

# **GOOD EPIDEMIOLOGICAL PRACTICE (GEP)**

## **IEA GUIDELINES FOR PROPER CONDUCT OF EPIDEMIOLOGICAL RESEARCH**

### **SUMMARY**

In these guidelines, we begin by outlining the background to epidemiological research and the role of ethics committees. We then summarise the four general ethical principles for research and the important concept of informed consent. The second section provides suggested rules for good research behaviour under the headings of working with personal data, data documentation, publication, and exercise of judgment with a final note on scientific misconduct. It is our intention that these guidelines will be kept under regular review as new problems and opportunities emerge.

## **GOOD EPIDEMIOLOGICAL PRACTICE (GEP) IEA GUIDELINES FOR PROPER CONDUCT OF EPIDEMIOLOGICAL RESEARCH<sup>1</sup>**

### **BACKGROUND**

Research should be an activity devoted to the exploration of the laws of nature driven only by a desire to know the truth. In the real world, other factors often interfere with this ideal aspiration and can result in conflicts of interest. Research has to be funded, conducted and published, and researchers like to promote their reputations. Research is, therefore, often carried out amid many competing elements.

Research findings in public health should serve the public good but may not be welcomed by all. Findings of serious side-effects of a given drug, for example, may be welcomed by those taking the drug and their physicians, but may seriously reduce sales and the expected profits of the manufacturer. Alternatively, a promising hypothesis may not be supported by new data. Opposing forces may divert the researcher and may even, in extreme circumstances, lead to a violation of ethical codes.

Good Epidemiological Practice (GEP) guidelines recommended by a scientific organisation cannot prevent these problems but are intended to promote discussion and to inform and educate young epidemiologists. We need a code of practice when we do research and when we take part in the evaluation of research and of each other's work.

We must also be sure to obtain a reasonable balance between ethical constraints and the opportunities for legitimate research of importance to public health. The aim of this document is to provide a set of guidelines, recommended by the IEA, for the conduct of high quality epidemiological research and proper collegiate behaviour. It has no legal status.

Guidelines should change with time as new problems and new opportunities emerge and any document on GEP should thus be regularly re-visited, particularly when it covers epidemiological practice in all parts of the world.

### **THE ROLE OF ETHICS COMMITTEES**

The IEA fully respects the important role of ethics committees and all research should be based on accepted ethical standards and be of high quality. Poor research may do more harm than no research at all. There must, however, be flexibility and an acknowledgement that different types of research will require different levels of ethical appraisal. One size definitely does not fit all.

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<sup>1</sup> These updated guidelines are based on a document developed for the IEA-European Federation by Jørn Olsen, modified by IEA members at the IEA Meeting in Brazil in April 2007, and edited by Charles du V Florey, Neil Pearce and Susie Stewart.

Much epidemiological research requires simple observation of populations and study participants and does not involve risky or invasive procedures. Such research can be threatened by time-consuming, over-exhaustive and costly ethical appraisal that may only be necessary for research that involves invasive and/or risky procedures.

It is our contention that ethical evaluation criteria should be appropriate to the type of study under consideration. Criteria governing randomised clinical trials, which involve invasive interventions, should not be the same as those applied to simple observational studies where the sole risk to participants might be that of unwanted disclosure of personal data. It seems unreasonable to treat all protocols alike for ethical appraisal purposes, regardless of risks and benefits.

Experience has also shown that standards vary widely between different ethical committees and large multi-centre studies must follow procedures acceptable to all relevant committees. This rigid approach can threaten the validity and conduct of a study. We would argue for procedures in this area to be streamlined, especially for research that covers several geographical regions and, is, therefore, subject to a multiplicity of ethics committees. We would further suggest that ethical approval for observational epidemiological research might be more appropriately addressed by experts in data protection and that consent to participate in research can be given in a broad sense without the need for repeated consents in studies with repeated analyses over time.

It is an unfortunate fact that there are rare instances where researchers have violated important ethical standards. This should not, however, result in unduly bureaucratic procedures that absorb unreasonable amounts of time and resources and impoverish epidemiological research as a whole.

The role of ethics committees should be to ensure that high quality epidemiological research of benefit to the public health can be carried out, after a level of scrutiny appropriate to the particular protocol involved.

## **ETHICAL PRINCIPLES OF RESEARCH**

There are four general ethical principles for research:

- . • Autonomy (Respect for individual rights)
- . • Beneficence (Do good)
- . • Non-maleficence (Do no harm)
- . • Justice

Although these principles are well accepted, they must be seen in a broader context. Research is needed because people have the right to know about hazards to their health and to make evidence-based choices concerning treatment and prevention. From an ethical point of view, it may sometimes be preferable that no research is done, but this is not normally the case. There are many epidemiological research projects in which the ethical concerns of not doing the study far outweigh

those of doing it. Research must also be of good quality. Bad research may lead to wrong decisions that may have a profound impact on people's health.

