REGULAR EVALUATION SELF-EVALUATION FORM

Evaluation of R&D activities in Estonia 2024

Institution:	University of Tartu
Evaluated field of research:	Medical and health sciences
Evaluation period:	2018–2023
Person responsible:	Maris Laan, Vice Dean for Research, Faculty of Medicine

General information

Short introduction of the evaluated field of research

Structural units, current number of staff, share of academic staff, number of students, main research directions, other relevant information about the field.

The major hub for medical and health sciences at the University of Tartu (UT) is the Faculty of Medicine (FM) that is solely responsible for the academic education in medicine, dentistry, pharmacy, physiotherapy and nursing science in Estonia. The FM consists of six institutes: Institute of Biomedicine and Translational Medicine, Institute of Clinical Medicine, Institute of Family Medicine and Public Health, Institute of Pharmacy, Institute of Dentistry, Institute of Sport Sciences and Physiotherapy. FM is a leader in health policymaking in Estonia and responsible for providing quality education and R&D in medical and health sciences that meets the needs of the healthcare sector, including personalised medicine and e-medicine. In autumn 2023, the number of students enrolled in FM was 1,882 at undergraduate or MSc-level, and 206 PhD students. Both the education and research benefit from the broad collaborative network of health service providers (e.g. Tartu University Hospital, North Estonia Medical Centre) and institutions (e.g. the National Institute for Health Development) in the Estonian medical sector.

In 2023, the total number of employees in FM was 678, including ~100 junior research fellows enrolled in the doctoral programmes, ~400 academic staff and the rest representing various non-academic personnel. Due to specific educational setting in training all the MD-level clinicians for the country, most of the teaching in FM is in the Estonian language. The overall proportion of academic personnel ~70%, reflecting the high teaching load in FM. Another special feature is the relatively high proportion of part-time academic positions as clinical training of students and residents is provided by medical practitioners with dual roles, the hospital and UT.

Research activities at the FM are organised into eight focus areas:

- psychiatric and neurodegenerative disorders, combining complementary research on clinical aspects and their utility, and molecular mechanisms using *in vitro* and *in vivo* disease models;
- immune-inflammatory chronic disorders and their pathogenesis, including variety of molecular models and clinical research on diabetes, cardiovascular and dermatological conditions;
- infectious diseases with the focus on paediatric and immunocompromised populations, pharmacokinetics and -dynamics of antibiotics, microbiota research, development of probiotics;
- reproductive (bio)medicine, including pre-clinical, clinical and epidemiological research on infertility, pregnancy-related disorders and other sex-specific health conditions;
- public health related research, including focus on epidemiology, risk-taking health related behaviours, environmental and occupational health risks, health technology assessment;
- pharmaceutical research on drug development, multifunctional nanofibrous medicines and bioscaffolds for wound therapy, printed nanomaterial substrates and drug delivery systems;
- sports science combining research from psychology to mechanisms of muscle contraction in athletes, physical activity and its promotion in general population, and physiotherapy;

• oral disorders and health, including prevention, development of treatment options, social aspects and genetic determinants of congenital conditions such as orofacial clefts.

The strength of FM research is a consensus view that using a complementary toolbox of experimental, clinical, analytical and computational approaches will create synergies and lead to the best outcomes in solving the postulated study questions. Additionally, special attention in all areas of medical science is given to translational approach.

Health-related research is also implemented in other UT units. **Institute of Genomics** (151 staff members, 31 PhD students; mainly research-oriented activities) with the affiliated Estonian Biobank (EstBB) has been focused on genome-wide association studies in international consortia investigating the role of common genetic variation to various health conditions. Another focus area has been developing and analysing the utility of polygenic risk scores to prognose the risk to chronic diseases.

The research at **Institute of Computer Science** (242 staff; ~1500 students, 98 PhD students) and the affiliated Health Informatics research group includes computation analysis of health datasets to better understand the mechanisms of the disease development and competence in computational tools for the mining of the electronic patient records, facilitating public health-related research.

Institute of Technology (152 staff; 390 students; 73 PhD students) has special interests in developing novel therapeutic tools such as cell-penetrating peptides, and in molecular biology research of antibiotic resistance and human viruses, capable of causing pandemics.

Additionally, the **Faculty of Social Sciences** has some contribution to epidemiological studies of health behaviour and its social determinants, studies of factors affecting mental health, cognition and obesity, and health-related educational research.

Broad professional competence in medical and health sciences at UT has been highly supportive to active participation in high-level international research, evidenced by increasing number of competitive collaborative grants received from the EU calls and other external funders.

1. Scientific Impact of Research

1.1. Institution's description of the 10 most impactful R&D results of the evaluation period (incl. explanation why they are considered the most impactful).

In 2018–2023, seven outstanding research teams of FM received annual Estonian National Research Awards, whereby the awardees are competitively selected by the committee led by the President of the Estonian Academy of Sciences. These achievements are summarised below with reference to the most impactful paper(s) of each team.

1. Prof. Joel Starkopf and Dr Annika Reintam Blaser (Anaesthesiology and Intensive Care) received the Research Award in Medicine in 2018 for their research "Intra-abdominal pressure and gastrointestinal failure in intensive care patients".

The Estonian team led an international clinical research team including 15 centres from Europe, Australia and the USA aiming to identify the prevalence, risk factors, and outcomes of intra-abdominal hypertension and gastrointestinal tract complications in intensive care unit (ICU) population. Evidence-based definitions to describe feeding intolerance in ICU patients were developed and their reliability was tested. As a result, ICU clinical practice has changed significantly worldwide.

Lead paper: Reintam Blaser, A et al. Incidence, Risk Factors, and Outcomes of Intra-Abdominal Hypertension in Critically III Patients-A Prospective Multicenter Study (IROI Study). *Crit Care Med.* 2019; 47(4):535-542.

2. **Prof. Allen Kaasik** (Pharmacology) received the Research Award in Medicine in 2019 for his research "**The role of mitochondria in diseases of the nervous system**".

Allen Kaasik has shown a critical contribution of cellular energy crisis due to damaged mitochondrial function in the development of neurodegenerative diseases such as Parkinson's disease. His research

brought novel insights into how to stimulate the formation of new mitochondria in nerve cells and how to guarantee the critical energy reservoir necessary for cellular growth. His discovery study uncovered the role of mitochondrial outer membrane protein Miro1 in sensoring mitochondrial damage and protecting neurons from glutamate-induced mitophagy.

Lead paper: Safiulina, D et al. Miro proteins prime mitochondria for Parkin translocation and mitophagy. *The EMBO Journal.* 2019; 38(2):e99384.

3. **Prof. Ana Rebane** (Molecular Medicine) received the Research Award in Medicine in 2020 for her research "**MicroRNAs in chronic immune diseases**".

