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First Steps

The purpose of most investigations in community medicine, and in the health field generally, is the collection of information that will provide a basis for action, whether immediately or in the long run. The investigator perceives a problem that requires solution, decides that a particular study will contribute to this end, and embarks upon the study. Sound planning – and maybe a smile or two from Lady Luck – will ensure that the findings will be useful, and possibly even of wide scientific interest. Only if the problem has neither theoretical nor practical significance and the findings serve no end but self-gratification may sound planning be unnecessary.

Before planning can start, a problem must be identified. It has been said that 'if necessity is the mother of invention, the awareness of problems is the mother of research'.[1] The investigator's interest in the problem may arise from a concern with practical matters or from intellectual curiosity, from an intuitive 'hunch' or from careful reasoning, from personal experience or from that of others. Inspiration often comes from reading, not only about the topic in which the investigator is interested, but also about related topics. An idea for a study on alcoholism may arise from the results of studies on smoking (conceptually related to alcoholism, in that it is also an addiction) or delinquency (both it and alcoholism being, at least in certain cultures, forms of socially deviant behaviour).

While the main purpose is to collect information that will contribute to the solution of a problem, investigations may also have an educational function and may be carried out for this purpose. A survey can stimulate public interest in a particular topic (the interviewer is asked: 'Why are you asking me these questions?'), and can be a means of stimulating public action. A community self-survey, carried out by participant members of the community, may be set up as a means to community action; such a survey may collect useful information, although it is seldom very accurate or sophisticated.

This chapter deals with the purpose of the investigation, reviewing the literature, ethical aspects, and the formulation of the study topic.

First Steps

- Clarifying the purpose
- Reviewing the literature
- Ethical considerations
- Formulating the topic

Research Methods in Community Medicine: Surveys, Epidemiological Research, Programme Evaluation, Clinical Trials J. H. Abramson and Z. H. Abramson

Clarifying the Purpose

The first step then, before the study is planned, is to clarify its purpose: the 'why' of the study. (We are not speaking here of the researcher's psychological motivations – a quest for prestige, promotion, the gratifications of problem-solving, etc. – which may or may not be at a conscious level.) Is it 'pure' or 'basic' research with no immediate practical applications in health care, or is it 'applied' research? Is the purpose to obtain information that will be a basis for a decision on the utilization of resources, or is it to identify persons who are at special risk of contracting a specific disease in order that preventive action may be taken; or to add to existing knowledge by throwing light on (say) a specific aspect of aetiology; or to stimulate the public's interest in a topic of relevance to its health? If an evaluative study of health care is contemplated, is the motive a concern with the welfare of the people who are served by a specific practice, health centre or hospital, or is it to see whether a specific treatment or kind of health programme is good enough to be applied in other places also?

The reason for embarking on the study should be clear to the investigator. In most cases it will in fact be so from the outset, but sometimes the formulation of the problem to be solved may be less easy. In either instance, if an application is made for facilities or funds for the study it will be necessary to describe this purpose in some detail, so as to justify the performance of the study. The researcher will need to review previous work on the subject, describe the present state of knowledge, and explain the significance of the proposed investigation. This is the 'case for action'.

Preconceived ideas introduce a possibility of biased findings, and an honest self-examination is always desirable to clarify the purposes. If the reason for studying a health service is that the investigator thinks it is atrocious and wants to collect data that will condemn it, extra-special care should be taken to ensure objectivity in the collection and interpretation of information. In such a case, the researcher would be well advised to 'bend over backwards' and consciously set out to seek information to the credit of the service. Regrettably, not all evaluative studies are honest.[2]

To emphasize the importance of the study purpose, and maybe to make it clearer, let us restate it in the words of three other writers:

> The preliminary questions when planning a study are:
> 1. What is the question?
> 2. What will be done with the answer?[3]

> *Do not*: say that you will try to formulate a good subject.
> *Do*: tell what you want to accomplish with the subject.[4]

> Discover the 'latent objective' of a project. The latent objective is the meaning of the research for the researcher, and gives away his or her secret hopes of what (s)he will achieve. To detect this latent objective, it is often fruitful to 'begin at the end.' How will the world be changed after the research is published?[5]