## **RESPECT FOR INDIVIDUALS**

### ***Informed Consent***

Respect for individuals in research entails accepting an individual's right to refuse to participate; to be informed about the research subject; and to be properly equipped to make a decision based on the best possible information. The principle of informed consent rests on the principle of autonomy and respect for those who take part in research. Written informed consent should be obtained when the research involves risks – the purpose should be to inform the study participants, not to protect the researcher against possible claims for compensation if something goes wrong. Formal written consent is unnecessary if the research is carried out in settings that pose no threat to the potential participants, when it is stated that taking part is voluntary and it is obvious that no benefits are at risk of being lost if potential participants refuse to take part. Such situations often arise in studies based on self-administered questionnaires or telephone interviews where providing the data involves giving *de facto* consent. There may also be instances where informed consent is impossible, difficult, or even unethical to obtain. There may even be circumstances where requiring specific information poses a threat to the participants and to the validity of research - for example, in the use of already existing data.

The early guidelines of the Council for International Organisations of Medical Sciences (CIOMS) state that:

*Informed consent is a decision to participate in research, taken by a competent individual who has received the necessary information; who has adequately understood the information; and who, after considering the information, has arrived at a decision without having been subjected to coercion, undue influence or inducement, or intimidation.*

[http://www.cioms.ch/070516april\\_epi\\_revisions.pdf](http://www.cioms.ch/070516april_epi_revisions.pdf)

Informed consent thus includes three components – information, understanding and consent.

### ***Information***

There should be adequate disclosure of information to enable the potential participant in research to make an informed choice. There may, however, be times when consent has to be given in more general terms without knowledge of the detailed study hypothesis and design. In a case control study, for example, disclosure of the specific hypothesis may make it impossible to obtain reliable information from participants. Similarly, in much of contemporary genetic research, the meaning of being informed about the aims of the study is not clear since these aims are very broad and change rapidly with new research findings.

### ***Understanding***

Individuals should be able to understand what they are told and to make a reasoned choice based on that information. Experience shows that this ideal is difficult to achieve. Too much information may be given in excessive detail, mainly to protect the researcher and the institution. An understanding of the main ideas and risks of the study may be more important than being informed about all the specific scientific details.

### ***Consent***

There should be a voluntary decision or agreement on the part of a capable person. Research participants have the right to refuse to take part in a study but they also have the right to accept. As a general rule, only research ethics committees or similar authorities may deny participants the right to choose for themselves whether they will take part in the research or not and they should exercise that right with great caution. It is especially important that people who may be responsible for the potential harmful exposures under study cannot deny the exposed people the opportunity to have the possible health effects of the exposure studied. If a possible side-effect of a new drug is under investigation, for example, doctors who have prescribed this drug should provide access to those patients and allow them to take part in the study if they wish to do so.

Beneficence, non-maleficence and justice may all be involved when considering whether subjects should be informed about all aspects of a study. In general, sufficient information must be given so that, when the interview or examination is completed, or when the research results are published, participants do not feel they have been misled. Information was insufficient if, at that stage, participants express regret that they took part and think they would have made a different decision had they been better informed.

Participants must also have the right to withdraw their consent at any time during the study without being obliged to give their reasons. Non-participation or withdrawal of consent should never result in disadvantage for these individuals. Informed consent should be given freely without external pressure and without unreasonable inducements. There should always be an assessment of what incentives, if any, should be offered to potential respondents for participating in the study. Although the distinction is not clear-cut, a balance between reasonable reimbursements, such as travel costs, and unreasonable remuneration must be struck. Incentives that include more than payment for actual costs are acceptable only in studies that carry no risk for the participants. In the clinical setting, where patients may not feel free to refuse a request from their doctor to take part in a study, mechanisms to counteract undue influence must be established. These might include letting an outside person give the information or waiting until patients return to their own environment to ask for consent.

Although people have the right to say no, it should be permissible to try to contact people who do not respond to an invitation to take part.

Consent should not be required for use of information in the public domain, although countries and communities differ in their definition of what type of information about citizens is regarded as public. Data gathered for administrative purposes do not require consent from the subjects if obtaining consent could cause undue concerns, be impractical or too expensive. This type of research requires, however,

that standards of data protection are followed to reduce any possible risks of disclosure of personal data.

