

Conference Report

# Abstracts of the 2nd International Electronic Conference on Clinical Medicine (ECCM 2024) <sup>†</sup>

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**Abstract:** The 2nd International Electronic Conference on Clinical Medicine: Chronic Diseases—Current State and Future Trends (ECCM 2024) was organized by MDPI and MDPI *Journal of Clinical Medicine* and took place online from 13 to 15 November 2024. This conference report is an abstract collection from different sessions of ECCM 2024.

**Keywords:** telemedicine; cardiology; clinical psychology; dermatology; endocrinology; epidemiology; hematology; oncology; psychiatry

## 1. Introduction

The 2nd International Electronic Conference on Clinical Medicine (ECCM 2024) was an online event, chaired by Prof. Dr. Emmanuel Andrés and Prof. Dr. Kent Doi. This conference presented the latest studies in various fields of clinical medicine pertaining to the following general and related themes, including, but not limited to, the following:

- AI and Telemedicine;
- Cardiology;
- Clinical Psychology;
- Dermatology;
- Endocrinology and Metabolism;
- Epidemiology and Public Health;
- Gastroenterology and Hepatopancreatobiliary Medicine;
- Hematology;
- Infectious Diseases;
- Nephrology and Urology;
- Neurology and Stroke Neurology;
- Nuclear Medicine and Radiology;
- Obstetrics and Gynecology;
- Oncology;
- Ophthalmology;
- Orthopedics;
- Otolaryngology;
- Pharmacology;
- Psychiatry;
- Pulmonology;
- Stomatology.



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## 2. Cardiology

### 2.1. An Insight into the Interplay Between Immune Thrombocytopenic Purpura (ITP) and Heart Failure: A Retrospective Analysis of National Inpatient Data in the United States

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Patients admitted with autoimmune thrombocytopenic purpura (ITP) are high-risk due to their susceptibility to bleeding and limitations on medical interventions. Heart failure (HF) is a widespread condition that significantly impairs quality of life, complicating the management of ITP. These patients often use blood thinners, exacerbating their risk profile. This study analyzed the National Inpatient Sample database for 2019–2020 to examine the impact of HF on ITP patients. The cohort included 27,885 patients hospitalized with ITP, of which 1950 (7%) also had HF. Multivariate regression analysis was used to assess the outcomes. The results showed no significant difference in mortality (OR 1.1, 95% CI 0.52–2.29,  $p = 0.795$ ) and length of stay (+1.14 days, 95% CI 0.32–1.95,  $p = 0.006$ ) between the groups. However, hospitalization costs increased significantly for patients with HF (+17,762 USD, 95% CI 3439–35,439,  $p = 0.04$ ). HF patients had higher odds of acute respiratory failure (OR 2.44, 95% CI 1.31–4.52,  $p = 0.005$ ), ICU admission (OR 1.86, 95% CI 1.015–3.41,  $p = 0.044$ ), and acute coronary syndrome (OR 6.27, 95% CI 1.05–37.47,  $p = 0.04$ ). No significant differences were found in major (OR 1, 95% CI 0.66–1.51,  $p = 0.983$ ) and minor bleeding (OR 1.36, 95% CI 0.33–5.58,  $p = 0.666$ ), blood transfusions (OR 0.81, 95% CI 0.52–1.25,  $p = 0.352$ ), platelet transfusions (OR 0.98, 95% CI 0.73–1.30,  $p = 0.897$ ), venous thromboembolism (OR 0.93, 95% CI 0.36–2.38,  $p = 0.887$ ), mechanical ventilation (OR 1.79, 95% CI 0.92–3.48,  $p = 0.084$ ), cardiac arrest (OR 3.04, 95% CI 0.65–14.11,  $p = 0.156$ ), acute kidney injury (OR 1.07, 95% CI 0.77–1.47,  $p = 0.661$ ), and sepsis (OR 1.61, 95% CI 0.59–4.39,  $p = 0.346$ ). In summary, HF in ITP patients is associated with higher hospitalization costs, increased acute respiratory failure, ICU admissions, and cardiac events, but not mortality or bleeding. Effective HF management in ITP patients is crucial for mitigating adverse outcomes and optimizing care.

### 2.2. Analyzing Neurological and Cardiological Signals: Original vs. Bessel-Activated—Exploring Correlation and Anomalies

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**Background:** Accurate anomaly detection in brain and cardiac signals is essential for advancing diagnostic accuracy in neurological and cardiological research. Traditional signal processing methods often face challenges in preserving signal integrity while identifying anomalies.

**Objective:** This study investigates the application of Bessel activation functions in transforming brain and cardiac signals to facilitate effective anomaly detection and correlation analysis.

**Methods:** Bessel activation functions were applied to a dataset of brain and cardiac signals to transform the data. The transformed signals were then compared with the original signals using Pearson correlations to evaluate the preservation of signal integrity. Additionally, anomaly detection was performed by identifying peaks in the activated signals.

**Results:** The application of Bessel activation functions resulted in a significant improvement in the identification of anomalies, with the method effectively discerning peaks corresponding to signal anomalies. Pearson correlation analyses demonstrated that the

Bessel activation preserved signal integrity, with correlation coefficients consistently above 0.9 across all samples.

**Conclusion:** This study demonstrates the potential of Bessel activation functions in enhancing the accuracy of anomaly detection in brain and cardiac signals while maintaining the integrity of the original data. These findings contribute to the broader field of signal processing and offer promising implications for improving diagnostic approaches in medical and scientific research.

### 2.3. Cerebrovascular Pathology in Patients with Ischemic Heart Disease (Neuroimaging Results)

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**Background:** The aim of this study was to assess the neurological status and the condition of the brain in patients with ischemic heart disease.

**Methods:** We examined 170 patients, all men and middle age, with an average age of 58.6 years. All of them passed a neurological examination and a Mini-mental State Examination (MMSE) test. The brain examination was performed with the multi-spiral computer tomograph "Somatom Sensation 64 Siemens" (Germany). On a native multi-detector computed tomography (MDCT) of the brain, the ventriculocranial index Evance, the width of ventricle III, and the presence of leukoaraiosis, cysts, and gliosis were estimated.

**Results:** The frequency of vestibulopathy syndrome was 24%, that of asthenia syndrome was 56%, that of mild cognitive impairment was 46%, and the average of the MMSE test results was 27 [26; 28] points.

The width of ventricle III was  $7.6 \pm 2.0$  mm, the ventriculocranial index Evance was 3–4.2%, leukoaraiosis was found in 26% of the patients, signs of cortical atrophy were found in 19% of the patients, and cysts were found in 5% of the patients. The average age of our patients was no more than 60 years, but the width of ventricle III corresponded to the expected values for the age category of healthy persons over 60 years old, and the values of the ventriculocranial index Evance corresponded to the age norms for healthy subjects over 70 years old.

**Conclusions:** Mild cognitive impairment, asthenia syndrome, and vestibulopathy syndrome are very common among patients with ischemic heart disease. Signs of cerebral angiopathy (leukoaraiosis, cysts, width of ventricle III) indicate the vascular nature of neurological disorders.

### 2.4. Comparison of Novel vs. Standard Myocardial Dysfunction Biomarkers and Analysis of Their Relation with Diastolic Dysfunction Grade in Kidney Transplant Recipients

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**Introduction:** Compared to the general population, kidney transplant recipients have a significantly higher risk of contracting cardiovascular disease, which is one of the leading causes of death in these patients. The aim of this analysis is to compare some novel

myocardial damage biomarkers with standard ones and with cardiac ultrasonography measurements in this group of patients.

**Methods:** The study included 91 adult kidney transplant recipients whose data on cardiac ultrasound was compared with levels of the following cardiac damage biomarkers: galectin-3, soluble interleukin 1 receptor-like 1 (ST2), FK506-binding protein-like, procollagen type III N-terminal peptide, and periostin. Patients were divided into two groups based on diastolic dysfunction grade.

**Results:** The median age of patients was 43 years (interquartile range—IQR: 37–53). Galectin-3 showed a significant positive correlation with the systolic-to-diastolic velocity ratio ( $r = 0.300, p \leq 0.05$ ), while a negative correlation was found with the left atrium volume index ( $r = -0.377, p \leq 0.05$ ). ST2 showed a significant positive correlation with the left ventricular mass index ( $r = 0.318, p \leq 0.05$ ) and procollagen type III N-terminal peptide with peak velocity blood flow in late diastole caused by atrial contraction ( $r = 0.289, p \leq 0.05$ ). Serum periostin showed a significant positive correlation with the systolic-to-diastolic velocity ratio ( $r = 0.329, p \leq 0.05$ ), while a negative correlation was found with the peak velocity blood flow from left ventricular relaxation in early diastole ( $r = -0.343, p \leq 0.05$ ). A between-group comparison in terms of diastolic dysfunction grade showed that patients with diastolic dysfunction grades 0 and 1 had significantly higher levels of galectin-3 compared to the patients with grades 2 and 3 (17.53 vs. 15.92 ng/mL,  $p = 0.03$ ).

**Conclusion:** The analyzed biomarkers show significant potential in determining the level of cardiac function commonly measured by ultrasonographic methods. Given their correlation with some standard biomarkers and diastolic dysfunction grade observed in this analysis, these biomarkers could be utilized in procedures by evaluating cardiac function in kidney transplant recipients and contributing to the timely diagnosis of these conditions.

#### 2.5. Early Diagnostic Markers of Nephropathy with Hypertensive Disease in Patients with Type 2 Diabetes Mellitus

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In this study, we tried to assess whether the existing diagnostic criteria for chronic kidney disease are insufficient for practice and whether new early laboratory markers of chronic kidney disease exist. Chronic kidney disease (CKD) is an umbrella term that indicates damaged kidney tissue, regardless of etiological origin. Based on several large studies, experts have come to the decision that albuminuria is a high risk factor for death in cardiac and renal diseases, diabetes, and arterial hypertension. The participants in this study were divided into three groups based on the main etiological causes of chronic kidney disease: the first group comprised those with hypertension, the second group comprised those with type 2 diabetes mellitus, and the third group comprised those with comorbid conditions of these diseases. They were subjected to standard and special laboratory analyses, and the results of the analyses were compared. In the patients, nephrinuria and aldosterone in the blood were determined, indicating kidney podocyte dysfunction, along with collagen IV, indicating tubulointerstitial dysfunction, and these were compared with the standard diagnostic indicator albuminuria, and inter-group differences were assessed. It can be concluded that in all three groups, microalbuminuria did not serve as a predictor of chronic kidney disease, but it has now been replaced by more reliable urine nephrinuria and collagen IV analyses.

#### 2.6. Hematological Profile of Congenital Heart Disease Patients Undergoing Surgical Correction: A Cas–Control Observational Study from North India

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**Background:** Congenital heart disease (CHD) is a cardiac condition present from birth, contributing to ~28% of all birth defects and causing higher fetal and neonatal mortality worldwide. Complete blood count (CBC) is a routine diagnostic tool in clinical settings and has been suggested to be predictive of cardiovascular diseases and other metabolic disorders. This study investigates the correlation between CBC indices and CHD.

**Methods:** We analyzed preoperative CBC data from 238 CHD patients and 50 healthy controls. Statistical analyses, including the Student's *t*-test, chi-square test, and multivariate logistic regression, were employed to identify significant deviations and correlations.

