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The codex of science: honesty, precision, and truth—and its violations

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Science has made enormous achievements for our understanding of the world and for everyday life: we now know that we live on a spherical planet of the solar system, we understand the origin of the species, we can take a train, survive myocardial infarction, and fly to the moon. This has been made possible thanks to a persistent search for truth by great scientists and the scientific community at large. Our assumptions were often wrong, but the scientific process advanced by a productive interplay of conjectures and refutations. As in any profession, there is misconduct, i.e. sloppiness, plagiarism up to falsification, or even fabrication of data. Although eventually fraudulent science has and will be disproved, it is morally inappropriate, damages the reputation of research and journals in which its products are published, may endanger patients, and misuses grant money of federal and private institutions. Thus, as editors and readers, we should be aware of it based on its typical pattern, but we must avoid an atmosphere of distrust, as trust is the essence of scientific exchange and progress.

A historical vignette

In 1857 the Augustinian monk Gregor Mendel (1822–1884; *Figure 1A*) began to carry out experiments with peas in his monastery garden and reported the results at the Brünn Natural-History Society on 8 February and 8 March 1865,[1] and published them in the journal of the society in German,[2] as was common practice in the Austrian–Hungarian Empire. Although his findings later became the foundation of modern genetics, they were largely ignored. Only more than a decade after his death in 1900 was his seminal work appreciated by the plant biologists Hugo de Vries, Carl Correns, and Erich Tschermak who confirmed Mendel's findings—the rest is history.

In 1936, Aylmer Fisher, an English population geneticist, charged Mendel of fudging. While he acknowledged Mendel's role as a true pioneer, he claimed that Mendel's data were too good to be true. Indeed, Mendel's ratio of dominant to recessive traits was suspiciously close to the ideal values predicted by his hypothesis.

Was Mendel a fraudulent scientist? Although Fisher's case is convincing, we have no proof of misconduct; specifically, we are uncertain whether Mendel was selecting data intentionally or whether he felt that he was doing the right thing by omitting some experiments that he considered false for good reasons—in any case, he was right. Certainly, at the time, he was unaware of probability and statistics, penetrance of genes, and other factors that might have contributed to the higher than expected variability of his experiments.

Illustrations of scientific work have been changed by many outstanding scientists to make them more convincing ('the most representative figure..'), among them Charles Darwin (*Figure 1B*): in 1872, thirteen years after the appearence of his seminal work *On the origin of species*,[3] Darwin published *The Expression of the Emotions in Man and Animals*,[4] one of the earliest works in behavioural science.[5] The monograph included figures of people's facial expressions depicting emotions such as grief, joy, and anger, amongst others. Paul Ekman, a Darwinist teacher at the University of California in San Francisco, who was involved in the third edition of the book, acknowledged that some of the photographs had been altered. Darwin himself acknowledged that some of his pictures had been posed, modified, or retouched. Indeed, cameras of that time were slow and it was difficult to catch the right expressions. Is this fraudulent or rather smart? Again, Darwin was largely right, as were other icons such as Newton who tended to adjust his calculations to fit best with his models (*Figure 1C*).[6]

The mission of science

The goal of science is the continuous production and extension of certified knowledge. Certified knowledge is based on empirical observation, precise wording, consistent statements about facts[7] and their interaction, supported by appropriate statistics[8]—and it is continually up for confirmation or rather falsification as Sir Karl Popper taught us.[9]

Of note, the intention of the scientists—and this is not of lesser importance—must be the pursuit of truth and nothing but the truth. It is the intention that is crucial, not necessarily the results

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Figure 1 Giants of scientific discovery: (*A*) Gregor Mendel (1822–1884) who set the basis for modern genetics (reproduced by kind permission of Keystone), (*B*) Charles Darwin (1809– 1882), the father of evolution [reproduced with permission from John van Wyhe ed. The Complete Work of Charles Darwin Online. (http://darwin-online.org.uk/)], and (*C*) Isaac Newton (1642–1726), the discoverer of gravity and founder of modern physics (reproduced by kind permission of the Trustees of the Portsmouth Estates).

of their doing: as Immanuel Kant put it in his seminal work *Critique of Practical Reason* published in 1788,[10] there is nothing that is undisputedly good than a good will. We all may err (it is in fact said to be human), but is should not be based on intention, on the will to deceive. As the Scottish writer Samuel Smiles (1812–1904) put it 'He who never made a mistake, never made a discovery'. Nevertheless, honesty and truth must remain the foundations of the scientific process; without it, it must fail.

