

Truth, Ethics and Consensus - Their Relation to Medical Progress and the Quality of Patient Care

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EDITORIAL

This article describes the various thought modalities underlying the scientific process, and discusses their application to literature review, meta-analysis, consensus statements and position papers, with examples. Various pitfalls are discussed that can act as impediments to medical progress and the quality of care of patients.

Keywords: medical ethics, consensus statements, position papers, scientific method, medical progress, vested interests, patient care, philosophy, meta-analysis, literature review.

FIRST CONSIDERATIONS

At the time of being admitted as a member of the medical profession: I solemnly pledge, myself to consecrate my life to the service of humanity: I will give to my teachers the respect and gratitude which is their due: I will practice my profession with conscience and dignity: The health of my patient will be my first consideration.

Excerpt from the Declaration of Geneva [1]

The fundamental commitments set down in the Declaration of Geneva [1], with its obvious echo of the Hippocratic Oath, were in many ways a response to the atrocities of the Holocaust which may seem remote from current circumstances. They are simple statements of which all medical doctors should be constantly aware - when performing research or when writing for publication, just as much as in everyday practice. In medical research and the advancement of medical knowledge, though, the issues are more complex, and the necessary guidelines less straightforward than in the purely clinical context. At times, the requirements of science can conflict directly with the tenets of the Declaration of Geneva, particularly with "The health of my patient will be my first consideration". Fortunately, the Declaration of Helsinki [2] is available to guide us in the conduct of clinical research, and to protect the individual patient from the demands of scientific progress:

In the treatment of the sick person, the physician must be free to use a new diagnostic and therapeutic measure, if in his or her judgement it offers hope of saving life, re-establishing health or alleviating suffering.

The physician can combine medical research with professional care, the objective being the acquisition of new medical knowledge, only to the extent that medical research is justified by its potential diagnostic or therapeutic value for the patient.

Excerpts from the Declaration of Helsinki [2]

This, and the other principles laid down in the Declaration, can be seen to operate in the carrying out of medical research, from the requirement for informed consent and for ethical committee approval, to the need on occasion, to break the code prematurely in the interests of patients. However, medical research nowadays is a multimillion-dollar international industry, which generates more information and, inevitably, pseudo-information than a working doctor can ever hope to absorb.

ABSTRACTS, REVIEWS, META-ANALYSES AND CONSENSUS STATEMENTS

To assist us all in the endeavour of assimilating data, recent years have seen a rapid growth in the abstracting, reanalysis and integration of research findings. Most medical specialities are served by a variety of publications which contain abstracts or summaries of data for rapid assimilation, in many languages. Abstracting research findings is, of course, an art in itself (rather than a science), but assuming a basic degree of impartiality it is not a very difficult art to carry out effectively, though accuracy is of paramount importance.

Abstracts of research papers deal with single studies. When the aim is for the results of a number of studies, dissimilar in a variety of ways that may not be immediately obvious, to be brought together into a coherent whole, to make some form of overview, the challenges are far greater.

Even a straightforward review of the literature can be a hazardous undertaking: on the one hand, if the paper says nothing new, where is the point? There is a natural pressure to present a viewpoint, any viewpoint at all, and thus a danger of distorting the facts to fit the theory. On the other hand, there is an equal and opposite danger that if all the literature reviewed is not considered critically, the inaccuracies and inadequacies of past research - and worse, of past reviews - will be faithfully reproduced.

The same ethical principles described above evidently apply also when a group of physicians or scientists come together to review the current state of knowledge in a particular area of medicine and publish their conclusions. Any such consensus statements or "position papers", whoever the originators may be, and whatever credentials they present, should stem primarily from a concern as to how best to serve the interests of patients. This is the "gold standard", plainly stated in the Declarations of Geneva and Helsinki. Any paper which falls short of this standard should be viewed with suspicion, as there may be underlying and unstated motives which do not reflect a primary concern for the patient, but involve vested interests of one sort or another.

There are two methods of thus integrating data that have become important in recent years, with contrasting methodologies and outcomes - meta-analyses and consensus statements (position papers can be considered the same as consensus statements). As well as the problems described above for all reviews, these approaches also carry their own dangers.