**Results:** Our findings revealed that ~79% (11 out of 14) of CBC parameters differed significantly from those of healthy controls. Notably, lymphocytosis and a reduced platelet-to-lymphocyte ratio (PLR) were observed consistently across all CHD cases ( $p = 0.000$ ). Cyanotic patients exhibited erythrocytosis and higher hemoglobin levels despite their tendency towards anemia ( $p = 0.000$ ). Multivariate regression analysis demonstrated robust correlations: hematocrit was strongly associated with both hemoglobin ( $r = 0.92$ ) and SpO<sub>2</sub> ( $r = -0.76$ ), while red blood cell (RBC) counts correlated closely with hematocrit ( $r = 0.88$ ), hemoglobin ( $r = 0.83$ ), and SpO<sub>2</sub> ( $r = -0.78$ ). Elevated pulse rates, platelet counts, and lymphocyte levels, coupled with lower body mass index (BMI), mean corpuscular volume (MCV), hemoglobin, and mean corpuscular hemoglobin (MCH), could facilitate early CHD diagnosis ( $p = 0.05$ ). Additionally, reduced mean corpuscular hemoglobin concentration (MCHC) levels were linked to shorter ventilation times ( $p = 0.0004$ ).

**Conclusion:** Our study underlines the significant associations between CBC indices and CHD in a North Indian cohort, highlighting the potential of CBC parameters for the early diagnosis and management of CHD. Our findings suggest that specific CBC alterations are closely linked to the severity and type of CHD, offering valuable insights for improving patient care and outcomes.

### 2.7. Integrated Bioinformatic Analysis of Diabetes Mellitus and Cardiovascular Diseases' Shared Molecular Mechanisms

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#### Integrated Bioinformatic Analysis of Diabetes Mellitus and Cardiovascular Diseases' Shared Molecular Mechanisms

**Introduction:** Cardiovascular diseases (CVDs) and type 2 diabetes mellitus (T2DM) are closely interconnected, sharing several molecular mechanisms. Notably, insulin resistance and inflammation are common pathophysiological factors that contribute to the progression of both conditions. Given that CVD is the leading cause of mortality in individuals with T2DM, this study aims to explore these shared mechanisms to provide insights that could inform the development of more targeted therapeutic strategies.

**Aim:** The primary aim of this research is to identify the shared molecular pathways and mechanisms between CVDs and T2DM. Specifically, this study focuses on uncovering differentially expressed genes (DEGs), curated pathways, common miRNAs, and other related molecular factors that could contribute to the co-occurrence of these diseases.

**Methods:** A bioinformatic approach was utilized to analyze gene expression data, leading to the identification of DEGs and the isolation of curated pathways and genes. The analysis was also extended to miRNAs and other chemicals associated with both CVDs and T2DM.

**Results:** This study identified four differentially expressed genes (DEGs) and one shared miRNA, hsa-mir-223, which are potentially implicated in the development of both CVDs and T2DM. Additionally, the analysis uncovered 6 curated genes, 37 curated chemicals, and 253 inferred pathways. The statistical analysis confirmed the significance of these findings, with the DEGs showing a strong correlation ( $p = 0.05$ ) between the two diseases.

**Conclusion:** The results highlight potential molecular interconnections between CVDs and T2DM, providing a foundation for further research into the development of targeted therapies. The findings underscore the importance of collaborative efforts among researchers, clinicians, and the pharmaceutical industry to advance early detection, improve drug development, and refine treatment strategies for individuals at risk of or suffering from both conditions.

### *2.8. Optimizing Pattern Design and Standardizing Production for Abdominal Aortic Prostheses*

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**Introduction:** Abdominal aortic prostheses are crucial in surgical interventions where infected prostheses must be replaced. Though synthetic materials are commonly used, this study explores the use of bovine pericardium for its superior biocompatibility and reduced inflammatory response.

**Aim:** The objective of this research is to develop a standardized pattern construction for abdominal aortic prostheses to enhance fitting accuracy and reduce manufacturing time, specifically targeting the challenges faced by surgeons in the manual cutting and suturing process.

**Methods:** This study proposes an optimized cutting template using a sterilizable metal stencil to standardize and expedite the production process. New pattern constructions were created, and their manufacturing processes were formulated using CAD software for precision.

**Results:** Three pattern constructions were tested. The first two demonstrated improvements, reducing suturing time and simplifying handling during surgery. Clinical tests in a limited sample of patients confirmed the feasibility of the new designs, with no postoperative complications observed.

**Conclusions:** The use of a standardized cutting template for bovine pericardium prostheses offers improved clinical outcomes through reduced surgery time and enhanced prosthesis fitting. Further large-scale clinical trials are recommended to validate these findings.

### *2.9. Oral Bleeding: First Clinical Manifestation of Dentigerous Cyst in Geriatric Patient with Dabigatran Therapy and Systematic Literature Review*

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**Background:** Jaw cyst surgery is a common intervention in oral surgery. A cyst is an epithelium-lined sac containing fluid and/or semisolid material due to epithelial cell proliferation, degeneration, and liquefaction; the hypertonic solution withdraws liquids from the surrounding tissues, while internal pressure exerts an equal strength on the cyst walls. Dentigerous cysts are the second most common odontogenic cysts and commonly present no symptoms. Mandibular dentigerous cysts are common in children and adults and rare in elderly patients. Treatment usually involves the removal of the entire cyst and the associated unerupted tooth. This intervention may be more difficult if the cyst is large, the third molar is in contact with the mandibular nerve, and/or the patient has a medical history that may represent a relative or absolute contraindication.

**Materials and Methods:** The case of a dentigerous cyst in an elderly patient in treatment with dabigatran therapy is presented, with jaw cyst surgery and tooth extraction. A systematic literature review was performed to evaluate previous cases of dentigerous cysts in elderly patients.

Results: No complications, in particular excessive bleeding, occurred during the surgery or in the week after. Mandibular sensitivity returned with the pass of the dental anesthesia. One year after the surgery, a new panoramic radiograph was performed, revealing the complete healing of the site. The systematic literature review reported two previously documented cases, one treated with irrigation and the other one treated with cyst enucleation and tooth extraction.

Conclusions: This paper reports the first case of spontaneous oral bleeding as a first clinical sign of a dentigerous cyst in a geriatric patient, with one year of follow-up. Clinicians should consider the possibility of dentigerous cysts in elderly patients and, on the basis of multidisciplinary evaluation with cardiologists and geriatrician doctors, choose the most effective treatment to reduce the risks of surgery.

#### 2.10. Screening of Atrial Fibrillation in Dental Practices: A Qualitative Feasibility Study

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##### Introduction:

Atrial fibrillation (AF) is an abnormal, rapid, and irregular cardiac arrhythmia. AF is associated with a five-fold increase in stroke risk, but anticoagulation given to eligible patients can reduce this risk by 65%. Dental practices are increasingly seen as an appropriate healthcare environment in which to undertake healthcare prevention.

This qualitative study aimed to explore perceptions of and barriers faced by dental staff in screening for atrial fibrillation using a hand-held electronic device in a primary dental care setting.

##### Methods:

Purposive sampling was used to recruit participants from a large mixed NHS (National Health Service) and private dental practice. Interviews were semi-structured, face-to-face, audio-recorded, and transcribed verbatim amongst dental professionals within the practice. Interviews continued until no new themes or patterns emerged from the data and thematic saturation had been achieved.

##### Results:

Eleven participants were interviewed. Overall, the responses were positive. Four out of seven clinicians expressed concerns about time and remuneration. They felt screening would be well received but could heighten anxiety among patients. Seven out of eleven participants stressed their preference to refer the patients to their GP (general practitioner) for confirmation after the initial screening. Encouraging feedback regarding the simplicity of the portable screening device was given. Participants also proposed models of screening, such as using private screening booths.

##### Conclusions:

Overall, the AF screening was deemed to be a good concept amongst participants, but concerns were expressed about time, remuneration, and heightening anxiety among patients. A need for further research is indicated whilst evaluating the role of dental care professionals.

### 2.11. *The Activator Protein-1 Complex Governs a Vascular Degenerative Transcriptional Programme in Smooth Muscle Cells to Trigger Aortic Dissection and Rupture*

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**Background and aims:** Stanford type A aortic dissection (AD) is a degenerative aortic remodeling disease marked by exceedingly high mortality without effective pharmacologic therapies. Smooth muscle cells (SMCs) lining the tunica media adopt a range of states, and their transformation from contractile to synthetic phenotypes fundamentally triggers AD. However, the underlying pathomechanisms governing this population shift, and subsequent AD, particularly at distinct disease temporal stages, remain elusive.

**Methods:** Ascending aortas from nine patients undergoing ascending aorta replacement and five individuals undergoing heart transplantation were subjected to single-cell RNA sequencing. The pathogenic targets governing the phenotypic switch of SMCs were identified by trajectory inference, functional scoring, single-cell regulatory network inference, and clustering, regulon, and interactome analyses and confirmed using human ascending aortas, primary SMCs, and a  $\beta$ -aminopropionitrile monofumarate-induced AD model.

**Results:** The transcriptional profiles of 93,397 cells revealed a dynamic temporal-specific phenotypic transition and marked elevation of the activator protein-1 (AP-1) complex, actively enabling synthetic SMC expansion. Mechanistically, tumor necrosis factor signaling enhanced AP-1 transcriptional activity by dampening mitochondrial oxidative phosphorylation (OXPHOS). Targeting this axis with the OXPHOS enhancer coenzyme Q10 or AP-1-specific inhibitor T-5224 impedes phenotypic transition and aortic degeneration while improving survival by 42.88% (58.3–83.3% for coenzyme Q10 treatment), 150.15% (33.3–83.3% for 2-week T-5224), and 175.38% (33.3–91.7% for 3-week T-5224) in the  $\beta$ -aminopropionitrile monofumarate-induced AD model.

**Conclusions:** This cross-sectional compendium of cellular atlases of human ascending aortas during AD progression provides previously unappreciated insights into a transcriptional program permitting aortic degeneration, highlighting a translational proof of concept for an anti-remodeling intervention as an attractive strategy to manage temporal-specific AD by modulating the tumor necrosis factor–OXPHOS–AP-1 axis.

### 2.12. *The Effects of Multitask Cognitive Training on EEG Changes and Neurovascular Unit Markers in Cardiac Surgery Patients*

**Irina Tarasova, Darya Kupriyanova, Irina Kukhareva, Tatjana Temnikova, Evgenia Gorbatovskaya and Olga Trubnikova**

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**Background:** Understanding the neurophysiological mechanisms that contribute to better cognitive functioning is a research area that has been subject to growing interest. It is assumed that multitask interventions have better results in cognitive recovery. This study aimed to evaluate the effects of multitask cognitive training (MCT) on electroencephalographic (EEG) changes and markers of the neurovascular unit (NVU) in cardiac surgery patients.

**Methods:** A prospective cohort study was conducted on 62 cardiac surgery patients between 45 and 75 years old, with 30 of them going through a 5–7-day MCT course. The groups had similar clinical indicators at baseline. Before and after cardiac surgery, EEG studies were carried out. The NVU indicators (S100, NSE, and BDNF) were analyzed in three stages: before surgery, during the first 24 h after surgery, and 11–12 days after CABG.

**Results:** After CABG, patients with an MCT course and controls had higher theta1 power values as compared to preoperative data. The indicator of relative changes confirmed that the control group had more significant changes ( $p = 0.001$ ). The increase in S100 concentrations was only observed in the control patients during the first 24 h after CABG. At the end of the training course, the MCT group had an increase in BDNF levels compared to their preoperative values. The control group had a low serum BDNF concentration.

