Epidemiology for the Uninitiated

What is a case? Dichotomy or continuum?

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In clinical practice the definition of "a case" generally assumes that in any disease people are divided into two discrete classes—the affected and the unaffected. This assumption works well enough in the hospital ward, and at one time it was thought appropriate also for populations. Cholera, for instance, was identified only by an attack of profuse watery diarrhoea, often fatal; but we now know that infection may also be subclinical, or cause only mild diarrhoea. Similarly in non-infectious diseases today we recognise the importance of premalignant dysplasias, in-situ carcinoma, mild hypertension, presymptomatic airways obstruction in smokers. Increasingly it appears that disease in populations exists as a continuum of severity rather than as an all-or-none phenomenon. The rare exceptions are mainly genetic disorders with high penetrance, like achondroplasia; for most acquired diseases the real question in population studies is not "Has he got it?" but "How much of it has he got?"

In the first place quantitative results should always be reported quantitatively, as distributions of their relevant statistics—for example, mean and standard deviation. Arbitrary cut-off points waste information and can prevent communication. In one study (table I) estimates of diabetes prevalence ranged from 7% to 32%, depending on which of various "standard" definitions was adopted.

TABLE I—Bedford diabetes survey: effect on prevalence estimate of different criteria for glucose tolerance test results

Criterion	Prevalence
≥ 120 mg/100 ml (6.7 mmol/l) @ 2 h	16%
≥ 140 mg/100 ml (7.8 mmol/l) @ 2 h	7%
≥ 180 mg/100 ml (10 mmol/l) @ peak	32%
≥ 120 mg/100 ml @ 2 h and > 180 mg/100 ml @ peak	11%

What is abnormal?

For practical reasons at some stage even quantitative results must often be divided into acceptable and unacceptable. In defining cut-off points four approaches may be considered:

Statistical—"Normal" may be defined as within two standard deviations of the age-specific mean, following conventional laboratory

practice. This is acceptable as a simple guide to the limits of what is common; but it must not be given any other significance, for it fixes the frequency of "abnormal" values of every variable at around 5% in every age and population. More importantly, what is common is not necessarily good.

Clinical—Clinical significance may be defined as the level of a variable above which symptoms and complications become more frequent. This level may be hard to identify. Anaemia is traditionally associated with tiredness, and so a woman attending her doctor with this complaint is likely to have a blood count. In this way anaemia is more likely to be discovered in tired than in other patients, and the association becomes a self-fulfilling prophecy. In a population survey employing uniform standards of ascertainment it was impossible to prove any overall excess of symptoms among those with anaemia having haemoglobin concentrations down to 8 g/dl.

Prognostic—In a man of 50 a systolic pressure of 150 mm Hg is common (that is, "statistically normal"), and it is clinically normal, in the sense of being symptomless; but his risk of fatal heart attack is about twice that of his contemporary with a low blood pressure. In fact, the prognostically ideal blood pressure seems to be "as low as possible," and in this sense the concept of "a case of hypertension" becomes inappropriate.

Sometimes, as with glucose tolerance, there is a threshold value below which level and prognosis are unrelated. "Prognostically abnormal" is then definable by this level. In other instances, as with body weight, the relation to prognosis is U-shaped: the highest mortality rates occur at the two extremes of the distribution, creating categories both "abnormally high" and "abnormally low."

Operational—The research worker may be content to describe his distributions, but for the man of action dichotomy is unavoidable: however arbitrary may be the definitions of hypertension or diabetes, a decision has to be taken that at some level patients should be treated. This operational definition will take into account the clinical and prognostic definitions, but it may well differ from either: a person may be symptom free yet benefit by treatment, or, alternatively, he may have an increased risk which cannot be remedied. For screening, a case should be defined in relation to that level of disease above which action will improve either symptoms or prognosis.

Each of these four approaches to case definition is suitable for a different purpose, so the investigator may need to define his purpose before he can define his cases.

Definitions and descriptions

A standard textbook of cardiology proposes these electrocardiographic criteria for left bundle-branch block: "The duration of QRS *commonly* measures 0.12 to 0.16 seconds . . . V5 or V6 exhibits a *large widened* R wave . . ." (*our italics*). As a basis for epidemiological comparisons this is potentially disastrous, since each investigator could interpret the italicised words in his own way. By contrast, the epidemiological "Minnesota Code" defines it like this: "QRS duration ≥ 0.12 seconds in any one or more limb leads *and* R peak duration ≥ 0.06 seconds in any one or more of leads I, II, aVL, V5 or V6; each criterion to be met in a majority of technically adequate beats." If different studies are to be compared, case definitions must be

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rigorously standardised and free of ambiguity. Conventional clinical descriptions do not meet this requirement.