Meta-analyses use formal statistical techniques to combine the results from similar trials not only to increase numbers but also to generalize conclusions to a more varied range of patients and treatment protocols [3]. In other words, meta-analysis pools data from several studies and applies statistical methods to extract a generalization of sorts. The problems associated with it are therefore largely of a statistical nature, and include the necessary assumption that if the results of one study are representative in some way of the population at large, the combined results of several must be more so. Studies of publication bias, for example, have shown that papers with positive findings are more likely to be published than those with negative outcome, so simply bringing together all the available published papers on a treatment effect does not guarantee a representative sample. Nevertheless, statistical techniques are available at least for evaluating, if not eliminating, such weaknesses, and it is reasonable to conclude, that: "meta-analysis cannot tell clinicians how to treat an individual patient, but it can provide information that helps decision-making" [3]. These issues have been discussed in this journal [4] and elsewhere [5].

Consensus statements raise different and greater problems. Such a statement is produced by a group of experts and/or interested parties coming together to seek agreement on a scientific topic, and formulating a statement which embodies that agreement. Although such a statement has to refer to the published evidence, it is not data that is pooled, but the opinion of the group, in contrast to meta-analysis, and herein lie two major weaknesses. First, because it is opinions that are pooled, rather than data, such a statement is not based on, nor does it refer to, the scientific method. Secondly, the composition of the group is clearly of importance in determining the outcome of its deliberations. When, as is often the

case, such a group is self-selected, the outcome is largely predetermined at that point and the bias set. That bias is likely to be evident from an examination of the membership of the group.

From the outset, therefore, it is clear that the process of consensus statements, or position papers, is not necessarily a scientific one; in some instances it is clearly a political one. How does this approach to the advancement of knowledge match up to the scientific method?

THE BACONIAN METHOD

That which we now term the scientific method is based on the ideas of Francis Bacon (1561-1626) who, in *The New Organon* [6], described the process of inductive logic. Faced with a phenomenon which requires explanation, one formulates a hypothesis, then conducts an experiment to prove the hypothesis. That much we can all remember from school or college. But there is more to it. Bacon termed crucial experiments "Instances of the Fingerpost", in reference to crossroad signposts; the purpose of an experiment is not to seek evidence which supports a pet theory, but to discriminate between alternative hypotheses. At each step in this model, science advances by eliminating alternatives so that the remaining hypothesis must be nearer to the "truth". The following step eliminates more possible explanations, and so on.

Bacon was clear that, as Popper [7] has pointed out, there is no such thing as a proof, only a disproof, once conclusively rejected, a theory is forever dead, but a theory that is alive will live only as long as it takes to replace it by a better one. Medicine, though, is very much an applied science, as witnessed by the declarations quoted earlier. We are frequently concerned with whether something works rather than why it works so the null hypothesis is introduced to give us something to disprove. We hypothesize that a treatment will not work, then seek to disprove that hypothesis. Thus, we believe, science progresses.

MULTIPLE WORKING HYPOTHESES

For better or worse, though, all scientists and all physicians are human. Our humanity can get in the way of our scientific clarity. In this issue of the journal we reprint three papers, the youngest two years old and the eldest over 90, all of which we believe to be important contributions to the philosophy of science, particularly in relation to the emerging field of nutritional medicine. The oldest paper, published in 1897, is by a geologist, T. C. Chamberlin. It identifies a human failing and proposes a solution. The failing is that we can become attached to our theories, particularly if our reputation depends on them, or is augmented by them; "as the explanation grows into a definite theory his parental affections cluster about his offspring and it grows more and more dear to him.... There springs up also unwittingly a pressing of the theory to make it fit the facts and a pressing of the facts to make them fit the theory" [8]. Chamberlin's solution is the method of "multiple working hypotheses". This could be described as open-mindedness in operation. Good detective work can be likened to good science. In detection, holding on to a fixed theory despite the facts will inevitably lead to injustice, and in medicine will lead to a compromised quality of patient care. In both fields of endeavour the use of multiple working hypotheses is superior to attachment to a single hypothesis. Superior in outcome, in that it speeds the advancement of scientific knowledge; superior for emotional reasons, because career or self-esteem is not at stake; and superior for intellectual reasons in that it encourages "a mode of thought of its own kind which may be designated the habit of parallel thought or of complex thought". As the second of the three reprinted papers says, the conflict of ideas which is "all too often a conflict between men ... becomes purely a conflict between ideas".