Importance of the problem

This all sounds obvious, but it is not. As editors, reviewers, and authors, we have to be particularly concerned about the issue; indeed, it is the mission of publishing to provide the best science. The published data should eventually influence the practice of medicine. Thus, fraudulent data not only endanger the mission of science and the reputation of journals and authors, they may damage patients, cause unnecessary costs for fruitless studies trying to reproduce fabricated findings, and they misuse federal grants—enough good reasons to consider the matter.

How common is scientific misconduct? While data on the incidence and prevalence of fraudulent investigations are difficult to obtain, it appears that the behaviour is much more common than expected. Fanelli reported that 2% of scientists admitted fabricating data, and up to a third admitted other misconduct such as dropping data points that did not fit their expectations, changing study designs retrospectively, using inappropriate methodologies, and/or altering results in response to pressures from competitors or funding sources.[11]

Moreover, it appears that the number of papers retracted from prestigious journals has increased recently[12]—the *New York Times* even proclaimed an epidemic of retraction.[13] Indeed, Steen reported that rates of retractions increased markedly between 2000 and 2010.[14] Disturbingly, more than a quarter of retractions were for scientific fraud, and many retracted papers involved high impact journals. In a subsequent analysis by Fang and Casadevall,[15] rates of retractions by prestigious journals correlated well with their impact factors, i.e. higher impact journals had higher retraction rates.[14]

Furthermore, some very recent fraud scandals in The Netherlands[16–18] and Japan[19–21] nourished the discussion about the issue. Why would fraud become more common? If true, several explanations might be possible: first, the prestige associated with publishing in higher impact journals and the impact such papers have on their careers may promote risk-taking behaviour by investigators. Secondly, the increasing competiveness in obtaining grants from funding agencies may lead to scientific misconduct, as will bonuses that certain universities provide to their faculty members who are able to publish in high impact journals. On the other hand, the high visibility of papers published in high impact journals may facilitate detection of fraudulent data.

The spectrum of misconduct

Fraud is a harsh word—it can damage institutions, halt research programmes, and destroy careers. When using it, we should do so with care—we should be conscious of what the word means.[22] The spectrum of its connotations is indeed broad: it ranges from double publication, self-plagiarism, sloppiness, and data suppression, to true plagiarism, data theft, hoaxing, forging, trimming, and cooking (*Figure 2*). Not all types of misconduct are of similar severity; indeed, some—such as data suppression—are everyday practice under certain circumstances. Indeed, there are good reasons to exclude data of a study such as technical problems with an assay, contamination of cultured cells, and mislabelling of patients, among others. Sloppiness such as different numbers in the results and tables, and inappropriate description of methods and other aspects of a study are certainly misconduct, but is it fraud or just mistakes that we all can make unintentionally? Finally, in clinical science, informed consent may not have been obtained in all patients and other ethical standards may have been neglected—again, inappropriate, but not fraud in the proper sense.

Thus, deviations from accepted practice in obtaining, analysing, and reporting results may be of a lesser or greater degree, with

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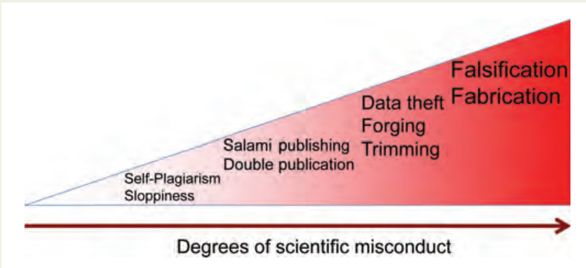

Figure 2 The spectrum of scientific misconduct.

falsification, fabrication, and invention at the top. If truth and fraud have no distinct border, how can we separate the two? It is the intention to deceive that is essential; it is this mind-set that separates omission from trimming and sloppiness from fraud. Similarly, if the work of others is used or even incorporated, but not cited, it is done with an intention to deceive—while citing is acknowledging the work of others. Thus, from a moral standpoint, scientific misconduct may be minimal or severe—aspects that we have to consider.

