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STATISTICAL CONSULTING IN CLINICAL RESEARCH: THE TWO-WAY STREET

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SUMMARY

Clinical research often rests on statistical interpretation of numerical data. Thus, effective collaboration between clinician and statistician can have central importance. Interaction in the planning phases of a project can identify tractable scientific and statistical problems that will need attention and can help avoid intractable ones. The central need is for clear, broad, specific two-way communication on scientific issues and research roles.

KEY WORDS Statistical consulting Communication Collaboration

INTRODUCTION

Proverbial among statisticians is the incoming telephone call that starts out 'I have a simple statistical problem that should take only a minute of your time'. Not only is the estimated time likely to be off by some orders of magnitude, but the statement seems to reflect a view of the statistician as some kind of equipment installer (or maybe interior decorator). The view taken in this paper is that the natural relationship between clinical researcher and statistician is inherently *collaborative*, that the logic of the situation demands that. Collaboration is a two-way street.

We address our remarks here to people at both ends of that street—clinical researchers and statisticians. We do not aim to tell either party how to 'cope' with the other; rather we point to ways of working together that we believe help to make the collaboration fruitful.

We focus neither on the consultative interaction that actually does take only five minutes, nor on the mature relationship between a clinical and a statistical investigator that has developed through joint work on several projects. Rather, we address situations where the integrity of the research effort may depend on sound statistical design, analysis and interpretation, needing a joint effort extending at least for several weeks. The merit of such a co-operative undertaking rests largely on

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success in dealing with two classes of activities, which we call scientific interaction and co-ordination of affairs.

Boen and Zahn[1] and Finney[2] discuss some of these aspects of statistical consultation, and Baskerville[3] proposes a plan for training consulting statisticians. Louis[4] and Moses[5] discuss broad concepts of the statistical approach. All these works are bountiful sources of examples of the consultative and statistical processes and of additional references.

SCIENTIFIC INTERACTION

The consulting transaction may start with a question that looks small:

> Would you give me a reference to the Mann–Whitney test?
> What computer package can do a logistic regression on our computer?

Or the question may look (and be) large:

> We are preparing a research proposal. Would you look over the statistics part? May we name you as a consultant?
> A journal has just rejected this paper because of the statistics. Will you help me prepare it for resubmission?

However the transaction may begin, its sound progress depends crucially on one thing: that the clinician and statistical consultant (ultimately) deal with the same problem. At the beginning the consultant is unaware of the scientific problem. Before he can be helpful, he must correctly understand the investigation, its purposes, its motivating questions, its materials, techniques and measurements. If he offers advice based on a misapprehension, the advice may be wrong and useless, or even damaging. So clear, mutual understanding of the problem is the single most important element.

Step-by-step communication is the necessary pattern. The statistician must first gain correct understanding of the substantive problem. When a point appears understood, he should check it by saying, 'Now, let me tell *you*—the clinician—about this point and see if I have it right.' This step may require repetition. Similarly, the clinician needs to acquire a correct grip on the essential statistical features, and can best check a concept by explaining it to a colleague and/or the statistician.

Effective communication is likely if each partner has high expectations of understandability from the other. The iterative communication style helps realize these high expectations. Of course, jargon is an unacceptable encumbrance. Neither party should use it or accept it.

The understanding needs to be specific within a broad construction of the problem. The broad construction may lead more quickly to a correct understanding of a highly specific concept than may a narrowly focused treatment of that topic alone. This principle of breadth applies to both clinical and statistical issues with the following consequences. First, each collaborator should anticipate some reading in the other's field. (Review articles and those leading up to the current research are ideal.) Secondly, each partner should be wary of 'protecting' the other by avoiding mention of topics which might have relevance merely to avoid 'needless' complication. Although in everyday life we may ease communication by omission of details that seem inessential or hard to explain, that practice can lead to trouble in scientific collaboration.

The understanding of the problem needs to be specific about details; the worth of a study may turn on them. For example, the difference between a sound randomized clinical trial and a collection of anecdotal material rests on the answers to questions such as: How were the patients for this investigation chosen? How was it decided which ones got which treatment? Did the person assessing post-treatment status know which treatment the patient had received? Did the patient know? DerSimonian *et al.*[6] give a bare-bones list.

A similar specific knowledge about the measurement process can be essential. Measurements of the same phenomenon may vary from day to day; to assess that possibility in a study, the consultant must know which observations were made on which days, on which piece of apparatus, or by which technician or interviewer. Some 'measurements' are actually composites of others, and the variability of the composite will depend on the variability of its components. An understanding of the details may permit more efficient experimental design (if the collaboration concerns the planning of an investigation). Both partners should take pains to ensure that incorrect *assumptions* about how the data were acquired do not creep in and vitiate the analysis and interpretation.

The importance of understanding measurements is highlighted by the following simple example. On two successive days a researcher records a phase angle; data = 10° and 350°. The statistician averages these to produce the 'typical' angle of 180°. A little thought will reveal that the typical angle is 0° (or equivalently 360°).

Broad, specific and iterative communication is the central necessity. But additional measures can help the collaboration succeed. At an appropriate stage there may be some utility in one of the partners' attendance at a meeting of the other's colleagues, a meeting addressed to the subject of the investigation. Thus, the clinician may invite the statistician to staff meetings or receive an invitation to attend a seminar of statistical staff and students. From such meetings, new ideas and helpful criticism often emerge.

