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FROM IDEA TO PUBLICATION

THE RESEARCH HANDBOOK

ANNETINE STAFF AND KARIN C. LØDRUP CARLSEN

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Anne Flem Jacobsen and Ernst Omenaas

Oslo University Hospital in collaboration with Haukeland University Hospital

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1 Preface

This is the 10th edition of The Research Handbook, published for the first time in 2003. It was published in paper from the first to sixth editions (2003-2012), and as well as in web format from 2014. From the 7th edition (2017) both the English and Norwegian editions of the book are published online on Oslo University Hospital's (OUS) website. The Research Handbook is also available at Research Support and at NORCRIN (Norwegian Clinical Research Infrastructure Network). The Research Handbook can be downloaded in pdf format.

The Research Handbook is designed to provide guidance to hospital personnel interested in research, health researchers and biomedical researchers. It covers a variety of topics that are essential when translating an idea into a research project with publishable results. Many of the suggestions are based on the authors' own experiences in basic and clinical research in hospitals. The book can be adapted for each clinic, hospital and research institution, and this version provides several local tips from OUS.

Any comments from the reader, including ideas or suggestions for Handbook improvement, would be appreciated. These are invaluable to us in our efforts to improve and update the Handbook on a continuous basis. Comments can be sent to Web Editor Ana Lobato or Editors Annetine Staff or Karin C. Lødrup Carlsen.

We thank those who have contributed ideas for updates. Significant contributors are acknowledged in the Appendix. A special thanks to the Research Directors at OUS for their support. We hope that the Research Handbook will be useful for both experienced and less experienced researchers at any stage of the research process, at Oslo University Hospital, Haukeland University Hospital, Helse-Sør-Øst or at other research institutions in Norway.

Oslo, August 2024

Annetine Staff and Karin C. Lødrup Carlsen

Editors of the Research Handbook

Harald Arnesen, Anne Grete Bechensteen, Anne Flem Jacobsen, Ernst Omenaas

Co-authors of the Research Handbook

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2 Why perform research at Norwegian hospitals?

Medicine and health sciences are developing rapidly, and there are many good reasons to actively pursue research at Norwegian hospitals.

1. To increase our *level of knowledge* and hence our *clinical competency.* We can acquire new knowledge directly through our own research. The stability of our population and general good resources make conducting clinical research in Norway particularly feasible. Comprehensive Norwegian national health registries have a considerable epidemiological potential as a basis for developing diagnostic and therapeutic guidelines. Studies of disease mechanisms and intervention effects facilitate optimal diagnosis and treatment. Basic science medical research studying pathological conditions or diseases, so-called patient-related basic science research, or translational research, is crucial to the process of improving how we practice medicine in an evidence-based manner.

2. Research leads to *improved diagnostics and treatment of patients, and increases the researchers' qualifications for teaching posts at the highest academic level*. Own research provides training in academic thinking. By carrying out our own research, we become more skilled in interpreting international research results and applying them locally. Research requires a high level of documentation and precision. Clinical research influences the precision and quality of clinical work and contributes significantly to quality improvement.

3. Under the Act of Specialist Health Services hospitals are obliged to conduct research.

4. We, as *members of an international research community*, are obliged to contribute to research. Norway, as a healthy and stable economy, has a *moral obligation* to participate in generating new knowledge that can improve health and quality of life, both in Norway and globally.

5. *Research provides professional satisfaction and pleasure.* It gives us the pleasure of nurturing our academic curiosity through systematic research work. Presenting our own

research results at international meetings will also enable us to gain valuable international research contacts.

3 How to develop ideas for a research project

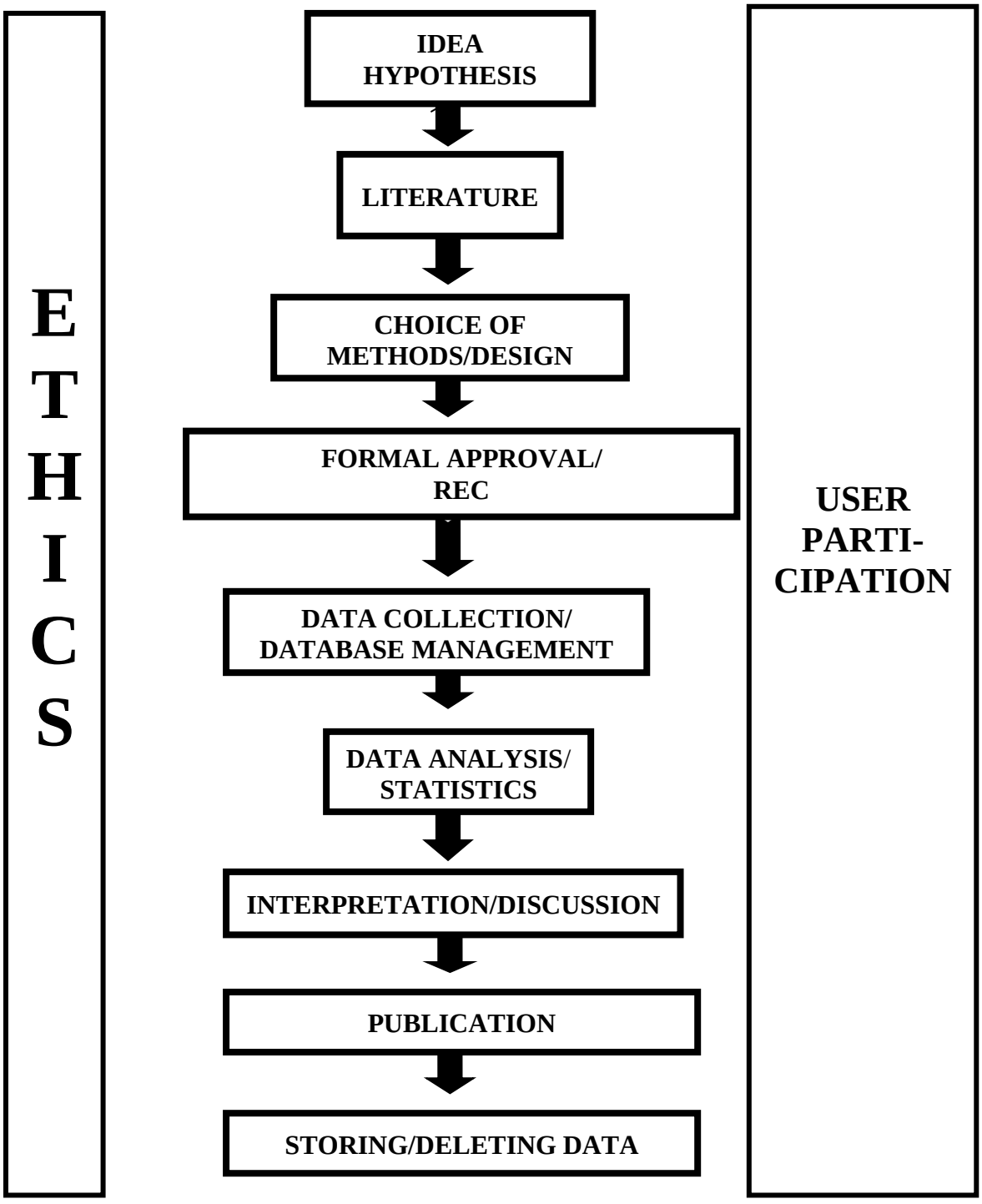
Hospital employees engaged in clinical activities are aware of unsolved problems or suboptimal diagnostic methods in patient management. Are the disease mechanisms sufficiently understood to ensure that medicine is practiced in a firmly evidence-based manner? Are current methods adequate? Do we have new methods that could shed light on problems to which there were previously no solutions? Could there be alternative solutions or could new methods be developed? Can existing patient data be used for more in-depth assessment of the underlying pathophysiology? Changes in disease epidemiology may also necessitate new research. Healthcare professionals with ideas for scientific projects should contact researchers with the necessary relevant academic expertise at the appropriate unit or institution.

The flow chart on the following page is designed as a tool to aid research planning and to clarify the different phases of the research process. The chart can be applied both for qualitative and quantitative research projects.

Idea →Hypothesis

Write down the idea and develop the hypothesis. Putting things in writing clarifies one's ideas and makes it easier to state the objective of the project, as well as any supplementary aims. A clear definition of the question being raised increases the likelihood of valuable scientific results and is vital for further planning and efficient project work.

This first creative phase of a research project may be the most challenging for many researchers. Although developing new ideas is critical to creating new and good research, there is little focus on how biomedical researchers can streamline and optimize this important phase of a research project. This book provides tips on how to become more adept at this process: *Ness, R:* Innovation Generation: How to Produce Creative and Useful Scientific Ideas; Oxford University Press 2012.


ETHICS
IDEA HYPOTHESIS
LITERATURE
CHOICE OF METHODS/DESIGN
FORMAL APPROVAL/ REC
DATA COLLECTION/ DATABASE MANAGEMENT
DATA ANALYSIS/ STATISTICS
INTERPRETATION/DISCUSSION
PUBLICATION
STORING/DELETING DATA
USER PARTI-CIPATION

Literature

A thorough literature search pertaining to the relevant field and research question is essential. This process supplements and develops the original idea and helps determine whether the project may shed light on the research question. Literature searches may be performed using various bibliographical databases, potentially with librarian assistance (see Chapter 5). The Norwegian Institute of Public Health has designed checklists for evaluating research articles, systematic reviews and guidelines.

Choice of methods and design

Determine which type of investigation could help answering the research question. A pilot study or use of retrospective data may be required in order to have sufficient basis for planning prospective studies. Randomized controlled trials are the "gold standard" for clinical studies. Studies may also employ a cohort or case control design, or be purely observational.

It is particularly important to calculate the number of patients/ subjects/ experimental animals/ cell experiments that must be included in order to provide a reliable answer, i.e.: perform a statistical power/sample size analysis. A study that does not have the statistical power to answer the question at hand should not be started, unless it is a pilot study. A new literature search may be useful at this stage. Contact experts within the fields of epidemiology or biostatistics at the planning stage of the study (see Chapter 8).

User participation in research projects

User participation in research is becoming increasingly more important and is often required at an international, national, regional, and hospital level (e.g. User participation in research at OUS). User participation (Brukerutvalg) is integrated in all the hospital's tasks, also in research and development. It might be useful for many research projects to get advice from relevant user groups, both in the planning and follow-up of research projects. For instance, user groups could review the information to research participants/patients before starting a research project.

For applications for research funding in Norway, the researchers must explain how user participation and organizations are involved in the research process and application. The flow chart illustrates that user involvement is important in all phases of the research project.

Formal approval

All research projects under the Health Research Act, involving human subjects, human biological material and health data are subject to review and approval. This includes approval by REK (the Regional Committee for Medical and Health Research Ethics, "Regional komité for medisinsk og helsefaglig forskningsetikk", the Norwegian Medical Products Agency ("Direktoratet for medisinske produkter") and the Norwegian Directorate of Health ("Helsedirektoratet"), as well as local approvals at the home institution, notification to the local Data Protection Officer, and in the case of multi-center studies, the partner institutions.

For studies involving medicinal products, approvals are applied for by using the new platform CTIS - EMA (euclinicaltrials.eu), which replaces previous separate applications to the Norwegian Medical Products and REK. Till 30 January 2025, trials conducted in the EU are regulated either under directive 2001/20/EC (old legislation) or under a new regulatory framework, the EU Clinical Trials Regulation no. 536/2014. From the 31st of January 2025, all clinical trials will have to follow the Regulation no. 536/2014.

The following must be clarified well in advance of project commencement (for details, see Chapter 6):

Local approval of the project (usually at the Departmental/Clinical or Divisional level): We strongly recommend that institutional approvals are obtained prior to submitting an application to the relevant authority (REK through REK portal/REK KULMU, and Norwegian Medical Products Agency through EU – CTIS portal). Normally, the Head of the Department, (or the equivalent) where the project is academically grounded, will be the person who evaluates and approves the project professionally and resource-wise on behalf of the institution. As part of the local approval process, it is also recommended that relevant research support staff at your institution is contacted for further clarification of regulatory issues. A Data Protection Officer ("personvernombud") or other similar research support entities are currently established at most institutions where research on human beings is

performed, which may include biological material or health information. For University employees, local guidelines for formal approval prior to project start may apply, such as described in the University of Oslo guidelines (The Quality System).

External approval that must be obtained for your project (REK and other agencies):
The need for external review and approval will largely depend on the purpose of the project, what (and whom) is being studied and if the study includes the use of drugs or medical devices, gene therapy and/or genetic testing. Remember that if it is mandatory to submit your type of study to REK (see Chapter 6), the project should not start before REK has reviewed and finally approved it. For projects that do not require an approval from REK, but that include the use of personal or health data, it is required to notify the Data Protection Officer.

Research Director ("Forskningsansvarlig"): Familiarize yourself with how this role is *defined in practice* at your institution.

Research Protocols: Be thorough when you describe the project's purpose in your project protocols and consent forms. Any approval / license you obtain is limited to the research purpose/aim that you provide in the application / consent form.

Participant consent: informed consent is mandated for almost all clinical trials involving human subjects, although exceptions apply for emergency research and low-risk trials. Participant information and consent forms should be prepared and include all required information (including the purpose of the study) and the rights of the study participants (more on templates and consent requirements in Chapter 6).

Registration of the project in a public database (such as Clinical Trials in the European Union - EMA (euclinicaltrials.eu), clinicaltrials.gov and helsenorge.no) may be required prior to the study (see Chapter 9).

Collection of Data and Database Management

Ensure that data collection is as thorough and rational as possible. A logical and tidy database is essential.

For research projects that involve the recruitment of test subjects and involve many collaborators / institutions, a regular update of the study's development could be especially important to motivate everyone to collect sufficient material or include sufficient numbers of study subjects. A positive project leader will automatically stimulate the research group and thus increase the likelihood of successful completion of the project.

Data sources: In medical research, patient information (health information), patient test results and health services data (for example data on patient progression through the healthcare system) are often essential data sources. Patient information can be obtained through the medical record systems, various quality control registries, including local, regional, and national health registries, or by using questionnaires. Patient biological samples can, in some circumstances, be retrieved from existing diagnostic biobanks or can be collected and stored in a research biobank for a specific project.

Database construction can be easy in smaller projects, but may include thousands of variables and a large number of databases in large, complex, long-term studies. This can present major challenges to the development and maintenance of databases, particularly as projects grow and an increasing number of researchers gain access to different parts of the data. Most hospitals and research institutions have their own research computer servers. It should be decided early in the process which persons will be given access to the different levels of the research data. Generally, a *"master file*" containing all the collected raw data, is established. Master files should not be changed after proofing and file cleansing is performed against the source data (the source data may for example be made up of the files of individual research subjects, often called a Case Report Form, CRF). Any subsequent changes should be documented (in a separate file or other document), where corrected variables / data in the database are used for subsequent analyzes.

It is recommended to make a *variable list with correlating codes* at the start of the project. This simplifies the job later when you or others need to find which variables are related to each question in the research folder (Case Report Form: CRF). Since projects may contain many variables (both collected and constructed variables) and different (master) databases, it may be an advantage to have smaller and more focused datasets for each individual research question. Pay attention to use the correct version of the variables, especially for the constructed variables. Database construction must provide a basis for subsequent quality control of data and final statistical analysis. It is strongly recommended to seek advice from experienced statisticians / researchers both before data collection is begun, and preferably during the construction of the complete dataset. In addition, transparency in the construction of datasets reduces the risk of fraud and misconduct in research, see Chapter 16. Be aware of the possibility of incompatibility between database and statistics programs. Programs that can handle the transition between databases and statistics programs are available, see Chapter 8.

At some health trusts, like OUS, registry support and help desk services for data handling in clinical studies is offered. At OUS, the Research Support Services offers registry support, including technical advice and guidance in planning, for the start and maintenance phase, and with extracting data from the registries. At the Clinical Trials Unit (CTU), similar services for clinical studies are offered, including guidance in creation of databases and randomization strategies, control of research data and processing of necessary documentation. Advising on the above topics is free, and there is a charge for this service if one or more operational tasks is to be performed by the research support unit.

Also, University employees may benefit from locally provided IT systems and support for clinical study handling, such as TSD ("Tjeneste for sikker datalagring") at University of Oslo/USIT.

Data analysis and statistics

A wide variety of statistics programs are available. Each hospital/research institution may have its own preferences. Contact a statistician in advance, for choice of method and design (see Chapter 8).

Interpretation and discussion

Interpret the results carefully. Critically evaluate your own results, and compare with those reported by others. Discuss possible reasons for discrepancies with previously reported findings, including methodological issues (see Chapter 8).

Publication

See Chapter 9.

Storing/deleting data

Already in the planning phase of the study, it is important to clarify how research data is stored. This applies not only during data collection, processing, and any associated analyses, but also how and when data is deleted or anonymized after completion of studies. For OUS employees, see Storing, archiving and deleting health and personal information. Such information is included in applications to REK and the Data Protection Officer ("personvernombudet"), and must be adapted to the study's character and external requirements. For drug trials under the directive 2001/20/EC all documentation must be kept for at least 15 after project completion, whereas for those following Regulation 536/2014, 25 years apply. For medical devices, a minimum of 10 years is required, and 15 years for implantable devices after the last device is placed in the market. The formal requirements for storage of de-identified study data (and link key) are otherwise variable. A general rule is that study's essential documentation and research data (in the form corresponding to REK / PVO approvals and study participant consents) should be able to be verified in the event an institution needs access or an inspection occurs (for example, after PhD disputation, even where other formal requirements for study data storage are missing). Essential documents permit the evaluation of the conduct of a trial and the quality of the data produced.

Ethics

See Chapter 16 for relevant links to the Research Ethics Library. Ethical questions and issues are important in all stages of a research project, from the planning stage to the end of the project (e.g. how to publish the research data).

First and foremost, one must attend to the individual test subject's interests and integrity. This applies to both the patient-related research, but also when the project exclusively involves the use of human biological material and/or health data. Potential scientific results and possible public benefit that can be achieved must always be weighed against the interests of the research participants. For example, research participants should never be given poorer examination or treatment than the presumed best. All experimental diagnostics and treatment must therefore be assumed to be beneficial and have a solid rationale supporting the assumption.

Research-related or commercial interests must not unduly influence data collection, database construction, or analysis. As a researcher, you have the responsibility to ensure that your research is based on objectivity and impartiality, regardless of who initiated the project. In addition, you should not collect more data/samples than what is necessary to carry out the study.

It may be unethical to start a (quantitative) research study that does not have adequate statistical power to answer the study questions. In many studies, the databases should also undergo an independent audit prior to analysis. Research support Departments at large institutions can advise on how to carry this out. In addition, it is often necessary to have objective documentation of the study endpoints. Special guidelines apply to such independent evaluation of clinical drug trials. In the interpretation and discussion of data, all data must be made available for review, especially if there are adverse or unintended effects. Be open about and discuss the strengths and weaknesses of your study.

The research must be of academically high quality. It is unethical to use resources and research participants for studies that do not reach a sufficient level of quality. It is also unethical to fail to communicate research results, including negative results, either as reports or scientific publications. Both the researcher and the research institution are responsible for making sure that research projects are carried out with good research ethics.

Literature:

Tone Rustøen og Anners Lerdal (red): Klinisk Forskning innen helsefag. Hvordan utvikle god forskning - sentrale elementer. Fagbokforlaget 2021.

Laake P, Benestad HB, and Reino Olsen B (editors.): Research in Medical and Biological Sciences. From Planning and Preparation to Grant Application and Publication. Elsevier Academic Press 2015.

Ness, R: Innovation Generation: How to Produce Creative and Useful Scientific Ideas. Oxford University Press 2012.

Laake P, Reino Olsen B og Benestad HB (red.): Forskning i medisin og biofag. Gyldendal Akademisk 2008.

Friis S og Vaglum P: Fra idé til prosjekt. En innføring i klinisk forskning. Tano Aschehoug 1999.

4 Project descriptions and protocols

According to the Health Research Act, research involving human subjects, human biological material and health data must be described in a research protocol. It is the research protocol, along with the application to the Regional Committee for Medical Research Ethics (REK, see Chapter 6) that forms the basis for the committee's research ethics review and approval.

Project descriptions may also have other purposes, for example:

- To inform and get approval for the project at your institution.
- To apply for funding.
- As a working tool in relation to planning and implementation.
- When applying to other agencies, see Chapter 6

What a protocol should contain

In the Regulation appended to the Act on the organization of medical and health research it is specified what a research protocol (to be written in Norwegian or English) should contain. This includes:

- The project leader's name.
- A scientifically designed project plan (documenting the need for the research, project aims, materials and methods, likelihood of the study design to answer the research question, and the time frame).
- Sources of health data and a description of the processing of these data (including whether this is to occur in other countries/at other institutions).
- Sources of biological material (including whether these are to be sent abroad).
- Research-related ethical challenges.
- Assessment of risks and benefits for the research participants.
- Financing, conflicts of interest, dependency, and economy.
- A plan for the publication of the results etc.

Clinical drug trials must be conducted according to Good Clinical Practice (GCP) and have special requirements for the protocol and project implementation. A template protocol for clinical drug trials is available at NorCRIN (a Norwegian national research infrastructure body). It may be sensible to follow the GCP requirements in other types of research studies too. GCP requires that the protocol and other relevant study documents be dated, paginated, and signed if relevant (or the leader/principal investigator in exempt cases). All study documents must have a version number, in which updates should be made clear. Formal approvals of clinical research studies apply to the dated version submitted for review.

For projects that are neither subject to disclosure to REK nor a clinical drug trial, there are no corresponding formal requirements for what a research protocol should contain. It is still recommended that you follow the same requirements that REK uses since these requirements are based on well-established standards for the preparation of scientific protocols. For clinical investigations of medical devices, the setup of the study protocol (Clinical Investigational Plan, CIP) for human research shall follow ISO14155, Annex A.

The protocol should be a detailed project work description that forms the basis for applications to all the relevant bodies for approval, a tool to be used whilst implementing the study, and the document against which results are evaluated (in a publication or report). The more thorough the protocol is, the easier it is to write scientific articles based on the study. The table on the next page shows the contents of a typical research protocol, as well as additional factors which may be relevant to some research projects. Supervisors should be able to give advice on any other specific items of relevance to the proposed study. Qualitative research may emphasize other aspects than quantitative projects in their protocols. Among other things, power calculations may not be applicable.

All studies	Useful in many studies	Relevant to some studies
Date, version, pagination		
Title/working title		
Summary	Information to participants	
Project participants Project manager, Project staff, (Supervisor), Collaborators	Delegating authority (especially in GCP–studies)	Steering committee/panel Reference committee
Introduction What is known today and what do we need more knowledge about?		Publication committee
Hypothesis aim/objective "Aim" or "objective", preferably also hypotheses. Aim of Study Material and methods	Endpoints (primary/secondary)	Safety committee (some studies)
Participants Inclusion and exclusion criteria Recruitment, information, data protection	Procedures for handling of protocol deviations (should participants be included in any analysis, which?) "Intention to treat"	Flow chart Randomization procedures
Methods Which methods Administration of health data and biological samples	Securing of methods Design: type and justification registration form (Case Report Form (CRF)) Data Handling Procedures Procedure for collection / storage	Safety/ what if unexpected side effects? "Patient compliance"
Statistics Samples size and reason for this	Calculation of sample size / power analysis (relative to the main endpoint) Planned statistical methods	
Implementation Plan Publication Schedule Publishing of results, including the plan for publications / reports	Schedule ("milestones") Data management plan Tentative author order	Handling of resources Handling of deviations from the planned progress
Research ethics considerations Risk-benefit for participants Conflicts of interest/dependency	Plan for application to relevant bodies (see Chapter 6) Research participant information Informed consent	User participation (relevant and often mandatory to address in health-related studies)
Storage, anonymization, data handling, during and after study completion		
Relevant literature		
Budget and Funding	Insurance Financing/Sponsors	Priority of analyses
	Signature of project manager and collaborators	

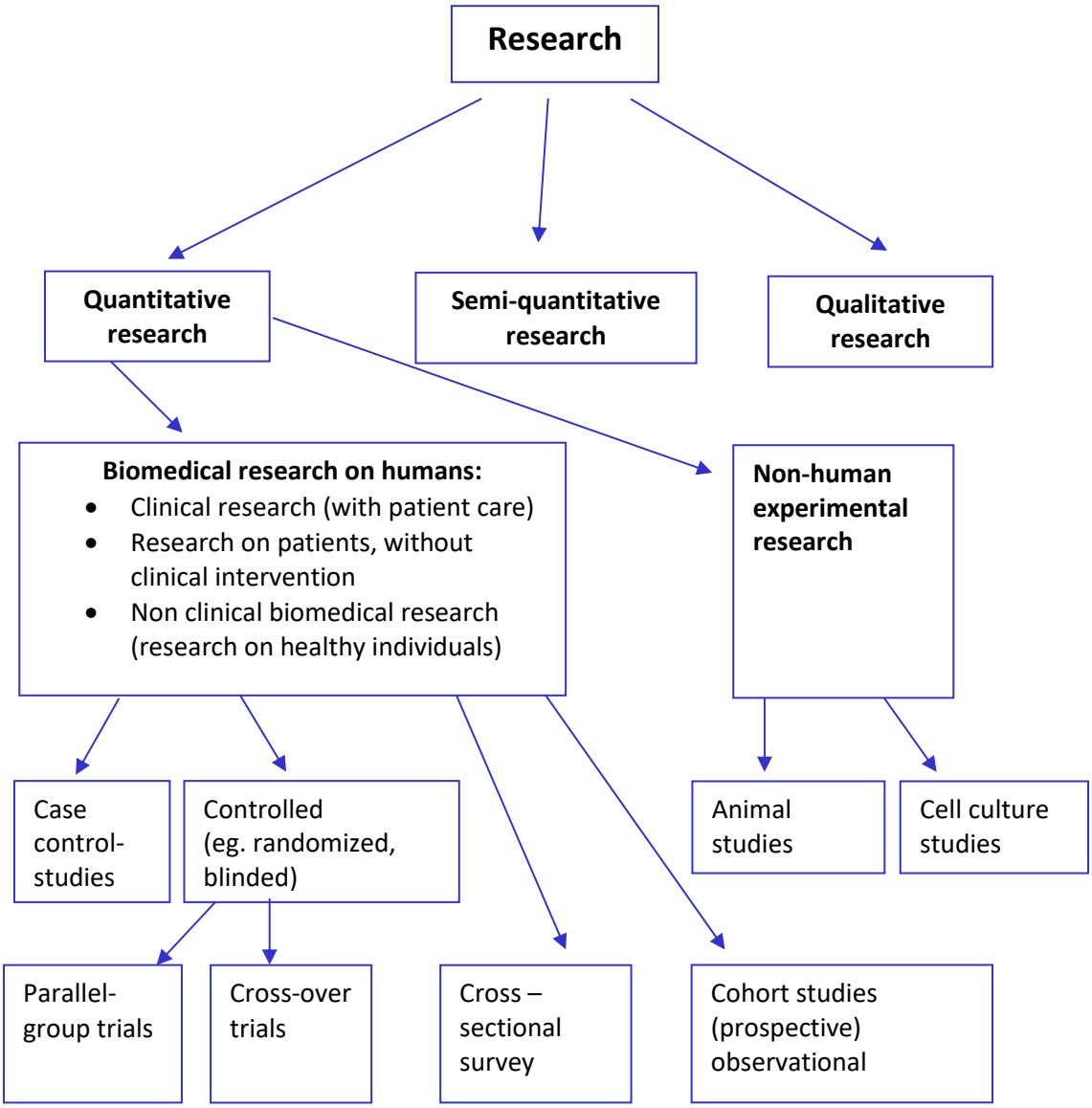
Changes to the research protocol

If (substantial) changes are to be made to the study after formal approval is given, the changes must be approved by the REK and any other relevant bodies before they can be implemented. Remember that the research institutions' own requirements and needs for updating research must be followed. It is important that the research protocol is updated in parallel with the research project changes. This is usually done in the form of an "amendment" ("addition") to the protocol in addition to the notifications to the relevant bodies of these changes.