Case studies

In 1971, William T. Summerlin, a transplant immunologist, claimed that in skin grafts rejection could be avoided, if the material is treated by a form of tissue culture before transplantation. This was breakthrough news that brought him a position at the Sloan-Kettering Institute in New York as chief of transplantation immunology. Unfortunately, in New York, he could not reproduce his previous experiments—obviously this can happen, as any scientists knows. In desperation, he painted some of the grafts of his white mice with black felt-tip pen. The unravelling of this misconduct followed instantly, and during the inquiry doubts also fell on his previous work. As it turned out he had already extensively misrepresented his results in the past. His fall followed a few days later.[23]

The case of the cardiologist John Darsee had a similar pattern.[24,25] Intellectually brilliant and charming, he had published, by the age of 33, a total of 133 research articles in the *New England Journal of Medicine* and *Circulation*, among others. At some point, his colleagues in the Cardiac Research Laboratory at the Brigham had growing suspicions and went to their head Robert Kloner stating that they believed that Darsee was fabricating data—several months later his abstracts and papers had to be withdrawn. Eventually he was dismissed from his position and relieved of his medical licence.

Elias A.K. Alsabti used another technique: he took articles from less well known journals, changed their titles, put himself as the first author with partly non-existent co-authors, and sent them off to other journals. This form of blunt plagiarism appears unique; was there not a similar case which shed light on fraud during the review process. On 9 November 1978, Helena Wachslicht-Rodbard submitted a paper to the *New England Journal of Medicine* about insulin receptors in anorexia nervosa.[26] Arnold Relman, then editor of the journal, sent the paper to reviewers, among them to Philip Feig, Vice-Chairman of the Department of Medicine at Yale, who forwarded it to his post-doc Vijay Soman. Their review was negative and Relman, with three reviews at hand, asked for major revision. Meanwhile, Vijay Soman who worked on the same topic, submitted a paper with Philip Feig as a co-author to the *American Journal of Medicine* where his supervisor was an associate editor. As it happened, the editor of that journal sent the paper out for review to Helena Wachslicht-Rodbard, among others.[27] It goes without saying that this unfortunate accident led to the uncovering of a major fraud. Soman was found to have fabricated most of the results, and he even had copied parts of the article of the Wachslicht-Rodbard paper into his own without citing it.

Most recently, on 17 November 2011, Erasmus University fired their internationally recognized expert in perioperative cardiovascular care, Don Poldermans.[16–18] The Investigative Committee found Polderman to have committed misconduct on several accounts: the first studies that have been questioned were four of the Dutch Echocardiographic Cardiac Risk Evaluation Applying Stress Echocardiography (DECREASE) studies, particularly DECREASE VI,[28] IV,[29] III,[30] and II.[31] Specifically, the committee found that Poldermans did not adhere to the proper procedures of informed consent. Although none of the patients was harmed and in this case the data appeared solid, Poldermans' actions were considered a breach of today's requirements of scientific conduct. Furthermore, the committee concluded that he had not collected data according to protocol. In two cases examined, i.e. DECREASE II[31] and DECREASE VI,[28] there were serious errors. Finally, in several cases, Poldermans apparently fabricated data. As a consequence, the *Journal of the American College of Cardiology* announced concerns about the scientific validity of three papers.[16]

The *European Heart Journal* has published 11 papers in which Polderman is an author; among them he was first or senior author in seven of them (*Table 1*;[32–38]). A conversation with the chairman of the investigative committee, Professor B. Löwenberg,[39] made it clear that the vast amount of publications led by Poldermans over the last decades made it impossible to assess their scientific validity in all cases. The editors of the *European Heart Journal* therefore would like to make an expression of concern related to the papers where Poldermans was the responsible author (*Table 1*). Although missing informed consent is now considered an ethically unacceptable behaviour by investigators, this as such would not invalidate the data. However, the finding of the committee that, at least in some studies, reported events could not be confirmed in all investigated cases, is a major concern.

In December 2012 in Japan,[20–23] concerns arose about the Jikei Heart Study involving publications in *Hypertension*, *Circulation Research*, *Circulation*, the *Circulation Journal*, as well as the *European Heart Journal* (*Table 2*). Again, also in this case it has not been clarified whether it was sloppiness or fraud, but it certainly affects the validity of the papers.