Ana Rebane has shown that microRNA-146a suppresses keratinocyte proliferation and inflammatory responses in atopic dermatitis and psoriasis, as well as exhibits anti-inflammatory effect in rhinovirus infection of bronchial epithelial cells. These studies have led to translational research developing protocols for therapeutic delivery of miRNAs in inflammatory skin diseases.

Lead paper: Carreras-Badosa, G, et al. NickFect type of cell-penetrating peptides present enhanced efficiency for microRNA-146a delivery into dendritic cells and during skin inflammation. *Biomaterials.* 2020; 262:120316.

4. The research team of Prof. Eero Vasar, Dr Mari-Anne Philips (Physiology), Dr Mario Plaas (Laboratory Animal Centre), and Dr Liina Haring (Psychiatry) received the Research Award in Medicine in 2021 for their research "Translational research in neuropsychiatry: from genetically modified experimental animals to human schizophrenia spectrum disorders".

The team of Eero Vasar has uncovered the potential of the IgLON family of neural adhesion proteins in treatment of neuropsychiatric diseases. The team has also used the *Wfs1 -/-* rat model to show a neuroprotective effect of liraglutide in the Wolfram syndrome. Their studies in schizophrenia have suggested that tryptophan-metabolites have a likely contribution and in contrast, diabetes medications may prevent the development of obesity and metabolic syndrome in these patients.

Lead paper: Kuuskmäe, C et al. Kynurenine pathway dynamics in patients with schizophrenia spectrum disorders across the disease trajectory. *Psychiatry Res.* 2023; 328:115423.

5. **Prof. Pärt Peterson** and **Prof. Kai Kisand** (Molecular Pathology) received the Research Award in Medicine in 2022 for their research **"Studies on aging immune system and Covid-19".**

Pärt Peterson and Kai Kisand have demonstrated age-related changes in monocyte metabolic fitness and signs of increased oxidative stress and DNA damage. Their highly influential paper resulting from the collaboratory team of Estonian researchers showed that at 6 months after the second dose of SARS-CoV-2 mRNA vaccine BNT162b2, the antibody levels had dropped to 7% of the baseline. They also showed that antibody response correlated negatively with age and positively with the total score of vaccination side effects.

Lead papers: Naaber, P et al. Dynamics of antibody response to BNT162b2 vaccine after six months: a longitudinal prospective study. *The Lancet Reg Health Eur.* 2021; 10:100208.

Naaber, P et al. Protective antibodies and T cell responses to Omicron variant after the booster dose of BNT162b2 vaccine. *Cell Rep Med.* 2022; 3(8):100716

6. **Prof. Irja Lutsar** (Medical Microbiology) and **Prof. Tuuli Metsvaht** (Paediatric Intensive Care and Pharmacotherapy) received the Research Award in Medicine in 2023 for their research "Interdisciplinary management of neonatal sepsis".

Their research on neonatal sepsis has pointed to early colonisation of the gastrointestinal tract by virulent microbes as one of the main reservoirs of sepsis agents, whereas appropriate measures at the family ICU reduce the risk, e.g. feeding with breast milk. The team has participated in multicentre studies on pharmacokinetics and clinical efficacy of antibacterial drugs in newborns. This has resulted in international recommendations on drug selection and dosage, successfully introduced to neonatal care units in Estonian hospitals. The infant mortality rate in Estonia, 2.2 per 1,000 births, is <u>one of the lowest in the world</u>.

Lead paper: Lutsar, I et al. Meropenem vs standard of care for treatment of neonatal late onset sepsis (NeoMero1): A randomised controlled trial. *PLoS One.* 2020;15(3):e0229380.

In 2020, Prof. Irja Lutsar was also awarded the Karl Schlossmann medal of the Estonian Academy of Sciences for her impactful interdisciplinary contributions to medical research in Estonia.

7. **Prof. Karin Kogermann** (Physical Pharmacy) received the Research Award in Chemistry and Molecular Biology in 2023 with the Institute of Technology (Prof. Tanel Tenson's team) for the jointly executed research "**Mechanisms of action and resistance to antibiotics**".

Researchers studied biochemical mechanisms of antibiotic action and their effects on bacterial cells. Karin Kogermann contributed in the field of pharmaceutical nanotechnology – investigating innovative formulations and manufacturing technologies for nanomedicines with a specific focus to novel local drug delivery systems that enable to improve the specificity and bioactivity of antibacterial and antimicrobial agents and reduce the probability of possible side-effects.

Lead paper: Zupančič, Š et al. Impact of PCL nanofiber mat structural properties on hydrophilic drug release and antibacterial activity on periodontal pathogens. *Eur J Pharm Sci.* 2018; 122:347-358. In 2018, Prof. Kogermann also received the L'Oreal Baltic "For Women in Science 2018" award for her innovative research on new types of antibacterial nanofibrous dressings for local wound healing.

Further impactful R&D results in medical and health sciences at UT:

8. **Impactful research in public health.** Epidemiological research at UT has significantly increased at national and international level, including identifying risks for disease and comorbidities, evaluating preventive measures and treatments, providing evidence-based information for public health decisions. Examples of important papers with **Prof. Anneli Uusküla** as the leading author:

- Uusküla, A et al. Long-term mortality following SARS-CoV-2 infection: A national cohort study from Estonia. *Lancet Reg Health Eur.* 2022; 18:100394.
- Uusküla, A et al. Prevaccination Prevalence of Type-Specific Human Papillomavirus Infection by Grade of Cervical Cytology in Estonia. *JAMA Netw Open.* 2023; 6(2):e2254075.

9. Sports medicine fighting the decreasing physical activity among young people. This internationally impactful research by the sports medicine group showed that the intrinsic motivation in physical education was the only significant mediator among the support from teachers, students' experiences of basic psychological need satisfaction and objectively measured physical activity. This outcome has practical implications highlighting the need to feed students' intrinsic motivation in physical education to increase physical activity behaviour during their leisure time. *Lead paper:* Kalajas-Tilga, H et al. Motivational processes in physical education and objectively measured physical activity among adolescents. *J Sport Health Sci.* 2020; 9(5):462-471.

10. Medical genetics discoveries improving diagnostics and personalised medicine. The past 6 years have enourmously expanded the discovery and translational research on human congenital diseases, including the characterisation of novel rare genetic disorders. Medical genetics discoveries have facilitated a wide usage of genetic testing in Estonian health care system.

Examples of impactful contributions with leading authors from the Faculty of Medicine:

• Kasak, L et al. Bi-allelic Recessive Loss-of-Function Variants in *FANCM* Cause Non-obstructive Azoospermia. *Am J Hum Genet.* 2018; 103:200-212.