Useful link for University of Oslo employees: The Quality System.

5 Research methodology and literature search

It is important that research methods are reliable and valid. A reliable method is one, which can be standardized, and is specific, sensitive, reproducible and accurate. There are a number of approaches to the design of studies and research projects, all of which may be equally valid. Below is an overview of the most common research methods used in research projects within the fields of health science and medicine.



Quantitative versus qualitative research

Medical research has traditionally been of a quantitative nature. This type of research measures amounts, degrees and frequencies and provides answers to questions such as: *How much? How often?* The emphasis is on "hard data", distance and objectivity. This approach is particularly suited to testing hypotheses. However, it is less appropriate for the study of "soft data" such as thoughts, experiences, attitudes and processes, for which qualitative methods are more appropriate. While quantitative methods analyze numbers and provide results in the form of tables and diagrams, qualitative methods deal with text (transcribed from interviews) and lead to results in the form of categorization of content and quotations. While quantitative research often tests hypotheses, qualitative research is often descriptive and tends to generate hypotheses. Although qualitative research is often descriptive and quantitative research analytical, this distinction is far from absolute. Qualitative research has gradually developed into a significant and distinct scientific area (Malterud 2017 and Kvale 2015). It is the nature of the research questions that should determine the appropriate scientific methods to be used (Lorensen 2006), and many research projects may benefit from both qualitative and quantitative methodologies.

Tools have been developed to measure patient-reported endpoints (PROM) for numerical assessment of "soft" data (see Chapter 8). Graduated scales based on interviews or self-reporting allow scoring of items such as symptom levels, satisfaction with treatment or quality of life. Parametric statistics may be used since, in practice, such scales function as interval scales (Campbell & Machin 2003). Validated scales such as these, allow researchers to use powerful statistical methods for the analysis of major clinical problems relating to patients'/informants' symptoms, experiences and considerations.

Patient-reported outcome measures (PROM) provides a patient's health information directly from the patient. PROM includes e.g. health-related quality of life (HRQL) and symptom measurements. Valid results in a study depend on choosing the right outcome, and thoroughly assessing whether the outcome measure is suitable to assess what is intended in the chosen population. The regional research support network PROMiNET assists researchers by facilitating access to updated knowledge, valid research methods, and outcome measures.

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Qualitative Health Research, an international, interdisciplinary journal for qualitative research in health-care settings.

Literature search

Bibliographical databases contain references to journal articles (often with abstracts), books and other publications. Some databases and journals are available free of charge, while others require a subscription. As a rule, institutional libraries subscribe to the most important databases, as well as to the key journals within most of the medical specialties. Please contact your library to get an overview of what you have access to, as well as what can be obtained beyond that which is included in print or electronic collections.

In Norway, many databases and journals are freely available through The Norwegian Electronic Health Library - a national online resource in medicine and health sciences. The National Health Library website also contains other useful information, including a separate page with links to helpful resources for researchers.

In order to perform a comprehensive literature search, multiple databases are usually needed because they vary in scope and organization. Ample knowledge of the various databases is necessary in order to ensure the quality of the literature search. Most libraries offer guidance on literature searches, and many also organize courses on the use of the different databases. One of the most widely used bibliographic databases in medicine and the health sciences is Medline. PubMed is the free version of Medline. There are several other relevant databases, such as EMBASE, which are important supplements to PubMed/Medline. A direct link to the full text articles may be available through local library websites, provided they have a subscription for the relevant Journal.

A personal library of articles of particular interest for your personal use can be created in various ways. Today most researchers prefer electronic reference management programs. The most common reference manager today is EndNote, which is available for students and employees at many research institutions. Zotero is another reference manager provided free of charge by Firefox. Mendeley is a reference manager which is also available from several research institutions. The programs are used to create a personal reference archive either by importing references from bibliographic databases such as PubMed, or by manual entry. The reference managers can be connected to word processors (typically Microsoft's Word) and used to create citations and reference lists in articles. Hundreds of output styles are included, and by a few keystrokes the formatted reference list can be altered in compliance with the requirements of a specific journal. Please contact your medical library for information regarding which programs your research institution offers and opportunities for courses and guidance.

6 Research projects: The formalities

This chapter will explain the formalities (approvals, etc.) that should be in place before a research project involving human beings, human biological material and health data can begin. Bear in mind that the Project Manager ("prosjektleder") is responsible for obtaining the necessary approvals for the research project.

Like hospital staff, university employees have local guidelines for formal approval before project start, as described in UiO's guidelines (The Quality System).

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6.1 Legislation and background

The Health Research Act

The Health Research Act from 2009 determines that REK (Regional Committee for Medical Research Ethics) is the only external body that preapproves medical and health research projects (with the exception of The Norwegian Medical Products Agency and The Norwegian Directorate of Health, see below). The Project Manager ("prosjektleder") usually has to deal with only one external authority (REK), in addition to the research institution, for formalization and anchoring of a research project.

The role of *The Data Protection Officer ("personvernombudet")* in medical and health research is largely maintained as part of the research institution's internal review and systems responsibilities. The Data Protection Officer for Research is a significant resource for obtaining advice and quality assurance in connection with processing and storage of health data in research. The Data Protection Officer is either internal to the institution or external.

Obtaining assistance and advice from a Data Protection Officer for Research or equivalent support (e.g. from a competence center), is an important and central part of the research administrator's responsibility to 1) perform review within the organization, and 2) ensure privacy and information security in all research involving the use of health data and other sensitive information. The Norwegian Data Protection Authority is still regulator for all processing of health data, also in research (§ 47 of the Health Research Act).

The Regional Committees for Medical and Health Research Ethics (REK) consists of seven committees: REK South East (4 committees: A, B, C and D), REK West, REK Central, and REK North. The Project Manager's ("prosjektleder") place of work usually determines which REK will receive the application, but another committee may also process the application. For ordinary applications, you may expect an answer from REK within three weeks after the upcoming meeting in the committee that receives your application. REK KULMU (Norwegian Ethics Committees for Clinical Trials on Medicinal Products and Medical Devices) was established in 2020 to aid in the implementation of the new EU regulations: Clinical Trials Regulation 536/2014 (CTR), Medical Device Regulation 2017/745 (MDR), and In Vitro

Diagnostic Medical Device Regulation 2017/746 (IVDR). REK KULMU's work is dedicated to projects regarding research ethics assessments of clinical trial applications on medicinal products and medical devices.

The committee members of REK are appointed for a period of 4 years by the Ministry of Education and Research ("Kunnskapsdepartementet") on the basis of nominations submitted by the following specialties: medicine (Chair and Deputy Chair), psychology, nursing, law and ethics. A lay representative, a representative for patient organizations, and a representative for the hospital owner or public health authority are also appointed. The activities undertaken by REK follow the provisions of the Research Ethics Act and Health Research Act. In addition, the work of the Ethics Committees is based on a number of conventions, as well as commonly accepted ethical principles. Authors, who wish to refer to REK's study approval, when writing articles in English, may use the term "Regional Committee for Medical and Health Research Ethics" (the corresponding American institution is the Institutional Review Board, IRB).

The National Committee for Medical and Health Research Ethics ("Den nasjonale forskningsetiske komité for medisin og helsefag", NEM) is an advisory body that coordinates the work of the regional committees (the REKs). Among other things, NEM addresses complaints under the Health Research Act on decisions in REK, with a unique responsibility of promoting equal treatment. At NEMs websites you can also find The Research Ethics Library, including information and articles on ethics, integrity and collegiality, co-authorship, privacy and responsibility of the individual, research on specific groups, research on human biological material, the relationship between society and research, science and the environment, as well as an overview of ethical research entities, laws and policies.

The Helsinki Declaration is of fundamental importance to ethical research work within medical and health-related research. The Declaration was drawn up under the direction of and approval by the World Health Organization in 1964. The Declaration has been revised several times, most recently in 2013. In 2008 it was revised with special mention of new guidelines for research involving children and the use of placebo in research. The most recent editions of the declaration emphasize transparency of research funding. The need for

transparency surrounding funding is important, because studies have shown that the research results and publication willingness may differ depending on who is paying for the research (Laine et al 2007). The Declaration also emphasizes the obligation researchers have to publish their own research results irrespective of positive, neutral or negative findings. The Declaration of Helsinki is under revision in 2024, a new update will soon be published.

The European Data Protection Regulation (GDPR)

The EU Privacy Regulation (GDPR) is a regulation that aims to strengthen and harmonize privacy in the processing of personal data in the European Union (EU). The regulation applies if the data controller or data processor (a business) or the registered (individual) is in the EU (or EEA). The regulation also deals to some extent with processing that takes place outside the EU or the transfer of personal data out of the EU/EEA. In Norway, the regulation entered into force on July 20th 2018.

If the controller is a public authority (with certain exceptions for the courts, etc.) or an undertaking with more than 250 employees, it is mandatory to appoint a privacy officer. The same applies to data processors where the core task is the processing of personal data. This means that having a Data Protection Officer (Personvernombud) at research institutions that process personal data is now again required by law. GDPR requires that it must be considered whether a Data Protection Impact Assessment (DPIA) should be made. OUS has a guide, written in accordance with Regulation (EU) No. 2016/679 (General Data Protection Regulation) Art. 35 on the need to carry out a privacy impact assessment.

You can read more about Research Ethics on chapter 16.

6.2 Projects that must be submitted to REK

The Health Research Act applies to "medical and health research on humans, human biological material or health information". This also includes pilot studies and experimental treatment.

The requirement to apply to REK is limited to projects *with the objective of acquiring new knowledge on health and illness*; in other words, projects must have an explicit medical or health objective. The decisive factor is thus not whether the project deals with humans, human biological material, whether there is a considerable amount of information, or very sensitive information, or whether the project is to be carried out within the healthcare service already in place or by particular healthcare personnel.
For projects that fall outside REK's mandate, it is usually required that the project is formalized internally by the data controller and reported to the Data Protection Officer (Personvernombud) who determines the grounds for processing according to the GDPR (see section 6.3). The transition between projects that are required to be submitted to REK and studies that require other formalization to be carried out is discussed in more detail in section 6.4.
For clinical drug trials, the new Clinical Trial Regulation 536/2014 applies - These must be approved via the Clinical Trials Information System, CTIS, see Chapter 6.8.

Use of health data in research

Prior approval from REK is both necessary and it provides a sufficient basis for the use and processing of health data in research. But REK's approval is not synonymous with having the right to conduct the research project, as it is also necessary to obtain approval from (and in collaboration with) the relevant institution(s) from where the data are to be obtained, before the project can begin. This is discussed later in this chapter and in Chapter 7.

Requirements for REK approval also include research on pseudonymous data, i.e. where it is possible to link the information back to individuals by using a code key, even if the researcher does not have access to the code key. From 2023, the application procedures for access to health information have been changed. The Directorate of e-health through the Health Data Service is given the authority to make decisions about making health information available and dispensation from the duty of confidentiality. REK has made an overview in Norwegian about which body that should receive the application and make the decision (Health Data Service, "Helsedirektoratet" or REK).

In The Health Research Act there is a special provision for research studies that only use data from one of the Norwegian national health registries listed in the Health Registry Act §11. Such registries include The Medical Birth Registry, Cancer Registry of Norway, Norwegian Prescription Database, the Cause of Death Registry, SYSVAK (national immunization registry) and NPR (Norwegian Patient Registry). Evaluation and approval from Directorate of e-health is not required if the data are equivalent to anonymous before being handed over to the researcher. This means that approval is not required if personal identifiers have been removed such that the data are only indirectly linked to personal identifiers when handed over to the researcher (in other words the data has been anonymized). This exemption also pertains to research projects that link data between these central health registries. However, other medical and health-related research projects that involve linking to registries other than the central registry (e.g. health records, medical records and other public registries), must be evaluated and preapproved by REK. For example, the Project Manager ("prosjektleder") must apply to REK if data from the Cancer Registry is planned to be linked to information obtained from medical records of a health institution.

Research projects using genuinely anonymous information and anonymous human biological material are not required to notify REK either, assuming the data is anonymized before it is disclosed to the researcher. If the health data is first collected, and then anonymized, approval from REK is required.

Bear in mind that the Health Research Act and the requirements for prior approval from REK exclusively cover the use of health information for a specific research protocol. If you are planning the establishment of health records for future research (quality registers/research registers), the register is formalized via notification to the Data Protection Officer. The Data Protection Officer will be able to guide regarding requirements for establishing different types of registers.

Research Biobank and use of human biological material for research

The definition of a research biobank is "a collection of human biological material used in a research project or which is to be used for research" (the Health Research Act). All projects involving the use of biological material must be approved by the REK. Unlike anonymous

information, the disclosure obligation also applies to the use of anonymous biological material from a biobank. However, test results and information that can be derived from biological material are not part of the biobank. These should be treated as health data (Chapter 7 of the Health Research Act).

The Health Research Act allows, however, for the establishment of a general research biobank that is not linked to a specific research project (§ 25). This is classified as a prospective research biobank where the recruitment happens prior to commencement of the research project. Such samples may be used in multiple future research projects. In such cases, the application to REK for establishing a general research biobank is to be submitted through REK's web portal. The application for the establishment of a general research biobank will often be based on a "broad consent" from the study participant (see the Health Research Act, § 14). Every research project that uses material from such a biobank must apply for REK approval and provide the informed consent form.

The Health Research Act (§ 28) allows the use of biological material obtained in a healthcare setting in research, including research on biological material from diagnostic or treatment biobanks. REK may approve research projects for which *the patient's consent is not mandatory* in this setting, if "such research is of substantial interest to society and the participants' welfare and integrity are assured". One of the conditions for such REK approval is that "patients have to be informed in advance that human biological material gathered for clinical purposes can in certain cases also be used for research, and they must be given the opportunity to reserve the use of their own human biological material in research studies" (§ 28).

A registry has been established for persons who wish to withhold their biological material from being used for research ("Reservasjonsregisteret", i.e The Reservation Registry). The Project Manager ("prosjektleder") must ensure that potential project participants are not on this list. The Reservation Registry is administered by the Norwegian Institute of Public Health ('Folkehelseinstituttet'), and relevant information for researchers is presented on their website. These websites also include information for patients on how to register to withhold their own biological material from future use in research. However, this reservation is not

absolute. The Project Manager can ask for and obtain consent from a potential participant for a specific project even if the person is listed in the reservation registry. The Health Research Act (§ 8) states, "commercial exploitation of research participants, human biological material, or health information as such is prohibited".

Dispatch of human research material to foreign countries

As a rule, a research biobank or parts of a research biobank can only be shared with other researchers and projects and sent abroad if approved by REK, and if the donor of the material (the study participant) consents to it (the Health Research Act, § 29). If human biological material from a research biobank or treatment biobank is to be used for research by other external researchers (§ 31 of the Health Research Act and § 15 of the Treatment Biobank Act, Behandlingsbiobankloven), those responsible for the Biobank (the Research Director/"forskningsansvarlig"/ the person in charge) have to ensure that the necessary approvals have been attained before sending the material. This is normally based on REK approval granted to the external Project Manager. Such sharing of biobank material is followed by a mutually signed material transfer agreement and is anchored internally at the research institution.

New and altered use of existing research biobanks

In order to make new and altered use of an existing research biobank, a new REK evaluation and approval is needed. This can be achieved either as part of a new application to REK for a project (a specific research biobank), or as a separate application for the establishment of a general research biobank unrelated to a specific project.

If significant changes are to be made to the use of human biological material in a specific research project or significant changes to an already established general research biobank, the amendment should be approved by the REK in a change notification form.

How to apply to REK

Applications to the REK should be submitted electronically. Deadlines and meeting dates are listed on the web portal. The document "Regulations on the organization of medical and

health research" contains comprehensive information about the roles and responsibilities when applying to REK.

The application form to REK must include information about the Research Director ("forskningsansvarlig"), "Project Manager ("prosjektleder") (including her/his qualifications), the aim and rationale of the project, materials, methods, assessment of the probability that the study design will yield answers to the research questions, timeframe, selection criteria for research participants, recruitment of participants, information/personal data security for participants, obtaining consent, ethical research challenges, research subject safety, interests, sources of finance, conflicts of interest, and publication of results. As a rule, the application for approval should be written in Norwegian. A research protocol should be attached in either English or Norwegian (more about research protocols in Chapter 4).

REK decisions

REK approves or does not approve research projects and can stipulate conditions for approval. REK must provide grounds for their decisions. REK may use external experts in difficult cases and is free to determine the emphasis they place on any such expert advice. A list of approved REK projects is presented in a new public research information and science archive platform (CRIS/NVA) from late 2024. Previously, projects could be accessed via CRISTIN (Current Research Information System In Norway). However, CRISTIN will continue to be accessible (reading-only) for a period.

Most projects are approved after some or several changes. Often the written information for study participants is incomplete and requires improvement. A lot of time is saved by thorough preparation of the application. The Research Handbook's authors therefore strongly recommend all researchers who are not familiar with the REK applications to obtain advice and guidance from research staff and experienced researchers/advisors before applying.

In their evaluation, REK carefully considers any potential benefits and risks/inconvenience/discomfort to the study participants or the community at large. REK also considers whether the Project Manager and collaborators have the expertise needed and

whether the proposed selection of participants is appropriate with respect to the research question. Other central components of REK's evaluation are the manner in which consent is obtained, and the question of whether exemption from obtaining consent may be acceptable for a specific project.

Grounds for appeal to NEM

The Project Manager may appeal final decisions made by REK to NEM (National Committee for Medical and Health Research). This applies both to a rejection of the application ("non-approval") and to any specific conditions put forth by REK in order to grant approval. If REK rejects the application because they do not consider the project to be medical or healthcare-related, the Project Manager may also appeal this to NEM. The Project Manager should send any complaints about REKs verdict to REK. REK will then assess the basis for the appeal and may either change its original decision or forward the appeal and the case to NEM.

6.3 Quality control studies and other types of research projects

Quality control studies and other research projects should apply to the REK if privacy and collected health data will be used to obtain new general knowledge about disease and health. Whether the study is intended for publication does not decide if preapproval by REK is required. Projects that involve the use of personal and health data, but do not require REK approval, must notify the Data Protection Officer. Chapter 6.4 discusses the grey zone between quality control studies / other research projects (that are exempt from disclosure to REK) and research for which disclosure is mandatory.

Either way, researchers and healthcare professionals are always personally responsible for protecting the study participants' interests, including medical, health, and privacy issues, regardless of which approvals. Anyone involved in research must have sufficient expertise to comply with the procedures and institutional requirements that apply regarding personal and health data. Requirements for a high level of security when handling data, applies regardless of whether the project is a quality control study, other type of research, or requires approval from REK. The local Data Protection Officer or Information Security Officer

at your research institution will have established routines and will assist in ensuring proper handling of the data in the research project.

When publishing the results of a quality control study, where REK has stated that the project does not require their approval, the researcher (author) could attach this statement at manuscript submission ("exempt from IRB (Institutional Review Board) evaluation"). This can be a convenient solution when you want to publish in a journal that requires all results to be based on a prior ethical review by the IRB. This is a requirement that all the reputable scientific journals have adopted and is based on Article 35 of the Helsinki Declaration.

6.4 The demarcation between research projects that need approval from REK, quality studies and other research projects

Research projects that must be approved by REK versus Quality control studies.
The Norwegian term “kvalitetssikring” (quality control studies) is an ambiguous term, and it may be difficult to determine whether a project should be defined as a research- or a quality control study. It is not the scientific methodology, whether the results are to be published, or whether the project is a type of research that is exempt from REKs mandate that determines whether a project should be defined as "research" or "quality control. REK’s practice shows that a number of projects are considered to be quality control studies based on the project aims. Studies with a primary aim of evaluating a treatment program or healthcare services are considered an integral part of the healthcare service. As a result, these studies are subject to the overall health legislation, and the framework of the Health Research Act does not apply.

The REKs have identified some characteristics that define whether the projects are deemed as research (requiring REK approval) or quality control projects. These characteristics are summarized by the Joint Committee for REK (“Fellesorganet for REK”; FREK).

Among the key factors indicating that a study should be defined as *"research",* thereby requiring evaluation and approval from REK are:

- Does the project involve risks to the participants? In clinical follow-up studies, diagnostic procedures may for example involve risks that are acceptable for obtaining a correct diagnosis, but that are not acceptable for use in a research follow-up study.
- Does the project involve extra procedures for the participants, which would not otherwise be done as part of regular clinical follow-up?
- Will the project generate new general knowledge that may be of general interest? (A quality control project may also generate "new" knowledge, but may still be exempt from mandatory REK evaluation, if the project has other obvious quality control study characteristics).
- Methodology development. If a study involves new diagnostic or therapeutic approaches tested in humans, this is deemed as “research”, and will require a REK evaluation and approval.
- Randomization of research participants argues for application to REK.
- If the study involves recruitment of a control group of healthy subjects, REK approval is required; as such participants are not covered by the regulations that apply to patients in the healthcare system.

Characteristics of a *"quality assurance project"* according to REK:

- Is the project retrospective? This does not mean that a quality assurance project cannot be prospective; study design may involve the collection of new data based on information from retrospective data, typically as part of a follow-up of a treatment program without specific research questions. This applies regardless of whether the data are collected from several institutions.
- Are different methods being compared? If the project aims to compare two established methods that are commonly used, and both are acceptable alternatives, this may indicate that the project should be defined as a quality assurance study. This does not apply to the testing of drugs.
- Projects evaluating patient experience and satisfaction combined with a retrospective evaluation of clinical practice may also be considered an integral part of the institution’s quality assurance.

- Implementation and use of questionnaires, with the aim of structuring a regular clinical interview and using the data gathered to evaluate the service offered, will generally also be considered as quality assurance projects.

The decision of where to draw the line distinguishing projects that need REK evaluation and research that is exempt from this evaluation, is primarily related to the purpose of the project. This evaluation is not dependent on whether the project involves patients, health information or human biological material. If the purpose is not to generate new knowledge about health and disease, the project is not covered by the Health Research Act and does not require evaluation and approval from REK.

Examples of research projects that are not encompassed by the Health Research Act, but where health data are used, are projects aiming to study the organization and efficient use of resources in healthcare services (Health Services Research, "*helsetjenesteforskning*"). It is somewhat more challenging to evaluate where to draw the line as to which studies require REK approval, when looking at studies that involve elements of socio-economic issues related to a defined patient group. One way to determine this is to question whether the patient group's health and diseases are the basis for the study or if the purpose is to evaluate socio-economic conditions, such as examining how some patient groups function at work, socially, etc. As a general rule, if the project involves patients and the purpose is in some way related to their health condition, an application should be submitted to the REK for review (on a special form in the REK web portal).

Even if REK characterizes a project as a quality assurance study, and it is thus exempt from the REK mandate, this does not imply that the requirement for informed consent can be waived. There is a distinction between quality studies and internal quality assurance according to the Health Personnel Act ("helsepersonelloven", § 26). The latter does not require informed consent, but is not defined as "research" since the purpose is related to the internal institutional activity and needs, such as improving quality of care. These distinctions can be clarified with the local Data Protection Officer ("personvernombudet").

6.5 Patient/participant information and consent

General rule of consent

*The main rule in research is that informed consent from each study participant is required***.** For the consent to be valid, it must be explicit, voluntary, and documented. However, the Health Research Act allows collection of information and biological material that has already been obtained in a healthcare setting, without patient consent specific to using the information for research. However, this must be evaluated by REK. If REK determines that the project does not need to obtain consent from all or part of the recruited population, the Committee will consider whether to set different privacy terms as a result of this exemption. For example, it may be considered appropriate to inform potential study participants about the research project and then give them the option of opting out of participating, as opposed to obtaining active informed consent. In postal questionnaires of a minimally invasive character, for example, REK may rule that returning a completed questionnaire (without the person's signature) is a sufficient documentation of “consent”.

Broad consent (“Bredt samtykke”)

The Health Research Act (§ 14) allows for the option to obtain *broad consent* in research, defined as consent to a "broadly defined research objective that is to be specified in greater detail at a later time". This entails research participants giving broad consent to research, on human biological material and health information that includes one or more overall research objectives and fields of research. Please note that other countries do not necessarily accept broad consent, including projects funded by the EU.

The Health Research Act provides “cancer research” as an example of how one might state the purpose of a study for which broad consent is to be used. In most cases, the purpose might be narrowed down more than this, e.g. "lung cancer research". Under the Health Research Act, participants giving broad consent have a right to receive information about project progression on a regular basis, but REK can also require that the Project Manager must meet other terms. The use of broad consent is often convenient when establishing a general research biobank or a research registry (see Chapter 6.2). REK may be reluctant to

approve the use of broad consent for research that includes children or persons that are legally incompetent with respect to consent.

New and altered use of human biological material that has already been collected

In the case of new or altered use of human biological material that has already been gathered for research, REK will usually require that new consent is obtained. However, REK may consider that such consent is unnecessary, as long as "the research is of significant interest for the community at large and the participants' welfare and integrity is maintained."

Who can consent to research participation?

Obtaining consent from children and adolescents

Under the Health Research Act all persons over the age of 16 years have the right to give consent to medical and health research. For clinical drug trials or surgery, parental consent is always required (this includes adolescents aged 16-18 years). For children and adolescents under the age of 16, parents must give their consent to participation in research. However, REK does have the ability to determine that only consent from the child is required without involving the parents, if there are particular reasons for this and the child is between the ages of 12 and 16 years. It is advisable to contact REK early in the research planning for advice and guidance on how such studies could be handled. One example is a questionnaire looking at alcohol consumption amongst 15- year-olds, where it is up to the adolescents to decide whether to inform their parents if they answered the questionnaire. Regardless of informed consent, children over 12 years have the right to give their opinion as to whether they want to participate or not in a research project.