Reviewing the Literature

The published experiences and thoughts of others may not only indicate the presence and nature of the research problem, but may be of great help in all aspects of planning and in the interpretation of the study findings. At the outset of the study the investigator should be or should become acquainted with the important relevant literature, and should continue with directed reading throughout. References should be filed in an organized way, manually or in a computerized database.[6] It is of limited use to wait until a report has to be written, and then read and cite (or only cite) a long list of publications to impress the reader with one's erudition – a procedure that may defeat its own ends, since it is often quite apparent that the papers and books listed in the extensive bibliography have had no impact on the investigation.

Papers should be read with a healthy scepticism; in Francis Bacon's words, 'Read not to contradict and confute, not to believe and take for granted … but to weigh and consider'.[7] Several guides to critical reading are available.[8] Remember that studies that have negative or uninteresting findings are less likely to be published than those with striking findings.[9]

If the title and abstract suggest that the paper may be of interest, then you should appraise the methods used in the study (which requires the kind of familiarity with research methods and their pitfalls that this book attempts to impart), assess the accuracy of the findings, judge whether the inferences are valid, and decide whether the study has relevance to your own needs and interests. Do not expect any study to be completely convincing, and do not reject a study because it is not completely convincing; avoid 'I am an epidemiologist' bias (repudiation of any study containing any flaw in its design, analysis or interpretation) and other forms of what has been called 'reader bias'.[10]

Search engines such as Google Scholar, and the increasing tendency to provide free access on the Internet to the full text of publications, have made it very much easier to find relevant literature. Google Scholar not only finds publications, it also finds subsequent publications that have cited them, and related publications, and it provides links to local library catalogues.

But, at the same time, the explosive growth in published material in recent years means that a computer search may find so many references (and so many of them irrelevant) that sifting them can be a demanding chore, to the extent that one may be misguidedly tempted to rely only on review articles, or on the abstracts provided by most databases, instead of tracking papers down and reading them.

Conducting a computer search in such a way that you get what you want – and don't get what you don't want – is not always easy. It is particularly difficult to get *all* of what you want. Investigators who wish to perform a systematic review of all previous published researches on a particular topic, for example, may be well advised to enlist the help of a librarian. A biomedical librarian advises the use of regular Google as well as Google Scholar if hard-to-find government or conference papers are sought, and also advises use of PubMed and other databases if the aim is an exhaustive search.[11] Most users find Google Scholar easy to use and very helpful – the answer to a maiden's prayer – but its coverage (in its present incarnation) is incomplete,[12] and in terms of

accuracy, thoroughness, and up-to-dateness it falls short of PubMed, which provides access to over 16 million citations, mainly from MedLine, back to the 1950s. The way to use PubMed is explained on the website (http://?www.ncbi.nlm.nih.gov/entrez), and it is easy to use if requirements are simple; but otherwise, it has been said, 'If you enjoy puzzles, MedLine is great fun'.[13] A user-friendly simplified interface, SLIM, is now available.[14]

Ethical Considerations

Before embarking on a study the investigator should be convinced that it is ethically justifiable, and that it can be done in an ethical way. Ethical questions arise in both experimental and nonexperimental studies.

There is an obvious ethical problem whenever an experiment to test the benefits or hazards of a treatment is contemplated. However beneficial the trial may turn out to be for humanity at large, some subjects may be harmed either by the experimental treatment or by its being withheld. There is also an ethical problem in not performing a clinical trial, since this may lead to the introduction or continued use of an ineffective or hazardous treatment. 'Where the value of a treatment, new or old, is doubtful, there may be a higher moral obligation to test it critically than to continue to prescribe it year-in-year-out with the support merely of custom or wishful thinking.'[15] But, it has been pointed out, 'this ethical imperative can only be maintained if, and to the extent that, it is possible to conduct controlled trials in an ethically justifiable way'.[16] The heinous medical experiments conducted on helpless victims by Nazi physicians in the first part of the 20th century should never be forgotten.[17]

