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MEDICINA
Volume 57, Supplement 1, 2021
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CONTENTS

MEDICINA
Volume 57, Supplement 1, 2021
ISSN 1648-9233
Issued since 1920

MEDICINA
ISSN 1648-9233
Issued since 1920
Volume 57, Supplement 1, 2021

MEDICINA
Volume 57, Supplement 1, 2021
ISSN 1648-9233
Issued since 1920

MEDICINA
Volume 57, Supplement 1, 2020
ISSN 1648-9233
Issued since 1921

MEDICINA
Volume 57, Supplement 1, 2021
ISSN 1648-9233
Issued since 1920

MEDICINA
ISSN 1648-9233
Issued since 1920
Volume 57, Supplement 1, 2021

MEDICINA
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Issued since 1920

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ISSN 1648-9233
Issued since 1920
Volume 57, Supplement 1, 2021

MEDICINA
ISSN 1648-9233
Issued since 1920
Volume 57, Supplement 1, 2021

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Volume 57, Supplement 1, 2021

Oral presentations

BASIC MEDICAL SCIENCE & PHARMACY

Mitochondrial oxygen consumption and ROS emission demonstrated in a *mouse model* of *ischemic stroke*

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Background. Cerebral ischemia, a condition caused by an insufficient blood flow to the brain, is the most common form of stroke. Worldwide, stroke is the second leading cause of death (Johnson et al., 2016). Mitochondria are critical for the maintenance of cellular homeostasis and their dysfunction play an essential role in the ischemic neuronal death. Mitochondria-generated reactive oxygen species (ROS) are involved in physiological signalling and in mediating tissue injury after ischemia-reperfusion (Stepanova and Galkin, 2020).

Aim. To investigate the mitochondrial respiration and ROS emission in both cerebral hemispheres 1 hour after the middle cerebral artery occlusion and 24, 72, 168 hours after reperfusion in stroke model mice.

Methods. The intraluminal monofilament model of 60 minutes middle cerebral artery occlusion (fMCAo) and followed by reperfusion was performed in C57BL/6NHsd male mice (10–12 weeks old; n=6–8 per group). Mitochondrial Complex I, II and III linked respiration and ROS emission in the form of hydrogen peroxide were analysed in the tissue homogenates of both hemispheres by using the high-resolution fluorespirometry.

Results. The oxygen consumption data obtained directly after 1-hour artery occlusion procedure revealed that the complex I, II and III linked respiration rate and OXPHOS state capacity was significantly lower in fMCAo mice ipsilateral hemisphere (ischemic hemisphere) compared to contralateral hemisphere (non-ischemic hemisphere). The maximal oxygen flux in the ipsilateral hemisphere of fMCAo mice was observed 168 hours after procedure, but the minimal – 24 hours after procedure. The ROS production in the ipsilateral hemisphere of fMCAo mice was the highest 1 hour after stroke and the lowest – 24 hours after.

Conclusions. Dysfunction of the mitochondrial oxidative phosphorylation system and increased ROS release are early markers seen in the ischemic stroke.

Acknowledgements. This study was supported by the ERA-NET project "Multi-scale investigation of synaptic dysfunction after stroke (MISST)" No. ES RTD/2018/29 and the UL Research Grant "Research of biomarkers and natural substances for acute and chronic diseases, diagnostics and personalized treatment".

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COX-LOX inhibition: current evidence for anti-inflammatory *Vaccinium* spp. berry extract properties *in vitro*

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Background. The arachidonic acid (AA) pathway is the root cause of several inflammatory diseases, including asthma, atherosclerosis, irritable bowel syndrome, rheumatoid arthritis, and cancer. AA metabolites are biosynthesized by cyclooxygenase (COX) and lipoxygenase (LOX) enzyme pathways. Recently, we published data on the polyphenol content and profile in five *Vaccinium* spp. berry pomace extracts (Muceniece et al., 2019), as well as showed that these extracts inhibit NF-kB pathway in LPS-stimulated THP-1 monocytes and COX2 activity (Kunrade et al., 2020). However, the effects of the berry pomace extracts on the AA metabolism are not fully researched.

Objective. The aim of the current study was to evaluate effects of five *Vaccinium* spp. berry pomace extracts on AA metabolism *in vitro*.

Methods. Inhibition of COX1, COX2, LOX5 and LOX15 activity by bilberry, blueberry, American cranberry, cranberry and lingonberry pomace extracts was assessed in parallel with corresponding enzyme inhibiting reference drugs such as SC560, celecoxib, zileuton and NDGA. Enzyme activities were measured using commercial enzyme inhibitor screening fluorometric kits (BioVision Inc. and Cayman Chem, USA). Fluorescence was measured using a Tecan Infinite 200 PRO plate reader and i-control software.

Results. Extracts did not influence LOX15 activity but showed concentration-dependent inhibition of other enzyme activities. 30% to 50% of COX1 inhibition was reached at 1 mg/ml concentration of extracts, whereas COX2 inhibition was much stronger than that of COX1. All extracts at concentration 1 mg/ml showed more than 50% to 80% inhibition of COX2 activity. American cranberry extract showed the most powerful LOX5 inhibitory effect (76% inhibition at 1 mg/ml) whereas lingonberry, blueberry and bog cranberry extracts possess similar effects (60–65% inhibition). A strong, positive correlation was found between the content of polyphenols with the extract ability to inhibit LOX5, whereas the content of anthocyanins correlated with an increased extract inhibitory effect on COX2 and COX1 activity.

Conclusion. Inhibition of both LOX5 and COX enzyme activities shows that the extracts affect two metabolic pathways of arachidonic acid. Dual inhibition of COX2/LOX5 enzyme is currently considered to be a new direction in the development of novel anti-inflammatory drugs with a better therapeutic safety profile.

Acknowledgements. The study has been supported by fundamental research grant in Biomedicine and Pharmacy "Research of biomarkers and natural substances for acute and chronic diseases' diagnostics and personalized treatment", the Faculty of Medicine, University of Latvia.

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The impact of Sigma 1 receptor on the adipogenesis and osteogenesis of mouse adipose-derived mesenchymal stromal cells

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Background. Sigma-1 receptor (S1R) is a chaperone protein at the endoplasmic reticulum. S1R dysfunction has been associated with neurodegenerative phenotypes and its ligands display neuroprotective effects (Ryskam et al. 2019). Recently it has been reported that adipogenesis is impaired in S1R-/- mouse embryonic fibroblast cells indicating that S1R might play a role in the regulation of adipogenesis (Yang et al. 2020).

Aim. The aim of the current study was to investigate the role of S1R in mesenchymal stromal cell (MSC) fate decision towards adipogenesis and osteogenesis.

Methods. Stromal vascular fraction (SVF) cells were isolated from adipose tissue of CD1 background wild-type (wt) and S1R knock-out (-/-) mice. Cell cultures were expanded in the presence of EGF and FGF2 and characterized for MSC marker CD44, CD29, SCA-1, CD105 expression and lack of hematopoietic marker CD45 using flow cytometry. Three S1R-/- and four wt cell lines were selected for further adipodifferentiation and osteodifferentiation. Adipogenesis was induced by indomethacin, 3-isobutyl-1-methylxanthine, dexamethasone and insulin for 2 weeks, osteogenesis was induced by β-glycerolphosphate, dexamethasone and vitamin C for 3 weeks. Cytochemical staining was performed to assess lipid accumulation by Oil Red O stain while calcium accumulation was assessed by Alizarin Red staining. Gene expression of adipogenesis markers *CEBBPA, PPARG, FABP4, Adiponectin* and osteogenesis markers *Runx2, Osteopontin, Osterix* and *Osteocalcin* was analysed by qPCR.

Results. MSC markers were expressed on wt and S1R-/- MSCs. The authors observed decreased adipogenesis marker expression in S1R-/- MSCs comparing to wt MSCs. After adipodifferentiation *CEBPA* expression was decreased on average six fold in S1R-/- cells. Lipid accumulation was unchanged in S1R-/- adipodifferentiated cells comparing to wt.

Osteogenesis marker expression was induced in three out of four tested cell lines of wt as shown by increase in *Runx2* and *Osteocalcin* expression. However, in S1R-/- cells osteogenesis marker expression remained unchanged following osteodifferentiation. Interestingly *Osterix* expression was remarkably induced in all S1R-/- MSC lines comparing to differentiated wt MSCs.

Conclusion. The authors conclude that S1R has an impact on the interplay between upstream transcription factors *CEBPA* and *Osterix*, which suggests that S1R might influence the fate decision in adipose stromal vascular fraction MSCs.

Acknowledgements. The authors declare the absence of conflict of interest. This study was supported by UL fundamental research grant "Research of biomarkers and natural substances for acute and chronic diseases' diagnostics and personalized treatment".

Target protein identification of MDA-MB-231 cell line selective aptamer

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Background. Triple-negative breast cancer cell line MDA-MB-231 selective aptamer Seq36 has been previously identified by our group using cell-SELEX approach. Further screening of aptamer selectivity on multiple cell lines was done using flow cytometry. Before any further development of Seq36 aptamer as a targeting ligand for the use in vivo, it is important to understand the molecular mechanism of action.

Aim. The aim of the current study was to determine the target protein for breast cancer cell line selective aptamer Seq36.

Methods. Adherent cells grown in a monolayer in T150 flask were lysed using 500 µL of 50 mM Tris pH 8.0, 150 mM NaCl, 1% NP-40 for 1 h on ice. Randomized aptamer library labelled with biotin and Seq36 aptamer labelled with biotin were folded at 1 µM concentration by heating at 95°C for 5 minutes followed by cooling on ice for 15 minutes. Aptamers were immobilized on 100 µL of Dynabeads™ MyOne™ Streptavidin C1(ThermoFisher) beads for 1 h at room temperature. Excess aptamers were washed away using PBS/0.025% Tween-20. Cell lysate was added to magnetic beads and incubated at 4 °C overnight. Beads were washed 8 times with PBS/0.025% Tween-20 and bound proteins were eluted with 1 µM random aptamer or Seq36 aptamer without biotin. Samples were run on 10% SDS-PAGE and stained using SilverQuest™ Silver Staining Kit (ThermoFisher). Protein bands of interest were cut out and sent for mass spectrometry proteomics analysis at Proteomics core facility at the University of Tartu.

Results. Based on the comparison between control and target samples from mass spectrometry proteomics results using emPAI values, heterogeneous nuclear ribonucleoprotein A1 (HNRNPA1) and heterogeneous nuclear ribonucleoprotein A2/B1 (HNRNPA2B1) were the most abundant proteins present in the Seq36 aptamer bound samples.

Conclusion. Seq36 aptamer interaction with target cells is likely to depend on the binding to hnRNP proteins. Further siRNA knock-down experiments are necessary to validate the target.

Acknowledgements. This work was supported by UL fundamental research grant "Research of biomarkers and natural substances for acute and chronic diseases' diagnostics and personalized treatment". K. Pleiko was supported by PhD research scholarship administered by the University of Latvia Foundation and funded by "Mikrotīkls" Ltd. and ERASMUS scholarship.

Protein quantification in green microalgae *Monoraphidium griffithii* biomass using Lowry and Bradford methods

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Background. Novel green microalgae *Monoraphidium griffithii* is still a very little investigated object which in its chemical composition contains various active substances. In studies, the proteins in *M. griffithii* have showed anticancer and anti-inflammatory activity. These proteins also have demonstrated antioxidant activity, and, consequently, they can be used in prevention or treatment of such globally widespread illnesses as various cardiovascular and liver diseases and cancer.

Aim. The aim of this study was to assess protein content in green microalgae *Monoraphidium griffithii* biomass (Kursiu marios were sampled for *Monoraphidium griffithii* in 2012).

Methods. Lowry and Bradford methods were used to determine the protein content in biomass. Using Lowry method, the protein extract from Monoraphidium griffithii was treated with Lowry reagent (copper sulphate, sodium tartrate, sodium carbonate and distilled water) and 1N Folin reagent. To determine the protein content of the biomass, the light absorption of solution was measured with a photometer at 650 nm. Using Bradford method, the same protein extract which was used in Lowry method was treated with Bradford reagent (Coomassie brilliant blue dye Roti®-Quant (Carl Roth, Germany)). The light absorption of solution was measured with a photometer at 595 nm. The protein content was calculated using MS Excel program® for both methods. Each evaluation was repeated three times and expressed as an average with standard deviation (x±SD).

Results. The protein concentration determined using Lowry method was 0.8±0.07 g/mL, and compared to concentration determined using Bradford method (0.36±0.07 g/mL), it was much higher. In regards of protein content per raw material (mg) using Lowry method was almost twice as high compared to Bradford method. Accordingly, there was 2.71 mg/g and 1.24 mg/g of protein content per raw material.

Conclusion. The differences between measured protein quantification with both methods could be caused by interfering substances in the reagents. It is known that, when using Bradford method for protein quantification, some of the proteins could not be measured because compounds in the dye interfere with light absorption. Despite the fact that Lowry method is much more complicated and time-demanding in comparison with Bradford method, it shows a much higher protein content and therefore a much wider qualitative spectrum of proteins could be found in chemical composition of *Monoraphidium griffithii* biomass.

Acknowledgements. The research was implemented in Lithuanian University of Health Sciences as a part of master's thesis. The authors declare the absence of conflict of interest.

Human organoid model to study the role of peripheral nervous system in pancreatic cancer

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Background. If placed in right culture conditions, mammalian cells can self-organise in 3D structures called organoids that recapitulate some of the structural and functional properties of the tissue of origin. They can be established from various human tissues that contain adult stem cells and provide an opportunity to study the aspects of development, regeneration and disease in a personalized way. Over the last few years, the use of organoids in pre-clinical studies has emerged as a widely accepted alternative to 2D *in vitro* cultures. There is an increasing public need for therapies for pancreas-related conditions like diabetes, exocrine pancreatic insufficiency and cancer. Organoid systems are already used to model pancreatic cancer and to study morphogenesis and differentiation of this organ. Lately, protocols to obtain adult human pancreatic tissue organoids (hPOs) and maintain them for long periods in culture have been described.

Aim. The aim of the current study is to derive hPOs from pancreatic tumour tissue, characterise them and establish a co-culture setup with peripheral nervous system (PNS) glial cells.

Methods. Primary tissue digestion and subsequent culture in a basement membrane matrix is performed. Cells within the organoids are characterised using immunofluorescence based on characteristic markers. Pre-aggregation of hPO cells and glial cells to establish co-culture organoid structures is tested.

Results. We will present the data on organoid derivation and co-culture attempts, including organoid expansion, morphology and expression of pancreatic epithelial (KRT19, SOX9), progenitor (PDX1, GATA6), tumorigenic marker (MUC5AC) and glial markers (in co-culture setup).

Conclusion. Successful hPO derivation and co-culture with glia provide opportunity for further validation of the organoid model and studies on the role of PNS in pancreatic deficiencies.

Acknowledgements. Authors declare the absence of conflict of interest. The study is funded by Latvian Council of Science project No. lzp-2020/2-0208 and a postdoctoral research project No. 1.1.1.2/VIAA/4/20/623.

Antimicrobial effect of Latvian polyherbal formulation in combination with essential oils

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Background. In recent years, polyherbal formulations have gained a greater interest due to their potential to cure wound infections and as an alternative to antibiotics. New polyherbal formulation "*Velvet*" from Latvian vulnerary plants was prepared, and its antibacterial efficacy was studied. In addition, essential oil (EO) combinations with "*Velvet*" were tested in hope to enhance antimicrobial effect on Gram(-) bacteria.

Aim. The aim for this study was to examine whether polyherbal formulation "*Velvet*" can potentially inhibit the growth of bacteria and can be used to treat skin infections. When it became clear that "*Velvet*" is effective only on Gram(+) bacteria, our aim was to test if EO could reduce Gram(-) resistance to "*Velvet*" alone.

Methods. Agar dilution method was used. We incorporated polyherbal combination into liquefied agar. After mixture solidified, bacteria were inoculated and Petri plates were incubated overnight at 35°C. After that, colonies were counted and compared with controls.

We used laboratory microorganism strains from microbial collection most frequently involved in wound infections, such as *S. aureus, E. faecalis, P. aeruginosa. K. pneumoniae, E. coli and P. mirabilis.*

In the study, the following EO were used: *Origanum Vulgare L., Pinus Sylvestris L., Mentha Piperita L.* and *Thymus Vulgaris*.

Formulation is considered bacteriostatic if growth of 99.5% of colonies is suppressed.

Results. "Velvet" without any additional compounds showed bacteriostatic properties on both tested Gram(+) bacteria (*S. aureus, E. faecalis*), but it was effective only on one out of four tested Gram(-) microorganisms.

Bacteriostatic effect on *S. aureus* reached 99.99%; SD 0.01. For *E faecalis*, it was 99.99%; SD 0.005, and for *P. aeruginosa* it was 99.75%; SD 0.14. However, Gram(-) bacteria, *K. pneumoniae, E. coli and P. mirabilis* were not inhibited by the "Velvet".

When combined with "Velvet", essential oils of *Origanum Vulgare L., Pinus Sylvestris L., Mentha Piperita L.* and *Thymus Vulgaris* were effective and suppressed *E. coli* and *S. aureus* growth by 100 % in all trials.

Conclusions. The study showed that polyherbal formulation "Velvet" possesses bacteriostatic properties on Gram(+) bacteria, but does not inhibit growth of Gram(-) bacteria.

All of the used EOs in combination with "Velvet" suppressed growth of *E. coli*, which supports our hypothesis that "Velvet" could be combined with EO in order to make it efficient for combined skin infections.

Acknowledgements. The research was a part of project supported by Latvian Academy of Sciences "Studies on Latvian candidate herbs in combination and the efficacy of chronic wound healing".

Towards safe medication use among geriatric patients: a combined tool for identification of potential drug-related problems

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Background. Drug-related problems (DRP), including potentially inappropriate medications (PIMs), are a common problem in older people with multi-morbidity and polypharmacy. It is important to identify appropriate tools, preferably adjusted to specific patient groups, to deal effectively with potential or existing DRPs. Our hypothesis is that combining PIM identification tools enables to significantly enhance the determination of DRPs.

Aim. To develop a combined tool for identification of DRPs in geriatric multi-morbid and polypharmacy patients, using the EU(7)-PIM and EURO-FORTA lists, with a focus on high-risk medications.

Methods. The combined PIM identification tool used the information on PIM active ingredients in the EU(7)-PIM and EURO-FORTA databases. The PIMs were classified into four colour groups based on risk profile: very significant PIMs (should be avoided in older patients) as red, significant PIMs (require dose and/or treatment duration adjustment) as yellow, non-significant PIMs/non-PIMs (low DRP risk) as green, and questionable PIMs (incomplete/missing information) as grey.

Results. The summarized list of the red PIMs contains 34 active ingredients, including one combination of two medications and one medication class. According to the ATC (Anatomical Therapeutic Chemical) classification, most of the red PIMs (n=27, 79.4%) belong to the A, C and N medication groups, and only 41.2% of the red PIMs have marketing authorization in Estonia. In 2019 more frequently used red PIMs in Estonia were sodium picosulfate (DDD=4.3637), propafenone (DDD=3.5699), ginkgo biloba (DDD=2.3355), magnesium hydroxide (DDD=1.187), and dextromethorphan (DDD=0.6223). The approximate number of the yellow and green PIMs is 248, but sub-classification of this category into one or another group depends mainly on an individual patient´s clinical characteristics. The complete list of the grey PIMs will be developed in the future

Conclusion. The combined PIM tool based on the EU(7)-PIM and EURO-FORTA criteria was created to address the need for more efficient identification of DRP in geriatric multi-morbid patients. The tool was developed with a focus on the high-risk medications for older adults and taking into consideration the availability of the PIMs in Estonia. The tool could potentially be applied as a screen to identify DRPs in different health care settings.

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Individualised assessment of primary central nervous system lymphoma: the role of immunohistochemistry

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Background. Primary central nervous system lymphoma (PCNSL) is defined as an aggressive, rare, mostly diffuse large B-cell (DLBCL) type, with no evidence of dissemination outside the CNS. With no disease-specific criteria, current PCNSL prognostic models are still used to determine patient's prognosis and treatment options. In contrary to the old models, immunohistochemistry allows to reveal the unique molecular features of PCNSL, biologically distinct from the systemic counterpart, to make a PCNSL prognosis more accurate and case-specific.

Aim. The objective of this study was to perform an immunohistochemical phenotype analysis of patients diagnosed with PCNSL. To determine the DLBCL subtype, to evaluate its correlation with clinical outcomes, aggressiveness of the disease and to identify important prognostic features.

Methods. Cases of immunocompetent adults diagnosed with PCNSL were retrospectively analysed. Clinical data including age, sex, immunologic status, imaging and biopsy results, treatment method, and outcome were obtained from medical records. Patients were subclassified to a germinal centre B-cell (GCB) and activated B-cell (ABC) subtype based on immunohistochemical phenotype. Clinical outcomes, mortality rate, deep regions' involvement, Ki67 and other markers' expression were compared between the subtypes. Descriptive statistical analysis was completed using R studio, p-values<0,05 were considered as statistically significant.

Results. A total of 36 patients were included in the sample. 44% of them were males (n=16) and 56% were females (n=20). The average age of patients was 61.08 (SD±9.47 years). 54% of the cases had a non–germinal centre B-cell phenotype (ABC) and 49% were identified as a germinal centre B-cell PCNS type based on CD10, BCL6 and MUM1 expression. BCL2 and MYC coexpression (53%) was frequent. 33% had multiple brain lesions, 61% had deep brain regions involved, statistically significantly (p-value=0,02) more often in the ABC subtype. The total of 8 patients died (n=6 in ABC and n=2 in GCB subgroup), 75% due to progression of the tumour. High Ki67 (>90%) was statistically significantly more often in the ABC subtype (p-value=0.03).

Conclusion. PCNSL ABC subtype dominated insignificantly. Half of patients had MYC/BCL2 coexpression regarding its reported contribution to the inferior survival. Single lesions were dominant. Higher Ki67 expression and involvement of deep brain regions were statistically significantly more often observed in the ABC subtype.

Acknowledgements. The authors declare the absence of conflict of interest and confirm that no funding has been received for the study.

Structural aspects of neuroimmune interactions in the intestinal mucosa

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Background. Mucosal sentinel cells, including epithelial cells, intraepithelial lymphocytes (IEL), dendritic cells and mast cells continuously sense the environment and coordinate defences for the protection of mucosal tissues. However, the immune system does not work in isolation. It acts in concert with nervous system.

Aim. The aim of this research was to study the structural relationships between mucosal sentinel cells and nerve fibres.

Methods. Duodenal biopsies from 12 patients with symptoms of malabsorption were studied. Biopsies were obtained from grossly normal areas of the mucosa. Tissue sections were stained for S100 protein to demonstrate nerve fibres and myeloid dendritic cells (MDC), for calretinin (nerve fibres), for CD8 to demonstrate intraepithelial lymphocytes (IEL) and lymphoid dendritic cells (LDC), and for mast cell tryptase.

Results. CD8 positive IEL and LDC are distributed in the intestinal epithelium and found both along the basement membrane and between epithelial cells in the lateral intercellular space. LDC often extend their processes through the intercellular spaces between absorptive enterocytes and goblet cells. It is known that soluble antigen is transported through the goblet cell from the apical to basolateral membrane where it is passed to closely adherent underlying LDC.

Both calretinin positive and S100 positive fibres were observed in subepithelial stroma. In this area they were devoid of Schwann cells. After reaching the basement membrane, axons then abruptly turn 90° and run adjacent to it, suggesting that within this area they are structurally connected to the IEL, LDC and goblet cells. Indeed, their localization adjacent to axons favours coordinated actions in response to the antigen invasion. Likewise, mast cells and MDC are closely apposed to nerve fibres in the *lamina propria*.

Conclusion. Our study showed close spatial relationships between nervous and immune system in the intestinal mucosa. It facilitates neuroimmune crosstalk to maximize survival. Thus, during immune responses (e.g., allergic responses) in mucosal tissues, nerve fibres effectively stimulated by numerous local sentinel cells send signals to parasympathetic ganglia and CNS and initiate "protective reflexes", which are associated with nausea, diarrhoea and vomiting.

Role of *IL-10* polymorphisms and IL-10 serum levels in laryngeal squamous cell carcinoma carcinogenesis and impact on survival rate

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Background. In all respiratory tract malignancies, laryngeal squamous cell carcinoma (LSCC) ranks the second in terms of the highest mortality rate. Results of LSCC treatment and the five-year survival rate of these patients remain poor. To clarify therapeutic targets and improve survival rate, identification of new specific and prognostic biomarkers of LSCC is required.

Aim. The study aimed to evaluate the impact of *IL-10:* rs1800871, rs1800872, and rs1800896 single nucleotide polymorphisms (SNPs), and IL-10 serum levels on LSCC development and analyse associations of selected SNPs with patient survival rate.

Methods. A total of 833 subjects (300 h*istologically verifed LSCC* patients and 533 control subjects) were included in this study. The genotyping of *IL-10:* rs1800871, rs1800872, and rs1800896 was carried out using the real-time polymerase chain reaction; IL-10 serum concentrations were measured in 20 subjects of the control group and 20 patients of the LSCC group and were analysed by Enzyme-Linked ImmunoSorbent Assay (ELISA).

Results. Significant associations were identified between *IL-10* rs1800871 variants and advanced stage of LSCC patients' group in the codominant, recessive and additive models (OR=0.473, p=0.027; OR=0.510, p=0.040; and OR=0.733; p=0.037). Significant variants of IL-10 rs1800872 were determined in the codominant, recessive and additive models (OR=0.473, p=0.027; OR=0.510, p=0.040; and OR=0.733, p=0.037). No statistically significant differences of IL-10 serum concentration between the control and LSCC groups (10.3 pg/ml ±15.99 vs. 14.6 pg/ml ±2.61; p=0.579) were identified.

Conclusion. *IL-10:* rs1800871 and rs1800872 SNPs are associated with the development of advanced stages of LSCC. The genotypic distribution of *IL-10:* rs1800871, rs1800872, and rs1800896 SNPs did not impact survival rate of LSCC patients (respectively, p=0.952; p=0.952; p=0.991).

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Evaluation of biochemical and genetic parameters as potential biomarkers for multiple sclerosis

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Background. Previous studies indicate various possible reasons for multiple sclerosis (MS). DNA damage and products of lipid peroxidation are some of the most potent biomarkers for oxidative stress. Overproduction of nitric oxide synthases (NOS) is associated with many disorders, including inflammation and MS. The most potent way to detect NOS activity is by evaluating levels of nitrites and nitrates in physiological fluids. Some studies also correlate MS with polymorphisms in ATM, PARP1, XPC, XPA, and XRCC1 genes.

Aim. This study aimed to evaluate different potential biomarkers in whole blood, plasma, and serum of patients with MS.

Methods. 25 randomly selected patients with MS and 25 healthy subjects were chosen for this study. Nitrates and nitrites were analysed by chemiluminescence on Sievers NOA 280i in plasma and serum samples. Enzymatic alkaline comet assay was performed on isolated PBMNC samples. Levels of MDA were measured with TBARS assay. Polymorphisms were evaluated by genotyping ATM, PARP1, XPC, XPA, and XRCC1 genes of 96 patients, including 25 patients from the initial selection.

Results and conclusion. Patients with MS had a significant increase in nitrate, nitrate, and MDA concentrations in plasma and serum. Single-strand DNA breaks evaluated by conventional and enzymatic comet assay were higher in isolated PBMNCs of patients with MS. On the other hand, genotyping results have shown a typical polymorphism pattern compared to the European population. Few correlations between genotype and other parameters were also observed. One-way ANOVA statistical analysis was performed after each experiment, and statistical significance ($p<0.05$) was proved.

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Evaluation of hematopoietic progenitor cells potential in patients with myeloproliferative diseases *in vitro*

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Background. Myeloproliferative diseases are clonal diseases of the hematopoietic system, which are associated with damage to the hematopoietic system at the molecular and cellular levels. Since the mechanisms of pathological effects realization are complex and difficult to elucidate, the role of hematopoietic stem cell and its progenitors in the development of the leukemic process is controversial. Therefore, it is important to investigate the behaviour of hematopoietic progenitor cells in patients with myelodysplastic syndrome (MDS), chronic myeloid leukaemia (CML), and normal control bone marrow in the model of semi-liquid agar conditions of cultivation *in vitro*.

Aim. The aim of the study was to determine the functional activity of hematopoietic bone marrow progenitor cells in myeloproliferative diseases in comparison with the normal control bone marrow-derived hematopoietic stem cells.

Methods. Bone marrow samples were derived from 23 patients with MDS, 10 patients with newly diagnosed CML and 6 healthy donor patients. The mononuclear fraction was cultured in DMEM medium with 20% FBS, L-glutamine and 50 ng/ml GM-CSF in 0.33% agar Difco under conditions of near absolute humidity in CO_2 incubator at 37°C. Analysis of the obtained cell aggregates was performed on the 14th day of cultivation under an inverted microscope. To visualize the morphological features of cells, Pappenheim staining method was used.

Results. It was demonstrated that hematopoietic progenitor cells of the bone marrow of patients with MDS have a reduced ability to form colonies (4.2±1.1 per 1x10^5 of explanted cells), accompanied by the appearance of distorted forms of cell aggregates. A completely different picture was observed in the study process of progenitor cells in patients with CML and samples of normal bone marrow. Patients with CML and healthy patients showed an increased (61.0±2.4 per 1x10^5 of explanted cells) and normal (37.3±3.2 per 1x10^5 of explanted cells) number of colonies of the classical form, respectively. In the morphological analysis of cell aggregates in CML, the prevalence of immature cell forms proliferation was observed.

Conclusion. Therefore, low colony-forming activity of bone marrow of patients with MDS compared with increased ability to form cell aggregates in CML on the background of classical bone marrow colony formation in healthy patients indicates the role of hematopoietic progenitor cells in the pathogenesis of leukemic process and reveals various heterogeneous pathologies.

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Investigation of genetic variants of vitamin D receptor gene polymorphisms in Latvian population

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Background. Vitamin D is a nutrient and hormone that has a critical role of calcium and phosphate metabolism. It plays an important role in pathogenesis of different allergic diseases, such as asthma and food allergy. Vitamin D acts through binding to special vitamin D receptors (VDRs), which are expressed in a variety of tissues. Genetic variants of VDR have also been studied as a potential factor of autoimmune diseases and allergic diseases since they may affect VDR activity. Among the known VDR polymorphisms, the most common that influence VDR expression within the immune system are Bmsl (rs1544410), ApaI (rs7975232), TaqI (rs731236) and FokI (rs10735810) (Kamel et al. 2014).

Aim. To determine the prevalence of VDR genetic polymorphisms in Latvian population and to evaluate its possible functionality of in order to analyse their applicability as molecular markers.

Methods. Literature and sequence data on VDRs genetic polymorphisms (Bmsl (rs1544410), ApaI (rs7975232) and TaqI (rs731236) were analysed using meta-analysis and bioinformatical tools for DNA and RNA secondary structure, DNA bending and transcription factor binding sites. Genotyping of 253 samples of Latvian population was made using allele specific PCR and restriction enzyme site polymorphism method.

Results. The majority of studied SNPs demonstrated allele-dependent alternative secondary structures. Differential structures of DNA and/or RNA were found. Marked differences in simulated DNA curvature and bendability depending on allele were observed.

In European population, the prevalence of all SNPs is at least 34%, and there is information on their associations or linkage with different diseases in different populations. Minor allele frequencies in Latvian population are close to data of European population in average.

Conclusion. Meta and bioinformatic analysis of selected VDRs genetic polymorphisms (Bmsl (rs1544410), ApaI (rs7975232), TaqI (rs731236), and FokI (rs10735810) illustrate the potential of using them as possible molecular markers by genotyping in association study.

Interactions of these polymorphisms with the gut microbiome and vitamin D levels in various disease cohorts in Latvians are planned in future studies.

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A fifteen-year prospective audit of LASIK outcomes for myopia patients

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Background. Laser *in situ* keratomileusis (LASIK) was introduced in early 1990s and became the most performed refractive surgery modality in the 2000. Refractive surgery is mostly performed on young and healthy eyes of patients with high expectations, and long-term safety and efficacy is the biggest concern. However, there is little knowledge about the general changes in visual acuity, refractive tendencies, and the anatomic parameter changes of patients without post-operative problems.

Aim. To assess and evaluate the long-term clinical outcomes of laser *in situ* keratomileusis (LASIK) for myopia patients in 15-year period.

Methods. In our research, we evaluated 60 preoperative myopic eyes (mean spherical equivalent (SE) of -5.91±2.54 D) treated with LASIK. Patient data were separated in three groups divided by myopic grade – low (11 eyes), moderate (23 eyes), high (26 eyes). All patients were evaluated one day, three months, one year, five years, ten to twelve and thirteen-to-fifteen-year period post-operatively. The main outcome measures were objective refractive power, subjective refraction, uncorrected (UCVA) and best corrected visual acuity (BCVA), central corneal pachymetry and axial length. The data was analysed using ANOVA difference test (significance level (p) 0.05).

Results. Subjective refractive power of eyes with low grade myopia increased by +0.28±0.26 D, objective for -0.39±0.36 D. UCVA reduced by -0,20±0,15 decimal units (mean UCVA after 15 years 0.80±0.17 decimal units), BCVA by -0.12±0.22 decimal units (mean BCVA after 15 years 0.99±0.03 decimal units). Corneal thickness changed by 6.22±13.03 μm, axial length 0.01±0.05 mm. Medium eyes UCVA reduced by -0.31±0.34 decimal units (mean UCVA 0.77±0.33 decimal units), BCVA decreased by -0.01±0.10 decimal units (mean BCVA fifteen years after the surgery 0.99±0.11 decimal units). The mean corneal pachymetry change was 5.60±17.12 μm). Axial length had increased for 0.06±0.04 mm. 15 years after LASIK surgery preoperative high grade myopic eyes mean UCVA was 0.32±0.30 decimal units, with a correction of 0.85±0.15 decimal units. UCVA change was -0.63±0.29 decimal units, BCVA -0.09±0.13 decimal units. The corneal thickness changed for 18.02±25.42 μm, axial length 0.20±0.26 mm.

Conclusion. The eyes with low and medium grade myopia do not show statistically significant difference (p>0.05) in UCVA, BCVA, subjective and objective refraction power fifteen years after LASIK surgery. High grade myopia progresses during lifetime due axial length growth, corneal thickness thickening and showed statistical significance in all the parameters.

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Assessment of human sensitivity to cigarette smoke

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Background. Cigarette smoking is associated with a high risk of lung cancer and chronic obstructive pulmonary disease (COPD). However, COPD and lung cancer affect only 20–40% of smokers. Predisposition to smoking-related diseases is determined by several factors, including the ability to metabolize toxic products contained in tobacco smoke.

Aim. The aim of the current study was to develop a method for assessing the body's resistance to tobacco smoke.

Methods. The study involved 20 volunteer smokers. Participants abstained from smoking for at least 8 hours and then smoked one cigarette. Exhaled air at different time intervals was collected and analysed for 24 different volatile organic compounds (VOCs). Before sampling, people breathed high purity synthetic air for one minute to clean out the lungs from ambient air.

Results. Immediately after smoking, the exhaled air contained high concentrations of aromatic compounds such as benzene, toluene, xylene, styrene, as well as various aldehydes and ketones. The degradation rate of these compounds varied between individuals. Some compounds' clearance curves were characterized by two wave patterns. Each individual reproduced similar pattern of response in repeated trials.

Conclusion. We assume that the rate of degradation of toxic products and clearance patterns contain information that characterizes individuals' resistance to tobacco smoke. Further data collection is needed, especially for smokers with lung cancer and COPD patients, to clarify the specific response patterns characteristic to these diseases.

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Measurement of total antioxidant activity of tear and serum samples of the patients with hypertensive retinopathy

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Background. The chosen topic is of an exceptional importance, since hypertension ranks first in the leading causes of morbidity and mortality worldwide, causing the development of one of the most complex visual impairments known as hypertensive retinopathy (HR). The HR pathogenesis encloses many mechanisms, among them oxidative stress (OS). The inability of the antioxidant protection system to counteract OS could be among the causes of the development and progression of HR.

Aim. The aim of the study was to evaluate the serum and tear total antioxidant activity (TAA) and to determine whether there is are correlations between: a) TAA level and the degree of HR; b) the TAA levels in tear and serum.

Methods. Altogether 90 hypertensive patients were enrolled in the study being divided according to the Keith-Wagner-Barker grading system of HR into three groups: GI–36 patients; GII–35 patients; GIII–19 patients. The TAA determination in tears and serum was based on the ABTS neutralization method. The results were analysed in SPSS Statistics by ANOVA, followed by Bonferroni's post-hoc comparisons test. In addition, the Spearman correlation coefficient was determined. $p \leqslant 0.05$ was considered statistically significant.

Results. In the tear samples of the patients with HR was determined a statistically significant enhancement in TAA values as HR advanced in grade (p=0.008). Serum TAA level showed just a tendency of reduction (p=0.319). Tear TAA levels correlate significantly with medium power with HR grade (r=0.357, p=0.001). A significant negative, low power correlation was established between serum and tear TAA levels (r=-0.226, p=0.032).

TAA (μM/L)	HR grade			P value		
	I	II	III	GI vs GII	GI vs GIII	GII vs GIII
in tear	100%	159%	169%	p=0.026	p=0.028	p=1.00
in serum	100%	99,7%	98%	p=1.0	p=0.454	p=0.594

Conclusion. The results of the research reveal an enhanced capacity of local protection against OS in patients with HR, due to the increase of the TAA level in tear. The level of protection increases along with the increase in the HR grade. This fact potentially explains the apparent resistance of the retina to the effects of high blood pressure induced damage and the slow progression of retinopathy.

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Evaluating the immuno-expression patterns of HHV-6 and CD68 in *Substantia Nigra* in the background of excessive alcohol use: a histo-pathological analysis

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Background. HHV-6 (Human Herpesvirus 6) is an omnipresent double stranded DNA virus that can reside in multiple organs including the brain. The virus has been previously shown to infect vascular cells, thereby evoking an immune response. Furthermore, excessive alcohol use has also been associated with endothelial cell dysfunction. The role of activated microglia as protector of homeostasis has been long established. Hence, it becomes essential to investigate the potential synergistic role of the HHV-6 infection and excessive alcohol intake in the dysregulation of homeostasis leading to cellular immune response mediated by activated microglia.

Aim. The present study aimed to evaluate HHV-6 antigens in micro-vessel walls and activated microglia/macrophages in the *Substantia Nigra* (SN) in the setting of the excessive alcohol use.

Methods. Grey and white matter in the SN region from 14 brain autopsy samples with history of alcohol addiction (alcoholics) were investigated in the present study, which were age-matched with 15 non-alcoholics (controls). Quantitative estimation of the HHV-6 positive micro-vessels was done using anti-HHV-6 antibody along with activated microglia/macrophages using anti-CD68 antibody. The immuno-expression was analysed using a light microscope (40×) and the results were analysed using Excel and R.

Results. The median age in the alcoholics group was 33.5±6.17 years compared with 26±5.75 years in the controls. HHV-6+ blood vessels were observed in 8 samples – 4 each in alcoholics and controls. Significantly more ($p < 0.05$) HHV-6+ micro-vessels were found in both grey and white matter in the alcoholics when compared with controls. More CD68+ cells were observed peri-vascularly in the alcoholics when compared with controls in the white matter while controls showed more CD68+ cells peri-vascularly in the grey matter. However, when adjusted for number of activated microglia/macrophages per 10 vessels per visual field, higher number of activated microglia were noted for alcoholics in both grey (10 activated microglia/10 vessels/visual field in alcoholics compared with 9 activated microglia/10 vessels/visual field) and white matter (11 activated microglia/10 vessels/visual field in alcoholics compared with 9 activated microglia/10 vessels/visual field).

Conclusion. An increased presence of CD68+ cells per 10 vessels per visual field peri-vascularly coupled with a higher number of HHV-6+ vessels in the alcoholics group indicates a role of both excessive alcohol use and HHV-6 infection in mediating the immune response via activation of perivascular microglia.

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GASTROENTEROLOGY, NUTRITION, GASTROINTESTINAL ONCOLOGY & MICROBIOTA

Association between CT and clinical parameters of pancreatic ductal adenocarcinomas

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Background. Pancreatic ductal adenocarcinoma (PDA) is the most common pancreatic neoplasm, it has poor prognosis and high mortality. CT is one of the main diagnostic tests and histological analysis is the gold standard, so to improve diagnostic accuracy, it is important to determine if there is any association between these parameters.

Objective. To explore available clinical, radiological and histological information about patients with PDA in CPTAC-PDA database and to determine association between these parameters.

Methods. Retrospective study was conducted to analyse 165 patients from Cancer Imaging Archive CPTAC-PDA database with histologically confirmed PDA. CT scans of the abdomen of 60 patients were evaluated and density was measured. Data were collected from 24.08.2020. to 01.12.2020. Data were analysed using IBM SPSS 23.0.

Results. Median age was 65.0 years (IQR 60.0–71.0 years). 53.9% (n=89) were males and 46.1% (n=76) females. Median tumour size was 3.5 cm (IQR 2.8–4.5 cm). There were no statistically significant correlations between tumour size and density in CT phases ($p>0.05$; $r<-0.3$). There was no statistically significant association between tumour size and presence of metastasis ($p>0.05$), but the mean tumour size was larger for patients with distal metastasis (pM1 4.2±1.5 cm vs. pM0 is 3.8±1.5 cm). There was no statistically significant association between tumour grade (G) and tumour density in CT phases ($p>0.05$). G I tumour mean density in native CT scan was 19.9 HU vs. 28.7±5.4 HU for G II and 29.3±6.3 HU for G III tumours. G I tumour mean density in arterial phase was 42.4±8.7 HU vs. 58.8±15.2 HU for G II and 61.6±20.4 HU for G III tumours. There was statistically significant association between male gender and presence of metastasis ($p<0.05$). There was statistically significant association between R1, R2 resection lines and presence of metastasis ($p<0.05$).

Conclusion. To diagnose PDA, it is necessary to perform contrast-enhanced CT, because most tumours become hypodense only in arterial and venous phase scans. Tumour density was increasing with higher grade tumours in native and arterial phase.

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Eosinophilic oesophagitis as an underlying cause of patients admitted with food bolus obstruction to Ear, Nose and Throat Department in Ninewells Hospital, Dundee, Scotland in period 2016–2019

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Background. Patients with food bolus obstruction (FBO) are admitted under Ear, Nose and Throat (ENT), Medical or Surgical teams. In Ninewells Hospital, patients with FBO above sternal notch are admitted to ENT. Resolving FBO is the main aim during acute admission, nevertheless, the underlying cause for FBO should be investigated. In literature, eosinophilic oesophagitis (EoE) is the single most common cause for FBO.

Aim. The objective of this study was to investigate the underlying cause, such as EoE, that can only be diagnosed early with biopsies by analysing ENT FBO admissions, type of interventions and investigations used.

Methods. Retrospective study of adult FBO admissions to ENT inpatient ward from January 2016 to December 2019. Electronic and paper notes examined for information gathering on type of food bolus, interventions performed to resolve FBO and investigations and follow up used to look for the underlying cause of FBO.

Results. 120 FBO admissions in total. Men admitted 2.16 times more often than women. 87% FBO caused by animal-based food. A half required surgical intervention, of those 31% rigid oesophagoscopy (RO) and 69% oesophagogastroduodenoscopy (OGD). Biopsies were taken in half of OGD and <10% in RO. Of all biopsies, 50% had histopathological diagnosis of EoE, although potentially some were EoE negative due to inadequate number of biopsies taken. In all the patients diagnosed with EoE, food bolus was animal-based food.

Conclusion. Biopsies were not taken in all FBO patients undergoing oesophagoscopy, leaving EoE underdiagnosed. Follow up arrangements often are suboptimal. ENT doctors and OGD endoscopists need to be better informed on significance of EoE in patients presenting with FBO acutely and with dysphagia in outpatient clinics. Not much is known about the cause of EoE, therefore we speculate that animal-based food, especially chicken, plays a role in development of EoE, as it affects people born after 1970, and the annual poultry consumption per capita in the United Kingdom since then has increased by 300%.

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Application of sensor breath analyser for non-invasive detection of gastric cancer

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Background. Gastric cancer (GC) is one of the most common, as well as deadliest cancers worldwide. It is important to detect GC in early stages to provide successful treatment. A promising and non-invasive cancer screening method is exhaled breath analysis. It is based on the detection of volatile organic compounds (VOCs) in exhaled breath using the sensors.

Aim. To evaluate the ability of sensor breath analyser to differentiate between GC patients and subjects without cancer.

Methods. The study group included 146 subjects. A portable sensor-based breath analysis device was tested in a group of 77 GC patients and 69 non-cancer subjects. The sensor breath analyser consisted of two different type of sensors – gold nanoparticle sensors (GNP) and metal oxide sensors (MOX). The readings of each type of sensors were analysed separately. The breath samples were collected by the study subjects breathing directly into the aperture of the instrument for at least ten seconds. Baseline measurements were used for the standardization. All sensors were compared in both study groups using a nonparametric Mann-Whitney test. The difference was considered statistically significant at $p<0.05$.

Results. The average age of participants in control group was 54.3±14.9 years. In gastric cancer patients, the average age was 62.2±10.8 years. There were 59.4% (n=41) females and 40.6% (n=28) males in the control group, while the gastric cancer patient group encompassed 36.4% (n=28) females and 63.6% (n=49) males.

The GNP sensors showed convincing results – out of 8 GNP sensors, all sensors showed statistically reliable results in detecting the disease ($p<0.001$). Most of the MOX sensors were able to differentiate GC patients from the control group: out of 22 MOX sensors, 18 sensors showed statistically significant results in detecting GC patients ($p<0.001$).

Conclusion. The GNP sensors provide convincing results in differentiating GC patients from the control group. Overall sensor breath analyser has shown high efficiency in detecting gastric cancer patients. It has a future potential to detect other malignant diseases.

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Findings from the surveillance upper endoscopies in patients with gastric mucosal dysplasia at the baseline

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Background. Regular surveillance of patients with gastric precancerous lesions, in particular, those with dysplasia, is essential for timely recognition of progression of the lesion towards gastric cancer. Surveillance strategies and intervals are recommended by the European (MAPS) guidelines.

Here we are reporting the initial results of surveillance in GISTAR subjects who were initially diagnosed with dysplasia.

Aim. The aim of the study was to evaluate findings of the surveillance upper gastrointestinal (GI) tract endoscopy in patients from the GISTAR cohort having been diagnosed dysplasia at the baseline endoscopy.

Methods. Upper endoscopies were performed according to the GISTAR study protocol, obtaining 5 non-targeted biopsies plus targeted biopsies if any lesions were identified.

Indications and timing of the surveillance were applied according to the MAPS guideline, i.e., subjects at baseline being diagnosed with dysplasia (indefinite for dysplasia, low- and high-grade dysplasia) were included to the evaluation.

The current study was a subset of the overall GISTAR study, in which a total of 1345 subjects underwent upper endoscopy by the end of 2020.

Results. Out of 98 subjects, the surveillance endoscopy results were available of 60. Of those, 28 had low-grade dysplasia, 32 were diagnosed as indefinite for dysplasia, but none were diagnosed high-grade dysplasia at baseline. *H. pylori* infection was detected at the baseline endoscopy in 45 subjects (75%), and eradication therapy was completed in 36 of them.

One patient developed gastric cancer during surveillance (Stage 0; $TisN_0M_0$)

In six patients, dysplasia progressed to a higher grade (i.e., from indefinite for dysplasia to low grade). In three subjects, dysplasia remained in the same grade. Altogether, 50 study subjects were not found to have dysplasia at the follow-up endoscopy; 28 of those have had received eradication following the baseline endoscopy. Of these 50 subjects, 16 had lesions requiring further surveillance endoscopy, while 34 did not have lesions that required surveillance endoscopy.

Conclusion. Endoscopic surveillance of patients with gastric dysplasia is important in order to identify those progressing to more advanced lesions, even though during the surveillance a significant proportion of subjects may be found without dysplastic lesions, in particular after having undergone *H. pylori* eradication. It remains unclear whether patients with dysplasia at the baseline endoscopy, but without high-risk lesions at the first surveillance endoscopy still require additional endoscopic surveillance.

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Acute upper gastrointestinal bleeding in patients with and without non-steroidal anti-inflammatory drug therapy: patient profile and outcomes

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Background. Non-steroidal anti-inflammatory drugs (NSAIDs), including aspirin, are among the most commonly used drugs in the world. However, NSAID use is associated with increased risk of peptic ulcer disease and acute upper gastrointestinal bleeding (AUGIB).

Aim. The aim of the study was to compare outcomes in hospitalized patients with acute peptic ulcer bleeding with and without prior NSAID therapy.

Methods. Prospective study of patients aged 18 and over admitted consecutively to the Riga East Clinical University Hospital in 2019 and 2020 with acute peptic ulcer bleeding (PUB). Data were collected from interviews and medical records from 36 patients: age, gender, history of NSAID use, Forrest classification, hospitalization time, number of hospitalisations due to AUGIB within the last year, admission to intensive care unit (ICU), need for surgical treatment and outcome. Bleeding severity on endoscopy was evaluated according to Forrest classification (classes IA, IB and IIA). Patients who had Forrest IIB, IIC and III class PUB or used NSAIDs with anticoagulants were excluded from the study. The level of significance was set at $p<0.05$. Data were analysed using IBM SPSS 26.0.

Results. Of the 36 patients, 21 (58.3%) were female and 15 (41.7%) were male. NSAID users were 61.1% (n=22; Me=59 years, IQR=32.8 years), non-users 38.9% (n=14; Me=75 years, IQR=28 years). No statistically significant difference was found between the two groups regarding severity of Forrest classification (FIA, Fisher's exact test, p=1; FIB Fisher's exact test, p=0.65; FIIA, Fisher's exact test, p=1), length of hospitalization (Mann-Whitney U test=72.0, p=0.19), number of hospitalisations due to AUGIB within the last year (Mann-Whitney U test=128.5, p=0.41), admission to ICU (Fisher's exact test, p=0.27), need for surgical treatment (Chi- square test (1, n=33)=0.3, p=0.55), mortality (Fisher's exact test, p=1).

Conclusion. No statistically significant difference was detected between patients suffering acute PUB with or without prior non-steroidal anti-inflammatory drug use regarding severity of Forrest classification stage, length of hospitalisation, number of hospitalisations due to AUGIB within the previous year, admission to ICU, need for surgical treatment or mortality. Further clinical studies with an increased sample size of NSAID users and non-users are necessary for additional evaluation.

Profiling of microRNAs and their isoforms in differentiated and undifferentiated colonic epithelial cells of patients with active and inactive ulcerative colitis

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Background. Ulcerative colitis (UC) is a chronic, relapsing condition defined by the intestinal inflammation and epithelial injury (Lee et al., 2015). To date, diagnosis of UC is based on clinical, endoscopic, histological features and biochemical markers. However, in certain proportion of clinical situations they do not correlate with the activity and severity of the disease (Gisbert et al., 2009). MicroRNAs (miRNAs) are poised to contribute to etiopathogenesis of UC and are being studied as potential biomarkers to discriminate patients with active (aUC) and inactive UC (iUC) (Peck et al., 2015).

Aim. To determine the changes in expression profiles of miRNA and their isoforms (isomiRNA) in differentiated and undifferentiated colonic epithelial cells (CEpCs) during aUC and iUC.

Methods. Differentiated and undifferentiated CEpCs were sorted from biopsies of healthy control (HC) individuals (n=19), patients with aUC (n=17) and iUC (n=15) using FACS technology (Dalerba et al., 2011). Total RNA was extracted, small RNA sequencing libraries were prepared and sequenced using *Illumina* platform. Sequencing data was processed with *nextfbw-core/smrnaseq* pipeline to generate miRNA count table. Differential expression, comparative, correlation analyses and data visualisation were performed using *Rstudio* software packages *DESeq2*, *isomiRs*, etc.

Results. 432 unique miRNAs and 518 unique isomiRNAs were identified in samples. Changes of expression profile during aUC were identified in undifferentiated CEpCs (compared to: (i) HC – 24 miRNAs and 53 isomiRNAs, (ii) iUC – 26 miRNAs and 34 isomiRNAs ($p_{adj}<0.05$)) and in differentiated CEpCs (compared to: (i) HC – 28 miRNAs and 40 isomiRNAs, (ii) iUC – 9 miRNAs and 19 isomiRNAs ($p_{adj}<0.05$)). Also, 7 miRNAs and 13 isomiRNAs ($p_{adj}<0.05$) were differentially expressed in undifferentiated CEpCs and 3 miRNAs and 1 isomiRNA ($p_{adj}<0.05$) in differentiated CEpCs during iUC compared to HC. 5 miRNAs and 17 isomiRNAs ($p_{adj}<0.05$) were identified to be differentially expressed during aUC, 2 miRNAs and 2 isomiRNAs ($p_{adj}<0.05$) – during iUC, and 11 miRNAs and 31 isomiRNAs ($p_{adj}<0.05$) in HC when comparing expression profiles of undifferentiated and differentiated CEpCs. We also identified 12 miRNAs and 12 isomiRNAs which expression in differentiated and undifferentiated CEpCs moderately (0.5<rho<0.7) correlated with Mayo score.

Conclusion. The changes of expression profiles of miRNAs and isomiRNAs revealed that differentiated and undifferentiated CEpCs respond to inflammation differently, and the expression of these miRNAs and their isoforms reflected disease activity.

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TP53 and PIC3CA gene mutations as targets for circulating tumour DNA detection in colorectal and breast cancer patients

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Background. At the moment, liquid biopsy is at the peak of attention, challenging scientists with many questions. One of them is the determination of appropriate targets for ctDNA detection. A lot of variants have already been suggested for different localizations, but we decided to propose at once two equivalent targets for two different localizations in this study. We suppose that such an approach in future research can help to create a universal panel for detection and monitoring of different cancer types and, as a result, liquid biopsy could be made more available and convenient to general use in clinical practice.

Aim. Our study aimed to compare frequency of TP53 and PIC3CA mutations in patients with colorectal cancer (CRC) and breast cancer (BC) and determine their role in treatment monitoring of these cancers.

Methods and materials. 29 patients with histologically verified BC and 19 patients with CRC were screened for study participation. All of 48 patients underwent radical surgery for the underlying disease. Quantification of TP53 and PIC3CA gene mutations was performed using the QuantStudio 3D Digital PCR System (Applied Biosystems, USA). Both FFPE tumour tissue samples and patients' blood plasma samples taken before and after surgery were tested for the above mutations.

Results. Target mutations were detected in 78.9% of patients with CRC. 52.6% of CRC patients had mutation of TP53 gene, 10.5% – of PIK3CA, and 15.8% had both mutations simultaneously. In patients with BC, mutation of TP53 gene was detected in 20.7%, PIK3CA gene mutation – in 17.2%. The results of detecting mutations in FPPE samples were comparable with the results of plasma samples analysis. There was a significant decrease in ctDNA in patients' blood in the postoperative period, compared with the samples taken before surgery.

Conclusion. The obtained results show the significant importance of TP53 and PIK3CA gene mutations for CRC patients. In BC patients, these mutations appear less but also have a clinical significance. We suppose that mutations in the TP53 and PIK3CA genes, determined at different stages of treatment of patients with BC and CRC, can help to monitor the effectiveness of their treatment. Further research is needed for in-depth analysis.

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Non-invasive diagnosis of pancreatic fibrosis in chronic pancreatitis: a new approach

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Background. Pancreatic fibrosis is a major histological feature of chronic pancreatitis (CP), which abundant increase leads to CP severity accretion. Non-invasive pancreatic fibrosis measurement can help to estimate CP process precisely and predict CP progression.

Aim. The aim was to study new approaches to non-invasive diagnosis of pancreatic fibrosis in patients with CP.

Methods. We examined 43 patients: 22 (51.2%) with calcifying CP and 21 (48.8%) with CP after pancreatic necrosis (the mean age 47.8±11.9; 35–82) between January 2018 and December 2019. We collected the results of contrast-enhanced multidetector 128-row computed tomography (MDCT), as well as fibronectin (FN), C-peptide and faecal pancreatic elastase-1 rates. We calculated normalized contrast enhancement ratio during the pancreatic (PP)and venous phases (VP), as well as contrast enhancement ratio between VP and non-contrast MDCT. ANOVA, Mann-Whitney pair tests, and Spearman correlation (r) were used for data analysis.

Results. There were no differences in C-peptide ($p=0.18$) and normalized contrast enhancement ratios during PP and VP ($p>0.05$) between the studied groups. Faecal pancreatic elastase-1 concentration (108.36±144 μg/g) was significantly lower in calcifying CP ($p=0.03$) vs. patients with CP after pancreatic necrosis (185.67±145.1 μg/g). Blood FN level negatively correlated with CP severity according to M-ANNHEIM classification ($r=-0.36$, $p=0.018$). In patients with calcifying CP median contrast enhancement ratio (1.01±0.06) was significantly higher ($p=0.033$) than in patients with CP after pancreatic necrosis (0.95±0.14). Weak tendency to increase of median contrast enhancement ratio of the whole pancreas ($r=0.31$, $p=0.04$) and the pancreatic head separately ($r=0.36$, $p=0.02$) with CP duration was revealed.

Conclusion. FN level decrease in patients with severe CP is highly likely and occurs due to long-term increased FN intake because of pancreatic fibrosis. Thus, FN level increase can be an additional marker of pancreatic fibrosis.

Pancreatic fibrosis due to CP affects the characteristics of pancreas contrast enhancement, which leads to an increase in contrast enhancement ratio. Therefore, contrast enhancement ratio could be a useful method in non-invasive pancreatic fibrosis diagnosis based on MDCT results, which highly likely will lead to CP treatment improvement.

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Clostridium difficile infection as a cause of severe outcomes in patients with inflammatory bowel disease

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Background. The prevalence of *Clostridium difficile* infection (CDI) in patients with inflammatory bowel disease (IBD) is higher than in general population.

Aim. To define the frequency of *Clostridium* infection (CDI) in patients with IBD and to study the risk factors that predict severe outcomes associated with CDI in IBD patients.

Methods. 1278 medical records were analysed in a retrospective study of patients with IBD, of which 808 patients met the inclusion criteria. Patients were divided into 2 groups based on the presence of a preliminary diagnosis of CDI. Our primary outcome was time to total colectomy or death with follow-up censored at 180 days after CDI. Cox proportional hazards models were used to identify predictors of the primary outcome from among demographic, disease-related, laboratory and medication variables.

Results. The frequency of CDI in patients with IBD was 17.6%. The mean age of occurrence of CDI in patients with IBD was 37.8±12.9, 85.3% of infections were community-acquired and only 4.9% occurred in medical institutions. The first group included 143 patients CDI+IBD, and the second group – 665 patients IBD without CDI. In the first group, C-reactive protein, erythrocyte sedimentation rate and faecal calprotectin levels were significantly higher and albumin level was lower than in the second group ($p<0.05$). Only 25.3% of all patients with CDI had a history of antibiotic use, and 30.4% had previously used steroids. Long-term immunosuppressive therapy in patients with IBD has an impact on the development of CDI: among patients with CDI 48.7% long-term received azathioprine/6-mercaptopurine, in patients without IBD – 18.3% ($p<0.001$). Only 19% of patients with CDI had control of the disease with salicylate therapy, while 62% of patients without CDI achieved remission by taking salicylates ($p<0.05$). Of these, 7 patients (4.9%) met our primary outcome (1 death, 6 colectomy) at a median of 21 days. On multivariate analysis, serum albumin<22 mg/L (HR 7.93, 95% CI 1.006-62.57), was independent predictors of our primary outcome.

Conclusion. The study shows that patients with IBD are more sensitive to the development of CDI at a young age, while not having such traditional risk factors as recent hospitalization or antibiotic use. Patients with IBD with CDI in history often noted the ineffectiveness of therapy with salicylates; often require the assignment of biological therapy. Serum albumin<22 mg/L was an independent predictor of severe outcomes in hospitalized IBD patients with CDI.

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Long-term follow-up after faecal microbiome transplantation: results from consecutive case series

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Background. Many studies have shown high effectiveness of faecal microbiota transplantation (FMT) in treatment of recurrent or refractory *Clostridium difficile* infection (CDI). Nevertheless, data on long term outcomes and complications after FMT are still lacking.

Aim. In this study, we aimed to evaluate efficacy of FMT treatment for recurrent CDI and investigate short and long-term FMT safety.

Methods. Our study included 60 consecutive patients that were treated in Lithuanian University of Health Sciences Hospital Kauno Klinikos from 2015 to 2019 for recurrent CDI infection. In all patients, FMT was performed through nasoenteric tube placed during upper GI endoscopy. Fresh donor faeces were used for FMT from unrelated donors. Pre-FMT preparation included CDI treatment with oral vancomycin 500 mg q.i.d. for at least five days and proton pump inhibitor (PPI) administration before FMT. Follow-up data included information about recurrent CDI episodes, early and late complications, health status at 3, 12 and 24 months after FMT.

Results. FMT was performed for 60 patients with recurrent CDI. The mean age of the patients was 69.3±15.1 years. Clinical improvement after the first FMT procedure was observed in 48 patients (80%). 10 of 12 initially non-responding patients had clinical resolution after a second FMT leading to an increased overall cure rate of 96.7%. Remaining two patients needed a third FMT with a final overall cure rate of 100%. Nine of 60 patients were under immunosuppressive therapy. Six immunosuppressed patients were in the initial responders' group and remaining three – in non-responders' group. We observed a very low rate of serious adverse events (SAE) in short and long term after FMT. During the first 8 weeks after FMT procedure, death of three patients occurred, however, it was not related to FMT procedure. After FMT, patients were followed for a median of 20 months, with a range from one to 55 months. During follow-up period, no long-term SAEs were documented.

Conclusion. Our study confirms a very high rate of FMT efficacy in the treatment of recurrent CDI with an overall cure rate of 100%. Our study also shows that compliance with a very stringent peri-procedural patient follow-up protocol enables avoiding short term SAE, when FMT is administered via nasoenteric tube. FMT shows good safety results with low risk of long- and short-term adverse events. Within our cohort of patients, immunosuppression was not associated with reduced primary non-efficacy of FMT in CDI treatment.

Screening for celiac disease among gastroenterological patients

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Background. Celiac disease (CD) is defined as a systemic immune-mediated disorder caused by gluten and related prolamins in genetically predisposed individuals. The prevalence of CD is not well established, but in most of the Western world it affects approximately 1–2% of the population. It is important to understand the prevalence of CD in the risk group, such as patients with gastroenterological symptoms.

Aim. The aim of the study is to determine the frequency of celiac disease among patients with digestive pathology and criteria for its active detection.

Materials and methods. A retrospective cohort study was conducted, involving 1 358 patients referred for consultation by a gastroenterologist from 2016 to 2019, of which 140 were previously diagnosed with celiac disease, encompassing 339 males (24.9%) and 1019 females (75.1%). The average age of the subjects was 40.4±15.4 years (18-86 years). All patients were determined in serum antibodies to tissue transglutaminase (anti-TTG) IgA, IgG, and also analysed the clinical symptoms of celiac disease and laboratory parameters of the examined patients. The obtained results were subjected to statistical processing using parametric and nonparametric analysis methods, using the program *Statistica* 13.3 (*StatSoft Inc*., USA).

Results. Among the examined gastroenterological patients without celiac disease (1218 people), an increase in the level of at Tg IgA and IgG was observed in 59 (4.8%), an increase in anti-TTG IgA – in 54 (4.4%), and anti-TTG IgG - in 38 patients (3.1%). The diagnosis of celiac disease, confirmed by a morphological study of mucosa, was established in 51 patients (4.2%). It was found that the main symptoms in gastroenterological patients were diarrhoea (88%), abdominal pain (60.7%), bloating and rumbling in the abdomen (73.8%) and nausea (40.3%). Also, 44.3% of patients had progressive weight loss.

The analysis of laboratory parameters revealed that a decrease in haemoglobin was determined in 31.6% of patients, a decrease in serum iron levels – in 33% of patients, hypoproteinaemia – in 12.6%, and hypoalbuminemia – in 12%. Electrolyte disorders, such as hypokalaemia was observed in 5.48%, hypocalcaemia – in 21.9%. An increase in the level of liver transaminases was recorded in 14% of patients (AST – 14.54%, ALT – 14.6%).

Conclusion. The incidence of celiac disease among patients with gastroenterological symptoms was 4.2%, which is higher than in the general population (1%). Analysis of clinical and laboratory data has shown that a comprehensive analysis of clinical symptoms and laboratory indicators at the stage of primary treatment will allow timely identification of patients with celiac disease and prescribe gluten-free diet.

The effect on physical and mental health with most common gastrointestinal tract symptoms using four-week course nutritional supplement with humic substances

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Background. Intensive farming practices of the modern world have reduced soil's (S) capacity to regenerate itself. S is deficient in humic substances (HS) and cannot provide sufficient quantities of needed to living organisms. Organic part of the S contains humic and fulvic acid, and polyphenols which are necessary for normal human diet. Nutritional supplement (NS) used in the study is a natural compound of birch and chaga mushroom extract that contains large amounts of HS.

Aim. The purpose of this study was to evaluate the effect on individual's, who have gastrointestinal tract symptoms (GTS), physical health (PH) and mental health (MH) with four-week course NS.

Methods. A pilot study was performed on participants in age group 18–80 between September 1 to December 31. Participants were given a 30 g package of NS powder for the duration of study, surveyed using two questionnaires in a four-week period – at 0, 14 (+7) and 30 (+7) days. Data were summarized using *MS Excel* and statistically analysed with SPSS. Spearman's correlation analysis was used for determination of associations between NS effect on PH and MH at 0, 14 and 30 days.

Results. 31 participants were included in the study – 58.1% women [95% CI: 41.9–74.2] and 41.9% men [25.8–58.1]. The mean age group was 20–39 years [41.9–77.4]. The most common answers to GTS impact on PH ranging from 0 to 10 (none – very bad) were 1 and 3 (16.1% [3.2–29]) at 0 days and 0 after 4 weeks (48.4% [32.3–64.5]), showing a moderate positive correlation at 0 days vs. 4 weeks (r_s=0.634, p<0.001). Impact on MH ranging from 0 to 10 (none – very disturbing) was 1 (16.1% [3.2–29]) at 0 days and 0 after 4 weeks (54.8% [38.7–71]) showing a moderate positive correlation between 0 days vs. 4 weeks (r_s=0.622, p<0.001).

Conclusion. The findings of this study show that NS containing HS has a positive effect on both PH and MH, with moderate positive correlations between PH rate at 0 days vs. 4 weeks (r_s=0.634, p<0.001) and between impact on MH at 0 days vs. 4 weeks (r_s=0.622, p<0.001). Further research should be conducted to assess the study's outcomes in a more general population.

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SURGERY

Critical evaluation of mathematical formulas describing the nasal air stream used in commercial rhinomanometry by air flow simulation and computational fluid dynamics

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Background. Rhinomanometry is the standard technique for measuring nasal airway resistance, pressure and airflow during breathing. Preoperative rhinomanometry is necessary before nasal surgeries.

Aim. The aim of the current study was to evaluate whether the law of Hagen-Poiseuille correctly describes the relation between nasal resistance, width and length of the nasal channel.

A further objective was to determine by measurement whether the law for 2 parallel electric resistors is applicable for the calculation of the total nasal resistance.

Methods. A simulator for the nasal airstream generating a reproducible flow (ARNO 5) was constructed, consisting of spirometry calibration pump, a linear actuator and a digital control unit. The simulator generates trapezoid breathing curves, where top fluxes of 250, 375 and 500 ccm/s have been chosen. Since the nasal airway can be compared with a diaphragm, a tube or an elastic resistor (Starling-resistor), models have been created by 3D-printing, representing either holes between 2.5 and 8 mm diameter or tubes of 20, 40, 60 and 80 mm length. They have been tested either as single concentric tubes or side by side, simulating the bilateral nasal air stream (Centre of Experimental Surgery, UL).

The measurements for pressure and flux have been carried out by the rhinomanometer 4RHINO in a special edition with extended pressure range.

In a next step, the applied geometric forms have been simulated by Computational Fluid Dynamics (Institute of Aerodynamics, RWTH Aachen/Germany). The results of physical and computational simulation of the airway have been compared.

Results. The physical simulation and simulation by CFD show very similar results. In all ranges in geometric forms, the measurements showed that the nasal resistance depends exponentially on the diameter of the resistor, but not on the 4th power as given in the law of Hagen-Poiseuille, the nose works more effectively than predicted by this basic law of aerodynamics. The interpretation of the results has to consider general principle of aerodynamics, i.e., the interpretation of non-steady air streams. Also, the rule of Kirchhoff for parallel resistors is not simply applicable for the nose, which is not surprising after earlier measurements of the total nasal resistance and 2 unilateral resistances: the average error for clinical applications in rhinomanometry will be evaluated and shown.

Conclusion. The nasal cavity is not simply comparable with tubes or diaphragms. CFD simulations are giving detailed information about the pressure behaviour in the nose.

Acknowledgements. The authors declare the absence of conflict of interest.

Increased numbers of CD8+ T-lymphocytes and FOXP3 T-lymphocytes correlated with HPV infection in patients with cervical intraepithelial neoplasia

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Background. The problem viewed in the current paper is of an outstanding importance, since cervical cancer is among the most common cancers in women worldwide, and also one of the leading causes of cancer-related deaths. Cervical cancer usually develops from the precancerous lesions, namely, cervical intraepithelial neoplasia (CIN).

Human papillomavirus (HPV) infection is the most important risk factor for cervical cancer and precancerous lesions.

Regulatory (FOXP3+) T cells (Tregs) comprise a subpopulation of CD4+ T cells that suppress autoreactive immune cells, thereby protecting organs and tissues from autoimmunity.

Aim. The aim of the current study was to analyse the role of T regulatory cells (Tregs), CD4 and CD8 T lymphocytes in CIN I, CIN II and CIN III patients with and without HPV infection.

Methods. Patients with CIN I (n=20), CIN II (n=14) and CIN III (n=18) and 10 subjects of control group were retrospectively enrolled in the study. Each patient underwent a colposcopy-guided cervical biopsy. The histopathological examination of tissue was performed. The slides were stained with hematoxylin-eosin. The immunostaining for CD4, CD8 and FOXP3 was performed. HPV testing was performed by *Aptima HPV* assay.

Differences between groups were analysed using Chi-squared test (the numbers of positive cases) and Kruskal-Wallis test with Dunns post-test for morphological data.

Results. Obtained results showed that the numbers of CD4 T-lymphocytes did not differed between the patients with CIN I, CIN II and CIN III. However, patients with CIN II and CIN III had significant CD8 T-lymphocytes upregulation compared to patients with CIN I.

The numbers of FOXP3 T regulatory lymphocytes did nod differed between the patients with CIN I and control group. However, in patients with CIN II and CIN III the numbers of FOXP3 T-lymphocytes were significantly upregulated compared to patients with control group (respectively, 15 (6-32) vs. 3 (2–7) cells/mm^2, $p<0.0001$; and 17 (2–23) vs. 3 (2–7) cells/mm^2, $p=0.0002$. In addition, the positive correlation between the HPV status and the numbers of FOXP3 T regulatory lymphocytes was revealed.

Conclusion. Up-regulation of T regulatory lymphocytes in patients with HSIL suggested the pivotal role of Tregs for counteracting the host immune response for the progression from LSIL to HSIL.

Acknowledgements. The authors declare the absence of conflict of interest.

Histological and ultrasonographical evaluation of skin in the region of scapular and thigh anterolateral flaps

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Background. The loss of soft tissue of the sole represents a challenging problem due to the lack of locally available tissue for transposition and the weight-bearing requirement of the region. We compared histological and ultrasonographical differences of skin in the region of scapular and thigh anterolateral (ALT) flaps.

Aim. To find a more suitable flap for covering of sole defects.

Methods. Thirty participants underwent cutaneous punch biopsies (3 mm) and ultrasonography studies of the scapular, ALT, and sole regions. The study included 15 males and 15 females, the mean age – 27 years, with normal body mass index, without chronic co-morbidities. Results were evaluated semiquantitatively. The Wilcoxon signed-ranks test was used to comparison skin features between regions.

Results.

Histological findings.

The corneal layer of ALT region is thicker than in scapular region (z=-3.207; p=0.001) and the corneal layer of sole is thicker than in scapular and ALT region (z=-5.109; p=0.000) and (z=-4.853; p=0.000). The epidermal layer of sole is thicker than in scapular and ALT region (z=-4.786; p=0.000) and (z=-4.850; p=0.000). The papillary layer of sole is thicker in comparison with scapular and ALT region (z=-3.984; p=0.000) and (z=-4.104; p=0.000).

Ultrasonographical findings.

Median of epidermal and dermal thickness in the scapular region was 2.57 mm (IQR 2.48 – 3.03 mm), in the ALT region it was 1.72 mm (IQR 1.52 – 1.90 mm). The median of the epidermal and dermal thickness of the sole was 5,00 mm (IQR 4.31 – 5.13 mm). The epidermal and dermal layers in the scapular region are thicker than in the ALT region (z=-4.76; p=0.001). These layers are thicker in the sole if compared with scapular and ALT regions (z =-4.20; p=0.001). Median of subcutaneous tissue thickness in the scapular region was 3.57 mm (IQR 2.64 – 5.08 mm) and in the ALT region 10.20 mm (IQR 4.72 – 12.06 mm). The hypodermal layer in the scapular region is statistically significantly thinner than in the ALT region (z=-4.50; p<0.05).

Conclusion. Histological and ultrasonographical examinations showed controversial results. Presumably, the thicker dermal layer in the ultrasonography study is due to the reticular dermis. The tinner hypodermal layer of the scapular region has a better blood supply which decreases the risks of bedsore formation. Considering our study results, we suggest a scapular flap for covering sole defects.

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Infection risk factors and systemic infection rates with antibiotic prophylaxis

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Background. Systemic infection after major surgery is a serious and deadly complication. It greatly affects length of hospital stay and mortality. Systemic infection is caused by multiple factors. It is important to explore, identify and limit these potential risk factors.

Aim. This study was aimed to determine antibiotic prophylaxis against set risk factors of postoperative systemic infection.

Methods. This randomised prospective study included lower limb amputation patients in Riga East University Hospital, Riga, Latvia. Control group received preoperative prophylaxis (2g cefazolin). Experimental group received additional 2g cefazolin for 7 days. Recent hospitalization (<3 months), local haematoma, local seroma, anaemia, hyperglycaemia, blood transfusion, prolonged stay before operation (>3 days), jaundice, use of immunosuppressant drugs and systemic infection rate was assessed. Each group was compared to set count of risk factors: 1 or less risk factors and 2 or more risk factors. Statistical analysis using SPSS 22 software was done for Chi-squared test. Statistical significance level was set at $p<0.05$.

Results. 152 patients participated: 58% (n=88) males, 42% (n=64) females, the mean age 72.2 years. Total systemic infection count was 11.2% (n=17). Pearson's Chi-square test between systemic infections and amount of risk factors ($\leqslant 1$ or $\geqslant 2$) in prophylaxis group was statistically insignificant ($p=0.14$). Similarly, the same test proved statistically insignificant difference in therapeutic group between systemic infections and amount of risk factors ($p=0.63$).

Conclusion. Additional antibiotic use against systemic infection prevention in lower limb amputation patients is ineffective. Still, removal of preoperative antibiotic prophylaxis is not recommended. Therefore, proactive action towards risk elimination may give best results.

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The first experience in Riga East University Hospital with slowly resorbable biosynthetic mesh Phasix™ used in hernia repair surgery in patients with symptomatic hiatal hernia

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Background. The problem is of an outstanding importance, since patients with large and symptomatic hiatal hernias require surgical treatment for gastroesophageal reflux symptom release and better quality of life. The research regarding hiatal hernia repair surgeries using a new slowly resorbable biosynthetic mesh Phasix™ is still scarce.

Aim. The current study aimed to compare gastroesophageal reflux disease symptoms before and after hiatal hernia operation using GERD-Health Related Quality of Life Questionnaire (GERD-HRQL) for patients in whom hernia repair surgery was done using a new slowly resorbable biosynthetic mesh Phasix™.

