For the most part, it is not the commercial activity or links per se that have become the target for criticism, but the perceived influence of for-profit enterprises on clinical decision-making or on messages conveyed by professional medical organisations.

What is a conflict of interest? The word, “conflict”, derived from the Latin confligere, means to come into collision, to clash [6]. In a conflict of the kind under discussion here, two sets of interests collide: scientific integrity and the desire for personal or financial success. Such desires may be conscious or not, but may lead to biases. “Bias” means tending or leaning towards a particular outcome [7]. Obviously, numerous biases can arise in the scientific process, in publishing and clinical practice. First and foremost, authors may want to prove preconceived notions and advance their careers. Indeed, although Sir Karl Popper saw the scientific process evolving between conjectures and refutations [8], scientists truly strive to prove rather than falsify their own notions and hypotheses. This behaviour reflects the basic motivation of researchers as well as the incentives of the academic rewards system as a
whole. This must not create a real problem as long as editors and their peers ensure that the enthusiasm of authors for their findings is supported by appropriately obtained and analysed data, and that the results and conclusions are discussed in a balanced manner (see page 122 of the current issue).

Such requirements are particularly important for guidelines published by the ESC and other medical societies. Indeed, such publications are among the most cited: the European Heart Journal has published a large number of guidelines in the last five years. With 252 citations and some 28600 cumulative downloads, the best cited guideline was that on the Diagnosis and Treatment of Pulmonary Hypertension [9] under the chairmanship of Nazzareno Galie and a meta-analysis of randomised controlled trials in pulmonary arterial hypertension by the same author [10] also attracted 114 citations. The second most cited guideline in 2009 was on the Diagnosis and Management of Syncope [11] with 130 citations and some 21800 downloads. Also much cited were the Guidelines for Pre-operative Cardiac Risk Assessment and Perioperative Cardiac Management in Non-Cardiac Surgery [12], with 127 citations and some 17200 downloads, and the Guidelines for Prevention, Diagnosis, and Treatment of Infective Endocarditis [13], with 119 citations and an impressive 48500 downloads. Thus, proper and balanced statements are of the utmost importance in such documents since they immediately influence the care of patients. Authors involved in such documents should therefore be particularly aware of potential conflicts, and avoid and disclose them as much as possible.

Should conflicted authors be allowed to be involved in guideline committees? Indeed, in some instances authors may want to gain direct or indirect financial benefit from their publications. An increasing number of findings result in patents, and obviously such results are intended to translate into marketable products. Under such circumstances, it cannot be ruled out that the statements made are biased and potentially inadequate. Since financial ties are not visible, full disclosure of such relations must be required, as again outlined by the ESC White Paper. However, it should be noted that most real experts are conflicted: he who achieves something in medicine and research is a target for industry. For good reasons: the most experienced are needed for the development of new tools and remedies – who else should they ask for advice? If we exclude those, we may hinder innovation and the translation of knowledge into practice. The ESC decided not to follow the American way and also allow such experts to remain active in guideline committees and to nominate co-chairpersons from another field to assure balanced documents on the management of cardiovascular disease.

Is too much of a good thing wonderful?

Mae West’s saying may apply for natural goods to which she was referring, but not necessarily to medicine and research. Rather, Paracelsus’ (Theophrastus Bombastus von Hohenheim, 1493–1541) words are appropriate in this context: All things are poison and not without poison; only the dose makes a thing not a poison. Too many rules are poisonous as well: indeed, too much ethics may become unethical, may hinder innovation and in turn economic and academic development, and not least optimal care of the patients of the future. In spite of the current belief in transparency as a remedy for biases and conflicts, we should not forget that science is primarily based on trust: if researchers do not report what they truly found, the entire process cannot work. However, even if the results are described properly, the interpretation of the data may be flawed: are the findings important or are they clinically meaningless? Are the findings useful for clinical practice or too complicated or expensive to use? These are the crucial questions and we must force ourselves to remain balanced in spite of our enthusiasm for our findings. Eventually, however, only time will tell: as Karl Popper taught us: useless information will not stand the test of time, it will be falsified and substituted by novel findings – a true Darwinian principle in the intellectual world. The ESC White Paper does strive for an intermediate way in the jungle of conflicts we encounter today: we should report potential conflicts to those involved, to our supervisors, directors and rectors. But a Sunshine Act destroying any privacy may only satisfy the needs of investigative journalists and not those truly interested in the progress of science and medicine.

In search of the white doctor

Are we striving for perfection with the ESC White Paper? Probably not, but we should under all circumstances ensure that working with industry does not become a sin. Conflicts are not black spots on our white coat, but the result of a necessary and useful collaboration between two partners. However, we must be conscious of the fact that the incentives differ in industry and academia, and that this may create biases that we must avoid as much as possible. We should go back to the basic principles of Hippocrates, keeping honesty, the patients and those we teach in mind and avoiding an inflation of rules beyond those absolutely necessary. Without rules we cannot work, and with too many neither.
References


2  Relations between professional medical associations and the healthcare industry, concerning scientific communication and continuing medical education – a Policy Statement from the European Society of Cardiology. Eur Heart J. 2012;33:666–74.


