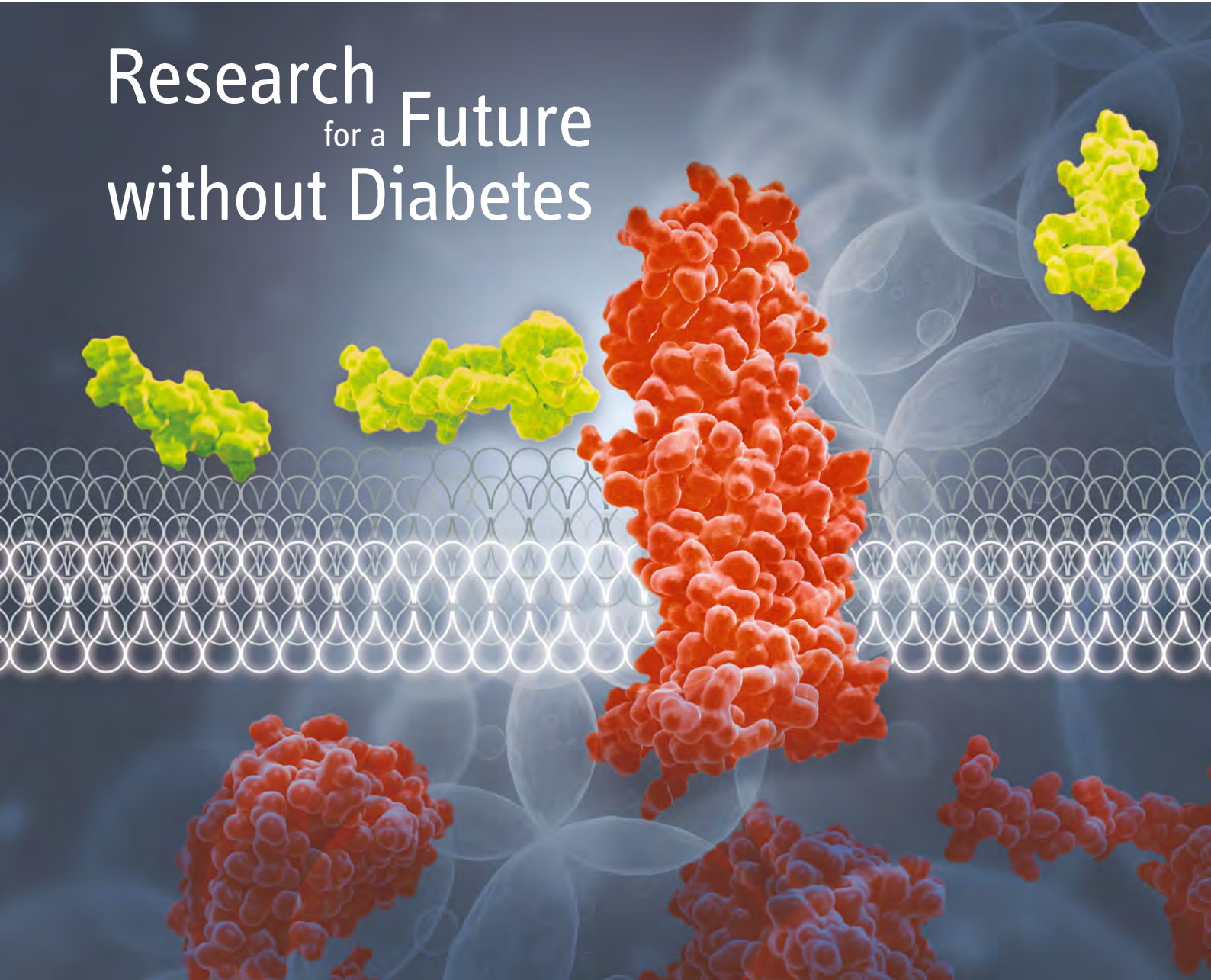
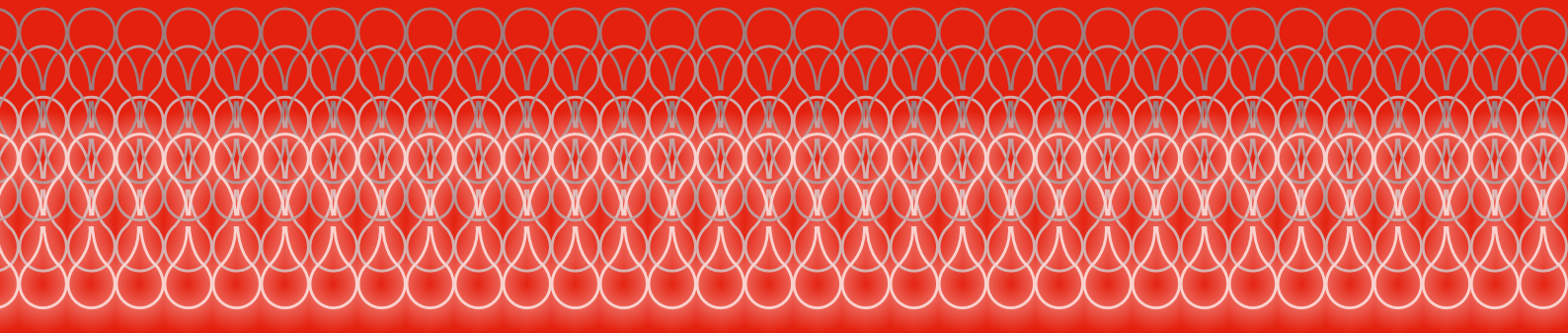
DZD
German Center for
Diabetes Research

