An introduction to clinical epidemiology

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Summary

Clinical epidemiology is defined and its influence on methods of diagnosing and treating patients assessed. A plea is made for the wider application of such methods.

Epidemiology is the science that determines the distribution and control of diseases in populations. Its role in research has been detailed elsewhere, but it is also relevant to the practice of clinical medicine because it relates to the care of the individual patient. Epidemiological methods enable clinicians to solve a wide range of common problems in clinical practice, some of which will be reviewed here. The need for such a review was expressed by participants in a recent workshop on epidemiology organised by the authors that was attended by clinicians from Groote Schuur Hospital.

The classic clinical process entails making decisions based on the best available data that clinicians have at their disposal. These data comprise both information about the individual patient and the previous experiences of a single clinician, or other clinicians. In making a decision clinicians have to assess whether their combined previous experiences have any relevance to the treatment of individual patients under their care. They have to make decisions on diagnosis and treatment in the following way:

In taking a history they must ask appropriate questions and assess the relevance of the answers. The physical examination should include both positive and negative findings and the relevance of both must be taken into account. There are many special examinations available and the doctor must decide which should be done for the patient and assess the results in the light of the problem presented.

On the basis of the information collected he must consider the alternative diagnostic possibilities and the probability of each of them being correct.

The presumptive diagnosis having been made, the prognosis is assessed, the therapeutic options are considered, and a treatment regimen is recommended that will achieve the maximal benefit to the patient with the minimal harm. Follow-up of the patient is necessary to determine the response of the disease to the treatment.

It is clear that each of these decisions is taken in relation to the specific circumstances of a specific patient, but almost all the actions taken by clinicians require them to relate prior experience obtained from groups of patients in similar circumstances to the individual patient. For example, how has a particular clinical finding, symptom, sign or test helped similar patients? How have similar patients fared on a particular treatment or total therapeutic regimen?

If, therefore, rational clinical practice requires the projection of diagnostic findings, therapeutic responses, or the effectiveness of treatment from the group to the individual, then those basic sciences that provide the specialised strategies and tactics used to assess groups of patients (epidemiology and biostatistics) must be part of the armamentarium that each clinician requires in dealing with the individual patient. This is the link between clinical medicine and epidemiology - clinical epidemiology. In this review we highlight selected clinical aspects and illustrate how epidemiological methods can be applied to them.

Recently there have been several important contributors to the development of clinical epidemiology. We all recognise the pioneering thoughts that were generated by Paul in his book published in 1958. Although there are differences in the approaches that these scientists have brought to the subject, they all view epidemiology as a discipline critical to the understanding of the way that clinical decisions are made.

There is a major difference between clinical and community-based epidemiology. The patient in hospital is usually in a short phase of the clinical history of his disease. In addition, he will illustrate only a single example of the range of severity of the disease, and this usually at the more severe end. This will affect the relevance of most clinical questions and limit the extent to which the experience of patients in hospital can be generalised to the community as a whole.

Steps in clinical management

Diagnosis

The clinical diagnosis is dependent on information collected by history, examination, and special tests. Before considering the problems arising from this, it should be noted that studies have shown that an adequate history and clinical examination enable a general practitioner to reach a diagnosis for about 90% of his patients. In a general medical outpatient clinic, this is so for 73% of patients. In the latter study 56% of the correct diagnoses had been reached by the time the history had been taken. Although advances in diagnostic ability and precision (for example, computed tomography) provide an important extension to clinical capabilities, an overreliance on special tests has developed that has often obscured the importance of the history and physical examination.

Any clinical decision may be incorrect or correct. Incorrect decisions are made because any single clinical observation (or set of them) may not reflect the 'true' situation, either by chance or because of bias. Chance errors occur because of the random variation that is a feature of all biological measurement and this is illustrated by repeating a measure many times and seeing that the results vary randomly around the 'true' value. Bias has been defined as 'any process, at any stage of inference, which tends to produce results or conclusions that differ systematically from the truth'. Selection bias has already been referred to. Measurement bias occurs when the methods of measurement used in different groups of patients are not the same. Confounding bias occurs when some other factor (related to the characteristic being considered) is the actual reason for the association identified.
The association and difference between bias and chance is well illustrated by the measurement of blood pressure. Although the 'true' intra-arterial blood pressure is measured through a cannula in the artery, it is measured in the clinical situation by using a sphygmomanometer and a cuff. If this instrument is consistently measuring blood pressures higher than the true value this will be considered to be bias. There is, however, an additional random variation of the sphygmomanometer measurement around the correct value. A single measurement of the blood pressure might vary by chance from the accurate measurement. The clinical epidemiologist must discover these errors and assess their extent and the possible relevance to diagnosis.