Methods. Altogether 10 patients were enrolled in the study and were treated surgically for their hiatal hernias using a new slowly resorbable biosynthetic mesh Phasix™. Surgeries were performed in Riga East University Hospital from 2018 to 2020. Statistical analysis was performed using IBM SPSS Statistics 23.

Results. 80% of all patients were female, 20% were male. Age distribution was from 42 years of age to 81 years of age. One patient had hiatal hernia I, seven patients had hiatal hernia III and two patients had hiatal hernia IV. Eight hiatal hernia surgeries using Phasix™ mesh were done laparoscopically, whereas two were done using upper midline laparotomy incision. For all patients, fundoplication was done modo Toupet. Most patients before surgery had noticeable symptoms or symptoms that were incapacitating them in their daily activities with a mean score of 3.4±0.84 and after surgery with no or minimal symptoms with a mean score 1.0±0.94. The total mean score of the questionnaire before surgery was 14.90±6.67 and after surgery 3.30±3.74. Mean score of regurgitation symptoms before surgery was 13.80±7.96 and after 1.30±1.77. All patients after surgery were satisfied with their present condition, but before surgery one patient had a neutral opinion, and all the others were dissatisfied.

Conclusion. The approach of using slowly resorbable biosynthetic mesh Phasix™ in hiatal hernia repair surgery proved to be a sufficient method in improving patients' GERD symptoms and can be used in further surgeries.

Acknowledgments. The authors declare the absence of conflict of interest.

Laparoscopic Heller myotomy with Dor fundoplication – upper gastrointestinal quality of life before and after the surgery

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Background. Achalasia is a rare esophageal motility disorder characterized by aperistalsis of the esophageal body and impaired lower esophageal sphincter relaxation. Clinical manifestations include dysphagia, regurgitation, chest pain, weight loss, etc. Current treatment modalities of achalasia include pharmacologic agents, endoscopic methods and surgery.

Aim. The aim of the study is to access the short-term efficacy and quality of life (QoL) of patients with achalasia after laparoscopic Heller myotomy and Dor fundoplication.

Methods. Prospective case-controlled study was carried out in Riga East University Hospital (Latvia). Fifteen achalasia patients underwent laparoscopic Heller myotomy and Dor fundoplication from July 2016 to June 2020. The data on clinical evaluation and QoL before therapy and 6 months after operation was collected and analysed. Eckardt clinical scoring system and Gastrointestinal Quality of Life Index (GIQLI) scores were used. A standardized quality of life assessment questionnaire, which contained 36 questions with 5-point Likert scale (0- 1- 2- 3- 4), each with a score of 0–4 points was used in the study. Calculation of the score: the most desirable option – 4 points, the least desirable option – 0 points; GIQLI score: sum of the points. Global score: 0–144 points; higher score means better QoL; normal = 125 points.

Results. All the fifteen patients underwent laparoscopic Heller myotomy and anterior fundoplication successfully. One patient was excluded from the study because of mortality, which was not due to the operation. By comparing the data of the preoperative and 6 months postoperative period after Heller myotomy, we found that the mean Eckardt score decreased from 2.125 to 0.285 ($p<0.05$) and postoperative QoL scores were higher than those of preoperative. There were no complications. 10 out of 15 patients noted major improvement in emotional and social factors such as coping with stress, nervousness and managing daily activities. 60% remarked not only a total absence of gastrointestinal symptoms, but also an improvement in physical factors. In 53%, the 6 month-follow up GIQLI scores were more than two times higher than those obtained in preoperative period. All patients had normal or above normal GIQLI score (range: 127–139). None of the patients had more than mild intensity of any of the most common symptoms of achalasia.

Conclusion. Laparoscopic Heller myotomy with Dor fundoplication is safe and effective method for treating achalasia in the short-term, it can relieve clinic symptoms, as well as improve patients' QoL.

Acknowledgements. The authors declare the absence of conflict of interest.

Inguinal hernia transabdominal preperitoneal repair using Senhance robotic platform: first multicenter report from the TRUST registry

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Background. Inguinal hernia repair is one of the most common surgical procedures worldwide, and over the last couple of decades, minimally invasive techniques are being widely introduced in clinical practice. Minimally invasive transabdominal preperitoneal approach appears to have a reduced rate of complications, although it is more technically challenging compared to other methods. However, the robotic platform has a three-dimensional view and flexible instruments that facilitate the work of a surgeon. So far, there was a lack of broad robotic inguinal hernia repair studies, thus, the major strength of our study is the data from the few largest centers from different countries covering registry.

Aim. The purpose of this article was to provide feasibility and safety results of robotic inguinal hernia transabdominal preperitoneal (TAPP) repair.

Methods. We included 271 cases of robotic inguinal hernia TAPP repair using Senhance® robotic platform from four different centers between March 2017 and March 2020. Key data points were intraoperative and postoperative complication rate, operative time, length of hospital stay, postoperative pain score and time required to get back to daily routine tasks that were inserted in the TRUST registry.

Results. We report 203 cases of unilateral and 68 cases of bilateral inguinal hernia repairs. Mean operative time was 74±35 minutes (range 32–265 min.), while average docking and console time were 7±3 minutes (range 1–90 min.) and 48±28 minutes (range 11–225 min.), respectively. Postoperative complications occurred in five (1.85%) cases, intraoperative complication rate was five (1.85%). Average subjective patient-related pain score after the procedure was 3±1.9 (range 1–9), length of hospital stay was 39±28 hours (range 4–288 hours), and recovery time was 9.65±8 days (range 1–36 days).

Conclusion. Robotic inguinal hernia TAPP repair shows inspiring results. It is a safe and feasible procedure. However, cost analysis should be performed in future to show the superiority over other techniques.

Acknowledgements: The authors declare the absence of conflict of interest. The current study required no specific funding. All the performed procedures were in compliance with ethical standards of the responsible committees on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, revised in 2000. Informed consent was obtained from all patients included in this study.

Long-term outcomes and quality of life after inguinal hernioplasty p–Lichtenstein versus Transabdominal preperitoneal repair with self-gripping mesh

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Background. Inguinal hernioplasty is one of the most common manipulations performed in general surgery. There are many techniques known today for management of inguinal hernias that can be divided into two groups – Laparoscopic and open surgery. Both have their advantages and disadvantages. The main problem is differentiating how each method affects patients' quality of life in long term.

Aim. The aim of this study was to compare long-term (3 years postoperatively) outcomes and quality of life after Lichtenstein hernioplasty and Transabdominal preperitoneal inguinal hernioplasty with self-gripping mesh.

Methods. A prospective case control study was performed at Riga East University Hospital (Latvia) in 2016–2020. Ninety patients were allocated into two groups: 35 patients in the LICHT group and 55 patients in the TAPP group. In the LICHT group, Lichtenstein hernioplasty with polypropylene mesh was performed, in the TAPP group – Transabdominal preperitoneal hernioplasty with polypropylene self-fixating Progrip mesh without additional fixation was done. Follow-up was carried out at 3 years after surgery by telephone and if necessary, by visit. Complications, discomfort, pain, recurrence and satisfaction with the operation were assessed.

Results. Ultimately, 84 patients (33 in the Open group and 51 in the TAPP group) were included in the study, representing 93% of the selected patients during the study period. Both groups were comparable by body mass index, gender, hernia size. None of patients had postoperative complications or recurrence in both groups. Both groups were comparable in terms of pain in rest: LICHT 1 (3.0%) patients vs. TAPP 0 (0%) (p=0.393) and pain on movement LICHT 5 (15.1%) vs. TAPP 5 (9.8%) (p=0.504). Significantly more patients had discomfort during physical activity in LICHT group 11 (33.3%) as compared to TAPP group 7 (13.7%) (p=0.035). Significantly more patients had restrictions of routine daily physical activity in LICHT group 7 (21.2%) vs. TAPP 3 (5.9%) (p=0.048). Maximal aesthetic satisfaction (10 points of 10 possible) with the operation was higher in TAPP group 43 (84.3%) patients as compared to LICHT group 16 (48.5%) patients (p<0.001). Maximal overall satisfaction with the operation also was significantly higher in TAPP group 44 (86.3%) patients vs. 16 (48.5%) patients in LICHT group (p=0.001).

Conclusion. Both Lichtenstein and TAPP inguinal hernioplasty have comparable long-term results in terms of complication, recurrency rate and pain in rest. Patients after TAPP have less discomfort during movement and less restriction s of daily physical activity. Satisfaction with the operation is higher after TAPP hernioplasty as compared to Lichtenstein hernioplasty.

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Urodynamics referral pathways: Are we over-investigating? An audit of the appropriateness of urodynamic investigation in NHS Tayside

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Background. Urodynamic studies (UDS) are an investigation used in the assessment of people with urinary incontinence (UI). UDS is an invasive test with documented complications and NICE* specify criteria for when it should be performed. UDS has become standard clinical care without solid evidence for its routine use. It is a relatively expensive, embarrassing investigation, which can cause physical complications such as urinary tract infections. UDS should be judiciously used in patients with failed conservative therapy where there is diagnostic uncertainty before embarking on invasive treatment.

Aim. To audit the use of UDS in NHS Tayside against the NICE guidelines over the period of one year.

Methods. Audit of females undergoing UDS in the gynaecology department of NHS Tayside between November 2017 and November 2018. A pro forma was used to collect the patients' data retrospectively using the Clinical Portal, an electronic database.

Results. The majority of patients were referred for UDS without a full appropriate conservative treatment. 72.9% (n-78) of the females presenting for UDS (n-107) had urge or mixed UI symptoms, but only 10% of them were suitable to undergo invasive treatment (botox, neuromodulation) post UDS. 18% were not suitable for UDS. It is recommended that UDS should not be performed in females with pure stress UI, but we found that 22% of patients presenting for UDS had symptoms of pure stress UI. There was great variability in conservative treatment started by different healthcare professionals before UDS referral.

Conclusion. Overall, this audit identified that the NICE guidelines were not adhered to in NHS Tayside. Performing UDS only after failed conservative treatment, and before surgery is more cost effective and spares patients an invasive test that does not influence further management of their condition.

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Usage of bilateral retromuscular rectus sheath block catheters for early postoperative analgesia after laparotomic gastrectomy

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Background. In early postoperative period, the occurrence of severe pain after open major upper GI surgery is a significant issue. The study was aimed to assess the efficiency of rectus sheet block with continuous bupivacaine infusion catheters into retromuscular space in providing an effective pain relief, decreasing opioid consumption and enhancing postoperative recovery.

Aim. Continuous retromuscular rectus sheath infiltration of 0.125% bupivacaine through rectus sheath catheter after laparotomic gastrectomy provides effective postoperative analgesia, significantly reduces opioid consumption and facilitates bowel movement.

Methods. This prospective case-control cohort experimental study was conducted in Riga East University Hospital (Latvia). 39 patients with laparotomic gastrectomy were divided into two groups – 21 patients in the Block Group and 18 patients in the Control Group. Only in the Block group, retromuscular catheters in the m. rectus abdominis sheath were placed before fascia closure on both sides of the incision under the direct supervision of a surgeon.

After surgery, the patients in the Block Group received continuous 0.125% (10–12 mg/h) bupivacaine infusion through rectus sheath catheters for 72h in addition to fentanyl i/v infusion on postoperative day 0, and ketorolac or trimeperidine injection on postoperative day 1–2. The patients in the Control Group received only fentanyl i/v infusion on postoperative day 0 and ketorolac or trimeperidine injection on postoperative day 1–2.

Pain intensity was assessed in both groups Visual Analog Scale (VAS) at 24-, 48- and 72-hour intervals after surgery at rest and during movement. Postoperative complications, hospital stay, comorbidities were all examined.

Results. The demographic profile of the two groups was comparable. Postoperative pain (VAS) at rest was significantly lower in the Block Group at the time period 48 hours – median 20 vs. 40 ($p=0.006$) and 72 hours after surgery – median 10 vs. 30 ($p=0.01$). Pain on movement in the Block Group was significantly lower in all measurements: at 24 hours ($p=0.006$), at 48 hours ($p<0.001$) and 72 hours postoperatively ($p<0.001$). There were no complications related to the rectus sheath catheter insertion and bupivacaine infusion.

Conclusion. Continuous retromuscular rectus sheath infiltration of 0.125% bupivacaine after laparotomic gastrectomy provides effective postoperative analgesia in early postoperative period.

CARDIOVASCULAR MEDICINE

Percutaneous transcatheter left atrial appendage occlusion (LAAO), procedural success and safety. Data from Latvian Centre of Cardiology (LCC) during 2010–2020

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Background. Each year, twenty-six million people worldwide suffer from stroke, the leading cause of long-term disability globally. Cardioembolic stroke accounts for 20–30% of ischaemic strokes. Cardiac embolism incidence has a tendency to increase. Cardioembolic stroke carries a worse prognosis regarding clinical outcome, disability and stroke reoccurrence rate, compared to atherosclerotic aetiology. Atrial fibrillation comprises a fivefold increase in the risk of ischemic stroke. Treatment with oral anticoagulation (OAC) has been demonstrated to significantly reduce stroke in patients with atrial fibrillation, however, up to 12% of atrial fibrillation patients have contraindications for oral anticoagulant use. Left atrial appendage occlusion (LAAO) is a non-pharmacological method to prevent cardioembolic stroke in patients with atrial fibrillation and contraindications for long-term oral anticoagulant use.

Aim. To analyse transcatheter percutaneous left atrial appendage occlusion (LAAO) method safety and procedural success.

Methods. Data on all LAAO procedures performed at the Latvian Centre of Cardiology from May 2010 to October 2020 was collected using LCC registry of LAAO procedures.

Results. A total of 74 LAAO procedures were performed during 2010–2020. Patients aged 72±7 years, 63% (n=46) were woman. CHA_2DS_2-VASc score was 5.6±1.7 and HAS-BLED score was 3.0±1.1. A total 48% (n=36) had a prior bleeding 42% (n=15), of which gastrointestinal bleeding makes up 21% (n=15). Noncompliance to OAC use composed 18% (n=13) and recurrent stroke 14% (n=10). Device used for majority of cases was *Amplatzer Amulet* ® 55% (n=41). *Amplatzer* ® cardiac plug used in 26% (n=19) and *Watchman* ® device 20% (n=15). Implant success rate was 96% (n=72, p=<0.05) No major in- hospital adverse events including stroke, death, myocardial infarction, pulmonary embolism or significant bleeding occured. Insignificant bleeding was detected in 2.8% (n=2), and vascular access complications was seen in 8% (n=6) of all cases. Device embolization occurred in 4% (n=3) of cases. In one case, the device was retrieved by transcatheter approach. In two cases, an open heart surgery was required.

Conclusion. Our ten-year experience performing LAAO has showed high success rate, which coincides with other studies. CHA_2DS_2-VASc score represented in our study was generally higher and major in-hospital adverse event rate compared to other studies was lower, except device embolization rate 4% (n=3). LAAO is a safe procedure with low complication rate.

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Comparison of early intrahospital results of total arterial revascularization using BIMA composite Y-grafts versus other surgical revascularization techniques

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Background. Several studies have shown an improvement in long-term mortality using bilateral mammary arteries (BIMA) in coronary artery bypass grafting (CABG). Concern was raised that use of BIMA grafting is technically more demanding and could increase surgery time, as well as the risk of sternal wound infection. A debate continues regarding BIMA technical aspects to achieve full myocardial revascularization.

Aim. The aim of the current study is to determine whether it is possible to obtain complete revascularization using the BIMA Y anastomosis configuration and whether it does not prolong the total duration of surgery and aortic occlusion time.

Methods. This is a retrospective single centre study, where we analysed intraoperative and pre-discharge data between two surgical myocardial revascularization techniques. The first group included all the patients who underwent CABG using BIMA as a composite graft in Y configuration as the only graft material (BIMA Y). The second group comprised all patients who arrived in in 2018 and underwent other configurations of CABG (other CABG).

Results. 61 patients were included in the BIMA Y group, and 157 patients – in the other CABG group. BIMA Y group included fewer female patients – 23% compared to other CABG group – 37% (p=0.049) and less diabetic patients (16% vs. 29%, p=0.048). We observed no significant changes in total aortic cross-clamp time (BIMA Y vs. other CABG; 63.44 ±19.28 min. and 60.07±20.38 min., p=0.96), but CPB time was shorter in the BIMA Y group (76.57±23.49 min. vs. 81.86±29.34 min.). In both groups, a similar number of coronary anastomoses per patient were done (BIMA Y vs. other CABG; 3.05±0.8 and 3.13±0.76; p=0.11) to achieve complete revascularization. The mean total operation time was slightly longer in BIMA Y group (218.2±40.45 min. and 176.67±52.6 min.), albeit not reaching statistical significance, p=0.09. There was no significant difference either in deep wound infection rate (BIMA Y vs. other CABG; 7% vs. 5%, p=0.56), or in postoperative stay (10.02±6.90 days vs. 9.99±6.32 days, p=0.96).

Conclusion. With using BIMA in Y configuration, it is possible to achieve total arterial revascularization with no increase in aortic cross-clamp time, the total CPB time and with only insignificantly longer total operative time. Our study has not shown a higher rate of deep wound infection or prolonged postoperative stay using BIMA in Y technique.

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Analysis of most important cardiovascular disease drivers based on cross-sectional study of cardiovascular risk factors in population of Latvia

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Background. Public health is a continuously changing system that can be understood by keeping track of its dynamics data. It is necessary to watch trends, reacting proactively to them, and to detect possible future challenges to be prepared beforehand. The data can be obtained in epidemiological studies that meet two main criteria: a wide cross-section of the population and the right methodology.

Aim. One of the aims of the "Population based cross-sectional study of cardiovascular risk factors in Latvia" was to determine the prevalence of most common cardiovascular disease (CVD) risk factors (RF). In this sub-study, we analysed three of them: arterial blood pressure (BP), blood lipid profile (BLP) and smoking to use data in health policymaking according to European Society of Cardiology (ESC) guidelines.

Methods. 4070 inhabitants of Latvia were enrolled. The statistical sample (6000 pers.) was formed by random selection from the Housing Register of the Central Statistical Bureau (1 209 756 pers.) representing a cross-section of Latvia's inhabitants (age 25–74). Study interviews and physical measurements were taken, and the objective examination included: double measurement of BP, body weight, height, BLP, blood glucose. The data were processed using *Microsoft Excel* and R.

Results. The response rate was 67.8% (n=4070) of the sample respondents (SRs). Blood samples were taken from 37.0% (n=2218) of the SRs. BP (SRs with objective measurements): <120/80 mm/Hg – 34.3% (n=761); BP 120–129 and/or 80–84 mm/Hg – 30.1% (n=667); BP ⩾130/85mm/Hg – 35.6% (n=790). BLP (SRs with objective measurements): total cholesterol ⩾5 mmol/l – 63.2% (n=1402); low-density lipoprotein cholesterol: ⩽1.4 mmol/l – 1.4% (n=31); 1.41–1.79 mmol/l – 3.7% (n=82); 1.8–2.99 mmol/l – 18.5% (n=410); 2.6–2.99 mmol/l – 14.5% (n=322); ⩾3 mmol/l – 62.0% (n=1375); high-density lipoprotein cholesterol >1.0 mmol/l in men and >1.2 in women – 86.0% (n=1907); triglyceride <1.7 mmol/l – 75.3% (n=1670). Smoking: 30.4% (n=1237) of the SRs smoked on regular basis and occasionally; 49.7% (n=2023) had been regular smokers for at least 1 year; 82.2% (n=1663) of the SRs who had been smokers for at least 1 year had started smoking aged less than 20 years.

Conclusion. This methodological approach allowed us to establish the prevalence and measures of three most common RF of CVD in the Latvian population. A scrupulous analysis of the data shows us the level of discrepancy between the real-time CV profile of the population and the recommendations of ESC guidelines.

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Arterial stiffening process may be affected by dietary habits in metabolic patients with hyperuricaemia

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Background. Hyperuricaemia has been classically associated with purine rich diet and metabolic syndrome, however, association to cardiovascular (CV) health is still not well established.

Aim. The aim of this study was to examine the differences of early atherosclerosis parameters between hyperuricaemic and non-hyperuricaemic patients and examine the associations between UA, arterial stiffness, and eating habits in a large group of patients with metabolic syndrome.

Methods. This cross-sectional study included 709 (445 women and 264 men) participants with previously diagnosed metabolic syndrome. We evaluated associations between uric acid (UA) and non-invasive vascular stiffness parameters of early artherosclerosis: mean blood pressure, augmentation index (AIx), pulse wave velocity (PWV), flow mediated dilatation (FMD) and carotid artery intima media thickness (IMT). The blood samples were taken for biochemical evaluations of UA and serum cholesterol and triglycerides. In addition, the participants completed the specialized nutrition profile questionnaire.

Results. 239 persons (33.71%) were found to be hyperuricaemic. Comparing the two groups dichotomized by UA level, both mean blood pressure and cfPWV (carotid femoral PWV) were higher in group with elevated UA, while AIx was evidently lower. Significant but weak association was found between UA and AIx. The negative correlation showed the indirect relationship: with elevation of UA the AIx tended to decrease showing arteries being less responsive to pulse wave.

Conclusion. Based on bivariate and multivariate models we conclude that hyperuricaemia is related to arterial stiffness by increasing the cfPWV and diminishing AIx. Dairy products, drinking water around 1.5 litre per day may have a beneficial impact on vascular health. Lowering the serum UA may also benefit vascular health, although the mechanisms are not known yet. The effect of sociodemographic factors, namely, senior age, parallels higher cfPWV, while female gender has some protective role, as women tend to have higher AIx, meaning more elastic arteries than men.

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Acute ischemic stroke's clinical outcome and ASPECTS value based on hyperdense artery sign

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Background. Acute ischemic stroke is one of the leading causes of death and disability in adults and elderly. The burden of the disease can be eased by recognising the stroke early and setting an appropriate treatment plan. Therefore, knowledge of radiographic acute stroke signs is a valuable clinical tool.

Aim. The aim of the study is to analyse occurrence of hyperdense MCA (Middle Cerebral Artery) sign at the time of admission and on follow-up CT scan and its association with clinical outcome of acute ischemic stroke. The study also aimed to analyse the HMCA (hyperdense MCA) impact of decreasing Alberts Stroke Programme Early CT Score (ASPECTS) value on a follow-up scan.

Methods. A retrospective analysis of 63 patients with acute middle cerebral artery ischemic stroke was done. Patient evaluation was implemented by using NIHSS scale (The National Institutes of Health Stroke Scale) and non-contrast CT scan was done at the time of admission and on follow-up after 24 to 48 hours. Patients were divided in two groups based on the presence of HMCA sign on the initial CT scan. Both study groups were compared by the clinical outcome graded with NIHSS and ASPECTS scale.

Results. 57% (n=34) of the initial non-contrast CT scans revealed hyperdense MCA. Patients with HMCA compared to patients with normal density MCA showed higher NIHSS score in both CT scans – the initial mean NIHSS score in hyperdense artery group was 13.765±5.308 and in normal density group it was 8.138±4.282; the follow-up mean NIHSS score in hyperdense MCA group was 8.676±5.574 and in normal density group it was 3.828±3.464. NIHSS score differences between study groups were statistically significant on follow-up evaluation (Mann-Whitney U test, n= 63, u= 211.500, $p<0.001$).

Patients with HMCA showed a noticeable decrease of ASPECTS value – 9.529±1.134 on the initial and 6.088±2.108 on follow-up CT scan; while patients with normal density MCA showed 9.552±0.948 and 7.793±1.235. ASPECTS score differences between the groups were also statistically significant on follow-up scan (Mann-Whitney U test, n= 63, u= 256.500, $p<0.01$).

Conclusion. Hyperdense MCA both in admission's non-contrast CT scan is associated with poor clinical outcome compared with normal density MCA findings. Finding HMCA at the time of admission points to significant ASPECTS value decrease in the following hours, days.

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Differences of unstable angina's clinical presentation based on sex

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Background. Evidence of sex-based differences in the pathophysiology, management and outcomes of unstable angina (UA) were reported more than 30 years ago and yet there is still an issue of making preliminary diagnosis according to clinical symptoms which differ between sexes. Increasing awareness of distinct clinical presentation may help to individualise diagnosis and treatment for each patient.

Aim. We aimed to find the main differences of UA clinical presentation while comparing duration, type, irradiation, localisation, previous incidence of pain, incidence of dyspnoea and previous myocardial infarction (MI) between men and women.

Methods. Data of 715 patients who were diagnosed with UA and hospitalised in Vilnius University Santaros Klinikos over the period of 2017–2018 and had undergone troponin test and coronarography were analysed retrospectively using *MS Excel* and *R-Commander*. P-value <0.05 was used to determine if findings were significant.

Results. Out of 715 analysed patients with UA, 458 (64.05%; median age of 65.81[17]) were men and 257 (35.94%; 70.65[14]) were women. Out of all patients who had previous MI (237), men (174) had it more often than women (63) ($p<0.05$). Although duration, type, incidence of dyspnoea and ECG findings did not differ significantly between sexes, it was realised that men more frequently experienced pain during physical activity. Pain tended to irradiate more often for women compared to men. Males were also reported to have experienced previous pain especially located in the chest more often than women ($p<0.05$). Previous MI and therefore following percutaneous coronary intervention (PCI) and coronary artery bypass graft (CABG) surgery were also significantly more frequent in males. According to the records of the coronarography, men are more likely to have obstruction (⩾50% diameter stenosis) in their coronary arteries, especially in the right coronary (RCA) and right circumflex (RCA) arteries.

Conclusion. There were significantly more men with UA diagnosis and they were 4.64 years younger than women. Males were more likely to experience chest pain during physical activity. For women, pain irradiated more often compared to men. Males were also more prone to having had previous incidences of pain, MI and coronary interventions, especially due to higher incidence of obstructive coronary artery disease.

Long-term outcomes after true bifurcation stenting

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Background. Bifurcation percutaneous coronary intervention (PCI) is challenging and associated with a lower rate of procedural success and a higher risk of complications. The optimal management of bifurcation lesions is a matter of considerable debate.

Aim. The aim of this study was to evaluate long-term outcomes of patients who underwent PCI for bifurcation lesions involving both main vessel and side branch, with a diameter exceeding or equal to 2.5 mm.

Methods. A prospective analysis of the ongoing Coronary Bifurcation Treatment registry (PCI performed from 01.01.2017. to 30.09.2020). Patients with STEMI in last 24 hours and lesions involving Left Main were excluded. A total of 469 patients with true bifurcations were included in this study. 1-year follow-up was possible in 386 patients Study population was divided into two groups: provisional single-stenting and systematic double-stenting. Long-term complication rates were compared between groups. 325 (84.2%) patients were treated using provisional single-stenting technique (1 stent) and 61 (15.8%) with systematic double-stenting technique (2 stent). Creatine kinase-MB levels 24h after PCI were measured in 169 patients.

Results. There were cases of death (total 2.3% (n=9); 1 stent 2.2% (n=7) vs. 2 stent 3.3% (n=2), p=0.638), hospitalization because of MI (total 0.8% (n=3); 1 stent 0.9% (n=3) vs. 2 stent 0%, p=0.455), target lesion revascularization (total 0.5% (n=2); 1 stent 0.6% (n=2) vs. 2 stent 0%, p=0.534) and target vessel revascularization (total 1.8% (n=7); 1 stent 1.8% (n=6) vs. 2 stent 1.6% (n=1), p=0.894). There were no cases of definite late stent thrombosis. Creatine kinase-MB levels more than 3 times above upper normal limit (total 14.8% (n=25); 1 stent 13.0% (n=22) vs. 2 stent 1.8% (n=3), p=0.897).

Conclusion. Long-term complication rate in the treatment of true coronary bifurcation lesions was low and there was no significant difference between one or two stent strategy groups.

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Personalized FSI-modelling of the aortic segment for its mechanical behaviour prediction and loads during the heart cycle assessment

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Background. Hemodymanics modelling is important in understanding the physiological processes in the cardiovascular system.

Aim. The objective of the current study was to create a personalized aortic segment FSI simulation to predict the mechanical behaviour of the aorta during the cardiac cycle.

Methods. The data of functional MSCT coronary angiography were used to model the aortic segment. Multiplanar and three-dimensional reconstructions of the ROI were generated, including the anatomical structures of the heart and aorta. Editing and reverse engineering of the 3D-reconstruction was carried out in *SolidWorks*. The preprocessing of the CAD model for FSI analysis was performed in *HyperMesh*. The calculated FE mesh was generated taking into account the anatomical and morphological features of the aortic wall. For the subsequent formulation of the FSI problem, a flow-through region was simulated. To simulate the anisotropic properties of the aortic structures, we applied the «Holzapfel-Gasser-Ogden material» anisotropic model. To evaluate the proposed model, FSI analysis of the aortic arch was carried out during systole. The results of the analysis were compared with the fMSCT-CA data and analysed by expert control method. The deformed states of the FSI model were compared with displacements on fMSCT-CA at the corresponding moments of systole. Aortic valve stenosis was modelled by varying the area and peak flow rate during systole.

Results. Plots of displacements, pressure and stress according to Mises for the aortic wall were obtained. Changes in blood flow characteristics are described. All initial conditions were simulated for systole at time t=0 in accordance with fMSCT-CA data. FSI analysis predicted the behaviour of the aortic wall during systole of 0.23 seconds. The result of prediction was compared with fMSCT-CA at time t=0.1s, and t=0.23s corresponding to the peak of systole. We carried out a study of geometric deviations of FSI modelling from fMSCT-CA data by imposing and analysing STL grids extracted from the output file of the solver at t=0, 0.1s, 0.23s, on 3D fMSCT-CA reconstruction for the corresponding times. For precise imposition of the resulting meshes, we used the rigid image registration method. The prediction accuracy estimation was calculated using the IoU metric, as the arithmetic mean of the IoU of all 2D images. The maximum value of the coefficient for two predictions of the FSI model is 0.96, minimum-0.73. The average IoU for two FSI model predictions is 0.92.

Conclusion. The accuracy of predicting based on FSI modelling is about 92%.

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Requalification of unstable angina diagnosis according to fourth universal definition of myocardial infarction

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Background. The troponin level is the only criteria in MI without ST segment elevation and UA differential diagnosis – it is increased in MI without ST elevation. Despite troponin level cut point that differentiates these two diagnoses, the problem of distinction between unstable angina (UA) and acute myocardial infarction (MI), as well as risk of misdiagnosis has been observed.

Aim. We aimed to evaluate peculiarities of diagnosing UA in Vilnius University Hospital Santaros Klinikos over the period of 2017 to 2018, and find out if it was possible to alter UA diagnosis to acute MI according to Fourth Universal Definition of Myocardial Infarction.

Methods. We analysed data of 840 patients with UA diagnosis and used Fourth Universal Definition of Myocardial Infarction to re-evaluate diagnosis. Normal value of high sensitivity cardiac troponin-I (cTnI) was referred as ⩽15.6 ng/l in women and ⩽35.2 ng/l in men. The increase of cTnI⩾5 times above upper limit was considered to be definite indication for requalification to type 1 myocardial infarction (MI1) if accompanied by changes (⩾50% diameter stenosis) of coronary angiography (CAG), or to type 2 myocardial infarction (MI2) if no changes of CAG were found. cTnI, increased more than normal range but <5 times, was considered as a possible indication for requalification to MI1 (with CAG changes) or MI2 (without). *MS Excel* and *R-Commander* were used for statistical analysis. P-value <0.05 indicates significant findings.

Results. There were 840 patients with UA diagnosis, of which 528 (62.86%) were men (median age of 66[16]) and 312 (37.14%) women (73[15]). 151 (18.02%) had a definite indication for requalification to MI1 and 25 (2.98%) to MI2. There were 180 (21.48%) patients who had a possible indication to be retrained to MI1 diagnosis, 36 patients (4.3%) with a possible retrain to MI2 diagnosis. 361 (43.08%) patients were correctly diagnosed with UA. In the group of patients who should be definitely reclassified to MI1 or MI2 median levels of cTnI on arrival were 187.7 [261,15] and 171.45 [156.93] respectively, and for those with a possible retrain to MI1 and MI2 median levels of cTnI on arrival were 47.20 [66.70] and 46.95 [28.45] respectively.

Conclusion. Only less than a half of analysed patients were correctly diagnosed with UA. One fifth of patients with a diagnosis of UA could have been definitely reclassified to MI. Every fourth patient could have been classified as a possible MI patient.

Impact of on admission leukocyte count on coronary blood flow and in hospital mortality in patients diagnosed with STEMI

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Background. Currently it is believed that atherosclerotic plaque formation and coronary artery thrombosis is a result of a cascade of inflammatory processes. Myocardial necrosis induces the release of proinflammatory markers. It may even lead to tissue damage and eventually to the development of undesirable events such as heart failure and death, if released excessively. No data are currently available on the impact of leukocyte count on coronary blood flow after successful reperfusion.

Aim. The aim of this study was to assess the correlation between leukocyte count and thrombolysis in myocardial infarction (TIMI) flow before and after successful reperfusion. Moreover, to assess the impact of leukocyte count on in-hospital mortality in patients diagnosed with STEMI.

Methods. This retrospective study included 835 consecutive patients diagnosed with STEMI. They were admitted to our centre from January 2014 to December 2015 and underwent diagnostic coronary angiography and Percutaneous Coronary Intervention (PCI) within 60 minutes from the time of admission. Coronary angiograms were evaluated with respect to TIMI flow grade. Patients were divided into two groups: Leuk I (count, $<10\times103$ cells/mL), and Leuk II (count, $\geqslant10\times103$ cells/mL). Study end points were defined as myocardial adverse cardiac event (MACE) and all-cause mortality at in-hospital period. Statistical analyses were performed to determine correlation using the SPSS 25.0 software. The value of $p<0.05$ was considered as statistically significant.

Results. Average age was 66.7±12.6 years and 77% were men. Women were statistically significantly older than men ($p<0.05$).

It was detected that TIMI flow grades were statistically significantly different depending on leukocyte count. We have noticed that TIMI flow <3 in the culprit vessel was most frequent in the Leuk II group ($p<0.05$).

50 patients (6,5%) died during in-hospital period. Using Mann-Whitney U test, patients in the Leuk II group had worse in-hospital prognosis and higher rate of in-hospital mortality (8.9%) than patients in Leuk I group (4.2%) ($p<0.05$).

Conclusion. High leukocyte count on admission is associated with impaired coronary flow (TIMI<3). High leukocyte levels are a strong and independent predictor of in-hospital mortality in patients diagnosed with STEMI.

Acknowledgements. The authors declare the absence of conflict of interest.

PAEDIATRICS

The severity of acute gastroenteritis among children with rotavirus vaccination compared to non-vaccinated 3 to 6-year-olds

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Background. Acute gastroenteritis (AG) is one of the most common infectious diseases worldwide among children under five years of age. The leading cause of dehydration and hospitalization due to diarrhoea is AG, which is mainly caused by rotavirus infection. In 2019, total number of 3445 cases of viral intestinal infections in Latvia were reported, with the highest prevalence among children aged 1 to 6 years. Vaccination is one way to prevent rotavirus infection as there is no specific treatment for rotavirus gastroenteritis. Since 2006, two vaccines against rotavirus have been available in Latvia. Since January 1, 2015, rotavirus vaccination has been included in the Latvian National Immunization Programme.

Aim. The aim of this study was to investigate the rotavirus vaccination efficiency on frequency and severity of acute gastroenteritis among children aged 3 to 6 years.

Methods. In cross-sectional cohort study, 102 children aged 3 to 6 years from Latvia were included. Parents filled in information about their children in an anonymous questionnaire of 34 questions. This study was conducted in family doctors' offices and through internet forums from November to December 2020. All data were collected and then analysed using "Microsoft Excel", "IBM SPSS 2.0" and "MedCalc" programs.

Results. Overall, 102 children were included in this study – 57.8% (n=59) girls and 42.2% (n=43) boys. The mean children's age was 57.41 months (SD ± 12.82 months). 71.6% (n=73) of children have had at least one episode of AG compared to 28.4% (n=29), who did not have AG. Rotavirus vaccine had been received by 67.6% (n=69) children, exclusive breastfeeding for 6 months had been received by 41.2% (n=42) children. There was no statistically significant association between Rotavirus vaccine (χ^2 test, p=0.77) and exclusive breastfeeding for 6 months (χ^2 test, p=0.63), and frequency of AG. There was statistically significant association of rotavirus-vaccinated children who did not have elevated temperature during AG compared to non-vaccinated children with AG (χ^2 test, p=0.04). Non-vaccinated children had significantly more frequent and liquid bowel movements (χ^2 test, p=0.05), compared to rotavirus-vaccinated children with AG.

Conclusion. Rotavirus vaccination is associated with less severe disease – non-elevated or lower body temperature and less frequent bowel movements during acute gastroenteritis, confirming the positive effect.

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Epidemiology and clinical characteristics of von Willebrand disease in Latvian paediatric population

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Background. Von Willebrand disease (VWD) is the most commonly inherited bleeding disorder, yet its diagnostic and management remain challenging. This is the first study that has evaluated epidemiology, clinical features, and diagnostic tools of VWD in Latvia.

Aim. To collect data on epidemiological and clinical characteristics and diagnostic approach of paediatric VWD patients in Latvia.

Methods. A retrospective descriptive study included paediatric patients with confirmed VWD who were diagnosed in Children's Clinical University Hospital. Data were collected from electronic medical records and outpatient reports and further analysed using *SPSS v21*.

Results. From November 2019 to March 2020, 48 VWD paediatric patients were included in this research. The mean age at the time of diagnosis was 8.1 ± 7.9 years. 26 patients were boys (54%), 22 patients – girls (26%).

The epidemiological distribution of Latvian paediatric patients with VWD is, as follows: 16 patients (35.4%) were from Riga, 12 patients (25%) – the district of Valmiera, 5 patients (10.4%) - the district of Riga, 3 patients (6.3%) – the districts of Daugavpils and Valka, 2 patients (4.2%) – the districts of Limbaži and Jelgava, 1 patient (2.1%) – Jūrmala and the districts of Talsi, Rēzekne, and Cēsis.

21 patients suffered from epistaxis and mucocutaneous bleeding (44%), 15 patients (31%) – from isolated epistaxis, 4 patients (8%) – from mucocutaneous bleeding and epistaxis, and GI bleeding, 3 patients (6%) – from mucocutaneous bleeding, 1 patient (2%) presented with each pattern: epistaxis + mucocutaneous bleeding + intracerebral hepatoma; epistaxis + menorrhagias; epistaxis + GI bleeding; mucocutaneous bleeding + menorrhagias; isolated menorrhagias.

A VWF:RCo/VWF:Ag ratio was calculated for 34 patients, it was <0.7 in 17 patients (50%). Of them, 8 patients (47.1%) received a therapeutical trial with desmopressin with a good response in 6 patients (75%), 1 patient was unresponsive and 1 patient had a slight rise in VWD factors.

Conclusion. The regional prevalence of the VWD differs among all regions, emphasizing the need for a more detailed genetic research in the affected areas.

Most patients suffer from epistaxis and mucocutaneous bleeding (44%) and only epistaxis (31%), that are the most common clinical manifestations of von Willebrand disease.

The calculated VWF:RCo/VWF:Ag ratio <0.7 indicates a possible Type 2 disease, for its classification a further multimer analysis is critical. It could provide accurate VWD diagnostic for a half of the research participants, enabling the choice of an appropriate treatment without avoidable adverse effects.

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Analysis of new potential biomarkers from CBC in distinguishing SBI versus bacterial/viral infections in paediatric emergency

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Background. Sepsis is the leading cause of morbidity and mortality in children worldwide. Primary diagnostics and treatment are crucial for preventing progression to more severe forms and lethal outcomes. Specific early SIRS markers are still missing.

Aim. The aim of the current study was to investigate the diagnostics value for standard infection biomarkers, such as CRP, WBC, neutrophils, monocytes, platelets (PLT) as well as PLT/MPV to discriminate between bacterial and viral infections.

Methods. We performed a perspective single-centre study. Children with SIRS criteria and fever of <48h were enrolled into the study. Exclusion criteria: chronic conditions, immunodeficiency, recent antibiotic use or if complete blood count (CBC), CRP were not performed. Finally, 179 children from 1 to 5 years of age were enrolled and further divided into three groups: severe bacterial infection (SBI) (n=22), bacterial infection (BI) (n=37) and viral infection (VI) (n=120) patients. For all study participants, blood was drawn, CBC and CRP levels were assessed and PLT/MPV was calculated. Data analysis was performed using GraphPad Prism. P value of <0.05 was considered significant.

Results. There was no significant difference in children's age or gender between SBI, BI and VI groups (median- 30 months, male (55.86%)). SBI and BI participants demonstrated significantly higher white blood cells (WBC) than VI patients ($18.7\pm8.55\times10^9$/l vs. $15.4\pm5.46\times10^9$/l vs. 10.91±7.47 p<0.001) and neutrophils count ($13.17\pm7.08\times10^9$/l vs. $11.06\pm4.78\times10^9$/l vs. 7.152±3.82) p<0.001). CRP level were significantly higher in SBI and BI vs. VI patients (56.61±61.32 mg/l vs. 54.52±41.9 mg/l vs. 16.84±28.35 p<0.001). We observed a significant difference in monocytes count between SBI, BI and VI ($2.11\pm0.98\times10^9$/l; $1.64\pm0.63\times10^9$ vs. $1.37\pm0.66\times10^9$/l p<0.0002). Also, PLT showed to be significantly higher between SBI compared to BI and VI patients ($340.4\pm115.3\times10^9$/l vs. 275.6±84.65 and $265\pm74\times10^9$/l, p= 0.0079). There was a significant difference in children's PLT/MPV between SBI vs. BI and VI (47.15±18.09 vs. 38.46±13.96 and 36.30±11.98 p=0.0241). With a cut-off value of 40.65, PLT/MPV identified subjects with SBI with the sensitivity (62.5%) and specificity (66.23%) (AUC of 0.677 (CI 95%, p=0.0137).

Conclusion. Our study showed that absolute monocytes count can help to discriminate between SBI, BI and VI. PLT/MPV could be a biomarker used in clinical practice to differentiate SBI, BI and VI in all children 1 to 5 years of age. However, further studies are necessary to identify more sensitive and specific markers.

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Diagnostic informativeness of ultrasonography examinations in paediatric appendectomy patients during 2018–2020 at Children's Clinical University Hospital of Riga, Latvia

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Background. Acute appendicitis (AA) is the most common surgical emergency in children. Due to psychological characteristics and pain intolerance in paediatric patients, visual diagnostics may be difficult, leading to errors in the interpretation of results.

Aim. The aim of the study was to analyse the informativeness of the performed ultrasonography (US) examinations in appendectomy patients at the Children's Clinical University Hospital (CCUH) during last two years.

Methods. This retrospective study includes 361 patients hospitalized in CCUH between December 2018 and December 2020 with performed diagnostic US examination and appendectomy, along with its histopathological evaluation. The degree of informativeness of US was classified as 'positive', 'ambiguous' and 'non-diagnostic'. Histopathological findings were classified as 'no appendicitis', catarrhal AA and phlegmonous/gangrenous AA with no perforation, with micro-perforation and macro-perforation. Pearson Chi-Square test of independence was used to determine the statistical significance between US findings and AA stages in children under and above 7 years. Statistical analysis was performed using Stata/IC.

Results. There was no difference between US and histopathological findings in either the total children population, χ^2 (4, N=361) = 9.49, p=0.30, nor in the age groups <7 years, χ^2 (4, N=49) = 2.87, p=0.83, and >7 years, χ^2 (4, 310) = 8.96 (p=0.35).

Conclusion. The informativeness of US does not change depending on whether AA is catarrhal, phlegmonous/gangrenous without perforation, with micro-perforation, or with macro-perforation in either the general patient population or the age groups under and above 7 years.

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Association of the HLA locus intergenic rs9275596 polymorphism with bronchial asthma in the Latvian population

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Background. Bronchial asthma (BA) is a chronic inflammatory, genetically complex, heterogeneous disease. Specific genes or gene combinations that could be used in the early diagnosis of BA have not yet been identified. Human leukocyte antigen (HLA) genes encode functionally important proteins, that are responsible for regulating the immune system. Mutations in intergenic region of this locus can affect the regulatory functions of the genes in the way the immune system works. The studied SNP rs9275596 (chr6:32713854) is localized between the *HLA-DQB1* and *HLA-DQA2* genes. Full genome studies have shown that this SNP is significantly associated with the risk of various autoimmune diseases (Sawcer et al., 2011) and was found to be in association with multiple sclerosis in Latvians (Paramonova et al., 2020).

Aim. The study was aimed at determining the potential association of SNP *rs9275596* located in the human leukocyte antigen locus with bronchial asthma in Latvian children.

Methods. The case/control group included 117 children diagnosed with asthma and 208 individuals without asthma and any other autoimmune and chronic disease/condition. The *rs9275596* were genotyped by restriction enzyme site polymorphism on BA main and sex-specific association. Statistical analysis was performed with SPSS.25 Statistical Package. The c^2 tests was used to determine the association with the disease and the difference between the results in two groups; odds ratio was used to determine clinical significance.

Results. In both MS and Latvian population cohorts, the SNP rs9275596 genotyping call rate was 100%, and the marker was found to be in the HWE ($p>0.05$). Statistical analysis revealed a statistically significant association with BA for common allele genotype TT (OR = 2.63, CI 95% [1.18–5.86]). The heterozygote genotype TC and rare allele C were found to be clinical protective factors in affected women (OR = 0.37, CI 95% [0.15–0.92]) and OR = 0.49, CI 95% [0.25–0.94], respectively).

Conclusion. We present evidence that the intergenic SNP rs9275596 of the HLA locus may contribute to the risk of bronchial asthma in Latvian children, and thus plan to analyse the interaction of this polymorphism with the clinical characteristics of BA in future studies.

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Effectiveness of the new patronage model in breastfeeding

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Background. Exclusive breastfeeding is critical to the development of every child. WHO is supporting countries to implement and monitor "Comprehensive implementation plan on maternal, infant and young child nutrition", approved by the Member State in May 2012. The plan includes 6 goals. One of these is to increase the exclusive breastfeeding rate for the first 6 months by at least 50% by 2025. WHO and UNICEF have developed courses to train health-care workers to provide skilled support to nursing mothers to help them overcome child growth problems.

Aim. This study aims to reduce the problems associated with exclusively breastfeeding infants up to 6 months of age. The introduction of a new model of patronage services into the work of PHC enables increasing the percentage of mothers committed to exclusive breastfeeding.

Methods. Currently, the work of the traditional patronage service was assessed by anonymous survey of 168 mothers with children under 6 months of age. Moreover, a descriptive analysis was carried out. 29 women with a gestational age of 32 weeks for patronage were taken under observation and patronage, according to the universally progressive patronage model (UPPM) before and after childbirth, as well as until their children reach 6 months of age.

Results. According to the results of the survey, it was revealed that 86% of mothers breastfeed, whereas 87% of women with newborns under 6 months of age provide additional food for the child. 62% had problems with breastfeeding in the first weeks after giving birth. Only 35% out of the 168 women received home visits at 32 weeks. Of the women undergoing patronage, only 47% were explained the benefits of breastfeeding, and showed the techniques of breastfeeding. Now, out of the children taken for patronage 11 have reached the age of 6 months, they have received medical assistance: 8 women according to the universal package and 3 according to the progressive package until the problems were eliminated.

Conclusion. The introduction of a new model of patronage services into the work of PHC enables increasing the percentage of mothers committed to exclusive breastfeeding of children up to 6 months. The UPPM showed the highest efficiency compared to the traditional model. According to the new model, the involvement of all family members increased, which affected the favourable development of the child.

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Asthma control level and quality of life in children

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Background. Asthma is the most prevalent chronic disease in pediatric population, it affects many aspects of children`s lives. Asthma control level is the most meaningful determinant of children`s quality of life (Petsios et al., 2013). The results of some studies indicated that children with asthma have a significantly lower quality of life compared with healthy children of the same age (Kouzegaran et al., 2018), it is important that we apprise these values in order to asses physical and psychoemotional well-being of children.

Aim. The objective of this study was to analyse asthma control level and quality of life in children ages 4-18.

The aim of the study was to find out how asthma control level and severity correlates with children's living standards and daily activity.

Methods. In this study, children with asthma aged 4–18 years were surveyed in social networking platforms (*Facebook*, *Twitter*, etc.). The participants voluntarily completed a questionnaire that included several asthma-related dimensions encompassing asthma control level, severity, treatment, vitamin D level, frequency of exacerbations and quality of life which included 3 domains – symptoms, emotional function, and activity limitations.

Test used to assess quality of life – miniPAQLQ (*mini Pediatric asthma quality of life questionnaire*)*. Statistical analysis was performed with SPSS statistics by using Mann-Whitney test. The level of statistical significance was set at $p<0.05$.

Results. Overall, 30 participants were surveyed. All of them (100%) had asthma. The mean children's age was 9.57±3.9 (4–18) years. 73.3% (n=22) had well-controlled asthma, 48.3% (n=14) had intermittent asthma. The mean quality of life in children with well-controlled asthma 6.5 ± 0.5, children with poorly controlled asthma 5.2 ± 0.4 (max value 7.0), emotional function 5.2 ± 0.4, symptoms 5.5 ± 0.8, activity limitations 5.3 ± 0.9.

Children were divided in 2 groups based on asthma control level – well-controlled and poorly controlled asthma. Using Mann-Whitney test, it was found that there was a statistically significant difference ($p<0.001$) between these 2 groups in quality of life overall and in all 3 domains – symptoms ($p=0.002$), emotional function ($p<0.001$) and activity limitations ($p=0.002$).

Conclusion. Patients with well-controlled asthma have a better quality of life than children with a poor asthma control. Asthma has an effect of all aspects of children`s life. For better understanding of dimensions in which asthma affects children, we need to continue the study, increasing the sample size of patients.

Rehabilitation as immunomodulation approach for children with cerebral palsy (CP)

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Background. CP is a group of motor disabilities with predominantly spastic forms. The morbidity and mortality were reported to associate with respiratory infection. There are also studies on 2-fold enhanced pro-inflammatory TNF-a level, and possible link between altered immune status and spastic muscle modifications in children with CP. So, we decided to verify effect of rehabilitation on immune system components.

Aim. To test effect of rehabilitation-induced motor improvement on immune system components in children with CP.

Methods. Lymphocyte status (CD22+ B-cells, IgA, IgM) was evaluated (n=22) 3 times: before rehabilitation, after 3 weeks of rehabilitation and after 6 weeks of rehabilitation.

Results. There was a trend in CD22+ B-cells decline. IgA levels dropped after 15 days of rehabilitation, while IgM after 15 days of rehabilitation showed a slight decrease, reaching 7.35% drop in levels after 30 days of rehabilitation.

Conclusion. Rehabilitation exerts immunomodulation effect on immune status of children with CP.

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Accuracy of the flexible flatfoot measurement in a Paediatric Population. Results of a cross-sectional study

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Background. Flatfoot is a common posture in children's feet. The posture of the foot depends on age, and the time when the longitudinal arch is formed is not yet known precisely. Mostly, non-dynamic assessment of children's feet is performed in clinical practice to classify foot posture and excluding pathological feet. This includes: visual assessment, anthropometric measurements (resting calcaneal stance position angle (RCSP), Navicular Drop Test (ND)), Foot Posture Index (FPI-6), various footprint-based analyses (Chippaux-Smirak Index (CSI), Staheli Arch Index (SI), etc.) and radiological examinations – calcaneal pitch angle (CP), talocalcaneal angle (TCA), lateral first metatarsal angle (TMA). However, there is no concensus in clinical practice and researcher's community as to whether FPI-6, ND, RCSP, SI, CSI or X-ray measurements and clinical measurements could be used as a best clinical, radiological measuring tools for paediatric flat foot.

Aim. To investigate the relationship between the 6-item version of the foot posture index and other clinical, foot anthropometric, radiological measurements for foot position in children at 5–8 years.

Methods. A total of 300 participants with a mean age of 6.4 ± 1.14 years were enrolled in the study. Children were examined physically, clinically, radiologically to measure Foot Posture Index and Navicular Drop Test, resting calcaneal stance position angle, Chippaux-Smirak Index, Staheli Index, calcaneal pitch angle, talocalcaneal angle, lateral first metatarsal angle. Tibial torsions, internal rotation of hip as an indirect method of femoral anteversion and Beighton Scale were analysed for factors associated with flat foot prevalence.

Results. The study included children with normal and flexible flat feet. Statistical analysis showed a significant FPI score correlation with other parameters (SI, CSI, RCSP, ND, CP, TMA, TCA showed strong and moderate correlations, $p<0.001$). Overall, the strongest associates are Chippaux-Smirak Index ($\beta=0.34$) and ND ($\beta=0.28$). Other indicators have relatively inconsiderable relationships with the foot posture index.

Conclusion. There is a strong correlation between FPI-6 and Navicular Drop Test, Chippaux-Smirak Index in children at 5–8 years.. All three prominent foot posture indicators (FPI-6, ND, CSI) might be used as a primary or preferred tool in clinical practice.

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US screening in the 1st trimester of pregnancy and congenital anomalies at births

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Background. Ultrasound-based screening (US) has been an integral part of routine prenatal care for decades. The prenatal detection of fetal anomalies allows for optimal perinatal management.

Aim. The objective of the study was to analyse US examination and frequency of congenital anomalies at births between urban and rural area.

Methods. Data source – Health Care Monitoring Datalink (HCMD). We used two data sources: Medical Birth Register and ambulatory care data provided by public and private health care providers about US. US screening was detected by manipulation code: 50694 – routine US screening in the 1st trimester of pregnancy. All singleton birth in 2018 (n=12955) were included in the data analysis. Place of residence was categorized in three groups: Riga, other biggest cities and rural area (including regional cities).

Results. A total 39.5% (n=5121) birth data in Riga, 38.7% (n=5011) other cities and 21.8% (n=2823) in rural regions were analysed. The mean mothers' age was 30.3 years (SD 5.4). During the study time, US scan once in the 1st trimester was 85.3% (n=11051), 2 times 12.4% (n=1603) and 3 times and more 2.3% (n=301). 91.7% (n=11880) of births were also the 1st trimester genetic screening. Higher proportion of genetic screening by 6 percent points was observed in Riga ($p<0.001$) than rural regions (93.3% to 87.0%). The use of ICD-10 code O28 – abnormal findings on antenatal screening of mother – was observed in a small number of cases. 2.4% (n=305) abnormal findings on antenatal screening of mother were detected at ambulatory care visits. From these cases 6.8% (n=21) were diagnosed congenital anomalies at birth. Totally 2% (n=265) of births were registered congenital anomalies. The higher proportion by 2 percent points ($p<0.001$) of congenital anomalies were in Riga 3.2% (n=162) than in other cities 1.3% (n=64) and rural regions 1.4% (n=39). Most often were registered congenital malformations and deformations of the musculoskeletal system (Q65–Q79) 26.8% (n=71) and congenital malformations of the circulatory system (Q20–Q28) 24.2% (n=64) at births.

Conclusion. Higher proportion of congenital anomalies were observed in Riga. There is not enough information of US screening results in existing data bases. There are need more studies to analyse frequency of anomalies that prenatally diagnosed in the first-trimester screening.

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Child and youth mortality trends in respect to macroeconomic factors in the Baltic states 2008-2018

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Background. Child mortality in two of the three Baltic states historically has been high for EU standards. Previous research suggests there may be economic factors contributing to this. The primary objective of this study is to expand on the previous research by investigating the relationship between rates of mortality stratified by age groups; Perinatal, Neonatal, Infant, Under-Five and Youth (5–14) in the Baltic states; Latvia, Estonia, and Lithuania with their corresponding macroeconomic indicators. By analysing a time period mindful of recent economic history, from 2008 to 2018, it allows us to see in detail the effects, if any, that the global financial crisis had on child mortality in the region.

Aim. To expand on the previous research by investigating the relationship between rates of mortality in several age groups and their corresponding macroeconomic indicators in the Baltic states.

Methods. Statistical data was gathered from national and international databases for rates of child mortality and macroeconomic indicators. This data was then analysed using a multivariate regression analysis in SPSS.

Results. Statistically significant correlations were found between GDP per capita for under-five and youth (5–14) mortality for Latvia ($p<0.001$), Lithuania ($p=0.001$ and $p=0.004$, respectively) and Estonia ($p<0.001$ and $p=0.002$, respectively). Additionally, an association was found between healthcare expenditure and Neonatal, Under-Five and Youth mortality in Estonia, and Under-Five mortality in Latvia. Moreover, an association was uncovered between the rate of unemployment and the Under-Five and Youth mortalities in Lithuania. No further associations were found.

Conclusion. The mortality of children between the ages of 1–14 is tied to the economic stability of the Baltic states. Furthermore, Estonian health care spending policies are responsible, at least partly, for the low levels of mortality recorded in Estonia. If similarly effective policies were to be applied, comparably low rates of child mortality could be achieved across the Baltics states.

Acknowledgements. The authors declare the absence of conflict of interest.

ETHICAL, SOCIAL & LEGAL ASPECTS OF MEDICINE

Organ procurement and donation in Latvia: is law reform needed?

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Background. Organ transplantation has become a common lifesaving procedure. However, the gap between the number of patients waiting for a transplant and the number of patients who actually receive a transplant is increasing each year. Despite the fact that Latvia has adopted the policy of presumed consent, also known as the "opt-out" policy, important limitations still remain. Families are always approached to understand what the wishes of the deceased were on donation and to ask for consent to proceed with organ recovery in the event that the wishes of the deceased were unknown and not communicated. In case of any contradiction the decision of the family is usually respected.

Aim. The aim of this study was to find consensus on organ procurement and donation among Latvian students.

Methods. An anonymous survey that included questions about organ procurement and donation was conducted among Latvian students. The results were collected and statistically analysed using Microsoft Excel and IBM SPSS.

Results. Overall, 857 responses were received. Of these, 73.6% (n=631) respondents were women and 26.4% (n=226) were – men. When asked if the informed consent should be signed at the moment of obtaining driver's license, remarkable 61% (n=523) agreed with the statement, while 34.5% (n=296) disagreed and 4.5% (n=38) had no opinion on this matter. The majority of respondents (76%; n=651) denied that signing such agreement could alter the equity and accessibility of proper healthcare. Even though 79.5% (n=681) of respondents stated that they would donate their organs in case of their death to a stranger, astonishing 92.5% (n=793) had not signed informed consent for organ donation after death. In addition, 83.9% (n=719) admitted to not having enough information and knowledge regarding organ procurement and donation in Latvia.

Conclusion. The study shows that Latvian students express favorable views towards organ donation. However, the majority has not officially signed informed consent for organ procurement and donation upon their death. Therefore, if the wishes of the deceased are unknown and have not been communicated during their lifetime, it complicates the procedure of organ procurement and adds additional pressure on the family to make a decision when the family is approached.

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Constitutional law framework for building a human rights-based approach to mental health care in Latvia

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Background. The previous UN Special Rapporteur on the right of everyone to the enjoyment of the highest attainable standard of physical and mental health Dr. *Dainius Pūras*, stated: "A human rights-based approach would allow the international community to abandon the sad legacy of mental health" (UN, 2017). The human rights approach is considered as a way forward in response to global, as well as national and local health crisis in mental health (Porsdam Mann et. al., 2016). Knowledge concerning the national constitutional law framework is an essential prerequisite for development of human rights-based approach to mental health care in Latvia.

Aim. The aim of the current paper is to explore Latvian national framework of the constitutional law applicable in development of a human rights-based approach to mental health care.

Methods. This study is a part of the national research project "Towards a human rights-based approach for mental health patients with a limited capacity: a legal, ethical and clinical perspective" No. lzp-2020/1-0397. The research has been implemented by applying doctrinal legal research methods, such as in-depth study of statutes, regulations, case law and policy documents.

Results. The study analyses the scope of Latvian constitutional law applicable to provision of mental health care services. It explores how legal norms contained in the Constitution of Latvia (*Satversme*) and legal principles established by the case law of the Constitutional Court of Latvia (*Satversmes tiesa*) should be applied in development and application of mental health care legislation, policies, and strategies. The paper reveals the existing legal gaps and limitations in application of constitutional law regulating provision of mental health care in Latvia.

Conclusion. Legislation and provision of mental health care services should be substantiated by principles of national and international human rights. The Latvian Constitution – *Satversme*, and international human rights treaties ratified by Latvia form a well-founded base for building and developing a human rights-based approach to mental health care. Existing legal gaps and limitations revealed by this study can be mitigated by knowledgeable and consistent application of constitutional law.

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Defendants with intellectual disability in criminal proceedings – analysis of case law

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Background. Criminal proceedings where persons with intellectual disabilities are accused must be conducted in conformity with internationally recognized principles of human rights. That requires proper assessment of person's mental capacity, provision and protection of procedural rights of the accused in line with diminished capacity because of one's intellectual disability.

In Latvia, the proportion of intellectually disabled among the incarcerated persons with limited capacity to work is 18.4%, whereas of those with mental health disorders – 19.6% (The Prison Administration of Latvia, 2020). The number of inpatients with intellectual disability in prison hospital has risen from 17 in 2015 to 47 in 2018.

Aim. To evaluate practices concerning the protection of human rights of the accused with marked intellectual disability in criminal procedures in Latvian courts.

Methods. Anonymized criminal court decisions containing key words "intellectual disability" were searched in the information system of court decisions (2013 – June 2020). Overall, 324 court decisions were found, and 37 of them corresponded the inclusion criteria – the accused had the diagnosis of moderate or mild to moderate intellectual disability. The case law analysis was performed, applying descriptive and analytical method. The results of forensic psychiatric assessment and the concordance thereof with court decision were analysed. The presence of a representative of the accused had been established.

Results. All the accused were found to be capable to participate in court hearings, to give evidence and all the adults – to participate in their own defence.

No defendants had insanity defence. Forensic psychiatric assessment was performed in 35 (94.5%) cases: 19 of the accused (51.4%) were considered to be in a state of diminished mental capacity during the offense and court supported this statement (100% concordance with expert's conclusion).

The remaining16 defendants (43.2% of all the accused) were found to be in a state of full mental capacity during the offense and it was completely supported by court (i.e., 100% concordance).

Conclusion. The study results call into question the quality of forensic psychiatric examination – the assessment of mental state during the offense and criminal competencies of the accused. The protective legal instruments appear to be underused in Latvia – defendants with marked intellectual disability participate in criminal proceedings without forensic examination and a representative. Courts appear to fully rely on the conclusion of the psychiatric expert.

There is a need for research to explore the methodology of forensic psychiatric assessment and court decision making in cases against persons with marked intellectual disabilities.

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Ability to understand or control actions as precondition for capacity assessment in health care

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Background. The concept of one's capacity to enter into a contract is underdeveloped in the legal system of Latvia, including entering into contracts in health care. The current legal framework stipulates that legal transactions may be concluded by natural and legal persons having the appropriate capacity to act. However, in circumstances where a person has the legal capacity to enter into a transaction, there may be disturbance of consciousness and will, in which the ability to understand the meaning of their action or control their action is limited. There is a need for research in the field of capacity assessment and expression of intent both in civil and health law.

Aim. The aim of the current study is to develop a unified, capacity-based approach for the assessment of one's expression of intent for civil law contracts in health care.

Methods. The theoretical basis of the research is formed by literature review methodology for collecting and analysing data from research in legal sciences; normative legal basis – law and regulations of the Republic of Latvia and foreign countries and case law. Within the framework of the study, such research methods as doctrinal, historical, comparative legal norms, as well as theoretical approach research method is being used.

Results. As the result of the study, the extent of the ability required to enter into a legal transaction is being assessed, including determining capacity to act, as well as the meaning of ability to understand or control actions in the legal transaction. The effect of disturbance of consciousness and will in conclusion of the contract and its legal force is being discussed.

Conclusion. This paper firstly explores the legal interpretation of Latvian national framework for capacity to act. Secondly, the role of the expression of intent and ability to understand or control actions both in civil and health law is being examined. Thirdly, it highlights the importance of the need to establish a common approach for assessing capacity and abilities in both legal and medical context to protect the rights of transaction participants, including patient rights.

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Pilot study of surgeons' attitude towards patients' right to refuse treatment

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Background. Discharge against medical advice is reported to have negative consequences not only for patients (prolonged hospitalization, higher risk for complications) but also for physicians due to a moral conflict. However, not enough studies have been conducted about physicians' attitude towards the refusal of the treatment.

Aim. We aimed to find out how and why would surgeons act if a patient who needs an urgent treatment does not give a written consent.

Methods. Surgeons of four University Hospitals in Lithuania were asked to fill anonymous questionnaire with four theorical clinical situations including appendicitis, oncological case and blood transfusion, which requires a fast decision making. Respondents were also asked about the main reasons why, in their opinion, some patients refuse a treatment. MS Excel and R-Commander were used for statistical analysis. Findings were considered statistically significant, if p-value was <0.05.

Results. Out of 53 surgeons, 33 (62.3%) were men and 20 (37.7%) were women. The average age was 44.7±12.5 and the average work experience was 19.0±13.4 years. 23 (43.4%) surgeons tended to make interventions for patients who did not want to be treated in more than 50% of given situations, 15 (28.3%) in 50% and 15 (28.3%) in less than 50% of given situations. The most common reason (41.6%) for intervention without consent was surgeons' opinion that patients cannot estimate the situation and consequences of their disease adequately. There was no significant correlation between decision to treat patients who did not want to be treated and surgeons' sex, age or work experience. It was also realised that, according to surgeons, the most important grounds to refuse treatment was the lack of information (19.0%), level of patient's education (12.2%) and age (11.7%). Poor socioeconomical status and long wait for medical services were considered the least important reasons.

Conclusion. Surgeons' decision about treating patients without consent does not depend on surgeons' sex, age or work experience. Surgeons tend to treat patients without consent if it is suspected that the patients cannot make the decision adequately. Lack of information, level of patients' education and age are thought to be the most important reasons behind rejecting recommendations for a necessary treatment.

Ethically and socially responsible governance of research biobanks: evidence-based recommendations for stakeholders

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Background. The present-day research excellence in medicine to a large extent depends on the development of research biobanks – collections of human biological samples and associated information. At the same time, the existing legal framework and state policies have significant gaps preventing the successful functioning of biobanks in Latvia.

Aim. The overall aim of the research project was to contribute to ethically and socially responsible governance of research biobanks in Latvia by analysing attitudes, concerns, and needs of the general public, donors and researchers.

Methods. Methodology of the research project combined quantitative and qualitative research methods and included three quantitative surveys (representative survey of general public (n=1017), survey of biobank donors (n=297) and survey of researchers who collaborate with biobanks (n=76)) and series of qualitative semi-structured interviews (20 interviews with biobank donors and 20 interviews with researchers).

Results. In comparison with 2010, the awareness of research biobanks among the general public in Latvia has decreased, however, the public is slightly more willing to participate in research biobanks by donating biological samples and personal data. Younger people with higher educational levels who are more engaged in searching information about biobanks are more willing to donate samples. The preferred and ethically most justifiable type of informed consent remains one of the most discussed ethical issues in the context of biobanking. Researchers in Latvia face ethical questions and dilemmas about returning research results and incidental findings to donors and their relatives, and donors need more information on sharing research results with relatives during the informed consent process.

Conclusion. Based on the research results, we developed recommendations for stakeholders. The ongoing process of developing the new Biobank law in Latvia should include diverse forms of consultations with stakeholders (general public, scientists, industry, non-governmental organizations etc). Biobanks should not only promote donors' awareness, but also increase willingness to donate biological samples and to engage in biobank-based research by active participation. More information on biobanks and biobank-based research should be made available to the public in Latvia to demonstrate the results and benefits of donations.

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MENTAL HEALTH

Association of somatic complaints and externalizing/internalizing mental health difficulties in Latvian adolescents

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Background. Various physical symptoms and complaints are a common experience in paediatric and child psychiatric practice. Adolescents suffering from somatic symptoms perform worse in school, are more often absent from school, and more frequently tend to have problematic social relations. Somatic symptoms in children and adolescents are also associated with mental health disorders (Bohman, 2018). There is increasing evidence that somatic health complaints in combination with mental health complaints are important components of mental disorders (Potrebny, 2017). So far, there have been no studies to investigate association of somatic complaints and externalizing (behavioural) and internalizing (emotional) mental health difficulties in adolescents in Latvia.

Aim. To investigate association of somatic complaints and externalizing and internalizing mental health difficulties in adolescents.

Methods. The study was conducted using data from the international Health Behaviour in School-Aged Children (HBSC) study year 2017/2018 database. HBSC in 2017/2018 included a mental health-screening instrument – the Strengths and Difficulties Questionnaire (SDQ), which is a brief behavioural screening questionnaire for 3–16-year-olds. SDQ results were defined as abnormal, and indicative of significant mental health difficulties, if 22 points and higher were reached on the total difficulties score (results above the 90th centile). Separate binomial logistic regression models were performed in SPSS to explore the link between headaches, backaches, stomach aches and the risk of externalizing and internalizing difficulties, adjusted for sex, age and socioeconomic status.

Results. The sample consisted of 4412 adolescents aged 11, 13 and 15, of these, 2224 (50.4%) were girls. Girls had 1.33 times higher odds of having an abnormal SDQ score (CI=1.07–1.66). Adolescents who evaluated their socioeconomic status as poor had 2,44 times higher odds of having an abnormal SDQ score (CI=1.62–3.69). Frequent aches were defined as any aches at least once a week in the past 6 months. The most frequent aches that were reported in the sample were headaches (30.1%), following by backaches (22.6%) and stomach aches (20%). Adolescents reporting any frequent aches had 2.63 times higher odds of having an abnormal SDQ score (CI=2.09–3.30).

Conclusion. Self-reported aches indicate a higher risk of having internalizing and externalizing difficulties. Therefore, it is recommended in general practice to screen adolescents reporting any frequent aches for mental health difficulties.

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Selection criteria of the psychotherapist at the urban outpatient psychotherapy service

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Background. When an individual has decided to seek help from a psychotherapist, he or she is faced with a number of different questions, starting from which method of psychotherapy to choose and how to choose a particular psychotherapist? Surveys show that nearly half of people who begin psychotherapy, quit. Private and painful topics are discussed in the psychotherapy process, therefore, trust is of the utmost importance for the psychotherapy to take place at all.

Aim. To evaluate the criteria which patients use to choose a psychotherapist and to determine whether patients have found a psychotherapist who meets their expectations.

Methods. A cross-sectional study was conducted at a private health centre. Only adult patients who are involved in an ongoing psychotherapy for at least 3 weeks were included. 40 patients were enrolled in the study and filled out the questionnaire: a 5-point (1 – not affected, 5 – fully affected) scale to evaluate the significance of criteria and some multichoice questions about the psychotherapist and the process. The data is statistically processed in *Microsoft Excel* and SPSS Statistics 23 using chi-squared test, descriptive statistics and Spearman's correlation coefficient analysis. Statistical significance level was determined at $p<0.05$.

Results. Patients were 18 to 57 years old (mean 33.15±3.07), of them 17.5 % (n=7) were men and 82.5% (n=33) – women. More than one psychotherapist has seen 50% of the respondents. 55% had sought help regarding depression and anxiety. Additionally, the second most common reason was relationship issues.

The data showed that the most significant choosing criteria were the psychotherapist's knowledge and previous experience ($p<0.001$). Psychotherapist's location and pricing were more relevant for younger respondents. Spearman's correlation coefficient analysis showed that for the patients who choose a psychotherapist by the location, the consultation price has a more significant impact on their decision. The data indicated that women are more likely to choose a psychotherapist by gender and by the suggestion of a friend/family or a doctor ($p<0.05$).

85% of respondents felt safe talking to their psychotherapist. 65% felt understood by the psychotherapist, however, 32.5% answered that the psychotherapist understands them only partly. No statistically significant difference was found in patients who had visited one or several psychotherapists ($p>0.05$).

Conclusion. The criteria for choosing a psychotherapist are not unambiguous, however, some correlations were found. Regardless of the criteria patients use to choose a psychotherapist, most patients feel safe and understood during the psychotherapy.

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Depression and somatization in 9th grade adolescents at the beginning and at the end of the final school year

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Background. At the end of the final school year (the 9th year of studies), many adolescents experience multiple stresses, some adolescents suffer from depressive or somatic symptoms.

Aim. The aim of the study was to investigate differences in the level of depressive symptoms and somatization in the 9th grade adolescents of Riga's schools at the beginning and at the end of the final school year, and to compare these factors between genders.

Methods. We assessed the level of depressive symptoms and somatization using Achenbach System of Empirically Based Assessment (ASEBA) youth self-reported scale at the beginning and at the end of the final school year. According to the local norms, the level that indicates the presence of depressive symptoms for girls is ⩾9, and for boys – ⩾8. A range of ASEBA classification of somatization is from 0 (no somatization) to seven (multiple somatizations). Differences between time points were investigated using Wilcoxon test, and between genders were investigated using Mann-Whitney test. Correlation between depression and somatization was checked using Spearman's rho test. Differences of $p<0.05$ were considered as statistically significant.

Results. 286 adolescents took part in the longitudinal prospective study performed in seven schools. The mean age of participants was 15.0 (± standard deviation 0.3); 50.5% were boys. The mean level of depression for the entire study sample was 7.0±4.8 at the beginning, 6.0±5.1 at the end of the final school year ($p=0.30$). The mean level of somatization did not differ at the first and at the second time points (2.0±2.3 at both time points; $p=0.08$). We observed significant differences between genders at both time points: 48.1% of girls and 20.2% of boys ($p<0.01$) and 44.4% of girls and 18.3% of boys ($p<0.01$) had depressive symptoms at the beginning and at the end of the final school year, respectively. Level of somatization was higher in girls (mean 3±2.3) than in boys (mean 1±2.3) ($p<0.01$ at both time points). The level of depressive symptoms significantly correlated with the level of somatization ($r=0.46$; $p<0.01$ and $r=0.58$; $p<0.01$ for the first and the second time point, respectively).

Conclusion. Adolescent girls need a particular attention during the final school year due to higher levels of depression and somatization.

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Six years with gender identity disorder – a study of case series

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Background. As gender variant youth seeks medical help at an increasing rate, efforts should be directed towards preventing adverse outcomes and ensuring adequate care by prompt diagnostic tactics and fitting treatment of comorbid pathologies, as well as the underlying cause. An assessment of existing experience is essential for suitable methods to be implemented.

Aim. The aim was to summarize the current data and analyse the dynamic of gender identity disorder (GID) patient care in Latvia.

Methods. With medical records provided by Children's Clinical University Hospital, all clinical cases of child/adolescent patients diagnosed with gender identity or other sexual disorders (ICD-10, F64, F66) during years 2015–2020 were analysed.

Results. 28 patient records were analysed. 10.71% (n=3) were diagnosed in 2015 with the rest spread steadily over the following years and an upswing in 2020, diagnosing 50% (n=14). In 2015–2016, 50% (n=2) of the diagnosed patients were assigned females at birth, subsequently 83.33% (n=5) in 2017–2018 and 83.33% (n=15) in 2019–2020.

75% (n=3) of the patients diagnosed in 2015–2016 were hospitalized in their first contact with psychiatric care, followed by 66.67% (n=4) and 33.33% (n=6) in the following time periods, respectively. Suicidal ideation/attempt was the most commonly described reason for seeking psychiatric help – found in 75% (n=3) of the diagnosed during 2015–2016, 33.33% (n=2) and 33.33% (n=6) in the subsequent years. An opposite trend is seen with newly presenting patients claiming GID as the primary concern – 7 new cases since 2018, none in the previous years.

Nearly all the patients (85.71%, n=24) have at least one psychiatric comorbidity, however, patients presenting with GID as the primary concern, seem less likely to be diagnosed with a coexisting mental disorder, i.e., 4 out of 7 patients initially presenting with GID have no comorbid disorders.

Conclusion. The number of newly diagnosed GID patients is rapidly increasing. During the analysed years, patients of female-assigned gender are presented more frequently. GID patient hospitalization rates, alongside suicidal ideation/attempt at the initial presentation, although still remaining prominent, tend to decrease. Consequently, more patients seem to seek GID directed psychiatric help in an outpatient clinic and appear to have a slightly lesser likelihood of having additional mental health issues at the time of presentation.