DZG

Research for a Future without Diabetes





The mission of the DZD is to discover and develop innovative, precise strategies for the prevention, early detection and treatment of individuals with prediabetes or diabetes. Our goal is to improve quality of life and reduce diabetes-related comorbidities, complications and premature mortality.

Foreword

Research for a future without diabetes is the ambitious guiding principle of the German Center for Diabetes Research (DZD). Our incentive is to bring the results of diabetes research from the laboratory to society as quickly as possible through translational applications.

More than 450 experts from various disciplines in translational diabetes research, epidemiology, health-care research, bioinformatics and clinical practice are working together on new precise prevention and therapy concepts. State-of-the-art infrastructures, clinical multicenter studies, biobanks and the use of innovative IT and artificial intelligence enable excellent research. This culminates to much success: the DZD's research work not only helps to better understand the development of the metabolic disease, but also lays important foundations for innovative prevention and treatment methods. Some examples are new diabetes drugs, improved prevention and the introduction of precise diabetes therapy.

With its attractive training program, DZD NEXT, the DZD is able to attract and train young talents for diabetes research. The DZD collaborates with the leading organizations in diabetes research both on a national and an international level. It is one of the eight German Centers for Health Research (DZG).

These successes would not have been possible without the outstanding achievements of all those involved nor without the support of the federal and state governments. People will continue to be the focus of our work in the future – and they should benefit from our research results as quickly as possible.

Prof. Dr. Martin Hrabě de Angelis
DZD Board Member

Prof. Dr. Andreas Birkenfeld
DZD Board Member

Prof. Dr. Annette Schürmann
DZD Board Member

Prof. Dr. Michael Roden
DZD Speaker

Prof. Dr. Dr. Michele Solimena
DZD Speaker

Dr. Astrid Glaser
DZD Managing Director

Diabetes – A Growing Threat

In 2023, at least

8.9 million

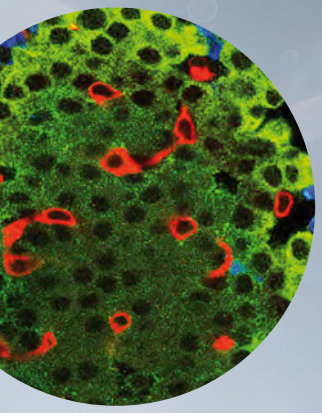
people in Germany had type 2 diabetes. In addition, the estimated number of unreported cases is at least 2 million.

Almost **12%** of adults in Germany have been diagnosed with diabetes.

Type 2

Obesity – A Risk Factor for Type 2 Diabetes

Every second adult in Germany is overweight, one in four is obese.



16%

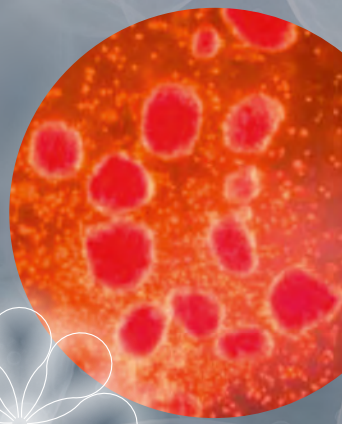
Around one in five deaths in Germany (16 percent) is associated with type 2 diabetes – due to complications and concomitant diseases such as cardiovascular diseases.

Type 1

37,000 children and adolescents and 340,000 adults have type 1 diabetes.

Complications of diabetes:

Heart attack
Diabetic foot syndrome
Hypertension
Stroke
Retinal disease
Psyche
Obesity
Disorders of lipid metabolism
Poly-neuropathy
Kidney diseases
Nerve damage
Vascular diseases
Renal insufficiency
Heart diseases



On average, the life expectancy of people with diabetes is around four to six years less than that of people of the same age without diabetes (Germany).