Research ethics committees and other appropriate authorities should specify the conditions for setting up biological research banks. If the samples are to be used for research not covered by the original consent, an ethics committee should decide under what conditions renewed consent is required.

Research ethics committee or a similar authority could, under special conditions, give consent for children and other individuals who are temporarily or permanently unable to give informed consent by themselves.

It has been suggested that research data should be made available to participants but there must be some caveats to this idea. It could present a threat to data security and would require stringent identity checks. Furthermore, research tests are usually not of the same quality as diagnostic tests so providing uncertain data might do more harm than good. In genetic epidemiology, for example, many thousands of gene mutations are often examined simultaneously without any prior knowledge of the role or importance these genes may have. This makes it impossible to explain the findings in any meaningful way.

## **DO GOOD, DO NO HARM**

A central aim of epidemiological research is to improve people's opportunities for making choices that will improve their health. Individuals have the right to choose between different preventive and therapeutic actions. To do this effectively, they need to know about health hazards related to the different procedures in order to obtain optimal treatment in the health care system. Without research they cannot exercise these rights.

The most basic ethical principle is the moral obligation to cause no harm, whether physical or psychological, to participants in epidemiological research. Although the risk of harm to those who take part in an epidemiological investigation is usually minimal, most participants gain no personal benefit and often do not have a disease that needs treatment. In recognition of this altruism, they should be treated well and with respect. Important findings from the research should, therefore, be made available in an understandable form. Results may reveal information on individual participants that is of importance and value for these individuals alone and such data should be made available to them. In research that does not involve risky invasive procedures, the greatest risk to individuals is a disclosure of personal data that could be misused by the media, an employee, an insurance company or someone else.

## **RULES FOR GOOD RESEARCH BEHAVIOUR**

Data collection and recruitment of volunteers for research in many countries are subject to legal controls but many other areas of activities are not guided by legal principles. In the following section we present IEA guidelines for these activities under four headings: working with personal data, data documentation, publication, exercise of judgment. There is also a short section on scientific misconduct. The list should be regarded as a starting point to which new elements may be added.

### **WORKING WITH PERSONAL DATA**

Working with personal information given by participants in research is a privilege that should be respected by making the best possible scientific use of the data and by making sure confidentiality is observed.

Do not work with data that have overt personal identifiers. Such data are only needed during data collection and as part of the data cleaning process. Use a study-specific running number to identify your data and keep the link between overt personal identifiers (such as names, addresses, phone numbers, social security numbers) locked in a safe with access limited to the person responsible for data security. This person should also make sure that all back-up copies are kept safe. On completion of the study, data should be kept in a safe for the time period required by law to document published results. Exchange and sharing of data, or reuse of existing data, will usually require additional permissions from the relevant authorities.

Data analyses should be conducted in designated areas where doors and windows can be locked.

As a researcher you are bound by professional secrecy. You must not reveal personal information obtained by having access to research data to anyone outside the scientific research team. All researchers on the project should sign a contract of professional secrecy and should agree in writing to adhere strictly to the national rules set for working with data. The principal investigator is responsible for making sure that all members of the team are aware of these rules.

Identifiable personal data should never be stored on computers outside research establishments and the files containing personal identifier should be stored in locked cabinets or rooms separated from the data used for analysis. Back-up copies must be subject to the same degree of data security and personal data should only be sent from one place to another by secure methods. Do not send personal data by ordinary mail or in any electronic form unless they are encrypted. Data should be sent by personal courier or as special delivery mail.

Those working with data should be identified throughout the study period. They are responsible for ensuring that legal conditions are followed correctly and for the implementation of good practice rules.

Publication of data should only be in the form of anonymous tables where individuals cannot be identified.

Epidemiologists often use personal data, and people's rights to privacy are paramount and must be respected. Working with personal data is a privilege that calls for a high degree of data protection, especially in situations where data are used without personal consent. Over and above the requirements set up by the data protection agencies, epidemiologists should set up a working standard that secures as little risk of disclosure of personal information as possible.

We encourage each country to set up standards for data protection for all research organisations that have access to personal data, since unintended disclosure of personal data can harm individuals. Public disclosure of personal data is a violation of the trust that must exist between the epidemiologists and the people who take part in research and a violation of this agreement may impair future options for other researchers.

Particular care should be taken to avoid publication of data that may lead to discrimination against vulnerable groups in society. Publication of unfavourable data from small vulnerable groups may stigmatise these groups and cause harm.

## **DATA DOCUMENTATION**

Data documentation includes all phases of the study, from its planning, through conduct to publication. The research protocol is the key document.