With the observed increase in patients diagnosed with GID, further improvement of management and care is required; application of clear guidelines regarding diagnostic and treatment process is needed.

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The impact of colour on taste perception and its potential applications in health care

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Background. Disliking and avoidance of medication is a topical problem today, eventually leading to disease progression or poor recovery outcome. Modelling taste based on colours can provide a support in motivation to use the medication. Within the research on crossmodal perception, systematic colour associations linking visual and gustatory perception were examined.

Aim. The aim of this study is to explore how perception of colour interacts with taste to provide a support in solving problems such as refusal of hospital meals or prescribed medications.

Methods. In three quasi-experimental between-groups experiments (n1=67, n2=63, n3=32) associations between colours and tastes were examined. According to hedonic rating scale, the most preferred colours were determined and their emotional and associative links were examined.

Results. The highest positive taste/flavour ratings were for yellow, red, green, and orange (average values 5.8, 5.6, 5.5, and 5.4), followed by pink, white and purple (5.2, 5.1, and 5.1) on a 7-point Likert scale. Negative ratings were for blue, brown and grey (4.6, 4.1, and 3.9). The typical associations (25–35% of participants) for the colours with the highest ratings were 'aromatic', 'exotic', 'refreshening', and 'summer', whereas the typical associations for negatively rated colours were 'unsafe' and 'disappointment'. Red, pink, orange, and purple (3.7, 3.7, 3.6, and 3.6) were rated as the sweetest according to 5-point Likert scale and are also among the colours rated as the most tasteful. Yellow, green, and white are rated as the sourest (3.4, 3.2, and 3.0), and – with the exception of white – also as the colours with the crossmodal links to sweet-sour (also orange belongs to this group; the average values – 3.6, 3.3, and 3.4). Grey, blue, and white (2.7, 2.6, and 2.6) are most typically rated as the salty colours, whereas white, grey, and brown (2.9, 2.8, and 2.7) – as the bitter ones. Colours that were rated as tasteless (and also negatively rated in respect to their taste/flavour) were grey (average value 3.3), brown (2.9), blue (2.8), and white (2.8). Our results indicate that the actual tasting decreased likeability but colour could increase preference for it.

Conclusion. According to our results, there are systematic emotional and associative links between flavours, colours, and their preferences. Our findings can be used to improve the likeability of medication and food.

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Inpatient treatment and rehabilitation of children and adolescents with Autism spectrum disorders (ASD) and intellectual disability (ID)

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Background. The development of intellectual abilities can be very different in children with autism spectrum disorders. According to populational studies, as much as 30–45% of people with ASD have some form of comorbid ID. There are currently no effective pharmacological treatments for core symptoms of ASD independent of their intellect level, and the goal of treatment and rehabilitation is to increase functional independence and quality of life through learning and development, improved communication, and social skills.

Aim. The aim of this study was to investigate the patterns of uses of pharmacological treatment and psychosocial rehabilitation in children and adolescents with ASD and comorbid ID in Latvia.

Methods. A retrospective study based on analysis of medical records of patients with a diagnosis of ASD (F84*, ICD-10) who received inpatient psychiatric care in Children's Clinical University Hospital in the period from January 2015 to December 2019.

Results. The study included 316 admissions of which 252 (79.7%) patients were boys. In this study, 181 (57.3%) patients with ASD had comorbid ID. 40 (12.7%) patients had mild ID, 82 (25.9%) moderate ID, 33 (10.4%) severe ID. The mean age of patients was 6.55 (SD=4.03) years, and there was a significant difference between ID and non-ID groups, patients with comorbid ID tended to be older (difference of means 1,22 years, p=0.01). The mean duration of hospital stay was 6.76 (SD=4.62) days, and there were no significant differences between patients with and without ID. 71 (39.2%) of patients with ASD and ID received pharmacotherapy, while only 29 (21.5%) of the patients without ID (p=0.00). 131 (97.0%) patients without ID have received psychosocial rehabilitation interventions, but only 151 (83.4%) patients with ID (p=0.00) have benefitted from this support.

Conclusion. In the inpatient child and adolescent population of patients with ASD, the prevalence of comorbid ID is high, – even higher than could be expected based on the published populational prevalence estimates. The patients with comorbid ID are more likely to be treated with medication, and less likely to receive psychosocial rehabilitation. Efforts should be made to increase the use of evidence-based non-pharmacological interventions in children with ASD and comorbid ID.

Self-assessment of depression and anxiety symptoms among patients with epilepsy

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Background. Around one-third of people with epilepsy suffer from depression and/or anxiety. These conditions may have a negative impact on the quality of life and may lead to suicidal ideation or attempts. Both conditions are generally underdiagnosed and undertreated. In many countries, self-assessment scales are validated and used as screening instruments, including Patient Health Questionnaire-9 (PHQ-9) for assessing depression symptoms, and Generalized Anxiety Disorder-7 (GAD-7) scale for detecting anxiety symptoms. Both are frequently used in research and are suitable for general population and risk groups, including epilepsy patients. Recently, PHQ-9 has been validated in Latvia.

Aim. To determine the prevalence of depression and anxiety symptoms among people with epilepsy in comparison to people without epilepsy based on self-assessment.

Methods. The study took place at Riga East Clinical University Hospital, where patients were interviewed using PHQ-9 and GAD-7 scales. *MS Excel* database was created for data collection and basic statistics. IBM SPSS was used for data analysis. Fisher's exact probability test was used to compare results, p value below 0.05 was considered statistically significant.

Results. 42 participants (21 with and 21 without epilepsy) were included. In the epilepsy group, the mean age was 45.4 years (SD±16.8), 61.9% (n=13) were male. In the control group, the mean age was 41.5 years (SD±14.9) and 57.1% (n=12) were male. 66.7% (n=14) of people with epilepsy and 23.8% (n=5) in the control group showed at least mild depression symptoms (PHQ-9 score >4 points), with no statistical significance between results in both groups (p=0.062). According to GAD-7 results, 57.4% (n=12) of participants with epilepsy and 4.8% (n=1) without epilepsy had at least mild anxiety symptoms (>4 points). GAD-7 results were significantly different (p<0.005) between both groups. Three participants with epilepsy had been previously diagnosed with depression, one with both conditions (one received antidepressants). None in the control group had been diagnosed with either condition. Seven epilepsy patients (33.3%) and none of participants (0%) in the control group had suicidal ideation based on their PHQ-9 answers.

Conclusion. Depression and anxiety symptoms, as well as suicidal ideation are highly prevalent among people with epilepsy. Compared with people without epilepsy, anxiety symptoms were significantly more prevalent among epilepsy patients. Screening for both conditions should be performed. Simple instruments like self-report questionnaires used in this study could be useful in identifying patients in need for further evaluation to ensure that they would ultimately receive the necessary support and treatment.

Occupational burnout among Vilnius University residents

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Background. Occupational burnout is defined as a physical and emotional exhaustion caused by prolonged emotional work. Occupational burnout is characterized by high prevalence rates of burnout among the medical workers. The prevalence of burnout in residents has shown the largest burnout results of all medical workers. It is important to analyse occupational burnout to identify the prevalence of it. Research deficiency of occupational burnout among residents in Lithuania determined the aim of this study.

Aim. The aim of the current study was to determine occupational burnout prevalence among Vilnius University residents.

Methods. The survey was conducted through an anonymous questionnaire in 2019. 243 Vilnius University residents were involved in research analysis. Occupational burnout prevalence was measured using the Copenhagen Burnout Inventory (CBI). The CBI questionnaire identifies three components of occupational burnout – personal burnout (the degree of physical and psychological fatigue and exhaustion experienced by the person), work-related burnout (the degree of physical and psychological fatigue and exhaustion that is perceived by the person as related to his/her work), and patient-related burnout (the degree of physical and psychological fatigue and exhaustion that is perceived by the person as related to his/her work with patient). The questionnaire also included socio-demographic questions.

Results. 62.9% of the residents experienced a work-related burnout, 48.1% suffered from patient-related burnout and 32.5% experienced a personal burnout. The overall prevalence of occupational burnout components was 59.7%. Personal and work-related burnout scores were higher for females. The trend test has shown that personal burnout increases with age. 53.6% of respondents who were not satisfied with residency studies experienced personal burnout, 85.5% were affected by work-related burnout, and 68.1% were affected by patient-related burnout. 76.2% of residents who assessed their health as bad were affected by personal burnout, 85.7% were affected by work-related burnout, and 71.4% were affected by patient-related burnout.

Conclusion. More than a half of Vilnius University residents experience work-related burnout, nearly half residents experience patient-related burnout and more than one-third of residents experience personal burnout. The survey revealed that women were more likely to experience personal and work-related burnouts. It was found that personal burnout increased with age. Personal burnout, work-related burnout and patient-related burnout is related to satisfaction with the residency studies and health assessment.

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Parent reports on externalizing difficulties in child-adolescent psychiatric outpatient setting using SDQ and their relation to clinical diagnosis

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Background. Externalizing symptoms in child-adolescent psychiatry include various impulsive, hyperactive, disruptive, and aggressive behaviours. Externalizing problems is the most common reason leading children and adolescents to be referred for mental health treatment (Frick, Thornton et al, 2017). In Latvia, there are no official screening instruments that have been validated and regularly used in child-adolescent psychiatry setting. The Strengths and Difficulties Questionnaire (SDQ) is currently one of the most widely used screening instruments in child-adolescent psychiatry (Goodman et al, 1997).

Aim. The aim of this study was to examine the prevalence of parent-reported externalizing difficulties in outpatient child-adolescent psychiatry setting using SDQ and to explore the relation between parent-reported results and clinical diagnosis set by a child-adolescent psychiatry specialist.

Methods. The study was conducted in two outpatient centres in Latvia. The study group was 370 patients, 2–17 years old, who received outpatient child-adolescent psychiatry care, and their parents. Parent-reported externalizing difficulties were assessed using SDQ parent version – hyperactivity/inattention and conduct problems subscale (combined – externalizing difficulties scale). Externalizing disorders in this study were F1x, F90, F91 – according to ICD-10. When analysing the score, 4-band categorization was used, 3rd and 4th band were defined as "high".

Results. 344 valid parent reports were analysed. At least one externalizing disorder was diagnosed in 27.3% (N=94) of patients. The levels of parent reported externalizing difficulties by SDQ were high, with 47.7% of parents reporting high level of conduct problems and 31.7% of parents reporting high level of hyperactivity/inattention problems. Patients with externalizing disorder diagnosis had higher parent reported results in conduct subscale (mean – 4.49 points vs. 3.23), $p<0.001$, hyperactivity scale (7.76 vs. 5.30), $p<0.001$, externalizing disorder scale (mean – 12.27 points vs. 8.5), $p<0.001$, and total disorder scale (20.26 vs. 17.31), $p<0.001$. Patients with an externalizing disorder diagnosis showed lower results in emotional disorder subscale (3.89 vs. 4.8) than those who did not have the diagnosis, $p=0.004$.

Conclusion. Parents reported high levels of externalizing difficulties, higher than the prevalence of diagnosed disorders. Patients with externalizing diagnosis had higher parent reported results in concordant scales – conduct, hyperactivity/inattention, and external difficulties scale. This suggests SDQ could be a useful instrument for screening patients in child and adolescent psychiatry in Latvian population. In further research, SDQ validity and reliability should be explored, and for implementing this instrument in clinical practice, cut-off values for Latvian population should be explored.

Relationship between health system evaluation and anxiety, depression and assessment of their own health state in multimorbid patients

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Background. Multimorbid patients spend a lot of time in Primary Care (PC). Visits to PC physicians tend to get shorter, so it is important that each appointment's time would be used as effectively as possible. Although it is known that the quality of visit impacts health state control, the literature is limited as to whether insufficient patient's information about his condition affects his mental health or his health condition.

Aim. To investigate the correlation between health system assessment and depression, anxiety in patients with multimorbidity and find out whether this affects the assessment of their own health condition.

Methods. A single cross-sectional study was performed by the method of an anonymous questionnaire. Inclusion criteria: patients over 18 years of age and diagnosed with two or more chronic diseases from two different organ systems. The questionnaires were completed by 65 (25 females and 40 males; age 62.54±8.537) multimorbid patients. Health system was evaluated using 5 statements with 5 possible answers (1 – almost never, 2 – generally not, 3 – sometimes, 4 – most of the time; 5 – almost always):

- I was...
- asked for my ideas when we made a treatment plan;
- satisfied that my care was well-organized;
- shown how what I did to take care of my illness influenced my condition;
- helped to make a treatment plan that I could implement in my daily life;
- asked how my chronic illness affects my life.

Anxiety and depression were assessed using the Hospital Anxiety and Depression Scale. Health condition was evaluated with the visual analogue European Quality of Life Scale (EQ-VAS) from 0 (worst condition) to 100 (best condition). Data analysis was performed using the SPSS 24.0 program. Correlation was significant, if $p<0.05$.

Results. In this research, only one statement "Satisfied that my care was well organized" correlated with anxiety ($r=-0.278$; $p=0.025$). It showed that if there is a lack of satisfaction in a patient's health care, it promotes an increase of the patient's anxiety. There were no correlations among health system evaluation and depression or patient's health state.

Conclusion. The clinicians should pay attention that dissatisfaction of not well-organized health care can cause more anxiety for the patients.

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INTERNAL MEDICINE

Itch in psoriasis and its contributing factors

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Background. Psoriasis is a chronic inflammatory dermatosis, frequently presenting with chronic itch. Pruritus may be severe and seriously affect the quality of life of patients. Most of the psoriatic patients have a defective protective barrier that is easily permeable to allergens in the environment, including those that can cause itching. The study evaluated objective, molecular factors and laboratory parameters associated with the disease.

Aim. To find out what laboratory parameters indicate the loss of skin protective barrier functions that can clinically cause itching, which would allow to adjust the choice of treatment for patients with psoriasis.

Methods. Retrospective study – review and analysis of laboratory examinations from the patient histories of Prof. Jānis Ķīsis patients who were diagnosed with psoriasis in the period from January 2015 to November 2020. In the prospective part in 2021, we will conduct a survey of psoriasis patients to find out their quality of life in relation to itching before starting treatment.

Results. The study included 435 patients- men (n=245) and women (n=190). The groups of men and women were further divided into age groups. The first group included patients aged 18 to 50, while the second group included patients aged 51 and older. 18 laboratory parameters were analysed from patient medical histories. According to the obtained data, a correlation was observed that for both women (35.7%) and men (38.3%) the ASO values in the age group 18 to 50 are above the norm (p= 0.002), compared to the age group 51 and older (p=0.026). Low levels of HDL contribute to weakening of protective gear, for both women and men aged 18 to 51, HDL was below normal (women=86.1%; men=83%) and for age group 51 and older (women=76.5%; men=86.2%).

Conclusion. Following a summary of the data performed, it may be encouraged that itching may be increased by abnormalities in laboratory parameters, that indicates a reduction in the functions of protective barriers, a systemic inflammation that allows personalized medicine in psoriasis patients to reduce the severity of psoriasis and pruritus.

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Prevalence and dermatoscopic features of non-infectious balanitis

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Background. Chronic recurrent balanitis is a common, although underrecognized medical concern among male patients. Clinical signs are unspecific, and therefore clinicians commonly treat these conditions empirically, e.g., using antifungal medication against *Candida spp*. Nevertheless, up to a half of balanitis cases have a non-infectious aetiology. Dermatoscopy could potentially help in differentiating between different types of balanitis.

Aim. The aim of the current study was to describe the prevalence of different non-infectious balanitis, as well as their dermatoscopic features in a single clinical centre.

Methods. Approval of Riga Stradiņš University Ethics Committee (No. 6-3/82 29.11.2018) was acquired. Patients with a chronic recurrent balanitis (N=49) that presented to a single clinical centre over a period of 18 months had been enrolled in this study. Patients with sexually transmitted diseases were excluded from the study. Digital dermatoscopy (20x magnification, Medicam 1000, FotoFinder Systems GmbH, Germany) and a 3 mm punch biopsy has been performed. Dermatoscopic and histopathological evaluation has been performed. Candidal balanitis was diagnosed according to a positive culture for *Candida spp.* and a clinical response to an antifungal treatment.

Results. Lichen sclerosus (N=18 (28.6%)), lichen planus (N=13 (26.5%)), non-specific balanitis (N=10 (20.4%)), psoriasis (N=9 (18.4%)) and Zoon's balanitis (N=3 (6.1%)) were histopathologically confirmed among the enrolled patients. Each type of balanitis had characteristic dermatoscopic features, including Wichkam's striae in case of lichen planus balanitis, dotted vessels and diffuse scaling in psoriatic balanitis, white structureless areas with peripheral linear vessels in lichen sclerosus, red to orange structureless area and curved vessels in Zoon's balanitis.

Conclusion. Five non-infectious balanitis types have been documented over a period of 18 months in a single clinical centre. Dermatoscopy can help in differentiating among these entities.

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Primary healthcare practitioners' knowledge and beliefs in pain management with opioid medications

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Background. Pain management is a daily work for primary healthcare practitioners (PHP). Numerous studies showed the lack of adequate knowledge about pain diagnosing and management, which, in turn, led to undertreatment of pain.

Aim. The aim of the current study was to analyse primary healthcare practitioners' knowledge and beliefs in opioid prescription for pain management.

Methods. The study was performed through a survey. Along with questions about geodemographic data, modified KnowPain-50 questionnaire was used. The survey assessed PHP knowledge, attitudes and beliefs in: 1) initial pain assessment; 2) defining goals and expectations; 3) development of a treatment plan; 4) implementation of a treatment plan; 5) reassessment and management of longitudinal care; 6) management of environmental issues. *IBM SPSSv23* was applied for the statistical analysis.

Results. In total, 100 participants (the mean age 46.2 years, SD±14.1) were included in the analysis, predominantly females (89.0% vs. 11.0%). Work experience as a doctor ranged from less than a year to 45 years. Most of the patients of the interviewed doctors were adults (71.0%). At least every fourth PHP did not consider himself/herself sufficiently competent in diagnosing the type of pain (24.0%) and every fifth doctor – in prescribing adequate pain therapy (20.0%). Meanwhile, up to 42.0% PHP disagreed with the statement that he/she could pass opioid therapy prescription exam tomorrow, and 61.0% did not feel comfortable calculating conversion doses of commonly used opioids. The presence of a physiologic basis for pain should be the primary factor to prescribe opiates for 43.0% PHP, and 60.0% believed that chronic pain of unknown cause should not be treated with opioids, even if this is the only way to obtain pain relief. Almost half of PHP (46.0%) thought that persons who fit the profile of a likely drug abuser should never be treated with opioids and even more – it was not lawful to prescribe an opioid to treat pain in a patient with a diagnosed substance use disorder (44.0%). At varying degrees, 64.0% of professionals were confident that there was a "ceiling" to the dosage of pure agonist opioids, and long-term use of nonsteroidal anti-inflammatory drugs in the management of chronic pain had a higher risk of tissue damage, morbidity, and mortality than long-term use of opioids (56.0%).

Conclusion. The study results indicated insufficient knowledge in pain assessment and management, especially in opioid prescription. More attention should be paid on PHP's education on pain management.

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Analysis of the hospitalized patients with systemic sclerosis in Pauls Stradiņš Clinical University Hospital Rheumatology department during 2017–2020

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Background. Systemic sclerosis is one of the most severe autoimmune rheumatic diseases with high morbidity and mortality rates. Frequently, the disease progression is very fast and unresponsive to immunosuppression therapy, especially in later stages.

Aim. The aim of the current study was to evaluate demographic data, immunological peripheral blood tests and organ involvement in patients with systemic sclerosis, who were hospitalized in rheumatology department from 2017 to 2020, comparing with worldwide statistics.

Methods. Altogether, 82 patients were enrolled in this study. All of them met diagnostic criteria for systemic sclerosis (The ACR/EULAR 2013). Retrospective study was performed where were analysed hospital data of clinical histories and immunological blood tests of these patients during 2017-2020.

Results. Altogether 82 patients were enrolled in the study. 67 of them females (82%), 15 males (18%). The average age in time of hospitalisation was 61 years. The youngest patient was 20 years old, the oldest one – 86 years of age. 23 patients had positive *anti-Scl 70* antibodies (anti-topoisomerase I) and 28 patients had positive anti-centromere antibodies. We found no significant correlation between specific antibodies and gender. Raynaud's syndrome was observed in 71 patients (87%), 26 of them anti-centromere positive, 21 of them *anti-Scl 70* positive. 26 of 28 anticentromere positive patients had Raynaud's syndrome (93%). Pulmonary hypertension was observed in 25 patients (30%) – by transthoracic echocardiography or by right heart catheterization. 11 of them with positive anti-centromere antibodies, 5 of them with positive *anti–Scl 70*. 11 of 28 anticentromere positive patients had pulmonary hypertension (39%). Interstitial lung disease was observed in 43 patients (52%), 8 of them with positive anti-centromere antibodies, 18 of them with positive *anti–Scl 70*. 18 of 23 *anti-Scl 70* positive patients had interstitial lung disease (78%).

Conclusion. In our study, it was found that systemic sclerosis predominately affected females, with female: male ratio 4.5:1 similar to worldwide data. Raynaud's syndrome was the most common manifestation of systemic sclerosis and was diagnosed in all patients with positive anticentromere antibodies. We found a significant correlation between anti-centromere positive patients and a development of pulmonary hypertension, as well as in *anti-Scl 70* positive patients and interstitial lung disease. We observed similar data when comparing with worldwide studies.

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Hereditary angioedema in Latvia and Lithuania

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Background. Hereditary angioedema (HAE) is a rare, life-threatening, inborn error of immunity disease, characterized by recurrent episodes of subcutaneous or submucosal edema. There are known C1 inhibitor associated (I/II) and non-associated types of HAE. I/II HAE are mainly caused by pathogenic variations in the *SERPING1* gene, that results in deficient or dysfunctional C1-INH, leading to overproduction of bradykinin and the development of massive local edema. The aetiology and pathogenesis of HAE with normal C1-INH is associated with gain-of-function pathogenic variants in genes involved in the quinine (incl. bradykinin) system (*F12, PLG, ANGPT1, KNG1*).

Aim. To assess a prevalence and clinical diversity of HAE in two Baltic countries – Latvia and Lithuania.

Methods. 43 HAE patients (according to the WAO/EAACI definition 2017) from Latvia and Lithuania were included in the study. Retrospective study was performed, where immunological peripheral blood tests, epidemiological and clinical data were analysed.

Results. 12 patients (11 women and 1 man) from Latvia, 31 – from Lithuania (16 women, 14 men, one child – girl) were diagnosed of HAE during the period from 2004 to 2020. Almost all patients (42/43) were diagnosed with C1-INH associated HAE (I/II types). The diagnosis was most commonly made in adults between the ages of 31 and 70 years. 2 patients died. Genetical analysis was done in 5/13 patients from Lithuania (pathogenic variations in the *SERPING1* gene were detected in 2 cases). 11/43 of examined patients had uncontrolled relapses of disease with severe angioedema attacks including abdominal and airway edema on average 2–4 times per month.

Conclusion. Prevalence of HAE is about 1 in 15 000–50 000 people worldwide. In Latvia, the expected amount of HAE is 38–100 patients versus 12 patients diagnosed now. In Lithuania, provisionally 50–160 HAE patients versus 31 diagnosed. HAE is often poorly recognized because of its nonspecific signs. Low awareness of HAE as a primary immunodeficiency among non-allergists and non-immunologists is one of the most likely explanations for the low prevalence of diagnosed HAE in both countries, especially in Latvia.

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Diagnostic challenges in patients with suspicions for primary immunodeficiencies in Latvia

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Background. The immunological tests are not informative in all the cases of patients with suspicions of primary immunodeficiencies (PID). Genetic testing is used for better diagnostics of primary immunodeficiencies. More than 430 genes are known as causes of inborn errors of immunity. The yield of NGS testing in PID in various reports show a high variability (15–79%) and is dependent on the patient selection criteria and the gene content of the analysed panel.

Aim. To characterize clinical phenotypes and data of next generation sequencing (NGS) test results of consulted patients with suspected primary immunodeficiencies in Latvia.

Methods. Retrospective data of 21 clinical histories and genetic testing NGS from the Children's Clinical University Hospital Clinic of Medical Genetics and Prenatal Diagnostics were analysed during 2018–2020.

Results. DNA of 21 patients (aged from 3 months to 31 years) were tested for suspicion of primary immunodeficiencies. Clinically, there was a heterogenous group of patients: 5 patients with unclear periodic fevers, 6 – recurrent pyogenic infections, 1 – recurrent Herpes simplex virus encephalitis, 1 – chronic urticaria with infections, 1 – suspicion of hyper IgE syndrome, 1 – recurrent severe osteomyelitis and sepsis, early recurrent viral infections, 1 – recurrent multifocal osteomyelitis, 1 – severe autoimmune disorders, 2 – recurrent candidiasis, 1 – meningitis and aspergillosis, 1 – Burkitt lymphoma. All were sent for the analysis of a selected PID genes panel (274 genes in 2018, updated to 298 in 2019), and in 3 cases analysis was later expanded to whole exome sequencing. In 17 (81 %) patients, the results were negative; in two (10%) patients – a variant of uncertain significance (VUS) was identified of whom one patient had *PLCG2*:c.3682C>T, p.(Arg1228Trp) in homozygous state and in another patient *PIK3CD*:c.2905C>T, p.(Arg969Cys) in heterozygous state. In four (20%) patients – pathogenic or likely pathogenic variants in different genes were identified: *PIK3CD*:c.1573G>A,p.(Glu525Lys) causing immunodeficiency-14; *CYBB*:c.676C>T,p.(Arg226*) confirming X-linked chronic granulomatous disease; *STAT1*:c.812A>C,p.(Gln271Pro) causing immunodeficiency-31 and *SH2D1A*:c.5A>G,p.(Asp2Gly) confirming X-linked lymphoproliferative syndrome. **Conclusion.** In our study of genetic results for suspicions of PID, pathogenic variants were found in 19% (4/21) of the patients. We suggest that the whole genome and transcriptome sequencing approaches may be useful in other individual cases, where a definitive diagnosis is not reached.

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Neurofilament light chain in the serum of patients with multiple sclerosis

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Background. Multiple sclerosis (MS) is a chronic autoimmune inflammatory and neurodegenerative disease of central nervous system. Neurofilament light chain (NfL) represents neuronal cytoskeleton and its level increases in serum when there is neuro-axonal damage.

Aim. We aimed at comparing serum neurofilament light chain levels in multiple sclerosis patients and healthy controls and determined its association with the clinical course of the disease.

Methods. In this cross-sectional study, we collected serum samples of 68 multiple sclerosis patients and 70 respondents in healthy control group. Neurofilament light chain was measured by Single Molecular Array (SiMoA) technology. We analysed the level of serum neurofilament light chains in both groups. The patient`s clinical condition was determined by medical documentation. The neurological examination data was defined by Expanded Disability Status Scale (EDSS).

Results. NfL levels were measured in serum of 139 participants: 70 were in the healthy control group and 69 were MS patients. In the healthy control group 28 were male and 42 – female, in MS group – 29 male and 39 female. The mean age of respondents in the healthy control group was 37.94±12.96 years and 38.76±10.4 years in MS group. The mean level of neurofilament light chain in the healthy control group was 5.95±3.12 ng/L but in the MS group 7.74±4.9 ng/L and it was statistically significantly different ($P_{MV}=4.37x10^{-2}$). We confirmed statistically significant correlation between age and serum NfL level in both groups (MS group $\varrho=0.35$; healthy control group $\varrho=0.62$), neurofilament light chain level increase with respondent`s age. Patients under the age of 45 with EDSS score $\leqslant 3.0$ had lower NfL level than patients with EDSS score from 3.5 to 6.0.

Conclusion. The serum level of NfL increases with age in all population groups, but it is significantly higher for MS patients with severe functional disability. The higher serum level of NfL shows neurodegeneration with disease progression.

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Calpain-3-related limb-girdle muscular dystrophy: complex genetics for a rare disease

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Background. Calpainopathy is a rare disease characterized by progressive weakness of proximal limb-girdle muscles, hyperCKemia and myopathic pattern in electromyography. Magnetic resonance imaging of muscle shows wasting of the posterior compartment of the thighs, sparing sartorius and gracilis. This characteristic pattern in MRI allows using it in the differential diagnosis. The prevalence of all limb girdle muscle dystrophies is 1:100 000, 30% of them being calpainopathies. They are caused by disease-associated variants in the *CAPN3* gene.

Aim. The objective of the study was to identify and describe genetic variants in calpainopathy patients.

Methods. Patients were recruited from the Neurology and Genetics Clinics at BKUS and from the outpatient clinic for neurological diseases at PSKUS. Testing for common disease associated variants in the *CAPN3*, whole exome sequencing and transcriptome analysis were performed at the Latvian Biomedical Research and Study Centre (BMC). Whole exome/genome sequencing was also performed in collaboration with the Myo-Seq project and at Prof. C. Bonnemann's laboratory. Genetic testing was also done at private laboratories as a part of routine diagnostic performed at the Genetics Clinic at BKUS. Allelic frequency of variants was obtained from the Genome Database of Latvian population.

Results and conclusion. BMC has been involved in solving unidentified neuromuscular diagnosis for more than a decade. Combined efforts with our collaborators have allowed us to find genetic aetiology in more than 80 patients with rare neuromuscular diseases. Nine of these patients have calpainopathy. The following variants in the *CAPN3* have caused an autosomal recessive type of inheritance and a non-uniform phenotype in our patients: NM_000070.3c.550del p.Thr184fs, c.643T>C (p.Ser215Pro), c.1043del (p.Gly348fs) and c.1079G>A (p.Trp360Ter).

The variant c.1333G>A (p.Gly445Arg) was associated with an autosomal dominant type of inheritance and an early asymptomatic hyperCKemia, which later complicates with myalgias and proximal weakness. We have observed this variant alone in three persons with dominant pattern of inheritance and in combination with the second disease causing allele in two persons, suggesting autosomal recessive inheritance.

Conflicting evidence has been reported previously regarding the effect of variant c.1746-20C>G on splicing and RNA expression. We have confirmed that mRNA analysis from the muscle biopsy showed altered splice site and new isoforms of CAPN3. The GnomAD reports allelic frequency 0.01 from the individuals of European background, in Latvian population it is 0.02, a significant increase over the average for Europe.

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Dynamics of multiple sclerosis progression in Latvian population

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Background. Multiple sclerosis (MS) is a lifelong demyelinating disease, an autoimmune disorder triggered in genetically predisposed subjects by environmental factors. Most MS patients go from RRMS (relapsing-remitting) to SPMS (secondary progressive MS form), but it is not clear why and how this transition occurs. Preventing disease progression in MS remains a serious challenge. Improved conditions of incidence research on a population-based level would offer new possibilities for more objective studying of MS progression dynamics.

Aim. The objective of the study was to estimate the dynamics of MS progression in Latvian population, analysing the clinical indicators in MS patient cohort and their changes in the period of 15–20 years from the first visit.

Methods. We conducted a descriptive incidence longitudinal study using the clinical data from collection of 288 MS patients, started at 2011 (disease duration of 1–51 years), on the basis of the Latvian Maritime Medical Centre. Socio-demographic and clinical data of time period first visit to 15/20 years was analysed to describe MS cohort in Latvians. T-test or Mann-Whitney test, Kruskal-Wallis H-test, Friedman test, χ^2 tests, Spearman correlation test were used for statistical analysis.

Results. At 2011, 1558 MS patients were registered in Latvia. Accordingly, the collection created in 2011 accounted for 18.48% of the Latvian MS cohort. 213 patients were required to consider the collection as representative of the MS population with sufficient reliability and study power. In the collection of MS patients, 70.83% are women, which corresponds to an average gender ratio of 2.4:1. The average age at diagnosis in the presence of the first symptoms of the disease was 29.40 years (95% CI 28.31–30.49) with most common first symptoms as visual (25.18%) or sensory (20.21%); the rate of progression (transition of patients from RRMS to SPMS group) was 13.35 years (95% CI 11.78–14.92); but the approximate age for this transition was 42.98 years (95% CI 41.15–44.82). The distribution of main clinical indicators associated with MS did not correlate with gender among the Latvian population.

Conclusion. To better understand the incidence rate and dynamics of MS progression in Latvian population we need to continue our research by increasing the sample size of patients and analyse their clinical parameters.

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The relationship between cognitive failures and human speech hearing difficulties

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Background. Individuals with hearing difficulties have a greater risk for cognitive failures (CF) and the development of dementia.

Aim. This study aimed to find a relationship between CF and the subjective human speech hearing difficulties (HSHD) among middle-aged females.

Methods. 310 females aged from 26 to 59 years (M=38.6) took part in an online study. They filled in the Cognitive Failures Questionnaire (CFQ). Answers about subjective HSHD were also registered. Results were compared using Fisher's exact test.

Results. Respondents with cognitive failures (CF+ group) more often had HSHD compared to those without cognitive failures (CF- group) (35.3% vs. 12.3%, p=.001). CF+ group more often reported to better understand the voice of male than female compared to CF- group (17.6% vs. 1.4%, p<0.001). CF+ group were more likely to get recommendations for checking their hearing by family or friends than CF- group (50.0% vs. 22.1%, p=0.001). CF+ group had more difficulties understanding everything when several people spoke than CF- group (47.1% vs. 10.9%, p<0.001). More prompt onset of fatigue when communicating was reported by more respondents in CF+ group than in CF- group (55.9% vs. 16.3%, p<0.001). Females in CF+ group more frequently had to make an effort when listening to a companion than CF- group (41.2% vs. 9.8%, p<0.001). Greater difficulties with understanding children's voice were reported by CF+ group than CF- group (32.4% vs. 2.2%, p<.001).

Conclusion. Cognitive failures in middle-aged females are related to a HSHD.

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Thyroid nodule malignancy risk stratification by numerous TIRADS systems – can we define the best one?

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Background. Thyroid ultrasound (US) is a key examination for management of thyroid nodules. Numerous TIRADS systems aim to improve interobserver reproducibility of descriptions, but the existing different stratification criteria maintain accuracy in suboptimal levels.

Aim. The purpose of the study was to assess, which of the four TIRADS systems (L-TIRADS, EU-TIRADS, K-TIRADS or ACR-TIRADS) is more accurate and sensitive, and to evaluate, which of the systems have the strongest association with malignancy and in which categories of these systems is the stronger association with malignancy.

Methods. The prospective study in which thyroid ultrasound and FNA biopsy were done to 200 patients (23 to 85 years, the mean age 54 years) with 213 nodules according to the national thyroid nodule biopsy guidelines. The majority of patients were women 186 (87.3%) and 27 (12.7%) men. Each nodule was classified by all four TIRADS systems and nodule malignancy risk stratification comparison was accomplished based on malignant pattern defined by certified radiologist and approved by cytology results (Bethesda).

Results. Of the 213 thyroid nodules, 149 nodules (69.95%) were benign, 9 (4.23%) nodules were suspicious of malignancy and 20 (9.39%) were malignant. All of the systems showed high sensitivity (100%), however, L-TIRADS appeared with higher accuracy (68%) and area under ROC curve (81%). All systems had a high sensitivity (100%), however, L-TIRADS showed a better accuracy (ACC=68%, $p<0.001$) than other systems – EU-TIRADS (ACC=40%, $p<0.001$), K-TIRADS (ACC=47%, $p<0.001$) and ACR-TIRADS (ACC=39%, $p<0.001$). Evaluation of L-TIRADS 4A-5 categories individually reveals that there is a statistically significant association between L-TIRADS 4C and malignancy ($p <0.001$) with a moderately high AUC value (0.63) and between L-TIRADS 5 and malignancy ($p<0.001$) with AUC of 0.60 L-TIRADS 4A (one sign) and 4B (two signs) categories did not show difference in malignancy risk ($p=0.63$ and $p=0.99$), respectively.

Conclusion. Although different TIRADS systems show high sensitivity, there are significant differences in accuracy among the intermediate and malignant subcategories (TIRADS 3–5). Simplified L-TIRADS system categorization by count of malignant signs was recognized as the most accurate in comparison to EU-TIRADS, K-TIRADS or ACR-TIRADS systems.

CD63 and DNA mismatch repair protein expression in prostate cancer

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Background. Protein expression levels in immunohistochemistry and molecular biomarkers are reported for their ability to predict recurrence, progression, development of metastases, or patient survival. The molecular features in low- and high-grade prostate cancer could be different, thus influencing treatment decision and prognosis.

Aim. The objective of the current study was to compare the expression of exosomal biomarkers CD63 and mismatch repair proteins (MSH2, MSH6, MLH1, and PMS2) by immunohistochemistry (IHC) in the tissue of patients with prostate cancer and benign hyperplasia.

Methods and material. The study was retrospective. Altogether, 62 patients with prostate acinar adenocarcinoma and 20 patients with prostate benign hyperplasia were enrolled in the study. The CD63, MSH2, MSH6, MLH1, and PMS2 expression was analysed by immunohistochemistry.

Results. Obtained results showed that CD63 expression was significantly higher in patients with prostate cancer Grade III–V compared to Grade I–II, respectively, 2.23 (1–3) vs. 0.92 (0–2) score, p=0.001. In addition, the significant positive correlation between the CD63 expression and Grade groups was revealed (Rho=+0.54; p<0.0001). Furthermore, the progression-free survival was significantly higher in patients with low CD63 expression, compared to high CD63 expression (p=0.0007).

MMR expression was absent in 14 patients (four patients with Grade I–II cancer and 10 patients with Grade III cancer). MMR was present in all cases of benign prostate hyperplasia (mild to moderate staining).

Conclusion. High grade prostate cancer (Grade group 3–5) characterized by increased CD63 expression, which correlated with progression-free survival.

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Clinical usefulness of FDG-PET/CT parameters in detecting of superficial oesophageal cancer

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Background. Oesophageal cancer is a major leading cause of death and has a poor prognosis. The high incidence of oesophageal cancer demonstrates the need for modern methods of detection and early treatment to improve patient prognosis.

Aim. The purpose of this study was to determine the clinical utility and importance of the use of ^{18}F-FDG-PET/CT for differentiating superficial oesophageal cancer.

Methods and materials. A retrospective cohort study of 98 patients with superficial oesophageal cancer at the Nagasaki University, between 2010 and 2020 an ^{18}F-FDG PET/CT image was taken. The images are visually and quantitatively analysed using special software (Metavol). To measure the effectiveness of PET/CT with FDG in predicting overall survival, we examined medical records and survival rates for all patients. Long-Rank and Wilcoxon methods were used to analyse survival. The JMP15 program was used for statistical analysis.

Results. On visual classification, FDG-negative patients had a better prognosis than FDG-positive patients with $p>0.0204$ using the Wilcoxon test, although the Log-Rank test did not reach statistical significance. In terms of quantitative parameters, FDG-negative patients had a significantly better prognosis than FDG-positive patients with both the Long-Rank $p>0.0280$ and Wilcoxon test $p>0.006$.

Conclusion. We analysed and differentiated the effectiveness of qualitative and quantitative parameters using high accuracy ^{18}F-FDG-PET/CT for detecting early stage of oesophageal cancer. Quantitative parameters have been shown to be effective in identifying asymptomatic patients with superficial oesophageal cancer that are difficult to detect using visual parameters alone.^{18}F-FDG-PET/CT may provide powerful predictive parameters for superficial oesophageal cancer.

Architectural distortion on mammography: multimodality radiologic imaging using standard and novel diagnostic tools in Oncology Centre of Latvia – correlation with histopathology

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Background. In mammography (MG), architectural distortion (AD) is defined by BI-RADS scoring system as normal breast architecture distortion with no definite mass visible, including spiculations radiating from a point and focal retraction or distortion at the edge of the parenchyma. AD is most often rated as BI-RADS 4 or 5 lesions (suspicious or highly suggestive of malignancy). If cancer is detected as a cause of AD, additional functional imaging tools (magnetic resonance (MR) or contrast-enhanced spectral mammography (CESM)) are recommended. Radial scar often mimics malignancy and because of association with high-risk lesions excisional biopsy is recommended.

Aim. To evaluate AD radiological characteristics, to determine the frequency of malignant, atypical lesions and radial scar lesions, as well as to detect if there is any enlargement of pathological area using functional methods.

Methods. This retrospective study included 35 patients who met AD criteria on mammography and had biopsy performed in Oncology Centre of Latvia from 1.01.2020 to 31.12.2020. Diagnostic standard mammographic, tomosynthesis and CESM images were obtained, US and MR examinations were performed. On MG imaging exclusion criteria were deformation with visible mass or multifocal lesions, malignant type calcifications and prior surgery. Diagnostic imaging and biopsy histopathological results were analysed using *IBM SPSS Statistics 25*.

Results. In total, 35 cases of AD detected on MG were rated as BI-RADS 3, 4 or 5 in 34%, 48% and 5% respectively, all of radial scars were classified as BIRADS 3 or 4 lesions. The most common density of the breast was category C in 65%, AD was detected on right breast in 54%. On standard MG, AD was detected in 88% of cases, while in 100% on tomosynthesis. 34 core ultrasound biopsies and 1 stereotactic biopsy were made. Breast carcinoma was detected in 51%, radial scar in 31%, atypical changes in 5.7%. CESM was performed for 12 patients (4 with radial scar, 8 with carcinoma), which showed contrast-enhancement in both groups (in 11 cases). Functional imaging methods were performed for 20 patients, presenting 4 malignant lesion cases with pathological area enlargement, comparing to MG data.

Conclusion. According to data obtained in this study, tomosynthesis is an excellent method for AD detection. Radial scar may mimic malignancy in radiological imaging and was rated as suspicious lesion, demanding further examination. Breast carcinoma was detected in 51 % of cases, and functional imaging (MR, CESM) showed increased extent of tumour in some cases.

Contrast-enhanced spectral mammography in pre-surgical evaluation of breast malignant lesions at Oncology Centre of Latvia – first-year experience

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Background. Contrast-enhanced spectral mammography (CESM) combines digital mammography with the intravenous administration of contrast material. Similarly to magnetic resonance imaging (MRI), it depicts enhanced differences between neoplastic and normal tissue, and has recently gained momentum as an innovative and clinically useful method for pre-surgical breast assessment.

Aim. The aim of this study was to evaluate the first-year experience – performance and benefits of CESM at Oncology Centre of Latvia.

Methods. This retrospective study included 97 women with histologically proven breast cancer, who underwent CESM at Oncology Centre of Latvia between 01.01.2020 and 31.12.2020. We reviewed CESM findings and assessed correlation by histopathological type and treatment data. We made statistical analysis of compiled data with *IBM SPSS Statistics 26*.

Results. Our study included 97 females with mean age 58.73 (range 37 to 85). Breast density BI-RADS classification was B, C, A and D for 62.9%, 32.0%, 3.1% and 2.1% respectively. 93 cases were invasive lesions and 4 were in situ lesions. The most common finding on low-energy images was mass with or without (±) calcifications in 68% (n=66), followed by architectural distortion ± calcifications in 16.5% (n=16), microcalcifications alone in 9.3% (n=9) and asymmetry ± calcifications in 4.1% (n=4). 2 patients (2.1%) had no findings on low-energy images due to dense breast parenchyma, however, multifocal cancer was observed on high-energy images in both cases. The majority of lesions were ⩾15 mm in 85.6% (n=83), 10–14 mm in 11.3% (n=11) and 1–9 mm in only 3.1% (n=3) of cases. CESM identified 99% (n=96/97) of malignant lesions, with strong enhancement observed in 80.4% (n=78) and weak enhancement in 18.6% (n=14). The only lesion not identified was a small (1–9 mm) mass. On CESM, we saw increased extent of tumour in 34% of patients (n=33), from those multifocality in 84.8% (n=28). As a result, 34% (n=33) of patients had changes in treatment strategy – 72.7% (n=24) had more extensive surgery, and 27.3% (n=9) had neo-adjuvant chemotherapy (p=0.008). Along with CESM, 16.5% (n=16) patients also underwent breast MRI – we observed correlation of findings in 93.8% (n=15) cases, and overdiagnosis on MRI in 1 case.

Conclusion. CESM provides high sensitivity for identifying breast cancer and the real extent of it, especially for lesions ⩾10 mm, and lead to changed treatment strategy in 34% of cases. Our data suggests that CESM is comparable to MRI in terms of cancer detection and size estimation.

Impact of targeted molecular imaging with ^{18}F-PSMA-1007 PET/CT in multimodal evaluation of prostate cancer

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Background. According to the European Urology Association, prostate cancer remains the second most commonly diagnosed cancer in men, accounting for 15% of all cancers diagnosed. Accurate localization of recurrent prostate cancer is a major challenge, it can be assessed by magnetic resonance imaging (MRI) and positron emission tomography in combination with computer tomography (PET/CT).

Aim. The aim of this study was to compare the diagnostic tools – ^{18}F-PSMA-1007 PET/CT and MRI for evaluation of local recurrence and regional lymph nodes. Radiopharmaceutical ^{18}F-PSMA-1007 is a ligand, used in PET/CT, and it has some advantageous characteristics in recurrent prostate cancer diagnostics.

Methods. This comparative prospective study included 29 prostate cancer patients (mean age 66.83±6.76 years) with biochemical relapse referred for ^{18}F-PSMA PET/CT, who were previously treated with radical prostatectomy and/or radiation therapy of the prostate bed. The probability of a ^{18}F-PSMA-1007 PET/CT scan suggestive of pathology was compared with MRI Imaging results, PSA level and Gleason score (GS). Clinical data of patients and/or follow-up information were used as the reference standard.

Results. PET/CT confirmed pathological findings in 20/29 patients, 69%, respectively. The overall mean PSA level in the study group was 2.48 ng/ml (range 0.16–13.1 ng/ml). The mean PSA level in PET-positive finding group was higher than in PET-negative finding group (3 ng/ml vs. 1.3 ng/ml), but without statistically significant correlation (r_s=0,33; p=0,08). The mean PSA doubling time – 10.4 months, the median Gleason score was 7 (range 5–9), and 72% (N=21) had a score above 7 (with prevalence of 3+4), the rate of pathological scans in these patients was 80% (N=17).

Local recurrence findings were detected by PET/CT in 35 % (n=10/29), in MRI – 31% (n=9/29). Nodal involvement was evaluated by PET/CT and MRI in 48% (n=14/29) and 28% (n=8/29). Overall method sensitivity was for ^{18}F -PSMA-1007 PET/CT and MRI for local recurrence 90.9% vs. 81.8% and for regional lymph nodes sensitivity 92.9% vs. 57.1%.

Conclusion. This study results revealed ^{18}F -PSMA-1007 PET/CT as superior diagnostic tool to MRI for evaluation of recurrent prostate cancer. Results are highly dependent on PSA level increase and Gleason score, confirming result stability in the groups with GS >7.

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Incidence of acute and chronic complications in patients with pancreatogenic, type 1 and type 2 diabetes mellitus

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Background. Because pancreatogenic diabetes mellitus (PDM) is rarely associated with absolute insulin deficiency, diabetic ketoacidosis occurs not so frequently in PDM patients, as well as in type 2 diabetes mellitus (2TDM) patients in comparison with type 1 diabetes mellitus (1TDM) patients. Additionally, destruction of glucagon-producing α cells and increased peripheral insulin sensitivity seen in the case of PDM results in the high risk of hypoglycaemia. Chronic diabetic complications as diabetic neuropathy, nephropathy and retinopathy are observed in all three types of diabetes mellitus (DM).

Aim. To detect difference in the incidence of acute and chronic complications in PDM, 1TDM and 2TDM patients.

Methods. 1087 patients with 1TDM, 2TDM and PDM who had been treated in departments of endocrinology, gastroenterology and surgery at the Pauls Stradiņš Clinical University Hospital for period 2018–2019 were retrospectively analysed. 90 patients were randomly selected – 30 patients with 1TDM, 30 patients with 2TDM and 30 patients with PDM. The incidence of acute and chronic complications was studied and compared between the patients.

Results. Diabetic ketoacidosis occurred in 11 patients (36.7%) with 1TDM, in 2 patients (6.7%) with 2TDM and in 4 patients with PDM (13.3%). There was statistically significant difference in the incidence of diabetic ketoacidosis comparing these three types of DM (p=0.008). However, the prevalence of hypoglycaemia was not significantly different – 7 (23.3%) cases of 1TDM, 3 (10%) cases of 2TDM and 8 (26.7%) cases of PDM (p=0.233). Our results showed statistically significant difference in the incidence of diabetic nephropathy and retinopathy – diabetic nephropathy was observed in 9 1TDM patients (30%), in 17 2TDM patients (56.7%) and in 3 PDM patients (10%) (p=0.001) and diabetic retinopathy occurred in 11 1TDM (36.7%) patients, in 7 (23.3%) patients and nobody with PDM had this complication (p=0.002). However, there was not statistically significant difference in the prevalence of diabetic neuropathy – 15 cases (50%) of 1TDM, 18 cases (60%) of 2TDM and 9 cases (30%) of PDM (p=0.06).

Conclusion. Diabetic ketoacidosis occurred less often in PDM and 2TDM patients in comparison with 1TDM patients, however, the incidence of hypoglycaemia was not significantly different. There was difference in the prevalence of diabetic retinopathy and nephropathy but diabetic neuropathy was equally common complication seen in the patients with these types of DM

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Hypoglycaemia and its association with metabolic compensation in patients with type I diabetes mellitus, preliminary data

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Background. Hypoglycaemia is the most common acute complication of diabetes mellitus. Severe hypoglycaemia can cause accidents, injuries, coma, and may even prove fatal. It also causes glycaemic variability. Long-term fluctuations in glycemia contribute to the development of chronic complications of diabetes.

Aim. The aim of this study was to analyse the frequency of hypoglycaemia in patients with type I diabetes (T1DM), as well as its association with HbA1c and duration of diabetes.

Methods. A retrospective study of 29 patients with T1DM. Data were received from SIA University of Latvia Medical Postgraduate Education Institute. Depending on the level of HbA1c, participants of this study were divided into the following groups: group I – good compensation of diabetes (HbA1c<6.5%), group II – satisfactory compensation of diabetes (HbA1c=6.5-7.5), group III – poor diabetic compensation (HbA1c>7.5%). Additional information was obtained through a questionnaire.

Results. The average age of the interviewed participants was 36.10±12.32 years. Most of them (21 participants or 72.4%) have poor metabolic compensation. The mean HbA1c among participants was 8.32±1.27%. Median diabetes duration was 14.85±9.79 years. In our study, all respondents experienced mild hypoglycaemia, 7 respondents (24.1%) had experienced moderate hypoglycaemia, 4 respondents (13.7%) – severe hypoglycaemia in the past year. Hypoglycaemia occurred more frequently in the third group, but this study did not find a statistically significant difference between groups and mild (p=0.819), moderate (p=0.061) or severe (p=0.540) episodes of hypoglycaemia. Moderate hypoglycaemia episodes were strongly associated with diabetes duration (p=0.043), with 51.7% of those with diabetes ⩾10 years having an event in the past 12 months. It is likely that the increased risk with longer duration is related to the development of autonomic neuropathy, impaired counterregulatory hormone responses to hypoglycaemia and altered renal function. No significant correlation was found between the frequencies of all and severe hypoglycaemia with the mean HbA1c and *self-monitoring blood glucose*.

Conclusion. In our study, there was no strong association between hypoglycaemia and HbA1c, but further research is needed. Hypoglycaemia can occur at any level of HbA1c. Isolated HbA1c cannot be used as a surrogate marker for hypoglycaemia. Early recognition of hypoglycaemia risk factors, self-monitoring of blood glucose and appropriate educational programs for healthcare professionals and patients with diabetes are the major ways forward to maintain good glycaemic control, minimize the risk of hypoglycaemia and thereby prevent long-term complications.

Assessing quality of life in type 1 diabetes and type 1 diabetes-associated autoimmune diseases

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Background. Type 1 diabetes (T1D) is one of the most common chronic diseases in the population under 18 years of age. It requires extensive self-management to avoid complications and may have negative effects on the everyday life of children with the disease. T1D results from the autoimmune destruction of pancreatic beta cells. Thence, it is often associated with other autoimmune diseases. Most common comorbidities include celiac disease, autoimmune thyroid disease, autoimmune gastritis, pernicious anaemia and vitiligo. These diseases may decline glycaemic control, lead to an increase rate of hypoglycaemia, can cause malabsorption and anaemia, which additionally impair the quality of life (QoL) in patients with T1D.

Aim. To evaluate and compare QoL and glycaemic control in children with T1D and associated autoimmune diseases with T1D only.

Methods. This case control study included 94 children ranging from 2 to 17 years of age with diagnosed T1D. QoL was assessed in participants and parents using Pediatric Quality of Life Inventory Generic Core Scale (PedsQL). Questionnaires were scored from 0 to 100; higher scores indicate better QoL or well-being. Glycaemic control was evaluated by using data of most recent haemoglobin A1c. Scores were compared between children with T1D (n=70) and T1D with associated autoimmune disease (n=24). Data was evaluated using *IBM SPSS Statistics* software.

Results. Based on PedsQL survey data among children with T1D, statistically significantly lower total score of general well-being was obtained from children with T1D and associated autoimmune disease (p=0.016). Children with T1D and associated autoimmune disease reported lower physical functioning score (p=0.034) and lower emotional functioning score (p=0.038). Social and school functioning scores didn't differ in those with and without T1D associated autoimmune disease. There were no statistically significant differences in haemoglobin A1c between children with T1D and autoimmune disease and T1D only. Furthermore, results submitted by children and parents presented similar generic PedsQL survey data.

Conclusion. Children with T1D and associated autoimmune disease have lower QoL. Nevertheless, there is no statistically significant correlation between T1D-associated autoimmune diseases and lower glycaemic control. Novel strategies are required to understand and improve adherence in those with both conditions.

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Retrospective analysis on the efficacy of GLP-1 receptor agonists in outpatient clinic

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Background. GLP-1 receptor agonists (RA) as an add-on therapy to oral hypoglycaemic drugs and basal insulin, their effect on glycemia, BMI and kidney function require further evaluation in Latvia.

Aim. To evaluate efficacy of GLP-1 RA in obese patients of type 2 diabetes with poor glycaemic control (BMI $\geqslant$ 35 kg/m^2, HbA1c $\geqslant$ 7%) and to compare the effectiveness of specific drugs in GLP-1 RA group.

Methods. We retrospectively analysed data of 94 patients who were started on dulaglutide or semaglutide as a single injectable agent or basal insulin in combination with liraglutide or lixisenatide at the Jaunliepāja Primary Health Care Centre from January 2019 to November 2020. Glycated haemoglobin (HbA1c) was evaluated at three, six and 12 months after initiation of GLP-1 RA. Body mass index (BMI), creatinine and fasting plasma glucose (FPG) were determined prior to administration of GLP-1 RA and after six months. To assess normality in distribution Shapiro-Wilk and Kolmogorov-Smirnov tests were used. In order to compare categorical risk factors, Chi-squared test or Fisher's exact test was applied and the association between two categorical variables was determined with Cramer's V test. All statistical analysis were performed using *IBM SPSS Statistics* version 25.0 software.

Results. The known diabetes duration in patients was 11.4±8.1 years. The majority of patients (69.5%) were female. All GLP-1 RA agents showed improvement of HbA1c, FBG and reduction in BMI. GLP-1 RA treatment reduced HbA1c levels by 0.79% (P_χ=2.23x10^{-10}) over three-month period, by 1.71% (P_χ=1.14x10^{-11}) and 1.35% (P_χ=7.00x10^{-7}) over six months and 12 months respectively. Fasting blood glucose decreased by 1.87 mmol/L (P_χ= 4,78x10^{-15}). The mean weight reduction was 5.10 kg (P_χ= 7.51x10^{-5}), and BMI decreased by 1.8 kg/m^2(P_χ= 9.59x10^{-5}). Creatinine reduced by 3.43 μmol/L (P_χ= 5.69x10^{-6}). The patients were divided in two groups based on their self-reported adherence to lifestyle regiments of healthy diet and regular physical exercise. We did not observe statistically significant difference on HbA1c after three and six months of treatment but after 12 months in group with better adherence to healthy lifestyle HbA1c decreased by 1% more (P_χ=1.72x10^{-2}).

Conclusion. The retrospective analysis confirms that GLP-1 RA treatment is effectively reducing glycaemia and weight in outpatients with type 2 diabetes mellitus.

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Risk factor analysis for lower extremity amputation in diabetic and non-diabetic patients

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Background. Awareness of risk factors helps in preventive education of medical professionals and patients, thus reducing the number of amputations.

Aim. To evaluate lower limb amputation risk factors in diabetic and nondiabetic patients.

Methods. In a retrospective cohort study 3-year data from Riga East University Hospital on 574 patients, including 223 with diabetes mellitus who had undergone leg amputation was evaluated for amputation risk factors in diabetic and non-diabetic groups, in particular sex, age, also presence of peripheral artery disease, osteomyelitis and chronic kidney disease. To assess normality in distribution Shapiro-Wilk and Kolmogorov-Smirnov tests were used. To compare categorical risk factors, Chi-squared test or Fisher's exact test was applied and the association between two categorical variables was established with Cramer's V test. Analysis was performed using *IBM SPSS Statistics* version 25.0 software.

Results. Among 210 women, the patients' mean age was by 10 years older than in 364 men (77 years vs. 67; $P_{\chi}=4.92x10^{-12}$). Also, one-year postoperative mortality was higher in women (28.57% vs. 17.58%; $P_{\chi}=2.06x10^{-3}$). In diabetic patients, a higher incidence of chronic kidney disease ($P_{\chi}=1.04x10^{-4}$) and osteomyelitis ($P_{\chi}=2.06x10^{-12}$) was observed. Out of diabetic patients with osteomyelitis, only 13.33% ($P_{\chi}=1.83x10^{-10}$) did not have prior diabetic foot ulcer. Only 10.8% of diabetic patients had no prior history of peripheral artery disease. In diabetic patients, amputations were performed more distally at transtibial level compared to more proximal transfemoral amputations in nondiabetic patients ($P_{\chi}=2.18x10^{-4}$). Occlusion of *a. femoralis* was more in nondiabetic patients, whereas in diabetic patients the occlusion was more distal at the level of *a. tibialis* or none ($P_{\chi}=2.61x10^{-5}$).

Conclusion. Lower limb amputation risk is overall higher in men, but in women it increases with advanced age. In diabetic patients, lower extremity amputations are performed due to more distal occlusions in leg arteries or osteomyelitis caused by pathogens of infected foot ulcer. Chronic kidney disease is more frequently observed in diabetic patients.

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Telomere length and serum proteasome concentration in patients with type 1 diabetes and different severity of diabetic retinopathy in Latvia and Lithuania

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Background. Diabetic retinopathy is the leading cause of blindness in working-age adults in developed world. Derangements of ubiquitine-proteasome system and telomere length have been associated with microangiopathy in diabetes. Until now, limited data are available on the above markers in diabetic retinopathy in type 1 diabetes (T1D).

Aim. The aim of this work was to compare serum proteasome concentration and telomere length in patients with different stages of diabetic retinopathy and T1D in Latvia and Lithuania.

Methods. 186 Latvian and 120 Lithuanian patients with type 1 diabetes were enrolled in the study. Patients were stratified according to severity of diabetic retinopathy. The group of severe retinopathy included patients with proliferative retinopathy and status post laser-photocoagulation. "No retinopathy" group included patients with nonproliferative/no retinopathy. Proteasome concentration was measured by ELISA. Telomeres were evaluated by real-time qPCR with a relative telomere length method using a reference gene and expressed as (ΔCT). Statistical analysis was performed in programme R. Wilcoxon rank sum test followed by Ancova on ranks was used to compare the locations of biomarkers distributions between the groups of retinopathy and to adjust for covariates (diabetes duration, waist/hip ratio, serum triglycerides, estimated glomerular filtration rate (eGFR), country).

Results. Subjects in the group of severe retinopathy (n=119) compared to "no retinopathy" (n=187) were statistically significantly older (44 (35–53.5) vs. 31 (24.5–44) years), had longer duration of diabetes (28 (22–36) vs. 16 (12–21.5) years), higher serum creatinine concentration and lower estimated glomerular filtration rate, higher serum triglyceride and waist-hip ratio, as well as higher prevalence of other complications of diabetes. We observed lower serum proteasome concentration in the group of severe retinopathy (130 (90–210) ng/ml, vs. "no retinopathy" 150 (100–240) ng/ml), difference was significant after adjustment for covariates, p=0.024. Median telomere length was higher in the group of severe retinopathy (ΔCT 0.21 (0.12–0.28 vs. "no retinopathy" 0.18 (0.1–0.28), the difference was significant after adjustment for covariates, p=0.036.

Conclusion. In this study, we demonstrated differences in proteasome concentration and telomere length between patients with different stages of diabetic retinopathy.

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COVID-19 pneumonia in elderly patients

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Background. First COVID-19 cases were registered in Kazakhstan in March 2020. As of January 1, 2021, there were 203 562 cases of COVID-19 patients and 2 771 of these patients died.

Aim. The aim of the study is to evaluate the clinical and radiological features of the course of coronavirus pneumonia in elderly patients. Is advanced age a bad prognostic sign of the disease?

Methods. We examined 20 patients with pneumonia over 60 years old with PCR confirmed SARS-CoV-2. By gender there were more women in the study group (60%). The patients underwent PCR to identify the RNA of the SARS-CoV-2 virus, chest CT scan, CBA, urine test, blood coagulation table, the biochemical profile, the D-dimer and the oxygen saturation level tests.

Results. Cough (75%), fever (50%), chest pain (30%) prevailed amongst the clinical manifestations in the group of elderly patients. The chest CT scan determined the percentage of lung damage, which was an important prognostic sign. In 41% of elderly patients with COVID-19 pneumonia, 25% of the lesion was detected; in 41% of patients up to 50% of the lesion was detected; and in 18% of the elderly patients, significant lung damage was revealed up to 75% and over 75%. Elderly patients had extensive lung damage of over 50% or more, and low saturation indicators were found. All elderly patients (100%) were hospitalized and treated in a hospital. In this age group, leucocytosis, increased D-dimer, lymphopenia were present, which is considered a poor prognostic sign. However, there were no deaths in this study group. The patients had concomitant hypertension, diabetes mellitus, ischemic disease.

Conclusion. In this sample, the elderly patients had COVID-19 pneumonia with a high percentage of damage over 50% or more. All patients in this group were hospitalized. Cough, fever, sore throat prevailed among the clinical manifestations. The CT scan revealed multifocal lesions. Concomitant diseases such as hypertension, ischemic heart disease, diabetes mellitus aggravate the course of the disease of the elderly patients. Thus, COVID-19 pneumonia in the elderly is characterized by a more severe course.

Prognostic clinical indicators of COVID-19 pneumonia

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Background. As of October 31, 2020, 136 271 cases of COVID-19 infection were detected in Kazakhstan and 2 067 patients died.

Aim. The target of the study is to assess the features: of the course of COVID-19; of tomographic and radiological manifestations of the disease; and prognostic signs of severity of the disease.

Methods. In the group of 40 patients with confirmed PCR test of COVID-19, 27 had pneumonia and 13 did not have it. Patients underwent a PCR test to identify the RNA of the SARS-CoV-2 virus; a CT scan; a CBA; a urine test; the blood coagulation, the biochemical profile, the D-dimer and the oxygen saturation.

Results. Clinical manifestations were more pronounced in the PCR-positive patients with pneumonia, among those: cough (71%), fever (50%), chest pain (25%) predominated. Out of 55% of patients with pneumonia ,25% revealed lesions; for 25% of the patients, the number was up to 50%, and 20% of the patients showed significant lung damage of 75% and more. A large percentage of the damage (50 or more) of the lung was more common in the group of patients over 60 years of age. High percentage of lung damage was reflected in the lower oxygen saturation levels (less than 95%). In the group of older patients with CVD and DM with large damage of lung leucocytosis, increased D-dimer, lymphopenia have been detected more often, which is a sign of negative prognosis. Two patients (38 and 59 years old) died in the hospital from respiratory failure. In both cases, pronounced leucocytosis (60x109) and lymphopenia (1x103) were revealed.

Conclusion. In this sample, COVID pneumonia was detected in 70% of the patients and in other 30% the course of the disease was mild. A CT sign of COVID pneumonia was manifested in diffuse multifocal lesions. The CT scan is more informative than PCR. In some cases, with negative PCR, the CT scan showed signs of COVID pneumonia. GGO effect is the main symptom of COVID lung lesion. The vast lung damage (more than 75%) correlates with a leucocytosis, a lymphopenia and increased D-dimer, which are indicators of poor prognosis of the expected development of COVID pneumonia.

Application of whole-genome sequencing in studying cases of prolonged and recurrent tuberculosis caused by *Mycobacterium tuberculosis* Beijing (SIT1) genotype

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Background. *Mycobacterium tuberculosis* (Mtb) strains vary in multiple aspects, including geographical distribution, virulence, and drug-resistance. Mtb Beijing family is frequently associated with multiple drug resistance, as well as with a high risk of unfavourable tuberculosis (TB) treatment outcome and disease relapse. Spoligotype SIT1 is a typical genotype of the Beijing family and is prevalent in Latvia. However, limited data about the propensity and rate of genomic mutations of SIT1 Mtb during human infection are available.

Aim. The aim of this research was to explore drug-resistance pattern and pairwise SNP-distance in available SIT1 Mtb isolates of prolonged and recurrent TB cases, and to decipher the aetiology of relapse cases.

Methods. In total, 16 Mtb isolate pairs were studied. These pairs consisted of an initial isolate and second isolate taken from patients with prolonged (N=4) or recurrent (N=12) TB cases. Whole-genome sequencing (WGS) of Mtb DNA samples was conducted using Ion Torrent technologies. Galaxy web platform and TB Profiler tool was used for bioinformatic analysis of WGS data, genotypic drug-susceptibility testing, and determination of pairwise SNP-distances.

Results. In 5 recurrent TB cases, reinfection is thought to be the cause of TB relapse: (A) In one case, paired isolates had different drug-resistance profiles and 169 SNP-distance. (B) 38 and 122 SNP-distance was found in two TB cases, with second episodes showing additional resistance-associated mutations. (C) In two other cases, despite a small pairwise distance of 2 and 7 SNPs and identical drug-resistance profiles, SNP pattern of the paired isolates did not match.

In 7 recurrent TB cases, paired Mtb isolates had 0–3 SNP difference with a mutation rate 0.14–0.62 SNP/genome/year, which indicates endogenous disease reactivation. Only two patients in this group had drug-susceptible strain infection; in two other cases, multi-drug resistant (MDR) Mtb isolates became extensively drug-resistant (XDR); acquired SNPs associated with this event were identified.

Among 4 TB patients with prolonged disease, three Mtb isolate pairs were drug resistant. In three cases 0 SNPs were accumulated. In one case, XDR Mtb isolate acquired 7 *de novo* SNPs within 3-year period, and it is known, that the person was therapy non-compliant, which could provoke such high mutation rate.

Conclusion. This study highlights diversity in drug-resistance profile, SNP patterns and molecular clock of studied Mtb SIT1 strains involved in prolonged and recurrent TB cases.

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Bloodstream infections in multidisciplinary teaching hospital in Latvia: characteristics, outcomes and utility for sepsis surveillance

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Background. Bloodstream infections (BSIs) are among the leading causes of morbidity and mortality worldwide and may lead to sepsis, which is a medical emergency characterized by dysregulated inflammatory immune response and organ failure due to infection. Sepsis in an elusive clinical syndrome, often poorly documented in medical records, underreported and underrepresented in administrative data. Improving methods of identification of sepsis cases may benefit sepsis surveillance.

Aim. The aim of the study was to analyse the clinical characteristics and mortality of the patients with community-onset BSIs admitted to Pauls Stradiņš Clinical University Hospital (PSCUH) and to assess the representation of BSI and sepsis in diagnosis upon discharge.

Methods. In retrospective cohort study, we identified 525 adult patients with clinically significant bacteremias admitted to PSCUH between September 2017 and September 2018. Further analysis was performed on 242 community-onset BSI cases. Data on demographics, clinical presentation, comorbidities, blood cultures, mortality were collected, and diagnoses upon discharge were evaluated.

Results. The median age of the cohort patients was 71 years (IQR 56–79) with median Charlson Comorbidity index (CCI) of 6 points (IQR 3–7), 53.3% were male. Intrahospital mortality was 34.7% with diagnosis of septic shock present in 10.3% of cases. Mortality was significantly higher in older patients ($p=0.001$) and patients with higher CCI ($p<0.001$). The reason of hospitalization was documented as infectious disease for 59.5% of community-onset BSI cases, followed by cardiovascular and neurological causes (both 9.9%). Urinary tract infection (28.5%) and pneumonia (21.1%) were the most common sites of origin, followed by primary BSI in 12.8% of the cases. *Staphylococcus aureus* and *Escherichia coli* were isolated in 28.9% and 24.4% of BSI cases, respectively. Sepsis/BSI was mentioned among the discharge diagnoses in 75.6% of bacteremia cases. In no-diagnosis subgroup (N=59) 64.4% of episodes had clinical signs and laboratory parameters attributable to sepsis documented in medical records. However, in 45.8% of the cases in no-diagnosis subgroup the blood culture results returned after the discharge. Any notion of infection was missing in 18.6% of cases without BSI/sepsis diagnosis upon discharge. Patients had lower CCI in no-diagnosis subgroup ($p=0.046$). Absence of diagnosis had no statistically significant correlation with the patients' age, outcome, reason of hospitalization or source of infection.

Conclusion. Bloodstream infections are underrepresented upon discharge. Surveillance of bacteremias may provide additional benefit to using ICD-10 (International Classification of Diseases, 10th revision) diagnosis codes in identifying sepsis cases.

Acknowledgements. The authors declare the absence of conflict of interest.

Can SARS-CoV-2 infection induced liver damage be assessed and quantified using advanced ultrasound methods?

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Background. Since the start of the Covid-19 pandemic, multiple studies focused on examining the long-term health effects that the disease had on different organ systems, however, to the authors' knowledge, no such investigations had been carried out regarding the use of advanced ultrasound methods in the assessment and quantification of liver damage in Covid-19 patients post-infection.

Aim. The study aimed to assess and quantify liver damage in patients who had SARS-CoV-2 by using advanced ultrasound (US) methods.

Methods. 90 patients were enrolled in a prospective cross-sectional study. 56 patients had proven SARS-CoV-19 infection in the 3–9 months preceding the study and 34 were randomly selected as a control group. An ultrasound exam using advanced liver assessment programmes (2D shear-wave elastography measurements, attenuation and dispersion imaging to quantify fibrosis, steatosis and viscosity respectively) was performed for all patients. Ultrasound findings were then correlated with biochemical markers of liver damage (LDH, GGT, AlAT) and inflammation (CRP, ESR), and compared between the groups. Disease severity and progression in the study group were in correlation to the ultrasound findings.

Results. Measurements of liver fibrosis differed significantly between the Covid-19 and control group, with especially higher fibrosis scores (F2, F3) in the study group ($p<0.001$), also observed in patients with no previous history of liver damage. Although no correlation between infection status and viscosity and attenuation scores was observed, altered biochemical markers of liver damage and inflammation had a statistically significant correlation with changes in all ultrasound findings ($p<0.05$). Almost a third of study group patients with Covid-19 had been hospitalised (59%, n=33), and steatosis grades in patients with a more severe disease course were found to have been significantly higher ($F= 9.1$, $p<0.01$).

Conclusion. Biochemically proven liver damage was found to be more common among patients post-SARS-CoV-2 infection than a randomised control group, and these changes were mirrored by altered ultrasound findings using advanced ultrasound liver imaging techniques. Covid-19 patients with a more severe disease course had higher steatosis grades.

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Detection of antimicrobial resistance in *Klebsiella pneumoniae* strains

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Background. *Klebsiella pneumoniae* accounts for a significant proportion of hospital-acquired pneumonia, urinary tract infections, septicaemias, and soft tissue infections. It is one of the most common causes of severe nosocomial infections all over the world, it is estimated that *Klebsiella spp*. cause 8% of all nosocomial bacterial infections in the United States and in Europe. *K. pneumoniae* resistance to antibacterial agents, including extend spectrum beta lactamases, is growing rapidly. That, in fact, significantly increases the duration of hospitalization, financial burden on the patients and the government, and it escalates the patient mortality rate all over the world.

Aim. The aim of the current study was to isolate, identify and detect *K. pneumoniae* resistance to antibacterial agents, to detect frequency of resistance and number of ESBL (extended spectrum beta lactamases) producing *K. pneumoniae* strains.

Methods. *K. pneumoniae* samples were isolated and species identification was performed at Riga East University Hospital "The Centre of Tuberculosis and Lung Diseases" Laboratory of Mycobacteriology. The specimens of *K. pneumoniae* were collected and analysed in the time period of 01.01.2018–31.12.2018. The following methods were used in the study: Kirby-Bauer disc diffusion tests, E-test and for ESBL determination-double disc method. Overall, 234 *K. pneumoniae* isolates were analysed, and antimicrobial resistance was detected to the following antimicrobial agents – amikacin, ceftazidime, ciprofloxacin, imipenem and meropenem.

Results. Out of all 234 *K. pneumoniae* isolates, the most common *K. pneumoniae* resistance was detected to ceftazidime- 9.83% (n-23), the next – to ciprofloxacin – 8.55 % (n_23). 0.85% (n-23) of the analysed samples were amikacin resistant. There was no resistance to carbapenems – imipenem and meropenem, so 100% susceptibility was determined. The total number of ESBL cases (n-23), compiling 9.83%.

Conclusion. The antimicrobial resistance in *K. pneumoniae* remains problematic. Although the detected resistance was moderate, we still need continuous monitoring and greater effort to avoid this increase. An increasing threat is carbapenem resistance mediated by a range of carbapenemases, which may confer resistance to all beta-lactam antibacterial drugs. In other European countries, carbapenem resistance was almost always combined with resistance to several other antimicrobial groups, limiting the treatment options for infections caused by *K.* pneumoniae.

Acknowledgements. The authors declare the absence of conflict of interest.

REGENERATIVE MEDICINE

Assessment of effect of chamomile *(Matricaria recutita)* flower extract on human endothelial cell proliferation

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Background. Cardiovascular diseases are known to be amongst the prevalent causes of death worldwide. The main risk of atherosclerosis is disruption of normal activity and functions of the vascular endothelium that can lead to impaired blood circulation or infarction.

Studies of chamomile flower extract properties in animal models have shown a significant positive effect on triglycerides, cholesterol including LDL/HDL ratio and mitigation of atherosclerosis progression. In addition to these findings, inhibition of proliferation of certain cell lines was observed.

Proliferation inhibition properties of chamomile flower extract on vascular endothelium are still unknown.

Aim. The aim of study was to evaluate the effect of chamomile flower extract on human endothelial cell proliferation.

Methods. The human endothelial cell line HBEC-5i (ATCC®) was utilised as a test system. The xCELLigence (Roche) real-time proliferation assay were applied. The chamomile flower aqueous extract was obtained from *Matricaria recutita v. Zloty Lan.*

Results. The chamomile flower extract was obtained in previous stages of study and contained: 0.82 mg/ml total polyphenols, 0.18 mg/ml flavonoids and 0.1 mg/ml apigenin, respectively.

Prior to exposition, endothelial cells were seeded in test plate and cultured within incubator at 37°C with 95% humidity and 5% CO^2 for 24h. After adhesion cells were exposed to five different concentrations of chamomile flower extract – 50, 150, 350, 750 and 1000 μg/mL for 72 h. Control specimens contained the same cells and an extract-free culture medium.

No statistically significant proliferation activity differences between control and exposition specimens were observed.

Conclusion. Conducted assessment of chamomile flower extract activity on proliferation of human endothelial cells lead to conclusion that previously observed cytotoxic and proliferation inhibiting activity on cancer cell lines at the same dose range do not have an effect on normal cells.

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Evaluation of technical design performance of bioreactor system

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Background. Diverse human cell lines are in use for scientific, applied research and cell-based product medical applications, prompting industry towards more cost-effective, time-effective and labour-effective cell expansion methods. The main challenge during cell expansion process is related to bioreactor system contamination. To find a solution for these aspects, our study is focusing on novel approach in construction of bioreactor systems, mitigating labour and technical construction-related contaminations.

Aim. The aim of this particular stage of the study is to evaluate the bioreactor systems' design capability to ensure appropriate breeder internal environment.