4 – 6 years

537

Around 537 million adults (aged 20–79) worldwide live with diabetes.

The total number of people with diabetes is expected to rise to 643 million by 2030 and to 783 million by 2045.

Every year, around 50,000 women in Germany develop gestational diabetes, which is almost 7 percent of all pregnant women. Their risk to develop type 2 diabetes later in life is seven times higher.

For sources see imprint page 31

Focus on Translational Research

Preventing diabetes effectively, treating it more efficiently and even averting it in the future – these are the ambitious goals of the DZD.

Diabetes is a pervasive global health issue. There will be a growing number of individuals affected by diabetes. Studies assume that the number of cases of diabetes in Germany will rise from the current 8.7 million to more than 12 million by 2040.

Interdisciplinary Collaboration

The research and development of innovative, precise strategies for the prevention, early detection and treatment of people with prediabetes and diabetes is the mission of the DZD. We aim at improving the quality of life and reduce diabetes-related complications and premature mortality. To this end, we are combining the expertise of leading German research institutions and universities in the field of metabolism and diabetes research. The additional value of the DZD is based on the broad technical expertise and the cross-departmental and cross-institutional collaboration of experts in diabetes research, clinical medicine, epidemiology, bioinformatics and healthcare research. This enables us to quickly transfer diabetes research findings from the laboratory to clinical studies and ultimately to society.

Successful Research

With the identification of the subtypes of prediabetes and type 2 diabetes, the DZD has achieved an important breakthrough towards precise diabetes therapies in the future. The DZD is successfully working on the discovery, validation and refinement of new drug candidates and targets for innovative drugs. Researchers at the DZD have developed a new class of drugs for the treatment of diabetes and severe obesity that combines several hormones. In population studies, DZD researchers are investigating the effects of environment, lifestyle and genetics on the development of diabetes.

The DZD's research into the early stages of type 1 diabetes provides an important basis for the development of innovative therapies that can delay or even prevent the development of the autoimmune disease type 1 diabetes. The DZD Academies focus their diabetes research on the most pressing questions: What is the influence of the liver or brain on diabetes? How can beta cells be protected? Which diseases are associated with diabetes? How do genetics and epigenetics contribute to the development of disease?

Translation: Quickly from Bench to Bedside

Thanks to the effective translation of research findings into practice by the DZD, numerous people are already benefiting from improved prevention, new types of medication and more precise diagnoses and therapies. The following examples present some of the DZD's translational research successes.

Weight Control: New Drugs for Obesity and Diabetes

A new generation of drugs, the polyagonists, is making a decisive breakthrough in the treatment of obesity and type 2 diabetes.

Instead of costly operations, polyagonists help overweight people to significantly reduce their weight and improve their blood sugar levels.

These drugs combine the effect of endogenous hormones such as GLP-1, GIP and glucagon to regulate the metabolism and curb one's appetite. The first approved drug, a dual agonist, impressively reduces body weight by up to more than 20 percent.

This innovative concept was developed by DZD researchers, among others. They are working on further combinations of active ingredients, including triple polyagonists, which show even stronger effects on body weight. The development of such drugs has the potential to become relevant for other diseases as well. This can be attributed to the fact that the combination of further hormones makes it possible to transport the drug specifically to certain organs and thus minimize potential side effects.

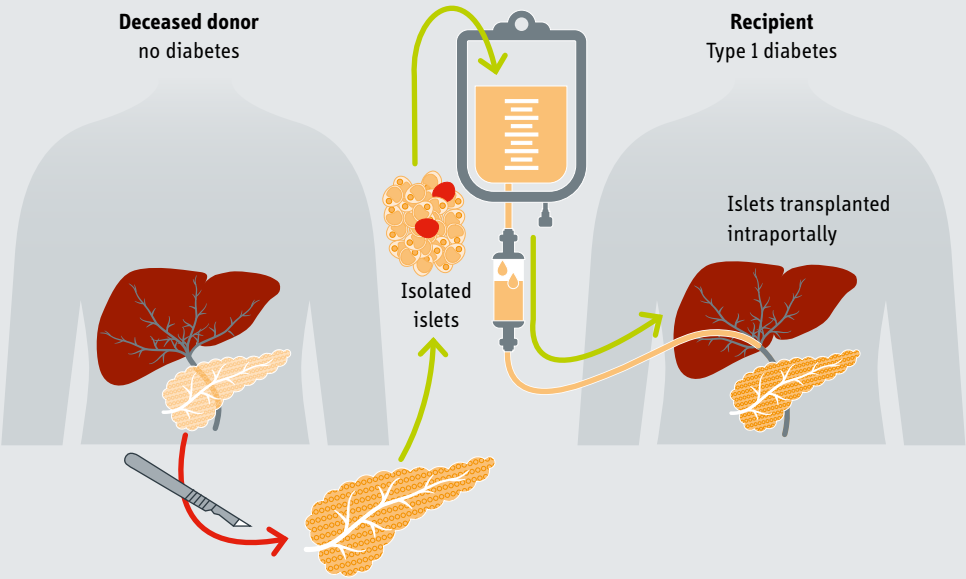
Publications: Science Translational Medicine 2013 | Cell 2016 | Nature 2023

