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What can Epidemiological Methods Mean to Surgical Research?

Hans-Olov Adami

Department of Surgery, University Hospital, Uppsala, Sweden

ABSTRACT

Traditionally, the aim of epidemiological research has been to determine and explain the incidence of a disease and thereby ultimately to reveal its causative mechanisms. Clinical research, or clinical epidemiology, on the other hand, has been devoted primarily to the evaluation of diagnostic and therapeutic techniques and to investigation of the course of a disease after its diagnosis. The aim of this brief discussion is to illustrate how these two areas of research - epidemiological and clinical - have the same methodological roots and use similar biostatistical tools. Whether they are carried out as experimental or as observational studies, the fundamental problem in the scientific method is to achieve validity by attenuating or controlling the effects of extraneous factors that influence the outcome under study. In modern epidemiology powerful methods of reaching this goal have been developed and thus a sound basis has been provided for drawing reliable conclusions concerning causal relations between "exposures" and outcomes. If surgical researchers become aware that epidemiological and clinical researchers obtain their scientific tools from the same conceptual domain and become familiar with the methods used in traditional epidemiology, this will probably result in fruitful scientific expansion in clinical surgery.

INTRODUCTION

We live in a research tradition in which it is now and then considered more sophisticated, indeed even more surgical, to study physiological effects in experimental systems than to try to identify the factors affecting the origin and course of surgical diseases in man. This tradition has had consequences for the scope and quality of clinical, surgical research that are sometimes easy to distinguish. It is my difficult task today to try to demonstrate why a great deal of surgical research can and should at the same

time be epidemiological, and why truth-seeking surgeons should thus to some extent simultaneously be epidemiologists.

Surgeons appreciate the idea that there is a causal connection between measures that we take and the subsequent course of the disease, particularly when the treatment is operative and the outcome favourable. The doubt expressed by David Hume (1) as early as at the beginning of the 18th century regarding the possibility of relating cause and effect worries us but little. With good reason we start from the idea that the gall-bladder or the appendix, for example, is removed in consequence of our intervention and that this causal connection will also apply in the future.

THE SCIENTIFIC PARADIGM

It may be stated in general that analogous considerations are the basis of all our diagnostic decisions and therapeutic measures even if the causal connections are not always as evident as in the example of the gall-bladder and the appendix. The idea is that one has chosen the alternative with the greatest probability of success. The overall goal of clinical research is to prove such assumptions. Remarks of this kind are, of course, trivial but they take us to the first principal point of the scientific paradigm, i.e. the idea that a hypothesis is tested through an experiment (3).

Under ideal circumstances this means that one furnishes oneself with two sets of observations, exactly identical in every conceivable respect except regarding the factor one wishes to study. Let us call this factor an "exposure" and define this concept in the broadest sense. Manipulations of an experimental system, the adminstration of medicines, operative interventions, a call to a health examination of cancer screening are thus "exposures", as also are air pollutions, tobacco-smoking, sexual habits, or the life of a Mormon, of a decided open-air type or of a fastidious gourmet.

We hypothesize that the probability that a certain event will occur is influenced by the exposure studied - i.e. that lung cancer can develop as a consequence of cigarette smoking. Sometimes one is only interested in the magniture of this influence. However, more often the time dimension is of interest. One wishes to find out both whether and when an event occurs. The main measure of an effect will then be the incidence or number of events per unit of time. The incidence is the quotient between the number of occurred events, e.g. numbers of individuals being taken ill or recovering, and the total person-years that are determined by the number of individuals and by

the length of time for which they have been observed. The difference between two groups can be expressed both in absolute terms and in relative ones, i.e. as the quotient between the incidences of the compared groups.

In practice, the "exposure" in the whole group of patients or in the background population is generally unknown. This situations arises, for example, when a patient develops an unexpected postoperative complication and one attempts to find a causal connection between this event and the preoperative characteristics; analogously, when a smoker is affected with lung cancer and a causal connection is sought with his habits of life; or when a cancer of the stomach is found in a patient who has previously undergone a parital gastrectomy, and one tries to find a causal connection with earlier operation. It is often ethically unfeasible to test such hypotheses in an experiment in man and moreover it is time-consuming and costly to delineate the exposure in the whole population. In this situation there remains one possibility, which is in fact the fundamental principle in case-control studies; that is, to assess the prevalency of the "exposure" of interest (preoperative characteristic, smoking, partial gastrectomy) in the cases and in a sample of individuals from the population that gave rise to the cases.

All this, of course, seems simple and it is exactly this that is interesting and fascinating, for what we have just briefly summarized are not only the central principles of clinical research, of controlled clinical trials, and of studies of prognostic factors and of survival in the broadest sense. They constitute at the same time the scientific outline of the cohort and case-control studies of traditional epidemiology. Before going on to consider the close connections between the methods and concepts of epidemiological and traditionally clinical research, we must further discuss the problems inherent in controlled observations.