Methods. The breeder and its supply compartment internal environment airborne particle quality were tested by automatic particle counter. Particles in size of 0.5 μm and 5.0 μm were counted in 28.3 L air and calculated to 1 m^3.

The breeder and supply compartment internal air microbiological conditions were accessed by sedimentation method, utilising tryptic soy agar (TSA) 90 mm plates, exposition time 4h. Surface microbiological condition was accessed by TSA 50 mm contact plates, exposition time – 10 sec. Air flow velocity was accessed by anemometer after HEPA filters perpendicular to airflow.

Results. The average airborne particle counts in breeder compartment reached 2789 – 0.5 μm and 26 – 5.0 μm particles. The average airborne particle counts in supply compartment reached 3560 – 0.5 μm and 32 – 5.0 μm particles. Air microbiological condition tests in breeder showed >1 colony forming units (CFU) in all samples. One sample taken in supply compartment during opening of maintenance lid showed presence of 2 CFU. The surface microbiological assessment showed >1 CFU in all tested locations. The airflow velocity in breeder variated in ±5.4% range comparing to designed value and supply compartment ±6.6% respectively.

Conclusion. All the tested parameters comply with acceptance criteria and lead to conclusion that proposed solution – to construct supply compartment equipped with separate air circulation and HEPA filter – could benefit mitigation of risks. Despite UV treatment of circulating air during opening maintenance lid, any intervention could be potentially critical.

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Validation of supercritical carbon dioxide extraction protocols of Sea buckthorn (Hippophae rhamnoides L.) berry residues, pulp and seeds

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Background. Conventional methods to isolate biologically active ingredients from natural sources are distillation, solvent extraction, maceration and others. Utilisation of conventional methods are usually associated with significant impact to purity and quality of final product. Supercritical carbon dioxide extraction technology is shown to be superior compared to conventional extraction methods, as it is not causing chemical modification and leaves no solvent residues in product.

Carbon dioxide is the most frequently used solvent in supercritical fluid extraction to isolate fatty acids, sterols, pro-vitamins and other natural fat-soluble compounds. Definition and validation of extraction process parameters are crucial to obtain optimal yield of target substance for specified natural materials.

Aim. The aim of this study was to validate supercritical carbon dioxide extraction protocols for Latvian origin Sea buckthorn (SBT) fruit residues, pulp and seeds in order to determine optimal extraction profile and yields.

Methods. The SBT fruit residues (SBTr), pulp (SBTp) and seeds (SBTs) were extracted by supercritical carbon dioxide, using pre-existing extraction parameters. The extraction parameters range: time 90–180 min (T), pressure 300–330 bar (P), temperature +45°C–+50°C (t), solvent flow rate 70–90 l/h (SFR). The obtained extracts were analysed by GC and HPLC methods. The content of polyunsaturated fatty acids (PUFA), Omega-3, Omega-6, total carotenoids, total tocopherols and total sterols were analysed.

Results. In total, 45 parameter combinations were tested. Optimum extraction yield in SBTr group was obtained at 90 min (T), 330 bar (P), temperature +50°C (t), 90 l/h (SFR) and reached 12.96% from initial material. Optimum extraction yield in SBTp group was obtained at 90 min (T), 300 bar (P), temperature +50°C (t), 90 l/h (SFR) and reached 18.00% from initial material. Optimum extraction yield in SBTs group was obtained at 90 min (T), 330 bar (P), temperature +50°C (t), 90 l/h (SFR) and reached 9.97% from initial material.

Conclusion. Doubling exposition time do not correlate to doubling of extraction yield. This finding reduces energy consumption during extraction cycles and enhance production capacity. Lower temperature and solvent flow rate in extraction chamber are associated with a higher total tocopherol yield and can be applied to produce tocopherol-enriched products.

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Phytosterols and fatty acids extracted from sea buckthorn seeds can serve as a means for cardiovascular disease prevention

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Background. Carbon dioxide is the most frequently used solvent in supercritical fluid extraction to isolate fatty acids, sterols, pro-vitamins and other natural fat-soluble compounds. One of most important target substances are phytosterols. Beta-sitosterol is one of many sterols that come from plants (phytosterols) and have a structure like the cholesterol produced in the body. Research supports the fact that phytosterols, including beta-sitosterol, can reduce cholesterol levels. Sea buckthorn seeds (SBS) are recognized as one of the best candidates to extract above mentioned target substances. In addition, SBS oil extraction using supercritical CO_2 technology from sea buckthorns harvested in Latvia has been intensively developed over the last year.

Aim. The aim of the current study was to develop and improve oil extraction protocol, using supercritical CO_2 to obtain phytosterols, including beta-sitosterol, from SBS grown in Latvia.

Methods. After juice pressing, sea buckthorn press cake was freeze-dried (residual moisture content – 5.99%). SBS were separated (using blender and vibrating sieves) and grinded (particle size: 0.80–1.10 mm). SBS was extracted using supercritical CO_2 (extraction parameters 3 h /310 bar/40°C). Extracted SBS oil composition was analysed by GC and HPLC methods. Five different samples were obtained by changing the temperature (45 or 50°C), CO_2 flow rate (70 or 80 kg/h) and humidity (5, 5.5 or 6%).

Results. Table. Most important oil components % (m±SD)

Sample number	No.001	No.002	No.003	No.004	No.005
USFA*	88.1±2.9	88.7±2.9	87.7±2.9	88.0±2.9	87.3±2.9
Omega 3	32.9±1.6	33.6±1.7	32.8±1.6	33.2±1.6	32.4±1.6
Omega 6	36.4±1.8	36.3±1.8	35.8±1.8	36.0±1.7	35.4±1.8
Omega 9	16.6±1.5	16,5±1.5	16.8±1.5	16.6±1.5	17.2±1.6
C 18:2**	0.1±0.0	0.1±0.0	0.1±0.0	0.1±0.0	0.1±0.0
Phytosterols, beta-sitosterol mg/g	27.99±4.4	29.3±5.7	27.56±4.2	27.75±5.5	31.54±4.4

*USFA: unsaturated fatty acids
**Trans fatty acid isomer
Presented results show a high level of USFA in SBS oil, and practically an absence of trans fatty acids. The content of phytosterols, including beta-sitosterols, is comparatively high and stable in all samples.

Conclusion. SBS oil extraction using supercritical CO_2 technology has proven the presence of phytosterols in SBS, which is very promising in terms of cardiovascular disease prevention.

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PUBLIC HEALTH & EPIDEMIOLOGY

Smoking initiation among young adults, teens, grade-schoolers – one of the main public health challenges in Latvia

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Background. Smoking is responsible for 50% of all avoidable deaths in smokers, half of these due to cardiovascular diseases (CVD). The 10-year risk of fatal CVD is approximately doubled in smokers. CVD risk in former smokers is in between that of current and never smokers. According to World Health Organization data, in Latvia, 2018, 3% girls and 10% boys had ever smoked at age 11y; 23% girls and 24% boys – at age 13y; 48% girls and 46% boys – at age 15y.

Aim. The aim of the Population Based Cross-Sectional Study of Cardiovascular Risk Factors in Latvia was to determine the prevalence of CVD risk factors (RF), including smoking, to use the data in accurate health policymaking and targeted public health campaigns in near future.

Methods. 4070 inhabitants of Latvia were enrolled in the study out of the initial statistical sample (6000), formed by random selection from the Housing Register of the Central Statistical Bureau (1 209 756 pers.) representing a cross-section of Latvia's inhabitants (age 25–74). Data on the socio-economic status, prevalence of smoking, alcohol consumption, diet, physical activity, mental health etc. was obtained using CINDI and HADS questionnaire in face-to-face interviews. The data were processed using *Microsoft Excel* and R.

Results. 30.4% (n=1237) of respondents smoked during the study period on regular basis or occasionally. 49.7% (n=2023) had been regular smokers for at least 1 year during their lives. The respondents – smokers smoked 13 cigarettes with a filter per day on average. 18.6% (n=376) of the respondents who had been smokers for at least 1 year had begun smoking aged less than 16y; 63.6% (n=1286) had started smoking aged 16 to 20y; 12.5% (n=252) – aged 21 to 25y; 5.4% (n=109) – older than 26y. 52,8% (n=653) of smokers would like to stop smoking. 27.5% (n=1119) of the respondents were exposed to passive smoking at work, home, or elsewhere.

Conclusion. 82,2% of the respondents who had been smokers for at least 1 year during their lives had started smoking before age of 21, when buying cigarettes is prohibited by law. The data indicate urgent need for exact changes in the public health policy, for the target groups and in the tactics of anti-smoking campaigns for adults to young adults, teens and grade-schoolers to prevent the first cigarette at a young age or ever.

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Prescribed dose assumption in evaluation of medication adherence and persistence from administrative data: a study of myocardial infarction patients

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Background. Insufficient adherence to prescribed medications is a known problem in health care. Pharmacy databases are often used to measure medication adherence in different settings and populations. However, due to different approaches, comparison between studies might not be straightforward. Crucial component in adherence estimation is days' supply (number of days covered) information for each dispense. Assumptions have to be made when such information is not available.

Aim. The aim of the current study was: 1) to compare adherence and persistence estimates between two prescribed dose assumptions, namely, the defined daily dose (DDD) per day or tablet per day; 2) to offer a relatively easy visual inspection for a validity of chosen dosage assumption.

Methods. Latvian nationwide medication refill data submitted for reimbursement (2014 to 2018), linked to hospitalization database, was used. Patients discharged alive after the hospitalization with acute myocardial infarction with ST-segment elevation were selected and followed for 1 year as a subgroup with generally standardized recommendations for further pharmaceutical therapy. In total, n=8 061 patients were selected from a database and 281 609 dispensing events were analysed. We compared the distribution of the number of days between subsequent dispensing events with the distribution of days' supply to investigate dosage assumption validity. Patient-level 360-day adherence was computed as a proportion of days covered and persistence as a time until the last medication usage episode ended. Boxplots were used for visual comparison and medians (interquartile range) as numeric summaries.

Results. Distributions of days between subsequent refills and days' supplies computed using either DDD/day or tablet/day (see figure below) dosage indicate that tablet/day is a more realistic dosage than DDD/day.

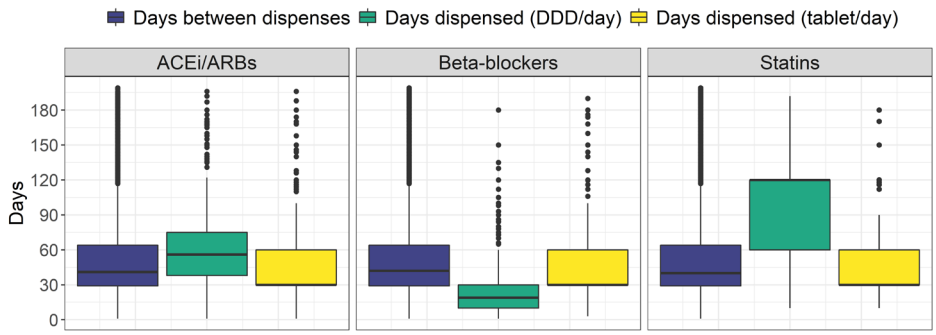

Fig. Distributions of days between dispenses and days' supplies.

Median adherence was 66% (IQR 39%, 90%) for ACEi/ARBs, 68% (IQR 42%, 93%) for beta-blockers, and 67% (IQR 36%, 88%) for statins. Adherences were higher when computed with DDD/day for ACEi/ARBs, 85% (IQR 50%, 100%), and statins, 100% (IQR 83%, 100%), but lower for beta-blockers, 31% (IQR 17%, 50%).

Conclusion. This national validation study for adherence and persistence calculations showed that resulting estimates strongly depend on dosage assumptions. These assumptions may not only bias medication adherence estimates for each medication separately, but also comparison between medications, as adherence might be biased in different directions.

Analysis of Latvian cancer care infrastructure in relation to criteria established in European Union

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Background. Latvia lacks an accredited cancer centre, while the EU recommendations suggest at least one accredited comprehensive cancer infrastructure in each of the EU Member States.

Aim. The aim of the current study was to determine whether the Latvian Oncology Centre/Riga East University Hospital can meet the requirements that are put forward by different accreditation programmes in EU, and consequently to find out how close Latvia is to fulfilling the new EU recommendations.

Methods. We searched for cancer infrastructure accreditation bodies in Europe, and analysed the criteria set for cancer centre accreditation. Furthermore, we evaluated is the compliance of the infrastructure in Latvia to these criteria in general aspects.

Results. The following accreditation bodies were identified: Organisation of European Cancer Institutes (OECI), European Society for Medical Oncology (ESMO), European Cancer Centres (ECC) currently perform accreditation of 'cancer centres' and 'comprehensive cancer centres'.

The principal criteria of accreditation include organisation of quality system, patient involvement programmes, multidisciplinary approach in diagnosis and treatment, research and education independent program, as well as number of specialists, number of primary diagnosed patients per year, number of hospital beds, annual budget for cancer research (no difference in the required research funding amount to be allocated for research was revealed between the high-performing EU countries and widening countries).

The principal difference in accreditation was revealed as to whether the accreditation was related to general factors covering major aspects of cancer care or it was organ-specific.

The most advanced accreditation is being offered by OECI.

While matching the criteria to the situation in Latvia, we have recognized that the funding for research and training is not included in the routine healthcare budgets.

Conclusion. With the current set-up, it would be difficult for Latvia to comply with the recommendations of the European Commission, mainly due to underdeveloped clinical research infrastructure. As a result, patients in Latvia currently do not have an access to and cannot benefit from high-quality cancer research and care, which can be offered only through interventions in context of clinical studies.

Actual body size and body size perception using Stunkard's scale in elderly people from Lithuania

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Background. Self-perception of one's body is one of the factors that determine the quality of life and it has been widely studied among younger age groups. With the rapid ageing of many countries due to a longer lifespan, elderly people are becoming one of the largest categories in the society and yet they remain among the least studied.

Aim. The aim of this study was to determine associations between the actual body size and the perceived body image in elderly people.

Methods. In total, 183 (147 women and 36 men) elderly people were investigated in hospices and leisure centres for senior citizens. The age varied from 64 to 99 years (M=77; SD+/-8). Weight and height were measured using an electronic scale and Martin type anthropometer (GPM – Siber Hegner, Zurich). The participants answered questions about their body size – how they perceive their body size and which one body size and shape they wish to have, using Stunkard's scale with 9 different body figures (1983). Actual (real) body mass index (BMI), "declared" and "desired" BMI were calculated. Statistical analysis was done using Microsoft Excel 2010, R Commander. Differences between results were deemed statistically significant when $p<0.05$.

Results. The mean of "actual" BMI was 27.82, "declared" – 25.65, "desired" – 24.48. Half of respondents perceived their BMI as lower, 13.5% – as higher, 36.5% – similarly to their actual (real) BMI (+/-1). In total, 88.89 % with normal BMI, 60.71% of overweight and 44% obese people assumed their BMI correctly. When asked to choose the most similar figure to their bodies, obese participants chose No. 6, overweight – No. 5, those with normal weight – No.4 ($p<0.05$). Stunkard's figures did not correlate with the overall assessments of health or appearance. A correlation was found between the choice of a larger Stunkard's figure and poorer evaluation of appearance. The most desired Stunkard's figure was No. 4 despite BMI category. In total, 57% chose a thinner figure as the most beautiful than the one they chose for themselves. Younger participants (64-70 y.) chose slimmer figures ($p<0.05$). People who only had a secondary school education chose a larger figure as their ideal.

Conclusion. Most seniors care about their appearance and want a smaller body size. It is important to consider the body image of older people as a part of their psychological well-being.

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Drowning associated risk groups in a five-year time period in Riga and Riga planning region: gender and alcohol concentration in blood

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Background. Drowning is the 3rd leading cause of unintentional injury of death worldwide. These deaths are often unintentional, classified as accidents and instantaneous. However, they are potentially preventable. There are several factors that could be associated with risk groups within our population.

Aim. The aim of this study is to determine whether male gender and elevated alcohol consumption is associated with higher chance that individual will drown.

Methods. A study was carried out involving fatal drowning victim cases from January 1, 2015 to December 31, 2019 at the State Centre for Forensic Medical Examination of the Republic of Latvia. All recorded data were analysed using *MS Excel* and *IBM SPSS*.

Results. In total, 215 victim cases were included in this study, of which 64 involved females and 151-males. 58% (n=124) of victims had an elevated alcohol concentration in blood, out of which 93% (n=115) of victims had a concentration above 1‰. 42% (n=90) of victims had no alcohol concentration in blood, 1 victim was in decomposition stage, blood alcohol level was not obtained. In males, the mean alcohol concentration in blood was 1.61‰ (95% CI 1.38-1.83, $p<0.0001$), meanwhile, in females it was only 0.74‰ (95% CI 0.46-1.03, $p<0.0001$).

Conclusion. Elevated alcohol concentration (especially above 1‰) and male gender can be identified as predisposing factors for drowning in population of Riga and its surroundings.

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Factors influencing willingness to pay for compulsory social health insurance among informal sector workers in Oskemen city of Kazakhstan

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Background. Defining the demand or willingness to join and pay for health insurance is crucial in exploring the feasibility of such schemes, establishing prices, and setting potential contribution levels. In order to improve the quality health care services and to achieve universal health coverage without financial burden on households' health insurance scheme was introduced in Kazakhstan. As a classic form of social health insurance, the health services will be paid through payroll contributions from employer and employee, self-employed individuals and the government. The main problem is the large number of self-employed people, for whom contributions are not made.

Aim. The main objective of this study was to assess informal workers' willingness to join a social health insurance (SHI) model in Oskemen, East Part of Kazakhstan, and to determine factors influencing this willingness. A second objective was to identify informal workers willingness to pay (WTP) according contribution level and their payment ability

Methods. The study was cross-sectional in design and conducted between August 2019 and October 2019 in Oskemen city. We elicit the WTP using the double-bounded dichotomous choice elicitation method was used to estimate respondents WTP for proposed health insurance premium. The study participants were randomly selected by two-stage cluster sampling. From the 195 participants, 161 participated in the interview, thus, the achieved response rate was 82%.

Results. Willingness to pay for social health insurance was found to be predicted by SHI awareness, SHI Trust Income per month, Monthly expenditure. Informal workers who are aware, are 2.5 times more likely to pay (p-value 0.022) the second instalment than a person lacking awareness. Also, Trust level for SHI was significant and the person who did not trust SHI system and improvement in the Health Care system after introducing SHI, was 4.2 times less likely to pay (p-value 0.021) the contribution rates compared to those who did. The majority of the informal workers were willing to enrol in the social health insurance scheme, with the mean of WTP of 2% of their average monthly salary. This was lower than the premium proposed by the government (35%).

Conclusion. Our results suggest that the contribution rate for informal workers should be revised according to income level of regions and geographical location of informal workers. Also, it is important to provide Educational Campaigns for rural dwellers and for people who do not have access to media equipment.

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First-time diagnosed with diabetes within hospitalised for acute myocardial infarction: administrative data analysis

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Background. It is known that type 2 diabetes mellitus (T2DM) is common in patients hospitalized for acute myocardial infarction (AMI). In some cases, T2DM is for the first time recognized during the hospitalization. A high proportion of such cases can indirectly indicate systemic problems in primary care thought to be responsible for timely diagnosis and proper management of chronic conditions. Although the knowledge about T2DM is essential to reduce the risk of AMI, in reality, prevention of T2DM in Latvian population is still insufficient. In part of patients, T2DM is discovered only at the time of their hospitalization for AMI, however, the real proportion of such patients is still underestimated.

Aim. The aim of the current study was to investigate the first-time diagnosis of T2DM within the patients that were hospitalized for AMI.

Methods. Latvian administrative health data was used for this analysis. We analysed all hospitalizations with a primary diagnosis for AMI (ICD-10 code I21, I22) for years 2015–2018. The presence of T2DM diagnosis (ICD-10 codes E11, E11.1, E11.2, E11.3, E11.4, E11.5, E11.6., E.11.7, E.11.8., E.11.9) was assessed in actual AMI hospitalization and for the period of one year prior to it by screening through registered diagnoses of all records for received outpatient care and for medication prescriptions in the national reimbursement system.

Results. 15 084 hospitalization episodes (12 253 unique patients) with a primary diagnosis of AMI were registered since 2015. Of these patients, 20.7% were diagnosed with T2DM including 12.9% of patients who had not been diagnosed before the actual hospitalization for AMI. From all the patients hospitalized for AMI and having T2DM, 26.4% patients had not used the drugs prescribed for treatment of T2DM during the last year before AMI.

Conclusion. A significant proportion of T2DM patients were not diagnosed with T2DM before the AMI episode and were not receiving the appropriate treatment and medication before the AMI episode. This data can be used to improve the systemic problems in primary care and to ensure the timely diagnosis and management of T2DM.

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Component analysis of changes in incidence of lungs cancer in Kazakhstan

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Background. Lung cancer has transformed from a rare disease into a global problem and public health issue, with 2 206 771 newly diagnosed people in the world (IARC, 2020). Lung cancer is the world's leading cause of cancer-related death. Accordingly, 1 796 144 cases of death are recorded annually.

Aim. The purpose is to study the dynamics of lung cancer incidence in Kazakhstan (2009 to 2018).

Methods. Retrospective study, mainly using Dvoirin and Aksel guidelines on component analysis.

Results. The annual average incidence rate of LC (IDC-10 C34) in Kazakhstan amounted to $21.6\pm0.2^0/_{0000}$ (95% CI=21.1–22.0) per 100,000 all population. Over time, the index decreased from $22.4\pm0.4^0/_{0000}$ (95% CI=21.6–23.1) in 2009 to $20.6\pm\mathbf{0.3}^0/_{0000}$ (95% CI=19.9–21.3) in 2018, with a statistically significant difference (t=3.60; p=0.00; R^2=0.750).

According to the study results, the decrease in the number of new LC cases could be mainly associated with the following components:

1. Population growth (Δ_P=+289.4%).
2. Changes in the age structure (Δ_A=+232.8%).
3. The combined effect of changes in the population and its age structure (Δ_{PA}=+31.7%).
4. Changes in the risk of acquiring illness (Δ_R=−349.1%).
5. The combined effect of changes in the risk of acquiring illness and changes in the population (Δ_{RP}=−47.5%).
6. The combined effect of changes in the risk of acquiring illness and changes in the population age structure (Δ_{RA}=−50.4%).
7. The combined effect of changes in the risk of the population to acquire illness and the population age structure (Δ_{RPA}=−6.9%).

The number of patients with LC in Kazakhstan is decreasing. Carrying out this component analysis, we confirmed the decline in patients' number mainly due to changes in the risk of acquiring illness, the combined effect of changes in the risk of acquiring illness and changes in the population, the combined effect of changes in the risk of acquiring illness and changes in the population age structure.

Conclusion. The study showed that a decrease in the incidence of lung cancer is characteristic of a relatively young contingent of the population. Through primary prevention, screening programs, new and less invasive technologies, good success is being achieved in the treatment of LC. Studies on the epidemiologic characteristics of lung cancer and its relative risk factors have played an important role in the primary prevention of lung cancer and in exploring new ways of diagnosis and treatment.

The prevalence and risk factors of *Staphylococcus aureus* carriage in patients undergoing hemodialysis

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Background. *Staphylococcus aureus* carriage, present in up to 80% of hemodialyzed (HD) patients, and is considered as a major risk factor for *S. aureus* bloodstream infection (SAB) in this population. Moreover, the carriage is associated with 20-fold increase in mortality in the case of sepsis comparing to general population.

Aim. The aim of this study was to determine the prevalence of *S. aureus* carriage and its associated potential risk factors in HD outpatients.

Methods. 61 HD patient were examined in terms of *S. aureus* carriage during the period of October 2018 - March 2019. The selected patients were receiving HD for at least two months. 66 healthy subjects were taken as control group. Bacterial culture samples for the presence of *S. aureus* were taken from the anterior nares and throat with cotton-wool swabs. Respondents were interviewed to evaluate *S. aureus* carriage risk factors. Antimicrobial susceptibility testing was performed using the disk diffusion and gradient methods according to the EUCAST guidelines. Statistical analysis was done by SPSS 25.0 program. p-values below 0.05 were considered statistically significant.

Results. This study included 47.2% (n=60) male and 52.8% (n=67) female respondents with mean age of 60.0 years (range: 19–90 years). The HD group consisted of 37 (60.7%) male and 24 (39.3%) female patients. HD vintage was 2-300 months (average 43.13 ± 59.51 months). 49.2% (n=30) patients were identified as *S. aureus* carriers, 43.3% of them carried *S. aureus* in the nose, 16.7% in their throat and 40.0% in both sites. In the control group, which has been matched with the patient group in terms of age, *S. aureus* carriage was 28.7% (n=19). There was a statistically significant difference in carriage rate between the patient and control groups (p=0.018). When we classified the patients into three groups depending on their dialysis vintage (⩽12, 13–24, ⩾25 months), *S. aureus* isolation ratio was statistically higher in the vintage group of ⩾25 months (p=0.08). Moreover, carriage ratio was 4.69-fold higher in patients with arteriovenous fistula compared to central venous catheter (CVC) patients (p=0.013). Recent antimicrobial therapy and hospitalization also showed significant association with *S. aureus* carriage (p=0.027 and 0.031, respectively). We found no methicillin-resistant *S. aureus* (MRSA) carriers in both groups. All isolated strains were sensitive to vancomycin, mupirocin and rifampin.

Conclusion. 49.2% of HD outpatients were *S. aureus* carriers. Dialysis access, vintage, recent hospitalization and antimicrobial therapy were significantly associated with the carriage. MRSA carriers were not determined.

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Corpus uteri cancer in Kazakhstan: component analysis of incidence dynamics

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Background. Corpus uteri cancer is the most common gynaecological malignancy in high-income countries, with 417 367 newly diagnosed women in the world (IARC, 2020). Every year, high rates are detected in countries in Asia (167 310; 40.1%), Europe (130 051; 31.2%) and North America (68 402–16.4%).

Aim. The purpose is to study the dynamics of corpus uteri cancer incidence in Kazakhstan (2009 to 2018).

Methods. Retrospective study, mainly using Dvoirin and Aksel guidelines on component analysis. This method of analysis allows segmenting the number of patients within the same population in different time periods. The component method was used to analyse the dynamics of CUC incidence based on the number of cases that occurred from 2009 to 2018 throughout Kazakhstan.

Results. The annual average incidence rate of CUC in Kazakhstan amounted to $11.9\pm0.3^0/_{0000}$ (95% CI=10.7–11.6) per 100,000 female population. Over time, the index increased from $10.7\pm0.4^0/_{0000}$ (95% CI=10.0–11.5) in 2009 to $11.6\pm0.4^0/_{0000}$ (95% CI=11.0–12.3) in 2018, with a statistically insignificant difference ($t=1.59$; $p=0.11$; $R^2=0.083$).

According to the study results, the increase in the number of new CUC cases could be mainly associated with the following components:

1. Population growth ($\Delta_P=+57.9\%$).
2. Changes in the age structure ($\Delta_A=+52.5\%$).
3. The combined effect of changes in the population and its age structure ($\Delta_{PA}=+6.9\%$).
4. Changes in the risk of acquiring illness ($\Delta_R=-5.8\%$).
5. The combined effect of changes in the risk of acquiring illness and changes in the population ($\Delta_{RP}=-0.8\%$).
6. The combined effect of changes in the risk of acquiring illness and changes in the population age structure ($\Delta_{RA}=-9.4\%$).
7. The combined effect of changes in the risk of the population to acquire illness and the population age structure ($\Delta_{RPA}=-1.2\%$).

The number of patients with CUC in Kazakhstan is increasing. Carrying out this component analysis, we confirmed the growth of patients' number mainly due to population growth and changes in the age structure.

Conclusion. Based on these results, an increase in the proportion of people over the age of fifty, in turn, led to an increase in the number of people diagnosed with CUC, which, accordingly, is mainly a disease of postmenopausal women. The provided data complement our knowledge and are recommended for the monitoring of anti-cancer activities.

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ANESTHESIOLOGY, REANIMATOLOGY & INTENSIVE CARE

Outpatient behaviour characteristics in Regional Hospital Endoscopy Department

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Background. Endoscopic procedure is performed under sedation. *Propofol* is administered for a sedation which can induce cardiorespiratory depression. Patients sign an informed consent that they accept the sedation and will not drive a car for the next 24 hours.

Aim. To examine patient knowledge about sedation, restrictions and their behaviour. Another purpose is to assess condition of patients 2 hours after the procedure to make sure it is safe for discharge.

Methods. Prospective research, interviewing and observing the patients who have had sedation before and after endoscopic procedure during the authors' practical training in Vidzeme Hospital in the period from December 07, 2020 to December 18, 2020.

Results. Forty-two patients were interviewed and observed, of these, 26 (62%) women and 16 (38%) men. 10 (24%) patients had esophagogastroduodenoscopy, 26 (62%) – fibrocolonoscopy, 6 (14%) – both. Age ranged from 19 to 84 years. The most common age group was from 50 to 59 years, the total of 12 (29%). 28 (67%) had a driving licence and 12 (43%) of them got to the hospital by car, while others had a reliable person who provided support. From those who drove themselves, 4 (33%) had knowledge about restrictions. Only 2 (5%) knew the meaning of sedation because they were medical employees, others were informed by the authors. All patients signed an informed consent and agreed for anaesthesia. After 2 hours, when the procedure was completed, all of them were conscious. Patients had no serious side effects except in 3 (7%) cases, when blood pressure difference between before and after sedation was ⩾50 mmHg.

Pearson Correlation test showed that there was interdependence of variable quantities between administered *Propofol* dose and blood pressure difference before and after sedation ($p=0.052$). Increasing the medication dose led to significant blood pressure drop (See the graph below).

After discharging, 32 (76%) patients were picked up by relatives, 7 (17%) drove a car themselves and 3 (7%) used public transport.

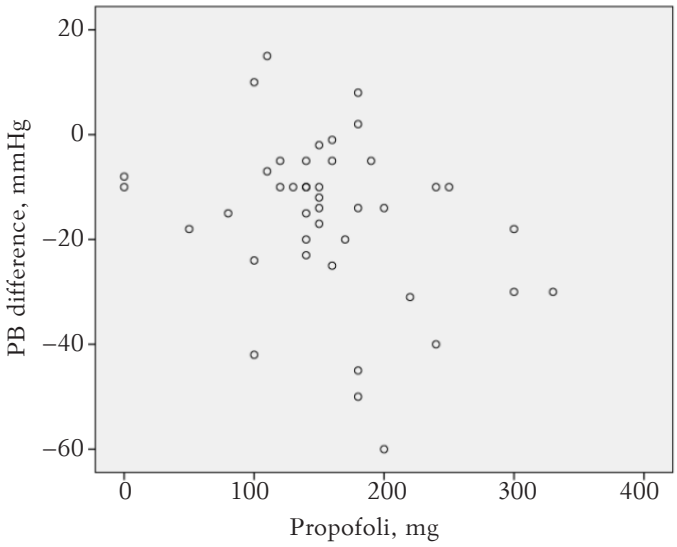

Fig. Correlation between BP difference and *Propofol* dose

Conclusion. Patients should be more thoroughly informed by medical workers about sedation and restrictions.

Acknowledgements. Vidzeme Hospital administration granted permission to authors to conduct the current study.

Analgesia Nociception Index potential use for chronic shoulder pain detection

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Background. Analgesia Nociception Index (ANI) is a new method used to measure acute pain while the patient is unconscious. ANI's greatest benefits include measuring surgical stress and preventing intensive pain in surgical and intensive care patients. ANI detection principle is monitoring heart rate variability by using electrocardiography. Technology uses algorithms analysing R-R complexes and breathing rate therefore assesses patient condition and his sympathetic and parasympathetic nervous systems activity. This innovative technology allows doctors to create an individual technique for dosing analgesic drugs to every patient. Although ANI shows good results in the detection of acute pain when the patient is being unconscious, currently the trials for chronic pain detection are still in progress.

Aim. The aim of this pilot study was to determine the usefulness of ANI for chronic pain intensity detection. It was hypothesized that ANI may be used for chronic pain detection and as an indicator of the effectiveness of therapy.

Methods. The pilot study was conducted in Hospital of Traumatology and Orthopaedics. Riga, Latvia, after approval by Ethics Committee on July 2020. Nine patients suffering from chronic shoulder pain participated in this study. ANI was monitored for a total of 40 minutes for each patient in dedicated time cuts (while rested, after pain provocations tests, before and after suprascapular nerve blockade). Medication for every patient suprascapular nerve block was similar to similar doses: sol. Bupivacaine (20 mg), sol. Methylprednisolone (80 mg).

Results. In eight (88.8%) out of nine patients, significant changes took place (95% CI [-27, -7.4]). Analgesia Nociception Index significantly increased 20 minutes after peripheral nerve block: 58±7 comparing with results before peripheral nerve blockade 40.8±11 ($p=0.004$). On average, ANI scores before blockade were -17.2 lower than after blockade that shows good peripheral nerve blockade effectiveness for chronic pain treatment.

Conclusion. In summary, it has been concluded that ANI technology at pain detection works effectively and could be a potentially useful tool for measurement and treatment of chronic pain. However, to apply it to patients in conscious state, a much broader and more detailed study is needed to be able to objectively assess all aspects affecting ANI. This study theoretically could encounter problems with the patient's psychoemotional state and stress about the procedure, which might give false-positive results by initially increasing heart rate and decreasing ANI. Also, variable ANI values before and after blockade affect patients' etiological reasons for chronic pain.

Safety and effectiveness of different spinal morphine doses for postoperative analgesia after primary hip replacement

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Background. Intrathecal morphine combined with bupivacaine effectively relieves postoperative pain, but has opioid-related side effects (nausea, pruritus, urinary retention, respiratory depression), that could depend on the dose of morphine.

Aim. The aim of our study was to find the best dose of intrathecal morphine giving the maximal effect at the minimal side effects after total hip replacement.

Methods. This prospective randomized study includes 69 patients meeting the inclusion criteria. All patients underwent total hip replacement surgery under spinal anaesthesia with Bupivacaine 0.5% 10–15mg. The 1st group – control. The 2nd group received 0.1mg morphine intrathecally. The 3rd group received 0.2 mg morphine intrathecally. All patients received multimodal analgesia after surgery using morphine 10 mg subcutaneously as a rescue medication (if pain >5 by NRS). Outcome evaluation focused on 24 h measurement: Morphine consumption (primary outcome); pain level in rest and on movement 4 h, 7 h, 12 h and 24 h after surgery (by NRS); oxygen saturation (%); respiratory rate (x/min) and the incidence of nausea and itching. Data were analysed using SPSS program.

Results. Groups were comparable before surgery. During 24 h after surgery:

- The amount of s/c morphine was statistically significantly higher in the 1st group=75% of all patient (doses 10–20mg), the 2nd group 25% (10–20mg) and the 3rd group 10% (10mg), ($p<0.001$).
- There were no statistically significant differences in mean (min;max) respiratory rate between groups: the 1st – 16.1 (13.0; 20.0); the 2nd – 15.2 (13.0;19.0); the 3rd – 15.4 (11.5; 21.5) ($p>0.05$),
- and oxygen saturation between groups: the 1st group – 96,7% (92,0%; 100,0%); the 2nd group – 95.5% (92.0%;99.0%), the 3rd group – 95.7% (91.0%;100.0%), ($p>0.05$).
- The mean NRS pain scores in the 1st, 2nd and 3rd group, accordingly, were at 4 h after surgery: 0.95 vs. 0.68 vs. 0.00 ($p=0.089$); at 7 h: 2.79 vs. 1.20 vs. 0.20 ($p<0.001$); at 12 h: 3.31 vs. 1.00 vs. 0.25 ($p<0.001$); at 24 h: 2.45 vs. 1.32 vs. 0.00 ($p<0.001$).
- The patients in the 2nd and 3rd group had statistically significantly lower pain level in rest than in the control group at 7 h, 12 h after surgery and 3rd group in 24 h ($p<0.005$).
- No statistically significant difference in nausea and vomiting incidence between groups: 10.3% (1st), 20% (2nd), 15% (3rd). The itching incidence was statistically significantly higher in the 3rd group: 25% patients ($p<0.005$).

Conclusion. Intrathecal morphine in a dose 0.2 mg provides the most effective pain relief without significant side effects.

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Prehospital care of paediatric burn patients in 2015–2018

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Background. In Latvia, an average of 160 children per year are hospitalized with complicated burns, most of them under the age of two. Some patients have to spend more than a month in hospital undergoing complex surgeries (Children's Clinical University Hospital, 2017). The process of treating patients is technically complicated (repeated surgeries, skin graft, rehabilitation), patients suffer from severe pain and emotional stress, scars and movement restrictions often persist for the rest of their lives.

Aim. To analyse information from ECC of SEMS paediatric burn patients from 2015 to 2018.

Methods. Document analysis was used as a research method in the study, evaluating 2 658 SEMS call cards for children with burn injuries in the period from 2015 to 2018. The research protocol included the following criteria: age, gender, the reason for the call, primary diagnosis made by the EMS team, call outcome (patient hospitalised/non-hospitalised), medical manipulation and use of analgesics.

Results. In the period from 2015 to 2018, EMS specialists provided assistance to a total of 2 658 children with burn injuries, including 61% boys. The most critical age for children with burn injuries was identified as spanning from birth to 3 years of age, the proportion of which was 64%. In 35% of calls, the area of burns was not indicated, in 48% the area of burns was less than 10%, whereas burns with an area above 50% occurred in 0.5% or 12 children over the given period.

The most common thermal and chemical burns in children identified by EMS physicians were the following: body (17%), wrist and hands (16%), head and neck (14%) burns.

Conclusion. From 2015 to 2018, EMS specialists provided assistance to a total of 2 658 children with burn injuries, including 1 944 (73%) children who were hospitalized. The greatest risk of burns was identified for children until the age of three. The most commonly used painkillers for burns were *Paracetamolum* as rectal suppositories (33%) or tablets, and *Fentanylum* 0.05 mg/ml solution administered intravenously or intranasally (17%). Other opiate medication was used very rarely: *Morphini Hydrochloridum* was reported once throughout the period, while the usage of *Tramadol Hydrochloridum* was recorded on four occasions.

Over the given period, EMS physicians encountered only thermal and chemical burns in children. No calls were received for paediatric electrical injuries. Finally, there were no fatalities while transporting patients to hospitals during that time.

Delirium in patients with myocardial infarction in the cardiovascular intensive care unit setting: occurrence and prognosis

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Background. Delirium is a common issue in non-intensive care settings. However, the prevalence of this confusional state is especially high among intensive care unit patients where it can develop in up to 80% of mechanically ventilated and up to 50% of non-mechanically ventilated subjects. The most common condition in the cardiovascular intensive care unit (CICU) is an acute myocardial infarction (AMI).

Aim. We aimed to describe the occurrence and outcomes of delirium in a cohort of AMI patients in the CICU setting.

Methods. An observational retrospective study was carried out to investigate patients who were admitted to the CICU of Vilnius University Hospital Santaros Clinics, Vilnius, Lithuania. All included patients had a documented delirium diagnosis through liaison and consultation with a psychiatrist.

Results. Our analysis included 142 patients who had a confirmed delirium episode in the CICU setting after experiencing AMI. 104 (73.2%) patients had an ST-elevation myocardial infarction (STEMI) (78.7% of women and 69.1% of men) and 38 (26.8%) presented with a non-ST-elevation myocardial infarction (NSTEMI) (21.3% of women and 30.9% of men). There was no significant difference in delirium incidence in terms of gender and the type of AMI. Delirium occurred on average after 7.31 days after hospitalization among STEMI patients and after 6.18 days after hospitalization among NSTEMI patients. Neither percutaneous coronary intervention (PCI), nor coronary artery bypass surgery had a significant impact on the prevalence of delirium nor patients' lethality ($p>0.05$). The in-hospital mortality analysis revealed no correlation between the type of AMI and delirium manifestation time. CICU patients with AMI and a concomitant infection on average developed delirium later (10.3 days) than those without infection (4.1 days) ($p<0.05$).

Conclusion. Delirium was more prevalent between CICU patients with STEMI, however, delirium manifested earlier in those with NSTEMI. Neither the type of AMI nor the invasive treatment option had a significant impact on the occurrence time of delirium. On the other hand, those with concomitant infection developed delirium later compared to those with no concomitant infection.

Bedside multimodal somatosensory testing for prediction of positive treatment effect after transforaminal epidural steroid injection in patients with lumbosacral radicular pain

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Background. Transforaminal epidural steroid injection (TFESI) is widely practiced for the treatment of radicular pain. As its effectiveness is still subject to debate, an improvement in patient selection for TFESI is necessary.

Aim. We aimed to test the relation between sensory disturbances detected by bedside multimodal somatosensory testing and the early positive effects of TFESI in patients with lumbosacral radicular pain.

Methods. We evaluated patients with chronic unilateral lumbosacral radicular pain appointed for pain treatment with TFESI in a prospective observational study (#158200-15-772-289). Before the intervention, patients were assessed using a battery of bedside-suitable sensory testing instruments (10 g monofilament, 200–400 mN brush, Lindblom rollers with controlled 25°C and 40°C temperature, 40 g neurological pin, and moderate force finger pressure). Participants had to rate their sensory perceptions on the painful leg comparing with the non-painful at multiple symmetrical test points along the affected dermatomes. Sensory perceptions were rated as normosensitivity, hyposensitivity, or hypersensitivity. Pain and related characteristics were evaluated before and 4 weeks after TFESI.

Results. Thirty-six patients (26 women, 10 men; the mean age (± SD): 58.7 (±10.3), range 38–78 years) completed the study. Tactile static testing detected hyposensitivity in 25 (69%), hypersensitivity in 4 (11%) and normosensitivity in 7 (19%) patients. Tactile dynamic, respectively – 9 (25%), 4 (11%), 23 (64%). Pinprick testing – 22 (61%), 4 (11%), 10 (28%). Innocuous cold – 22 (61%), 4 (11%), 10 (28%). Innocuous warmth – 21 (58%), 4 (11%), 11 (31%). Deep pressure – hypoesthesia in 6 (17%), hyperesthesia in 17 (47%), mixed hypo/hyperesthesia in 7 (19%), normal sensitivity in 6 (17%) patients. The whole study group showed significant improvements in most outcome measurements. However, individual results between study participants varied. The univariate linear regression model showed some sensory testing modalities to be independent parameters in predicting statistically significant better results after 4 weeks in the following domains: leg pain intensity (measured with BPI-SF pain intensity items), patient-reported outcome measurements (measured with Global Impression of Change Scale and Global Pain Change Scale), some impact on functioning items (measured with BPI-SF impact on functioning items). In the latter cases, normosensitivity detection was related to the greatest improvements. Sensory testing had no predicting effect for improvement in anxiety and depression evaluation (measured with HADS) and neuropathic pain component (measured with painDETECT).

Conclusion. Bedside-suitable multimodal somatosensory testing shows a potential to predict better early effects of radicular pain treatment by TFESI.

A new add-on device for treatment of COVID-19 pneumonia

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Background. COVID-19 patients usually do not require mechanical lung ventilation in the first stages of disease. Initially treatment requires constant positive airway pressure (CPAP) with increased oxygen concentration (SpO2). Typical hospital equipment for mechanical ventilation is able to work in different modes, including CPAP with high SpO2. However, the cost of such a device is high (>10 000 EUR) and production time is several months. There are home care CPAP devices that are less expensive (<1 000 EUR) and widely available with short production time, but they cannot be used with high oxygen concentration. CPAP can supply additional oxygen directly to the patient's mask with constant flow, without concentration control, which leads to decreased treatment efficiency.

Aim. To develop a home care CPAP add-on device, capable to maintain precise inhaled oxygen concentration without altering CPAP device structure. That will allow fast supply of these devices in short time.

Methods. We designed a prototype of a new add-on device for treatment of COVID-19 pneumonia, that can be produced in high volume and at low cost. Additionally, device has all crucial safety features and could go through clinical trials and become certified.

Results. We have created a new add-on device for CPAP device allowing to administer additional oxygen and to measure more precisely inhaled oxygen concentration. The main challenge was to maintain stable oxygen concentration at any phase of inhalation, which was achieved by using of a 2-liter buffer tank. Multiple simulations were performed to find optimal volume and form of the buffer. Clinicians see FiO2 level on the LCD touchscreen and change it according to the therapy. Device has alarm and logging capabilities to monitor patient condition and store data for further analysis.

Simulations shown 41% maximal oxygen concentration. X-type mixer created good oxygen homogeneity but increased hydraulic resistance significantly (11.6%).

All the necessary documents have been prepared and submitted to receive a permit of the Regional European Medical Agency for conducting a trial. The clinical protocol and hospital infrastructure have been prepared for clinical trials.

Conclusion. The add-on device for CPAP creates a precise FiO2 measurements with <1% error. The FiO2 (max) strongly correlates with CPAP generated positive pressure resulting in 50–60% concentration of oxygen in inhaled air.

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NURSING

Quality of life for patients with chronic noncommunicable disease

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Background. The achievements of modern medicine that increase life expectancy without completely eliminating the disease contribute to the progression of patients with chronic conditions. Type 2 diabetes has a high risk of disability, death, and reduced quality of life, and therefore obliges patients to change their usual lifestyle. In addition to preventive measures, our country has implemented a Disease Management Program (DMP).

Aim. To study the quality of life of patients with type 2 diabetes to determine the effectiveness of the DMP.

Methods. A cross-sectional study was conducted with 187 patients with type 2 diabetes aged 35–74 years. The official adapted version of the Medical Outcomes Study 36 was used to survey patients.

Results. All respondents are divided into two groups: Group 1 included 100 patients who were participants in the new Disease Management Program; group 2 included 87 patients who were not included in the DMP, were under dynamic medical supervision.

The results are presented in points on 8 scales, forming two indicators: physical and psychological components. The scale indicators are modified between 0–100 points, a higher score indicates a high quality of life, and indicators closer to 0 – a low quality of life. For the physical component, the maximum indicator in Group 1 on the scale of "Bodily pain" is 67.27, the minimum on the scale of "Role functioning" is 61.2. Among patients under the supervision of a doctor, the highest value is marked on the scale of "Physical functioning" – 65.7, the lowest – "General health" – 56.3. The mental component in the group of the DMP has the highest score on the "Social functioning" scale – 75.16, the lowest score on the "Viability" scale – 60.8.

In Group 2, the record indicator of "Social functioning" is 66, and the minimum indicator of "Viability" is 55.1.

The effectiveness of the DMP was analysed between groups using the $\chi 2$ (Chi-square) criterion. Analysing the critical value of $\chi 2$ at the significance level $p<0.05$ was 14.067. The relationship between the features is not statistically significant ($p>0.05$).

Conclusion. After two years of operation, the DMP has not achieved significant results, since it is not designed for short-term results, and the effectiveness of work can be observed after 5–10 years.

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Influence of the type of attitude towards disease in course of diabetes

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Background. Any chronic disease is characterized by great psychological trauma, which leads to development of lasting emotional defects. Type 2 diabetes is not a fatal disease, but the chronic course obliges patients to change their usual lifestyle. The relevance of the current study is a comprehensive research of the internal picture of the disease, the manifestation of which is reflected in the attitude towards the disease. Awareness of the presence of an incurable disease manifests itself in different ways.

Aim. To study the prevailing types of attitudes towards the disease among patients with type 2 diabetes.

Methods. A cross-sectional study was conducted on the basis of 2 polyclinics in the city of Nursultan. The respondents were 82 patients (38 men and 44 women) with type 2 diabetes mellitus aged 35 to 78 years, who were under dynamic observation by a doctor. The personal questionnaire developed by Bekhterevsky Institute (LOBI) was used to correctly determine the type.

Results. Among all respondents, the lowest value of 2.5% was scored by patients with a sensitive and egocentric type of attitude to the disease. A harmonious attitude to diabetes was observed in 3.7% of respondents. Apathetic attitude was expressed by 3.7% of patients. 6.2% of the respondents revealed prevailing anosognosia and neurasthenic types. Hypochondria was typical for 7.2% of the subjects. Paranoid attitude was diagnosed in 8.6% of patients. The highest value, 27.2% of subjects belonged to a euphoric type. When interpreting the questionnaire, 32% of respondents were diagnosed with 2 or more types at the same time, which we combined into a mixed type.

Conclusion. The data obtained suggest that patients with type 2 diabetes in most cases have a "vague" attitude towards the disease, which can negatively affect the course of the disease, its treatment, and lead to serious consequences. Focusing on mental health and properly selected psychological assistance will help a person to quickly adapt to the disease, and can have a significant positive effect, even if there are complications.

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Quality of sleep of nurses during fight against COVID-19

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Background. In the context of a widespread acute infectious disease, nurses around the world who are in close contact with patients can experience various psychological problems. In most cases, there are problems with sleep.

Aim. To assess the quality of sleep of nurses working on the front line in the fight against COVID-19.

Methods. A cross-sectional study was conducted, involving 472 secondary health workers aged 18 to 74 years. All respondents were divided into 2 groups: Group 1 – the experimental group, which included 319 people who worked with COVID-patients, Group 2 – the control group, which included 153 medical workers who had no access to COVID-patients. The Pittsburgh Sleep Quality Index was used to study sleep quality. The questionnaire consisted of 19 items, each item could be rated from 0 to 3. The results are presented by summing the scores of 7 components, which gives a total score from 0 to 21, lower scores mean a better, healthier sleep quality.

Results. The results of the study showed that the total value for all components in the experimental group was 7.89±0.19, in the control group – 5.92±0.24 (p=0.000). In the experimental group, the highest rates were recorded for the following components: "Sleep latency" (1.60±0.051) and "Sleep duration" (1.59±0.049). Of the 321 nurses from Group 1, for 173 the quality of sleep was higher (53.9 %) with a total score of from 6 to 10, whereas 56 of them had a poor sleep quality with a score of 11 to 15 (17.4%), and 7 nurses observed a very poor sleep quality (or 2.2%) with a total score of 16 to 18. The differences in "Duration of sleep" (t=11.08, p=0.000), "Sleep efficiency" (t=10.76, p=0.000) and in "Disruption of the daily operation" (t=5.34, p=0.000) between the two groups was statistically significant (p<0.01). 20 persons (to 6.2%) in the basic group took sleeping pills more than three times a week because of problems with sleep. The overall score in the experimental group was 7.89, which indicated a poor sleep quality.

Conclusion. Nurses involved in the fight against COVID-19 have problems with sleep, because since the study indicates significant differences in the PSQI test between the two groups. Health care managers should pay due attention and strengthen psychological counselling for frontline nurses to improve sleep quality and mental health.

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Necessity to amend Article No 43 of the Code of Civil Procedure to ensure patients' rights of exceptions to general provisions regarding court expenses

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Background. Article No 43 of the Latvian Code of Civil Procedure does not provide a direct opportunity for the patients to enjoy exceptions to the general provisions regarding court expenses, however, Latvian court practice indicates that disputes between hospitals and patients or their relatives occur on a regular basis. The existing regulation states that plaintiffs shall be exempt from the payment of court expenses in claims arising from personal injuries that have resulted in mutilation or other damage to health, or the death of a person, or in claims regarding compensation for financial losses and moral damage resulting from criminal offences. This regulation does not cover all the possible damages that could be incurred to the patients. Taking into account the significant role of civil disputes in healthcare and earnest impact thereof not only on individuals and hospitals but also on the public, it is essential to find an appropriate legal solution to guarantee patients' rights to enjoy exceptions regarding court expenses.

Aim. The aim of this research is to expand the understanding of the exception of general provisions regarding court expenses and patients' rights to the court free of charge. The author has chosen to analyse the existing regulation and possible modernization of the Latvian Code of Civil Procedure to ensure more open and just system both for regular cases regarding personal injuries, damage to health (also moral), or the death of a person within or without framework of criminal offence and medical treatment.

Methods. For the interpretation of the Latvian Code of Civil Procedure, the author has used the grammatical, historical, systemic and teleological methods. In addition, the author has analysed modern and historical Latvian court practices and legal literature on this topic from various periods.

Results. Research results are: 1) expanded understanding of the necessity of specific procedural regulation that provides exceptions to the general provisions regarding court expenses; 2) more precisely illuminated legislative task to ensure protection of patients' rights; 3) identified proposal to the legislator to improve regulation.

Conclusion. Article No 43 of the Latvian Code of Civil Procedure should be supplemented with a new regulation which clearly stipulates that patients enjoy exceptions to the general provisions regarding court expenses – patients are entitled to a fair trial free of charge.

Psychological well-being of patients in the intensive care unit

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Background. Patients in the Intensive Care Unit (ICU) experience sudden and unexpected deterioration in their health, resulting in severe physical suffering, extreme stress and sometimes altered states of consciousness. According to *MedicineNet* data, 1 of 3 patients staying in the ICU for more than 5 days experience psychosis. These experiences can cause suffering in the future. In order to help patients to recover faster, reduce the development of complications and shorten the time of rehabilitation, it is important to take care also of patients' psychological well-being.

Aim. To study the psychological well-being of patients in Intensive Care Unit.

Methods. Qualitative method was used for the research, – a content analysis, the tool – interview questions. The instrument was developed on the basis of the analysis of the literature and the theory of Carol D. Ryff. The study was conducted remotely, during 05.04.2020–30.04.2020, using the *Facebook* video call feature. Respondents were selected according to the convenience method, in total, 6 respondents were interviewed – 3 men and 3 women, aged 30–61, who had spent at least 2 days in ICU.

Results. We found that the respondents in the ICU experience both positive and negative feelings. Limited opportunities to communicate with loved ones caused more emotional suffering for women than for men. While privacy in ICU is ensured, the independence is suspended by the severity of the situation and insufficient staff communication. Being in the ICU without clothes and personal belongings promotes the development of negative emotions, the lack of a mobile phone creates a feeling of isolation. Half of the participants remember the harassing thoughts, nightmares or hallucinations, and some of them had experienced auditory or visual altered states of consciousness of other patients, which had caused confusion and fear. Some praised the care and professionalism of the staff. Respondents who have felt unheard or have not received answers to their questions give a more negative assessment of care.

Conclusion. ICU patients experience fear, ignorance, powerlessness, and the main contributing factor is insufficient staff communication with the patient. Effective communication could facilitate acceptance of the status quo, create a sense of security and foster trust in staff. Respondents acknowledge that the quality of staff communication with the patient is the most important element of ICU care and indicate that it promotes patient independence, provides psychological support and better opportunities to communicate with relatives.

Performance of nursing staff in taking care of children with a congenital heart defect

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Background. The congenital heart defect accounts for 26% of all congenital anomalies in Lithuania and ranks second after the congenital anomalies of the central nervous system.

Aim. To assess the performance of the nursing staff in taking care of the children with a congenital heart defect.

Methods. A total of 90 nurses from the Cardiac Surgery Centre of one University Hospital in Vilnius participated in the investigation. The questionnaire survey (32 closed-ended questions) was carried out in the course of three months (the responses constituted 69.2%). The performance of the nursing staff was assessed during the preoperative, perioperative and postoperative periods.

Results. The *preoperative* period: the majority of nurses (93.3%) measured the pulse and breathing frequency quite often; others (6.7%) indicated drug administration. The majority of nurses (60.0%) assessed changes in arterial blood pressure, the pulse, temperature more often than the patient's irritability ($p<0.05$). Correlations ($p<0.01$) between a frequent assessment of vital functions and preserving the safe environment were established. During the *perioperative* period: the majority (82.3%) of the respondents gave more priority to oxygen saturation, arterial blood pressure than to changes in skin colour ($p<0.05$) regarding the performance of the nurses. One the fifth of the respondents stated that assessing changes in the pulse and temperature were a frequent practice of the nursing staff. During the *postoperative* period: a half of the respondents (50.0%) attributed the observation of diuresis to very important acts performed by the nurses, especially when the production of urine was 0.5 ml/kg/hour or less. The majority of the respondents (73.3%) correctly assessed four physical factors that caused the formation of pressure ulcers; one fourth of the respondents specified three physical factors (moisture, friction and movement); 2.3% indicated two factors that caused the formation of pressure ulcers ($p<0.05$). One fourth of the respondents (24.4%) attributed lung ventilation disorders, infection, bleeding to frequent complications, a half of the respondents (50.0%) indicated a blockage of the urinary catheter, the position of an intubation tube, suctioning secretions; others (20.0%) specified cardiac tamponade; 5.6% said that intestinal peristalsis, changes in skin were the rarest causes of complications.

Conclusion. During every period, the performance of the nurses was directed towards the assessment and maintenance of vital functions. During the postoperative period, actions were more often intended for the prevention of complications and physical factors that caused the formation of pressure ulcers.

Acknowledgments. The authors declare the absence of conflict of interest.

Risk factors influencing hand skin damage

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Background. Hand skin damage increases the risk of occupational contact dermatitis for the medical staff by about 80%.

Aim. To evaluate risk factors causing hand skin damage.

Methods. The research was performed online for one month and involved 64 nurses working in surgical, therapy departments and an outpatient clinic. The average age of the nurses was 40.26±12.69 years, the average working time per week – 45.46±8.89 hours. The study assessed the effect of the application frequency of external irritants (soap, hand sanitizer, medication, gloves) on the skin of hand.

Results. The majority (77.8%) of surgical nurses washed their hands more than 18 times per shift, a decreasing trend (53.8%) was observed in therapy nurses and 15.2% of outpatient clinic nurses. *Hand sanitizer.* Outpatient clinic nurses (30.3%) used hand sanitizers 10 times per shift, surgical (38.8 %) and therapy nurses (30.8%) – more than 18 times per shift. *Gloves.* In performing nursing actions, the majority of surgical nurses (77.8%), 53.8 % of therapy and a quarter of outpatient nurses changed gloves more than 18 times per shift. One the third of therapy and a quarter of outpatient nurses wore gloves for 10 minutes, one the third of surgical nurses – for 15 minutes and 16.7% – for more than 20 minutes. To avoid skin, contact with medications, 72.3% of surgical nurses, 72.7% of therapy and 53.8% of outpatient nurses put on gloves. *Emollients.* A third of therapy nurses and more than a quarter of surgical nurses and outpatient nurses used hand emollients 6 times per day, surgical nurses (5.5%) – 10 times per day, therapy and outpatient nurses (8.6%) – 3 times per day. *Skin condition.* At the end of a work shift, 12.1% of outpatient nurses reported itching on the back of hands and appearance of fissure. Other surgical nurses (16.7%) reported redness, stretching of skin and itching on fingers and wrists. One third (30.8%) of therapy nurses reported dryness of hand skin, redness and swelling. Other respondents (40.4%) did not notice any changes ($p<0.5$). A frequent (>18 times) use of sanitizers damage hand skin more than soap ($p=0.0001$). The glove type ($p=0.001$) inflicted more damage than glove wearing time.

Conclusion. The effect of the emollients on hand skin was underestimated. Hand sanitizers are frequent irritants. Common symptoms of hand damage are redness, itching, dryness of skin. The type of gloves is an important risk factor.

Acknowledgments. The authors declare the absence of conflict of interest.

Evaluation of patients' quality of life aspects after cardiac pacemaker implantation

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Background. The number of people with heart rhythm disorders in Lithuania is constantly increasing. The number of threatening cases is also on the rise; the patients are getting younger. Pacemaker implantation not only saves the lives of these people, but also affects their quality of life.

Aim. To evaluate patients' quality of life aspects after pacemaker implantation relating to gender, age, social status, body weight and implantation timespan.

Methods. A total of 176 clinically stable patients of both genders (51.1% women and 48.9% men) over 18 years old (average 66.9±12.6 years) were evaluated. We used the SF–36 (*Medical Outcomes Study 36-items Short Form)* questionnaire to assess the quality of life.

Results. The domains characterising the quality of life such as physical activities, social functions, energy/vitality, presence of pain, physical and psychical health were assessed higher by men ($p<0.05$). The assessment of the domains pertaining to the quality of life such as physical activity, the restriction of the activity due to the physical problems, pain and physical health dropped when answered by older people ($p<0.05$). The quality of life was assessed with fewer points by the disabled, pensioners, widowed and the less educated. The respondents with normal body weight gave the highest assessment to such domains of the quality of life as energy/vitality, presence of pain, general health, physical and psychical health ($p<0.05$). Patients suffering from heart rhythm disorders and other diseases for a longer time, gave a lower assessment to all the domains pertaining to the quality of life. The longer was the implantation time of a pacemaker, the worse the assessment of such domains as the restriction of the activity due to physical problems, social functions, energy/vitality, pain, physical and mental health ($p<0.05$).

Conclusion. Many domains pertaining to the quality of life are rated higher by younger, higher-educated subjects, men, and those with normal body weights. The assessment of quality of life depended on the general state of health.

Acknowledgments. The authors declare the absence of conflict of interest.

Type 2 diabetes and quality of life

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Background. In the case of diabetes, the number of cases is growing rapidly in all countries of the world. Long-term development of the disease and complications of the disease are a frequent occurrence. In halting the progression of the disease, the treatment regimen and diverse lifestyle are of a particular importance. These factors require changes in many spheres of life, thus bearing a close connection with the quality of life of patients. Factors related to diabetes and their impact on the quality of life of patients have been investigated in this aspect

Aim. The objective of the study was to evaluate the disease factors related to diabetes, changes in quality of life.

Methods. The study included 101 patients with type 2 diabetes. Quality of life was assessed using the SF-36 questionnaire.

Results. The lowest scores were given by all the subjects in terms of general health, whereas the higher scores were allocated to social functioning and mental condition. Physical condition, activity limitations due to physical disorders, general health, energy, mental condition, and overall quality of life deteriorated with age. Disabled people and pensioners rated their quality of life lower. BMI, gender, marital status, and education had no effect on quality of life assessment. Most areas of quality of life were rated higher on pill-treated scores. The incidence of arterial hypertension and CD complications affect various areas of quality of life – deteriorating general health, energy, mental state, social functioning, activity limitation due to physical disorders and the overall quality of life. Restrictions of activity due to physical disorders have a direct impact on the quality of life – an increase of one point in the assessment of performance restrictions due to physical disorders increases the assessment of quality of life by 0.290 points.

Conclusion. Physical condition, activity limitations due to physical disorders, general health condition, energy, mental condition, and overall quality of life is affected by type 2 diabetes depending on the duration of illness.

Acknowledgments. The authors declare the absence of conflict of interest.

Patients' opinion on the most frequent factors affecting quality of primary care

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Background. Quality health services offer real opportunities to meet patients' needs, save resources, promote employee responsibility, develop knowledge and excellence. Therefore, the analysis of the availability and quality of primary health care services and the assessment of patients' motivation in choosing a provider are among the most frequent and important studies in Lithuania.

Aim. The objective of the current study was to evaluate patients' attitudes towards services provided by the primary personal health care institution.

Methods. The study was performed in one outpatient clinic in Vilnius. 187 patients participated in a survey. A questionnaire prepared by the authors was used for the research. We evaluated socio-demographic data of subjects and the assessment of service quality.

Results. The most common criteria for choosing an institution providing primary personal health care were: comfort – close to the place of residence (39%), quality service (21.4%), recommendations of relatives and acquaintances (20.9%). Patients gave assessment "good" and "very good" to the quality of treatment (80.7%) and nursing care (76.5%), and gave these domains of services higher scores. Almost two thirds of the respondents gave assessment "good" and "very good" to both medical services and receptionists' work, 73.8% and 70% of the respondents accordingly. One third of the surveyed were of the opinion that nurses did not inform them about a healthy diet and side effects of the drugs (33.7% and 31.5%), 29.4 interviewees were missing an individual attention of nurses.

Conclusion. The most common criteria for choosing an institution providing primary personal health care was comfort – proximity to the place of residence. The highest assessments were given to the quality of service organization, the lowest – to the functional quality of services. Patients were most satisfied with the neat and appropriate clothing of staff, competency and quality of the procedures.

Acknowledgments. The authors declare the absence of conflict of interest.

Poster presentations

MENTAL HEALTH

Childhood risk factors for substance abuse in a clinical sample of adult outpatients in Riga Psychiatry and Addiction Medicine Centre

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Background. Studies conducted in clinical populations suggest a strong connection between different childhood risk factors and substance use disorder (SUD) in adulthood.

Aim. To examine the associations between self-reported weak academic performance, repetition of a grade, single-parent family, self–reported quality of parent–child relationship, conduct problems in childhood and SUD in adulthood in a sample of outpatients in the Addiction Outpatient Clinic in Riga, Latvia.

Methods. Adult outpatients of addiction clinic were asked to complete a self-report survey. Healthy control subjects (adults without addiction, formally assessed for fitness to drive, firearms licensing etc.) and patients with substance use disorder were examined in relation to self-reported childhood risk factors.

Results. Self-report surveys were completed by 334 outpatients (mean age 37.4; SD=10.1), including 97 healthy control subjects. 76.3 % of participants were male. The acquired data show significant connections between poor academic performance ($p<0.000$), repetition of a grade ($p=0.001$), conduct problems in childhood ($p<0.000$) and SUD in adulthood. Associations between single-parent family, low quality of parent–child relationship and substance abuse were insignificant. Males were found to be 1.5-fold more likely to have substance use disorder comparing to females ($p=0.000$).

Conclusion. According to the obtained data, poor academic performance, repetition of a grade and conduct problems in childhood might be risk factors for developing SUD in adulthood. Children with these risk factors should be the target population for primary prevention of substance abuse.

Acknowledgements. The authors declare the absence of conflict of interest.

Communication between physiotherapist and patient with chronic pain – qualitative analysis

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Background. Communication is the basis of therapeutic relationships that plays a crucial role in treatment of any person. Physiotherapists have a great opportunity to make a positive impact on the pain experience of people with chronic pain. Communication between a physiotherapist and a patient has so far been given insufficient attention in Latvia, thus, the understanding of this issue is vague at best.

Aim. The aim of the current qualitative study was to find out how communication is constructed between physiotherapists and patients with chronic pain.

Methods. Grounded Theory approach by Charmaz was applied. Ethnographic observations and audio recordings of conversations during the interaction between five physiotherapists and 10 patients with chronic pain were made, starting with the first consultation. Audio recordings and observation notes were transcribed verbatim and analysed by creating simple and focused codes, using constant comparison and writing memos, forming categories and sub-categories. Throughout this analytical process, the explaining theoretical framework was created. The study was approved by Riga Stradiņš University Ethics Committee (No. 26/28.06.2018.).

Results. During the data analysis, a number of processes emerged that occurred in different sequences during interactions. Two basic processes, the Introduction of Clarity and the Search for Words, came to the forefront. The Introduction of Clarity describes processes that are based on uncertainty. The Search for Words describes processes related to looking for best words to match the experience. One cannot reach the clarity until the correct words have been found. These two processes interact with each other and share common features that manifest through smaller communication actions, identified as: Expressing the Nature of Physiotherapy (defining the roles and the nature of the cooperation), Putting Forward and Verifying Hypotheses (setting and revising hypothesis from the first point of contact), Disclosing Information (the way patients express their uncertainties and opinions), Justifying and Explaining Information (physiotherapists explaining theoretical rationale behind their actions), and Giving Advice and Training (directing and giving instructions).

Conclusion. There are communication differences that physiotherapists should be aware of to minimize potential risk of miscommunication: interaction, that is itself permeated by uncertainties and search of words, is largely dominated by physiotherapists, using closed-ended questions to focus on hypotheses about patient's problem, whereas patients engage by bringing forward their own experience (all that has happened and has been felt), thereby explaining and justifying their condition.

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Emotional state of first-year medical students and contributing social factors

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Background. All over the world, medical students experience high levels of depression, anxiety and psychological distress.

Aim. The aim of our study was to evaluate self-reported emotional state of first-year medical students and investigate, which social factors could have an effect thereon.

Methods. The target group was the first-year local medical students at the Vilnius University Faculty of Medicine. Anonymous questionnaire created by the authors was used to collect data about self-perceived emotional state and about social factors which may affect it (change of the city/town of residence, living in parents' house, having regular hobbies). The study involved 97 local medical students. SPSS 17.0 was used for statistical data analysis.

Results. The study included 73.2% female and 26.8% male students. 42.3% of students had to move to another city because of their studies. 40.2% of students remained at their parents' house after entering the university. Half of the students reported that they had a regular hobby (53.6%) while 46.5% reported not having any particular hobbies besides their studies. 69.1% of the students reported that the studies had a negative impact on their emotional condition. We did not find any statistically significant correlation between self-perceived emotional condition of students and the aforementioned social factors.

Conclusion. The majority of the first-year medical students reported that studies had a negative impact on their emotional condition. However, further research is needed to investigate, which social factors could affect their emotional condition.

Assessment and analysis of psychological abuse in the information technology (IT) sector

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Background. Psychological abuse at work (mobbing) is one of the most relevant public health problems at present. In Lithuania and other countries, the expression of mobbing has been widely studied in different sectors. However, the expressions of psychological abuse at work among IT specialists have not been studied in practice. Therefore, the aim of this study was to determine whether we reasonably believe that the expressions of psychological abuse in the IT sector are insignificant and we do not consider them.

Aim. The study was conducted to assess the prevalence of psychological abuse at work and its links to subjective health assessment and productivity among IT professionals.

Methods. The study was conducted in 2020 March. An anonymous survey of respondents was conducted online. A standardized Negative Acts Questionnaire (NAQ) was used (24 questions in total). 114 questionnaires were selected for data analysis. The χ^2 criterion and Fisher's exact test were used for data analysis.

Results. Results of the study indicate that employees have difficulties in recognizing the expression of abuse in staff. Only 10.5% (n=114) respondents experienced manifestations of psychological abuse at work. However, up to 30% of the surveyed IT professionals indicated that they systematically faced individual forms of abuse (were ordered to perform work of lower competence, were gossiped about, experienced offensive remarks, etc.). Almost 92% of the respondents who often experienced psychological abuse indicated that, as a result, they were less able to work. The relationship between psychological abuse at work and subjective health assessment has been established, as well. It has been found that 8.3% of IT specialists who experience frequent or systematic psychological abuse at work rate their health as bad, compared to respondents who have never experienced psychological abuse at work (2%). This difference is statistically significant, p=0.048.

Conclusion. The study shows that IT professionals face difficulties in recognizing the expression of abuse in staff. Only 10% of respondents indicated that they had experienced psychological abuse at work, but up to 30% indicated that they systematically faced individual forms of abuse.

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Actions of healthcare workers in cases of violence and the impact of violence on their quality of life and workplace experience in Rokiskis mental institutions

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Background. Violence in the workplace, most commonly experienced in the healthcare sector, is a global problem and a cause for concern, but it is rarely reported. Violence caused by the mentally ill disturbs healthcare workers, therefore, in order to solve the problem of violence at work, it is important to find out the actions of healthcare workers in cases of violence and assess the impact of violence on their quality of life and general workplace experience.

Aim. To find out the actions of healthcare workers in cases of workplace violence and to assess the impact of workplace violence on the quality of life and workplace experience of healthcare workers in Rokiskis mental institutions.

Methods. The study was based on anonymous questionnaires and comprised healthcare workers of two Rokiskis mental institutions. The analysis of 58 questionnaires was performed.

Results. The mean age of the respondents was 47.4±12.2 years. Subjects included 98.3% women and 1.7% men, 91.4% nurses, 8.6% psychiatrists. The results of the study indicate that at least one type of violence was experienced by 70.6% of the respondents. The majority of respondents reacted to the violence by telling the abuser to stop (42.3%) and calling for help (26.8%). Fewer respondents reported doing nothing in violent incidents (12.2%) or trying to pretend that nothing had happened (15.5%). After the violence 37.4% of the respondents told colleagues about the incident, 36.5% reported it to a superior, 8.4% filled out an accident form, and 10.3% took no action. Both physical and psychological violence affected the quality of life and workplace experience of medical staff. It was found that physical violence and sexual harassment have a long-term, 2–4-month or one-year (61.5%) negative impact on employee well-being and workplace environment. Results showed that 47.1% of subjects had experienced violence, 36.9% had suffered from poorer well-being (insomnia, tension, anxiety, fear, etc.), 24.3% were accompanied by unpleasant memories after experiencing violence.

Conclusion. Respondents who experienced any kind of violence were usually inclined to seek social support from colleagues, defended themselves by telling the abuser to stop, called for help. Physical violence and sexual harassment have a long-term negative impact on employee well-being and workplace environment.

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Latvian translation and adaptation for ASRS v1.1. symptoms checklist

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Background. Many studies show a link between attention deficit disorder (ADHD) and substance use disorders (SUD). SUD patients with ADHD tend to have worse treatment prognosis and higher relapse risk. Adult ADHD might be underdiagnosed among SUD patients in Latvia, as there are no diagnostic screening instruments for adult ADHD in Latvian. Identifying ADHD symptoms in SUD patients could help improve their treatment outcome and quality of life.

Aim. To develop a Latvian translation and adaptation for Adult ADHD Self Report Scale (ASRS) v1.1. symptoms checklist

Methods. A translation of ASRSv1.1 symptoms checklist from English to Latvian was made by a linguist naive to the purpose of translation and a psychiatrist. The translations were merged under guidance of a third linguist. Afterwards a backwards translation was made by a professor in English philology also blind to the purpose. An overall consensus was reached by an expert team to merge a polished translation. The instrument was given to focus group (Minnesota program psychotherapy ward patients) and university students to give a written feedback on clarity and comprehensibility of the translation and fill the first 6 screener questions from ASRSv1.1.

Results. Of the 42 participants 31 were male, 11 – female, the mean age was 31.1. Out of 22 focus group patients, 5 (22%) screened positive for ADHD, out of 20 university students, 1 screened positive for ADHD. None expressed any difficulty in understanding or comprehending the instrument.

Conclusion. Latvian version is a feasible adaptation of ASRSv1.1 symptoms checklist for the participants. Treatment-seeking SUD patients show to be a good focus group for further scientific research on ADHD. Further research should be carried out to validate the adapted versions of the instrument.

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One-item self-assessment tool for screening of depression in cardiovascular patients

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Background. According to recent European and American cardiovascular disease prevention guidelines, it is highly recommended to assess psychosocial risk factors, including depression as it may result in premature death and a more severe psychopathology. Several validated screening instruments are developed, but there is a need for quick, easy and suitable tool in daily clinician practice.

Aim. To explore single self-assessment Likert-type item for detecting depression symptoms in cardiovascular patients comparing with validated Patient Health Questionnaire (PHQ-9).

Methods. The authors implemented a cross-sectional analysis of 879 patients hospitalized in 2 hospitals of Riga, Latvia with several cardiovascular diseases, aged 18–80 years. All the patients were classified in 3 groups: acute coronary syndrome, percutaneous coronary intervention group and atrial fibrillation group. Upon enrolment, participants completed a baseline questionnaire of general socio-demographic information and measures of somatic and psychological health. Depressive symptoms were assessed with PHQ-9. Self-rating one-item Likert-type scales were filled as well; each item was followed by a string of 11 points from 0 to 10. Continuous data are expressed as median values with interquartile range (IQR). Receiver-operating characteristics (ROC) curve was constructed to determine the cut-off value that optimized sensitivity (Se) and specificity (Sp), and area under curve (AUC) was calculated, the positive predicted and negative predicted values (PPV, NPV) were calculated as well, with 95% confidence interval (CI). A value of $p<0.05$ was considered statistically significant. Statistical analyses were conducted using R 4.0.3 (R Foundation for Statistical Computing, Vienna, Austria).

Results. The median age of patients was 66 [IQR: 59–73]. Mild depression was observed in 323 (36.7%) patients, moderate to severe depression in 132 (15.0%) patients by PHQ-9. There were statistically significant differences found between the 3 groups of patients by PHQ-9 questionnaire ($p<0.01$). ROC curve analysis showed that happiness, sleep, life satisfaction, pain were poor classifiers for depression (AUC less than 0.70), but self-assessment of depression was fair predictor for diagnosis of depression (AUC=0.74 (CI: 0.71–0.78)), the most appropriate cut-off value was 3 (Se=52% (CI: 46–57); Sp=88% (CI: 85–91); NPV=72% (CI: 70–74); PPV=76% (CI: 71–80)), and predictive accuracy was 73% (CI: 70–76).

Conclusion. Likert-type single-item tool for self-assessment of depression can be used in clinical settings for primary screening of depression. Additional work is needed to exclude other modifiers and to improve the predictability of depression.