For an experimental study to be ethical, the subjects should be aware that they are to participate in an experiment, should know how their treatment will be decided and what the possible consequences are, should be told that they may withdraw from the trial at any time, and should freely give their informed consent. These requirements are not always easily accepted in clinical settings, and they are sometimes circumvented by medical investigators who feel that they have a right to decide their patient's treatment. Studies have shown that patients (especially poorly educated ones) who sign consent forms are often ignorant of the most basic facts. Special problems concerning consent may arise in cluster-randomized trials,[18] where clusters of people (e.g. the patients in different family practices) are randomly allocated to treatment or control groups (see p. 351), or where a total community is exposed to an experimental procedure or programme, or when experiments (such as trials of new vaccines) are performed in developing countries.[19]

Ethical objections to clinical trials are reduced if there is genuine uncertainty about the value of the treatment tested or the relative value of the treatments compared (*equipoise*) – for some investigators, it is sufficient that there is genuine uncertainty in the health profession as a whole, whatever their own views – and if controls are given the best established treatment. 'The essential feature of a controlled trial is that it must be ethically possible to give each patient any of the treatments involved'.[19]

Decisions on the ethicality of trials may not be simple.[20] Bradford Hill has said that there is only one Golden Rule, namely 'that one can make no generalization … the problem must be faced afresh with every proposed trial'.

The goals of the research should always be secondary to the wellbeing of the participants. The Helsinki declaration states:

> Concern for the interests of the subject must always prevail over the interests of science and society … every patient – including those of a control group, if any – should be assured of the best proven diagnostic and therapeutic method.

But researchers sometimes argue that obtaining an answer to the research question is the primary ethical obligation, so that they then 'find themselves slipping across a line that prohibits treating human subjects as means to an end. When that line is crossed, there is very little left to protect patients from a callous disregard of their welfare for the sake of research goals'.[21] This has raised debates about possible 'scientific imperialism', characterized by the performance of trials, sometimes with lowered ethical standards, in countries that are unlikely to benefit from the findings: 'Are poor people in developing countries being exploited in research for the benefit of patients in the developed world where subject recruitment to a randomized trial would be difficult?'[22]

In 1997, a furore was aroused at the disclosure that, in developing countries, controls were receiving placebos in trials, sponsored by the USA, of regimens to prevent the transmission of human immunodeficiency virus (HIV) from mothers to their unborn children, although there was an effective treatment that had been recommended for all HIV-infected pregnant women in the USA and some other countries. A debate ensued, the main issue being whether the Helsinki declaration's requirement that controls should be given the best current treatment was outweighed by the claims that a comparison with placebo was the best way of finding out whether the relatively cheap experimental regimens would be helpful in countries that cannot afford optimal care, and that the investigators were simply observing what would happen to the infants of the controls, who would anyway not have received treatment if there had been no study.

How well the trial is planned and performed is also important:

> Scientifically unsound studies are unethical. It may be accepted as a maxim that a poorly or improperly designed study involving human subjects – one that could not possibly yield scientific facts (that is, reproducible observations) relevant to the question under study – is by definition unethical. When a study is in itself scientifically invalid, all other ethical considerations become irrelevant. There is no point in obtaining 'informed consent' to perform a useless study.[23]

It is generally accepted that a study that is too small to provide clear results is *ipso facto* unethical. But it is has been argued that this is not necessarily so, since a larger sample size would impose the burden of participation on more subjects, without having a proportionate effect on the trial's capacity to yield clear results.[24]

Other ethical considerations may arise after the trial has started. If it is found to be in a subject's interest to stop or modify the treatment, or to start treating a control subject, then there should be no hesitation in doing so. If there is reason to think that continuation of

the trial may be harmful, then it should be stopped forthwith. For example, the first randomized controlled trial of the protective effect against HIV infection of the performance of circumcision of young men, conducted in Orange Farm, a region close to Johannesburg in South Africa, was stopped as soon as an interim analysis revealed that the incidence of HIV infection was much higher in the controls than in the circumcised group.[25]

In nonexperimental studies[26] ethical problems are usually less acute, unless the study involves hazardous test procedures or intrusions on privacy. But here, too, there is a need for informed consent[27] if participants are required to answer questions, undergo tests that carry a risk (however small), or permit access to confidential records. The investigators should give an honest explanation of the purpose of the survey when enlisting subjects, and respondents should be told what their participation entails, and assured that they are free to refuse to answer questions or continue their participation. Pains should be taken to keep information confidential. Any promises made to participants, e.g. about anonymity or the provision of test results, should of course be kept.