### ***The research protocol***

The protocol is the cornerstone of any epidemiological research project. In this the purpose of the study, the hypotheses, the design, the source population, and the planned analyses are described. Administrative issues, ethical considerations and possible problems and limitations are also addressed in the protocol.

The primary objectives of the protocol are fourfold:

- 1 to justify the need for the study – that is, why the study should be conducted, given the current state of knowledge;
- 2 to demonstrate the appropriateness of the proposed methods for testing the stated hypothesis;
- 3 to demonstrate the feasibility of doing the study as proposed - that is, that the study can be completed successfully in the specified time and with the available resources;
- 4 to demonstrate that the investigator(s) have the ability and skills to conduct the proposed study and are aware of all limitations in the design.

The protocol serves:

- as an instrument to justify that the project is practicable when applying for money or permissions;
- as documentation for those conducting the study - usually a more detailed protocol will be needed for that purpose and this should be updated over the course of the study to record all changes in the original protocol over time.

A study protocol should always be available before the study starts. Since epidemiological studies may involve many different study designs, it is not possible to present a standard structure for a protocol that could be used in all situations. Nevertheless, the protocol should be sufficiently detailed to serve as documentation for the study. The protocol should demonstrate that the researcher knows the literature well. It is often useful to include power calculations, but in some instances it is acceptable to do studies with smaller numbers than the power calculations indicate are required. Even a small study may collect valuable data that may, in combination with other published data, be used to reach conclusions. In any case, single studies are rarely sufficient to make decisions and consensus is usually reached by gradually obtaining information that modifies previous beliefs until the evidence becomes sufficient.

It is also advisable to include agreements on time schedule, publications and authorship in the protocol.

The protocol is the intellectual property of the investigators and should be treated as such. It should be considered as confidential by those who read or review it. It should also be stored and kept after the study has ended. For randomised studies there are now procedures for archiving protocols before data collection begins, partly to document that study hypotheses were made before the data analyses.

### ***Storage of data***

Once data have been collected, the process of data cleaning starts. This process may involve recoding some data and it is, therefore, important that this process is transparent. Data cleaning should involve as little recoding as possible, the recoding rules should be stated in the protocol, and raw data, without any manipulations, should always be stored together with the cleaned data.

These data files should then be stored in locked cabinets and kept for a time period of not less than five years after the results are published. The data documentation is part of this archiving procedure and the IEA supports the establishment of public archives for research data.

Data documentation should be sufficiently detailed to enable others not involved in the study to replicate its published findings.

### **PUBLICATION**

The general principle is that research of importance for other people's health should be published, unless the researchers find the study to be of insufficient quality. Sometimes a good design described on paper does not work in practice. If the researchers themselves have no confidence in their results, the results should probably remain unpublished. This should be a rare exception, however, and it is always unacceptable to avoid publishing results if they do not fit with expectation and hypothesis, or if

they do not fit the financial interests of the sponsor. Before a study starts it should be made clear to all members of the research team that the research is being done with the aim of being published. Many colleagues have experienced substantial pressure from private funding sources with an economic interest in certain results when these results were not reached. This had led to a widespread debate about “conflicts of interest”. The IEA supports disclosure of “conflicts of interest”, as well as “conflicts of financial interest.”

Researchers should have no undisclosed conflict of interest with their collaborators, editors, sponsors or participants in research. Thus, researchers must disclose actual, apparent or potential conflicts of interest to the Ethical Review Committee. All sponsorship of research should be publicly acknowledged – it is difficult to justify secrecy. All results of a study, whether government or industry-sponsored, should be the intellectual property of the investigators, not the sponsor. Requests to withhold findings, to change or tone down the content of a report to produce a misleading or delayed publication should be categorically refused.

It is essential to acknowledge these issues at the start of negotiations with the sponsor, whether private or governmental. There should be a written document that states that the results will be submitted for publication regardless of outcome. The sponsor must acknowledge the independence of the investigators and this relationship must be maintained throughout the study.

The IEA recommends that, when research of public health importance is sponsored by a private contractor that has a personal interest in a given result, a buffer funding structure should be established. The buffer could be to act through a government-funded research organisation, the purpose of which would be to ensure the data are analysed, interpreted and reported in good faith and that the researchers publish results without pressure to deviate from what the data actually show.

The epidemiologist should not inform the press about the findings of a particular study, unless the full scientific report is available to the public. It is unacceptable to inform the public at a stage when no one has had the opportunity to read the full report and to challenge the findings. Under normal circumstances no information should be given to the media before the findings have been subject to peer review. Only for a limited set of good reasons (emergency, epidemic, and so on) can this principle be waived. Investigators, for example, may discover health hazards that demand rapid intervention and thus have an obligation to protect and restore health. In this event, their advocacy must be based on objective, scientific data only, and these data should be made available for others to scrutinise.