Broad research consent from children is unlikely to be approved by REK. Increasing emphasis is placed on the child’s own thoughts about taking part in research projects, based on increasing age and maturity level. Children have a right to receive project information that is tailored to their maturity level. Information procedures and written information should be adapted to different age groups and degrees of maturity, using for example cartoons for very young children. Children's right to be heard does not imply that they are to sign a consent form (children give passive consent unless they themselves wish to give active

consent), while parents (or others with parental responsibility such as the Child Welfare Services, 'Barnevernet') give explicit surrogate consent (“stedfortredende samtykke”).

Obtaining consent from incompetent adults

The Health Research Act states that where persons without powers of consent (as defined by the Patient and User Rights Act § 4) participate in a research project, their next of kin are to be asked and, where necessary, give consent on behalf of the incompetent person.

Research on minors or adults without powers of consent

Conducting research involving children and people without competency to consent is not just a wish to fulfill curiosity on the subject; it is a necessary right that these groups have. The safety and efficacy of drugs used for children must be documented. It is not sufficient to extrapolate conclusions about treatment of children based on knowledge gained from studies on adults. Children are different from adults concerning pharmacokinetics, immunology and organ plasticity. Furthermore, these and other factors change through various stages of childhood.

In agreement with international principles, the Health Research Act stipulates many requirements, which must be fulfilled before research projects can be carried out on persons without powers of consent (§ 18). This includes the requirement that the research must imply no more than negligible risk or disadvantage to the individual participant and that the person herself/himself is not opposed to participating. Another requirement is for it to be reasonable to assume that the research results will be of use to the individual person or patient group. In general, REK will consider whether a 'significant' expected benefit of a project is in reasonable proportion to any potential risks or disadvantages. In addition, scientific arguments must be presented for why the research project needs to be carried out on this specific group of patients lacking legal competence to consent.

Research in clinical emergencies

The Health Research Act (§ 19) also stipulates multiple requirements particular to research projects that involve persons in clinical emergencies in which the patients themselves or their next of kin cannot give consent. The potential risk or disadvantage to each individual

participant must be no greater than negligible. The participants themselves must not be opposed to the research project (or would assumedly not oppose the project had they been competent to give consent). The research can only be carried out in clinical emergency situations. The result must be expected to be of great preventive, therapeutic or diagnostic value. The research participant or next of kin are to be given information about the project as soon as possible and, where applicable, must provide consent in order for further research to continue.

Template for study information and obtaining informed consent

In the REK web portal you will find templates for information and consent forms. In addition, institutions often provide templates of different kind, see OUS guidance. The templates have been created to ensure that the information presented meets the requirements specified in the biomedical research legislation. The information in the consent forms aims to help ensure that potential research participants understand what they are being asked to consent to. The information is divided into a main section and additional chapters. The main section should be a maximum of two pages, while chapters A and B should not exceed four pages in total. The most important information should be presented in the main section, and the following information chapters are meant to elaborate. The information must be adapted to the type of project and the target population, especially if this population consists of children or adults with reduced or lacking legal competence to consent (more information in Norwegian here). In studies involving children, especially from the age of 12, information must not only be given to the parents, but also to the child, and in a format that matches the child's level of maturity and understanding.

The likelihood of a rapid application process by all bodies is increased when following a consent information template. If the template is not followed and the participant information letter deviates substantially from the requirements in terms of content or length, REK may return the project application to the Project Manager for rewriting. Information letters and consent forms should be formulated in such a manner that they satisfy both legal and ethical requirements regarding content, as exemplified in the templates. It is important to note that many information letters to study participants become so long and complex, that recipients may well have difficulty comprehending the

content, and REK will in such cases recommend changes to the information letter prior to approving the study.

Information letters are frequently insufficiently prepared. In general, they should be written in a neutral tone. Careful consideration should be given to the title of the study and the heading of the information letter. Examples of information requiring specification (the templates from REK also cover these points) are:

- The aim of the project (the objectives of the project and reason why this particular person has been asked to participate)
- Which health trust/institution is responsible for the project (including names and addresses)
- The voluntary nature of participation in the project must be explicitly stated and, where appropriate, whether participation will affect any treatment the patient may be undergoing at the study hospital
- The sources of data being gathered; e.g. medical records, the Cancer Registry of Norway etc. and whether the patient is expected to make an active contribution in any way, for example by undergoing additional tests or filling in a questionnaire
- Whether the information used is connected to or derived from biological material and, if so, which analyses will be conducted on the material
- When information is to be deleted/anonymized (date)
- In cases where information is to be released to external parties (for example in collaborations between universities/colleges or other regional authorities), the names of these parties must be provided. If any collaborators are located abroad, permission must be sought to transfer biological material or health information. Where relevant, state which form the material will be sent in, anonymously or de-identified etc.
- Information allowing patients to make use of their rights. This includes rights of access so that they may find out what information has been registered and the option of recalling consent given previously (deleting information and destruction of biological material). Please note the limitations on withdrawal of test results in pharmaceutical trials, see information on the Norwegian Medical Products Agency in this chapter.
- Any financial ties to sponsors, such as pharmaceutical companies, should be declared

- Final date for deletion of any audio or video recordings used in the project.
- It is advisable to set the date for when consent for inclusion in the health records are adopted. Such consent forms are often updated, and it may be important to keep track of which patients have agreed to what.

Some study information letters describe the role of the Project Manager and her/his research expertise in too much detail. This should be downplayed and the information letter should instead focus on the role of the study participant, what consent is being requested for and the scientific aim (objective) of the study. It is recommended that information letters are written in the first person plural rather than first person singular ('we' rather than 'I'), cf. the fact that research is being carried out under the direction of the relevant employer (Do *not* start the letter in the following manner: "My name is XX and I am a PhD candidate at the University of Oslo. I am writing to ask if you would consider participating in this study…").

The language used in the information letter should be simple and easy to understand. Technical details, which have not been modified to suit the recipient, should be avoided. In complex studies, a one-page flow chart illustrating the course of the study, in addition to the information letter, may be useful for a potential study participant.

The consent form itself should not contain any new or detailed information, but simply state that the informant (study participant) consents to taking part in the study, as described in the information. In accordance with international regulations, clinical drug trial consents must also include the name and signature of the person who has provided information to the study participant. Such a signature may also be relevant for other types of research projects.

The information letter and consent form in clinical drug trials must be dated and have a version number. Bear in mind that without documented obtained informed, dated, and signed consent (where this is a requirement), a person cannot be included in the study and the person's data cannot be used. Data from non-participating individuals (individuals which have not been asked to consent or have said no) can in general not be used for dropout analysis. An exception to this rule requires REK approval.

Dispensation from access to confidential information in research projects

Since 2023, the application procedures for access to health information has changed. The Health Data Service has been given the authority to make decisions about making health information available and dispensation from the duty of confidentiality. This applies to health information for use in statistics, health analyses, research, quality improvement, planning, management and preparedness. In some cases, when the access to data is required for research purposes, the Directorate of Health and REK (the Regional Committees for Medical and Health Research Ethics) will still have the authority to make decisions on dispensation from confidentiality.

Applications for dispensation are necessary for research based on confidential health and personal data information obtained by the healthcare service without consent from each individual patient. According to The Health Research Act, REK is responsible for deciding if confidential health information may be provided by health personnel for use in research. REK has the option of giving dispensation, allowing access to such information, only if the research project is deemed to be of substantial interest to society and only if the welfare and integrity of the participants are maintained.

When applying for dispensation to allow access to confidential information in quality research studies and other research studies that use health data, the legislation is complicated. According to the Health Personnel Act § 29, REK is the delegated authority for determining whether dispensation from confidentiality may be given, also in types of research studies that are not included under the Health Research Act. However, in quality research studies (see Chapter 6.4), the Directorate of Health determines whether exemption from confidentiality may be given. It is recommended to clarify such questions with the Data Protection Officer at your institution before a dispensation application is submitted.

If the researcher is to have access only to anonymous data, it is not necessary to apply for a dispensation. This presupposes, however, that those who disclose the health data have legal access to the relevant information. An example of this is where healthcare officers and others with legitimate access to the data retrieve information from a medical chart or other health registries, then anonymize, and disclose the data to the researcher. Such retrieval of

clinical data may imply added costs for the institution, and researchers, even with REK approval, cannot expect the health institution to take on this extra cost without compensation.

For internal quality assurance studies of health services within a health trust/hospital, there is no requirement for approval from any external authority (The Health Personnel Act § 26). Internal quality registries are subject to notification to the local Data Protection Officer. More information can be found in the "Regulation of access to health data registers" in Norwegian.

6.6 The roles of the supervisory authorities

Under the Health Research Act, the Norwegian Board of Health Supervision ("Statens helsetilsyn") is responsible for supervising medical and health research and the management of biobanks, while the Data Protection Agency ("Datatilsynet") is responsible for supervising the use of health information. The Research Director ("forskningsansvarlig"), the Data Processing Director ("Behandlingsansvarlig"), the Project Manager ("prosjektleder"), and other personnel involved in a research project have a duty to provide information to the supervisory authorities.

The Norwegian Board of Health Supervision can rule that a project must be stopped or change the conditions for research projects and research biobanks if these have detrimental consequences for research participants or others, or are considered inappropriate or unjustifiable. The Norwegian Board of Health Supervision should be notified in writing in cases of "serious, unwanted and unexpected medical events that are believed to be related to the research." This is in addition to the standard obligation to report clinical incidents and injuries both internally to the institution as well as externally (cf the Health Research Act Chapter 5, and the Research Handbook, Chapter 14). In clinical pharmaceutical drug trials, the Norwegian Medical Products Agency is the body that oversees the implementation of the study, and that ensures the establishment of internal control procedures (Standard Operating Procedures, SOP), which include rules for "Good Clinical Practice" (GCP).

The Data Protection Agency can rule that any processing of health information opposing the provisions of the Health Research Act must cease. Alternatively, the Data Inspectorate can stipulate conditions to be fulfilled before the processing of health information may be initiated/continued in a research project. Willful or grossly negligent violations can lead to a fine or prison sentence.

6.7 Report and final study report to REK

Project Managers are legally obliged to submit a final report to REK at the end of a research project (the Health Research Act § 12), no later than 6 months after the approval period has expired. REK specifies that the final report should be submitted when the project is finished and published, or of other reasons completed/ended. In other words, the period from last patient contact to publication of the results must be a part of the application period. REK can make specific demands with respect to the content in the final report. REK can instruct the Project Manager to provide annual or extraordinary reports where deemed necessary by the committee. Instructions for filling in the final report form are available on the REK web portal.

6.8 Clinical Trials on Medicinal Products for Human Use and the Norwegian Medical Products Agency ("Direktoratet for medisinske produkter")

All ongoing clinical drug trials are or will be regulated by national legislation (Forskrift om klinisk utprøving av legemidler til mennesker) and European laws (European Regulation EU No 536/2014). There are strict requirements for the implementation of drug trials regardless of whether it is an early testing phase or the medicinal product has previously been approved and used in clinical therapy. The studies must be conducted in accordance with Good Clinical Practice (GCP), which includes that all those involved in the study must possess an updated GCP certification. Participation in the GCP courses held by NorCRIN partners qualifies for a GCP certificate. A number of national procedures (SOPs) are available, including templates and checklists, and in accordance with the regulations for pharmaceutical drug testing (see NorCRIN).

NorCRIN and NorTrials have worked together to produce a short introductory course to clinical studies, briefly explaining the different types of studies, budgeting, roles and regulations among other. The course is available at the institutions' Learning portals. For OUS employees, it can be accessed at the course catalogue site.

For all clinical trials on medicinal products on humans, both patients and healthy subjects, applications must be submitted via the EU portal "Clinical Trials Information System" (CTIS). CTIS applications are assessed by Norwegian Medical Products Agency and REK KULMU.

Studies of drugs defined as advanced therapy medicinal products (ATMPs) include somatic-cell therapy medicines, gene therapy medicines and tissue-engineered medicines. These have their own GCP guideline that sets requirements for protocol content, patient information and additional requirements such as traceability and documentation (30 years instead of 15/25 years, which applies to regular drug studies). The Norwegian Medical Products Agency reviews applications for gene therapy studies (see Chapter 6.9).

Clinical Trial Information System (CTIS): Clinical trials approved under or transferred to Clinical Trial Regulation 536/2014 are publicly available through the Clinical Trials Information System (CTIS). Older studies approved in accordance with the Clinical Trials Directive 2001/20/EC and initiated before 31 January 2022, as well as all studies conducted outside the EEA that are part of a Pediatric Investigation Plan (PIP) and/or are conducted in accordance with Article 45 or 46 of Regulation (EC) No. 1901/2006, are registered in the EU Clinical Trials Register (EU CTR). Drug trials where the last participant/patient visit will take place after 30 January 2025 must be transferred to the Clinical Trial Information System (CTIS) and follow regulation 536/2014. Within 90 days after the last patient contact, a final report is sent to CTIS. The results of the study (including any side effects) must be registered in CTIS within 12 months of the last patient contact (6 months for paediatrics). The requirement applies regardless of whether/when the results are published. The registration in this database also meets requirements from the journals for such studies before they can be considered for publication.

International clinical drug trials to be conducted in Norway: Under the CTR, a national coordinating site (NC) is no longer defined. Sponsors (researchers or companies) who apply via CTIS take over responsibility for many of the previous NC tasks. However, some tasks that previously fell under the NC are not covered by the legislation, e.g. registration of the study on the hospitals' websites/Helsenorge. If the sponsor is a foreign company or CRO (Contract Research Organization), they may lack familiarity with REK's consent templates and Norwegian conditions. It is recommended that the sponsor assigns a Norwegian Principal Investigator the task of quality-assuring the consent form and other information for the study participants, as well as registering the study on the hospitals' websites/Helsenorge, on behalf of all participating centers in Norway.

The collected research data in a multicenter study will be stored and analyzed with an external sponsor (e.g. commissioned research), the sponsor will be responsible for this part of the project. In such cases, however, it is important that the disclosure of health information from each center is carried out in accordance with the provisions of the Personal Data Act on information security and that such disclosure is based on an agreement between the collaborating institutions. In addition, in these cases it is important to obtain the necessary advice and assistance from the Data Protection Officer or equivalent support functions. Some institutions have implemented their own internal forms for such data exchange. These forms are normally managed by the Data Protection Officer.

The Clinical Trial Units offer monitoring of investigator-initiated clinical pharmaceutical drug studies, see Monitoring - www.norcrin.no. The aim is to assure that the research follows national and international guidelines. The guidelines for Good Clinical Practice (GCP) state that the requirements for monitoring should take place before, under, and after a study/project. Quality assurance must commence before the first research participant enters the study and involves documenting the training of study personnel, GCP certification, and practical aspects surrounding performance of the study.

A study participant in a clinical drug trial may withdraw from the study at any time. Patient data and biological material collected up to this point may, however, be used in the study. For safety reasons, all documentation for a clinical trial, including research data, must be

stored for 25 years after project completion (15 years for trials governed by the old Directive 2001/20/EC, see the Regulation on clinical trials of drugs in humans § 8). This applies to each of the participating centers (Research Directors/"forskningsansvarlige").

Adverse events in clinical drugs trials must be reported to the Norwegian Medical Products Agency as Annual Safety Reports. Suspected unexpected serious adverse reactions have to be reported to the EudraVigilance database and can be facilitated by the clinical trials units. See also Chapter. 17 on the obligation to report to the Norwegian Board of Health Supervision in cases of severe, adverse, and unexpected events in research projects.

6.9 Clinical Medical Device trials and the Norwegian Medical Products Agency ("Direktoratet for medisinske produkter")

Clinical trials testing medical equipment are to be reported to the Norwegian Medical Products Agency if the clinical trial is carried out for one of the purposes of MDR Article 62 (1) or is carried out for other purposes as described in Article 82 of the MDR and where the medical device is not CE marked or where it is to be tested for applications other than those specified by the manufacturer for the device. Medical device manufacturers looking to manage and perform an EU clinical trial must follow ISO 14155:2020 in addition to the regulatory requirements set out by Medical Device Regulation (MDR). For more information about which clinical trials requiring an application to the Norwegian Medical Products Agency (NOMA), see NOMA website. The new EU regulation Medical Device Regulation (MDR) 2017/745 came into force in 2021. Clinical trials testing medical equipment which is covered in the MDR have to apply to REK KULMU and to the Norwegian Medical Products Agency at the same time (more information on MDR at the Norwegian Medical Products Agency and REK websites).

6.10 The role of The Norwegian Directorate of Health ("Helsedirektoratet")

From the 1st of January 2024, The Norwegian Directorate of Health has merged with the Directorate for e-Health, and has taken over tasks from the Norwegian Institute of Public Health. The digitization work that has been carried out in the Directorate for e-Health is now continuing in the Norwegian Directorate of Health (NDH). The Health registers are moved from NDH to the Norwegian Institute of Public Health. The Norwegian Medical Products Agency takes over the areas of medical products, blood, cells and tissue.

For gene therapy studies, questions about the interpretation of the Biotechnology Act's provisions on gene therapy can be addressed to the Department of Health Law and Biotechnology (postmottak@helsedir.no). Questions about the approval of clinical studies with gene therapy can be addressed to the Norwegian Medical Products Agency and the Regional Committees for Medical and Health Research Ethics (REK).

Artificial intelligence studies

The Norwegian Directorate of Health offers guidance and information that is relevant for research or development of products based on artificial intelligence within healthcare, for an acquisition or for usage of equipment that is based on artificial intelligence.

The University of Oslo has a dedicated page to aid in the use of tools based on AI for learning. Pay special attention to the legal guidelines.

6.11 Use of research animals

Regulations on the use of animals in experiments (FOR-2015-06-18) came into force in 2015 and are based on directive 2010/63/EU. All breeders, intermediaries and users, including the premises they use, must be approved by the Norwegian Food Safety Authority (§5, FOR-2015-06-18). Each laboratory animal department must appoint personnel with special control responsibility (personell med særskilt kontrollansvar, PMSK), who is responsible for controlling animal welfare and ensuring that all personnel have the necessary competence. PMSK carries out local assessment of applications (following orders from the Norwegian

Food Safety Authority) and the Norwegian Food Safety Authority processes and approves applications for animal testing. The project manager is responsible for ensuring that trials are carried out in accordance with the approval granted by the Norwegian Food Safety Authority.

Everyone who plans, designs, or carries out experiments, cares for animals or kills laboratory animals must have undergone training in accordance with the regulations (Appendix E, FOR-2015-06-18). Several universities in Norway offer a joint theoretical course in laboratory animal studies, CAREiN, which is adapted to new regulations and the use of the animal species mouse, rat, pig and fish. Everyone who carries out experiments, cares for and euthanizes experimental animals must also complete practical training with the relevant animal species. UiO offers practical training in handling and basic procedures with rodents (MF9495). MF9495 is a mandatory course for all users who perform experiments, look after and euthanize laboratory animals at OUS. The complete MF9495 course consists of a theoretical part (MF9495T; Function A+B+D) and practical training (MF9495P; Function A+D). Students must sign up for both MF9495T and MF9495P to obtain a CAREiN Diploma certifying training required for working with research animals.

For animal experiments at Oslo University Hospital (OUS) see eHandbook SOP 83692 for further descriptions of roles, responsibilities and implementation of animal experiments.

7 Project organization and management

This chapter covers terminology and leadership roles in research projects. The chapter also includes practical advice on how to organize and lead a project in order to best facilitate project progression and to increase the likelihood of completing the project. If the most common "project management tools" are employed, a number of pitfalls can hopefully be avoided. This chapter is specifically directed at those who have not worked much with projects earlier.

Research projects differ from standard clinical medical practice because they are limited in terms of time and resources, and have very specific goals.. By defining the research as “a project” (see Chapter 4 about research protocols), the work is viewed as "a unique task which leads to a definite result, which requires a variety of resources, and is limited to a finite amount of time" (Andersen ES, Grude VK and Haug T. Målrettet prosjektstyring. Fagbokforlaget 2022). Literature on efficient management of a project may prove useful in this setting.

Roles and responsibilities in project organization

A number of terms are used in the field of project work, although their use vary substantially according to context. The Appendix includes a summary of some Norwegian terms and their English translation. Important terms are ”Research Director” (“forskningsansvarlig”), "Project Director" ("prosjektansvarlig"), ”Project Manager" ("prosjektleder"), and ”Data Processing Director” (“behandlingsansvarlig”). These distinctions must be clarified before the project commences so that all participants agree on their rights and responsibilities. The division of responsibility in research projects is regulated by formal Norwegian legislation and by the institutions’ own routines and guidelines (e.g. the OUS guidelines). The researchers' responsibilities, roles, and rights in relation to co-authorship, tasks, and finances should also be clarified in advance. Role clarification is also important in order to know which agreements are needed between the various parties in a research project.

University employees and hospital staff may find relevant information on roles and responsibilities relevant for their institution, such as at the University of Oslo website (The Quality System).

Research Director ("forskningsansvarlig")

A Research Director ("forskningsansvarlig") is defined by the Health Research Act as *«The institution, or another legal entity or individual, who has overall responsibility for the research project, and who has the necessary qualifications to fulfill the research administrator's duties under this Act".* In Norwegian health trusts ("helseforetak"), it is the hospital, by way of the CEO (Chief Executive Officer) that is formally responsible for research and acts as "Research Director".

The duties of the Research Director are defined in separate regulations specific to the organization of medical and healthcare research. The Research Director possesses the overall responsibility for the research project and must through the establishment of systems and routines (internal control) ensure that the institutions' own researchers are made capable of maintaining the ethical, medical, healthcare-related, scientific, confidentiality- and privacy-related aspects of a project. The Research Director should also facilitate proper organization, initiation, implementation, dissemination, closure and follow-up management of research projects. At larger institutions, i.e. health trusts, universities, and university colleges, the tasks (but not the responsibilities) entrusted to the Research Director, are usually delegated to Department Chairs or Heads of Institutes.

In collaborative projects that take place at several institutions simultaneously and follow the same research protocol, each participating institution is responsible for the part of the research project carried out at their own institution (multi- studies). When processing personal health information in a (multi-) research project, the role as Research Director ("forskningsansvarlig") and Data Processing Director ("behandlingsansvarlig") will normally coincide.

Many researchers have double employment at a University and a Health Trust (e.g. hospital). If a research project is mainly carried out at a Health Trust, or it involves the use of biological samples and health information obtained by the healthcare system, it is reasonable that the Health Trust, not the University, is defined as the responsible research entity (and carries the role as “Research Director” i.e. “forskningsansvarlig”). As a matter of fact, OUS is always the responsible entity for research where clinical data is to be processed, see Collaboration Agreement with UiO.

Project Director (i.e. “prosjektansvarlig”)

The role of the *Project Director* (i.e. “prosjektansvarlig”) is not defined in the Health Research Act; clarification of this concept is still needed for some projects. In the corporate business world, a “Project Director" is often the client, whether the client is a representative from the business itself, or a single customer. In The Research Council of Norway’s (RCN) General Conditions of Contract, "Project Director" is defined as "*The institution, company or business that to the Research Council is responsible for ensuring that the project is carried out in accordance with the contract*." This means that in a RCN funded project that is subject to disclosure to REK, one and the same institution may be defined as the Research Director according to Health Research Act and as the Project Director relative to the Research Council. In multi-center studies there is often a "project responsible researcher" (“prosjektansvarlig forsker”, in English often called the “Principal Investigator”, PI) from each institution. In clinical drug trials, the PI position is held by the person known as the ”Investigator” (“utprøver”), but for other types of studies one must clarify who is defined as the “local project responsible”.

The commissioning entity ("oppdragsgiveren") may be the Project Director (“prosjektansvarlig”) in the case of commissioned research (oppdragsforskning). However, this may vary according to the type of contract with the hospital and must therefore be clarified with one's immediate superior, as well as with the Research Director (i.e. “forskningsansvarlig”).

Sponsor

In the clinical drug trial regulations, a *sponsor* is defined as *"a person, company, institution, or organization that is responsible for the initiation, management, and / or financing of a clinical trial."* Similarly to the terms Research Director and Project Director, “sponsor” normally refers to an institution (legal entity). In a clinical drug trial organized as a multi-study, there can be only one sponsor. This means that while each participating study center is individually responsible for conducting their portion of the research study at their own institution, only one institution carries the role as sponsor. As a rule, for clinical drug trials performed on behalf of the pharmaceutical industry, the pharmaceutical company in question acts as the sponsor, whereas for investigator initiated clinical drug trials the institution leading the study is defined as "the sponsor".

Investigator

The term “Investigator” (“utprøver”) is defined specifically for clinical drug trials and in separate regulations for testing drugs on humans. It is important to clarify the roles and tasks of the Project Manager (and/or supervisor), PhD student, and other key study personnel, by using a delegated authority log. The role descriptions must include information on which tasks the participant has both in the project management, and relative to the local investigators.

Data Processing Director

The Data Controller must be specified for projects involving the use of personal and health data. According to the Personal Data Protection Regulation, a Data Processor is a natural or legal person, public authority, institution or any other body that processes personal data on behalf of the Data Controller. In practice, the institution has the overall responsibility for the processing of the data in the project through the senior manager. The tasks of the Data Controller can be delegated to others at the institution, which is common in research where the project manager is in practice responsible for compliance with the regulations. In cases where a Data Processor is used, the Controller will be responsible for the processing of personal and health data that takes place with the Data Processor. Processing responsibility must be clarified in the planning of a project.

Person responsible for a research biobank

According to the Norwegian Health Research Act, the *person responsible for a research biobank* (“*biobankansvarlig*”) should be "*a person with a higher degree either in medicine or biology*", and the Research Director at the institution appoints him or her. In your role as researcher, you should familiarize yourself with how this is organized at your research institution. In collaborative or multi- studies, the person responsible could be from an institution other than your own. In some cases, biobanks have a board or a steering committee, in addition to the person responsible for the biobank. For general research biobanks across clinics, the establishment of a supervisory board is recommended.. Members of the board should consist of representatives from the relevant academic community and the institution in charge of research.