The pattern of fraud

The fraudulent scientist is typically a highly ambitious and talented post-doctoral fellow or assistant professor, charming, sometimes even charismatic, with a brilliant intellect and an impressive

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Table 1 Papers by Don Poldermans as first or last author published in the *European Heart Journal*

Manuscript	Title	Role
EURHEARTJ-D-03-00665	Dobutamine echocardiography: a diagnostic tool comes of age	First author
EURHEARTJ-D-05-01491	Should the ACC/AHA guidelines be changed in patients undergoing vascular surgery?	Last author
EURHEARTJ-D-06-01716	Selecting optimal non-invasive cardiac imaging stress test in intermediate-risk patients using cost effectiveness analysis.	First author
EURHEARTJ-D-07-00137	Indications of prophylactic coronary revascularization in patients undergoing major vascular surgery; the saga continues.	Last author
EURHEARTJ-D-07-02341	Pre-operative cardiac risk assessment in vascular surgery patients; seeing beyond the perioperative period.	Last author
EURHEARTJ-D-09-01732	Three-dimensional speckle tracking echocardiography: a novel approach in the assessment of left ventricular volume and function?	Last author
EURHEARTJ-D-09-02037	Long-term prognosis of patients with peripheral arterial disease with or without polyvascular atherosclerotic disease.	Last author

The Editors wish to mention that this table is provided only as a reference and out of an expression of concern.
[1]Poldermans D, Bax JJ. Dobutamine echocardiography: a diagnostic tool comes of age. *Eur Heart J* 2003;**24**:1541–1542.
[2]Hoeks SE, Bax JJ, Poldermans D. Should the ACC/AHA guidelines be changed in patients undergoing vascular surgery? *Eur Heart J* 2005;**26**:2358–2360.
[3]Poldermans D, Bax JJ. Selecting optimal non-invasive cardiac imaging stress test in intermediate-risk patients using cost effectiveness analysis. *Eur Heart J* 2006;**27**:2378–2379.
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publication record. Usually, he or she—based on his or her remarkable achievements—has been highly recommended to a prolific lab at a prestigious institution led by a well-known mentor. The atmosphere of such labs is highly competitive: positive results, if not breakthroughs, are expected. To fulfil such expectations, fraudulent scientists exhibit a remarkable, if not unusual productivity, and have typically published > 100 papers already at a young age. Often, their papers are full of guest authors, preferably notable scientists, a strategy used to give credibility to their paper. Numerous collaborations with their previous and other institutions make it difficult for invited authors to assess the quality, if not the actual existence, of the data. Duplicate publications with similar or identical figures and tables are also not uncommon—a practice that can easily be detected with today's search engines. Indeed, the editors of the *European Heart Journal* check novelty and the degree of overlap with previous publications of each paper considered for publication using a Medline search.

Usually, sooner or later, fraud comes to an end: colleagues, other post-docs, or technicians become suspicious at some point—indeed whistle-blowers and the scientific process itself play a crucial role in uncovering fraudulent research. As other scientists are unable to reproduce the data, doubts about the validity of such data arise. That's the good news: lies don't live long in science.

Who is an author?

Nevertheless, we have to consider a few things when reviewing papers as editors and experts. In the days of Mendel and Darwin, there was commonly only one author. The complexity of modern science as well as the structure of academic institutions no longer allows single authorships. As a consequence, we witness an inflation of authors in published manuscripts. Indeed, large trials list up to 20 authors, and genome-wide analyses may even go further. This raises the question: who is an author? As we saw, guest authorships, particularly those of great stature, can be abused to provide credibility to questionable data. Thus, whenever we accept an authorship, we must be aware of the responsibility associated with it. At best we should be able to defend the entire study, if required, or at least that part to which we contributed, e.g. statistical analysis, specific assays, etc. At the very least, we should have proofread the last version of the manuscript—anything else is inappropriate.

The peer review process

Can the peer review process detect scientific misconduct? Obviously, it has not been designed to do so—peer review assumes honesty as a prerequisite of scientific working. Peer review is meant to improve the submitted work, if possible. It is not designed to be an inquiry; suspicion is not its mind-set.

