JG|U UNIVERSITÄTSmedizin. MAINZ

Clinical Epidemiology and Systems Medicine

Embedded in a Strong Institution

University Medical Center of the Johannes Gutenberg University Mainz

The University Medical Center of the Johannes Gutenberg University Mainz is the only medical institution offering supra-maximum care in the German state of Rhineland-Palatinate and is internationally recognized for its scientific achievements.

Specialists in medicine and life sciences at 60 clinics, institutes and departments work together on an interdisciplinary basis, treating 300,000 inpatients and outpatients annually.

Highly specialized patient care, research and teaching are inseparably intertwined. Around 3,000 medical and dental students as well as more than 600 medical, commercial and technical professionals are trained in Mainz.

With a workforce of approximately 8,600 colleagues the University Medical Center Mainz is one of the largest employers in the region and an important driver of growth and innovation.

304,607 Patients

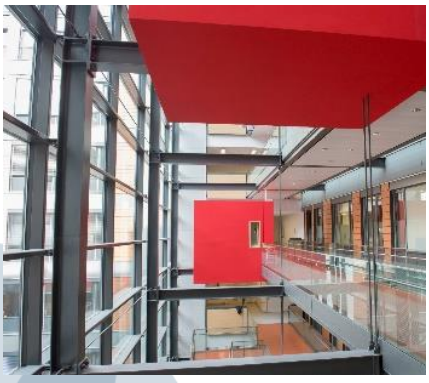
2,965 Students

8,580 Employees

Research and Patient Care

Our focus is on performing cutting-edge translational research that benefits patients, while also delivering the state of the art in patient care. This philosophy is translated in practice in a research arm - the Clinical Epidemiology and Systems Medicine (CESM) – and a clinical arm – the department of Preventive Cardiology and Medical Prevention, Department of Cardiology, at the University Medical Center of the Johannes Gutenberg University Mainz.

Organizational Affiliations



PREVENTIVE CARDIOLOGY AND MEDICAL PREVENTION AT THE DEPARTMENT OF CARDIOLOGY

The Department of Cardiology at the University Medical Center Mainz is the leading cardiology center in Rhineland-Palatinate and the Rhine-Main metropolitan region. Clinical focuses comprise the acute coronary syndrome and chronic cardiovascular disease. With Europe's first Heart Valve Unit the center is a leading center in Germany in interventional heart valve therapy. A dedicated team of approximately 400 ensures care at the highest international standards to more than 11,000 inpatients and 20,000 outpatients annually.

CLINICAL EPIDEMIOLOGY AND SYSTEMS MEDICINE AT THE CENTER FOR THROMBOSIS AND HEMOSTASIS

The Center for Thrombosis and Hemostasis Mainz (CTH) was established in 2010 as an Integrated Research and Treatment Center funded by the German Ministry for Education and Research. The CTH provides a unique interdisciplinary environment that facilitates basic research, innovative patient care and the development of new diagnostics and therapies.

CTH
Centrum für Thrombose und Hämostase Mainz

PARTNER SITE RHINE-MAIN AT THE GERMAN CENTRE FOR CARDIOVASCULAR RESEARCH (DZHK)

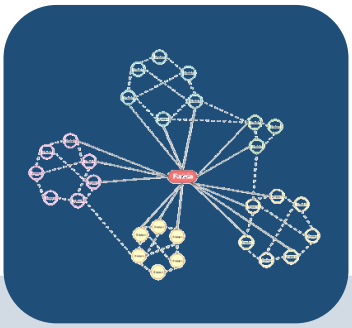
DZHK
DEUTSCHES ZENTRUM FÜR HERZ-KREISLAUF-FORSCHUNG E.V.

The DZHK was established in 2012 on the initiative of the Federal Ministry of Education and Research. The objective of the DZHK is to rapidly and efficiently transfer results from basic research in cardiovascular disease into clinical practice.

Our Focus and Research Aims

What We Do

A focus on complex common diseases with high burden in society



Systems medicine with epidemiological principles of causal inference

Patient-oriented research geared towards clinical translation

Our Objectives

Identifying and understanding clinical and subclinical phenotypes (e.g. intermediate organ damage) by investigating molecular patterns in deeply phenotyped human subjects