This study led by the Estonian team uncovered a novel gene in male infertility, resulting in a novel entry to the <u>NCBI OMIM database</u>, Spermatogenic failure 28.

Prof. Maris Laan (Human Genetics), the senior author of this study was awarded the Baltic Academies of Sciences medal in 2019 for her research in reproductive biomedicine.

• Engal, E*, Oja, KT * et al. Bi-allelic loss-of-function variants in WBP4, encoding a spliceosome protein, result in a variable neurodevelopmental syndrome. *Am J Hum Genet*. 2023; 110:2112-19.

This study linked loss-of-function mutations in *WBP4* to a severe neurodevelopmental syndrome. Coleader of the project, **Prof. Katrin Õunap** (Clinical Genetics) was awarded in 2019–2022 the Neinar Seli prize of Tartu University Hospital for her significant clinical research.

Example study of EstBB from the Institute of Genomics, Faculty of Science and Technology:

• Reisberg, S et al. Translating genotype data of 44,000 biobank participants into clinical pharmacogenetic recommendations: challenges and solutions. *Genet Med.* 2019; 21:1345-1354. The last author of this study, **Prof. Lili Milani** (Epi- and Pharmacogenomics) received as the member of the research team the National Research Award in Chemistry and Molecular Biology in 2020.

1.2. Description of intellectual property granted.

During 2018–2023, four patents in medical and health research were granted (priority dates 2012–2017), including two to **Prof. Andres Merits** (Institute of Technology) related to his research on vaccine development using recombinant alphaviruses. An approved patent to the clinical biochemistry and clinical microbiology teams (first author **Assoc. prof. Tiiu Kullisaar**, co-PIs: **Prof. Marika Mikelsaar**, **Prof. Mihkel Zilmer**) covered the use of *Lactobacillus fermentum* ME-3 strain DSM 14241 in preventing, alleviating the symptoms of, or treating a metabolic syndrome and its related disorders. A patent in biomechanics of skeletal muscles was granted to **Dr Arved Vain and colleagues** for the invention in sports sciences – a mechano-therapeutic device for monitoring the progress in treating and correcting the posture of body parts.

In total, 23 patents were applied for during the evaluation period (priority dates 2017–2021), including methods related to the development of virus vaccines (**Prof. Merits' team**), for drug delivery using cell-penetrating peptides (**Prof. Tambet Teesalu's team**) and for the encapsulation of bioactive entities, and formation into solid materials (**Prof. Karin Kogermann's team in collaboration with Prof. Tanel Tenson's team**). Protection of two inventions in reproductive medicine were applied – method development for In Vitro Fertilisation (IVF) to evaluate embryo viability (**Prof. Andres Salumets' team**) and biomarker assay for preeclampsia risk prediction (**Prof. Maris Laan's team**).

1.3. Institution's opinion regarding aspects that need to be improved in the field of scientific impact of research.

Aspects to be improved:

- Further broadened spectrum of funding sources from industry, EU, international grant agencies;
- Increased proportion of high-impact research publications in terms of international visibility;
- Targeted attention to R&D in less developed research fields, e.g. physiotherapy or dentistry;
- Promoted awareness and training about the importance of intellectual property protection and encouragement of the academic staff to apply for patents for their innovations.

2. Sustainability

2.1. Institution's description of the most important facts showing sustainability and potential of R&D.

- 1. UT is among the 1% of the world's most influential research institutions in the fields of clinical medicine, immunology, biology and biochemistry, microbiology, molecular biology and genetics, neuroscience and behaviour, psychiatry/psychology, pharmacology and toxicology. The average number of citations per article published by Estonian researchers in clinical medicine is 67 vs 16 worldwide (Clarivate, Essential Science Indicators). In the molecular biology and genetics category, these numbers are 87 vs 28, and in immunology, 42 vs 22.
- 2. There is an overall positive trend of increasing number of publications in high-impact medical and health science and interdisciplinary journals lead by the researchers of UT; the Category Normalised Citation Impact has increased from 1.6 in 2018 to 2.4 in 2023.
- 3. Medical and health research at UT is supported by efficient inter- and multidisciplinary network within the institution and medical sector in Estonia, within Europe and overseas.
- 4. High proportion of academic staff (74%) among all the personnel working in FM; increase in academic staff members (excluding doctoral students enrolled as junior research fellows) from 385 in 2018 to 405 in 2023, including 72% with a PhD.
- 5. Two top researchers in medical sciences were elected to the Estonian Academy of Sciences, Prof. Maris Laan (2021, public health) and Prof. Pärt Peterson (2023, biomedicine).

- 6. New professorships for middle-career medical researchers were opened in Molecular Medicine, Clinical Neurology, Andrology, Paediatric Intensive Care and Pharmacotherapy, Vasology, Reproductive Medicine, Oncology and Obstetrics, Gynecology and Genetics.
- In 2018–2023, a total of 158 PhD theses in medical and health sciences were completed this is a significant, 1.5-fold increase compared to the previous evaluation period covering 2010–2015, when 109 doctoral theses were defended; likewise, the number of defended MSc thesis has increased from 315 (2010–2015) to 387 (2018–2023).
- In total 312 PhD students are currently enrolled to research related to medical and health sciences

 a notable 37% increase compared to 228 doctoral students in 2015 at the time of the previous research evaluation; the recruitment of all PhD students as junior research fellows in 2022 marked a trend of growing numbers, as this position, compared to the student status, provides social guarantees and promotes their scientific career.
- 9. Successful application for competitive funding the total sum of funding from research grants received in UT during 2018–2023 in the category of medical and health sciences was €186m, including over €95m allocated to the Faculty of Medicine, and the rest to the other faculties of UT, including Institute of Genomics receiving the major fraction (€57m); annual research funding nearly doubled from €13,014,119 in 2018 to €20,792,543 in 2023 (see Quantitave indicators).
- 10. The number of funded projects in medical and health sciences has increased from 453 to 484, compared to the previous evaluation period; funding by EU and international foundations nearly tripled, from €2,857,749 in 2018 to €7,223,854 in 2023. Likewise, there was a two-fold increase in medical research funding from Estonian private sector.
- 11. Health science research at UT is promoted by the EU Horizon Europe Teaming for Excellence grant – <u>TeamPerMed "Centre for Data Enriched Medicine"</u> (2023–2028, €30m). The partners Erasmus Medical Center, the Erasmus University Rotterdam, and Helsinki University facilitate knowledge transfer to UT.
- 12. Large clinical and population-based sample sets along with detailed clinical and epidemiological datasets that promote growing trends for cutting-edge research.
- 13. An increasing number of completed and ongoing successful translational research projects in clinical medicine, biomedicine, public health, sports medicine, and pharmaceutical science that provide added value to the health of individual subjects and national health care.
- 14. Continuous oversight and updating the research infrastructure to ensure the state-of-the-art research implementation conditions.
- 15. Active international mobility of the R&D staff in scientific conferences and training events.
- 2.2. Description of R&D infrastructure (sufficiency and condition).