Conclusions: Theta activity changes and S100 and BDNF markers showed a slight decrease in the severity of brain damage in cardiac surgery patients after a short MCT course. Monitoring the process of cognitive rehabilitation in cardiac surgery patients can be made more informative using EEG and NVU markers.

### 3. Gastroenterology and Hepatopancreatobiliary Medicine

#### 3.1. Early Detection of Pancreatic and Colorectal Cancers via Ultra-Sensitive Circulating Tumor DNA (ctDNA) Analysis

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Pancreatic and colorectal cancers are often diagnosed at advanced stages, which limits therapeutic options and drastically reduces survival rates. To address this critical issue, we propose a novel, non-invasive early detection method that leverages the analysis of circulating tumor DNA (ctDNA) for identifying tumor-specific genetic mutations in plasma. ctDNA analysis offers a high-precision, dynamic approach to detecting molecular signatures of cancer at much earlier stages compared to traditional diagnostic tools such as endoscopy, imaging, or biopsy, which typically identify tumors when they are already advanced. This review analyzes current research pertaining to next-generation sequencing (NGS) and highly sensitive digital PCR to detect minimal amounts of ctDNA shed by cancer cells into the bloodstream. The novelty of this approach lies in its capacity for the continuous monitoring of ctDNA fluctuations, enabling not only early detection but also real-time assessment of tumor progression or response to therapy. This technology holds promise for significantly improving early diagnosis, particularly for high-risk populations with a genetic predisposition to these cancers. However, further research is required to enhance the sensitivity and specificity of ctDNA detection, especially in distinguishing between benign and malignant alterations, and to evaluate its effectiveness in larger, more diverse cohorts. Ultimately, ctDNA-based early detection could revolutionize cancer screening and patient management, providing a personalized, molecular-level approach to identifying and monitoring these deadly cancers.

#### 3.2. Genetic Variations and Drug Response in Gastroesophageal Reflux Disease (GERD): The Role of Pharmacogenomic Testing in Optimizing Proton Pump Inhibitor (PPI) Therapy

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The influence of genetic variations on drug efficacy has become an area of growing interest in the treatment of gastrointestinal (GI) disorders, particularly gastroesophageal reflux disease (GERD). Proton pump inhibitors (PPIs), the cornerstone of GERD management, are metabolized by the cytochrome P450 enzyme CYP2C19, whose activity is highly

variable due to genetic polymorphisms. Patients with CYP2C19 loss-of-function alleles (poor metabolizers) exhibit prolonged PPI exposure, leading to enhanced acid suppression, while those with gain-of-function alleles (ultra-rapid metabolizers) may experience suboptimal therapeutic effects. This variability in drug metabolism highlights the importance of personalized treatment approaches in GERD. Pharmacogenomic testing provides a novel and clinically relevant tool for identifying these genetic variants, allowing for tailored PPI dosing to maximize efficacy and minimize adverse effects, such as increased risks of *Clostridium difficile* infection or nutrient malabsorption associated with long-term PPI use. Recent clinical trials and observational studies underscore the benefits of incorporating pharmacogenomic testing into routine practice, where it has shown improved patient outcomes and medication adherence. Future research should focus on expanding pharmacogenomic testing to include other GI disorders and medications while addressing implementation barriers, including cost-effectiveness and clinician education. Integrating pharmacogenomics into clinical practice offers a promising pathway to personalized GI care, optimizing drug response, and enhancing therapeutic outcomes for patients with GERD.

### *3.3. Integrating Single-Cell RNA Sequencing and Microbial Metabolomics for Predictive Biomarker Discovery in Inflammatory Bowel Disease*

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Inflammatory bowel disease (IBD) treatment remains challenging due to the unpredictable therapeutic responses observed in patients with Crohn's disease and ulcerative colitis. In this analysis, we explore a review of combining single-cell RNA sequencing (scRNA-seq) and microbial metabolomics to identify biomarkers predictive of therapeutic response. scRNA-seq allows for detailed gene expression analysis of immune cells, such as T cells and macrophages, within intestinal biopsies, providing insights into cellular drivers of inflammation and potential treatment outcomes. Concurrently, microbial metabolomics analyzes gut-derived metabolites like short-chain fatty acids (SCFAs) and bile acids, which influence immune modulation and therapeutic efficacy. This integrated approach offers a highly specific, dual-layered method for predicting patient responses to therapies such as TNF inhibitors and IL-23 blockers. The combination of these cutting-edge technologies allows for an unprecedented level of precision in predicting patient-specific treatment responses. Future research should focus on longitudinal studies to track these biomarkers before and after therapy initiation, validating their utility in large, multicenter trials with the potential to personalize IBD treatment and shift clinical practice towards precision medicine. This approach could dramatically shift the paradigm toward precision medicine in IBD, reducing treatment failures and improving patient outcomes by tailoring therapies to individual molecular and microbial profiles.

### *3.4. Safety, Feasibility, and Preliminary Results of a Multicenter Randomized Trial Comparing Fat-Free Versus Balanced (WHO) Diet in Gallstone Disease (The Rationale Diet for Gallstones (RADIGAL) Study)*

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**Rationale:**

There is no high-level-of-evidence data to support the general notion that a fat-free diet is beneficial to patients with gallstone disease. Herein, we assess the feasibility and safety of a randomized study to assess the effect of recommending a fat-free diet versus a balanced WHO diet on the quality of life (QoL) in symptomatic patients with gallstones (RADIGAL-1) and in patients undergoing cholecystectomy for gallstone disease (RADIGAL-2).

**Methods:**

This is a multicenter, randomized, single-blind, parallel-arm, non-inferiority trial. Patients presenting with biliary colic or acute cholecystitis or undergoing cholecystectomy for gallstones are randomly assigned to recommending either a fat-free or a balanced WHO diet. A follow-up at 3 months will appraise patient adherence and outcomes. A validated quality-of-life questionnaire (GIQLI) will be administered both at baseline and during follow-up. A total of 136 patients will be recruited for RADIGAL-1 and 106 for RADIGAL-2 according to sample size calculation based on the mean clinically important difference of GIQLI scores.

**Results:**

The rate of recruitment in the participating centers is eight patients per month for RADIGAL-1 and twenty for RADIGAL-2. In RADIGAL-1, full compliance was recorded in 87.8% of the patients. Additionally, 2.4% of the patients followed the diet for more than 50% of the follow-up time, while 4.8% followed it for less than 50% of the time. In RADIGAL-2, full compliance was recorded in 88.3% of the patients. Moreover, 8.3% of the patients followed the diet for more than 50% of the follow-up time, and 3.3% followed it for less than 50% of the time. Drop-off rates are 2.4% for RADIGAL-1 and 1.7% for RADIGAL-2. No adverse events such as hospital admissions or biliary colic have occurred in excess in the control groups.

**Conclusion:**

These data support the safety and the feasibility of the RADIGAL trial (NCT06405906).

### *3.5. The Role of AI-Enhanced Optical Coherence Tomography in the Early Detection and Treatment of Gastrointestinal Cancers*

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The integration of artificial intelligence (AI) into optical coherence tomography (OCT) technology represents a novel frontier in the early diagnosis and treatment of gastrointestinal (GI) cancers, particularly esophageal and colorectal cancers. OCT, a high-resolution imaging modality that provides cross-sectional views of tissue microstructure, has shown promise in identifying dysplastic and early cancerous changes in the GI tract. When combined with AI-driven algorithms, OCT enables real-time automated analysis of tissue patterns, increasing diagnostic accuracy and reducing the likelihood of missed lesions. This AI-assisted technology is particularly effective in distinguishing between benign and malignant tissues, which can be challenging using traditional imaging techniques alone. As AI models continue to evolve, their ability to recognize subtle histopathological features can potentially reduce reliance on biopsies, speeding up the diagnostic process and facilitating immediate therapeutic interventions, such as endoscopic mucosal resection (EMR). However, future research is needed to further refine these AI algorithms and ensure their applicability across diverse patient populations. Additionally, cost-effective strategies must be developed to make this technology more accessible in routine clinical settings. The fusion of AI with OCT holds immense potential to revolutionize the management

of early GI cancers, offering a pathway to more personalized and minimally invasive treatment options.

#### 4. Epidemiology and Public Health

##### 4.1. Aromatic Microbial Metabolites in the Cerebrospinal Fluid Determined by Gas Chromatography–Mass Spectrometry as Promising Markers of Secondary Bacterial Meningitis

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**Introduction:** The diagnosis of infectious complications, in particular secondary bacterial meningitis, in patients who have undergone neurosurgical interventions is an urgent task, since, regardless of the cause of their occurrence, their differential diagnosis is an important factor in the successful treatment of patients. Aromatic metabolites of tyrosine, phenylalanine, and tryptophan, determined by chromatography–mass spectrometry, are promising markers of infectious complications in patients of different groups. The goal of this study was to identify the aromatic metabolites that are clinically significant for the diagnosis of secondary bacterial meningitis in patients who have undergone neurosurgical interventions.

**Methods:** Residual cerebrospinal fluid (CSF) samples obtained from neurosurgical patients after routine laboratory analysis were analyzed by gas chromatography–mass spectrometry ( $n = 82$ ) and high-performance liquid chromatography–tandem mass spectrometry ( $n = 29$ ). The levels of 11 phenyl- and indole-containing acids were determined. Patients were divided into two groups depending on the presence or absence of signs of secondary meningitis based on the clinical picture and clinical and laboratory analysis of CSF.

**Results:** Chromatography–mass spectrometry methods were used to determine the levels of aromatic metabolites in CSF samples of neurosurgical patients at the level of  $\mu\text{mol/L}$  and  $\text{nmol/L}$ . Metabolite profiles were compared in groups of patients with or without signs of secondary meningitis. Statistically higher levels of 4-hydroxyphenyllactic ( $p = 0.005$ ), phenyllactic ( $p = 0.002$ ), 3-indolelactic ( $p = 0.006$ ), and 3-indolecarboxylic ( $p = 0.027$ ) acids were found in patients with signs of secondary meningitis.

**Conclusions:** CSF levels of aromatic microbial metabolites may be potential markers of secondary bacterial meningitis in patients undergoing neurosurgery.

##### 4.2. Application of Bacteriophages in Clinical Practice

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**Introduction:** Among the issues related to the use of medical care in intensive care units (ICUs), the leading place is occupied by hospital or ventilator-associated pneumonia. One of the promising methods of preventing respiratory infectious diseases in the ICU may be adaptive phage therapy.

**Methods:** The study included patients ( $n = 41$ ) with an average age of 54 years (28% men) and a control group ( $n = 38$ ) with an average age 59 of years (19% men). Adaptive phage therapy was administered by inhalation (5.0 mL, 3 times a day) from the first day of stay of patients of the main group ( $n = 41$ ) for at least 21 days in the intensive care unit of the Federal Research and Clinical Center of Intensive Care Medicine and Rehabilitology. The control group ( $n = 38$ ) consisted of patients who received standard therapy in accordance with current recommendations for pneumonia. The taxonomic composition and resistance genes of endotracheal aspirate were assessed via PCR testing using Amplisens reagents (Russia) on CFX 96 (BioRad; USA).

**Results:** Over the entire study period, 24 (58.5%) patients in the main group ( $n = 41$ ) had no recurrence of nosocomial pneumonia and did not require antibiotics, while in the control group ( $n = 38$ ), only 11 (26.3%) patients did not need antibiotic therapy. A statistically significant decrease in the number of pathogens in the study group compared

to the control ( $p = 0.008$ ) suggests the possibility of the effective use of a complex preparation of bacteriophages.

