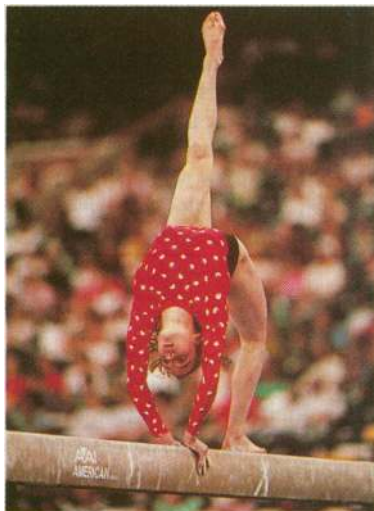


## Flexibility



Flexibility allows the safe use of a wide range of movements.

Flexibility is an essential part of training because it allows us to use a wide range of movements safely. In some sports such as gymnastics, flexibility is high on the list of training priorities. Coaches of such sports have their own methods of assessing improvements in flexibility. Comprehensive and reproducible assessment is difficult to achieve, however, because of the complex nature of movement. Nevertheless, carefully controlled measurements, albeit in limited ranges of movements, can be used to assess flexibility with a simple set of goniometers. It is particularly important that the measurements are standardised and that in longitudinal studies the same person performs all the measurements. The results can contribute useful information in assessing overall fitness when this strict code of practice is followed.

## Conclusion

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Fitness is a complex physiological characteristic that is difficult to describe comprehensively. Nevertheless, we can assess the central elements of fitness in reliable and reproducible ways. Through assessing athletes fitness we can extend health care by advising them on their ability to cope with the exercise demands of their chosen sport.

The photographs of the javelin thrower (Tessa Sanderson) and of the woman gymnast (Jackie Brady) were taken by Supersport Photographs.

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## Medical ethics: four principles plus attention to scope

Raanan Gillon

**The “four principles plus scope” approach provides a simple, accessible, and culturally neutral approach to thinking about ethical issues in health care. The approach, developed in the United States, is based on four common, basic prima facie moral commitments—respect for autonomy, beneficence, non-maleficence, and justice—plus concern for their scope of application. It offers a common, basic moral analytical framework and a common, basic moral language. Although they do not provide ordered rules, these principles can help doctors and other health care workers to make decisions when reflecting on moral issues that arise at work.**

Nine years ago the *BMJ* allowed me to introduce to its readers<sup>1</sup> an approach to medical ethics developed by the Americans Beauchamp and Childress,<sup>2</sup> which is based on four prima facie moral principles and attention to these principles' scope of application. Since then I have often been asked for a summary of this approach by doctors and other health care workers who find it helpful for organising their thoughts about medical ethics. This paper, based on the preface of a large multiauthor textbook on medical ethics,<sup>3</sup> offers a brief account of this “four principles plus scope” approach.

The four principles plus scope approach claims that whatever our personal philosophy, politics, religion, moral theory, or life stance, we will find no difficulty

in committing ourselves to four prima facie moral principles plus a reflective concern about their scope of application. Moreover, these four principles, plus attention to their scope of application, encompass most of the moral issues that arise in health care.

The four prima facie principles are respect for autonomy, beneficence, non-maleficence, and justice. “Prima facie,” a term introduced by the English philosopher W D Ross, means that the principle is binding unless it conflicts with another moral principle—if it does we have to choose between them. The four principles approach does not provide a method for choosing, which is a source of dissatisfaction to people who suppose that ethics merely comprises a set of ordered rules and that once the relevant information is fed into an algorithm or computer out will pop the answer. What the principles plus scope approach can provide, however, is a common set of moral commitments, a common moral language, and a common set of moral issues. We should consider these in each case before coming to our own answer using our preferred moral theory or other approach to choose between these principles when they conflict.