The condition of infrastructure for medical and health science research at UT is up-to-date and supportive to a broad range of medical disciplines. The heart of the medical and health sciences research is the **Maarjamõisa campus**, bringing together and facilitating synergies between research teams in preclinical, clinical, and public health medicine, pharmacy, and dentistry. It also houses collaborative research teams in natural (e.g. virology, proteomics, molecular biology) and social (e.g. behavioural neuroscience) sciences, such as the Institutes of Technology and Chemistry.

Maarjamõisa is also the home for Tartu University Hospital (TUH), the only university hospital in Estonia and the core partner in clinical research and education (https://www.kliinikum.ee/en/about-the-hospital/). TUH is the largest provider of medical care in Estonia and meets the highest clinical research standards; during the evaluation period, it was enlarged with new up-to-date units. The departments of the **Institute of Clinical Medicine** are located in the buildings of TUH. Clinics have infrastructure for proof-of-concept clinical studies. TUH is also the bases for the studies in physiotherapy and nursing science. The infrastructure of the **Institute of Dentistry**, located at TUH, was reconstructed in 2020 and provides an updated modern medical environment, including interactions with clinical research. Current facilities include 24 fully equipped dental units for clinical

practice and 20 for preclinical training. The department of oral and maxillofacial surgery was reconstructed in 2023, serving as a training base for dental surgery practice.

The **Biomedicum** houses most of our departments for preclinical and public health research. Laboratories and other facilities of the **Institute of Biomedicine and Translational Medicine** are annually assessed for the need of renovations. In addition to the experimental and analytical equipment in each of the nine departments, equipment for preclinical research includes shared facilities, such as autoclaves, ultracentrifuges, walk-in cold and freezer rooms; centrally managed dedicated space and secured alarm system for -80°/-90° C freezers for the secured storage of biological samples; laboratories for advanced-level DNA, RNA, protein and primary tissue culture and pathology research; dedicated facilities for radioactive and bacterial work. The institute houses core facilities for medical genetics, metabolomics, and microscopy (light, fluorescence, confocal, electron microscopes), high throughput screening (fluorimeter FlexStation and luminescence/scintillation counter TriLux Beta, LSR Fortessa FACS). The **Institute of Family Medicine and Public Health** is the core unit for the epidemiological research at UT, equipped with respective necessary facilities. It also houses and supports the infrastructure and activities of the **Clinical Guideline Unit** (*see section 3.8*) and the <u>Health Technology Assessment Centre</u>, both affiliated to the Estonian Health Insurance Fund.

The **Centre of Translational Medicine**, affiliated with the Institute of Biomedicine and Translational Medicine, includes a modern 3,000 m² animal house with ABSL laboratories, facilities to produce transgenic animals, in vivo imaging (9.4T small animal MRI and two-photon microscope), specialised laboratories for behavioural research and preclinical toxicity studies. The centre is certified according to ISO and GLP standards, allowing to perform the most demanding research.

The **Institute of Pharmacy** offers infrastructure for the analysis of pharmaceutical materials and physical solid-state characterisation methods, such as polarised light microscopy, Raman, NIR, FT-IR, and UV-Vis spectrophotometers, HPLC, gas chromatography, differential scanning calorimetry, etc. For the production of nanofibrous structures, needle-based, and needleless electrospinning systems are available. including a jointly patented technology with University of Helsinki – ultrasound-enhanced electrospinning. Diverse additional equipment includes 3D printers, cryogenic ball-mill, coating tools, rotary tablet press, high-shear granulator and rotary evaporator, climate chambers for testing of materials' stability, fully set up tissue culture and BSL II labs for antibacterial studies.

The new facilities (built in 2019) of the **Institute of Sports Sciences and Physiotherapy** are located next to the University of Tartu Academic Sports Club in the city centre, with all its diverse physical training facilities for indoor and outdoor sports, including water sports. All necessary equipment is in place for measuring physical performance or condition through life circle, from recreational to high-performance level, as well as in physiotherapeutic patients. Available equipment for physical activity measurements includes oxygen consumption sensors, different treadmills, isokinetic dynamographs etc. The institute holds a unique climate laboratory, which aims to study the resistance and adaptation of the human body to different extreme climatic conditions. There is also a Move Lab that focuses on the stimulation and measurement of mobility and physical activity of schoolchildren.

The National Centre of Translational and Clinical Research (CTM) represents a consolidated research infrastructure network shared by UT, TUH and the Estonian University of Life Sciences (PI: Prof. Külli Kingo, Dean, FM). The Clinical Research Centre (a joint unit of UT and TUH) is the national competence centre ensuring high-level medical experimental studies, academic clinical and pharmaceutical industry trials with the goal to further expand national and international competitiveness and cooperation in all aspects of healthcare. The centre provides ethical and data protection inputs for the proposals of biomedical and clinical studies, monitors the QC in clinical trials, and organises training courses, and is the primary national contact for international clinical studies.

Additional infrastructure for medical and health sciences-related research is available at the the **Institute of Genomics** and its affiliated **Estonian Biobank**, located in the Omicum building in the centre of Tartu. Various genotyping and sequencing core laboratory services are accessible to other academic units of UT. Core facilities for DNA analysis offer service for genome-wide genotyping

(Illumina iScan system) and Sanger Sequencing (Applied Biosystems 3730xl DNA Analysers; 3500xl Dx Genetic Analyser, also in compliance with IVD-R regulations). Service for short-read NGS is offered on Illumina HiSeq2500, MiSeq and NextSeq500 platforms. In 2023, Illumina NextSeq2000 was introduced, providing enhanced throughput, as well as Oxford Nanopore MinION and Oxford Nanopore PromethION 2 for long-range sequencing. The Genetics and Personalized Medicine Clinic of TUH houses the medical genetics laboratory (ISO15189 certified) with high-throughput Illumina NovaSeq X plus sequencers and a wide range of other platforms available to UT researchers.

For secure management and analysis of large-scale datasets, the UT central computational service facility <u>High-Performance Computing Centre</u> offers data storage, large computer clusters and shared memory servers, and more special dedicated GPU-based platforms to enable deep learning on large data. The storage service includes backup protocols to prevent any data loss or corruption. In addition, researchers in medical sciences have access to various other core service labs at the UT institutes, including proteomics and epigenomics research.