Conclusions: In the long term, the use of bacteriophages helps to improve the quality of treatment, reduce the number of recurrent infections, and reduce the use of antibiotics.

#### 4.3. Assessment of Metformin Treatment in Type 2 Diabetic Patients in Cape Coast

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Metformin, a first-line anti-diabetic medication, is used in the management of type 2 diabetes worldwide. Defects in insulin secretion, insulin activity, or both in diabetic patients affect the metabolism of carbohydrates, fat, and protein (which causes high blood glucose levels and obesity). Metformin decreases glucose production, increases insulin sensitivity, and enhances peripheral glucose uptake. Its effectiveness in managing blood glucose levels is well documented; however, the association between metformin treatment and blood glucose levels and body weight remains a subject of investigation. This study aims to assess the association between the dosage and duration of metformin treatment and the fasting blood glucose (FBS) level and body mass index (BMI) of diabetic patients. A cross-sectional study was conducted with 162 type 2 diabetic patients on routine checkup at Cape Coast Teaching Hospital in Ghana. Information on FBS level and BMI, metformin treatment, and demographic characteristics were obtained from records and face-to-face-interviews using a structured questionnaire. Pearson's correlation was used to analyze the association between dosage and duration of metformin treatment and the FBS level and BMI. The dosage of metformin treatment showed a significant positive correlation with the FBS level ( $r = 0.165$ ,  $p = 0.036^*$ ), and the duration of metformin treatment showed a highly significant negative correlation with the FBS level ( $r = -0.204$ ,  $p = 0.01^{**}$ ). However, there was no significant correlation between the dosage of metformin treatment and BMI ( $r = 0.109$ ,  $p = 0.168$ ) and between the duration of metformin treatment and BMI ( $r = 0.0790$ ,  $p = 0.319$ ). These results indicate that the dosage and duration of metformin treatment significantly affect fasting blood glucose levels. Monitoring metformin treatment based on fasting glucose levels is more effective for managing diabetes than using body mass index as a guide.

#### 4.4. Effectiveness of Hypochlorous Acid in Hospital Disinfection

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##### Introduction

Hospital disinfection is crucial for infection prevention, especially with rising bacterial resistance. Effective disinfectants compliant with European biocide regulations (528/2012 CE) are needed. At Clínica Universidad de Navarra, we started using Hypochlorous acid (Klorxitol<sup>®</sup>) in March 2022. We conducted a study to verify its efficacy by taking surface cultures before and after its application.

##### Methods

Hypochlorous acid (Klorxitol<sup>®</sup>) was applied via nebulization in wards and misting in operating theatres. We cultured five surfaces before and after disinfection on nine occasions. Nebulization used the BYOPLANET<sup>®</sup> Electrostatic Sprayer System, which requires no PPE or ventilation sealing. The high-touch surfaces sampled included patient armchairs, toilet flushes, nurse call bells, bed trays, and bed controls. In operating rooms, a mist system sprayed Klorxitol<sup>®</sup> for 15 s, followed by a 5 min settling time. The sampled surfaces included the surgical table, keyboards, instrument tables, and door elbow push pads. Statistical analysis was conducted using IBM SPSS, calculating the absolute reduction in Colony-Forming Units (CFU) pre- and post-disinfection. Paired Student's *t*-tests and confidence interval calculations were used, with results presented in BoxPlot diagrams.

##### Results

Both application methods demonstrated significant efficacy. The BYOPLANET® Electrostatic Sprayer System showed a significant reduction in CFU ( $p = 0.001$ ). Specific surfaces with significant reductions included the bed rail ( $p = 0.002$ ) and table edge ( $p = 0.019$ ), though the cistern handle was not significant ( $p = 0.171$ ). The mist system also showed a significant CFU reduction. The mean CFU count decreased from 20.17 (95% CI  $-2.05$ – $62.39$ ) with an SD of 30.7 before disinfection to 8.33 (95% CI  $-11.59$ – $28.25$ ) with an SD of 18.98 after disinfection ( $p = 0.031$ ).

#### Conclusion

Hypochlorous acid (Klorxitol®) effectively reduces bacterial contamination on hospital surfaces, meeting disinfection standards and supporting its use as a reliable disinfectant in healthcare settings.

#### 4.5. Hospitalizations of Patients with Atrial Fibrillation (AF) in Poland: A Nationwide Study Based on over One Million AF Hospitalizations in 2017–2021

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**Introduction:** Atrial fibrillation (AF) is one of the most common forms of persistent arrhythmia in adults worldwide. Given the increasing prevalence of AF worldwide, aging populations, improved methods of diagnosis, and an increasing burden of comorbidities, AF poses a significant burden on healthcare systems.

**Methods:** This is a retrospective population-based study conducted using hospital discharge records. Data covered 1,225,424 cases of AF hospitalization reported in 2017–2021.

**Results:** The study group consisted of 51.36% men and 48.64% women. The mean and median ages were 73.6 and 74 years, respectively. Women were significantly older than men (77 vs. 70 years,  $p = 0.001$ ). The mean and median lengths of hospitalization were 6.9 and 4 days. The mean annual hospitalization rate was 640.0 per 100,000 person-years. In the group of patients aged  $\geq 65$  years, the hospitalization rate was 2870.4 per 100,000 person-years. Men were hospitalized more frequently than women ( $p = 0.001$ ). The total in-hospital mortality rate was 37.7 per 100,000 person-years, and it was higher in women than in men ( $p = 0.001$ ). There was a significant downward trend in first-time hospitalizations during the analyzed period and a significant downward trend in mortality rates with a marked increase in the years 2020–2021 (during the COVID-19 pandemic).

**Conclusions:** To the best of the authors' knowledge, this study presents the aspects of AF based on the national hospital morbidity register and it presents the latest data on AF epidemiology in Poland. AF remains a significant public health problem in Poland. Although women are less frequently hospitalized for AF, they show a higher risk of fatal hospitalizations. The pandemic may have reduced new AF diagnoses and increased mortality in this group of patients. The results of this study may be helpful in performing comparative analyses in the European and global context and taking actions aimed at improving the health of the Polish population.

#### 4.6. Integrative RNA-Seq and DEG Analysis for the Identification of Clinical Biomarkers in Tuberculosis Infectious Disease

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Tuberculosis (TB) continues to be a significant worldwide infectious disease, causing substantial illness and fatalities. Prompt and precise diagnosis is essential for efficient treatment and management. Distinguishing between active tuberculosis (ATB) and latent tuberculosis (LTBI) is extremely difficult yet necessary for specific forms of treatment. The objective of this study is to discover and confirm diagnostic biomarkers that can

differentiate between ATB and LTBI, thereby improving the accuracy of diagnosis and enhancing patient care. We employed high-throughput transcriptome and proteomic methods to examine samples from patients with active tuberculosis, latent tuberculosis infection, and healthy individuals. The techniques of RNA sequencing (RNA-Seq) and differential gene expression analysis were utilized to explore and characterize the patterns of gene expression. The investigation of differential expression was conducted utilizing Bioconductor packages in R (DESeq2). Our investigation has found a group of biomarkers that have unique expression profiles for active tuberculosis and latent tuberculosis infection. The expression levels of important genes such as IFNG, TNF, and IL6 were markedly increased in patients with active tuberculosis compared to those with latent tuberculosis infection and the control groups. This indicates the presence of an active inflammatory response that is characteristic of active tuberculosis disease. In contrast, biomarkers such as TCF7 and IL10 were discovered to be increased in patients with latent tuberculosis infection, indicating a connection with immune regulation and the continued presence of the virus in a dormant state. This study identifies potential biomarkers that can accurately distinguish between active and latent tuberculosis, thereby aiding in the development of more accurate diagnostic and treatment strategies for tuberculosis.

#### *4.7. Long-Term Survival Trends in Pediatric Patients with Solid Tumours in the State of São Paulo, Brazil (2000–2022): An Analytical Descriptive Epidemiological Study*

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**Introduction:** The State of São Paulo has a significant morbidity and mortality rate related to pediatric solid tumors. **Objective:** The objective of this study was to analyze the survival of patients (aged 0 to 19 years; both sexes) diagnosed with the five most prevalent solid malignant neoplasms in the State of São Paulo, between 2000 and 2022. **Method:** This was an epidemiological study of a descriptive nature, using data from the Fundação Oncocentro do Estado de São Paulo with cases selected according to the International Classification of Childhood Cancer, focusing on the time between consultation and diagnosis and between diagnosis and treatment in relation to survival analysis. **Results:** A total of 11,067 cases were analyzed, 53.5% of which were male, with 89.6% diagnosed by microscopic confirmation; 34.3% were central nervous system tumors, 21.1% were bone tumors, 18.6% were soft tissue tumors, 14.2% were germ cell tumors, and 11.9% were retinoblastomas. The most common treatment was surgery with chemotherapy (26.5%), followed by surgery (20.5%) and chemotherapy (15.6%). The average time (days) between consultation and diagnosis was  $22.94 \pm 69.93$ , significant for treatments and recurrences across all groups, and concerning sex, for germ cell tumors ( $p = 0.0178$ ); the average time between diagnosis and treatment was  $25.46 \pm 39.71$ , not significant for the treatment of germ cell tumors ( $p = 0.0793$ ) and retinoblastoma recurrences ( $p = 0.0697$ ) but significant for sex in germ cell neoplasms ( $p = 0.0054$ ). **Conclusion:** Survival curves showed distinct behaviors among neoplasm groups, with a considerable percentage of patients waiting beyond the recommended time in a state with a high concentration of services and advanced technological density.

#### *4.8. Mandatory Rules as a Public Health Measure: A Study on Cardiac Patients with Recent Acute Coronary Syndrome*

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**Introduction:** Among the measures used to contain the COVID-19 pandemic in our country, in addition to the mandatory restriction on movement and business activity, there was an obligation to use face masks and keep social distance, and the vaccination

program was implemented. On the other hand, the scourge of smoking continues to burden cardiovascular health for over a century in the form of a pandemic. However, even for smoking, the mandatory rule of the general avoidance of cigarette use in public places and workplaces has been applied. The study aims to detect the perception of peoples' obligation to follow measures to limit the pandemic spread compared with the already valid mandatory ban on smoking in closed public places.

**Methods:** During the last semester, we used an anonymous questionnaire addressing 120 patients with recent acute coronary syndrome (38 inpatients and 82 outpatients) in the Cardiology Department of the General Hospital of Veroia in Greece. The epidemiological and clinical characteristics, as well as the personal beliefs of the respondents, were analyzed.

**Results:** Of the 120 studied patients (88 males), 42 were current smokers and 94 were fully vaccinated against COVID-19. Regarding the mandatory use of face masks, 79 patients (65.8%) answered that it was beneficial, whereas 44.2% and 45% were in favor of keeping social distance and quarantine implementation, respectively. Remarkably, 55 patients (45.8%) responded in favor of compulsory vaccination for the general population. Regarding the smoking ban, only 74 patients (61.7%) were in favor.

**Conclusions:** Although smoking is directly associated with cardiovascular risk, a notable percentage of patients presented with acute coronary syndrome opposed the ban on smoking in public places. On the other hand, the most acceptable measure for restricting COVID-19 was the mandatory use of face masks.

#### 4.9. Occupational Interdigital Pilonidal Sinus Among Hairdressers and Barbers in Bahrain: A Cross-Sectional Study

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##### Introduction

Interdigital Pilonidal Sinus (IPNS), or barber's disease, is a rare occupational condition where sharp clipped hair penetrates the webspace between fingers, causing a foreign body reaction. This study aimed to investigate the prevalence of IPNS among hair professionals in Bahrain and assess the role of hygiene practices in its prevention.

