

**Guidelines and Recommendations
to Assure
Good Epidemiologic Practice
(GEP)**

Long Version

**German Society for Epidemiology
(DGEpi)**

In Collaboration with the
German Association for Medical Informatics, Biometrics, and Epidemiology
(GMDS),
German Association for Social Medicine and Prevention
(DGSMP)
German Region of the International Biometrics Association
(DR-IBS)

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Foreword

In December of 1997, an international commission, assembled by a mandate of the chair of the German Research Foundation (DFG), formulated the following offer: "Scientific Professional societies should, as part of their scope of action, develop and publish standards of good scientific practice on which their members are to be obliged."

As a result, during a membership meeting on March 17th, 1998, the German Epidemiological Foundation (DAE) authorized its Working Group on Epidemiological Methods to develop a blueprint for Guidelines and Recommendations to Assure Good Epidemiological Practice (GEP). A first draft of these recommendations was openly discussed during a two-day workshop in May, 1999 at the Robert Koch Institute in Berlin. The corrections and modifications that arose from this discussion were applied by an editorial committee and presented to the boards of directors of the DAE, the GMDS and the DGSMP, and the German Region of the International Biometrics Association. In an extensive consensus-building process, the current recommendations were adopted by all participating professional associations in February, 2000.

The Guidelines and Recommendations to Assure Good Epidemiological Practice (GEP) will be available in both a short and a long version. The short version is intended to provide a concise overview and comprises therefore only the 11 guidelines and associated recommendations. The long version contains additional commentary regarding each guideline. It is intended that the capacity of the guidelines to assure Good Epidemiological Practice will be evaluated during a two-year trial period, after which the document will be revised if necessary.

These guidelines and recommendations are addressed to everyone involved in the planning, preparation, execution, analysis, and evaluation of epidemiological research, as well as research institutes and funding bodies. The guidelines and recommendations presented here are based on current widely accepted standards of epidemiological research already in international use, and were arrived at as a result of the above-mentioned consensus process.

The purpose of epidemiological research is to investigate the determinants of health, as well as the causes, incidence, progression and outcomes of diseases in human populations, or rather in well-defined population groups. Epidemiological studies are primarily observational, and are therefore to be differentiated from randomized intervention studies in clinical research.

The guidelines presented here should serve to establish standards of quality for epidemiological research in Germany. They should help to eliminate scientific fraud, to ensure transparency in research, and to promote trusting collaborations among scientists. The guidelines, however, should not be as limiting or inflexible as to threaten the freedom of scientific research in Epidemiology. Rather, the guidelines should define the framework within which epidemiological research can be used to its fullest benefit, in all of its facets and relating to all of its areas of application.

It is quite possible that in special cases reasonable deviations of the guidelines can and sometimes even ought to be made. Such cases are capable of remaining consistent with good epidemiological practice via explicit description of the nature of the deviation and its valid justification. Although many of the elements described here are already accepted as

good scientific practice in Epidemiology, these guidelines will be particularly important with regard to both the execution of upcoming studies and the planning of future ones.

It is important for all people involved in the practice of Epidemiology to be aware of the main features of good scientific practice and to implement them in daily practice. Serious cases of scientific fraud threaten the value of Science itself, as they erode the public's trust in Science as well as the relationships of scientists among one another. Epidemiology, however, depends on both of these basic elements, which should therefore be safeguarded for the future by the Guidelines and Recommendations to Assure Good Epidemiologic Practice presented here.

December 1999

Foreword to the Revised Edition

As stated in the preamble, upon the adoption of the guidelines, it was decided that an evaluation would be conducted after two years of use and the recommendations would be revised if necessary. In September of 2001, the DAE assigned the Working Group on Epidemiological Methods in conducting this evaluation. The Joint (Cross-Sectional) Working Group for the Evaluation of the Guidelines for Good Epidemiological Practice was established to develop the content and format of the evaluation instrument; this group consisted of members representing the Epidemiological Methods Working Group, as well as members of other workgroups of the DAE and its umbrella organizations. The objective was to obtain the most representative overview possible of the recognition, application, and usefulness of the guidelines from a wide range of people involved in epidemiological research in Germany. All participants were requested to suggest improvements or rather provide feedback on the formulation of the individual guidelines and recommendations.