Project Manager ("prosjektleder")

According to *the Health Research Act* a Project Manager is *"A physical person who is responsible for the day-to-day operation of the research project and who has the necessary research qualifications and experience to be able to fulfill the duties ascribed to the project manager pursuant to this Act".* In a separate regulation on the organization of medical and health research, criteria for the qualifications of the Project Manager are specified, including the requirement of having the "technical and scientific expertise that the research project requires for proper implementation." This means that students, PhD candidates, as well as others who wish to perform research, but do not have doctoral qualifications, most often cannot be defined as a project manager based on legal requirements. For student projects or PhD work, the supervisor or co-supervisor usually acts as the Project Manager. In addition, the Universities set other requirements for the supervisor (see Chapter 10).

The Project Manager is responsible for (as described in the Health Research Regulations):

- That ethical, medical, healthcare, privacy and information security issues is dealt with in the daily management of the project
- That the project is established and approved by the Research Director before commencing
- That necessary approvals by REK, the Norwegian Medical Products Agency, and any other relevant bodies is obtained prior to commencement

- That the project is carried out in accordance with the approved research protocol
- Communication with public institutions and Research Director (“forskningsansvarlig”)

The Project Manager will also be responsible for the financial aspects of the project and the follow-up on any project financier's reporting requirements.

For any research project, there can be only one Project Manager and this person is responsible for obtaining the necessary approvals (REK, Norwegian Medical Products Agency). However, in multinational non-drug non-medical device studies, there will be as many project managers as there are countries. For medicinal product trials there will be one sponsor for the entire trial that will apply to DMP and ECs (REK for Norway). In the NorCRIN SOP “Roles and responsibilities in clinical trials” (for non-commercial sponsors) the sponsor task is delegated to the coordinating investigator, a function that is defined in the SOP.

Clarification of common misconceptions regarding the Project Manager’s role:

- Being a Project Manager is not synonymous with having ownership of the data. Intellectual rights with respect to ownership of data should be specified in the research protocol.
- Being a Project Manager is not synonymous with authorship. Authorship is regulated by the Vancouver Conventions (see Chapter 9).

Though the concept of a Project Manager is not clearly defined for other types of research (i.e. research that is not governed by the Health Research Act and where disclosure to REK is not required), it is probably wise to use the general guidelines described above.

Project management ("prosjektstyring")

Some tasks associated with research project management may not be directly related to research in particular. Therefore, it may be helpful to make use of the experience and academic insights of project management to ensure an efficiently run research project. Project management involves running a project in accordance with agreed standards of quality, within the agreed period of time and using the resources available. Projects are divided into phases in order to clarify how and when to utilize specific resources. The phases

in a project are typically: start-up, planning, implementation, winding down and termination. Although it may seem time-consuming to plan each of these phases, it cannot be overemphasized that thorough planning will save time and frustration.

According to project management theory, the Project Manager is responsible for:

- Planning and developing a progress schedule
- Determining what is to be done, how, and when
- Defining who is to do what (and does everyone agree?)
- Acquiring sufficient resources for the project
- Designing a follow-up- and information system for the project
- Organizing and following up the implementation of the project
- Ensuring that the tasks are carried out according to plan and in the correct manner
- Ensuring adequate follow-up and information to all parties involved (progress reports, superiors, steering groups etc.)
- Evaluating the project at its conclusion (publications or reports).

Project objectives

- One of the first, and most important tasks in a research project is to define specific project objectives. Without clear objectives, the protocol, grant application, methods, and publications are unlikely to be of good quality. When applying to REK (see Chapter 6) it is particularly important to outline and define the aims of the project well, as the aims provide the boundaries for the restriction REK sets on data usage.
- Aims must be verifiable. In quantitative research, this often means formulating hypotheses that can lead to yes/no answers. In scientific terms, it is the null hypothesis that is to be rejected or confirmed.

Implementation, activity plan and milestones

- An activity plan is a plan showing what is to be done when. This is of particular relevance in grant applications, since the likelihood of the project success is evaluated according to how realistic the implementation of the plan appears to be.
- Milestones are "checkpoints" en route with allotted dates (for example, when a questionnaire on lifestyle factors will be validated and approved for printing). A

milestone plan provides a useful means of checking if the research project is on schedule. If this is not the case, the consequences must be assessed.

Project work as a topic, may be studied further at several institutions, including BI and the Norwegian Center of Project Management (Prosjekt Norge).
Other useful information may be provided by local institution, such as at OUS.

The formalization of a research project

According to the Health Research Act, the responsible research institution (i.e. the Research Director) is required to maintain an updated overview of ongoing medical and health research projects. This is in line with the requirement that the Project Manager ("prosjektleder") involves the Research Director ("forskningsansvarlig") in the project prior to its commencement. Consequently, most research institutions have established systems for how research projects should be formally organized within the institution. In addition, the GDPR requires the Data controller to keep an overview of all processing of personal data. This means that the responsible research institution must keep an overview of all projects where personal data is processed, including health research, registers, research outside REK's mandate, etc. In general, the internal institutional formalization process of a research project will be based on the steps on the next page.

For Oslo University Hospital (OUS) see eHandbook SOP 60 and eHandbook SOP 61 for further descriptions of roles, responsibilities and implementation of studies.

Step 1: Planning and internal approval (included organizational approvals)

1. Local discussions and internal approval of the project within the Department(s). This will normally be based on the discussion of:

- Draft of research protocol (or REK application)
- Draft of participant information sheet and consent form
- Project budget

2. For institutions with their own research administration or Data Protection Officer ("personvernombud"): it may be required for the researcher to seek advice and guidance in the planning phase

Step 2: Approvals (REK, Norwegian Medical Products Agency, Data Protection Officer)

The Project Manager ("prosjektleder") is responsible for obtaining the necessary approvals before the project can start. Normally the research institution requires that the application (including relevant appendices) is registered and filed in the institution's administrative systems.

At OUS, studies with all attachments are to be reported to the OUS Data Protection Officer (Personvernombudet) (following project approval by REK, whe8re this is needed) via this form.

Step 3: Study start and implementation

Once necessary approvals are obtained, the Project Manager's responsibility is to:

- Follow up the terms that underlie the approval
- Follow up the institution's procedures for access, storage and dispensing research data. If the project is a collaboration between several institutions (multicenter study), a data transfer agreement between the involved institutions is commonly made. The Project Manager has a particular responsibility to ensure that such agreements are in place.

The study is formalized and can start after approval from institutional leader with the mandatory responsibilities

8 Statistics and data analysis

Data must be analyzed in order for research results to be evaluated. A sound understanding of data processing is required in the planning, execution, and completion phases of all studies. This is essential as statistical evaluation can demonstrate whether or not the study has a sufficient number of subjects e.g. patients, or experimental animals.

The number of subjects or cell cultures required in a study depends upon a number of factors, the key term in this context being "minimum clinically relevant difference". In order to determine the "minimum clinically relevant difference" one needs to know the internal variation of the variable measured, i.e. the intrinsic variation present prior to comparing two groups. During the planning phase, the effect of the relevant variable as demonstrated in previously published papers may be used as a proxy for the "minimum clinically relevant difference". The number of participants required can be calculated using power analysis. This reduces the risk of conducting a study leading to results from which no conclusions may be drawn (i.e. an inconclusive study).

Planning and hypothesis testing

Many studies propose two competing hypotheses (for example: "The treatment provides an improvement" vs. "the treatment provides no improvement"). The hypothesis called *the null hypothesis (H0)* is the hypothesis to be rejected. The other hypothesis is called *the alternative hypothesis (HA or H1).* The hypotheses must be well defined in order to conduct *a statistical hypothesis test*. A hypothesis test determines whether the null hypothesis should be accepted or rejected. When performing the test, two types of errors may occur: a rejection error *(i.e. a type I error),* or an acceptance error *(i.e. a type II error)*:

		Test result	
		H0 accepted	H0 rejected
Reality	H0 true	Correct	**type I mistake**
	H0 false	**type II mistake**	Correct

The goal is to reduce the risk of both types of errors. These risks can be calculated for a given data set and a given test. Studies are often planned such that *the risk of a rejection error (significance level, α)* is set for example at 5%, and *the risk of an acceptance error (β)* is set for example at 10%. Increasing the number of observations (patients, cell cultures etc.) will often reduce the risk of erroneous conclusions. The necessary number of observations may be calculated by power analysis. This calculation requires an estimate of the least amount of change observed that would still equal a relevant difference between the groups being compared, the known or anticipated variation in outcome, and the predetermined significance level, α, and acceptance level, β.

Once the necessary data has been collected, a statistical hypothesis test may be carried out. This is usually performed using a statistical program, and the result is provided in the form of *a p-value (the probability that the result could have occurred randomly, p=probability).* The rule is that the null hypothesis *is not rejected* if the p-value equals or is larger than the significance level ($p \geq \alpha$), but is rejected if $p < \alpha$, for example if $p < 0.05$. The statistical test examines the probability of the obtained results (or more extreme results) if the null hypothesis were true. This probability is expressed by the p-value; the lower value- the less likely that the null hypothesis is true (Laake P et al. Epidemiologiske og kliniske forskningsmetoder. Gyldendal Akademisk 2007). If the null hypothesis is rejected, we express that there is a statistically significant difference between the tested groups. It is recommended that statistical significance is assessed by confidence intervals and to avoid relying solely on p-values (Veierød MB et al. Medical statistics in clinical and Epidemiological research. Gyldendal Akademisk 2012).

Statistical Analysis Plan (SAP)

A description of statistical analyses, including interim analyses are often gathered in a protocol or statistical analysis plan (SAP). Many attractive journals will favor articles submitted with a SAP (Gamble C et al. Guidelines for the Content of Statistical Analysis Plans in Clinical Trials. JAMA 2017;318(23):2337-43).

Selection of statistical tests

The type of statistical hypothesis test that is appropriate to use depends on the type of data as well as the scientific question. One must know whether to use parametric tests (in the case of a Gaussian distribution of a variable i.e. with a normal distribution), or non-parametric tests (for variables that do not have a normal distribution in the observed population).

It is necessary to be critical when determining what constitutes a clinically or biologically significant difference between groups. A statistically significant difference is frequently found between groups, without a biological significance. If a large number of individuals or experimental subjects are included, a small and unimportant biological difference may result in a statistically significant difference. Likewise, statistically significant associations or differences may arise if many variables are tested after completing a study, simply because of the large number of parameters being analyzed. The requirements for statistical significance increase if multiple variables are tested (cf. the Bonferroni correction). If multiple hypotheses are to be tested, this needs to be considered at the planning stage as well as when determining the significance level and the size of the study.

Most biomedical publications contain a section describing the use of statistical analyses, detailing the above mentioned factors. The choice of experimental study design (e.g. randomized, controlled, blinded, open - see Chapter 8), data analysis methods (e.g. t-test, non-parametric tests, ANOVA), data tools (e.g. SPSS, Excel, SAS, EpiData), choice of significance level (α), and how the size of the sample has been calculated (based on power analysis) should be discussed in this section. Such statistical considerations must be completed before the study commences. The researcher him/herself should have a good grasp of this information. However, in planning large studies, it is important to seek advice early from statisticians or epidemiologists.

Courses

Universities arrange research courses for their PhD students. Many of the newly established "research schools" (forskningsskoler) will offer research courses of a more specific nature. Some of these courses focus solely on statistics and include training in data processing.

Other courses provide more general insights into research, including information on how to plan a research study.

Literature

There are a number of books available, spanning a wide range in terms of difficulty and detail. Books may be used as reference works and as a means of learning and understanding statistical terms and methods. The following books are frequently used by medical and health science researchers:

Svend Juul et al. Epidemiologi Og Evidens – 3rd Edition 2017, Munksgaard Denmark. (in Danish).

Altman DG. Practical statistics for medical research. Chapman & Hall 1991.

Aalen O et al. Statistiske metoder i medisin og helsefag. Gyldendal Akademiske Forlag. New Edition 2018.

Ejlertsson G. Grundläggande statistik med tillämpingar inom sjukvården. Studentlitteratur; last Edition 1998.

Field A. Discovering statistics using IBM SPSS Statistics. SAGE Publications 2017 (also available for the statistical programs R and SAS).

Gamble C et al. Guidelines for the Content of Statistical Analysis Plans in Clinical Trials. JAMA 2017;318(23):2337-43

Kirkwood BR and Sterne JAC. Essential Medical Statistics. Wiley 2003.

Laake P et al. Epidemiologiske og kliniske forskningsmetoder. Gyldendal Akademisk 2007.

Rothman K. Epidemiology; An introduction. Oxford University Press 2012.

Veierød MB et al. Medical statistics in clinical and epidemiological research. Gyldendal Akademisk 2012.

Data programs for setting up databases and analyzing results

A number of software programs are available for storing and processing data. The programs used depend on factors such as availability at the institution the researchers are affiliated with, personal preferences, and the nature of the study.

At OUS, Viedoc is the only approved IT solution for data collection which meets the ICH-GCP requirements. Viedoc is suited for research projects, but not for quality registries. Please contact CTU at OUS Research Support Department if you wish to use this clinical data management solution.

Microsoft Excel is available at most institutions. The program is easy to learn and use, and courses on Microsoft Excel are frequently arranged. The program is, however, not suitable for advanced statistical analyses, and the graphics program is not ideal.
SPSS (originally Statistical Package for the Social Sciences) software is user-friendly, high in quality, and comes with the appropriate manuals. Universities in Norway now favor teaching STATA instead of SPSS at any PhD statistical courses. *STATA* (a syllabic abbreviation of the words statistics and data) is taught at the statistical introductory PhD courses in Norway .
See more: Resources for learning Stata.

EpiData is the database recommended by WHO. It is well suited for most clinical studies and can be downloaded free of charge here.
EPI Info is another useful program well suited for questionnaires, database building and some types of statistical analyses in epidemiological studies. The program can be downloaded free of charge here.

Other statistical programs:

The Comprehensive R Archive Network

Medcalc

NCSS

SAS

Tibco Spotfire

Some statistics programs also contain excellent graphic tools. However, specific scientific graphic tools can be purchased separately, such as *Sigmaplot* and *Graphpad Prism.*
NVivo is a program for analysis and presentation of data obtained using qualitative methods.

Assistance from statisticians or epidemiologists

University hospitals and other research institutions have qualified statisticians and epidemiologists with medical expertise. It is recommended that researchers contact such

specialists as early as possible in the planning stage of a study and continue to seek advice from a statistician as the study progresses. It should be discussed and agreed upon in advance whether the statistician is to be a co-author (the Vancouver “rules” on co-authorship must be followed, see Chapter 9), receive payment or be acknowledged in the planned publication(s). Oslo Centre for Biostatistics & Epidemiology (OCBE), a part of Regional Research Support, offers assistance to researchers in the south-eastern health region of Norway.

Bioinformatics

Many research projects within biomedicine utilize biotechnological methods that generate large amounts of research data, requiring sophisticated biostatistical work. Specific expertise in the field is often available at the major research institutions.

9 Publication

Publication forms

Scientists have a moral obligation to share their results with others, also when study results differ from those expected. This is made clear in the Declaration of Helsinki: *"Negative as well as positive results should be published or otherwise made publicly available"* (§36). The Health Research Act also requires that the Research Director ("forskningsansvarlig") and Project Manager ("prosjektleder") ensure transparency in research by making research results publicly available (§ 39).

Publishing scientific results is a significant part of the research process and in doing so researchers contribute to the common fund of knowledge. The publication of results and methodology is a prerequisite for scientific debate. Publishing enables replication of a study and comparison of results with those of other studies.

During the process of writing and summarizing results it is important to bear in mind the context in which the results are to be presented. Publishing a scientific paper is not the aim of every research project. Some may wish to report the results in a local setting or at an internal meeting only, whereas many researchers will present a poster or oral presentation at international conferences and submit a scientific paper to a medical or health sciences journal. The content of a lecture and the type of presentation will also differ according to whether it is to be a relatively comprehensive lecture in a hospital department setting or a ten-minute presentation at a scientific conference.

It is important to consider to which journal the paper will be submitted. Follow the guidelines of the journal or the conference organizer at all times, as this will make the paper formatting easier. Also bear in mind the reader of the paper; i.e. whether it will be the world's leading researchers in the scientific field or colleagues in a hospital department who have never heard of the subject before. Adapt the form and content of the message accordingly.

Writing a scientific paper

Scientific papers follow a standard format (e.g. requirements regarding characters and number of words etc.), which is described in the "Instructions to Authors", usually on the website of the relevant journal. These must be adhered to. Reading other papers in the journal is of benefit with respect to becoming familiar with the required format. The Vancouver Convention ("rules") describes authorship with respect to publication of articles.

Title

The title should indicate the content of the manuscript, attract the attention of the reader and must be in the format of the journal in question.

Abstract (summary)

Follow the format in the journal's "Instructions to Authors". See this overview with links to the Guidelines for Authors of a number of journals.

Introduction

Describe the background for the study and the scientific question being investigated. What information is currently known and where are the knowledge gaps? The introduction should culminate in the main question being posed by the study. "The aim of the study" should be concise and describe in concrete terms how the question is to be answered (see Chapters 4 and 6 about aims). This is perhaps the most important part of the paper and will govern how information is presented throughout the remaining part of the article. The aim of the study may be divided it into a primary objective (aim) and secondary aims. A description of the study's hypothesis is often desirable.

Materials and methods

These need to be described in sufficient detail for other researchers to be able to replicate the reported findings. Laboratory methods should indicate the coefficient of variation of the applied method. Describe which patients/informants/experimental animals/cells etc. were included in the study, the number of included subjects, the inclusion and exclusion criteria, and the outcomes being measured. Choice of statistical analysis method should also be indicated; this is often done in a separate paragraph. Many journals restrict the length of the

methods section, making it difficult to describe the methods in sufficient detail. In such cases, including supplemental materials might be a way to cover details that do not fit in the manuscript itself; check the “Instructions to authors” to see if this is possible.

Results

First, present the main findings of the study, potentially with important background data for the study population. Next, present the results of the secondary (or following) aims. The main findings can often be presented in a figure (demonstrating the most interesting points), but bear in mind that figures, tables and text are meant to complement each other, not overlap. Do not include too many figures and tables. Consult the “Instructions to Authors.” Findings should be presented objectively and not be discussed; the latter is reserved for the *discussion*.

Figures

The “Instructions to authors” will define how the figures should be presented, but tips are also available in several books and articles on how to best illustrate one’s major research findings, and how to avoid common mistakes (see literature list).

Discussion

Give a brief description of the major findings of the study. Compare them with prior relevant studies. Alternative explanations should be discussed if the results are inconsistent with previous findings. Discuss possible sources of error and potential biological mechanisms that may underlie associations demonstrated by the study. It is advisable to include a discussion of the strengths and limitations of the present study. Conclude by restating the main findings and discuss the impact these may have within the related scientific field.

Acknowledgements

In this section gratitude is expressed to colleagues who do not fulfill the criteria for co-authorship. Note that many journals require a "substantial contribution" for a person to be acknowledged. Some also require that all those acknowledged have agreed in writing to appear in the acknowledgements section. Consult the “Instructions to authors”. Financial

and other contributions (e.g. technical support) are also mentioned in this section. For cases where the researcher has financial ties to a company that is involved in the study, there are rules on how this should be disclosed.

References

Regulations governing the references one should choose in one's publications are generally lacking, except the restrictions applicable to plagiarism (see Chapter 16). It is important to refer to high quality studies that provide a balanced account of the background for your research question, preferably reporting the original studies that first described the findings. Studies that confirm such findings may also be mentioned, but not without including the original paper. Reporting thoughts, ideas and statements from others, as if they were your own, is considered plagiarism. The Norwegian Committees of Research Ethics ("forskningsetiske komiteer") has published a paper on plagiarism. Plagiarism is intellectual theft, and is regulated in Norway by "åndsverkloven", as well as by "universitets- og høyskoleloven",

A trap some researchers fall into is to cite someone else's citation without reading the original paper or checking whether corrections to the article have been published. As a result, incorrect citations may be "inherited" from one paper to the next, and in the worst case, erroneous information is presented as fact. To complement the general unwritten consensus on use of references in science, some institutions have developed specific guidelines for their employees and students.

The way (style) in which references are presented, both within the body of the article and in the list of references, varies by journal. Adhere to the format of the relevant journal. Software programs such as "Reference Manager"/ "Endnote" are useful as they generate a database, which can be used as a source of citations during paper preparation. By choosing the appropriate "output style" for the relevant journal, the list of references and "in-text" citations is adjusted in the correct format. A new "output style" can be generated and saved for later use, by editing an existing similar format (see Chapter 5).

Reporting guidelines

The guidelines listed below should be followed where appropriate, and to structure your article.

CONSORT Statement

For reporting of randomized controlled trials: please use the appropriate extension to the CONSORT statement, including the extension for writing abstracts

SRQR

For reporting qualitative research

COREQ

For reporting qualitative research

STARD

For reporting of diagnostic accuracy studies

STROBE

For reporting of observational studies in epidemiology

Checklist for cohort, case-control, and cross-sectional studies (combined)

Checklist for cohort studies

Checklist for case-control studies Checklist for cross-sectional studies

PRISMA

For reporting of systematic reviews

PRISMA-P

For reporting of systematic review and meta-analysis protocols

PRISMA-ScR

For reporting of scoping reviews

MOOSE

For reporting of meta-analyses of observational studies

SPIRIT

For reporting protocols for RCTs

STREGA

For reporting of gene-disease association studies

TRIPOD

For reporting of studies developing, validating, or updating a prediction model, whether for diagnostic or prognostic purposes.

ACCORD

For reporting of consensus studies

CHEERS

For reporting of health economic evaluations. The EQUATOR Network (Enhancing the Quality and Transparency Of Health Research) provides a comprehensive list of reporting guidelines.

Choice of journal and Open Access

A supervisor will often have valuable insight with the scientific profiles of relevant journals and what target audiences a paper should aim towards. Many consider the "impact factor" of a journal to be important, since this indicates citation frequency and number readers. However, high impact factor is not synonymous with high scientific quality. Although many journals catering to narrow clinical subspecialties may be of very high quality, they will have a lower impact factor than journals with a wider audience (such as journals on cardiovascular disease, cancer etc.). Which journals you publish in plays a role in the evaluation of future applications for grants and academic posts; and research institutions receive research funding based on the journal and number of publications (see below). Information about the impact factor of various journals is found in the JCR (Journal Citation Reports), which contains all journals that are part of Web of Science, a comprehensive article and citations database.

The DORA Declaration (the San Francisco Declaration on Research Assessment) was signed in 2018 by many research institutions in Norway, including OUS and the Research Council of Norway. The Declaration aims to improve the evaluation of research results by avoiding the use of the journal`s Impact Factor or other magazine-based indicators as a measure of the quality of individual articles. So far, the statement has been signed by institutions in 145 countries and by more than 19,000 single researchers.

Publication in "**Open Access**" journals has been rapidly increasing since the 2000s, and means that articles are freely available online without subscription. These journals also use peer review, and the quality of journals and articles vary, in the same way as subscription-

based (and printed) journals. It is becoming a requirement in many parts of the world that research conducted using public funds should be freely available on the web. However, someone has to pay the costs of publishing these Open Access journals, and often it is the authors themselves (or their employers) who have to pay. UiO requires Open Access available papers from their scientists. One way to achieve this is for UiO to publish the "postprint" version (the latest version from the author to the journal before the final version) after the agreed embargo time. The Research Council of Norway supports Plan S, which requires full "Open Access" publication without embargo time from 2021 and onwards. In the mandate for the Regional Health Authorities in 2019, the Ministry of Health and Care Services has stated the following, as a follow-up of Plan S: "The Regional Health Authorities shall ensure that all scientific articles based on research funding from the Regional Health Authorities shall be openly available from 1st of January 2021". See also Openscience.no (Norwegian site), that provides guidance on how to identify relevant Open Access journals in relevant fields for the researcher, through "advanced" search in "kanalregisteret".

From 2019, the University Libraries in Norway have negotiated agreements with several publishers, meaning that many researchers in Norway (including employees at OUS and UiO) can publish "Open Access" at no extra (personal) cost. The number of agreements is constantly expanding and the University Libraries can be contacted for updated information. The agreements contain a yearly number of articles where the publishing costs, the Article Processing Charges (APC), is covered. For example, agreements are negotiated with the major publishers (Elsevier, Wiley, IOP, Taylor & Francis and Springer Compact). The University Library provides details of the individual agreements.

Research data management and archiving

The University of Oslo provides help and services on managing research data. In addition to dealing with data protection and privacy, data management also encompasses documentation, organization, licensing, sharing, and archiving data. It helps improve reuse of data, reproducibility and can contribute to making your research more visible. In order for research data to be understood and used by more people and also in the future, they must be described and stored in such a way that this is possible. FAIR

(Findability, Accessibility, Interoperability, and Reuse of digital assets) is a set of principles that will ensure that this is possible to the greatest extent possible. Useful tools for data management can be found at the Norwegian Research Council and NorCRIN.

Authorship

The Vancouver criteria for authorship (Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals), published by the International Committee of Medical Journal Editors (ICMJE), contains guidelines regarding authorship rights in biomedical journals. Over 500 medical journals follow these rules on authorship.

ICMJE defines an "author" in a biomedical journal as "*someone who has made substantive intellectual contributions to a published study*…". To be defined as an author, the following four criteria must be satisfied:

1. "*Substantial contributions to conception and (or) design of the work, or the acquisition or interpretation of data for the work, or analysis and interpretation of data".*

2. "Drafting the work article or revising it critically for important intellectual content".

3. "Final approval of the version to be published".

4. "*Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved".*

Each author must fulfill all the criteria. Please note the requirement for "substantial contributions" in criterion 1.

According to the Vancouver Convention, authors are recommended to submit a description of each author's contribution to the editor (in the submission of a PhD thesis a detailed description of authorships such as this will be required by the University). For details, consult the Guidelines for Authors for the relevant journal.

Any person contributing significantly to the work without fulfilling authorship requirements may be acknowledged, and their contribution briefly described. Multi-centre authors must individually satisfy requirements for authorship. According to the Vancouver “rules”, the order of the authors should be decided jointly by the co-authors. Authors must also be prepared to explain the order of authors and the contribution of each co-author. A spirit of positive collaboration is essential should any problems arise in discussions on authorship. PhD candidates should have a contract defining their relationship with their supervisor. In addition, a supervisory institution that can assist if any problems arise, should be named (for example the Director of a research department). Other than this, there are few rules and little formalized support structure governing cases of conflict. However, discussions of authorship early in the research process may prevent conflicts by avoiding misunderstandings, shattering of expectations, and damage to the scientific collaboration (see Chapter 14).

In general, it may be wise to be generous in offering co-authorship, and similarly wise to decline such offers if the requirements for co-authorship are not fulfilled. Co-authorship entails not merely prestige, but also responsibility for the scientific content of a scientific paper. Shared authorship (for example, first or last authorship) can be used if this is appropriate in papers with a large scope of work. The Vancouver rules do not provide specific guidelines regarding shared authorship. However, the Universities in Norway have set limits on the number of papers that can be used in more than one doctoral dissertation. This should be clarified between the supervisor and the PhD candidate at an early stage.

