MINISTERSTVO ZDRAVOTNICTVÍ
ČESKÉ REPUBLIKY

Health Research Concept to 2030

Contents

Preamble

Pursuant to the Competence Act No 2/1969 Coll., as amended on 01/ 01/ 2022, the Ministry of Health of the Czech Republic is responsible for health-related scientific research activities. It establishes the Czech Health Research Council (CHRC) with the basic purpose of supporting applied research in the health sector pursuant to Act No 130/2002 Coll.

The Frascati Manual of 2015, as amended, divides research into basic, applied and experimental. Applied research is defined as original research carried out with the aim of acquiring new knowledge and is primarily directed towards a specific practical aim or objective. In the case of applied health research, this is logically directed towards the health sector. Nevertheless, Medical and Health Sciences include basic medicine, clinical medicine, health sciences, medical biotechnology and other medical sciences. All these areas are, in applied research, covered by CHRC expert evaluation panels under the responsibility of the Ministry of Health of the Czech Republic. On the other hand, the P304, P305 and P30G evaluation panels of the The Czech Science Foundation are clearly focused on basic health research.

The current Health Research Concept approved by the Government of the Czech Republic in 2014, valid until the end of this year, abandoned the original expert character and reflected a multidisciplinary approach. In this respect, the current approach remains unchanged.

The presented Health Research Concept responds to current healthcare needs in the Czech Republic and is based on both a detailed evaluation of the past period and defined thematic priorities.

1. Introduction

At present (i.e. in 2022), the "Health Research Concept to 2022" (approved by the Government of the Czech Republic through Resolution No 58 of 22 January 2014) is still in force. The 2014 concept was based on the documents relevant at the time. Since many significant changes have occurred in research, development and innovation in recent years, this "Health Research Concept to 2022" needs replacing with a new document that will better reflect current conditions and define such basic strategic directions that will be related to, and better reflect, the current conceptual documents of the European Union and the Czech Republic applicable to research, development and innovation.

The "Health Research Concept to 2030" (hereinafter the "Concept") is directly related to the "Health Research Concept to 2022" and further develops it. Therefore, an integral part of the Concept is an evaluation of how the existing concept has been implemented, along with chapter 6 "Evaluation of the Implementation of the Existing Concept for 2016 to 2022", then in detail in Annex 1 "Conclusions of the Interim Evaluation of the Programme to Support Applied Health Research for 2015-2022 and the Health Research Concept to 2022". The findings and recommendations of this evaluation are reflected in the new Concept. It must be stressed that this is an issue implemented by a number of institutions under different founders on the beneficiary side and a number of budget chapters on the provider side. A detailed analysis of the financing of health research is presented in Annex 2 "Analysis of Support for Health Research in the Czech Republic".

The Health Research Concept is based primarily on the needs of the development of the health system in the Czech Republic and the objectives set out in strategic documents for the healthcare sector. The basic direction for the strategic orientation of the Concept is primarily the Strategic Framework for Healthcare Development in the Czech Republic to 2030, the National Research, Development and Innovation Policy of the Czech Republic 2021+, the National Priorities of Oriented Research, Experimental Development and Innovation (hereinafter the "R&D&I Priorities") and the National Research and Innovation Strategy for Smart Specialization of the Czech Republic 2021-2027. In terms of the international context and related international commitments, the Concept contributes to the 2030 Agenda for Sustainable Development in the area of the Sustainable Development Goal "Ensure healthy lives and improve their quality for all at all ages". The Concept also reflects the objectives for the development of the European Research Area and the related objectives of the Horizon Europe support framework programme. Consistency and links to strategic documents of the Czech Republic and the EU are elaborated in Chapter 4 "Links of the Concept to Other Strategic Documents and Securing their Objectives".

The thematic priorities of research, development and innovation (R&D&I) for the Concept (Chapter 7) were defined by the members of the Commission for the Preparation of the Concept and the Panel of Guarantors of Thematic Priorities.

These identified the most important research areas and themes for individual disciplines in the Czech Republic. From the point of view of the Concept, there is one priority in the National Priorities of Oriented Research, Experimental Development and Innovation, Priority 5: Healthy population, focused on health, especially applied, research and development. Priority 5 themes are significantly reflected and developed in the Concept. Some sub-themes of Priority 5,

focused on the development of new materials and technologies for use in healthcare, are and will be implemented through Technology Agency of the Czech Republic programmes. The procedure for preparing the Concept is described in detail in Chapter 11 "Procedure for Preparing the Concept". In addition to updating and expanding the content of the thematic priorities already contained in the existing Concept, some completely new priorities have been included in the new Concept. As an example, the inclusion of the Public Health thematic priority as a response to the situation facing the whole world in the context of the COVID-19 pandemic.

The Concept also reflects the strategies to support health research in developed countries, which are described in Chapter 5 "Analysis of Health Research Abroad" and in more detail in Annex 3 "Foreign Approaches to Supporting Health Research". Chapter 8 "Ensuring Concept Implementation" is devoted to the implementation of the Concept which, *inter alia*, points to the need to increase support for health research in the Czech Republic. The Concept fulfilment indicators and evaluation system are defined in Chapter 10 "Concept Implementation Control and Evaluation".

2. Thematic focus of the Concept

The thematic focus of the Concept is based on the National Priorities of Oriented Research, Experimental Development and Innovation, specifically on Priority 5: Healthy Population, Thematic Priorities of the Strategic Framework for Healthcare Development in the Czech Republic to 2030, other strategic documents and the current needs of health research arising, for example, from the situation presented by the COVID-19 pandemic. Also from European policies such as Europe's Beating Cancer Plan, etc. The thematic priorities of the Concept are divided into three areas (1. Public Health; 2. Pathogenesis and Development of Diseases; 3. Innovative Solutions for Medicine), which are further divided into 24 sub-areas and 89 sub-objectives.

A separate thematic sub-area of the Concept focuses on the COVID-19 pandemic and infectious diseases in general. However, despite the existence of the pandemic and its reflection in a number of thematic priorities in the Concept, it is necessary to focus on the most common and dangerous areas: chronic non-communicable diseases such as cardiovascular and cerebrovascular diseases, lung diseases, oncological diseases, metabolic diseases, neurodegenerative diseases, psychological diseases, chronic diseases of the musculoskeletal system, etc. Research on these diseases should then not be limited to high-incidence adult diseases but should cover all ages, including patients with rare diseases, paediatric patients, adolescents and the polymorbid elderly. Diseases of the perinatal period and childhood represent a separate sub-area in the Concept.

Prevention is the most effective tool to achieve a healthy population, so attention must be paid to population behaviour and their poor nutritional, addictive, physical and other negative behavioural patterns. Attention must also be paid to external environmental influences, which are undergoing significant changes. Here, the role of primary prevention of diseases related to environmental and work environment determinants/quality is indispensable, and represented by the fields of hygiene, epidemiology, occupational medicine and public health in general.

However, as the COVID-19 pandemic demonstrated, public health cannot be reduced to hygiene, epidemiology and occupational medicine. Acute public health interventions that have significant economic and societal impacts must be effectively implemented not only in healthcare but also in other areas of public life. This is where we need to invest in communication research, in combating misinformation and in different types of motivational campaigns. Therefore, a completely new thematic area of the Concept is Public Health, which includes sub-chapters such as health economics, digitalisation of healthcare, demographic changes, but also global health, etc.

The cross-dimensional themes are summarised in the area of the Concept labelled Innovative Solutions for Medicine. Key topics here include personalised medicine. The use of high-capacity molecular biology methods and modern imaging techniques and the development of bioinformatics approaches in the field of "big data" will enable more detailed characterization of diseases individual level. This will also lead to a better understanding of human diseases and a higher degree of medicine personalisation. In the follow-up translational research, it is necessary to focus on effective use of the acquired knowledge for the development of innovative diagnostic, therapeutic and theranostic tools usable in clinical practice both at the individual level and for more stratified sets of patients within individual diagnostic units.

Technological development should then focus primarily on the wider application of personalised medicine principles across the health system.

In addition to sub-areas such as research on low molecular weight drugs, biologics and vaccines, and new drug formulations, cross-dimensional themes include research and development of medical devices and equipment and innovative research in surgery, including transplants. Compared to the current concept, topics such as research and development in medicines for advanced therapies (somatic cell therapies, gene therapies, tissue engineering products), research in telemedicine and e-health, and the development of innovative procedures in palliative and supportive care have been added.

The health system and related fields must be able to adapt to the dynamic evolution of knowledge to maintain access to quality prevention, treatment and promotion of good health and healthy lifestyles for the entire population. Since our healthcare system is at a very good level, we need to look for ways to apply and promote both basic and applied research. Research in this area should seek better connections with local industry. For this reason, the Concept also responds, through its thematic priorities, to the National Research and Innovation Strategy for Smart Specialisation of the Czech Republic 2021-2027 (specifically to the Advanced Medicine and Pharmaceuticals domain of specialisation).

3. General objective of the Concept

3.1. Basic demographic characteristics and state of health of the population

The basic characteristics and state of health of the population are taken from Chapter 2 ("Analytical Part") of the Strategic Framework for Healthcare Development in the Czech Republic to 2030. According to this analysis, **ageing** is clearly the most important factor determining the state of health of the Czech population. The population structure, with a high proportion of elderly people in both men and women, is an important factor determining the future development of Czech healthcare and the expected demands on health and social services. The average age of the Czech male population is 40.8, and 43.6 for the female population. The proportion of people aged over 60 is approximately 25%. Demographic predictions show that the proportion of the population over 60 and the population over 65 will increase significantly over the next 30 years. This development will inevitably be associated with the higher morbidity typical of the elderly population. Population models show an expected increase in the numbers of patients with malignant tumours, circulatory musculoskeletal disorders, lung diseases, connective tissue diseases and diabetes. The numbers of elderly patients with neurodegenerative diseases (dementia, Alzheimer's Disease, etc.) will also grow significantly. This substantial part of the population will need long-term and almost all-day health and social care. The future demographic development of the Czech population will be a challenge for the palliative medicine segment and for the end-of-life health and social services segment in general.

The relative structure of the population of the Czech Republic clearly shows three major age groups whose further shift over time will have significant impacts on the health system. This concerns the very large group of people aged 40-50, and especially those aged 30-40. These population categories will age to 60 and over in the next 15 or 20-25 years, and will inevitably multiply the need for health and social services significantly. The decline in the population between the ages of 10 and 25 is very significant and, together with the rising average age of first-time mothers, is creating a demographic risk of a shortage of people of working age in the next 15-30 years.

The predicted increase in life expectancy will further increase the pressure to change the structure of health and social services on offer. The median variant of the Czech Statistical Office demographic projection indicates that life expectancy at birth will increase and in 2050 should reach 82.1 for men and 86.7 for women. This positive development needs to be supported by increasing health literacy and citizens' responsibility for their health. It is essential to increase the period of healthy life alongside life expectancy. However, longer life expectancy will also bring a new dimension to the health problems of an ageing population.

Life expectancy by year of birth in the Czech population has been increasing for a long time. However, the values for Czech men and women are still lower than the EU average. In 2017, life expectancy at birth for women was 82, 1.8 years more than in 2007 but 1.5 years less than the EU average in 2017. For men, life expectancy at birth was 76.1 in 2017, 2.3 years more than in 2007 but 2.2 years less than the EU average for men in 2017.

In terms of healthcare, **healthy life expectancy** is an important parameter, and the Czech Republic improved this significantly between 2006 and 2016. On the positive side, the healthy life expectancy of the Czech population surpasses almost all Central and Eastern European

countries. However, these values are still lower than those typical for populations in more developed EU countries. The positive development in life expectancy and healthy life expectancy is clearly the result of improving healthcare in the Czech Republic.

The overall mortality rate showed a slightly increasing trend in the 2010-2017 period, largely due to the ageing of the population. A total of 62% of all deaths in the Czech Republic are deaths of long-term ill patients without acute causes. This represents over 66,000 patients per year who may potentially need long-term or palliative care.

Pursuant to the EUROSTAT methodology, some deaths can be considered **premature or preventable**.

In accordance with this methodology, we can define 25.9% of all deaths in the Czech Republic between 2007 and 2017 as premature. Although the premature mortality rate in the Czech Republic is not as high as in Lithuania, Hungary or Latvia, it is still well above the EU average and cannot be compared with Western European countries. Although demographic ageing is the main factor increasing population morbidity, poor lifestyles and the strong influence of risk factors such as alcohol consumption, tobacco use, poor dietary habits, etc. also play major roles. The Czech Republic clearly has a higher rate of deaths from preventable diseases (285 per 100,000 people) than the EU28 average (216 per 100,000 people).

A slight downward trend in premature deaths can however be observed, especially in the last decade. Their share of mortality in both men and women is declining. Ischaemic heart disease accounts for the largest proportion of premature deaths in the Czech Republic (7% of total deaths), followed by lung cancer (3.7%) and accidents (2.7%). For men, the proportion of premature deaths is 31.9% of total deaths, while for women it is only 16.7%. The significant imbalance between men and women in the proportion of preventable deaths is largely due to lifestyle and can therefore be greatly influenced by increasing health literacy and effective prevention programmes.

Essential indicators of the state of health of the population undoubtedly include **population reproductive health indicators**. Prenatal care for pregnant women in the Czech Republic has long been at a high level. This is evidenced, for example, by the timing of the first pregnancy-related visits to a gynaecologist. More than 80% of women have their first check-up sometime in the first 12 weeks of pregnancy. Among other indicators for this segment of the population's health, the following can be selected:

- The **infant mortality rate,** i.e. the number of deaths of children under one year of age per 1,000 births in the Czech Republic, is one of the lowest of all European countries. The infant mortality rate in the Czech Republic has been lower than the EU average since 1985.
- **Birth weight** is one of the basic indicators of the viability of a newborn baby and largely determines the baby's postnatal adaptation. The proportion of babies with a birth weight of less than 2,500 g ("preterm") has been declining slightly in recent years, but remains above 7% of births. Risky births, i.e. births of low-birth-weight babies, are highly centralised in perinatology and intermediate centres in the Czech Republic. This is a very positive phenomenon that significantly contributes to the quality of care for these children.

The Czech Republic is also outperforming other Central and Eastern European states in terms of overall **healthcare outcomes,** such as survival rates after hospitalisation for ischaemic strokes. The overall hospital mortality rate in the Czech Republic is already relatively low at under 3%. This is a constant value over time, fluctuating between 2.7% and 2.9%. Improving

healthcare outcomes in the Czech Republic are best illustrated through international comparative studies quantifying survival achieved for cancer patients. The EUROCARE-5 study published in 2014 was positive news for Czech oncology. The success rate for cancer patients is generally increasing, with 5-year relative survival rates close to or just below the European average for most diagnoses. They are also well above the values achieved in other former Eastern Bloc countries. Significant positive trends are observed especially in patients diagnosed with prostate cancer of the kidney and in patients with colon cancer, as well as in patients with breast cancer, skin melanoma and thyroid cancer.

The temporal evolution of the values of the above population health indicators can clearly be interpreted as a result of the improving level of healthcare in the Czech Republic. At the same time, it must be emphasized that there is significant room for further improvement in a number of indicators, and this challenge does not represent only an absolute improvement in population average values.

3.2. Basic objective of the Concept

The Health Research Concept is based on the National Priorities for Oriented Research, Experimental Development and Innovation, specifically on Priority 5: Healthy Population, from the Thematic Priorities of the Strategic Framework for Healthcare Development in the Czech Republic to 2030, from the National Research and Innovation Strategy for Intelligent Specialization of the Czech Republic 2021-2027 (specifically from the domain of specialisation Advanced Medicine and Pharmaceuticals) and other strategic documents and the current needs of health research arising, for example, from the situation presented by the COVID-19 pandemic. Its aim is to ensure health research and, subsequently, the development of practically usable research results for the needs of healthcare in the field of public health, the elucidation of pathogenesis and development of diseases, and the search for innovative solutions for medicine, while maintaining maximum efficiency in the use of public funds.

Objective:

The basic, and at the same time the main, objective of the Concept is to ensure and further develop internationally competent health research and the use of its results to improve human health with an impact on healthcare both in the Czech Republic and worldwide.

The presented Concept sets out strategic areas of health research, identifies expected results, and defines indicators so that health research in the Czech Republic does not lag behind current global trends, especially within the European Union.

The horizontal objectives of the Concept include:

- increase the relative share of public support for health research,
- strengthen international cooperation in health research,
- improve the quality of health research,
- involve young researchers in health research,
- use health research findings to implement new clinical and laboratory procedures,
- improve connections and continuities between basic and applied health research,
- translate the current assessment of the state of health of our population and current health threats into health research priorities, with special focus on vulnerable

and disadvantaged groups (children, seniors, people with disabilities, foreigners, socially excluded people, LGBTIQ people, etc.)

- use the results of research in the pre- and post-graduate education of doctors and other health professionals,
- use the results of health research to present research organisations and to popularise health science,
- reflect sex and gender in health research at all stages (from the design of the methodology to its outputs),
- ensure quality working conditions for all people working in health research, including carers and other potentially disadvantaged groups.

The Concept is elaborated in the following sub-areas:

- Socio-economic aspects of healthcare
- Digitalisation of healthcare
- Demographic changes and care for the elderly
- Healthcare
- Health literacy and patient orientation
- Health promotion and prevention
- Global health
- Metabolic and endocrine diseases
- Diseases of the circulatory system
- Cancer
- Chronic pulmonary diseases
- Diseases of the blood
- Mental illness and diseases of the nervous system
- Diseases of the musculoskeletal system
- Diseases of the immune system
- Infectious diseases
- Childhood diseases and rare disorders
- Personalised medicine and new diagnostic and theranostic procedures
- Low molecular weight drugs
- Biological medicines, including therapeutic and preventive vaccines
- New drug formulations
- Advanced Therapy Medicinal Products (ATMPs)
- Development of new medical devices and equipment
- Innovative surgical procedures, including transplants
- Telemedicine and e-health
- Innovative practices in palliative and supportive care

4. Linking the Concept to other strategic documents and securing their objectives

The Health Research Concept is based primarily on needs related to the development of the health system in the Czech Republic and the objectives set out in strategic documents for the healthcare sector. The basic direction for the strategic orientation of the Concept is primarily the Strategic Framework for Healthcare Development in the Czech Republic to 2030, the National Research, Development and Innovation Policy of the Czech Republic 2021+, and the National Research and Innovation Strategy for Smart Specialization of the Czech Republic 2021-2027.

In terms of the international context and related international commitments, the Concept contributes to the 2030 Agenda for Sustainable Development in the area of the Sustainable Development Goal "Ensure healthy lives and improve their quality for all at all ages". The Concept also reflects the objectives for the development of the European Research Area and the related objectives of the Horizon Europe support framework programme. The Concept is complementary to the National Recovery Plan funded by the European Union through the Recovery and Resilience Facility.

Strategic Framework for Healthcare Development in the Czech Republic to 2030

The Strategic Framework for Healthcare Development in the Czech Republic to 2030 (hereinafter "Health 2030") is conceptual material with an inter-ministerial overlap setting the direction for the development of healthcare for citizens of the Czech Republic to 2030. This strategic framework was approved by Government Resolution No 743 of 13 July 2020. The Health 2030 strategic framework reflects the specific objectives of the Czech Republic 2030 Strategic Framework in the field of health and concentrates them into three strategic objectives: 1) Protecting and improving the health of the population, 2) Optimizing the healthcare system, 3) Supporting science and research.

In the area of the objective Supporting research and development, the Health 2030 strategic framework focuses primarily on the development of the following research activities:

- Research in fields focusing on new diagnostic and therapeutic methods
- Verification of new effective procedures in primary prevention
- Improving the diagnosis and treatment of diseases related to climate change
- Behavioural research in relation to health and health literacy
- Preclinical and clinical research in biotechnology
- Searching for new molecules with therapeutic effects
- Clinical trials with a non-commercial sponsor
- Innovative scientific-research base for the digitalisation of healthcare
- Research focusing on information and communication technologies (ICT) and artificial intelligence (AI) in healthcare and telemedicine

This orientation of health research is directly reflected in the thematic definition of the priorities of the Concept. In addition, the Health 2030 strategic framework also addresses the systemic conditions for the effective development of health research in the Czech Republic, which are

also included among the systemic objectives of the Concept. Specifically, this includes the development of cooperation with the Council for Research, Development and Innovation on the creation of a new Health Research Concept, the effective implementation of the special-purpose support programme for health research, the implementation of the Methodology for the Evaluation of Research Organisations and Programmes of Special-Purpose Support for Research, Development and Innovation (Methodology 17+) in research organisations financed from the budget chapter of the Ministry of Health of the Czech Republic, the setting up of a system of institutional support for these institutions that sufficiently takes into account the evaluation of organisations according to Methodology 17+, the transfer of funds from national sustainability programmes and current research needs, e.g. the involvement of young scientists and the more intensive involvement of healthcare users in the development and implementation of new solutions.

National Research, Development and Innovation Policy of the Czech Republic 2021+

The National Research, Development and Innovation Policy of the Czech Republic 2021+ (hereinafter the "NP R&D&I 2021+") is an overarching national-level strategic document for research, development and innovation. The NP R&D&I 2021+ was approved by Government Resolution No 759 of 20 July 2020.

The vision of the NP R&D&I 2021+ is to contribute, through effective support for and targeting of research, development and innovation, to the prosperity of the Czech Republic as a country with an economy based on knowledge and the ability to innovate, whose citizens have quality living conditions and with the Czech Republic as a recognized partner both in the community of European countries and globally.

The NP R&D&I 2021+ should contribute to development and progress in five key areas:

- managing and financing the research, development and innovation system
- motivating people to pursue research careers and developing human capacity for R&D&I
- quality and international excellence in research and development
- cooperation between the research and application spheres
- innovation potential of the Czech Republic

The Concept is directly related to the NP R&D&I 2021+ and seeks to fulfil the objectives in the above dimensions in health research. Like the NP R&D&I 2021+, the Concept also aims at the effective managing and financing of health research, developing qualified people for health research, increasing the quality of health research, and strengthening international cooperation and, last but not least, effectively transferring health research results into practice.

National Research and Innovation Strategy for Smart Specialisation of the Czech Republic 2021-2027

The National Research and Innovation Strategy for Smart Specialisation of the Czech Republic 2021-2027 (hereinafter the "National RIS3") is a strategic document ensuring the effective targeting of European, national, regional and private resources to support oriented and applied research and innovation. The National RIS3 was approved by Government Resolution No 66 of 25 January 2021.

The Concept builds on the horizontal objectives and thematic priorities of the National RIS3. The horizontal objectives of the National RIS3 include increasing the innovation performance of firms, increasing the quality of public research, increasing the availability of qualified people for R&D&I and increasing the use of new technologies and digitalisation. Among the thematic priorities, the Concept is mainly related to the domain of research and innovation specialisation "Advanced Medicine and Pharmaceuticals" focusing on the development of research and innovation activities in medicine, diagnostic technology and medical devices using advanced materials, electronic and optoelectronic elements and progressive digital technologies, including artificial intelligence. It also focuses on R&D of innovative drugs and their use in medicine. An integral part of progress in this domain is a systematic effort to eliminate the potential negative consequences of the development of new biological and medical methods and to prevent their misuse (e.g. in genetic engineering).

National Priorities for Oriented Research, Experimental Development and Innovation

The National Priorities for Oriented Research, Experimental Development and Innovation (hereinafter the "NPOR") approved by Government Resolution No 552 of 19 July 2012, represent the basic framework for thematic targeting of support for research, development and innovation in the Czech Republic.

The Concept reflects the R&D&I priority themes set out in the NPOR, particularly Priority 5 "Healthy Population". Thematically, the Concept focuses on the fulfilment of the research objectives set out in the NPOR and aimed at the clarification of the "Origin and Development of Diseases", the development of "New Diagnostic and Therapeutic Methods" and the development of "Epidemiology and Prevention of the Most Serious Diseases". These objectives are elaborated in the Concept in three priority themes: "Public Health", "Pathogenesis and Development of Diseases" and "Innovative Solutions for Medicine".

In accordance with the NPOR, these thematic priorities will be implemented through targeted and institutional support instruments. The focus of R&D&I support on priority topics is aimed at improving the quality of prevention, diagnosis and treatment of diseases, and also at improving the flexibility and resilience of the health system in the Czech Republic.

European strategies relevant to health research

In addition to the national strategies, the Concept also builds on European strategies aimed at the development of the European Health Union. Among the most relevant in this context are the European Cancer Action Plan, the Pharmaceutical Strategy for Europe and, of course, the Horizon Europe Framework Programme.

The *Europe's Beating Cancer Plan* aims to address all aspects of the disease in the following areas: 1) prevention; 2) early detection; 3) diagnosis and treatment; and 4) quality of life for current and former cancer patients. In the coming years, the focus will be on research and innovation and on exploiting the potential offered by digitalisation and new technologies to tackle various aspects of cancer.

The *Pharmaceutical Strategy for Europe* aims to create a permanent regulatory framework and support the pharmaceutical industry in research and technologies that will actually reach

patients and improve their health. The strategy is based on four pillars that include legislative and non-legislative measures:

- ensure patients have access to affordable medicines and address treatment gaps (e.g. in antimicrobial resistance and rare diseases)
- promote the competitiveness, innovation and sustainability of the EU pharmaceutical industry and the development of quality, safe, effective and environmentally friendly medicines
- improve crisis preparedness and response mechanisms, diversify and secure supply chains, address drug shortages
- ensure the EU has a strong global voice by promoting high standards of quality, efficiency and safety.

The *Horizon Europe Framework Programme* is the EU's flagship instrument for supporting research and innovation activities in Europe and for strengthening European research cooperation. In addition to the pillar supporting the development of excellent science and the pillar supporting the development of innovation, Horizon Europe also emphasises support for research and innovation activities aimed at tackling global challenges. One of these is in health (Horizon Europe Cluster 1), which focuses on finding solutions to persistent health inequalities between and within EU countries, and responds to the rise of certain types of diseases such as cancer, non-communicable diseases, mental illnesses and infectious diseases. Improving the promotion of disease prevention, including vaccination, is another challenge for the research supported in this cluster. Other areas of focus under the Health theme of Horizon Europe include the impact of increasing environmental pollution on human health, growing resistance to antimicrobial drugs, and demographic changes, including within the context of an ageing population.

A new element of the Horizon Europe framework programme is the so-called missions, or portfolios of research and innovation actions with major impacts across disciplines and sectors, and which should be relevant to a significant part of the European population. The six core mission areas include the Cancer Mission, which seeks to reverse the negative trend in the increase of newly diagnosed cancers. In line with the Europe's Beating Cancer Plan, the Cancer Mission focuses on a comprehensive approach to tackling the different aspects of the disease, including: Understanding Cancer Diseases at the Preclinical Level, Prevention, Optimizing Diagnosis and Therapy, and Supporting Patient Quality of Life.

National Recovery Plan

The Concept is complementary to the National Recovery Plan (NRP), which the Czech Republic is implementing under the EU Recovery and Resilience Facility. The follow-up concerns in particular component 5.1 Excellent Research and Development in Priority Areas of Public Interest in the Health Sector.

Component 5.1 of the NRP, Excellent Research and Development in Priority Areas of Public Interest in the Health Sector

Component 5.1 of the NRP aims to modernise and renovate the scientific infrastructure in the Czech Republic to meet European standards. Furthermore, the aim is to develop a network structure in the field of research and development, to reduce fragmentation in the research

sector in the Czech Republic to improve its management and to support basic research in specific, state-defined health fields. This investment in the science base in priority areas of health research will also bring about a systemic change in the form of at least four research consortia focusing on areas with high mortality, in particular infectious diseases, neuroscience, cancer, metabolic disorders and cardiovascular diseases, including research on the socio-economic impact of health risks.

The main implementation instrument of component 5.1 is the Programme to Support Excellent Research in Priority Areas of Public Interest in Healthcare - EXCELES, approved by Government Resolution No 796 of 13 September 2021. The EXCELES programme was prepared and is administered by the Ministry of Education, Youth and Sports of the Czech Republic. Representatives of the Ministry of Health of the Czech Republic are represented in the programme advisory bodies, tasked with, *inter alia*, drawing attention to possible overlaps with other programmes focusing on health research and the risks of double funding, and at the same time mediating communication between the ministry that owns the component (the Ministry of Education, Youth and Sports of the Czech Republic) and the ministry that is responsible for research in healthcare.

The programme is intended to support the establishment of national scientific authorities in areas falling mainly under the main thematic priority Pathogenesis and Development of Diseases, namely metabolic and endocrine diseases, diseases of the circulatory system, cancer and infectious diseases. The thematic priority of Public Health is then linked to the national scientific authority for social and economic research on the impact of systemic health risks, which will analyse and further develop already implemented public policies in cooperation with the Government of the Czech Republic, thus preventing major failures in the implementation of public policies or in cooperation with public authorities. The creation of such a national scientific authority is consistent with the Government's commitment to address the lack of implementation of an "evidence-based policy" approach to strategic governance and strategic management in the Czech Republic and reflects the Government's commitment to create sufficient institutional and analytical capacity to ensure policy coherence for sustainable development.

The specific form of incorporation of the newly established national scientific authorities into the research and development system in the Czech Republic is being jointly discussed by the two ministries.

Five projects have been selected for support under the EXCELES programme in 2022, with an allocation of approximately CZK 5 billion from European Union funds. Under the selected projects, the following five national scientific authorities will be established in the Czech Republic: National Institute of Virology and Bacteriology, National Cancer Institute, National Institute of Neurological Research, National Institute of Metabolic and Cardiovascular Diseases Research, National Institute of Socio-economic Impacts of Disease and Systemic Risk Research.

Component 5.1 of the National Recovery Plan and the Exceles programme is thus one of the instruments through which the Concept will be implemented.

Gender Equality Strategy 2021-2030 (Strategy 2021+)

Strategy 2021+ aims to eliminate persistent gender inequalities and builds on existing policy in this area. Although equality between men and women is a fundamental value of the Czech Republic expressed, *inter alia*, in the Charter of Fundamental Rights and Freedoms, many gender inequalities persist in Czech society. Various international and European comparisons show that the Czech Republic is below the EU average in terms of gender equality (see below). The main problems include inequalities in the labour market (including the high difference in average incomes between men and women), economic inequalities (women's higher risk of poverty), the very low representation of women in decision-making positions, horizontal gender segregation in education, and the stereotypical division of roles in terms of household and family care. The incidence of sexual and domestic violence is a specific problem related to gender inequality. Gender inequalities have a negative impact primarily on the position of women in Czech society. Many of these inequalities, however, also negatively affect men's lives - especially in the areas of health and gender stereotypes about men's roles. The strategy is the second framework government document for the implementation of the gender equality policy in the Czech Republic. The aim of the strategy is to formulate a framework for state administration measures that will contribute to achieving gender equality in the Czech Republic. The purpose of these measures is to build on the positive changes that have been achieved in some areas of gender equality and to reverse negative trends where they persist or worsen.