The Joint (Cross-Sectional) Working Group produced a six-page, 34-item questionnaire to evaluate the guidelines. The Department of Epidemiology of Health Care and Community Health of the Institute for Community Medicine at the Ernst-Moritz-Arndt University Greifswald coordinated the data collection. After consulting with the board of directors of the DAE and its umbrella organizations, the questionnaire was sent by mail to all members of the DAE and to the members of the professional association of Epidemiology of the DGSMP. The evaluation form was sent to a total of 457 members, of whom 138 (30%) responded.

The participants of the members' poll from the DAE and DGSMP were, as an alternative to the paper version, given the option of filling out the questionnaire online, with an individualized password for access to a secured webpage. This was created by the department of Epidemiology at the German Institute for Nutrition Research.

In consultation with the boards of directors of the supporting organizations, the members of the German Association for Medical Informatics, Biometrics and Epidemiology (GMDS) and those of the International Biometrics Association – German Region (IBG-DR) were provided the option of using a printable version of the questionnaire that was made available on the homepages of their respective professional associations.

The compilation of the raw data from both the paper and internet versions of the questionnaires into a single database was carried out by the Institute for Epidemiology and

Social Medicine of Westfälische Wilhelms-University Münster. In September 2003, the Joint (Cross-Sectional) Working Group coordinated the analysis. The findings of the evaluation were presented in a plenary session of the 11th Annual Meeting of the DAE and subsequently put to discussion. The resulting changes to the formulation of the Guidelines and Recommendations to Assure Good Epidemiological Practice have been incorporated into this revised version.

Adopted by the Board of Directors of the DAE on

August 19th, 2004

Supplement of the Guidelines for Good Epidemiological Practice (GEP) by specific regulatory statutes for several sub-specialties in Epidemiology

The extensive application of the GEP in any area of Epidemiology was encouraged by the further development of the GEP based on the evaluation and the following discussion in the participating scientific societies. The GEP is today accepted by the great majority of the epidemiological researchers, the public and many private sponsors as well as evaluators, peer reviewers and editors of scientific journals. The application comprises all areas of descriptive and analytic Epidemiology and covers the whole spectrum of epidemiological topics. This wide application requires to increasingly apply and adapt the general recommendations of the GEP to specific research questions, data bases and methodological contexts of the different specialties in Epidemiology. Here it might happen that for a certain epidemiologic area a GEP guideline or selected recommendations are inapplicable or relevant requirements of specific areas are not explicitly addressed in the guidelines. As a consequence the GEP may be supplemented by "implementation rules" to ensure the conceptual and methodological coverage of the different requirements of all epidemiological specialties as well as to achieve the necessary level of detail. In these implementation rules the relevant guidelines and recommendations of the GEP will be specified and interpreted for the use in different areas of Epidemiology as praxis-oriented recommendations. Proposed additions will be formulated in a process of discussion and coordination and will be presented for review to the participating scientific societies. Accepted additions will be incorporated in the attachment of the latest version of the GEP and thereby become integral parts of the GEP.

Based on a proposal of the working group Secondary data analysis (AGENS) of the DGSMP the GEP was supplemented by the implementation rule "Good Practice Secondary Data Analysis". For the applications in the field of the epidemiologic analysis of secondary data the Good Practice Secondary Data Analysis (GPS) specifies and supplements the guidelines and recommendations of the GEP. The current version of the GEP was formulated in a process of cooperation and reconciliation between the representatives of the AGENS (board of representatives Enno Swart, Magdeburg, and Peter Ihle, Cologne), the working group epidemiologic methods (board of representatives Stefanie Klug and Thomas Lampert), and the board of the DGEpi (Wolfgang Hoffmann) with active contribution from many other colleagues.

The current supplemented version has been accepted by the boards of the DGEpi, the gmds, the DGSMP and the DR-IBS.

July 29th, 2008

Guideline 1 (Ethics)

Epidemiological research must be conducted in accordance with ethical principles and must respect human dignity as well as human rights.