### Respect for autonomy

Autonomy—literally, self rule, but probably better described as deliberated self rule—is a special attribute

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*BMJ* 1994;309:184-8

of all moral agents. If we have autonomy we can make our own decisions on the basis of deliberation; sometimes we can intend to do things as a result of those decisions; and sometimes we can do those things to implement the decisions (what I previously described as autonomy of thought, of will or intention, and of action). Respect for autonomy is the moral obligation to respect the autonomy of others in so far as such respect is compatible with equal respect for the autonomy of all potentially affected. Respect for autonomy is also sometimes described, in Kantian terms, as treating others as ends in themselves and never merely as means—one of Kant's formulations of his "categorical imperative."

In health care respecting people's autonomy has many prima facie implications. It requires us to consult people and obtain their agreement before we do things to them—hence the obligation to obtain informed consent from patients before we do things to try to help them. Medical confidentiality is another implication of respecting people's autonomy. We do not have any general obligation to keep other people's secrets, but health care workers explicitly or implicitly promise their patients and clients that they will keep confidential the information confided to them. Keeping promises is a way of respecting people's autonomy; an aspect of running our own life depends on being able to rely on the promises made to us by others. Without such promises of confidentiality patients are also far less likely to divulge the often highly private and sensitive information that is needed for their optimal care; thus maintaining confidentiality not only respects patients' autonomy but also increases the likelihood of our being able to help them.

Respect for autonomy also requires us not to deceive each other (except in circumstances in which deceit is agreed to be permissible, such as when playing poker) as the absence of deceit is part of the implicit agreement among moral agents when they communicate with each other. They organise their lives on the assumption that people will not deceive them; their autonomy is infringed if they are deceived. Respect for patients' autonomy prima facie requires us, therefore, not to deceive patients, for example, about their diagnosed illness unless they clearly wish to be deceived. Respect for autonomy even requires us to be on time for appointments as an agreed appointment is a kind of mutual promise and if we do not keep an appointment we break the promise.

To exercise respect for autonomy health care workers must be able to communicate well with their patients and clients. Good communication requires, most importantly, listening (and not just with the ears) as well as telling (and not just with the lips or a wordprocessor) and is usually necessary for giving patients adequate information about any proposed intervention and for finding out whether patients want that intervention. Good communication is also usually necessary for finding out when patients do not want a lot of information; some patients do not want to be told about a bad prognosis or to participate in deciding which of several treatments to have, preferring to leave this decision to their doctors. Respecting such attitudes shows just as much respect for a patient's autonomy as does giving patients information that they do want. In my experience, however, most patients want more not less information and want to participate in deciding their medical care.

#### **Benevolence and non-malevolence**

Whenever we try to help others we inevitably risk harming them; health care workers, who are committed to helping others, must therefore consider the principles of benevolence and non-malevolence together and

aim at producing net benefit over harm. None the less, we must keep the two principles separate for those circumstances in which we have or recognise no obligation of benevolence to others (as we still have an obligation not to harm them). Thus the traditional Hippocratic moral obligation of medicine is to provide net medical benefit to patients with minimal harm—that is, benevolence with non-malevolence. To achieve these moral objectives health care workers are committed to a wide range of prima facie obligations.

We need to ensure that we can provide the benefits we profess (thus "professional") to be able to provide. Hence we need rigorous and effective education and training both before and during our professional lives. We also need to make sure that we are offering each patient net benefit. Interestingly, to do this we must respect the patient's autonomy for what constitutes benefit for one patient may be harm for another. For example, a mastectomy may constitute a prospective net benefit for one woman with breast cancer, while for another the destruction of an aspect of her feminine identity may be so harmful that it cannot be outweighed even by the prospect of an extended life expectancy.

The obligation to provide net benefit to patients also requires us to be clear about risk and probability when we make our assessments of harm and benefit. Clearly, a low probability of great harm such as death or severe disability is of less moral importance in the context of non-malevolence than is a high probability of such harm, and a high probability of great benefit such as cure of a life threatening disease is of more moral importance in the context of benevolence than is a low probability of such benefit. We therefore need empirical information about the probabilities of the various harms and benefits that may result from proposed health care interventions. This information has to come from effective medical research, which is also therefore a prima facie moral obligation. The obligation to produce net benefit, however, also requires us to define whose benefit and whose harms are likely to result from a proposed intervention. This problem of moral scope is particularly important in medical research and population medicine.