Crediting/addressing

In 2024, a new national platform, CRISTIN/NVA (Norsk vitenarkiv), will be launched in Norway, replacing CRISTIN and the local science archives. The purpose of this state-funded platform is to make openly accessible scientific literature financed by public funds. This new system will provide with an overview of Norwegian research, make publications openly available and also facilitate the reuse of metadata. The existing research documentation system, CRISTIN (Current Research Information System in Norway) will be replaced but still be accessible for a period in reading-only access. Scientific publications and doctoral degrees

will be reported through this new system. Data from this joint system is the basis for results-based research funding in the healthcare and institute sectors.

This database will also list REK- approved projects. However it will be accessible from the CRISTIN site during the transition period.

Researchers are responsible for their publications being registered in Cristin/NVA (Norwegian Science Archive). Each year, the research institutions are responsible for checking affiliation and metadata for their articles within certain deadlines. Researchers in the university and university college sectors often have the 31st of January as the deadline for logging in, checking and finalizing the publication list for the previous year in Cristin/NVA.

Researchers credit institutions for their work by publishing the address of the relevant involved institution(s) on the scientific work and publication. It is important to note that such credit can be given regardless of employment.

The National Strategy Group for Health Research (“Nasjonal samarbeidsgruppe for helseforskning”, NSG) has discussed guidelines for publication crediting, and has concluded that it is the author who decides crediting, on the basis of the following general rules:

1. *An institution should be credited and its address included in the publication if it has provided a necessary and essential contribution to the performed work.*
2. *The same author should also provide addresses of other institutions if they also meet these requirements. Other contributors may be named in "Acknowledgements".*

It is appropriate to provide the address to a hospital if the research is conducted at and/or funded by the regional health authority and/or health trust (e.g. hospital). In assessing whether the research is "conducted at" a specific hospital, the use of biological materials and/or health data from hospital patients (e.g. medical records), use of medical equipment at the hospital and other infrastructure such as IT equipment and facilities should be heavily weighed. If the research is fully or partially funded by a regional health trust, the corresponding hospital’s address should be included, thereby crediting it.

Some research institutions have signed local collaboration agreements for scientists who work both at the university and at the health trust, such as OUS and UiO. Researchers should check what is considered the correct address to use before submitting a paper for publication. When crediting several institutions, the crediting must for practical reasons either stand as separate addresses, or have a *semicolon* or *and* between the two addresses (e.g. Oslo University Hospital and University of Oslo). The general rule is that all PhD candidates who are accepted at the UiO PhD program must credit UiO as at least one of their affiliation in all publications. The candidate may have several affiliations, but UiO must be one of them.

Duplicate publication

Duplicate publication refers to publication of original results twice. Usually this would entail publication in two journals. However, some journals do not even accept published abstract reports prior to publication in the journal. This must therefore be verified in advance to avoid spoiling one's chances of publication in the more prestigious journals. Most journals will however accept a poster or oral presentation at international conferences prior to publication of a paper. Bear in mind that if journals suspect or discover attempts of duplicate publication, this will lead to sanctions such as barring further submissions in the relevant journal for a specified period of time. Some journals accept duplicate publication (often known as secondary publication), as long as this is stated up-front. One example is the Journal of the Norwegian Medical Association, which may be interested in a Norwegian language version of interesting data previously published in an international journal.

Guidelines regarding duplicate publication/overlapping publication are found in the Vancouver agreements. In addition, most journals have clarified their views on duplicate publication, e.g. what is acceptable in terms of abstracts at international meetings etc. prior to publication. Read the Instructions to Authors carefully before submitting a paper to a journal.

Commercial industry ("sponsors"), conflict of interest, and publication

Most research institutions have standard contracts for collaboration with sponsors in research projects, and you should get familiar with the guidelines at your institution. At UiO and “Helse Sør-Øst”, as well as Nordland Hospital Trust and the University Hospital of North Norway, Inven2 negotiates and manages contracts with the sponsor, in collaboration with the Principal Investigator/Project Manager. Inven2, or similar Technology Transfer Offices (TTOs at other Norwegian universities, could help assessing contracts with sponsors, particularly with respect to the rights of access and publication of results. The researcher may otherwise find that their attempt to publish is hampered by the sponsor if the latter does not wish to have the results published.

According to the Helsinki Declaration, both authors and publishers have ethical obligations with respect to publishing research results. Both negative and positive results must be published or otherwise made available to the public. Disclosure of funding, institutional links and any possible conflict of interest must be stated in the publication. Disclosure of ”Conflicts of Interest” includes more than possible financial ties, see the recommendations made by the Vancouver group. In general, it is preferable to openly present any possible factors that may impact one’s ability to be objective and neutral in one’s research and publications, and rather enable the journal (and its readers) to decide whether these factors could have influenced the research. The ethical reflection on any potential ”conflicts of interest” should be undertaken by the researchers already during the planning phase of the research project, and not solely as presented as a ”disclosure” when submitting the paper to a scientific journal. Bear in mind that REK does not approve studies with publication restrictions, such as restrictions imposed by a "sponsor", where the committee evaluates such restrictions to be in conflict with the Helsinki Declaration (§36).

Peer review

Peer review of submitted papers is standard for all renowned journals within medical research. Peer reviewing implies that the editors ask independent peers (not employed by the academic journal) within the field of research to evaluate critically the submitted manuscripts. Many consider this form of evaluation to be an extension of their academic work and a means by which to receive considerable useful feedback to improve the paper.

The aim of peer review is to assist the editor in deciding if the manuscript is suitable for publication, and also whether further information is required or other analyses are necessary prior to publication. The number of peer reviewers used for each manuscript and the emphasis placed on their judgment varies between journals, and depends upon the submitted paper. The Vancouver group has a description of the peer review system and recommendations.

There are no uniform conventions on how authors should respond to feedback from editors and to the judgments of peer reviewers. Naturally, many researchers are disappointed if their paper is rejected. In the cases where the authors are given the opportunity to reply to questions and amend the paper accordingly, many find that their manuscripts eventually are approved for publication. All questions should be answered in detail, and the Instructions to Authors will often outline how to do this. Keep in mind that most papers improve after revisions based on peer reviews.

Registering clinical trials

Internationally

The journals affiliated with The International Committee of Medical Journal Editors (the Vancouver-group) require all clinical trials that prospectively randomize research participants in treatment or control groups, to be registered prior to study start. Drug trials submitted and approved under the Clinical Trials Regulation (CTR) will automatically be registered in the Clinical Trials Information System (CTIS), which is one of several internationally recognized databases (see section 6.8). All other types of clinical trials are also expected to be published in databases, and the most common database/website is ClinicalTrials.gov (directed by NIH; US National Library of Medicine). Familiarize yourself with the guidelines at your institution. Note that the participation of patients in the US may require the study to be registered in ClinicalTrials.gov even if the study is already registered in CTIS.

The Project Manager should also register the results of the study in the same database within a year after study completion (last patient last visit). In the EU Clinical Trials Register,

the Project Manager has to remember to register the results by his/her own (see section 6.8).

ClinicalTrials.gov labels the study with a reminder, informing that the study is not completed if the researcher does not submit the main results. Publishing results improves data transparency, and reduces the risk of hiding “unwanted” findings.
Certain research funders, e.g. Stiftelsen Dam, assumes that a study financially supported by them will be registered and peer-reviewed in a journal that will later publish the results, a so-called "Registered report".

Nationally

The national registry of research projects is available at CRISTIN (the information is imported from REK) until the new information system Cris/NVA replaces it. In addition, the Data Protection Officer (“personvernombudet”) has its own registry of ongoing studies in the institution, which is automatically updated when the project is submitted to the Data Protection Officer. All studies that recruit patients should also be publically announced by one of the participating hospitals in the study, making it available through the Norwegian hospitals’ websites search function, and at helsenorge.no. Registration should happen before inclusion of the first patient, at the latest, by filling out and sending a form to the Department of Communication at your hospital. The same department should also be notified when inclusion is completed, or if there are changes in the study, for instance in participating (Norwegian) institutions. Studies that are not recruiting patients may also be registered.

Literature

Scientific writing

Booth WC, Colomb GG og Williams JM. The Craft of Research. Third Edition University of Chicago Press 2016.

Friis S og Vaglum P. Fra idé til prosjekt. En innføring i klinisk forskning. Tano Aschehoug 1999.

Hofmann A. Scientific. Writing and Communication: Papers, Proposals and Presentations. Oxford University Press 5.utgave 2023.

Laake P, Reino Olsen B og Benestad HB (red.). Forskning i medisin og biofag. Gyldendal Akademisk 2008.

Moher D, Schultz KF, Altman DG. The CONSORT statement: revised recommendations for improving the quality of reports of parallel-group randomised trials. The Lancet 2001; 357: 1191-4.

Schultz KF, Altman DG, Mother D. CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. PLoS Med 7(3): e1000251.

Turabian KL. A. Manual for Writers of Research Papers, Theses, and Dissertations. University of Chicago Press 9. utgave 2018.

von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for improving observational studies. The Lancet 2007; 370: 1453-7.

Other relevant reading

Nylenna M. Publisere & presentere - Medisinsk fagformidling i teori og praksis. Gyldendal forlag 2015, 2.utgave. ISBN: 978-82-05-49012-3.

Weissgerber TL, Milic NM, Winham SJ, Garovic VD (2015) Beyond Bar and Line Graphs: Time for a New Data Presentation Paradigm. PLoS Biol 2015; 13(4): e1002128

10 Research supervision

Aim

The purpose of research project supervision is to ensure that the person being supervised, regardless of the candidate's background or level of ambition, will be able to carry out the project in the best possible manner. A supervisor should give expert advice, already during the early stages of the project. Although not all research projects are designed to lead to a doctoral degree, formalized agreements on PhD supervision could serve as a good example for other types of supervision.

Most universities and university colleges have specific supervision agreements and programs; see for example the regulations for PhD at the University of Oslo. Supervision should lay the foundation for the development of a PhD thesis that will prepare the candidate for future independent research activities and work in the scientific community at large, both of which require academic expertise. Doctoral studies require independent research within a specialty field, and the goal is to produce a thesis of high academic quality. In addition, doctoral candidates are to receive advanced training in methodology and theory to ensure academic depth and width and to provide a framework for the field at hand. The doctoral candidate should also receive training in how to communicate academic work and scientific results. The training program should be planned and carried out in consultation with the supervisor.

Candidates are expected to fulfill certain requirements with respect to work effort, PhD course attendance etc., as well as complying with deadlines from the supervisor for efficient progression of the project. Both parties, the candidate and the supervisor, can terminate an agreement if the terms are not being met, but flexibility and skillful consideration is an advantage.

Contracts

Acceptance to a doctoral program is formalized in a written agreement. The agreement between the doctoral candidate, the supervisor(s) and the school/faculty/institute states the rights and duties of the respective parties. The agreement states the subject of the thesis,

the time period of the agreement, a plan for financing, the nature of the supervision, the place of work, and possibly also a PhD course plan.

Choosing a supervisor

PhD work is to be supervised by a main supervisor, and one or several co-supervisors. At UiO the main supervisor is normally a UiO employee, and affiliated with the faculty where the candidate is admitted. If relevant arguments are presented, an external main supervisor may be appointed. In such cases, an internal co-supervisor must also be appointed. Supervisor(s) must have a PhD or the equivalent expertise. The candidate and supervisor(s) are expected to maintain regular contact, in line with the guidelines for candidate supervision. In general, doctoral candidates should also be given the opportunity to have their thesis work discussed at a seminar, within the research group or in other relevant forums.

During the process of selecting a project and supervisors, we recommend that you check bibliographical databases such as PubMed to find the articles the supervisor(s) have produced as well as to identify number of doctorates they have supervised during the last five years. If the main supervisor has not been particularly active in this respect or is new as a supervisor, the co-supervisor should have a reasonable level of research activity. In addition to the question of expertise, it is important to know something about the supervisor's character, as well as her/his abilities to create a good working environment. Ample supervisor expertise and research activities are of little benefit to the PhD student if the supervisor has no time to supervise the candidate. Paired with the candidate's own abilities and motivation, a motivated supervisor is the best basis for carrying out a successful doctorate project.

Supervision

Regular contact is important in order to meet the planned deadlines. Most PhD students have regular appointments to meet with their supervisor, often approximately one hour a week. The candidates usually prepare an agenda for the meeting; they might prepare a draft of a manuscript, a table or a topic for follow-up discussion. This provides the basis for the supervisory discussion and further work. It is the supervisor's duty to give feedback and general comments about the work and progress of the project. The co-supervisor often plays

a specific role, often of methodological nature. He/she may for instance act as a biostatistical supervisor. In case of difficulties or conflicts, it is recommended that all the supervisors and the candidate meet jointly to clarify the situation and find a way forward. In some cases, supervision can also be given in groups. Good supervision is one of the most important prerequisites for a successful research project. More information about the universities' requirements for supervision and follow-up of students are found on their websites.

National Research Schools

The National Graduate-level Research Schools, supported by the Research Council of Norway, are designed to improve the quality of the PhD education by collaboration between institutions. These schools are a supplement to existing doctoral degree programs at the various institutions. In addition, the research schools should contribute to the internationalization of research education in Norway. Each Research School consists of a network of institutions that have entered into a binding cooperation on PhD education in a specific academic field. The participating institutions collaborate on PhD courses, seminars, summer schools and such, with reciprocal use of their respective laboratory facilities in fields where this is relevant. The schools can thus provide broader-based research education than each individual institution can on its own.

Conflicts

In case of conflicts of a personal and/or academic nature between the supervisor and the candidate in a PhD program, a person who has been designated to take on responsibility for resolving such matters is available at each institution. Any conflicts are generally handled with the nearest superior. The Institute leader is responsible for follow-up of such cases, and the medical school (faculty) has the final responsibility. This only applies to formal agreements for PhD studies. Sometimes problems arise regarding supervision or questions about authorship, credits, and other difficulties that need an unbiased assessment.

More information

- **University of Oslo:** information about PhD supervisor roles.
  More about the PhD-program at UiO.
- **Courses on University-level pedagogy** are offered at all Universities.
- **Courses on research leadership** are held at several Universities in Norway (such as at UiO, as well as at Copenhagen Business School).
- **Courses on ethics**: See Chapter 16 of this Research Handbook, and the Research Ethics Library.
- **Research regulations and responsibilities:** See Chapters 6 and 10 of this Research Handbook and the Norwegian Health Research Act guidelines.
- "**Successful Supervision, A Dialogue Facilitator**" from the Karolinska Institutet, Sweden. This is a practical guide, made to help the supervisor and PhD candidate to define expectations and roles and to help develop realistic research project plans.
- **Research supervision books in Norwegian**
  Lauvås P and Handal G. Forskningsveilederen. Cappelen Akademisk forlag 2006.
  Dysthe O and Samara A. Forskningsveiledning på master- og doktorgradsnivå. Abstrakt forlag 2006.
- **"Downhill tracks" for PhD students and for supervisors**, see Appendix 8 and 9, based on slalom ski-tracks; includes tips for all stages of a PhD research project.

"Forskningsombud" at the Institute of Clinical Medicine, UiO and the Oslo and Akershus University Hospitals: provides guidance and advice to researchers that are in difficult research ethics situations, including PhD student conflicts. See Chapter 14.

11 Financial support and resources

A number of institutions, grants and endowments can finance research projects, completely or partly. There are four levels in Norway for these sources of funding: an international (e.g. EU), a national, a regional (health regions, universities) and a local level (hospitals, institutions, departments). International, national and regional sources of funding have in general greater financial resources than local funding sources. However, local sources of funding for research projects should also be pursued.

The numbers of grants for research funding are declining in Norway, as several funding sources increase the grant money per project. The regional health trusts and the Dam Foundation (previously named Extrastiftelsen) still provide individual grant opportunities. In general, there are several types of calls, and the availability of these grants vary between institutions and regions:

- Personal grants (for example PhD grants or recruitment grants)
- Grants to a research group (may also be PhD grants - the research supervisor or the research group is awarded a grant before a PhD candidate is identified)
- Short-term special grants (e.g. to buy time off from clinical work to enable completion of a project)
- Postdoctoral grants (grants awarded after a PhD has been completed)
- Career grants (grants for research above the level of postdoctoral work to support talented researchers; top-level research)
- International mobility grants (grants to promote international collaboration through training and methodological development)
- Grants specifically for expenditures (often called operations costs and equipment costs) and/or to cover technical/nursing staff (often a supplementary or secondary section in most applications, but may also be the main section of applications for endowments and funds)
- Grants for attending conferences: often towards travel expenses, living costs and conference registration fees; may be a supplementary or secondary section in many

types of grant applications, but may be the main section of applications for small endowments and funds. A researcher's own institution may often finance this.

International sources of funding

The European Commission has grants available for international (European) collaborative research projects and for research leadership. The EU also has grants for mobility and career development (Marie Sklodowska Curie Actions), as well as for individual and collaborative research projects (see European Research Council).

Horizon Europe, EUs framework program for research and innovation, aims to ensure that European research, technological advances, and innovation lead to good solutions to shared challenges in the future. Cancer, adaptation to climate change, climate-neutral cities, healthy oceans and waters, and soil health and food are the five mission areas in Horizon Europe. Horizon Europe builds on the previous EU program Horizon 2020, with a budget of 95 billion euro for the 2021-2027 period. Norwegian researchers can apply for these grants on equal footing as researchers elsewhere in Europe. The Norwegian authorities and the Research Council of Norway strongly encourage Norwegian researchers to apply for such funding. It is possible to apply for both individual project grants/stipends as well as for grants for collaborative projects between various research groups in various countries. Large research institutions receive help with the application process.

Other international grant websites

- https://www.nordforsk.org/no
- http://www.novonordisk.com/
- https://era.gv.at/directory/143
- http://eeagrants.org/
- http://www.cost.eu/
- http://www.gatesfoundation.org/
- https://www.nih.gov/grants-funding (the world's largest public sponsor of biomedical studies).

National sources of funding

1. The Research Council of Norway **("Forskningsrådet")** finances research at all levels. The primary emphasis is on large-scale, self-initiated projects (with total budgets of approx. NOK 10-12 million) including top-level research programs and postdoctoral grants. Larger projects may include PhD grants, although these are now mainly channeled through universities and regional health authorities. See their website for further details.

2. National Program for Clinical Treatment Research in the Specialist Health Service **(KLINBEFORSK)** is a national initiative for clinical multicenter studies in the Health Trusts. The main objectives are to offer more Norwegian patients participation in treatment testing research project, to contribute to increased coordination of competence, resources and infrastructure and to strengthen the basis for providing effective, safe and good quality health services. The program announces funding annually for multi-center studies where all health regions are represented, and with a budgetary framework of approx. 5 - 20 million NOK.

3. The Dam Foundation **(former Extrastiftelsen)** consists of 38 health and rehabilitation organizations. Some of the profits from Norsk Tipping goes to voluntary organizations' projects in prevention, rehabilitation and research. It is not necessary to be a member of the foundation in order to apply for funding, but the applications must be submitted through one of the approved applicant organizations. More information about application types and requirements can be found on the website. The Dam Foundation requires that the applicant organization cover any "overhead" of its own funds.

4. Although many of the **voluntary charitable organizations** participate in the The Dam Foundation, most of them also have their own grants and call deadlines. Applications may be made for both small and large research grant amounts. Contact the charitable organizations directly; updated links to patient organizations may be found on the webpage felleskatalogen.no.

5. There are several **international grants** administered by the universities and the Research Council of Norway, with the purpose to stimulate collaboration and exchange of ideas and research competencies with researchers in other countries (see for instance UiO websites). Often, applications for foreign grants and for postdoctoral grants will support each other, increasing the odds of acceptance. Various academic organizations (internationally), have their own grants for shorter or longer research stays abroad. Search for these within the individual "societies". Additionally, at UNIFOR you can find foundations supporting research stays abroad.

6. **Center grants**. Various national and international prizes/grants are also awarded for excellence in research at an internationally recognized high academic level. At regular intervals, grants are awarded to Norwegian Centers of Excellence (SFF), and Centers for Research-Driven Innovation (SFI), and those who achieve such support are allocated multi-year financial resources, and are offered significant assistance for application writing, project descriptions and budgeting. More information on Forskningsrådet.no. Other large research center grants include KGB Jebsen.

7. **Other stipends**. There are various endowments and stipends that support research endeavors. Stipends are often limited in terms of extent and specify certain requirements for the application. See UNIFOR and Legathåndboken.

8. **Regional research grants**. The Norwegian Health Authorities have varying practices for how they advertise available grants. Most Regional Health Authorities advertise both earmarked national research grants, as well as specific regional financing, on a yearly basis. See for instance Helse Sør-Øst. In the last years, the Health Authorities have contributed with major financial support towards research at a regional level, and they collaborate with the universities in each health region. In addition, other regional funding sources exist, such as RBUP ("regionsentrene for barn og unges psykiske helse," i.e. the regional centers for child and adolescent mental health").

9. **The Universities** support research in many ways, including through funding of PhD and post-doctoral positions. The universities also give out several grants.

Research grant application support

All large research institutions in Norway provide local assistance in external fund applications. At OUS, the regional Research Support provides information about calls and funding opportunities, and helps with reviewing applications and budgets, administrative formalities, contracts and more (grants@ous-hf.no). The universities are also offering support for applications (med-funding@medisin.uio.no).

Local financial support in own research institution

Local regulations for anchoring of applications for research funding vary between research institutions. It is therefore recommended that all applicants contact local research support and financial manager for clarification, including assistance with budget proposals that take into account any rental of equipment, consumables, and salary levels (the latter including social costs and potential overhead costs). Different sources of research grants also have different rules regarding the inclusion of overhead costs, sometimes these must be guaranteed by the applicant's own institution in the application.

Useful links to UiO and OUS websites for grant announcements:

- http://www.tiki-toki.com/timeline/entry/736150/External-grant-deadlines/
- http://www.med.uio.no/english/research/news-and-events/funding/
- http://ous-research.no/calls/

Stepwise guidance from UiO and OUS on grant application:

- https://www.uio.no/english/for-employees/support/research/research-project/
- In Norwegian: https://www.uio.no/for-ansatte/arbeidsstotte/fa/forskningsprosjekt/

Tips on how to write grant applications:

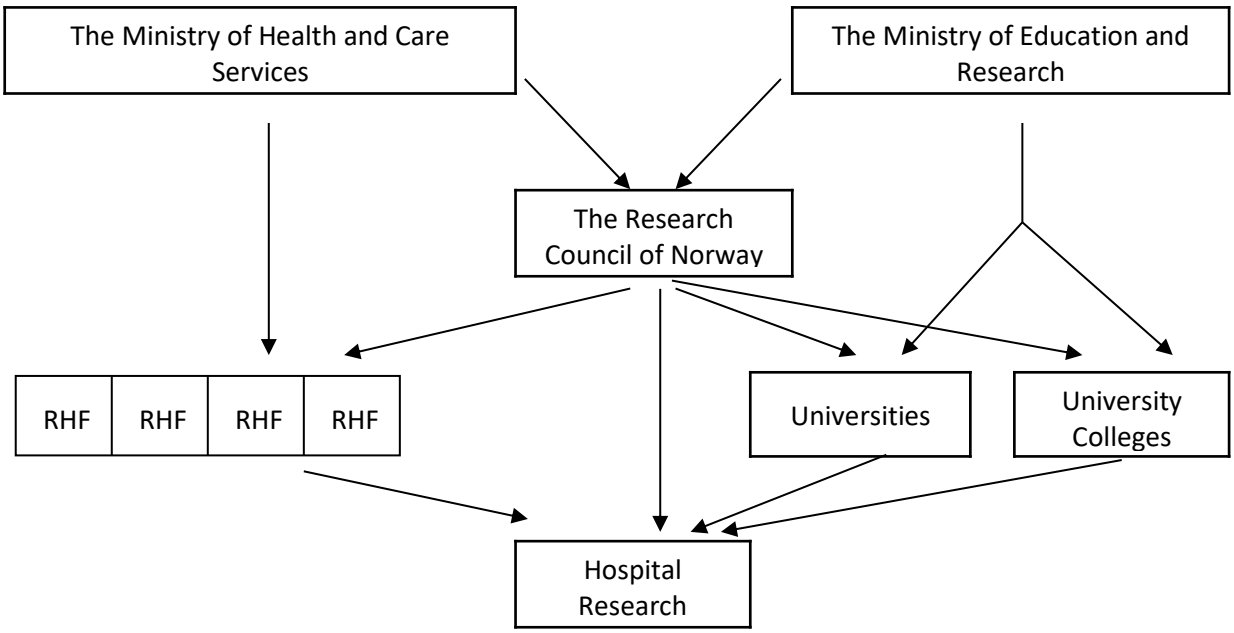
*Chasan-Taber L***.** Writing dissertation and grant proposals. CRC Press, Taylor and Francis 2014.

Regional Research Support (OUS): tips for writing applications (English text): www.ous-research.no/faq

12 Organization of research

Research is one of the four main responsibilities of health trusts in Norway, (cf. the Act on Specialist Health Services). Research activities should therefore be apparent in the business plans, budgets, and activity reports of health trusts and regional health authorities, as well as individual hospitals. The Ministry of Health and Care Services in Norway (”Helse- og omsorgsdepartementet”) provides research funding for health trusts and university hospitals of several hundred million kroner per annum. These funds are administered by the regional health authorities and cooperative bodies (”Det regionale samarbeidsorganet”) in each region. The size of the results-based portion of the funding granted to each health region (currently 70% of total funding), is based on “publication points” awarded for the number of completed PhD theses and publications in scientific journals. The research meriting system uses CRISTIN and the Norwegian Science Index (NVI), a national database on academic publishing (see Chapter 9 for more details). These will be replaced in 2024 with a new research information and science archive (Cris/NVA-Norsk vitenarkiv).

Strategies for research linked to health trusts and universities are developed both at a local and a regional level. The regional research strategies can be found on the websites of the regional health authorities. Additional national research strategies may also affect the field of medical research.



The Ministry of Health and Care Services ("Helse- og omsorgsdepartementet") is responsible for research at the health trusts, whereas the Ministry of Education and Research (”Kunnskapsdepartementet”) is responsible for research at the universities. This division of responsibility for medical research in Norway has led to several challenges.

At the organizational level below The Ministry of Health and Care Services are the four regional health authorities in Norway (RHF, "regionale helseforetak"), which have the overall responsibility for individual health trusts ("helseforetak"- HF). The Ministry of Education and Research has overall responsibility for university schools/ faculties (e.g. “medisinske fakultet”) and university colleges (“høyskoler”). Reporting procedures for the utilization of research funds allocated to the regional health authorities are established. The Ministry of Education and Research is responsible for the funding allocated to universities and university colleges (“høyskoler”). The Research Council of Norway (”Forskningsrådet”) has an intermediate position; receiving funding from several ministries, as well as from other sources.