Ethical principles arise from national and international law governing human and civil rights as well as the rights of patients, research subjects and investigators. These ethical principles are also to be applied in epidemiological research even in the absence of an explicit legal obligation.

Recommendation 1.1

Before conducting an epidemiological investigation, approval should be obtained from an ethics commission.

Basic requirements of ethical appraisals have been stipulated in the Checklist for Ethical Assessments of Epidemiological Studies of the German Epidemiological Foundation (DAE) (1999 draft).

Guideline 2 (Research Question)

The planning of every epidemiological study requires explicit and operationalizable research questions that are to be formulated as specifically and precisely as possible. The selection of the study population must be justified on the basis of the main research question.

The research question is indispensable, as it forms the basis upon which the potential use of an epidemiological study can be identified. Based on the research question, it must be obvious if and to what extent the research project seeks to serve medical, scientific, disease prevention, health promotion, socio-political or other comparable social or corporate interests.

The explicit formulation of the research question is a fundamental pre-requisite for the planning and evaluation not only of the study design and instruments, but also of the timeline and budget of the planned research. The operationalizability of the research question enables the selection, design, and application of the most suitable methodological elements for a given epidemiological study (selection of the research sample, survey instrument, estimate of sample size given a predefined level of precision, etc.).

The specification and focusing of the research question requires the existing scientific evidence for being amassed and evaluated at the beginning of a research project. Therefore it helps to avoid the use of obsolete hypotheses and/or accidental duplicate investigations.

Recommendation 2.1

In the description of a research question, hypothesis-testing and hypothesis-generating (exploratory) research questions must be distinguishable from one another.

Recommendation 2.2

If hypotheses are to be tested in a study, these hypotheses have to be formulated previous to the beginning of the study.

The application of statistical methods to confirm a hypothesis requires the a priori formulation of the hypothesis that is to be tested. Those hypotheses have to be based on an operational and quantifiable research question. In hypothesis-testing studies, the selection of the study participants must be carried out in a manner that satisfies the theoretical assumptions of the used statistical methods.

Recommendation 2.3

The testing of hypotheses not defined a priori (secondary data analyses) can be justified.

The implementation of secondary data analyses can be justified. These analyses, however, are to be considered statistically explorative. This stipulation is to be indicated in the presentation of the results and to be kept in mind during the interpretation.

Guideline 3 (Study protocol)

An epidemiological study is based on a detailed and binding study protocol, in which the study elements are defined in writing.

The creation of a study protocol (study plan) before the beginning of a study is a fundamental methodological requirement for ensuring the quality of the study. The study protocol is a compilation of the most important information necessary for the implementation, application, and evaluation of the study.

The study protocol should include:

- Research question(s) and working hypotheses
- Study design
- Target population and study population
- Sample size of the study and its rationale
- Sampling procedure and recruitment methods for study participants
- Definition of, measurement methods and survey procedures for the dependent variables (outcome variables)
- Independent variables (risk factors)
- Potential confounders and effect modifiers
- Data collection and storage methods
- Analysis strategy, including statistical models
- Quality assurance methods
- Methods to ensure data protection and safety and compliance with ethical principles
- Timeline with predefinition of accountability

Recommendation 3.1

The study design should be described and its selection adequately justified.

The choice of study design is dependent on the methodological framework that is adopted (incidence of considered disease and of the independent variables of interest, scaling of the dependent variables, possibilities for the prevention of falsification of data) – which is itself dependent on the research question – as well as on the available resources (accessibility of data sources, patients and cohorts, costs, duration). It is also valuable to consult published studies with comparable objectives.

Recommendation 3.2

The target population and the sampling methods for the study participants should be described and adequately justified.

Both the internal validity and the generalizability of the study results are highly dependent on the choice of the target population and the sampling of the study

participants. Differences in the incidence of the diseases being studied or of its risk factors as well as the availability or the comparability of collected information often require the target population to be narrowed down to a well-defined study population. Inclusion as well as exclusion criteria should be defined and adequately justified a priori. As an example, the study design and research methodology are to be designed so that gender differences can be adequately detected. For research questions pertaining to both sexes, a justification is required if participants of only one sex are to be included in the study.

Recommendation 3.3

Already during the design of epidemiological studies, possible biases toward the results should be identified and addressed.