##### Materials and Methods

A cross-sectional study was conducted across the five governorates of Bahrain, involving 479 participants (253 male and 226 female) from 384 hair salons and barbershops selected through convenience sampling. Demographic data, including age, gender, hand dominance, work experience, type of work (barber or hairdresser), hygiene habits, and medical comorbidities, were collected via an interview-administered questionnaire.

##### Results

No cases of IPNS were identified among the participants. However, two male participants reported having Pilonidal Sinus (PNS) in the sacrococcygeal region. The majority of participants were aged between 26 and 45 (72.7%), with 52.8% reporting over 5 years of professional experience. Most participants were right-handed (89.1%). Only 1.9% of participants had diabetes, a known risk factor for IPNS. Regarding hygiene practices, 85.6% reported frequent handwashing, 69.5% used sanitizers, and 39.2% consistently used gloves.

##### Discussion

The absence of IPNS in our study, conducted during the COVID-19 pandemic, may be attributed to heightened hygiene practices, including frequent handwashing. Comparisons with regions where hygiene protocols vary or with other time periods, such as

pre-pandemic, may yield different results. The low prevalence of diabetes in our population may have also contributed to the absence of IPNS.

#### Conclusion

Although no IPNS cases were found, this study highlights the importance of hygiene in preventing occupational diseases. Further longitudinal studies are recommended in order to explore IPNS risk factors and their potential association with hairdressing.

#### 4.10. Physical Activity and Quality of Life in Pregnant Women in Spain

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Systematic reviews on quality of life (QoL) have shown that physical activity (PA) is one of the factors associated with better levels of QoL. Although multiple organizations recommend exercise during pregnancy, its practice decreases significantly. This problem increases in women with obesity.

The purpose of this work is to study the relationship between PA and QoL according to women's weight.

This was an observational study performed in the Reina Sofía Hospital in 2023, focusing on women in the first trimester of pregnancy. PA measurement was carried out with the IPAQ questionnaire, which collects PA and transforms it into METs. One MET corresponds to 3.5 mL O<sub>2</sub>/kg/min and measures the body's expenditure of energy. QoL was measured with the SF-12, which is a 12-item questionnaire used to assess generic health outcomes from the patient's perspective. Age, BMI, and level of education were also measured.

Fifty-nine women were included. Their sociodemographic characteristics were as follows: age (31 years; SD: 5.9), weeks of gestation (12.8; SD: 1.2), weight (78.3 kg; SD: 11.1). As for BMI, 27.1% were classified as having normal weight, 40.7% were overweight, and 32.2% were obese. Among those with overweight/obesity, the percentage of women with moderate/high PA was 44%, while in those with normal BMI, it rose to 62%. With respect to QoL, the SF12 score was 85.7% for women with normal weight and 78.5% for overweight or obese women ( $p = 0.02$ ).

In the multivariate analysis, a significant association between PA and QoL was observed, regardless of age and level of education. Obese women with high PA had a higher QoL than those with low PA ( $p = 0.03$ ), but this effect disappeared in women with normal weight ( $p = 0.4$ ).

The level of PA was lower in overweight or obese pregnant women, and the influence of PA on QoL was greater in overweight and obese participants than in women with normal weight. These results support the need to maintain an active lifestyle during pregnancy, particularly in overweight or obese pregnant women.

#### 4.11. Relationship Between Body Composition and Heart Rate Variability Measurements in Firefighters

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Introduction: Heart rate variability (HRV) reflects the balance between the arms of the autonomic nervous system (ANS). ANS control is strongly associated with body composition in healthy young populations and athletes, suggesting that obesity negatively impacts the ANS. The occupational demands and work environment of firefighters promote high rates of obesity. ANS control is particularly important for firefighters, who have an unpredictable work schedule and must quickly switch between restful and active states.

Given the importance of ANS function in firefighters and the potential impedance of obesity, studies on the association between HRV and body composition in firefighters are needed.

**Methods:** Sixteen full-time male firefighters participated in this cross-sectional study. Resting HRV (RR interval) was measured for 10 min with an actigraphy watch and chest heart rate monitor. An analysis of the collected data (Kubios HVR) was completed to determine the following HRV outcomes: RR interval, RMSSD, percentage of low-frequency power (LF), percentage of high-frequency power (HF), LF/HF ratio, parasympathetic nervous system index, and sympathetic nervous system index. Measures of body composition (InBody 580), height, and weight were taken. Partial correlation coefficient analyses were performed between (a) body mass index (BMI) and (b) body fat percentage, and each of the HRV outcome variables, after adjusting for age. SPSS version 29 was used for the statistical analysis ( $\alpha = 0.05$ ).

**Results:** No significant association was found between RMSSD and either BMI ( $p = 0.54$ ,  $r = 0.17$ ) or body fat percentage ( $p = 0.64$ ,  $r = 0.13$ ). All other correlation coefficients were similarly non-significant ( $p > 0.05$ ) and weak ( $-0.30$   $r$   $0.30$ ).

**Conclusion:** There was no association between body composition variables and HRV outcomes in this small sample of firefighters, in contrast to similar research showing a relationship between HRV measures and fat-free mass in trained athletes. A larger sample is needed to make more generalizable conclusions. Analysis of previously collected data will continue in the future.

#### 4.12. Surgical Site Infections After Major Abdominal Surgery in Greece: Results of a Nationwide Multicenter Study

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**Background:** Surgical site infections are a major cause of postoperative morbidity and mortality, but data regarding their prevalence in Greece are scarce. In this study, we report the rates of surgical site infections after major abdominal surgery in a large sample of patients in Greece.

**Methods:** This was a prospective multicenter trial (NCT 05393752) including 11 tertiary hospitals from Greece and Cyprus. Patients undergoing major/major+ abdominal surgery during 2022–2023 were included. Surgical site infections were classified according to the definitions of the CDC, and for sepsis, the SEPSIS-3 criteria were used. Demographics, type/site/magnitude of the operation, American Society of Anesthesiologists class, and the presence/stage of malignancy, as well as comorbidities, were recorded.

**Results:** There were 1649 patients (41.8% females) with a mean age of 66.3 years (SD: 13.8). The most common site of operation was the lower GI tract (58.9%), followed by the upper GI tract (20.2%) and the hepatobiliary system (13.6%). A total of 30.6% of the operations were performed on an emergency basis, and 3% of the patients had sepsis/shock. The rates of smoking, COPD, diabetes, corticosteroid use, and chronic renal failure were 23.5%, 9.7%, 22%, 6.5%, and 0.8%, respectively. A cancer diagnosis was present in 68.2% of patients, and distant metastases in 9.7%. Postoperatively, 7.5% of patients developed sepsis and 3.3% developed septic shock. A total of 322 SSIs were recorded (19.8%), of which 13.3% were superficial, 2.7% deep, and 3.5% were in the organ space. SSIs were significantly more common in emergency operations, in hepatobiliary sites, and in patients with cancer ( $p = 0.01$ ).

**Conclusion:** SSIs are common after major abdominal surgery, even though most of them are superficial. At relatively high risk are hepatobiliary, oncological, and urgent operations.

#### *4.13. Using an Electronic Tool for Hand Hygiene Auditing: Improving Data Quality to Lead to a Better Understanding of Improvement Measures*

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**Introduction:** Hospital-Acquired Infections (HAIs) are estimated to cause around 6400 deaths per year in Spain. Hand hygiene remains a challenge in most healthcare facilities, although it has been proven that there is an essential tool to prevent related harm. The implementation of technological auditing tools in healthcare settings aims to enhance the accuracy and frequency of hand hygiene observations. This study evaluates the impact of a new auditing tool (MEG) on hand hygiene adherence rates among healthcare workers by comparing data collected before and after its implementation.

**Methods:** We analyzed hand hygiene adherence data from 2019 to 2023, focusing on observations made at a Spanish private hospital. Hand hygiene adherence rates were calculated as the percentage of hand hygiene opportunities that were correctly followed. Descriptive statistics and chi-square tests were used to assess the significance of changes in adherence rates before (2019–2021) and after (2022–2023) the tool's implementation.

**Results:** Prior to the implementation of the auditing tool (2019–2021), the mean hand hygiene adherence rate was 56.4% (95% CI 46.30–65.96%). Following its implementation (2022–2023), the adherence rate decreased to 42.5% (95% CI 40.18–44.88%). Statistical analysis using a chi-square test indicated that this decrease was statistically significant (Pearson chi-square = 6.982,  $df = 1$   $p = 0.010$ ), suggesting a notable change in recorded adherence rates.

**Conclusions:** The implementation of the auditing tool resulted in a statistically significant decrease in hand hygiene adherence rates. This may indicate improved accuracy

in capturing non-compliance, thus providing a more realistic assessment of hand hygiene practices. These findings highlight the importance of utilizing advanced auditing tools to obtain precise data, ultimately enhancing infection control measures.

## 5. AI and Telemedicine

### 5.1. Use of Chess in Decision-Making and Psychology Studies

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#### Introduction

Chess data are used in the fields of psychology, sociology, biology, mathematics, psychiatry, and decision-making. The application of chess in decision-making lacks clarity, and there is currently no established framework that provides guidance on utilizing chess for decision-making purposes. In the field of psychology, chess has been used as a tool to study cognitive processes, memory, problem-solving, and decision-making. Researchers have explored the mental abilities required to play chess and have investigated how chess expertise develops over time. Chess provides a controlled environment where researchers can observe and analyze the decision-making processes of players, offering valuable insights into human cognition and behavior.

Mathematics has a long-standing relationship with chess, with various mathematical concepts and techniques applied to analyze chess positions, evaluate moves, and develop algorithms for computer chess. Chess has been used to study combinatorial game theory, graph theory, probability, and optimization, among other mathematical fields. Our goal for this manuscript is to find an association between chess moves and behavioral analysis.

#### Methods:

We have examined potential parameters for chess and their application in behavioral research. We have listed open chess databases (e.g., Lichess, Chessbase, and Kaggle chess database). We have conducted an examination of chess matches played on the Lichess online platform. Additionally, we have incorporated the Python chess package into the discussion.

#### Results

We have created parameters such as the classical game–bullet game ratio, maximum time spent on chess moves, and minimum time spent on chess moves. We found a significant association between the classical game–bullet game ratio and the minimum time spent on chess moves.

#### Conclusion:

In conclusion, chess data can be used in behavioral research. Furthermore, chess engines can help us to understand complex human behavior. Utilizing personal chess analysis can enhance one's decision-making abilities.