Finally, among European organisations relevant to the medical and health research, UT is a national contact point and responsible organisation of the European Strategy Forum on Research Infrastructures (**ESFRI**) objects: European Translational Research Infrastructure in Medicine (EATRIS), Biobanking and Biomolecular Resources Research Infrastructure (BBMRI) and The European Life-Science Infrastructure for Biological Information (**ELIXIR**).

2.3. Description of databases and collections.

Clinical and biomedical sample collections and respective databases at the Faculty of Medicine: The Institute of Biomedicine and Translational Medicine, and the Clinical Research Centre at the Institute of Clinical Medicine / TUH jointly house a diverse array of sample collections gathered over ~30 years and vital for biomedical research and innovative medical advancements. The cohort biosamples have been collected with TUH and other hospitals in Estonia. Notable examples:

The Human Microbiota Biobank (HUMB) with >30,000 biosamples for studying the properties of beneficial bacteria, opportunistic infections, and development of novel probiotics. The studies on HIV and HCV are bolstered by a collection of 30,000 serums. Research of E-HIV and COVID-19 are facilitated by the collection of 13,079 PBMC, 14,232 plasma, 13,178 serum and 28,124 RNA samples. The **Reproductive Biomedicine** biobank collected by the Chair of Human Genetics together with the Women's Clinic and Andrology Clinic is focused on the research of pregnancy disorders (HAPPY PREGNANCY and REPROMETA cohorts), andrological conditions (ESTAND cohort), and hypertension (HYPEST study). The biobank has an extensive collection of >167,000 diverse samples (DNA, RNA, serum, plasma, whole blood, urine, and placenta). Immunology biobank has been focused on the subtypes of diabetes (T1D, T2D, GDM) and includes over 6,500 biosamples (serum, plasma, gDNA, blood cell RNA, and PBMCs). Various clinical cohorts have recruited thousands of paediatric (e.g. DIABIMMUNE) and adult cases of cardiovascular conditions (stroke, peripheral vascular disease), dermatological and neurodegenerative (e.g. Parkinson's disease) disorders etc. A repository in pathophysiology houses 20,000 clinical biosamples from patients with skeletal and joint, dermatological, oncological, vascular, neurological, and mental health diseases. In addition, the neurophysiology research team has a collection of over 4,600 biosamples from patients with schizophrenia and respective mouse models, and a unique sample set of 500 human brain biopsies collected by the team of Pathological Anatomy and Forensic Medicine. Datasets in sports medicine include longitudinal monitoring of the physical activity and fitness, body composition and diverse health related parameters in children from puberty to adolescence.

Biomedical sample collections and databases in the Faculty of Science and Technology:

The Estonian Biobank (EstBB) collection housed at the Institute of Genomics includes samples and data from about 212,200 biobank participants. The biobank constitutes a single broad database, which can be subdivided into different subsets, all of which can provide useful input to R&D activities. Detailed data on the composition and accessibility of the EstBB dataset and samples is

provided <u>here</u>. The database of EstBB participants' health data is being updated annually and includes data from national registries, such as e-Health (EMR), Health Insurance Fund, Population Register, Causes of Death Registry, Cancer Registry, as well as registries of the Tartu University Hospital and North Estonia Medical Center.

As an affiliated sample set to EstBB, **Estonian Microbiome Cohort (EstMB)** has been collected, including samples (oral and fecal samples for microbiome studies, microbial DNA) and shotgun metagenomics sequences and health data from 2,509 participants and about 300 follow-up visits.

2.4. Connections between R&D activities and doctoral studies (where relevant).

FM has currently one PhD programme, Medicine and Sports (annual competitive admission 25–30 students) with 4 specialisations: Medicine, Pharmacy, Neuroscience, Exercise and Sports Sciences. In 2022, Estonia reformed the status of doctoral students, who are now hired as junior research fellows at UT. FM has offered the same status to all PhD students, irrespective of their enrolment year, and has supported their research and training from the faculty resources.

All PhD students are actively involved in nationally and/or internationally funded R&D projects, being closely integrated into scientific work – participating in research design, conducting independent experiments/analyses, interpretation and publishing the results. The PhD thesis in FM must be based on at least three articles published in peer-reviewed international journals with the doctoral candidate as the first author in two papers. Participation in project meetings and discussions fosters their research skills, sense of contribution, and prepares them for future success.

Doctoral studies in FM are among the most efficient PhD programmes in UT with a low dropout rate – 158 PhD theses in medical and health sciences were completed in 2018–2023. This is a noteworthy achievement as ~50% of PhD students continue working as clinical practitioners to maintain their professional competence. Several PhD students have two or more supervisors guaranteeing the quality of mentoring, especially in multidisciplinary projects. If relevant, doctoral projects may also have foreign co-supervisors, providing additional competence. PhD studies are supported by various activities such as research networking and transferable skills training, coordinated 2016–2023 by the Doctoral School in Clinical Medicine targeted not only to PhD students in FM, but also junior researchers in health sciences at the Faculty of Science and Technology. Since 2024 all PhD students belong to the Estonian Doctoral School.

High motivation and quality of the students' research at FM is evidenced by numerous National Awards for Doctoral studies. The Grand Prix across all PhD theses in Estonia in 2022 was awarded to Rasmus Pind (Sports Science). The 1st prize for the best doctoral thesis in medicine was awarded in 2019, to Mari-Anne Vals, and in 2020, to Pille-Riin Soodla for their top-level clinical research; in 2022, to Liis Preem for pharmaceutical research, and in 2023, to Anni Lepland for biomedical studies.

In 2018–2023, an additional 7 PhD theses related to health sciences and mostly based on the EstBB datasets were defended at the Institute of Genomics, Faculty of Science and Technology.

2.5.Principles of ensuring equal opportunities in the institution (if possible, please add a link to an English-language document).

UT aims to ensure the well-being of its members and guarantee that they have good working and learning conditions and are protected from unfair and unequal treatment. Acknowledging diversity, respecting the rights of the university members, and promoting equal treatment contributes to achieving the UT strategic goals, supports an encouraging learning and work environment, and values employees and students. If a member of UT (staff or student) suspects unequal treatment or bullying, they can turn to a <u>network of equal treatment support staff</u>, following the <u>Guidelines for equal treatment</u>. UT has adopted the <u>gender equality plan</u>, which is the first bigger step towards a broader and more systematic approach to gender equality. There are four goals, the implementation and progress of which will be monitored in the years 2022–2025. Both employees and students can use our <u>equal treatment webpage</u>, which collects explanations, guidelines, other important information, and further references.

Four of six FM institutes are led by female professors; also the dean and 3 of 4 vice deans are women. 2.6.Institution's opinion regarding aspects that need to be improved in the field of sustainability.