Restoring Insulin Production

In people with type 1 diabetes, the insulin-producing beta cells in the islets of Langerhans (islet cells) in the pancreas die.

In this case, transplanting islet cells to restore the body's own insulin production is a promising treatment option. The DZD laid important foundations for islet cell transplantation and is the leader in this therapy.

However, the low willingness to donate organs and the need for lifelong immunosuppression inhibit the widespread use of islet cell transplantation. Researchers at the DZD are therefore working on alternatives, including an artificial pancreas. This therapy is special in that, although a Teflon membrane protects the islet cells from destructive contact with the body's own immune cells, the insulin produced can enter the body. DZD researchers are driving forward the development of an artificial pancreas with cells of human or animal origin. In addition, islet cells from human stem cells are being developed as an alternative source.



Publications: PNAS 2017 | Nature Scientific Reports 2018 | Nat Rev Endocrinol. 2022

Diabetes Prevention: Know Your Own Risk

Prevention is better than cure. But how do I know if I am at risk of developing type 2 diabetes? Important information on individual diabetes risk is provided by the DIfE – Deutscher Diabetes-Risiko-Test® (DRT, German Diabetes Risk Test).

Adults can determine their individual risk of developing diabetes in the next ten years free of charge. The test takes into account modifiable (e.g., waist circumference, smoking) and non-modifiable (e.g., age, family history) factors and provides specific recommendations for action to reduce a possible risk. The DRT is available as a self-test questionnaire, an interactive online test and a patient questionnaire for healthcare professionals.

The risk test was developed based on research data from the DZD and is being continuously improved. It now also considers the risk of cardiovascular disease. The DRT is part of the national education and communication strategy for diabetes, featured on diabinfo.de, and utilized by various stakeholders including health insurers, pharmacies, corporations, and the media.

Publications: Diabetes Research and Clinical Practice 2014 | Nature Scientific Reports 2021

Subtypes Discovered in Preliminary Stage of Diabetes

Diabetes has many causes. Accordingly, the health consequences of this metabolic disorder and the risk of severe courses are multifaceted.

As a result of the Prediabetes Lifestyle Intervention Study (PLIS), DZD scientists discovered six subtypes that can be clearly distinguished as early as in the preliminary stages of diabetes (prediabetes). This enables a more precise assessment of the risk of developing diabetes. This risk can be reduced through targeted prevention.

The suptype makes a big difference for people suffering from prediabetes: Three of the newly identified subtypes are characterized by a low risk of diabetes, three by an increased risk. People who belong to the high-risk subtypes are more likely to develop type 2 diabetes, fatty liver or damage to the kidneys and cardiovascular system. A new study argues in favor of remission of prediabetes as a therapeutic goal, i.e., a reduction in symptoms. This approach protects against the development of type 2 diabetes and leads to improved kidney and vascular function in the long term.

Publications: Nature Medicine 2021 | Lancet Diabetes Endocrinology 2023

On the Way to Precise Diabetes Therapy

Diabetes is more diverse than the classification into type 1 and type 2 diabetes would suggest. Researchers show the heterogeneity of the disease. They therefore propose a classification into five diabetes subtypes.

These groups were confirmed in analyses of the German Diabetes Study (GDS) that was conducted by the DZD. Depending on the subtype, the risk of developing complications such as fatty liver and damage to the eyes, nerves or kidneys varies in people with diabetes.

Algorithm for Precise Diabetes Diagnosis

With the help of mathematical algorithms, routinely collected variables can be used to find out which people produce less insulin or are prone to high blood pressure or lipid metabolism disorders within the first five years after they have been diagnosed with diabetes. As has been shown in a DZD study, these formulas also reveal other risks such as earlier death and specific diabetes complications.

These research findings have the potential to change the way type 2 diabetes is understood and treated and make it possible to enter the world of precision diabetology.