STRONG INFERENCE

The second paper is "Strong Inference" by J. R. Platt [9], published in 1964. He refers to Popper's point, cited above, that there is no such thing as a proof, and suggests a working method based on the Baconian one, but accepting that what emerges from the elimination of alternative hypotheses is the inference that the remaining hypothesis is nearer to the truth. It is then possible to move swiftly to the next experiment and the next hypothesis. When we cease looking for proofs, we can concentrate on the more scientific approach of successive disproofs. Platt considers the use of this logic a yardstick with which to judge a discipline and its exponents. Those areas of research which exhibit the most rapid advances are those in which the method of strong inference is widely used: he cites molecular biology as an example.

The third paper [10] by Horrobin, was published in 1990 as part of a Journal of the American Medical Association symposium on peer review. It describes the "necessary creative tension between innovation and quality control. The innovators who generate the future, are often impatient with the precision and the systematic approach of the quality controllers. The quality controllers are often exasperated by the apparent indiscipline and unpredictability of the innovators". The relevance of this dynamic to publishing has been discussed before in these pages [11]; it is just as relevant to the advancement of science at large. The paper provides preliminary evidence with which to evaluate medicine by Platt's yardstick. It uses the example of psychiatric drugs, and points out that the five major types of drug in use -neuroleptics, tricyclics, benzodiazepines, monoamine oxidase inhibitors and lithium -were all discovered before 1960. In the 30 plus years since then, despite vast expenditure on research, no major new drug therapies have been developed. This could be because we have done the easy part, and "the problems have become inherently more difficult", or it could be because innovation is being suppressed. However, as Horrobin points out, how can we know about advances if they are being suppressed? He nevertheless manages to cite a number of instances of suppression which failed, including Krebs' description of the citric acid cycle.

CONSENSUS - FUNDAMENTALLY FLAWED

Even when the thinking of individuals is guided by these principles, the consensus of the group can be a far more stubborn beast. As Kuhn [12] pointed out in 1970, "scientific consensus shifts not when new facts are established, but when younger people advance in scientific rank upon the retirement of their elders". Such a shift is "generally preceded by a period of pronounced professional insecurity". Viewed in this light, consensus can be seen as a dangerously unscientific response to the threat of change. At the risk of repetition, we quote again from our letters pages: "decision by self-selected consensus provides such intellectual focus that divergent scientific advances are not 'seen'.... Colleagues have told me that their interest in scientific thinking that diverges from the consensus is actively dissuaded by their seniors and mentors as dangerous to their career advancement and hazardous to their receiving grant support" [13].

This is hardly a new problem- Ninety-five years ago Sir William Osler, writing on the "vice of authority", quoted Stokes:

Though the hair be grey and his authority high, he is but a child in knowledge, and his reputation an error. On a level with a child so far as correct appreciation of the great truths of medicine is concerned, he is very different in other respects; his powers of doing mischief are greater: he is far more dangerous. Oh, that men would stoop to learn, or at least cease to destroy [14].

Consensus is also maintained by the almost universal illusion of intellectual autonomy; if we are told something often enough we come to believe it, despite ourselves. In society this is borne out by the power of advertising, and of the media in general. In medicine, there is a very specific instance; the constant very heavy exposure of all physicians to pharmaceutical

advertising, promotion and influence fosters the illusion that there are no other therapeutic choices available. Medical research is primarily and predominantly funded by the pharmaceutical industry, with little or no resources being channelled into researching other treatment options. Medical students are taught by doctors whose career advancement is dependent on such medical research, and so the "invisibility" of other choices is perpetuated.