THE PROBLEMS OF THE CONTROLLED OBSERVATION

When scientific hypotheses are to be tested, we are confronted with a measuring exercise with two fundamental problems. The first is to achieve precision by limiting and estimating the random errors. This aspect will not be touched upon further here. The other and really difficult problem is that of accomplishing validity by checking systematic mistakes and, after all, it is this factor that governs the methodology of biological research. A myriad of known - and probably still more unknown - factors affect biological courses of events beyond and often in complex interaction with the exposure in question. The idea of being able to provide oneself with two sets of ob-

servations, completely identical except for the factor (exposure) whose effects one wishes to study is, therefore, quite unrealistic in biological experiments (3).

To be able to relate an effect to a cause and draw probable conclusions as to the causability, the influence of other interfering factors will have to be brought under control. This can be achieved e.g. by "diluting" their influence, i.e. by providing oneself with two sets of observations where there is reason to suppose that they have manifested themselves to the same extent, or by checking the effects of interfering factors during the actual data analyses. Which approach one chooses depends, among other things, on whether the reality can be manipulated in an experiment of whether one is reduced to observing what has already occurred and to trying to elucidate the causes.

For natural reasons, experimental studies are the most preferable. Experimental animals, patients or healthy individuals are randomly allocated to the groups that are later to be compared when one of them has become the subject of intervention. Randomization optimizes the probability that interfering factors will be equally distributed among the groups. This is the reason why the controlled randomized trial is now generally considered the safest, often the only acceptable path to reliable knowledge of the effectiveness and reliability of new methods of treatment (2).

There are many limitations, however, associated with both clinical trials and - to a still greater extent - experimental studies in healthy human subjects. In an experimental trial allocation to different groups is not undertaken for the sake of the patient or the healthy subject but for that of the study. This involves important limitations. The exposure can be tested only if it is expected to prevent the onset of disease or alleviate the course of the disease. Only the best available methods can be included in the trial and they should preferably be equally acceptable to the subject after he or she has been informed and given consent.

Another impediment to experimental studies is encountered when the effects appear only after a very long induction time. The alternative at hand is to carry out observational, i.e. non-experimental, studies. The aim is to simulate the results of an experiment had this been feasible. This is the field of traditional epidemiological research. All its methodology and concepts are centred around the problem of relating, without experiments, cause and effect by eliminating the interfering influence of other factors. The

overall purposes of the methodology of traditional clinical and epidemiological research are thus identical. It is a matter of achieving validity by avoiding systematic mistakes. With this we are approaching the main item in this discussion, i.e. why, in surgical research, great importance should be attached to epidemiological methodology.

TRADITIONAL EPIDEMIOLOGY AND CLINICAL EPIDEMIOLOGY

The traditional purpose of epidemiology has been to describe and elucidate the incidence of diseases in different groups of a population. One cannot experimentally expose healthy individuals to a factor that is suspected to increase the risk of disease. This part of the epidemiology is therefore chiefly non-experimental. Prospective (cohort) and retrospective (case-control) studies are its principal tools.

The concept of clinical epidemiology has quite recently been introduced as a summarizing combination of different methods of studying the course of a disease after an individual has been taken ill (6). Clinical epidemiology includes not only controlled treatment studies but also studies of prognostic factors and of survival, decision analyses, meta-analyses (5), and a number of other procedures (4).

It would be to the detriment of surgical research if one did not adopt and utilize methods from both these traditionally separate research areas in order to investige the causes of disease and their courses. There are two major reasons for uniting them into one joint concept. We have previously touched upon the first reason: these different techniques can often be traced back to one and the same, in principle very simple concept and this becomes particularly obvious when one begins to use modern multivariate methods of controlling confounding factors or of illustrating interactions. The methods are then similar in, for example, cohort studies, clinical trials, and studies of prognostic factors and of survival. The second major reason is that now, just as in the future, we will probably have to acquire most of our new knowledge in surgery from non-experimental observations. For this, the concepts and methods of analysis of cohort and case-control studies will be most useful even if so far they have been utilized very little in surgery.

CONCLUSIONS

1. There is no reason methodologically to separate clinical research or clinical epidemiology from traditional epidemiological research; they

obtain their tools from the same conceptual and biostatistical domain.

2. Modern epidemiology can bring into traditional clinical research a number of powerful methods that can be applied both to experimental and observational studies.

3. Research training in epidemiology will therefore become an invaluable asset to the clinical researcher.

4. By applying a wide methodological repertoire and simultaneously making use of both the large number of hypotheses that are generated naturally in all clinical work and the extremely favourable conditions available in Sweden it is possible to create unique opportunities for fruitful scientific expansion.

5. Each patient has a history that may contribute to the knowledge about his or her disease. This can be utilized in epidemiological studies whose purpose is to elucidate the aetiology of surgical disease and illustrate the possibilities of predicting and affecting their course.

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Address for reprints:

Hans-Olov Adami, M.D.
Department of Surgery
University Hospital
S-751 85 Uppsala, Sweden