Beginning in the planning stages of a study, measures should already be taken to defend against biases that may arise through selection, confounding, etc. Such measures could include, for example, participant matching (during sampling) or a limitation of the variability of potential confounders, or rather the collection of information required for control of confounding. Sensitivity analyses can be planned as extra investigations to estimate the impact of measurement errors on the results of the study.

Recommendation 3.4

The concept of the minimization and control of potential selection biases due to non-participation and unavailability of data for selected study participants should be addressed in the study protocol.

Such a concept implies a proband-oriented documentation of the reasons for non-participation or one's subsequent exclusion from the study. During the study, basic information should be obtained from non-participants as well. The objective in collecting such information is to estimate the direction and magnitude of a possible selection bias due to non-response. In order to document such non-participation, the various categories of non-participation must be defined in advance. To ensure a detailed response-analysis, successful as well as unsuccessful contact-attempts should be documented according to type, content, and date/time.

In order to be able to better estimate possible biases due to selective nonparticipation and to better compare between studies, at least the following categories of probands should be included in the reporting of the results of an epidemiological study:

Number of probands:

- with complete participation
- with incomplete participation
- who refused participation
- who were too sick to participate
- who were ineligible as a result of the study protocol, due to not fulfilling the inclusion criteria and/or fulfilling the exclusion criteria

- who were not reached (separated into those removed from the study and those who died during the study)

A stratified analysis of the participants, for example by gender, may be necessary to prevent selection effects. When conducting cohort studies, reasons for the premature/early withdrawal from the study are to be recorded as well.

Recommendation 3.5

All variables of interest should be precisely defined and operationalized as much as possible according to professional standards. Measurement and survey instruments that are as valid and reliable as possible are to be used.

In addition to the qualitative description of variables, and particularly for exposure data, the quantitative magnitude and temporal distribution of the variables should be measured. Diseases or causes of death should be defined and be encoded according to international accepted diagnostic standards. In addition, for classifications of diagnoses and degree of severity of diseases internationally accepted codes / classifications (e.g. ICD, TNM, NYHA-classification etc.) should be used.

The validity and reliability of the used instruments should be differentially described (e.g. according to sex), or rather demonstrated. As far as possible, standardized and validated instruments are to be employed. The choice of the measurement and survey instruments should always be justified.

Basically, all data sources from which information about the study population is gathered should be described (hospital discharge diagnoses, death certificates, proband surveys, workplace reports of occupational medicine sites, etc.).

Recommendation 3.6

A justification for and quantitative estimation of the size of the study is to be provided in the study protocol.

The estimation of the study size (sample size, and in cohort studies also duration of observation) is not only used for quantifying the estimated expenses (costs, working time, etc.) to answer the epidemiological study question. It should, however, also be demonstrated that an appropriate and optimal balance exists between expenses and methodology (in order to the anticipated accuracy of the conclusion from the chosen statistical analytical methods).

The acceptance of this estimation should be justified, for example based on the expected effect size, the prevalence of the exposures, the alpha- and beta-errors etc.

Recommendation 3.7

In addition to the study protocol, all organizational specifications relevant to the planning and implementation of the study, including the survey instruments, should be documented in an operation manual.

In all epidemiological studies an operation manual should be drawn up. In addition to the survey instruments, organizational specifications relevant to the timeline, process, human resources, methods for the contact and recruitment of study participants, and technical procedures (i.e. laboratory tests) of the study should be formulated. Furthermore, the scheduling of interviewer training, the measures of quality assurance and control, as well as the accompanying evaluation should be described.

Recommendation 3.8

Adequate time and human resources are to be provided during the analysis phase of the study.

The appropriate analysis of the data of epidemiological studies is only possible if there is enough time and an adequate number of technically qualified employees available. That way “data graveyards” are avoidable.

Guideline 4 (Biological Sample Banks)

In many epidemiological studies, the creation of a biological sample bank is both necessary and reasonable. The documented consent of all probands is required for this as well as for all current and intended future uses of the collected samples.