One moral concept that in recent years has become popular in health care is that of empowerment—that is, doing things to help patients and clients to be more in control of their health and health care. Sometimes empowerment is even proposed as a new moral obligation. On reflection I think that empowerment is, however, essentially an action that combines the two moral obligations of benevolence and respect for autonomy to help patients in ways that not only respect but also enhance their autonomy.

#### **Justice**

The fourth prima facie moral principle is justice. Justice is often regarded as being synonymous with fairness and can be summarised as the moral obligation to act on the basis of fair adjudication between competing claims. In health care ethics I have found it useful to subdivide obligations of justice into three categories: fair distribution of scarce resources (distributive justice), respect for people's rights (rights based justice) and respect for morally acceptable laws (legal justice).

Equality is at the heart of justice, but, as Aristotle argued so long ago, justice is more than mere equality—people can be treated unjustly even if they are treated equally.<sup>45</sup> He argued that it was important to treat equals equally (what health economists are increasingly calling horizontal equity) and to treat unequals unequally in proportion to the morally relevant inequalities (vertical equity). People have argued ever since about the morally relevant criteria for

regarding and treating people as equals and those for regarding and treating them as unequals. The debate flourishes in moral, religious, philosophical, and political contexts, and we are no closer to agreement than we were in Aristotle's time.

Pending such agreement health care workers need to tread warily as we have no special justification for imposing our own personal or professional views about justice on others. We certainly need to recognise and acknowledge the competing moral concerns. For example, in the context of the allocation of resources conflicts exist between several common moral concerns: to provide sufficient health care to meet the needs of all who need it; when this is impossible, to distribute health care resources in proportion to the extent of people's needs for health care; to allow health care workers to give priority to the needs of "their" patients; to provide equal access to health care; to allow people as much choice as possible in selecting their health care; to maximise the benefit produced by the available resources; to respect the autonomy of the people who provide those resources and thus to limit the cost to taxpayers and subscribers to health insurance schemes. All these criteria for justly allocating health care resources can be morally justified but not all can be fully met simultaneously.

Similar moral conflicts arise in the context of rights based justice and legal justice.

#### PERSONAL DECISION MAKING

The best moral strategy for justice that I have found for myself as a health care worker is first to distinguish whether it is I or an organisation, profession, or society itself that has to make a decision. For example, "how should I respond to a particular patient who wants an abortion?" is distinct from, "what is this hospital's organisational view on abortion?" and "what is the medical profession's collective view on abortion?" and "what is society's view as expressed in law and practice?"

Firstly, for decisions that I must take myself I must try to exclude decisions that have no moral basis or justification. Neither pursuit of my own self interest—for example, accepting bribes from patients, hospitals, or drug manufacturers—nor action that discriminates against patients on the basis of personal preference or prejudice can provide a just or morally acceptable basis for allocating scarce health care resources or for any other category of justice. Moreover, it is not my role as a doctor to punish patients; withholding antibiotics from smokers who do not give up smoking or refusing to refer heavy drinkers with liver damage induced by alcohol for specialist assessment on the grounds that they are at fault is not a just or morally acceptable basis for rationing my medical resources.

Secondly, I should not waste the resources at my disposal; so if a cheaper drug is likely to produce as much benefit as a more expensive one I should prescribe the cheaper one. Cost and its team mate opportunity cost are moral issues and central to distributive justice. If I believe, however, that an expensive drug is clearly and significantly better for my patient than a cheaper alternative and I am allowed to prescribe it then I believe that I should do so. Thus, like many British general practitioners, I try oxytetracycline first when treating acne, but if it does not work well I prescribe the more expensive minocycline; for depression I usually start with tricyclic antidepressants, but if they do not work well or the side effects are unacceptable I prescribe the new and expensive 5-hydroxytryptamine uptake inhibitors.