Chance variation may be evaluated by estimating the reproducibility of a measure — that is, the degree to which the same results are obtained when the same observer repeats the measurement (intra-observer variation) or when another observer repeats it (inter-observer variation).\(^2\) This degree of agreement on the repeated performance of any action can be quantified and the question that must be answered is whether the agreement is greater than that which could be expected by chance alone.

The validity of a measure is the degree to which the 'test' is measuring what the physician really wants to measure. For example, if a decision (whether a patient has a certain disease) is made on the results of a number of tests, is that disease really what the tests are measuring? This can be examined using a 2 x 2 table (Table I). Two questions must be asked: firstly, to what extent is the test identifying the patients with the disease as being sick (the sensitivity of the test), and to what extent is the test identifying those who are free of the disease as healthy (specificity of a test)?

### TABLE I. MEASURING THE VALIDITY OF A DIAGNOSTIC TEST

<table>
<thead>
<tr>
<th>Test</th>
<th>Disease</th>
<th>Present</th>
<th>Absent</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>a</td>
<td>c</td>
<td>a + c</td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>b</td>
<td>d</td>
<td>a + b + c + d</td>
<td></td>
</tr>
</tbody>
</table>

Sensitivity of test = \(a/(a+c)\); specificity of test = \(d/(a+d)\); positive predictive value = \(a/(a+b)\); negative predictive value = \(d/(b+d)\); prevalence of disease = \((a+b)/(a+b+c+d)\).

Estimates of the power of these indices are sometimes available from research studies and are valuable in deciding whether to use a diagnostic procedure. They do not, however, mirror what happens clinically, when the doctor does not know who has or has not got a disease. Secondly, therefore, we need to know how many of those with positive results actually have the disease (positive predictive value)? Of those with negative results, how many are free of the disease (negative predictive value)? These two measures indicate to physicians what is the approximate accuracy of the test that they are performing.

At this point it is important to stress the importance of the prevalence\(^2\) of the disease in the population from which the patient comes. The lower the prevalence the lower the positive predictive value and the higher the negative predictive value for a test with set sensitivity and specificity. An example of this using an exercise ECG as a test in patients with different clinical likelihoods of disease\(^6\) is shown in Table II, and the method for calculation is shown in Table III. In all instances the sensitivity (60%) and specificity (91%) are the same but the positive and negative predictive values of the likelihood of disease given the test results vary depending on the pretest clinical likelihood, or prevalence, of disease. Clearly the test is not useful when clinicians are virtually certain of the diagnosis, and most useful when they are uncertain.

The predictive values of non-invasive tests for peripheral arterial disease were reported recently.\(^13\) The authors showed that in their defined sample of the general population the positive predictive value for the tests was considerably lower than that reported by Marinelli et al.,\(^15\) in a group of diabetics with a far higher incidence of peripheral arterial disease. From

### TABLE III. EXAMPLE OF CALCULATION OF POSITIVE AND NEGATIVE PREDICTIVE VALUES

To estimate positive and negative predictive values for patient A; construct a 2 x 2 table (Table I) as follows:

1. Disease = coronary heart disease
2. Test = exercise ECG
3. Assume \(a + b + c + d = 1000\) patients
4. If pretest probability = 90%, then the prevalence of coronary heart disease in 1000 such subjects is likely to be 900 — that is, \(a = b = 900, c = 100, d = 100\)
5. Then apply given sensitivity (60%) and specificity (91%), i.e.
   \[a = 60\% \times 900 = 540, \text{ therefore } b = 900 - 540 = 360, d = 91\% \times 100 = 91, c = 100 - 91 = 9\]
6. Therefore positive predictive value = \(540/(540 + 9) = 98\%\), negative predictive value = \(91/(100 - 360) = 20\%\), and therefore 100% — negative predictive value = 100% — 20% = 80%.