Strategy 2021+ is primarily concerned with the Concept in the Health and Knowledge chapters. The Health chapter is relevant to the Concept in all strategic objectives. The Knowledge chapter of the Concept refers primarily to specific objective 2.4 Reducing inequalities resulting from gender-insensitive research, development and innovation, and strategic objective 3, Applying a gender perspective in the operation and management of educational and scientific research institutions.

5. Analysis of support for health research abroad

An international comparison of state budget expenditures on health research and development shows that state support for health research and development in the Czech Republic lags behind not only more developed EU countries such as the Netherlands, Sweden, Austria and Germany, but also in relative terms behind neighbouring countries in Central and Southern Europe, namely Slovakia, Slovenia and Croatia. As regards dynamics, the decline in the share of state budget expenditure on health R&D in the total state budget expenditure on R&D over the last ten years from 14% in 2010 to 12% in 2020, is also negative for the Czech Republic.

For a more detailed comparison of the status and trends in support for health research abroad, four countries were selected - Germany, Austria, the Netherlands and the USA (more detailed information on support for health research in these countries is described in **Annex 3**). The selection was based on several aspects. To compare the level of support for health research, economically developed countries with well-functioning research systems producing excellent results were selected. Differences in the size, historical development and state structures of individual countries are a prerequisite for a certain diversity of research and development (hereinafter R&D) support systems, including health R&D. The EU countries selected for this study also represent two neighbouring, culturally close countries (Germany, Austria) and countries of similar population size (Austria, the Netherlands).

A review of the approaches taken abroad has shown that health research policy objectives and instruments focus on supporting other areas of health research, whether oriented towards specific population groups (seniors, socio-economically disadvantaged people, etc.) or defined as systemic topics (health services, use of digital technologies, big data, ethics in healthcare, animal testing, transfer of research results into practice, support for start-ups, support for research education, support for young researchers, etc.).

The thematic focus shows a clear orientation of health research towards new solutions for the application of digital technologies in healthcare and health systems, the development of artificial intelligence applications in healthcare, the use of the potential of big data in prevention and diagnostics, and research on new materials for healthcare. A separate major area of health research is the development of personalised medicine and e-health.

Among systemic issues, health research abroad is also strengthening its emphasis on issues related to the behaviour of society and individual population groups, the relationship between health and the environment and, in relation to the COVID-19 pandemic, the socio-economic impact of pandemics.

Among the horizontal themes, an emphasis on supporting interdisciplinary research and the related networking of university and non-university research, in some key areas also with corporate partners, is also gaining importance. Furthermore, emphasis is being placed on developing quality working conditions in health research, focusing on supporting training and further education, as well as on introducing systemic solutions for career advancement or the involvement of doctors in clinical research.

Last but not least, in the case of support for applied research, the importance of supporting projects that clearly define their focus on application already at the project application and approval stage is emphasised, and where emphasis will be placed primarily on the potential and method of transfer of research results into clinical practice.

6. Evaluation of the implementation of the current Concept for the years 2016 to 2022

The interim evaluation of the Health Research Concept to 2022 was carried out by an external evaluator in the first half of 2021 (the conclusions of this evaluation are described in more detail in **Annex 1**). This evaluation concludes that the spectrum of research directions set out in the Concept is relevant to the needs of the healthcare system in the Czech Republic and reflects all the main areas that need to be continuously developed through research activities. At the same time, this evaluation shows that the research system in the Czech Republic has the capacity to develop the majority of the clinical fields of health research at a quality level corresponding to the global average and, in selected fields, even significantly exceeds this average (e.g. in oncology, haematology, cardiology and cardiovascular systems). On the other hand, the Concept focuses more narrowly on the development of laboratory disciplines, which are an important prerequisite for the implementation of applied health research in clinical disciplines. These areas include, for example, genetics, pathology, biochemistry, microbiology and biomedical technology.

However, the existing Concept has only to a limited extent reflected current foreign trends in the strategic focus of support for health research, where there is a gradual shift away from defining strategic goals in relation to the structure of clinical disciplines, while setting the goals of health research in the broader context of the links between the health system and society is gaining importance. Among these themes, important areas of health research related to the development of digital technologies and new systems of healthcare organisation are emerging, and are the focus of European programmes to support collaborative research and development, notably Horizon 2020 and more recently Horizon Europe. These topics include personalized medicine, rapid and digital diagnostics, the application of artificial intelligence in public health and healthcare, the digital transformation of the healthcare system, cybersecurity in healthcare and more. There is also an emphasis on secure data sharing in health research and healthcare.

The main instrument for fulfilling the Concept objectives was the Programme to Support Applied Health Research 2015-2022 (hereinafter the "Programme"). The interim evaluation of the Programme and the related analysis of the projects' disciplinary focus and their results have shown that the Programme supports all areas of health research defined as key Concept areas. The highest number of projects and results are supported in oncology, cardiology and cardiovascular systems, neurology and neurosciences, and endocrinology and metabolic disorders. These fields are also among the largest fields of health research in the Czech Republic in terms of the total number of publications.

The Programme also supports all core institutional health research segments, i.e. universities (and especially their medical faculties), teaching hospitals and other medical institutions, and Academy of Sciences institutes (especially in the field of natural sciences). Cooperation with businesses is rather sporadic, but this is not an immediate objective of the Concept.

Among the horizontal themes, the Concept aims to develop cooperation among the individual departments of the health research system in the Czech Republic and to develop international cooperation in health research and development. In terms of national cooperation, the Programme contributes to the development of collaboration between individual departments, as evidenced by scientometric maps of collaboration on health research projects supported by

the Programme. The most important role in the development of cooperation is played by teaching hospitals which, together with medical faculties, are natural hubs for the development of inter-institutional cooperation in health research and development in the Czech Republic.
In addition to the Programme itself, other support instruments have contributed to fulfilling the objectives of the Concept, such as support for the long-term conceptual development of research organisations (institutional support), earmarked support provided by the Czech Science Foundation, the Technology Agency of the Czech Republic and, to a limited extent, other providers, support from the Operational Programme Research, Development and Education for the development of infrastructural conditions for the development of health research and, last but not least, support for the development of research infrastructures and international cooperation provided from the funds of the Ministry of Education, Youth and Sports of the Czech Republic.
Thanks to the funds from operational programmes and national funds for the development of large research infrastructures, the necessary infrastructural conditions for the implementation of quality health research have been developed. Among the biomedical disciplines, infrastructure capacities in life sciences, health sciences and basic medicine have received the most significant support since 2015.
In terms of thematic focus, all Concept priority topics are covered by the support for health research. These topics mainly cover key clinical research areas.
The interim evaluation further states that the current Concept does not allow for a responsible assessment of the degree of fulfilment of the set objectives, as the chosen indicators reflect rather contextual conditions of the development of population health and the health system. The existing Concept contained a very broadly defined indicator system, which enabled the development of the environment in which health research is carried out to be monitored to some extent yet did not enable evaluation of how specifically supporting health research helped meet the set objectives. In the course of the evaluation, it was also found that some indicators set out in the Framework were not systematically monitored by any health system departments and were therefore not detectable.
Following the evaluation of the relevance and implementation of the Concept, the interim evaluation provided the following main recommendations:

- The new Concept should set out a realistic but sufficiently ambitious plan for the future financing of health research in the Czech Republic, increasing the share of support for health research in the system to the level of more developed European countries.
- In line with international approaches and the focus of Horizon Europe, new emphasis should also be placed on the strategic targeting of new health research areas related to the development of digital technologies and new healthcare organisation systems.
- In addition to the redefinition of thematic objectives, it is useful to explicitly set horizontal objectives for health research development that reflect current systemic issues. Such areas include, for example, the applicability and effective transfer of health research results into clinical practice, the effective training and involvement of young researchers in health research, the development and sharing of infrastructure for health research, and strengthening the internationalisation of Czech workplaces and their involvement in international health research projects.

- Building on the experience with the COVID-19 pandemic, the new approach should allow for timely and effective targeting of support to new unforeseen health research needs.
- In the new Concept, attention should also be paid to the legislative conditions for the implementation of health research and a more consistent and dynamic implementation of European directives into Czech law.
- The new Concept and follow-up programmes should emphasise interdisciplinary research and the development of collaboration between interdisciplinary teams.
- For the effective management of the Health Research Concept and its implementation, it will be useful to set up an evaluation system linking the strategic level (concept), the programme level and the project level. Only by setting up a coherent indicator system from projects through programmes to the Concept will it be possible to responsibly monitor and evaluate the contribution of support instruments to the fulfilment of the Concept objectives.
- In addition to assessing the links to the Concept thematic objectives, it will also be useful to monitor the contribution of the supporting instruments to the horizontal (systemic) objectives, which include the development of research infrastructure, strengthening cooperation and the internationalisation of health research.

7. Main thematic priorities

7.1. Public health

7.1.1. Socio-economic aspects of healthcare

Focus

Improving healthcare quality through empirical evaluation of the cost-effectiveness of care and health policy impacts

Health economics, as practised in developed countries, offers methodological tools for evaluating pilot public health policy measures as well as for ex post evaluation of the impact of reforms and incentives in the health system on the effectiveness of healthcare, and for comparing the effectiveness of alternative measures. These include cost-effectiveness evaluation, impact assessment and the causal impact analysis of measures, as well as comparative analysis. However, these tools are not systematically used in the Czech Republic. Without a systematic assessment of the impact of health policy and the subsequent use of empirical evidence to inform health policy formulation and resource allocation, the health system cannot be expected to be able to provide the same or higher quality of care in the future, when the main trends of the coming decades will be population ageing and the accompanying increasing health and social care spending and growing pressure on public budget sustainability.

Public health policy is defined here as a set of public administration measures that influence the behaviour of individuals, and public and private organisations in the health sector, with the aim of improving population health.

Study of population behaviour in support of preventive care and epidemiological modelling; optimisation of health communication with significant economic and societal impacts in normal times and in times of crisis

Many public health problems (in the areas of lifestyle and primary prevention, as well as in situations of acute epidemic threats) are behavioural or sociological issues. To solve theses problems, it is necessary to combine tools from different disciplines. Health policy and communication measures should be designed taking into account the latest evidence. The methodological tools described above could be used to measure the impact of emerging health policies and communication measures, where data tools are needed to track contacts or willingness to vaccinate and the effectiveness of both economic and health measures and incentives. Evaluating the effectiveness of communication tools is a natural part of optimising primary prevention as well as epidemiological measures. It is also appropriate to incorporate the findings of behavioural economics into communication tool design.

As demonstrated by the COVID-19 pandemic, acute public health interventions with significant economic and societal impacts need to be effectively implemented in both healthcare and other areas of public life, but also require investments in communication, countering misinformation and in different types of motivational campaigns.

In the long term, improving the quality of life and life expectancy across the Czech population will require systematic data collection and strategies for implementing measures that allow empirical quantification of their impact on behavioural change (e.g. healthy lifestyle

incentives). In this area, there is significant interaction between public health policy and family, employment, social and tax policies, and there is a need to link their evaluation and implementation.

The impact of population health and total healthcare costs on economic levels and growth

Just as population health depends on other public policies and the economic situation, health policy and the cost of healthcare (both public and private) impact economic development and socio-economic inequalities in society. This should also be evaluated, as health policy significantly impacts social cohesion and the economic performance of a country, as the COVID-19 pandemic has shown. Evaluating health policy settings with the aim of improving care quality and efficiency can also help alleviate the staffing crisis in the health sector, especially as a result of the ageing of the Czech population, and also improve the quality of life in view of our country's below-average performance in comparison with other European countries.

The main objective

The emergence of an institutional setting in which a new type of interdisciplinary collaboration between medical and social science disciplines takes place

Given the currently undeveloped state of public health, including health economics, in the Czech Republic, addressing research topics in public health and health economics will require the creation of a new institutional setting that would allow researchers from clinical, social science, and technical disciplines to collaborate, e.g., in experiments and clinical studies, data collection on (un)healthy behaviour, administrative data on the impact of public policies, personal preferences and the impact of health communication, and the acquisition and use of information from specific groups of patients and care providers. Related to this is the need to develop educational and research capacities in public health, health economics, and related disciplines to strengthen staff capacity in this area in the coming decades: to strengthen the capacities of existing institutions in public health (the National Institute of Public Health, Regional Hygiene Stations, etc.) and to modernise their structure and focus, as well as to create new study programmes that will produce experts for this system with insight not only in epidemiology, hygiene and prevention, but also in health economics, management and evaluation. Due to the current lack of personnel (due to many years of absence of support for this sphere), the emergence of large research centres in the first half of this period is not very realistic, and it will first be necessary to expand the base by educating a new generation of experts. It will be advisable to closely link key existing institutions (e.g. the National Institute of Public Health and the Institute of Health Information and Statistics) and, by strengthening their role and their cooperation, provide a basis for the development of the whole field.

Sub-objectives

Sub-objective 1 Collection, quality and the application of data on healthcare and population behaviour

Develop data collection on the quality of care and its effectiveness across regions and providers, integrate with registry data and share in a transparent format while maintaining privacy requirements. **Collaborate with hygiene stations and other actors on data collection and analysis in the areas of prevention and public health protection**, including the use of

psychometric methods and real-time data collection, for example from social networks. Emphasise disinformation campaigns and defence against them. Support research on the epidemiology of infectious diseases (see chapter 7.1.8) through collecting data on human behaviour during a pandemic, and developing research on addictive behaviour (see chapter 7.1.6.7).

Develop a database for care coordination in the health and social sectors (collection and analysis of data on the needs and preferences of patients and carers) and in end-of-life care (hospice, informal, medical care).

Sub-objective 2 Measurement of programme impacts and analysis of new programmes or legislative proposals by government and independent experts

Analysis of longitudinal registry data, work with natural and controlled (artificial) experiments (pilot measures), recommendations for improving the effectiveness of current programmes and creating new ones.

Comparative analysis of capacity and investment (cost-benefit analysis) in technology, staff capacity and access to care at regional level.

Measuring the indirect economic and social impacts of healthcare costs, measuring the economic impacts of negative health trends and epidemics. The economic impact of spontaneous curtailment of economic activity will make it possible to assess whether, for example, widespread testing or improved diagnostics are economically fiscally viable, even if a burden on the budget in question.

Systematic measurement of the impact of incentives (e.g. the setting of the Reimbursement Decree) on the efficiency of providers and the quality of care, or the impact of new technologies on the organisation of care.

Sub-objective 3 Develop new methodologies and interdisciplinary collaboration in healthcare

Develop methods and implement health technology assessment.

Developments in health technology assessment (HTA), a formal evaluation of the cost-effectiveness of different types of drugs, procedures or diagnostic technologies for specific patients. The results of these trials should be applied in clinical practice. A specific approach will be needed, for example, for rare diseases.

Analyse and implement health communication strategies, including the effectiveness of campaigns targeting primary and secondary prevention and healthy lifestyles (early testing and diagnosis of diseases) or willingness to be vaccinated. Evaluation of alternative approaches to communication and motivation for individuals and institutions, use of modern methods (data integration across datasets, pilot validations, experiments, communication strategies, etc.) using insights from sociology and behavioural sciences.

Sub-objective 4 Social determinants of health and gender dimensions

Research in this area will specifically focus on the social determinants of health and will look more closely at, *inter alia*, the gender aspects of health. This approach is in line with the main objective of the Concept, which assumes the creation of an institutional background for interdisciplinary cooperation. Research in this area should then emphasise, *inter alia*, the

gender dimension of health and disease and will be in line with Strategy 2021+, chapter 'Health', which contains a number of relevant measures in this area.

7.1.2. Digitalisation of healthcare

Focus

Digitalisation represents the advanced use of information and communication technologies in healthcare. The possibilities of modern technologies already exceed the ingrained perception of computer and telecommunication technology and rationalize, accelerate and refine processes originally designed for manual, classical processing and information storage - historically often using paper or analogue recording means. Originally, the computerization of processes had no ambition to propose such changes/reforms, creating completely new procedures and methods, while the alternative, a return to classical processing, is ineffective or even impossible. Development is heading towards digital health, where procedures and methods are fully dependent on digital technologies, accompanying the patient and the healthcare provider in various forms from first contact to the return to everyday life.

Digitalisation is essential to meet the challenges posed by the growing demand for health services due to the ageing population and the associated chronic diseases, while at the same time accommodating the efforts of modern and health-literate people to take care of their own health, including prevention and the timely use of health services.

The importance of using experience and practices from abroad in digitalisation is growing, but it is necessary to consider the national conditions in the Czech Republic or to propose appropriate reforms to adjust them. The available state of scientific knowledge and the inspiration of disseminated practices and experiences abroad, including respecting the European Union's digitisation initiatives, are important elements that should be respected, together with the Health 2030 Framework Programme priorities and objectives, when setting the objectives of research projects on digitalisation in healthcare.

In the context of public health, research and development in digitalisation is particularly focused on the following areas: (i) population health (especially chronic disease management, improved prevention and treatment effectiveness), (ii) patient empowerment, health literacy, improved patient compliance, (iii) quality of patient services (especially accuracy, more valid information, personalised medicine, early detection of deterioration, patient care in the home environment), (iv) accessibility of health services (time and place), (v) efficiency (changes in procedures, reduction of costs, capacity and resources needed - also in the event of economic pressures such as increasing demand for health services x limited capacity and resources), (vi) integration within healthcare (collaboration among multiple healthcare providers, (vii) use of available data resources in the Czech health system to improve and streamline the development of the Czech healthcare system, (viii) use of available data resources in the clinical setting to improve care in different medical specialisations and improve procedures through diagnosis, design optimal procedures, safe and effective implementation of new types of interventions and operations, (ix) use for clinical trials and clinical studies.

The main objective

Research in the development of digital technologies will lead to improved population health, patient empowerment and patient services quality. Innovative solutions for integrating digital technologies into health services will improve their accessibility and efficiency. The use of available data sources will enable the improvement and streamlining of healthcare development and the improvement of quality of care. There will be developments at the level of innovative tools using artificial intelligence.

Sub-objectives

Sub-objective 1 Digitalisation will improve population health and health services quality

Research in digitalisation and its implementation in healthcare will lead to improved population health (especially in terms of chronic disease management and higher prevention and treatment efficiency),
patient empowerment, health literacy, better patient compliance and also patient services quality (in particular accuracy, more valid information, personalised medicine, early detection of deterioration, home care).

Sub-objective 2 Digitalisation will lead to improved health services accessibility and efficiency and a higher level of data integration within the healthcare provider system

Research in digitalisation and its implementation will enable better health services accessibility (time and place), higher efficiency (changes in procedures, reduction of costs, required capacities and resources - also in the event of economic pressures such as increasing demand for health services vs. limited capacities and resources) and a higher level of data integration within the healthcare system (collaboration amount multiple health service providers).

Sub-objective 3 Increased use of data sources in the Czech health system

More intensive use of available data sources in the Czech health system will enable improved Czech health system quality and efficiency. The use of available data sources in the clinical environment will enable improved quality of care in various medical specialisations and improved procedures according to diagnoses, improved design of optimal procedures, and the safe and effective implementation of new types of interventions and operations.

7.1.3. Demographic changes and care for the elderly

Focus

Throughout the second half of the 21st century, there will be 2.5 times more seniors than children in the Czech Republic. The cause is the ageing population, manifested by an accelerating increase in the absolute and relative number of elderly people due to increasing life expectancy. In relative terms this is a stable trend, and one that is irreversible even with massive migration or slightly higher fertility levels. In 2018, the average age of the Czech population increased by one tenth of a year to 42.3 (40.9 for men and 43.7 for women) and was thus two years higher than in 2008 (e.g. in the South Moravian Region it reached 42.5 in 2019, an increase of 5.8 years since 1991). At the end of 2019, almost 239,000 people in this age category lived in the region, i.e. one fifth of the population (Czech Statistical Office data). The

number of people aged over 85 and over 90 has also increased significantly. The health and well-being of today's and tomorrow's seniors is a key challenge in modern societies with changing demographics. The WHO has declared 2021-2030 as the Decade of Healthy Ageing and a necessary collaborative action to promote health, care and respect for the rights of older people.

Although ageing in itself is not a health problem, older age can pose significant health risks. Probably as a result of better diagnostics, we are already witnessing a sharp increase in the number of patients with neurocognitive deficits, Alzheimer's, Parkinson's disease, etc. Also, in connection with the SARS-CoV-2 virus infection, which causes COVID-19 and, according to research, also affects the brain and other CNS structures, cognitive loss can occur even earlier than as a result of natural involution several years after infection.

These trends are also reflected in the use of health services, and the structure and frequency of hospital admissions are significantly co-determined by patient age and gender. The average age of hospitalized patients in 2019 was 69.3. As their age increases, the average treatment time also increases, especially for women. In terms of gender, in 2019 we recorded 240.8 cases of hospitalizations per thousand women compared to 202.5 per thousand men, i.e. one fifth more. The reasons for the higher number and duration of hospitalizations include the older age structure of women, their higher life expectancy, selected socio-economic characteristics, and hospitalizations associated with women's reproductive health. However, even after removing the effect of age differences from the calculation through standardization, women still account for 7.1% more hospital admissions than men.

Demographic changes in society are leading to the geriatricisation of medicine and healthcare. Healthcare professionals no longer encounter elderly patients only in specialised geriatric and gerontology units, but in all specialisations and disciplines. Similarly, there are increasing demands on residential social service facilities and on primary care (the burden on general practitioners and outpatient specialists) and demands on community coexistence and the provision of care for the elderly in a natural social environment (home healthcare, charity services), including long-term and aftercare, rehabilitation and respite care, especially with regard to the still unresolved issue of the social-health border. With the increasing need for health services, it is not possible to give up on health protection for seniors, and especially secondary prevention, as well as on increasing the quality and safety of healthcare and social care and comprehensive improvement of the quality of life of seniors and carers, even in the context of temperature extremes manifested especially in the summer months. An important area is the protection of public health in times of emergency (e.g. pandemics) and the promotion of media literacy, which is linked to health and financial literacy.

The main objective

Deliver the highest possible standard of quality in health and social care at every contact point (primary care, outreach services, inpatient acute and follow-up care, respite care), including through the use of data-based and evidence-based decision-making and health outcome evaluation using smart data and applied knowledge. A robust database, analysis of available resources and identification of stakeholder needs, along with the implementation of smart virtual care tools that include mental healthcare and chronic condition management, will lead

to the protection and promotion of health and improve the quality of life for all involved, including:
- the ageing population;
- the chronically ill;
- lay carers (especially older carers and the so-called sandwich generation);
- professional carers (health and social workers).

Sub-objectives

Sub-objective 1 Analyse the structure of providers and social healthcare provided to the elderly population

Robust analyses of the data sources of the National Health Information System and the sources of social service providers will be carried out to monitor the manifestations and impacts of demographic changes on the health and social care system. The current state of provision of health and social services for the elderly population will be identified in relation to its geographical distribution within the Czech Republic and taking into account the use of health services, social services in residential facilities, and the availability of care by region of the Czech Republic. Innovative procedures will be based on the analysis of resources on health and social services, morbidity, hospitalizations, mortality and other demographic indicators in relation to capacity indicators of the socio-health border. Data will be analysed in relation to specific ICD-10 diagnosis groups. The effectiveness of use of services, staffing and structural capacities will be evaluated, and methodologies for cost analysis of care for the elderly will be defined. The result will be a description of the current situation in the provision of health and social services to the elderly. The structural analysis will be followed by sub-objective 2, which will enable the definition of needs in the field of social and health care for the elderly and the planning of institutional care capacities in relation to the identified needs of care recipients and providers. The analyses will take into account possible variable development scenarios and changes in the health and social needs of future seniors and their provision.

Sub-objective 2 Analyse and address the social and healthcare needs of the elderly (especially the very elderly)

Research activities will lead to the identification and subsequent addressing of the needs of the elderly in terms of social and health care. The output should be evidence-based recommendations (guidance and guidelines) to identify the appropriate scope of care, criteria parameters for specific types of care, and interventions for a holistic approach in elderly care for both lay and professional caregivers. An integral part will be the acquisition of knowledge and skills to strengthen evidence-based decision-making in elderly care for both professional and lay caregivers. Emphasis will be placed on developing soft skills (communication skills for identifying needs, recognizing early warning signs of a change in an elderly person's condition, dealing with crises and sudden changes). The result will be methodological and curricular documents for the professional training of caregivers for the elderly with regard to patient-centred care and the prevention of ageism. The research will include finding ways to effectively support health and care staff in age-sensitive patient handling, to prevent cop-out and burn-out syndrome with consequences for labour migration and turnover, and to support their work longevity.

Sub-objective 3 Early prevention of the emergence and mitigation of the impacts of involutional changes, including the use of modern technologies

The aim is to prepare comprehensive methodological documents and guidelines for the implementation of tools to mitigate the manifestations and impacts of involutional changes. Research activities will focus on evaluation of the impact of living conditions and lifestyle on involution, evaluation of the use and effectiveness of appropriate preventive procedures (in the physical and psycho-social areas: physical activity, mental training, memory training, support for social interaction, support for work longevity, etc.), and anti-ageing in the sense of compressing negative involutional changes into shorter periods of time (prolongation of healthy life).

Evidence-based practices will include the promotion of intergenerational coexistence and tools to ensure quality care by lay and professional caregivers using modern technologies. The result will be the establishment of a stable and continuously developing infrastructure, the creation of a "System of integrated telemonitoring and telemedicine in health and social services" which, with the use of modern digital technologies not only in the field of telemedicine but also in human resource management systems, will create a quality functioning platform supporting further research and development of technologies in this area.

Sub-objective 4 Promote quality and safe patient care with regard to age-specific risks and prevent adverse events in the provision of long-term medical and nursing care

Research in this area will lead to the identification of the most important risk factors affecting the quality and safety of care for the elderly. Methodological procedures for risk prevention in institutional care (health and social care), early warning systems and signals for ensuring follow-up care will be developed. Educational activities will focus on the implementation and translation of knowledge into clinical practice to ensure safe and quality care. Education of lay and professional caregivers in risk recognition, development and the implementation of proactive and retroactive measures and communication strategies to promote quality and safety will form an integral part. The output will be summary methodological material covering the most common adverse events, appropriate preventive and corrective measures, and a description of stakeholder competences, including an evaluation system for quality of care, systemic measures and protection of the individual.

7.1.4. Healthcare

Focus

Improving the quality and efficiency of healthcare provision, ensuring capacities and a legal framework to ensure access to quality healthcare

Health Services Research (HSR) is a multidisciplinary field of scientific research that studies how societal factors, financing systems, organisational structures and processes, health technologies and individual behaviour influence access to, and the quality and cost of, healthcare. HSR examines individuals, families, organizations, institutions, communities and populations. It examines how people gain access to healthcare, how much healthcare costs, and

what the outcome of that care has been for patients. The main HSR objectives include identifying the most effective ways to organise, manage, finance and deliver quality care, reduce medical errors and improve patient safety.

The basic condition for a functioning health system, which should ensure the availability of quality health services with regard to the available capacity, is in our conditions the ensuring of **sufficient qualified health personnel**. The causes of the global health and nursing workforce crisis are diverse, intricate and complex. It is therefore necessary to identify and analyse the causes leading (or that may lead in the near future) to a shortage of health personnel, especially in certain professions and specialisms of doctors and non-medical health professionals, to identify the areas where this shortage leads to a reduction in the availability of healthcare, and to find tools to improve this situation in the future. The complexity of the issue is due to the many factors that may influence current and future numbers of health workers. For example, the **attractiveness of the medical profession**. Surveys indicate the overall prestige of physicians in our society remains high. As a career choice, medicine maintains its attractiveness (as evidenced by the numbers of applications that are many times higher than the actual capacity of medical faculties). Therefore, the recent increase in the capacity of medical faculties was the right step and should be continued in the future, including an increase in capacities for studying non-medical health professions (general nursing and other professions). The attractiveness of health professions is not as much limited by salary issues as in the past, but rather by the enormous time and psychological burden on health professionals and the high demands for postgraduate and lifelong learning, the increasingly real threat of forensic implications, the time demands of the profession, etc. The attractiveness of individual medical disciplines and their expected future development also differ. In the case of women working in healthcare, especially nurses, the near impossibility of balancing their professional and personal lives plays a significant role. The lack of childcare facilities at health facilities and shift work that does not allow for flexibility may be among the reasons for women leaving the sector. This topic was discussed during the COVID-19 pandemic and, given the lack of capacity in the health sector, it is desirable to conduct further research to bring the needs of these workers and their motivations for staying in the profession into focus.

In the case of non-medical health workers (especially nurses), numerous international findings confirm that the most important negative factors include stress from heavy workloads, long and irregular working hours, the social status of the profession, complex relationships at work, problems in fulfilling professional roles, and the various health risks in the workplace. The link between **job satisfaction for nurses** and motivation to leave, which is more easily done especially in larger urban areas with low unemployment and a greater supply of often better-paid jobs, needs to be addressed.

Considerable attention has recently been paid to the impact of **demographic ageing** on the provision and uptake of health services, as this factor may play a very significant role in the coming years. As the population ages, the range of health services that will need to be provided to the ageing population will change. At the same time, the health service providers will also be ageing.

The future numbers of health workers will be influenced by **the system for their training**. In the case of doctors, this issue is mainly the very complex and opaque system of postgraduate education. Frequent changes to it (new laws and decrees issued every few years) have done

great damage.
It is essential that changes in the structure of medical disciplines should only take place in very long cycles (e.g. not less than after 10 years) and that the development should not be in the direction of an increase in the number of fields (which often leads to dead ends where not enough specialists can be trained for small fields). In the case of non-medical health professionals, it is very likely that the education system is not able to produce them in sufficient numbers (see above).
Of course, the numbers of health professionals will continue to be affected by **migration**: both the emigration of our doctors and nurses and the immigration of health professionals from abroad (mainly from Ukraine and Russia). Since it is not only about salaries but also about the working conditions offered to our health workers abroad, it is necessary to analyse all the factors that lead to the departure of our health workers abroad.
Another factor that needs to be analysed is the **expected development of the various medical disciplines**. In examining this factor, it will be necessary to draw on updated concepts of individual disciplines, analyse experience abroad, and conduct a survey of experts and representatives of individual disciplines using qualitative methods.
Although the provision of health services is subject to private law relations between providers and patients, it is an area in which contractual freedom is significantly restricted and at the same time there is considerable scope for public regulation. The law here reflects the risks associated with interference with bodily integrity in the provision of healthcare and sets out rules to eliminate them as much as possible. At the same time, however, it also imposes other obligations to ensure that citizens in general have real access to healthcare and thus create the conditions for them to live in dignity, even if they could not afford to pay for healthcare from their own resources. (Pl. ÚS 19/13).