In many epidemiological studies it is both necessary and reasonable to create banks of biological samples (e.g. serum, blood, other bodily fluids and tissues). Even when samples are analyzed immediately during the primary implementation of the study, a simultaneous analysis of all samples after the completion of the proband recruitment is usually required in order to assure consistent laboratory procedures as a part of the quality assurance process. As the recruitment of the probands in most epidemiological studies occurs over a long period of time, the collection of biological samples almost always requires the existence of a sample bank at least over the primary study period.

Furthermore, it is reasonable in many cases to store biological samples in the sample bank beyond the primary study period. This allows, among other, the re-analysis and verification of the reproducibility of the results in case of doubts regarding the validity of the primary laboratory analyses. Such long-term storage can also allow for the later implementation of more reliable or more detailed analyses over and above the primary research questions via the use of more elaborate and/or improved laboratory techniques, as well as for the analysis of additional, newly identified markers that can be potential risk factors, effect modifiers or confounders. The requirement to secure long-term storage along with the possibility of later investigations of the biological probes arises particularly in prospective long-term cohort studies, whose analyses occur in many cases decades after the primary collection of the biological samples.

At the same time, it is to be assured that the probands are comprehensively informed about the storage and the current and planned future uses of the biological samples. The methods of the eventual notification of the results of laboratory analyses to the probands as well as the securing of the confidentiality of the results are to be explicitly regulated. This applies particularly to parameters with higher, more individual meaning for disease risk, diagnosis, prophylaxis and therapy, for example specific genetic analyses.

Recommendation 4.1

The institution and individuals who are responsible for the management of the sample bank should be made known to the probands. In doing so, the type and quantity of the collected biological materials should be described, along with the storage method, place, and duration. The probands are also to be made aware of the ownership of the collected samples.

Conflicts of interest, for example in the setting of commercial cooperation, are to be declared. Where complete anonymization is not carried out, the proband consent should always include the option to withdraw one's sample from the sample bank at any time.

Recommendation 4.2

Where preserved samples are to be used for primary, unplanned research questions, the guidelines for GEP are to be applied again.

Before conducting later investigations that were not yet foreseeable when proband consent was first obtained (for example data pooling, consolidation of samples in the scope of international studies), the requirements regarding obtaining a new informed consent, degree of anonymization, and notification of the results to the probands etc. are to be clarified with a new involvement of an appropriate ethics commission. One possible way to assure this would be to irreversibly destroy identifying links between samples and probands, so that no possibility exists any longer for samples to be re-identified.

Guideline 5 (Quality Assurance)

In epidemiological studies, an accompanying quality assurance of all relevant instruments and procedures is to be guaranteed.

An internal quality assurance is an indispensable element of every epidemiological study. This is to be assured by the description of its methods and the designation of the responsible people. The scope of the quality assurance based on its associated costs has to be related to the entire scope and costs of the study. The targets of the quality assurance are set by the chronological, organizational and technical rules of conduct that are described in the study protocol and operations manual.

Recommendation 5.1

In every epidemiological investigation obtaining primary data, it is to be examined if a separate pilot study is required prior to the start of the main study.

Pilot studies are defined as a simulation of the main study or the testing of essential elements of the main study. A pilot study differs from a pilot-phase (run-in-phase). Procedures, including survey methods are tested and used in identical ways as in the planned main study, simply on a smaller scale. A pilot study will be required in every case when, for example, a new survey instrument is to be used, a specific sample has been drawn, unusual contact requirements made, or when any other aspects relevant to the study methodology remain unproven. As required, a validation of instruments can also be carried out in the scope of a pilot phase to a planned study.

The pilot study should be evaluated and documented prior to the beginning of the main study so that required modifications to the study protocol and operations manual of the main study can be implemented.

Recommendation 5.2

If during the conduct of a study the necessity arises to change the pre-determined procedures (to make an amendment), these changes are to be justified, documented, and to be announced in time to all study personnel

Recommendation 5.3

Prior to the beginning of the fieldwork, all persons involved in the data-collection are to be extensively skilled and trained.

The data-collection personnel are to be carefully selected and their social and professional qualifications assured. During the process of the data collection, they should be retrained whenever necessary.

Recommendation 5.4

Rules for and comments on the conduct of the data-collection should be fixed in a written form of a data collection handbook and made available to the data collection personnel. The data collection handbook becomes a component of the operations manual.