Of particular importance is the question of what action should be taken if a survey reveals that participants would benefit from medical care or other intervention. In studies involving HIV antibody testing, subjects with positive results should obviously be notified, even if this affects the soundness of the study.[28]

The notorious Tuskegee study in Alabama is a horrible illustration of an unethical survey.[29] It began in 1932, with the aim of throwing light on the effects of untreated syphilis. Some 400 untreated Black syphilitics (mostly poor and uneducated) were identified and then followed up; their course was compared with that of apparently syphilis-free age-matched controls. Treatment of syphilis was withheld. By 1938–1939 it was found that a number of the men had received sporadic treatment with arsenic or mercury, and a very few had had more intensive treatment. In the interests of science 'fourteen young untreated syphilitics were added to the study to compensate for this'. Treatment was withheld even when penicillin was found to be effective and became easily available in the late 1940s and early 1950s. Participants received free benefits, such as free treatment (except for syphilis), free hot lunches, and free burial (after a free autopsy). By 1954 it was apparent that the life expectancy of the untreated men aged 25–50 was reduced by 17%. By 1963, 14 more men per 100 had died in the syphilitic group than in the control group. In 1972 there was a public outcry, and compensation payments were later made.

There are those who say that political decisions that may involve risk to human life, e.g. the raising of speed limits on interurban roads, without setting cut-off points for early termination in the case of adverse results, are unethical before–after experiments.[30]

In many countries informed consent is mandatory for studies of human subjects unless there are valid contraindications, such as qualms about alarming fatally ill patients with doubts about the efficacy of treatment. Many institutions have ethical committees that review and sanction proposed studies. Some investigators feel that this control is too permissive, but there are some who think it is too restrictive (it 'stops worthwhile research').[31] A fanciful account of the rise and fall of epidemiology between 1950 and 2000 (printed in 1981)[32] attributed the fall to ethical committees and regulations designed to protect the confidentiality of records.

At a different ethical level, consideration should be given to the justification for any proposed study in the light of the availability of resources and the alternative ways in which these might be used. Does the possible benefit warrant the required expenditure of time, manpower and money? Is it ethical to perform the study at the expense of other activities, especially those that might directly promote the community's health?

An honest endeavour to clarify the purpose of the study may lead to second thoughts: is the study really worth doing? A great deal of useless research is conducted. This wastes time and resources, and exposes the scientific method to ridicule.[33]

Formulating the Topic

When the purpose and moral justification of the study are clear, the investigator can formulate the topic he or she proposes to study, in general terms. In many cases this is easily done and almost tautological. For example, if the reason for setting up the study is that infant mortality is unduly high in a given population and there is insufficient information on its causes for the planning of an action programme, the topic of the study can be broadly stated as 'the causes of infant mortality in a defined population in a given time period'. If the reason for the investigation is that health education on smoking has been having little effect, and that it is considered that certain new methods may be more effective, the investigation will be a comparative study of defined educational techniques for the reduction of smoking.

In other instances the formulation of the topic may be less easy, since the researcher may have difficulty in deciding precisely what study is needed to solve the research problem, taking account of practical limitations. As an illustration, a problem arose in a tuberculosis programme; the extent of public participation in X-ray screening activities fell short of what was desired, and there were indications that the tuberculosis rate was higher among people who did not come for screening. It was decided to seek information that would help to improve the situation, but considerable thought was required before a study topic could be formulated. The alternative topics were the reasons for nonparticipation and those for participation. For a variety of reasons, it was decided that the latter approach would be more useful.[34]

As another example, a researcher interested in a possible association between eating fish and coronary heart disease has several alternative approaches. One, for example, is to study the previous dietary habits of people with and without coronary heart disease; another is to follow up groups of people whose diets differ, and determine the occurrence of the disease during a defined period; and a third is to examine statistics on the disease rates and average fish consumption of different countries. The decision will be based both on the ease with which the required information can be obtained and on the probability of obtaining convincing evidence, one way or the other.