Research at health trusts is by nature often based within research groups at university hospitals where expertise and equipment required for translational and basic science research is available. However, small hospital trusts are also required to conduct research. In addition, national or regional research competency centers are located at the university hospitals.

The regional health authorities receive instructions from the Ministry of Health and Care Services, which outline the framework and principles for research activities and regulate collaboration between regional health authorities and universities in key areas. Collaborative bodies ("Samarbeidsorganer") between the regional health authorities and the universities/university colleges exist in each region.

13 PhD studies and research options for hospital employees with a PhD

Why "do" a PhD

Over the last 10-15 years in Norway, there have been few career inducements for physicians to pursue a PhD in Medicine. Within most specialties, senior hospital positions have been relatively easy to obtain without a PhD, even at university hospitals. Furthermore, it has been more financially rewarding to be a clinician rather than a researcher. Three years as a PhD student can result in a large income drop as compared to the salary of an attending physician/consultant with on call duties. In prior years, a PhD was often a prerequisite for permanent senior employment at a university hospital.

A number of measures have been taken to increase the interest in medical research. Many hospitals have introduced an annual salary bonus for physicians with a PhD. In addition, some hospitals provide combined clinical/research posts to physicians, where a minimum of 50% of paid working hours is spent on research. This type of position secures clinical salary levels, while allowing the individual designated time for research.

The most substantial reason for embarking on a PhD program however, should be the personal motivation and your wish to enjoy the challenges involved. A PhD provides you the opportunity for in depth study of an exciting subject of your choice. Such study gives rise to a deeper understanding of a field and enables you to more effectively take in, comprehend and disseminate novel scientific ideas and knowledge in general. In addition to yielding many pleasures, research is a source of numerous challenges, not only scientific, but also personal, that one must be prepared to face. Although colleagues, supervisors and family can be a great source of support during PhD studies, a strong inner drive is essential to tackling the challenges that are likely to arise.

How to "do" a PhD

Common practice is to find a PhD supervisor, and then to apply for a PhD program at the university where he or she is employed. Formally, supervisors are appointed by the medical school after suggestions from the candidate and research groups at the institution (or the

supervisor herself/himself). In order to be admitted to a PhD program, an applicant is required to hold a relevant Master's Degree or the equivalent (5 years). For admission to a PhD program at a medical school, the applicant must have either a ”cand. med.”, ”cand. san.”, "cand. scient.", or relevant master’s degree. Applicants that possess equivalent qualifications may also be accepted; this is evaluated on an individual basis. To get accepted to a PhD program at the UiO, the average grade at the Bachelor’s degree should not be lower than C, and the average grade at the Master’s degree (and the Master Thesis) should not be lower than B. An overall assessment of the applicants’ competence and planned PhD project is made for applications from educations with none or few grades.

Approved completion of a PhD program, which includes the trial lecture and thesis defense, gives the individual the right to use the title PhD. For admission to a PhD program, universities often require documentation of research financing for at least 50% of ordinary work-hours.

The most tangible result of a PhD is usually the publication of papers in international peer-reviewed journals. The PhD work is gathered in a comprehensive, independent compilation (“avhandling”). The PhD program also includes mandatory courses/credits. The standard timeline of a Norwegian PhD program is three years. The timeline may be extended to allow for prescribed training, for instance teaching medical students. However, funding institutions usually provide funds for three years only. This is a limited period of time to complete a PhD, particularly for prospective clinical studies or animal studies.

Additional information on PhD studies

More information about the different PhD programs and requirements is available at the universities’ websites, such as at the University of Oslo.

PhD on track: a resource for new PhD students. This website is a collaboration between several contributors, including the University Library of Oslo, the University of Bergen and the Norwegian School of Economics (”Norges Handelshøyskole”).

PhD and supervisor tracks

The Research Handbook has made a "PhD track" for PhD students at the Faculty of Medicine (i.e. the medical school) at the UiO, presented in the Appendix. The track outlines the major steps on the road to the PhD disputation and can easily be adapted to other Norwegian universities and other faculties. In addition, the Appendix presents a "Supervisor track" in the Appendix, with tips for supervision and distribution of tasks between the supervisor and the PhD student.

PhD points/credit

NIFU ("Nordisk institutt for studier av innovasjon, forskning og utdanning") awards PhD points to an institution or health trust based on the following criteria: "The criterion for reporting a PhD degree, is that 50 percent or more of the PhD work is performed at or financed by the institution. This criterion implies that two or more institutions partaking in the pole cannot report the same PhD. Normally, employment and funding is stated in the supervision contract. It is the candidate's, not the supervisor's, work and effort that must meet the PhD criterion for affiliation to the institution. The PhD work may be both internally and externally financed. The criterion means that one PhD thesis normally only can be credited to one institution. The exception is when the PhD studies have involved equal cooperation between two institutions, in which case, the PhD degree points may be shared".

Awareness of the rules for awarding credit for a PhD is important when starting a collaborative PhD project. The intent of two collaborating institutions to share the credit for a PhD thesis should be included in the contract between the institutions.

Research possibilities after completing a PhD

There are several alternatives for healthcare professionals seeking positions in which they can perform research:

- A full clinical position with research "on the side": attempted by many, but it is difficult and often results in spare time being "eaten up" by research. Funded time off from clinical work is possible with combined clinical/research positions, or through grants that may be either locally awarded (by the hospital) or by the regional health authorities.

- Full research grants (see Chapter 11): For physicians this often involves reduced income. To compensate, some doctors work extra shifts.

Possible academic research positions after a PhD:

- *Postdoctoral grants* (from 3-4 years) from the universities, the Research Council of Norway (see Chapter 11), the regional health authorities or the individual health trusts/hospitals. All postdocs at UiO should have a career plan; see the template here. The Research Council of Norway also requires such a plan for postdocs. OUS recommends similar plan.
- *Associate Professorships* ("Amanuensis-stillinger"): involves teaching.
- *Qualifying Grants* ("Kvalifiseringsstipendier")/Career Grants ("karrierestipendier") at the universities: (usually 3 years): for work used to qualify for professorship.
- *Professor II*: Usually a 20-50% position divided between research and teaching. The balance between clinical work and the professorship may be tailored.
- *Professor I*: Full-time professorship, where the main emphasis is on research and facilitating research. A 10-30% part-time clinical post at a health trust is not unusual, but this can vary.

Few positions are available at universities and university hospitals for researchers between a postdoctoral level (fixed term of years) and a professor. Very few Professor I and limited numbers of Professor II positions exist.

Career Assessment Matrix (CAM) is a tool to assist researchers in career development following a PhD, based on the European Commission guidelines. A postdoc career plan is required for grantees at the Research Council of Norway. Oslo University Hospital has revised the recommendations into an OUS-CAM tool, which may help early researchers and their research environment to prioritize their academic goals. This includes simplified tools in Norwegian and English, which can be used by postdocs and any early career researchers.

14 What problems may arise during the research process?

Hopefully, researchers at hospitals and biomedical- or healthcare research institutions in Norway experience research as a source of intellectual and personal fulfillment. Although this chapter focuses on some of the problems that can and do arise, the pursuit of ideas is undoubtedly exciting, challenging and rewarding. In short - research is fun. At times research will be challenging, fun and sometimes even euphoric, whilst at other times it can be tiring, frustrating and difficult. Attitude plays a significant role in determining «quality of life" as a researcher.

Pessimists will maintain that there are endless possibilities for things to go wrong in any research project. In addition to all problems one can foresee, things go wrong even after safeguarding. For example, the freezer (containing irreplaceable patient biological samples) and two separate alarms malfunction simultaneously, resulting in destroyed samples and three years of research wasted (a piece of advice: put the samples in two separate freezers. That way only half the batch will be lost next time).

Optimists, on the other hand, will say that one can learn from one's mistakes and that skills improve with every project (not to mention with respect to backing up data compilations electronically; not doing so has led to many research crises). Personal drive and enthusiasm, background knowledge and a willingness to implement new information and skills are important factors in promoting research. Usually more than one person is required to carry out a research project (resources, supervisors, other research collaborators etc.). The data collection stage in a collaborative project is often (relatively) unproblematic, if everyone involved displays basic politeness and has reasonable social IQ. Then the time comes for analysis and publication. Experience dictates that this is when conflicts between collaborators tend to arise.

Possible conflicts regarding authorship

Disagreement about authorship rights and the order of authorship in scientific publications is probably the most common cause of interpersonal conflict in research. The reasons for, and consequences of this, may vary. The authors of this Handbook refer to the definition and

guidelines for authorship provided in the Vancouver Conventions ("rules") and our own interpretation of these guidelines (see Chapter 7). The Norwegian Health Research Act does not regulate the question of scientific authorship. The Act's definition of rights and duties of the Project Manager ("prosjektleder") has no implications regarding options for and rights to co-authorship (see Chapter 7).

The Vancouver Conventions (see Chapter 9) state that no one is to be listed as a co-author without having made a *significant contribution* to the research. Although the Vancouver "rules" specify *who* satisfies authorship requirements for a scientific paper, they do not say anything about the *order of authors*. Usually the order reflects the contributions made by each individual to the research and the publication. However, different traditions and unwritten rules apply in different countries and research settings.

The first author is usually the person who formulated the hypotheses, performed/was responsible for the analysis/ data processing and who has contributed most to writing the manuscript.

The second author is usually the person who made the second largest contribution, and any remaining authors are listed after this. Note that some research groups write authors subsequent to the first author in alphabetic order.

The last author is usually the person who carried the overall scientific responsibility for the project. In some research institutions, leaders of research groups or heads of institutes are listed as last authors of publications, regardless of the nature of their contribution to the project. There is no support for this practice under the Vancouver Convention, unless there has been real scientific contribution to the project concerned.

A statement regarding the contribution of each author to the paper will, hopefully, reduce any conflict surrounding authorship. The Vancouver Conventions recommend that each author's contribution should be described at time of submission of an article, and some journals also publish this information with the manuscript (see Chapter 9).

The pursuit of research engenders few financial benefits in Norway and *academic recognition* and publication of results are therefore of great significance. This partially explains why conflicts that are damaging to both the research projects and the research

community may occur. Many researchers are concerned about their potential to obtain research grants in the future, and the chances of doing so are reduced if their names do not appear in a key position in the order of authors on the journal publication (either number one, two or last).

How to reduce conflicts about authorship

- Come to an agreement about the order of authors before the study commences or as soon as the aim for a study has been formulated (contingent on their contributions actually qualifying for authorship). It may seem awkward to raise the matter at such an early stage, but experience has shown it to be even more awkward later. Doing so will also clarify the roles in the project so that all parties have realistic expectations with respect to their own contribution and their "rewards" as an author.
- Be generous in offering co-authorship and equally generous in refusing any co-authorship offered. Remember that, as co-author, one must be able to justify the content of the article and declare responsibility for specific parts of the paper.
- If the premise for the research or the research activities themselves is altered in the course of the project, the question of authorship should be discussed again. It is quite common for new methods and aims to be introduced and it is thus quite reasonable to review authorship.
- Authorship is an area in which etiquette plays an important role and much is to be gained from playing with an open hand. The question of the order of authorship is, in essence, about "giving credit where credit is due". As long as collaborators agree about each individual researcher's contribution to a project, they should be able to reach agreement about the order of authors in any publication.

Potential conflicts with a supervisor

See Chapter 10 on supervision (including contracts, university involvement in supervising conflict resolution, and supervisor courses). No fool proof recipe exists for how to avoid conflicts between supervisor and candidates, nor for what type of relationship is the most productive, promotes the most independence, or is the "best". Personal characteristics clearly affect any collaboration, and it is likely fruitful to make use of potential complementary strengths. The potential for conflict can be reduced by making clear

agreements and giving reciprocal feedback. An agreed level of ambition is also important (what is the time frame of the project and do both the candidate and supervisor(s) agree on plans for project progress?). Clarify in advance how much time the supervisor has available for the candidate and whether the candidate is to have free access or access at fixed times. Schedule a set time for feedback on drafts of papers; stick to appointments to avoid wasting time and causing unnecessary irritation.

Access to research data and biobank after the PhD period

A number of factors determine continued access to research data and biological material in a research biobank after the PhD period is over:

- The nature of the employment contract and whether the employer remains the same during and after the PhD period
- The nature of the information to and consent given by the study participants who have provided data and/or biological samples to the project
- Conditions for obtaining information from existing databases (such as a medical charts and external registries), as well as conditions for use and collection of sample from existing biobanks
- Conditions determined by public authorities such as the Data Inspectorate, the Regional Committee for Medical and Health Research Ethics (REK) and the Directorate for Health Affairs.

Many research institutions have their own guidelines on access to data in health registries and biological samples. In principle, the ideal condition is that research data and biological samples should be accessible for future research by other parties. However, "protection from competitors" must also be considered. In practice the ”Data Processing Director” (“behandlingsansvarlig”) and the person in charge of the research biobanks (in the case of large research institutions this responsibility often lies at an administrative level above that of the project manager) will determine whether continued access will be granted. Proposals for new use of existing research data and/or material from research biobanks must always be submitted to REK etc., as specified by the laws and regulations described in greater detail in Chapter 6. The Vancouver Convention also places restrictions on publications based on existing biobank material. Collection of biological samples alone is not considered to be a

"substantial contribution", and is therefore not sufficient to satisfy criteria for authorship under these regulations.

What if a paper is rejected for publication?

Why are articles rejected? Identify the key problem. Peer reviewers usually provide useful comments on why they have criticized a paper and sometimes the editor will add her/his own comments. Go through the stages outlined in Chapter 3 to identify where the research project went wrong. If the study has not been sufficiently well designed, there is little chance of having papers published after the study is completed. If it is only a matter of additional analysis being required, it is common to follow the advice of the reviewers or alternatively attempt submitting the article to another journal. Whatever journal is chosen, including those with the highest impact factor (The Lancet, Cell, Nature etc.); the authors should always check the profile of the journal before submitting a manuscript, in order to avoid wasting time on submitting a paper to a journal with a different scope than the paper.

Insurance and research projects

In biomedical and healthcare research projects that involve human participants, insurance may be required.

The Norwegian System of Compensation to Patients (Norsk Pasientskadeerstatning, NPE)

The Norwegian System of Compensation to Patients is an independent government agency under the Ministry of Health and Care Services. NPE processes compensation claims made by patients and study participants who believe they have suffered an injury resulting from treatment within the private and public healthcare system. The NPE system also covers research projects in these settings.

Product Liability Act ("Lov om produktansvar") and clinical trials

The Product Liability Act safeguards the interests of patients/study participants in pharmaceutical trials. *The sponsor of a clinical drug trial is legally obliged to purchase insurance through membership in the* Drug Liability Association ("Legemiddelansvarsforeningen"), unless the project is covered by the insurance policies of a potentially involved pharmaceutical company. Insurance is obtained by contacting

unedv@bahr.no. The fee is calculated based on the number of patients included per year and may add up to a substantial amount. Confirmation of existing insurance must be sent to The Norwegian Medical Products Agency (”Direktoratet for medisinske produkter”), when applying for a clinical drug trial.

Separate insurance

If the research project is not covered by the Product Liability Act or the Norwegian System of Compensation to Patients (NPE), alternative insurance must be purchased. The relevant insurance policy should cover liability and damages regardless of culpability.

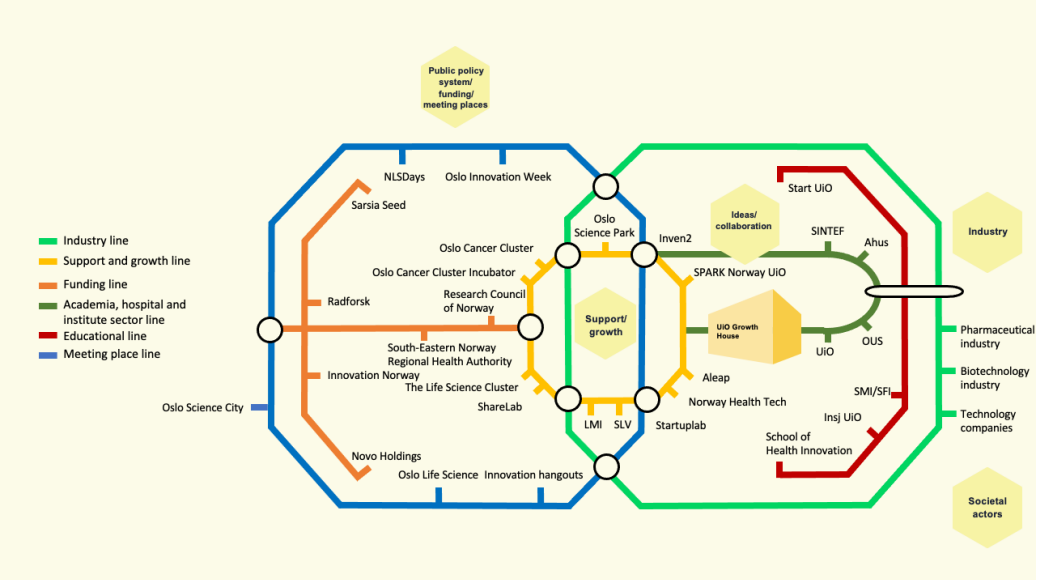
Duty to report to “Statens helsetilsyn” (Norwegian Board of Health Supervision) in cases of serious, undesirable and unexpected events in research projects

The Norwegian Health Research Act has a provision for mandatory reporting to “Statens helsetilsyn” in cases of accidents in clinical research. The act declares that "*The project manager shall promptly give written notice to the Supervisory authorities in cases of severe and unwanted or unexpected medical events that are believed to be related to the research. The project manager, other researchers, and other personnel should on their own initiative provide the Supervisory authorities information about conditions that may endanger the safety of the research participants. In cases of unnatural deaths the Police is to be notified immediately.”* The obligation to notify the Norwegian Board of Health Supervision is in addition to the regular compulsory reporting of adverse medical events internally and externally. The Norwegian Board of Health Supervision may, following inspection, give orders for the suspension of or change to the terms of a research project and research biobanks, provided they be thought to have harmful consequences for the study participants or others, or are otherwise unsuitable or unsatisfactory.

15 Commercialization and obtaining patents

At research institutions, ideas are constantly being developed, which in addition to being of great scientific interest also have commercial potential. Society has a need for research results and projects that benefit society as a whole, and in recent years, assessment of potential for innovation has become a higher priority. As a result, universities and university colleges ("høyskoler") have worked more actively in developing organizations, systems and routines that enable research results to be commercialized. There are now a number of "Technology Transfer Offices" (TTO) and research parks in Norway whose mission is to promote research ideas to the business sector in order to realize their market potential. If an idea results in commercialization, it may also provide a possible income for further research funding.

OUS and UiO employees are encouraged to engage in the development of new pharmaceutical compounds, medical devices, and other innovative solutions that can directly benefit not only the patient, but also improve the healthcare provider work tools and methodologies. In addition, an emphasis has been made during the past years for following the framework of Responsible Research and Innovation (RRI). Employees of OUS and UiO can benefit from programs aimed at facilitating the implementation and development of innovation techniques and processes, see Innovation – Knowledge in use.



The actors in the innovation system, credit UiO.

Commercialization regulations

As of January 2003, the Act on Universities and University Colleges ("Universitets- og høgskoleloven") and the Act on Employee Inventions ("Loven om arbeidstakeroppfinnelser") got a greater emphasis on commercialization of university research. Institutions may claim ownership-rights to research results that are patentable.

Guidelines exist at OUS for patenting and commercialization of innovations emerging from work carried at OUS, see eHåndbok - Kommersiell utnyttelse av innovasjoner. Employees at UiO have to follow similar steps.

InnoMed - Innovation and business development in the health sector

InnoMed, the National Network for Need-based Innovation in Healthcare ("Nasjonalt nettverk for behovsdrevet innovasjon i helsesektoren", is owned and run by the regional health authorities and KS ("Kommunesektorens interesse- og arbeidsgiverorganisasjon").

InnoMed's vision is health-based value creation that is to benefit patients and society. InnoMed's aim is to increase efficacy and quality in the healthcare sector through the development of new solutions. These should be based on national needs and have international market opportunities. The solutions are developed in close collaboration between healthcare recipients, Norwegian companies and health professionals. The Directorate of Health ("Helsedirektoratet") and Innovation Norway fund InnoMed's activities.

Patenting inventions

A patent awards the owner exclusive rights to commercial exploitation of a patented invention for a period of 20 years. For pharmaceuticals, the patent period is 25 years due to the length of time involved in the process of approving pharmaceuticals. In order to be patented, inventions must be recent and differ significantly from previous inventions. The principle purpose of a patent is to ensure competitive advantage and thereby safeguard any future revenue for the owner. Inventors have the right to a reasonable share of the revenue generated by commercialization of a patent. A patent is thus a means of rewarding researchers for their efforts and encouraging new and current inventors. Patent law protects a patented product, method or an application. However, the law prohibits patenting of

methods used in surgical treatment, therapy, or diagnostics carried out on humans or animals. Pharmaceutical products and methods of analysis may be patented. The patent law does not regulate the use of inventions in research or development settings. Norwegian patents are not automatically valid abroad and vice versa.

The primary function of the Patent Board ("Patentstyret"), a government authority organized under the Ministry of Trade and Industry, is to process applications for patent protection. On their home page you will find a guide for beginners, information on patents, forms, and patenting laws. The Patent Board offers introductory courses on patent protection at regular intervals.

For further information on applying for patents on research results, contact your local TTO (see Appendix for TTO addresses).

Useful innovation links relevant for UiO and OUS employees

http://www.med.uio.no/english/about/innovation/

http://www.uio.no/english/for-employees/support/research/innovation/index.html

Home - UiO Growth House

Innovasjon - Oslo universitetssykehus (oslo-universitetssykehus.no)

Health2B (established by Norway Health Tech, Oslo Science Park and Oslo University Hospital)

16 Research ethics, misconduct and fraud

Research ethics

Research ethics is focused on raising awareness among researchers in particular, and society at large with respect to issues that arise in modern research. There are three important research ethics categories applicable to the field of medical and healthcare research:

- Ethical standards for good scientific practice (concerning the research process).
- Ethical norms for proper research (often called protection ethics).
- Ethical standards for publication of research results (publication ethics).

Sound research ethics will increase the population's confidence in research results, individual researchers, and the research community in general. The confidence that society has in researchers and their results is a prerequisite for research funding and, in addition, it is likely to affect the recruitment of new researchers and study participants. In other words, ethical reflection and sound research ethics are a prerequisite for allowing researchers opportunities to realize their aims.

The Norwegian Health Research Act shows how central research ethics is, as the purpose of the Act is to promote sound and ethical medical and healthcare research. The Research Ethics Act from 2017 shall contribute to that research in public and private sector is conducted in accordance with recognized ethical norms. The act requires that every Research Institution has an Ethical Research Committee ("Redelighetsutvalg", see own section in this chapter).

Sound research ethics could also include giving study participants the opportunity to get information about the study results and publications of the study they participate in, for example provided by study specific web sites.

Requirements for responsible research (protection ethics)

The main purpose of regulating research that involves human beings, human biological material and health information, is to protect the individual's basic rights (i.e. the rights of the study participants). It is worth noting that the laws and regulations that have been

established in this research area are largely based on the ethical principles that the researchers themselves have been promoting in their respective fields (professional norms). The Helsinki Declaration, developed by the World Medical Association (first edition in 1964, most recently revised in 2013), is particularly important for the field of medical and healthcare research. Several international agreements that build on the principles of the Declaration of Helsinki have later emerged. Central to this context are:

- The European Convention on Human Rights and Biomedicine; Additional Protocol on the Convention on Human Rights and Biomedicine, concerning Biomedical Research
- EU Directive on Pharmaceuticals;
- ICH guideline for good clinical practice E6 (R2), (GCP). Please note a new revision R3 is ongoing drafting and will be published soon.
- The Council for International Organizations of Medical Sciences (CIOMS)
- GDPR- General Data Protection Regulation from 2018
- All European Academies: The European Code of Conduct for Research Integrity. – ALLEA (2017); these European guidelines for research integrity are a common framework for all scientific disciplines
- Montreal Statement on Research Integrity in Cross-Boundary Research Collaborations; issued by the World Conference on Research Integrity in 2013 and is a statement on integrity related to collaborative projects across national borders.

The Health Research Act is largely based on the ethical principles that we are governed by under international agreements. These principles are fundamental:

- Research is to be based on respect for the participants' human rights and dignity.
- The participants' welfare and integrity should be placed before the interests of science and society.
- Medical and healthcare research shall respect ethical, medical, healthcare, scientific, and personal data issues.

Similarly, through international and national privacy laws, there have been established some basic principles for the use of personal health information. Particularly important are the following principles:

- Utilization of personal health information in medical and healthcare research should have an explicitly stated purpose.
- Use of personal health information must be *relevant and necessary* to achieving the research objectives of the project.
- The degree of personal identification of the relevant health information shall not be greater than what is necessary to achieve the research objectives.
- Information shall not be kept longer than is necessary in order to complete the research project.

The Norwegian Health Research Act requires that medical and healthcare research is to be organized and practiced properly, thereby applying the central principles of protection ethics.
Based on several of the above-mentioned documents, and similar guidelines at the University of Oslo, Oslo University Hospital has drawn up a guideline for Research Ethics and Research Integrity in medical and healthcare research projects.

Risk-benefit assessment in research

In medical and healthcare research involving patients, the legal requirement of "soundness" ("forsvarlighet") is based on a thorough and balanced assessment of anticipated additional risk of harm to participants, compared with the expected benefits of participation. A sound research projects implies that no one should be asked to consent to participate in a project before a risk-benefit assessment is carried out, including an evaluation of the balance between these factors. It is also an important step in the planning of a research project to identify possible measures to reduce any potential risks to the participants. Such measures could include establishing study monitoring, performing interim analysis, making a contingency plan and select criteria for when a research study should be stopped.

Risk in a project is defined as a product of probability and grade of severity. In this context, it is important to remember that consequences are weighted more heavily than probabilities. This implies that the more severe the potential consequences, the more stringent the requirements for potential benefit must be. Severe harm that is foreseeable, even if it is

likely to affect only very few of the participants, is therefore given much weight in the evaluation of such projects. This assessment should be communicated clearly and evident in the REK application, in the research protocol, and in the information letter to potential study participants.

What is considered as acceptable risk in research?