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Beliefs about influence of psychological factors on the recovery from lower back pain

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Background. Low back pain (LBP) is the most common musculoskeletal problem globally and a reason for seeking medical treatment (Hoy D., 2017). Psychological factors like fear-avoidance behaviour, depressive mood, somatization, passive coping, expectation of passive treatment and negative pain beliefs are known as risk factors for the development of chronic LBP.

Aim. The aim of the current study was to analyse opinion regarding influence of psychological factors on the recovery from LBP.

Methods. A retrospective study was performed through a survey. The questionnaire used in the study contained sociodemographic data, pain characteristics and the Back-Pain Attitudes Questionnaire (Darlow et al., 2014). In this study, only the questions regarding beliefs about recovering from the LBP were selected. The obtained results were compared between healthcare professionals (HCP) and non-HCP. IBM SPSSv23 was applied for the statistical analysis.

Results. In total, 126 participants (mean age 40.8 years, SD±11.9) were included in the analysis, predominantly females (88.9% vs. 11.1%). Almost a third part of participants (27.0%, N=34) were HCP. Both analysed groups (non-HCP and HCP) were unsure or disagreed to varying degrees with the statement that thoughts and feelings can influence the intensity of back pain – 60.7% vs. 38.2% (56/92 vs. 13/34). The non-HCP group was more unsure or disagreed in comparison to HCP group, that stress in their life can make back pain worse – 52.2% vs. 23.5% (48/92 vs. 8/34). The vast majority of HCP in comparison to the non-HCP group agreed that worrying about their back can delay recovery from LBP – 82.3% vs. 50.0% (28/34 vs. 46/92). Non-HCP were more unsure or disagreed that focusing on things other than their back and expecting LBP to get better accelerate recovery – 65.2% and 69.6% (60/92 and 64/92), respectively. HCP were slightly less unsure or disagreed with the aforementioned statements – 47.0% and 44.2% (16/34 and 15/34), respectively. More than a half of non-HCP group in contrast to HCP thought that if once you have a back problem, there is not a lot you can do about it – 55.4% vs. 29.4% (51/92 vs. 10/34).

Conclusion. HCP are better educated and knowledgeable, however, the third part of them still disagree that subjective psychoemotional factors influence attitude to LBP. HCP should pay more attention to patient psychoeducation.

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Can depression, anxiety, chronic pain or health state lead to suspect self-care maintenance problems in multimorbid patients?

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Background. Due to aging society, the numbers of the multimorbid patients increase. The main gap of this situation is that these patients demand multicomplex care. Patients with multimorbidity suffer from different health conditions and little is known whether the impairment of one factor affects others. In literature, there is a lack of information about self-care maintenance in multimorbid patients and how it affects patients in general.

Aim. To investigate the correlation between self-care maintenance, depression, anxiety, chronic pain and whether it affects health state in patients with multimorbidity.

Methods. In 2019–2020, a study was performed by the method of an anonymous questionnaire at the Family Medicine Center of Vilnius University Hospital Santaros Klinikos. Inclusion criteria: patients over 18 years of age, who have been diagnosed with two or more chronic diseases in two different organ systems. 71 (46 male and 25 female, age 64.49±7.85) patients completed four questionnaires. The patient self-care maintenance was assessed according to the sum of the results presented in the section "self-care maintenance" of the questionnaire of independence and self-care maintenance (from 6 to 30 points). Anxiety and depression were assessed using the Hospital Anxiety and Depression Scale. Chronic pain was assessed using section "Pain" (1 – no pain; 2 – mild pain; 3 – severe pain) of European Quality of Life Scale (EQ-5D-3L). Health state was evaluated on the visual analogue European Quality of Life Scale (EQ-VAS) from 0 (worst possible health condition) to 100 (best possible health condition). Data analysis was performed using the SPSS 24.0 program. Correlation was significant if $p<0.05$.

Results. All 71 multimorbid patients completed the questionnaires correctly. Using Pearson's correlation test, difficulty of self-care maintenance was associated with increased depression ($r=0.498$; $p<0.001$), anxiety ($r=0.361$; $p=0.002$) and decreased health state evaluation ($r=-0.576$; $p<0.001$) in multimorbid patients. Using Spearman's test the correlation between self-care maintenance and chronic pain was significant, too ($r=0.480$; $p<0.001$). Increased chronic pain results in difficulty of self-care maintenance.

Conclusion. These results show that different factors indeed affect others in multimorbid patients. Clinicians must be aware that pain worsens patient's self-care maintenance and despite the presence of pain decreased self-care maintenance can cause depression and anxiety. These facts are important in the preparation and application of multicomplex care.

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Cognitive failures in everyday life: how to prevent them?

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Background. The rising cognitive impairment (CI) among younger adults calls for establishing preventive factors to timely manage situations.

Aim. The study aimed to evaluate factors that can predict cognitive failures (CF) among females.

Methods. 310 females from 26 to 59 years of age (M=38.6) took part in an online study. They filled Cognitive Failures Questionnaire (CFQ), Geriatric Depression Scale (GDS), and Shirom-Melamed Burnout Measure (SMBM). Smoking, alcohol usage, usage of supplements and vitamins, sleep patterns were registered. Student t-test, Chi-square test, and logistic regression analysis (LRA) were used for data analysis.

Results. 34 females (11%) had CF in perception, memory, and motor function (CF+ group). They had higher GDS scores compared to those without CF (CF- group) (M=6.88 vs. M=3.78, p<0.001), also had a higher level of burnout: physical fatigue (M=4.33 vs. M=3.26, p<0.001), cognitive weariness (M=4.07 vs. M=2.46, p<0.001), emotional exhaustion (M=3.38 vs. M=2.15, p<0.001). Both groups did not differ in smoking habits, alcohol usage, usage of supplements and vitamins. The CF+ group more often than the CF- group complained about insomnia (41.2% vs 20.3%, p=0.006) and used sedatives (26.5% vs. 10.5%, p=0.007). LRA with all study variables revealed that CI by CFQ could be predicted only by cognitive weariness (Negelkerke R2=0.245, correct classification of data is 88.7%) by the SMBM.

Conclusion. Out of the analysed variables, only reducing cognitive weariness could be a preventive factor of CF among middle-aged females.

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Psychological correlates of COVID-19-related fear among medical students

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Background. According to the WHO, the COVID-19 pandemic may have negative impacts on mental health, including those caused by COVID-19-associated fear (FCV). A study conducted by the authors in March 2020 found that FCV was observed in 44.4% of medical students and was associated with sleep disorders and headaches [1].

Aim. To assess the impact of FCV on the psychological state of medical students.

Methods. In August 2020, FCV was assessed using the Fear of COVID-19 Scale (FCV-19s) with a 16.5 cut-off point [2] among 1–6-year students of Astana Medical University (Nur-Sultan, Kazakhstan), the level of depression, anxiety and stress was assessed using the DASS-21. Statistical analysis included measures of descriptive statistics, correlation, and regression analysis.

Results. Overall, 437 students participated in the study: 331 (75.7%) females and 106 (24.3%) males. FCV observed in 49.4% of students: among males in 30.2%, females – 55.6% (1.8 times more often). Female students had more pronounced level of both the emotional (11.19±3.98 vs. 9.18±4.02) and physiological (6.28±2.85 vs. 5.15±2.87) components of fear ($p \leqslant 0.001$). In general, there was no significant difference in FCV depending on the year of study. FCV positively correlated with the level of anxiety ($r=0.361$), stress ($r=0.292$) and depression ($r=0.255$), $p<0.01$. The degree of correlation of FCV with anxiety, stress, and depression was also higher in females compared to males, 0.552 vs. 0.379, 0.405 vs. 0.308, 0.381 vs. 0.271, respectively. A more pronounced level of fear was noted among students living with people at high risk (senile age, with comorbid conditions; 17.50±6.99 vs. 15.91±5.92, $p<0.05$). Emotional response to FCV was a predictor of social distancing ($\beta=0.121$, $p<0.05$), emotional support ($\beta=0.126$, $p<0.05$), physical support ($\beta=0.145$, $p<0.05$), and educational support ($\beta=0.176$, $p<0.001$). The physiological response to fear was a predictor of physical support ($\beta=0.116$, $p<0.05$).

Conclusion. FCV observed in half of the respondents, 1.8 times more often in females, and positively correlated with anxiety, stress and depression. Fear was a predictor of preventive and altruistic behaviour during the COVID-19 pandemic.

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Mental health and occupational safety of seafarers

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Background. The issue of mental health of seafarers is extremely important in relation to their health and to the occupational safety onboard. The safe operation of the shipping industry is crucial not only for its workforce but for the international economic and environmental order and safe delivery of goods. However, the mental health of seafarers and its impact on the occupational safety lacks attention. Recently, it was affected by the COVID-19 pandemic: the number of suicides among crews on-board the ships increased, constituting a great threat. Thus, the COVID-19 pandemic raised the concern related to the subject, as the working conditions of seafarers was extremely disturbed, mainly regarding their psychological condition.

Aim. The aim of the current study was to investigate the factors affecting mental health of seafarers and their impact to the occupational safety in order to explore possibilities to improve their occupational health and safety.

Methods. The theoretical framework was consisted by the existent literature related to the subject and presentation of definitions and features of mental health and well-being according to international recognized entities such as WHO (World Health Organization). A quantitative analysis of the online survey created for the study with a representative sample of 100 seafarers was performed. The research mainly investigated the determinant factors affecting mental health and well-being on-board, the perception of seafarers regarding the importance of mental health as an aspect of their general health, and the current status of specific training related to mental health and well-being of seafarers.

Results. The findings of the responses of 100 seafarers (n=100) suggested that the most influencing factors on-board regarding mental health and well-being are: being away from family and friends (59%), limited access to the internet (58%), relationships with colleagues and atmosphere onboard (53%), leadership style (52%) which point out aspects related with the occupational environment that affect mental health onboard. 99% of respondents consider mental health as the key aspect to general health (3% – moderately important, 21% – very important, 75% – extremely important). Only 53% of respondents acquired some training on mental health, however the importance of such a training was highlighted by 85% of the respondents.

Conclusion. Our research highlights the importance of mental health regarding general health and occupational safety. Appropriate training on mental health awareness can help to develop healthy workplaces onboard and maintain a balanced mental health of seafarers.

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PUBLIC HEALTH & EPIDEMIOLOGY

Association of alcohol consumption level changes in general population with occupation during Covid-19 pandemic in Latvia

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Background. Due to COVID-19 epidemiological restrictions, the availability of several services was limited or excluded. Accordingly, people previously holding an employment were fired. Alcohol use is one of the most common unhealthiest coping strategies in crisis situations. This study uncovers alcohol consumption association with the change of occupation status during COVID-19 pandemic in Latvia.

Aim. The aim of this study was to find association of alcohol consumption level changes in general population with occupation during COVID-19 pandemic in Latvia.

Methods. The data was collected by using behavioural cross-sectional online survey that was conducted as a part of international multi-country study I-SHARE (International Sexual Health and Reproductive Health Survey) realized in Latvia as a component of the National Research Programme project (No. VPP-COVID-2020/1-0011). Data was analysed, using *MS Excel* and *IBM SPSS 26.0*. The results have been defined as statistically significant, if $p<0.05$.

Results. Distribution by employment status during the pandemic (n=926): 49.7% (n=460) continue to work at their workplace, 9.3% (n=96) at their workplace and partly from home, 7.9% (n=73) remotely, while 3.2% (n=30) are unemployed indefinitely, 2.9% (n=27) lost their jobs. Alcohol consumption remained mostly the same in 62.5% (n=579) and slightly increased in 19.9% (n=185). Relationship between the difference in alcohol consumption and the change in employment status during the pandemic: alcohol consumption decreased significantly for persons without changes at work 34.1% (n = 30) and for those working from home by 15.9% (n=14); slightly decreased for persons without changes at work by 50.0% (n=37) and for persons who changed workplace by 9.5% (n=7); consumption slightly increased (n=185) for persons without changes at work 54.4% (n=95), those partially working from home 10.8% (n=20), people who lost their job 6.5% (n=12). On the other hand, comparing the changes in alcohol consumption after the changes in work status, the group of losing jobs is distinguished (n=27), where alcohol consumption has increased most markedly by 44% (n=12).

Conclusion. The observed results of this study showed that the changes in higher alcohol consumption are not directly related to job loss. It shows that there are other possible factors that affect alcohol consumption changes. However, job loss is associated with the highest proportional increase in alcohol use among the study groups.

Ranking of medical universities in Kazakhstan as a tool of stimulating scientific activity

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Background. One of the reasons behind the low competitiveness of medical universities in Kazakhstan is their low level of scientific activity. In this regard, the system of scientific activity ranking of medical universities has been implemented in the Republic of Kazakhstan. It is based on international indicators acquired from global university rankings.

Aim. The aim of the current study was the analysis of effectiveness of the scientific activity ranking system of medical universities.

Methods. Study of the qualitative and quantitative characteristics of the employees in medical universities (faculty members, researchers and doctors of university hospitals), amount of funding, number of articles, citations, patents, international co-authorship.

Results. Analysis of the results of the implementation of the ranking system for the period from 2013 to 2018 showed the growth of all key indicators of the scientific activity. Despite the decrease of in the total number of employees in medical universities by 4.1%, there is an increase of staff with scientific degree (Doctors and Candidates of Sciences, PhD) by 8.4% and funding in 1.4 times, the number of publications by 3.1 times, citations in 14.3 times, patents in 16.7 times. The number of articles published in journals indexed in authoritative international databases (Web of Science and Scopus) increased in 3.6 times (121%). The average impact factor (IF) for journals indexed in the Web of Science and the SCImago Journal Ranking (SJR) for journals indexed in Scopus increased in 2.4 times. The share of articles published in co-authorship increased from 64.7% to 74.3%. In general, the total performance indicator for the analysed years increased in medical universities by 664.2%

Conclusion. The analysis of scientific activities of medical universities in dynamics showed an increase in the main performance indicators, thereby proving the stimulating nature of the scientific activity ranking system of medical universities.

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Control and surveillance health problems during training in military environment

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Background. Combat training course (CTC) is a compulsory module of study programme in National Defence Academy. It focuses on training participants in military environment with high physical, psychological load, and using teamwork skills in decision-making process and solution military tasks. Standardized nature of stressors provides a unique opportunity to examine changes simultaneously occurring in condition of individual adaptation to a military environment close to real situation.

Aim. The aim of the study was to provide surveillance and assessment of medical problems of participants during the training course to contribute to planning and improvement of pre-course training methods.

Methods. The research group included participants of CTC in 2017 (n=59), in 2019 (n=56), in 2020 (n=70) in aged from 22 to 34. Participants passed through rigorous physical and mental pre-course training, including loaded road marching, obstacle exercises, swim survival exercises, confidence exercises. All participants passed enhanced medical examination of health status. During the course, participants completed rigorous physical and mental training, including loaded road marching, obstacle exercises, swim survival exercises, confidence exercises. Medical team specialists controlled the health status during the CTC.

Results. The main problems during courses were dermatological problems of feet, musculoskeletal disorders, acute respiratory disease, and gastrointestinal problems. According to data analyses, about 80% of participants had visited medical specialists' team. Assessment of health problems during the course showed that the incidence of foot health problems (foot blisters) remained at a high level and comprised about 50% of all the visits to medical specialists. Problems in conducted course were revealed, such as traumatic injuries (strain, skin chafe), that composed 24.3% to 27.2% of visits trauma; skeletal muscular disorders accounted for 1.2% to 7.1% of visits; number of gastrointestinal disorders occurred in 1.3 % to 4.3%, and general problems were recorded in 3.7% to 7.6% of cases. Pre-course training programme (physical exercises, marches, tactical exercises etc.) increased the adaptation level and allowed to reduce acute respiratory diseases from 11.1% to 0.5% of visits, but in risk surrounding.

Conclusion. Military environment increased health risks of participants. Pre-course training programme provided for retaining and elevating physical fitness and preparedness level, which is essential for supporting health capacity and successful processing of CTC. Training participants must take care of foot health problems, since it is an important part of pre-course training programme.

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Effectiveness of biocide in daily disinfection and its impact on hands skin

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Background. Recently, skin disinfection became a part of daily routine for all people. A lot of disinfectants contain irritating chemicals which cause development of allergic and irritant skin diseases. One of disinfectant options is the formulation that contains biocide. Applying sanitizer that combines qualities of skin protector together with disinfectant is important for skin's health. It is critical to prove efficiency of such sanitizer to provide evidence-based conclusion of its disinfection qualities.

Aim. The aim of the study was to evaluate biocide-based disinfectant's effectiveness against pathogenic flora on hand's skin surface.

Methods. The study contained data of 30 randomly selected patients from general population. Each selected patient answered a questionnaire prepared for study. Bacterial swabs from hand surface were performed before and after disinfection with biocide-based sanitizer with contain Aloe Vera and D-panthenol. Bacterial swab was performed in compliance with European Standards (EN1500). All the received data were statistically analysed by SPSS v.23. Non-parametric tests (Pearson's χ^2, MANOVA) were used to analyse demographics and other data from questionnaire. Parametric statistical tests (Student's t-test, ANOVA) were used to evaluate microbiological culture results.

Results. The study included data of 30 participants, from those 66.7% (n=20) were female and 33.3% (n=10) male. The majority of participants were aged from 40 to 49 years – (n=11). Coagulase-negative *staphylococcus* (46.0%), *Bacillus spp.* (14.0%), *Acinetobacter spp.* (14.0%), *Enterobacter spp.* (16.0%), *Pseudomonas spp.* (2.0%), *Klebsiellas spp.* (2.0%) and *Candida albicans* (2.0%) were established after the first swab. After hand disinfection with biocide-based disinfectant, the number of colonies on participant's skin decreased or completely disappeared, and significant correlation was found between number of colonies before and after disinfection. In some cases, Coagulase-negative *staphylococcus* was still detected, but the number of colony-forming unit (CFU) decreased significantly [$p<0.001$]. Similarly, *Bacillus ssp.* and *Acinetobacter spp.* still were found in 17.6% (n=3) of all cases after disinfection, but the number of colonies had decreased [$p=0.001$; $p=0.008$].

Conclusion. The primary results show that hand sanitizer based on biocide is effective in daily hand disinfection.

Acknowledgements. All the included patients signed informed consent form. The authors declare the absence of conflict of interest.

Association of physical activity with metabolic syndrome and its components in Lithuanian urban population

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Background. The problem is of outstanding importance, since insufficient physical activities (PA) are a dominant risk factor for noncommunicable diseases, such as cardiovascular diseases, diabetes and cancer [1]. Metabolic syndrome (MS) is a cluster of conditions that occur together, increasing risk of noncommunicable diseases [2].

Aim. The aim of this study was to evaluate the association of PA with MS and its components.

Methods. The study presents data from the survey conducted within the framework of the international project Health, Alcohol and Psychosocial Factors in Eastern Europe (HAPIEE) [3]. A random sample of 6752 participants (3051 men; 3701 women) aged 45–72 years were selected for statistical analysis. MS components were evaluated according to ATP III criteria [2]. PA was determined by the mean length of time spent per week during leisure time in winter and summer for walking, moderate and hard work like gardening and other PA. The respondents were categorized into three tertiles according to their PA in leisure time: 1st tertile (physically inactive; ⩽10 hours/week), 2nd tertile (moderate physically active; 10.5–20.0 hours/week) and 3rd tertile (physically active; >20 hours/week). Multivariable logistic regression analysis was performed to determine the independent associations between the PA and MS and its components expressed as odds ratio (OR) with 95% CI (data adjusted for age, education level, smoking status).

Results. MS was identified for 37.9% of men and for 27.8% of women ($p<0.001$). The multivariable logistic regression analysis results showed that the increase of PA level (2nd and 3rd tertiles compared with 1st tertile) could be associated with a lower risk of MS: in men group (2nd tertile OR=0.78; p=0,014 and 3rd tertile OR=0.60; $p<0.001$); in women group (2nd tertile OR=0.82; p=0.017 and 3rd tertile OR=0.81; p=0,016). Furthermore, physically active men had lower odds of arterial hypertension (OR=0.75; p=0.019), central obesity (OR=0.61; $p<0.001$), hyperglycaemia (OR=0.60; $p<0.001$), and reduced HDL level (OR=0.59; $p<0.001$) in comparison with physically inactive men. Physically active women had lower odds of hyperglycaemia (OR=0.84; p=0.039) and central obesity (OR=0.81; p=0.01) in comparison with physically inactive women.

Conclusion. PA is related to a lower MS risk among men and women aged 45–72 years.

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Correlation between COVID-19 extraordinary measures issued by Czech government and practical implementation at an oncology healthcare facility

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Background. In March 2020, the Czech Republic, similarly to the rest of Europe, faced a pandemic spread of COVID-19 virus. According to available data, persons of higher age categories and persons with reduced immunity were generally more susceptible to infection. Thus, patients with oncologic profile were immediately considered to belong to a risk group with possible severe consequences. Masaryk Memorial Cancer Institute is a facility located in the city of Brno, Czech Republic. The institute is completely dedicated to cancer treatment and research; it serves nearly 70 thousand patients per year. The patients of the Masaryk Memorial Cancer Institute were considered to be at a risk group for the infection with COVID-19. The facility had to take special measures that were implemented in several stages, as the pandemic extended through the country and the region. Such preventive measures were based on interpretation of national regulations. A group of colleagues from the institute prepared a summary showing the correlation between government-issued Protective measures and practical implementation in the institution.

Aim. The correlation was processed into a clear simple table. The aim of this table is to make the correlation easier on first sight. This may be useful for comparison with other healthcare institutions and countries.

Methods. The table contains information on each relevant national regulation. Next to each regulation, short description and implementation methods at the Institute are presented.

Results. Comparison between national regulations and their parallel within the facility is showing that the regulations within the institute were implemented in a phase adequate to the rest of the country. However, some of the institute's regulations were approved even earlier than the national ones. These institutional restrictions were more limiting than ones issued for public. As a result, the number of positive patients and staff members remained very low until the end of the first wave of the pandemic.

Conclusion. Limitation and regulation of epidemiologic conditions and human factors is extremely important in facilities that treat oncologic patients. Implementation of very harsh restrictions, such as the Masaryk Memorial Cancer Institute, from first days of outbreak decreases the number of COVID-19 positive patients and staff.

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Analysis of risk factors for multiantibiotic-resistant infections among Ukrainian patients at a children's hospital

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Background. The World Health Organization has named antibiotic resistance as one of the most important public health threats of the 21st century. Multidrug-resistant infections are associated with increased mortality compared to those caused by susceptible bacteria and they carry an important economic burden. Obtaining knowledge about risk factors may provide possible evidence for prevention and control strategies of multiantibiotic-resistant infections.-

Aim. To identify the potential risk factors for multiantibiotic-resistant infections among Ukrainian paediatric patients.

Methods. Altogether 211 patients at Sumy Regional Children's Clinical Hospital, at period from January to December 2020, were enrolled in the study: 39% (n=82) were multiantibiotic-resistant infection cases (average age±SD 6.34±5.153 years, 71 girls and 58 boys); 61% (n=129) – were cases without multiantibiotic resistance (average age 9.02±4.832 years, 37 girls and 45 boys). The clinical laboratory information monitoring system and the medical record system were used to collect patient information regarding age, disease, prescribed treatment, department and season of hospitalization. *Microsoft Excel* and SPSS 25.0 (Chicago, IL, USA) software were used for the statistical analysis. To predict the occurrence of multi-antibiotic resistance infections among paediatric patients, a logistic regression model was created. With the help of it possible risk factors: age, department and season of hospitalization were checked. The value of $p<0.05$ was considered statistically significant.

Results. Among patients with multiantibiotic-resistant infection 52% (n=43) were from somatic departments and 48% (n=39) from surgical departments; 54% (n=44) were hospitalized in the fall-winter season. Among patients without multi-antibiotic-resistant infection 75% (n=97) were from somatic departments and 25% (n=32) from surgical departments; 63% (n=81) were hospitalized in the spring-summer season. According to binary logistic regression data, a higher risk of developing multi-antibiotic-resistant infections have patients from surgical departments (p=0.01, OR=2.749, 95% CI=0.202-0.656) and who were hospitalized in the fall-winter season (p=0.019, OR=1.954, 95% CI=1.114-3.428). Older children have a lower risk of developing multi-antibiotic resistance compared to younger children ($p<0.001$, OR=0.897, 95% CI=0.846-0.951).

Conclusion. This study suggests the inclusion of younger age, surgical type of department and fall-winter hospitalization season as risk factors for multiantibiotic-resistant infections among Ukrainian paediatric patients.

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Development of population-based cancer registry model in Uzbekistan: opportunities and challenges

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Background. For the first time, a cancer registration system has been already created to process data on cancer patients in the Republican Specialized Scientific and Practical Medical Center of Oncology and Radiology (RSSPMCOR) and in its several branches. However, the existing system was found to be insufficient for data management across the regions of Uzbekistan. Along with the growth of cancer morbidity and the increase in the need for cancer care, it is necessary to develop a perfect model for registering cancer in Uzbekistan.

Aim. The aim of this study is to analyse the requirements for registering cancer in Uzbekistan in a network of RSSMPCOR and its regional branches.

Methods. This study was conducted by a method classified as a qualitative study, without experimental methods and without data processing. Information for planning the creation of a cancer registration system model, as well as an architectural plan was obtained from interviews of RSSMPCOR staff, its branches and district oncologists whose work was related with cancer registration. The questions in the questionnaire were created on the basis of elements for developing a cancer registration system.

Results. Each regional branch is responsible for a specific area, where data is collected, compiled and initially analysed which are sent to the RSSMPCOR. It is possible to avoid duplication, poorly collected data, as well as ensure regular collection and monitoring of filling in data from regional areas. This model has several advantages: it is possible to analyse the epidemiological characteristics in each region. This study outlined six main components necessary to develop a cancer registry. Standard technical resources among all medical institutions of the oncology registry were found only in RSSMPCOR and its several branches (Samarkand, Bukhara, Andijan and Khorezm regions), while organizational structure and job responsibilities were found in district polyclinics. The unique part of the cancer registration system in this design is the operation of a virtual private network. This technology uses hubs that will provide connectivity from/to the main centre to all departments including doctors and staff.

Conclusion. The results of this study are the formation of a network plan of oncologic medical institutions for a cancer registration system with special protection for data transmission, as well as the formation of a technical structure for recording cancer patients.

Acknowledgements. The authors declare the absence of conflict of interest.

Analysis of emergency medical care calls of Nur-Sultan polyclinics population

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Background. Emergency care of Nur-Sultan is provided by teams that consist of two medical assistants and a driver of ambulance vehicle. Assistance is provided for calls of the fourth category of urgency.

Aim. The main objective of the substation is to provide the population that is attached territorially to primary health care centres with round-the-clock timely and qualified emergency medical care for both adults and children.

Methods. In this study, the analysis and structure of the circulation of the attached population were carried out for the period from 01.01.2018 to 01.01.2019.

Results. After analysing gender, it was revealed that female patients account for 9600 (60%), male patients – for 6400 (40%) of the number of emergency responders. After analysing the age, it was revealed that 6224 (38.9%) calls were made in cases where patients were in the age range between 0 and 10 years, 1552 (9.7%) – between 11 and 20 years, 3024 (18.9%) – between 21 and 30 years, 1968 (12.3%) – between 31 and 40 years, 960 (6%) – between 41 and 50 years, 1072 (6.7%) – between 51 and 60 years, 672 (4.2%) – between 61 and 70 years, 432 (2.7%) – between 71 and 80 years, and 96 (0.6%) – 80 years old and above. Analysis of the distribution by age showed that the most frequently calling age group was the patients under 40 years old (80% of all calls), and the most seldom called the patients over 60 years of age (7.5% of all calls).

Analysis of the structure revealed 5 main classes of diseases, which are 78% of all the causes for ambulance calls during the aforementioned period:

- respiratory diseases (RD): 33–61% of the total number of call causes, the peak is distinct from January to March;
- digestive system diseases (DSD): 8–29%, the peak can be observed from July to September;
- nervous system diseases (NSD): 5-8%;
- circulatory system diseases (CSD): 5-8%;
- skin and subcutaneous tissue disease (SSTD): 3-8%, the peak is distinguished in July and August.

Conclusion. This result matches the fourth category of calls, because it involves assisting in the absence of diseases with an immediate threat to the patient's life. On calls of the fourth category of urgency, assistance is provided by the ambulance station of primary health care. Respiratory diseases prevail in the structure of ambulance calls.

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Computer-related work and physical activity at home environment in university students during pandemic

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Background. Students' physical inactivity and sedentary behaviours have increased due to immense escalation of computer use during lockdown. It is a rising disaster in young people, leading to deterioration their health condition. Therefore, investigating computer-related working environment and physical inactivity in young people is of importance.

Aim. The aim of the study was to investigate computer-related work and physical activity at home environment in university students during pandemic.

Methods. The study was performed in 2020, in Lithuania, after the first wave of pandemic. 201 university students participated in the survey. Chi-square test was applied and the significance level $p \leqslant 0.05$ was considered statistically significant.

Results. 98 male (48.8%) and 103 female (51.2%) students participated in the survey. The study revealed that 50.2% of all investigated young people have spent by computer 6–10 hours per day, 35.8% – 3–5 hours per day, and 11.9% – even over 10 hours per day. Young men and women have spent similar time by computer (Chi square=4.569; df=3; p=0.206). 68.7% of students used uncomfortable work chair, 68.2% – complained of insufficient computer table area, 65.7% –had insufficient working space. 22.9% of respondents used computer at very good illumination, 55.2% – at good, 21.4% – at moderate illumination. While working with computer, 40.8% of respondents were disturbed by other people, 21.4% – by noise. Over half of the respondents suffered from the pain in the neck, shoulders, and back area. 10.9% of students self-rated their physical health as very good, 49.3% – as good, 33.8% – as moderate, and 6% – as bad. 32.8% of respondents self-reported that they had enough knowledge about impact of physical activities on health. 11.9% of students exercised or did a sports training for at least 30 minutes daily, 24.9% – 2–3 times per week, 19.4% – 2–3 times per month. 62.2% of young people agreed that they should be more physically active. 38% of young people had regular breaks during their work with computer. 68.3% of students would like to exercise together with peers and friends, 19.1% – with family members.

Conclusion. The study showed that during pandemic most of young people used computer for too many hours per day, with irregular breaks. They experienced insufficient working equipment and poor working environment, and suffered from the pains in different parts of the body. The majority of students self-reported too little effort regarding physical activities. Students prefer to exercise with peers and friends. More attention must be dedicated to creating a healthy environment and promoting physical activities.

Acknowledgements. The authors declare the absence of conflict of interest.

Perception of patient safety climate in Latvian healthcare personnel: the effect of patient safety training

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Background. The problem is of outstanding importance since patient safety (PS) gained its place in the international spotlight. The studies suggest possible relationships between PS culture, climate, individual's behaviour and medical errors. A range of training materials have been developed by World Health Organization (WHO) to support training of healthcare professionals to improve their understanding and knowledge of PS. The first Latvian concept for PS was accepted in 2017, however, only few hospitals have recommended learning systems, but postgraduate PS training is occasional. Patient safety training (PST) effect on perception of safety climate are not fully investigated yet.

Aim. The aim of the current study was to investigate differences between Latvian health care professionals in assessment of safety climate according to their participation in PST programmes.

Methods. Altogether, 744 healthcare professionals were enrolled in the study. We assessed PS climate using a previously validated Staff Survey for Measuring of PS (SSMPS) questionnaire. In addition, information regarding socio-demographic, work-related conditions were assessed. We investigated the differences between healthcare professionals that participated in PST programs in their assessment of domains of SSMPS using Mann-Whitney test.

Results. Most of the study participants were women (92.1%) aged 45–54 (36.4%) working full time (91.5%). 390 (52.4%) of them never attended PS training, or attended only one lecture. For the entire study population, we did not observe significant differences between those who had attended and those who did not attend PST at all or attended only one of lectures (N=390, 52.4%) in their assessment of PS climate for four investigated SSMPS domains (Safety Climate, Teamwork Climate, Job Satisfaction and Stress Recognition). From the entire study population, 47% were nurses, and the difference between those who had attended and did not attend PST was observed in Stress Recognition domain of SSMPS ($p<0.01$): Those, who had passed more than one PST (N=148, 47.6%) assessed work stress impact on patient safety more critically than those who had not attended PST or attended only one lecture (mean ± standard deviation 3.56±0.66 and 3.85±0.86, respectively).

Conclusion. PST shows an effect on nurses' acknowledgement of how performance is influenced by stressors. Stress, high workload, staff shortage are usual factors in healthcare, therefore human factors training should be part of PST. Physicians' perception of human ability to work safely in stressful conditions should have attention. No PST differences in other investigated SSMPS domains indicate that PS climate should be improved through PS culture and reporting-learning systems as recommended internationally.

Cartogram of Down syndrome incidence in Kazakhstan

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Background. Down syndrome (DS) is one of the most common birth defects, which, according to various sources, affects 1 child in 800–1100 and it occurs in people of all races, both boys and girls. Analysis of the epidemiological situation by drawing up cartograms permits to acquire a spatial assessment and use the data obtained to monitor the current situation.

Aim. To create a cartogram of the incidence of DS in Kazakhstan.

Methods. When compiling cartograms, indicators of Down syndrome morbidity (ICD 10–Q90) for 10 years (2009–2018) were used and a method of compiling cartograms was used, based on determining the standard deviation (σ) from the mean (x).

Results. During the study period, 5 689 new cases of DS were registered. The average annual incidence of diabetes was 11.0±0.4 per 100 000 population. To compile cartograms, at the beginning, the incidence rates of DS were determined, which corresponded to the following criteria: low – up to $8.4^0/_{0000}$, medium – from 8.4 to $13.5^0/_{0000}$, high – above $13.5^0/_{0000}$. On the basis of which the following groups of areas were determined:

1. Regions with low rates (up to $8.4^0/_{0000}$) – Karaganda ($4.4\pm0.5^0/_{0000}$), West Kazakhstan ($6.3\pm0.4^0/_{0000}$), Kyzylorda ($7.6\pm1.2^0/_{0000}$), Mangistau ($7.9\pm0.9^0/_{0000}$) area.
2. Regions with average indicators (from 8.4 to $13.5^0/_{0000}$) – Kostanay ($8.9\pm0.9^0/_{0000}$), Aktobe ($9.2\pm0.5^0/_{0000}$), Akmola ($9.3\pm0.8^0/_{0000}$), North Kazakhstan ($9.4\pm0.8^0/_{0000}$), South Kazakhstan ($9.4\pm0.7^0/_{0000}$), Almaty ($9.5\pm0.5^0/_{0000}$), East Kazakhstan ($9.6\pm0.5^0/_{0000}$), Atyrau ($9.8\pm0.4^0/_{0000}$) and Pavlodar ($11.4\pm1.1^0/_{0000}$) area.
3. Regions with high rates ($13.5^0/_{0000}$ and higher) – Zhambyl region ($19.1\pm0.9^0/_{0000}$), as well as the city of Almaty ($20.4\pm1.0^0/_{0000}$) and Astana ($22.6\pm1.8^0/_{0000}$).

The cartogram more clearly reflects the spatial distribution of DS, while the discrepancy between the theoretical and actual distribution of morbidity in the studied regions is small ($\chi^2=19.4$, which is more than the tabular value of 0.5398 at k=7), i.e., the actual distribution is close to normal.

Conclusion. Thus, the established regional features of the incidence of diabetes indicate variability with territorial differentiation in terms of incidence rates. The obtained results will allow healthcare organizers to have a clear spatial picture of the incidence of DS, which is necessary for carrying out treatment and preventive measures.

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Cartogram of heart attack incidence in Kazakhstan

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Background. According to the current statistics, 17.5 million people perish annually because of the CVD, 80% of them from heart attack/myocardial infarction (hereafter MI) and strokes. MI continues to lead among economically developed countries, despite the significant progress of surgical and endovascular revascularization methods. A dimensionless assessment of the incidence is needed for diagnosis and prevention, which can dramatically reduce the risk of development in these regions.

Aim. To study the regional features of incidence of MI in Kazakhstan by compiling cartograms.

Methods. A dimensional assessment of the MI (IDC-10 I21-22) incidence is presented using the cartogram, which was carried out after preliminary determination of the average annual indicators in individual medical-geographical regions, then the arithmetic mean coefficients and standard deviations were calculated, also on their basis, the steps scale of the cartogram was determined.

Results. During the study period (2009–2018), over 82 809 new cases of MI were registered. The average annual incidence of the heart attack was 69.0±5.1 per 100 000 people. In dynamics, the incidence rates tended to increase from 56.8±0.7$^0/_{0000}$ in 2009 to 116.2±1.0$^0/_{0000}$ in 2018, the established difference is significant (t=60.96, p=0.000). The average annual growth rate of the equalized indicator was T=+9.3 %. On this basis, the following groups of areas were defined:

1. Regions with low indicators (up to 53.2$^0/_{0000}$) included Kyzylorda (36.5±8.7$^0/_{0000}$), Zhambyl (44.7±7.9$^0/_{0000}$), Mangystau (48.2±8.1$^0/_{0000}$), Atyrau (50.9±5.3$^0/_{0000}$), Almaty (50.9±5.3$^0/_{0000}$) regions and as well as the cities Almaty (53.2±5.9$^0/_{0000}$) and Nur-Sultan (40.9±7.9$^0/_{0000}$).
2. Regions with average indicators (from 53.2 to 72.5$^0/_{0000}$) included Kostanay (58.4±4.0$^0/_{0000}$), Aktobe (58.2±10.8$^0/_{0000}$), South Kazakhstan (58.8±7.8$^0/_{0000}$), West Kazakhstan (63.7±9.0$^0/_{0000}$) and Pavlodar (72.5±5.3$^0/_{0000}$) regions.
3. Regions with high indicators (72.5$^0/_{0000}$ and above) included Karaganda (85.7±3.2$^0/_{0000}$), Akmola (107.6±7.3$^0/_{0000}$), East Kazakhstan (128.8±6.5$^0/_{0000}$) and North Kazakhstan (130.5±7.6$^0/_{0000}$) regions.

Conclusion. European countries such as Finland, England, Germany, as well as the USA and Australia had the highest death rates owing to MI around the world at the last century. Due to the large-scale measures of primary prevention, surgical interventions, and well-designed programs which had been taken at the state level, these countries achieved success. Thus, the cartogram brings scientific and practical value to the field of medicine, since the studies in this aspect make it possible to assess the influence of the risk factors and preventive measures.

Changes in indicators of ovarian cancer in Kazakhstan

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Background. Ovarian cancer is among the most deadly gynaecologic malignancies worldwide and annually about 207 252 lives are lost to this disease in the world (IARC, 2020). Furthermore, with increasing life-expectancy, the number of cases diagnosed each year is increasing, and about 313 959 new cases of ovarian cancer (OC) are registered.

Aim. To evaluate the tendencies in OC incidence in Kazakhstan.

Methods. The material of the study was the data of the Ministry of Health (MoH)of the Republic of Kazakhstan, concerning OC (form 35). The retrospective study employed descriptive and analytical methods of epidemiology.

Results. In 2009, 835 people were registered with the first-ever diagnosis of OC and the incidence (crude rate) was 10.08±0.4$^0/_{0000}$. In 2018, 1095 new cases of OC were registered (table), and the incidence increased to 11.69±0.4$^0/_{0000}$ (t=3.25; p=0.001; T=+0.1%).

Table. OC indicators in Kazakhstan, 2009–2018

Indicators	2009	2012	2015	2018
New cases (%)	835 (100%)	986 (100%)	1,095 (100%)	1,095 (100%)
Morphological verification (%)	773(92.6%)	906 (91.9%)	1,036 (94.6%)	1,016 (92.8%)
I–II stage (%)	293 (35.1%)	363 (36.8%)	473 (43.2%)	447 (40.8%)
III–IV stage (%)	541 (64.8%)	620 (62.9%)	598 (54.6%)	642 (58.7%)

The rate of morphological verification of OC in the researched years increased from 92.6% in 2009 to 92.8% in 2018. In dynamics, the indicators of early diagnosis (I–II stage) increased from 35.1% (2009) to 40.8% in 2018, and the incidence of the female population of stage I–II in these years was 3.54±0.2$^0/_{0000}$ and 4.77±0.2$^0/_{0000}$ accordingly (t=3.95; p=0.000). The incidence of stage III tended to increase from 4.84±0.24 $^0/_{0000}$ (2009) to 6.06±0.25$^0/_{0000}$ in 2018 (t=3.52; p=0.000), and the incidence of stage IV in these years has decreased significantly and amounted to 1.69±0.14$^0/_{0000}$ and 0.79±0.09$^0/_{0000}$, respectively (t=5.41; p=0.000).

Conclusion. Kazakhstan reflects the global trend of rise in the incidence of ovarian cancer. According to the available data, morphological verification practically remains at the same level, there is no obvious improvement. Despite the decrease in the proportion of patients with stage III-IV, an increase in the incidence of patients with stage III is alarming. To adequately fight ovarian cancer, you need to know the risk factors and control them. The data obtained permits to objectively assess the state of cancer care.

Acknowledgments. The authors declare the absence of conflict of interest and express their gratitude to the MoH for provided data and supporting the public association "Central Asian Cancer Institute".

Tendency of ovarian cancer morbidity and mortality in Uzbekistan according to the cancer registry system

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Background. According to World Health Organization, ovarian cancer takes seventh place among all types of cancer and the third place among malignant neoplasms of female reproductive system after cancer of the cervix and uterus. According to the International Agency for Research on Cancer, more than 165 000 new cases of ovarian cancer are registered annually in the world, with a mortality rate of over 100 thousand cases per year. In Uzbekistan in 2017 year in the structure of cancer incidence among women ovarian cancer took the third place with an incidence rate of 2.4 and a mortality rate of 1.3 per 100 000 population.

Aim. Study of the trends in morbidity and mortality in ovarian cancer in the Republic of Uzbekistan from 2013 to 2017.

Methods. The materials and methods of this study were the main statistical indicators for the Republic for the period 2013–2017 according to the cancer register.

Results. In 2013, in the structure of the incidence rate by Uzbekistan regions the 1st, 2nd and 3rd places were taken by Bukhara region, Tashkent city and Ferghana regions with incidence rates of 2.6, 2.2 and 2.1 per 100 000 populations respectively. At the same time, in 2017, leading positions were taken by Bukhara, Tashkent and Jizakh regions with incidence rates of 3.9, 3.3 and 3.1 per 100 000 population accordingly. In 2013, there were 573 newly diagnosed cases of ovarian cancer in the Republic of Uzbekistan with incidence rate of 1.9, and 268 women died from ovarian cancer at the same year, with mortality rate of 0.9. To compare the same indicators in 2017, it can be concluded that the rate of morbidity and mortality over the past five years had increased by 0.5 and 0.4 respectively. Moreover, from the number of women newly diagnosed with ovarian cancer from 2013 to 2017, it was revealed that 52.9% of patients were rural residents. The percentage of patients with stages III–IV in 2013 was 67.9%, and in 2017 this percentage decreased to 53.2%.

Conclusion. As can be seen from the study, over the past 5 years there have been recorded trends in the growth of morbidity and mortality in the Republic of Uzbekistan. Based on this study, ovarian cancer requires more attention of oncologists in terms of timely diagnosis at the early stages of malignant growth.

Acknowledgements. The authors declare the absence of conflict of interest.

On incidence of type 2 diabetes mellitus in Kazakhstan

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Background. According to International Diabetes Federation, type 2 diabetes mellitus (T2DM) accounts for almost 90% of all diabetes cases. It is a chronic metabolic disorder that is the matter of immense concern of healthcare system due to its rapidly increasing prevalence worldwide. Referring to WHO, approximately 463 million adults (20–79 years) are living with diabetes and it is expected that by 2045 this number will rise to 700 million.

Aim. The objective is to study the incidence of T2DM in Kazakhstan and highlight emerging epidemiologic trends.

Methods and materials. The study period was 10 years (2009–2018), the data of the Ministry of Health (MoH) of Kazakhstan on new cases of T2DM (ICD – E11) in children, adolescents, adults and the entire population. Incidence rates on 100,000 population, 95% confidence interval, equalized indicator of the average annual growth rate have been analysed using the generally accepted methods of descriptive and analytical epidemiology.

Results. Over the period of study, 283 331 new cases of T2DM were registered, of which 99.9% were adults (table).

Table. Type 2 diabetes mellitus in Kazakhstan

Age group	Number (%)	P±m, $^0/_{0000}$	95 % CI, $^0/_{0000}$	T, %
Children (under 15)	249 (0.09)	0.6±0.05	0.5-0.6	+3.2
Adolescent (15–17)	143 (0.05)	2.0±0.2	1.6-2.4	+0.8
Adults (18+)	282 939 (99.86)	236.6±9.8	217.4-255.8	+5.0
Total	283 331 (100.0)	165.3±6.4	152.8-177.7	+4.7

The average annual incidence rate was 165.3 cases per 100 000 of the total population. In the dynamics, the indicators tended to grow from 131.6±0.9 (2009) to 198.9±1.1 in 2018 (t=47.35, p=0.00), while equalized indicator of the average annual growth rate was T=+4.7% (R^2=0.9011). In the studied groups the highest rates were found among adults – 236.6$^0/_{0000}$ (T=+5.0%, R^2=0.9054), while children (0.6$^0/_{0000}$) and adolescent (2.0$^0/_{0000}$) groups have the lowest rates. At the same time, differences in the incidence among these population groups were statistically significant (t=7.00; p=0.00).

Conclusion. The analysis of the data proved that the dynamics of the growth rate indicator and very high level of approximation cause concern. The results of the study show that T2DM is a problem in the adult population mainly, and more detailed study of age groups is necessary. Moreover, high growth rates in children under 14 years of age are alarming. Therefore, it should be noted that this issue requires further study.

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Seasonal and climatic variations in mortality in ischemic heart disease

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Background. There is an increase in the incidence of ischemic heart disease (IHD) in the period 2001–2018 in the Republic of Kazakhstan (RK) and Nur-Sultan, rising from 321.5 and 201.5 (2001) to 529.0 and 377.0 (2018) per 100 000 population, respectively. However, the mortality from IHD decreased in Kazakhstan from 157.4 (2009) to 62.3 (2018) and in Nur-Sultan from 124.5 to 51.4.

Aim. Assessment of the influence of seasonal climatic and meteorological factors (CMF) on the mortality of patients with IHD in Nur-Sultan.

Methods. The daily mortality of the population of Nur-Sultan for 2009–2018 from IHD in comparison with the daily CMF was grouped by days, months, seasons, analysed by gender and age groups: young (18–44 years old), middle-aged (45–59 years old), young-old (60–74 years old) and the aged (>75).

Results. During 2009–2018, 5865 deaths from IHD were registered in Nur-Sultan: 3332 males (56.8%), 2533 females (43.2%). Mortality decreased from 842 to 541 cases and had pronounced gender-age differences. There is an increase in mortality: 5.4%–21.1%–31.9%–41.6% of cases, respectively, in age groups. In the first three age groups, there were 4.7, 5.3 and 1.6 times more males, respectively, and in the aged group there were 1.8 times more females. The highest mortality was in spring (1609) and winter (1527), autumn (1381), and the lowest in summer (1348) with the same gender-age characteristics noted above in all seasons. The increase in mortality in the spring-winter period is confirmed by an increase in the seasonality index (SI), calculated as the ratio of mortality in a given month or season to the average for all years of the analysed period. SI value more than 100% considered that seasonal factors intensified in this month (season). SI was above 100% from January to May (102.9–124.7), more pronounced in females. The IS mortality for winter was 105.4%, spring 108.9%, autumn 94.5%, and summer 91.2%.

Conclusion. In 2009–2018 in Nur-Sultan there was a decrease in the MR from IHD. The mortality was higher in the spring-winter season, it grew with the age and showed the prevalence of males among young, middle-aged, and young-old people, and females among the aged. The noted seasonal and gender-age specificities of mortality should be taken into account when carrying out management and prophylactic measures for patients with IHD.

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Retrospective epidemiological analysis of incidence of Congo-Crimean fever 2009–2018 in the Republic of Kazakhstan

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Background. Congo-Crimean haemorrhagic fever (CCHF) is a disease that is common on three continents – in Europe, Asia and Africa, and causes a high proportion of deaths, varying in different years from 10 to 50%, and in some cases, when the pathogen is transmitted from person to person, reaching 80%.

Aim. The objective of the study was to find out the patterns and features of the trend in the incidence of Congo-Crimean fever in the Republic of Kazakhstan for 2009–2018, to analyse the long-term dynamics of this nosological form.

Methods. Materials for the study included statistical data of the Committee for the protection of public health.

Results. Data for the period from 2009 to 2018, for the Republic of Kazakhstan, showed that the incidence of Congo-Crimean fever is characterized by cyclical, undulating flow, periodic rises are observed at intervals of 2–3 years, the highest peak of cases occurs in 2016, 2017, 2018, similar indicators were 25%, 64%, 14.7%, respectively.

Characterising the incidence of Congo-Crimean fever in the Republic of Kazakhstan in 2016–2018, 159 cases of Congo-Crimean fever were registered in the Republic in advance of 2018, 198 cases were detected in 2017, including 102 predicted cases (64%) and 57 probable cases (35.8%). From the Congo-Crimean fever, 12 out of 159 cases registered in the city of Shymkent were suspected. In Turkestan region 71, Kyzylorda region 13, Zhambyl region 63 cases.

In general, in the Republic in 2018, 153 (2.2%) people were diagnosed with tick bites and were hospitalized for medical observation.

Conclusion. The dynamics of the epidemiological process of the incidence of Congo-Crimean fever in the Republic of Kazakhstan is characterized by a slight downward trend. The reasons for the summer seasonality of CCL require further study. The most effective methods of controlling the infection are improving sanitary and hygienic conditions, strengthening supervision over the quality of food and water, introducing expanded vaccination, as well as raising public awareness about the ways of spread and preventive measures against this disease.

Regional aspects of incidence diseases of pancreas in Kazakhstan

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Background. Diseases of pancreas (DP) have great impact on quality of life, risk of developing cancer of pancreas. The incidence of acute pancreatitis ranges from 13 to 45 per 100 000 population-years and that of chronic pancreatitis ranges from 5 to 12 per 100 000 population-years worldwide. Thus, pancreatitis remains a critical public health issue.

Aim. To study DP incidence age trends in Kazakhstan in 2008–2017.

Methods. The retrospective study covered the data of the Ministry of Health of the Republic of Kazakhstan (MoH RK) for 2008–2017 – the annual form No.12 related to the new cases of DP (ICD 10–K85-K86). Descriptive and analytical methods of medical and biologic statistics were used to define annual averages (P, $^0/_{0000}$), mean error (m), 95% confidential interval (95% CI), annual average aligned increase/decrease (T, %). The alignment was made according to the formula: $y=a+bx$.

Results. In the study period, 203 449 new cases of DP were registered. The annual average crude incidence rate of DP in Kazakhstan amounted to 119.9 (95% CI=101.0–138.8) per 100 000 total population. Over time, the crude rate decreased from 95.6±0.8$^0/_{0000}$ (95% CI=94.1–97.1) in 2008 to 194.5±1.0$^0/_{0000}$ (95% CI=192.5–196.6) in 2017, with a statistically significant difference (R^2=0.7524). The aligned index was also growing, with an annual average rate of T=+9.5%.

Then, we reviewed the regional trends in the DP incidence. The upward trends were registered in the city of Astana (T=+2.3%; R^2=0.226; P=145.1$^0/_{0000}$), Kostanay (T=+2.8%; R^2=0.038; P=69.4$^0/_{0000}$), Aktobe (T=+3.3%; R^2=0.6597; P=50.3$^0/_{0000}$), Almaty (T=+3.6%; R^2=0.4927; P=135.6$^0/_{0000}$), West Kazakhstan (T=+4.9%; R^2=0.4416; P=21.5$^0/_{0000}$), Mangistau (T=+6.4%; R^2=0.4333; P=217.3$^0/_{0000}$), North Kazakhstan (T=+7.5%; R^2=0.7775; P=101.1$^0/_{0000}$), Atyrau (T=+7.8%; R^2=0.6406; P=42.0$^0/_{0000}$), East Kazakhstan (T=+9.0%; R^2=0.5819; P=126.6$^0/_{0000}$), Zhambyl (T=+11.0%; R^2=0.6745; P=116.5$^0/_{0000}$), Kyzylorda (T=+11.1%; R^2=0.6783; P=30.4$^0/_{0000}$) regions, the city of Almaty (T=+11.7%; R^2=0.6034; P=216.5$^0/_{0000}$), Pavlodar (T=+12.7%; R^2=0.5899; P=120.7$^0/_{0000}$), South Kazakhstan (T=+29.7%; R^2=0.648; P=156.6$^0/_{0000}$) regions. The downward trends were registered only in Akmola (T=–1.0%; R^2=0.0598; P=99.2$^0/_{0000}$) and Karaganda (T=–7.7%; R^2=0.4296; P=73.5$^0/_{0000}$) regions.

Conclusion. Trends of rates DP incidence are growing in all regions except for Akmola and Karaganda regions. Sharply increased indicators in South Kazakhstan require special attention. Accurate information about the burden of pancreatitis from different regions is valuable for policy makers to decrease its burden.

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Cerebrovascular mortality in seasonal and climatic conditions of Shymkent and Nur-Sultan cities

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Background. In connection with global warming, the problems of cerebrovascular diseases (CVD) in the climatic conditions of the population are of particular relevance and high social significance.

Aim. Comparative characteristics of seasonal and climatic features of the distribution of mortality of patients with cerebrovascular diseases in the conditions of the Southern and Northern regions of Kazakhstan on the example of two cities.

Methods. The data of the Committee of Statistics on daily mortality of patients with CVD among the adult population of Shymkent and Nur-Sultan for 2009–2018 are analysed. Climate and meteorological factors (CMF) data were obtained from «Kazhydromet».

Results. In 2009–2018, there was an increase in daily mortality from CVD in Shymkent from 490 (2009) to 528 (2018), and in Nursultan from 299 to 307 cases. In Shymkent, higher mortality rates are observed in winter (1334), then in summer (1261), spring (1228) and autumn (1218). In Nur-Sultan in winter (847), autumn (846), spring (824) and the lowest in summer (738).

Mortality in the cold period (CP) (November–March) in Shymkent accounted for 2232, in the warm period (WP) (April–October) – 2809 deaths from CVD. In Nur-Sultan in CP-1426 and WP-1829 cases. In both cities, the mortality rate in CP is less than in TP of the year. However, the calculation of deaths on day 1 of each period showed that CP in Shymkent accounted for 1.49 with 1.31 in WP, in Nur-Sultan 0.95 and 0.85, respectively. Consequently, the absolute mortality rates from CVD in both cities are higher in the CP of the year.

There is a certain dependence of mortality rates of CVD patients on the degree of climate comfort rating (CCR), which is more pronounced in Nur-Sultan (CCR from November to February was 2.5 points out of 5 possible), while in Shymkent in July-August CCR was 3.5 points.

In both cities, mortality rates increase with age: in the young 4.7% and 5.3%, on average 19.8% and 18.7%, in the elderly 35.7% and 35.0%, senile 39.8% and 41.0%, respectively. In 3 age groups, men predominate, in senile, more than twice the mortality rate among women.

Conclusion. In the cities of Shymkent and Nur-Sultan, there is an increase in mortality from CVD, and in Shymkent, the mortality rate is 1.5 times lower than in Nur-Sultan. Mortality from CVD increases with the age of patients and in the cold period of the year.

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Cartogram of peptic ulcer disease of stomach and duodenum incidence in Kazakhstan

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Background. The incidence of peptic ulcer disease of stomach and duodenum (PUD) is declining, possibly due to decreasing prevalence of *H. pylori* infection. However, it continues to be a source of significant morbidity and mortality worldwide.

Aim. To study the regional features of PUD incidence in Kazakhstan by compiling cartogram.

Methods. We used the incidence rates for 10 years (2009-2018) provided by the Ministry of Health of Kazakhstan (MoHK) and applied the method of compiling cartograms based on the determination of the standard deviation (σ) from the mean (x) to compile cartogram.

Results. During the study period, 174,641 cases of PUD were recorded in country. The average annual incidence was 102.7±3.0 per 100,000 population. In dynamics, the incidence rates tended to decrease from 99.2±0.8$^0/_{0000}$ in 2009 to 85.1±0.7$^0/_{0000}$ in 2018, the established difference is statistically significant (t=13.26; p=0.000; T=–2.6).

To do the cartogram, we determined the levels of PUD incidence based on the following criteria: low – up to 87.1$^0/_{0000}$, average – from 87.1 to 123.8$^0/_{0000}$, high – above 123.8$^0/_{0000}$. As a result, the following groups of regions were made:

1. Regions with low indicators (up to 87.1$^0/_{0000}$) – Mangistau (60.7$^0/_{0000}$), Aktobe (74.6$^0/_{0000}$), Atyrau (76.4$^0/_{0000}$), West Kazakhstan (83.5$^0/_{0000}$), and regions.
2. Regions with average indicators (from 87.1 to 123.8$^0/_{0000}$) – Kyzylorda (87.1$^0/_{0000}$), Karaganda (90.4$^0/_{0000}$), North Kazakhstan (90.7$^0/_{0000}$), Almaty (91.0$^0/_{0000}$), East Kazakhstan (91.3$^0/_{0000}$), Akmola (94.2$^0/_{0000}$), Pavlodar (100.1$^0/_{0000}$), Kostanay (101.9$^0/_{0000}$) regions and the city of Astana (109.6$^0/_{0000}$).
3. Regions with high indicators (123.8$^0/_{0000}$ and above) – South Kazakhstan (123.8$^0/_{0000}$) region, the city of Almaty (128.9$^0/_{0000}$) and Zhambyl (164.9$^0/_{0000}$) region.

Conclusion. Thus, the established epidemiological peculiarities of incidence of peptic ulcer disease of stomach and duodenum indicate its geographic variability, with a territorial differentiation of loci with low values in the western regions and high values in the mainly southern regions. The obtained results will provide the public health managers a clear spatial picture of PUD frequency and incidence, which must be used to monitor and assess the treatment, to conduct proper prevention and further research.

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Regional trends of varicose veins incidence in Kazakhstan

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Background. Varicose veins of the lower extremities (hereinafter VLE) are a very common problem, which occurs due to the incompletion of recognition of primary and secondary VLE, which is often overlooked by healthcare professionals. The prevalence of this pathology is higher in socio-economically developed countries than in underdeveloped ones.

Aim. To study of VLE incidence trends in Kazakhstan in 2009–2018.

Methods. The retrospective study covered the data of the Ministry of Health of the Republic of Kazakhstan for 2009–2018 – the annual form No.12 related to the new cases of VLE (ICD10–I83). Extensive and rough indicators of morbidity are determined by the generally accepted methodology used in modern statistics. The mean value (M), the mean error (m) and the average annual rates of increase and decrease ($T_{pr/lo}$,%), 95% confidence intervals (95% CI) were calculated.

Results. In the study period, 158 151 cases of VLE were registered for the first time in the republic in which 37 670 (23.8%) and 120 481 (76.2%) cases are among men and women, respectively. The average annual incidence rate of VLE (both sexes) in the republic was 91.6±9.6 per 100 000 of the total population (95% CI=72.8-110.3$^0/_{0000}$). In the dynamics, the incidence rates tended to grow from 69.2$^0/_{0000}$ in 2009 to 138.7$^0/_{0000}$ in 2018. The average annual growth rate was T_{pr}=+12.5%, R^2=0.7821. Then, we reviewed the regional VLE incidence trends. The upward trends were registered in the South Kazakhstan (T_{pr}=+40.6, R^2=0.7599), Kyzylorda (T_{pr}=+28.3, R^2=0.5900), Mangystau (T_{pr}=+22.4, R^2=0.156), Almaty city (T_{pr}=+20.2, R^2=0.7119), Zhambyl (T_{pr}=+18.0, R^2=0.8689), East Kazakhstan (T_{pr}=+16.5, R^2=0.6908), Astana city (T_{pr}=+9.7, R^2=0.5299), Almaty (T_{pr}=+20.2, R^2=0.5567). The downward trends were registered in Atyrau (T_{lo}=–22.8, R^2=0.5741), Aktobe (T_{pr}=+2.2, R^2=0.1117), Akmola (T_{pr}=+3.8, R^2=0.3554), Kostanay (T_{pr}=+4.5, R^2=0.3095), Pavlodar (T_{pr}=+4.6, R^2=0.4451), North Kazakhstan (T_{pr}=+5.6, R^2=0.5315), Karaganda (T_{pr}=+5.7, R^2=0.5491) and West Kazakhstan (T_{pr}=+8.4, R^2=0.5119).

Conclusion. Thus, the established regional trends in the incidence of VLE indicate high rates in regions with a developed industry. The high incidence of VLE in our country emphasizes the importance of timely diagnosis and prevention, the need for new treatment technologies that can be used not only by cardiovascular doctors, but also by general surgeons and even doctors of other specialties.

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Cartogram of the incidence of Parkinson's disease in Kazakhstan

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Background. One of the leading methods of scientific analysis of the epidemiological situation is mapping, which allows conducting spatial analysis and monitoring the current situation of morbidity. One of the most relevant diseases is diseases of the nervous system, as they affect the functioning of the main regulatory systems of the body. Among these diseases, a separate large group consists of neurodegenerative diseases, one of which is Parkinson's disease.

Aim. Make a cartogram of the incidence of Parkinson's disease in Kazakhstan.

Methods. In the preparation of cartograms, the indicators of the incidence of Parkinson's disease (ICD 10 – G20) for 6 years (2013–2018) were used and the method of mapping was applied, based on the determination of the standard deviation (σ) from the average (x).

Results. During the study period, 5 130 new cases of Parkinson's disease were registered. The average annual incidence of Parkinson's disease was 6.9±0.1 per 100 000 population. For mapping purposes, Parkinson's disease incidence levels were determined at the beginning, which meet the following criteria: low – up to $8.4^0/_{0000}$, medium – from 8.4 to $13.5^0/_{0000}$, high – above $13.5^0/_{0000}$. On the basis of which the following groups of areas were defined:

1. Regions with low indicators (up to $8.4^0/_{0000}$ – Kostanay ($3.3\pm0.2^0/_{0000}$), Karaganda ($3.4\pm0.3^0/_{0000}$), West Kazakhstan ($4.3\pm0.2^0/_{0000}$), Pavlodar ($5.9\pm0.2^0/_{0000}$) regions.
2. Regions with average indicators (from 8.4 to $13.5^0/_{0000}$) – Kyzylorda ($6.3\pm0.7^0/_{0000}$), Almaty city ($6.8\pm0.3^0/_{0000}$), Atyrau ($6.9\pm0.2^0/_{0000}$), Aktobe ($7.1\pm0.5^0/_{0000}$), Zhambyl ($7.4\pm0.3^0/_{0000}$), South Kazakhstan ($7.5\pm0.5^0/_{0000}$), East Kazakhstan ($7.5\pm0.4^0/_{0000}$) Almaty ($7.6\pm0.3^0/_{0000}$) and North Kazakhstan ($7.9\pm0.5^0/_{0000}$) regions.
3. Regions with high indicators ($13.5^0/_{0000}$ and above) – the city of Astana ($8.6\pm1.1^0/_{0000}$), Mangistau ($11.3\pm1.6^0/_{0000}$) and Akmola ($11.8\pm0.5^0/_{0000}$) regions.

The cartogram more clearly reflects the spatial distribution of Parkinson's disease, while the discrepancy between the theoretical and actual distribution of morbidity in the studied regions is small ($\chi^2=8.4$, which is greater than the table value of 0.5398 at k=7), i.e., the actual distribution is close to normal.

Conclusion. Thus, the established regional features of the incidence of Parkinson's disease indicate variability with territorial differentiation by incidence levels. The obtained results will allow health care organizers to have a clear spatial picture of the incidence of Parkinson's disease, which is necessary for the implementation of therapeutic and preventive measures.

Acknowledgments. The authors declare the absence of conflict of interest and express their gratitude to the Ministry of Health of the Republic of Kazakhstan for the provided primary material.

30-day mortality after myocardial infarction in men with type 2 diabetes mellitus in Latvia

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Background. Prevalence of diabetes has been rising all over the world, more rapidly in low- and middle-income countries. In Latvia, in 2017 there were 86 639 patients registered of type 2 diabetes mellitus (T2DM) with the prevalence of 4 478.9/100 000. T2DM can be related to exceeded mortality after acute myocardial infarction (AMI).

Aim. The aim of the current study was to investigate the 30-day mortality after AMI in patients with T2DM and without T2DM in Latvia in 2017.

Methods. 2466 patients from AMI administrative dataset available in Latvian Centre for Disease Prevention and Control database for year 2017were analysed. Patients with T2DM were identified by information from state paid outpatient, inpatient services, and state-reimbursed medications retrospectively one year before AMI hospitalization. In a cross-sectional analysis, odds ratio (ORs) and 95% confidence intervals (CIs) for 30-day mortality after hospitalization as a result of AMI were calculated using direct age-adjustment and stratifying each gender in 6 groups (0–39, 40–49, 50–59, 60–69, 70–79, 80+ years). Mean age (M) and standard deviation (SD) were calculated. A p-value of <0.05 was considered significant.

Results. From the total number of AMI hospitalization cases, T2DM was diagnosed in 22% of patients, 52% of them were men. The mean age of men with T2DM was 68.2 (SD=11.4) years, and for men without T2DM M=65.4 (SD=12.6) years, p<0.01. For women, the mean age was 75.6 (SD=9.9) years for those with T2DM, and M=76.3 (SD=11.4) years for those without T2DM, p=0.35. Twenty one percent of those with T2DM and 17% for patients without T2DM died in 30 days after the hospitalization for AMI. 30-day mortality rate in men with T2DM was higher than that in women with T2DM: for men – 6.8/100 000, for women – 4.6/100 000. For men with T2DM, the 30-day mortality was by 21% higher (OR=1.21, 95% CI 0.84–1.76) than for men who had not been diagnosed with T2DM. For women, the 30-day mortality was by 12% higher (OR=1.12, 95% CI 0.80–1.57) in those with T2DM than in women who had not been diagnosed with T2DM.

Conclusion. Gender differences should be considered by treating T2DM patients with AMI.

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Inpatient incidence of intracranial injury in Kazakhstan: spatial assessment

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Background. It has been estimated that traumatic brain injury affects over 54 to 60 million people annually, leading to either hospitalisation or mortality. Of all types of injury, those to the brain are among the most likely to result in death or permanent disability. According to the Global Burden of Disease Study 2016, there were 27.08 million new cases of traumatic brain injury, with age-standardised incidence rates of 369 per 100 000 population, per year.

Aim. Make a cartogram of the incidence of intracranial injury (II) in Kazakhstan.

Methods. When compiling cartograms, indicators of II morbidity (ICD 10–S06) for 10 years (2009–2018) were used and a method of compiling cartograms was used, based on determining the standard deviation (σ) from the mean (x).

Results. During the study period, 473 440 new cases of II were registered. The average annual incidence of intracranial injury was 279.1±11.6 per 100 000 population. To compile cartograms, at the beginning, the incidence rates of II were determined, which corresponded to the following criteria: low – up to $233.1^0/_{0000}$, medium – from 233.1 to $292.4^0/_{0000}$, high – above $292.4^0/_{0000}$. On the basis of these, the following groups of areas were determined:

1. Regions with low rates (up to $233.1^0/_{0000}$) – North Kazakhstan ($168.4\pm7.4^0/_{0000}$), Kostanay ($186.8\pm10.4^0/_{0000}$), Mangistau ($203.3\pm11.3^0/_{0000}$), Atyrau ($203.4\pm7.5^0/_{0000}$), West Kazakhstan ($209.9\pm13.5^0/_{0000}$) areas, as well as the city of Astana ($229.9\pm21.5^0/_{0000}$).
2. Regions with average indicators (from 233.1 to $292.4^0/_{0000}$) – Karaganda ($242.1\pm19.3^0/_{0000}$), Kyzylorda ($250.5\pm11.6^0/_{0000}$), Aktobe ($278.8\pm15.0^0/_{0000}$), Akmola ($284.7\pm19.7^0/_{0000}$) areas.
3. Regions with high rates ($292.4^0/_{0000}$ and higher) – East Kazakhstan ($296.5\pm6.2^0/_{0000}$), South Kazakhstan ($304.1\pm7.8^0/_{0000}$), Zhambyl region ($313.4\pm19.1^0/_{0000}$), Almaty ($341.9\pm17.4^0/_{0000}$), and Pavlodar ($363.3\pm13.8^0/_{0000}$) areas, as well as the city of Almaty ($326.6\pm18.3^0/_{0000}$).

The cartogram more clearly reflects the spatial distribution of II, while the discrepancy between the theoretical and actual distribution of morbidity in the studied regions is small ($\chi^2=1.6$, which is more than the tabular value of 0.4405 at k=10), i.e., the actual distribution is close to normal.

Conclusion.. Thus, the established regional features of the incidence of intracranial injury indicate variability with territorial differentiation in terms of incidence rates. The obtained results will allow healthcare organizers to have a clear spatial picture of the incidence of II, which is necessary for carrying out treatment and preventive measures.

Acknowledgments. The authors declare the absence of conflict of interest and wish to express their gratitude to the Ministry of Health of the Republic of Kazakhstan for the provided primary material.

Crohn's disease prevalence in Kazakhstan

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Background. Crohn's disease, a subtype of inflammatory bowel disease (IBD), has been increasing in incidence over the last few decades. The prevalence of CD has an incidence of 3 to 20 cases per 100 000. Crohn's disease is more common in the industrialized world, particularly in North America and Western Europe, although the incidence is also rising in Asia and South America.

Objective. The aim is to study the prevalence of Crohn's disease in Kazakhstan and highlight emerging epidemiologic trends.

Materials and methods. The study period was 6 years (2013–2018), the data of the Ministry of Health of Kazakhstan (MoHK) on new cases of Crohn's disease (ICD–K50) in children, adolescents, adults and the entire population. Prevalence per 100 000 population, 95% confidence interval, equalized indicator of the average annual growth rate have been analysed using the generally accepted methods of descriptive and analytical epidemiology.

Results. Over the period of study, a total of 12 495 cases of Crohn's disease were registered, of which 92.5% were adults (table).

Table. Crohn's disease in Kazakhstan

Age group	Number (%)	P±m, $^0/_{0000}$	95 % CI, $^0/_{0000}$	T, % (R^2)
Children (under 15)	727 (5.8)	2.6±0.4	1.9-3.4	–14.8 (0.327)
Adolescent (15–17)	206 (1.6)	5.2±0.5	4.2–6.3	–8.3 (0.169)
Adults (18+)	11 562 (92.5)	17.2±2.5	12.4–22.1	–25.2 (0.808)
Total	12 495 (100.0)	13.0±1.8	9.4–16.6	–24.6 (0.816)

The average annual prevalence was 13.0 cases per 100,000 of the total population. In the dynamics, the indicators tended to decline from 22.8±0.4 (2009) to 7.1±0.2 in 2018 (t=35.1, p=0.00), while equalized indicator of the average annual growth rate was T=–24.6% (R^2=0.816). In the studied groups the highest rates were found among adults – 17.2$^0/_{0000}$, but at the same time, there is a downward trend (T=–25.2%, R^2=0.808). While children (2.6$^0/_{0000}$) and adolescent (5.2$^0/_{0000}$) groups have the lowest rates. At the same time, differences in the prevalence among these population groups were statistically significant (t=4.06; p=0.00).

Conclusion. It is worth paying attention to the analysis of the data obtained, which showed the dynamics of the rate of decline and a very high level of approximation. The results of the study show that Crohn's disease is a problem in the adult population mainly, and more detailed study of age groups is necessary.

Acknowledgments. The authors declare the absence of conflict of interest and express their gratitude to the MoHK.

Prevalence of *Trichomonas vaginalis* in oncocytological smears collected from Latvian women of different age groups in 2020

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Background. *Trichomonas vaginalis* infection is the most commonly spread non-viral infectious disease acquired during sexual contact with an infected partner. The number of undiagnosed and untreated cases in women creates a risk factor for the development of precancerous condition of the cervix and premature birth.

Aim. The objective of this study was to determine the prevalence of urogenital Trichomonas infection cases in women of different age groups in the regions of Latvia in 2020.

Methods. A retrospective study was performed, and the data on registered cases of urogenital Trichomonas infection within the period from January 1, 2020 to December 31, 2020 were collected at the Department of Cytology of the Central Laboratory. The data obtained for 260 patients were analysed using *Microsoft Excel* and *IBM SPSS Statistics* software, taking into account the distribution by age groups, regions, seasonality, confirmed pregnancy and precancerous condition of the cervix.

Results. Data analysis confirmed that the age group among women with the highest recorded rates of urogenital Trichomoniasis was 40–50 years (n=70; 26.9%). The highest morbidity was observed in Vidzeme (n=155; 59.6%). The highest number of registered cases was observed in spring (n=76). Specific for Trichomoniasis microscopic findings were observed in women with confirmed pregnancy (n=22; 8.5%) and precancerous conditions of the cervix (n=15; 5.8%).

Conclusions. Urogenital Trichomoniasis is found in Latvian women of all ages, but most often from 40 to 50 years. The disease is characterized by seasonality. The highest morbidity is observed in Riga region. The future perspective is to compare the bacterioscopic laboratory examination method with the liquid cytology method in the diagnosis of *Trichomonas vaginalis*.

INTERNAL MEDICINE

Outcomes of strabismus surgery in case of congenital and acquired esotropia and exotropia

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Background. Strabismus has not only a cosmetic burden, but also has a crucial impact upon the development of fully functional sight, especially in terms of stereoscopic vision.

Stereoscopic vision is achieved when images from both eyes are combined into one whole three-dimensional picture. In the case of strabismus, this process is altered. Brain blocks the worst-seeing eye from the image formation process. As a consequence, the person looks only with one eye, the situation which has potentially detrimental ramifications in the full development of both sensory and motor functions.

Aim. To compare binocular alignment, angle of strabismus, before and after the surgery (right after the procedure and with a three-month interval). To perform a statistical analysis in order to calculate the percentage of the positive outcome.

Methods. Patients with the relevant criteria were selected. 105 subjects were divided in four groups.

Results. According to the data obtained, there is statistically significant difference ($p<0.05$) between the first measurements before and after the surgery and between the follow-up measurements after the surgery. Furthermore, the difference between the first post-surgical measurement and the follow-up is not statistically significant ($p>0.05$).

In all groups, monocular or alternating monocular vision was the dominant form of vision. In the first postoperative day, near binocular vision was achieved in 31% of subjects and distance in 22.9% of subjects.

In the group:

- with congenital esotropia on a follow-up visit near binocular vision was observed in 50% and with distance binocular vision in 16.7% of patients.
- with acquired esotropia near and distant binocular vision was reported in 52% and 43.5% of patients, respectively.
- with congenital exotropia, on a follow-up visit, near and distant binocular vision was achieved in 33.3% and 50% of patients, respectively.
- with acquired exotropia, on a follow-up visit near and distant binocular vision was observed in 72% and 64% of patients, respectively.

Stereoscopic vision before the surgery was observed only in patients with acquired exotropia (19.2%). On a follow-up visit, stereoscopic vision was achieved in patients with acquired esotropia (10.6%), acquired exotropia (38.5%), congenital exotropia (14.3%).

Conclusion. It is evident that the outcome of the surgery in terms of achievement of binocular and stereoscopic vision is more beneficial for those with acquired strabismus forms.

The data confirms that operation results in major decrease of the angle of both esotropia and exophoria, and has an overall positive outcome.

Acknowledgements. The authors declare the absence of conflict of interest.

Loss of sensation and symptoms of varicose veins related neuropathy: what does the evidence say?

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Background. Primarily clinicians most often associate peripheral neuropathy (PN) with diabetes. Although not widely recognized clinically, evidence of PN in patients with venous insufficiency (VI) has been reported. PN and painful varicose veins can be distinguished from each other based on a physical examination, however, the statement that varicose veins do not cause a change in sensation, is debated. VI may provoke not only the onset of various symptoms but also a significant elevation of the threshold of sensation in the extremities.