At this early stage, the formulation of the topic of study may be regarded as a provisional one. The feasibility of a valid study still has to be determined. When planning and the pretesting of methods get under way, it frequently happens that unpredicted

difficulties come to light, requiring a modification of the topic or even leading to a decision that there is no practicable way of solving the research problem.

Notes and References

1. Geitgey DA, Metz EA. Nursing Research 1969; 18: 339.
2. A dishonest evaluation of health care may be *eyewash* (an appraisal limited to aspects that look good), *whitewash* (covering up failure by avoiding objectivity, e.g. by soliciting testimonials), *submarine* (aimed at torpedoing a programme, regardless of its worth), a *postponement ploy* (noting the need to seek facts, in the hope that the crisis will be over by the time the facts are available), etc. Providers of care who evaluate services that they themselves provide should take pains to confute the criticism that this is like 'letting the fox guard the chicken house' (Spiegel AD, Hyman HH. Basic health planning methods. Aspen Systems; 1978).
3. Feinstein A. Clinical epidemiology: the architecture of clinical research. Philadelphia: W.B. Saunders; 1985. Cited by Vandenbroucke JP. Alvan Feinstein and the art of consulting: how to define a research question. Journal of Clinical Epidemiology 2002; 55: 1176.
4. Verschuren PJM. De probleemstelling van een ondersoek. Utrecht: Aula; 1986. Extract translated and cited by Vandenbroucke JP (2002; see note 3).
5. Vandenbroucke JP (2002; see note 3).
6. Numerous computer programs for *storing and managing references* are available. Google Scholar and other programs can automatically add citations to databases. For free reference managers, see Appendix C.

   For investigators loath to use computers, a card index is a substitute (one reference per card), with full bibliographic details (names of all authors, first and last page numbers, etc.) to avoid another hunt when a bibliography is prepared for the report.

   If printouts, photocopies, reprints or tear-out copies of articles or abstracts are collected, then they should be filed and indexed in an orderly way. The planning of a filing system is described in detail by Haynes RB, McKibbon KA, Fitzgerald D, Guyatt GH, Walker CJ, Sackett DL (How to keep up with the medical literature. Annals of Internal Medicine 1986; 105: 149, 309, 574, 636, 810, 978).
7. Bacon F. 1620 Novum organum. English translation. Open Court Publishing; 1994.
8. *Guides to critical reading* include: (a) Greenhalgh T (How to read a paper: the basics of evidence based medicine, 2nd edn. London: BMJ Books; 2001). Ten excerpts from a previous version that appeared in successive issues of the British Medical Journal [vol 315] from 19 July 1997 are available on the Internet at http://www.bmj.com/collections/read.dtl. (b) Sackett DL, Straus SE, Glasziou P, Richardson WS, Rosenberg W, Haynes RB (Evidence-based medicine: how to practice and teach EBM, 3rd edn. New York: Churchill Livingstone; 2005. pp. 81–117). (c) A series of 'Users' Guides to the Medical Literature' occasionally published in the Journal of the American Medical Association between 3 November 1993 and 13 September 2000.

   Also, see Crombie IK (A pocket guide to critical appraisal, 2nd edn. Blackwell Publishing; 2007) and Abramson JH, Abramson ZH (Making sense of data: a self-instruction manual on the interpretation of epidemiologic data, 3rd edn. New York: Oxford University Press; 2001).
9. *Publication bias* is an established fact in the health field: negative or inconclusive studies are often 'tucked away in desk drawers' or rejected; e.g. see: Easterbrook PJ, Berlin JA, Gopalan R, Matthews DR (Publication bias in clinical research. Lancet 1991; 337: 867), Dickersin K, Min YI (Publication bias: the problem that won't go away. Annals of the New York Academy of Sciences 1993; 703: 135), Stern JM, Simes RJ (Publication bias: evidence of delayed publication in a cohort study of clinical research projects. British Medical Journal 1997; 315: 640).