Publications: Lancet Diabetes Endocrinology 2019 | Lancet Diabetes Endocrinology 2024

A Ray of Hope for a Future Without Type 1 Diabetes

With its research work, the DZD has made unique progress in the early detection and prevention of type 1 diabetes (T1D).

Type 1 diabetes often occurs in childhood and adolescence. T1D is an autoimmune disease in which the immune system destroys the insulin-producing cells. DZD researchers have developed a test that can be used to detect an increased risk of T1D in infants.

The autoimmune disease T1D usually begins with a misdirected immune reaction against insulin. To delay or even prevent the onset of the disease in children with an increased genetic risk, DZD researchers are working on therapies to suppress the autoimmune reactions, for example by administering insulin powder or probiotics. Babies with an increased risk can take part in prevention studies.

Current studies show that T1D is an unexpectedly heterogeneous disease. The DZD has defined different subtypes in which the disease progresses differently. This may enable more precise treatment in the future.

Publications: JAMA 2013, 2020 | Nature Communications 2016 | eBioMedicine | 2022, ClinicalMedicine 2023

Excellent Infrastructures for Research

By establishing its own sustainable infrastructures, the DZD has created an important basis for translational diabetes research in a network.

The DZD's clinical research platform offers comprehensive services for conducting clinical multicenter studies and for collecting biosamples and medical data. Quality assurance and quality control measures in accordance with the Good Clinical Practice (GCP) and a standardized data management ensure high-quality and efficient processes in clinical research at the DZD.

For the DZD, it is particularly important that its research data management is secure, and that medical data can be reused. To achieve standardized data collection, the DZD has defined a core data set for diabetes which is also available to researchers outside the DZD. As a result, it is easier to analyze data across studies.

Leveraging artificial intelligence (AI) and machine learning (ML), the DZD Computational Core Unit develops cutting-edge methods for analyzing data from the DZD's clinical and translational research.

The DZD Biobank comprises several collections of biosamples from people with a preliminary stage of diabetes (prediabetes), type 1 or type 2 diabetes and gestational diabetes. The extensive medical data combined with the samples make the DZD Biobank a unique resource for diabetes research.

The DZD promotes the development of key infrastructures for efficient translational research at its sites, including preclinical models, geno- and phenotyping as well as high-throughput screening platforms and GMP laboratories that meet the quality standards for Good Manufacturing Practice (GMP) for medicinal products.

Clinical Diabetes Research: Precise Therapy and Prevention

Clinical studies on diabetes are not only crucial to the approval of new active substances or therapies, but they also provide new insights into the causes and mechanisms of the different courses of diabetes and its complications.

The DZD studies focus on type 1 and type 2 diabetes, gestational diabetes, complications, treatment of fatty liver in diabetes and insulin resistance in the brain as well as the effect of lifestyle changes or certain drugs. The results of the studies provide an important basis for precise prevention and therapy measures, i.e., the right treatment for the right patient group at the right time. The DZD has succeeded in identifying different subtypes of prediabetes and diabetes (see pages 12 + 13).

Thanks to the Germany-wide cooperation within the research network and together with university hospitals, the DZD is able to initiate large multicenter studies and recruit the required number of participants

Important information for translational diabetes research in the DZD is also provided by the data collection of the DPV (Diabetes-Patienten-Verlaufsdokumentation, Diabetes Patient Follow-up Documentation) and large population studies such as the Cooperative Health Research in the Augsburg Region (KORA), the European Prospective Investigation into Cancer and Nutrition Study (EPIC-Potsdam) and the National Cohort (NAKO), an important health study in Germany.

Promoting Up-And-Coming Talent

With the DZD NEXT program for the promotion of young talents, the DZD trains internationally competitive young diabetes researchers.

Professional training courses for core competence in translational research, events with top-class speakers and the active interdisciplinary network of DZD NEXT form a sustainable basis for scientific careers in the DZD. Being DZD NEXT members, more than 250 aspiring doctoral students, postdocs and clinician scientists in biomedical disciplines currently benefit from this offer.

The annual highlight is the international DZD Diabetes Research School for young talents in diabetes research, which comprises two days full of informative presentations by outstanding diabetes researchers. Participants benefit not only from exciting discussions in front of posters where they present their own research work, but also from new contacts among like-minded people.

DZD NEXT works successfully with the training programs of its partner sites and with national and international organizations, including the Danish Diabetes and Endocrine Academy (DDEA), the Lund University Diabetes Center (LUDC), the German Diabetes Association (DDG) and the German Centers for Health Research (DZG).

DZD NEXT

- Imparts specialized knowledge in translational research
- Professional national and international networks
- Promotes individual career paths

Translation Through Cooperation

Intensive interdisciplinary exchange is the basis for successful translational research.