The main objective

A key objective of healthcare research is to provide patients with evidence-based, timely and quality healthcare delivered in a cost-effective manner (see chapter 7.1.1.). An important aspect for assessing the availability and quality of health services is sufficient provision of material capacities. In our conditions, this especially applies to the capacities of qualified health workers. Healthcare must be provided with respect for patients' human rights, on the basis of equality, and taking into account patients' limited social and financial resources.

Sub-objectives

Sub-objective 1 Analyse the need and consumption (use) of healthcare by people with chronic diseases

There is a significant gap between healthcare needs, demand for healthcare and actual healthcare consumption (use). This discrepancy can have a serious impact, especially for people with chronic conditions. The aim is to have studies available that address the often hidden health needs of individuals, communities and populations. At the same time, knowledge of needs must be linked to research recommending ways in which these needs can be met within existing organisational, financial and other constraints.

Sub-objective 2 Measurability of healthcare outcomes

Research activities should lead to improved quality, performance and safety in the delivery of healthcare, with an emphasis on verifiability and measurability. The ultimate goal is the measurability of both medically objective healthcare outcomes and subjective outcomes (change in quality of life from the patient's perspective). For this, it is necessary to have both medical information from existing databases and to obtain data through questionnaires (see chapter 7.1.2).

Sub-objective 3 Healthcare capacities, consumption and availability
The aim of this sub-objective is to assess the availability of healthcare capacities and to identify any capacity gaps that may exist for selected diseases or specific geographical locations. This includes analysis of healthcare consumption (utilisation), including problems of equal access to care, which can be influenced by various factors such as geographical accessibility, population social structure, patient nationality and migrant status, patient co-payments including poverty problems, a poorly designed reimbursement system, the configuration of public and private health insurance, etc.

Sub-objective 4 Human resources in healthcare
The aim is to carry out multidisciplinary research (with the participation of health professionals, sociologists, demographers, geographers, statisticians and lawyers) in human resources in healthcare, leading to a detailed analysis of all the important factors determining the number of health professionals in each profession, including the weighting of their influence. It is necessary to analyse which professions are affected, which workplaces are more at risk and in which areas. The task of applied research should then be to propose specific solutions that can be used by healthcare organisers.

Sub-objective 5 Patient participation rights and respect for patients' autonomy of will
Detecting the values and rights protected in the provision of healthcare, with a focus on the personal autonomy and self-determination of individual patient groups, especially vulnerable people (in terms of age or disability) or people in a specific position (e.g. in the field of obstetrics or vaccination) in the context of the interests of the individual, but also in the public interest, defining barriers and developing proposals for legislative solutions.

Sub-objective 6 Means of protecting the rights of persons in healthcare negligence
Legal analysis of and research in procedural mechanisms for investigating suspicions of healthcare negligence and means of protecting the civil and criminal rights of vulnerable groups (especially in terms of age, ethnicity, physical or sensory handicap) in the legal environment of the Czech Republic, including in the context of ECHR case law, defining barriers, creating proposals for legislative and non-legislative (methodological) solutions.

7.1.5. Promoting health literacy and patient orientation

Focus

Health literacy is defined as "people's knowledge, motivation and skills to acquire, understand, evaluate and use health-related information so that they are able to make informed decisions in their daily lives about healthcare, disease prevention and health promotion with the intention of maintaining and improving quality of life across the course of their lives." (Kickbusch,I. et al.: Health Literacy: The Solid Facts, Copenhagen, WHO 2013, p. 4) A number of international studies point to the fact that reduced levels of health literacy significantly increase healthcare costs. According to the WHO, this burden accounts for 3%-5% of health expenditure; other studies suggest it may be as high as 8%. People with higher levels of health literacy are generally healthier and consume less healthcare.

Two representative surveys were carried out in the Czech Republic, the first in 2015 and the second in 2020. Since in both cases the methodology used in other countries of the European region was used, comparison is possible. In both cases, the Czech Republic was shown to be lagging behind other comparable European countries. The situation is particularly critical for some social groups, namely children and youths, socially and economically deprived groups and the elderly.

With this second representative survey, the Czech Republic is among the 17 countries that have joined the international M-POHL (Monitoring of Personal and Organizational Health Literacy) initiative, which aims to regularly monitor health literacy in the European region. This initiative, coordinated by the International Coordination Centre in Vienna and supported by the WHO, has the ambitious goal of conducting surveys in regular cycles and complementing them with specifically targeted studies.

The regular monitoring of health literacy, including research on specific population groups and sub-aspects and components of health literacy, will enable the Czech Republic to repay the debt it owes in comparison to other countries in the region through the creation and approval of a National Health Literacy Programme. Regular surveys will enable monitoring of the implementation of the individual components of the programme and the fulfilment of its objectives. The creation and monitoring of the implementation of the National Health Literacy Programme is one of the objectives of the Strategic Framework for Healthcare Development in the Czech Republic - Health 2030 (Implementation Plan 1.2. Disease prevention, health promotion and protection; improving health literacy). Health literacy is also the focus of a specific objective of the Strategy for Gender Equality 2021-2030 in the ‘Health’ chapter, 1.3 Improving health literacy unencumbered by gender stereotypes. Although efforts to improve health literacy are increasing, the necessary coordination, methodological clarification and evaluation are still lacking. It is therefore desirable to improve research, coordination, the methodological framework and mutual information and cooperation between actors, while major organisational and conceptual changes also need to be prepared.

The main benefit of the research and the measures arising from it is to strengthen the effectiveness of public administration in public health, strengthening health literacy, informing and increasing the confidence of the population in information, decisions and measures of the state health authorities.

The benefit for the target groups will be the creation of optimal processes based on the analytical part of the strategy and on the strategic management of the individual organisations that will be involved in the implementation of the strategy.

The main objective

A National Health Literacy Programme will be developed based on the research and using the experience of other European countries. The programme will contribute to optimising government processes through strategic planning and strategic management of organisations to ensure increased health literacy. This goal will be achieved by ensuring systemic support for the development of health literacy in the Czech Republic through new strategic management of state administration organisations in all the relevant ministries and a strategically set system of long-term awareness and education of the Czech population in this area. The implementation of the National Health Literacy Programme will be monitored through representative surveys and validation studies of the individual programme components.

Sub-objectives

Sub-objective 1 Monitoring health literacy in the Czech Republic

The Czech Republic, as an active member of the group of countries associated in the M-POHL initiative, should continue to cooperate in this association and, using the methodology developed by experts from these countries, carry out, in particular, national representative surveys to provide essential feedback on the implementation of the programme's objectives. The data obtained will be used to modify or refine the programme objectives.

Sub-objective 2 Research on the competences and needs of health literacy actors

Using specific methodologies, the competences and needs of the different actors involved in health literacy will be regularly monitored. These include health workers, educators, journalists and others. The training of these actors will include specifically designed tools to identify their needs and competences.

Sub-objective 3 Research on specific target groups of the National Health Literacy Programme

Existing research on health literacy has revealed a strong social gradient: socio-demographic and socio-economic characteristics such as age, gender, education, place of residence and level of financial deprivation significantly influence health literacy levels. The National Health Literacy Programme will emphasize these specific contexts and include projects targeting population groups defined by these attributes. Specific data collection methods will be designed and used to monitor health literacy levels.

Sub-objective 4 Research on specific areas of health literacy

The M-POHL survey proposed specific indicators and tools to measure health literacy in the areas of (a) navigating the healthcare system, (b) digital health literacy, or the ability to obtain and use information from online environments, (c) health communication literacy, or competence in interacting with physicians, and (d) vaccine literacy, or competence in obtaining and making decisions regarding vaccinations. In all these areas, sub-projects will be included in the National Programme, while targets will be set and monitored.

Sub-objective 5 Competence of health professionals in health literacy

Research in this area will lead to the development of evidence-based practices to strengthen health professionals' competences in communication, working with emotions, and addressing ethically challenging situations and gender sensitivity. The aim is to improve the ability of healthcare professionals to communicate sensitively and effectively about serious diagnoses, prognoses, end-of-life care, limitations of care, and other topics related to palliative care. It also aims to improve the ability of health professionals to provide gender-sensitive services at the level of diagnosis, communication and treatment.

Sub-objective 6 Combating unscientific views in healthcare

The National Health Literacy Programme will address unscientific views held by the population and health professionals, and a system will be developed to target appropriate population groups to reduce the percentage of people promoting or practising unscientific approaches to treating patients.

Sub-objective 7 Strengthen health literacy unencumbered by gender stereotypes

Analyses will be conducted on the influence of gender stereotypes on self-assessment and health beliefs, and the influence of gender on lower/higher incidences of disease in women and men. Based on the conclusions, recommendations will be formulated to strengthen health literacy, focusing specifically on the needs of various vulnerable groups in the healthcare system that often have poor healthcare access, such as ethnic minorities, foreigners and socially excluded persons, and whose specifics need to be taken into account when including them in healthcare.

7.1.6. Health promotion and prevention

7.1.6.1. Metabolic and endocrine diseases

Focus

Epidemiological data on the evolution of prevalence and changes in incidence of the most common metabolic disorders such as type 2 diabetes mellitus, prediabetes, obesity, dyslipidemia and other components of metabolic syndromes are worrying. They impair quality of life and increase mortality, especially from cardiovascular diseases and cancers. Accurate data on environmental, social, socio-economic, biological and behavioural determinants, including dietary and exercise habits, are lacking. The reasons for regional differences in the incidence of these diseases and their complications are unclear. Regional differences in treatment and patient adherence to preventive measures and treatment are also likely to be significant.

The application of measures to prevent complications of endocrine and metabolic diseases is equally important. In the Czech Republic, there are suitable conditions for research and development in pharmacotherapy and especially immunotherapy for this group of diseases to contribute to preventing complications. Industry can be involved in this way, where - in addition to the development of drugs and immunotherapies - new technologies, including telemedicine devices, can be developed and used.

The main objective

To obtain validated epidemiological data on (i) the prevalence, trends, health and economic consequences of especially metabolic and endocrine disorders and their complications, (ii) their treatment and its effectiveness for the prevention of complications, and (iii) their social, socio-economic, behavioural and biological determinants and consequences. These data are crucial for basic preventive procedures influencing the development of this group of diseases and their complications.

In diabetology and other disciplines, the flow of patients between GPs, specialists and specialised centres will be analysed, as well as the possibilities of catching the first signs of the disease and its complications. The priority is not only to monitor the genetic determinants of disease development but also interactions between genetic makeup and the environment, e.g. diet and exercise. In view of the ongoing pandemic, research on preventing infectious complications and analysing immune disorders and cytokine deficiencies in diabetics and patients with metabolic syndrome is also a priority. Research on preventing increased cardiovascular complications following infection is important. In the coming years, health research on diabetes prevention will focus on the following topics, for example: Artificial intelligence - e.g. screening for early forms of the disease e.g. diabetic retinopathy. Personalized medicine enabling the discovery of predictors of the effectiveness of type 2 diabetes mellitus therapy in relation to diabetes complications. Diabetes prevention and research on the early stages of diabetes - the detection of early pathogenetic markers, including the use of imaging methods. Longitudinal pathogenetic research in the prevention and treatment of diabetes complications. Nutritional interventions in diabetes prevention, including research on nutrigenetic and nutrigenomic factors.

Sub-objectives

Sub-objective 1 Definition of a set of markers for the most common metabolic disorders and their complications

One sub-priority should be the creation of a national diabetes registry and other registries for metabolic and endocrine diseases, including rare disorders, and the setting of rules on who can analyse data from the registry of Czech patients and under what conditions, while the rules determining access to data from the registry should be set up to make it user-friendly for a wide group of researchers. The design of the parameters to be monitored should incorporate a range of clinical (including treatment) and social (e.g. community and regional influences, lifestyle, nutrition) indicators and other factors with potential impact on the development of metabolic and endocrine diseases and their complications. A proposal of factors for the evaluation of the development of complications depending on both the pharmacological and non-pharmacological procedures used.

These epidemiological and clinical data are crucial for the genetic and biochemical analysis of patient biological material. Given the significant heterogeneity of metabolic and, to a large extent, endocrine diseases, clearly defined homogeneous subsets must be analysed.

In endocrinology, a focus on early markers for the diagnosis of endocrinopathies and endocrine-active tumours and effective treatment, including new drugs and immunotherapy, are necessary to prevent complications and the progression of endocrine diseases. Evaluation

of the development of complications must also focus on treatment innovations and regional differences in the treatment of these diseases

7.1.6.2. Diseases of the circulatory system

Focus

Cardiovascular disease (CVD) is the leading cause of mortality in developed countries, accounting for more than 50% of all deaths, half of which are attributable to a single disease, coronary heart disease, and its acute form, myocardial infarction. Strokes are the second leading cause of death in both developing and developed countries (more than 5 million deaths/year, or about 10% of all deaths). Cerebral infarction mortality rates range from 20%-30% and for cerebral haemorrhage up to 50%. Strokes leave permanent disability in almost 30% of surviving patients. The occurrence and development of these diseases is conditioned by the interaction of factors resulting from both uncontrollable unique characteristics of the organism (e.g. age, sex, personal and family history), its structural, functional and biochemical characteristics, and controllable factors resulting from lifestyle and environmental influences. Since the vast majority of the major risk factors for cardiovascular disease are controllable, research in the prevention of existing and emerging risk factors for these diseases is needed, as prevention is still the most effective form of treatment. One essential prerequisite for the success of prevention programmes is broad interdisciplinary cooperation at national and international level, involving experts from medicine, nursing, sociology, psychology, media, biostatistics and other disciplines.

The main objective

Identifying and influencing the cardiovascular and cerebrovascular diseases risk factors to reduce the incidence of these diseases in the Czech Republic and to reduce their mortality and morbidity rates. Prevention programmes need to be made more attractive and accessible to the general population. It is necessary to focus both on primary prevention (which alone can reduce the prevalence and incidence of these diseases in the population) and on secondary prevention, which can significantly reduce mortality and morbidity rates. Primary prevention must be targeted at the whole population and should start from school age - promoting healthy eating habits, encouraging active participation in sport and physical activity, and combating smoking and obesity. Secondary prevention is aimed at reducing mortality and morbidity rates in people who have already developed the disease. The goal must be to slow or stop disease progression. This can be achieved by modern procedures, both regime-based (analogous to primary prevention procedures) as well as pharmacological and interventional (catheterisation or surgical methods). The public health system should work closely with epidemiologists, hygienists, cardiologists, diabetologists, neurologists, and other experts to maximise implementation of a wide range of practices affecting primary and secondary prevention.

Sub-objectives

Sub-objective 1 Population studies: data on the evolution of key diseases over time

Collection and processing of data on the incidence and prevalence of cardiovascular and cerebrovascular diseases and their risk factors, with a focus on the temporal evolution and

evaluation of the effect of specific measures implemented in secondary prevention. A cost-effectiveness assessment would also be appropriate.

Sub-objective 2 Population intervention, assessment of the impact of preventive measures
Verification of intervention procedures leading to (a) a reduction in the incidence, and social and economic impact of cardiovascular and cerebrovascular diseases and their risk factors, (b) population education with the aim of early recognition of symptoms by the patient, allowing for early diagnosis and treatment. Population studies evaluating the effectiveness (including cost-effectiveness) of measures implemented as part of primary prevention.

7.1.6.3. Cancers

Focus

More than 85,000 people in the Czech Republic get cancer each year, and approximately 27,000 die as a result. One in three Czech citizens is diagnosed with cancer during their lifetime. Malignant tumours are the second leading cause of death. The incidence of cancer, which is still rising, and the rate of cancer deaths in the Czech Republic are already higher than the EU28 average. Cancer will be the leading cause of death in the EU by 2035. This development is mainly due to the ageing population, declining health literacy (see chapter 7.1.5) and unhealthy lifestyles. At the same time, the Czech population is more burdened by risk factors and has a lower level of health literacy, while a part of the population also exhibits greater resistance to preventive programmes. Despite significant improvements in healthcare in this area, the burden of cancer in the Czech population is very high from both national and international perspectives, and has been steadily increasing over time (the annual prevalence increase is 3% to 4%). Even relatively conservative predictive models show that by 2030, the annual number of newly diagnosed cancers could increase to 110,000, while 790,000 is even possible. The available data show that, in addition to the growing overall epidemiological burden of cancer in the population, late detection of these diseases is another problem in the Czech Republic. A high percentage of cancers (even in diagnoses with organised screening) continue to be caught at an advanced stage, when treatment is very expensive and the likelihood of a cure is significantly reduced.
The Czech Republic was significantly affected by the COVID-19 pandemic. During the pandemic, only emergency healthcare was provided and there was a reduction in preventive examinations and check-ups for cancer patients. The prioritisation of dealing with the pandemic consequences caused delays in cancer diagnosis. Anti-epidemic measures also negatively affected the lives of a significant part of the population and increased the amount of stress placed on people. This may translate into an increase in cancer incidence and progression, with higher treatment costs.
Cancer epidemiology is a traditionally well-developed area of research in the Czech Republic, mainly thanks to the mandatory reporting of cancer and the existence of the National Oncology Registry since 1976. Future research in cancer epidemiology and prevention will build on these historical foundations and focus on identifying factors involved in the occurrence and development of cancer, risk factors in the population (especially genetic, environmental,

physical, addictive, nutritional, exercise and infectious), and monitoring cancer incidence, mortality and prevalence in international, national and regional contexts. The information obtained will be used to shape strategies to reduce cancer incidence and mortality, as well as to rationalise screening, diagnosis and treatment costs. Attention will also be paid to emerging threats in oncology, such as the increasing incidence and prevalence of recurrent and secondary malignancies caused by previous anticancer treatment, and the monitoring of the long-term consequences of complex anticancer therapy with regard to the patient's quality of life. Research on cancer risk factors will primarily rely on well-designed longitudinal cohort studies. In cancer molecular epidemiology, new molecular diagnostics possibilities for the detection of early stages of cancer in the population will be studied. Emphasis will be placed on the use of diagnostic registries in the study of cancer epidemiology and the use of modern laboratory methods in the elucidation of etiopathogenetic factors of cancer. Genetic predisposition to childhood and adult cancers will be studied using modern molecular genetics and genomics methods. Emphasis will be placed on participation in large-scale genomic studies as well as individual case studies with additional diagnostic, therapeutic and preventive implications.

In **prevention of cancer formation and development**, research will focus on primary, secondary and tertiary prevention. Important cancer risk factors include an inappropriate lifestyle (obesity, smoking, alcohol consumption, lack of exercise, stress, etc.) which, on the other hand, is a modifiable factor. Around one third of cancer-related deaths are caused by inappropriate lifestyles. In primary specific prevention programmes, priority will be given to studying risk factors in the population, and in non-specific primary prevention, methods generally leading to a healthier lifestyle, including effective, data-based education. Secondary prevention research will focus on early cancer detection, with a particular focus on screening programmes in at-risk populations to increase the percentage of treatable and curable patients. Tertiary prevention research will focus on early detection of cancer recurrence and the side effects of anticancer treatment using molecular diagnostics and advanced imaging techniques. Here, priority will be given to studies working with data from clinical practice (real-world data). Special attention will be paid to the possibilities of chemoprevention of tumours, the strengthening and refinement of existing and the introduction of new, highly sensitive, specific, non-invasive or minimally invasive screening programmes to enhance the early detection of cancer in the general population or at-risk groups. Attention will also be paid to quality of life for patients in relation to the type of anticancer treatment. The need for specialised palliative care and treatment effectiveness for particularly strong symptoms will be determined in patients who have exhausted specific anti-cancer treatment options.

By supporting cancer epidemiology and prevention research, the national concept also reflects the European Commission's priorities in oncology as set out in Europe's Beating Cancer Plan.

The main objective

Cancer epidemiological data will be collected and analysed in regional, national and international contexts. Risk factors in individual populations will be identified and specific and non-specific prevention methods (primary prevention) will be proposed. Methods of accurate and specific screening will be further developed and tested, ultimately leading to the identification of at-risk individuals, early detection of tumours, their recurrence and side effects of treatment, with implications for reduced mortality and morbidity rates, and reduced costs of

anti-cancer treatment with respect to subjective assessment of patient quality of life. The need for specialised palliative care for patients who have exhausted options for specific anti-cancer treatment will be recognised. The number of high-quality clinical trials in the above areas and the availability of their outputs will increase.

Sub-objectives

Sub-objective 1: Screening and secondary prevention

Screening programmes are an effective secondary prevention tool to reduce cancer morbidity and mortality rates. Early disease detection reduces the cost of very expensive treatment at advanced stages of the disease and also prolongs life expectancy and improves quality of life. It is therefore essential to ensure the further development, quality and availability of screening and secondary prevention, following the evidence of these benefits. Research activities should therefore focus primarily on strengthening and refining existing, as well as introducing new, highly sensitive, specific, non-invasive or minimally invasive screening programmes that can be used for early cancer detection in the general population and in high-risk groups.

Sub-objective 2: Identification of risk factors and at-risk individuals in populations

Research in this area will focus primarily on identifying etiological factors involved in the occurrence and development of cancer, and risk factors in the population (especially genetic, environmental, physical, addictive, nutritional, exercise and infectious). The data obtained should allow the formulation of specific preventive measures, but should also become the basis for further experimental research on cancer pathogenesis.

7.1.6.4. Chronic lung diseases

Focus

Lung disease ranks among the top ten causes of morbidity, mortality and disability. It is clearly related to an unhealthy lifestyle, especially smoking tobacco-based products. Lung cancer ranks first in mortality, but chronic obstructive pulmonary disease (COPD) is no less serious, causing high financial costs due to its severity but also patient numbers, morbidity, treatment, loss of work capacity and loss of life. Another serious, though less frequent, disease is pulmonary fibrosis, the incidence of which rises with increasing age, while ageing is also a factor in its development in addition to smoking. Asthma is a very common disease that is easily treatable. However, in some patients the disease is severe and disabling and difficult to control with medication, and here individualized targeted treatment can help. Extensive research from France and the UK has confirmed that women are more at risk of COPD, lung cancer and other serious lung diseases than men. The incidence of lung cancer is slowly declining in men, while it is increasing in women. Surveys mapping lung cancer incidence in the Czech Republic from 1977 to 2016 show that the annual incidence of this malignant disease in men fell by 9.9%. For women, on the other hand, it increased by 32.8% over the same period. Smoking is the cause of almost 90% of lung cancers, while both active and passive smoking can contribute. Treatment outcomes for lung cancer are disappointing, mainly due to late detection of the disease.

For this reason, the Czech Republic launched a pilot lung cancer screening trial from the beginning of 2022. The aim is early detection and therefore a higher lung cancer operability rate, and this will go hand-in-hand with early detection of chronic obstructive pulmonary disease and pulmonary fibrosis. The pilot screening programme provides an opportunity to highlight lung health and the harmfulness of smoking, and will be linked to anti-smoking programmes. It will also provide an opportunity to study at-risk populations and to conduct research on the epidemiology and preventability of chronic lung diseases with the aim of improving lung health in the entire Czech population. It will also become a base for research on molecular genetic risk factors for chronic lung diseases, the search for new risk markers for determining the risk of these diseases, and for personalized targeted treatment.

The main objective

Early serious chronic lung disease detection - research in risk factors for the development of these diseases and their prognosis, whether COPD, severe asthma, lung cancer or fibrotic lung processes. To combat factors affecting lung health and that causally contribute directly to the development of chronic lung disease, especially the smoking of tobacco products. To improve the lung health of the Czech population.

Sub-objective

Sub-objective 1: To increase awareness of lung health and factors affecting it

Improving lung health in the Czech Republic is not possible without the active cooperation of an informed population, but also without the cooperation of the public and private industrial sector, which can be a source of pollution in the working and living environments. However, the major factors influencing lung disease development are related to the risky behaviour of individuals, particularly smoking, but also poor nutrition and physical inactivity.

7.1.6.5. Diseases of the blood

Focus

The incidence of serious blood diseases (leukaemia, lymphoma, myelodysplastic syndrome, bleeding disorders and bone marrow failure) is a significant group of diseases with an incidence of over 25 cases per 100,000 people per year (only the most serious conditions) and which are also very expensive to treat. Moreover, these are diseases where incidence increases with age, and therefore increasing incidence of these diseases can be expected in the near future (see chapter 7.1.3). The prevalence of these diseases has been gradually increasing over the last 20 years (numbers almost double those of 20 years ago). The rising prevalence is due to the increasingly successful treatment of these diseases, but is leading to an increase in the burden on healthcare facilities and an increase in the cost of treating these diseases. Most of these diseases are treated over a long period of time, so patients have to visit specialists for treatment on a long-term basis.

The Czech Republic is one of the most successful countries in Europe when it comes to the treatment and monitoring of patients with blood diseases. Many of these diseases are very well

covered by registries maintained by specialist associations. Unfortunately, none of the registries are publicly funded, although the data they produce are used on a very regular basis, for example, to calculate treatment costs and monitor treatment effectiveness.
As mentioned in the previous chapter, the Czech Republic was significantly affected by the COVID-19 pandemic. There was also a reduction in checks on haematology patients during the pandemic. In addition, the seriousness of the infection was very often severe in COVID-19 patients (e.g. mortality rates of more than 20% in patients with chronic lymphocytic leukaemia).
Epidemiology of haematological diseases is one of the traditionally well-developed areas in the Czech Republic thanks to the above-mentioned registries (real-world data) of these diseases. Research in blood disease epidemiology and prevention already builds on data from these registries and is already used to predict the prevalence, treatment and mortality of these diseases.
In the area of **prevention of blood diseases**, research will focus primarily on the innate predisposition to blood diseases and on programmes to reduce the risk of blood disease recurrence and quality of life issues.

The main objective

Additional epidemiological data on blood diseases will be collected and analysed from regional, national and international perspectives. Risk factors will be identified, new treatment strategies will be tested, and strategies to reduce the risk of disease relapse (including follow-up after treatment) will be tested.

Sub-objective

Sub-objective 1: To identify risk factors and individuals at risk in populations

Research in this area will focus primarily on the identification of aetiological factors involved in the development of blood diseases, risk factors in the population (especially genetic, environmental, nutritional and infectious). The data obtained should allow the formulation of specific preventive measures, and also become the basis for further experimental research on blood disease pathogenesis.

7.1.6.6. Mental illness and diseases of the nervous system

Focus

Brain diseases (mental disorders, neurological diseases and addictions) affect more than 300 million people in Europe (in the Czech Republic, the Institute of Health Information and Statistics indicates that almost 650,000 people were treated for mental disorders in 2019 in the outpatient sector alone, and 35,000 hospitalisations were recorded; data are not available for neurological disorders) and represent the largest health and economic burden (mental disorders are responsible for 20%-30% of negatively impacted years lived with a disease - YLD; mental disorders alone are associated with direct and indirect losses and costs of 4% of GDP in Europe). These are usually long-term chronic illnesses such as affective disorders, anxiety disorders, psychotic disorders, dementia, alcohol abuse, stroke and complications of perinatal

disability. A significant proportion of these diseases affect people of working age and lead to disability (e.g. psychotic illnesses, affective disorders). Patients with severe mental disorders are significantly more likely to suffer from somatic comorbidities, especially diabetes, cardiovascular disorders, obesity and smoking, and their life expectancy is found to be reduced by 15 to 25 years compared to the population not receiving psychiatric treatment. Environmental and lifestyle risk factors or trauma at different stages of life play an important role in the development of some neurological and psychological diseases. Environmental risk factors, along with genetic risk factors, contribute to the development of multiple sclerosis, Parkinson's disease, most mental disorders, while perinatal complications contribute to the development of neurological diseases and behavioural and emotional disorders with onset in childhood and adolescence, and the level of mental and physical activity also plays a role in the development of Alzheimer's disease. A variety of severe stressful situations directly trigger severe mental disorders (post-traumatic stress disorder), while psycho-social stressors lead to relapses and a generally adverse illness course, with loss of functional skills and the ability to live independently in the community. Thus, preventive interventions include both the primary prevention of the development of the disease, as well as the adverse course and mutual negative influence of the environment and the disease. It is therefore necessary to study the adequacy of the health service system and the impact of its changes - and thus to evaluate the use of individual services and therapeutic interventions with regard to the prevalence of adverse effects of disease and quality of life for patients.

In particular, projects with the following focus are expected: Epidemiology of both neurological (e.g. epilepsy, multiple sclerosis, Alzheimer's disease, stroke, brain trauma, perinatal asphyxia) and psychiatric diseases (e.g. mood disorders, psychotic and anxiety disorders, dementia) maps the prevalence of these diseases; demographic studies describe population trends, prevalence, incidence and associations of individual disorder prevalence (by region, by occupation, by environmental conditions, etc.). Studies focused on the use of health and social services, drugs and medical devices, economic analysis for streamlining the healthcare system to improve quality of life for patients with mental and CNS disorders.

Such studies will form a basis for (a) policy decisions, (b) priority adjustment, (c) generation of hypotheses about the causes and protective factors of brain disease, and (d) creation of prevention and care programmes. Furthermore, the organisation of multi-year longitudinal studies in at-risk patients - with risk factors, with prodromal stages of the disease - is a priority.

The main objective

The main demographic and epidemiological characteristics of diseases of the nervous system will be mapped, and their associations (e.g. age, gender, geographical and environmental, developmental, genetic, and co-morbidities) found and predicted, along with linkages to health service utilization, while there will be evaluation of preventive measures, new services and programmes to reduce the prevalence and incidence of nervous system diseases, including mental disorders, recidivism (frequency and length of hospital admissions) will be reduced, as will the socio-economic burden and impairment of quality of life that diseases of the nervous system represent. At the same time, research in the effectiveness and efficiency of interventions and services will be carried out to optimize the supply and coordination of these interventions.

Sub-objectives

Sub-objective 1 Population study: disease data

The creation of registries (mental and nervous system diseases, suicides, somatic comorbidities, early and late morbidity in at-risk newborns, etc.) and support for longitudinal studies will form the basis for databases on which preventive interventions will be based.