Aim. To evaluate whether peripheral critical sensation disorder determining anaesthesia in legs is associated with VI, diabetes and age in ambulatory practice patients (APP).

Methods. 238 APP (176 male and 62 female; 58.9±14.9 years) were evaluated for sensation disorder by current perception test (CPT) with the Neurometer® on both legs' toes at different frequencies: 2000, 250 and 5 Hz. The stimulus was presented with increasing intensity ranging from 0.01 to 9.99 mA until the patient reported that felt the current. At least in one measure having no response to the maximal stimulus at a CPT value of 9.99 mA indicated anaesthesia. Patients were divided into two groups: those with anaesthesia (WA) (n=23; 9.7%) and without anaesthesia (WoA) (n=215; 90.3%). All patients anonymously filled the Varicose Veins Symptoms Questionnaire (VVSymQ®) (heaviness, achiness, swelling, throbbing and itching), also self-reported having (n=114; 47.9 %) or no (n=124; 52.1%) diabetes, having (n=75; 31.5%) or no (n=163; 68.5%) varicose veins (VV). Results were compared using Student t and Fisher Exact tests.

Results. WA patients compared to WoA patients had higher VVSymQ® results (7.48 vs. 4.44; p=0.012), felt more often heaviness (65.2% vs. 42.8%; p=0.033) and throbbing (52.2% vs 27.4%; p=0.016) in legs. There were no differences between self-reported patients with or without diabetes, also with or without VV. WA patients were older (65.26 vs. 58.24; p=0.032).

Conclusion. There is a discrepancy between the critical loss of peripheral sensation with self-reported diabetes or VV. The results indicating that patients with anaesthesia more often feel leg heaviness and throbbing symptoms may be important for clinicians on suspicion of critical sensation loss in APP. More studies are needed to better understand VI and diabetes-related neuropathy.

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Diagnostic purpose of bronchoalveolar lavage cell differential count

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Background. Bronchoalveolar lavage is a method for assessment of diffuse parenchymal lung diseases. Information about cell differential count gives important information about processes in lungs.

Aim. The purpose of the study was to compare normal bronchoalveolar lavage cell differential counts with diffuse parenchymal lung disease patients and patients' group with other diseases, who had undergone lavage for exclusion of diffuse parenchymal lung diseases.

Methods. In this retrospective study, the data were collected from bronchoalveolar lavage from 2019to 2020. 195 samples were analysed for agranulocyte, neutrophil, eosinophil, and alveolar macrophage percentual count. Patients were divided in two groups, in the first group – the patients with diffuse parenchymal lung diseases, and in the second (control) group – the patients who had undergone bronchoalveolar lavage due to other reasons or for exclusion of diffuse parenchymal lung disease. Both groups were compared with healthy non-smoking person cells count parameters from literature data and cells count criteria for concrete patient diagnosis.

Results. In period of 2019–2020, 195 bronchoscopies with bronchoalveolar lavage sampling were carried out in Pauls Stradiņš Clinical University Hospital. From all the materials: 78 (40%) were from the control group and 117 (60%) from the patients with diffuse parenchymal lung disease. From the control group only 12 (15%) samples had cell parameters that corresponded to a healthy person (agranulocytes $\leqslant$15%, neutrophil $\leqslant$3%, eosinophil $\leqslant$1%, and alveolar macrophage $\geqslant$85%), in 38 % cases lavage sample did not meet the cell differential count criteria for patient diagnosis, in 62% the results were appropriate for illness. In the group with diffuse parenchymal lung disease patients, 14 (12%) had normal bronchoalveolar lavage, 33% had no diagnostic value, whereas in 67% the lavage test met criteria for diffuse parenchymal lung disease.

Conclusion. Bronchoalveolar lavage is a method with a high diagnostic value. Only in 13% cases, the material had normal cell differential count ranges, in other cases the samples were changed, but also an unchanged test sometimes had a diagnostic significance. In 65 %, the test had diagnostic value to confirm diagnosis.

Acknowledgements. The authors declare the absence of conflict of interest.

Material quality of bronchoalveolar lavage

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Background. Bronchoalveolar lavage is a gold standard in evaluation of diffuse parenchymal lung diseases, but to use this method in daily practice, the quality of material needs to be good, otherwise the results could be interpreted falsely.

Aim. The purpose of the study was to detect how many of the performed bronchoalveolar lavage are of sufficient quality to be examined for diagnostic goal.

Methods. In this study, retrospective data from 88 materials of bronchoalveolar lavage during bronchoscopy were collected. Filled fluid volume and percent of its withdrawn was analysed following the bronchoscopy protocol. Bronchoalveolar lavage was sent for evaluation in laboratory, where cells were counted. Bronchoalveolar lavage withdrawn fluid volume and total nucleated immune cell count were analysed to obtain information about quality of procedure.

Results. 88 bronchoscopies with bronchoalveolar lavage were carried out in Pauls Stradiņš Clinical University Hospital in 2020. From all the materials, in 70 (80%) bronchoscopy protocols, there was a known difference between injected and recovered fluid volume. Only in 6 (9%) cases the withdrawn volume was less than 30%, which can be misleading factor in cell differential counts. There was no significant correlation between the percentage of withdrawn fluid volume in patients with diffuse parenchymal lung diseases or with other disease. From all samples, in 5 (6%) cases the total cell count was not calculated, but from other materials only in 41 cases the total cell count was more than 300 cells. Consequently, 49% of the cases were of a good quality. There was no significant correlation in total cell count in bronchoalveolar lavage between patients with or without diffuse parenchymal lung diseases. To summarise, both quality parameters in 17 (19%) cases lacked information about both data parameters, but good material was only in 36%.

Conclusion. To use bronchoalveolar lavage as diagnostic tool, the quality of this method needs to be good. The current study demonstrated that only 36% of the cases are with a good withdrawn fluid volume and sufficiently high total immune cell count. To identify causes of low-quality lavage, further investigation is needed.

Acknowledgements. The authors declare the absence of conflict of interest.

The rate of subjective cognitive complaints and relationship with chronic diseases in middle-aged females

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Background. Substantial evidence exists that cognitive decline may begin in women at a middle age causing a higher risk to develop dementia. Chronic diseases (ChD) have a significant impact on dementia risk.

Aim. Study aimed to evaluate the rate of subjective cognitive complaints (SCCs) and to determine if ChD are related to SCCs in population of middle-aged females.

Methods. 310 females from 26 to 59 years (M=38.6) took part in an online study. They filled in Subjective Cognitive Complaints (SCCs) questionnaire. Self-reported ChD were registered. Results were compared using Fisher's exact test.

Results. 28.7% (N= 89) had SCCs (SCCs+ group) and 71.3% did not have SCCs (SCCs- group). 30.6% (N=95) females reported they had ChD and 69.4% (N=215) did not have ChD. 46 respondents in SCC+ group reported to have no ChD, 33 – one ChD, 5 – two ChD, 2 had three ChD, also 2 had four ChD and 1 had five ChD. Most often self-reported the ChD in SCC+ group was hypothyroidism (18.03%, N=11) (Fig.) and that was the only disease where differences between SCC+ and SCC- groups were found (12.4% vs. 4.5%, p=.022). Both groups did not differ when compared by other self-reported diseases.

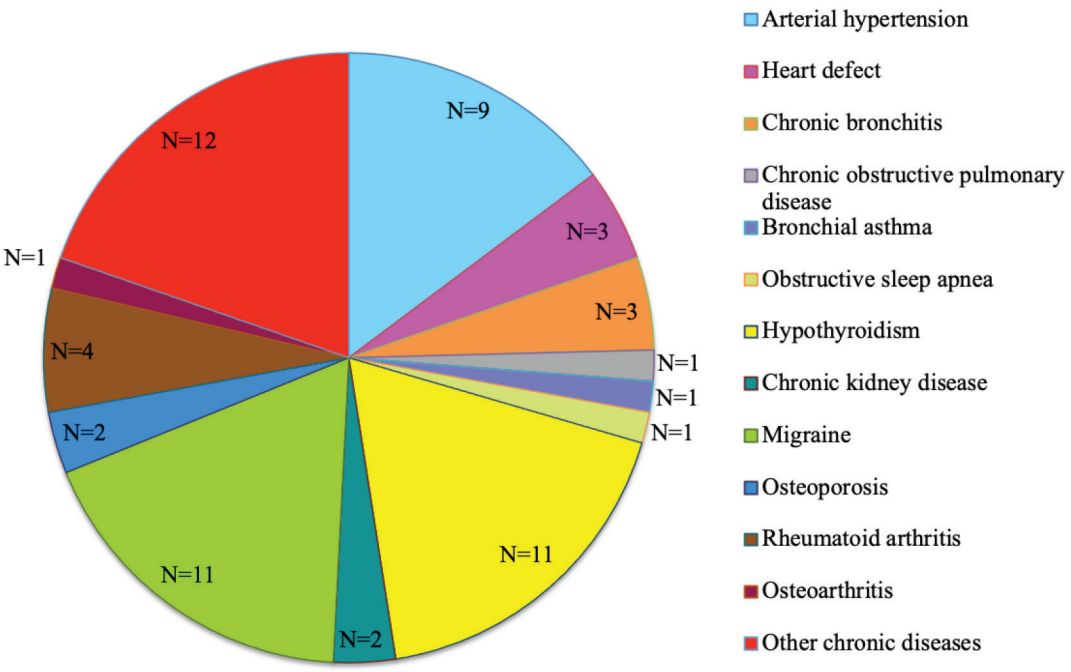

Fig. Distribution of chronic diseases among those with cognitive complaints

Conclusion. SCCs are related to hypothyroidism in middle-aged females.

Acknowledgements. The authors declare the absence if conflict of interest.

Genotype – phenotype associations in Charcot-Marie-Tooth disease

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Background. Charcot-Marie-Tooth (CMT) disease is the most common inherited neurological disorder and affects peripheral nervous system. Disease is caused by mutations in more than 80 genes and most patients have a "classical" CMT phenotype characterized by onset in the first two decades of life, distal weakness, sensory loss, foot deformities (*pes cavus* and hammer toes), and absent ankle reflexes. However, the frequency of these disease manifestations and the variability between CMT types is poorly understood.

Aim. The goal of the study was to evaluate clinical phenotype differences in three CMT subtypes – CMT1A, CMTX1 and other CMT type.

Methods. 21 CMT patients were enrolled in the study. Patients completed a sociodemographic questionnaire. Clinical severity was assessed using the Charcot-Marie-Tooth neuropathy score (CMTNSv2) and 6-minute walk distance (6MWD).

Results. In our study group, (n=21) the mean age was 37.3±12.5 years, there was a slight female predominance: 62% (n=13) were females, and 38% (n=8) were males. The majority of patients 42.9% (n=9) had CMT1A type, 23.8% (n=5) had CMTX1 type and 33.3% (n=7) had other CMT type. The mean age of first symptom development in CMTX1 type was 11.6±4.9 years, it was earlier in CMT1A patients (10.8±4.7 years), and later in other CMT type patients (12.4±6.5 years). CMTNSv2 revealed more severe clinical phenotype in CMTX1 type patients (21.2±7.6), in CMT1A group it was 14.2±3.8 and for other CMT types – 9.0±9.1, differences were statistically significant ($p<0.05$). The shortest 6MWD was in CMTX1 type group (326.0±114.6 m), it was 445.8±59.8 m in CMT1A group and 420.0±139.4 m in other CMT types, differences were statistically significant ($p<0.05$).

Conclusion. CMTX1 type patients had a significantly more severe clinical phenotype compared to CMT1A and other CMT type assessed by CMTNSv2 and 6MWD. Further characterising of the variability of disease severity between CMT types is important to increase genotype-phenotype association knowledge and improve our understanding of the prognosis of this disorder.

Sympathetic skin response in Kennedy disease patients

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Background. Spinal and bulbar muscular atrophy (SBMA), also known as Kennedy disease, is a rare X-linked neuromuscular disease, caused by a CAG repeat expansion >35CAGs in the exon 1 of the androgen receptor gene. SBMA classically manifests with lower-motor neuron symptoms. Patients commonly present with muscle cramps, tremor, leg weakness, dysarthria and dysphagia. Autonomic nervous system involvement in SBMA is not well studied nor fully known. Sympathetic skin response (SSR) is used in diagnosing the impairment of non-myelinated sympathetic fibres in peripheral neuropathies.

Aim. The aim of the study was to investigate the autonomic nervous system's involvement in SBMA by using sympathetic skin response test.

Methods. All Kennedy disease patients in Latvia (n=5) took part in this study – five unrelated Caucasian male patients. We deeply phenotyped all patients and carried out sympathetic skin response test as a non-invasive approach to investigate the sympathetic system, as well as nerve conduction studies.

Results. The study included all patients with Kennedy disease in Latvia (n=5) that were 34 to 68 years old. Neurological examination revealed typical manifestations of lower-motor neuron damage. Motor and sensory nerve conduction velocities and compound muscle action potentials and sensory action potential amplitudes were abnormal for two out of five patients indicating peripheral large nerve fibre neuropathy. All patients had complaints about sweating disturbances – 3 patients complained about increased sweating and 2 patients about decreased sweating. Sympathetic skin response test results indicated that three of five patients had peripheral sympathetic nervous system dysfunctions. All of those three patients demonstrated an increased latency and two of them also had a decreased amplitude during examination.

Conclusion. Our data supports the evidence that Kennedy disease is multisystemic disease with peripheral nervous system involvement, including sympathetic nervous system. However, our study group size was limited and bigger SBMA patient cohorts should be evaluated for autonomic nervous system involvement.

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A newly characterized *HPDL*-associated neurodegenerative disease: two cases representing the variability of clinical spectrum

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Background. Last year, a new neurodegenerative disorder was described by two international collaborator groups. An association has been revealed between loss-of-function variants affecting the *HPDL* gene and a variable phenotype ranging from neonatal encephalopathy to adolescent-onset spastic paraplegia.

Aim. Here we describe a new phenotype arising from mutations in the recently published disease-associated gene.

Methods. The patients were recruited in scientific research projects after clinical genetic testing failed to identify the cause of patients' clinical features. One patient was referred from Children's Clinical University Hospital (Latvia), and one from Centre Hospitalier du Quebec (Canada). The genetic testing performed in this project involved *duo* and *trio* whole exome/genome sequencing analysis.

Results. Case one. Three years old boy had burst suppression convulsions since birth, followed by demyelinating leukodystrophy and elevated lactic acid peak. Now he has severe global developmental delay and spasticity. Whole exome sequencing identified a homozygous variant c.1013T>C p. (Leu338Pro) in the *HPDL* gene (NM_032756.2).

Case two. A boy, 11 years old. First presented at 6 weeks of age due to hypertonia and seizures. Head MRI was done and the changes were attributed to hypoxic-ischemic encephalopathy. EEG showed mild focal epileptiform activity and he received treatment with valproic acid for one year. His further development was mildly delayed and he started walking at 18 months. At 4 years, increased clumsiness was noted. At 6 years, the gait progressively deteriorated and he was referred for further investigations. IQ result was 70. Neurological examination revealed spastic gait, hyperreflexia, polykinetic reflexes, intention tremor, dysarthria and intermittent enuresis, and he was diagnosed with hereditary spastic paraplegia. During next year he developed pronounced ataxia and tremor, and lost ambulation at the age of 7.5 years. Additional features are microcephaly and unilateral cryptorchidism. Whole genome sequencing revealed a homozygous variant c.599delG, (p.Gly200Alafs*4).

Conclusions. Our patients add to the 34 reported patients and represent the severe and intermediate range of the reported clinical spectrum. The function of the *HPDL*-encoded protein is yet unknown, however, it has been shown to be expressed in multiple tissues, including brain, and to localize in mitochondria. Notably, the mitochondrial dysfunction is well-known to have a wide range of clinical effects. It is likely that the characterization of the phenotype is not yet complete, as our patient two exhibits pronounced ataxia that has not been noted in the published cases.

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Blood serum HER2 as predictive marker for treatment effect assessment in patients with breast cancer undergoing neoadjuvant systemic treatment

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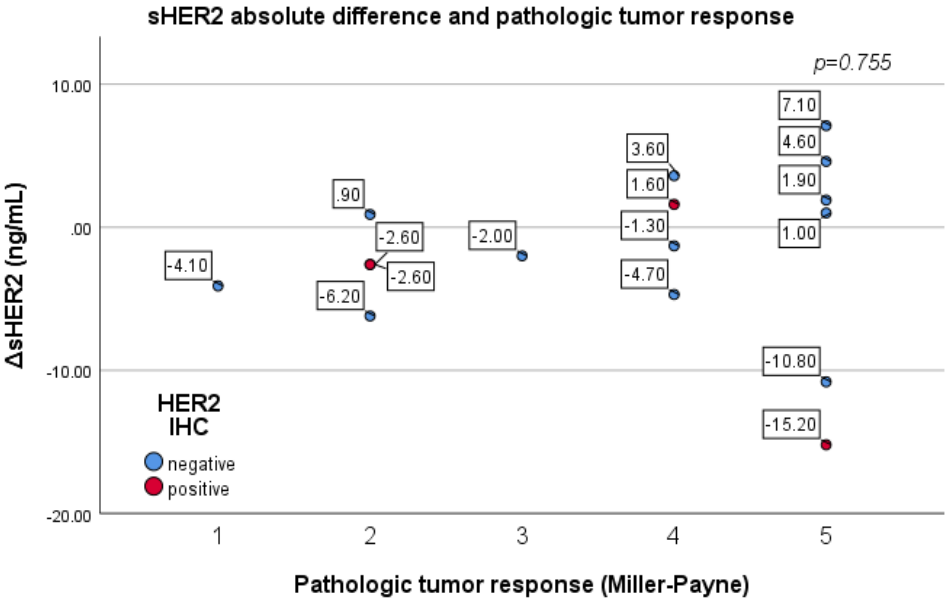
Background. About 20% breast carcinomas overexpress human epidermal growth factor receptor-2 (HER2) [1,2]. The extracellular domain of the HER2 protein can be detected in peripheral blood as serum HER2 (*sHER2*) [1,2]. A decrease in *sHER2* was associated with pathologic complete response, increased disease-free and overall survival [2]. Significant positive association between pCR and elevated *sHER2* levels, and a decrease of *sHER2* levels during NAT in HER2-positive, but not in HER2-negative breast cancer, was found [3,4]. Clinical relevance of *sHER2* is still unclear and being investigated [1].

Aim. Measure *sHER2* levels in non-metastatic breast cancer patients before NAT and before surgery; compare *sHER2* during NAT in HER2-positive and HER2-negative tumors; evaluate association of pathologic response with *sHER2* changes.

Methods. This is prospective observational single-centre cohort study. Before each NAT cycle patient's specimen of blood was tested for *sHER2* with chemiluminescence method (@Siemens). The cut-off value for *sHER2* was 15 ng/mL. Tumour biopsy specimen was analysed by immunohistochemistry (IHC) for HER2 expression. After the surgical treatment pathologic response was evaluated. Data was analysed with IBM SPSS26 software.

Results. Overall, 16 of 76 enrolled patients, all women (median age 46.0, range 32.0–63.0), underwent breast surgery after NAT from April 2020 till January 2021. Median baseline *sHER2* was 18.0 ng/mL [CI95% 18.0–32.3] in HER2-positive and slightly lower, 15.4 ng/mL [CI95% 19.4–20.8], in HER2-negative tumors (p=0.146). Median difference of *sHER2* before the first and the last courses of NAT was -2.6 ng/mL [CI95% -2.6–1.6] in HER-2 positive and -1.3 [CI95% 3.6–7.1] in HER2-negative tumors (p=0.439). pCR rates were 33% in HER2-positive and 38% in HER-2 negative tumors (p=0.696).



Conclusion.

No significant association was found between *sHER2* dynamics and pathologic tumor response. However, positive tendency found in the only HER2-positive patient with pCR.

No significant difference in baseline *sHER2* and its dynamics found between HER2-positive and HER2-negative tumors.

This innovative test was studied for the first time in Latvia. Study population was small and representes initial trends. Larger, better distributed groups of patients will show more precise data in the future.

I125 low-dose-rate brachytherapy in localized prostate cancer: preliminary results after 4 years

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Background. Prostatic brachytherapy by permanent implant of I125 is a therapeutic option in the treatment of organ-confined prostate cancer. We analyse preliminary results and complications after four years in the group of patients who received I125 low-dose-rate brachytherapy as the only intention-to-cure treatment and evaluate the differences with the standard treatment (surgery).

Aim. The evaluate results of I125 low-dose-rate brachytherapy treatment for localized prostate cancer.

Methods. The study group includes 69 patients enrolled between 2008 and 2011. The mean follow-up is 48 months. Biochemical failure was defined in accordance to the EAU criteria. Statistical survival analysis was carried out with the SPSS statistical software using the Kaplan Meyer method. Urinary and gastrointestinal complications were evaluated in accordance to the RTOG criteria.

Results. The mean age was 61 years (range 46–78 years). 100% of the patients presented a clinical stage < or =T2a with 97.2% of the cases having a PSA < or =10 ng/ml. Gleason score was < or =6 in 100% of the cases. All cases had a prostate volume <50 cc. Overall, 4-year survival was 100%, with a 100% disease-free survival and a 100% biochemical failure-free survival.

Conclusion. Low-dose brachytherapy offers good short-term cancer control in selected men with localized PCa. The further studies are needed for safety analyses and for comparison with other treatment modalities.

Evaluation of HER-2 serum concentration in breast cancer patients receiving neoadjuvant chemotherapy

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Background. Breast cancer is the most common cancer type in the world with incidence 47,8 per 100 000 of the population and the second leading cancer related mortality (*Globocan,* 2020). New diagnostic and prognostic methods should be investigated to improve early detection and survival of breast cancer patients. HER-2 (human epidermal factor 2) is protooncogene that is overexpressed in certain types of breast cancer and is used as biomarker and target of therapy. Commonly it is detected by immunohistochemistry performing tumour core biopsy.

Aim. The aim of the current study is to analyse HER-2 serum concentration in breast cancer patients and to conclude about serum HER-2 correlation with the stage of the disease and grade of the tumour.

Methods. A prospective study was conducted at the Pauls Stradiņš Clinical University Hospital Cancer clinic. HER-2 serum concentration was analysed in breast cancer patients receiving neoadjuvant chemotherapy. 20 breast cancer patients were selected, 10 patients with HER-2 positive and 10 patients with HER-2 negative breast cancer. Data analysis was performed using *SPSS 22.0* and *Microsoft Excel* programs. Nonparametric Spearman's correlations were used to determine correlation coefficient between HER-2 serum concentration and tumour grade and stage.

Results. The patients' age ranged 37 to 72 years. The median age was 46.5 years. 60% patients with HER-2 positive tumour had grade 2, 40% grade 3. 60% patients with HER-2 negative tumour had grade 3 and 40% grade 2. 60% patients with HER-2 positive tumour had stage III, 30% had stage II, 10% patients had stage I. 60% patients with HER-2 negative tumour had stage III, 40% had stage II. Statistically significant correlation between HER-2 serum concentration and tumour stage was not observed ($p=0.379$). Also, no correlation between serum HER-2 and tumour grade ($p=1$) was found.

Conclusion. Serum HER-2 does not correlate with grade and stage of the breast cancer in patients receiving neoadjuvant chemotherapy. More patients should be involved to evaluate HER-2 serum concentration changes and their role in monitoring the course of breast cancer.

Acknowledgements. The authors confirm the absence of conflict of interest.

Influencing factors that contribute to bone metastasis in breast cancer patients

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Background. Bones are the first site of metastasis for breast cancer patients. Bone metastasis is extremely common in women with breast cancer. Breast cancer cells can spread to any bone. The most common anatomical location are the spine, pelvis, ribs and long bones. Clinically it manifests with severe pain, pathologic fractures and spinal cord compression.

Aim. To find out the factors that influence development of bone metastasis in breast cancer patients.

Methods. The study is retrospective, including 25 patients. Data were collected from Pauls Stradiņš Clinical University Hospital, Department of Oncology archive and patient cards. All patients have been diagnosed with breast cancer with bone metastases. The following data were collected: age at diagnosis, stage, TNM classification, breast cancer grade, histological types of breast cancer, breast sector resection or mastectomy was performed, adjuvant or neoadjuvant radiotherapy, location of bone metastases, time when bone metastases were diagnosed, prescribed drug therapy, time when the palliative radiotherapy was launched, the gray (Gy) therapy dose and fractions, alkaline phosphatase before and after pain relief radiotherapy. Analysis was performed using *IBM SPSS Statistics* version 25.0 software.

Results. Among 25 patients who had breast cancer with bone metastases, the average age is 54 years. The youngest patient was 28 years old, while the oldest – 74 years old. 6 patients who were diagnosed with bone metastasis had Stage IV (24%), 5 patients Stage IIIB (20%), 4 patients Stage IIIA (16%), 3 patients Stage IB (12%), 3 patients Stage IIA (3%). Among 25 patients Grade 2 had 14 patients (56.0%), Grade 3–9 patients (36.0%) and Grade 1–2 patients (8.0%). The average time when breast cancer was diagnosed until bone metastasis with Grade 2 – 54.38 months, Grade 3 – 30.08 months, but Grade 1 – 12.3 months. Statistically significant differences were found between Grade 1, 2, 3 and the time from diagnosis to metastasis ($p = 0.049$).

Conclusion. The most frequent stage in patients with bone metastasis is Stage IV and Stage IIIB. Both stages describe invasive breast cancer that has spread beyond the breast and nearby lymph nodes. Grade 2 patients have a longer time from diagnosis to metastasis than those of Grade 1 and 3.

Effectiveness of breast cancer screening in women: case of Latvia

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Background. Breast cancer is the most frequently diagnosed oncological disease in women in Latvia. It is often detected at an advanced stage hampering the effectiveness of treatment and reducing life expectancy. In 2009, a state-funded breast cancer screening was introduced in Latvia for women aged between 50-69. This study seeks to assess the effectiveness of breast cancer screening by analysing changes in two critical measurements: women attendance rate and breast cancer stage in the detection moment between 2010 and 2017/2019.

Aim. The aim of the current study is to:

- assess attendance of women at breast cancer screening in Latvia;
- analyse, what impact had introduction of breast cancer screening on the early detection of breast cancer in women in Latvia.

Methods. Statistical data of the Latvian Centre for Disease Prevention and Control (LCDPC) on attendance of women at the state-funded breast cancer screening from 2010 to 2019 and statistical data of LCDPC on the stages of breast cancer diagnosed from 2010 to 2017 were used for statistical analysis.

Results. From 2010 to 2019, between 130 205 as minimum (2012) and 196 578 as maximum (2010) screening invitations were sent to women. In other research years, on average 140 000 invitations were sent annually. Between 2010 and 2019, women attendance fluctuated between 38 148 as minimum (2010), i.e., 19.4% of all sent invitations and 62 455 as maximum (2017), i.e., 44%. From 2017 to 2019, attendance reached its highest rate 44–39% respectively. In none of the years, attendance reached 50% of the sent invitations.

From 2010 to 2017, the lowest percentage of stage I, II breast cancer was detected in 2011, i.e., 61.7% (741) of all cancer cases, the highest was in 2017, i.e., 67.7% (767). From 2015 to 2017, the percentage increased annually from 61.8% (729) to 67.7% (767) respectively. The highest percentage of stage III, IV was detected in 2013, i.e., 33% (348), the lowest in 2017 (314), i.e., 27.7%. From 2015 to 2017, percentage decreased annually from 31.5% (472) to 27.7 (314) respectively. In addition, between 2013 and 2017, the number of stage III cases were decreasing annually (from 269 to 204 respectively).

Conclusion. The attendance of breast cancer screening by women in Latvia is low, and lags behind the EU recommendations (70–75% attendance). Screening has shown its effectiveness for the early detection of breast cancer. Promotion of attendance can further facilitate early detection of cancer in larger number of women.

Structural changes in retina after cataract surgery in patients with type 2 diabetes mellitus using optical coherence tomography angiography

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Background. Optical coherence tomography angiography (OCTA) is a relatively new non-invasive diagnostic device mostly used in ophthalmology to diagnose vascular abnormalities. Studies investigating exact parameters that can be obtained using this device in patients after cataract surgery and diabetes are scarce.

Aim. To evaluate changes in retinal structures – diabetic maculopathy, changes in central retinal thickness, foveolar avascular zone (FAZ) enlargement and vascular density (VD) reduction – after phacoemulsification cataract surgery among patients with type 2 diabetes mellitus (T2DM).

Methods. A longitudinal prospective study was held in Pauls Stradiņš Clinical University Hospital from October 2020 to December 2020. All participants included in the study underwent OCTA with *Optovue AngioVueHD (USA) device.* Individual 3x3 mm^2 and 6x6mm^2 OCTA images of the superficial and deep layer were obtained at baseline and one month after cataract surgery. Automated measurements of FAZ, VD parafoveal density, and perifoveal density were analysed. A *Wilcoxon signed-rank* test was used to compare measures in two time-points. Statistical significance of $p<0.05$ was considered for this study.

Results. A total of 12 eyes from 12 patients (83.3% women, 16.7% men) with type 2 diabetes mellitus followed up for 1 month. Median duration T2DM was 20.00; interquartile range (IQR) 11.25–21.75 years. Median duration of insulin use was 7.00; IQR 2.50–10.00 years. Median metabolic compensation of diabetes was 8.50; IQR 7.09–9.3%. There were no statistically significant differences in FAZ before and after cataract surgery (mean (M)=0.40, standard deviation (SD)=10mm^2 and M=50, SD=0.92mm^2, respectively, p=0.43). FAZ perimeter did not differ at two time points (M=2.58, SD=0.38 mm before and M=2.65, SD=0.42 mm after cataract surgery, p=0.31). No differences were observed in perifoveal density (M=40.90, SD=5.65µm before and M=39.42, SD=5.40µm after cataract surgery, p=0.38). In parafoveal density the difference was not significant at 0.05 level, but significant in 0.1 level which is acceptable considering a small sample size (M=41.27, SD=5.04% before and M=38.20, SD=7.52% after cataract surgery, p=0.07).

Conclusion. Larger sample size and longer research are necessary to observe the difference before and after cataract surgery in most of parameters.

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Comorbidity in type 2 diabetes in persons exposed to ionizing radiation

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Background. In comorbidity, type 2 diabetes mellitus (DM) is of clinical interest due to the increasing frequency of this pathology and the systemic nature of organ damage. The main studies of comorbidity in type 2 DM were carried out in patients with traditional FR: lifestyle, heredity, without affecting professional, environmental factors.

Aim. To study the structure of comorbid pathology in patients with type 2 diabetes, exposed to ionizing radiation.

Methods. The prospective study included 57 patients with type 2 diabetes (50 men, 7 women), the mean age – 60.9±5.8 years, including 38 patients exposed to ionizing radiation in the Semipalatinsk nuclear test site, 19 – liquidators of the Chernobyl accident. All the subjects underwent a comprehensive clinical and instrumental, laboratory examination: Holter monitoring of ECG, EchoCG, ABPM, USDG of brain vessels, limb vessels, U/S, FGDs; according to indications – CAG, EP heart test, head MRI.

Results. A high prevalence of metabolic syndrome was found in 43 (75.4%) patients. The structure of comorbidity was dominated by cerebrovascular diseases in the form of dyscirculatory encephalopathy (II–III-degree) in 50 (87.7%) patients and peripheral polyneuropathy in 55 (96.5%). The following finding was a cardiovascular pathology: hypertension was in 40 (70.2%) patients, CHD was observed in 19 (33.3%), MI occurred in 5 (7.0%) cases, 9.1% of patients had CHF II-III FC. A few patients had various arrhythmias: 5 (8.8%) patients had AF, 22 (38.6%) had high-grade PVCs, and 4 (7.2%) patients had II–III-degree AV block. 40 (70.2%) patients had gastrointestinal diseases, including 25 (43.8%) chronic cholecystitis and pancreatitis, fatty liver disease in 7 (12.3%), and 8 (14.0%) patients with GERD. Joint pathology in the form of polyosteoarthritis was observed in 59.6% of patients. Diseases of the urinary system were in 33 (57.9%) patients, while 36.8% were diagnosed with CKD. The pathology of the bronchopulmonary system was represented by chronic bronchitis (31.6%) and COPD (5.3%).

Conclusion. Analysis of comorbidity in patients with type 2 diabetes exposed to ecological, technogenic, professional and superstress factors revealed a complex structure of association of this pathology with a number of cerebrovascular, cardiovascular diseases, and lesions of gastrointestinal tract and urinary system, including CKD as a prognostically unfavourable complication of diabetes. The close association of type 2 diabetes with these diseases requires a comprehensive approach to diagnosis, selection of therapy, and rehabilitation measures in this cohort of patients.

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Assessing the impact of supervised interval training on cardiovascular autonomic status in type 2 diabetes patients

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Background. Cardiac autonomic neuropathy (CAN) is a serious complication of diabetes mellitus (DM) that is strongly associated with increased risk of cardiovascular mortality. The significance of CAN has not been fully appreciated. Treatment of CAN includes physical activity.

Aim. To detect CAN status and measure the influence of physical activity on the autonomic nervous system using cardiovascular autonomic reflex tests (CARTs).

Methods. The study included 51 patients with type 2 diabetes: 30 were allocated to the control group (Con, n=30) and the rest to the interval training (IT, n=21) group. IT group exercised 3 times a week for 60 minutes for 4 months, using a mobile device application. CAN was assessed on tilt table testing using 5 CARTs proposed by Ewing et al. (1985): parasympathetic function: heart rate (HR) response to the Valsalva manoeuvre (Valsalva ratio), HR response to deep breathing (E/I ratio) and HR response to standing (30 s/15 s ratio). Sympathetic function was measured by blood pressure (BP) responses to lying & standing, as well as BP response to a sustained handgrip. Each test was assessed with a score of 0 for normal, 0.5 for borderline, and 1 for an abnormal result. Patients who had Ewing score ⩾2 were classified as CAN positive.

Results. At baseline, CAN was detected in 33 (65%) patients. Ewing score in the CAN positive patients was 2.61±0.74 and in CAN negative patients 1.08±0.58. Probability of CAN before and after the intervention was 0.65 (95%CI-0.38, 0.85) and 0.48 (0.22, 0.76) in the control group and 0.80 (0.48, 0.94) and 0.58 (0.27, 0.84) in the IT group. After the intervention between group (Con versus IT) change in CARTs and Ewing score was: Valsalva ratio 1.13 to 1.17 mm versus 1.12 to 1.25 mm (p=0.091); E/L ratio 12.85 to 12.51 mm versus 13.09 to 12.88 mm (p=0.902); 30s/15s ratio 1.04 to 1.06 mm versus 1.03 to 1.09 mm (p=0.233); BP response to lying & standing 8.69 to 9.45 mmHg versus 11.91 to 15.54 mmHg (p=0.420); BP response to handgrip 25.03 to 26.30 mmHg versus 26.76 to 22.70 mmHg (p=0.268); Ewing score 1.94 to 1.69 versus 2.04 to 1.74 (p=0.885).

Conclusion. CAN is a common complication of diabetes that often goes unrecognized. Physical activities can improve autonomic status.

Therapeutic opportunities to reduce the symptoms of premenstrual syndrome in women aged 20 to 30 years

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Background. One of the most common problems affecting quality of life for women of reproductive age is premenstrual syndrome (PMS). It is therefore important to inform both women and medical practitioners about the course of this syndrome, symptoms and the principles of possible treatment. Emotional and physical symptoms usually appear several days before menstruation and disappear as they begin. The severity of symptoms differs among women in different age groups. Most women have mild to moderate symptoms, but a small number of women experience severe symptoms. In the case of mild symptoms, women tend to use non-pharmacological therapy, such as rest, physical activity, meditation, etc. However, when experiencing moderate and severe symptoms women use pharmacotherapy.

Aim. The aim of this study is to determine the prevalence of PMS in Latvia among women aged 20 to 30 years, as well as the therapy chosen by women to reduce the PMS symptoms.

Methods. The study included an electronic questionnaire of 20 questions on PMS symptoms, the first choice of therapy and the effectiveness of the therapy. The survey involved 118 women from different regions of Latvia aged 20 to 30 years.

Results.

1) Of all women who participated in the survey, 89.8% admitted that they experience PMS symptoms.

2) The most common symptoms that women noted were increased emotionality, changes in breast tenderness, gastrointestinal disorders, back pain and headaches.

3) 55% of the surveyed women who experience PMS symptoms indicated that the symptoms make daily lives difficult, while 20% of women reached out to medical professionals for help.

4) 32.1% of women use therapy to reduce the PMS symptoms which 5.9% noted that the therapy they chose was ineffective.

5) The most common type of therapy is analgesics such as Ibuprofen, while some women choose to also use spasmolytic and homeopathic therapy.

Conclusion.

1. Despite the fact that most women have PMS symptoms that interfere with their daily life, they do not seek professional help, which indicates the lack of information provided to women about this syndrome.

2. If women have symptoms that interfere with their daily life, they should consult a doctor to consider an adequate treatment to reduce the symptoms.

3. Although some of the women surveyed note that they have emotional state changes, none of them reported using antidepressants, which in some cases are the treatment of choice.

Prevalence of menstrual migraine in Latvia among women aged 20 to 35 years

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Background. Nowadays, people most frequently complain of headaches caused by migraine, which are defined as one of the most frequent neurological disorders. Migraine headaches are more common in women, since approximately 50% of cases are closely related to hormonal changes during menstrual cycle. Menstrual migraines are headaches that occur two days before or first three days during menstruation due to changes in oestrogen levels. Menstrual migraines can appear with (MA) or without (MO) aura. Menstrual migraines without aura are more common in women. Menstrual migraine therapy is no different from any other type of migraine, most often using triptans and hormonal therapy.

Aim. The aim of the study is to investigate the prevalence of menstrual migraine in Latvia among women aged 20 to 35 years and the most common type of menstrual migraine (with or without aura), as well as to identify treatment chosen by women to reduce its symptoms.

Methods. The study included an electronic questionnaire with 21 questions on menstrual migraine – its type and first choice of therapy. The survey involved 144 women from different regions of Latvia aged between 20 and 35 years.

Results.

1) 42.4% of women surveyed experience severe headaches shortly before and during menstruations.

2) 76.6% of women experience menstrual migraines without aura, while 23.4% – with aura.

3) 74.2% of women who have menstrual migraine use prescribed medications to reduce the severity of headaches.

4) Medications, most often used by women surveyed, are non-steroidal anti-inflammatory drugs.

5) Only 19.5% of women, who use pharmacotherapy, use triptan group medications, which is the appropriate therapy for migraines.

Conclusion.

Menstrual migraine headaches should be distinguished from other types of headaches because without adequate treatment they can become chronic and affect the quality of life of a woman.

Menstrual migraines in women aged 20 to 35 years most often occur without an aura.

Only 1/5 of women surveyed in the study who have been diagnosed with menstrual migraine use adequate therapy.

Women should be informed about the specificity of menstrual migraine headaches and the need for adequate treatment.

Tick-borne encephalitis in children treated in Kaunas Hospital during 2012–2019

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Background. Lithuania has the highest tick-borne encephalitis (TBE) rate in Europe. Even though TBE incidence in children is lower, it may still cause long-term consequences. Therefore, it is essential to further investigate its clinical and epidemiological characteristics in children.

Aim. To evaluate epidemiological and clinical characteristics of children with TBE.

Methods. We performed a retrospective analysis of 87 cases of children with confirmed TBE who were hospitalized in Kaunas Hospital of the Lithuanian University of Health Sciences from 2012 to 2019. Each case of TBE was identified with neurological symptoms and positive serological tests.

Results. 87 children (55.2% male, 44.8% female) aged from 1 to 17 years old were involved in this study. Around half of them (50.6%) reported having a tick bite, while 6.9% stated having exposure to unpasteurized milk. Incubation period varied between 1 to 60 days (19 days on average) in case of a known tick bite. Biphasic course of the disease occurred in 70.1% of the cases with an average of 13 days (5 to 25 days) between the two phases. The most common clinical symptoms were headache (100%, N=87), nausea (85.1%, N=74), vomiting (78.2%, N=68), drowsiness (67.8%, N=59) and general weakness (66.7%, N=58). Meningeal symptoms were present in 93.1% of the cases and 93.1% of the children had at least one focal neurological sign (tremor 82.3%, impaired balance 73.6%). Isolated meningitis was diagnosed in 57.5%, meningoencephalitis – in 41.4% and meningoencephalomyelitis in 1.1% of the cases. Majority of younger children (1–8 years old) had meningitis (77.3%) while 49.2% of older children (9–17 years old) had more severe forms of TBE. Pleocytosis was found in 94.3% of cases (average WBC count – 111.7 per µL, protein – 0.5 g/l). Duration of the symptomatic disease lasted for approximately 12 days. Early residual signs were observed in 75.9% of all cases. Most commonly they included tremor of the tongue, eyelids and fingers, asthenia, headache, balance or coordination disorders, and fatigue.

Conclusion. Only a half of the subjects reported having a tick bite. Younger children tend to suffer from moderate to severe forms of TBE less frequently than older ones. The majority of children had residual signs of TBE upon discharge from the hospital, which shows the need for them to be followed up.

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Detection of SARS-CoV-2 virus in saliva samples: lateral flow immunoassay prototype development

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Background. Global SARS-CoV-2 pandemic confirms the importance of diagnostic testing in preventing the transmission of the infection. Although RT-PCR is the gold standard in SARS-CoV-2 diagnostics and can detect low viral loads, the use of rapid tests can be beneficial for high-throughput screening, for example, in hospitals and airports.

Aim. This study was aimed to develop lateral flow assay (LFA)-based test prototype for the qualitative detection of SARS-CoV-2 proteins in saliva samples.

Methods. Polyclonal antibodies (PAbs) were produced by mice immunization with recombinant receptor-binding domain (RBD) of SARS-CoV-2 spike protein. An indirect ELISA was performed to determine antibody titre. The anti-RBD PAbs and commercial antibodies directed against different SARS-CoV-2 spike protein epitopes were used as capture or detection antibodies for sandwich ELISA, while the entire spike ectodomain was used as the antigen. Based on the spectrophotometric results, antibody pairs for antigen detection were identified and tested in LFA format. The LFA concept for selected antibody combinations was evaluated using artificial antigen spiked into blank saliva samples from healthy volunteers and saliva samples from individuals (n=10) with SARS-CoV-2 symptoms 3–5 days before sample collection. The performance of LFA was compared to an in-house RT-PCR reference method.

Results. Of the various antibody combinations tested, 6 antibody pairs produced an intensive signal ($A \geqslant 1.5$) and were selected for the LFA assay. The optimal detection antibody and capture antibody titres in sandwich ELISA were 1:1000 and 1:5000, respectively. The lowest detectable antigen concentration ranged from 0.16–1.25 µg/mL. The LFA prototype comprised dual labelled antibodies to ensure antibody-antigen complex binding to the test strip and visualization of the result. The developed assay exhibited acceptable sensitivity in the saliva samples obtained from patients in the acute phase of infection. Moreover, the result was obtained within 30 minutes without the introduction of laboratory equipment for sample preparation, analysis, and result interpretation.

Conclusion. After passing the validation procedure, the LFA prototype developed in this study has the potential to be applied in screening programs for rapid detection of SARS-CoV-2 in acute patients with high viral loads. The advantage of this assay is the use of easy-to-collect saliva as a testing material.

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Characteristics of patients with hepatitis C and distribution of viral genotypes in Lithuania

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Background. In 2016, the World Health Assembly passed a resolution to eliminate hepatitis C as a public health threat by 2030. Effective drugs are now available; however, most patients remain unaware of the hepatitis C virus (HCV) infection, which may be recognized only in the late stages when the complications have occurred. Different virus genotypes may affect the pathobiology of disease. Thus, identifying patients at high risk of HCV infection and ensure proper treatment is a health care challenge.

Aim. This study aimed to evaluate the characteristics of patients with hepatitis C and HCV genotype distribution in Lithuania.

Methods. The study was carried out in three hospitals, which are the inpatient and outpatient centres consulting and treating the patients with HCV infection. All patients who attended a routine visit at each hospital within 6 months and fulfilled the selection criteria (diagnosis of chronic HCV infection confirmed with a positive HCV-RNA test, defined HCV genotype and age ⩾18 years) were selected. Altogether, 201 patients (51.7% men and 48.3% women) were involved in the study. Information was collected from patient's medical documentation and include demographic data, alcohol consumption and substance use, suspected mode of infection, duration of HCV infection, genotype, liver fibrosis stage, and hepatocellular carcinoma status.

Results. One (0,5%) patient was an active drug user and 10 (5%) were former drug users. Alcohol was consumed by 30 (14.9%) patients. The main suspected route of HCV transmission was blood transfusion (26.4%). Injection drug use was recorded by 5% of patients. The highest proportion (38.8%) of patients was with a disease duration of 3 years or less. Almost every fifth patient (19.4%) had diseases duration of 10 years or more. Fibrosis grade 4 (liver cirrhosis) was diagnosed in 30.1% of patients and fibrosis grade 3 – in 24.9%. Hepatocellular carcinoma was found in 4 (2%) patients. Genotype 1 was most common, accounting for 69.7% of all infections, followed by genotype 3 (22.4%). Genotype 2 was found in 5% and mixed genotypes – in 3% of patients. Subtype 1b accounted for 74.3% of all genotype 1 infections.

Conclusion. Genotype 1 is the most common HCV genotype in Lithuania. In contrast to Western countries, intravenous drug use was not the main mode of transmission of the infection. A high proportion of fibrosis grade 3 and 4 indicates the need for screening for this latent infection in the general population, especially in risk groups.

Correlation between the production of specific antibodies against Borrelia burgdorferi and particular HLA genotypes

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Background. A small subset of patients infected with *Borrelia burgdorferi (Bb)* does not produce *Bb* specific antibody. Our research provides additional evidence of a genetic predisposition for seronegativity in some individuals with Lyme disease.

Aim. The aim of the current study was evaluation of associations between the production of specific antibodies against *Borrelia burgdorferi* and particular HLA class II.

Methods. The study included 204 patients with an established diagnosis of Lyme borreliosis (LB) and 282 healthy (control) people. The LB diagnosis was confirmed clinically, serology was tested and imposed in the Infectology Center of Latvia. Tests of *Bb*-specific immunoglobulin G (IgG) and IgM antibodies were performed using *Bb* IgG/IgM Enzyme-Linked Immunosorbent Assay (ELISA) and *Bb* IgG/IgM Westernblot test (WB) (Siemens, Germany), according to the manufacturer's instructions. HLA genotyping was performed by PCR with sequence-specific primers (PCR–SSP) in the Riga Stradiņš University, Laboratory of Clinical Immunology and Immunogenetics.

Results. The study revealed a statistically significant relationship in the production of specific IgG antibodies in carriers of the *DRB1*07* allele ($p< 0.001$). Moreover, a high level of antibodies (from 165U/ml to 255U/ml) was observed starting from the second week and remains until the sixth. There were also significant differences ($p <0.001$) for *DRB1*04, DRB1*17(03), DRB1*15(02),* but the IgG level was not as high as of carriers of the *DRB1*07* allele. No statistically significant associations in the production of antibodies with the *-DQB1*, *-DQA1* loci were found. We analyzed an IgM seronegative group (IgMab-) separately from IgM seropositive group (IgMab+) to detect allelic correlations. Out of 204 patients, 18 were IgM negative (8.8%; 95% CI 5.5-13.3%), all of those patients had an active phase of the disease, analyses were performed in the period from second to fourth week. At the same time, all 18 patients had IgG antibodies in low titers (from 78U/ml to 100 U/ml). Study showed differences between IgMab- and IgMab+ LB patients for the following alleles: *HLA-DRB1*01* (IgMab- 27.7%, IgMab+ 9,9%; $p= 0.002$), *-DQA1*0301* (IgMab- 50%, IgMab+ 22.6%; $p= 0.017$), *-DQB1*0502-4* (IgMab- 33.3%, IgMab+ 11.3%; $p= 0.011$), *-DQB1*0602-8* (IgMab- 44.4%, IgMab+ 19.4%; $p= 0.020$).

Conclusion. A high level of *Borrelia burgdorferi* specific IgG antibodies statistically significantly correlates with *HLA-DRB1*07* in LB group.

Acknowledgements. The authors declare that they have no competing interests.

CARDIOVASCULAR MEDICINE

The impact of the left atrium appendage volume and morphology found in computed tomography on characteristics of P wave morphology in electrocardiogram

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Background. Electrocardiography is a gold standard test for patients with any type of heart disorder, graphically visualising electrical activity of the heart by voltage versus time. Multi-slice cardiac computed tomography (CT) scan is more specific for anatomical and volume evaluation of the heart and requires specifically educated personnel to be performed. This study was performed as a multidimensional approach to connection between left atrium appendage (LAA) anatomical variations and electrical activity in the left atrium, demonstrated by electrocardiogram (ECG) P wave.

Aim. The aim of the study was to find statistically significant correlations between LAA morphology and volume found in cardiac CT in relation to ECG P wave characteristics in high coronary risk patients.

Methods. The retrospective study included 145 patients, all of them were hospitalized for surgical treatment of peripheral artery disease. Data were collected from perioperatively made medical tests. Cardiac multi-slice CT scan analysis was performed by making 3D reconstruction models of the left atrium and analysing the volume and morphology of the LAA. The IBM SPSS was used for statistical analysis.

Results. The mean age of patients was 66.9 years (SD=7.9), 75.2% (109) were men. The distribution of the LAA morphologies was chicken wing (65.5%), cactus (17.9%), cauliflower (13.1%) and windsock (3.4%). The mean LAA volume was 12.1 ml (SD=4.8), and distribution of the LAA mean volume among morphology groups was chicken wing 12.2 ml (SD=5.1), cactus 12.1 ml (SD=4.4), cauliflower 12.9 ml (SD=3.5) and windsock 6.5 ml (SD=2.2).

No statistically significant differences of ECG P wave duration (p=0.956), amplitude (p=0.860) and axis (p=0.127) among LAA morphology groups. The morphology of the ECG P wave found in lead V1 showed no statistically significant differences among LAA morphology groups (p=0.105), there was not found any association between LAA morphology and P wave notching in lead II (p=0.082).

There was not identified any statistically significant correlation between LAA volume and ECG P wave duration (p=0.634), P wave amplitude (p=0.659) and P wave axis (p=0.894). The distribution of LAA volume showed no statistically significant differences among P wave notching groups in lead II (p=0.747) and P wave morphology in lead V1 (p=0.589).

Conclusion. The morphology and volume parameters of the LAA showed no statistically significant impact on the ECG P wave characteristics.

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Survival of patients after myocardial revascularization for coronary heart disease

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Background. The choice of the optimal tactics for the treatment of coronary heart disease has remained an urgent issue for many years. The choice of revascularization strategy is influenced by the continuous development of pharmacology and invasive techniques. According to the results of various studies, it has been shown that coronary artery bypass grafting (CABG) has advantages for patients with multivessel coronary artery disease. To date, there are few studies that show long-term patient survival for more than 7–8 years. In most studies, the observation period is 5 years or less.

Aim. To analyse the survival rate of patients who underwent myocardial revascularization by stenting of the coronary arteries and coronary bypass grafting in the conditions of the city cardiological center in Almaty, Republic of Kazakhstan.

Methods. Statistical processing of the database of patients of the Almaty City Clinical Center, who underwent treatment in the period from 2012 to 2017 was carried out. The statistical analysis was implemented using the software *IBM SPSS Statistics*, *Microsoft Office 2019*.

Results. In total, 989 patients underwent treatment during the presented period. Of these, myocardial revascularization by stenting of the coronary arteries was performed in 853 patients (86.24%), and myocardial revascularization by CABG was performed in 136 patients (13.75%).

- The minimum age of patients in the PCI (Percutaneous coronary intervention) group was 28 years, the maximum – 92 years. Average age – 61.52 years; men – 58.92 years; women – 68.01 years;
- The minimum age of patients in the CABG group was 44 years, the maximum – 84 years. Average age – 63.71 years; men – 62.30 years; women – 68.93 years;
- The survival rate of patients after PCI for 8 years was 65.2%. The average survival time is 85.53 months. (CI 83.27–87.69). The maximum observation time of patients was 103 months.
- The survival rate of patients after CABG for 8 years was 50.9%. The average survival time is 71.25 months. (CI 64.25 - 78.25). The maximum observation time of patients was 103 months.

Conclusion. Presumably, the survival rates obtained in our study can be associated with a number of reasons, for example, urgent revascularization due to the development of myocardial infarction, the lack of proper cardiological rehabilitation both at the stage of inpatient treatment and at the level of primary health care.

The role of intraoperative 2D foot perfusion during percutaneous infrainguinal angioplasty in patients with critical limb ischemia

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Background. Critical limb ischemia (CLI) is an end stage of peripheral arterial disease. Percutaneous transluminal angioplasty (PTA) has gained a mainstream position in treatment of CLI. Frequently, multilevel hemodynamically significant atherosclerotic lesions are detected during PTA in patients with CLI. Therefore, intraoperative decision of intervention level and amount has to be undertaken based on macrovascular images acquired during intraoperative digital subtraction angiography (DSA) analysed by eye. Intraoperative 2D foot perfusion angiography (2DFPA) is a novel post-processing tool integrated in newest generation DSA equipment. It offers an objective quantitative analysis of different flow and contrast density parameters within region of interest (ROI). Consequently, it might become an additional objective intraoperative tool in estimation of operation volume.

Aim. To establish basic protocol for 2DFPA in Riga East University Hospital and perform pilot evaluation of the parameters acquired during 2DFPA.

Methods. In this case, the control study performed during June to November of 2020, and included 7 patients with CLI and intraoperative 2DFPA. 2DFPA performed through antegrade 6F 23 cm sheath in superficial femoral artery with automated injection volume/rate 15 ml/6 ml/s and fixed position of the foot during procedure. Following pre-intervention and post-intervention perfusion parameters analysed in whole foot ROI: arrival time (AT), time-to-peak (TTP), area under the curve (AuC), peak density (PD);

Results. The mean age – 71.5 (54–85) years, 4 males, 3 females. CLI Rutherford class V in all patients. One patient excluded due to foot movements during procedure and noncomparable 2DFPA results. 3 patients underwent PTA of superficial femoral artery, 3 patients – infrageniculate PTA. In 4 PTA procedures defined by operator as successful based on DSA, the following 2DFPA parameters were acquired: decrease of AT and TTP, and increase of PD and AuC was found corresponding with good technical result. 2DFPA showed no improvement of parameters in one PTA defined by operator as successful and in one PTA defined by operator as not successful.

Conclusion. 2DFPA is an easy and safe intraoperative analysis tool to be applied, although adaptation of protocol and patient positioning is required. Acquisition of intraoperative perfusion parameters pre- and post-treatment might serve as a marker for operation volume, if the desired perfusion goals are not achieved. Following larger scale trials have to be conducted to establish specific perfusion value ranges as treatment end-points.

The role of Transcranial Doppler sonography for neuromonitoring in cardiac surgery with cardiopulmonary bypass

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Background. In patients undergoing cardiac surgery with cardiopulmonary bypass (CPB), blood pressure (BP) excursions outside the limits of cerebral autoregulation are associated with organ and brain dysfunction. The use of TCD has been reported in intraoperative monitoring of cerebral blood flow and air emboli by providing instant visual feedback. Individualized mean arterial pressure (MAP) management targeted to optimize cerebral autoregulation by TCD might provide a more neuroprotective approach to patient care during CPB than standardized BP management.

Aim. The study aimed to analyse MAP excursions during non-pulsatile CPB effects on cerebral blood flow parameters and primary postoperative outcomes. As well as identify possible other factors affecting TCD.

Methods. 50 elective cardiac surgeries with CBP performed in a University Clinical Hospital. The right and left middle cerebral artery blood flow velocity was assessed using TCD and analysed for spectrum.

Measurement intervals: after anaesthesia induction, 15 minutes after aortic cross-clamping, and 15 minutes after CBP. The average pulsatility index (PI), time-averaged peak velocity (TAPV), resistance index (RI), end-diastolic velocity (EDV), peak systolic velocity (PSV) were recorded and compared.

Results and discussion. A total of 50 patients were included. The mean age 64.76 (42–81) years; CPB 101.14 (54–184) minutes; Ejection fraction 52.50 (20–72); Body mass index 29.08 (19.48–44.41);

Diabetes occurred in 38 patients; Pulmonary arterial hypertension (PAH) I occurred in 18 patients, 21 patients – PAH II;

Blood transfusions were performed in 22 patients; Catecholamines was required in 21 patients;

Patients who stayed longer in the ICU had more comorbidities – nine patients stayed in the ICU for 9–65 days (median 4.64).

MAP during CPB was 66.18 (50–80).

The blood transfusion rate showed no significant differences.

Hematocrit was decreased postoperatively (mean 29) compared to preoperative values (mean 37.7); during CPB 25.6.

CPB during cardiac surgery has been demonstrated to cause alterations of the cerebral blood flow.

RI was affected by gender ($p=0.08$), type of operation ($p=0.09$) and CHF ($p=0.08$);

PI was affected by gender ($p=0.02$), diabetes ($p=0.06$) and PAH ($p=0.02$);

PSV was affected by presence of diabetes ($p=0.04$), PAH ($p=0.006$), heart rate ($p=0.04$), TAPV ($p=0.05$);

Conclusion. TCD method can be considered for multimodal neuromonitoring in cardiac surgery.

TCD can be a useful guiding instrument for adequate hemodynamic parameters, confirming the adequacy of cerebral perfusion strategy or the need for its optimization.

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Evaluation of STEMI caused by the atherosclerotic disorder of the specific coronary artery

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Background. ST-elevation myocardial infarction (STEMI) is an acute condition best treated by percutaneous coronary artery (CA) intervention. This retrospective study attempted to assess the association between STEMI caused by CA and disease risk factors, studies conducted and treatment data.

Aim. To evaluate the connections between CA and of STEMI – experienced patients' data of those admitted to the Lithuanian University of Health Sciences Department of Cardiology.

Methods. A retrospective single-centre study was conducted of 745 STEMI patients. Patients were divided into four groups, depending on CA induced STEMI: right coronary artery (RCA), left main artery (LM), left anterior descending (LAD), left circumflex (LCx). Gender, age, history of smoking, diabetes mellitus (DM), obesity, arterial hypertension (AH), TIMI flow before and after reperfusion, total number, length and diameters of stents used, initial laboratory tests: haemoglobin, glucose, creatinine, troponin I (TnI), potassium, leukocytes, total (TC), high (HDC) and low (LDC) – density cholesterol, triglyceride levels (TG) and mortality were evaluated. Chi-square test, Student's t-test, independent – samples Kruskal-Wallis test, ANOVA were used for analysis. The value of $p \leqslant 0.05$ was considered statistically significant.

Results. The study evaluated 756 STEMI patients. No statistical significance was found between the CA and data: gender (p=0.217), age (p=0.466), smoking (p=0.378), DM (p=0.296), obesity (p=0.095), AH (p=0.194), TIMI flow before (p=0.173) and after intervention (p=0.488), number of stents used (p=0.629), initial laboratory tests: glucose (p=0.690), creatinine (p=0.156), TnI (p=0.808), potassium (p=0.185), leukocytes (p=0.912), TC (p=0.217), LDC (p=0.187), TG (p=0.4) and mortality (p=0.461). The statistical significance of the following data was determined: the total length of stents used in RCA was longer than LCx (p=0.03), the total diameter of the stents used in LAD was larger than RCA (p=0.02), the initial haemoglobin concentration was lower in LAD than RCA (p=0.02), HDC was found to be higher in LAD than in RCA (p=0.004).

Conclusion. For the RCA, longer stents were used in general than the LCx, but the total stents' diameter for the LAD was larger than in case of the RCA. The haemoglobin concentration was lower in the LAD than in the RCA. HDC was found in higher concentration among LAD than the RCA.

Platelet activity and its correlation with inflammation and cell count readings in chronic heart failure patients with reduced ejection fraction

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Background. There has been an increasing interest in the role of inflammation in thrombosis complications in chronic heart failure (HF) patients. The incidence of thrombosis in HF is shown to be the highest in patients classified as NYHA IV. It is stated that inflammation is regulated by platelet-induced activation of blood leukocytes.

Aim. The objective of the current study was to compare the platelet and cell count readings in chronic HF with reduced ejection fraction (HFrEF) patients according to NYHA functional class and to evaluate the correlation between those readings.

Methods. Total of 185 patients were examined in complete blood cell count, platelet aggregation, C reactive protein (CRP), NT-proBNP, cortisol, fibrinogen concentration.

Results. Mean platelet volume (MPV) increased with deterioration of a patient's state ($p<0.005$). Lymphocyte count and percent were the lowest in NYHA IV group ($p<0.005$). Neutrophil percent and count, monocyte percent and count were the highest ($p<0.045$) in NYHA IV. ADP and ADR-induced platelet aggregation was higher in NYHA III group compared to NYHA II and I group ($p<0.023$). NYHA functional class correlated with MPV ($r=0.311$, $p=0.0001$), lymphocyte count ($r=-0.186$, $p=0.026$), monocyte count ($p=0.172$, $p=0.041$), and percent ($r=0.212$, $p=0.011$). CRP concentration correlated with NT-proBNP ($r=0.203$, $p=0.005$). MPV correlated with fibrinogen concentration ($r=0.244$, $p=0.004$). Neutrophil count correlated with fibrinogen concentration ($r=0.308$, $p=0.0001$), evening cortisol concentration ($r=0.256$, $p=0.009$), and CRP ($r=0.378$, $p=0.0001$). Lymphocyte percent correlated with fibrinogen concentration ($r=-0.174$, $p=0.03$), CRP ($r=-0.220$, $p=0.028$), and evening cortisol concentration ($r=-0.246$, $p=0.012$). Monocyte percent correlated with fibrinogen concentration ($r=0.175$, $p=0.03$). Monocyte count correlated with morning cortisol, fibrinogen concentration ($r=0.279$, $p=0.004$ and $r=0.315$, $p=0.0001$, respectively) and CRP ($r=0.315$, $p=0.0001$).

Conclusion. 1) MPV could be considered as additional reading reflecting patient's condition; use of MPV identifying patients at risk of hypercoagulable state should be evaluated in more extensive studies; 2) increasing neutrophil and monocyte count could indicate a higher inflammatory state in chronic HFrEF.

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The difference of complete blood count, inflammation and platelet readings in chronic heart failure with reduced ejection fraction patients according to neutrophil count

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Background. As stated in the literature, neutrophils exhibit a greater proinflammatory profile and a significant role in the pathophysiology of heart failure (HF). However, there is a lack of information about neutrophil participation in patients with chronic HF. The results provided in the literature are obtained from heterogeneous population and measurement of blood cell count methods.

Aim. The objective of the current study was to compare complete lymphocytes, monocytes, platelets count, platelet (MPV, platelet aggregation) and inflammation (CRP, fibrinogen concentration) readings in very narrow CVD patients' groups (those who had had ischemic heart disease with chronic heart failure with reduced ejection fraction) according to neutrophil count investigated in one laboratory according to study-wide protocol.

Methods. Chronic heart failure with reduced ejection fraction (CHFrEF) patients (n=180) were investigated. The patients were divided into two groups according to neutrophil count: with $\geqslant 4.37 \times 10^9$ L (n=97) and with $<4.38 \times 10^9$ L (n=83).

Results. CRP, fibrinogen, morning cortisol ($cortisol_m$), and evening cortisol ($cortisol_e$) concentration were statistically significant higher in the group with higher neutrophil count (p=0.012, p=0.028, p=0.029, p=0.001 respectively). Neither of cholesterol concentration and platelet aggregation readings differed between the groups. Platelet (PLT), leukocyte and monocyte count were higher in the group with higher neutrophil count (p=0.032, p=0.0001, p=0.0001 respectively). PLT correlated with other cell type count and CRP (r=0.280, p=0.013). Neutrophil count correlated with fibrinogen, $cortisol_e$ and CRP concentration (r=0.204, p=0.007, and r=0.192, p=0.046, and (r=0.338, p=0.0001 respectively).

Conclusion. Neutrophil maintained low inflammation in CHFrEF patients. The greater the inflammation environment, the more stressful the condition of patients.

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Correlations between plasma cortisol levels and changes in local earth magnetic fields during acute myocardial infarction

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Background. Acute myocardial infarction (AMI) is a stress-inducing situation, which triggers a cascade of physiological and physiopathological events, leading to the activation of the hypothalamic-pituitary-adrenal axis. Biological effects of local earth magnetic fields (LEMF) and their consequences on human health have become the subject of important and recurrent public debate.

Aim. The aim of the current study was to determine the correlation between LEMF and serum cortisol levels in patients diagnosed with AMI.

Methods. The prospective, observational study was conducted in the Lithuanian University of Health Sciences Kaunas Clinics, including all patients admitted in 2017 to the CCU with a diagnosis of AMI. Total serum cortisol levels were measured on admission. The intensity of the time varying LEMF intensity was measured by the Global Coherence Monitoring Network magnetometer located in Lithuania. The LEMF was observed in five frequency intervals obtained from Schumann resonances: SDelta [0–3.5], STheta [3.5–7], SAlpha [7–15], SBeta [15–32], SGamma [32–65]. We formed [0–65] group, where all frequency intervals were combined together. The electromagnetic fields frequencies average during week days was assigned as [0–3.5], [3.5–7], [7–15], [15–32], [32–65], [0–65]. The strength of the magnetic field is measured in two directions: north-south (NS) and east-west (EW) axis.

Results. 94 patients were included. The mean age of the patients was 63.9±11.6 years and 65% were males. Average of plasma cortisol level for patients admitted during the day time (5–12:59 hours) (n=37) showed no significant difference in comparison with patients admitted during the evening time (13–4:59 hours) (n=86) [743.9±309.7 vs. 715.2±374.9; p=0.683].

Table. Correlation of studied LEMF frequency with plasma cortisol level for patients admitted during the day

LEMF frequency intervals [Hz]	LEMF frequency intervals average during a week	NS	EW
0-3.5	r=0.526, p=0.001	r=0.48, p=0.003	r=0.458, p=0.004
3.5-7	*r=0.466, p=0.004	r=0.385, p=0.019	*r=0.327, p=0.048
7-15	*r=0.396, p=0.015	r=0.257, p=0.125	r=0.185, p=0.273
15-32	r=0.391, p=0.017	r=0.307, p=0.065	r=0.158, p=0.352
32-65	*r=-0.206, p=0.222	r=-0.238, p=0.156	r=-0.23, p=0.171
0-65	*r=0.334, p=0.043	r=0.243, p=0.147	r=0.151, p=0.372

r- the Pearson correlation coefficient, *r – the Spearman correlation coefficient.

Conclusion. Our study reveals a significant interdependence between plasma cortisol level for patients admitted during the morning time and LEMF Delta, theta frequencies in the NS and EW directions during AMI.

Acknowledgments. The authors have no conflict of interest to declare.

The most common risk factors for deep vein thrombosis in female population

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Background. Risk factors for the development of deep vein thrombosis have been extensively described in the world literature, however, most studies analyse these factors in the general population and therefore there is not enough information on the prevalence of risk factors for deep vein thrombosis separately in the male and female populations.

Aim. To find out the most common possible risk factors for deep vein thrombosis in the female population.

Methods. The retrospective study included data on 100 female patients aged 18–90 years who were diagnosed with "deep vein thrombosis" (ICD-10 code I80.1, I80.2) and was conducted at the Riga East Clinical University Hospital. Data from medical cards were recorded in *Microsoft Excel 2016* program, for processing using *IBM SPSS Statistics 22* and *Microsoft Excel 2016* program. The most common risk factors for deep vein thrombosis in women, the frequency of certain risk factors and the incidence of risk factors in certain age groups were determined.

Results. In total, 23 individual risk factors were identified in patients diagnosed with "deep vein thrombosis". The most common were smoking (25%), obesity (24%), history of pulmonary embolism (23%) and history of deep vein thrombosis (22%). It was found that the most common risk factors differ between the two age groups – the most common risk factors for women of childbearing potential (from 18 to 49 years old) were a history of deep vein thrombosis (42.5%), a history of pulmonary embolism (22.5%), use of hormonal contraception (17.5%), May-Thurner syndrome (15%) and smoking (14%). In contrast, in menopausal and postmenopausal women (from 50 to 90 years old), the most common risk factors were obesity (31.7%), chronic heart failure (28.3%), a history of pulmonary embolism (23.3%), smoking (18.3%) and oncological disease (11.6%).

Conclusion. The most common possible risk factors for deep vein thrombosis in the female population of age group 18–90 are smoking, obesity and a history of pulmonary embolism, however, the risk factors differ between certain age groups. In women of reproductive period (18 to 49 years old), these are a history of DVT, a history of pulmonary embolism and the use of hormonal contraception, while in menopausal and postmenopausal women (50 to 90 years old) these are obesity, chronic heart failure and a history of pulmonary embolism.

Acknowledgements. The authors declare the absence of conflict of interest.

Relation between dyslipidaemia and in-hospital complications of STEMI patients

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Background. Dyslipidaemia is abnormality in the serum lipids level. Abnormal lipid profile may include high total cholesterol, high triglycerides, low high density lipoprotein cholesterol and raised low density lipoprotein cholesterol concentration. This condition is a major risk factor for developing ST-elevated myocardial infarction (STEMI), which is the leading cause of death among men and women worldwide. This study attempted to compare the incidence of STEMI complications between those with dyslipidaemia and those without.

Aim. To evaluate the incidence of early in-hospital complications in patients with STEMI who had dyslipidaemia and those, who had not.

Methods. This retrospective study involved 734 patients diagnosed with STEMI in the LUHS Department of Cardiology. Patients were considered to have dyslipidaemia, if they were diagnosed prior to STEMI. Patients were divided into two groups according to their dyslipidaemia status: with dyslipidaemia and without dyslipidaemia. The endpoints of the study were defined as early complications during in-hospital period (stroke, pulmonary venous stasis (PVS), death, atrial fibrillation (AF), ventricular extrasystole (VE), ventricular fibrillation (VF), and atrioventricular disease II-III° block (AVB)). Statistical analysis was performed using IBM SPSS version 25.0. Chi-square (χ^2) criteria was used to compare qualitative characteristics and study correlations. Student's T-test was used to compare the average of two variable parameters in independent samples. Compare the average values of two nonparametric variables in independent samples – Mann-Whitney U-test. The value of $p \leqslant 0.05$ was considered as statistically significant.

Results. The majority of patients had dyslipidaemia prior to the onset of STEMI 594 (80.1%). The presence of PVS on chest roentgenogram was statistically significant among patients with dyslipidaemia (p=0.005). Among STEMI patients with dyslipidaemia grade I venous stasis 205 (27.6%) is the most common. There is statistical significance between dyslipidaemic STEMI patients and in-hospital mortality (p=0.01). AF, stroke, II-III ° AVB, VE, VF frequency were not statistically significant (p=0.163, p=0.08, p=0.583, p=0.156, p=0.795 accordingly).

Conclusion. There is a statistical significance that dyslipidaemia increases the incidence of pulmonary venous stasis, death in STEMI patients. Meanwhile, the association of dyslipidaemia with atrial fibrillation, II-III ° atrioventricular block, ventricular fibrillation, ventricular extrasystoles, and strokes of in-hospital STEMI patients were not statistically significant.

Acknowledgements. The authors declare the absence of conflict of interest.

SURGERY

Gallstone disease: the cause of acute intestinal obstruction

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Background. Acute intestinal obstruction is a complex of symptoms that combines various diseases, which are characterized primarily by a disruption of the passage through the gastrointestinal tract. The causes of this pathology are divided into two groups: a mechanical obstacle, or a lack of intestinal motor function. In rare cases, gallstone disease can also become the cause of this pathology. This work is devoted to the role of biliary ileus in the structure of non-standard situations in biliary surgery, the timeliness of patients' referral to a round-the-clock surgical hospital, the timeliness of diagnosis of this pathology, and the results of treatment of patients with biliary ileus.

Aim. Our work is devoted to ileus, which develops as a complication of gallstone disease. A rare cause of acute small bowel obstruction (1.0%–4.0%), with high mortality (12.0%–18.0%). We also present 3 case reports related to the aforementioned problem.

Methods. We have analysed the data for 5 years of a round-the-clock surgical hospital of urgent medical care "Severodvinsk City Clinical Hospital No. 2 Emergency Medical Care" and "Karpogorsk Central District Hospital". Statistical analysis is carried out using the STATA12.1 application package for small numbers.

Results. For 5 years, 5 patients with biliary ileus, including 1 case of Bouveret's syndrome, have been treated at the Severodvinsk City Clinical Hospital No. 2 of the SMP JSC. The time from the onset of the disease to hospitalization was more than 24 hours. All patients were operated on, in 2 cases, the diagnosis was established before the operation. One patient with Bouveret's syndrome has been treated in the Karpogorsk Central District Hospital in the last 5 years.

Conclusion. Despite the fact that biliary ileus, like one of its manifestations, Bouveret's syndrome, is a rare pathology, it is necessary to remember this cause of intestinal obstruction. Elderly patients with bowel obstruction deserve special attention. The operation should be performed as early as possible from the onset of the disease. A timely performed planned cholecystectomy in patients with gallstone disease, before complications occur, is an important aspect in the work of the surgical service.

Analysis of Trifocal IOL implantation in Femtosecond Laser-Assisted Cataract Surgery

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Background. The problem is of outstanding importance since of the presbiopic problems in the peoples eyes, after the age of 40.

Aim. The aim of the current study was the analysis of the trifocal intraocular lenses (IOL) implantations in femtosecond laser-assisted cataract surgery.

Methods. Altogether 64 patients (128 eyes) were enrolled in the study, after the implantation n of the Acrysoft IQ Panoptix trifocal lenses.All patients underwent femtosecond laser-assisted cataract surgery. The following data was evaluated: uncorrected distance visual acuity (UCDVA), uncorrected near visual acuity, and at discharge, after 14 days, 1 and 3 months after the surgery under photopic and mesopic lighting conditions.

Results. It was shown that the Acrysoft IQ Panoptix lens provided high uncorrected distance and near visual acuity in photopic lighting conditions, and at the same time show significantly better visual acuity also at an intermediate distance.

Conclusion. The use of the Acrysoft IQ Panoptix lens made it possible to obtain maximum visual acuity at different distances, regardless of the level of illumination.

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The effect of the degree of compensation for type 2 diabetes on visual acuity and central retinal thickness in patients after cataract surgery

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Background. The incidence of type 2 diabetes has increased worldwide. Preoperative glycaemic control in diabetic patients remains a controversial issue among surgeons, including ophthalmologists.

Aim. The objective of the current study was to evaluate the effect of the degree of compensation for type 2 diabetes on visual acuity and central retinal thickness in patients after cataract surgery.

Methods. A prospective study was conducted. 60 patients were enrolled in the study (30 patients were diagnosed with type 2 diabetes). Glycated haemoglobin (HbA1c) was previously detected in diabetic patients. Patients were evaluated and compared for best corrected visual acuity (BVCA) and central retinal thickness (CRT) before and after cataract surgery. Statistical analyses were performed using the SPSS 26.0 software.

Results. The mean age was 73.92 years ± 6.73. A statistically significant increase in CRT was observed in both groups at week 4 postoperatively ($p<0.001$). A statistically significant improvement in visual acuity was observed in both groups. ($p<0.001$). There were no statistically significant differences between the control and study groups in both visual acuity (preoperatively ($p=0.376$) and postoperatively ($p=0.524$)) and CRT (preoperatively ($p=0.415$), postoperatively ($p=0.105$)). The Correlations between HbA1c and preoperative CTB ($R=-0.079$; $p=0.680$) and postoperative CRT ($R=-0.102$; $p=0.591$) were not statistically significant. The correlation between HbA1c and best corrected visual acuity was not statistically significant both preoperatively ($R=0.040$; $p=0.833$) and postoperatively ($R=0.109$; $p = 0.567$).

Conclusion. After surgery, patients with type 2 diabetes have improved visual acuity and changed CRT almost as much as patients without diabetes. HbA1c does not affect the postoperative outcome of cataracts, which means that elevated HbA1c levels are not a contraindication to cataract surgery.

The histopathological features of breast radial scar and adenosis stratified according to BI-RADS-3: a pilot study

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Background. Over 40% of women undergoing breast screening have mammographically dense breast tissue. Elevated mammographic breast density is an established breast cancer risk factor and could mask tumours within the dense tissue. Therefore, the precise recognition and stratification of benign breast lesions is of particular importance.