The DZD stands for close interconnectedness and short communication channels. The continuous open exchange not only enables the development of innovative research approaches, but also the effective implementation of new findings from the laboratory into practice.

The DZD actively contributes to Germany-wide interconnectedness in medical research. Among others, we work closely with the German Centers for Health Research (DZG), the German Diabetes Association (DDG), the BZgA (future Federal Institute for Prevention and Education in Medicine) and the University Medicine Network.

The German Centers for Health Research

The DZD is one of the eight German Centers for Health Research (DZG). They were founded by the Federal Ministry of Education and Research (BMBF) to combat the widespread diseases such as diabetes, infections, cancer, cardiovascular, pulmonary, neurodegenerative and mental illnesses more effectively and to strengthen the health of children and young people. Throughout Germany, more than 100 universities, university hospitals and non-university research institutions are involved in the DZG. Cooperation across disciplinary and institutional boundaries is a particular strength of the DZG and is indispensable for successful translation from the laboratory to the clinic.

At international level, the DZD collaborates with leading organizations in the field of diabetes and metabolic research. DZD researchers are active on the boards of these organizations and organize international conferences. DZD research results are incorporated into guidelines.

One of the DZD's important cooperation partners is the healthcare industry. Spin-offs and patents contribute to the transfer of research results into applications. By involving all members of the value chain in the development of new drugs, the DZD makes optimum use of existing resources and can quickly bring new findings into practice and to the people.

Taking Advantage of Broad Expertise

The DZD is advised on the strategic development of the research program by a scientific advisory board.

Seven renowned experts from academic, clinical and industrial diabetes research form the Scientific Advisory Board (SAB).

The advisory board consists of:

- Prof. Dr. Domenico Accili is a physician working on the mechanisms of beta cell function and its disorders in the pancreas at Columbia University in the U.S.A.
- Prof. Dr. Johan Auwerx conducts research on metabolism, mitochondria, genetics, systems biology, diabetes, arteriosclerosis, obesity and transcription factors at the École Polytechnique Fédérale de Lausanne in Switzerland.
- Prof. Dr. Fatima Bosch is Professor of Biochemistry and Molecular Biology at the Universitat Autònoma Barcelona (UAB) in Spain and works on gene therapies, among other things.
- Prof. Dr. Marit Jørgensen is a medical researcher in the field of clinical epidemiology with a special focus on diabetes and cardiovascular diseases at the Steno Diabetes Center, Greenland, Denmark.
- Dr. Heike Neubauer is Director of the “External Innovation Cardio-Metabolic Diseases” department at Boehringer Ingelheim in Germany.
- Prof. Dr. Ulf Smith is Professor of Internal Medicine and Director of the Lundberg Laboratory for Diabetes Research at the Sahlgrenska Academy of the University of Gothenburg in Sweden (Spokesman of the Advisory Board).
- Prof. Dr. Karsten Suhre is working at Weill Cornell Medicine in Qatar to translate discoveries from metabolomics and genomics into clinical and biomedical applications.

Actively Involving People With Diabetes

People with diabetes and their relatives have a wealth of experience and can thus provide new impetus for research and communication with people. Both scientists and patients benefit from their active involvement in the DZD.

Consulting

A Citizens' and Patients' Advisory Board has been supporting the DZD since 2021. It advises the DZD on the translational research strategy and on research projects from the perspective of citizens and patients. The committee consists of nine people with type 1 and type 2 diabetes, relatives and interested citizens. The expertise of the advisory board has already been incorporated into the development of a new multicenter study and the further development of the national diabetes information portal *diabinfo.de*.

Active Participation

Clinical studies play a decisive role in medical progress. Patients are often involved as study participants. The DZD actively integrates the test subjects into the process and informs them regularly about the study results through newsletters or annual meetings.

diabinfo.de
Reliable Information on Diabetes

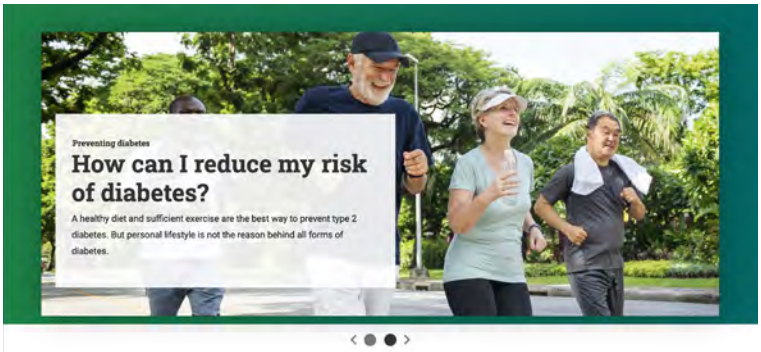
The online-based national diabetes information portal *www.diabinfo.de* offers independent, neutral, generally understandable and quality-assured information on prevention and treatment relating to all aspects of diabetes and its complications.