Sub-objective 2 Population intervention, evaluation of the impact of new services and preventive measures

Above all, primary preventative population-wide interventions will focus on the destigmatization of individuals suffering from brain disease: stigmatization represents a stressor potentially worsening the course of the disease and results in delaying the search for therapeutic assistance, while delaying may adversely affect the patient's outcome. Primary prevention programmes will further target at-risk sectors of the population, such as perinatally at-risk children and individuals at increased risk of developing psychotic disorders, stroke or dementia. The most modern methods will be used, including, for example, telemedicine. At the same time, research into the effectiveness and efficiency of interventions and services will be carried out to optimize the supply and coordination of these interventions.

7.1.6.7. Diseases of the musculoskeletal system and inflammatory and immunological diseases

Focus

Inflammatory rheumatic diseases

Immune-mediated inflammatory rheumatic diseases are relatively rare and based on an abnormal reaction of the immune system against its own tissues and organs. These are autoimmune and autoinflammatory diseases, which can be simply divided into four major groups of arthritis, inflammatory diseases of the spine, systemic connective tissue diseases and vasculitis. Within these groups there are several different diseases, e.g. rheumatoid arthritis, crystal-induced arthropathies, spondyloarthritis, systemic lupus erythematosus, Sjogren's syndrome, idiopathic inflammatory myopathies, systemic scleroderma, various types of vasculitis and other rare rheumatic diseases. These conditions are common causes of disability and place a huge financial burden on health and social security systems.

The cause of inflammatory and systemic rheumatic diseases is not precisely known, but a genetic predisposition is assumed, usually a polygenic inheritance that interacts with environmental factors to induce changes in immune processes that become fixed and cause disease manifestation. The breaking of immune tolerance can be conditioned by microbial antigens, and the role of the gut microbiome is considered in the development of immune-mediated rheumatic diseases, for example. An important role is played by dendritic cells, which link the natural and adaptive immune systems, activate lymphocytes and stimulate the production of cytokines and autoantibodies, which in many cases are characteristic of specific autoimmune diseases. In addition to genetic causes, there are so-called epigenetic regulatory mechanisms able to modify gene expression without affecting the DNA sequence, using DNA methylation and histone acetylation, and using non-coding RNAs. These changes contribute to

the activation of the immune system and the pathogenesis of rheumatic diseases and may have diagnostic, prognostic and therapeutic potential.

Early diagnosis and treatment of immune-mediated rheumatic diseases can prevent damage and the need to go through the entire course of the disease. Thus, urgent needs include early diagnosis of inflammatory rheumatic diseases, as well as efforts to identify preclinical stages, risk factors and preventive measures that can help delay and alleviate, or even cure, rheumatic diseases. Due to the frequent association of rheumatic diseases with extra-articular manifestations and increased incidence of comorbidities such as cardiovascular disease, diabetes and depression, interdisciplinary collaboration is essential.

Degenerative and non-inflammatory diseases of the musculoskeletal system

Osteoarthritis is the most common arthropathy, affecting up to 50% of the population aged over 60. It reduces quality of life, increases morbidity and mortality rates, and imposes significant socio-economic costs on society as a whole. The number of major joint replacements required using endoprostheses is increasing every year.

The aim of the research will be to describe the epidemiological context of arthritis and to address both genetic and environmental factors. Genetic factors mainly include gene mutations related to components of the hyaline articular cartilage. Biomechanical factors (joint incongruence, congenital dysplasia, postoperative conditions) will be studied. Among other systemic predisposing factors of osteoarthritis, endocrinological influences and metabolic factors (e.g. adiponectins) will be determined. Biomarkers of cartilage degradation and their relationship to disease progression and effectiveness of therapeutic intervention will be monitored. New imaging techniques will be developed to visualise cartilage and soft-tissue changes, based on MRI techniques and techniques combining multiple imaging modalities. The efficacy of therapeutic interventions, including arthroscopic and cartilage salvage methodologies, will be monitored.

Osteoporosis is a chronic, mass-onset disease, and a major health-economic consequence of osteoporosis is low-trauma fractures that impair the health of half of women and one fifth of men aged over 50. In the Czech Republic, around 70,000 people suffer a new bone fracture every year, of which 12,000 have a hip fracture. The number of fractures is expected to be one-third higher in 2025 than in 2010, when 2.1% of women (43,700 out of 2.09 million) and 1.6% of men (28,500 out of 1.71 million) aged over 50 suffered a fracture.

In 2010, the cost of osteoporosis treatment was almost CZK 1.4 billion, and only one tenth of men and one quarter of women with densitometrically diagnosed osteoporosis were treated. As the treatment of people with a previous fracture does not address the economic burden associated with the increasing number of osteoporotic fractures, the aim of the research will be to prevent osteoporosis in the population. This will be done using epidemiological data on the association of fracture risk, physical activity, nutritional factors and indicators of moderate chronic inflammation in people aged 50 to 70. Among nutritional factors, the anti-inflammatory value of the diet and the supply of vitamin D and calcium and their association with the gut microbiota will be highlighted. The association of physical activity and metabolic characteristics of muscle cells, osteocytes, osteoblasts, osteoclasts and calcium phosphate metabolism with muscle and bone mass will be investigated as a function of age and the degree of chronic inflammation. Attention will be paid to the influence of hypercortisolism and

hypogonadism on these indicators. The effectiveness of preventive interventions (probiotics, selective estrogen receptor modulators, vitamin D fortification of foods) will be monitored.

Other immunopathological diseases

Immunopathological diseases can be broadly divided into allergic, autoimmune and immunodeficiency disorders. In terms of frequency, diseases where different types of allergic conditions play a major role are definitely dominant. According to current statistics, various forms of atopic hypersensitivity affect up to 30% of the population, with bronchial asthma found in 5% of people and atopic eczema in up to 30% of children under 3 years of age. Yet these are diseases whose prevalence has risen significantly in the last 50 years, a rise linked to "western" lifestyles. The so-called hygiene hypothesis emphasizes the influence of insufficient stimulation by microbes and microbial products in preventing the development of allergic diseases. The mechanisms that lead to an atopic disposition are unknown, but are both genetic and environmental influences. In addition to pharmacological treatment, regime measures play an important role in allergic disease. The aim of the research will be to investigate the influence of hereditary and environmental influences on the development of allergic diseases and to compare the possibilities of influencing these factors in both the prevention and treatment of allergic diseases.

Autoimmune diseases affect an estimated 5%-10% of the population. Both genetic and environmental influences play an important role in these diseases. The most common autoimmune diseases include the aforementioned inflammatory rheumatic diseases, autoimmune diseases of the endocrine glands (pancreas, thyroid), and autoimmune disorders of the intestines (especially non-specific intestinal inflammation, celiac disease). However, virtually any organ can be affected by autoimmune disease. From the point of view of the section's focus, it is necessary to monitor especially endogenous and environmental influences that lead to the development of these diseases on a population-wide scale. Once again, it is important to stress that the incidence of these immunopathologies is also increasing. However, the mechanism for this rise has not been elucidated and should be an important topic of research.

In terms of occurrence in the general population, various primary and secondary immunodeficiencies are probably equally common immunopathological diseases. The problem of primary immunodeficiencies from a societal perspective is early diagnosis to prevent the development of severe subsequent conditions, as well as appropriate treatment, which is usually very costly. Secondary immunodeficiencies are a relatively common side effect of treatments, especially cancer or immunosuppressive treatments, or are the result of serious medical conditions. In particular, due to the heterogeneity of these conditions, the epidemiology of secondary immunodeficiencies is not sufficiently studied compared to other immunopathological diseases, and the methodologies for searching and monitoring these conditions, as well as monitoring the necessary treatment, are unclear.

Influence on immune-system function

Approaches to influencing immune-system function should play an important role in research. From the point of view of disease prevention, vaccination is certainly the most important issue, both in terms of the development of new vaccines and adjuvants, but also in the search for optimal vaccination schedules and the avoidance of adverse reactions. Immunology is also about fighting the anti-vaccination movement, and explaining the benefits of vaccination for

individuals and society. In addition to vaccination, the development of drugs and procedures that positively stimulate the immune system should be encouraged for the treatment and prevention of cancer, infections and immunodeficiencies. Immunosuppressive therapy is used in the treatment of many diseases.

The main objective

Not only prevalence and incidence factors, but also other important environmental factors involved in the aetiopathogenesis of these diseases will become known. Among the most important are the relationship between infection and the development of autoimmune diseases, endocrine factors, the effects of ageing, environmental pollution, and the effects of smoking and other addictive substances.

Sub-objectives

Sub-objective 1 Epidemiology of degenerative and metabolic diseases of the musculoskeletal system and autoimmune-mediated diseases of the gastrointestinal tract

Describe the epidemiological context of external causes for the development of degenerative joint and spine diseases, such as joint dysplasia, obesity, trauma, inflammation, lifestyle factors and exercise. Map the epidemiologically important connections leading to the formation of various types of metabolic osteopathies, such as nutritional factors, calcium and vitamin intake, the effects of physical activity, the effects of smoking and addictive substances, the influence of various drugs (e.g. glucocorticoids) and the development of idiopathic intestinal inflammation and celiac disease.

7.1.6.8. Addictions

Focus

Addictions (the need to compulsively repeat certain behaviours regardless of the consequences) include:

(a) dependence on addictive substances with psychoactive effects,

(b) addictive disorders in the context of the eating disorder spectrum,

(c) process addictions such as pathological gambling, including the need to play games (including computer games), internet addiction disorder, kleptomania (the need to steal), etc.

(d) other pathological addictions and manifestations of addictive behaviour.

Dependence on addictive substances (drugs) is currently one of the most common causes of health and social complications, either alone or as a comorbidity of other related disorders or diseases, and the incidence trend is rising. An addictive substance (drug) is defined here as any psychotropic substance capable of inducing a state of compulsion, dependence or other serious negative health or social effects associated with its use. We do not distinguish between the past and current state of regulation for these substances, meaning we include nicotine, alcohol, illegal addictive substances, toluene, the so-called new synthetic drugs, etc.

The annual report of the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) highlighted in particular the growing trend in the use and interception of new

synthetic drugs (a total of 24 brand-new substances for recreational use have been identified in the EU). In addition, other documents (e.g. the WHO Alcohol Strategy, the EU Alcohol Action Plan, etc.) have identified groups of substances with the most significant health and wider societal impacts as priority areas. These are mainly tobacco, alcohol, cannabis-based drugs, stimulants and the above-mentioned new synthetic drugs. These areas form a priority axis for research and development of preventive and treatment measures.

Treatment of drug addiction is relatively expensive for chronic patients (also due to highly problematic psychiatric and somatic comorbidities) and has only a partial or short-term effect in many patients. This area forms the **first focus of priorities**, where the key focus is on research on effective treatment factors and their application, research on the phenomenon of non-institutional forms of assistance (self-help elements, etc.), research on motivation to undergo treatment (in the context of voluntary and involuntary treatment), and the development and application of complex treatments and programmes targeted at specific target groups and their needs (e.g. studying the possibilities of substitution therapy for methamphetamine addicts).

Prevention is **the second focus of priorities**. The aim of the programme is to develop and test prevention and intervention programmes to prevent, delay the onset of, or halt the progression of substance use, including alcohol, in children and adolescents.

The **priority target groups** for both programme focus points include children and adolescents, high-risk (vulnerable groups) and comorbidity patients, and groups for whom use poses high health, social and safety risks. The epidemiology of addiction describes the structure and evolution of addiction in the general population as well as in predefined population sectors (children and adolescents, men vs. women, persons at risk, criminal subculture) and maps the association with other risks (HIV, hepatitis in IV use, cirrhosis with alcoholism, hepatitis).

The main objective

The programme aims to reduce the prevalence and incidence of addictions and their health and socio-economic impacts, to reduce the harms associated with substance use (including smoking and alcohol use), gambling, digital addiction and other addictive behaviours, and to test the effectiveness of treatment and preventative interventions. A prerequisite for achieving these goals is to map the epidemiology, development risks, societal burden and predictors of addiction treatment, and to prepare the basis for prevention measures and programmes and for political, legislative and economic decisions.

Sub-objectives

Sub-objective 1 Links

Establish the genetic, epigenetic, environmental, public-health, behavioural and social links of addiction, including their links to other related diseases.

Sub-objective 2 Social impact

Reduce the social and economic impact of addictive behaviour.

Sub-objective 3 Use of e-health and ICT assisted technology in addiction treatment and prevention

Obtain more evidence on the effectiveness of using e-health and ICT assisted technology in addiction treatment and prevention.

7.1.7. Global health

Focus

The term **global health** refers to the level of physical, mental and social well-being of people on a global basis. Global health builds on national public health systems but emphasizes transnational research, activities and broad strategies that lead to improved health for the majority of the population. Given that the rapid development of civilization often has adverse effects on health, in that many civilizational factors directly and indirectly increase health risks and healthcare costs, it is essential to focus on studies, research and practices that emphasize improving health and achieving health equity for all people from a global perspective. Therefore, it is essential to focus on reducing excess mortality and disability rates, promoting healthy lifestyles, developing health systems that equitably improve the state of health of the population, and creating a framework for an effective health policy that promotes primary prevention and health promotion in particular, including an emphasis on the underlying social, economic, environmental, behavioural and political determinants of health.
At present, the issue of primary prevention and health promotion is legislatively anchored in Act No 258/2000 Coll., on the protection of public health, and in its implementing regulations. Protecting and promoting public health is a priority not only for the European Union and its Member States, but is also emphasised, including the improvement of global health, by the World Health Organisation in all its documents and strategies. The Health in All Policies strategy is enshrined in the Treaty on European Union, and commits all policies to this approach.
In addition to medicine and public health approaches, global health uses tools from other disciplines such as epidemiology, hygiene, demography, economics and sociology to analyse and influence the determinants and promote health in society. This is the only way to identify risk factors and causes of health problems and to seek measures with regard to the cost-effectiveness and optimal allocation of health resources. Global health therefore refers to all health-improvement strategies, whether population-wide or individual health measures, and across all sectors, not just the health sector.

The main objective

Use objective indicators to characterise the state of global health, describe trends and quantify the health impact of different interventions and policy approaches. Recognize the risky influences of new technologies, new chemicals, from exponential increases in electromagnetic fields, increased noise pollution, light emissions, etc. as well as biological agents, physical and psychosocial environmental and work environment factors on health, and mitigate them through a combination of preventive and corrective protective measures.
Describe toxic chemicals and their mixtures from the environment and workplace or everyday objects where they are added to maintain and improve performance. The occurrence of

developmental and organ toxicity, reprotoxicity, neurotoxicity, carcinogenicity and sensitising and endocrine disrupting effects have been proven for a number of these substances.
Using disease surveillance and biological monitoring, which is the link between all exposure pathways, it is possible to assess levels of toxic and other contaminants, and to assess the magnitude of the health impacts as a basis for necessary action. Improve the assessment of health risks and health impacts arising mainly from chronic population exposure to environmental and dietary toxicants, thus providing an objective, evidence-based foundation for health-risk management. This is the most effective way leading to targeted measures to protect public health in the sense of reducing and/or gradually eliminating the most serious exposures and thus improving population health. Drinking water from public water supplies and outdoor recreational water can be sources of exposure to health-risk contaminants. However, in addition to the quality indicators monitored, a number of other potentially hazardous substances may be present in drinking and bathing water that may pose a health risk. Adaptation and mitigation to climate change refers in particular to research, monitoring and measures to prevent infectious and non-communicable diseases and to prevent health threats caused by extreme weather events. Due to the many natural and anthropogenic influences, the human living and working environment is continuously changing, and while some traditional and well-known health risks are becoming irrelevant, many new ones are emerging or waiting to be discovered.

Sub-objectives

Sub-objective 1 Environmental and occupational health effects

Research on health risks from **exposure to environmental risk factors**, especially ultrafine particles, which are the most serious fraction of aerosol particles from the health point of view due to the possibility of their penetration into the alveoli. Improve knowledge of the **health risks associated with drinking tap water and swimming in pools or in open water**, and assessing and managing the associated health risks of newly discovered potentially hazardous factors in these environmental components.
In particular, nationwide biomonitoring of exposure to toxic substances in different population groups **is a systematic tool for data collection**.

Sub-objective 2 Impact of nutrition and diet on health

Statistical data and estimates show that approximately 48% of all deaths in the Czech Republic can be attributed to risky behavioural factors. These include poor dietary habits, high alcohol consumption and low physical activity. Risky eating habits such as low fruit and vegetable consumption and high salt consumption contributed to more than a quarter of all deaths (27%), well above the EU average (18%). The adult obesity rate in the Czech Republic is among the highest in the EU. It has grown by more than 30% in the last 15 years. Around 20% of adults were obese, which is higher than the EU average (15%). Primary prevention in public health can significantly reduce the economic cost of acute healthcare and improve quality of life. Negative facts require the development of research, the production of relevant data and their interpretation in relation to health. Obtaining **epidemiological data on individual consumption, nutrition and food** in accordance with what is required by EU and national legislation will be essential. Completely missing data or older existing data do not allow an up-

to-date assessment of the food consumption of individual population groups, including at-risk groups such as children, the elderly, pregnant women, and people with diseases. The data are currently inaccurate, weakening the **health risk assessments** required by food control authorities in the Czech Republic and the EU in administrative and judicial proceedings. Research in this area of public health covers four main areas: (i) creating an environment for healthy diets, (ii) promoting whole-life healthy diets, (iii) strengthening health systems to promote healthy diets, and (iv) surveillance, monitoring and evaluation.

Sub-objective 3 Infectious diseases

Infectious diseases are of great importance to global health because they recognise and have no borders. Therefore, in today's globalised and interconnected world, the threat of disease in one place can very quickly become a health threat anywhere else, including the Czech Republic. Given the increase in population, the simplification and speed of global travel, along with rapidly expanding global trade and the long-distance movement of goods, animals and plants, it is more important than ever to set and follow binding rules and procedures that minimize the spread of serious human infectious diseases and zoonoses in the Czech Republic. Epidemiological surveillance, monitoring, early warning and combating serious cross-border health threats are proving increasingly important, as the experience gained during the ongoing COVID-19 pandemic has shown.

To maintain global health in the area of infectious diseases it is important to:

- obtain more knowledge in the prevention, diagnosis and control of communicable diseases, including cooperation and exchange of scientific information at all levels,
- improve the quality of early detection and reporting systems for communicable diseases, in particular taking into account the global context, creating automated systems using modern technologies to strengthen capacity, especially for contact tracing, while complying with Regulation (EU) 2016/6791a of the European Parliament and of the Council,
- improve methodologies and strengthen capacity in epidemiological surveillance, and promote long-term and systematic data collection,
- support research on emerging diseases, re-emerging diseases and neglected diseases (see also chapter 7.2.7),
- study the emergence, selection and spread of pathogens with respect to their resistance to anti-infectives, in particular antibiotics and vaccines, and to research and implement methods to enable the targeted and accurate detection of infectious agents.
- study and obtain information on the risks arising from changes in the epidemiological situation in relation to the impact of climate change on infection rates
- improve the monitoring system (surveillance), in particular focusing on preventable infections, climate-sensitive pathogens and their animal vectors and reservoirs

Sub-objective 4 Toxicology and health safety

Chemicals pose a direct risk to health. There are more than 100,000 different chemicals on the market today, with around 1,500 new ones added each year. Chemicals are used in all human activities and in all products, including those intended directly for consumers, such as food. Many chemicals have not yet been studied for their effects on human health, especially the harmful effects of long-term, chronic exposure.

Given the need to protect the population from the harmful effects of chemicals, it is essential to focus on the following: (i) research aimed at unravelling the mechanisms of chemical carcinogenesis and tumorigenesis, (ii) toxicological studies, (iii) development and application of sensitive and innovative toxicological methods, (iv) monitoring determinants of healthy environmental and living conditions.

Sub-objective 5 Occupational medicine and occupational diseases

The choice of research topics in occupational medicine must be based on demographic changes in society, changes brought about by globalisation, new technologies that introduce new, previously unexplored risks in the work environment, including exposures to new chemicals, biological agents, physical factors, and the impact of information technology and digitalisation.

Sub-objective 6 Innovative approaches to the promotion of health and intervention programmes in primary prevention

The key objectives are the need for very specific and systematic work that sees the individual in the whole context and to focus interventions on the whole organism and any possible illnesses or harmful consequences of exposure to various harmful influences or substances.

The priority steps are: (i) Strengthening primary prevention and the whole primary prevention pillar, techniques and interventions related to it**,** (ii) increasing health literacy among the general population, primary school pupils and secondary and university students (see chapter 7.1.5), (iii) raising awareness of addiction among the general and professional public, and (iv) promoting behavioural surveillance for infectious and non-communicable diseases at national and international levels.

7.2. Pathogenesis and development of diseases

7.2.1. Metabolic and endocrine diseases

Characteristics

Metabolic diseases and endocrinopathies are a major cause of population mortality and morbidity. Serious impacts are present in diseases that arise already in childhood and early adulthood. Diseases grouped under the term metabolic syndrome (obesity, dyslipidemia, hypertension, prediabetes and type 2 diabetes mellitus) have a common pathogenesis, in particular systemic inflammation, insulin resistance, fat accumulation, lack of exercise and the interaction of these factors with the genetic makeup of the individual. The pathogenesis of metabolic syndrome is undoubtedly related to the development of serious complications classified in other fields such as cardiology, angiology, oncology, immunology, nephrology, neurology and pneumology. Diabetes itself currently affects about 10% of the Czech population (some from childhood) and another 5% of the population has prediabetes. The pathogenesis of endocrinopathies and endocrine active tumours is partly similar yet partly different. Again, this is largely an interaction of environmental influences and genetic causes. In any case, research in the pathogenesis of endocrine and metabolic disorders is key to prevention and the development of new treatments for these diseases. One serious finding is the increasing prevalence of diabetes-related complications which, rather than decreasing, are increasing, despite new therapeutic standards. Diabetes is the most common cause of cardiovascular events, chronic renal insufficiency, non-traumatic limb amputation and blindness in adulthood in the Czech Republic. The cost of treating type 2 diabetes mellitus accounts for over 10% of all healthcare costs, with the majority spent on inpatient treatment of organ complications.

Type 1 diabetes mellitus is a specific problem that occurs mostly in children and young people and affects about 4% of the population in the Czech Republic. Better knowledge of its pathogenesis would help in the development of preventive or early-intervention procedures, the principles of which aimed at preservation or regeneration of insulin-producing cells could find application in the treatment of type 2 diabetes mellitus.

Thyroid diseases are common and affect more than 10% of the population. Special attention should be paid to autoimmune and non-autoimmune thyreopathies and their complications. Pituitary diseases usually lead to significant disability and are expensive to diagnose and treat. Particular attention should be paid to research on the aetiology and pathogenesis of pituitary tumours and their complications. Diseases of the adrenal glands are quite common. If we include all adrenal tumours, they affect more than 10% of the population. Adrenal tumours with hyperfunction syndromes are serious conditions with significantly increased morbidity and mortality. Attention should be paid to their etiology and pathogenesis and the pathogenesis of their complications. Many diseases of other endocrine glands, especially parathyroid and gonadal diseases, are also socially and economically important.

Attention should also be paid to developing methods for the early diagnosis and study of the etiopathogenesis of inherited metabolic disorders, which are not so common but where early diagnosis and treatment can prevent the development of irreversible consequences with extremely expensive treatment.

The main objective

The etiology and pathogenesis of major metabolic and endocrine disorders in the current population will be elucidated, thereby preventing their progression, mitigating their course and, in particular, reducing their consequences, which affect almost all medical areas and contribute to overall mortality rates. This will not only increase the length, but also improve the quality, of active life for a wide group of the population and have a corresponding social and economic impact.

Sub-objectives

Sub-objective 1 Etiology and pathophysiology of insulin resistance and metabolic syndrome

Elucidate the pathogenesis of the interrelationships between congenital, developmental and environmental factors in the development of obesity, metabolic syndrome, and metabolic disorders leading to type 2 diabetes mellitus and related diseases. Research the role of muscle and adipose tissue hormones - myokines and adipokines. Investigate the distribution of adipose tissue and the influence of its distribution in the body using modern imaging methods. Investigate nutrigenomic and nutrigenetic relationships in metabolic syndrome.

Sub-objective 2 Etiology and pathogenesis of immune-mediated endocrine diseases

Identify inducing factors and mechanisms of autoimmune-mediated endocrine disorders, particularly type 1 diabetes mellitus, thyroid disease, adrenal and pituitary gland disease, as well as diseases of other endocrine glands and polyglandular autoimmune syndromes. The role of viral infections in the pathogenesis of autoimmune endocrinopathies and support for research in rare forms of diabetes and endocrinopathies should also be a subject of research.
Identify etiological and pathogenetic factors involved in the development of other endocrine diseases, their complications and associated diseases. There is also a need to support the study of the etiopathogenesis of inherited metabolic disorders and to develop new diagnostic and therapeutic approaches based on this knowledge.

Sub-objective 3 Pathogenesis and treatment of diabetes complications

Identify mechanisms for the development of chronic diabetes complications such as diabetic nephropathy, retinopathy, polyneuropathy, diabetic foot syndrome and diabetic macroangiopathy, and the introduction of new prevention and therapy methods. This implies many unknowns in the pathogenesis of metabolic and endocrine disorders and our still limited knowledge of the pathogenesis of complications of these diseases. Technology will dominate the treatment of type 1 diabetes in particular, with research in automatic insulin delivery systems ('artificial pancreas') playing a major role. Glycaemic variability is an important factor in the development of diabetes complications and this is being significantly reduced by new technologies. Here again, genome-environment interaction in disease pathogenesis is an important subject of research.

7.2.2. Diseases of the circulatory system

Focus

Cardiovascular disease (CVD) is the leading cause of mortality in developed countries, accounting for more than 50% of all deaths (44.6% in men, 54.3% in women), half of which are attributable to a single disease, coronary heart disease and its acute form, myocardial infarction. Despite all the successes achieved by Czech cardiology in the past 15 years, especially in research on the pathogenesis, prevention, diagnosis and treatment of coronary heart disease and its risk factors, atherosclerosis and hypertension, in the treatment of acute coronary syndromes, heart failure, heart rhythm disorders, congenital heart disease and other CVDs, these diseases remain the leading cause of mortality in the Czech Republic. According to data from the Czech Society of Cardiology, the mortality rate from CVD in the Czech Republic is still significantly higher than in Western European countries, with approximately 600 deaths per 100,000 inhabitants each year. Cardiovascular morbidity is also high, expressed in terms of the number of hospital admissions for cardiovascular diseases (more than 50% of all hospital admissions in internal medicine departments); it has increased by 25% over the last 10 years. Heart attack is the most common cause of death and disability in men of working age, the incidence of heart failure is increasing, and all the risks and complications arising from the increase in atrial fibrillation will have to be addressed. There are still great opportunities in the early diagnosis and prevention of CVD, as well as in the problem of thoracic and abdominal aortic aneurysms, the occurrence of which is increasing due to the ageing population and improving diagnostics, and also in issues related to CLI and diabetic foot.

According to World Health Organization criteria, strokes are defined as rapidly developing clinical signs of focal or diffuse brain damage, presumed to be of vascular origin, lasting more than 24 hours or leading to death. Strokes are the second leading cause of death in both developing and developed countries. Strokes affect about 15 million people worldwide each year and are responsible for more than 5 million deaths/year, accounting for about 10% of all deaths. Data from the Institute of Health Information and Statistics in the Czech Republic in 2010 indicate that the number of stroke-related hospitalizations (dg. I60-I69) in the Czech Republic was 46,374 people with a total of 57,484 incidents and an average hospital stay duration of 14.8 days. Of these, 5,826 people died in hospital. A total of 11,567 people died from these diseases in the Czech Republic in that year, which is 11% of all deaths. Mortality rates for cerebral infarction range from 20%-30% and for cerebral haemorrhage up to 50%. The incidence of strokes according to the National Stroke Registry of the Czech Republic was 300 cases per 100,000 people in 2011.

Strokes leave permanent effects in 70% of surviving patients, and severe permanent disability in more than 30% - strokes are the most common cause of disability, especially in the elderly. In addition, cerebrovascular diseases are the second most common cause of dementia and the most common cause of epilepsy in the elderly. A large proportion of post-stroke patients suffer from depression and other psychological problems or incontinence. Collectively, of all diseases in general, strokes have one of the greatest health and socio-economic impacts on society. According to the WHO, strokes are the second most common cause of loss of years of life.

The main objective

Major progress in the prognosis, diagnosis, and therapy of coronary heart disease, its risk factors, and other cardiovascular disorders would be unthinkable without the close cooperation of theoretical and clinical cardiologists, cardiac surgeons, angiologists, and vascular surgeons. This cooperation has a long tradition in our country and is the driving force of scientific progress. The aim of the research will be to contribute to the elucidation of etiological factors and molecular and cellular pathogenetic mechanisms involved in the development of coronary heart disease and its risk factors, heart failure, heart rhythm disorders, structural and inflammatory heart disease, congenital heart defects and diseases of the arterial and venous system, with particular attention to improving their prevention, early diagnosis and highly individualized treatment. New etiological factors and new pathophysiological mechanisms affecting the onset and progression of cardiovascular diseases, in particular ischaemic heart disease, heart failure, heart rhythm disorders, hypertension, structural heart disease, CIHD, aortic aneurysms, chronic venous insufficiency, inflammatory heart disease and other diseases of the arterial and venous system will be identified with a clear impact on improving their prevention, early diagnosis and highly individualized treatment.

The etiopathogenetic mechanisms that cause stroke and the possibilities of influencing them will be recognized, especially in the area of "non-traditional" risk factors. In addition, mechanisms that lead to neurological disability in patients with cerebral infarction, spontaneous cerebral haemorrhage, and spontaneous subarachnoid haemorrhage will be recognized and the potential to influence them will be elucidated. The reasons for the success and failure of therapeutic procedures in patients with stroke will be explained. Regenerative mechanisms that are responses to nervous system disorders, including mechanisms of brain plasticity and brain tissue regeneration in neurorehabilitation will be understood.

Sub-objectives

Sub-objective 1 Clarification of etiological factors and pathophysiological processes affecting the onset and course of cardiovascular and cerebrovascular diseases

Multi-disciplinary biohealth research will be preferred, bringing qualitatively new insights into the causes and mechanisms affecting the development and course of cardiovascular and cerebrovascular disease, with clearly defined clinical benefits improving their prevention, diagnosis and treatment. In cerebrovascular disease research, it is necessary to remove the existing interdisciplinary barriers and significantly deepen the collaboration between neurologists and cardiologists with the participation of other disciplines such as radiology, neurosurgery and angiology.