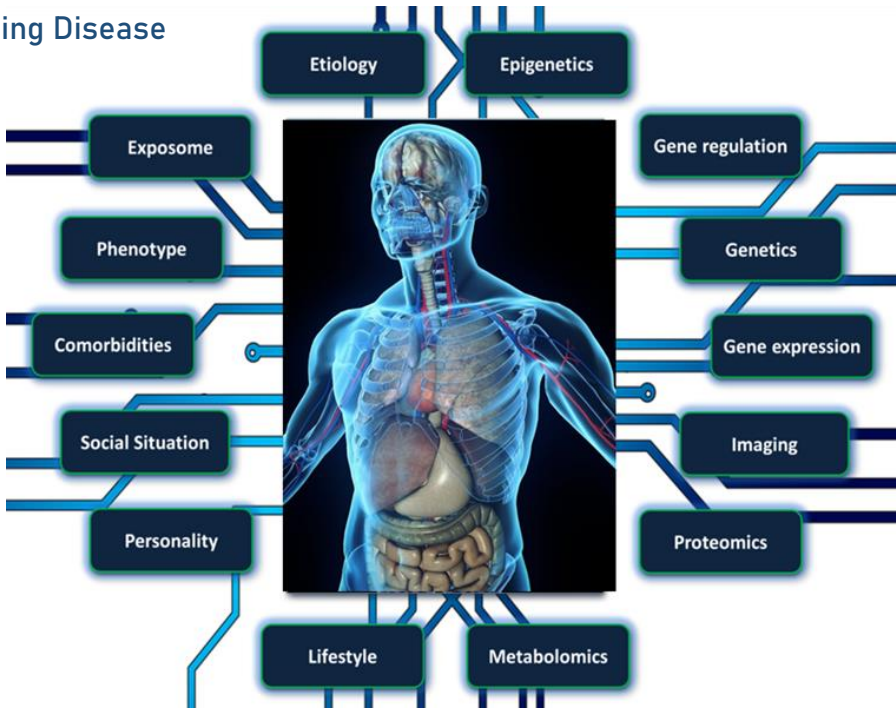
Screening and prioritizing therapeutic targets by relating pathophysiological processes to clinical outcome

Forming a bridge between bench and bedside by generating molecular hypotheses that are testable in experimental (phase I-II) and clinical settings (phase III-IV)

Our Systems-oriented Approach

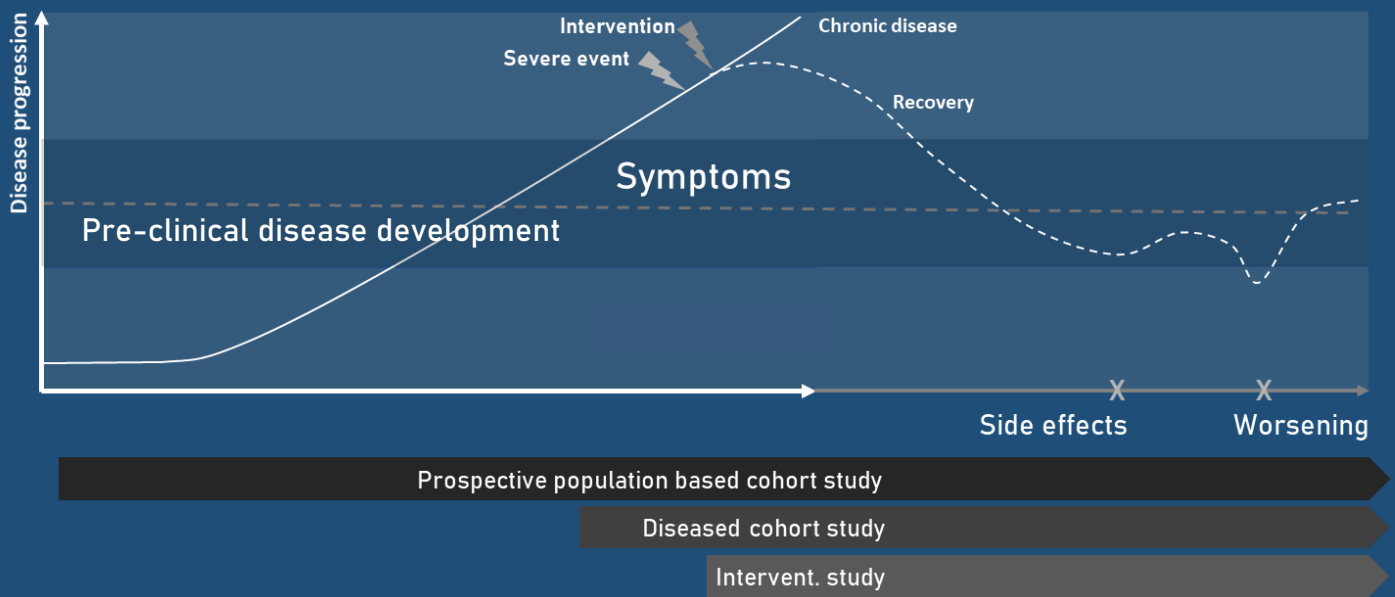
A Holistic Approach to Understanding Disease

The CESM concentrates on patient-oriented, translational, cardiovascular research. The focus is on conducting prospective cohort studies and clinical trials to improve the prevention, diagnosis, treatment and prognosis of common, especially cardiovascular, diseases. To achieve this, we take a holistic approach that reflects all levels that influence disease — from genetics, to lifestyle, social situation and other environmental exposures.