National epidemiological societies or IEA regions could assume responsibility for performing ad hoc reviews in situations where findings have a public health interest that overrides the principle of the normal review process.

Epidemiologists with access to information of major public health interest should not delay public release of such information, once the evidence has been reviewed by a competent body, usually a journal with a peer review procedure. Withholding such information is a violation of the principles of non-maleficence and autonomy.

Epidemiologists should not exaggerate their research results with the aim of increasing the likelihood of obtaining future research funding or making their paper more attractive to editors. We also

encourage editors not to highlight key findings in a manner that obscures critical reservation. We strongly stress the need for caution when writing press releases or when communicating directly with the public. Epidemiologists should be wary of publishing poorly supported conclusions. History shows that many research results are wrong or not fully right, and epidemiology is no exception to this rule.

Published results are usually only a small part of the information available and it is important that what is selected is selected in good faith. It is poor scientific practice and misleading to select only what agrees with the point of view of the investigator while omitting parts, which contradict previous beliefs.

It is advisable to publish the main results in a form that reaches the participants of the study and other interested members of the community where the study took place – for example, a newsletter, local newspapers. As stated, this type of publication should await publication in peer reviewed journals.

Raw data should be made available to journal editors if requested and to colleagues who want to verify already published results. Conditions for external access to data must of course respect rules for data protection and intellectual property for those who collected the data, and any other conditions imposed by the ethics committee that approved the study.

Authorship should follow the Vancouver rules, which state that all authors have taken an active part in several phases of the research and are willing to take responsibility for the final report.

<http://www.icmje.org/>

## **EXERCISE OF JUDGMENT**

Conflicts of interest can arise when researchers have or could have a private or personal interest sufficient to influence the objective exercise of their professional judgment towards their official duties. These potential conflicts of interest should be taken into consideration when epidemiologists are asked to provide advice or opinions.

Experienced epidemiologists spend a substantial part of their working time evaluating the work of others whether for editors, funding agencies, or users of epidemiological studies.

External reviewers of epidemiological manuscripts and applications for funding should recognise that they play an important role as guardians of scientific standards and advisors to journal editors and funding agencies. Referees judge the originality, scientific reliability, clinical or public health importance, and overall suitability of the paper for publication in the journal or for the funding agency. This peer review process is of fundamental importance for the quality of epidemiological research in general.

Epidemiologists who review research protocols, manuscripts in draft or the work of colleagues should ask themselves if they are suitably skilled to perform the review. Reviewers should not accept an invitation to do peer reviews if they lack competence in the area of research or have a conflict of interest from working too closely with one or more of the authors or being a competitor in the field. Reviewers should respect the intellectual property of the author's research ideas and should not delay

the review process or try to stop a project or a grant for personal gain. The review should respect the intellectual property rights of those who wrote the paper or the grant proposal.

It is important that we do not pretend to be experts in areas where we are not. One of the cornerstones of public and collegiate confidence in epidemiological research and in epidemiologists is the assumption that epidemiologists will judge their own work and ideas, and those of colleagues, impartially with skills, knowledge, and in good faith.

Research serves important tasks in a democracy and everybody should be given the opportunity to contribute with their experience. The IEA does not support the view that epidemiological research should be restricted to people with certain educational backgrounds. Scientific findings should be reviewed on their own merits. There are general guidelines for referees, which have been adopted by several scientific journals. [website link](#).

## **SCIENTIFIC MISCONDUCT**

Any large-scale study provides ample opportunity for manipulation and interpretation of data. Scientific misconduct is any deviation from an interpretation not reached in good faith and with the aim of objectivity. External pressures to publish and to get research funding are strong risk factors for scientific misconduct, as are editors' desires for simple 'take home messages'. In spite of these risk factors, the whole specialty relies on scientific integrity, supported by severe sanctions for documented misconduct. We encourage all countries to implement safeguards against misconduct by making research data available for other researchers and to remind co-authors and supervisors of their responsibility. Recent examples indicate that epidemiological research is not immune to the most severe form of misconduct - namely, fabrication of data. More information is available at [www.ieaweb.org](http://www.ieaweb.org).

## **CONCLUSIONS**

Epidemiological research is needed in health care, disease prevention and health promotion. This research should be of good quality, done in a timely manner and follow recognised ethical standards. Ethical evaluations should take into consideration the risk of not doing as well as the risk of doing research.

The IEA hopes that these guidelines, which will continue to be kept under review, will provide a useful template for high quality epidemiological research and proper collegiate behaviour.