Frequently the collaboration advances by *watching*. The statistician may move more quickly toward a fuller understanding as a result of his seeing the apparatus in use, observing the diagnostic procedure, looking at the recording processes. Similarly, the clinician who undertakes to follow the data-editing steps and statistical calculations may gain from doing so.

Written communication may advance the work notably. Questions, requests, information and tentative proposals all tend to gain specificity when posed in written form. Memoranda are not subject to memory decay. They exist tangibly and are amenable to discussion with knowledgeable colleagues of the recipient (and the sender). Memoranda may advantageously record: the current stage in the thinking; an issue that urgently demands resolution; or a proposal that will need consultative work. It pays to be aware of those situations where a memorandum constitutes the preferred mode of communication.

Thorough communication may take time, but one must avoid short cuts. This recommendation parallels good medical practice, which calls for taking a medical history before deciding on treatment. The parallel reaches further; it may be that the analysis (or treatment) remains ultimately unchanged by the fuller understanding (or history). In that case the payoff is the confidence that the right course was taken. Boen and Zahn[1] express a similar view of the consulting role.

CO-ORDINATION OF AFFAIRS

When two or more people share a task, chances for difficulties may arise as the work progresses. Forethought can eliminate many such problems, especially when willing participants have joined together to accomplish a mutually attractive piece of work. Problems are likely to be smaller when partners have worked together before. In a collaboration between clinician and statistician, the following questions may benefit from advance consideration and agreement:

1. Schedule

What is the schedule for the project? Are there deadlines, and can they be met? Most clinicians, and many statisticians, grossly underestimate the personal and chronological time necessary, and overestimate that available for a project. Data management, data analysis and report writing must all follow data acquisition, and they each take time.

If one foresees work as coming in stages, how much time should one allow for each, and what parties have responsibility for completing each stage? For example, data require preparation, computer entry, and once entered, necessitate validity checks before analysis can begin. Generally the clinician will be involved in the first and third of these activities, especially by providing feedback on acceptable ranges for data and checking on numbers that are out of range.

2. Resources

Are the resources (budget, computer time, personnel) adequate, or are some changes needed? Many long-term projects require a statistical collaborator, not simply an occasional consultant. It is important to identify early a person trained to use statistical computing packages and who can carry out analysis recommended by the statistician. Frequently standard computing packages cannot perform appropriate analyses, and the data analyst must obtain access to special-purpose routines or write new programs.

If financial aspects attach to the work, then clarity about them matters. Are there to be charges for consultation? What are the arrangements for funding of services of programmers? Computing costs? Keypunching? Secretarial support?

3. Acknowledgement/authorship

Sooner or later authorship will need a decision. Quality statistical input in the design and analysis phases of a project can constitute as important a scientific contribution as that provided by the medical team. Early discussion may wisely lead either to agreeing to defer decision until relative contributions can be assessed by hindsight, or to a tentative decision subject to change.

Co-authorship may not be the road taken. Then acknowledgement is in order. The statistician merits acknowledgement for his advice, if taken, establishing his responsibility as well as providing him with credit. Acknowledgements that are over-broad or otherwise inaccurate can be unfair; it follows that the statistician should review and accept any acknowledgement.

4. Data use

It may be wise to agree on arrangements concerning possible future uses of the study's data (and statistical analyses). Either party may some day wish to use the material in other articles, or in textbooks. What steps should the collaborators take if such an occasion arises?

The main message of this section is not that there are many ways to get into difficulty, but that it is well to consider *early*, and mutually, the essentials of getting the work completed. The collaborators should talk about the logistics, resolve quickly any immediate problems, and be aware of potential needs not yet settled. Recording the results of these discussions in a joint memorandum may bring to light some unnoticed misunderstandings. We see disadvantages too; sometimes the utterance, 'Let's put that in writing', chills the air. But the possibility of a memorandum about logistics deserves explicit consideration.

BENEFITS AND TIMING

This article began by observing that clinical investigations often present problems that demand statistical treatment—correct statistical treatment. Of course, collaboration with the biostatistician will usually help with that. Interaction in the planning phases of project can identify tractable scientific and statistical problems that will need attention and can help avoid intractable ones.

Statistical attention after the data are in can be too late. As a colleague* has remarked,

> If consultation is at the *post hoc* stage, it may be that objectives cannot be accomplished (sampling bias, poor design, etc.). It is the statistician's responsibility to state this frankly. We cannot do magic, and we can't participate in cover-ups. It is as well that researchers know our limitations in advance. This is a particular problem when the first consultation takes place after a research paper is rejected for publication because of poor methodology. Not much one can do!

Although statisticians can make mistakes and though many fine studies are designed and conducted without statistical collaboration, a study planned in the light of statistical considerations is less likely to have statistical and scientific flaws. In addition it can occasionally be much more cost-effective. (Admittedly, a good study often costs more than a poor one.) Sometimes the collaboration can broaden the scope of a study at little or no cost by exploiting familiar patterns of statistical design of experiments. The Canadian Aspirin Study[7] is a prime example. Using a factorial design allowed adding aspirin to a placebo study of sulfinpyrazone at little additional cost. Aspirin proved to be the superior treatment.

Finally there are often intellectual benefits that may flow to either collaborator (or both), and to their students and co-workers.

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