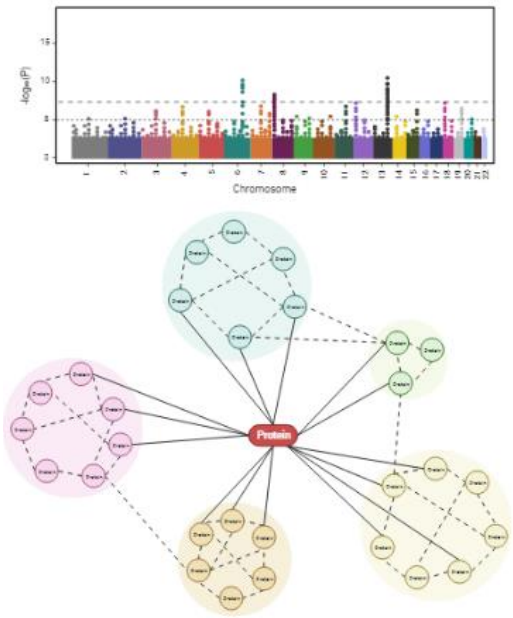
Detailed Monitoring of Disease Development, Expression and Progression

Studies in the clinical context usually enroll participants at the time of presentation to hospital with symptoms. Beyond potential selection biases, this means that it is not possible to observe individuals in the pre-disease period, in which subclinical disease first develops. Population-based cohort studies circumvent this by enrolling participants randomly, independent of their indication. Conversely, clinical studies are ideal for diseases with an important acute-phase component. The combination of population-based and clinical studies allows the investigation of disease at all stages, which is why the CESM conducts both types of studies.



Systems Medicine to Unravel the Molecular Mechanisms of Disease

Understanding Disease Pathophysiology at the Molecular Level



The Clinical Epidemiology and Systems Medicine (CESM) uses a combination of modern systems medicine methods and fundamental concepts from clinical epidemiology to gain new vantage points on complex disease. Data from all biological levels — from DNA, to the transcriptome, proteome and metabolome, as well as regulatory layers including DNA methylation — are holistically integrated with detailed clinical phenotype data to realistically depict the biological system in context of the disease of interest. A transdisciplinary team of experts works together to understand if and how these processes are causally related to the disease.

Sequential Multi-Omics Data

The Gutenberg cohorts managed by the CESM all share the feature that biomaterial is sequentially collected at several time points. Multi-omics profiling is conducted on biosamples and post-processing performed according to highly standardized procedures. This provides a high-resolution window into disease pathophysiology at all stages — from pre-disease to acute disease, its progression and resolution.

Examples of Multi-Omics Profiling in the Gutenberg Cohorts

Setting	Genomics	Transcript-omics	Proteomics	Lipidomics	Metabo-lomics	Regulatory levels (e.g. epigenetics)
Population-based	X	X	X	X	X	X
Cardiovascular	X	X	X	X	X	X
Diabetes mellitus	X		X	X	X	
Venous thrombosis	X		X			X
Arterial thrombosis	X		X			

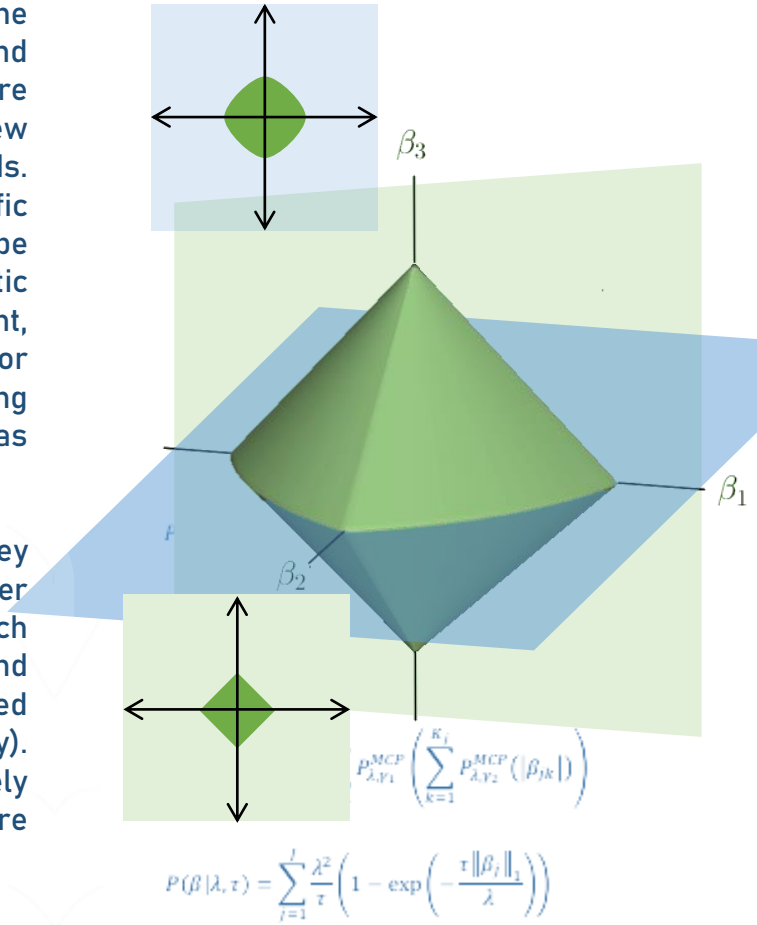
*Multi-omics profiling of sequential biosamples is ongoing in all cohorts, including those not shown above

Methods Development in Biostatistics and Artificial Intelligence (AI)

Advancing Analytic Methods to Promote Knowledge Generation

To support innovative systems medicine research, the CESM employs statisticians and machine learning researchers who are dedicated to the development of new biostatistical and machine learning methods. These methods are optimized to the specific purpose of each investigation, whether it be drug target discovery, mechanistic explorations of pathway involvement, monitoring disease development over time, or integrative multi-omics approaches including less well-characterized data levels such as the lipidome.