Aspects to be improved:

- Supporting the academic career of promising early-career researchers in medicine, health and sports sciences, e.g. by assisting their return to Estonia after a PhD or postdoctoral training abroad, in starting their own research groups and overcoming the challenges in combining work in a clinical, pharmaceutical or sports institution vs academic work;
- Finding solutions for competitive salaries in academia compared to the health sector in Estonia;
- Increasing the number of PhD candidate positions by seeking alternative available measures, e.g. industrial doctorates healthcare institution- or research project-funded PhD students;
- More effective involvement of international medical scientists at UT in the research and teaching;
- Investing into the competence and capacity of managing and analysing large datasets in (bio)medicine and public health research, including taking advantage of artificial intelligence.

3. Societal Impact of Research

3.1.Institution's description of the most important evidence-based examples of the societal impact of R&D activities.

Educating Estonian healthcare professionals:

- UT partners with the Ministry of Education and Research and the Ministry of Social Affairs in the development of medical curricula educating medical doctors (incl. residents) and pharmacists.
- In 2018–2023, FM delivered 745 continuing education courses in clinical medicine, pharmaceutics, health, and sports sciences to 29,135 participants from healthcare and the general public.

Translational research in medical and health sciences:

- The academic staff of FM has a key role in bringing the advances of medical sciences into clinical practice. This has a direct influence on the development of medical care in the entire country.
- R&D in cooperation in pharmaceutical and clinical studies with hospitals and private companies.

Managing the COVID-19 pandemic:

- UT made substantial contributions to addressing the health crises and making scientifically sound decisions during the COVID-19 pandemic, including Prof. **Irja Lutsar** (FM) serving 2020–2021 as the Head of the National Scientific Advisory Board to the Estonian government.
- Interdisciplinary research on COVID-19 development of facial masks and nasal spray against SARS-CoV-2 (**Prof. Karin Kogermann**), studies on immune reactions to SARS-CoV-2 (**Prof. Pärt Peterson**, **Prof. Kai Kisand**) and epidemiology of the pandemic (**Prof. Krista Fischer, Prof. Anneli Uusküla**).

Contribution to national decision-making and counselling bodies:

- UT is the principal partner with the Ministry of Social Affairs in the working groups of primary healthcare, and the development and implementation of the National Health Plan 2020–2030.
- UT is the principal partner with the Ministry of Culture in physical activity promotion and interventions and in the development of the physical education curricula in schools.
- Prof. Irja Lutsar, the leading spokesperson during the COVID-19 pandemic, was elected in 2023 to the Riigikogu, contributing to healthcare as a member of the Social Affairs Commission.
- Availability to stakeholders for advice on science-based innovation in health research and practice; **FM has** <u>66 spokespersons</u> (list available only in Estonian).
- FM and other UT faculties have conducted numerous public health-related <u>studies and analyses for</u> <u>the Estonian government</u> (list available only in Estonian).

Contribution to professional scientific bodies and events:

- Academic staff members of FM are involved at the highest level of EU scientific organisations or belong to the steering committees; UT medical researchers have contributed to European and Estonian Research Councils and act as expert-evaluators in different EU research calls.
- Societal impact through professional channels includes participation in the boards of professional societies in Estonia and internationally; contribution as (co)-editors or editorial board members of international scientific journals or programme committees of international scientific conferences.
- 11 (of 75) members of the Estonian Academy of Sciences, as well as nine (of 33) members of the Estonian Young Academy of Sciences are UT researchers active in the field of health and medicine.

Cooperation and contribution to patient organisations:

• FM has a tight collaboration with the Estonian Chamber of People with Disabilities and patient organisations in oncology, cardiology, neurology, rheumatology, pulmonology, nephrology, diabetes, and other diseases. The activities include educational events and creating materials for patients, and on the other hand, participation of patients in clinical research – clinical cohort studies, epidemiology and population registries, and preclinical biomarker studies. Patients are involved in the process of creating guidelines for disease management, and of applications and proposals for legal stakeholder institutions to develop innovative strategies and interventions.

Public outreach:

- During 04/2019 12/2023), in total ~<u>1500 media coverages</u> (~30 per month) (list available only in Estonian) by the academic staff of FM were delivered in the major newspapers and online news portals, on radio and TV; on most occasions, these communications were echoed in social media.
- 3.2. Generalised description of continuing education courses and consultations aimed at the general public.

The Faculty of Medicine is the main provider of continuing education courses and professional consultations in medical science and health-related topics in Estonia. During 2018–2023, the academic personnel of FM organised and delivered in total 745 educational courses (22,025 teaching hours; 3,670 teaching hours annually) aimed at a broad range of health professionals in Estonia and/or the general public. The number of different courses per annum ranged from 122 to 142. Overall, 249 online training courses (9545 hrs) and 496 onsite auditorial courses (12480 hrs) were taught. Notably, the number of participants nearly doubled during the evaluation period, from 3,128 in 2018 to 6,122 in 2023. Training opportunities included continuing education courses for practising health professionals; academic micro-credential programmes; and courses targeting the non-expert audience.

The continuing education courses targeting physicians and other healthcare professionals are mainly organised by the FM Centre of Continuing Education, offering a wide range of seminars, hands-oncourses, online courses, annual multidisciplinary conference KLIINIK to promote lifelong learning and increase knowledge, skills, and professional performance. In total, 470 training activities were offered and 19,000 learners received certificates.

FM is also offering micro-credential programmes delivering systematic training in specific medical topics: "Principles in health sciences" (12 ECTS, 312 hrs; online course); "Histology and fundamentals of histological techniques" (12 ECTS, 312 hrs; online and onsite); "Pharmacognosy" (12 ECTS, 312 hrs; online and onsite); "Genetics in Personalised Medicine" (24 ECTS, 754 hrs; onsite).

Other examples of targeted educational courses with broader impact are "Reintroducing medical doctors back to healthcare" (208 hrs), "Clinical pharmacy" (910 hrs), "Psychiatry in court proceedings" (104 hrs), "Advanced diagnostic methods and procedures" (104 hrs), "Physical activity education for leisure and physical literacy – training series" (94 hrs), "Congenital functional abnormalities of the face and jaw region. Teamwork" (78 hrs), "Training for staff of sexual violence crisis centres" (78 hrs), "Nutrition analysis. Self-restricted diets, different diets, and their evidence base" (45 h).

Additionally, the Institute of Genomics (Faculty of Science and Technology) organised the course "Implementation of Personalised Medicine in Estonia" in 2019–2023 targeting >900 healthcare professionals of various levels (8 hrs online, 8 hrs onsite; funded by the European Regional Development Fund).