Thirdly, I should respect patients' rights. For example, my disapproval of a patient's lifestyle would not be a morally acceptable justification for refusing to

provide a certificate of sickness if he or she cannot work because of sickness. I have no special privilege as a health care worker, however, to create societal rights for my patients. For example, while I might think that all my unemployed patients should receive sickness benefit, in Britain they have a right to receive it only if they cannot work because of sickness; I have a right, therefore, to provide a certificate of sickness only if this is the case.

Fourthly, I ought to obey morally acceptable laws. Thus, even though I may disapprove of breaking a patient's confidence, if he or she has one of several infectious diseases I am legally obliged to notify the relevant authorities. If I believe that the law is morally unjustified I am morally entitled to break the law; but this gives me no legal entitlement to break the law, and I should be prepared to face the legal consequences of disobeying it. I should also decide exactly what I mean by a morally unjustified law. I suggest, though here do not argue, that it is the processes through which laws are enacted that confer moral legitimacy not the content of the laws. Thus if a law is enacted through a democratic political system—and hence one that fundamentally respects autonomy—which represents conflicting views within its population and makes laws on the basis of certain common moral values that reflect the four principles then that law is morally acceptable, and *prima facie* we are morally required to obey it.

#### ORGANISATIONAL, PROFESSIONAL, AND SOCIETAL DECISIONS

My role in taking decisions about justice that are organisational, professional, or societal should only be as a member of the relevant organisation, profession, or society. It is therefore morally consistent to pursue at different levels objectives that are mutually inconsistent. The medical directorate at the hospital where I work may have decided to prohibit the prescription of a particularly expensive drug. As a member of that directorate I may have argued in favour of prescribing the drug in special cases, but my arguments were rejected. It is morally proper for me as a clinician to accept the directorate's decision and act accordingly even when faced with an exceptional case in which I believe the expensive drug would be preferable. It is also morally legitimate for me to point to such cases ("shroud waving") in my political role as a member of a democratic society, arguing, for example, for more resources for health care than, say, for defence.

As members of society we are still feeling our way even at the level of defining what the competing moral concerns of justice are. We must be particularly wary of apparently simple solutions to what have been perceived as highly complex problems for at least 2500 years. For example, populist solutions in distributive justice such as have occurred in Oregon in the United States<sup>6</sup> and technical and simplistic economic solutions such as the system of costed quality adjusted life years (QALYs)<sup>7</sup> are tempting in their definitiveness and simplicity; they fail, however, to give value to the wide range of other potentially relevant moral concerns. Until there is far greater social agreement and understanding of these exceedingly complex issues I believe it is morally safer to seek gradual improvement in our current methods of trying to reconcile the competing moral concerns—to seek ways of "muddling through elegantly" as Hunter advocates<sup>8</sup>—than to be seduced by systems that seek to convert these essentially moral choices into apparently scientific, numerical methods and formulas.

As Calabresi and Bobbitt suggested in the 1970s, rationing scarce resources that prolong life and enhance health often entails tragic choices—choices between

people and between values. Societies seek strategies to minimise the destructive effect of such choices, including tendencies to change their strategies over time.<sup>9</sup> Calabresi suggests that we are like a juggler trying to keep too many balls in the air; like the juggler we must do our best to improve our juggling skills to keep more balls in the air for more of the time and to avoid letting any ball stay on the ground for too long. We must accept, however, that in the context of competing and mutually incompatible claims there will always be some balls on the ground. Moreover, we should not be surprised that there will always be some people dissatisfied after justice has been done because by definition not everyone's claims can be met.