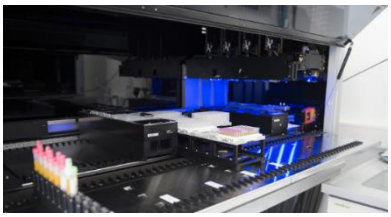
In all applications, it is important that key features of the biological system under investigation are adequately captured, such as non-linear relationships, interactions, and grouping structures (e.g. based on shared pathways, functions or sequence homology). To accommodate these needs in extremely high-dimensional settings, new methods are continuously proposed and implemented.



Deep Learning for Enhanced Feature Extraction from Clinical Imaging

A large amount of clinical imaging data is produced on a daily basis in clinics. Despite recent progress, only a fraction of this data is currently leveraged for clinical or research applications. New developments in artificial intelligence (AI), especially in the subfield of deep learning, open up the possibility of exploiting the large potential of this untapped resource. CESM researchers and affiliates work together to optimize deep learning architectures to automate and improve clinical imaging pipelines as well as to extract novel features that could enhance and accelerate individualized risk prediction.

Biobanking – The Basis for Cutting-Edge Biomedical Research



- Quality and Standardization
- Availability of data
- Ethics and legal requirements

Biobanking – one of "10 ideas changing the world right now" (TIME magazine, 2009)

BIOBANK MAINZ

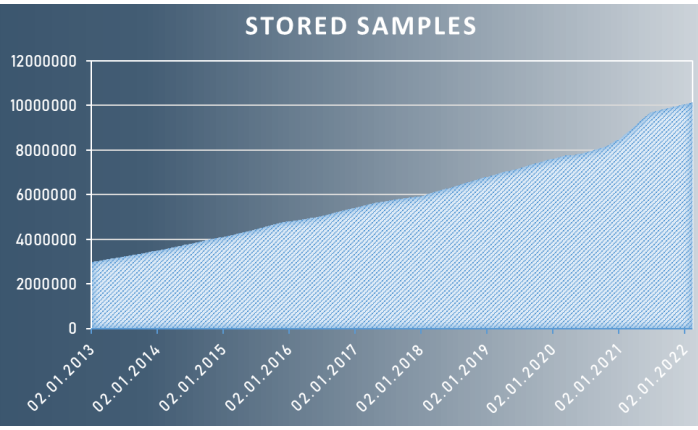
bbm

a strong partner within

Alliance Partner German Biobank Node bbmri.de

BBMRI-ERIC®

The BioBank Mainz (BBM) at the Mainz University Medical Center represents one of the largest collections of human biological samples in Germany. It offers professional support to partners within and outside the University Medical Center Mainz for the archiving, management and analysis of biospecimens.



-80°C -196°C	>15	>10M	>40	>20
Storage	Years	Samples	Studies	Biomaterial Qualities

Quality Management – Highest Standards for Data Quality

Standardized Data Collection

Standard Operating Procedures (SOPs) which clearly define procedures for investigations and data collection ensure comparable and uniform data collection.
Regular staff trainings and SOPs for training new team members guarantee that the quality of data in our studies remains at a consistently high level.

Standardized Biosample Collection

To guarantee the highest level of biomaterial measurement especially with respect to biobanking, all workflows from sample collection over processing and storage have been standardized with SOPs documenting all processing steps. In addition, pipetting robots prepare samples and with the aid of standardized sample management (sorting by quality, mirrored storage) the samples are then stored in temperature-monitored freezers (biobanking).

Transparency and Documentation

To ensure transparency regarding procedures and data collection, variable dictionaries are available for each study visit comprising detailed information about instruments/devices used for data collection, response formats, reference values etc. Variable dictionaries are accessible for scientists for planning of evaluations and research projects.
Any adjustments or changes with respect to data collection methods or to data throughout quality control are documented so that changes can be traced at any time.

Data Management– From Data Collection to Quality-Controlled Data

Our data management team monitors, controls., and supports the process from data collection to the final data sets for statistical analysis. This includes the provision and renewal of survey forms (electronic Case Report Form, eCRFs), programming query reports for automated real-time control of raw data with respect to completeness and plausibility, managing and documenting queries, and maintaining the study databases. The quality-controlled (QC) databases, which are stored in the firewall-secured, departmental server landscape, build the basis for creating data sets used for statistical analyses and research.

Scientific Expertise

Systems Medicine	Cardio-vascular Medicine	Clinical Epidemiology	Molecular Epidemiology	Molecular Biology and Biochemistry
Deep Clinical Phenotyping	Multi-Omics (e.g. Genetics, Proteomics, Metabolomics)	Biology and Bioinformatics	Artificial Intelligence (Machine learning, Deep learning)	Biostatistics
Conducting and implementing large scale studies	Quality Management	Digital data assessment (Apps, wearables)	Biobanking	Technology Platforms as a Service

Our Team – Interdisciplinary, Professional, and Passionate about Science

Our team currently comprises over 150 staff members and combines expertise from several scientific disciplines and professions to jointly conduct cutting-edge clinical and epidemiological research and excellent medical treatment.