Radial scar and sclerosing adenosis are characterized by increased breast cancer risk. These lesions could also coexist. However, the risk of breast cancer for proliferative adenosis is unclear and not defined.

Sclerosing adenosis was characterized by lobulocentric proliferation of acini and stromal fibrosis, whereas radial scar consisted of fibroelastostotic stroma and entrapped glandular structures, with or without proliferative epithelial lesions.

Aim. The aim of the current pilot study was to evaluate the findings in patients with sclerosing adenosis with and without radial scar stratified to BI-RADS-3.

Methods. 12 patients undergoing breast mammographic examination with subsequent needle core biopsy in Latvian Oncology Centre in 2020 were prospectively enrolled in the study.

The breast density according to Breast Imaging Reporting and Data System (BI-RADS) was assessed. The core needle biopsy samples were stained with hematoxylin and eosin to evaluate the histopathological features. Chi-square test were performed to evaluate the relationship between clinical and histopathological characteristics.

Results. 12 patients were enrolled in the pilot study. The median age of patients were 47 (37–68) years, the median size of mammographic detected lesion was 3.0 (1.8–4.9) cm.

7 patients had radial scar; 8 patients had breast adenosis.

The obtained results showed the significant correlation between the subtype of adenosis and radial scar ($p=0.02$). The patients with breast radial scar in 57% of cases demonstrated the coexistence of sclerosing adenosis. The histological features observed in patients with radial scar with and without adenosis were usual ductal hyperplasia, cystic ductal changes, stromal fibrosis, hyalinosis, microcalcification, apocrine metaplasia, mild lymphocyte infiltration. These features did not differ between patients with radial scar with sclerosing adenosis and patients with adenosis without radial scar.

Conclusion. The histopathological findings in patients with sclerosing adenosis with and without radial scar stratified to BI-RADS-3 are similar, however, in vast majority of cases, the patients with radial scar demonstrated concomitant sclerosing adenosis.

Since all the lesions corresponded to BI-RADS 3, the histopathological examinations still remain the gold standard for the differentiation between radial scar with and without sclerosing adenosis.

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Comparison of magnetic resonance imaging and arthroscopy in the evaluation of shoulder pathology in patients with chronic shoulder pain

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Background. The third most common reason why patients turn to a doctor traumatologist-orthopaedist is a shoulder joint pain. Most frequently, chronic shoulder pain is caused by impingement syndrome, however, patients often develop various types of joint component damage. Magnetic resonance imaging (MRI) is the most accurate non-invasive radiological examination method, nevertheless, mistakes sometimes occur while using it.

Aim. The aim of the research is to find out the sensitivity and specificity of MRI in diagnostics of shoulder joint pathologies, comparing it to the arthroscopy finding, which is the gold standard.

Methods and material. Retrospective study involved 50 patients aged 22–73 years, who had a shoulder joint pain for at least 6 month and who had MR examinations and arthroscopy performed. MR and the arthroscopy findings were compared. The collected data was presented in the form of tables. We calculated true positive (TP), true negative (TN), false positive (FP) and false negative (FN) values, sensitivity and specificity.

Results. 66% out of 50 patients (n=33) were male and 34% (n=17) – female. The average age of the analysed patients was 47.1 ±10.9 years. It was established that almost all of the patients had subacromial bursitis (94.0% of patients, n=47) and acromioclavicular (AC) joint arthrosis (92% of patients, n=46). The most common pathologies are summarized in the table below.

Table. Sensitivity and specificity of MR in diagnostics of most common pathologies

Pathology	TP	TN	FP	FN	Sensitivity	Specificity
Subacromial bursitis	47	3	0	0	1	1
AC joint osteoarthritis	46	3	1	0	1	0,75
Labral tear	10	27	2	11	0,48	0,93
Rotator cuff tear	15	30	1	4	0,79	0,97

Pathologies such as calcinate in tendons (MR n=5, arthroscopy n=6), biceps long head tendon tear or subluxation (MR n=4, arthroscopy n=4), calcinate in subacromial bursa (MR n=2, arthroscopy n=2) and adhesive capsulitis (MR n=1, arthroscopy n=2) were diagnosed rarely.

Conclusion. Magnetic resonance showed an excellent sensitivity in diagnostics of subacromial bursitis and AC joint osteoarthritis, good sensitivity in rotator cuff tear case, but poor sensitivity in labral tear case. However, specificity was high in detection of all of these pathologies, using MR. The rest of the findings are relatively rare; therefore, it is not proper to evaluate sensitivity and specificity data.

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Clinical experience with microwave ablation of kidney lesions in Santaros Clinics

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Background. Microwave ablation is a new method for treating kidney tumors or cysts less than 4 cm in size that cannot be treated surgically due to the patient's comorbidity status.

Aim. To evaluate microwave ablation as a new treatment method for small kidney tumors or cysts.

Methods. On October 10, 2015, the first ultrasound-guided microwave ablation (MWA) of renal cancer was performed in Vilnius University Hospital Santariskiu Clinics, Lithuania. This procedure was performed for five patients with renal cell carcinoma and two patients with renal cysts until March 6, 2018.

The first 61-year-old patient diagnosed with renal cell carcinoma size 11 mm and R.E.N.A.L. 6p received a total MWA power output of 60W for 2 minutes. The second 83-year-old patient with an initial diagnosis of renal cell carcinoma size 26mm and R.E.N.A.L. 6a received a MWA of total 100W power for 4 minutes. The third 53-year-old patient with renal cyst sized 13 mm and Bosniak 3 received a MWA of total 60W power output for 3 minutes. The fourth 62-year-old patient was diagnosed with (15 mm size) renal cell carcinoma and with R.E.N.A.L. 8a. She had a MWA of 100W power for 4 minutes. The fifth 54-year-old patient was diagnosed with renal cyst, Bosniak 3 (cyst size 20 mm). During the MWA a power output of 100W for 2 minutes was used. The sixth 84-year-old patient with diagnosis of a 16 mm renal cell carcinoma and R.E.N.A.L 5p had a MWA of 60W power for 3 minutes.

The last 78-year-old patient diagnosed with renal cell carcinoma size 34mm and R.E.N.A.L. 8h received a total MWA power output of 100W for 4 minutes.

Results. Complete ablation was achieved in 5 out of 7 (71.4%) lesions after 1 MWA session. The patient comorbidity status did not change in any of the patients. No severe complications occurred during the MWA, only one patient had kidney hematoma after the MWA. No significant elevation of renal function was observed after the MWA.

Conclusion. MWA is a safe and effective treatment option for patients who suffer from inoperable kidney lesions less than 4 cm in size. The complication rate is low and excellent tumor control can be achieved without deterioration of the residual renal function in experienced centers. Because of low patient number, our MWA results are lower than reported in other studies.

Prediction of chronic kidney disease after partial nephrectomy using preoperative estimated glomerular filtration rate and acute kidney injury criteria

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Background. Partial nephrectomy (PN) has a "Strong" recommendation according to Strength Rating in European Association of Urology Guidelines, since it is considered an ideal treatment option for tumours less than 7 cm in size, maintaining part of the renal parenchyma and lowering the possible risk of glomerular filtration decrease [1–3]. Retrospective data on chronic kidney disease (CKD) after PN shows acceleration of disease onset, however, the prospective data is lacking [4].

Aim. To evaluate *estimated glomerular fltration rate* (eGFR) and acute kidney injury (AKI) as factors that determine the development of CKD after PN.

Methods. A prospective study analysing the data of 63 patients without CKD and albuminuria before partial nephrectomy for a single cT1 N0 M0 renal mass was performed. Patients were divided into two groups according to CKD status by KDIGO criteria after 12 months since surgery: CKD group and non-CKD group. CKD group was evaluated by AKI AKIN and RIFLE criteria persistence.

Results. After 12 months since surgery, 4 (6.3%) patients were with CKD. CKD group had decreased preoperative eGFR (67.8±8.7 vs 92.5±12.1, ml/min, p<0.001), higher hypotension time during PN (31.2±22.5 vs 11.9±17.7, min, p=0.042), lower postoperative eGFR after 48h (40.2±13.4 vs 77.5±17.7, ml/min, p<0.001) and 2 months since surgery (49.0±7.9 vs 85.3±12.4, ml/min, p<0.001), higher AKI by RIFLE serum creatinine (sCr) cases after 48 h since surgery (75% vs 15.3%, p=0.022).

Table. AKI persistence in CKD patients

Patient, No	AKI after 48 h		
	AKIN, stage	RIFLE sCr, class	RIFLE eGFR, class
1.	1	Risk	Risk
2.	-	-	-
3.	2	Injury	Injury
4.	1	Risk	Injury

Conclusion. AKI by RIFLE serum creatinine and lower preoperative eGFR may predict CKD after PN.

Intraocular pressure changes after the intravitreal antivascular endothelial growth factor therapy

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Background. Over the recent years, intravitreal injections of anti-vascular growth factor (anti-VEGF) agents have been the primary treatment for age-related macular degeneration (AMD) and diabetic maculopathy (DM). Over 8 million intravitreal anti-VEGF agents' injections are performed worldwide annually. It has been well expressed in literature that intravitreal anti-VEGF agents can lead to a transient elevation of IOP, which usually normalizes within 30–60 minutes in majority of the eyes. The increased IOP and, in particular, its sharp rise in the first minutes after the injection can pose a risk to the patient eye health.

Aim. The aim of the prospective study is to evaluate and compare the dynamics of IOP changes in the eyes with DM and AMD, following intravitreal administration of the anti-VEGF agent Bevacizumab.

Methods. The study included 63 patients who received intravitreal injections of the anti-VEGF agent Bevacizumab (1.25 mg/0.05 ml). Patients were divided into two groups, with 35 (56 %) patients with AMD in the first group and 28 (44 %) patients with DM in the second one. Patients IOP was measured using the "Icare ic100" tonometer before the intravitreal injection, as well as 2 minutes and 30 minutes after that.

Results. The analysis of the data obtained showed that in patients who received i/v injections in one eye, the IOP increased by an average of 27.5 mm/Hg 2 minutes after i/v administration. In contrast, in patients who received injections in both eyes, IOP increased by 21.8 mm/Hg in the right eye and by 25.2 mm/Hg in the left eye A slightly higher mean increase in IOP was observed in DM patients, i.e., by 28.4 mm/Hg for injections in one eye and by 21.4 mm/Hg in the right eye and 26.1 mm/Hg in the left eye in the case of bilateral injections. In the majority of patients, IOP returned to normal 30 minutes after the intravenous administration. The statistical significance of the impact on IOP fluctuations of other analysed factors was not confirmed.

Conclusion. Following intravenous administration of the anti-VEGF agent Bevacizumab, the patient IOP tends to increase rapidly and return to the base level within 30 minutes. The mean dynamics of IOP changes are similar in both AMD and DM patients. Factors such as the family history of glaucoma, the lens status and the number of previous injections do not affect the change in IOP at a statistically significant level.

First experience of postoperative MRI following arthroscopic primary anterior cruciate ligament repair in Latvia

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Background. Although the gold standard for repairing an anterior cruciate ligament (ACL) rupture is graft replacement, arthroscopic primary suturing of the ACL has become relevant in recent years. In the last two years, surgeons in Latvia have also started using it, however, no study in Latvia to date has assessed post-operative magnetic resonance imaging, and there is also little information in foreign literature.

Primary repair is only used in patients with proximal ligament rupture and good outcome is associated with minimally invasive techniques and early postoperative mobilization.

Aim. To evaluate short-term MRI postoperative findings – ACL integrity and maturation.

The future goal is to compare the MRI findings 1 year and 2 years after surgery.

Methods. A retrospective search was performed in the database of the surgeon for patients who underwent arthroscopic primary ACL repair. All postoperative MRIs were included.

The radiologist first graded the ligament as continuous or not continuous (reruptured). Then, ligament maturation was graded as hypointense (similar to intact posterior cruciate ligament (PCL)), isointense (>50% similar to PCL) or hyperintense (<50% similar to PCL).

Results. In two year period (from 2018–2020), 25 patients underwent primary ACL repair, 7 postoperative MRIs from 5 patients were included (only 5 patients had a clinical need for repeated MRI).

The mean age of patients was 38 years (range: 31–47). The mean surgery-MRI interval was 5 months (range: 1 month–14 months).

Within one year of surgery, ligaments were hyperintense in 100%, but ACL intensity decreased 14 months after surgery. At least one of the causes of hyperintensity is postoperative edema, which complicates MRI interpretation and may be mistaken for rerupture.

Additional ligament fixation with internal brace was used during surgery in all the studied patients. This finding helps the radiologist to understand that there has been an ACL plastic. However, due to its small size, there will be no or minimal bone swelling around it, which makes fixation less noticeable.

Only one patient had a postoperative complication – arthrofibrosis, however, this complication is not specific to the arthroscopic primary ACL repair (ACL was the same as in the other patients).

Conclusion. For a correct radiological evaluation of ACL, it is important to know the patient's history, the time interval after the operation and the clinical finding, whether the knee movements are stable.

The MR sequence pd tse sagittal and axial is recommended for ACL continuity assessment, but pd fs sagittal – for maturation assessment.

PEDIATRICS

The comparison of diagnostic reference levels for paediatric CT examinations

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Background. CT imaging delivers a substantially higher ionizing radiation dose than other imaging methods and causes an increased lifetime risk of cancer. Children's developing organs and tissues are inherently more vulnerable to cellular damage than those of adults, therefore it is important to ensure the optimal patient doses. Diagnostic reference levels (DRLs) are an important tool for monitoring and optimizing patient exposure, however, a great number of countries has not established them for at least a limited set of common paediatric examinations yet.

Aim. To perform literature analysis on paediatric national DRLs for head CT examinations in other countries and compare the collected data with Lithuanian established national DRLs.

Methods. Literature analysis was performed on *PubMed* search engine on inclusion criteria: publication date 2015–2020, used keywords *paediatric computed tomography, paediatric CT, national diagnostic reference levels (DRLs)*. The 23 articles discussing paediatric national DRLs were further analysed.

Results. Data analysis shows that different countries examine patients using relatively different values of scan parameters (tube current (mAs), tube voltage (kV), scan length (mm), slice thickness (mm) and pitch), which results in varying exposure doses (CTDI, DLP) for the same CT examinations. The national DRLs reported in Lithuania were compared with data of other 8 countries based on the same age grouping method (<1, 1–5, 5–10 and 10–15 years) (Fig.). The results of our study show that the established national DRLs (DLP values) for head CT are generally higher than in other countries except Jordan and Japan.

Conclusion. There is a limited number of publications on this topic at European level, therefore it is imperative to establish national and local DRLs. The results of our study indicate that further research on patient exposure optimization is highly significant and setting new DRLs for Lithuania and establishment of local DRLs in hospitals is required.

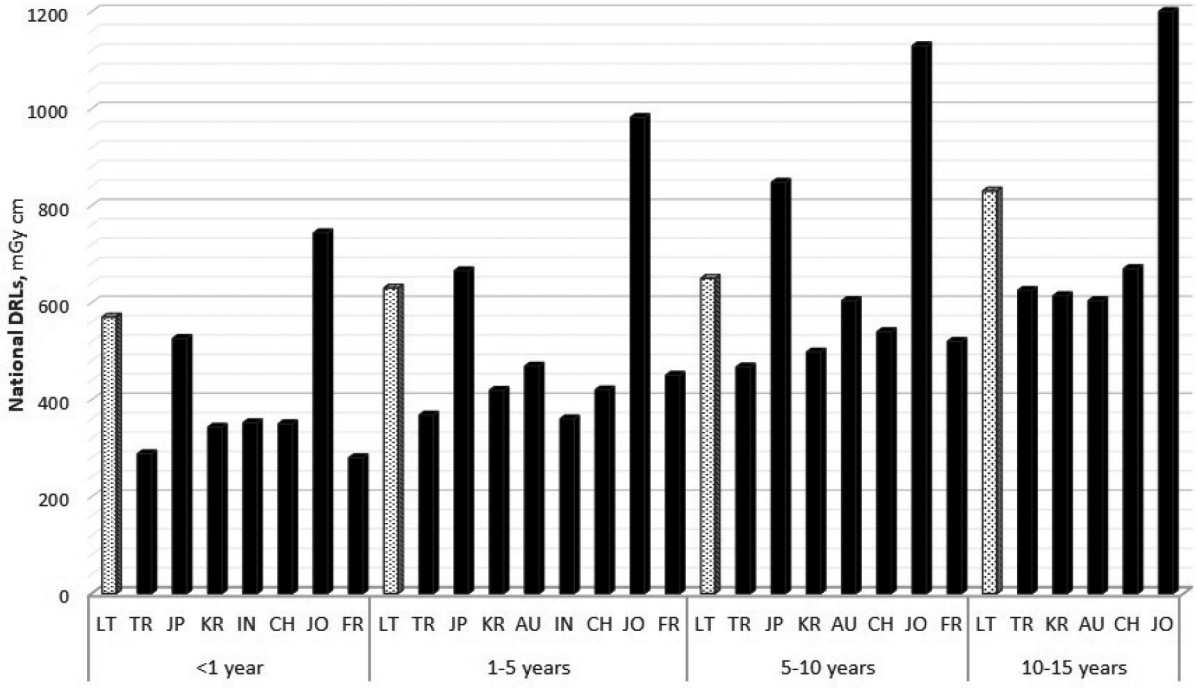

Fig. Comparison of paediatric national DRLs for head CT examinations
Note: LT – Lithuania, TR – Turkey, JP – Japan, KR – South Korea, AU – Australia, IN – India, CH – Switzerland, JO – Jordan, FR – France.

Assessment of exposure from paediatric head CT procedures

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Background. Children are particularly sensitive to ionizing radiation, therefore it is important to monitor and optimize radiation exposure during CT procedures. However, patient dose monitoring presents a challenge for healthcare facilities and a limited number of hospitals has published data on exposure evaluation and local diagnostic reference levels (DRLs) as a tool for patient exposure optimization.

Aim. The aim of this study is to evaluate exposure of paediatric head CT scans, estimate local diagnostic reference levels (DRLs) for head CT examinations and compare them with national and European DRLs.

Methods. Scan parameters of single-phase CT examinations of the head performed over a 2-year period were collected. Relationships between dose parameters (effective dose and DLP) and patients' age were evaluated. Patients were grouped by age in the following intervals: <1, 1–5, 5–10, 10–15 and 15–18 years. Local age based DRLs set as the 3rd quartile of the median dose-length product (DLP) were calculated.

Results. Data was collected from 596 paediatric head CT examinations. The median DLP values for head CT were 140, 215, 247, 272, 297 for <1, 1–5, 5–10, 10–15 and 15–18 years. For head CT local DRLs (180, 242, 287, 313, 335 mGy*cm for <1, 1–5, 5–10, 10–15 and 15–18 years, respectively) were 2–4 times lower than national DRLs and about 2 times lower than European DRLs (178, 179, 249, 314 mGy*cm for 0–3 months, 3 months–1 y, 1–6 y and ⩾ 6 y respectively).

Conclusion. The estimated children's exposure shows that paediatric head CT doses are lower in comparison with those indicated in the majority of published articles from other hospitals over the last 6 years and when compared with national and European DRLs. Our initiative via the estimation exposure and determination of local DRLs for paediatric head CT must be a starting point to expand this investigation to include other examinations and imaging modalities, as well as re-establishing the current national DRLs.

Phenotypes and baseline risk factors of acute kidney injury in children after allogeneic hematopoietic stem cell transplantation

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Background. Acute kidney injury (AKI) is a frequent and widely recognized complication of allogeneic hematopoietic stem cell transplantation (allo-HSCT). Despite relatively high prevalence, AKI after allo-HSCT and its risk factors in children remain obscure.

Aim. The aim of this study was to describe the prevalence and course of AKI during the first 100 days after allo-HSCT in children and to investigate its associations with baseline characteristics.

Methods. Retrospective single-centre chart review of all patients under 18 who underwent allo-HSCT during 2011–2017 was performed. AKI was defined using the paediatric RIFLE criteria and only the patients with pRIFLE stage I (eGFR decrease by 50% or more) or higher were considered for the analysis. Recurrent AKI and acute kidney disease (AKD) were defined according to the Acute Disease Quality Initiative consensus. Demographic, clinical, and procedure-related characteristics were recorded at the day of HSCT.

Results. Fifty-one patients (68.6% boys) with a median age of 9 years (range: 0.25–17) were included. During a median follow-up of 82 (IQR, 60–98) days, 27 (52.9%) patients experienced a total of 39 AKI episodes, translating into one AKI episode per 100 patient days. Multiple AKIs occurred in 11 (21.6%) patients and 18 (35.3%) progressed to AKD. Four patients died, all with an ongoing or previous AKI. Patients with AKD were, on average, older (10 vs. 6 years; p=0.03) and had higher baseline body mass index (BMI) [standard deviation score (SDS) 0.83 vs. 0.04, p=0.05], whereas patients with recurrent AKI had higher baseline estimated glomerular filtration rate (eGFR) (244.1 vs. 193.9 ml/min/1.73 m2, p=0.02). In the adjusted Cox models (HR; 95% CI), older age (1.10; 1.01–1.20) was associated with a higher risk of overall AKI and higher eGFR (1.02; 1.01–1.04) was associated with a higher risk of recurrent AKI, while older age (1.17; 1.04–1.31), higher eGFR (HR 1.01; 1.0–1.02), and higher BMI SDS (1.66; 1.01–2.72) were associated with a higher risk of AKD.

Conclusion. AKI is a frequent early complication of allo-HSCT in children, and approximately one fifth experience AKI recurrence and one third develop AKD. Older age, higher BMI, and higher eGFR at the day of transplant may have an effect on the risk of AKI development and its course.

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Significance of urinary Aminopeptidase N in early diagnosis of kidney damage in children with type 1 diabetes mellitus

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Background. Diabetes mellitus is a global health problem resulting in social and economic effects. The age-sex standardized incidence rate of T1DM in Ukrainian children and adolescents aged 0–14 years lies between 5-10 per 100,000 population per annum, and it is not as high as in the other EU countries such as Finland (62.3) or Sweden (43.2). However, the possibility of early formation (in five years of disease duration) of micro and macrovascular complications makes the problem of T1DM extremely actual. Diabetic nephropathy is one of the common complications of diabetes. Aminopeptidase N (ANPEP) is an exopeptidase that is expressed by glomerular, mesangial, and renal tubular cells. ANPEP is involved in the conversion of angiotensin III to angiotensin IV. ANPEP in urine is one of the first markers of renal damage when microglobulin levels are within normal limits.

Aim. The aim of the current study was to investigate the features ANPEP levels in urine of children depending on the duration of diabetes.

Methods. We analysed 3 groups of children with type 1 diabetes mellitus and comparison group of children without diabetes from Regional Children's Clinical Hospital in Sumy. ANPEP was measured by ELISA using a Proteome Profiler Human Kidney Biomarker Antibody Array (R&D Systems, Minneapolis, MN, USA). Results were detected with BioRad ChemiDoc Touch. The arrays were analysed semi-quantitatively, using BioRad Image Lab Software.

Results. The study included 47 children with diabetes and 8 children without diabetes. The level of ANPEP in urine increased 2.6-fold in children with the duration of diabetes below one year compared to the control group. ANPEP levels were elevated 3.2-fold in children with duration of diabetes from one to five years. In children with duration of diabetes duration, the marker increased 2.7 times.

Conclusion. Increase urinary ANPEP was observed in the first year of diabetes in children. Measuring the level of ANPEP in urine may be useful for the diagnosis of diabetic nephropathy.

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Causes of impaired heat balance in children in the postnatal period at home

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Background. For the first 28 days of life, children are characterized by various transitional states due to the adaptation of a newborn to postnatal life. One of the transient conditions of newborns is a feature of the heat regulation process – a high heat loss in relation to heat production.

Aim. The study was aimed at providing an analysis of the causes of infractions in heat regulation in newborns in the postnatal period.

Methods. 30 full-term newborns were under observation. All were discharged from the maternity hospital on the 2nd day of life after birth. The children were examined daily at home, all were exclusively breastfed and healthy. The early clinical signs of hypothermia were assessed: cold feet to the touch (become cold before body temperature drops), poor sucking, decreased activity, weak cry, and "marbling" of the skin. The body temperature in the armpit was measured 3 times a day. Signs of overheating were also taken into account.

Results. In 25 (83.3%) newborns, especially during the first 7 days of life, the following was noted: cold feet to the touch, decreased activity, and "marbling" of the skin. Clinical signs of hypothermia did not persist throughout the day. At the same time, the body temperature remained in the range of 36.50°C–36.70°C. In five (16.6%) newborns, during the first 7 days of life, a mild hypothermia was noted during the day. Periodically, the body temperature remained within the range from 36.04°C to 36.00°C, periodically there was also poor sucking, decreased activity, and cold feet to the touch. In 5 (16.6%) newborns, mainly during the first 7 days of life, an increase in body temperature from 37.50°C to 38.00°C was revealed, moderate dryness of the mucous lips, anxiety were noted. However, during the day, after normalization of body temperature, there could also be clinical signs of hypothermia: cold feet to the touch of the "marbling" of the skin.

Conclusion. The period of adaptation is characterized by imperfect heat regulation processes. Physiological processes for newborns in the postnatal period, if certain temperature conditions of the external environment, humidity, care, feeding are not observed, can assume pathological features. It was revealed that the main reason for the appearance of early clinical signs of hypothermia, overheating and mild hypothermia are infringements of thermal comfort, as well as humidity conditions, and flawed child care at home. A correct thermal regime, humidity, care and breastfeeding are the key to the successful development of a child at home.

Attitude of physicians to sleep medicine and sleep disorders in paediatric patients

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Background. Sleep medicine is a rapidly evolving field of medicine that covers a variety of diseases. Sleep disturbance is one of the most common problems causing concern to parents. However, patients with sleep disorders often remain undiagnosed, because health care providers have limited knowledge about sleep medicine.

Aim. The aim of the study was to find out attitude, interest and existing knowledge regarding sleep medicine and sleep disorders in children among Latvian primary care physicians, as well as to obtain a view about the prevalence of children's sleep disorders in doctors' practices in Latvia.

Methods. A prospective descriptive cross-sectional survey was carried out from April 2019 to August 2020. The respondents completed anonymous questionnaires during professional conferences in Riga or an electronic questionnaire. The questionnaire contained questions about socio-demographic factors (gender, specialty, work experience), attitude and knowledge about sleep medicine terminology, sleep disorders and prevalence of sleep disorders among respondents' patients. Data were analysed by a statistical program MedCalc (descriptive statistics, x^2 test).

Results. Sample for analysis contained the data obtained from 259 respondents (general practitioners, paediatricians, neurologists and residents). Most of the doctors 87% (221/259) - were working in cities; 50% (130/259) respondents had a work experience of more than 20 years. Only 41% of physicians (81/259) often asked about sleep disorders. The most common reasons why doctors did not ask about their patients' sleep were lack of knowledge and limited time. The majority (84% (214/259)) of respondents admitted that sleep problems were reported in 0–25% of all patient visits per year.

The most common sleep disorders were waking up during the night (58% (150/254)), difficulty to fall asleep (55% (141/254)) and difficulty to wake up in the morning (47% (121/254)).

Conclusion. The majority of doctors note that sleep disorders only occur in ¼ of patients. Doctors who have reported that they often ask about sleep disorders are more likely to have experience with sleep disorders.

GASTROENTEROLOGY, NUTRITION, GASTROINTESTINAL ONCOLOGY & MICROBIOTA

Gallstone disease in patients with non-alcoholic fatty liver disease: metabolic risks

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Background. Non-alcoholic fatty liver disease (NAFLD) and gallstone disease (GD) are widespread throughout societies worldwide. Moreover, there is a high percentage of NAFLD and GD combination cases. It remains unclear whether NAFLD is a precursor to GD or if GD reveals signs of a metabolic syndrome that accelerates the progression of NAFLD.

Objective. To assess metabolic risks of patients with NAFLD with/without GD to improve the quality of management and treatment.

Methods. A total of 183 patients with NAFLD were included in this case control study. The main group was represented by patients with NAFLD and GD (n = 88), of which 53 underwent cholecystectomy. The comparison group was represented by patients with NAFLD without GD (n = 95). All patients underwent standard laboratory testing to assess level of related hormones (*i.e.* leptin, its soluble receptor, adiponectin, and insulin) and instrumental examinations to assess fatty liver and stage of liver fibrosis (*i.e.* elastometry). Processing of research results was conducted with the Python programming language and the specialized data analysis libraries (NumPy and Pandas). Fuzzy logic and fuzzy rules were used to describe the relationship between risks and disease course.

Results. Compared to patients with NAFLD without GD, those with NAFLD and GD presented greater general weakness (χ^2 = 11.33, r_s = 0.234, $P \leqslant 0.01$), fatigue (χ^2 = 15.68, r_s = 0.281, $P \leqslant 0.01$), bitter taste in the mouth (χ^2 = 11.66, r_s = 0.147, $P \leqslant 0.01$), coronary heart disease (9.47% *vs* 25%, $P \leqslant 0.01$), and type 2 diabetes (r_s = 0.164, $P \leqslant 0.01$). Individuals suffering from GD after cholecystectomy showed higher levels of low-density lipoprotein cholesterol (r_s = 0.228, $P \leqslant 0.01$) and gamma-glutamyl transferase (r_s = 0.298, $P \leqslant 0.01$). Leptin level was positively correlated with cholecystectomy (r_s = 0.336, $P \leqslant 0.01$). The NAFLD and GD patients also showed greater advanced fibrosis (26.31%), especially those who had undergone cholecystectomy (30.18%). Stage of liver fibrosis was also positively correlated with cholecystectomy (r_s = 0.366, $P \leqslant 0.01$).

Conclusion. Comorbid course of NAFLD and GD is characterized by clinical and laboratory features that may be associated with metabolic disorders, particularly imbalanced adipose tissue hormones.

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Role of anxiety and depression in formation of gastrointestinal symptoms and eating behaviour disorders among students (according to survey results)

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Background. University students experience significant changes in their social environment, which contribute to higher levels of anxiety and depression. Psychosocial disturbances occurring during this period can persist into adulthood.

Aim. To assess the role of anxiety and depression in the formation of eating behaviour disorders and gastrointestinal symptoms among students.

Methods. Anonymous survey was carried out by filling out online questionnaire forms, like MINIMULT, GSRS and WHO CINDI program questionnaire among students of the Omsk State Medical University. The sample size was 53% (3634 students). The respondents included 709 (19.51%) males and 2925 (80.49%) females.

Results. The presence of depressive symptoms was revealed in 985 (27.11%), anxiety – in 1304 (35.88%), a combination of anxiety and depression – in 526 (14.47%) respondents. Depressive mood background is associated with an increase in the consumption of sweet (2I=16.22, p<0.001) and flour products (2I=13.14, p<0.001), the formation of gastrointestinal symptoms of constipation (2I=38.27, p<0.001) and abdominal distention (2I=47.69, p<0.001). A positive association with a decrease in the frequency of food intake up to 1–2 times a day was established in persons with anxiety dominance, also revealing a deficit in the consumption of vegetables and fruit up to 214.3 [107.1; 398.8] g/day, with gastrointestinal symptoms of epigastric burning (47.93%), abdominal pain (43.94%). A combination of anxiety-depressive symptoms is associated with increased consumption of coffee (U=1544300.5, p=0.0048), spicy food (2I=7.76, p<0.001), low consumption of vegetables and fruit (U=1323404.0, p=0.000), the habit of adding salt to cooked food (2I=18.85, p<0.001), a high incidence of abdominal pain (62.16%) and dyspepsia syndrome (55.7%).

Conclusion. The study shows the role of anxiety and depression in predicting student dietary choices. The obtained results substantiate the necessity of screening students for psychological disorders, taking into account the consequences for the behavioural lifestyle and health.

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Effect of the cytoprotector rebamipide on the activity of enzymes of the small intestine mucosa in patients with impaired membrane digestion

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Background. Enteropathy with impaired membrane digestion (ENMP) is a disease characterized by poor food tolerance due to a decrease in the enzymatic activity of the small intestine mucosa (SSC).

Aim. To display the effect of the cytoprotector rebamipide on the activity of enzymes of the small intestine in patients with enteropathy with impaired membrane digestion

Methods. 24 patients with ENMP were examined. The average age of patients was 35.6+9.9 years (among them 7 men (29%), 17 women (71%). In all the examined patients (24), in addition to the classical therapy regimen, a course of the cytoprotector rebamipide was added (4 weeks, 300 mg/day).

Results. As a result of the treatment, an increase was observed in activity of all the studied enzymes: 17 patients out of 24 increase the level of glucoamylase (which accounted for 70.8% of total), the activity increased by 84% ($p<0.0036$). An increase in maltase activity was observed in 16 patients (66.6%), an increase of 33% ($p<0.0184$), sucrose in 17 patients (70.8%), activity increased by 92% ($p<0.0239$), lactase in 17 patients (70.8%), an increase of 94% ($p<0.0036$).

A persistent increase in the activity of small intestine enzymes was observed in a patient whose course of treatment was 12 weeks. Against the background of long-term treatment, there was an increase in the activity of glucoamylase by 6 times, maltase by 2 times, sucrose by 2 times, lactase by 4 times.

In 13 patients (54.1%), the drug was well tolerated. Of these, 3 (12.5% of the total number of patients taking cytoprotector) improved the tolerance of carbohydrate-containing products.

Conclusion. The basis of pathogenetic therapy of ENMP is rebamipide, which increases the activity of carbohydrases and reduces the clinical symptoms associated with food intolerance. The positive effect of rebamipide was observed 4 weeks after the start of taking the drug in patients with ENMP who received the drug at a dose of 300 mg/day. In most patients, there was an improved tolerance of food products and decrease or ceasing of flatulence, pain, abdominal discomfort and disorders of the chair. The impact of rebamipide therapy was particularly well-pronounced in patients who took the drug for 12 weeks.

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Dynamics of colorectal cancer indicators in Kazakhstan

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Background. In 2020, 1 931 590 cases of colorectal cancer (CRC) were registered worldwide accounting for 10% of all cancer cases (gco.iarc.fr). According to American Cancer Society, the lifetime risk of developing colorectal cancer is about 1 in 23 (4.4%) for men and 1 in 25 (4.1%) for women.

Aim. To estimate the tendencies in CRC incidence in Kazakhstan.

Methods. The material of the study was the data of the Ministry of Health of Kazakhstan (MoHK), concerning CRC (form 35). The retrospective study employed descriptive and analytical methods of epidemiology.

Results. In 2009, 2364 people were registered with the first-ever diagnosis of CRC and the incidence (crude rate) was 14.37±0.30$^0/_{0000}$. In 2018, 3218 new cases of CRC were registered (table), and the incidence increased to 16.87±0.30$^0/_{0000}$ (t=5.890; p=0.000; T=+1.1%).

Table. CRC indicators in Kazakhstan, 2009–2018

Indicators	New cases	Morphologically verified	I-II stage	III-IV stage
2009	2364 (100.0%)	2023 (88.1%)	985 (42.9%)	1309 (57.0%)
2012	2766 (100.0%)	2505 (93.3%)	1308 (48.7%)	1375 (51.2%)
2015	3148 (100.0%)	2843 (95.3%)	1694 (56.8%)	1258 (42.2%)
2018	3218 (100.0%)	2951 (96.3%)	1935 (63.2%)	1120 (36.6%)

The rate of morphological verification of CRC in the studied years increased from 88.1% in 2009 to 96.3% in 2018 (T=+1.1%). In the dynamics, the indicators of early diagnosis (I-II stage) increased from 42.9% (2009) to 63.2% in 2018, and the incidence of stage I-II in these years was 6.16±0.20$^0/_{0000}$ and 10.66±0.24$^0/_{0000}$ respectively (t=14.400; p=0.000; T=+4.7%). The incidence of stage III tended to slightly decrease from 5.79±0.19$^0/_{0000}$ (2009) to 4.04±0.15$^0/_{0000}$ in 2018 (t=7.230; p=0.000; T=–6.2%), and the incidence of stage IV in these years has amounted to 2.40±0.12$^0/_{0000}$ and 2.13±0.11$^0/_{0000}$, respectively (t=1.660; p=0.098; T=–3.1%).

Conclusion. The incidence rates of CRC in Kazakhstan tend to rise. However, the analysis of the collected data allows us to draw positive conclusions about improved diagnosis in country. Despite the fact that a colorectal cancer screening program already exists, early diagnosis must receive a thorough attention.

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Comparison of endoscopic data, clinical symptoms and risk factors in Gastroesophageal reflux disease and Barrett's esophagus

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Background. The most important pathogenicity factor in the development of Barrett's esophagus is Gastroesophageal reflux disease (GERD). However, only a small proportion of patients with reflux disease have a Barrett's esophagus (BBV), which is the only known precursor of the esophageal adenocarcinoma. It is therefore even more important to identify the inherent clinical manifestations and potential risk factors for the development of these diseases.

Aim:

- compare the relationship between GERD and BBV endoscopic deposits and clinical symptoms using the GERDQ;
- assess the relationship of their endoscopic findings with common risk factors such as age, adiposity and smoking;
- consider their relationship with the size of hiatal hernia.

Methods. Patient survey was performed in time period from March to August of 2020. Patients with reflux esophagitis or Barrett's esophagus were invited to participate in the study after gastroduodenoscopy and signed informed consent.

Results. Of the 62 patients with reflux esophagitis and BBV, 35 had never smoked, 14 regularly smoked, 13 had quit smoking. 3 patients consumed alcohol at least once a day. In 19 patients (31%), the body mass index was normal, 24 (40%) were overweight, 16 (26%) had grade 1 obesity, 1 (1%) had grade 2 obesity, 2 (3%) females – grade 3. There were 32 (52%) patients with esophagitis A, 8 (13%) – B, 7 (11%) – C. No one was identified with esophagitis D. 15 (24%) patients had BBV, of whom 4 were younger and 11 older than 50 years of age, with a ratio of 1:2.75. In the BBV group, one patient did not have a hiatal hernia, with others ranging from 2 cm to 6 cm, an average of 2.96 cm. In women ($p=0.025$), non-obese patients ($p=0.01$) and patients $\geqslant$ 50 years of age ($p=0.01$), complaints about heartburn, regurgitation, epigastric pain and nausea were more common than in men, patients with obesity and those under 50 years of age, respectively.

Conclusions. Esophagitis A and B were more common than C and D (5.7:1), and patients with small esophageal defect complained more frequently about the typical symptoms of GERD, such as heartburn, regurgitation, epigastric pain, nausea. BBV was 4 times more common in men, 93.3% of patients had hiatal hernia. BBV on average was diagnosed at the age of 54.33.

Pancreatic cancer indicator changes in Kazakhstan

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Background. The incidence of pancreatic cancer (PC) in many countries remains high and tends to increase worldwide. PC is the seventh leading cause of cancer-related deaths in the world. According to IARC (gco.iarc.fr) assessments, this intractable malignancy has ranked the 11th most common cancer in the world counting 458 918 new cases and causing 432 242 deaths in 2018.

Aim. To evaluate the tendencies in PC incidence in Kazakhstan.

Methods. The material of the study was the data of the Ministry of Health of Kazakhstan, concerning PC (form 35). The retrospective study employed descriptive and analytical methods of epidemiology.

Results. In 2009, 845 people were registered with the first-ever diagnosis of PC and the incidence (crude rate) was 5.04±0.18$^0/_{0000}$. In 2018, 1096 new cases of PC were registered (see table below), and the incidence increased to 5.68±0.18$^0/_{0000}$ (t=2.51; p=0.012; T=+5.5%).

Table. PC indicators in Kazakhstan, 2009–2018

Indicators	New cases	Morphologically verified	I-II stage	III-IV stage
2009	845 (100.0%)	320 (39.7%)	109 (13.5%)	697 (86.5%)
2012	929 (100.0%)	423 (48.0%)	155 (17.6%)	598 (82.2%)
2015	958 (100.0%)	553 (62.1%)	182 (20.4%)	254 (77.6%)
2018	1096 (100.0%)	598 (58.0%)	692 (24.6%)	776 (75.3%)

The rate of morphological verification of PC in the studied years increased from 39.7% in 2009 to 58.0% in 2018 (T=+5.5%). In the dynamics, the indicators of early diagnosis (I-II stage) increased from 13.5% (2009) to 24.6% in 2018, and the incidence of stage I-II in these years was 0.68±0.07$^0/_{0000}$ and 1.40±0.09$^0/_{0000}$ respectively (t=6.31; p=0.000; T=+6.2%). The incidence of stage III tended to slightly decrease from 2.35±0.12$^0/_{0000}$ (2009) to 2.17±0.11$^0/_{0000}$ in 2018 (t=1.11; p=0.269; T=−1.6%), and the incidence of stage IV in these years has amounted to 2.01±0.11$^0/_{0000}$ and 2.10±0.11$^0/_{0000}$, respectively (t=0.580; p=0.563; T=−1.2%).

Conclusion. The incidence rates of PC in Kazakhstan are rising as well as in the world. The obtained data show that special attention should be paid to the state of morphological verification. Since the indicator for 10 years amounted to only 52.3%, work on improving the level of morphological verification is still required. Also, the level of early diagnosis is poor. What is connected with the lack of screening. Ultrasound, CT and MRI are available as screening methods. Overall, measures for prevention and better learning of risk factors of PC are needed.

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Body muscle mass association with Chrohn's disease activity

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Background. IBD has become a global disease in industrialized countries, and the incidence of CD has risen significantly over the past half century (Levine, 2020). Malnutrition is a common complication of Crohn's disease (CD) patients and it is correlated with alterations of the body composition and disease activity (Balestrieri, 2020; Argiles, 2015).

Aim. Our aim of this study was to analyse body muscle mass metabolic data in association with Crohn's disease, identifying patients with low and high disease clinical activity.

Methods. This prospective pilot study included twenty-three hospitalised patients aged ⩾18 years, with an established diagnosis of CD, with no medical history of surgical interventions. CD patients were divided into those with low and high clinical activity indexes, according to CD activity index (CDAI). Patients were assessed using the Nutritional Risk Score (NRS2002) and Malnutrition Universal Screening Tool (MUST), recommended by the European Society of Clinical Nutrition and Metabolism. To evaluate body composition Body bioelectrical impedance analysis (BIA) measurements were performed.

Results. Twenty-three hospitalised patients (median age 36.5 IQR: 28.5–51.5 years) were enrolled, 61% (n=14) male. The median CDAI was 128 (IQR=6.0-207.0). The study group comprised 48% (n=11) patients with low CD activity and 52% (n=12) of patients with high disease activity. According to NRS2002 and MUST, 70% (n=16) CD patients were nutritionally at risk and in need of nutritional support. From twelve patients with high disease activity 92% (n=11) has a risk of malnutrition, from eleven patients with low disease activity only 45% (n=5) has a risk of malnutrition with statistical significance p=0.027. Comparing BIA results between CD patients and the control group, the median BMI was lower for the CD (21.10 [IQR=19.2–23.3]) than for the control group (23.4 [IQR=21.5–25.8]) (p=0.014). In addition, visceral fat mass was lower in CD (–4,00 [IQR=–12.1 to 5.6]) than in the control group (7.85 [IQR=-0.9–18.2]) (p=0.003). Reduced muscle mass was observed in 48% (n=11) of CD patients.

Conclusion. CD patients with high disease activity had a noticeably increased risk of malnutrition. 48% of CD patients in both the low and high disease activity groups had a reduction in muscle mass. Identification of the reduction in soft lean muscle mass in CD patients can be used as an indicator of disease activity. Patients that have BMI within normal values also have a high chance of having imbalance in body composition.

Carbohydrase activity of duodenum mucosa in adult celiac disease patients

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Background. Some celiac disease (CD) patients, provided they have a normal histological structure of the small intestine mucosa and follow a gluten-free diet, may complain of symptoms of rumbling, bloating, diarrhoea. Impaired activity of small intestine enzymes may be the cause of these symptoms.

Aim. To determine the activity of carbohydrases (glucoamylase, maltase, sucrase and lactase) in patients with celiac disease.

Methods. Thirty-five patients with newly diagnosed celiac disease were examined: 29 women and 6 men (mean age 31.6±15.4 years) and 60 patients with previously diagnosed celiac disease: 38 women and 12 men (mean age 42.6±17.2 years). The diagnosis of celiac disease was based in addition to the clinical picture, by serological indicators and duodenal biopsy. The histological changes in the duodenum biopsy were classified according to the Marsh criteria. The activity of carbohydrases (glucoamylase, maltase, sucrase, lactase) was measured in the small intestine mucosa by the modified Dahlquist method. Statistical processing of the results was carried out using parametric and nonparametric criteria

Results. In patients with newly diagnosed celiac disease, the activity of all the investigated carbohydrates was reduced by 91.6%, in the group of patients followed gluten-free diet – by 35% ($p<0.05$). It was found that total atrophy (Marsh IIIc) was associated with a decrease in the activity of all small intestine carbohydrases in patients. The recovery of the histological structure of the small intestine mucosa showed an improvement in the activity of all the studied carbohydrases. However, in the group of patients with normal small intestine mucosa, a decrease in glucoamylase activity was observed by 53.1%, a decrease in maltase activity – by 40.6%, sucrase activity decreased by 56.2%, and lactase activity – by 34.3%. A decrease in the activity of all carbohydrases was detected in 37.5% of patients with normal structure of the small intestine mucosa. A weak correlation was found between the degree of atrophy and the activity of sucrase and maltase.

Conclusion. Approximately one third (37.5%) of adult patients with celiac disease who follow a gluten-free diet and have a normal morphological structure of the small intestine mucosa may experience a decrease in the activity of intestinal carbohydrates, which may be one of the reasons for the persistence of symptoms of fermentation dyspepsia.

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The impact of regulatory molecules of hepato-biliary synthesis of bile acids on developing diarrhoea after cholecystectomy

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Background. Bile acid malabsorption is one of the frequent reasons for the persistent chronic diarrhoea cases after cholecystectomy (CCY). Its mechanism is very complex, it is not yet fully known and remains under study. Diarrhoea may follow an individual limited ability to reabsorb bile in the distal ileum due to a defect in the link of farnesoid X-receptor (FXR) – fibroblast growth factor 19 (FGF-19).

Aim. The aim of the current study was to determine the role of the fibroblast growth factor-19 (FGF-19) in the blood serum and bile acids (BA) in stools in pathogenesis of bile acid diarrhoea (BAD) of the patients who underwent cholecystectomy (CCY).

Methods. Patients who underwent cholecystectomy were examined at various periods of time, 30 of them with chronic diarrhoea, which appeared after CCY (group 1) and 31 patients with normal stools (group 2). All the patients were studied for FGF-19 concentration in the blood serum and the daily excretion of bile acids in the stools. The control group consisted of 28 practically healthy people.

Results. Patients form group 1 had the FGF-19 concentration in the blood serum equal to 86.2 ng/mL (67.8; 117.8), in comparison with the group 2 that showed 259 ng/mL (170.6;3 18.8), $p<0.001$, meanwhile, the daily excretion of bile acids in stools of the group 1 patients was 657.4 mg/day (524.6; 830.1), which on average was two times higher than the numbers of the group 2 and the control group. The inverse correlation was detected between FGF-19 and daily excretion of bile acids (Kendall'sTau: – 0.355, $p<0.001$), reflecting the reabsorption defect of bile acids in the distal ileum, patients with reduced concentration of FGF-19 had high daily excretion of bile acids with stools. The comparative analysis of FGF-19 concentration indicators in blood serum in patients who underwent cholecystectomy in different periods of time after surgery did not show significant differences within the group depending on the time of surgery, yet showed the remaining difference between groups 1 and 2.

Conclusion. One of the most probable reasons for the BAD in patients who underwent cholecystectomy lies in the decrease of the FGF-19 level besides the increase of the bile acids level, which can be used to diagnose BAD after cholecystectomy.

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Visceral hypersensitivity correction in patients with severe irritable bowel syndrome

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Background. Irritable bowel syndrome (IBS) is implicated in more than 50% of all functional diseases. It has achieved a great social relevance due to high spread among the working-age population and poor standard of living. Visceral hypersensitivity is the chief mechanism in the IBS pathogenesis. The drugs of choice to treat such patients are antidepressants from the serotonin and noradrenaline reuptake inhibitor type, such as duloxetine.

Aim. The aim of the current study was to examine the effect of duloxetine in the treatment of gastrointestinal and emotional-behavioural symptoms in patients with severe IBS.

Methods. The total of 35 patients with IBS and diarrhoea (IBS-D) were examined, including 17 men (45.5%) with an average age of 34±5 years, 18 women (51.5%) at the age of 32±4 years. The Rome Consensus IV served as the diagnostic criteria. The clinical symptoms of IBS were assessed using the VAS Pain, and the quality of life using the SF-36 questionnaire. Visceral sensitivity index (VIS) according to the Labus J. questionnaire (2004) and the Balloon Dilatation. Psychometric research included determination of the depression level (Beck 1961), actual and personal anxiety (Spielberger-Khanin 1976). All the patients were taking 60 mg of duloxetine for 16 weeks. Statistical results management was carried out by nonparametric methods according to the Wilcoxon criterion.

Results. All the 35 patients received the treatment with duloxetine. Against the background of 16-week therapy, the findings included the decrease of pain syndrome from 8±1 to 2±1 points ($p<0.01$), the change of defecation frequency and form (1–2 times a day, stool formed), the decrease of VIS from 46.3 to 12.01 ($p<0.01$), as well as tendency towards the increase in the maximum tolerated volume from 105.1 to 152.9 mL ($p<0.06$). Further findings included the decrease of the depression level from 21 to 5 points ($p<0.01$), the level of personal anxiety from 46 to 24 points ($p<0.01$), and situational anxiety from 49 to 28 points ($p<0.01$), as well as mental component improvement of the quality of life from 24.2% to 58.6% ($p<0.01$).

Conclusion. Patients with IBS-D under duloxetine therapy showed regression of clinical complaints for gastrointestinal tract and the severity of somatoform disorders, which led to improvement of their quality of life.

Acknowledgements. The authors declare the absence of conflict of interest.

Predisposition of inflammatory bowel disease in menopausal and postmenopausal women

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Background. Inflammatory bowel disease (IBD) is a group of intestinal disorders that manifest as inflammation of the different parts of digestive tract, which is a serious condition and has an impact on person's quality of life. Decreased oestrogen levels in menopausal and postmenopausal women are mentioned in the world literature as one of the IBD etiological factors, however, there are conflicting data and studies, and it is not entirely clear whether physiological decrease in oestrogen level in menopausal and postmenopausal women affect the development of IBD.

Aim. To investigate if menopause has an impact on IBD development.

Methods. A retrospective study was conducted at Riga East University Hospital and it included data from medical cards of 150 women over 45 years old with menopause and diagnosis "Crohn's disease" (ICD-10 code K50) or "Ulcerative colitis" (ICD-10 code K51), which were hospitalized from January 2013 to November 2020. For data collection and analysis, *Microsoft Excel 2016* was used. Statistical significance was considered as $p<0.05$. Fisher's test and T-test were used.

Results. The mean age was 63.84±10.6 years (median 64, mode 64). 61.3% (n=92) had an ulcerative colitis. 8.7% (n=13) had smoking factor in the anamnesis, of which 69.2% (n=9) had Crohn's disease. 87.3% (n=131) had at least one comorbidity. 16.7% (n=25) used hormonal replacement therapy (HRT), the mean age was 54.20±8.75 years. Statistically significantly, a relapse of IBD more often was found in women that used HRT (32.8%) compared to those who did not (4.7%) ($p<0.001$). There was no statistically significant difference between severity level of ulcerative colitis (Mayo score) and using or not using HRT ($p=0.645$).

Conclusion. The study did not find that hormone replacement therapy had a protective role for IBD, so menopause impact on IBD development is questionable. Using of the HRT had no effect on the severity of IBD, but increased the chance of disease relapse. Further investigations with a larger number of patients and control groups are required.

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Hepatocellular carcinoma in Lithuanian University of Health Sciences Gastroenterology Department in Kaunas

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Background. Hepatocellular carcinoma (HCC) is the fifth most common cancer and one of the most frequent causes of cancer-related deaths worldwide, constituting a major health problem. HCC prevention, diagnosis and treatment usually require a team of experienced medical specialists and are based on international guidelines.

Aim. Data analysis of HCC patients treated in Gastroenterology Department of Hospital of Lithuanian University of Health Sciences (HLUHS) Kauno Klinikos, Lithuania.

Methods. 46 patients with HCC, diagnosed and treated in Gastroenterology Department of HLUHS Kauno klinikos during 2012–2020, were enrolled in this study. The data of these patients were analysed using *Microsoft Excel*.

Results. A vast majority of HCC patients in our department were male (82.6%) with median age of 61.5 years. The most frequently chronic liver disease and HCC were caused by viral hepatitis C (47.8%) and viral hepatitis B (15.2%). Only 2 cases primarily were reported as HCC without underlying chronic liver damage. Every third case (32.5%) was classified as Barcelona Clinic Liver Cancer score (BCLC) stage 0 to A at the time of diagnosis that ensured the possibility of radical treatment. HCC of BCLC stage B were also diagnosed in every third case (37%), while remaining cases (30.4%) were associated with either extrahepatic spread (n=7) or end-stage liver function (n=7). 45.65% of diagnosis were proven histologically. In most cases, alpha-foetoprotein was assessed, but only in half of the cases (18/36) it was elevated above the upper limit of normal at the time of diagnosis. The methods of treatment were chosen according to the stage of HCC or its course. All the main HCC treatment methods were used in our centre: thermal ablation (8), resection (4), transarterial chemoembolization (TACE) (17), bland transcatheter embolization (TAE) (1), ethanol injection (3), transplantation (4), and systemic therapy (14). 11 patients were enlisted to liver transplant waiting list, out of which 4 patients underwent transplantation. Tumour recurrence after radical treatment was reported in 4 cases. All patients received sorafenib for systemic therapy as the first agent. Several patients were treated with second-line therapy: cabozantinib (3) and regorafenib (2). More than a half of patients (58.7%) received supportive care at some point of treatment.

Conclusion. Data analysis of HCC patients in Gastroenterology Department of HLUHS Kauno Klinikos showed tendencies of HCC diagnosis and treatment similar to international experience.

Frequency of hereditary and acquired thromboembolic complications in patients with inflammatory bowel diseases in Moscow

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Background. Thromboembolic complications (TC) are among the characteristic manifestations of inflammatory bowel diseases (IBD).

Aim. To identify the frequency of acquired and inherited hypercoagulation factors that contribute to the development of TC in patients with IBD.

Methods. The clinical status of 1238 IBD patients undergoing treatment in 2019 was evaluated in the Department of IBD. 748 patients with ulcerative colitis (UC) and 490 patients with Crohn's disease (CD). In 112 patients with IBD (9.0%), clinically significant TC (venous thrombosis of the lower extremities, upper extremities and others) was detected. In patients with clinically significant feasibility studies, DNA isolated from peripheral blood lymphocytes was examined to identify molecular genetic mutations that lead to hypercoagulation.

Results. Of the 112 patients with TC, 76 (67.8%) patients had UC, and 36 (32.2%) patients had Crohn's disease. Of 112 IBD patients with clinically significant TC, 45 (40.2%) had genetic mutations that increase affinity for fibrinogen, increase platelet aggregation, disrupt folic acid metabolism, and reduce the activity of the methylenetetrahydrofolate reductase enzyme, which may be manifested by a moderate increase in homocysteine levels. 67 patients with IBD (59.8%) did not have genetic mutations that lead to hypercoagulation. Of the 45 IBD patients with clinically significant feasibility studies due to hereditary factors, 30 (66.6%) patients had UC, 15 (33.7%) patients had CD (HR-1.038, 95% CI 0.746-1.444; x2-0.049; p=0.83921).

Conclusion. Clinically significant feasibility studies were found in 9.0% of IBD patients. More than 40% of patients with clinically significant feasibility studies (n=112) have inherited factors that contribute to the development of feasibility studies. About 60 % of IBD patients with clinically significant feasibility studies do not have hereditary factors that lead to the development of feasibility studies.

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Disaccharidase deficiency can cause the symptoms of irritable bowel syndrome

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Background. The decrease in disaccharidase activity of the membrane digestion in the small intestine providing digestion of carbohydrates can cause clinical symptoms of irritable bowel syndrome (IBS).

Aim. The aim of the current study was to estimate the enzymes activity of the membrane digestion of carbohydrates, namely glucoamylase, maltase, sucrase and lactase in patients with IBS and the effect of their activity in long-term therapy with rebamipide.

Methods. 102 patients with IBS, 41 men and 61 women were examined. According to Rome IV criteria (2016), 68 patients had IBS with predominance of diarrhoea, 20 patients had IBS with predominant constipation and 14 patients showed mixed type of IBS. The activity of glucoamylase, maltase, sucrose and lactase were determined by Dahlquist-Trinder method in duodenal biopsies obtained during esophagogastroduodenoscopy. The control group consisted of 20 healthy people aged 23–47. They showed following enzyme activity: lactase – 42±13 ng glucose/mg tissue x min, glucoamylase – 509±176, maltase – 1735±446, sucrase – 136±35 ng glucose/mg tissue x min. These figures were taken as the norm.

Results. 10.8% of the study group showed normal disaccharidase activity of the membrane digestion (11 out of 102 patients), 32.3% had decreased activity of all studied enzymes and 58.8% had selective reduction of disaccharidase activity. Twenty patients with disaccharidase deficiency were recommended the FODMAP diet and ingest rebamipide 3 times a day x 200 mg for 3 months. Before the treatment, the activity of glucoamylase 83±78, maltase – 417±221, sucrase – 32 ±17, lactase – 11±17 ng glucose/mg tissue x min. After the treatment 16 patients reported a decreased or no flatulence, abdominal pain, stool disorder; 4 people reported no change. The activity of glucoamylase increased to an average of 149±82 (by 78%, p=0.016), maltase to 864±472 (by 131%, p=0.0019), sucrase – 63±35 (by 95%, p=0.0041) and lactase – 10±8 ng glucose/mg tissue x min. (the activity did not change significantly).

Conclusion. In 89.2% of patients with IBS, there was a decrease of disaccharidase activity in the small intestine providing digestion of carbohydrates. The 3-month treatment with rebamipide helped reduce clinical symptoms of IBS and increase disaccharidase activity of the membrane digestion of carbohydrates in small intestine.

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Possibilities of acoustic myography for assessing functional condition of lower esophageal sphincter

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Background. Acoustic myography (AMG) is a method of detecting and measuring muscle sounds, the essence of which is that during contraction the muscles create an acoustic wave, which is recorded using a special microphone. The use of AMG for the diagnosis of smooth muscle (GM) of the lower esophageal sphincter (LES) is proposed in our work.

Aim. The aim of the current study was to investigate the possibility of non-invasive assessment of the functional state of GM LES, using the AMG technique.

Methods. Two volunteers, 19-year-old men, weighing 67 kg and 74 kg, height – 181 cm and 182 cm, were included. The subjects excluded signs of GERD, using the GERDQ questionnaire. The hardware included a microphone, an amplifier, a filter, analogue-to-digital signal converters, and a personal computer. Piezoelectric, dynamic and optical microphones and low frequency electronic amplifiers with amplification of 6, 20, 40, 50 and 60 dB in various combinations were used. The microphone was placed under the xiphoid process, at the level of Th XI, along the midline of the body, coinciding with the projection zone of the LES. Frequency analysis was performed by calculating the spectrum of an audio signal lasting about 2.5 seconds using a fast Fourier transform algorithm and a Hamming window. The graph was created on the basis of the obtained values using interpolation. For each volunteer, the averaging of the spectra was performed, and it was based on the results of processing 12 implementations of the audio signal.

Results. Graphical recording of the received signals showed that the spectrum of local movements for muscle fibres during the opening and closing of the LES is characterized by a significant proportion of mechanical oscillations with frequencies mainly from 100 Hz to 300 Hz. The presence of only low-frequency components (from units of Hz to 15-20 Hz) is typically for the reduction of GM when the LES is in a state of closed and significant oscillations of muscle fibres were not recorded. Instead, the reduction of GM after the opening of the LES leads to the appearance of relatively high-amplitude components of the signal. Similar results were obtained using the other types of microphones mentioned above.

Conclusion. Using the method of non-invasive diagnosis of the functional state of GM LES, applying the AMG technique, we obtained and analysed a graphical recording of the sound signal from the reduction of GM LES and the spectra of local displacements of GM.

Reasons for refusing further endoscopic surveillance in patients with diagnosed precancerous gastric lesions

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Background. Atrophic gastritis, intestinal metaplasia and dysplasia are precancerous lesions of gastric cancer. Endoscopic surveillance of patients with precancerous lesions is crucial for timely identification of an early-stage cancer. The European (MAPS) guidelines are defining the groups of subjects to be subjected to surveillance as well as the intervals of control.

Aim. To evaluate the proportion of patients refusing to undergo surveillance endoscopy, and the reasons for refusing surveillance.

Methods. Altogether, 233 GISTAR study subjects in whom surveillance endoscopy was indicated according to the MAPS guidelines, were invited for upper endoscopy by a telephone call. Reasons for refusing the follow up endoscopy were categorised into 5 categories.

Results. 27.9% (n=65) out of 233 patients refused surveillance investigation after the initial or any of the follow-up upper endoscopies – 53.8% (n=35) in the very high-risk group (dysplasia), 7.7% (n=5) in the high-risk group (OLGA or OLGIM stage III-IV), and 38.5% (n=25) in the medium magnitude risk group (intestinal atrophy and metaplasia). The most common reason in all risk groups for refusing surveillance upper gastroscopy was "just did not want it" – 43.1% (n=28). The second most common (29.2%; 19 subjects) reason was "other", which mainly included reasons like health problems and transportation issues. The third most common reason was "financial problems" – 12.3% (n=8), followed by fourth category of reasons "find in unnecessary", meaning patients, who thought endoscopic surveillance was not useful – 9.3% (n=6), and the least common reason category – "lack of time" in patients who could not find time for the endoscopy, concluding 6.1% (n=4) patients.

Conclusion. Approximately in a quarter of cases surveillance upper endoscopies were refused; about a half of the patients, who refused endoscopic surveillance, were in a very high-risk group with dysplasia, which is a precancerous gastric lesion with the highest risk of developing into adenocarcinoma. Feeling healthy, lack of belief in surveillance procedures being among the main reasons for not being compliant are indicating the need for improved health literacy among the general population.

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The role of capsule endoscopy in diagnosis of celiac disease

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Background. Clinical picture in the setting of celiac disease does not always depend on the extent and character of pathological changes in the mucosa of the small bowel. Capsule endoscopy (CE) allows us to evaluate the small bowel and obtain information about the extent of the damage in small bowel mucosa in celiac patients.

Aim. To determine the indications for CE in patients with celiac disease.

Methods. The study included 10 patients (6 women, 4 men) with proven celiac disease. The median age was 42.4±17.5 years. In 3 patients, celiac disease was detected for the first time, in the rest – during the period of 3 months to 2 years.

Results. In 3 patients with newly diagnosed celiac disease, endoscopic signs of mucosal atrophy of the small bowel were more pronounced in the duodenum. In 3 patients, mucosal atrophy spread to the proximal parts of the small bowel. In 4 patients (with typical and refractory forms), mucosal atrophy extended to the distal ileum, and erosion and ulcers were found in the jejunum. In 3 of them, the clinical picture was characterized by a severe course, accompanied by a syndrome of malabsorption.

Conclusion. Clinical symptoms do not always coincide with the extent of the lesion of the mucosa of the small bowel, owing to its uneven distribution of the damaged mucosa, as well as its uneven ability to restore. The alternation of externally unchanged mucosal surface with areas of atrophy suggests a different time of contact of the chyme and small bowel lining in the lumen.

The indication for performing a CE in celiac disease patients is the lack of response to treatment, the assumption of erosive and ulcerative lesions of the mucosa of the small bowel and the refractory disease. CE allows us to establish the extent of atrophic changes in the mucosal lining, which makes it possible to use it to assess the effectiveness of treatment.

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COVID-19: changes in IL-10 and faecal markers in patients with IBD

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Background. COVID-19 may include symptoms of gastrointestinal tract damage, which can come to the fore in the clinical picture of the disease and precede the onset of respiratory symptoms. Patients with chronic inflammatory bowel disease (IBD) receiving immunosuppressive therapy are at increased risk of developing COVID-19. However, so far, there is no specific data on the features of changes in faecal markers and some interleukins (except for IL-6 and α-TNF).

Aim. To monitor the condition of patients with IBD who have undergone COVID-19 and to identify specific changes characteristic of this condition.

Methods. 48 (22 UC, 26 CD) patients with IBD (aged 18 to 58 (average age 34.2±1.2 years), who underwent COVID-19 were examined in the period from August 2020 to January 2021. The patients underwent a routine examination corresponding to their severity; monitoring included laboratory tests (hemogram and C-highly sensitive protein (h/s CRP), α-TNF and IL-1β,2,4,6,8,10,18; stool tests and faecal calprotectin, lactoferrin); endoscopic examination was prescribed for calprotectin values above 100 μg/g (N⩽50 μg/g). In 23 patients, COVID-19 was established based on a PCR test (there were clinical symptoms and/or there were contacts), and in 25 patients, COVID-19 was established based on data from serological studies (IgM, IgG).

Results. When studying the data of hemogram and h/s CRP, significant changes corresponding to the severity of the patients were not found, however, when studying the data on the interleukin profile and faecal markers, a definite relationship was found: all 48 patients, regardless of the severity of IBD, showed an increase in the level of IL-10 (13.5–59.2 pq/ml; N<20 pq/ml) (which was not previously observed in these patients) and the levels of faecal calprotectin (52.3–2500 μg/g) and lactoferrin (7.9–69.9 μg/g, N<7.25 μg/g); changes in lactoferrin levels were more pronounced than changes in calprotectin levels. There were no statistically significant differences between the groups of patients with UC and CD (p>0.05).

Conclusion. Monitoring in patients with IBD who underwent COVID-19 revealed a change in certain markers to the fore: an increase in the level of IL-10 and changes in the levels of faecal calprotectin and lactoferrin, and the changes in lactoferrin were more pronounced than changes in calprotectin, respectively, in terms of the severity of IBD.

The primary data obtained by the authors suggest that during the COVID-19 period, the inclusion of new markers, IL-10 and lactoferrin, is possible in the diagnostic package.

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Evaluation of the dietary habits of Jēkabpils inhabitants regarding adherence to Nordic diet recommendations

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Background. The Nordic diet (ND) is recommended as a healthy, sustainable diet, that mostly adheres to consumption of local products. Nordic Council is actively promoting ND in Scandinavia, however, the data is lacking about the adherence to ND dietary habits among Latvian citizens.

Aim. The aim of the study was to evaluate adherence to the ND in average Latvian population.

Methods. The study was carried out as a sub-study of the "Multicentric randomised study of *H. pylori* eradication and pepsinogen testing for prevention of gastric cancer mortality (the GISTAR study)". The individuals, 40 to 64 years of age, were invited to the study centre located in Jēkabpils from October 2019 to November 2020. The participants signed an informed consent and completed 22 item self-administered questionnaire in Latvian or Russian. Socioeconomic data were collected within the GISTAR study protocol. The questionnaire included translated and adapted New Nordic Diet score questions. One score point was assigned for each match according to the published references: adherence to ND: as low (score 0–3), medium (score 4–5) or high (score 6–10). Hi square test was used for statistic and was considered as significant with $p<0.05$.

Results. In total, the survey was completed by 988 participants (out of these, 134 were incomplete and excluded). 854 completed questionnaires were analysed. 602 (70.5%) questionnaires were completed by females. A high adherence to ND was reported by 157(18.4%), medium – by 365 (42.7%), and low – by 332 (38.9%) respondents.

The adherence to ND was associated with sex: a high adherence was observed in 23.3% of females compared to 6.7% of males; medium – in 49.0% females and 27.8% males; low – in 27.75% females and 65.5% males, respectively ($p<0.0001$). Respondents in the age group 50–54 years had the highest adherence to ND, while individuals up to 44 years of age demonstrated the lowest adherence ($p=0.012$).

Adherence to ND was associated with a higher educational status: adherence to ND was observed in 18.5% of respondents with higher education, 19.7% of respondents with professional technical education, 14.0% of respondents with secondary education ($p=0.038$). No difference in adherence was observed in respect to employment status.

Conclusion. The adherence to ND among 40–64 year-old general population in Jēkabpils is of a medium level. The differences in adherence in the context of sex, age and educational pattern should be taken into account promoting ND in Jēkabpils. Nevertheless, the assessment of factors influencing adherence to ND in other regions of Latvia should be studied.

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Analysis of blood microbiome in patients with gastric cancer

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Background. Gastric cancer (GC) is one of the most common cancers in the world and third leading cause of cancer-related death. Due to disease frequency, limited treatment and diagnostic possibilities GC remains an important health issue. Previous studies have shown that microbiome plays an important role in maintaining a healthy state, and their imbalance is associated with various diseases. Recently microbial DNA were detected in the circulated blood. It has been shown that bacterial DNA also corresponds to various states of human health.

Aim. The aim of the current study was to perform a microbiome analysis and identify possible circulating biomarkers for GC.

Methods. Plasma DNA samples from 35 GC patients and 43 controls were used. Additional 4 extraction control samples were used to verify the quality and avoid possible bacterial contamination. V1–V2 region of bacterial 16S rRNA gene was sequenced on an Illumina MiSeq platform. To construct sample-similarity matrices abundances of taxonomic ranks in each sample type were used by applying Bray-Curtis algorithm. For significant differences between the groups permutational multivariate analysis of variance (PERMANOVA) and Mann-Whitney test followed by false-discovery rate (FDR) test were used. Analysis included such clinical data as grading, tumour size, number of lymph nodes containing cancer cells, presence of metastases (TNM classification) and growing type (Lauren classification).

Results. Comparison between the global plasma bacterial assemblages revealed that the global structures at phylotype, order, family, and genus taxonomic ranks were significantly different between control and GC groups. Relative abundance of *Prevotella*, *Enterobacteriaceae, Corynebacteriaceae, Prevotellaceae, Corynebacterium* in GC patients' blood was significantly higher than in controls. Differences in *Prevotella* abundance were associated with intestinal tumour growing type, while *Enterobacteriaceae* – with diffuse tumour growing type and low cell differentiation.

Conclusion. Global circulating microbiome profile of GC patients differs from that of the control group. *Prevotella* and *Enterobacteriaceae* could presumably be used as clinical biomarker of GC.

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Study of the structural changes' dynamics in the patients with a *Helicobacter pylori*-related gastritis

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Background. The dynamics over the past 10 years in Kazakhstan has had a tendency for an increase in the incidence of malignant neoplasms by 9.5% and a decrease in the mortality rate by 28.5%. In the structure of morbidity, stomach cancer takes the third place – 8.6%. The main purposes of a research are to study the dynamics of atrophic changes of gastric mucosa (GM) within a long period (in 5 years' time) in the patients with *Helicobacter pylori* (HP)-related chronic atrophic gastritis, and to take cancer-preventive measures.

Aim. The aim of the current study was study of the structural changes' dynamics in the patients with a HP-related gastritis.

Methods. 835 patients with a dyspepsia were examined by a minimally invasive screening procedure "GastroPanel" (MCH PAA RK) in 2011–2013. Consequently, 118 patients (14.1%) were diagnosed with the HP-related chronic atrophic gastritis with a diverse location of GM. Among examined patients were 93 (78.8%) with the completed invasive study – esophagogastroduodenoscopy with a HP detection. Chronic atrophic gastritis was histologically confirmed within 46 among 93 (49.5%) patients according to the system OLGA (men – 14, women – 32, average age – 48.8±8.7, age range 26–67 years).

Results. Histologic study results of GM are shown in the table below.

	Antrum	Body of stomach	Multifocal disease
First Stage Atrophy	16	19	10
Second Stage Atrophy	25	3	1
Third Stage Atrophy	4	2	-
Colonic metaplasia	4	1	-
Mixed metaplasia	3	1	-

Conclusion. Thus, "GastroPanel" is a highly-sensitive research which helps to determine atrophic changes of GM by a minimally invasive method and to specify a risk group with a gastric cancer potential among patients. Therefore, it supports prevention of a gastro carcinogenesis or its diagnosis within remediable life stages.

In prospect, an advanced study is required among patients with precancerous changes in a stomach and those HP stocks, which lead to a gastro carcinogenesis. More specifically, with s1/m1 variant vacA genes and/or cagA genes. Analytical part of a research is in progress at this time, which will develop a deeper understanding of precancerous progression in GM within a long date and part of HP reinfection in a gastro carcinogenesis within the reviewed period.

Role of combined probiotic in treatment of lactase deficiency in adult population

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Background. Secondary lactase deficiency (SLD) is inability to digest lactose, the predominant sugar of milk. This inability results from decrease of lactase enzyme activity, which is produced in the small intestine.

Aim. The aim of the current study was to define the influence of SIBO in patients with SLD in adult patients.

Methods. In this study, 386 patients (the mean age – 33.9±9.09; F/M – 249/137) with postinfectious irritable bowel syndrome (IBS) were analysed concerning lactase deficiency. All patients underwent intestinal endoscopy with biopsies from the mucosa of the descending duodenum to determine lactase deficiency by means of lactose quick test (LQT). To diagnose small intestinal bacterial overgrowth (SIBO), all the patients underwent lactulose breath test.

Results. SLD was detected in 36.5% of patients with postinfectious IBS. Mild SLD was determined in 25.6% of patients, and severe SLD – in 10.9% of patients. The specific clinical symptoms of mild SLD were moderate flatulence with abdominal pain (80.7%); the majority of patients (73.7 %) had normal stool consistency, one time a day; the other patients had semi-liquid faeces, 2–3 times a day (26.3%). SLD in all cases was accompanied by SIBO (the average level of lactulose breath test was 80.3±28.3ppm, N<20ppm). It turned out that the degree of lactase deficiency depends on the severity of SIBO in the lumen of the small intestine. Thus, when mild SLD average value SIBO was 72.4 ± 25.1ppm, whereas severe SLD average indicators of SIBO achieved higher values, 99.3±26.9ppm (N<20ppm). To establish the degree of dependence of SIBO in the small intestine and the degree of deficiency of lactase in the small intestine biopsies performed a statistical analysis of the results by calculating the Spearman rank correlation coefficient to study a statistically significant link between the various phenomena. In this study, an inverse correlation between the degree of lactase deficiency in patients with the SLD and the severity of SIBO in the small intestine, i.e., the higher the hydrogen concentration in the exhaled air, the less activity of the enzyme lactase in the small intestine biopsy specimens ($r=-0.49$, $p<0.001$).

Conclusion. SIBO in all cases was accompanied by SLD. Thus, the high frequency of the SLD associated with SIBO in the small intestine in patients postinfectious IBS can be explained by the growth of pathogenic microflora in the small intestine.

Acknowledgements. The authors declare the absence of conflict of interest.

BASIC MEDICAL SCIENCE

Correlation of severity of atopic dermatitis with blood and urine laboratory data

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Background. Atopic dermatitis (AD) is a chronic allergic disease, which is diagnosed primarily clinically.

Aim. 1) to search for laboratory markers diagnostic for AD; 2) to examine, which of the commonly used laboratory analyses – blood and urine – are deviated (above or below the norm).

Methods. Patients with severe AD were included in the study after obtaining the informed consent. Severity of AD was measured using EASI scale. Blood was drawn and urine analyses were taken and processed according to the international laboratory standards.

Results. None of the patients had normal blood picture or chemistry. The most common abnormalities were elevated eosinophils and neutrophils, as well as LDH, IgE, and decreased lymphocytes in percentage (See Table 1.)

Conclusion. The primary results show that AD patients have changes in blood, but not in urine. Some of these results, e.g., LDH and eosinophils correlate with the disease severity. Larger group of patients is required to establish, if these changes are statistically significant.

Acknowledgements. The authors declare the absence of conflict of interest.

Table 1. Results of laboratory analysis.