<table>
<thead>
<tr>
<th>Exercise ECG</th>
<th>Positive</th>
<th>No</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>540</td>
<td>9</td>
<td>549</td>
</tr>
<tr>
<td>Negative</td>
<td>360</td>
<td>91</td>
<td>451</td>
</tr>
<tr>
<td>Total</td>
<td>900</td>
<td>100</td>
<td>1000</td>
</tr>
</tbody>
</table>

### TABLE II. USEFULNESS OF THE EXERCISE ECG IN THREE PATIENTS WITH VARYING LIKELIHOODS OF HAVING CORONARY HEART DISEASE BASED ON CLINICAL HISTORY AND PHYSICAL EXAMINATION

<table>
<thead>
<tr>
<th>Patient</th>
<th>Pretest clinical likelihood of disease (prevalence)</th>
<th>Post-test likelihood of disease given test result</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Positive predictive value</td>
<td>Negative predictive value</td>
</tr>
<tr>
<td>A</td>
<td>90%</td>
<td>98%</td>
</tr>
<tr>
<td>B</td>
<td>5%</td>
<td>26%</td>
</tr>
<tr>
<td>C</td>
<td>50%</td>
<td>87%</td>
</tr>
</tbody>
</table>

...
these examples it is clear that if a test is used that has a low positive predictive value in the population from which the specific patient comes it may be of little clinical value, whereas in a population in which this value is high its value is substantial. It should be stressed that this difference will occur even though the sensitivity and specificity of the test are the same in both populations.

These are only a few examples of the problems associated with the choice and interpretation of diagnostic tests. Further details are given elsewhere.21,28 The use and interpretation of commonly used diagnostic tests have recently been reviewed.23,28

Treatment

The prognosis depends on the answers to two questions: (i) how will the disease progress if nothing is done — that is, what is the predicted natural history of the disease from the time at which it was diagnosed? (ii) what will happen if treatment is started?

When physicians are faced with a question related to the prognosis they have to assess the relative probabilities of each possible outcome in the natural history of a disease. This is based firstly on the personal experience of the physician. This, however, is heavily influenced by degrees of recall; outstanding, recent, or memorable cases are more likely to be remembered. The individual physician may have only limited experience, having seen few cases of that specific disease. This raises the question of bias discussed previously.

Secondly, they must consider the views of others. Once again problems arise, as experts often disagree and their experiences often differ.

Thirdly, they must consider published reports on the subjects. Sackett et al.19 have suggested guidelines for assessing the suitability of an article in relation to prognosis. They refer mainly to the methods used in the reported studies and the possible sources of bias introduced by unsuitable population definition, inadequate follow-up, or problems related to the definition and identification of outcomes. The careful epidemiological assessment of these problems is a prerequisite for adequate evaluation of the probabilities of the outcomes of treatment of the disease. The detailed analysis by Sackett and Whelan20 of a study about the probability of patients with ulcerative colitis developing malignant disease21 is an example of the way in which methods used in studies can introduce bias into the results. This in turn can influence the physician when he is deciding what to do and may have far-reaching (negative) results for the patient.

Assessment of the effectiveness of treatment

A number of problems face physicians when they have to decide what treatment to recommend for a patient. Will the treatment be curative or perhaps only relieve pain? What is the best available treatment for that particular patient? How will the clinician measure whether the chosen treatment has succeeded or whether it should be stopped?

The reliance on randomised controlled clinical trials to help make decisions about treatment has been reviewed frequently, and there is little doubt that without it there is often little chance of coming to valid decisions. There is, however, a need to review carefully the methods used in the reported trial to be certain that they meet accepted standards.22,23

Even if this is so, there is another possible problem that needs to be considered. To what extent are the findings really applicable to the patient under discussion? A good example of this problem is found in the Veterans Administration studies on the value of treating hypertension.23,24 There is little doubt that these studies have probably done more than any others to influence our thinking about the management of hypertension. One needs to realise, however, that although the planning and execution were of the highest standard they included only white men (veterans) over the age of 40 with diastolic blood pressures of a certain level, and they excluded potential non-compliers. Can the results therefore be applied to younger men, blacks, women, people whose compliance may be doubtful, patients with lower levels of blood pressure, and so on? The lesson is that findings of a randomised controlled trial, however well performed, cannot automatically be applied to all other patients with the same condition.

Conclusions

This review has attempted to highlight some aspects of clinical practice in which epidemiology can make an important, and often essential, contribution. In almost all the decisions that clinicians must make, they need to assess the value and relevance of a grouped experience (either a personal one, that of a colleague, or that expressed in a scientific paper) to a specific patient. This provides the rationale and justification for the use of epidemiology in clinical medicine. There is an urgent need for those who train to become established in clinical teaching and practice in the RSA. Currently there are no departments or divisions of epidemiology in medical schools, only a few trained epidemiologists are working here, and there is only one course in clinical epidemiology available.25

REFERENCES

22. Department of Clinical Epidemiology and Biostatistics, McMaster University Health Sciences Centre. How to read clinical journals: V. To distinguish useful from useless or even harmful therapy. Can Med Assoc J 1981; 124: 1156-1164.