

An interdisciplinary institute

Professor Meinhard Kieser, Director of the Institute of Medical Biometry and Informatics, provides an overview of the Institute, discussing its structure, involvement in research and education, and plans for the future



STRUCTURE

The Institute of Medical Biometry and Informatics (IMBI) at the University of Heidelberg comprises the Department of Medical Biometry and the Section for Medical Informatics.

The Department has extensive expertise in the statistical support of projects covering all areas of medical research. The primary area of methodological research in the Department is the development and improvement of statistical methods to optimise the planning of medical experiments and analysis of data. The research aims to improve the biometrical planning and analysis of clinical trials, studies in health services and gene association and expression studies, as well as systematic reviews and meta-analyses.

In medical informatics, one of the most important research topics is the management and integration of medical data that arise from decentralised sources and are stored in heterogeneous formats. The Section has extensive expertise in the creation and implementation of platforms to integrate these data (eg. clinical, molecular, genetic and tissue data) in a common database, which is not only

challenging from the informatics perspective but also requires the latest knowledge on ethics and privacy.

DIVERSE ROLES

My main duties as Director are to guide, encourage, teach and support all of my collaborators at the Institute. I direct their research activities and conduct my own methodological research. I'm also responsible for all administrative aspects of the Institute, such as supervising finances and organisational structures. Last but not least, I enjoy teaching medical biometry and participating in clinical research projects as a biometrician.

APPLYING STATISTICS

Medical biometry is the science and application of mathematical methods and statistical design to aid in the efficient conduct of medical research projects and objective interpretation of data. It includes aspects of designing, conducting and analysing clinical studies and provides objective evidence for medical investigations, enabling the accurate interpretation of results. Furthermore, medical biometry contributes to the efficacy and safety of pharmaceuticals and to the success of novel therapies or interventions.

COLLABORATIVE RESEARCH PROJECTS

In all research that takes place at the IMBI, our biostatisticians work closely with data managers and IT specialists, who are highly experienced in data handling and computer-assisted statistical analysis. This means the full spectrum of biostatistics is covered, with both methodological expertise and practical experience. Our scientists and data managers play an active role in the clinical research process through close cooperation with hospitals and pharmaceutical companies. They are involved in the planning, execution, evaluation and publication of studies. We always work towards a high standard of quality, and approved Standard Operation Procedures

(SOP) ensure the efficiency of all stages of biometric support for clinical trials and registers.

The successful planning and realisation of medical research projects is only possible if the responsible biometrician has methodical and medical knowledge as well as interdisciplinary skills; therefore, the ability to integrate medical and statistical research is of great importance. Working groups at the IMBI are in close contact, and they exchange their experiences on a regular basis so they can learn from one another.

SUPPORTING NEXT-GENERATION RESEARCHERS

The IMBI employs biometricians and medical information scientists with years of experience in planning and conducting trials and registers. They work closely with younger colleagues, imparting their knowledge and educating them for future research projects. The IMBI also offers internships in pharmaceutical companies to give young researchers professional experience and conducts a Master's programme in Medical Biometry. The programme covers the theoretical aspect of the certificate 'Biometry in Medicine' which is awarded by the German Society of Medical Informatics, Biometry and Epidemiology (GMDS) and the German Region of the International Biometric Society (IBS-DR).

PLANS FOR DEVELOPMENT

The IMBI already offers a wide spectrum of biostatistical methods and services to support medical research. I aim to develop this further and add more focus areas. For example, I would like to emphasise the highly important issue of extending methodology to evaluate targeted therapies. We have recently received funding for research in this field and have begun our investigations with promising results. I feel sure that we will contribute a great deal to research in this area in the coming years.

High-level support of medical research

The Institute of Medical Biometry and Informatics at the University of Heidelberg in Germany offers critical support to medical research through method development, education and consultation

MEDICAL BIOMETRY IS the science of measuring and analysing biological data. It is crucial to the successful planning and implementation of medical research and is based on biostatistical methodology. It aids the design, conduct and evaluation of clinical trials and is a vital part of assessing new treatments, and an essential tool for all medical research projects. Alongside this, medical informatics is crucial for effectively organising, analysing, managing and using information generated through medical experiments.

Professor Dr Meinhard Kieser is the Director of the Institute of Medical Biometry and Informatics (IMBI) at the University of Heidelberg, which addresses both of these key, emerging areas through the Department of Medical Biometry and the Section of Medical Informatics.