'Health journals are … interested in news – they will always want to report the earthquake that happened and not all the places without earthquakes', (Lawlor DA. Editorial: Quality in epidemiological research: should we be submitting papers before we have the results and submitting more hypothesis-generating research? International Journal of Epidemiology 2007; 36: 940).

Investigators who conduct meta-analyses that combine the findings of different studies often appraise the validity of their conclusions by computing a *fail-safe N*, i.e. the number of unpublished negative studies that would be needed to render the overall finding nonsignificant or trivial (for software, see Appendix C). A number of registers of clinical trials have been set up, in the hope that this will permit unpublished results to be sought and taken into account.

10. Forms of *reader bias* include *rivalry bias* (pooh-poohing a study published by a rival), *personal habit bias* (overrating or underrating a study to justify the reader's habits, e.g. a jogger favouring a study showing the health benefits of running), *prestigious journal bias* (overrating results because the journal has an illustrious name), and *pro-technology* and *anti-technology* bias (overrating or underrating a study owing to the reader's enchantment or disenchantment with medical technology). (Owen R. Reader bias. Journal of the American Medical Association 1982; 247: 2533.)
11. Giustini D. How Google is changing medicine. British Medical Journal 2005; 331: 1487.

    Advanced search techniques for use with Google Scholar are described by Noruza A (Google Scholar: the new generation of citation indexes. Libri 2005; 55: 170).
12. Burright M. Database reviews and reports: Google Scholar – science & technology. 2006. Available at http://www.istl.org/06-winter/databases2.html.
13. Sackett *et al*. (2005; see note 8). For a simple guide to the use of Medline, see Greenhalgh T (How to read a paper: the Medline database. British Medical Journal 1997; 315: 180).

    Finding a specific article, or a few articles on a specific topic, is easy. But an exhaustive search is another story. According to the Cochrane Handbook, an exhaustive PubMed hunt for randomized controlled trials (for a meta-analysis) requires 26 search terms over and above those specifying the topic of the trials (Higgins JPT, Green S (eds), Cochrane handbook for systematic reviews of interventions [updated September 2006], appendix 5b.3. Available at http://www.cochrane.org/resources/handbook/hbook.htm).
14. SLIM (Slider Interface for MedLine/PubMed Searches), is available at http://pmi.nlm.nih.gov/slim.
15. Green FHK, cited by Hill (1997; see note 20).
16. Roy DJ. Controlled clinical trials: an ethical imperative. Journal of Chronic Diseases 1986; 39: 159.
17. Seidelman WE (Mengele Medicus: medicine's Nazi heritage. Milbank Quarterly 1988; 66: 221) cites the horrors committed by Mengele and other Nazi physicians as warnings against 'ethical compromise where human life and dignity become secondary to personal, professional, scientific, and political goals'. Also, see Seidelman WE (Nuremberg lamentation: for the forgotten victims of medical science. British Medical Journal 1996; 313: 1463) and Annas GJ, Grodin MA (eds) (The Nazi doctors and the Nuremberg Code: human rights in human experimentation. New York: Oxford University Press; 1995).

    Experiments on prisoners in the USA are described by Hornblum AM (They were cheap and available: prisoners as research subjects in twentieth century America. British Medical Journal 1997; 315: 1437).
18. In *cluster-randomized trials*, e.g. those in which communities or general practices are randomly assigned to treatment or control groups, it is generally impracticable to obtain informed consent for inclusion in the trial from every individual subject before assignment.

    However, in cluster-randomized trials in which intervention is targeted at individuals (e.g. if vitamin or placebo capsules are administered), subjects may be given the option of leaving the trial (after assignment) and choosing an alternative, e.g. routine care. And in studies where outcomes are measured at an individual level, subjects may be required to give their assent to

measurements or access to their medical records; this may be regarded as less important if outcomes are studied only at a group level (e.g. changes in hypertension prevalence).