### Scope

We may agree about our substantive moral commitments and our prima facie moral obligations of respect for autonomy, beneficence, non-maleficence, and justice, yet we may still disagree about their scope of application—that is, we may disagree radically about to what or to whom we owe these moral obligations. Interesting and important theoretical issues surround the scope of each of the four principles. We clearly do not owe a duty of beneficence to everyone and everything; so whom or what do we have a moral duty to help and how much should we help them? While we clearly have a prima facie obligation to avoid harming everyone, who and what count as everyone? Similarly, even if we agree that the scope of the principle of respect for autonomy is universal, encompassing all autonomous agents, who or what counts as an autonomous agent?

Who or what falls within the scope of our obligation to distribute scarce resources fairly according to the principle of justice? Is it everyone in the world? Future people? Just people in our own countries? And who or what has rights? Do plants have rights? Does the environment have rights? Does a work of art have rights? Do animals have rights and if so, which animals? Conversely, against whom may holders of rights claim the correlative moral obligation? Similar questions concern the scope of legal justice.

### SCOPE FOR HEALTH CARE WORKERS

Fortunately for health care workers some of these issues of scope have been clarified for them by their special relationship with their patients or clients. In particular, the controversial issue of who falls within the scope of beneficence is answered unambiguously for at least one category of people: all health care workers have a moral obligation to help their patients and clients. Patients or clients fall within the scope of the health care workers' duty of beneficence. This fact is established by the personal and professional commitments of the health care professionals and their organisations—they all profess a commitment to help their patients and clients, and to do so with minimal harm. This commitment is underwritten by the societies in which they practise, both informally and through legal rules and regulations that define the health care professionals' duties of care.

Two issues of scope are of particular practical importance for health care workers. The first is the question of who falls within the scope of the prima facie principle of respect for autonomy. The second is the question of what is the scope of the widely acknowledged "right to life"; who and what has a right to life?

Obviously the scope of the principle of respect for autonomy must include autonomous agents—we cannot respect the autonomy of a boot or anything else that is not autonomous. But who or what counts as an autonomous agent? When we disagree about whether

or not to respect the decision of a girl of 14 to take the oral contraceptive pill we are in effect disagreeing about the scope of application of the principle of respect for autonomy.

Similar questions about the scope of respect for autonomy arise in other paediatric contexts, in the care of severely mentally ill or mentally impaired people, and in the care of elderly people who are severely mentally impaired. Some patients clearly do not fall within the scope of respect for autonomy; newborn babies, for example, are not autonomous agents as autonomy requires the capacity to deliberate. But 7 year olds usually can deliberate to a degree. How much capacity for logical thought and deliberation and what other attributes are required for somebody to be an adequately autonomous agent? Possible other, necessary attributes include an adequately extensive and accurate knowledge base, including that born of experience and of accurate perception, on which to deliberate; an ability to conceive of and reflect on ourselves over time, both past and future; an ability to reason hypothetically—"what if" reasoning; an ability to defer gratification for ourselves as an aspect of self rule; and sufficient will power for self rule.

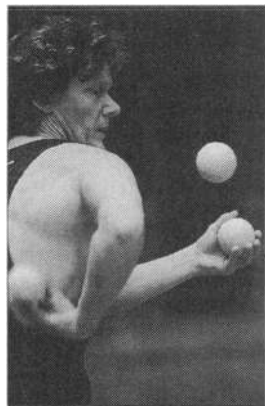
However these philosophical questions are answered, health care workers increasingly acknowledge that the autonomy of even young children and severely mentally impaired people should prima facie be respected unless there are good moral reasons not to do so. Moreover, those reasons will depend highly on the context; a young child or a severely mentally impaired person may not be autonomous enough to have his or her decision to reject an operation respected but be autonomous enough to decide what food to eat or clothes to wear. When patients who are not adequately autonomous for all their decisions to be respected make decisions that seem to be against their interests then important issues arise about who should be regarded as appropriate to make decisions on their behalf and about the criteria that they should use to do so.