Sub-objective 2 Development of the early diagnosis of cardiovascular and cerebrovascular diseases and finding treatment modalities and procedures in the treatment of cardiovascular and cerebrovascular diseases with higher therapeutic efficacy and greater patient friendliness

Multi-disciplinary research is preferred, as well as the development of new technologies, methods, drugs, and diagnostic and treatment procedures with clearly defined clinical benefits for the early diagnosis or highly effective targeted treatment of both types of diseases, while respecting each patient's uniqueness. In the development of modern treatment of cerebrovascular diseases, it is necessary to remove the existing interdisciplinary barriers and

significantly deepen the cooperation between neurologists and cardiologists in particular, but also with other disciplines such as radiology, neurosurgery and angiology. This area also includes research in identifying and validating regenerative, rehabilitation, re-socialization and educational procedures for patients with cardiovascular and cerebrovascular diseases to shorten recovery time and the duration of incapacity to work, and to improve their social welfare.

7.2.3. Cancer

Focus

Every year, 2.3 million more Europeans are diagnosed with cancer. Every year, 1 million Europeans die from cancer. In the context of demographic development - the ageing of the population - one in three citizens of the Czech Republic will get cancer during their lifetime. Cancer (27,699 cases in 2018) together with diseases of the heart and blood vessels (36,452 cases in 2018) is the most common cause of death in the Czech Republic. In addition, the COVID-19 pandemic is having a serious impact on cancer care, disrupting prevention and treatment, delaying diagnosis and vaccination, and affecting access to medicines. Since the onset of the pandemic, the number of cancer diagnoses has declined,which points to a future increase in cases.

The European Union's response to these needs is Europe's Beating Cancer Plan, intended to address all aspects of the disease.

It is structured around four key areas of action where the EU can make the biggest difference: 1) prevention; 2) early detection; 3) diagnosis and treatment; and 4) quality of life for current and former cancer patients. In the coming years, it will therefore focus on research and innovation, exploit the potential offered by digitalisation and new technologies, and unlock financial instruments to support member states. This mission against cancer, planned under Horizon Europe, will be the major component of the EU's investment in cancer research and innovation, and aims to deepen our understanding of the complexity of cancer.

The Czech Republic has a long history in the field of oncological research and there is potential, especially in research aimed at developing knowledge in cancer pathogenesis and research and development in diagnosis and treatment. In the Czech Republic, there are a number of top teams active in domestic and international research in these areas. At the same time, there are research centres with modern and high quality (and in many cases unique in the world) research infrastructure, enabling demanding multidisciplinary research and development linking disciplines seemingly far apart from each other.

The goals of cancer research in the Czech Republic for the coming period should be in line with Europe's Beating Cancer Plan and the Mission Against Cancer, i.e. (i) to increase our knowledge of cancer pathogenesis, (ii) to improve prevention, (iii) to improve cancer diagnosis and treatment, and (iv) to ensure better quality of life for patients (and their families) suffering from or affected by cancer. Research with the aim of meeting these objectives should not be limited to high-incidence cancers affecting adults, but should cover all ages, including patients suffering from rare forms of cancer, childhood cancer patients, adolescents, and polymorbid elderly. Research in improving prevention and screening programmes is covered separately in chapter 7.1.6.3.

The main objective

The main objectives of health research in the field of cancer are to deepen knowledge of the pathogenesis of cancer, improve diagnosis and treatment, and improve the quality of life of cancer patients. Individual projects will focus on the possibility of rapid implementation of research results into clinical practice. Research projects should be directed towards the development of new diagnostic methods and algorithms and the development of new therapeutic and preventive procedures.

Sub-objectives

Sub-objective 1 Deepen knowledge of the pathogenesis and development of cancer and identify new therapeutic targets

A detailed understanding of the biological processes accompanying tumour transformation and development is essential for the evolution of diagnostics, but especially for the identification of new therapeutic targets and the development of innovative therapies. Despite tremendous progress in the understanding of cancer pathogenesis and related developments in the molecular pathology of tumours, targeted therapies and immunotherapy, there are still cancers that are primarily resistant to all therapeutic approaches. On the other hand, there are very well characterized therapeutic targets against which effective drugs are still not available. Particular attention should be paid to tumours in children, adolescents and young adults, but also to tumours in older age groups. Tumours in these patient groups often have different biological and clinical characteristics compared to those in the general population. Attention should also be paid to the process of carcinogenesis and research on risk factors. This issue is addressed in chapter 7.1.6.3.

Sub-objective 2 Improve cancer diagnosis and treatment, especially through the implementation of precision medicine, medicines for modern therapies, targeted drugs and modern radiotherapy

Recent advances in cancer research and the development of modern targeted therapies have significantly advanced the therapeutic options for these diseases. The prognosis for cancer patients is improving, including for those with metastatic forms. Therefore, the logical goal of clinical research is to transform this disseminated disease from the category of fatal to chronic. However, a significant proportion of tumours that are diagnosed at late stages are those that are highly aggressive and primarily resistant to available drugs. The new knowledge gained under sub-objective 1 should enable improved diagnosis and treatment of these tumours through the discovery of new biomarkers and therapeutic targets. The focus will be on studies to enable the effective transfer of this knowledge into clinical practice. Studies to enable a higher degree of cancer treatment individualisation, so-called precision oncology, a concept based on the use of technology enabling comprehensive genomic profiling (next generation sequencing, NGS), are also considered important. An important advance in cancer treatment are definitely advanced therapy medicinal products (ATMPs, see chapter 7.3.3.), which we understand as products for gene therapy (e.g. T-lymphocytes with chimeric antigen receptor) or somatic cell therapy (e.g. immunotherapy based on dendritic cells). Studies focused on the development and evaluation of ATMPs in anticancer treatment are an important tool for meeting sub-objective 2. Research

in modern radiotherapy, which should reflect both the technological development (in IT and in irradiation instrumentation) and the development of knowledge in clinical radiobiology, will contribute to the fulfilment of the objective. The development of a new generation of highly selective receptor tyrosine kinase inhibitors (see chapter 7.3.2), oligonucleotide therapies, and drugs based on monoclonal antibodies (see chapter 7.3.4) will be important. Studies focused on the use of the principle known as Drug Repurposing or Drug Repositioning, or finding a new role for registered drugs, may bring new possibilities to anticancer treatment. In the coming period, it will be very important to optimize cancer treatment based on retrospective evaluation of real-world data/evidence (RWD/RWE) from clinical practice.

Sub-objective 3 Improve the quality of life of cancer patients through a better understanding of the factors that accompany cancer and its treatment

Improving the quality of life of cancer patients can only be achieved through a better understanding of the factors that accompany cancer and its treatment. For patients and survivors, these are mainly factors such as side effects (even late) of cancer treatment, disease symptoms, comorbidities, functional impairment (especially in older patients), mental health issues and reproductive problems. Many survivors also experience problems returning to work, due both to lingering effects of cancer treatment and their employers' attitudes. Studies aimed at analysing these factors, assessing their impact on quality of life and ways of preventing their negative effects will be considered important. Particular attention should be paid to patients who have had childhood cancer, as approximately two thirds of them suffer side effects related to treatment even in adulthood.

7.2.4. Chronic lung diseases

Focus

The most serious chronic non-cancerous lung diseases such as chronic obstructive pulmonary disease (COPD), pulmonary fibrotic processes and severe asthma are still not fully understood in terms of pathogenesis. Research is gradually developing to define pathogenetic subtypes of these diseases, and which will also guide targeted treatment. However, these diseases are still considered virtually incurable, and cause long-term or permanent disability and increased mortality rates. The identification of individual targets in the pathogenetic process of these diseases allows for better targeting of existing therapeutics at individual level and, in the context of research, the discovery of new treatment modalities

The main objective

Improved understanding of the pathogenesis of COPD, pulmonary fibrosis and severe asthma leading to better targeting of existing treatments, including biological therapy. Precise phenotyping of individual patients based on different biomarkers reflecting individually specific pathogenesis.

Sub-objectives

Sub-objective 1 Influencing hitherto incurable and progressive chronic diseases

in the sense of stopping progression or finding ways to reverse the process.

Sub-objective 2 Determination of new therapeutic procedures using already known targeted drugs within the framework of repurposing or a combination of existing drugs. Proposals for new treatment modalities based on phenotype-specific markers of pathogenesis.

7.2.5. Blood diseases

Focus

The occurrence of blood diseases will increase in the context of demographic change - the ageing population. Not only the incidence but especially the prevalence of these diseases will increase. Despite improving treatment, mortality rates for some blood diseases remain high (especially in the elderly). In addition, these mortality rates have also been adversely affected by the COVID-19 pandemic. The SARS-CoV-2 infection has a mortality rate of up to 20% in patients with blood diseases (especially malignancies).

To improve the care of patients with blood diseases, we need to improve 1) prevention (especially detection of congenital predisposition); 2) diagnosis and treatment; and 3) quality of life for patients with blood diseases. Quality of life and digitalisation of care for patients with blood diseases are already the focus of several projects, such as the MyPal project (H2020) focusing on chronic lymphocytic leukaemia and myelodysplastic syndrome. However, other blood diseases need to be approached in a similar way.

The Czech Republic has a long history in oncological research and there is potential especially in research in developing knowledge in the diagnostics and prognostic factors of blood diseases, and recently also research in predispositions to blood diseases. The Czech Republic has a number of top teams active in domestic and international research in these areas. At the same time, there are research centres with modern and high-quality (and in many cases unique in the world) research infrastructure, enabling demanding multidisciplinary research and development linking disciplines that are seemingly far apart from each other.

The goals of blood disease research in the Czech Republic for the coming period should include (i) improving knowledge of the pathogenesis of these diseases, (ii) improving diagnosis, treatment and monitoring of treatment responses, and (iii) ensuring a better quality of life for patients.

The main objective

The main goal of health research in blood diseases is to deepen knowledge of the pathogenesis of blood diseases, improve diagnosis and treatment, and improve quality of life for patients. Individual projects will focus on the possibility of rapid implementation of research results into clinical practice. Research projects should be directed towards the development of new diagnostic methods and algorithms and the development of new therapeutic and preventive procedures.

Sub-objectives

Sub-objective 1 Improve knowledge of the pathogenesis and development of blood diseases and identify new therapeutic objectives

A detailed understanding of the biological processes leading to the development of blood diseases is important to choose the best treatment strategy and for the development of new drugs for these patients.
It is primarily about improving the treatment of patients with resistant or relapsing blood diseases. Although we have a number of new drugs for these patients (including new immunotherapy options), they are far from being able to save all patients. The sequences in which to administer treatment and when to modify it according to molecular genetic findings in blood diseases are both also unclear.

Sub-objective 2 Improve the diagnosis and treatment of blood diseases, especially through the implementation of precision medicine, modern therapies, targeted drugs and modern radiotherapy

Recent advances have already made it possible to implement many of the new and innovative treatments for blood diseases (new targeted drugs, immunotherapy), but these treatments are not always successful. There are still patients for whom no effective therapy can be offered (especially elderly and comorbid patients with haematological malignancies). Procedures that allow a higher degree of individualization of blood disease treatment and the use of real-world data (RWD/RWE) from clinical practice are also considered important.

Sub-objective 3 Improve quality of life for patients with blood diseases by understanding the factors that accompany cancer and its treatment

Improving quality of life for patients with blood diseases can only be achieved through a better understanding of the factors that accompany cancer and its treatment - social, occupational and medical factors (risk of developing other malignancies after successful treatment of the blood disease in question).

7.2.6. Nervous and mental illnesses

Focus

Nervous and mental illnesses (NMIs) are one of society's greatest burdens. Their incidence and severity are increasing dramatically, not only in the context of increasing life expectancy, but also in the context of the growing problem of caring for newborns with extreme CNS immaturity. These are therefore diseases that affect both the neuropsychological development of young children and the mental and physical performance of individuals of working age, and in the context of an ageing population they are increasingly negatively affecting quality of life for the elderly.
Although in many cases these are sudden, life-threatening conditions, they are predominantly long-term, chronic diseases burdening society with direct healthcare costs and consequently high indirect costs related to reduced or lost work capacity, the need for long-term rehabilitation

and often lifelong social services. Although neuroscience research has been one of the fastest growing fields in recent years, many unanswered questions remain in the investigation of the complex multifactorial etiopathogenesis of NMIs.

The demographic composition of the world's population is fundamentally changing, with the elderly making up a significantly larger share. This demographic shift is being accompanied by an increase in the incidence and prevalence of many neurodegenerative diseases, including dementia. The most common form of dementia is Alzheimer's disease, which accounts for an estimated 50%-70% of all dementia. Alzheimer's disease is not an inevitable consequence of ageing, but its prevalence in the population is increasing as the proportion of people aged over 65 increases. Alzheimer's disease affects up to 5% of the population aged 65 and its prevalence increases with age, reaching over 40% in the 85-year-old age group.

Given the complexity, involving genetic, epigenetic, and environmental factors, multi-modal research is essential, including translational studies using animal and cellular models (including iPSCs and organoids), state-of-the-art molecular genetic and protein engineering methods, mathematical modelling, advanced data analysis incorporating psychosocial and demographic data, and the involvement of artificial intelligence methods, as well as recognition of regulatory processes, compensatory strategies, and the nature of neuroplastic changes. An interdisciplinary approach involving other biomedical and materials disciplines will be advantageous

Among **neurological diseases**, it is advisable to target early diagnosis and treatment not only for strokes, epilepsy, extrapyramidal syndromes, chronic pain, multiple sclerosis and other autoimmune diseases, but also for early recognition of functional neurological disorders and subsequent referral of patients to specialized centres with adequate diagnostic and therapeutic care. They also include a range of neurodevelopmental diseases, neurooncological issues including neurocutaneous syndromes and a wide spectrum of diseases of the spinal cord, peripheral nerves and muscles. One priority is undoubtedly the aforementioned neurodegenerative diseases such as Parkinson's and Alzheimer's disease which, together with the long-term motor and mental consequences of neurovascular, neuro-oncological and neurotraumatic disabilities, significantly increase the costs of both health and social care. A large number of rare diseases, intersecting across neurological sub-specialisations and comprehensively addressed in recent years under the auspices of the European reference networks (EpiCARE, EURO-NMD, RND) make up a separate group of neurological diseases. From this point of view, supporting basic and applied neuroscience research in aetiopathogenesis leading to early diagnosis and effective therapy is an investment that will clearly pay off in the long term.

Among **mental illnesses**, mood disorders (especially depression), anxiety disorders and psychotic disorders are associated with the greatest societal impacts. Research in psychiatric disorders in childhood and adolescence, particularly eating disorders, is increasingly important, and there is a need for early diagnosis based on clinical and biological subtypes of autistic disorders and hyperkinetic disorder. Some types of personality disorders, particularly borderline personality disorders, carry a significant clinical burden and new targets for effective interventions must be sought. Despite extensive research in biological psychiatry, just a small amount of knowledge of aetiopathogenesis and prevention has led to a clear shift in treatment practice and improved quality of life for patients. This contrasts with the expanding diagnostic

and therapeutic possibilities, and the monitoring of disease progression with new technologies and therapeutic approaches (including psychotherapy in general and, for example, research in the use of psychoactive substances - LSD, psilocybin, ketamine, ayahuasca, etc. - for assisted psychotherapy in the treatment of certain mental illnesses and addiction), which requires validation of their potential in diagnosis and treatment using standard evidence-based approaches. As therapeutic goals in mental illness shift from symptom control to improving quality of life and supporting functional capacity, studies need to focus on the impact of illnesses and interventions on real-life functioning and adapt data collection techniques to the phenomena under study (real-life data, the use of ICT technology for dense sampling of the functions under study, and use for individualized interventions). In the same vein, there is a need to test the impact of new services being developed as part of the current mental healthcare reforms. There is a need to increase the ecological validity of diagnostic and intervention tools using advanced technologies (augmented and virtual reality) and to refine the detection of significant signals in multidimensional datasets (using machine learning and bioinformatics methods).

An important part of this is the study of the relationships between physical (neuro-immuno-humoral regulation, study of the microbiome in relation to CNS function disorders and mental disorders) and psychological processes (body-brain-mind relationship) and the impact of their pathology within the bio-psycho-social concept of chronic somatic and mental diseases.

Neurotraumatology is a separate issue with the possibility of research in the replacement and reconstruction of nerve functions, but also with new forms of neurorehabilitation and resocialization. Neurostimulation and neuromodulation methodologies will play an important role, not only in bipolar disorder, depression, schizophrenia and anxiety neurotic disorders, but especially in untreatable pain, Parkinson's disease, epilepsy and even obesity.

A possible division into sub-areas, or circuits of neuropsychiatric disorders, which overlap and complement each other, is as follows:

Neurodevelopmental diseases (autism, hyperkinetic disorder, epileptic encephalopathies), neurodegenerative diseases including dementias, neurogenetic and neurometabolic disorders including mitochondrial disorders, psychotic diseases including depression and schizophrenia, psychosomatic, anxiety and neurotic disorders and eating disorders, personality disorders, the impact of physical illnesses on CNS disorders and psychopathology, hereditary neuromuscular and neuropathic diseases, neuroimmune diseases and, last but not least, neurotrauma and neurorehabilitation issues including neuropsychology and the social aspects of neurological and psychiatric disorders.

The main objective

The main objective is basic and applied research to elucidate the etiology and pathogenesis of major nervous system diseases to the extent that correct diagnosis can be established as soon as possible and personalized causal treatment initiated. The final outcome is the cure or minimization of difficulties and improvement of functional capacity and quality of life for patients. This will reduce the psychological, social and economic burden on the families of patients and on society in general. Part of the main goal is the early identification of at-risk individuals and preclinical conditions so that the most effective prediction and early prevention of neurological and psychological diseases is possible.

Sub-objectives

Sub-objective I Mental and neurological diseases

Clarifying genetic, epigenetic and environmental factors contributing to the emergence and development of mental and neurological diseases is a prerequisite for improving prevention, developing new therapies, and improving comprehensive care for patients with a wide range of diseases, including strokes, epilepsy, dementia, schizophrenia, depression, bipolar disorders, anxiety disorders, autism, hyperkinetic disorder, eating disorders, personality disorders, organic mental disorders (secondary), multiple sclerosis, extrapyramidal and cerebellar diseases, neuromuscular

and neuropathic disabilities and other nervous system disorders which manifest themselves as psychiatric or neurological illnesses.

Sub-objective 2 Diagnosis of diseases of the nervous system

Expansion and innovation of existing diagnostics, including molecular genetics (e.g. whole exome and genome sequencing), electrophysiological techniques of all modalities, structural and functional neuroimaging methods and technologies to elucidate physiological, developmental, and specific diagnosis of cerebral connectivity changes in patients with autism, epilepsy, schizophrenia, and other disorders connecting key areas of the brain. Diagnostics include the search for biological markers of individual diseases as well as new experimental and clinical neuropsychological tests to increase their accuracy and ecological validity.

Sub-objective 3 Increased effectiveness of treatments for diseases of the nervous system

Finding new therapeutic modalities and refining and upgrading existing treatments based on genotype or endophenotype, including pharmacogenetic analyzes to minimize adverse effects. Introduction of advanced artificial intelligence methods to detect not only diagnostic and predictive, but also therapeutic biomarkers for most psychiatric and neurological diseases. Optimization of modern interventional treatment in selected diseases (ischaemic icts, idiopathic Parkinson's disease, dystonia, epilepsy, etc.). Evaluation of the impact of new services in mental healthcare. The effectiveness criteria will be not only the curing or alleviation of clinical problems, but also the maximum possible quality of life, including a dignified psychosocial level of the patient and their family.

Sub-objective 4 Ensuring quality of life for patients with diseases of the nervous system

In the context of the previous objective, the main priority of neuroscientific research must be to ensure the highest possible quality of life for individuals suffering from diseases of the nervous system, not only through early diagnosis and therapy, but also continuous neurorehabilitation, psychotherapeutic and psychosocial care, psychoeducation and modern community social care, including stationary and respite services.

The aim is not only to increase functional capacity and quality of life with reduced revertance (frequency and duration of hospitalizations) and to strengthen the patient's resilience, but also to achieve economically significant savings associated with reducing sick leave and convalescence.

7.2.7. Musculoskeletal and inflammatory diseases

Focus

Systemic rheumatic diseases are among the most common autoimmune disorders, with an overall incidence of around 5% in the population. Young and middle-aged people are most commonly affected, including children. These are serious chronic diseases, currently incurable, which cause pain, joint deformities, functional limitations and even disability and in some cases irreversible organ damage to many other structures and organs such as muscles, bones, lungs, heart and the digestive system. Rheumatic diseases reduce life expectancy and significantly increase healthcare costs. The most common are rheumatoid arthritis, which affects approximately 1% of the adult population, while spondyloarthritis also affects 1% and gout arthritis 1%-2%. In childhood, the incidence of juvenile idiopathic arthritis is lower (approximately 1%), but the impact of the disease is all the more severe due to the developmental specifics of childhood and the consequences for the patient's entire family. Moreover, chronic inflammatory diseases are considered to be one of the important risk factors for the development of atherosclerosis. Rheumatic diseases of the musculoskeletal system in their fully developed forms are serious, often systemic, diseases that fundamentally affect the health of the individual. They are usually disabling, life-shortening, and take root not only in the musculoskeletal system, but in a variety of other organs such as muscles, bones, lungs, heart and the digestive system. Young and middle-aged people are most commonly affected, including children.

Symptomatic osteoarthritis is the most common joint disease, and its prevalence rises sharply with age, so it represents a significant medical and social problem in today's ageing population. There is no effective treatment yet, and the number of major joint replacements needed is increasing. A large proportion of the population - up to 80% - suffers from back pain, often caused by degenerative changes. The increased prevalence of obesity and unhealthy lifestyles are also contributing to the rising incidence of osteoarthritis. Attention should therefore be paid to the register of total replacements, including the long-term results of total replacements, and prevention and treatment of complications, including the prevention and treatment of post-traumatic arthrosis.

Osteoporosis, a chronic skeletal disease affecting one in three women and one in five men over the age of 50, is the leading cause of low-trauma fractures. There are around 13,500 hip fractures every year in the Czech Republic alone (more than a third in men), and the costs of their treatment and follow-up care alone are in the billions of koruna. Fractures are associated with high direct medical and non-medical costs and indirect costs (loss of ability to work, family care, institutional and social care). The importance of osteoporosis increases along with life expectancy.

Other immunopathological conditions are also increasing in prevalence. In the case of autoimmune processes which, in addition to systemic diseases of the connective tissue, also include non-specific intestinal inflammation, multiple sclerosis, autoimmune endocrinopathies, etc, these are often serious diseases with unclear prognosis and expensive treatment. In most immunopathological diseases, the pathogenetic mechanisms are not fully

understood and therefore cannot be causally treated. Exceptions are some units from the group of so-called autoinflammatory diseases whose etiopathogenesis is related to the dysregulation of innate immunity mechanisms, often associated with genetically determined overproduction of inflammatory mediators. Especially in the group of so-called monogenic fevers (e.g. cryopyrinopathy, hyperimmunoglobulinemia D syndrome), targeted blockade of these pro-inflammatory factors proves to be a highly effective therapeutic approach that can significantly improve quality of life for patients and prevent the development of life-threatening complications.

Studying the pathogenetic mechanisms of immunopathological diseases may identify optimal targets for safe and effective therapeutic intervention or even lead to regimens for inducing immunological tolerance to prevent autoimmune behaviour of immune system effector cells. Finding a therapeutic regimen to establish immunological tolerance would be a revolution not only in allergy and autoimmune diseases, but also in transplantation medicine, allowing patients to live a full life without permanent immunosuppressive treatment.

The main objective

Etiopathogenetic factors, both genetic and environmental, of autoimmune, inflammatory and rheumatic diseases, as well as metabolic diseases will be evaluated. Individual factors in the pathogenesis of these diseases will be evaluated and targets for new biological and targeted therapies identified. Biomarkers will be evaluated for early diagnosis and treatment efficacy assessment. In degenerative diseases, the factors of metabolic failure of chondrocytes, the influence of genetic factors and, among external factors, mainly biomechanical ones will be evaluated. Research in the field of musculoskeletal traumatology will answer key questions relating to trauma prevention and innovative treatments for selected target groups.

Sub-objectives

Sub-objective 1 Etiology and pathogenesis of degenerative and metabolic diseases of the musculoskeletal system

Study of the molecular biology of bone, cartilage and muscle cells. Study of genetic and metabolic polymorphisms and epigenetic factors in the development of autoimmune diseases. Monitoring environmental factors in the development of degenerative diseases such as spondylarthrosis, discopathy and instability. Further development of bone microstructure imaging methodologies to enable better assessment of bone quality. Development of imaging methodologies to assess the progression of osteoarthritis. Furthermore, the development of sonography and magnetic resonance techniques to detect sacroiliitis and soft tissue changes in the musculoskeletal system. Furthermore, imaging techniques to detect vasculitis (PET, CT and others). Understanding other factors that enable fracture healing. Development of tissue engineering methodologies for the preparation of artificial cartilage and bone. The study of chondrocyte and extracellular matrix metabolism, especially understanding the disbalance of degradation and repair processes that enable the synthesis of targeted preparations.

Sub-objective 2 Research in musculoskeletal traumatology

Attention will be paid to musculoskeletal traumatology, especially: (i) common fractures in the economically active population, the economic benefits of their proper treatment, reduction of

complications and late sequelae, (ii) in gerontotraumatology, optimal treatment of the most common fractures (proximal femur, proximal humerus, distal radius, spine), (iii) major injuries of the growing skeleton, (iv) the importance of a national fracture register (especially proximal femur) - such registers have been used in many countries for a long time (UK, Norway, etc.), and (v) the issue of polytrauma.

7.2.8. Immunopathological diseases

Focus

The immune system defends the body against dangerous antigens from the external and internal environments. From a medical point of view, not only is the study of the 'well-known' immunopathological diseases, in which various degrees of dysregulation and dysfunction of the immune system are present, very important, but it is also necessary to study the immunological mechanisms involved in the development of other diseases. Examples include the response to the development of cancer, and the need to study abnormal and body-damaging inflammatory responses during severe infectious complications or granulomatous diseases.

Of the 'well-known' immunopathological diseases, the most common are allergic diseases, especially allergies of the early, IGE-mediated type. In them, still not very clearly defined genetic and external influences lead to the release of pro-inflammatory mediators such as histamine and arachidonic acid metabolites with subsequent eosinophilic inflammation symptoms after allergen stimulation. The immunopathogenesis of atopic eczema is complicated and not yet fully understood. Elucidation of pathogenetic mechanisms as well as adequate diagnostics will enable the most targeted therapy of both relatively common allergic conditions and serious diseases that have so far escaped standard allergy treatment. Modern highly effective procedures include the use of monoclonal antibodies directed against IGE and cytokines involved in IGE and eosinophil production.

Autoimmune diseases affect 5%-10% of the population with significant geographical differences. The mechanisms for breaking immune tolerance in individual diseases are obviously different, resulting in different approaches for the diagnosis and treatment of different autoimmune diseases.

The most important organ autoimmune diseases from the societal point of view can be highlighted, especially those affecting the endocrine, nervous and gastrointestinal systems.

Immunodeficiency conditions can be divided into congenital and acquired. For congenital immunodeficiency diseases, the term 'innate immunodeficiency disorders' is preferred, which includes not only 'well-known' immunodeficiency diseases, but also diseases in which there is an innate dysregulation of the inflammatory process - the so-called autoinflammatory diseases. These are usually relatively rare diseases, and their impact on society as a whole lies mainly in the high costs currently associated with their treatment. However, it can be assumed that further research will allow more targeted, and consequently cheaper and more effective, treatment of such severely affected individuals. The issue of secondary immunodeficiencies affects many areas of medicine. Significant secondary immunodeficiencies mainly accompany immunosuppressive and oncological treatments, with a significant increase in secondary hypogammaglobulinemia after B-lymphocyte-targeted therapy.

The issue of research in the failure of immune surveillance over tumour growth and the possibilities of immunological diagnosis and, above all, cancer treatment will open up new aspects in care for patients with malignant tumours.
An important aspect of immunological research should be to gain an understanding of the mechanisms leading to inflammatory process dysregulation. As such, inflammation is an important defence mechanism, especially as a non-specific immune system component. However, at certain times, inflammation becomes an important pathogenetic mechanism leading to the deterioration of the patient's condition. Here one can name the abnormal activation of the immune system in sepsis, as well as the appearance of granulomatous inflammation of various etiologies. The mechanisms leading to the impaired regulation of the inflammatory process and the possibilities of influencing them should be an important topic of immunological research.

The main objective

The research will focus on identifying the mechanisms leading to the development of immunopathological diseases, and will investigate genetic and external disease triggers. A more precise understanding of these mechanisms will enable better-targeted diagnosis and treatment of immunopathological diseases in which the immune system plays an important role.

Sub-objectives

Sub-objective 1 Defining factors for immunopathological diseases and identifying new objectives for the diagnosis and targeted treatment of these diseases

Genetic and especially environmental mechanisms leading to immunopathological diseases as well as diseases with abnormal regulation of the inflammatory process will be studied with the aim of finding new diagnostic and therapeutic options for these diseases.

7.2.9. Infectious diseases

Focus

Infectious diseases caused by microorganisms (viruses, bacteria, yeasts, fungi and parasites) represent one of the most important statistical factors in terms of morbidity and mortality rates. Although it was assumed that 'well-known' infections had been contained, the opposite is true and it is quite clear that infectious diseases represent one of the most significant health problems and have a direct impact on national health systems and economies. Specific areas of public health concern can be defined as follows:

(1) **Emergence, selection and spread of microorganism resistance to anti-infectives, in particular bacteria resistance to antibiotics**. The WHO and ECDC have repeatedly and strongly warned that highly resistant bacterial strains combined with a declining number of new effective antibiotics could soon bring the world into a pre-antibiotic era, and the possibility of a pandemic of infectious diseases caused by multi- and pan-resistant bacteria is ever higher. An equally alarming problem is the increasing resistance of mycotic and viral pathogens to

antifungals and antivirals. Infections associated with biofilm formation on the surface of artificial materials (e.g. catheters, cannulas and implants) are also a serious problem.