Recommendation 5.5

Particularly with large, long-term and multicentre investigations it is to be determined, if a quality assurance of the methods should be carried out by an external person or institution.

An external quality assurance is no substitution for an internal quality assurance, but provides rather a verification of its processes, results, and consequences. In applications for external funding, a budget for an external quality assurance should be considered.

Guideline 6 (Data management and documentation)

A detailed concept is to be developed in advance for the compilation and management of all data collected during the study, including the editing, plausibility-verification, and coding of data, as well as the provision of data for transfer.

Recommendation 6.1

All data collected during the study (documentation, forms/questionnaires, measured values and laboratory values etc.) should be entered promptly in a database to assure its secure compilation and management.

A database structure is a requirement for data-auditing, and data entry must be conducted regularly and promptly in parallel to the fieldwork. That way, qualitative and quantitative shortcomings in the structure or use of the database can be discovered as early as possible during the conduct of the field-phase and corresponding interventions implemented. The original documents should be kept in appropriate form (original, microfilm, electronic scan, or similar) for a minimum of 10 years after the end of the study.

The collection of free-text responses enables the later testing of assigned codes and, in addition makes available the later detailed analyses of the free-text responses themselves.

Recommendation 6.2

A second, or rather verification entry should be carried out for numeric variables.

The verification-entry is conducted particularly to call attention to those variables that offer only limited opportunity for later plausibility-testing (e.g. age, date, calendar year).

Recommendation 6.3

The raw dataset obtained after the test-entry should be kept in unaltered form.

Recommendation 6.4

The coding of data has always to be carried out independent, which means in a manner that is blind to the respective status, or rather the group membership of the proband being referred to.

In many cases a categorization with subsequent coding is required. Every coding of free-text survey responses should be carried out using standard classifications (i.e. ICD-classification, occupational classification, industrial classification). As quality assurance measures, it is advisable that either an independent second coding or rather that, at minimum, a random sample of the data is repeat-coded by a previously uninvolved person. A complete repeat-coding of all raw data is preferable. Where this is not possible, the control of quality of the coding can be carried out with a random sample.

During the coding of data, and as much as possible, an extensive blinding with respect to the case-status and exposure-status is to be guaranteed.

Recommendation 6.5

Plausibility controls occur principally on the basis of the verified raw datasets. Any later required changes to the variable values or the formation of new variables are to be documented in writing in each individual case.

A part of the plausibility-testing can already be carried out during the data entry phase through suitable controls of data-entry masks, whereby particularly feasible ranges of values, as well as compliance with filtering of particular entries are tested, or rather demonstrated. In individual cases original data collection documents or other raw data sources (i.e. recordings of interviews) can be resorted to for the checking of particularly implausible entries.

The documentation of changes of the values of any variable should include at minimum the following specifications:

- Date of the change
- Variable identification
- Old variable value
- New variable value
- Type of mistake/reason for the change
- Person making the change

Recommendation 6.6

The revised dataset after plausibility-testing and data-correction is to be identified and stored as the analysis dataset, independently from the raw data file.

When circumstances require the compilation of updated analysis datasets after data correction or rather plausibility control this has to be clearly documented. Recourse to the raw data must be possible at all times for a later verification of attained results.

Guideline 7 (Analysis)

The analysis of epidemiological studies should be carried out using adequate methods and without unreasonable delays. The data underlying the results are to be kept for a minimum of 10 years in a complete reproducible form.

The analysis of epidemiological studies should occur in agreement with the analysis plan in the study protocol quickly, validly as well as transparently and this should be completely reproducible to a third (uninvolved) party. The requirement that analyses be carried out quickly after the conduct of epidemiological studies arises, in general, from public interest in these results.

Investigations, for example of risks at work or in conjunction with environmental impacts often occur in the health care policy context as a result of requests by public authorities, ministries, etc. These clients have a right to the earliest possible completion of the most important analyses in order for them to comply with their mandate to effectively protect the health of the public.

Recommendation 7.1

The analyses pertaining to the individual research questions should occur on the basis of an analysis plan developed before the commencement of the study.