	001	002	003	004	005
Erythrocytes (x10E12/L)	5.1	4.5 (L)	4.5	4.6	4.5 (L)
Haemoglobin (g/L)	158	134 (L)	132 (N)	142 (N)	122 (L)
Haematocrit (L/L)	0.52	0.45	0.40	0.48	0.40
MCV (fL)	103 (H)	101 (H)	89	103 (H)	88
Leucocytes (abs) (x10E9/L)	11.8 (H)	6.0	11.1 (H)	6.0	6.9
Neutrophils (%)	77 (H)	75 (H)	76 (H)	67	50
Lymphocytes (abs) (x10E9/L)	1.9	0.8 (L)	2.1	0.9 (L)	2.1
Lymphocytes (%)	16 (L)	14 (L)	18 (H)	15 (L)	30
Esosinophils (abs) (x10E9/L)	0.4	0.3	0.2	0.6	0.9 (H)
Eosinophils (%)	3	5	2	10 (H)	13 (H)
LDH (U/L)	290 (H)	204	164	300 (H)	317 (H)
IgE (IU/ml)	260.7 (H)	N	239 (H)	N	4163 (H)
EASI	52.1	27.6	47.4	37.7	38.4
Urine	N	Abnormal. but not clinically significant	N	N	N
Asthma	No	No	Yes	No	Yes

Metagenome analysis of archaeological teeth samples from Latvian Iron Age, 8th–11th centuries AD

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Background. Ancient teeth and dental pulps are not only valuable sources of DNA from humans and systemic infections, but also an open window for the study of ancient oral microbiomes. Oral microbiome is the second most studied human microbiome subtype after gut microbiome, and, based on culturing and sequencing work on modern dental plaque, is harbouring over 700 species of bacteria. However, still very little is known about the ancient oral microbial communities. The possibility to understand and reconstruct the microbiomes of pre-antibiotic lifestyles is highly valuable for understanding the evolution of human microbiome and its role in health and disease.

Aim. The aim of the study was to explore in detail the taxonomic composition of ancient dental samples dated to Iron Age Latvia (the 8th–11th centuries AD).

Methods. During this study, historic human teeth samples were examined representing the 8th–11th century burials in Latvia. Ancient DNA (aDNA) was isolated from complete ground teeth samples. Special protocols and precautions in order to eliminate all possible contamination from modern DNA sources were followed. For aDNA library preparation QIAseq Ultralow Input Library Kit (Qiagen) was used. Metagenomic data were generated by high-throughput sequencing using Illumina technologies. For microbiome analysis, read files were analysed using MALT 0.5.0 using all complete bacterial genomes available from NCBI Assembly in August 2020 as reference.

Results. In total, over 7000 OTUs were identified in microbiome datasets. The most abundant bacterial species were typical soil bacteria belonging to *Rhodanobacter*, *Baekduia*, *Rhodanobacter*, *Dyella*, *Conexibacter*, *Mesorhizobium*, *Amycolatopsis* and *Alloactinosynnema* genera. Oral microbiome signature was also present, but in significantly lower amounts. Nevertheless, molecular signatures of typical oral bacteria were identified, such as *Actinomyces* sp. oral taxon 414, *Desulfobulbus oralis*, *Lautropia mirabilis*, *Neisseria mucosa*, *Neisseria sicca*, *Olsenella* sp. oral taxon 807, *Pseudopropionibacterium propionicum*, *Streptococcus cristatus* and *Streptococcus sanguinis*.

Conclusion. Altogether, the obtained results indicate that, although ancient dental samples were invaded by environmental bacteria after death, they also conserve a record of the microbial communities that are naturally present in the oral cavity.

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Diversity and antimicrobial susceptibility of *Staphylococcus sp.* isolates on the facial skin of healthy volunteers

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Background. Most common bacterial colonizers of the skin, *Staphylococci*, are often involved in a rapidly developing global health concern that is antimicrobial resistance. Antibiotic resistant microorganisms cause significant morbidity and mortality, and situation only seems to increase in magnitude as new microbial resistance mechanisms emerge.

Aim. The fundamental aim of this research is to investigate healthy volunteers facial skin colonization with potentially pathogenic bacteria and to determine the susceptibility of *Staphylococcus sp.* to antibacterial agents.

Methods. Samples from skin microbiota were cultured in Tryptone soya broth. Bacterial cultures were identified using the BBL™ Crystal™ identification system and biochemical *characteristics were compared.* Antimicrobial susceptibility was tested by the *Bauer-Kirby* disc diffusion method according to the Clinical Laboratory Standards guidelines. The following international reference strains were used as controls: *S. epidermidis* ATCC 12228 and *S. aureus* ATCC 25923. Excel was used for data summary and statistical analysis.

Results. Out of all participants (n-40), the most common contaminant *S. epidermidis* was isolated in all 40 samples, 17 (43%) *Staphylococcus aureus*, two *Enterococcus sp.,* one *Propionibacterium acnes* and one *Streptococcus sp.* were also present. Among the 40 *S. epidermidis* isolates, 14 (35%) were beta-haemolysis-negative. Enzyme tests showed the following results: alkaline phosphatase-positive were 8 (20%), urease-positive - 29 (73%). Out of all: 7 (17%) were cefoxitin resistant, 37 (93%) were ampicillin sensitive, 35 (88%) were erythromycin sensitive, 36 (90%) were clindamycin sensitive, 38 (95%) were ciprofloxacin sensitive, 33 (83%) were cefoxitin sensitive and 40 (100%) were vancomycin sensitive.

Conclusion.

1. Methicillin resistance rate of *S. epidermidis* was determined to be 7 (17%) in total. Results show increase by 4.5% compared to study carried out in 2015, where 12.5% isolates of healthy volunteers were methicillin resistant.
2. The most effective antibiotic in *S. epidermidis* strains was identified as vancomycin. On the contrast, different data was collected during the 2015 study, where *S. epidermidis* strains were sensitive to all of the antibacterials.
3. Haemolytic activity was demonstrated in 26 (65%) out of total 40 *S. epidermidis* isolates, which is significantly less than in 2015 (haemolysis reaction was positive in 90% of isolates).
4. *S. epidermidis* showed urease positive reaction in total of 29 (73%) strains, only 8 (20%) strains were alkaline phosphatase positive. The percentage of urease-positive reactions decreased from 93 % (2015) to 73% and alkaline phosphatase from 48 % (2015) to 20%.

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Ultrastructural changes of the thymus' hemocapillares in the condition of mild general dehydration

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Background. The microvascular bed, along with stromal and hematopoietic elements, is one of the most important tissue components of a thymus.

The study of morphological changes of thymic hemocapillaries under the influence of various factors allows, in particular, better understanding of the hematothymic barrier function as a selective structure in the immunogenesis regulation and its role in the development of compensatory-adaptive responses under specific conditions.

Aim. The objective of the study was to establish features of ultrastructural changes of rats` thymus hemocapillaries under conditions of the mild general dehydration.

Methods. 12 rats were involved in the experiment. 6 rats formed the control group and were kept under normal vivarium conditions. The mild degree of dehydration was modelled in other 6 rats and achieved in 3 days. Rats were kept on a completely waterless diet and fed by granulated feed.

When animals were taken away from the experiment, we selected the thymus and prepared samples for investigating the organ ultrastructure by electron microscopy.

Results. Under experimental conditions of the mild general dehydration, we observed deformation and lumen narrowing of some hemocapillaries in the rat`s thymus. The nuclei of capillary endotheliocytes acquire an elongated shape with pronounced invaginations, directed both towards the lumen of the capillary and towards the basal membrane. Chromatin is redistributed, acquiring mainly the form of a peripherally thickened band located along the contour of the nucleus, but does not completely lose its diffuse distribution.

The nucleolus has a typical structure. Areas of cytolysis are noted in the cytoplasm, free ribosomes are found. Mitochondria are hypertrophied and characterized by decomplexation straightening of cristae and dissociation of membranes. The endoplasmic reticulum has the appearance of elongated cisterns. Golgi complexes in most cells are represented by flat cisterns with bound vesicles. The basement membrane has a different thickness. Narrowing of the subendothelial zone may be a sign of changes in pressure in the blood capillaries at the initial stage of hypoxic disorders.

Conclusion. Structural changes in the thymus under conditions of the general mild dehydration significantly affect the hemocapillaries and form the morphological basis for the development of endothelial dysfunction, which in turn contributes to the formation of compensatory-adaptive response of the body to dehydration.

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Investigation of microbial contamination of soft contact lenses and their care accessories among asymptomatic users

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Background. Contact lenses can act as a vector for potentially pathogenic microbes to adhere to and get on the ocular surface. With the increasing usage of contact lenses for cosmetical and therapeutic purposes, the incidence of corneal or conjunctival inflammation and infection is also on the rise. Contamination of contact lenses undoubtedly comes from hands, our surroundings and care products, such as cleaning solutions or storage cases. Appropriate hygiene habits have an undeniable therapeutical importance in preventing pathogen invasion.

Aim. The aim of this study was to evaluate the rate, level and profile related to microbiological contamination of contact lenses and care accessories in asymptomatic users.

Methods. The research was carried out at Vilnius University, Institute of Biomedical Sciences, Department of Microbiology in the period from September to December 2019. Samples from lenses and care accessories were collected from asymptomatic users in accordance with all sterility requirements. Isolated microorganisms from taken samples were identified using standard cultivation and identification methods. The association between microbiological contamination and lens hygiene behaviour was evaluated with anonymous survey. Participants filled the questionnaire about contact lens replacement, duration of use, smoking, swimming and sleeping while wearing contact lenses. The statistical analysis of the data was performed with IBM SPSS® Statistics 24.0.

Results. Four samples each from 56 (n=224) lens users were collected including from inner surface of lenses, storage containers, multipurpose solutions and their bottles. 83.9% (n=47) of participants were female and 16.1% (n=9) were male, participants aged 18 to 25. The most contaminated items were lens cases – 64.3%, the lowest incidence of contamination appeared in lens solutions – 12.5%. Lens cases demonstrated the widest range of bacterial isolates and 89.8% of those pathogens belonged to Gram-positive microbial bioburden. The most commonly isolated microorganism was Coagulase-negative staphylococci (42.3%), followed by Gram-positive rods (15.8%), *S. aureus* (3.9%), *P. aeruginosa* (3.1%) and *C. albicans* – 0.77%. 25% of respondents showed unsatisfactory lens hygiene skills. No statistically significant relation between contamination and hygiene behaviour were found.

Conclusion. It has been revealed that 78.6% of participants' samples were contaminated. 25% of respondents shown having poor skills of hygiene with contact lenses itself and lens care systems. Usage of contact lens is the primary key factor for developing ophthalmic complications, hence increasing awareness about proper use and maintenance is more relevant than ever.

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Positive allosteric modulator of sigma-1 receptor E1R alleviates generalised and chronic seizure severity

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Background. Epilepsy is one of the most common neurological diseases affecting more than 50 million people worldwide. Despite the wide range of medications to treat epilepsy, at least one third of patients do not respond to therapy. The heterogeneous etiology of epilepsy makes the choice of treatment more complicated, thus there is a need for new anti-seizure drugs.

Aim. Our previous research has demonstrated that the sigma-1 receptor (Sig-1R) is involved in epileptogenesis. E1R, a positive allosteric modulator of Sig-1R, protects against acute chemoconvulsant-induced seizures. Therefore, the aim of the present study was to investigate the efficacy of E1R in generalized (grand mal) and chronic (petit mal) seizure models.

Methods. Four-month-old Swiss Webster male mice were used in the experiment. The efficacy of E1R against generalized seizures of the tonic-clonic type was assessed in transcorneal and transauricular maximal electroshock-induced seizure (MES) tests. In addition, the anti-convulsive effect of E1R on chronic seizures during epileptogenesis was tested in the chronic pentylenetetrazole (PTZ) kindling model.

Results. Auricular MES test results demonstrated that E1R (25 and 50 mg/kg, *per os*) significantly reduced the development of tonic seizures, if compared with a control group (ED_{50} = 15.6 mg/kg). Furthermore, after using pre-treatment with E1R (50 mg/kg), clonic seizures were not observed at all in 1/3 of mice. E1R at doses of 25 and 50 mg/kg decreased development of tonic (ED_{50} = 23.7 mg/kg) but not clonic seizures in corneal MES test. In addition, E1R at doses of 25 and 50 mg/kg significantly reduced both the incidence, as well as severity of seizures occurring during the repeated administration of PTZ during the course of kindling period.

Conclusion. E1R exerts significant anti-convulsive activity against generalized tonic-clonic seizures and delays epileptogenesis. Taken together, our results demonstrate that E1R is a promising drug candidate for treating a wide range of seizures.

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The role of *S. Enteritidis* in the structure of microbiological monitoring in epidemiological surveillance system

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Background. Salmonellosis is one of the most common zoonosis in the world, most often registered in the children's population aged 1 – 7 years.

The validity of the study of the current trend to change clinically significant serotypes of *Salmonella spp*. in the structure of salmonellosis is due to the regularity of monitoring. The prevalence of *Salmonella enteritidis* has been widely discussed in the specialized literature for many years, and in many regions their own characteristics in the spectrum of salmonellosis pathogens have been noted.

Aim. to evaluate the frequency of bacteriological isolation of *S. enteritidis* as an etiological pathogen of salmonellosis over an 11-year period among children.

Methods. The study was conducted by analysing the annual statistical reporting forms of the bacteriological laboratory of the "City Children's Infectious Diseases Hospital" No. 1 in Almaty within the period from 2000 to 2019.

Results. The results of *S. enteritidis* verification from isolated salmonella cultures were analysed. Quantitative performance analysis on Salmonella infection, i.e., the load over the study period ranged from 45129 (2009) to 78665 (2019), and from 2009 -2011, some stability was observed already since 2012 (50032). In our work, for the period 2009 -2019 in the category of children aged 0 – 14 years, coprological strains in the structure of salmonellosis group D, *S. enteritidis* took the first place only in 18.1%, being registered only in 2009 – 36% and in 2012 – 39%, which can be interpreted as a regional feature. In comparison, isolates of *S. tyhymurium*, from the same group D, were notable only in 2011 – 38%, and *S. Virchow* for the analysed eleven-year period were leaders only in 2019 – 41%. Since the most common in the dynamic study among 4 types of salmonella, *Salmonella of other groups* were found quite often, amounting to 63.6%, which were recorded during 7 years: with 2010 – 40%, 2013 – 46%, 2014 – 44%, 2015 – 39%, 2016 – 36%, 2017 – 38% and 2019 – 41%.

Conclusion. Summarizing the obtained results of the species' diversity of clinical salmonella isolates for the studied period, microbiological monitoring showed periodic rises in the excretion, which we interpreted as sporadic cases of infection, excluding cyclicity with an unambiguous determination of the tendency to change the pathogens-leaders, due to *Salmonella other* categories. According to the results of microbiological monitoring of the etiological structure of salmonellosis pathogens detected from stool samples of sick children, the established proportion of *S. Enteritidis* was 18.2%.

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The effect of colour on the perception of sweetness in non-alcoholic beverages and its potential applications in healthcare

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Background Reducing sugar consumption is a core task to decrease the risk impacting heart attack and stroke derived from higher blood pressure, weight gain, diabetes, and fatty liver disease. Therefore, innovative principles of reduced sugar intake are of particular importance. Our study is elaborated within the framework of cross-modal perception where systematic links between different perceptual domains are experimentally explored.

Aim. The first aim of the current study is to determine the impact of colour on the perception of sweetness. The second aim is to elaborate principles enabling to reduce the amount of sugar without decreasing the flavour enjoyment.

Methods. In a between-group quasi-experimental setting hedonic, associative, and emotional ratings were measured regarding different colours and two different containers (n1=67, n2=63); additionally, the taste of two non-sweetened coloured drinks were tested (n=32).

Results. According to Likert 5-point scale red, pink, orange, and purple (average values 3.7, 3.7, 3.6 and 3.6) were the colours with the highest ratings of sweetness. These were followed by yellow and green with relatively similar proportions of participants agreeing/disagreeing about the statement that the visually presented drink is sweet (average values 3.1 and 3.0). As the least sweet were evaluated blue, brown, white, and grey drinks (average values 2.7, 2.6, 2.5 and 2.4). When testing the gustatory perception, the drinks were not evaluated as sweet (75% and 90% subjects disagreed with the statement that the drink is sweet; average values 1.7 and 1.6). However, the rating on a 9-point hedonic scale indicated that the drink evaluated as less sweet is more preferred (4.7 and 5.1). Also, the sense of freshness modulates the likeability of the flavour (40% of participants indicate this as an important feature for non-alcoholic beverages). The most refreshing colours for drinks are yellow, orange, red, white, and green (referred by 35–40 % participants as refreshing). Brown and grey are evaluated as relatively stable.

Conclusion. Applying orange and red, as well as pink and purple to non-alcoholic beverages can provide some crossmodal sense of sweetness. Green, yellow and white colours might increase the sense of refreshment. These two general findings can be used to improve the design of healthy food.

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On the issues of acquiring knowledge in fundamental sciences in medical universities of the Republic of Kazakhstan

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Background. The basis of providing qualified medical care is a high-quality medical education. Currently, the Republic of Kazakhstan is undergoing a reform in the system of medical education, which aims to train highly specialized professionals who have a good competitive ability and meet the requirements of society.

Fundamental sciences – microbiology, epidemiology and hygiene – are the basic sciences that provide a "bridge" between the theoretical and practical part of medicine.

Aim. Optimization of the educational process of medical students in fundamental sciences for the preparation of competent future doctors.

Methods. Since 2018, on the basis of the Department of Microbiology, Virology and General Immunology of the Kazakh Medical University of continuing education of the Republic of Kazakhstan, the teaching staff conducted the educational process, providing the full educational and methodological complex of the discipline. We have developed training manuals "Methodological recommendations for conducting practical classes in the discipline "Microbiology", "General Hygiene" and "Epidemiology", intended for students in the bachelor's degree programmes of medical universities.

Results. Each of these notebooks is a systematic document that includes a brief theoretical description of all types of classes and is intended for both online and offline training. It offers a rather fascinating volume of independent tasks: a terminological dictionary, leading questions on topics for independent search of information and filling out answers to them, presented tabular and schematic versions of tasks, solving which develops systematized knowledge, which gives easy and quick perception and is stored in memory. In addition, to consolidate the studied material, there are tests and situational tasks, when solving which probable pictures from the practice of a medical worker are played out. After each topic of the lesson, a list of the main and additional literature that are relevant for today is offered. This type of tasks provides for mandatory familiarization with the material independently, in order to form your own vision of the issue under consideration.

Conclusion. The use of manuals develops significant level of students' clinical and microbiological competence, that in the future will allow to organize and perform microbiological, epidemiological research, to interpret research results and thereby improve the organization of medical-diagnostic process, the organization of hygienic conditions of life and work, the algorithm of actions in the event of infectious diseases, and the implementation of specific preventive measures.

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Intense pulsed light and heated eye mask therapies for the treatment of dry eye syndrome

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Background. At present, 5–30% of the population 50 years and older suffer from dry eye disease (*DEWS*, 2007). The goal of the dry eye disease treatment is to improve tear film stability and eye surface condition, thus reducing the number of symptoms and their intensity.

Aim. The aim of the current study was to evaluate the effectiveness of intense pulsed light (IPL) and warm mask therapies as a treatment of dry eye syndrome.

Methods. It was analysed 12 patients (24 eyes); of those 9 were females and 3 – males. All the patients participating in the study had dry eye disease. Tear film diagnostics was performed using the SBM System Ocular Surface Analyzer. Different tests were carried out: interferometry, tear film non-invasive break up time NIBUT, tear meniscus height, eyelid meibography, slit lamp examination, corneal staining with fluorescein, OSDI questionnaire. Six participants underwent two IPL procedures, once a month. Another six participants received warming mask therapy for the duration of two weeks, seven minutes twice a day. Both participant groups used lubricant eye drops for one week.

Results. Following two IPL treatment sessions, improvements were observed in NIBUT (21%), lipid layer thickness (68 %), as well as decline in meibomian gland deficiency (31%), corneal staining (85%) and OSDI (34%). Warm mask therapy boosted lipid layer thickness (56%), reduced meibomian gland deficiency (49%) and corneal staining (100%), OSDI (21%). Comparing two therapies, it was found that they did not differ statistically significantly. There is no difference between changes in lipid layer thickness ($p=0.81$), changes in lower eyelid gland deficiency ($p=0.25$), changes in OSDI ($p=0.08$). IPL therapy improves the NIBUT rate ($p=0.02$), while warm mask therapy does not show a statistically significant improvement ($p=0.42$). Comparing therapies, they are not significantly different ($p=0.17$). Both therapies can be used in dry eye disease treatment.

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Visual performance of scleral lenses in patients with different stages of keratoconus

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Background. Keratoconus is a disorder of the eye, when the cornea becomes thinner and deforms causing blurry and double vision. Glasses in this case usually do not give a satisfactory visual acuity. Scleral lenses are used to improve visual acuity.

Aim. The aim of the current study was to evaluate the visual quality performance of scleral contact lenses in patients with keratoconus and analyse the factors that can affect visual performance.

Methods. For this retrospective study we investigated 17 eyes of 15 participants (1 female and 14 males, average age 30.3±8.1 years) with keratoconus (stage II, III and IV), which were fitted with scleral contact lenses. Two participants had intrastromal corneal rings. Uncorrected (UCVA) and best corrected (BCVA) visual acuity with spectacles were examined before contact lens fitting and visual acuity with scleral lens (SLVA)were examined after fitting. Keratometry (K1, K2) were examined by corneal topographer *Oculus Pentacam* before scleral lens fitting. UCVA, BCVA and SLVA were analysed.

Results. Mean UCVA, BCVA and SLVA were 0.15±0.12 (0.02-0.5), 0.44±0.23 (0.1-1.0), and 0.83±0.17 (0.5-1.2), respectively. A significant improvement in visual acuity was observed with scleral lenses compared to UCVA and BCVA ($p<0.05$). Best visual acuity improvements were observed for 3 participants, with scleral lenses they saw approximately 13 decimal lines more than without correction. No differences in SLVA were observed depending on the stage of keratoconus and apex position ($p<0.05$).

Conclusion. Scleral lenses are a good and effective visual correction method for keratoconus. A significant increase in visual acuity can improve their visual performance and life experience.

Acknowledgements. The authors declare the absence of conflict of interest relevant to this article.

The impact of rebamipide on functional topography of enzymes of the small intestine in rats in the norm

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Background. The functional topography of small intestine enzymes is variable and depends on many factors, both in normal and pathological conditions.

Aim. Research activity of maltase, glucoamylase, sucrase, lactase and alkaline phosphatase in the mucous membrane without and with the introduction of rebamipide.

Methods. Studies were conducted on two groups of animals: intact (n=5), intragastric administration of rebamipid at a dose of 50 mg/kg per day for 14 days.

Results. In the control group, the maximum activity of maltase, glucoamylase and alkaline phosphatase was observed in the second segment. The lowest activity of maltase, glucoamylase and alkaline phosphatase was observed in the ileum. The sucrose activity in animals of the control group was observed in the duodenum and gradually decreased in the caudal direction. The lactase activity in the control was maximum in the third OC segment. Under the influence of the introduction of rebamipide, changes in the functional topography of the activity of all the studied enzymes occurred. The highest activity was observed in the second segment – maltase activity increased by 45% ($p<0.05$), glucoamylase activity – by 70% ($p<0.05$), alkaline phosphatase activity in the first three segments decreased by a maximum of 30%, while in the ileum the enzyme activity increased by 140% ($p<0.05$). The sucrose activity was most pronounced in the second segment, but against the background of a decrease in the enzyme activity in the duodenum. The decrease in sucrose activity in the caudal direction was the same as in the control group. The lactase activity was maximum in the second segment with an increase in activity compared to that in the control group by 200% ($p<0.05$). These changes led to a redistribution of functional topography in the rebamipide-treated group compared to the control group.

Conclusion. Intragastric administration of rebamipide at a dose of 50 mg/kg per day led to a change in the functional topography of the activity of enzymes in the small intestine. The maximum level of activity of all studied enzymes in animals under the action of rebamipide was observed in the second segment, and for lactase – in the third segment. In addition to the change in the enzyme topography, an increase in the activity of maltase, glucoamylase and lactase was observed, while the activity of alkaline phosphatase decreased in the first three segments and increased in the ileum.

Acknowledgements. The authors declare the absence of conflict of interest.

Assessment of bacteriophage effect in the bacteria culture isolates from patients

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Background. Infections related with provision of medica care are one of the most important problems in the modern health-care system. The continuously growing resistance of infection causes against antibiotics requests that physicians apply alternative forms of fight. Bacteriophage (phage) therapy is one of them.

Aim. To evaluate bacteriophage lytic activity from clinical materials *in vitro*.

Methods. An experimental *in vitro* study was made. During the study period, 36 samples were collected, 12 KONS, 12 *E. coli* and 12 *S. aureus* samples. Two bacteriophage mixtures "Otofag" and "Dermofag" were used. The lytic effect of bacteriophages was determined using a microorganism sensitivity test. The presence of the lytic zone was assessed. Positive bacterial lysis and partial bacterial lysis were positive results. Lach of lytic zone or resistance of stem against phage was considered as negative result. Results were compiled in MS Excel 2016 and IBM SPSS Statistics v22, and later graphs were created. The place of the study is Joint Laboratory for Microbiology and Pathohistology, Hospital of Traumatology and Orthopedics.

Results and conclusion. The lytic effect of bacteriophages was different using mixtures of two types of bacteriophages. The greatest lytic effect was observed for the "Otofag" mixture (92% or n=22), while for the "Dermofag" mixture (88% or n=21). The greatest lytic effect was observed for gram-negative microorganisms. In all cases, complete bacterial lysis was observed (100% or n=12). Full bacterial lysis and partial bacterial lysis are considered a positive effect. Gram-positive microorganisms showed a positive lytic effect in 92% (Otofag) and 88% (Dermofag). Negative effects were observed in 8% of the cases. To investigate the lytic effect of bacteriophages further studies are needed using a larger number of bacterial cultures.

Clinical and pharmacogenomic implications of xanthine dehydrogenase genetic variation in Latvian tuberculosis patients

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Background. Xanthine dehydrogenase (XDH) is involved in the oxidative metabolism of purines and is encoded by the XDH gene. XDH can be converted to xanthine oxidase (XO) by reversible sulfhydryl oxidation or by irreversible proteolytic modification. XO is involved in the oxidative metabolism of clinically significant drugs, including an important antituberculosis agent pyrazinamide. XDH gene is highly polymorphic; several polymorphisms are related to the variability in enzyme activity and also enzyme deficiency, which leads to xanthinuria.

Genetic polymorphisms of XDH gene have been studied as modifiers of drug toxicity and/or efficacy. Recently, a single common tag SNP (rs17011368) located in Mo-pt domain of XDH has been shown to accurately predict high enzyme activity of an individual.

Aim. The aim of this study was to identify genetic polymorphisms of metabolic enzyme XDH in Latvian tuberculosis patients receiving pyrazinamide.

Methods. DNA was isolated from whole blood samples of tuberculosis patients. A 410-bp DNA fragment of the XDH gene which contains the rs17011368 SNP was amplified by PCR and subsequently sequenced on both strands by Sanger method. The sequence analysis and SNP identification were performed using CodonCode Aligner software with the sequence of human gene (EC 1.17.1.4) (GenBank: NG_008871.2) as the reference. Clinical information was obtained from the Centre of Tuberculosis and Lung Diseases, Riga East University Hospital, Latvia. The study protocol was approved by the Central Medical Committee of Ethics in Latvia.

Results. In total, 33 TB patients were included in our study, 10 (30.3%) women and 23 (69.7%) men, age range 19–82 years. Before the TB therapy, all individuals had normal ALAT/ASAT biochemical indicators, except 4 patients with insignificant increase of ALAT. Significant increase of ALAT/ASAT indicators after 10 days of therapy was observed in 21.21% (7/33) of individuals. Sequencing results showed that all but one patient carried the major rs17011368 T allele and were classified as a wild type. The second allele (rs17011368 C, p.Ile703Val) was present in one heterozygous patient; the frequency of the minor allele was 0.015. No significant associations with clinical characteristics were observed.

Conclusion. The observed frequency of missense T>C allele, which was associated with high XDH activity, was similar to other northern European populations. In order to assess the merits of pyrazinamide pharmacogenomis in the treatment of tuberculosis additional research is needed in a larger cohort.

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Detection of genes responsible for biofilm formation in blood of patients with ischaemic coronary artery disease

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Background. It is known that bacteria are involved in the development and progression of atherosclerosis by forming biofilms within arterial plaques. It may lead to a rupture of unstable plaque and myocardial ischaemia. Clinically important microorganisms forming biofilms on or inside the human body secrete bacterial DNA. It has been shown that *wcaF* gene encoded for colanic acid (a key polysaccharide in *E. coli* biofilm extracellular polymeric substance) is up-regulated in mature biofilms. Gene *papC* is essential for the formation of P fimbriae for adherence to uroepithelial cells when a gene *sdhC,* involved in the production of fumarate, has been reported to stimulate biofilm formation. A modern real-time PCR may allow to determine these genes rapidly.

Aim. The aim of the current study was to detect bacterial genes, responsible for a formation of a biofilm, in whole blood of patients with ischaemic coronary artery disease.

Methods. Altogether 80 blood samples of patients (40 women and 40 men) with cardiovascular diseases were tested for bacterial genes *wcaF, sdhC* and *papC*. Identification of a biofilm encoding genes was performed by using real-time PCR. Reference strain of *E. coli* ATCC 52922 was used as a positive control.

Results. Bacterial genes were detected in nearly 20% of whole blood samples (gene *wcaF* in 12.5%, gene *sdhC* in 7.5% of all samples analysed when *papC* gene was not detected). There were determined differences in genes prevalence (due to a low sample size differences were not significant) according to gender.

Conclusion. The data obtained suggest that bacterial genes responsible for a biofilm formation might be detected in patients with ischaemic coronary artery disease, more often in men than women.

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Functional activity of hematopoietic stem and progenitor cells under the acute and chronic exposure to ionizing radiation in different doses

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Background. The problem of ionizing radiation influence on the organism is rather significant due to the fact that radiation sources are widely spread in medicine, industry, and environment in general. Therefore, it is important to study the mechanisms, which underlie the radiation-induced processes in cell, as well as the consequences on the level of tissues, organs and systems.

Aim. The aim of the current study was investigation of functional properties of hematopoietic stem and progenitor cells of Balb/C mice under external acute and chronic exposure to irradiation in different doses.

Methods. The study was performed using original system of hematopoietic cells cultivation in diffusion chambers *in vivo*, which allows assessing their functional activity. Animals were divided into 5 groups: 1) acute irradiation in the sublethal dose of 5.95 Gy during 8.5 min; 2) acute irradiation in the dose of 0.19 Gy during 4 h; 3) chronic irradiation in the dose of 0.24 Gy during 6 months; 4) chronic irradiation in the dose of 1.5 Gy during 18 months; 5) control group. 25 mice were used as donors; their bone marrow was obtained from femoral bones and suspension for further cultivation was prepared based on cultural medium and semisolid agar. Suspension was injected in gel diffusion chambers, which were inserted into the intraperitoneal cavity of recipients (50 mice). After 11-day cultivation we performed the analysis of obtained cell aggregates.

Results. Assessment of the cell cultures allowed determining the essential differences between the investigated groups of animals. The most pronounced decrease in the functional activity of hematopoietic progenitor cells was revealed in the 1st group. We obtained only 17.1±0.8 colony-forming units (CFU) per 1×10^5 explanted cells, comparing to 36.4±1.8 in control group. In the 4th group we received 19.2±0.9 CFU; the 2nd and the 3rd groups were less affected – 29.1±1.4 and 25.6±1.1 CFU, respectively.

The obtained results are the evidence of high radiosensitivity of hematopoietic system, first of all, stem and progenitor cells. Besides, chronic long-lasting exposure to ionizing radiation causes the injury of not only hematopoietic cells, but also of hematopoietic microenvironment, and, as a result, impaired haematopoiesis.

Conclusion. The comparative analysis of obtained data has shown a pronounced influence of ionizing radiation on the functional properties of hematopoietic cells, depending on the accumulated doses. These findings can provide the basis for further development of radiation injury criteria in case of human radiation exposure.

Acknowledgements. The authors declare the absence of conflict of interest.

PHARMACY

Analysis of insomnia and remedies used to reduce it in the elderly

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Background: Structure and quality of sleep change with age, and it leads to the global problem – insomnia is the most common sleep-related complaint and the prevalence of it in the elderly population ranges between 30% and 60%.

Aim: To analyse prevalence of insomnia and the used remedies between genders and to find out the risk factors that may cause sleeplessness in the elderly.

Materials and methods: A sample of 429 elderly participants (aged 65–95 years) who voluntarily agreed to complete an anonymous questionnaire about their insomnia experience, various habits and remedies used to reduce insomnia was examined. Descriptive and comparative statistics were used. The results are presented in frequencies and percentages. Chi-square and odds ratio were executed to measure responses association with risk indicators. The study was approved by the Lithuanian University of Health Sciences Bioethics Center.

Results: Of all the respondents, 281 (65.5%) were women, the mean age (standard deviation) was 74.0 (6.7). Insomnia was reported by 258 (60.1%) respondents. More urban 236 (62.1%) than rural 22 (44.9%) people (p=0.021), as well more women than men (184 (65.5%) vs. 74 (50.0%), p=0.002) experienced insomnia. Stress had a significant effect on insomnia, i.e., individuals experiencing stress daily were 10.45 times more likely to have this problem (95% confidence interval: 5.123–21.3006, no difference between genders). Neither eating habits and use of electronic devices before bedtime, nor going to bed on time and sleeping during the day affected insomnia. Reading helped to avoid insomnia for 55 (44.7%) respondents comparing with non-readers 203 (66.3%) (p=0.000). Different measures were used to relieve insomnia, 33 (12.8%) respondents used non-pharmaceutical remedies and 29 (11.2%) did nothing. A greater number of men did nothing, compared to women (13 (17.6%) vs. 16 (8.7%), p=0.041). From the respondents using preparations, 55 (28.1%) used food supplements, 60 (30.6%) respondents used over-the-counter drugs, more men than women preferred prescription drugs (18 (38.3%) vs. 32 (21.5%), p=0.011), while more women chose prescription and nonprescription drugs at the same time (3 (6.4%) vs. 28 (18.8%), p=0.021). To improve sleep quality, 142 (55%) respondents engaged in physical activity. The most common activities were exercising (81 (31.4%)) and walking outdoors (83 (32.2%)), no difference between genders was observed.

Conclusion: This study shows that insomnia is a widespread problem in the elderly. The use of preparations to relieve sleeplessness dominates among respondents. The measures for stress reduction are recommended to respondents.

Acknowledgements. The authors declare the absence of conflict of interest.

Peganum harmala alkaloids positively affecting pain

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Background. *Peganum harmala* (Syrian rue) is widely used in traditional medicine against pain. For example, in Moroccan traditional medicine, *P. harmala* seeds are extensively utilised as a remedy for rheumatic pain, painful joints, and intestinal pain. The other confirmed pharmacologic properties of *P. harmala* mentioned in traditional Iranian medicine include analgesic effect for the management of sciatica, joints pain, coxalgia, chronic headache, and toothache. In forms such as joint pain, rheumatic pain, the seeds are predominantly used in the poultice form. *P. harmala* seeds are also effective in cases of painful and difficult menstruation, and for regulating menstruation cycle.

The researchers evaluated the effect of *P. harmala* on formalin-induced pain response in mice. As a result, alkaloid extract induced a significant reduction in pain response when compared to control, as follows.

In another study, different extracts of *P. harmala* seeds were evaluated for analgesic and anti-inflammatory activities using glacial acetic acid-induced writhing and carrageenan-induced rat paw edema models respectively. For analgesic and anti-inflammatory activities, aspirin and diclofenac were used as standard drugs respectively. The ethyl acetate extract showed significant analgesic and anti-inflammatory activities, thus it can be considered as a potential candidate for analgesic and anti-inflammatory activities.

Aim. The current study aimed to individually isolate *P. harmala* alkaloids, which have a positive effect on pain.

Methods. Powdered *P. harmala* seeds are extracted 3 times by 95% ethanol. Liquid extracts are evaporated until 10 mL on the water bath, then mixed with 5% hydrochloric acid (pH=2-3), and filtered. The solution is alkalized by 25% ammonia solution (pH=9-10) and extracted by liquid/liquid extraction with chloroform 4 times. A mixed and concentrated chloroform fraction was analysed by thin-layer chromatography (TLC). On TLC plates, 4 orange spots with R_f 0,69, 0,31, 0,2 and 0,1 (stationary phase "Sorbfil" (Russia), mobile phase chloroform/methanol, 9/1, v/v; revelator Dragendorff reagent) were observed. A preparative TLC plate was used for the purification process ("Machery-Nagel", Germany), mobile phase chloroform/methanol, 8.5/1.5, v/v). UV-, IR-, and NMR-spectroscopy of the compounds were realized.

Results. Harmine, harmaline, and vasicine alkaloids were identified individually.

Conclusion. *P. harmala* alkaloids can be evaluated in the pharmaceutical industry as painkillers.

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Deficient hippocampal neurogenesis and cortical angiogenesis in the chronic stages of ischemic stroke

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Background. Ischemic stroke is one the most common causes of death and disability worldwide. It is caused by the obstruction of cerebral blood vessels and insufficient cerebral blood flow, resulting in cell injury and death in the lesion area. In the chronic stages of ischemic stroke, generation of new neurons (neurogenesis) and blood vessels (angiogenesis) around the ischemic lesion occur as a part of the recovery process (Rajkovic et al., 2018). Nevertheless, these two processes have not yet been extensively studied in ischemic stroke model animals.

Aim. The objective of this study was to assess whether the number of doublecortin (DCX)-positive cells in the hippocampus and the expression of vascular endothelium growth factor (VEGF) in the cortex are altered two months after the ischemic stroke induction in model mice.

Methods. An endovascular filament-induced middle cerebral artery occlusion (fMCAo) was performed in male C57BL/6 mice (18-21 g, 10-12 w.o.). In Stroke group, fMCAo lasted for 60 min, whereas in Sham group filament was inserted in the vessel and immediately withdrawn. Two months after the surgery animals were euthanized and the number of DCX-positive cells and the density of VEGF were determined immunohistochemically in coronal brain slices. Statistical analysis was used to compare the measured values within group (ipsilateral or ischemized side vs. contralateral or non-ischemized side) and between groups (Sham vs. Stroke).

Results. The number of DCX-positive cells was markedly lower in the ipsi- and contralateral side of the brain in Stroke group compared to Sham group, respectively. VEGF density was remarkably lower in the ipsi- and contralateral sides of the cortex in Stroke mice compared to Sham subjects, respectively.

Conclusions. Obtained preliminary data show that two months after fMCAo induction, neurogenesis and angiogenesis are suppressed in both sides of the male mice brain – ipsi- and contralateral. A further research of neurogenesis and angiogenesis in other regions of the ischemic mice brain is imperative.

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Increased microglial activation in the chronic stages of experimental ischemic stroke

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Background. Neuroinflammation is a hallmark of many neurological deficits, including ischemic stroke, the top three morbidity cause worldwide. The central role in neuroinflammation, on the other hand, is played by microglia, resident immune cells of the brain (Zhang, 2019). Microglial activation, or microgliosis, is a complex process that can be both neuroprotective and neurotoxic in the ischemic brain. Therefore, investigating the rate of microgliosis in different stages of ischemic stroke is crucial to understand its role in the disease progression.

Aim. The aim of this study was to detect whether microglial activation and changes in microglial phenotype take place in ischemic stroke model mice in the chronic stages after stroke induction.

Methods. We modelled ischemic stroke using endovascular filament-induced middle cerebral artery occlusion (fMCAo) in naïve male C57BL/6 mice (18-21g) for 60 min. In sham controls, filament was briefly inserted into and removed from the blood vessel. Two months after fMCAo, controls (n=9) and stroke mice (n=5) were euthanised and free-floating slices were obtained from the whole brain samples. Optical density of ionized calcium-binding adapter molecule-1 (Iba-1) was determined after immunohistochemical analysis. Microglial phenotype was assessed based on the cellular shape. Data were analysed utilizing one-way analysis of variance followed by Holm-Šidák post hoc test within groups (ischemized versus non-ischemized brain hemisphere) and between groups (sham controls versus fMCAo mice).

Results. Striatal density Iba-1 was higher in the striatum of the ischemized and non-ischemized brain hemisphere in mice that underwent fMCAo when compared to the corresponding hemispheres in sham controls.

Conclusions. These preliminary results show that ischemic stroke produces chronic microglial activation in the infarct area two months after fMCAo, yet microglial phenotype does not seem to be affected. The observed changes can be associated with the length of fMCAo induction.

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Evaluation of the applicability of computer microtomography to study the internal structure of tablets containing trazodone hydrochloride. Safety of tablet subdivision

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Background. The incidence of depression increases year by year. It is estimated that soon it will be as common as ischemic heart disease. The practice of dividing tablets is popular both among patients and among doctors. In order to assess the safety of this practice and its influence on the uniformity of the dose of the drug substance in the resulting parts of the tablets, and at the same time on the effectiveness of the therapy, many modern research methods are used, including computer microtomography.

Aim. The two major objectives of the study were, as follows: a) to investigate the applicability of computer microtomography techniques supported by the methods of image analysis and processing to assess the homogeneity of the distribution of ingredients in tablets; b) to discuss already gathered data concerning the problems with tablet subdivision, such as precision and safety for the patient.

Methods. Prolonged release tablets containing 75 mg of trazodone hydrochloride were measured with a calliper and then weighed to check mass uniformity. After dividing into three parts using a kitchen knife, the mass of the resulting parts was weighed and checked for uniformity. Using a Phoenix v|tome|x microtomograph (GE, Germany), scans of the tablets were taken before and after subdividing the tablets. The calibration curve was determined based on the scans of the microtomograph calibration phantom containing areas of known density. Statistical analyses were performed using the IBM SPSS Statistics version 25.

Results. Tablets before and after splitting met the pharmacopoeia weight uniformity requirements. The loss of weight after dividing the tablets was found to be lower than 3% which is in compliance with FDA requirements. The weight significantly differentiated the parts of the tablet obtained after subdividing. The analysis of the pixel brightness along with the density correlated with it showed that both the tablets and their parts differed significantly from each other.

Conclusion. Computed microtomography supported by techniques of image analysis and processing can be successfully used to analyze the internal structure of tablets. Dividing the prolonged release tablets containing 75 mg of trazodone with a kitchen knife does not guarantee obtaining tablet fragments that have the same amount of the active substance. In addition, the weights of the obtained parts differ significantly from each other. This, in turn, creates a risk of large fluctuations in the dose of medication taken by the patient.

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Exploring the possibilities of implementing the Medication Use Review service in Eastern Europe and Iran

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Background. Polypharmacy and drug-related problems are common in both the elderly and patients with chronic diseases. Medication Use Review (MUR) is a structured evaluation of a patient's medicines to optimize the use of medicines and improve health outcomes. In the on-going international project (January 2019 – March 2021), the MUR standard adapted from Pharmaceutical Care Network Europe 2013 statement and amended in Estonia is piloted in community pharmacies in Estonia, Latvia, Lithuania, Poland, Croatia, Bosnia and Herzegovina, Hungary, Romania, Bulgaria, Slovakia, and Iran (MUR network).

Aim. The aim of this study was to gain insights into developments of the community pharmacy sector and map factors encouraging and hindering MUR service in Eastern European countries and Iran.

Methods. In September 2019, the MUR network countries performed document analysis and qualitative interviews to define community pharmacy sector indicators, current and future competencies and roles of community pharmacists, and factors encouraging and hindering MUR service in a particular country. The collected information together with the results of the piloting of MUR service enables the evaluation of the possibilities of implementing the service in the future.

Results. Current community pharmacist competencies in MUR network countries were more related to traditional services such as dispensing and counselling of prescription and OTC medicines and compounding of extemporaneous medicines. In most network countries reporting of adverse drug reactions, patient education on disease prevention and health promotion, and some point-of-care testing were available. Most frequently, the identified future competencies included provision of different extended services (e.g., medication review, immunization, diabetes screening, smoking cessation, INR measurements, and new medicines service).

The main factors encouraging MUR were increases in polypharmacy, pharmaceutical waste, and access to patients` health data by pharmacists. The main hindering factors were unfamiliarity of MUR to physicians, pharmacists and patients, financing of MUR and lack of private consultation facilities in some community pharmacies.

Conclusion. Key stakeholders in Eastern Europe and Iran are exploring possibilities to apply extended pharmacy services into practice. As polypharmacy is an increasing concern in MUR network countries, it is important to routinely assess patients' medication use. Pharmacists are well placed to provide MUR, however, more health professionals and patients need to be introduced to MUR and it is necessary to find a mechanism for financing the service in Eastern Europe and Iran.

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Do elderberry and elderflower extracts inhibit binding of SARS-CoV2 S1 protein receptor binding domain to cellular receptor ACE2 *in vitro*?

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Background. *Sambucus nigra* L. is a medicinal plant. Extract of elderberries are reported to exhibit anti-viral activity against influenza A and B viruses. In addition, anti-viral properties of elderberry extract against human immunodeficiency virus (HIV), dengue virus (DENV-2), human herpesvirus type 1 (HSV-1) and human coronavirus NL63 (HCoV-NL63) have previously been reported. Nevertheless, the effect of *S. nigra* berry and flower extracts on SARS-CoV2 surface protein S1 binding to cellular receptor ACE2 has not been evaluated before.

Aim. The aim of the current study was to assess inhibitory capacity of wild and cultivated *S. nigra* berry and flower extracts against SARS-CoV2 S1 protein RBD (receptor binding domain) binding to cellular receptor ACE2 *in vitro*.

Methods. Ethanol extracts of elderberries and elderflowers originating from 18 wild populations of *S. nigra* from Latvia were assessed for total flavonoid (TFC), total phenolic content (TPC) and anti-radical activity (ARA) using spectrophotometric microplate assays (Davis method, Folin-Ciocalteu's reagent and DPPH reagent respectively). Single best performing elderberry and elderflower extract was tested for inhibitory capacity against SARS-CoV2 S1 protein RBD binding to ACE2 using competitive ELISA (COVID-19 Spike-ACE2 binding assay kit CoV-SACE2-1, RayBiotech Inc).

Results. TPC, TFC and ARA of wild elderberries and elderflowers was significantly affected by sampling site. Although the average values of TPC, TFC and ARA of wild *S. nigra* populations from Latvia did not exceed corresponding values of widely-grown *S. nigra* cultivar 'Haschberg', several individual wild plants exhibited superior properties.

Wild elderberry and elderflower extracts exhibited significant concentration dependent inhibitory effect on SARS-CoV2 S1 protein RBD binding to ACE2 *in vitro*. IC50 of wild elderberry extract was estimated at 1.66 mg dry extract ml^{-1}. IC50 of wild elderflower extract was estimated at 0.532 mg dry extract ml^{-1}. Inhibitory effect of assessed wild elderberry extracts was significantly stronger (two-way ANOVA $F(1,2)=43.69$; $p=0.02$) compared to effect of cultivated elderberry extract (derived from cv 'Haschberg').

Conclusion. Results of the study serve as validation for further research of *S. nigra* anti-SARS-CoV2 applications.

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Extraction of biologically active substances from Lithuanian balsam poplar buds and research of their quality and antioxidant activity

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Background. The natural environment contains unlimited amounts of biologically active compounds. Balsam poplar buds (*Populus balsamifera*) are well known and appreciated in alternative medicine for their anti-inflammatory and antimicrobial effects. There are very few examples of research about the phytochemical composition of this raw material and its application to pharmaceutical ophthalmic preparations.

Aim. The aim of the study is to evaluate the predominant phenolic compounds in the extracts of balsam poplar buds and to assess the antioxidant activity of these extracts.

Methods. Extracts were prepared by extraction using ultrasonic bath of raw material and solvent with ratio 1:10. The extractants used were 70% ethanol (V/V), purified water, a mixture of polyethylene glycol 200 and purified water (20%), and a mixture of purified water and β-cyclodextrins (10%). Predominant phenolic compounds were evaluated by high performance liquid chromatography (HPLC). The antioxidant activity of the extracts was evaluated by the DPPH• radical scavenging method and the ABTS•+ radical cation binding capacity method *in vitro*. Reductive activity was evaluated by the FRAP method *in vitro*. The results were expressed as means, standard deviation of three measurements.

Results. *P*-coumaric acid, caffeic acid, apigenin, kaempferol, galangin and quercetin were found to be the predominant phenolic compounds in all extracts by HPLC. It was also found that the highest content of phenolic compounds was extracted by 70% ethanol (V/V), the lower content of phenolic compounds was found in the aqueous extracts. The extracts showed antioxidant activity, the extracts extracted with 70% ethanol (V/V) showed the highest antioxidant activity (65%) by DPPH• and ABTS•+ method, the lower radical scavenging capacity was characteristic to aqueous extracts (25%–42%). The reducing activity of the FRAP method was also best characterized by the ethanolic extract (95%), the aqueous extracts had lower reducing activity (37%–59%). The obtained results differed statistically significantly ($p<0.05$).

Conclusion. 70% ethanol extracts more phenolic compounds compared to aqueous mixtures of polyethylene glycol 200 and β-cyclodextrins, but these solvents are promising in the production of balsam poplar bud extracts. All extracts showed antioxidant activity, the results correlate with the concentrations of predominant phenolic compounds in the extracts of balsam poplar buds obtained by high performance liquid chromatography. From the obtained results it can be stated that Lithuanian balsam poplar buds are a promising plant raw material for pharmaceutical purposes.

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Study of herbal product use during pregnancy in Lithuania

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Background. Recently, the use of alternative and additional preparations has grown rapidly worldwide, because a lot of people consider that they are safe. The use of herbal products in pregnancy varies from 7% to 45% in different countries.

Aim. The objective of the study was to evaluate the prevalence of herbal preparation use among pregnant women.

Methods. 379 pregnant women completed an online questionnaire anonymously about consumption of herbal preparations and knowledge about them. Women's responses were analysed according to education (medical; other) and pregnancy (first; second; third and more). Descriptive and comparative statistics have been used – the results are presented in frequencies and percentages. Chi-square test was performed to find associations of the responses with medical education and pregnancy. Results are considered to be statistically significant, when $p<0.05$. The study was approved by the Bioethics Center of Lithuanian University of Health Sciences.

Results. Respondents' mean age (SD) was 28.7 (5.27). The 16.1% of respondents had medical education, most of the women (62.8%) had their first pregnancy, while 97 (25.6%) – their second and 44 (11.6%) – their third pregnancy and above. At least one herbal product was used by 57 (15%) of respondents, with no difference between groups. Herbal products were used to minimize symptoms of inflammation of the urinary tract (17, 29.8%), anxiety (14, 24.6%), insomnia (12, 21.19%), nausea and digestion disorders (10, 17.5% and 9, 15.8%, respectively) – no difference between the groups was identified. Mainly used herbal products contained cranberry, ginger, valerian and lemon balm.

Women with medical education were more concerned about the safety of herbal preparations in comparison to those respondents who had other education ($p<0.05$): herbal preparations are not safe for pregnant women (11 (18.0%) vs. 21 (6.6%)); can have a side effect (24 (39.3%) vs. 27 (8.5%)); possible interreactions with chemical medications (35 (57.4%) vs. 60 (18.9%)); safer than chemical preparations (30 (49.2%) vs. 203 (63.8%)); can be used without the medical advice (1 (1.6%) vs. 15 (4.7%)). No difference was noticed analysing safety questions according to pregnancy groups.

Conclusion. Use of herbal products during pregnancy was not popular in the analysed sample. Women's knowledge about the safety of these products for foetus and themselves remains incomplete. Pharmacist's consultation might be useful while dispensing the preparations to pregnant woman.

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The Synergistic Cytotoxic Effects of Combination Chlorophyllides and Doxorubicin

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Background. The purity of chlorophylls plays one of the key roles for the production of chlorophyllides. When the prepared chlorophyllides were applied to anticancer tests, they were active for multidrug resistant breast cancer cells. The results suggested that the prepared chlorophyllides could be a synergic effect of combination therapy with doxorubicin.

Aim. The aim of this study was production of chlorophyllides. The result illustrated that combination of chlorophyllides and doxorubicin showed synergistic cytotoxic effect, thus, it could be a potential candidate of combination therapy to multiple drug resistant breast cancers.

Methods. Fresh and clean leaves were weighted and ground in pestle with liquid nitrogen in the dark. Chlorophyll could be extracted by immersing in petroleum ether, diethyl ether, *n*-hexane, ethyl acetate, acetone, *n*-butanol, ethanol and methanol, respectively. After 48 h, each extract was centrifuged and then extracts of chlorophylls could be obtained. The ethanol extract of chlorophylls was sequentially extracted by *n*-hexane. After 48 h, the twice extract of chlorophylls was centrifuged and then purified chlorophylls from ethanol-hexane extracts could be obtained. To measure the concentrations of chlorophyll a/b, the filtrates were analysed by UV-Vis spectrophotometer. The reaction mixture contained 0.5 mg of recombinant chlorophyllase, 650 μL of the reaction buffer and 0.1 mL of 100 mM of chlorophylls extracts. After the organic phase removed, the chlorophyllides could be obtain in the aqueous phase. The identification of chlorophyllide a/b was examined by UPLC-Q-TOF-MS/MS. All measurements made in the 96-well plates were performed using five technical replicates. The combination effects of doxorubicin with chlorophyllides at different concentrations were analysed.

Results. The results showed that higher chlorophyllide a/b obtained when purified chlorophylls (ethanol-hexane extract) used as starting materials than that of crude chlorophylls (ethanol-only extract). The prepared chlorophyllides were used to test the cytotoxic effects in breast cancer cell lines, the combination therapy using doxorubicin and the prepared chlorophyllides were studied to identify synergistic or antagonistic effects. We demonstrated that the purified chlorophyllides could be a potential candidate of combination therapy to breast cancers with multiple drug resistance.

Conclusion. A new method for the production of chlorophyllides was successfully developed though twice extraction. The results illustrated that combination of chlorophyllides and doxorubicin showed synergistic cytotoxic effects, it could be a potential candidate of combination therapy in multiple drug resistant breast cancers.

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Amorphous calcium phosphate stimulates osteogenesis from bone marrow mesenchymal stromal cells

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Background. Mesenchymal stromal cells (MSCs) are fibroblast-shaped, plastic adherent cells residing in the stroma of the bone marrow, fat and other connective tissues. The function of MSCs is to maintain the tissue integrity and homeostasis by responding to the tissue damage through paracrine action and differentiation into mesodermal cell lineages. Owing to their regenerative properties, MSCs are being tested in numerous clinical trials for treatment of musculoskeletal disorders. Technologies that improve regenerative properties are rapidly evolving, aiming to satisfy the medical need for bone reconstruction. MSCs serve as a useful tool to confirm biocompatibility and evaluate osteoinductivity for different biomaterials. Amorphous calcium phosphate (ACP) is the first bone mineral phase to form in bone, and so provides the basis for investigation in this study.

Aim. To observe the biocompatibility and assess osteoinductivity from mesenchymal stromal cell seeded amorphous calcium phosphate coatings.

Methods. Human bone marrow derived MSCs (ATCC) were seeded onto ACP flame sprayed titanium coatings in serum supplemented alpha-Modified Eagles Medium (alpha-MEM, Sigma-Aldrich). MSC viability was assessed after 48 hours by colorimetric assay (CCK-8, Sigma-Aldrich). To induce osteogenesis during a three-week period, MSCs were propagated in serum supplemented alpha-MEM containing 0.1 μM dexamethasone, 10 mM sodium β-glycerophosphate, and 0.05 mM ascorbic acid-2-phosphate (Sigma-Aldrich). Subsequently, cells were fixed with 3.7% formalin and proceeded to immunocytochemical staining. Samples were incubated with primary rabbit osteocalcin polyclonal antibody and secondary donkey anti-rabbit antibody AlexaFluor555 conjugate, Phalloidin AlexaFluor488 (Invitrogen), and Hoechst 33342 (Sigma-Aldrich). Images were acquired with a Nikon C2 fluorescent microscope.

Results. After 48 hours, MSC viability on ACP was 31% compared to tissue culture polystyrene (TCPS) control. After three-week propagation on ACP coated discs in serum supplemented alpha-MEM, MSCs exhibited an adherent cell morphology and 80% confluence. On the contrary, MSCs on ACP displayed spheroid-like structures, highly positive for osteocalcin expression after propagation in osteodifferentiation medium.

Conclusion. MSC viability on ACP was lower than the respective TCPS control. Amorphous calcium phosphate favours osteogenesis, as observed by increased osteocalcin expression following MSCs propagation in osteodifferentiation medium.

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Impaired neuronal myelination occurs two months after ischemic stroke induction in mice

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Background. Ischemic diseases, including stroke, result in major mortality worldwide. Defining the detailed pathological cascade of ischemic stroke in preclinical models is highly warranted to understand the course of this disease in humans. One of the defining processes in stroke is the loss of myelination that is observed in acute stages of stroke and is associated with motor and cognitive impairments (Zhou et al., 2013), however, whether this process is impaired in the subacute stages of ischemic stroke remains unknown.

Aim. In this study, we determined whether myelination is altered in the infarct area, retrosplenial cortices and hippocampi of ischemic stroke model mice two months after stroke induction.

Methods. We performed an endovascular filament-induced middle cerebral artery occlusion in male C57BL/6 mice (18–21g) for 60 minutes (Stroke group, n=5). In Sham group, filament was briefly introduced into the blood vessel and immediately taken out. Two months after this procedure, we determined changes in the density of myelin basic protein (MBP) in the infarct area of the cortex, retrosplenial cortex and hippocampus of both brain hemispheres using immunohistochemistry with free-floating frozen sections. Density of MBP staining was analysed using analysis of variance within groups (ischemized versus non-ischemized hemisphere) and between groups (Sham versus Stroke).

Results. A significant decrease in MBP density in the infarct area of the ischemized brain hemisphere was seen in Stroke group mice. Hippocampal density of MBP in Stroke group mice was diminished in both ischemized and non-ischemized mice brain hemispheres.

Conclusions. Preliminary data demonstrate that ischemic stroke produces impairments in myelination of neurons in the infarct area and hippocampus. Identifying the association of myelination deficits with behavioural outcomes is the next step in our research.

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Green synthesis of silver nanoparticles using extract of common wormwood and hop fins, characterization and antimicrobial activity

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Background. Green synthesis provides advancement over chemical and physical methods, as it is cost effective, environment friendly, and does not require high pressure, temperature and toxic chemicals.

Aim. The aim of this study was designed with an objective to synthesize silver nanoparticles (AgNPs) using aqueous extracts of common wormwood and hop fins.

Methods. The morphology of particle size of the synthesized AgNPs was carried out by using a SEM microscope. Antioxidant activity was tested by different methods such as ABTS, $TFPH^{\bullet+}$, DPPH• ,CUPRAC and FRAP assay. Spectrophotometric studies were also used to determine phytochemical structure. The antimicrobial activity was investigated against gram-negative/positive bacteria cultures. Two methods, the agar disk diffusion test and minimal inhibitory concentration.

Results. The extracts of common wormwood and hop fins contain hydroxycinnamic acid, flavonoids and phenolic acid derivates that provide antimicrobial and antioxidant activity. After synthesis of AgNPs, the total amount of hydroxycinnamic acid derivatives' variation – from 2.05 to 2.34 and 1.64 to 0.64 mg CAE/g DW, similar variation of the total amount of flavonoids from 4.45 to 3.94 and 2.28 to 1.52 mg RE/g DW common wormwood and hop fins, respectively. The common wormwood and hop fins extracts differ in their phytochemical composition: in the hop fins, the amount of the proanthocyanidins is 17% higher than in the common wormwood, but the total amount of flavonoids is 1.94 times less than in hop fins. The AgNPs particle morphology is dependent on the type of plant. Common wormwood /AgNPs particles are of irregular shape, 35 – 70 nm in size, and tend to attach themselves to small aggregates. Hop fins/AgNPs particles are triangular in shape with sharp corners, 50 – 90 nm in size.

Conclusion. The antioxidant activity of the obtained extracts was very similar. Common wormwood / AgNPs and hop fins/AgNPs strongly inhibit the viability of gram-positive and gram-negative bacteria strains. The inhibition zone diameter increased by 0 to ~17 mm in both cases comparing common wormwood and hop fins and extract with AgNPs.

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The role of pituitary gland hormones in electrolyte imbalance in model of isolated porcine kidneys perfused with modified preservation solution

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Background. Organs obtained for transplantation are stored in cold preservation solution before they are implanted into the recipient's body. Currently, many scientific centres in the world are conducting research on the development of the fluid composition that will enable long-term storage of organs for several days outside the human body. In addition, it will allow the transport of organs over long distances, and even their treatment and regeneration in vitro. As a result, poor quality organs that are currently being rejected will be able to be included in the transplant procedure.

Objective. The aim of our study was to analyse the effect of prolactin (PRL) and lutropin (LH) as a component of the preservation solution on the maintenance of electrolyte homeostasis in a model of isolated and perfused porcine kidneys.

Methods. Kidneys from Polish "Large White" breed adult pigs were used for the study. The study was conducted with the consent of the II Local Ethics Commission for Animal Experiments in Cracow, Poland (number 1046/2013) and in accordance with the European Union Directive (EU guideline 93/119/EC) on the protection of animals during slaughter or killing. The reference solution Biolasol (FZNP "Biochefa", Poland) and modified solutions for preservation were used: Biolasol + p-LH (0.01 µg/l), Biolasol + p-PRL (0.1 mg/l). In the collected samples of perfusates, the concentrations of sodium and potassium were determined using spectrophotometric methods (Kits, Pointe Scientific, INC USA).

Results. LH and PRL as components of the preservation solution affect the degree of ischemia-reperfusion damage in isolated pig kidneys. Hormones ensure the optimal ratio of sodium and potassium concentration in the perfundate after 24/48 h storage of the grafts. Biolasol with 0.01 µg/l p-LH: K^+ 12±1 mEq/l vs Na^+: 162±11 mEq/l. Biolasol with 0.1 mg/l p-PRL: K^+: 14±3 mEq/l vs Na^+: 118±11 mEq/l.

Conclusion. The addition of lutropin (0.01 µg/l) and prolactin (0.1 mg/l) to the composition of the Biolasol solution play a vital role in maintaining electrolyte homeostasis.

The effects of *Cannabis sativa* L. extract on antioxidant status in mice blood and organs

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Background. *Cannabis sativa* L. extract is high in antioxidant components, including a wide range of terpenes, phenols, especially stilbenoids, lignanamides, and may play a role in reducing the risk of chronic diseases. Aluminium exposure-related neurotoxicity is implicated to have a role in the etiology of neurodegenerative disorders. However, there is accumulating evidence that natural phenolic compounds with strong antioxidant activities could alleviate neuronal oxidative damage and inflammation, and counteract metabolic disorders associated with these diseases.

Aim. The present study aimed to elucidate possible protective effects of *Cannabis sativa* L. extract (CE) in alleviating the toxicity of aluminium on glutathione (GSH) and malondialdehyde (MDA) concentrations, as well as catalase (CAT) and superoxide dismutase (SOD) activities in erythrocytes, brain and liver homogenates of BALB/c mice.

Methods. The experiments were done on 4–6-weeks old BALB/c mice weighing 20–25 g. 8 mice per group were assigned to 4 treatment groups: 0 mg CE and 0 mg $AlCl_3$/g body weight (control); 0.05 LD_{50} CE; 0.15 LD_{50} $AlCl_3$; 0.15 $LD_{50}AlCl_3$ plus 0.05 LD_{50} CE. CE were administered intragastrically to mice via a stomach tube for 21 days. The amount of intracellular antioxidant GSH was assessed based on GSH reaction with the 5.5'-dithiobis-(2-nitrobenzoic acid) which produces a yellow complex. The amount of MDA (marker of lipid peroxidation) was estimated by measuring thiobarbituric acid reactive substances. The activity of CAT was determined by the hydrogen peroxide reaction with ammonium molybdate, which produces a complex that absorbs light at 410 nm. The activity of SOD was determined according to the inhibition of nitroblue tetrazolium reduction rate in the non-enzymatic phenazine methosulfate-nicotinamide adenine dinucleotide system assessed spectrophotometrically at 540 nm. Results were expressed as the mean ± SEM.

Results. CE significantly decreased the concentration of reduced GSH in blood of mice affected with aluminium ions by 26.81% and stabilized the level of oxidative stress indicator to the level of these parameters in the control mice. CE significantly reduced MDA concentration in brain and liver of mice affected by aluminium ions, respectively, by 82.12% and 53.5%. CE significantly increased CAT in brain of control mice by 56.44 % and mice affected by aluminium by 64.79% and, respectively, in liver by 34.53% and 72.37%.

Conclusion. *Cannabis sativa* L. extract normalizes uncontrolled synthesis of reduced glutathione caused by aluminium ions, protects brain and liver lipids from peroxidation, and has a strong stimulating effect on the brain and liver antioxidant protection system.

Formulation and characterization of hard gelatine capsule with apple lyophilizate

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Background. In the healthy food chain, apples are an important source of phenolic compounds. The bioavailability of phenolic compounds is not particularly high (absorbed at a rate of 0.3%– 43%). Although on the pharmacy there are quite a number of food supplements, which use various plant extracts rich phenolic compounds in capsules, the use of lyophilized fruits in the production of hard capsules is still a rare phenomenon. It is appropriate to model capsules that would improve the release of phenolic compounds from capsules with lyophilized fruits powder.

Aim. The aim of our study was to model hard gelatine capsules with lyophilized apple powder by using different excipients.

Methods. Object of study the cultivar 'Ligol' of apple. The slices of apples were lyophilized. The samples of apples extracted with 70% (v/v) ethanol in the ultrasonic bath for 20 min at room temperature. The capsule dissolution test was performed using a dissolution tester. The acceptor medium was an ethanol-water mixture at the ratio of 1:1, the volume 250 ml. The temperature being 37.0 ± 0.5°C. Phenolic compounds analysis was performed by high performance liquid chromatography method.

Results. The phenolic compounds were identified and quantified in the analysed samples of the lyophilized apples: rutin, hyperoside, isoquercitrin, reynoutrin, avicularin, quercitrin, procyanidin B1, procyanidin B2, procyanidin C1, (+)-catechin, (-)-epicatechin, phloridzin, and chlorogenic acid. The total amount of phenolic compounds determined in the lyophilized sample of apples was 183.07 ± 8.23 µg/ml. The study showed that the selected excipients were suitable for the modelling of capsules with lyophilized apple powder, and the corresponding amount of hypromellose neither prolonged the disintegration of the capsules nor affected the dissolution rate of the active compounds. According to the results of the dissolution test, the capsules can be classified as fast-dissolving preparations, since more than 85% of the active substance was released within 15 minutes.

Conclusion. The phenolic compounds that were predominant in capsules with the lyophilized apple powder of the tested compositions were (-)-epicatechin and chlorogenic acid. Excipients and their amounts may affect the dissolution kinetics of the active compounds. The results of the solubility and disintegration tests proved that the capsules of the proposed composition are appropriate for internal use.

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Evaluation of the usefulness of computer microtomography for the analysis of subdivided prolonged release tablets containing carbamazepine

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Background. With the advancement of medicine, increasing attention is paid to the individualization of pharmacotherapy. Tablet splitting is a common practice among patients and doctors. However, such a practice should ensure that tablet halves/parts obtained are uniform in terms of weight, as well as in terms of distribution of the active pharmaceutical ingredient (API). Imaging techniques, such as x-ray computer microtomography, may be helpful in the assessment of API homogeneity.

Aim. To assess the usefulness of the x-ray computer microtomography in the analysis of homogenous distribution of ingredients in prolonged release tablets containing 200 mg of carbamazepine.

Methods. Tablets were evaluated according to the Polish Pharmacopoeia XI (FPXI) requirements in term of weight uniformity (20 randomly selected tablets) and dimensions (5 tablets). Next, tablets were divided into two parts using kitchen knife, which is one of the most common ways to split tablets. According to Food and Drug Administration (FDA), the mass loss after splitting should not exceed 3%. To assess the homogeneity of tablets' ingredients, scans of the tablets were performed both before and after subdivision using a Phoenix v|tome|x microtomograph (GE Germany). In the research model, "bright" pixels correspond to the high-density areas, while "dark" pixels represent the areas with low density. Based on the histograms obtained using ImageJ software, correlation between the density and the grayscale level was made. This allows the calibration of any area of the tablet scan in order to determine its density. To establish the reference density, the Micro-CT HA Phantom D32 was scanned and reconstructed under the same conditions as the analysed tablets.

Results. Whole tablets met the FPXI criteria in terms of weight uniformity. The mean weight of both parts of the tablets obtained after splitting differed significantly ($p=0.014$). The mass loss after subdivision showed that two of the analysed tablets did not meet the FDA criterion, i.e., the weight loss was greater than 3%. Based on the microtomographic scans and subsequent image processing, the density between whole analysed tablets demonstrated statistical difference ($p=0.008$), which may indicate the lack of homogeneity in the distribution of ingredients between tablets. In turn, no significant differences in density between both halves of the tablets obtained after subdivision ($p=0.093$) were observed, and therefore the parts were homogeneous.

Conclusion. Computer x-ray microtomography may be useful in the quantitative assessment of API distribution in halves of the tablets after splitting.

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Influence of the sodium alginate's concentration on the quality parameters of nutmeg essential oil-loaded microcapsules

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Background. Essential oils are volatile liquids that have many effects. One of them is pharmacological, however using the oils *per os*, the doses of essential oil are usually very small and some of the compounds evaporate when exposed to the environment. So, essential oils can lose their activity but the microencapsulation method can be applied to preserve it and microparticles could be used in the manufacture of pharmaceutical forms. Extrusion is one of the methods used for the protection of essential oil. It is a physical method which is described as an action of pushing out.

Aim. The aim of this study was to prepare nutmeg essential oil-loaded microcapsules with sodium alginate as a shell material and to evaluate its influence on the physical properties of microcapsules.

Methods. Sodium alginate, nutmeg essential oil, polysorbate 80, calcium chloride were used as materials and medical syringe as a device in microparticle technology. Nutmeg essential oil emulsion was prepared, as follows: 4 % of sodium alginate aqueous solution (5 g, 10 g, and 15 g) was diluted with distilled water until 15 g, then an emulsifier (1 g) and lastly, nutmeg essential oil (0.5 g) were added. A syringe was filled with manufactured emulsion and the microcapsules were formed into a crosslinker solution (5 % calcium chloride). Physical parameters of nutmeg essential oil loaded microcapsules were measured: diameter of wet and dry microcapsules, force for crushing (the capsules firmness), and encapsulation efficiency.

Results. Microcapsules of emulsion with 0.4 g and 0.6 g sodium alginate had a significantly higher stability than an emulsion with 0.2 g. A higher encapsulation efficiency (60.59±1.35 %) was determined in emulsion with 0.2 g of sodium alginate (encapsulation efficiency was carried out after 48 h of manufacturing). Force needed to crush the microparticles was from 5547.78±260 g to over 6500 g. Diameter of wet microcapsules ranged from 2.286±0.17 mm to 2.678±0.27 mm; dry microcapsules – from 0.951±0.10 mm to 1.348±0.17 mm.

Conclusion. A direct correlation was found between sodium alginate content and microcapsule size and firmness; it increases these parameters. Higher amounts of sodium alginate decrease the release of essential oil from nutmeg essential oil-loaded microcapsules.

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Antioxidant activity of phenolic fractions from *Vaccinium vitis-idaea* L. leaves

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Background. Lingonberry (*Vaccinium vitis-idaea* L.) leaves are regarded to be a good source of phenolic compounds, which are promising multi-targeting agents in the treatment of various diseases because of versatile antioxidant activity. However, the contribution of individual phenolics or particular groups to the antioxidant activity of lingonberry leaves has not been extensively studied directly. This complicates the identification of lingonberry's antioxidant activity markers.

Aim. The present study aimed at isolation and of phenolic fractions from lingonberry leaves and evaluation of their antioxidant activity.

Methods. Powder of crude dry extracts of lingonberry leaves (marked L1) was applied to a glass column (3×60cm) packed with already equilibrated Sephadex LH-20 and eluted successively with one column volume of water (to obtain L2), four volumes of 50% ethanol (to obtain L3) and two volumes of 70% acetone (to obtain L4). For each fraction phenolic composition was determined by validated HPLC-PDA method and the radical scavenging, reducing, and chelating activities were investigated, using ABTS, FRAP, and FIC assays, respectively. Results of antioxidant activity assays were expressed as micromolar of standard antioxidant – Trolox or strong chelating agent – EDTA equivalents per gram of dry weight of fractions (μM TE/g DW and μM EDTA/g DW, respectively).

Results. The radical scavenging activity assessed by ABTS assay ranged between 4204.1 and 7832.7 μM TE/g DW, with the lowest and highest ($p<0.05$) values determined in the fraction enriched with arbutin (L2) and fraction with predominant compounds of polymeric and mainly A-type dimeric proanthocyanidins (L4), respectively. In FRAP assay, L3 fraction with prevailing compounds of catechins and flavonols, surpassed all other fractions by the greatest ($p<0.05$) reducing activity of 5316.7 μM TE/g DW, followed by L4 fraction. FIC assay showed a similar trend to the results of ABTS and FRAP assays. The highest ($p<0.05$) chelating activity (126.4 μM EDTA/g DW) was expressed in the fraction of L4, and the lowest ($p<0.05$) one, approximately two times lower, in L2. Antioxidant activity of crude extract and obtained fractions according to average values of all antioxidant assays were in the following ascending order: L2<L1<L3<L4.

Conclusion. The purified fraction, obtained by the last fractionation step, possessed the greatest antioxidant activity. The predominant compounds of this fraction – proanthocyanidins – can be considered to be antioxidant activity markers of lingonberry leaves.

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Quantification of isoflavones aglycones in the late harvest aerial parts of *Trifolium pratense* L. using different hydrolysis methods

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Background. Red clover (*Trifolium pratense* L.) is a perennial legume that has received considerable amount of interest as an alternative valuable source of isoflavones endowed with a variety of health protective effects. Isoflavones found in the red clover possess estrogenic and antiproliferative effects. Conjugated isoflavones like daidzin and genistin are inactive but become active in aglycone (daidzein and genistein) form, when the glucose molecule is removed from the structure. To obtain the highest amounts of aglycones, the best method of hydrolysis must be determined.

Aim. The aim was to obtain the highest possible amounts of isoflavones genistein and daidzein from *Trifolium pratense* L. blossoms using different methods of hydrolysis.

Methods. Ultrasound-assisted extraction was performed using 1.0 g of dried and milled flower heads and 30 mL of 70 % ethanol. Ultrasound power 250 W, temperature 40°C, extraction time 10- and 30-min. Alkali hydrolysis was implemented using 25% NaOH. The pH was changed to 10.5 and then the extracts were sonicated. After hydrolysis, the samples were neutralized to pH 5.7 using 25% acetic acid. Acidic hydrolysis was performed after sonication. 37% HCl was added to the whole medium ratio 1:12 (v/v) and the flask was heated under reflux condenser for 1 h. Hydrolysed extracts pH was changed to ~2.5 by adding aqueous solution of 2 M NaOH while stirring. Thermal hydrolysis was performed after sonication placing extract under reflux for 1 h. Maceration results was used as control. Extraction samples for quantification of aglycones were investigated using HPLC.

Results. Ultrasound-assisted extraction without hydrolysis yielded lower levels of aglycones than simple maceration but using alkaline and thermal hydrolysis larger amounts of aglycones were obtained. The highest amounts of isoflavones were obtained throughout thermal hydrolysis: 1066.96 µg/g daidzein and 150.8 µg/g genistein. Small amounts (10.67 and 14.83 µg/g genistein and daidzein respectively) or no isoflavones were detected using acidic hydrolysis. Daidzein levels were found to be higher than genistein in all the samples except one (ultrasound extraction – 10 minutes, without hydrolysis).

Conclusion. Most isoflavones were detected in the sample, which was sonicated for 10 minutes, and hydrolysis was performed by heating the sample. No isoflavones were detected in the sample, which was sonicated for 10 minutes and hydrolysed with acid. Extending ultrasound processing time from 10 to 30 minutes, the concentrations of isoflavones aglycones in extracts increase.

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