The second important issue of scope for health care workers concerns the "right to life." Who or what has this right to life? To answer the question we have to determine what is meant by the right to life. Specifically, is it simply the right not to be unjustly killed or does it also include a right to be kept alive? The scope of the first right will clearly be greater than the scope of the latter: we have prima facie moral obligations not to kill all people but we have obligations to keep alive only some people. Even with the first definition of the right to life (a right not to be unjustly killed) a question of scope arises; although all people clearly fall within its scope, do (non-human) animals? And what do we mean by people? In response to this last question much debate, often extremely acrimonious, occurs in health care ethics over the right to life of human embryos, fetuses, newborn babies, and patients who are permanently unconscious or even brain dead.

It is salutary to reflect that these contentious issues are not about the content of our moral obligations but about to whom and what we owe them—that is, they are questions about the scope of our agreed moral obligations. Our answers are reasoned and carefully argued but deeply conflicting, either religiously or philosophically. Such disagreement about scope does not justify accusing those who disagree with us of bad faith or incompatible moral standards; in principle it is open to resolution within our shared moral commitment.

### Conclusion

The four principles plus scope approach is clearly not without its critics. And the approach does not



PETTITREX FEATURES

*Pursuit of justice—keeping all the balls in the air*

purport to offer a method of dealing with conflicts between the principles. But I have not found anyone who seriously argues that he or she cannot accept any of these prima facie principles or found plausible examples of concerns about health care ethics that require additional moral principles.

The four principles plus scope approach enables health care workers from totally disparate moral cultures to share a fairly basic, common moral commitment, common moral language, and common analytical framework for reflecting on problems in health care ethics. Such an approach, which is neutral between competing religious, political, cultural, and philosophical theories, can be shared by everyone regardless of their background. It is surely too important a moral prize to be rejected carelessly or ignorantly; for the

sake of mere opposition; or for the fun of being a philosophical "Socratic gadfly."

- 1 Gillon R. *Philosophical medical ethics*. Chichester: Wiley, 1986. (From a 26 part series in *BMJ* from 1985;290:1117-9 to 1986;292:543-5.)
- 2 Beauchamp TL, Childress JF. *Principles of biomedical ethics*. 3rd ed. New York, Oxford: Oxford University Press, 1989.
- 3 Gillon R, Lloyd A, eds. *Principles of health care ethics*. Chichester: Wiley, 1994.
- 4 Aristotle. *Nicomachean ethics*. Book 5. McKeon R, ed. *The basic works of Aristotle*. New York: Random House, 1941.
- 5 Aristotle. *Politics*. Book 3, chapter 9. McKeon R, ed. *The basic works of Aristotle*. New York: Random House, 1941.
- 6 Klein R. On the Oregon trail: rationing health care—more politics than science. *BMJ* 1991;302:1-2.
- 7 Williams A. Economics, society and health care ethics. In: Gillon R, Lloyd A, eds. *Principles of health care ethics*. Chichester: Wiley, 1994:829-42.
- 8 Hunter DJ. *Rationing dilemmas in health care*. Birmingham: National Association of Health Authorities and Trusts, 1993. (NAHAT research paper No 8.)
- 9 Calabresi G, Bobbitt P. *Tragic choices*. New York: Norton, 1978.

(Accepted 16 March 1994)

## Statistics Notes

### Diagnostic tests 3: receiver operating characteristic plots

Douglas G Altman, J Martin Bland

This is the seventh in a series of occasional notes on medical statistics.

We have previously considered diagnosis based on tests that give a yes or no answer.<sup>1,2</sup> Many diagnostic tests, however, are quantitative, notably in clinical chemistry. The same statistical approach can be used only if we can select a cut off point to distinguish "normal" from "abnormal," which is not a trivial problem. Firstly, we can investigate to what extent the test results differ among people who do or do not have the diagnosis of interest. The receiver operating characteristic (ROC) plot is one way to do this. These plots were developed in the 1950s for evaluating radar signal detection. Only recently have they become commonly used in medicine.