Research that does not imply any individual benefit, should not pose any more than a "minimal" risk to participants. Minimal risk is equivalent to what each of us encounter in everyday life. If the risks of participation in a project are deemed to be greater than minimal risk, prospects for direct benefit to the participants should be present. If the risk is "considerably" greater than "minimal", the prospect that the research will have "potential benefit for future patients and society" does not constitute justification for carrying out the project.

Even in projects with minimal or no risk to most participants, study participation may still have severe consequences for a few participants. It is therefore important to describe the project risks in a similar way as the likelihood of benefit, both in the REK application and in the participant information. This information is important to ensure adequate (legal) informed consent from the participants.

Value of consent

Participants in a research project shall receive relevant and truthful information about who will benefit from the project, and the risks and burdens that participation entails. No one should be asked to consent to a project before a risk-benefit assessment is performed, and the balance between the risks and benefits has been deemed reasonable. However, a study participant’s consent does not protect the participant against risk of damage. The assessment of a project's soundness will thus not be affected by whether it will be possible to get the participants' consent. An irresponsible research projects is, in other words, not justifiable even if potential participants consent to participating. The Project Manager (“prosjektleder”) and the Research Director (“forskningsansvarlig”) are responsible for ensuring that study participants are only exposed to “justifiable” risks in line with potential REK approval.

Misconduct and fraud in biomedical and healthcare research

In recent years, several cases of fraud in biomedical research have been revealed. The debate on co-authorship in scientific journals has thus become even more relevant; focusing on what qualifies a researcher for authorship and the responsibilities that co-authorship entails. Fraud in biomedical and healthcare research can have far-reaching consequences. In addition to affecting the reputation of medical research, cheating can lead to risk of great harm to patient groups exposed to new treatments implemented based on false information.

In practice, qualitatively poorly executed research and outright research fraud may be on the same sliding scale. This includes everything from unintentional mistakes and actions, such as incorrect observations, analytical errors, and missing credits, to plagiarism, false correction, or exclusion of "inappropriate" data, as well as fabrication of data. Some define the difference between fraud and error by stating that fraud entails a deliberate intention to cheat and deceive. The Research Ethics Library has published several relevant articles about the subject, for instance an article about bias (skewness) in research.

It is impossible to determine the exact extent of fraud within biomedical and healthcare research. This is partly because the definition of fraud is somewhat unclear. By its very nature, research fraud is based on factors that are concealed and denied, as in other forms of fraud and breaches of trust. It is uncertain whether scientific fraud is more prevalent than before and whether variation exists between disciplines.

There is an increasing pressure to publish ("publish or perish"), particularly within biomedical disciplines in which it is crucial for researchers to be the first to publish important findings. Publications have also become the basis of a merit system, both in terms of personal career and with respect to allocation of research grants. However, the pressure to publish cannot fully explain why a few researchers deliberately choose to commit fraud in research, for example fabricating research data. It is likely that personal characteristics of the individual researcher also play a role. For instance, some researchers exposed of committing fraud have been found to repeat their fraudulent behavior (in research). The desire for “honor and glory” may also represent a motivational that can lead to research fraud. A report from the University of Bergen on research ethics in Norway (RINO) from 2018 has mapped

researchers' attitudes and, among other things, revealed poor formal education in research ethics and lack of knowledge about how to report nonconformities.

What can be done to prevent research fraud?

A number of quality assurance systems are already in place to minimize research errors and improve the quality of research within research institutions. In reality, the most important elements of the quality assurance system are the research groups and the researchers themselves. Systematic errors can be prevented through sound research design and random errors can be corrected for by statistical analyses. All research institutions are required to have internal control routines so that they can carry out their activities in a responsible manner (cf. Health Personnel Act, "Helsepersonelloven", § 16 and the Health Research Act, §6). In addition, a number of public agencies have auditing and supervisory functions with respect to research (see Chapter 6). Advance audits are the most comprehensive, e.g. REK and the Data Inspectorate (applications for licenses). Audits of ongoing research and of completed research projects are likely to be more fragmentary, both at the level of individual research institutions and at higher levels. Many research institutions also have their own bodies and routines for monitoring ethical and quality aspects of ongoing research projects.

Once a research project has been completed, publishing become an important factor in revealing errors or deficiencies. Preliminary findings are often presented as lectures or posters, and manuscripts are revised according to feedback before submission to an academic journal. Methodological, ethical and presentational aspects of the study are evaluated through the peer review system of academic journals and, as a rule, articles have to be revised a number of times before they are published. The underlying assumption is that peer review improves the academic quality of published work, but there is general agreement that this system cannot guarantee exposure of fraudulent research. Peer reviewers are not close enough to the data sources to be able to check the validity of results, although they do sometimes discover irregularities, which may lead to suspicions of fraud. Editors may then request further information from the authors. It has become increasingly common for journals to require authors to declare the exact nature of the contribution they have made to the study and the publication. If a journal suspects there is something dubious

about the research, they have the option of rejecting the article or sending out a "warning". By requiring the publication of the main results in publicly available databases (such as clinicaltrials.gov, see Chapter 9), the opportunity to withhold results will also be reduced.

Plagiarism

Correct use of references to other researchers' articles/work shows academic integrity and avoids plagiarism. Presentation of results, thoughts, ideas or formulations made by others, as your own, is plagiarism. Plagiarism is intellectual theft, and is regulated by two Norwegian Acts ("åndsverkloven" and "universitet- og høyskoleloven"). The Norwegian National Research Ethics Committees has published an article about plagiarism in their Research Ethics Library (see Chapter 9).

Research institutions and journals use different tools to check plagiarism. Several of the universities in Norway use Uoriginal as a tool, while there are also freely available programs, such as Copyleaks. Neither program is perfect.

Current sanction imposed on fraudulent researchers

The regulation of scientific fraud and misconduct in research is inadequate in Norway. Sanctioning may have a general preventive effect and thereby reduce risk of fraud and misconduct in the research field. The sanction options include censure by colleagues and exclusion from academic circles, as well as withdrawal of research funding. In addition, fraudulent researchers may face administrative, disciplinary, civil or criminal action, risking imprisonment and fines. They may be given notice by their employer and sentenced to pay compensation to parties who have been duped or injured. Fraudulent researchers who are also healthcare workers risk receiving a warning from the Norwegian Board of Health Supervision ("Helsetilsynet"), and in extreme cases the authorization to practice clinically (e.g. as a medical doctor) may be withdrawn. In 2006 one researcher lost the PhD title ("dr. med.") and the approval of this researcher's doctoral thesis at the University of Oslo was withdrawn.

How to prevent fraud in research communities

Can fraud be prevented by more research bureaucracy? The opinion of the authors of this Handbook is that more bureaucracy and control could easily lead to research being paralyzed by over-regulation and may result in many researchers giving up their careers. In practice, the integrity of the researchers themselves and internal social research control are probably more important than external control, which is chiefly designed to expose the most serious cases of fraud. The opinion of the authors of this Handbook is that research institutions must continue to be the cornerstone of initiatives promoting sound research ethics and prevention of misconduct. This implies the need for clarification, simplification and streamlining of existing rules and development of internal and external control systems. Continued promotion of sound principles in research and ethical awareness in the research community and the PhD program is essential, as it would probably emphasize the moral, professional and legal responsibilities of the individual researchers. Open debate and communication in research groups regarding ongoing research projects as well as discussions of what is sound research practice and research ethics, should contribute to the promotion of sound research and help prevent misconduct and fraud.

Presentation of research data and methodology not only provides opportunities for improved scientific quality of projects, but also ensures openness in the research environment, which, in turn, makes fraud more difficult. Sound research behavior and sound research culture requires openness, honesty, trust and fruitful collaboration and are thus likely to contribute to reducing conflicts, misconduct and fraud. It is also important that a greater number of researchers in research groups have access to original data so that the data material, calculations and presentation of results may undergo a greater degree of quality control.

Some of the possible avenues for research institutions to explore in this context include further development of research training with greater emphasis on research ethics (see educational tips below) and improved supervision procedures, as well as closer follow-up of PhD-candidates and researchers.

In practice, the supervisors' role in research projects varies considerably. The opinion of the authors of this Handbook is that supervisors should be well acquainted with all aspects of a research project, including quality control of data collection, electronic data processing, and statistical analyses, in addition to contributing to the publication process itself.

The Norwegian Health Research Act emphasizes the research institutions' formal responsibility of all aspects of the research project. The duties of the Research Director ("forskningsansvarlig") are defined in the Act's regulations, including facilitation of ethical, privacy-related and information security issues and internal controls etc. The Project Manager's ("prosjektleder") responsibility for the daily operations of a research project is also defined, and should ensure that ethical, medical, and privacy considerations are taken into account in daily research operations. The Project Manager is also responsible for notifying and involving the Research Director before the research project commences, for obtaining the necessary approval from REK and any other relevant bodies, and for ensuring that the project is carried out according to the approved protocol (see Chapter 6).

The responsibility of the Research Director (at the research institution) is made clear in the Research Ethics Act of 2017, and entails a system responsibility for overall good research ethics, including the establishment of an Ethical Research Committee ("Redelighetsutvalg", see below), training opportunities and guidance, both by supervisors, fellows and other researchers. However, the overall responsibility of the research institution does not reduce the individual responsibility of promoting and conducting ethical research and sound research practice throughout all stages of the research project.

Protection of "whistleblowers" in the workplace

It is often difficult for a person who discovers or suspects fraud to know how best to deal with the situation. The closer the "fraudster" is to one's own research group, the more difficult it can be. In practice, inexperienced researchers should be able to discuss the matter with their supervisor, who can then take the matter further. If this is not possible, advice should be sought from another senior researcher in whom one has confidence. An institutional research system founded on sound ethical and research principles should reduce the need for "whistleblowers". The Norwegian Working Environment Act offers

protection of whistleblowers against retaliation. Employers should have routines for internal reporting of irregularities in the workplace. This law also applies to research.

New merit systems?

Some feel that reducing the pressure to publish would affect the motivation underlying research fraud. However, it is inconceivable that biomedical and healthcare research communities in Norway would choose other academic systems of merit and funding arrangements than the rest of the world, basing these merits largely on scientific publications.

Tips for training in research ethics

Training in good research ethics is important, also beyond the PhD program, and especially for supervisors, postdocs and research leaders. Good tips are to use concrete, subject-specific examples when teaching and learning legislation and rules. Researchers themselves should teach research ethics, which should be integrated as a topic as part of seminars in the academic field. The informal training in daily research activities plays a major role, and openness is an important premise here. The institutions should also facilitate discussion of ethical issues beyond the PhD level.

In the autumn of 2021, UiO adopted an ethical platform with a common training program for all employees at the university. The aim is to provide knowledge of norms, influence behavior and build a culture for research ethics. The Norwegian National Research Ethics Committees (FEK) have many resources available. They publish the magazine "Forskningsetikk", provide proposals for teaching sessions in research ethics, and have a large Research Ethics Library available online with various topics and articles related to them, as well as discussion examples.

Norwegian national panel for misconduct in research

The National Commission for the Investigation of Research Misconduct, ("Granskningsutvalget"), is a national resource for universities, research institutions, businesses and employers that deals with cases of misconduct in research, as a supplement

to local institutional systems. The Commission deals with cases of suspected fraud reported by either institutions or individuals. The Commission may open a case at their own initiative, but as a rule, the responsibility lies with the individual institution. There is no requirement for research institutions to submit serious cases to the committee; however it is expected that the panel should be informed if an institution is dealing with a case of misconduct/fraud on its own. The Commission is not to impose penalties or sanctions, this is left to the employer or, indirectly, to the funding agents. The research institution has the primary responsibility for prevention of and dealing with fraudulent research, including appropriate research ethics training for its candidates.

The Research Ethics Committee ("Redelighetsutvalg") and "Forskningsombud"

In accordance with the requirements of the Research Ethics Act, a joint Research Ethics Committee ("Redelighetsutvalg") for the Department of Clinical Medicine at the Faculty of Medicine, the University of Oslo, Oslo University Hospital HF and Akershus University Hospital HF has been established from 2019. The committee deals with cases of possible violation of recognized research ethics norms in accordance with Sections 6 and 8 of the Research Ethics Act. The Research Ethics Committee will review individual cases and contribute to the institutions' responsibility to ensure that research is conducted in accordance with recognized research ethics standards. On request, the Committee will also handle cases from other health institutions in the Region.

In addition, the Institute of Clinical Medicine, UiO and the Oslo and Akershus University Hospitals have a "Forskningsombud". It provides guidance and advice to researchers that are in difficult research ethics situations, and in addition contribute on solving ethical cases as early as possible.

Research Ethics Committee at UiO

The Research Ethics Committee at UiO is the University's advisory body for research ethics. The Committee may, on its own initiative, comment on research ethics. In addition, the committee addresses individual cases where there is suspicion of scientific fraud or breach of good scientific practice at UiO.

Research ethics courses for established academic employees can be found at UiO, Starting 2024 four courses will be offered per semester, two in Norwegian and two in English.

Useful links

Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine

NTNU: The Ethics Portal

Universitets- og høgskolerådet

University of Oslo: Centre for Medical Ethics

University of Oslo: Research ethics

University of Oslo: Standard for Research Integrity.

University of Oslo: Quality System for Research

The Act on Health and Research («Helseforskningsloven")

The Council for International Organizations of Medical Sciences (CIOMS)

The EU Directive on Pharmaceuticals (GCP: Good Clinical Practice)

The Helsinki Declaration

The National Committee for Medical and Health Research Ethics (NEM)

The Oviedo Convention

The Research Ethics Library

The Vancouver "rules" (see Chapter 9)

The role of supervisors in research ethics: a 2023 guideline from the National research ethics committees (NREC) in Norway.

A new 2023 guideline for the ethical responsibility for research institutions in Norway is published from the National research ethics committees (NREC) in Norwegian.

Norwegian books and literature on research ethics

Hofmann B, Myhr AI og Holm S. Scientific dishonesty- a nationwide survey of Doctoral students in Norway. BMC Medical Ethics 2013, 14:3.

Nydal R og Solberg B (red). Juks, uredelighet og god forskning. Tapir akademisk forlag 2006.

Ruyter KW (red.). Forskningsetikk: beskyttelse av enkeltpersoner og samfunn. Gyldendal akademisk 2003.

Ruyter KW, Førde R og Solbakk JH. Medisinsk etikk: en problembasert tilnærming. Gyldendal akademisk 2000.

Simonsen S og Nylenna M. Helseforskningsrett: den rettslige regulering av medisinsk og helsefaglig forskning. Gyldendal akademisk 2005.

17 Industry sponsored trials/studies

Industry sponsored trials and studies differ from other clinical studies in that the external sponsor, such as a pharmaceutical company or a medical-technical equipment company, takes the study initiative. The sponsor is responsible for the implementation of the study and pays the hospital/site for extra study work and expenses. The institution contributes with data, for instance health information and biological samples, after identification and recruitment of suitable study participants. In studies with a large, professional sponsor, such as in clinical drug trials, the research protocol is usually written by the sponsor. The sponsor also provides a ready-made "package" which includes training of study team members, monitoring and systems for registration of data (eCRF; electronic Case Report Form). In studies with smaller actors, for example smaller med-tech companies, it may be relevant to collaborate to a greater extent on the study development and research protocol. In this chapter, we will go through the steps in an industry sponsored study, from sponsor contact until the study is completed.

Why industry sponsored trials?

An investment in industry-sponsored studies helps to give more patients access to clinical studies. In 2021, the Norwegian government introduced the first "Action Plan for Clinical Studies 2021-2025". The goal is to double the number of clinical studies by 2025, and to give many more patients the opportunity to participate in clinical trials. In 2019, the Ministry of Health and Care Services (“Helse- og omsorgsdepartementet”) introduced an annual reporting on the number of new patients included in clinical trials (read more about reporting in Cristin and on the government web page).

Some industry-sponsored trials may provide major savings for the hospital in that study medicine replaces expensive drugs that patients otherwise would receive. Industry sponsored studies are also a good "research school". By investing in industry-sponsored studies, the institution can build up knowledge and resources (study staff, premises, and funds) to continue investing in self-initiated studies.

Feasibility / request from sponsor

The first contact is usually through a request from the sponsor, either directly from the company or via a CRO (Contract Research Organization), whether the study may be relevant for the investigator and the institution. This is called "feasibility". You will often have to fill in a detailed request form with a short response time. It is important to respond within the deadline in order to be assessed. This initial response to the sponsor is non-binding, unless otherwise stated. Sometimes the center needs to sign a confidentiality agreement (Confidential Disclosure Agreement, CDA) before they can get more information about the study.

The aim is to find out whether the study can be carried out at the institution. The form contains questions about patient background, access to necessary resources such as equipment and personnel, and expertise of the examiner, among other. If the study is relevant, in some cases it may be possible to provide valuable input to the sponsor, especially if the research protocol is not completely finished. In this early phase, it is important that you discuss the study with relevant colleagues responsible for the subject, the head of department and possibly cooperating departments such as lab or radiology, and get a preliminary "internal anchoring" at the institution. After the form has been submitted, the sponsor will contact the centers that are selected to join the study, but if they have gone out very widely, it is not certain that they will give feedback to out-of-date centers. The feasibility process can take time, often many months. If you do not hear anything within a reasonable time, you can try to contact the sponsor to find out how things are going.

More and more pharmaceutical companies are using data-driven feasibility with platforms such as the Shared Investigator Platform (SIP), to identify relevant sites. SIP is also a portal for the exchange of study documents and information in many studies, and in these studies, it is mandatory for study team members to register. Contact your local research support if you need to create a site/study center in SIP or register in the portal.

NorTrials is a partnership between the Regional Health Authorities and the pharmaceutical and medical equipment industry associations, established on behalf of the Ministry of Health and Care. NorTrials has created a feasibility portal where the industry can submit requests

for new studies. The requests are communicated to relevant hospitals throughout the country. Read more on NorTrials' website.

Planning of the study

Internal approval

All research, including industry sponsored studies, must be approved by all affected departments, both where study participants is recruited and where data is processed, as well as departments where the researchers are employed. The Principal Investigator (PI) is responsible for internal approvals (more about the concepts and internal "anchoring" in Chapter 7). An early clarification on whether the institution has the resources to carry out the study is important, for example available study nurses and doctors, as well as equipment and premises. If service departments such as radiology, pathology or the local laboratory are to contribute, written agreements must be made.

Employees at OUS can seek help from the Regional Research Support. Their website provides a form listing prices for various services from service departments at OUS, and this form can be submitted for available capacity enquiries.

Budget and legal agreement with sponsor

Usually, a third party takes care of agreements and financial matters with the industry in larger institutions. At "Helse Sør-Øst" and the Northern Norway University Hospital (UNN), Inven2 negotiates agreements with the sponsor, on behalf of the PI and the hospital. When the decision to start a new study is made and the research protocol is ready, the sponsor is responsible for reporting the study to Inven2. Inven2 sets up a budget template and sends it to the PI for preparation of the budget. The PI (or study nurse/coordinator) must, among other things, estimate the time spent on study visits and other study assignments, and include prices for procedures provided by service departments (e.g., local lab, Radiology Dept.). The hospital pharmacies are separate health trusts and must therefore enter into a separate agreement with the sponsor. There are separate agreement templates for pharmacy services in studies on Inven2's website.

Approvals (Data Protection Officer, Norwegian Medical Products Agency and REK KULMU)
From 31 January 2023 all new clinical trial applications in the EEA must be submitted under the Clinical Trials Regulation, CTR, (EU Regulation No. 536/2014) through the CTIS platform. The study sponsor is responsible for applying to get study approval. For studies regarding medical devices and in vitro diagnostic medical devices, now regulated under Medical Device Regulation 2017/745 and In Vitro Diagnostic Medical Device Regulation 2017/746), the REK portal can be used for submissions. As a guideline, templates for consent can be found in the REK portal. Be sure to use the correct template and follow the instructions. After the application has been submitted, a notification must also be sent to the local Data Protection Officer (at OUS, this is done using a web form). Medical device trials that are not CE-marked (or that are CE-marked, but are to be tested for new intended use) must also be submitted to the Norwegian Medical Products Agency. In addition some trials have to be notified to the Norwegian Medical Products Agency and REK.

After the application has been submitted, a notification must also be sent to the local data protection officer (at OUS this is done using an online form).

Registration of the study
All clinical studies must be registered in a publicly available approved database before commencement. For medical product trials that follow new the new regulation, this happens when the sponsor submits the study via CTIS. Other studies are registered in clinicaltrials.gov or a similar website (see chapter 9) before patients/participants are included in the study. Both CTIS and ClinicalTrials are part of WHO's International Clinical Trials Registry Portal, which is recommended as the primary source for searching for studies and results.

In addition, all clinical trials that are open to inclusion will be posted on the hospital's website. The studies are linked to current treatment texts so that patients who read about a treatment on the website of a hospital will see an overview of current clinical studies for this treatment at all the Norwegian hospitals. The studies are also advertised together on the hospital's website for clinical studies which are reflected on helsenorge.no. The information is written for patients, relatives and referring physicians. Previously, the national coordinating investigator was responsible for publishing the study information, but since this

role no longer exists within the new CTR, the investigators in a multicenter study must agree on who undertakes the task, possibly with the involvement of a sponsor.

More information

The Regional Research Support at OUS has a separate website on industry-sponsored trials, with information on all phases of industry-sponsored studies, including routines for industrial collaboration. The website includes a guide: "Veileder for oppdragsforskning" at OUS (in Norwegian only). For questions and other inquiries about industry-sponsored studies, you may also contact the Regional Research Support by e-mail.

Implementation of the study

Start-up meeting and "ready-to-go signal"

The study cannot start until the sponsor has given permission to proceed and all formal approvals have been obtained. In drug trials, GCP (Good Clinical Practice) courses and CVs from all study team members (investigator/nurse/coordinator) must be in place (see section 6.8). It is common for the sponsor to arrange a site initiation visit with the PI and the rest of the study team. At this meeting, the sponsor thoroughly reviews the entire study, and hands out the Investigator Site File (ISF, the folder for study documents) and the first patient binders. A number of documents must be filled out and signed, including a delegation log (describing who can do what in the study team) and a source data list (stating the places that are the source of patient data, this is often in the patient's medical record). In addition, the study team must usually complete several e-learning courses in, among other things, eCRF. For OUS studies, see the guide: "Veileder for oppdragsforskning" (in Norwegian only) to read more about the electronic study archive and other relevant information.

Practical implementation

Recruitment of study participants is often the most time consuming part of the study. Potential participants can be identified in several ways, for instance, by giving information to other doctors at the Department, collaborating Departments and general/private practitioners, or advertising for study participants in social media (the ad text must be pre-approved by REK). The sponsor expects that the number of recruited study participants specified in the agreement is reached. In addition to a financial incentive, good recruitment

and completion of the study is important to gain a "good reputation" and attract more studies to the site. It is a good idea to prepare separate flow charts and work sheets for each study visit, to promote overview of the study activities. In addition, a calendar/planner for study visits, and a mobile phone to stay in touch with study participants, are good tools.

The protocol describes the procedure of randomizing study participants. The systems used for randomization are usually reviewed during the site initiation visit with the sponsor. Side effects/adverse events are reported to the sponsor by the investigator, and the sponsor is responsible for reporting to the Norwegian Medical Products Agency. In addition to the mandatory duty to report internally and externally in cases of undesirable medical incidents, there is an independent duty to report to the Norwegian Board of Health Supervision ("Helsetilsynet") in the event of serious as well as undesirable and unexpected incidents in research projects (see Chapter 14).

There are separate procedures for drug handling in clinical drug trials. The sponsor will give information about what applies to the specific study. The routines should be followed and any deviations, such as temperature deviations during transport or storage, or errors when handed over to the study participant, should be reported to the sponsor immediately. Study participants must not receive medication that is perceived as a deviation before the sponsor has approved. See also NorCRIN's procedure. If a pharmacy is not involved in the study, it is especially important to familiarize yourself with ordering, delivery and storage of the study medication.

Monitoring

Monitoring is a requirement in clinical drug trials. The purpose is to check that the trial takes place in accordance with the research protocol, legislation and GCP guidelines. Monitor also checks if collected data matches source data. The sponsor is responsible for monitoring the study. Read more about monitoring specifically for OUS in the guide: "Veileder for oppdragsforskning" (in Norwegian only).

Financial follow-up

Invoices are sent regularly (preferably semi-annually) to the sponsor, and includes the number of study visits and other study-related activities that have been completed since the last reporting. For Helse Sør-Øst, Inven2 is responsible for the financial follow-up and sending invoices to the sponsor. The study team fills in the invoice basis supplied by Inven2 and returns it. Inven2 also follows up any expenses from study participants for travel and accommodation that are not covered by pasientreiser.no. Note that the companies only reimburse expenses if these have been agreed in advance.

Changes in the study

The sponsor must report significant changes to the research protocol to the authorities. For clinical trials that comply with CTR (EU Regulation No. 536/2014), amendments must be submitted via CTIS. Changes that apply to studies that follow Directive 2001/20 (old regulations), and studies on medical equipment are reported to REK and/or DMP depending on the type of change.

The changes must be approved before they are implemented, only changes that affect patient safety can be made immediately. Relevant protocol changes must also be reported to the local data protection officer.

Completion of the study

The study is terminated when the last patient has completed the last study visit (including all the sites, all data has been collected and the sponsor has no more questions (also called "queries"). The PI is responsible for ensuring that the study documents are stored in a suitable and safe location at the institution. For medicinal product trials, the documents must be stored for a minimum of 25 years according to the new CTR (EU Regulation No. 536/2014), (see chapter 3 on storage/deleting data). Studies still governed by the Directive 2001/20/EC have a 15 year period requirement. The study is formally concluded when the sponsor sends a final report via CTIS. The PI at each participating site must also inform the local Data Protection Officer and affected departments about the study's completion. The sponsor is responsible for sending a final report latest 1 year after completion via the CTIS platform. At Helse Sør-Øst, Inven2 is responsible for the final financial settlement.

Co-authorship in industry sponsored trials

The regulations for co-authorship are the same for this type of study as for other research studies. See Chapter 9 on publishing, especially the section on "Commercial industry (sponsors), conflicts of interest and publishing". Most institutions will have standards for agreements with sponsors in research projects. You should familiarize yourself with the guidelines of your research institution, preferably before discussing the conditions for publication and co-authorship with sponsors. Make sure that what you agree on is mentioned in the agreement with the sponsor.