Opinions differ on the importance of informed consent in cluster-randomized trials, especially in control groups receiving conventional care. However, especially if intervention or nonintervention carries risks, informed consent should probably always be requested from the groups' 'gatekeepers' (who can provide access to their members) – or, preferably, 'guardians' (who can be expected to protect the groups' interests), such as head teachers, community leaders, or local health or political authorities. Because of possible conflicts of guardians' interests, particularly if the guardians are health authorities, approval should always be obtained from an ethics committee.

For fuller discussions of ethical considerations in cluster-randomized studies, see Donner A, Klar N (Pitfalls of and controversies in cluster randomization trials. American Journal of Public Health 2004; 94: 416), Hutton JL (Are distinctive ethical principles required for cluster randomised clinical trials? Statistics in Medicine 2001; 20: 473), and Edwards SJL, Braunholtz DA, Lilford RJ, Stevens AJ (Ethical issues in the design and conduct of cluster randomised controlled trials. British Medical Journal 1999; 318: 1407).

The 1991 CIOMS International Guidelines for Ethical Review of Epidemiological Studies state: 'When it is not possible to request informed consent from every individual to be studied, the agreement of a representative of a community or group may be sought, but the representative should be chosen according to the nature, traditions and political philosophy of the community or group. Approval given by a community representative should be consistent with general ethical principles. When investigators work with communities, they will consider communal rights and protection as they would individual rights and protection. For communities in which collective decision-making is customary, communal leaders can express the collective will. However, the refusal of individuals to participate in a study has to be respected: a leader may express agreement on behalf of a community, but an individual's refusal of personal participation is binding.'(cited by Donner and Klar 2004, *op. cit.*)

19. Regarding *research in developing countries*, international guidelines state: 'Rural communities in developing countries may not be conversant with the concepts and techniques of experimental medicine … Where individual members of a community do not have the necessary awareness of the implications of participation in an experiment to give adequately informed consent directly to the investigators, it is desirable that the decision whether or not to participate should be elicited through the intermediary of a trusted community leader. The intermediary should make it clear that participation is entirely voluntary, and that any participant is free to abstain or withdraw at any time from the experiment'. (Proposed International Ethical Guidelines for Biomedical Research Involving Human Subjects published by the World Health Organization and the Council for International Organizations of Medical Sciences. Cited by Hutton JL (Ethics on medical research in developing countries: the role of international codes of conduct. Statistical Methods in Medical Research 2000; 9: 185)).

    It may also be practicable to obtain the subjects' informed consent as a second stage, after consent has been received from a community leader, as demonstrated in a vaccine trial in Senegal (Preziosi M-P, Yam A, Ndiaye M, Simaga A, Simondon F, Wassilak SGF. Practical experiences in obtaining informed consent for a vaccine trial in rural Africa. New England Journal of Medicine 1997; 336: 370).

    Ethical considerations in field trials in developing countries are reviewed by Smith PG, Morrow RH, (eds) (Methods for field trials of interventions against tropical diseases: a 'toolbox'. Oxford: Oxford University Press; 1991. pp. 71–94).

20. The *ethical aspects of clinical trials* were emphasized by Sir Austin Bradford Hill 1977 (A short textbook of medical statistics. London: Hodder and Stoughton. p. 223), who on his election to the Royal Society was recognized as 'the leader in the development in medicine of the precise experimental methods now used nationally and internationally'.

The basic principle is neatly summarized in the following exchange: 'Mr Ederer: "If you could give only one bit of advice to a clinician planning a clinical trial, what would you tell him?" Dr Davis: "A one-word answer might be 'don't'. If you are determined to do it, my advice would be from the beginning put yourself in the patient's position and develop the protocol so you would be happy to be one of the subjects. If you cannot do that, you'd better not start."' (Davis MD. American Journal of Ophthalmology 1975; 79: 779).

See the *Helsinki declaration*, available at http://www.wma.net/e/policy/b3.htm.