As pointed out earlier,[8] when selecting manuscripts based on their novelty, importance, and interest, editors must be aware of scientific misconduct in one form or another, or—to use a morally less pejorative expression—must assess the precision and consistency of the work submitted: are the data accurately reported? Precision and consistency refer to the principle that all

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Table 2 Papers regarding the Kyoto Heart Study retracted in 2012 and 2013

Authors	Title	Published in
Sawada T, Yamada H, Dahlöf B, Matsubara H; Kyoto Heart Study Group.	Effects of valsartan on morbidity and mortality in uncontrolled hypertensive patients with high cardiovascular risks: Kyoto Heart study.	*Eur Heart J* 2009 (see page 3)
Kimura S, Sawada T, Shiraishi J, Yamada H, Matsubara H; for the KYOTO HEART Study Group	Effects of valsartan on cardiovascular morbidity and mortality in high-risk hypertensive patients with new-onset diabetes mellitus.	*Circ J* 2012
Shiraishi J, Sawada T, Kimura S, Yamada H, Matsubara H; KYOTO HEART Study Group.	Enhanced cardiovascular protective effects of valsartan in high-risk hypertensive patients with left ventricular hypertrophy—sub-analysis of the KYOTO HEART study.	*Circ J* 2011
Shiraishi J, Sawada T, Koide M, Yamada H, Matsubara H; Kyoto Heart Study Group.	Cardio-cerebrovascular protective effects of valsartan in high-risk hypertensive patients with coronary artery disease (from the Kyoto Heart Study).	*Am J Cardiol* 2012
Irie H, Shiraishi J, Sawada T, Koide M, Yamada H, Matsubara H; for the KYOTO HEART Study Group.	Cardio-cerebrovascular protective effects of valsartan in high-risk hypertensive patients with overweight/obesity: a post-hoc analysis of the KYOTO HEART Study.	*Int J Cardiol* 2012
Amano K, Shiraishi J, Sawada T, Koide M, Yamada H, Matsubara H.	Enhanced cardio-renal protective effects of valsartan in high-risk hypertensive patients with chronic kidney disease: a sub-analysis of KYOTO HEART Study.	*Int J Cardiol* 2012

data have been obtained as described in the methods section, are consistent in the text, figures, and tables, and analysed with proper statistics. The latter must be assured by a mandatory statistical review, a practice followed by all top journals, including the *European Heart Journal*.[40] This is particularly important in clinical research where power calculations, superiority and non-inferiority designs,[41] as well as various types of analyses of variance including propensity analysis[42,43] must be used.

Are editors truly able to detect 'cooking', 'trimming', or blatant forgery? This is obviously challenging. What they can do is to use computer-assisted programmes not only to assess novelty, but to exclude plagiarism, auto-plagiarism, and 'salami' publishing. Further, inconsistency of numbers in the methods, results, tables, and figures were the first sign of misconduct—often overlooked by co-authors, reviewers, and editors. Finally, plausibility should not be forgotten. An embarrassing example is one of John Darsees' fabrications in which he described a rare form of familial taurin-related cardiomyopathy. In the paper published in 1981 in the *New England Journal of Medicine* and later retracted, any careful reader (or again dedicated co-authors, reviewers, or editors) should have noticed that a 17-year-old male could not possibly have had four children age 4, 5, 7, and 8.[26] This is a lesson to us all, to read papers we are involved in carefully.

Take-home message

What can we learn from these unfortunate events? Certainly, there are seven measures to sustain scientific integrity as much as possible (as already, at least in part, outlined by Colin Norman in 1984[44]): (i) trainees need supervision by an experienced mentor; (ii) the results obtained by researchers should be discussed regularly at research meetings with presentation of the raw data; (iii) all authors should carefully read and approve papers they are involved in; (iv) ethical and animal research approval should be available and checked by a responsible person in the department at the beginning of each study; (v) certified courses on good clinical practice and animal experimentation for clinical and basic researchers should be mandatory; (vi) creation of an ethical board composed of a few wise elder statesmen for the ESC journal family devoted to the promotion of proper scientific conduct and (vii) last, but not least, we must stress that science is a commitment to honesty and the pursuit of truth—nothing else.

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Retraction

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Retraction of: Effects of valsartan on morbidity and mortality in uncontrolled hypertensive patients with high cardiovascular risks: KYOTO HEART Study [*Eur Heart J* (2009) **30**:2461–2469, doi: 10.1093/eurheartj/ehp363].

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This article has been retracted by the journal. Critical problems existed with some of the data reported in the above paper. The editors of the European Heart Journal hereby retract this paper and discourage citations of it.

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