Is consensus then fundamentally flawed? Certainly there is a very real danger that it will be used only to shore up a 'fixed idea' - "an idea which is employed to defend a paradigm even in the face of overwhelming evidence to indicate the inadequacy of that paradigm" [15]. This is a common instinctive response to "pronounced professional insecurity". It has already been described in these pages as "selective perception that excludes and ignores scientific advance: the cause is a common reliance on academic scientific consensus rather than on the more truly scientific method of strong inference" [13], so we may see consensus as both a symptom and a cause. Fixed thinking, it must be said, may also be "overtly employed to protect a vested interest without any concern for scientific integrity" [15] - that is to say, not in defence of an inappropriately-held belief but in suppression of an acknowledged but threatening truth.

Viewed in this light, then, consensus statements have to be seen as an unscientific approach to science, with a strong tendency to bias that is probably inescapable. When such a statement includes an opinion, for that is all it can be, regarding what should be considered as good practice, the bias is exposed. If it goes further, and states, for instance, what techniques should and should not be eligible for reimbursement by medical insurance companies, then the vested interest underlying that bias is also made plain. At this point, if not earlier, the bounds of ethical behaviour are over-stepped, in that the concern for the interests of the patient specified in the Declarations of Geneva and Helsinki has been relegated.

Nevertheless, there are examples of well-conducted and honourable consensus papers. A notable recurring feature of them is that they acknowledge the central fallacy, the unscientific nature of consensus, by publishing a divergent minority opinion in the same publication as the majority view. The US National Academy of Sciences report "Lead in the Human Environment" 1161 is a good example. A small number of the panel felt that they could not put their names to the report, and Prepared a separate minority report which was published in the same volume. Similarly, the "Biomarkers in Immunotoxicology" [17] and its addendum "Multiple Chemical Sensitivities" [18] by the Board on Environmental Studies and Toxicology, Commission on Life Sciences of the US National Research Council acknowledged the dissent among its members by publishing in the addendum a compilation of papers representing divergent views.

The above examples are in sharp contrast to the recent report "Allergy: Conventional and Alternative Concepts" [19] published by the Committee on Clinical Immunology and Allergy of the UK Royal College of Physicians. The final version of this, released in April this year, devoted 24 pages to consideration of "conventional" approaches and nine to condemning "alternative" ones, employing a total of 24 references to dismiss everything from dental mercury problems to acupuncture.

INNOVATION

Many approaches in medicine clearly have not been comprehensively "proven" as either beneficial or effective-indeed, we must accept Karl Popper's point that there is no such thing as scientific proof, only successive disproofs. But consensus statements, by their nature, risk creating an appearance of certainty, where none exists. If statements are made on what innovative treatments should or should not be applied clinically, they also risk acting as inhibitors of clinical freedom-the freedom of the individual physician and individual patient to chose a treatment which may be beneficial. This important principle of ethical medical practice is made explicit in the Declaration of Helsinki:

In the treatment of the sick person, the physician must be free to use a new diagnostic and therapeutic measure, if in his or her judgement it offers hope of reestablishing health or alleviating suffering.

The primary concern for the patient must be given priority, at all times, over the considerations of whether or not a procedure is "proven".

VESTED INTERESTS

In the preparation of consensus statements, comprehensiveness, accuracy and integrity are of paramount importance, and steps should be taken to ensure that bias introduced as a result of the vested interests and political motives of individuals within the group is avoided as far as is possible. In medical consensus statements the need to maintain at all times a primary concern for the well-being of each individual patient must prevail. One reason why a consensus statement may fall short of these ideals, clearly, must be the "pronounced professional insecurity" described by Kuhn as a response to a developing shift in the intellectual ground upon which we stand.

More worrying, however, is that some, if not all, participants in a consensus process might seek deliberately and covertly to protect their vested interests, which they see as threatened by innovation. Such a suspicion cannot be dismissed out of hand; as Horrobin [10] warns, apropos of innovation and peer review: "never forget the possibility that even the most eminent and urbane of reviewers may occasionally be corrupt or malign or that lesser folk may be acting under duress".