21. Angell M. Editorial: The ethics of clinical research in the Third World. New England Journal of Medicine 1997; 337: 847.
22. Wilmshurst P. Editorial: Scientific imperialism. British Medical Journal 1997; 314: 840. Other extracts: 'Should research be conducted in a country where the people are unlikely to benefit from the findings because most of the population is too poor to buy effective treatment? … Drug companies have performed research on children and adults in countries such as Thailand and the Philippines that do not conform to the Declaration of Helsinki and could not be conducted in the developed world. Reasons quoted for conducting research in Africa rather than developed countries are lower costs, lower risk of litigation, less stringent ethical review, the availability of populations prepared to give unquestioning consent, anticipated underreporting of side effects because of lower consumer awareness … In some experiments in developing countries it is difficult for patients to refuse to participate … participation in a trial may be the only chance of receiving any treatment'.
23. Rutstein DD. In: Freund FA (ed), Experimentation with human subjects. London: George Allen & Unwin; 1972.
24. Bacchetti P, Wolf LE, Segal MR, McCulloch CE. Ethics and sample size. American Journal of Epidemiology 2005; 161: 105.
25. Auvert B, Taljaard D, Lagarde E, Sobngwi-Tambekou J, Sitta R, Puren A. Randomized, controlled intervention trial of male circumcision for reduction of HIV infection risk: the ANRS 1265 trial. PloS Medicine 2005; 2: 1112.
26. For *ethical aspects of epidemiological research*, see: Coughlin SS (Ethical issues in epidemiologic research and public health practice. Emerging Themes in Epidemiology 2006; 3: 16) and Susser M, Stein Z, Kline J (Ethics in epidemiology. Annals of the American Academy of Political and Social Science 1978; 437: 128 [reprinted in Susser M. Epidemiology, health and society: selected papers. New York: Oxford University Press; 1987. pp. 13–22]).
27. A specimen 'informed consent' form for use in an interview survey is provided by Stolley PD, Schlesselman JJ (Planning and conducting a study. In: Schlesselman JJ (ed), Case-control studies: design, conduct, analysis. New York: Oxford University Press; 1982. pp. 69–104).
28. The 'To tell or not to tell' dilemma in studies involving HIV testing, and possible solutions, are discussed by Avins A, Lo B (To tell or not to tell: the ethical dilemmas of HIV test notification in epidemiologic research. American Journal of Public Health 1989; 79: 1544), Kegeles S, Coates TJ, Lo B, Catania J (Mandatory reporting of HIV testing would deter men from being tested. Journal of the American Medical Association 1989; 261: 1989), and Avins A, Woods W, Lo B, Hulley S (A novel use of the link-file system for longitudinal studies of HIV infection: practical solution to an ethical dilemma. AIDS 1993; 7: 109).
29. Thomas SB, Quinn SC. The Tuskegee syphilis study, 1932 to 1972: implications for HIV education and AIDS risk education programs in the Black community. American Journal of Public Health 1991; 81: 1498.
30. Richter E, Barach P, Herman T, Ben-David G, Weinberger Z. Extending the boundaries of the Declaration of Helsinki: a case study of an unethical experiment in a non-medical setting. Journal of Medical Ethics 2001; 27: 126.
31. Waters WE. Ethics and epidemiological research. International Journal of Epidemiology 1985; 14: 48.

32. Rothman KJ. The rise and fall of epidemiology, 1950–2000 A.D. New England Journal of Medicine 1981; 304: 600.
33. 'Time, talent, and money are sometimes squandered on the measurement of the trivial, the irrelevant, and the obvious … A friend of mine who has a gift for felicitous expression has distinguished between "ideas" research on the one hand and "occupational therapy for the university staff" on the other, and once referred to a research project as "squeezing the last drop of blood out of a foregone conclusion"' (Lord Platt. Medical science: master or servant. British Medical Journal 1967; 2: 439).

See an amusing compilation by Hartston W (The drunken goldfish: a celebration of irrelevant research. Unwin Hyman; 1988) of actual research results (Do rats prefer tennis balls to other rats? Can pigeons tell Bach from Hindemith? Does holy water affect the growth of radishes?) that serves 'to drop a gentle hint that there might be too much research going on, and much of that is taken far too seriously'.

Useless research is satirized in the Journal of Irreproducible Results (for details and a sample of contents, visit www.jir.com on the Internet).
34. Rosenstock IM, Hochbaum GM. Some principles of research design in public health. American Journal of Public Health 1961; 51: 266.