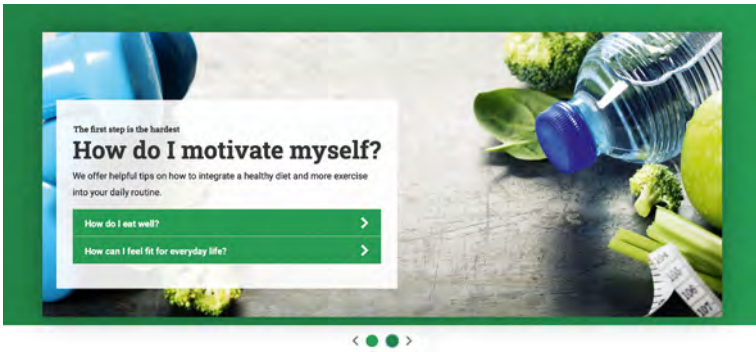
The portal is a joint service of the DZD and the DZD partners German Diabetes Center and Helmholtz Munich and is funded by the Federal Center for Health Education (BZgA).

In addition to basic knowledge, current news, background articles and the Diabetes Risk Test, the portal offers practical downloads, explanatory films, podcasts, infographics, quizzes and much more on the topics of prevention and living with diabetes. It also provides information for specialists. All content has been reviewed by doctors and scientists.

Large sections are offered in English, Turkish, Polish and Russian. In the German version, there are also pages in easy language and videos in sign language.

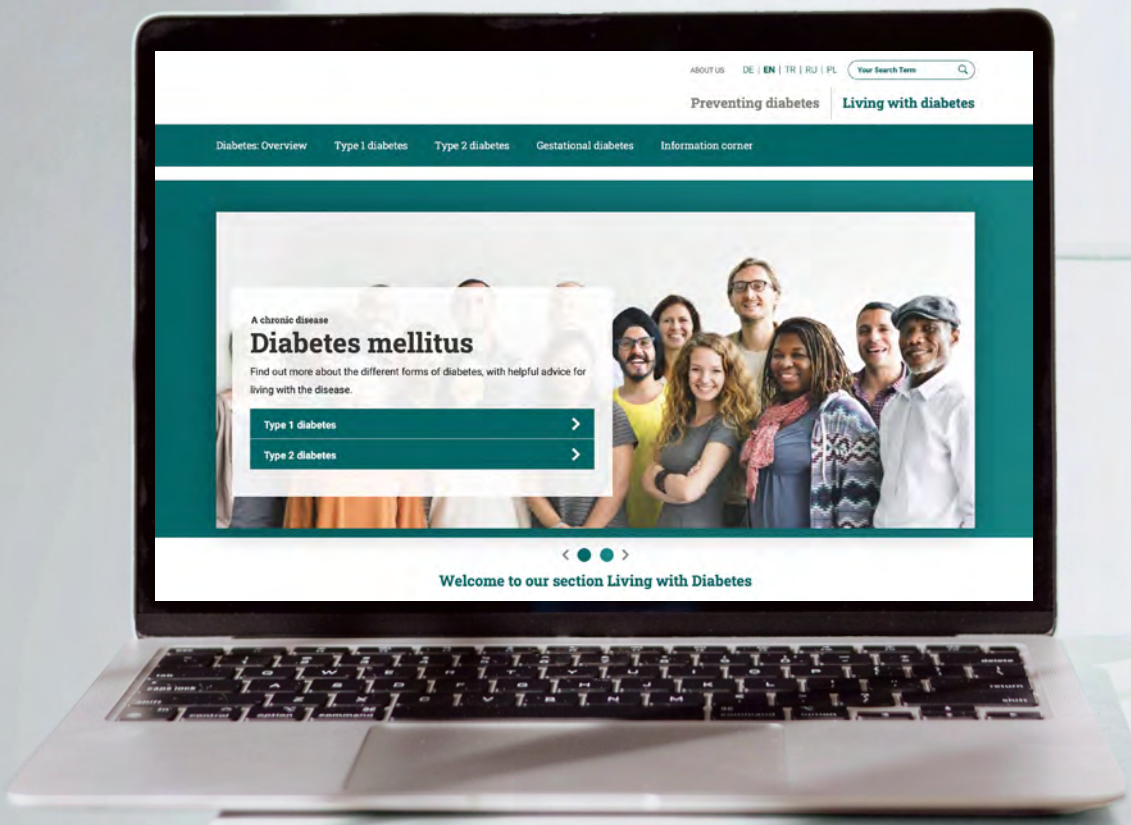
For people with diabetes, their relatives, teaching staff, the media and politicians, for professionals and for people at increased risk of developing diabetes and other non-communicable diseases, diabinfo.de is an important scientifically based source of information both as a website and on Instagram, X, YouTube and Spotify.