- Administration & Project management
- Lab staff
- Study assistants & Study nurses
- Student assistants
- IT & Technical staff
- Biostatistics & Bioinformatics
- Scientists, Clinician scientists
- Data management

Mission Statement

Our Values

Motivation and personal commitment
We identify with our tasks and work with heart and soul, since our findings benefit not only a few people, but the general public.

Appreciation and efficiency
We attach great importance to an appreciative and effective working atmosphere and enjoyment of our work.

Professionalism and reliability
We attach special importance to a very good cooperation and highest satisfaction in medical care and scientific cooperation. Therefore, professionalism, flexibility and reliability are of central importance to us.

What Sets Us Apart

Quality through diversity
Our interdisciplinary team enables us to provide high-quality research and excellent medicine through diverse approaches and complementary expertise.

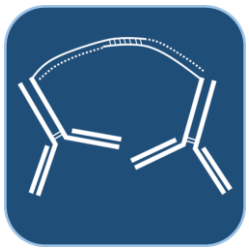
High standards and modern technologies
Standardization, quality management and the use of state-of-the-art technologies enable us to ensure the validity and reproducibility of innovative scientific findings.

Progress through continuous development
In order to provide the best research and care every day, we strive to continuously develop ourselves personally and as a team.

Technology Platforms

The CESM operates a number of state-of-the-art technology platforms, both for our own research as well as to facilitate the research of partners and affiliates. These platforms are available as a service, supported by highly trained staff qualified to optimize sample preparation, data pre- and post-processing, and data analysis using cutting edge methods.

Targeted Proteomics



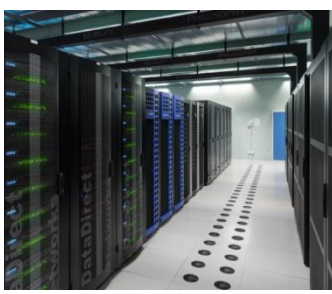
- High-throughput Proteomics
- Proximity Extension Assay (PEA) technique
- Combination of high specificity (dual antibody detection) and high sensitivity (PCR / NGS-based quantification)
- More than 3,000 plasmatic proteins per individual detectable in low sample volume
- Coverage of a wide range of biological processes

Platelet Phenotyping

- Platelet Function Analyzer (PFA)-200
- Light Transmission Aggregometry (LTA)
- Rotational Thromboelastometry (ROTEM)
- Calibrated Automated Thrombogram (CAT)
- Flow cytometry

Biostatistics and Applied Artificial Intelligence (AI)

- State-of-the art data analysis and interpretation
- Combination of traditional biostatistics with advanced methods including AI, encompassing supervised and unsupervised machine learning
- High Performance Computing (HPC)



Conducting Large-Scale Population Studies – The Gutenberg Health Study

Gutenberg Health Study

Gutenberg Health Study - Interdisciplinary prospective cohort study on population health in Rhineland-Palatinate

- Population-based (City of Mainz & District Mainz-Bingen, N = 15,010, age range at baseline 35-74 years)
- Baseline April 2007-April 2012
  Sequential follow-up investigations: 2.5, 5, 7.5, 10, 12.5y
  On-Site follow-up after 5y (N= 13,568) and 10y (ongoing)
- 5.5-hour medical–technical examination
- >11,000 data points per individual and visit
- >5M samples (blood, stool, tear liquid, PBMC, gum pocket swabs)

- Highly standardized medical-technical examinations
- Computer-assisted interviews
- Questionnaires
- Biomaterial
- Linkage to registry data (e.g. cancer registry)
- Validated and ICD-coded clinical endpoints

The Gutenberg Health Study (GHS) is the flagship population-based cohort study designed and conducted by the CESM, in concert with the consortial institutions. As the lead department in a multidisciplinary consortium of departments of the University Medical Center and the Johannes Gutenberg University Mainz, the CESM manages all aspects of the GHS. The combination of the age-stratified random sampling strategy (based on the local population registry), comprehensive deep phenotyping and follow-up (>10 years), and sequential multi-omics profiling renders the GHS a uniquely valuable resource for the study of disease development, progression and resolution in the population.

Study consortium

Department of Cardiology

Center for Thrombosis and Homeostasis

Institute for Clinic Chemistry and Laboratory Medicine

Department of Internal Medicine I

Department of Dermatology

Department of Psychiatry and Psychotherapy

Department of Psychosomatic Medicine and Psychotherapy

Institute of Medical Biostatistics, Epidemiology and Informatics

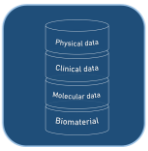
Department of Otolaryngology, Head and Neck Surgery

Department of Ophthalmology

University Cancer Center Mainz

The Gutenberg Cohorts – Systems-Oriented Research on Diseases

The Gutenberg Cohorts are prospective cohort studies spanning different clinical indications. Uniform, highly standardized methods of biobanking, deep phenotyping and serial multi-omics profiling across clinical and population-based cohorts enables direct comparison and external validation of results across indications.