APPENDIX 1: Links

(Translations to English from several Norwegian terms are presented **in Appendix 4**)

A

ADHD Norge

Adobe

Arbeidsmiljøloven

B

Bergen universitetsfond

BI

BMJ

Brukerutvalget ved OUS

C

CAREiN

ClinicalTrials.gov (National Institutes of Health)

Committee on Publication Ethics (COPE)

CORDIS: Community Research & Development Information Service

CRISTIN: Current Research Information System in Norway

Cris/NVA: Information about the new platform replacing CRISTIN

CTIS

D

Datatilsynet

Den norske legeforening

E

EpiData

EpiInfo

EUs legemiddeldirektiv (GCP: Good Clinical Practice)

Europarådets konvensjon om biomedisin og menneskerettigheter (Additional Protocol to the Convention on Human Rights and Biomedicine, concerning Biomedical Research)

European Clinical Trials Register

F

Fellesorganet for REK (FREK); kjennetegn ved kvalitetssikring vs fremleggelsespliktige forskningsprosjekter

Folkehelseinstituttet

Forbundet mot rusgift

Foreningen for hjertesyke barn

Forskningshåndboken

Forskningsparken AS

Forskningsrådet
Forskrift om forsøk med dyr
Forskrift om organisering av medisinsk og helsefaglig forskning
Funksjonshemmedes fellesorganisasjon

H
Health2B
Helsebiblioteket
Helsedirektoratet
Helse- og omsorgsdepartementet
Helse- og omsorgsdepartementet: system for måling av forskningsaktivitet
Helse Bergen, fag og forskning
Helse Bergen, forskning og innovasjon
Helse Sør-Øst
Helseforskningsloven
Helsinkideklarasjonen
Hørselshemmedes landsforbund

I
ICMJE, Uniform Requirements for Manuscripts Submitted to Biomedical Journals (Vancouver Convention)
InnoMed (Nasjonalt nettverk for behovsdrevet innovasjon i helsesektoren)
Innoventus Sør AS
Instructions to authors in the health sciences
Interactive statistical calculation pages
Inven2

K
Kreftforeningen
Kunnskapsdepartementet

L
Landsforeningen for hjerte- og lungesyke
Landsforeningen for nyrepasienter og transplanterte
Landsforeningen uventet barnedød
Legathåndboken
Leiv Eriksson Nyskaping AS
Lov om behandlingsbiobanker (behandlingsbiobankloven)
Lov om helseforetak (helseforetaksloven)
Lov om humanmedisinsk bruk av bioteknologi m.m. (bioteknologiloven)
Lov om organisering av forskningsetisk arbeid (forskningsetikkloven)

Lov om patenter (patentloven)
Lov om spesialisthelsetjenesten (spesialisthelsetjenesteloven)

M
Maler, informasjonsskriv (REK-portalen)
Mattilsynet
Meltzerfondet
Multippel sklerose-forbundet

N
Nasjonalforeningen for folkehelsen
National Institutes of Health, Grants and Funding Opportunities
NEM (Den nasjonale forskningsetiske komité for medisin og helsefag)
NorCRIN
Norges astma- og allergiforbund
Norges blindeforbund
Norges diabetesforbund
Norges døveforbund
Norges forskningsråd
Norges forskningsråd, utlysninger av forskningsmidler
Norges handikapforbund
Norges bedriftidrettsforbund
Norges teknisk-naturvitenskapelige universitet (NTNU), forskerutdanning
Norges teknisk-naturvitenskapelige universitet (NTNU), etikkportalen
NTNU Technology Transfer AS
Norges miljø- og biovitenskapelige universitet (NMBU)
Norinnova Technology Transfer AS
Norsk revmatikerforbund
Norsk folkehjelp
Norsk Pasientskadeerstatning
Norske kvinners sanitetsforening
Norsk Vitenskapsindeks (NVI)
NSD: Norsk senter for forskningsdata
Norwegian Medical Products Agency

O
Oslo universitetssykehus, forskning
Oslo universitetssykehus, medisinsk bibliotek
Oslo universitetssykehus, personvern
OUS, Regional forskningsstøtte

P

Patentstyret
PRISMA
PROMiNET
Prosjekt Norge
PubMed

R

Redd Barna
Regional forskningsstøtte, OUS
Regional komité for medisinsk og helsefaglig forskningsetikk (REK)
Regionsenter for barn og unges psykiske helse
Reservasjonsregisteret
Rådet for psykisk helse

S

SAS: Statistical Analysis Software
Simula Innovation AS
SINTEF TTO AS
Skattefunn
SPSS statistics
Stiftelsen Dam (former Extrastiftelsen)
Stiftelsen organdonasjon: Fond til fagutvikling
STROBE

T

Tidsskrift for Den norske Legeforening

U

UNIFOR - Forvaltningsstiftelsen for fond og legater ved Universitetet i Oslo
Universitetet i Bergen, ph.d.-utdanning ved det medisinske fakultet
Universitetet i Bergen, forskerskoler
Universitetet i Bergen, bibliotek for medisin
Universitetet i Oslo, ph.d.-programmet ved det medisinske fakultet
Universitetet i Oslo, medisinsk etikk
Universitetet i Oslo, forskning innen medisin og helse
Universitetet i Oslo, kvalitetssystem for medisinsk og helsefaglig forskning
Universitetet i Oslo, ledige vitenskapelige stillinger
Universitetet I Oslo, UiO Growth House
Universitetet i Tromsø
Universitetet i Stavanger

V

Vancouver-konvensjonen

Veilederen til helseforskningsloven

VIS innovasjon (former Innovest and BTO)

Vitenskapsombud UiO

APPENDIX 2: Overview over Norwegian TTOs (Technology Transfer Offices)

Inven2 (Universitetet i Oslo)
Gaustadallèen 21, 0,349 Oslo
Boks 1061 Blindern
N-0316 Oslo
Telephone: 22 84 00 80
Email: post@inven2.com
http://www.inven2.com/no

Vestlandets innovasjonsselskap (VIS) (Universitetet i Bergen)
Thormøhlensgate 51, 5006 Bergen
Telephone: 400 20 800
https://www.visinnovasjon.no/

Kjeller Innovasjon (OsloMet)
P.O. Box 102, N-2027 Kjeller
Telephone: 64 84 43 00
Email: post@kjellerinnovasjon.no
http://www.kjellerinnovasjon.no/

Norinnova (UiT Norges arktiske universitet)
Postboks 6413 Forskningsparken
9291 Tromsø
Telephone: 77 67 97 60
Email: post@norinnova.no
www.norinnova.no/

NTNU Technology transfer (NTNU)
Telephone: 90 05 11 11 / 73 55 11 81
Email: contact@tto.ntnu.no
http://www.tto.ntnu.no/

Sintef TTO
Postboks 4760 Sluppen
7465 Trondheim
Telephone: 73 59 30 00
Email: info@sintef.no
http://www.sintef.no/

Validé (Universitetet i Stavanger)
Postboks 8034, 4068 Stavanger
Telephone 51 87 40 00
Email: post@valide.no
https://www.valide.no/tto

ARD Innovation (NMBU)
Postboks 206, 1431 Ås
https://ardinnovation.no/en/employees-and-contact/

Innoventus Sør (UiA)
Gimlemoen 13, 4630 Stavanger
Telephone: 37 29 51 80
Email: post@innoventus.no
http://innoventus.no/

Nord innovasjon AS
Universitetsalleen 11, 8026 Bodø
Telephone: 75517148
Email: post@nordinnovasjon.no
https://www.nordinnovasjon.no/

APPENDIX 3: Local Research Support Oslo University Hospital, South-Eastern Norway Regional Health Authority and Haukeland University Hospital:

Oslo University Hospital (OUS):

OUS offers research support to all researchers within the South-Eastern Norway Regional Health Authority (Regional forskningsstøtte). In addition, OUS offers Data Protection Officer services ("Personvernombudet").

South-Eastern Norway Regional Health Authority:

"Samarbeidsorganet" advises decicion-making bodies in the South-Eastern Norway Regional Health Authority ("Helse Sør-Øst RHF") and co-operating universities in matters of common interest concerning research, innovation and education. "Samarbeidsorganet" shall promote co-operation between the South-Eastern Norway Regional Health Authority and co-operating universities within health research, innovation and education.

Haukeland University Hospital:

"Regionalt kompetansesenter for klinisk forskning" offers support in the planning, implementation, statistical analysis and publication of clinical research. The center is also responsible for coordinating networks within the regional health authority, and acts as a link to the university-based research groups.

APPENDIX 4: Norwegian and corresponding English terms in this handbook

Norwegian Terms	*English Terms or explanation*
Arbeidsmiljøloven	*The Norwegian Working Environment Act*
Barnevernet	*Child Welfare Services*
Behandlingsbiobankloven	*The Treatment Biobank Act*
Bioteknologiloven	*The Biotechnology Act*
Bredt samtykke	*Broad Consent*
Current Research Information System in Norway (CRISTIN)	*The Norwegian Research registration system (CRISTIN)*
Databehandlingsansvarlig	*Data Processing Director*
Datatilsynet	*The Data Protection Agency*
Den nasjonale forskningsetiske komité for medisin og helsefag	*The National Committee for Medical and Health Research Ethics*
Dødsårsakregisteret	*The Cause of Death Register*
Europarådets konvensjon om menneskerettigheter og biomedisin	*The European Convention on Human Rights and Biomedicine*
EUs legemiddeldirektiv	*EU Directive on Pharmaceuticals*
Folkehelseinstituttet	*The Norwegian Institute of Public Health*
Forskningsansvarlig	*Research Director*
Forskningsombudsman	*Research Ombudsman*
Forskningsrådet (Norges forskningsråd: NFR)	*The Research Council of Norway (NRC)*
Forsøksdyrutvalget	*The Institute for Nature Research*
Fødselsregisteret	*The Medical Birth Registry*
Førstemanuensis	*Associate Professor*
Helse- og omsorgsdepartementet (HOD)	*The Ministry of Health and Care Services*
Helsebiblioteket	*The Norwegian Electronic Health Library*
Helsedirektoratet	*The Norwegian Directorate of Health*
Helseforetak (f.eks. sykehus)	*Health Trust (e.g. a hospital)*
Helseforskningsloven	*The Norwegian Act on Medical and Health Research*
Helsepersonelloven	*The Health Personnel Act*
Helse-Sør-Øst (HSØ)	*The South-Eastern Norway Regional Health Authority*
Helsetjenesteforskning	*Health Services Research*
Helse Vest	*The Western Norway Regional Health Authority*
Helsinkideklarasjonen	*The Helsinki Declaration*
Kirke-, utdannings- og forskningsdepartementet	*The Ministry of Education and Research*
Klinisk forskningsstøtte (avdeling for), OUS	*The Department for Clinical Research Support, OUS*
Kreftregisteret	*The Cancer Registry of Norway*
KULMU-Komiteene for klinisk utprøving av legemidler og medisinsk utstyr	*Committees for Clinical Trials on Medicinal Products and Medical Devices*
Kunnskapssenteret	*The Norwegian Knowledge Center for Health Services*
Kvalifiseringsstipendier	*Qualifying Grants*
Kvalitetssikring	*Quality Control Studies*
Legemiddelansvarsforeninge	*The Drug Liability Association*
Lov om behandling av etikk og redelighet i forskningen	*The Act on Research Ethics*
Lov om produktansvar	*The Product Liability Act*
Loven om arbeidstakeroppfinnelser	*The Act on Employee Inventions*
Mattilsynet	*The Norwegian Safe Food Authority*
Nasjonabiblioteket	*The National Library*

Nasjonal strategigruppe for helseforskning (NSG)	*The National Strategy Group for Health Research*
Nasjonalt nettverk for behovsdrevet innovasjon i helsesektoren	The National Network for need-driven Innovation in Health care
Nasjonalt utvalg for gransking av uredelig forskning	The National Panel for Inquiry into Fraudulent Research
Norges veterinærhøgskole	The Norwegian School of Veterinary Science
Norsk pasientregister (NPR)	The Norwegian Patient Register
Norsk Pasientskadeerstatning (NPE)	The Norwegian System of Compensation to Patients
Norsk senter for prosjektledelse	The Norwegian Center of Project Management
Nærings- og handelsdepartementet	The Ministry of Trade and Industry
Oppdragsforskning	Commissioned Research
Oppdragsgiveren	The Commissioning Entity
Oslo Universitetssykehus (OUS)	Oslo University Hospital (OUS)
Patentstyret	The Patent Board
Personvernombud	Data Protection Officer
Phd. stipendiater	PhD candidates
Prosjektansvarlig (ikke definert i Helseforskningsloven)	Project Director (not defined in the Norwegian Act on Medical and Health Research)
Prosjektleder	Project Manager
Prosjektstyring	Project Management
Redelighetsutvalget	The research Ethics Committee
Regional komité for medisinsk og helsefaglig forskningsetikk (REK)	Regional Committees for Medical and Health Research Ethics (REK)
Regionalt helseforetak (f. eks. Helse Vest)	Regional Health Trust (e.g. Western Norway Regional Health Authority)
Reseptregisteret	The Norwegian Prescription Database
Reservasjonsregisteret	The Reservation Register
Spesialisthelseloven	The Norwegian Act on Specialist Health Services
Statens helsetilsyn	The Norwegian Board of Health Supervision
Direktoratet for medisinske produkter (DMP)	The Norwegian Medical Products Agency (DMP)
Stedfortredende samtykke	Surrogate Consent
SYSVAK	The National Immunization Registry
Tidsskrift for norsk legeforening	The Journal of The Norwegian Medical Association
Universitet i Oslo (UiO)	University of Oslo (UiO)
Universitets- og høgskoleloven	The Act on Universities and University Colleges
Veileder	Supervisor

APPENDIX 5: Acknowledgement

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Heidi Fjeldstad (OUS PhD fellow) contributed substantially to the English translation of the 2017 version. Any linguistic flaws in the 2024 version remain the responsibility of the Research handbook first author (Annetine Staff) and web editor (Ana Lobato Pascual).

APPENDIX 6: Registration of clinical studies

A clinical study will automatically be registered in national and possibly local databases because of REK and/or the Data Protection Officer ("Personvernombud"), but updates from the project manager may be necessary.

The REK portal

If the study cannot be completed or is stopped along the way, the project manager must send a notification to REK ("endringsmelding"). This also applies in the event for an extended project period or a change of project manager. In addition, a final report ("sluttmelding") is required no later than six months after the data has been analyzed (the project's end date in REK).

CRISTIN – national system for research projects and publication

In 2024 a new national platform replaces CRISTIN (Cris/NVA) and the local science archives. The purpose of this state-funded platform is to make openly accessible scientific literature financed by public funds. Information is imported from the REK portal, and information that requires a notification from REK cannot be edited by the project manager. The project manager, or others are given editing access, can, however, correct and expand the overview of project members, to ensure that the project is displayed on the member's profile in CRISTIN. Once articles related to the study have been published and are found in Cris/NVA, the articles can be linked to the project (manually).

The Data Protection Officer's database at OUS

The information in the application sent to the Data Protection Officer ("personvernombudet") at OUS is automatically stored in a separate database, which is also available to the Regional Research Support, research leaders and others in need for such access.

CTIS and the EU Clinical Trials Register

From January 2023, EU/EEA interventional clinical trials approved under or transitioned to the Clinical Trial Regulation 536/2014 are publicly accessible through the Clinical Trials Information System (CTIS). Older trials can be accessed through the EU Clinical Trials Register, EudraCT. This is the database used by national medicines regulators for data related to clinical trial protocols. The data on the results of these trials are entered into the database by the sponsors themselves and are published in this Register once the sponsors have validated the data. The Norwegian Medical Products Agency will register the study in the EU database when a Norwegian institution is sponsor. A final notification is sent to the Norwegian Medical Products Agency within 90 days after the last patient visit, and they will update the database. The results of the study (including any side effects), must be recorded in the database within 12 months after the last patient visit (6 months for pediatrics). This requirement applies regardless of whether / when the results are published. Registration in the database also meets the journal requirements for such studies before they can be considered for publication.

ClinicalTrials.gov – other studies

The project manager at the institution that is sponsor must register the study here, if it is not already registered in the EU database or another database that the journals approve of. The project manager must edit the project status (start/stop of inclusion, participating institutions etc.). The system has functionality for recording results (summary of main findings), and this should be done to ensure transparency and avoiding problems with US authorities. In addition, you may link to current research articles, automatically or manually.

The Hospital's websites/helsenorge.no

All clinical studies that are open to inclusion must be advertised from the hospital's website, and are then available for search from other hospital's websites and at helsenorge.no. The studies is also linked to current treatment texts. Registration must take place before inclusion of patients, by sending a separate form to the Department of Communication at the hospital. A notification is sent to the same place when inclusion is completed/terminated

or if there are changes in which (Norwegian) institutions that include patients. It is also possible to register studies that do not recruit hospital patients.

Annual reporting of included patients in clinical trials

The project manager should report the number of included (new) patients in the year or if the project has been completed, by a survey (web form). The project manager must ensure that the overview of relevant participants (institutions) is complete. The reporting provides the basis for the Ministry of Health and Care Services' assessment of whether the target number of studies and the proportion of included patients is reached (and for the distribution of research funds to the regional health authorities). An overview of active clinical trials and number of patients is published on CRISTIN (please be aware that this platform will be replaced in 2024 by a new science archive service).

APPENDIX 7: Author information

Annetine (Anne Cathrine) Staff: MD, PhD (2000); specialist in obstetrics and gynecology. Full-time professor (Professor I) at the University of Oslo since 2015, in combination with part-time clinical consultant work at Division of obstetrics and Gynaecology, Oslo University Hospital (OUS). Head of research, Division of obstetrics and Gynaecology since 2016. Deputy/Acting Head REK (Regional Committee for Medical and Health Research) Southern Norway 2001-2005. Member of NEM (National Committee for Medical and Health Research) 2006-9. Acting Director of Research and Development in South-East 2009-10.The research field comprises translational projects in the fields of obstetrics and gynecology, with emphasis on placenta, preeclampsia and associations with long-term maternal cardiovascular health.

Karin C. Lødrup Carlsen: MD, PhD. Head of Research 2010-2016 at the Women and Children's division, Oslo University Hospital. Head of Research Divison of Paediatric and Adolescent Medicine from 2016. Professor I at the University of Oslo, Faculty of Medicine from 2017 (Professor emeritus from autumn 2024). Consultant and specialist in pediatrics at the Children's Clinic. PhD in 1995, performing research projects related to lung function, asthma and allergic diseases in children. Head of the PreventAdall project and the ORAACLE research group (Oslo Research group of Asthma and Allergy in Childhood; the Lung and Environment).

Harald Arnesen: Professor Emeritus, MD, PhD. Clinical researcher for several decades. Main research focus include prospective randomized trials and translational research in the cardiovascular field and thrombo-cardiology. Professor in cardiology at the University of Oslo since 1992, Professor Emeritus since 2009. Previously Head of the Centre for Clinical Cardiovascular Research at OUS. Head of the Centre for Clinical Research at OUS until 2006. Chief of Cardiology at the outpatient section until 2009.

Anne Grete Bechensteen: MD, PhD. Consultant, specialist in pediatrics, currently Head of Children's Oncology section at OUS , localization Rikshospitalet. Performing research since

1988, PhD in 1997, including research projects within hematology, neonatal medicine and pediatric cancer.

Anne Flem Jacobsen: MD, PhD, specialist in obstetrics and gynecology, OUS, localization Ullevål. Performs clinical and epidemiological research on thrombo-embolism and pregnancy. Professor II at the University of Oslo since 2014.

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APPENDIX 8: Downhill skiing track

Downhill Skiing Track: PhD Track

Tips for PhD students, exemplified for the Faculty of Medicine, University of Oslo (UiO)

- Supervisor and project should be decided upon before submission of PhD application
- Do we fit together? See "Supervisor track" and Chapter 10 of the Research Handbook

PhD in medicine and health sciences UiO

Application of admission to the PhD program:

- Application form (information about the applicant, supervisor, co-supervisors, financing, PhD courses)
- Project description (maximum 10 pages)
- Certified copies of diplomas from completed degrees (medical, masters, graduate or equivalent)
- Confirmation of PhD project funding (≥ 1 year)
- Agreement with external parties (for external employees and / or candidates who make use of resources outside the University). A main supervisor from outside the University may be suggested, but should be justified
- Formal approvals (REK etc)

Project period

See "The Downhill Skiing Track for Research Projects" and Chapter 6 of the Research Handbook to ensure that the formalities are in place

Recommendations of the Committee

Within three months after receiving the thesis, the adjudication committee must submit a report. The committee must give notice within two months of whether revisions are required or if the dissertation will be rejected. The committee evaluation should be available 8 weeks before any agreed upon time of disputation

Preparations for disputation

UiO has made a list of tasks for the PhD candidate and The Faculty of Medicine

Booking of premises for disputation

The PhD student is responsible for booking the auditorium for the trial lecture and disputation. This is scheduled after the committee evaluation is received

Submission of a thesis to the UiO

- Submit the whole thesis, including:
- Application letter for evaluation of the thesis
- Confirmation of approved PhD courses
- Co-authorship declarations
- Declaration of research permits (REK etc)
- A form containing suggestions for members for the adjudication committee and Acting Dean
- Declaration of Impartiality

Printing of the thesis

After the thesis has been approved, it must be made publicly available at least two weeks before the disputation. Contact Reprosentralen (also assists in free electronic publishing in the UiO DUO electronic library).

A popularized scientific summary (in Norwegian and English) must be sent to UiO at least 4 weeks before the disputation

The big day: Trial lecture and disputation

The adjudication committee decides the title for the trial lecture, which lasts 45 minutes. The candidate is given the topic 10 working days before the trial lecture will take place

The disputation (2.5-3 hours) is chaired by the Dean or a deputy Dean. This "Acting Dean" first briefly describes the submission process and evaluation of the trial lecture. Thereafter, the PhD candidate gives a 20 minute popularized scientific account of the PhD research work performed. Subsequently, the first opponent has a maximum of 75 minutes for opposition, while the second opponent should limit the opposition to a maximum of 60 minutes

Congratulations,
you have passed your PhD exam!

PhD Party (optional)

Guidelines for the PhD dinner on the day of the disputation. A nice speech is expected of the candidate

Conferral of the PhD degree

After approved PhD disputation, the PhD degree is conferred upon the candidate by the University Dean on behalf of the University Board. This ceremony includes awarding of doctoral diplomas and usually occurs twice per semester. The PhD candidate may bring a limited number of guests

Useful documents for the PhD track:

- The PhD program
- How to apply
- Supervision
- Adjudication committee
- The chair of Defence
- "Med en doktor i magen"

Appendix in "The Research Handbook – from idea to publication", 10th. edition 2024, English version
by Annetine Staff (uxnnaf@ous-hf.no) and Karin C. Lødrup Carlsen (uxkclo@ous-hf.no) et al

Annetine Staff and Ana Lobato Pascual 2024

Downhill Skiing Track: Supervisor Track

Exemplified for PhD supervisors at the Faculty of Medicine, University of Oslo (UiO)

Basic information for supervisors:

- The PhD programme at the Faculty of Medicine: Admission to the PhD programme (with ethical guidelines for supervisors etc.) and rules and regulatory frameworks (including admission, supervision, thesis evaluation and public defence).
- Courses for academic staff at UiO: Teaching and Learning in Higher Education (25 h module).
- Ethics training programs: see this Research Handbook (RH) Chapter 16 and the Research Ethics Library.
- Research Formalities and responsibilities: see Chapters 6 and 10 (RH)
- Research Leadership Program: See Chapter 10 (RH), UiO Research leadership programmes and Copenhagen Business School.
- **Books on being a supervisor, in Norwegian**: Lauvås P and Handal G (Forskningsveilederen. Cappelen Akademisk Forlag 2006) and Dysthe O and Samara A (Forskningsveiledning på master- og doktorgradsnivå. Abstrakt Forlag 2006)
- **Successful Supervision, A Dialogue Facilitator**" from Karolinska Institutet: practical help for the supervisor and student: clarifies expectations and roles, and provides guidelines for creating realistic plans for the research project

Supervisor and candidate: a good match for this PhD project?

- Check CV and personal background information. For students: check with other PhD students/research group members
- Clarify expectations (it is the supervisor's responsibility to initiate the conversation): ambitions, responsibilities, roles, mutual expectations, collaborative format, co-supervisors' roles, PhD timeline, funding, publication rules (possible publications during and after PhD), potential access to data following PhD etc.

The main supervisor's tasks:

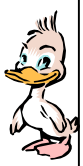
- Assistance with shaping the PhD project ideas and outline of the student's PhD application (ideas may be provided by the potential PhD student)
- Obtaining PhD grant
- Identify suitable co-supervisor(s)

START

Submit application for admission to the PhD program: see Chapter 13 of The Research handbook (RH), and "PhD Downhill Skiing Track"

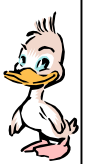
Project period:

- Conduct **the research projects**
- Attend PhD program **courses** and follow up meetings with the supervisor/ research group
- The PhD student has a personal responsibility to ensure that regulations and recognized ethical principles are followed, although the institution ("forskningsansvarlig" i.e. the Research Director) has the overall formal responsibility and the Project Manager has the day-to-day practical responsibility



Project period:

- **The supervisor is responsible for ensuring that formal** regulations are followed (during the entire project period) and should help the PhD candidate in understanding the rules for formalizing research projects. The Research Director is responsible at the institutional level and the Project Manager has the practical responsibility, according to The Health Research Act, see Chapters 6 and 10 (RH)
- **Formal preapproval of research projects** (at the institution and within REK etc): see "Research Project Downhill Track" and Chapter 6 and 10 (RH) to ensure that the formalities are in order for all research projects
- **Regular sessions with the supervisor:** Frequency, type and duration depends on the project type, and the candidate's/supervisor's background, experience and personality.
- **In case of conflict** between PhD student/supervisor (if a conflict cannot be resolved internally or at local institution): contact the PhD coordinators at the Faculty of Medicine, UiO.
- **Career guidance on future research options** after PhD completion



The End (of the PhD period):
Submission of PhD thesis, dissertation, PhD party (see Chapter 13 and the "PhD Downhill Skiing Track"). A nice speech to supervisors and everyone else that has assisted in the PhD period is expected

The End (of the PhD period):

- Guide the synopsis writing and submission of PhD thesis
- Provide suggestions to UiO on composition of the PhD evaluation (adjudication) committee (the head of the committee must be academically employed by UiO, both genders are to be represented)
- Deliver a nice supervisor speech at the PhD party

GOAL

Congratulations,
the student has been successfully supervised to a PhD degree!

Appendix in "The Research Handbook – from idea to publication", 10th. edition 2024, English version
by Annetine Staff (uxnnaf@ous-hf.no) and Karin C. Lødrup Carlsen (uxkclo@ous-hf.no) et al.

Annetine Staff and Ana Lobato Pascual 2024

THE RESEARCH HANDBOOK

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Oslo University Hospital: Harald Arnesen, Annetine Staff, Karin C. Lødrup Carlsen, Anne Flem Jacobsen og Anne Grete Bechensteen

Web edition available at Oslo University Hospital:
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