ADAPTIVE DESIGNS

The Department of Medical Biometry at the IMBI has unprecedented experience in biostatistical methodological research and biometrical consulting. It also has expertise in planning, conducting and analysing patient-orientated clinical trials, and is thus a valuable resource for the medical research community.

The IMBI undertakes biometrics methods research to address a range of different fields, each of which corresponds to a specific working group within the Department. For example, one such research area relates to the calculation, and re-calculation, of sample size. Determining the required number of test subjects is a crucial aspect of any clinical trial, but it can present a challenge when existing literature does not permit an accurate estimation of the parameters. The inability to reliably

estimate crucial parameters before a trial begins means there is a real risk of underestimating the sample size required to obtain meaningful results. To prevent this, the IMBI performs methodological research on the internal pilot study design that determines an initial sample size in the planning stage. It then takes in a portion of the data, re-estimates the parameters and adjusts the number of cases required accordingly. This innovative design meets several methodological challenges, and in recognition of this, the German Research Foundation has provided a six-year research grant for the project. Procedures have been developed for solving key problems in a broad range of study designs. Moreover, the methods have already been accepted and applied in a wide variety of cases.

Clinical trials are vital to provide evidence for the efficacy and safety of a new therapy or medicinal product. However, it was previously impossible to change the design of an ongoing trial without threatening its credibility – even if new data collected during the course of the trial suggested the study was flawed due to incorrect underlying assumptions. This is no longer the case with the development of adaptive trial designs. These enable data-driven modification of a study while the trial is ongoing. They form a major research area at the IMBI, acting as a powerful tool to maintain the integrity of a clinical trial. "Information from study data already obtained can be included in the second phase of the trial, while meeting the methodical standards," explains Kieser.

PROVEN TO INCREASE EFFICIENCY

Adaptive trial designs have been applied in the clinical trials working group as part of the DISPACT study, which was published in *The Lancet* and investigated the two most commonly used

closure techniques following a pancreatectomy. The multicentre trial included 450 patients and was planned using the IMBI's adaptive statistical design. The trial did not find a significant difference between the two treatment methods, but did show the effectiveness of adaptive designs to increase clinical trial efficiency.

SOUGHT-AFTER SKILLS

There is high demand for educated biometricians worldwide. This demand is especially being felt in Germany, where the gap between the number of required and available qualified biometricians is particularly prominent. The extra-occupational Master's programme in Medical Biometry at the IMBI is the only educational opportunity of its kind offered by a German university, making it an extremely valuable resource. This programme fosters sought-after skills in its students, and its structure has been adapted to ensure that the curriculum meets international standards. In fact, the degree is accepted all across Europe, allowing the programme to compete with the European market.

CONSULTING

The IMBI also has a biometric consulting service carried out by scientific staff at the department. The service offers methodological and statistical advice for projects and can, for example, assist in the selection of study design, sample size calculation and statistical interpretation of results.

The number and diversity of projects taking advantage of the service has rapidly increased during recent years. By offering biometric planning, data management and statistical analysis and interpretation, the IMBI is able to



Scope of projects

The IMBI is currently running 50 clinical trials and registers, with 6,568 recruited patients and 7,956 planned patients. Some of the most promising randomised, controlled trials include:

- **SYNCHRONOUS** – a multicentre trial to study the effects of resection of the primary tumour versus no resection prior to systemic therapy in patients with colon cancer and synchronous unresectable metastases. Performed in cooperation with the Study Centre of the German Surgical Society
- **PROUD** – a 1,200 patient examination of the efficacy of two sutures in preventing surgical

site infections after abdominal wall closure. Performed in cooperation with the Study Centre of the German Surgical Society

- **SOSTA-Net** – group based social skills training in children and adolescents with high functioning autism spectrum disorder, in cooperation with the University Hospital of Frankfurt
- **Malaria study** – investigation of the efficacy and safety of a combination therapy in the treatment of malaria in children, performed in Burkina Faso in cooperation with the Institute of Public Health, University of Heidelberg

provide important support to medical research projects to ensure methodologically optimal study design and analysis.

INFORMATICS AND MEDICINE

Running alongside the Department for Medical Biometry is the Section of Medical Informatics. The Section plays an important role in supporting biomedical research and clinical care, teaching, providing services for medical faculty and clinics at the University and fostering R&D.