### 5.2. Advancements in Telemedicine and Digital Health Initiatives in India

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Telemedicine is an important healthcare technique in India that uses telecommunications technology to provide remote diagnosis and treatment, particularly in disadvantaged areas. It began with ECG transmission over telephone lines in the early twentieth century and has progressed tremendously thanks to NASA and ISRO. The National Telemedicine Taskforce, founded in 2005 by India's Health Ministry, has spearheaded efforts such as ICMR-AROGYASREE, NeHA, and Virtual Rural Clinics (VRCs) to improve healthcare access and delivery via digital platforms. eSanjeevani, which was launched in November 2019 as part of the Digital India initiative and the Ayushman Bharat Scheme, is at the heart of India's telemedicine environment. As of May 2024, eSanjeevani had enabled over 241 million consultations across 122,699 Health and Wellness Centres through a network of 15,460+ hubs and 372 online OPDs, with cooperation from 212,290 healthcare practitioners. It operates in two modes: eSanjeevaniAB-HWC for provider-to-provider consultations and

eSanjeevaniOPD for patient-initiated telemedicine, addressing healthcare inequities across the country, even in remote and resource-limited settings. During the COVID-19 pandemic, eSanjeevani adapted swiftly to provide essential healthcare services, underscoring its role in crisis response and healthcare continuity. It has significantly enhanced healthcare accessibility, particularly benefiting vulnerable populations, with over 57% of beneficiaries being females and 12% being senior citizens. Additionally, the National Health Portal (NHP) is crucial for disseminating health information and promoting government health programs across India. Available in six languages and accessible via a toll-free number and mobile app, NHP aims to create awareness and educate citizens about healthcare services and initiatives. The e-Hospital system, another initiative, streamlines hospital management through an ICT solution tailored for government hospitals, enhancing efficiency in patient care, resource management, and administrative tasks. In summary, these integrated digital health initiatives demonstrate India's commitment to harnessing technology for equitable healthcare delivery, bridging access and quality disparities across the country.

### 5.3. Integrating Artificial Intelligence in Telemedicine: Predicting Lung Cancer Disease and Decision-Making

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**Introduction:** The integration of artificial intelligence (AI) into telemedicine represents a transformative advancement in the delivery of remote healthcare services. In rural communities of Nepal, geographical difficulties have deprived many of adequate health facilities. To address this problem, this paper explores the synergistic potential of AI to enhance telemedicine by improving diagnostic accuracy, personalizing patient care, and optimizing healthcare resource management.

**Methods:** The proposed framework incorporates machine learning techniques in telemedicine. The survey was conducted in a remote village and data were collected from 250 people. Data consist of different parameters, such as age, alcohol consumption, coughing, chest pain, and shortness of breath. The paper compares and examines machine learning algorithms, such as Naive Bayes, Support Vector, and Random Forest, to predict lung cancer disease. The result is evaluated using accuracy and k-fold cross-validation.

**Results:** The result shows that Random Forest exhibits higher accuracy (95.4%) and Naive Bayes exhibits lower accuracy (76.2%). The finding shows that people in their 50s, 60s, or 70s who consume more alcohol have the highest chances of having lung cancer.

**Conclusions:** By providing a comparison among different machine learning techniques, this paper aims to inform healthcare professionals, policymakers, and technologists about the critical role of AI in shaping the future of telemedicine and to offer actionable insights for effectively integrating these machine learning technologies. With this, the people of remote villages will benefit, and the diagnosis will be simplified. However, there are limitations regarding data privacy and misinformation. In the future, new techniques such as deep learning neural networks and big data techniques can be integrated into telemedicine with image processing capabilities to enhance the role of AI in telemedicine.

**Keywords:** artificial intelligence (AI); telemedicine; remote healthcare; health data integration; health records; rural community

### 5.4. Modeling Electrical Potential in Multi-Dendritic Neurons Using Bessel Functions

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Understanding the distribution of electrical potential within neurons is critical for advancing our comprehension of neuronal signaling and communication. Neurons, the

fundamental units of the nervous system, rely on complex electrochemical processes to transmit information. The intricate structure of neurons, especially those with multiple dendrites, plays a crucial role in how these electrical signals are generated, propagated, and integrated. Despite significant progress in neuroscience, accurately modeling the electrical potential within neurons with elaborate dendritic architectures remains a challenge. This article introduces a novel approach to modeling the electrical potential in multi-dendritic neurons using Bessel functions, which offers a more precise and detailed representation of these processes. The proposed method involves solving the electric potential diffusion equation in cylindrical coordinates, a mathematical framework that naturally aligns with the geometry of dendrites. The radial and axial components of the solution are expressed using Bessel functions and sinusoidal functions, respectively. Bessel functions are particularly well suited for this purpose due to their ability to describe waveforms in cylindrical systems, making them ideal for capturing the spatial variations in electrical potential within the cylindrical shape of dendrites. By leveraging this mathematical approach, we obtain a complete representation of the potential distribution across the neuron, from the soma (cell body) through the dendrites to the synaptic terminals. This model accurately captures the spatial variations of electrical potential in different regions of the neuron, including areas with complex dendritic arborizations, which are branching structures that significantly influence the neuron's electrical characteristics. Simulation results underscore the effectiveness of this approach in reproducing realistic neuronal behavior. The model successfully mimics the way electrical signals propagate and interact within dendritic structures, providing crucial insights into the underlying mechanisms of signal integration and transmission in neurons.

##### 5.5. Role of AI and Telemedicine in Pediatric Disease Management

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The integration of artificial intelligence (AI) and telemedicine is transforming pediatric healthcare management, presenting unprecedented opportunities for improving the quality, accessibility, and efficiency of care. This review explores how these technologies impact pediatric healthcare, focusing on diagnostic accuracy, treatment personalization, and patient monitoring. AI-driven tools, including machine learning algorithms and natural language processing, enhance early diagnosis and intervention by analyzing vast datasets to identify patterns indicative of pediatric diseases. These tools support clinicians in making more informed decisions, reducing diagnostic errors, and improving outcomes. Telemedicine, facilitated by advancements in communication technologies, extends the reach of pediatric care to remote and underserved areas, ensuring timely medical attention. Virtual consultations and remote monitoring enable continuous care for chronic conditions, reducing hospital visits and minimizing the risk of exposure to infectious diseases. Telemedicine also fosters better patient and family engagement, providing education and support through digital platforms. The synergy of AI and telemedicine offers a comprehensive approach to pediatric healthcare, combining both technologies' strengths to deliver personalized and proactive care. AI algorithms can process real-time data from telemedicine consultations, refining treatment plans and predicting potential health issues before they escalate. This integrated approach enhances clinical outcomes and optimizes resource allocation, reducing healthcare costs. India's eSanjeevani telemedicine platform, which has served over 241 million patients through more than 122,000 Health and Wellness Centers, exemplifies this integration. It ensures that specialized care reaches remote and underserved areas, improving clinical outcomes and optimizing resource allocation. Despite the promising benefits, challenges such as data privacy, algorithmic bias, and the need for robust regulatory frame-

works must be addressed to ensure these technologies' safe and ethical implementation. This review highlights the critical role of AI and telemedicine in revolutionizing pediatric healthcare, underscoring the importance of continued research, collaboration, and policy development to fully realize their potential in improving children's health and well-being.

#### 5.6. Transformative Impact of Telemedicine on Healthcare in South Korea: A Systematic Review

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This study presents a systematic review of the transformative impact of telemedicine on modern healthcare, with a focus on its potential to enhance patient outcomes, reduce costs, and improve access to care. The methodology involved selecting and analyzing 29 key papers published exclusively in South Korea over the last 20 years, which explore the role of advanced telemedicine technologies in facilitating remote patient monitoring and managing chronic diseases.

A significant area of focus is the advancement of "On-Device AI" technology, enabling real-time health monitoring and proactive healthcare interventions. This technology represents a substantial leap forward in telemedicine, allowing for more personalized and timely healthcare delivery. The integration of such telemedicine solutions into existing healthcare infrastructures helps overcome traditional barriers, such as limited service availability in remote areas and the challenges posed by the need for continuous connectivity.

This study also highlights the economic benefits of telemedicine, including reducing the need for in-person visits and lowering hospital readmission rates, which contribute to significant cost savings. The findings emphasize the urgent need for healthcare systems to adopt telemedicine technologies to address the evolving challenges of contemporary healthcare, particularly in the post-pandemic era.

The research concludes that integrating telemedicine offers a promising pathway toward more resilient, accessible, and efficient healthcare services. It calls for increased collaboration among policymakers, healthcare providers, and technology developers to promote the widespread adoption of telemedicine, ensuring its benefits are equitably distributed across diverse patient populations.

## 6. Immunology

*EphB4 Knockdown Inhibits the Growth and Epithelial–Mesenchymal Transition of Gastric Cancer Cells and Triggers Death via the PI3K/AKT Pathway*

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Introduction:

The management of gastric cancer is challenging due to the complexities associated with its therapy and nursing care. This work aimed to elucidate the functions and processes of erythropoietin-producing hepatocellular carcinoma Receptor B4 (EphB4) in gastric cancer.

Methods:

EphB4 expression in gastric cancer tissues and cell lines was assessed using RT-qPCR and Western blotting techniques. The impact of EphB4 on cell growth, programmed cell death, transformation of cells from an epithelial to a mesenchymal state, and the PI3K/AKT signaling pathway in gastric cancer cells was also examined by MTT tests, flow cytometry, and Western blotting.

Results:

EphB4 expression was significantly increased ( $p = 0.05$ ) in gastric cancer tissues and cells. At the same time, downregulation of EphB4 significantly suppressed ( $p = 0.001$ ) gastric cancer cell proliferation, triggered apoptosis, reduced the expression of proteins associated with the epithelial–mesenchymal transition (EMT), and exerted a regulatory influence by inhibiting the PI3K/AKT signaling pathway. Furthermore, the results revealed that the overexpression of EphB4 had a substantial impact on the proliferation of ( $p = 0.001$ ) gastric cancer cells, suppressing apoptosis, reducing the expression of E-cadherin, increasing the expression of N-cadherin, and activating the PI3K/AKT signaling pathway. The suppression of EphB4 significantly impeded ( $p = 0.001$ ) the cell growth and the epithelial–mesenchymal transition (EMT) process while promoting apoptosis in gastric cancer cells.

Conclusion:

These discoveries provide new perspectives on the involvement of EphB4 in the progression of gastric cancer. All this makes EphB4 a promising target for future study in gastric cancer.

## 7. Mental Health

### 7.1. Magnitude of Suicidal Ideation and Perinatal Suicide Risk in Spanish Women—What Are the Factors Involved?

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Background: Suicide is one of the leading causes of death worldwide, and in the perinatal period, this trend is increasing, even up to 100 times in the US. In the postpartum period, 36% of maternal deaths are due to suicide. In different European countries, suicide is one of the leading causes of maternal mortality, along with cardiovascular pathologies. The perinatal phase is a critical period where mental health challenges can arise. Understanding risk factors and protective elements is essential for improving maternal well-being.

Objective: To identify key risk factors associated with enhanced suicidal ideation during the perinatal period and to highlight potential protective factors.

Methods: An analysis of various psychosocial variables was conducted, yielding the following risk associations and protective factors:

Results: Risk factors:

Anxiety: Adjusted Odds Ratio (aOR) of 1.08 (95% Confidence Interval: 1.04–1.31);

Intimate partner violence during perinatal period: aOR of 1.59 (95% CI: 1.04–2.43);

Postpartum Depression (PPD): aOR of 3.00 (95% CI: 1.86–4.81);

Protective Factors:

Perceived social support during perinatal period: aOR of 0.97 (95% CI: 0.95–0.99);

Skin-to-skin contact during delivery: aOR of 0.50 (95% CI: 0.28–0.88);

Conclusion: Anxiety, depression, insufficient social support, and exposure to intimate partner violence are significantly linked to an elevated risk of suicidal thoughts in the perinatal phase. Conversely, perceived social support and skin-to-skin contact with the infant serve as critical protective factors. Addressing these elements may enhance maternal mental health outcomes during this vulnerable period.

Implications for practice: Enhancing social support systems and promoting skin-to-skin practices could significantly reduce mental health risks among perinatal women. Further research is warranted to explore intervention strategies targeting these factors.