(2) **New infectious diseases and the return of some known infections (Emerging (EID) and Re-emerging (R-EID) Infectious Diseases)**. Recent years have shown how inadequately supported research in this area is and how little ability society has to respond to EIDs (swine flu, EHEC, zoonoses), which can occur through genetic mutation of the agent (e.g. H5N1 virus) or the return of old types (e.g. H1N1, H2N2 viruses). This can be clearly demonstrated by the global COVID-19 pandemic caused by the SARS-CoV-2 virus. It is also evident that known infections are returning to our population (e.g. pertussis, epidemic parotitis) and the incidence of other known infections (e.g. sepsis, pneumonia, HIV/AIDS, viral hepatitis C) is increasing due to the increasing number of susceptible persons (ageing population, comorbidities, drug abuse). Infectious etiology is discussed in relation to many other diseases, ranging from obesity and cancer to neurodegenerative diseases.

(3) **Opportunistic infections**. These represent a major new phenomenon associated with increased healthcare and increasing numbers of immunosuppressed individuals. In particular, invasive bacterial, mycotic and viral infections affecting immunocompromised patients are currently associated with high morbidity and mortality rates. The main problems are early diagnosis, aetiopathogenesis of diseases (e.g. the importance of colonisation) and their prevention.

(4) **Neglected diseases**. Although these diseases are mostly associated with the tropics and subtropics (leprosy, Mycobacterium ulcerans, trachoma, Noma, cholera, ascariasis, ankylostomiasis, schistosomiasis, etc.), the conditions for the spread of some of them (e.g. Dengue fever) exist in Europe and need to be taken into account in view of climate change predictions.

(5) **Epidemiology**. Various legislative processes have restricted epidemiological studies throughout the EU, while the Czech Republic was one of the countries with the most sophisticated methodologies for monitoring and preventing the spread of infectious diseases. It is necessary to re-strengthen and develop this area. The importance of this requirement has been clearly demonstrated by the global COVID-19 pandemic.

(6) **There is a need to develop new methods, especially serological and molecular genetic (including proteomic) methods**, allowing targeted and accurate detection of infectious agents, including resistance to anti-infectives, and thus early and adequate therapy, which can significantly reduce morbidity and mortality rates for patients.

(7) **Pathogenesis of infectious diseases**. Research in understanding the pathogenesis of infectious diseases (interactions between pathogen and immune mechanisms), including the pathogenesis of organ-specific infections (neuroinfections, GIT infections, etc.).

(8) **The development of new antimicrobials** to enable the treatment of infections caused by microorganisms resistant to existing anti-infectives.

The main objective

Clarify the etiology, epidemiology, pathogenesis, treatment, and prevention of diseases in relation to new, re-emerging, opportunistic and overlooked infections, enabling the individualization of treatment and improving quality of life for patients and the population as

a whole. The development of new diagnostic methods for the early detection of infections and new treatments for important infectious diseases. Characteristics of molecular mechanisms of antimicrobial resistance, including the analysis of molecular-epidemiological resistance markers. Develop new antimicrobials and determine alternative objectives for the rational treatment of infectious diseases.

Sub-objectives

Sub-objective 1 Etiology and the treatment of major infectious diseases

Clarification of molecular-genetic mechanisms responsible for changes in the virulence and resistance of infectious agents. Determination of the pathogenic potential of microorganisms in the formation and development of infectious, metabolic (including endocrine), tumour, cardiovascular and neurodegenerative diseases and mechanisms/factors responsible for the activation of latent or opportunistic infections.

Sub-objective 2 Epidemiology of antimicrobial resistance

The definition of basic molecular epidemiological markers of the spread of multi-resistant bacteria, yeasts, fungi and viruses in the human population, with the aim of slowing their formation and spreading and maintaining the effectiveness of anti-infectives.

Sub-objective 3 New diagnostic methods

The development of new diagnostic methods for the early detection of infectious diseases and searching for new infectious disease markers as potential diagnostic and therapeutic targets.

Sub-objective 4 New anti-infectives

Develop new antimicrobial agents and their basic characteristics.

7.2.10. Diseases of the perinatal period and childhood

Focus

The development of the human individual from a single fertilized germ cell through the embryonic and foetal periods, the moment of birth, the infant, childhood and adolescent periods to early adulthood are extremely dynamic yet also fragmented phases of human life. Throughout the history of mankind, these periods of life have been burdened with high morbidity and mortality rates.

In recent decades, a number of nationwide prevention and screening programmes have been introduced in prenatal and postnatal care. Parallel to this, the diagnosis and therapy of a number of diseases and pathologies have been developed. As a result, the health burden of the developmental phase of human life has been eased and some problems have been almost completely eliminated. This is evidenced by some basic demographic indicators - for example, infant mortality, which places the Czech Republic among a small group of the most successful countries in the world. The socio-economic development of the country as a whole, and in particular the robust system of perinatological and paediatric care, both primary care (a network

of general practitioners for children and adolescents) and inpatient care in specialised centres, have contributed to this success.

Crucial in this regard is the development of current care for newborns, children and adolescents thus requires new approaches and a focus on new research areas, among which the pathology of intrauterine development, perinatal risks, risks of congenital developmental defects, rare diseases and immunopathological diseases with an environmental component.

Perinatal and early postnatal issues

A key area of paediatric research today is the prevention, diagnosis and treatment of the risks associated with the increasing proportion of low-birth-weight babies (from 5% 25 years ago to 8.5% today). The development of perinatology has meant the number of extremely immature newborns has increased, bringing new challenges related to postnatal adaptation and new clinical entities, research in which from pathogenesis to therapy requires scientific analysis. In addition, there is an increasing proportion of newborns with congenital developmental defects who have a chance of survival thanks to medical advances. The study of chronic diseases beginning in the earliest stages of life, from organ changes to social impact, provides further topics for scientific research. The issue of nutrition from infancy to adolescence is a perennial topic, with disorders in this area leading to consequences in both childhood and adulthood.

Rare diseases are the real domain of paediatrics and affect all its fields and subfields. Although each rare disease affects only a small number of individuals (a frequency of 1:2,000 or less), the sheer number of rare diseases (6,000 to 8,000 different rare diseases, with more being added every week) represents a significant population burden. These are almost always genetically determined conditions and the clarification of their causation, etiopathogenesis, diagnosis and therapy is a key challenge for contemporary health research. The vast majority of rare diseases clinically manifest prenatally, early postnatally or at the latest during childhood. Since the last decade, the European Union has included rare diseases among the key health problems of the European population, and has supported the establishment of the European Reference Network for Rare Diseases to ensure adequate access to the diagnosis and treatment of these conditions for all EU citizens.

Immunopathological diseases with an environmental component

The high and increasing frequency of immunopathological diseases of complex etiology (celiac disease, allergic diseases, type 1 diabetes mellitus) in our genetically stable population indicates that some environmental factors have changed fundamentally in recent decades. This change is apparently still ongoing. It is not clear whether these include, for example, nutritional exposures, exposure to common environmental toxicants, changing microbial exposures and colonisation of the gut, skin or other places in the body. These diseases, whose first laboratory markers can be detected years before clinical manifestation, cannot be effectively investigated except in large longitudinal birth cohorts. Such cohorts are completely lacking in the Czech Republic. The challenge for research is to construct effectively large birth cohorts with the availability of parental and environmental samples from the pregnancy period, cord blood samples, and regularly collected samples of biological material during the first years of life (blood, saliva, stool; diet; environmental samples) and samples allowing the detection of serological, biochemical and genetic markers in later life (including complex profiles of anti-infective immunity, toxins and others).

Such a cohort and its biobank, if established, should be a common resource for researchers across the country. It should be professionally managed and the use of the material should be controlled by a board of experienced clinical and laboratory experts. The existence and proper use of such a resource would place Czech paediatrics among those European countries where similar cohorts are already underway over the next decade. Our comparative advantage will be not only the different nature of exposures in our population, but also its relative homogeneity and, last but not least, the lessons available from other ongoing projects.

The main objective

The main objective of health research in this area is to deepen knowledge of the etiopathogenesis of serious rare diseases, developmental diseases of the prenatal period and perinatal complications, as well as immunopathological diseases with an environmental component. Individual projects will be directed towards the possibility of rapid implementation of research results into clinical practice, while the monitoring of longitudinal cohorts will require the continuous evaluation of results and the refinement of further research processes. The research will include the development of new diagnostic methods and algorithms and the development of new therapeutic and preventive procedures.

Sub-objectives

Sub-objective 1 Prenatal, perinatal and early childhood diseases

The study of prenatal, perinatal and early neonatal factors affecting long-term morbidity and population health (most common factors: immaturity, congenital developmental defects, congenital diseases, infections, perinatal hypoxia). The search for pathophysiological mechanisms affecting long-term morbidity rates, basic and then clinical research aimed at prevention, new therapeutic approaches and a positive impact on long-term care for these patients.

This area also includes further development of prenatal detection of urgent congenital heart disease with follow-up postnatal treatment as a key factor for achieving optimal therapeutic outcomes and minimizing mortality rates. Early detection of primary congenital arrhythmic syndromes and phenotype-genotype correlation will allow effective primary preventive treatment for probands and their family members, and will reduce the risk of sudden arrhythmic death in both children and adults.

Sub-objective 2 Rare diseases

The main priorities in this area are research in elucidating the etiology of diseases with unknown causes and the study of molecular, biochemical and cellular mechanisms in etiologically defined rare diseases (as a prerequisite for follow-up research in new diagnostic and therapeutic approaches). Another priority is to support research in their nosological classification (i.e. phenotypic ontology), epidemiology, the development of methods for the early prevention of these diseases, and research in the cost-effectiveness of diagnostic and therapeutic procedures for rare diseases.

Rare diseases also include most childhood cancers, including leukaemia. These are the most common cause of death from illness in children over one year of age. Research in the causes

of their occurrence, elucidation of predisposing genetic factors, and the introduction of modern diagnostic methods into clinical practice are among the key research goals.
Another area of rare disease research is the genetic basis of growth, development and pubertal maturation as a basis for understanding, diagnosing and treating conditions characterized by abnormal somatic, intellectual and psychosocial development in childhood.

Sub-objective 3 Chronic immunopathological diseases with an environmental component
The analysis of data from the longitudinal follow-up of large cohorts of patients will not only allow us to better understand the genetic and environmental influences and the possibilities of preventing further increases in the incidence of these diseases (allergic diseases, autoimmune diseases including type 1 diabetes and others), but also to optimize their therapy.
We will need to gain new knowledge about the mechanism of action of existing and potentially new drugs and their adverse effects. This knowledge will enable the use of treatments that are progressively more effective, more specific, and that reduce side effects. The aim is to find predictive treatment effect and risk factors so that therapy can be personalised. As the amount of data increases, they will need to be synthesised in an automated way using machine learning and artificial intelligence. Another goal is to increase the number of controlled double-blind studies in paediatric patients, which will enable the initiation of effective therapy in this age group, in which such data are noticeably lacking. By combining these research strategies, it will be possible to mitigate the significant impacts of these diseases on the growth and development of individuals, and avoid the high financial costs of caring for such patients throughout their lives.
This will also be helped by the introduction of nationwide therapeutic registers of common chronic and rare diseases, which will allow a more precise view of the effectiveness of diagnostic procedures and therapeutic interventions by specialists, with a clear overlap into personalised medicine and targeted reimbursement of modern medical devices. The excellent paediatric care system and a dense network of health facilities will allow the generation of robust data that will be competitive with major global registers.

7.3. Innovative solutions for medicine

7.3.1. Personalised medicine and new diagnostic and theranostic procedures

Focus

Personalized medicine is concerned with the biological factors that determine individual risk of disease development, the course of disease, and the therapeutic response to specific treatment approaches. Its boom began with the successful mapping of the human genome, and this concept brings new quality to medical care. At the beginning of therapeutic intervention, it is not only the diagnosis but also the individual biological characteristics of the patient or their disease, e.g. in the case of cancer, that is important. Implementing the personalised medicine principle requires the interplay of several sectors - medical and diagnostic technologies, healthcare information technology, legislation, education, data protection, health insurance and reimbursement. This is of course a very complex and expensive task, which is why personalised medicine is still not implemented in everyday practice to the extent that it should be.

The greatest advances are being made in the medical and diagnostic technology sector, particularly in the discovery of new genetic causes of rare diseases and genetic predispositions for multifactorial diseases, as well as new sets of candidate biomarkers for various diseases and pathologies, for example in predictive testing in oncology. The era of -omics technologies (genomics, transcriptomics, proteomics, metabolomics, etc.) is continuously generating entire sets of candidate genes and molecules for various diseases. However, for example, demonstrating pathogenicity in newly identified genetic variants requires further functional studies at both the cellular and individual level. The validation of these candidate genetic variants and candidate biomarkers in clinical practice remains a major challenge for the scientific and industrial community. The identification and experimental verification of new causal genes and pathogenic variants logically suggests new strategies in the development of targeted therapeutic approaches (chapters 7.3.2, 7.3.3 and 7.3.4). Currently, significant integration of diagnosis with treatment is taking place. The successful completion of the development of new drugs using or directly targeting specific DNA or protein damage requires the joint development of appropriate diagnostic technologies and reagents (companion diagnostics).

A key moment for the development of personalized medicine in research and clinical practice was the spread of next-generation sequencing (NGS) technology, which allows not only targeted sequencing by sequencing panels of hundreds of genes, whole-exome sequencing (WES) and whole-genome sequencing (WGS), but also the study of the transcriptome (RNA sequencing) and methylome. Third-generation sequencing such as real-time single-molecule sequencing and nanopore sequencing is being increasingly used in health research. The analysis of the genomes of entire populations (for example, that of the Czech Republic) is becoming a necessity and aims to define the spectrum of specific variants occurring in healthy individuals. The resulting database of gene variants can be used in molecular genetic diagnostics for comparison and identification of pathogenic germline gene variants. The A-C-G-T pilot project to sequence 1,000+ Czech genomes will be completed in 2024, and the database of identified gene variants will be published for the purpose of molecular genetic diagnostics. At the same time, the European 1+ Million Genomes Initiative is under way at European level, and the

Czech Republic became a founding signatory of this EU project in 2018. This implies that a total of 16,755 people in the Czech Republic are to supply sequencing data to the common European database by 2023. There is no doubt that the implementation of the European 1+ Million Genomes Initiative will be of fundamental importance for the entire molecular genetic diagnosis of all diseases with germline and somatic genome alterations.

An analogous situation to that of molecular biology technologies is observed in the field of functional imaging, where the rapid development of techniques based on ultrasound imaging, CT, MRI, PET and their combinations can be observed. The development of molecular genetic and imaging (diagnostic) and therapeutic techniques, for which the new term 'theranostics' is used, is a special chapter unto itself. A typical example of the theranostic approach is antibodies with PET-radio-pharmaceuticals. The development of new diagnostic methods and tools, both laboratory and imaging, is a natural response to the ever-increasing demands for the implementation of personalized medicine in clinical practice. Modern high-capacity, especially genomic, proteomic and metabolomic technologies, but also modern imaging methods generate enormous amounts of data ('big data', and their integration into clinical practice requires research and development in bioinformatics, which will be crucial for the successful application of personalized medicine in clinical practice. On the other hand, significant developments in, for example, microfluidic technologies are enabling instrumentation miniaturization along with ease of use, and increasing the number of applications of point-of-care tests (POCT) at the patient's bedside, thereby also increasing the availability of advanced diagnostic tools outside highly specialized centres. Key areas of medicine involving the implementation of personalized medicine, at both laboratory and imaging methods levels, are oncology, infectious diseases, cardiology, neurology and psychiatry, and hematological and immune disorders.

The main objective

The use of high-capacity molecular biology methods and modern imaging techniques and the development of systems biology and bioinformatics approaches in relation to 'big data' will enable more detailed characterization of disease at individual level, thus also enabling a better understanding of individual human diseases. Further translational research will lead to the effective use of the acquired knowledge for the development of innovative diagnostic, therapeutic and theranostic tools usable in clinical practice at both individual level and for more stratified sets of patients within individual diagnostic units. Technological developments will enable the wider application of personalised medicine principles across the health system.

Sub-objectives

Sub-objective 1 High-capacity molecular biology methods and bioinformatics tools for personalised medicine

High-capacity molecular biology methods generate a huge amount of data ('big data') and information that will need to be understood, and the clinical applicability of which will need to be systematically verified. One goal will be to develop *in vitro* technologies to enable rapid and efficient elucidation of the functional impact of genetic variants newly discovered, for example, in whole genome sequencing in patients with rare diseases. *In silico* bioinformatics and systems biology approaches will be developed for the effective analysis and identification

of clinically-relevant information from the data. Development will also be directed towards the simplification and standardization of methods with the aim of wider application of these advanced technologies and personalized medicine across the health system.

Sub-objective 2 Whole genome sequencing (WGS) of a selected sample of the Czech population

In accordance with the requirements of the European 1+ Million Genomes Initiative, of which the Czech Republic is a signatory and active member, perform whole genome sequencing and subsequent bioinformatic analysis of data for a selected part of the population so that the Czech Republic obtains data corresponding to the share of the Czech population in the EU. This activity will involve research infrastructures defined in the current Roadmap of Research Infrastructures - the National Centre for Medical Genomics and ELIXIR. The data obtained will be of key importance for molecular biology diagnostics as well as for research in genetic, cancer and other diseases.

Sub-objective 3 Research and development in innovative diagnostic and theranostic tools

New diagnostic and theranostic solutions will be developed to enable rapid, sensitive, specific, minimally invasive and non-invasive diagnosis or disease progression monitoring and, in the case of theranostics, treatment. These new tools will be based on analysis of biological material in the case of high-capacity molecular biology methods and patient examination in the case of functional imaging methods (MRI, PET-CT). Research in imaging methods will enable the preparation of new imaging enhancers and specific radiopharmaceuticals to enable the imaging of pathological processes (e.g. angiogenesis, specific localized metabolic processes, receptor imaging) in a specific patient over time. Some of these agents will have the character of theranostic tools, and will have a therapeutic function alongside their diagnostic function (e.g. antibodies with PET radiopharmaceuticals).

Sub-objective 4 Personalised disease prevention

Improving knowledge and the wider application of high-capacity molecular biology methods will enable the identification of individual risk factors. The aim is to prevent or delay the development of disease by taking appropriate measures based on knowledge of risk factors. The research will enable the use of new risk factors and their combination with standard prevention indicators such as lifestyle to create personalised prevention models. These models will allow the formulation of individually tailored preventive measures and reduction of the risk of developing the diseases in question.

Sub-objective 5 Personalised treatment

A higher degree of integration between diagnosis and treatment and the related identification and application of individually-tested predictive biomarkers as a prerequisite for the indication of targeted treatment will lead to better treatment outcomes and lower treatment toxicity rates. This approach will also prevent harm to the patient due to the delay between diagnosis and the start of effective treatment. Developments in advanced therapy medicinal products (ATMPs, see chapter 7.3.3) will allow the use of individually tailored medicines based on detailed

biological patient characterisation, for example in the form of gene therapy for patients with rare diseases.

7.3.2. Low molecular weight drugs

Focus

Research and the search for new low molecular weight drugs is currently a matter of organic synthesis carried out in the laboratories of chemical, natural science and pharmaceutical faculties and laboratories of the Academy of Sciences of the Czech Republic. This has created a new field (pharmaceutical chemistry) - integrating selected knowledge and methods of organic chemistry, biochemistry and pharmacology with the main goal of finding new substances with targeted pharmacological effects. These are organic molecules with an upper molecular weight limit of several thousand daltons (Da), i.e. substances that can in principle be prepared by chemical synthesis. Research and development in new drugs based on such molecules is on a downward trend in the commercial sphere worldwide, as it is no longer profitable for pharmaceutical companies. The high cost of research and development in new originator drugs remains a key issue - it is driven by the need to test up to 100,000 molecules per registered drug to succeed in clinical trials. The low predictability of routine pre-clinical tests in terms of efficacy and toxicity thus dramatically delays the progress of clinical trials and registration. The declining interest in small molecule drug research and development could have profound consequences for population health over the next 20 years. On the other hand, it is also an opportunity for basic research, as pharmaceutical companies are becoming more willing to collaborate with academic institutions. The existence of incurable diseases and the significant emergence of new diseases and indications will require the targeted conceptual orientation of research and development plans. For the research environment in the Czech Republic, it is essential that new active molecules have inappropriate pharma-kinetic properties ('druggability' - solubility, absorption, etc.). Thanks to collaboration among academic, university and corporate workplaces, the Czech Republic is a leader in the development of complex dosage forms for clinical testing and the market. It has extraordinary developmental capacities that enable the conversion of molecules of interest into a form that can be dissolved, absorbed, distributed and also excreted by the body without harming the patient, their microbiome and subsequently the environment. This is a unique opportunity for institutes of the Academy of Sciences, universities and other research institutions to intensify and expand the research already under way into these substances and how to evaluate them comprehensively and effectively, including using molecular biology, pharmacology and toxicology methods at the *in silico*, *in vitro* and *in vivo* levels. Ireland's phenomenal success in pharmaceutical chemistry should be a model and an example that this is possible. This activity will also involve large research infrastructures listed in the current Roadmap for Large-scale Research Infrastructures for Low Molecular Weight Drugs, such as OPENSCREEN-CZ and EATRIS-CZ. Research aimed at increasing our self-sufficiency in the development and production of generic low molecular weight active ingredients and pharmaceuticals should also be supported in order to reduce our dependence on imports from abroad, including the introduction of technologies and procedures that will lead to a reduction in energy intensity, an

overall increase in the efficiency of synthetic production and a reduction in environmental impacts.

The main objective

New biologically active low molecular weight compounds with therapeutic potential verified in proof-of-concept studies will be prepared. More effective procedures for monitoring the biological activity of drugs using a comprehensive approach to assessing the desirable, undesirable and toxic effects of new low molecular compounds (the improvement of biological tests, the introduction of new testing methods, prediction of biological activity, toxicity and side effects *in silico*) will lead to the timely elimination of non-active or toxic molecules. The identification of new leading structures and their modification, and the modification of clinically proven drugs, will enhance their pharmacotherapeutic utility. An essential part of the strategy must be the principle of investing in basic and technological research in parallel, without which support will only be reflected in interesting basic research results. Investments in research in new chemical structures of active substances and technologies enabling practical applications will significantly accelerate the transfer of basic research to the implementation phase and the creation of pharmaceutical start-ups.

Sub-objectives

Sub-objective 1 New low molecular weight compounds

The preparation of new low molecular weight compounds and structural motifs with relevant pharmacological effects. Research and development in new low molecular weight compounds to combat antimicrobial resistance. New molecules can be synthesized and discovered by studying the relationship between structure and activity, combinatorial chemistry, high throughput screening, and isolation from natural, especially plant, sources. In many areas (e.g. in high throughput screening (HTS)), the Czech Republic enjoys an internationally competitive level of infrastructure.

Sub-objective 2 Identification of new therapeutic targets, new methods and procedures for biological testing

New therapeutic targets will be generated based on basic research results, and new procedures and methods will be found for the evaluation of efficacy and toxicity *in vitro* to increase the likelihood of the clinical utility of small molecules. The selected candidate compounds, new methods and procedures will subsequently be validated at the preclinical *in vivo* level. To successfully address these challenges, it will be necessary to attract experts from abroad and create an optimal environment for them to work in.

7.3.3. Medicinal products for modern therapies

Focus

Scientific advances in biomedical technology have led to the development of highly innovative medicines, creating a new generation of biological medicines collectively called ‘advanced therapy medicinal products’ (ATMPs), combination medicinal products or ‘living drugs’.

Medicinal products for advanced therapies are defined as gene therapy, somatic cell therapy and tissue engineering products. **Gene therapy** is a biological medicinal product containing or consisting of a recombinant nucleic acid used or administered to humans to regulate, repair, replace, supplement or remove a genetic sequence, where the therapeutic, preventive or diagnostic effect of the medicinal product relates directly to the recombinant nucleic acid sequence or to a product of genetic expression of that sequence. Gene therapies also include gene-modified cell therapy, already used in the therapy of hematological malignancies (CAR-T cells) and, in the near future, with the contribution of techniques such as zinc finger nucleases (ZFNs), transcription-activator like effector nucleases (TALENs) and, especially more recently, CRISPR-Cas9, gene therapies using gene/genome editing (gene editing) will be included among them. **Somatic cell therapies** are human medicinal products using somatic cells whose biological properties have been significantly altered as a result of manipulation to achieve a therapeutic, diagnostic or preventive effect by metabolic, pharmacological or immunological means. It is essential that these medicinal products have undergone substantial manipulation to alter their physiological functions, biological or structural properties relevant to their intended clinical use, or are not intended for use in the recipient in the same essential function as the donor. **Tissue engineering products** contain engineered cells or tissues (i.e., substantially manipulated or in heterologous use - similar to somatic cell therapy), but unlike these, they are used to restore, repair or replace human tissues. This newly emerging and (in the last few years) very dynamically developing branch of biomedicine contributes and will contribute to new treatment options for a number of diseases, of course only after their systematic evaluation through clinical trials and administration pursuant to current European and national legislative requirements.

The essence of the development and production of these drugs is the manipulation of the cells of a specific patient or donor (autologous or allogeneic), or their use in a non-core function, *ex vivo* or *in vivo*, while all the drugs developed and registered so far work by influencing or manipulating somatic cells. The research, development and production of medicines for advanced therapies by large pharmaceutical companies faces a number of limitations, which are reflected in the small number of ATMPs registered so far (currently 14 ATMPs in the EU). One reason for this is that these drugs are very often used to treat rare diseases, including rare cancers. The investments made in research and development in drugs for these diseases make it not profitable for global pharmaceutical companies, and it appears that large companies will not develop these types of therapies in large numbers. Their development and production is also carried out worldwide through national channels at universities, research centres and smaller biotechnology companies. This is also reflected in the Pharmaceutical Strategy for Europe (https://ec.europa.eu/health/sites/default/files/human-use/docs/pharma-strategy_report_en.pdf), which supports the establishment of regional centres for research, development and GMP production of ATMPs. The proximity of the development and production sites and the specific patient for whom the drug is being prepared appears to be a major advantage. The collaboration of academia, research centres and teaching hospitals offers a suitable model and setting to enable a growing number of patients to access this ‘medicine for the next generation’. It also appears essential to address the issues of long-term financing, ethical, legislative and pharmacoeconomic studies, and technology transfer, and universities and other research centres in the Czech Republic must play an increasingly important role in

these areas. The research, development and GMP manufacturing of advanced therapeutics represents a unique opportunity for universities, academies of sciences and other research institutions, as well as medical facilities, to jointly participate in and expand some of the activities already under way in the development and manufacturing of these ATMPs, including their comprehensive and effective evaluation in clinical practice.

The main objective

Research, development and manufacture of advanced therapeutic medicinal products (ATMPs) with therapeutic potential validated in proof-of-concept Phase I/II clinical trials. Innovative monitoring of the biological activity of drugs using a comprehensive laboratory and clinical approach to assess safety and efficacy in clinical trials and evaluation of efficacy in real clinical practice (effectiveness). Predicting the effect of ATMPs and introducing precision genomics in the selection of suitable patients with the aim of optimal identification of patients suitable for personalized ATMP treatment. Innovative solutions in pharmacoeconomic models of reimbursement of medicines used in modern therapies, especially on the principle of outcome-based models; research in ATMP regulation and the ethical and legislative aspects of personalized ATMP pharmacotherapy.

Sub-objectives

Sub-objective 1 Research and development in medicinal products for gene therapy

Research and development in medicinal products for gene therapy, with particular focus on aspects of gene expression in the context of different gene transfer approaches. Optimization of viral or non-viral vectors for gene transfer, achieving tissue-specific and regulated expression of transferred genes and directing gene transfer to specific cell types. To address these important and technological concepts, the further development of animal models of disease for the preclinical testing of gene therapy, the study of biological behaviour in these models, and the use of advanced technologies such as organoids and organs-on-chips (OOC) are needed. In many of these research areas, cooperation with existing research infrastructures in biomedicine is envisaged.

Sub-objective 2 Research and development in medicinal products for somatic cell therapy

Research, development and optimization of autologous or allogeneic cells for drug development for somatic cell therapy. Research in the behaviour of mesenchymal stromal cells, stem cells, the biological properties of natural and artificial extracellular matrices, developmental manipulation of cells outside the organism (*ex vivo*). Validation of candidate drug production preparation at both the preclinical *in vivo* level and in early phase clinical trials. In many of these research areas, collaboration with existing biomedical research infrastructure is envisaged.

Sub-objective 3 Research and development in tissue engineered medicinal products

Research and development in stem/progenitor cell behaviour, responsible for the development and lifelong regeneration of the organism. Based on this knowledge, the finding and optimising of procedures allowing the properties and behaviour of these cells to be effectively and safely controlled. Research and development in artificial tissues and organs that can be used to help

study the aetiopathogenesis of disease and subsequently to replace human tissues and organs damaged by disease or injury. Development of induced pluripotent stem cell lines prepared from various somatic cell types (e.g. skin fibroblasts, vascular lining cells, peripheral white blood cells) for the development, validation and production of drugs in tissue engineering and regenerative medicine.

Sub-objective 4 Precision genomics as a tool for the optimization and stratification of patients suitable for gene and somatic cell therapy

Research in the areas of process optimization and clinical applications of precision genomics, based on research of innovative biomarkers for characterization of the most suitable patients in order to maximize the potential of ATMPs in personalized disease management, especially with respect to rare diseases and oncology. Identification and systematic testing of new biomarkers, bioinformatic analysis of complex transcriptomic and genomic data of patients who may be candidates for ATMPs or treated as such. Validation of biomarkers for precision medicine, development of prototypes for *in vitro* diagnostics.

Sub-objective 5 Support proof-of-concept Phase I/II clinical trials to evaluate the safety and efficacy of medicines for advanced therapies

The introduction of somatic cell and gene therapies into clinical practice should be implemented in the first phase through early phase clinical trials to verify in particular the safety and efficacy of these drugs in patients. Given the expected smaller cohorts of patients with genetically based, often rare diseases, research is needed in optimizing clinical trial design and innovative methodologies, including the concept of N-of-1 trials. Evaluation of short- and long-term safety through long-term laboratory and clinical monitoring of patients, including monitoring of minimal residual disease and immunomonitoring, especially in patients treated with gene CAR-based technologies.