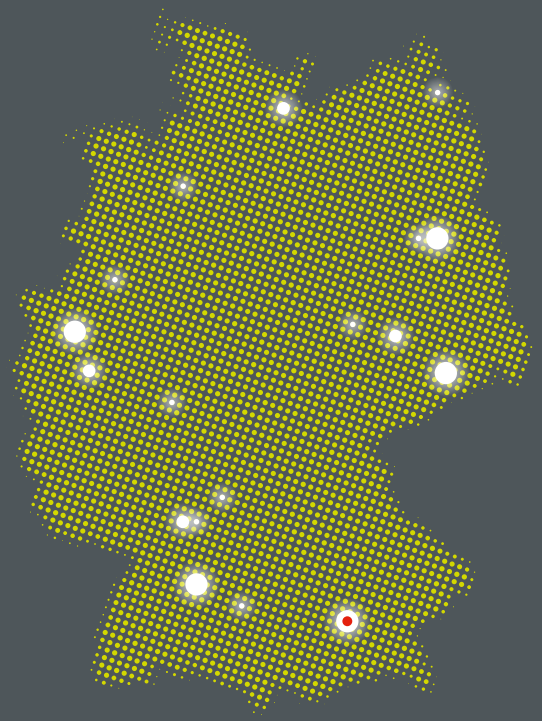


diabinfo

Das Diabetesinformationsportal



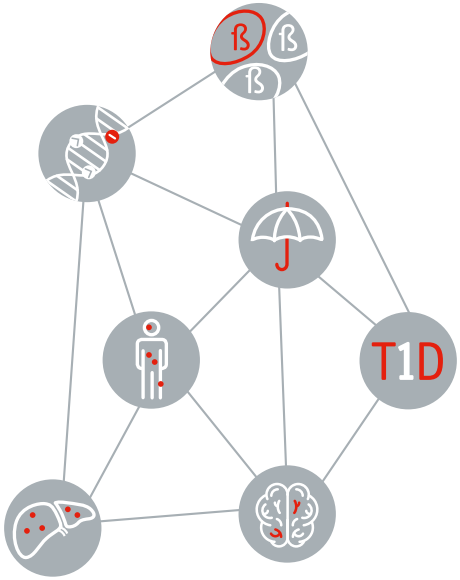
DZD at a Glance



> 450

scientists work together in the DZD across Germany on an interdisciplinary basis.

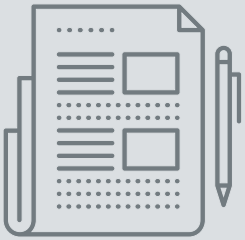
28 prizes and awards in 2023 for DZD researchers and projects.



The DZD is investigating the most pressing issues of diabetes research in seven key research areas.

> 500

publications per year in peer-reviewed journals.



> 5,800

people take part in clinical multicenter studies of the DZD.

The DZD is advised by a Scientific Advisory Board and, since 2021, also by a Citizens' and Patients' Advisory Board.

DZD NEXT

250

young talents take advantage of the DZD NEXT program, which focuses on translation.

Partners in the DZD

The German Center for Diabetes Research (DZD) e.V. is one of the eight German Centers for Health Research (DZG). It brings together experts in the field of diabetes research and interlinks translational research, epidemiology and clinical application.

Members

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German Institute of Human Nutrition in Potsdam-Rehbruecke (DIfE)
Speaker and member of the DZD Board of Directors:
Prof. Dr. Annette Schürmann

Helmholtz Munich
Speaker and member of the DZD Board of Directors:
Prof. Dr. Martin Hrabě de Angelis

Institute for Diabetes Research and Metabolic Diseases (IDM) of Helmholtz Munich at the Eberhard-Karls-University of Tuebingen
Speaker and member of the DZD Board of Directors:
Prof. Dr. Andreas Birkenfeld

Paul Langerhans Institute Dresden of Helmholtz Munich at the University Hospital Carl Gustav Carus of the TU Dresden
Speaker: Prof. Dr. Dr. Michele Solimena

Other partners

Associated partners of the DZD are diabetes research groups at the universities of Heidelberg, Cologne, Leipzig, Munich and Schleswig-Holstein. Other project partners are also part of the DZD.

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www.diabinfo.de/en

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