The analysis plan contains the specifications of the data and variables that are to be considered, furthermore procedures for model-selection and customization and the statistical methods to be used (i.e. exposure to missing data, outliers, etc.).

The main research questions are pre-defined and -formulated study hypotheses that are fixed via their specification in the study design and implementation (also: central or main hypotheses). Their answering eventually justifies and legitimates the conduct of the study, and they should be dealt with primarily. The differentiation of the plans for analyses must be in reasonable relation both to the objective of the study (i.e. explorative or confirmatory) and to prior knowledge.

Recommendation 7.2

Interim analyses should only be carried out when they can be justified.

Epidemiological studies should, with exception of long-term studies, as a rule, only be analyzed after the completion of the recruitment and data-collection. When analytical interim-analyses are planned, these should be described and justified in the study protocol. Unplanned interim analyses can, on the basis of pressing research questions, be meaningful in exceptional cases; however these are then to be explicitly justified ahead of time.

Excluded from this are interim analyses that serve to monitor the study and are therefore a part of the internal quality assurance.

Recommendation 7.3

The analyses of epidemiological study-data should be subjected to verification before publication. The underlying data and programs should subsequently be stored in completely reproducible form.

The co-authors should be given the opportunity to reproduce parts of the analyses themselves via provision of the underlying data. In order to prevent erroneous analyses from entry into a publication, it is advisable that all results are reproduced by a qualified person who previously remained uninvolved in the analyses. Inconsistencies in the results between original analyses and independent verifications require complete clarification; consistency on the other hand between these results attests to the reproducibility of the results based on the described procedures.

Before the verified analyses are publicized as scientific results (i.e. via lecture at national or international conferences, public available reports, original work in scientific journals), it must be ensured that the analyses and their results are reproducible by a third party. Therefore, a secure archiving of all publication-relevant datasets and programs on stable mediums (i.e. diskettes, CDs, tapes) as well as in paper-form is advised.

Furthermore there exists a duty to explicitly designate the analysis datasets with names, generation date, and storage location. An equivalent duty exists to document in a traceable manner all new variables and programs generated in the conduct of the analyses (transformations, operations).

Any analyses should be documented in such a way that exterior persons or institutions can understand and reproduce the conducted analysis and its results.

Guideline 8 (data protection)

In the planning and conduct of epidemiological studies, compliance with applicable data protection regulations are to be respected in order to protect the right to informational self-determination.

All persons involved in a research project who are exposed to personal data have to be informed about the relevant legal requirements. When personal data are used in research, laws are to be adhered to, including those protecting individual rights to informational self-determination, as well as those assuring freedom of scientific research and the acquisition of scientific knowledge which benefits the general public.

The storage, analysis, dissemination and publication of completely or anonymized data are not subject to legal restrictions regarding data protection, except for the obligation to restrict the use of such data to the purpose of scientific research, and, where required, the obligation to delete the underlying data upon the achievement of the research aims.

Guideline 9 (Contractual conditions/frameworks)

The conduct of an epidemiological study presumes certain defined legal and financial conditions. Therefore, legally binding agreements are to be sought between contractor (sponsor) and consignee (researcher), as well as between all partners of research collaborations.

Larger epidemiological studies are nowadays usually external funded, at least to a substantial degree. Contractors are often institutions of research promotion, as well as clients in public and private realm. The charters of some research institutes provide conditions for the conduct of externally funded research. Also, many contractors have qualifications for and restrictions on the allocation of the research-contracts that are to be fulfilled.

Recommendation 9.1

Transparent and realistic agreements should be reached with the contractor. Due to the diversity of conditions for different research contexts, various contract forms are possible.

The following aspects are to be considered:

- *Independence of research.* An ongoing research project can not be terminated by the contractor before completion, unless serious and impartial reasons exist. Responsible for compliance with the guidelines for good epidemiological practice are exclusively the study-leaders, or rather the scientists they have authorized.

- *Supervision and control/monitoring.* Type and scope of external supervision, monitoring, and testing-procedures by the contractors should be specified in the agreement.