Harmonized data assessment

Deep phenotyping

Standardized data and biomaterial collection

Homogeneous study population

>20

Clinical cohorts representing various indications

>30K

Study participants recruited across cohorts

>5M

Biosamples collected for multi-omics analysis

Our Contribution in the COVID-19 Pandemic

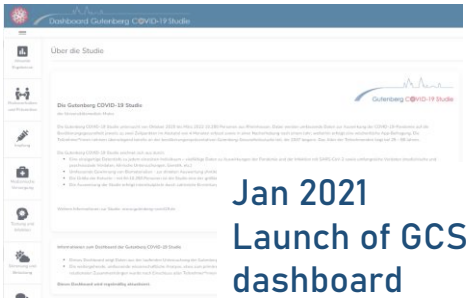
The Gutenberg COVID-19 Study (GCS)
A Case in Point of Rapid and Rigorous Science for the Benefit of Society

Mar 2020
WHO declared COVID-19 a pandemic

Mar 2020 – Oct 2020
Design, concept, establishment of two dedicated study centers

Oct 2020
Start of study including set-up of a population-based cell bank and app-based data recording

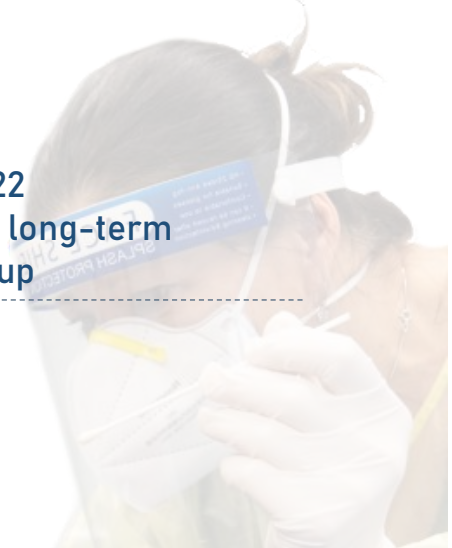
Oct 2020 – Apr 2021
Recruitment and baseline examination of 10,250 participants



Jan 2021
Launch of GCS dashboard

Mar 2021 – Jun 2021
Follow-up examination of 9,145 participants

Oct 2020 – Dec 2021
Continuous monitoring during the pandemic via GCS study app



Mar 2022
Start of long-term follow-up

Dec 2021
Start of the Gutenberg Long COVID Study

Translating Research into Patient Care: Our Knowledge for your Health

Preventive Cardiology and Preventive Medicine at the Department of Cardiology

A central motivation for CESM's research is to improve the health of the population by providing optimal treatment, taking into account the latest research findings and therapeutic options. In Preventive Cardiology and Medical Prevention, we offer a unique interdisciplinary environment for the diagnosis, treatment and prevention of cardiovascular diseases.

Preventive Medicine

- Comprehensive Medical Examination with a Focus on the Cardiovascular System
- Interdisciplinary Diagnostics and Treatment
- Individualized Consultation and Personalized Therapy Plans

Specialized Outpatient Centers

- Arterial Hypertension Clinic
- Clinic for Cardiovascular Sequelae after Childhood Cancer
- Lipid Clinic
- Pulmonary Embolism Clinic

Clinical Study Unit

- Access to latest Pharmaceutical Developments of Academia and Industry
- Conduct of and Participation in Clinical Trials and Registries across Cardiovascular-focused Indications

Training the Leaders of Tomorrow

We are committed to the promotion of young talent and teaching, as well as to the training and further education of the team in order to successfully meet the challenges of the present and the future.

In order to fulfil this mission we foster diversity and training in several multidisciplinary programs including postgraduate studies (e.g. (Bio)Medicine, Epidemiology), summer schools, structured programs for physician scientists and high-profile students and actively support efforts to overcome the gender gap and transform promotion of future leaders by fostering synergistic interaction across disciplines.

CESM offers talented students to participate in research schools and excellence networks facilitating access to structured training, mentoring and networking for individual career development:

TRANSMED
Mainz Research School
of Translational Biomedicine

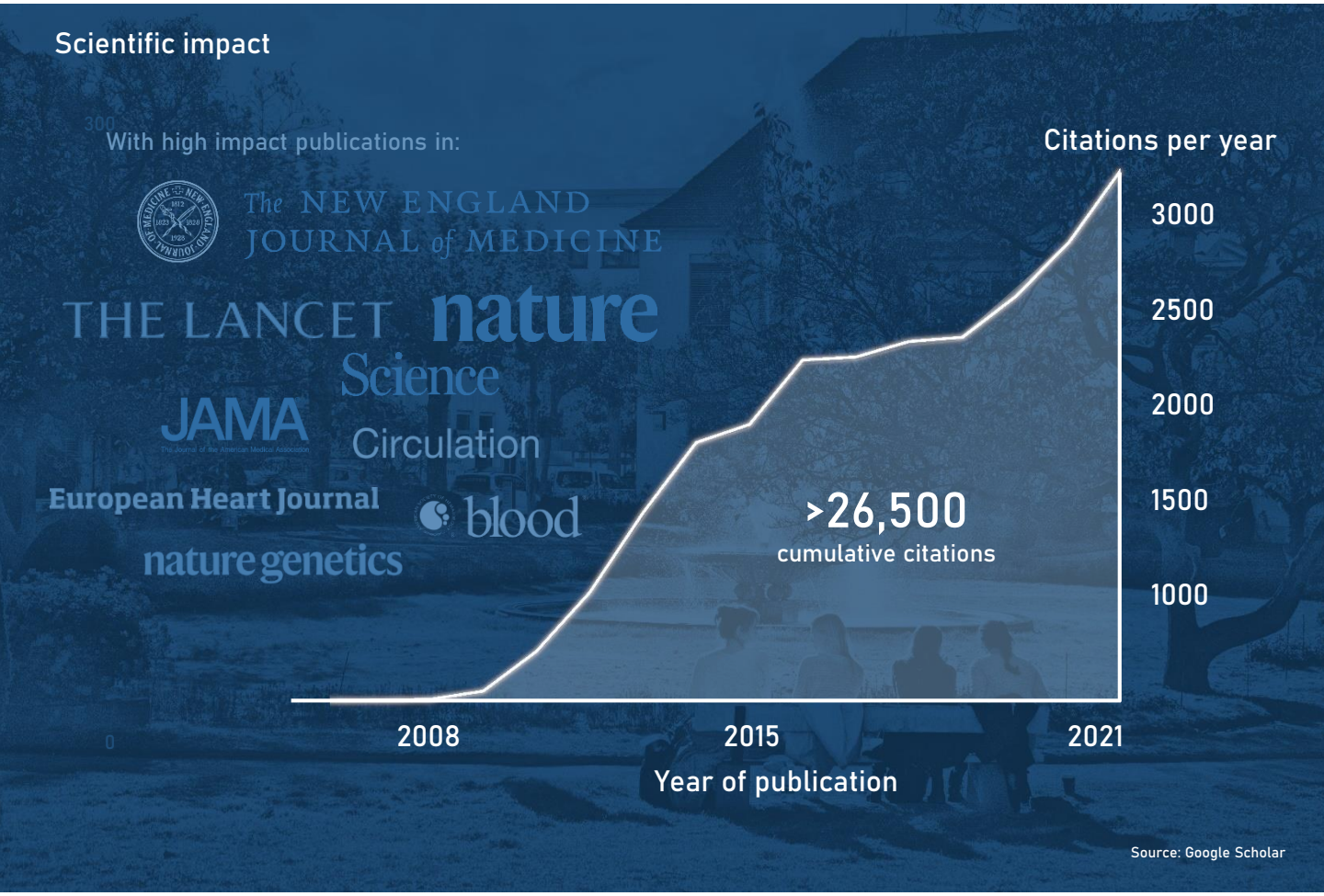
CTH
Centrum für Thrombose
und Hämostase
Mainz

imb
Institute of
Molecular Biology

INTERNATIONAL
PhD PROGRAMME
MAINZ

DZHK
DEUTSCHES ZENTRUM FÜR
HERZ-KREISLAUF-FORSCHUNG E.V.