3.3.Participation of R&D employees in state and/or business consultations related to R&D activities (e.g. participation in advisory bodies, administrative bodies, etc.); **counselling on important topics for the society.**

UT academic leaders play pivotal roles in advancing evidence-based medicine, driving innovation, making decisions in public health, and improving the quality of health and life in Estonia. Most of the academic staff in FM is involved in various professional committees and other bodies. Examples:

- UT academic staff served in the Scientific Advisory Board of the Estonian government during the COVID pandemic in 2020–2022 (Prof. Irja Lutsar, head of the board; Prof. Krista Fischer, Prof. Pärt Peterson and Prof. Ruth Kalda as the members).
- Prof. Irja Lutsar (Faculty of Medicine) was elected to the Riigikogu in 2023.
- 11 members of the Estonian Academy of Sciences are engaged in medical and health research: Prof. Mart Saarma (since 1990, molecular biology); Prof. Ain-Elmar Kaasik (1993; neurology), Prof. Raivo Uibo (2003, immunology), Prof. Eero Vasar (2010, physiology), Prof. Andres Metspalu (2010, genomics, biobanking), Prof. Toomas Asser (2011, neurosurgery; current Rector of UT), Prof. Jaak Vilo (2012, bioinformatics), Prof. Jaan Eha (2016, cardiology), Prof. Krista Fisher (2020, biostatistics), Prof. Maris Laan (2021, public health), Prof. Pärt Peterson (2023, biomedicine).
- Prof. Eero Vasar is the Head of the Committee on Medical Science and Health Strategy of the Estonian Academy of Science and a member of the council of Tartu University Hospital.
- Our staff consult the Ministry of Social Affairs of Estonia as advisors in pediatrics (Prof. Vallo Tillmann), neurology (Prof. Pille Taba), orthodontics (Dr Triin Jagomägi), forensic medicine (Prof. Marika Väli), primary health care (Prof. Ruth Kalda, Assoc. Prof Daisy Volmer), rare diseases (Prof. Katrin Õunap), dentistry (Dr Mare Saag); and hold critical roles in administrative bodies, e.g. immunoprophylaxis (Dr Marje Oona), nursing care (Dr Ere Uibu), disease screening programmes (Prof. Anneli Uusküla, Dr Kaja-Triin Laisaar), Estonian Board of Bioethics and Human Studies (Prof. Pärt Peterson, Dr Made Laanpere), working groups for the personalised medicine programme 2024–2034 (Prof. Ruth Kalda, Dr Sander Pajusalu, Dr Mikk Jürisson, Prof. Lili Milani, Dr Mait Metspalu, Prof. Jaak Vilo), patent safety and quality (Dr Liisi Mägi), steering group of the Estonian Cancer Action Plan (Prof. Jana Jaal, Dr Kadri Suija).
- Advisory committee on human rights, Estonian Chancellor of Justice (Dr Kai Part, Dr Made Laanpere as members)
- Contribution to the Clinical Guideline Unit in developing clinical guidelines and policy documents, e.g. the green papers on Alcohol Policy, Tobacco Policy, Nutrition and Physical Activity; to the Centre of Health Technology Assessment providing data for health policy discussions and decisions; and to various other working groups of the Estonian Health Insurance Fund for making decisions on nationally reimbursed healthcare services and medicinal products.
- Academic experts in pharmacy, pharmacology and clinical medicine participate in the committees of the Estonian State Agency of Medicines (Prof. Karin Kogermann, as the vice chair).
- Estonian Olympic Committee (Prof. Priit Kaasik, Vice-President; Prof. Jarek Mäestu, member)
- **3.4.Generalised description of participation of R&D employees in higher education activities** (number of lecture courses and students in the respective field, teaching of lectures, seminars and practicums both in and outside own institution and supervision of student theses).

Most R&D employees in FM are involved in academic teaching of future health professionals and/or coordinating clinical residency programmes, with the major contribution to healthcare quality in Estonia. Academic teaching load in FM staff during 2018–2023: 34,157 hours of lectures, 173,586 hours of practical classes, 63,323 hours of seminars.

In autumn 2023, FM was training a total of 1,882 undergraduate or master's students, and 206 PhD students. The total number of doctoral students in medical and health sciences is 312 – additional 106 PhD students iare enrolled in other faculties. In 2023, the number of medical students enrolled

in Estonian-taught integrated 6-year programme was nearly 980 and in English-taught programme, >140. The number of enrolled dentistry and pharmacy students (integrated 5-year programmes) was ~160 and ~100, respectively. The curricula "Physical education and sports" and "Physiotherapy" are divided into bachelor's and master's courses, both had ~140 BSc and 50 MSc students. In addition, the faculty offers special master's curricula "Public Health" (~40 enrolled students), "Nursing Science" (70 students) and "Clinical Nutrition" (English-taught, 7 students), as well as participates in the MSc programme "Biomedicine", jointly organised with the Institute of Molecular and Cell Biology (FST). Importantly, as the medical students' curriculum did not include student research thesis, a mandatory course "Research Work for Students" was developed for 2nd-year Medicine students and 4th-year Dentistry students aiming to promote their interest in sciences. Research-oriented students are encouraged to continue with a recently started elective course "Science track" providing additional knowledge and support in applying ethical permission, creation, and usage of medical datasets (e.g. in REDCap). The Pharmacy, Sports and Public Health medicine includes a mandatory course "Research Work", during which students must conduct research and write and defend their thesis (similarly to a master's thesis). For PhD student accomplishments, *see section 2.4*.

- **3.5.Organisation of cooperation events aimed at the society or community** (for example, an R&D institution as a partner that brings together parties from the private and public sectors to discuss topical issues).
- Various events introducing health related reports to the policymakers and society, e.g. "<u>Course</u> of the COVID-19 pandemic, measures implemented and lessons learned in Estonia" written and presented prof. Irja Lutsar.
- Participation at the <u>Annual Opinion Festival</u>
- School of oral health
- <u>Rare disease day</u>
- Involvement in national and international patient organisations
- Tartu Science Night as part of the Brain Awareness Week in Biomedicum (annually >300 visitors)
- The exhibition <u>"Gene-ius"</u> organised by the Institute of Genomics at the Tallinn TV Tower, won the "Nationally Recognised Science Communicator" title in 2020

3.6. Evidence-based examples of popularisation and dissemination of R&D results in society.

FM academic staff has <u>~30 media coverages monthly</u> (list available only in Estonian) (>2000 in 2018–2023) in major written media, online news portals, on radio and TV; on most occasions, these were echoed in social media. Examples:

During the **COVID-19 pandemic**, FM researchers were the major source in informing the public, stakeholders, and decisionmakers via all possible media channels about the progression and prognosis of the pandemic, vaccination against SARS-CoV-2, health-related behaviour during the pandemic and other relevant topics. Persons to be acknowledged from FM are **Prof. Irja Lutsar** (medical virology), **Prof. Pärt Peterson**, **Prof. Kai Kisand** (molecular immunology), **Prof. Joel Starkopf** (intensive care), **Prof. Ruth Kalda** (COVID-19 surveillance study). Additionally, **Prof. Krista Fischer** (statistics) from the Institute of Mathematics and Statistics, and **Prof. Tanel Tenson** and **Prof. Andres Merits** (molecular virology and microbiology) from the Institute of Technology were in the forefront of public outreach during COVID-19the pandemic.