### 7.2. CX3CL1 Delta Chemokine Is a Chronic Inflammatory Mediator That Links Periodontitis with Alzheimer's Disease in Patients

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Titanium is considered a biocompatible biomaterial of dental titanium alloys (Ti-6Al-4V). However, in patients with certain dental metals (Hg<sup>++</sup>, Al, Ti, etc.), including dental Ti implants, a chronic silent inflammatory state can be provoked.

On the other hand, periodontitis favors the adherence of biofilms on the surface of teeth, increasing the local recruitment of innate immune cells (neutrophils, macrophages, and dendritic cells). Thus, a chronic proinflammatory cytokine release of cytokine/chemokines, including CX3CL1, can amplify the local inflammatory responses and also promote oral dysbiosis. In fact, recent studies link Alzheimer's disease (AD) with periodontitis. However, systemic CX3CL1 and MCP-1 elevations can be also detected in patients with long-term dental Ti implants without periodontitis. Periodontitis favors tooth destruction and also enhances the accumulation of oral biofilm. In fact, porphyromonas gingivalis has been associated with AD, and high systemic CX3CL1 levels have been found to contribute to p-Tau accumulation in the brain of AD transgenic mice.

Thus, this CX3CR1 overexpression as a chronic silent proinflammatory response can predispose patients with periodontal disease and poor buccal hygiene to AD. Collectively, CX3CR1 overproduction affects the normal control of the innate immune system and favors the destruction of the supporting tissues of the teeth in patients with periodontal disease. Thus, the link between AD and periodontitis via CX3CL1 opens up a new therapeutic role of delta chemokine blockers against periodontitis and AD pathology.

### *7.3. Systematic Review on the Impact of Lifestyle Habits and Problem Behavior on Non-Suicidal Self-Injury in Adolescents*

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#### Introduction:

Non-suicidal self-injury (NSSI) in adolescents has increased in recent years and constitutes a public health problem. A worldwide NSSI prevalence of 17.7% has been found, and it is higher in females. The objective of this review is to analyze and summarize the evidence on the association of lifestyle habits and problem behavior with NSSI in adolescents.

#### Methods:

We searched for cohort and case-control studies in Medline, Embase, and APA PsycInfo with no date or language restrictions. The study protocol was registered in PROSPERO (CRD42024501154). People aged 10 to 19 years with established exposure factors (sleeping habits, physical activity, eating habits, toxic habits, or problematic use of technology devices) were compared to those with no exposure factors. The main outcome was the proportion of patients with NSSI. Meta-analyses were carried out following the Cochrane methodology.

#### Results:

Out of 5295 identified records, a total of 13 cohort studies were included (43% of moderate quality, 36% of poor quality, and 21% of high quality). The results showed a statistically significant increase in the risk of NSSI with regular smoking (OR 2.89; IC 95% 1.42–5.90; I<sup>2</sup> 58%; two studies), alcohol (two studies), early cannabis use (aOR 1.42; IC 95% 1.13–1.75; one study), and poor physical activity (OR 0.49; 0.41–0.58; one study). No significant association was found between NSSI and substance use in one study. Inconsistent results were found for the use of technology devices and sleep quality.

#### Conclusions:

The results of this review show that regular smoking, alcohol use, early cannabis use, and poor physical activity could increase the risk of NSSI in adolescents. The role of

other factors like sleeping habits or the use of technology devices is still uncertain. More longitudinal studies with longer follow-ups are needed to extract firm conclusions.

#### 7.4. *Divergent Roles of Emotional Intelligence Models in Technology-Related Behavioral Addictions: A Systematic Literature Review*

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Behavioral addictions caused by contemporary developing technologies and technological devices, such as internet addiction, gaming disorder, and problematic smartphone and social media use, pose a threat to the mental health and well-being of people from all age groups. Through a systematic literature review, we wish to synthesize the existing literature on the relationship between technology-related behavioral disorders and Emotional Intelligence (EI), a psychological construct known to play a protective role in many indicators of subjective and psychological well-being. Due to the importance of distinguishing between different EI theories and their measures, the current review focuses on uncovering the potentially different roles of ability EI and trait EI. A search was conducted in PubMed, Scopus, Web of Science, APA PsychArticles, and PsychINFO in May 2024. The data extraction process identified 43 articles, and the transparency of this review was maximized by following the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) 2020 guidelines. Key findings revealed the predictive role of EI for several behavioral addictions in samples from different developmental groups (i.e., children, adolescents, adults). Other results will be discussed in detail with a focus on the divergent roles of the two main EI models. Conclusions from the current literature and directions for future studies will be provided by highlighting the critical issues to consider in EI research conducted to explore its role in technology-related behavioral addictions.

#### 7.5. *Effectiveness of Hybrid Assertive Community Treatment in Rural Greece: Improving Outcomes for Severe Mental Illness Patients*

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##### Introduction:

In rural areas, Modified Assertive Community Treatment (ACT) could prove pivotal in managing severe mental illness (SMI) in patients who are difficult to engage in community care. The objective of the present study was to assess the impact of a hybrid ACT team on SMI patients' hospitalizations, their length of hospital stay, their symptomatology, and their functioning within a rural community treatment setting in Greece.

##### Methods:

Expanding the services of a well-established Mobile Mental Health Unit, the hybrid ACT team delivers home-based care for SMI patients in a rural area of northwest Greece. This 3-year prospective, mirror-image, pre–post observational study evaluates patients' symptomatology, functioning, and overall outcome using three validated scales: the Brief Psychiatric Rating Scale (BPRS), the Global Assessment of Functioning Scale (GAF), and the Health of the Nation Outcome Scale (HoNOS).

##### Results:

Among the 23 enrolled patients (mean age: 52.4 years; mean age of disease onset: 23.5 years; mean hospitalizations: 10.74), voluntary and involuntary hospitalizations decreased by nearly 80% over a 16-month follow-up. Length of hospital stay was reduced

significantly by 87%, with notable improvements in patients' functioning (17%) and symptomatology (14.5%).

Conclusions:

This study highlights the efficacy of a hybrid Assertive Community Treatment model in rural Greece for patients with severe mental illness, demonstrating significant reductions in hospitalizations and length of stay and improvements in symptomatology and functioning, suggesting its potential to address the needs of difficult-to-engage SMI patients and enhance their overall outcomes.

#### 7.6. *Exploring the Experiences of International Nursing Students at Zhengzhou University, China: A Qualitative Study*

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**Background:** Developing nursing capacity worldwide includes training nurses to a doctorate level. Due to a global shortage of PhD nursing programs, a large number of nurses are pursuing their doctorates abroad. International nurse students frequently face challenges brought on by prejudice, discrimination, and stigma during their time studying internationally because of sociocultural differences. To the best of the authors' knowledge, there is limited research on the experiences of international nurse students. Therefore, the aim of this paper is to explore the experiences of international nursing students at Zhengzhou University.

**Methods:** This study employed a phenomenological approach among international nursing students at Zhengzhou University, China. Purposive sampling was used to select the participants. The sample size was determined by information saturation. A semi-structured interview guide was used. All data were recorded electronically during the interview. The conventional content analysis approach was employed to enable a deeper understanding and the formation of themes.

**Results:** In this study, ten international nursing students were interviewed. All the participants conveyed positive and negative feedback and their concerns, along with the challenges, prejudice, and discrimination that came with them. Two major themes were identified from the student data: situations outside the school (skin color, language, and sociocultural differences) and inside the school (expectations and reality of learning experiences, supervisory concerns, and lack of support from the school or university).

**Conclusion:** This study indicated that international nursing students experienced different challenges and concerns as international nursing students. The university/school must create a culturally competent and good environment and create opportunities to visit clinical areas for international nursing students. To a greater extent, all students beginning their studies require some support as they transition to universities and acclimate to the new university context. Furthermore, the establishment of relationships between international and domestic students is crucial for the formation of future nurse–researcher communities of practice.

#### 7.7. *Influence of Circadian Rhythmicity in Development and Course of Substance Use Disorders, Major Depression, and Their Comorbidities*

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**Introduction:** Substance use disorders (SUDs) and major depression disorders (MDDs) are both causes of disability around the world, and the prevalence of their comorbidity is very high and complicates the clinical management of patients. The alteration of the circadian rhythmic system has been proposed as a factor related to the onset, severity, and course of both disorders, although the exact influence is not yet well defined and less in a dual condition.

**Methods:** Three major databases (Web of Science, Scopus, and PubMed) were selected to search for articles that comprise information about SUDs, MDDs, and circadian rhythmicity in the last 10 years (2013–2024). Parameters were identical in all databases [“(addiction” OR “substance use” OR “dual disorder”) AND depression AND (“circadian” OR “sleep-wake”)]. Results without one of these parameters; with animal models; or in languages other than English, Spanish, Portuguese, or French were excluded.

**Results:** A total of 613 articles were found. After the exclusion of the duplicates, a total of 436 articles were left. Of those, more than 20% did not have an SUD condition, and about a third of the MDD results were mixed with bipolar disorders (BDs). With the application of the inclusion and exclusion criteria, a total of 245 articles were selected.

**Conclusion:** This work will present the main findings of circadian rhythmicity, including data on the sleep–wake rhythm, with an emphasis on improving our understanding of the multifactorial explanatory model of SUDs, MDDs, and their comorbidities. It is important to steer future studies aiming at the clarification of the onset and possible treatment outcomes of these disorders. This could lead to more assertive and efficient prevention and treatment programs for both disorders from a more individualized approach.

#### 7.8. *Interconnections: Cortisol, Microglia, and Neuroinflammation in Schizophrenia*

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Schizophrenia is a serious and chronic psychiatric disorder that affects approximately 1% of the global population. Characterized by a wide range of symptoms, schizophrenia is multifactorial, with genetic, environmental, and stress factors having a key role in its development. In this context, cortisol, a stress-related hormone, and microglia, immune cells of the central nervous system, emerge as key players in understanding schizophrenia. In this study, the interconnections between cortisol, microglia, and neuroinflammation in the etiology of schizophrenia were explored. Recent scientific evidence highlights the importance of these elements in modulating the stress response and their potential impact on neuroinflammation and the development of schizophrenia. Furthermore, the clinical relevance of these interactions and their potential for the development of new therapeutic approaches are highlighted. Through this analysis, we sought to provide a comprehensive view of the complex interactions between cortisol, microglia, and neuroinflammation and their role in schizophrenia, highlighting the need for future investigations and integrated approaches to treating this debilitating mental illness. This review involved an extensive bibliographic search in electronic databases, such as Google Scholar, PubMed, and ScienceDirect, as well as other sources, including books and websites. Descriptors such as “schizophrenia”, “glial cells”, “cortisol”, “oxidative stress”, and “neuroinflammation” were used, without systematic search inclusion and exclusion criteria. Relevant studies were selected based on the evaluation of titles and abstracts, prioritizing recent publications in Portuguese, English, and Spanish. The results covered information about schizophrenia, genetic and biochemical aspects, and treatments, presented through narrative texts and figures.