Achievements and Scientific Output



15 Years of Research by the Numbers

>100M
Euros of third party funding obtained

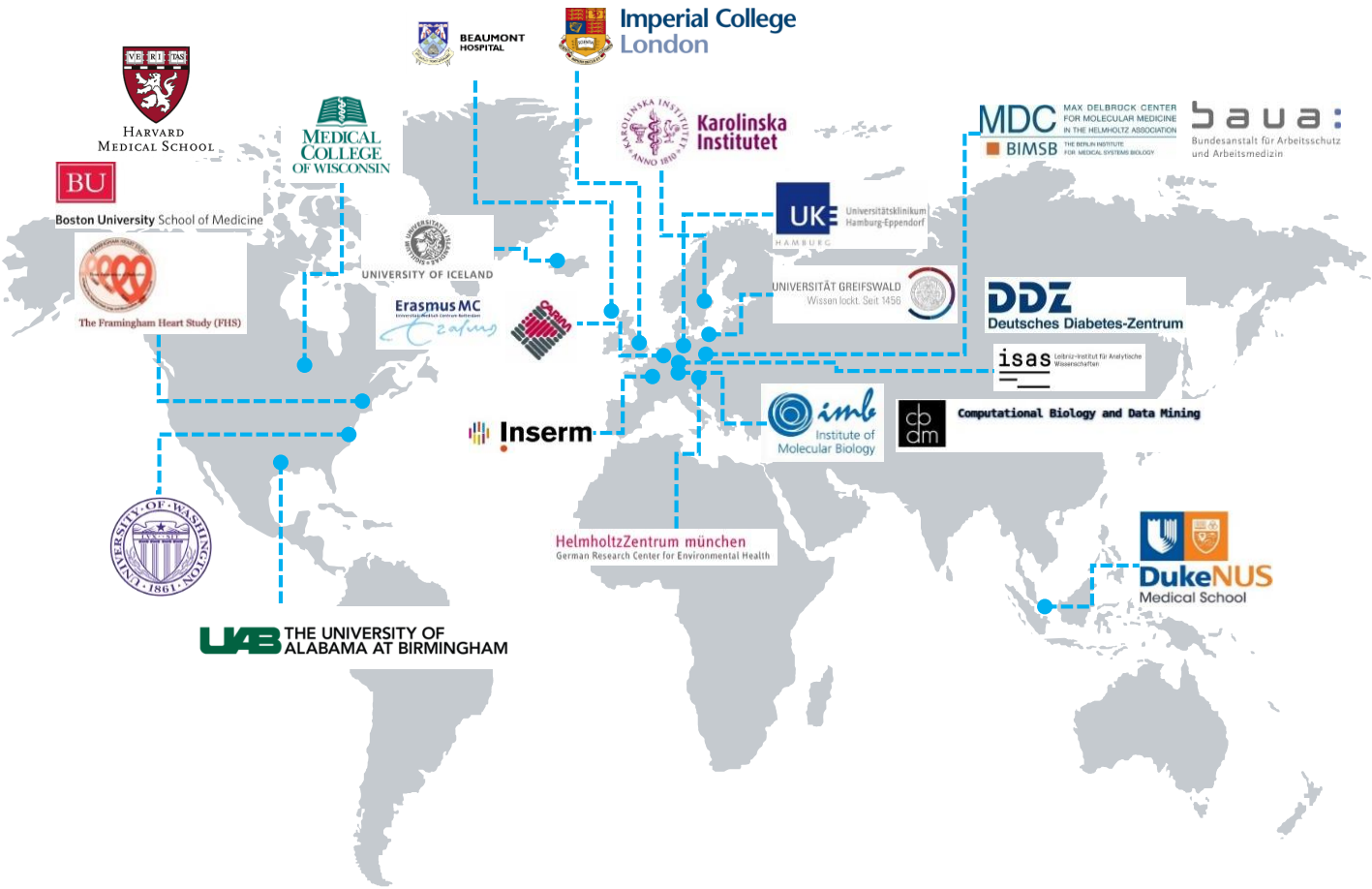
>350
Publications in peer-reviewed journals

>75
Citations per article

>26K
Citations across publications

The scientific footprint of the CESM is increasing year by year, and its high-quality work is recognized by publications in high-impact journals, high grant funding success rate, as well as the large amount of third party funding obtained.

Scientific Network



Scientific Networks and Consortia

curATime

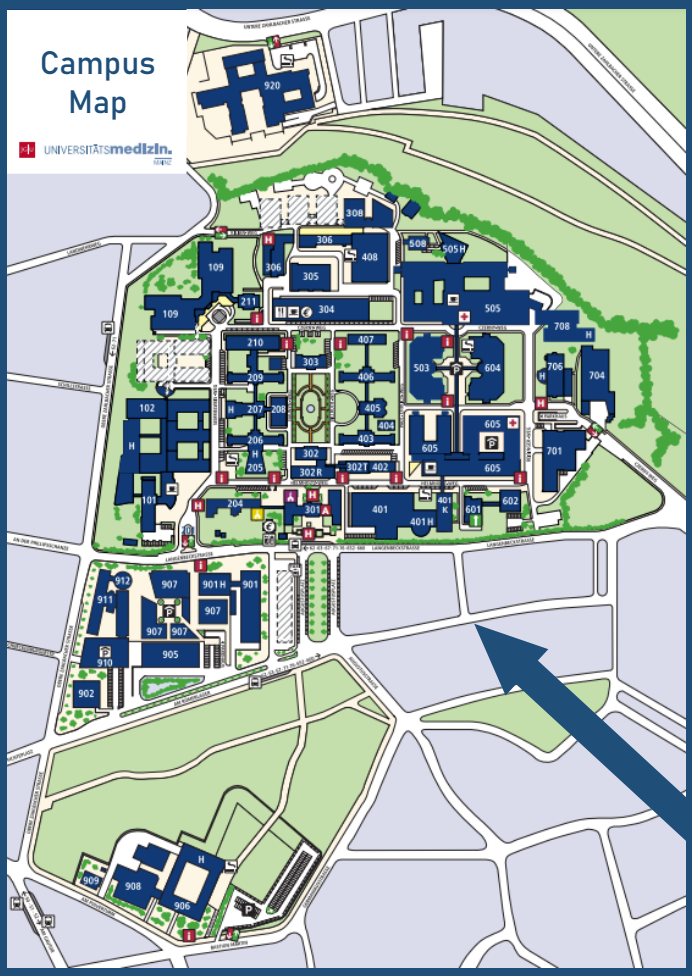
DIASYM

CHARGE Consortium

DZHK
Deutsches Zentrum für Herz-Kreislauf-Forschung e.V.

Industrial Collaborators

Bayer
Boehringer Ingelheim
Bristol-Myers Squibb
Daiichi-Sankyo
Novartis
Philips
Sanofi-Aventis
TRON



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Principal Investigator, German Center for Cardiovascular Research (DZHK)

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