- *Long-term access to the data.* Study-leaders and/or contractors must ensure that the underlying dataset to a publication remains available for a minimum of ten years after publication. Furthermore, the duration and extent allowed for the authorized person(s) to conduct further analyses, as well as a specification of who is entitled to this authorization, must be contractually regulated (institution-changeover, legal succession, secondary analyses, etc.).

Recommendation 9.2

The publication of the results of contracted research may not be prevented, obstructed or unreasonably delayed.

Retention periods and guarantees of cooperation required by the contractor must be explicitly itemized in the contracts and the agreements, and in terms of their scope specified and justified. For projects that are supported by public funds or that are to be carried out by scientists from public research institutions, it is to be assured that public discussion and scientific publication of the results can not be refused by the contractor (for

example, through the sponsor, the institution etc.) for more than a reasonable retention period. The writing of publications is the responsibility of the study-leaders. In other cases, the study-leaders are to be granted an unlimited guarantee of cooperation by the sponsor.

Recommendation 9.3

Written agreements should basically be made with all cooperating-partners. This holds independently of whether it is a matter of multiple study centres with equal rights in the context of a multicentre study, or a collaborating partner in the sense of a consignee working on one or multiple work-packages within the framework of a larger study project.

In the agreement, the following points should be considered:

- Structure and task-distribution within the research projects
- Common schedule for the research-protocols and time schedules of all cooperating partners
- Common financial plan and distribution of funds
- Duty to comply with the GEP
- Obligatory measures for quality control and quality assurance
- Used instruments and procedures
- Procedures and requirements for the awarding of sub-contracts to third parties
- External affairs, media, and public relations
- Access and utilization rights of the jointly collected data during data-acquisition and after the completion of the research plans
- Publication agreement
- Long-term storage of the raw data
- Procedures for analyses beyond the primary and secondary hypotheses of the research plans or the subject matter of the contract
- Procedures in case of disagreement or conflict
- Termination terms, rights and procedures, scope and form of the handover of partially completed contractual obligations
- Procedures in case that the study is aborted

Guideline 10 (Interpretation)

The interpretation of the results of an epidemiological study is the duty of the author(s) of the publication. The basis of every interpretation is a critical discussion of methods, data, and results of one's own research in the context of existing evidence. All publications should be subjected to an external review.

Personal integrity and objectivity, methodological rigor, comprehensive information, and adherence to scientific criteria are necessary prerequisites for a proper interpretation of the results of an epidemiological study. The evaluation of results may therefore not be left to the contractor, political decision-makers or the media itself. The interpretation is rather the duty of the responsible scientific leader of a research project and the authors of the respective publications. The reasoning and arguments underlying the interpretation must be transparently and reproducibly presented and discussed in writing by the epidemiological experts.

As a rule in general, research results should be subjected to an independent review by experts (peer review). Unlike to the internal verification of the reproducibility of the analyses, the external review has the task to evaluate the validity of the study design, analysis strategies and interpretations.

Guideline 11 (Communication and Public Health)

Epidemiological studies, which by nature concern the translation of results into real effects on health, should strive to adequately involve the affected population groups, and to report a qualified risk-communication to the interested public.

Recommendation 11.1

The author of a study may decide, based on his or her professional judgment, that the results of an epidemiologic study ought to be communicated to the public. In such a case, the health consequences of the study should be explicitly formulated, for example in the form of a recommendation. Where required to ensure an effective risk-communication, epidemiologists ought to engage in risk communication also with non-epidemiologists.

Epidemiological risk-assessments are often a cause of misinterpretation in the media as well as in the interested public. This has the potential to partly discredit Epidemiology itself as a science. An epidemiologist should generally open oneself to discussion and should make a contribution to the development of competent and objective risk-communication to the population.

Recommendation 11.2

The instruments used in a study should be made available to interested parties.

This is a confidence-building and quality assuring measure, in the sense that it encourages the reproducibility of epidemiological results and safeguarding against the manipulation of results.

Recommendation 11.3

In every study it should be examined if and to what extent the dataset of the investigation should be offered to the scientific community for research collaborations.

Generally, epidemiological studies are carried out with public funds and serve to test defined research questions. There exists far more information in the collected data than those conducting the study can make use of themselves. It should therefore be examined to what extent other scientific institutions can use this data, with appropriate contractual arrangements, if necessary.