Medicine nowadays is inextricably linked with the profit motive. The opportunities for doctors or scientists to live and work in "ivory towers" are few and far between. Science and medicine do not exist in a vacuum, but in personal, social, commercial, political and cultural contexts. There is always a danger that these contexts may adversely influence the scientific quality of any report.

It would not be right to condemn a physician for receiving research funds from a commercial interest, but when preparing a consensus statement, it is entirely desirable for those involved to disclose their financial interests. More personal vested interests of a non-financial nature, such as prestige, reputation or psychological factors, are, however, more difficult to document.

There is a further well-recognized factor involved in resistance to innovations. As a physician or scientist, magnanimity is required to contemplate the idea that particular advances in one's field might challenge the basis of one's life's work. The history of medicine provides many illustrations of this difficulty, such as the profession's response (an example of consensus!) to Harvey and his description of the circulation, Semmelweiss and childbed fever, Lister and sterile technique, to name but three.

In evaluating a study which shows a positive effect for a drug treatment, for example, the reader is entitled to weight the report differently according to whether or not the research was funded by the manufacturers, or performed by some independent body. In this journal, the policy is to ensure that any such ties on the part of authors, as of editors, are made plain, so that readers can form their own judgements. As in original research, so in reviews and consensus statements, such potential biases should be made plain.

It is inappropriate for academic bodies to include in their consensus statements any mention of what should and should not be reimbursable by medical insurance companies. This is something for each individual insurance company to decide upon, and not something on which academic bodies should make public statements, as it allies them too closely with financial and other vested interests, and may thus introduce bias, inhibit clinical freedom, and act as an impediment to medical progress as well as the quality of patient care. If the principles inherent in the scientific method of "strong inference" are applied, if a

comprehensive review is rigorously undertaken, and if a primary concern for the well-being of the patient is maintained, and if the financial vested interests of the participants are clearly stated, the potential for hidden bias should then be minimized.

TECHNIQUES OF DISTORTION

In evaluating a consensus statement or position paper, aside from maintaining an awareness of the biasing influence of vested interest, whether personal, financial, cultural, intellectual or political, it is helpful to bear in mind several techniques of distortion that may be employed to serve a particular bias, which can be fairly readily identified. These include the following.

Selective citation of the published literature, to serve a predetermined bias. This would also include failure to review the literature adequately, so that evidence which does not support the bias would thereby be excluded.

Citation of supposedly replicate studies to counter a hypothesis, which in fact are not true replications of the original work, by virtue of significant differences in methodology or design.

Misrepresentation or misemphasis of the contents of papers cited, either in support of a predetermined bias, or in an attempt to reduce the significance or scientific validity of those papers that do not support the majority opinion.

Denial of controversy when it exists, and failure to publish the fact that there may be valid opinions diverging from those of the majority.

Perjorative linking of unrelated concepts and techniques. It is a recognized journalistic technique to join two or more dissimilar items in a common description, thereby attributing the qualities of each to both.

Bias inherent in the structure of the committee or group; if the membership does not include those individuals who are thoroughly familiar with the finer technical details of the subject as well as those holding divergent but valid opinions on it, then crucial but troublesome questions may never be addressed. Thus, despite appearances, a thorough and valid peer review will not have been undertaken.

RESPONSES TO CRISIS

We are in an unprecedented crisis, as doctors and as human beings; the detritus of our industrial civilization has finally landed on our own doorstep, polluting our homes and poisoning our bodies. Because of the personal burden of assorted toxins that we each earn, medicine now is qualitatively different to medicine 100 years, 50 years, or even 25 years ago. Nutritional, environmental and alternative medicine are all responses to this crisis. None of them can be expected to provide all the answers, but at least they are asking some of the right questions - questions which many pre-eminent in "conventional" medicine appear, on the evidence considered here, to have failed to consider.

The majority of doctors, it is clear, are prepared to listen to intellectually sound arguments for any cause, however much of a "paradigm shift" they may represent. We believe that the three papers reprinted in this issue offer a means to enhance intellectual rigour and accelerate the advancement of medical knowledge. In Platt's words. this "offers the possibility of such great increases in effectiveness that it is unfortunate that it cannot be regarded as a challenge to learning rather than a challenge to combat".

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