The researchers of FM have delivered ~<u>60 interviews (20 min each) in the Kuku Radio series</u> <u>"Behind the Six Pillars"</u> (list available only in Estonian).

Prof. Mihkel Zilmer (medical biochemistry) has published highly demanded books "Normal eating" (updated version 2019), "Normal drinking" (e-book 2024) and a long list of other popular books on human biochemistry. In 2018, the Estonian Research Council awarded him the Lifetime achievement award for long-term systematic communication of science and technology. Also Prof. Ain Raal (pharmacy) has published popular books "Estonian medicinal plants 1–3" (2018–2020), among numerous other publications to lay public. In the National Science Communication Award

competition 2023, **Tiiu Rööp**, a junior research fellow in Medical Microbiology, was awarded **the** grand prize in the category "Popularisation of Science and Technology through Audiovisual and **Electronic Media**" as she has edited and hosted over **455 science-popularising radio programmes** in nine years.

Outside of FM, the Institute of Genomics has been also very active in public outreach. Their activities are communicated to media ~250- 300 times a year, and a notable subset of this outreach concerns analysis of the EstBB data on health-related topics. **Prof. Andres Metspalu** – the establisher and head (until 1 February 2024) of the EstBB, received the **Lifetime achievement award for long-term systematic communication of science and technology** in 2022.

3.7. Participation of R&D employees in national and international working groups and networks (list the names of the organisations and bodies).

Prof. Andres Metspalu – EU Cancer Mission Board (2019–2022); "1+ Million Genomes" initiative Prof. Helle Karro – European Board and College of Obstetrics and Gynaecology, Secretary-General Prof. Jaak Jürimäe – International Association of Sport Kinetics, Board Member; Baltic Sport Science Society, 2018–2021 President, 2021 – Vice-President

Prof. Janika Kõrv – Nordic Stroke Society, Chair 2015–2019; European Stroke Organisation; cocoordinator, <u>The Stroke Action Plan for Europe</u>

Prof. Jyrki Heinämäki – Steering Committee of the Nordic POP Researcher Network

Dr Kadri Medijainen – WHO Development group of the Package of Rehabilitation Interventions for Parkinson's disease, the European Reference Network for Rare Neurological Diseases Neurorehabilitation group

Dr Kadri Suija – Association of European Cancer Leagues, Patient Support Working Group Dr Kai Part – WHO sexuality education excellence group

Prof. Karin Kogermann – European Pharmacopoeia expert committee Group 12

Prof. Külli Kingo – European Union of Medical Specialists (UEMS), national representative in the Section of Dermatology and Venereology

Prof. Marika Väli – European Council of Legal Medicine, executive committee

Prof. Pille Taba – European Section of the International Parkinson and Movement Disorders Society, Chair; Movement Disorders Panel of the European Academy of Neurology, Co-Chair

Prof. Ruth Kalda – European Academy of Teachers of General Practice/Family medicine (EURACT), Council Member

Dr Triin Jagomägi – Academy of Applied Myofunctional Sciences (AAMS), Vice-President Dr Ülle Voog-Oras – Scandinavian Association for Dental Research, President

3.8. Publicly available publications, databases, products/services created as a result of R&D activities.

• Over 70 scholarly peer-reviewed articles in the Estonian language on various topics of medicine in the journal "Eesti Arst" (<u>Estonian Doctor</u>)

FM staff have been extensively contributing to national healthcare-related documents, for example:

- <u>Long-term Personalised Medicine Programme for 2024–2034</u> (Prof. Ruth Kalda as the PI), (available only in Estonian).
- Estonian Human Development Report 2023: Mental health and well-being.
- Estonian National Cancer Control Plan 2021–2030, (available only in Estonian).
- Analysis of COVID-19 cases and the risk groups, the CORIVA database.
- Nasal spray for bovine colostrum-derived antibodies against SARS-CoV-2.
- <u>COVID-19 preparedness plan for the 2022/2023 virus season</u> (only available in Estonian).
- At least eight national evidence-based clinical guidelines per year, coordinated by the <u>Clinical</u> <u>Guidelines Unit</u>.
- ~8 large-scale health technology assessments per year for the Estonian Health Insurance Fund and the Ministry of Social Affairs (a list of reports available <u>here</u>).
- 3.9. Other facts showing societal impact and cooperation of R&D.

Prof. Tambet Teesalu (nanomedicine), in collaboration with TUH, has initiated a Phase 2a proof-ofconcept, double-blind, placebo-controlled, randomised <u>study</u> evaluating the performance a novel developed drug LSTA1 (certepetide) for the treatment of solid tumours in subjects with newly diagnosed glioblastoma multiforme.

Prof. Maris Laan and **Prof. Kristiina Rull** are leading a <u>translational project</u> in three largest women's clinics of Estonia – "Estonian Pregnancy Research" (ESTPRE), evaluating the performance of a novel multimarker test in predicting the risk to preeclampsia in the first trimester already.

Prof. Külli Kingo has led the project "Comprehensive monitoring of psoriasis patients along the treatment pathway and prevention of relapses", supported by the Estonian Health Insurance Fund and performed together with the company Dermtest OÜ and a network of general practitioners.

3.10. Institution's opinion regarding aspects that need to be improved in the field of societal impact of research.

Aspects to be improved:

- Improve training and motivation of researchers to explain their R&D outside of academia;
- Strengthen engagement with policymakers and stakeholders to translate research findings into actionable policies that will enhance the quality and efficiency of healthcare;
- Expand online presence utilise social media and blogs to actively share research results and to bring evidence-based health information to general audience;
- Widen the societal impact of physiotherapy research, especially targeting the fitness and physical activity of the elderly people.
- Increase the academia industry collaboration to foster innovation and science-based business development, create added value in transferring scientific knowledge to practical applications, and drive economic growth.

The institution may ask the committee for feedback on up to three more specific R&D aspects that are important to the institution at the given time.

- 1. Advice on effective measures to promote the attractiveness of the academic career to MDs, both clinical practitioners and researchers outside of academia and abroad.
- 2. Recommendations on the communication strategies towards policymakers about the high value and urgent need for stable funding for longitudinal studies in clinical, biomedical, pharmaceutical, public health and sport medicine related research.
- 3. Advice on measures to further broaden the dissemination of medical research to the lay public to promote evidence-based health behaviour and disease prevention.