It is also essential to define and standardise the methods of measuring the chosen criteria. An important feature in diagnosing rheumatoid arthritis, for example, is early morning stiffness of the fingers; but two interviewers may emerge with different prevalence estimates if one takes an ordinary clinical history while the other uses a standard questionnaire. Cases in a survey are defined not by theoretical criteria, but in terms of response to specific investigative techniques. These, too, need to be defined, standardised, and adequately reported. As a result epidemiological case definitions are narrower and more rigid than clinical ones. This loss of flexibility has to be accepted as the price of standardisation.

Defining the source of cases

Cases derived from different sources cannot necessarily be compared, even if an identical case definition has been used. Table II shows the results from a large screening survey using rigorously standardised reporting: identical electrocardiographic

TABLE II—Prognosis of ECG findings at screening of 18 403 middle-aged men, according to whether they were already under medical care

	Five-year CHD mortality (%)	
	Not under care	Under care
Prominent Q-wave	3.4	6.3
S-T segment depression	3.2	13.3
Normal ECG	1.0	5.1

findings are seen to carry a very different prognosis according to whether they were first found at screening, or arose in men already under medical care. Before statements are made about disease and its outcome it is essential to define the source of the cases and the selective processes affecting entry to the study. Failure to do so, which is one of the commonest faults in epidemiological papers, prevents generalisation of the conclusions and comparison with other studies.

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Eventually this series will be collected into a book and hence no reprints will be available from the authors.

Letter from . . . Canada

Lament for Captain Cook

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Turning in the grave is an unlikely possibility, particularly if one has been the victim of a Polynesian barbecue. Otherwise, by now, Captain Cook would be rotating rapidly at the bottom of the sea.

Two hundred years ago, looking for something that did not exist, Captain Cook found British Columbia, or more precisely, Vancouver Island.

Always on the lookout for ways of increasing the flow of tourist dollars, the Provincial Government decided that a celebration was in order. Bunting, flags, logos, Captain Cook buttons, and even an actor, attired in full-dress eighteenth-century naval uniform, were soon much in evidence. A visit of tall ships was arranged—at least of two tall ships—and everything appeared set for a jolly and prosperous time. Things began to go astray when the ex-minister of health, now a member of Her Majesty's loyal opposition, publicly announced that the only thing Captain Cook should be remembered for was the spreading of venereal disease around the Pacific. The Minister in charge of the bicentennial celebrations, a forceful, red-headed lady, instead of blaming Bougainville and his Frenchmen—much more likely historically, and obviously much more likely to appeal to Western prejudice—decided to call a full press conference in refutation. We were then all treated to the

hilarious sight of Madam Minister, not only defending the personal serology of Captain Cook, but also stating publicly that he had daily inspected his men. The vision of a daily, eighteenth-century short-arm inspection left us all a little breathless, and distinguished academics were soon marshalled to bridge the credibility gap with the suggestion that Captain Cook really suffered from a vitamin deficiency—B, not C, of course.

Things might have settled if the native Indians had not entered the lists. Their spokesman stated forcibly that they had nothing to celebrate and that they had been much happier undiscovered. Furthermore, Captain Cook was lost and had to be told where he was, and he had overstayed his welcome in an orgy of pillage and rape, from which the Indians had never recovered. The celebrants were not allowed to land on the beach of Nootka Sound, Cook's anchorage, and some rather half-hearted anti-Cook demonstrations were arranged. Naturally, in such an atmosphere of controversy, the more scholastically minded turned to the record—and this does not help the image of Rousseau's "noble savage" one bit. Captain Clerke of HMS *Discovery* says flatly, "they are the dirtiest set of people I have ever yet met with. . . . The pulling of lice, and eating them passes away (seemingly very agreeably) many a leisure hour." As to rape, David Samwell, a surgeon aboard the *Resolution*, and obviously not subject to the squeamishness of a physician, wrote in his journal of 6 April 1778:

"Hitherto, we had seen none of their young women, though we had often given the men to understand how agreeable their company would be to us, and how profitable to themselves, in consequence of which, they about this time brought two or three girls to the ships. Though some of them had no bad faces, yet, as they were exceedingly dirty, their persons at first sight were not very inviting. However, our young gentlemen were not

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