Sub-objective 6 Ethical, legal, regulatory and socio-economic aspects of research, development and treatment of patients using ATMPs

Personalized therapy using gene or somatic cell drugs is a ground-breaking concept in 21st century pharmacotherapy that entails the need for national research in the socio-economic, ethical and legal aspects of these therapies, regulatory science and also, due to the significant costs, research in innovative concepts for determining reimbursement of ATMPs, involving risk-sharing reimbursement strategies, including financial and outcome-based schemes. The results of research in these areas will also be useful for the national regulatory authority for pharmaceuticals (the State Institute for Drug Control) and healthcare payers in the Czech Republic, as they will help identify necessary changes in decision-making and legislative processes with the aim of affordable treatment, while maintaining the principle of a sustainable national healthcare system.

7.3.4. Biological medicines, including prophylactic and therapeutic vaccines

Focus

Biological medicines are complex and structurally complicated substances produced, for example, by biotechnological processes using cell cultures in bioreactors. Unlike chemical drugs, they are products of living organisms. The production of these drugs began in the 1980s with simpler protein drugs like human insulin, interferons, growth factors and hormones, but at the beginning of the 21st century, the era of monoclonal antibodies in particular began, the development and production of which is progressing very rapidly: today they are the most commonly used form of biological medicine. They are mostly used in oncology, rheumatology, dermatology, gastroenterology, neurology and ophthalmology. Their entry into other therapeutic areas can be expected. The development of new therapeutic antibodies and recombinant proteins has huge therapeutic potential, but is accompanied by higher production costs, higher treatment prices and the restriction of the administration of these drugs to specialised centres. The key advantage of biological therapy is the possibility to specifically target a particular receptor, protein or other (macro)molecule, with associated high efficacy and relatively low toxicity. Current challenges include innovations in new generations of dosage forms, reduction in allergenic potential, reduction in neutralizing antibody production, and innovative routes of administration. Future research directions will focus mainly on the preparation of hybrid therapeutic proteins with novel properties, drugs with better stability, and improved pharmacokinetic profiles. Other humanized protein/polypeptide drugs (enzymes, binding proteins, transcription factors, etc.) will also be an important research area, as their presence in the phylogenetically broad spectrum of organisms (genomes, transcriptomes, cDNA libraries) represents an inexhaustible source of candidate molecules for biological treatment of humans with molecular factors (proteins/polypeptides) of non-human origin. The whole area of molecular taxonomic and phylogenetic research in biodiversity is thus becoming a huge inspiration in the search for new drugs and the development of modern vaccines ('trans-block vaccines') for biological therapy and immunotherapy.

In the area of vaccine development, research will be directed towards the preparation of effective and safe recombinant, often multi-component, vaccines, the identification of important patient-specific antigenic epitopes, and research in new immunoadjuvants that enable rapid induction of long-term or permanent immunity. These can be prophylactic vaccines with clinical vaccination application against infectious or cancer diseases through to therapeutic vaccines for the treatment of specific, already present diseases. The COVID-19 pandemic has also highlighted the enormous challenges in ensuring future preparedness and speed of development of innovative vaccines against emerging viral agents, including state-of-the-art development and manufacturing techniques such as mRNA technologies. Immunomodulatory therapy based on the use of specific antigens stimulates the immune system to fight specific tumour antigens and the progression of chronic infections such as hepatitis and HIV infections. In anti-tumour immunotherapy prepared by manipulation of autologous or allogeneic cells (e.g. dendritic cell vaccines, DNA/RNA vaccines), the emphasis is on highly individualised treatment tailored to each patient. A number of anti-cancer immunotherapy products under development are regulated under the advanced therapy medicinal products (ATMP) category, covered in Chapter 8.2.4.

The main objective

The research will mainly lead to the development of biological drugs and immunotherapy, especially in monoclonal antibodies and other humanised protein/polypeptide drugs. In the field of vaccines, research will focus mainly on prophylactic vaccines, especially against new infectious diseases, as well as innovative technologies including mRNA vaccines.

Sub-objectives

Sub-objective 1 New biological medicines

Innovative research, development, production and the wider use of biological therapies and immunotherapy, especially in monoclonal antibodies and other humanized protein/polypeptide drugs. Research in the identification and knowledge of the exact mechanism of action and specific target will be essential. Reducing manufacturing costs and new insights related to *in vivo* monitoring of the biological response to treatment are also important for the further development of biological medicines. New biological medicines with better pharmacokinetic profiles, higher stability, innovative dosage forms, and more appropriate safety profiles will be introduced.

Sub-objective 2 New vaccines for the prevention and treatment of diseases

In vaccine development, research and development must focus on the preparation of prophylactic vaccines, particularly against emerging infectious diseases, including innovative technologies and mRNA vaccines. Therapeutic antigen vaccines will be developed particularly for cancer and other chronic infectious diseases. New vaccination objectives will be developed (e.g. for the treatment and prevention of serious societal threats) and new vaccination approaches (reverse vaccinology - the development of vaccines using whole infectious agent genome sequences, desensitization, etc).

5.3.7. New drug formulations

Focus

Clinical practice and developments in pharmaceutical research and industry point to the importance and growing need for the development of controlled and targeted drugs in the form of modern drug delivery systems and innovative formulation methods. Research and development will focus on applications and dosage forms responding to the specific requirements of the patient and their disease, using formulations of modern pharmaceuticals with time- and place-specific release of biologically active substances, especially on the development of drugs enabling targeted distribution of the active component (drug, gene, radionuclide), targeting to specific organs, tissues or cells and its required release or activation at the time and place of the expected therapeutic effect. The focus will be on local, oral, injectable, inhalation and other dosage forms suitable for outpatient treatment of a specific patient or group of patients, characterized by specific release, absorption and action. In terms of materials, research will focus mainly on biocompatible carrier systems, intelligent and externally responsive polymeric materials, micellar and liposomal structures, microemulsions and suspensions, biodegradable thin films and micro- or nano-particle carriers, which will ensure the transport and subsequent active or passive release of the drugs and their

combinations (and possibly genes) in target tissues. Specifically, the issue of drug transfer through body barriers such as blood-brain, cerebrospinal, dermal, testicular and ocular barriers and the targeting of therapeutics to tissues and cells (including cancerous) expressing transport proteins will be addressed. Attention will also be paid to developing systems combining the therapeutic effect of the delivered drug with diagnostics (theranostics). The link between these efforts should be the goal of more effective, efficient, safe and patient-acceptable pharmacotherapy with an emphasis on the patient's specific requirements (personalization) and the possibility of outpatient application. Modern existing and currently being introduced technologies in pharmaceutical research and industry, such as printing technologies, chemical and physical preparations of micro- and nano-carrier structures, technologies enabling the stabilisation of sensitive biologically active substances, and their appropriate combination and precise deposition in substances administered at very low doses, should be used to make these efforts a success. Efforts to develop new dosage forms and modern drug delivery systems, e.g. drugs for rare diseases, should not remain in the background. New technologies to produce pharmaceuticals and new dosage forms, aimed at reducing production costs, are also an important research topic. This type of innovation will lead to cheaper therapies for the patient and contribute significantly to the overall sustainability of the healthcare system, ensuring the competitiveness of EU pharmaceutical production and strategic independence from Asian imports. Another relevant topic is research in the innovation of dosage forms in terms of the environmental impact of their production. Innovations in this area will lead to minimizing the product carbon footprint, reducing energy consumption and reducing the amount of active substances entering the environment through wastewater treatment plants.

The main objective

Innovative formulation approaches will be used to create and exploit new drug transport and delivery systems for drugs and their combinations, and even genes in the form of modern dosage forms, enabling therapy of target tissues and cells, the time-specific release of active substances, and the penetration of drugs in therapeutically significant concentrations into difficult to reach organ, tissue, cellular and subcellular structures. Research and development in new improved formulations of existing medicines should bring new added value to patients (value added medicine). For example, the elimination of side effects, improvement of patient compliance with the prescribed therapy (adherence to the actual application of drugs is generally very low and causes great economic damage and unnecessary deaths), improved therapeutic effect, etc.

Sub-objectives

Sub-objective 1 Development of new carriers for time- and site-specific drug release

New drug carriers formulated using biocompatible, mainly macromolecular, substances in the form of micro- and nano-structures will ensure time-controlled release of drugs in line with the requirements of the specific disease, and the targeted transport of active substances (drugs, genes) to specific tissues, and even cellular or subcellular structures. With the help of modern formulation techniques and innovative excipients, research will lead to the development of more effective, safer and more patient-acceptable drugs with more favourable pharmacokinetic and pharmacodynamic properties, allowing for highly precise dosing and personalized therapy.

Sub-objective 2 Systems for pharmacotherapy-resistant diseases and for overcoming biological barriers

Gradual elucidation of the nature of the functioning, structure and composition of biological, chemical and physical barriers in the organism (skin, hematoencephalic, testicular, ocular and others) leading to the development of ways to overcome them by means of new formulations and drug delivery systems, as well as to overcome drug-resistant phenotypes, etc. The outcomes of this sub-objective will have direct application in the treatment of patients with neurological, inflammatory, infectious, oncological, reproductive, ocular and other diseases, and ultimately in the treatment of diseases resistant to existing therapies.

Sub-objective 3 Introduce new formulation technologies into research, development and production of pharmaceutical forms

A partial goal is also to make more extensive use of existing and currently being introduced modern technologies in pharmaceutical research and production, such as printing technologies, the chemical and physical preparation of micro- and nano-carrier structures, technologies enabling the stabilization of sensitive biologically active substances, and the appropriate combination and precise deposition of substances administered in very low doses, etc. There will also be a focus on converting existing, often obsolete, dosage forms to modern drug delivery systems, e.g. in the case of medicines for rare diseases.

7.3.6. Research and development in new medical devices and equipment

Focus

Medicine in the 21st century is largely dependent on instrumentation, and this applies across medical disciplines. These include both diagnostic devices and devices used in treatment. In diagnostic devices, there is now a clear trend towards reducing the radiation dose from devices using ionising radiation, or replacing them with devices that use a different imaging principle. Examples could include the preference for magnetic resonance imaging (MRI) over CT if diagnostically feasible, or the extension of hybrid diagnostic devices for positron emission tomography (PET) from the now standard PET CT to PET MR.

With some devices, such as computed tomography (CT) and digital subtraction angiography (DSA), both are possible. Examples of the use of DSA can be diagnostic and therapeutic - interventional procedures, for example, in the treatment of ischaemic strokes, cerebral aneurysms and myocardial infarction or, more generally, in the treatment of arterial diseases in various parts of the body. The therapeutic use of CT devices finds application in the treatment of spinal diseases, for example in the infiltration of the affected nerve root by the pressure of a herniated disc (so-called root spraying), and the application of bone cement into a vertebral fracture - so-called vertebroplasty, and CT-guided interventions on the liver, kidneys or biopsies, and sampling of pathological material from various areas of the body.

The above examples also have an important aspect in terms of less invasiveness, higher patient comfort and lower subsequent morbidity compared to alternative surgical or more invasive procedures. In this sense, invasive catheterization techniques such as DSA and coronary

angiography have recently given way, albeit minimally, to completely non-invasive CT and MR examinations. Robotic surgical techniques are usually also more patient-friendly, and the same applies to navigation techniques in neurosurgery. Research and development in e-health and telemedicine enabling advances in the implementation of telemedicine monitoring in healthcare (e.g. continuous glucose monitoring and the application of decision-making algorithms and artificial intelligence (AI)) is described in Chapter 7.3.8 of this Concept.
In general, with the use of modern medical technology, contemporary medicine is moving towards more accurate and detailed diagnosis of diseases and less invasive approaches in their management with the aim of lower mortality and morbidity after surgery and generally higher patient comfort.

The main objective

The main objective will be development and research in diagnostic and therapeutic devices, improvement of their function, especially in the sense of the definition of modern procedures, the development of software and hardware, and result interpretation. A comparison of modern minimally invasive approaches with conventional methods will be an important parameter.

Sub-objectives

Sub-objective 1 Development and research in medical imaging techniques

Multidisciplinary research and development will be carried out in medical imaging techniques - MR with standard and high fields (7 Tesla), in both interdisciplinary and international terms with the involvement of grant projects and industry. The objectives are defined in terms of refining the diagnosis of nervous system diseases, cardiovascular diseases and oncological diseases. The inclusion of other medical disciplines is also possible. The focus will be, *inter alia*, on signal quantification, its modelling and development in the field of 'artificial intelligence' (AI) with the aim of refining diagnostics and, for example, predicting further development of a disease. Further research will be carried out, for example, in the emerging hybrid techniques of PET CT and PET MR, their mutual comparison and anchoring the role of PET MR in clinical fields.

Sub-objective 2 Development of minimally invasive treatment techniques and their comparison with conventional procedures

Research and development will be carried out in minimally invasive treatment techniques, whether catheter-based (DSA) in cardiology and interventional radiology, or focused on other methods - CT, ultrasound and MRI in the field of neurosurgery, cardiac surgery, gastroenterology and other fields. This research will also include research and development in radiosurgery and radiotherapy (Gamma Knife, Cyberknife, linear accelerators). One important element will be comparison of the results with conventional treatment methods (mostly open surgical approaches), in terms of morbidity and mortality, quality of life, and also the economic burden of both types of methods on the system.

Sub-objective 3 Development in navigation and robotic systems

There will be research and development in navigation and robotic systems, especially in neurosurgery, cardiovascular surgery, urology, abdominal and thoracic surgery. Another

element of research will be to compare the results to treatment methods without these techniques, in terms of morbidity and mortality, quality of life, and the economic burden of both methods on the system. The further expansion of navigation and robotic systems in other medical disciplines will be supported.

Sub-objective 4 Research and development in medical implants - neurostimulators and cardiac implants

The research will focus on standardizing and developing new procedures for implantation and follow-up of patients with neuromodulation and cardiac implants. Neuromodulation involves the use of neurostimulators primarily in the treatment of neurodegenerative diseases, most commonly Parkinson's disease. However, neuromodulation has wider application in other neurodegenerative diseases in the treatment of intractable pain, and in the future there is the prospect of treatment for psychiatric diseases as well. In cardiology, research targets a large group of continuously developed cardiac implants. Here too, international cooperation and collaboration not only with grant agencies but also with industry is planned.

7.3.7. Innovative research in surgery, including transplantation

Focus

The current development of surgical disciplines can be characterized as efforts to optimize the timing of surgery with respect to the specific disease and the necessary prehabilitation of the patient, minimizing the invasiveness of the procedure and the necessary hospitalization time, and adherence to the recommended onco-surgical radicality with respect to maintaining the maximum quality of life. Hence the development of surgical disciplines is directed both towards indication rationality (multidisciplinary teams with medicine personalisation, improvements in preparation for surgery) and reduction of the surgical burden, and towards increasing its safety.
This includes reducing the incidence of perioperative and especially postoperative complications.
On the one hand, there is a blurring of interdisciplinary boundaries, and on the other greater specialisation within surgical disciplines. This logically leads to the creation of specialised centres with a high frequency of procedures (high volume centres) as a requirement for the best results with the possibility of managing complications and providing comprehensive patient care.
In the majority of demanding operations, surgical disciplines are gradually getting to the limit of the possibilities of performing a specific surgical procedure in compliance with good clinical practice. Further improvements in outcomes will depend on close collaboration with neighbouring disciplines, both clinical and paraclinical. These efforts will lead to the development of hybrid therapeutic procedures - in some cases to more radical surgery or, on the contrary, to the favouring of non-operative treatment.
In transplantation, treatments are being optimised for individual organs: from bridging therapy, via living donor organ transplantation, to stem cell transplantation.

The application of new technical innovations and devices in some surgical fields is a chapter all to its own.

The main objective

The above indicates the appropriate focus of applied research in surgical disciplines as follows: (i) clinical and experimental research in new surgical procedures with regard to optimal preparation for surgery (prehabilitation depending on the operative and postoperative risk), minimizing the surgical burden, complications and length of hospitalization, (ii) clinical and experimental research focused on close collaboration with neighbouring clinical and paraclinical disciplines, (iii) clinical and experimental research in oncology aimed at optimising complex care within a multidisciplinary framework, with an increasing role of genetics and molecular biology, monitoring not only survival time but especially quality of life, (iv) clinical and experimental research on hybrid procedures, the role of individual disciplines, (v) clinical and experimental research in transplantology aimed at tissue culture, the creation of biological organ substitutes, and transplant tolerance.

Sub-objectives

Sub-objective 1 Non-invasive treatment

Focused radiation treatment, non-invasive local and loco-regional treatment (e.g. radiosurgery, lithotripsy, ultrasound treatment including sonotrombolysis). Multidisciplinary and multi-modal research is focused on non-invasive, but by nature surgical, techniques without penetration of the skin. Precise diagnostics and the development of new treatment methodologies will increase their use in the outpatient setting. The new modalities will be developed to the stage of clinically usable prototypes.

Sub-objective 2 Hybrid performance

Research in close collaboration with neighbouring disciplines in combined invasive approaches.

Sub-objective 3 Tissue and organ replacement

The emergence of artificial organs, neuroprostheses and the development of stem cell transplantation can be expected. It is necessary to mention the search for organ and tissue replacements for transplantation as another area of applied research.

Sub-objective 4 Treatment procedures

Optimization of treatment procedures using clinical and experimental models.

7.3.8. Telemedicine and e-health

Focus

E-health is a relatively new area of health data sharing - the use of information and communication technologies in healthcare. In addition to telemedicine, an important part of e-health is the sharing of health data between healthcare facilities and with the patient. It will

become a standard part of care delivery for patients. Part of the e-health infrastructure was created within the framework of IROP projects 19 and 26 (communication between the healthcare system and hospitals, communication between healthcare centres) in 2015 to 2019. Other system components, such as authorisation and authentication mechanisms for healthcare professionals and communication centres for interoperability and information exchange between healthcare facilities, will also be built as part of follow-up calls currently in the implementation phase. It can be imagined that the basic structure for communication will no longer be a subject of research and will be guaranteed by the state, insurance companies, or by the expansion and interconnection (interoperability) of existing information systems of healthcare institutions.

Therefore, the subject of research should be the three follow-up areas listed below and focusing mainly on early diagnosis and effective treatment leading to reduced incidence of disease complications.

Telemedical monitoring

The new trend of telemedicine monitoring is coming to healthcare. In addition to remote communication and remote data sharing and evaluation, this area is essential for streamlining work, improving quality of care and increasing patient safety. However, it is also a way of increasing access to care, which can be crucial in managing crisis situations caused by acute illnesses such as COVID-19. It can also be important in emerging fields (e.g. palliative care, home care, nutritional therapy). Priority may be given to extensions to e-health information systems for the individual monitoring of patients, e.g. non-invasive monitoring of selected vital signs of patients, especially temperature, heart rate, blood pressure, SpO_2 oxygen saturation, respiratory rate, other spirometric data, data from glucose sensors, sleep apnoea monitors and other devices under development enabling fully automated measurements and connected to a monitoring and surveillance centre. Intelligent alarm systems based on artificial intelligence may also be a priority. The results of such innovations can be used both in healthcare facilities, where they can help reduce the burden on staff, and outside, where patients can be monitored, for example after certain surgeries, but also in follow-up care for chronic patients. Monitoring the condition of indicated patients will allow patients in milder states of illness not to burden healthcare facilities and can reduce the duration of hospital stays. Continuous non-invasive monitoring of vital signs combined with continuous automatic assessment of the patient condition based on monitored values (EWSS - early warning scoring system) will allow the nurse or doctor to react earlier to any deteriorating condition of the patient and thus provide more timely assistance. This is important, for example, for many types of chronic patients. We can probably increase the capacity of healthcare facilities by at least 10%-20% through widespread adoption of this monitoring. As a result, patients who do not require acute care but need to be monitored will be monitored remotely at home. The introduction of this will make the work of nurses more efficient as they will not have to spend so much time measuring medical data and recording them in the medical records. This will save at least 30% of the time of medical staff. With telemetry, it will be possible to easily identify patients in a healthcare facility and almost immediately monitor a patient's deteriorating condition. The ability to mitigate the negative trends of ageing, namely the availability within the population and the increasing average age of PL/PLDD physicians, appears to be critical here. At a time when

75% of incidence is through these specialisations, this is a potential tool to flatten the negative growth curve in demand for healthcare over the next 10 years. Measurements using telemetry can be up to 90 times more frequent than conventional measurements. The cost-effectiveness of remote monitoring and remote care delivery is also at a similarly high level. This is the key to its inclusion in reimbursements, especially during the time of resource constraints that lie ahead. However, it is not only about cost-effectiveness, but also studies assessing how telemonitoring will best 'fit' organizationally into the existing provision of health services, i.e. what is acceptable, usable and required by patients and providers. According to AIPF research, there is reported demand from the largest patient organisations for the ability to make appointments for medical examinations. We are in a situation where there is legitimate demand for a telemedicine solution.

There will also be development and certification of new, innovative endpoint measurement/monitoring devices with the aim of achieving the necessary certification under the corresponding class of medical device. One benefit of the new devices will be the availability of new parameter measurements. One key aspect of the new types of devices will be their potential multifunctionality (measuring/monitoring multiple physiological values of the patient). Ease of operation, or simply no need for operation by the monitored patient, will be essential. For most of the devices that will be used for continuous monitoring, mobility and longevity will be other crucial parameters. In addition to this, supporting capacity, i.e. support for patients in operating telemetry devices (a classic e-health concept), should be considered during implementation. This technical support will be a prerequisite for the successful implementation of telemetry in remote performance.

Big data and telemedicine

Continuous monitoring will generate a huge amount of data in patient health records, and the resulting data will need to be transformed into information about important changes in the state of health of the monitored patient using other advanced techniques based on expert clinical practice.

Another huge advantage will be the possibility of analysing new categorizations of patients by groups, while such groups can be defined in acute care and in the care of selected types of chronic patients. This means that patients can be categorized according to the wards they are currently in, or they can be assigned to a virtual group that can monitor patients across wards on a single monitor and compare patients within the Czech Republic. It will be possible to effectively analyse and correct regional disparities in the Czech healthcare system. Artificial intelligence elements will be able to analyse procedures according to diagnoses and suggest optimal procedures. Analogous to Watson oncology systems, other applications can be developed.

Creation and clinical validation of new computational procedures that will allow current patient status to be determined in the care system from measured data and other clinical information, including data from imaging systems, and to recommend/adjust the further course of healthcare according to the expected development.

Here, in its conception e-health follows RWD/RWE, where it is necessary to start actively working with clinical practice data in conjunction with reimbursement data to ensure linkage, and sufficient linkage to preventive activities and their utilization. The ability to analyse big

data will create the necessary conditions for profiling patients, against which it will be possible to build standardized (clinical) treatment procedures, as well as to create study materials for young physicians.

Remote consultation, the effectiveness of care centralisation and decentralisation

Telemedicine can fulfil the complexity of healthcare visions. New analyses of effectiveness and quality of care are appropriate, for example in the following areas: Impacts on the effective use of health insurance. The impact of telemedicine consultations on the quality, safety and accessibility of healthcare. The impact of telemedicine on the effectiveness of prevention. Online analysis of care, including expert comparisons of the economic aspects of telemedicine and conventional care (market studies in telemedicine). Supporting primary care and small practices with telemedicine. Cybersecurity analysis of teleconsultation. Data protection and telemedicine security also require the legal and regulatory framework of these innovations to be researched.

Remote consultations can be provider-patient and provider-provider (physician) consultations. The first of these is not only important for patient comfort and effectiveness, but will become increasingly important in some regions of the country or in certain epidemiological situations to ensure accessibility. The second is essential for the division of labour between smaller and larger hospitals and specialist and general practitioner practices, in both normal operations and in times of crisis.

This opens up the possibility of territorial (community) health subsystems, e.g. in aftercare, where some facilities have abnormal occupancy rates compared to other facilities in the same locality. The ability to pro-actively manage bed occupancy during a pandemic (and at other times) also appears essential in terms of greater convenience for A&E and the ability to accommodate acute cases, with the potential to increase patient satisfaction and mitigate increases in bed occupancy for providers.

According to data from the World Health Organization, on average up to 10% of patients worldwide are harmed during the provision of healthcare. Mistakes are expensive, for both the patient and the system. Innovations to prevent risks in the provision of healthcare in hospitals include improved patient identification and continuous monitoring and evaluation of patient health through telemonitoring and teleconsultation.

Available statistics estimate that prevention is six times cheaper than treatment, if applied to patients without significant disease symptoms, and if monitoring innovations could catch health complications, worsening trends and adequate treatment at an early stage, this would save significant costs for subsequent treatment and patient care (e.g. nosocomial infections cost the health system tens of billions of koruna per year). The ability to mine and analyse data from the progress of detected infections can lead to recommended practices that can save a significant portion of these costs.

Web-based and especially mobile applications that increase patient compliance with treatment (especially for chronic diseases, typically diabetes) or are directly part of the treatment (for example for mental illness) will also be a subject of research. These are approved abroad through a process similar to that for new medical devices, and have one year to prove their effectiveness. If they can do so, they are included in the reimbursement system. Such innovations can be key to improving the effectiveness of diagnosis and treatment.

The main objective

Research and development in e-health and telemedicine will enable progress in the implementation of telemedicine monitoring in healthcare. New computational procedures will be developed and clinically validated, allowing the determination of current patient status from the measured data and other clinical information, including data from imaging systems in the care system, and the recommendation/adjustment of the further course of healthcare according to the expected development. These innovations will also enable remote consultations, which will increase the effectiveness and quality of healthcare. The field of e-health interventions, i.e., web-based and smartphone-based interventions, also represent a tool to support treatment and prevention, or direct stand-alone healthcare and preventive care. In the use and development of telemedicine and e-health technologies, emphasis will be placed on ensuring that these technologies are reliable for measuring different groups of people, while avoiding the introduction of bias based on, for example, gender, age or ethnicity.

Sub-objectives

Sub-objective 1 Creating a data environment that enables the fulfilment of the main objective

Letting data flow through the system is essential for the ability to deploy a functional telemedicine system.
This will require a certain level of integration of systems that must be able to communicate with each other.
Our healthcare system is currently lagging behind in all of these attributes. A quick analysis of why this is so is needed. A comprehensive strategy for system integration is needed, first at the level of the largest healthcare institutions but eventually also at the level of individual practices. The definition of communication interfaces is a key sub-objective for work to start on the main objective. Components of the system such as authorization and authentication mechanisms for healthcare professionals and communication centres for mutual interoperability and information exchange between healthcare facilities will also be built through follow-up calls, currently in the implementation phase. It can be imagined that the basic structure for communication will no longer be a subject of research and will be guaranteed by the state, insurance companies, or by the expansion and interconnection (interoperability) of existing information systems of healthcare institutions.

7.3.9. Innovative practices in palliative and supportive care

Focus

Palliative and supportive care is a dynamically developing branch of medicine that has long been neglected in the Czech healthcare system. This is one reason why there is currently a significant lack of data and evidence for the development of direct clinical palliative care and health policy in this area. This manifests itself, *inter alia*, in the ineffective use of care, where patients often consume expensive and demanding treatment that does not meet their needs and

priorities near the end of their lives. Caring for patients near the end of their lives also poses a challenge for healthcare professionals in terms of communication and dealing with emotions, and can lead to emotional exhaustion and burnout syndrome. Palliative care is evolving globally to provide adequate support to patients with serious and life-threatening illness, and their families, so that their quality of life is maintained and the care they receive is appropriate to their needs and values. It affects both adult and child patients alike. The modern approach to palliative care expands its scope from solely terminal care for dying patients to the early integration of palliative care with the potential to effectively coordinate the patient's trajectory through the health system even in the earlier stages of serious illness. The development of palliative care in non-cancer diagnoses, research in communication and effective tools for end-of-life care planning, effective models of health service organisation with an effort to appropriately link general and specialised palliative care are very current topics. In line with current priorities, palliative care also relies on a multidisciplinary approach involving medical and non-medical health professionals, as well as on the support of family members, who are an important part of the palliative care system. Another key challenge is to develop a robust methodology for the indication of general and specialised palliative care, not only based on prognosis but especially on the complexity of needs.

The main objective

The aim is to develop and validate innovative and methodologically robust practices in palliative and supportive care to ensure effective symptom management and good quality of life for patients with advanced and serious illness, and their families, to promote models of care that lead to more effective use and coordination of individual health services and health system resources as a whole, and to create evidence-based programmes to strengthen healthcare professionals' competencies in communicating about end-of-life care, working with emotions, and dealing with ethically challenging situations.

Sub-objectives

Sub-objective 1 Effective organisation of health services for patients in palliative care

New procedures will be developed for the early identification of palliative care needs of patients in primary, acute, follow-up and long-term care; and also tools for the effective planning of future care with an emphasis on harmonization of health service utilization and the needs and priorities of patients and their families. The goal is to minimize the use of healthcare that does not provide real benefit to patients and their families in the form of improved quality of life, life expectancy, or the meeting of other priorities. Specifically, this may include shorter hospital stays and the prevention of readmissions, less aggressive treatment in the last months of life, reduced terminal hospitalizations and use of end-of-life care, effective use of expert palliative care teams, and more timely and frequent transfer of patients to hospice care. To achieve this goal, methodological procedures, screening tools and comprehensive advance care planning methods will be developed and tested.

Sub-objective 2 Competence of health professionals in communication and ethics

Research in this area will lead to the development of evidence-based practices to strengthen health professionals' competencies in communication, dealing with emotions and ethically

challenging situations. The aim is to improve the ability of healthcare professionals to communicate sensitively and effectively about serious diagnoses, prognoses, end-of-life care, limitations of care and other topics related to palliative care. Verification is expected of the use of a multidisciplinary approach and the involvement of medical and non-medical health professionals, along with the development and verification of structured methodological procedures for communicating serious messages with patients and their families, and models and methodologies for dealing with ethically challenging situations, including the development of effective procedures for the implementation and transfer of these skills within clinical practice.

Sub-objective 3 Innovative approaches to symptom management in palliative care

The aim is to develop new approaches for the management of complicated clinical conditions in patients with advanced severe disease, including the establishment of optimal recommendations for individualized pharmacotherapy of symptoms (pharmacogenomics of opioids, antiemetics and other symptomatic drugs, advanced analysis of drug interactions using artificial intelligence systems), validation of the efficacy of some new treatments (medical cannabis, ketamine, psychedelics, traditional Chinese medicine, acupuncture) through methodologically sound clinical trials, and the testing of new drugs and new indications. Clinical recommendations for the treatment of refractory discomfort (palliative sedation) will be developed. The result will be a health system better prepared to effectively address the complex conditions that accompany advanced stages of chronic disease and the end of life.