We assume that high values are more likely among those dubbed "abnormal." Figure 1 shows the values of an index of mixed epidermal cell lymphocyte reactions in bone marrow transplant recipients who did or did not develop graft versus host disease.<sup>3</sup> The usefulness of the test for predicting graft versus host disease will clearly relate to the degree of non-overlap between the two distributions.

A receiver operating characteristic plot is obtained by calculating the sensitivity and specificity of every observed data value and plotting sensitivity against 1-specificity, as in Figure 2. A test that perfectly discriminates between the two groups would yield a

"curve" that coincided with the left and top sides of the plot. A test that is completely useless would give a straight line from the bottom left corner to the top right corner. In practice there is virtually always some overlap of the values in the two groups, so the curve will lie somewhere between these extremes.

A global assessment of the performance of the test (sometimes called diagnostic accuracy) is given by the area under the receiver operating characteristic curve. This area is equal to the probability that a random person with the disease has a higher value of the measurement than a random person without the disease. (This probability is a half for an uninformative test—equivalent to tossing a coin.)

No test will be clinically useful if it cannot discriminate,<sup>4</sup> so a global assessment of discriminatory power is an important step. Having determined that a test does provide good discrimination the choice can be made of the best cut off point for clinical use. This requires the choice of a particular point, and is thus a local assessment. The simple approach of minimising "errors" (equivalent to maximising the sum of the sensitivity and specificity) is not necessarily best. Consideration needs to be given to the costs (not just financial) of false negative and false positive diagnoses and to the prevalence of the disease in the subjects being tested.<sup>4</sup> For example, when screening the general population for cancer the cut off point would be chosen to ensure that most cases were detected (high sensitivity) at the cost of many false positives (low specificity), who could then be eliminated by a further test.

A receiver operating characteristic plot is particularly useful when comparing two or more measures. A test with a curve that lies wholly above the curve of another will be clearly better. Methods for comparing the areas under two curves for both paired and unpaired data are reviewed by Zweig and Campbell,<sup>4</sup> who give a full assessment of this method.

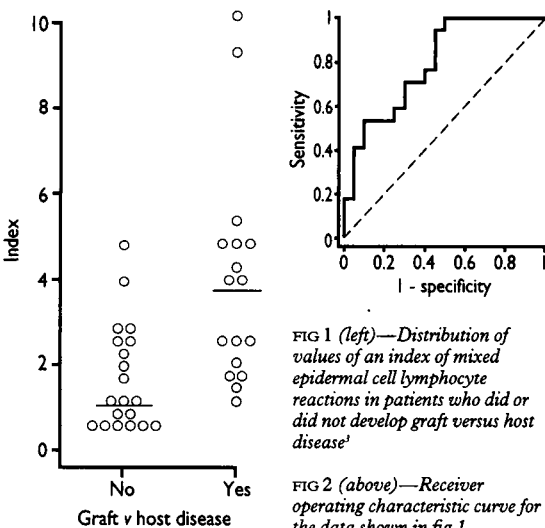


FIG 1 (left)—Distribution of values of an index of mixed epidermal cell lymphocyte reactions in patients who did or did not develop graft versus host disease<sup>3</sup>

FIG 2 (above)—Receiver operating characteristic curve for the data shown in fig 1

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BMJ 1994;309:188

- 1 Altman DG, Bland M. Diagnostic tests 1: sensitivity and specificity. *BMJ* 1994;308:1552.
- 2 Altman DG, Bland M. Diagnostic tests 2: predictive values. *BMJ* 1994;309:102.
- 3 Bagot M, Mary J-Y, Heslan M, et al. The mixed epidermal cell lymphocyte—reaction is the most predictive factor of acute graft-versus-host disease in bone marrow graft recipients. *Br J Haematol* 1988;70:403-9.
- 4 Zweig MH, Campbell G. Receiver-operating characteristic (ROC) plots: a fundamental evaluation tool in clinical medicine. *Clin Chem* 1993;39:561-77.