Research in the Section aims to identify challenges in medical data integration and develop tools to overcome these issues. Interdisciplinary collaboration is essential to this, and the Section maintains active partnerships with the Heidelberg University Hospital, internal and external research departments and local companies. Research is focused on three key areas: health data management, medical image processing and pattern recognition, and knowledge-based decision support. The team provides data, information and, most importantly, evidence to support decision making in diagnostics, therapy and preventative medicine.

IMPROVING METHODS FOR CANCER TRIALS

Most recently, the IMBI has been conducting groundbreaking work on phase II designs for cancer trials. It has published a number of papers

on the subject in highly regarded journals. The scientific community has received the papers with enthusiasm, and as a result, several national and international conferences have invited IMBI members to give lectures. Kieser explains why the cancer trial improvements have met with such success: "These methods allow for a more far-reaching flexibility for this type of clinical trial and thus considerably facilitate practical application. Moreover, these designs turned out to be more efficient than their classical counterparts – a real win-win situation". His team is currently implementing the methods within user-friendly and open-source software, which will further add to their benefit.

The IMBI has seen great success in recent years, as Kieser expounds: "IMBI scientists have published a huge variety of papers in high-ranking journals, both in the medical and the methodological field, and we have participated successfully in over 100 clinical studies so far. Additionally, we have substantially increased our third-party funding".

Furthermore, the IMBI has recently been confirmed to manage biometrics and data management within 'Neurobiology and Treatment of Adolescent Female Conduct Disorder: The Central Role of Emotional Processing', a research project managed by 17 Principal Investigators across nine different European countries. This underlines the Institute's role in ensuring the success of diverse medical research projects.

INTELLIGENCE

INSTITUTE OF MEDICAL BIOMETRY AND INFORMATICS

OBJECTIVES

The Institute of Medical Biometry and Informatics (IMBI) specialises in both biometric and bioinformatic methods development and consulting as well as planning, implementing and evaluating patient-orientated research projects. The working groups of IMBI cover the entire spectrum of medical research projects including clinical trials of all phases, genetic studies, health services research, systematic reviews, meta-analyses and clinical registries.

PARTNERS

Study Centre of the German Surgical Society • Coordination Centre for Clinical Trials Heidelberg • National Center for Tumor Diseases • Institute for Applied Quality Improvement and Research in Health Care • Research Network First-in-Man Heidelberg

FUNDING

In recent years, the IMBI received funding from the German Research Foundation, Federal Ministry of Education and Research, EC, public trusts, the pharmaceutical industry, medical engineering companies and others.

CONTACT

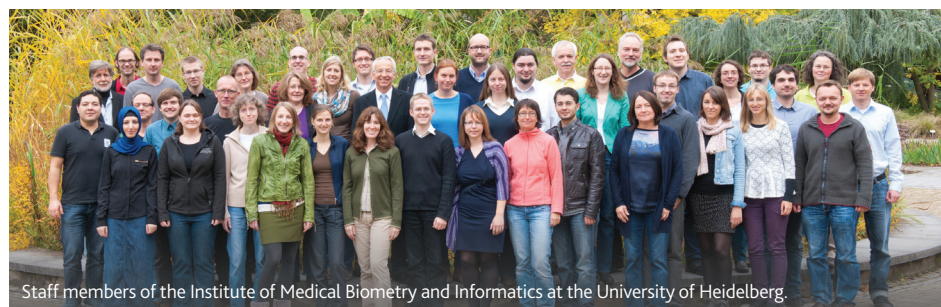
Professor Meinhard Kieser
Director

Institute of Medical Biometry and Informatics
Ruprecht-Karls University of Heidelberg
Im Neuenheimer Feld 305
D-69120 Heidelberg
Germany

T +49 6221 56 4140
E meinhard.kieser@imbi.uni-heidelberg.de

www.biometrie.uni-heidelberg.de

MEINHARD KIESER studied Mathematics and Physics and graduated in 1986. In 1991, he received his PhD, and his Habilitation ('*Venia legendi*') for Medical Biometry in 2001. After working as a research fellow at the universities of Mainz and Heidelberg, and as a biometrician in the pharmaceutical industry, he is now full Professor and has been Director of the IMBI since 2008.



Staff members of the Institute of Medical Biometry and Informatics at the University of Heidelberg.