8. Ensuring Concept implementation

8.1. Management, organisation and coordination, including staffing requirements

Several entities will be involved in the implementation of the Concept, providing management, coordination, implementation, monitoring, and the evaluation of objectives and individual measures and indicators.

Government commissioner for science and research in healthcare

In accordance with the statute (Government Resolution No 575 of 25 May 2020), the government commissioner for science and research in healthcare submits the National Health Research Concept and coordinates activities in science and research in healthcare in the Czech Republic.

In relation to the implementation of the Concept, the government commissioner for science and research in healthcare ensures the coordination of funding for health research through both institutional and targeted support. In the case of institutional support, they coordinate the provision of institutional support to eligible health facilities. In the case of targeted support, they cooperate with the Czech Health Research Council, the Grant Agency of the Czech Republic, the Technology Agency of the Czech Republic and other providers in setting up funding mechanisms for grant projects and R&D&I projects in areas contributing to the fulfilment of the objectives of the Concept.

The Ministry of Health of the Czech Republic

The Ministry of Health of the Czech Republic is the central state administration body for health scientific research activities.

The role of the Ministry of Health of the Czech Republic in relation to the implementation of the Concept is to provide financial support of an institutional and special-purpose nature for the implementation of the Concept. The Ministry of Health of the Czech Republic also continuously monitors and evaluates the fulfilment of the objectives of the Concept and, in cooperation with the government commissioner for science and research in healthcare and the Scientific Council of the Ministry of Health of the Czech Republic, proposes possible adjustments in the targeting of the Concept and individual measures to reflect the current needs of the healthcare system in the Czech Republic.

The Scientific Council of the Ministry of Health of the Czech Republic

The Scientific Council is established as an external advisory body to the Minister for Health to ensure the activities and effective implementation of the objectives of the Ministry of Health of the Czech Republic and to address expert issues within the Ministry's strategies in health service provision, education and scientific research activities and other issues of a conceptual nature at the Ministry of Health of the Czech Republic.

In relation to the Concept, the Scientific Council of the Ministry of Health of the Czech Republic cooperates in monitoring the fulfilment of the objectives of the Concept and in proposing adjustments to the set objectives and measures in relation to the current needs of the healthcare system in the Czech Republic.

Czech Health Research Council

The Czech Health Research Council (CHRC) is an organisational unit of the state under the direct competence of the Ministry of Health of the Czech Republic. Its primary purpose is to support applied research in the health sector. In this context, the CHRC ensures the preparation

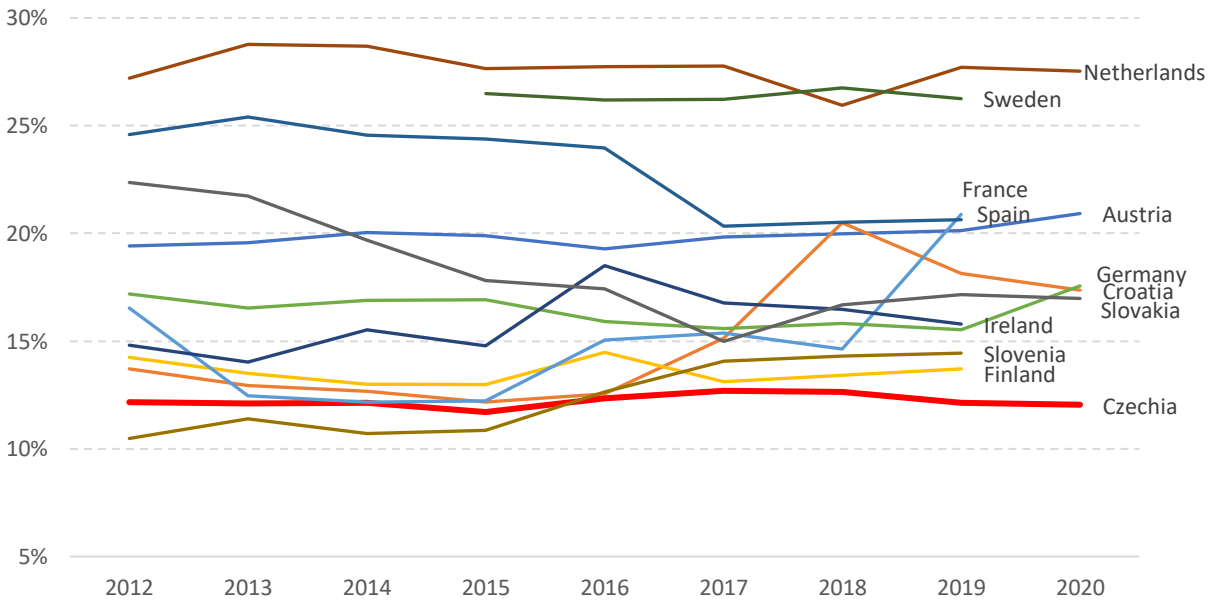
and implementation of programmes and other activities in applied biohealth research, and further develops cooperation with similar foreign agencies.
In relation to the Concept, the CHRC ensures the effective allocation of the dominant part of the resources for the purpose-oriented support of health research in relation to the thematic priorities and objectives set out in this Concept. It also cooperates in the monitoring and continuous evaluation of the fulfilment of the objectives of the Concept.

8.2. Financing of the Concept

8.2.1. Reference points

The analysis of the support for health research in the Czech Republic prepared in connection with the interim evaluation of the Health Research Concept to 2022 leads to the following conclusions (more detailed information is provided in **Annex 2**).
Support for health research and development in the Czech Republic is significantly lower than in more developed EU countries (e.g. the Netherlands, Austria, Sweden and Germany), both in absolute terms and relative to population and GDP. The relative share of support for health research and development in the total support for research and development from the state budget is the lowest among the compared countries at about 12%. Slovenia, Slovakia and Croatia all report higher shares of support for health research and development.

Share of state budget expenditure on health research and development (GBARD_Health and Medical)* in total state budget expenditure on research and development (GBARD). Source: Eurostat

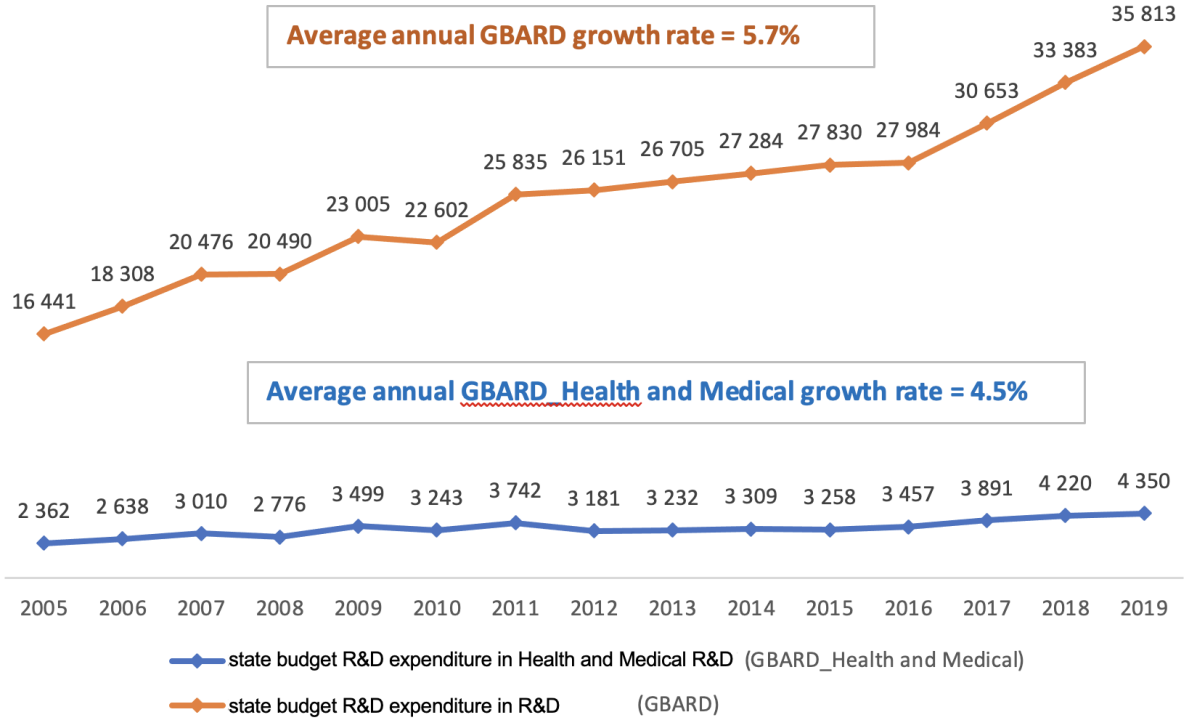


**Note: The GBARD_Health and Medical category includes state budget R&D expenditure in the areas NABS07, NABS123 and NABS133.*

Support for health research and development in the Czech Republic has been growing for the last 15 years, but the rate of growth of this support lags behind that of total state budget

expenditure on research and development. While the total state budget expenditure on R&D increased from CZK 16.441 million in 2005 to CZK 35.813 million in 2021, i.e. by an average of 5.7% per year, the state budget expenditure on health research and development increased from CZK 2.362 million in 2005 to CZK 4.350 million in 2021, i.e. by 4.5% per year on average. The share of the state budget expenditure on health research and development in the total state budget expenditure on research and development is thus decreasing in the Czech Republic.

Development of support for health research and development from the state budget of the Czech Republic (CZK million)*. Source: Czech Statistical Office - Direct public support for research and development - 2019

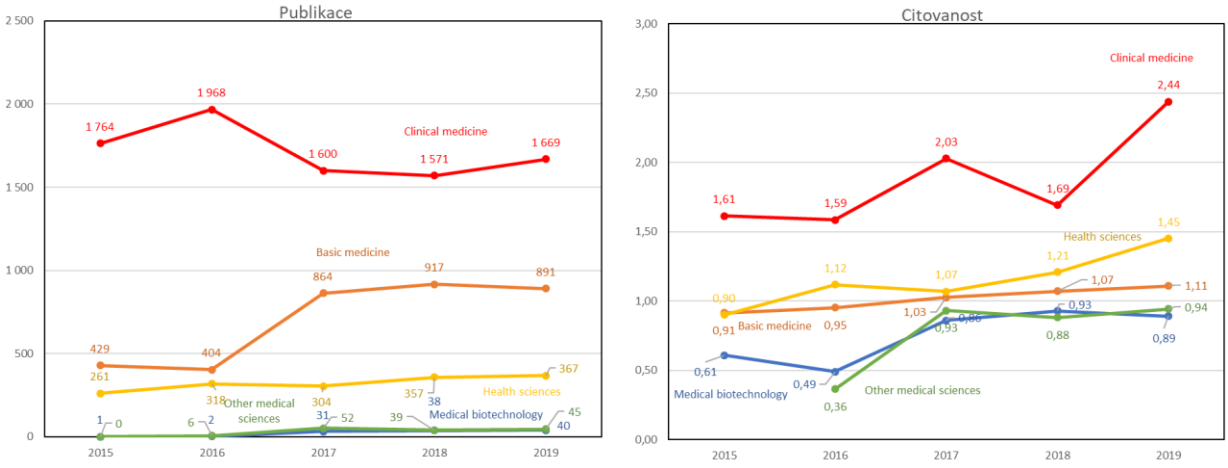


**Note: The GBARD_Health and Medical category includes state budget R&D expenditure in the areas NABS07, NABS123 and NABS133.*

In the structure of support for health research and development, the ratio of institutional to targeted support is 47:53 (in 2019). The share of institutional support is thus slightly lower than for the entire R&D support system in the Czech Republic, where institutional expenditure represented 49.5% of total R&D expenditure in 2019. Institutional support for health research and development is directed primarily at research and development in medical sciences at universities and institutes of the Czech Academy of Sciences, as well as at research and development in the socio-economic Health objective implemented in teaching hospitals. The targeted support is funding for research and development in the socio-economic Health objective. In terms of support for R&D for general knowledge development, the share of medical sciences research has fallen from 14% to 7% since 2010. On the other hand, the share of support for life sciences research, which helps develop knowledge for the health service and health research and development in certain areas, has increased.

In terms of results, nearly 14,000 publications were produced in the field of health research between 2015 and 2019. Most publications were produced in the field of *clinical medicine*, while a high number of publications were also produced in *basic medicine*. The total number of publications in the monitored fields of health research increased by about a quarter between 2015 and 2019. The number of publications is increasing slightly in most fields, with the greatest growth in *basic medicine*, where the number has approximately doubled over the period in question.

Annual numbers of publications produced in health research fields in 2015 to 2019 and their average citation rate. Source: IS VaVaI, Clarivate WoS.



The field-standardized citation rate of publications is above the global average in most of the monitored health research fields. Publications in *clinical medicine* have the highest field-standardized citation rate (almost 1.9 in 2019). The field-standardized citation rate of publications increased between 2014 and 2019, with a high increase particularly in the strongest field of publication - *clinical medicine* - where citation rates increased by approximately half.

Universities produced the highest number of publications in health research, with the highest number in *clinical medicine*. A high number of publications were also produced by teaching hospitals. Teaching hospitals also produced the highest number of publications in *clinical medicine*, and also a relatively high number in *basic medicine*. Institutes of the Czech Academy of Sciences publish mostly in *basic medicine*, with a relatively high proportion of publications also in *medical biotechnology*.

Approximately one sixth of publications in health research with a Czech author have at least one other co-author from a foreign institution. The largest share of publications produced with international collaboration is in *medical biotechnology*, where 65% of publications were produced with international cooperation. The highest proportion of publications produced with international collaboration have at least one co-author from the USA.

The analysis showed that there are a number of workplaces in the Czech Republic intensively involved in health research and producing very high quality publications with citation rates far exceeding the global average. A number of research institutes conducting health research also have the potential to engage in international collaboration.

On the basis of the analyses conducted, it can be concluded that there is potential for the effective increase in support for health research and development in the Czech Republic with an impact on the production of internationally competitive results contributing to improving the quality of health services in disease prevention, diagnosis and treatment.

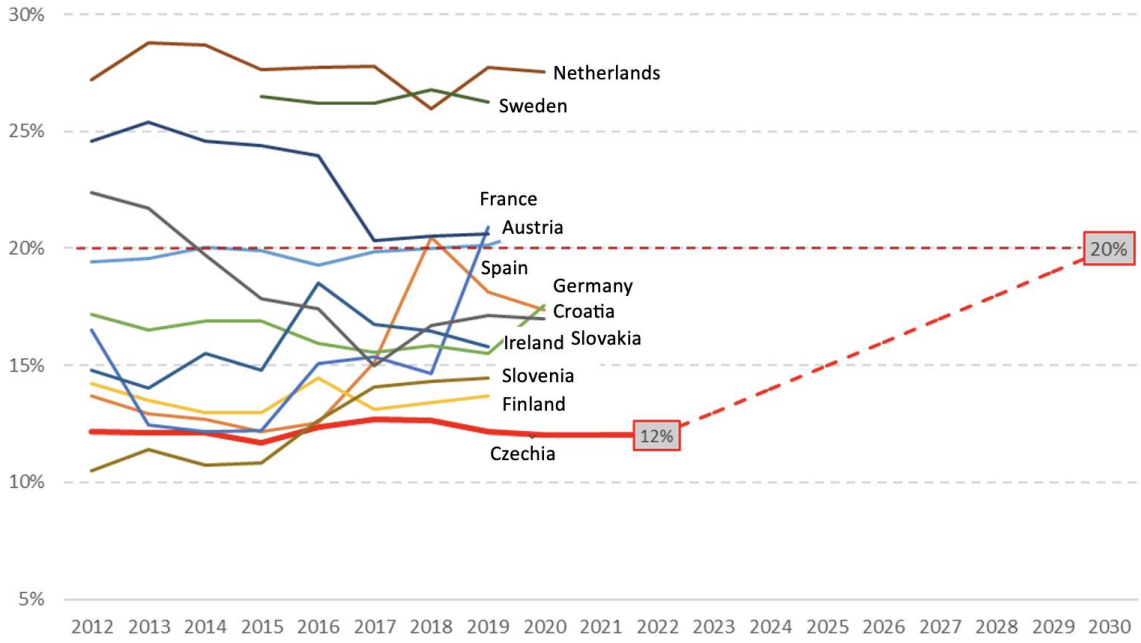
8.2.2. Support for health research and development

State budget expenditure in support of health R&D has grown at a slower rate than total state budget expenditure in support of R&D over the past 15 years, resulting in the relative underfunding of the development of health research as a whole. On the other hand, the quality of health research in the Czech Republic has been maintained and actually improved. The increasing demands placed on the healthcare system, including biohealth research, which is part of it, and the accelerating pace of development of health research are all increasing the cost of implementation and development of research activities in this segment. Therefore, in order for health research and development in the Czech Republic to keep pace with quality standards on a global level and to be able to effectively contribute to improving the quality of health services provided in the Czech Republic, it is necessary to proportionally increase the state budget expenditure on R&D.

In relation to this, the Concept aims to increase the relative share of state budget expenditure on health R&D in the total state budget expenditure on R&D from the current 12% to a target of 20% in 2030. This target corresponds to the relative share of support for health research provided by the state budget in more developed European countries such as Austria, France, Germany and Spain. At the same time, this share corresponds to the proposal for the allocation of funds for the priority area ‘Healthy population’ contained in the government-approved National Priorities for Oriented Research, Experimental Development and Innovation (Government Resolution No 552 of 19 July 2012).

To achieve the target, the share of support for health research will need to continuously increase by one percentage point per year from 2023 to 2030. The reason for gradually increasing the share of state budget expenditure on health research is primarily an effort to gradually adapt the health research system while maintaining its effective absorption capacity.

Projection of the development of the share of the state budget expenditure on health research and development (GBARD_Health and Medical)* in the total state budget expenditure on research and development (GBARD) in the Czech Republic compared to abroad.



Increasing the share of support for health research from the state budget will not automatically place additional demands on the state budget. The aim here is to focus existing R&D support from the state budget more on thematic priorities that can effectively contribute to the development of the healthcare system in the Czech Republic and to improving the quality of healthcare services in disease prevention, diagnosis and treatment.

The main financing instruments for the Concept are institutional support, special-purpose support provided by the Ministry of Health of the Czech Republic through the Czech Health Research Council, and special-purpose support provided by other support providers.

Institutional support

Institutional support for research organisations active in health research is currently provided mainly by the Ministry of Health of the Czech Republic (support for the long-term conceptual development of teaching hospitals and other research-oriented health facilities), the Ministry of Education, Youth and Sports of the Czech Republic (support for the long-term conceptual development of universities and their medical and science faculties) and the Czech Academy of Sciences (support for the long-term conceptual development of Czech Academy of Sciences institutes active in health research).

The main purpose of institutional support is to create stable and predictable conditions for the long-term conceptual development of research organisations (LCDRO). At the same time, the institutional support system must create certain incentives for the development of health research system components in line with the objectives of this Concept. In this context, regular evaluation of research organisations will be carried out pursuant to Methodology17+, with an emphasis on monitoring developments in research quality, international cooperation, the transfer of health research results into practice, and the creation of conditions for the development of personnel capacity for health research, specifically for the development of careers in science for young researchers. The results of the evaluation of research organisations carried out by the Ministry of Health of the Czech Republic will be taken into account in the allocation of support for the long-term conceptual development of research organisations to

ensure the evaluated research organisations are sufficiently motivated to implement the desired systemic changes, but at the same time so that the amount of institutional support remains sufficiently predictable for research organisations and enables the implementation of the longer-term strategic goals of research organisations.

Targeted support - Ministry of Health of the Czech Republic

As in the past, the dominant instrument of special-purpose support for health research will be the programme to support health research announced by the Ministry of Health of the Czech Republic and implemented by the **Czech Health Research Council (CHRC)**. This is a programme directly related to the objectives of the Concept and that comprehensively supports priority topics of health research. Furthermore, this programme will emphasize support for horizontal objectives of the development of the health research system, such as the transfer of health research results into practice, the involvement of young researchers in health research, strengthening the internationalization of Czech workplaces, and involving them in international health research projects.

Until 2026, the special-purpose support of the Ministry of Health of the Czech Republic will be provided through the Programme to Support Applied Health Research 2020-2026 (code "NU"), approved by Government Resolution No 171 of 11 March 2019. This programme is based on the Health Research Concept to 2022. However, given the continuity of the priority themes and strategic objectives of the previous and new Concepts, this programme will also contribute to the fulfilment of health research development objectives set out in this Concept.

Starting in 2024, a follow-up Ministry of Health of the Czech Republic programme for 2024-2030 will be implemented - it will be fully based on the objectives of this Concept and be one of the key instruments for its implementation.

Targeted support - other providers

In addition to the Ministry of Health of the Czech Republic's programme to support health research, the development of biohealth research is also supported by the budgets of other targeted support providers. According to the Analysis of Support for Health Research in the Czech Republic, the most important other providers of special-purpose support include the The Czech Science Foundation (GACR), the Technology Agency of the Czech Republic (TACR) and the Ministry of Education, Youth and Sports of the Czech Republic (MEYS). In line with the objective of increasing the share of public spending on health research, efforts will be made, in collaboration with these providers, to send more targeted support to research activities with the potential to contribute to improving the quality of health services in disease prevention, diagnosis and treatment.

The development of basic research in medical sciences will be coordinated in cooperation with the GACR, creating an indispensable knowledge base for further research and educational activities. The support provided by the Czech Health Research Council (CHRC) will be directed towards applied health research. At the same time, emphasis will be placed on the coordination of the activities of the GACR and CHRC in supporting translational research and research at the interface between basic and applied research to ensure the support effectively covers all health research phases.

As a provider, the TACR will focus primarily on supporting the more advanced phases of applied research and experimental development in healthcare. At the same time, mechanisms will be coordinated to ensure the effective use of results from projects supported by the CHRC in follow-up projects of the TACR aimed at bringing the results of applied research into practical applications and their use in practice.
The definition of individual research areas for each provider will be based on the **Frascati Manual** (OECD document). **Basic research** is experimental or theoretical work carried out primarily to obtain new knowledge about the fundamental principles of phenomena or observable facts, and not primarily aimed at any particular application or use in practice. **Applied research** is original research carried out with the aim of gaining new knowledge. However, it is primarily focused on a specific practical purpose or goal. In basic research, "new knowledge about the fundamental principles of phenomena or observable facts" will be directed towards the medical sciences, while in applied research "the specific practical aim and objective" will logically be directed towards the health sector. **Experimental development** is systematic work that draws on research findings and practical experience and produces further knowledge to create new products or processes or to improve existing products or processes, in this case for the health sector.
In cooperation with the MEYS, infrastructural conditions needed for cutting-edge health research will be systematically developed, both through investments from the **Operational Programme Johannes Amos Comenius** and through long-term support for the operation of **research infrastructure**. One important tool for the implementation of the Concept will also be the Programme to Support Excellent Research in Priority Areas of Public Interest in Healthcare - EXCELES aimed at concentrating research capacities in selected priority health research topics.

8.3. Development of international cooperation

International cooperation in health research (and research in general) is an essential prerequisite to improve the quality of research activities, transfer knowledge and strengthen the relevance of research carried out in the Czech Republic to address global population health challenges. Analyses to date show that health research in the Czech Republic is relatively well established abroad and that research teams from the Czech Republic are relatively strongly integrated into collaborative international research networks. Yet there is still room for greater involvement in research projects under the EU framework programmes for research and innovation - the new Horizon Europe programme. Therefore, emphasis will be placed on the development of international cooperation in health research in all existing and new institutional and targeted support instruments.
Specifically, the aim will be to increase the intensity of involvement of research teams from the Czech Republic in Horizon Europe framework programme projects and thus contribute to addressing challenges for health research at both European and global level. Another aim is to actively participate in projects in the Cancer mission area - the Czech Republic has a strong background in oncology research and it is also a highly relevant topic for the quality of life of Czech society.

9. Moral and ethical issues

At present (i.e. in 2022), each project proposal applying for special-purpose support under the "Programme to Support Applied Health Research 2015-2022" must obtain the approval of the ethics committee of the investigating institute and the ethics committees of the co-investigating institutes, according to the tender documents of the individual procedures. If none of the organisations involved in the project has its own ethics committee, it will obtain this opinion from the ethics committee of another authorised healthcare institution. Other providers contributing to the implementation of the current Concept will follow a similar approach. This approach will be maintained for the duration of the forthcoming Concept. Major problems will be solved in cooperation with the Ethics Committee of the Ministry of Health of the Czech Republic, possibly in cooperation with the Bioethics Committee of the Council for Research, Development and Innovation.

Ethical aspects of health research arise in particular from Article 16 (Protection of persons involved in scientific research) of the 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 of 4 April 1997 (No. 96/2001 Coll., Communication of the Ministry of Foreign Affairs of the Czech Republic).

10. Control and evaluation of the implementation of the Concept

10.1. Monitoring of the Concept

For the effective management and implementation of the Concept, an evaluation system will be set up to link the strategic level, programme level and project level. For this purpose, a coherent indicator system will be set up from projects through programmes to the Concept to ensure the contribution of support instruments to the fulfilment of the Concept objectives can be responsibly monitored and evaluated.

The monitoring of institutional support will be carried out through periodic reports submitted by research organisations to the Ministry of Health of the Czech Republic for control over the use of institutional support for each year and evaluation of projects implemented by the research organisations through institutional support. The monitoring of targeted support will be carried out through interim and final reports on targeted support projects for the past year and their assessment.

To monitor the implementation of the Concept and the progress in meeting its objectives, indicators are set at the level of both the thematic objectives and the horizontal objectives of the Concept.

Indicators for monitoring and evaluating thematic objectives

Objective	Indicator	Trend/Target value
Support research in the main thematic areas of the Concept	Number of calls for health research programmes focused on the main thematic areas of the Concept	Increase
	Number of supported health research projects (all providers)	Increase
	Volume of support for health research in the main thematic areas of the Concept	Increase
	Number and quality (percentage of publications in Q1 journals according to the WoS database) of health research results according to the main thematic areas of the Concept	Increase
	Degree of consistency of the material plan for institutional support from the relevant ministries with the thematic areas of the Concept	Increase
	Number of registered applied research results (production of a prototype, functional sample, software, utility/industrial design, semi-operation, verified technology, certified	Increase

	methodologies and procedures, patent application, patent, license)	

Indicators for monitoring and evaluating horizontal objectives

Objective	Indicator	Trend/Target value
Increase the relative share of public support for health research	Share of state budget expenditure on health research and development (GBARD_Health and Medical) in total state budget expenditure on research and development (GBARD)	20% in 2030
Strengthen international cooperation in health research	Number and financial volume of health research projects within Horizon Europe	Increase
	Share of scientific publications in health research published jointly with authors from foreign institutions	Growth (to about 60% on average)
	Number of research organisations involved in international health research projects	Increase
Improve the quality of health research	Share of health research publications in the top 10% of the globally most cited publications	Increase
	Number of health research results applied in practice (new procedures, methodologies, technologies, ...)	Increase
Involve young researchers in health research	Share of junior researchers in the total number of researchers	Increase
	Number and financial volume of health research projects carried out by junior researchers (in the role of principal researcher)	Increase
Utilize health research findings to implement new clinical procedures	Synergy with the Clinical Recommended Practices (CRP) project of the Ministry of Health of the Czech Republic	YES
Improve the links and continuities between basic and applied health research	Ensure the provision of support for basic and applied health research by one departmental provider	YES
Translate current assessments of the state of health of our population and current health threats into health research priorities	This is taken into account in the tender documentation for the procedures from various providers	YES

Use research results in the pre- and post-graduate education of physicians and other healthcare professionals	Subsidise the involvement of health professionals in pre- and post-graduate education in projects within the framework of the grant competitions of individual providers	YES
Use the results of health research to present research organizations and popularise health science	Media presentation of results obtained through health research, and the number of expert and popularising activities	Growth

10.2. Interim evaluation of the Concept

The interim evaluation of the implementation and fulfilment of the Concept's objectives will be carried out in the middle of the Concept's validity period, i.e. in the fifth year of its implementation. The evaluation will be carried out externally by an independent expert evaluator in cooperation with the Ministry of Health of the Czech Republic. The main aim of this evaluation will be to assess the relevance of the set objectives and strategic directions of the Concept, and the progress in meeting the set objectives, indicators and timetable of the Concept. The result will be an independent assessment and the formulation of recommendations for the next period of implementation of the Concept.

The information sources for the ongoing evaluation will include the outputs of the periodic evaluation of research organisations carried out by the Ministry of Health of the Czech Republic according to Methodology 17+ and the results of the evaluation of the Programme to Support Applied Health Research 2020-2026.

10.3. Evaluation of the results and impacts of the Concept

An evaluation of the results and impacts of the Concept will only be possible a certain time after its implementation. This evaluation will be carried out by an external evaluator in cooperation with the Ministry of Health of the Czech Republic three to five years after the end of the Concept implementation period, and will be based on the results of several periodic evaluations of research organisations carried out according to Methodology 17+, as well as on the evaluation of the results and impacts of the completed health research support programmes and other targeted support instruments used during the Health Research Concept period.

11. Concept preparation procedure

The Health Research Concept to 2030 is a national strategic document following on from the Health Research Concept to 2022. The Health Research Concept is based primarily on the needs of the development of the health system in the Czech Republic and the objectives set out in strategic documents for the healthcare sector. The basic direction for the strategic orientation of the Concept is primarily given by the Strategic Framework for Healthcare Development in the Czech Republic to 2030, the National Research, Development and Innovation Policy of the Czech Republic 2021+, the National Priorities of Oriented Research, Experimental Development and Innovation, and the National Research and Innovation Strategy for Smart Specialization of the Czech Republic 2021-2027.
The Concept preparation process is the responsibility of the Ministry of Health of the Czech Republic within the competence of the Department of Science and Medical Professions and the Czech Health Research Council. Coordination of the Concept preparation was provided by the Commission for the Preparation of the Health Research Concept, the preparation of individual thematic priorities was provided by the Panel of National Priorities Guarantors, and the Scientific Council of the Minister of Health provided an expert guarantee for the Concept. Annexes 1 to 3 were prepared by the Technology Centre of the Czech Academy of Sciences as part of the Interim Evaluation of the Programme to Support Applied Health Research 2015-2022 and the Health Research Concept to 2022.

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Annexes

Annex 1
Conclusions of the Interim Evaluation of the Programme to Support Applied Health Research 2015-2022 and the Health Research Concept to 2022

Annex 2
Analysis of Support for Health Research in the Czech Republic

Annex 3
Foreign Approaches to Supporting Health Research