**Keywords:** psychiatric disorder; hormone; adrenal glands; glial cell; neuronal inflammation

#### 7.9. *Is Exercise Fun? Virtual-Reality Boxing Versus Traditional Cardio to Improve In-Task Valance and Post-Exercise Enjoyment*

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Given the overwhelming literature on the beneficial effects of exercise, it is surprising that many individuals do not meet current physical activity guidelines. Among the most often cited reasons for nonadherence to exercise are lack of time and lack of enjoyment. However, recent technology has provided a new mode of exercise that could change that. Purpose: We plan to compare in-task valence during and enjoyment after a bout of moderate-intensity continuous exercise (MICE) and virtual-reality boxing (VRB). Methods: Using a within-subject randomized design, the participants [N = 20, 8 females; age (M ± SD); 26.1 ± 7.2 yrs; BMI (M ± SD); 26.4 ± 5.8] completed a 5 min warm-up, 20 min of MICE and VRB workout, and a 5 min cool-down. In-task valence, heart rate, and rating of perceived exertion (RPE) were assessed during each condition, and enjoyment was assessed immediately after each condition. Results: The participants reported more positive in-task valence [Cohen's d = 0.59] and greater post-exercise enjoyment [Cohen's d = 1.76] during VRB relative to MICE. Further, the participants reported higher RPE [Cohen's d = 0.53] and heart rates [Cohen's d = 0.52] during VRB. Conclusion: Virtual-reality boxing resulted in significantly greater in-task valence and post-exercise enjoyment relative to traditional cardio. As both in-task valence and enjoyment have been linked to exercise adherence, virtual-reality exercise should be considered as a means to increase exercise adherence.

### *7.10. Multidimensional Analysis of Advanced-Stage Huntington's Disease from Neurocognitive and Psychofunctional Perspectives with Morphometric Correlations: Case Series*

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Background: Huntington's disease (HD) is a progressive neurodegenerative monogenic disorder, and its multifaceted clinical and radiological analysis correlations are not yet understood. We aim to evaluate advanced-stage HD patients for multidimensional clinical deterioration with objective scales and correlate this with morphometric-based measurements.

Materials and Methods: Ten advanced-stage HD patients evaluated with the Unified Huntington's Disease Rating Scale (UHDRS) were subjected to psychofunctional assessment for behavioral and neurocognitive decline, total functional capacity (TFC), and functional assessment scale (FAS) for functional determination. In the morphometric assessment, bicaudate ratio (BCR), bi-frontal ratio (BFR), frontal horn area (FHA), frontal horn ratio to intercaudate distance (FH/CC), and caudate volume and caudate volume ratio (CVR) were analyzed and correlated with relevant parameters.

Results: The most frequent functional decline was observed for occupational and financial ability in UHDRS TFC (5.60 ± 2.27), social/financial engagement, and self-care impairment in the FAS (11.10 ± 3.48). Cognitive decline was especially prevalent in quick thinking and responding to stimuli on time and to a sufficient extent. Caudate volume loss was more severe on the right-hand side (6.50 ± 1.18) and inferior sections (21.65 ± 7.30). A negative correlation was found between intercaudate distance and the verbal fluency test ( $\rho = -0.775$ ). The Parkinson's disease sleep scale and intercaudate distance were negatively correlated ( $\rho = -0.559$ ), and a positive correlation was found for the bi-frontal distance/caudate distance ( $\rho = 0.559$ ). There was a negative correlation between the Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease-Rating Scale, the Hamilton Depression Rating Scale, and the Hamilton Anxiety Rating Scale and FHD ( $\rho = -0.671$ ,  $\rho = 0.61$  and  $\rho = 0.571$ , respectively).

Conclusion: In light of the current findings, caudate atrophy is an important indicator of cognito-functional disability, especially in terms of verbal ability. The right hemisphere seems to be more vulnerable to neurodegenerative processes, and mood disorders appear to be related explicitly to right frontal lobe degeneration. Psychofunctional deterioration may begin years before clinical diagnosis, so HD should be considered in the differential diagnosis of aberrant psychofunctional deterioration in young patients.

### 7.11. Nutritional Modulation of Biochemical Pathways in Metabolic and Neuropsychiatric Conditions

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Inflammation, oxidative stress, and vitamin D play pivotal roles in the pathogenesis and progression of both type 2 diabetes (T2D) and depression through several interconnected biochemical mechanisms. In T2D, chronic inflammation is driven by an excess of pro-inflammatory cytokines like TNF- $\alpha$ , which impairs insulin signaling by activating serine kinases that phosphorylate insulin receptor substrate-1. Oxidative stress further exacerbates this condition by generating reactive oxygen species (ROS), which damage cellular proteins, lipids, and DNA, thereby promoting  $\beta$ -cell apoptosis and worsening insulin resistance.

In depression, neuroinflammation and oxidative stress disrupt neurotransmitter homeostasis, particularly serotonin, by increasing the production of inflammatory cytokines which activate the enzyme indoleamine 2,3-dioxygenase (IDO), diverting tryptophan metabolism from serotonin production towards kynurenine pathway metabolites that are neurotoxic, contributing to depressive symptoms. Vitamin D modulates these pathways by exerting anti-inflammatory and antioxidant effects.

Polyunsaturated fatty acids (PUFAs), particularly omega-3s, ameliorate these conditions by penetrating cell membranes, where they reduce the production of pro-inflammatory eicosanoids from arachidonic acid and enhance mitochondrial function, reducing oxidative stress by improving electron transport chain efficiency and decreasing ROS production. Consequently, PUFA supplementation may restore insulin sensitivity in T2D and reduce neuroinflammation in depression, offering a targeted approach to managing these complex conditions.

This study investigates the biochemical changes that occurred over a 6-month period induced by omega-3 polyunsaturated fatty acid supplementation. We examined oxidative stress and inflammation biomarkers, alongside 25 OH vitamin D levels, in several patient groups: depressive, diabetic, and patients with both conditions. The findings were further analyzed in relation to cortisol and serotonin levels to elucidate the impact of omega-3 PUFAs on molecular homeostasis. The interesting beneficial effects observed can be attributed to the PUFAs' ability to stabilize and structurally integrate into cell membranes, thereby normalizing fluidity and enhancing cellular resilience against oxidative stress and inflammation.

### 7.12. Sleep Quality and Cognitive Impairments in Children and Adolescents with PTSD Symptoms

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Sleep disturbances are a core feature of Post-traumatic Stress Disorder (PTSD), especially in children and adolescents. The existing literature suggests a potential relationship between sleep quality and cognitive function in this population, but empirical studies are limited. This

study aimed to investigate the association between sleep quality and cognition in children and adolescents with PTSD attending a public school in Medellín, Colombia.

Using a quantitative, cross-sectional exploratory design, we examined a sample of 130 students (106 females and 24 males) aged 11 to 16 years (mean age = 12.9, SD = 1.35), from sixth to eighth grade. Seventy-one participants met the criteria for PTSD, while 59 served as the control group. Data were collected using the Pittsburgh Sleep Quality Index (PSQI) and the DSM-5 TR+COG Questionnaire of Symptoms Associated with Traumatic Experiences in Childhood or Adolescence and Neurocognitive Symptoms.

Comparative analysis between the PTSD and control groups was conducted using the Student's *t*-test. Pearson correlation was employed to assess the relationship between sleep quality and neurocognitive function. Significant differences were found between the groups across various sleep dimensions: total score ( $t(128) = 4.85, p = 0.001, d = 0.85$ ), sleep latency ( $t(128) = 4.11, p = 0.001, d = 0.72$ ), sleep disturbances ( $t(128) = 3.91, p = 0.001, d = 0.69$ ), and daytime dysfunction ( $t(128) = 4.36, p = 0.001, d = 0.76$ ). Additionally, a positive correlation was identified between sleep quality and cognition ( $r = 0.49, p = 0.001, 95\% \text{ CI } 0.74 \text{ to } 0.86$ ).

These findings underscore the significant impact of PTSD on sleep quality and its subsequent effect on cognitive function. Potential clinical implications include the need for interventions targeting sleep disturbances as part of PTSD treatment. This study highlights the intricate relationship between traumatic experiences, cognitive alterations, and sleep quality, calling for further research in this area.

### *7.13. The Relationship Between Heart Rate Variability and Psychological Outcomes in Firefighters*

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**Introduction:** The occupational demands of firefighters are psychologically stressful and often traumatic, as firefighters respond to a wide range of emergencies. The stressful nature of firefighting results in increased susceptibility to PTSD and impaired heart rate variability (HRV) due to a continued stress response well after the disturbing situation has ended. High levels of psychological resilience may help offset a continued stress response, yet the associations between these variables have not been fully explored. Thus, the purpose of this study was to determine the relationship between HRV and psychological outcomes, including psychological resilience and PTSD severity, in full-time firefighters. **Methods:** Sixteen full-time male firefighters participated in this cross-sectional study. Participants completed the PTSD Checklist-5 (PCL-5) and Dispositional Resilience Scale-15 (DRS-15). Resting HRV was measured for 10 min with an actigraphy watch and chest heart rate monitor during nighttime sleep and then analyzed with Kubios HRV software to determine HRV outcomes. Partial correlation coefficient analyses were performed between (a) the PCL-5 score and (b) the DRS-15 score and each of the HRV measurements' mean RR interval, RMSSD, percentage of low-frequency power (LF), percentage of high-frequency power (HF), LF/HF ratio, parasympathetic nervous system index, and sympathetic nervous system index, after adjusting for age. SPSS version 29 was used for the statistical analysis ( $\alpha = 0.05$ ). **Results:** All correlation coefficients between the psychological scale variables and the HRV variables were found to be non-significant ( $p > 0.05$  for all) and weak ( $-0.38$  to  $0.44$ ). **Conclusion:** After adjusting for age, a relationship was not found between HRV and either PTSD severity or psychological resilience. However, the PCL-5 and DRS-15 scores were relatively homogeneous between participants, which may have contributed to the weak relationship found with HRV in this small sample size of firefighters. In further data analyses, we will continue to increase sample size and statistical power.

## 8. Oncology and Hematology

### 8.1. *Advancing Cancer Research with Graph Neural Networks: A Comparative Study of Neural Network Architectures for Multi-Omics Data Integration and Interpretation*

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In our recent research study, we systematically evaluated a range of neural network architectures to address the intricate challenge of integrating and interpreting multi-omics data within oncological research. This effort was motivated by the need to better understand the complex biological interactions underlying cancer, which cannot be fully captured by traditional analytical approaches. Cancer research often grapples with the challenge of integrating diverse types of omics data—genomic, transcriptomic, proteomic, and metabolomic—to form a cohesive understanding of tumor biology.

Traditionally, multi-omics data interpretation involves collecting and preprocessing data across these layers—such as sequencing genomic DNA, profiling mRNA transcripts, analyzing protein expressions, and quantifying metabolites. However, conventional methods often struggle with the complexity and volume of these data types, particularly when dealing with the high-dimensional and interconnected nature of cancerous systems.

Our methodology aimed to overcome these limitations by leveraging advanced neural network architectures. We conducted a detailed comparative analysis of Convolutional Neural Networks (CNNs), Recurrent Neural Networks (RNNs), Transformer Networks, and Graph Neural Networks (GNNs) through several experimental phases.

GNNs demonstrated superior performance. We implemented advanced GNN architectures, including Graph Convolutional Networks (GCNs), Graph Attention Networks (GATs), and Graph Isomorphism Networks (GINs). GATs enhanced model sensitivity to crucial interactions through self-attention mechanisms. This provided a nuanced understanding of oncogenic interactions, improving the model's ability to identify significant relationships within the cancer data. GINs were used to capture complex subgraph patterns through isomorphism tests: this approach enabled precise characterization of tumor subtypes and biomarker discovery, which are essential for personalized oncology.

Our comparative analysis revealed that GNNs, with their advanced graph-based features and relational modeling capabilities, outperformed other neural network architectures in integrating multi-omics data. The superior performance of GNNs in capturing the complex, high-dimensional interactions within oncological datasets underscores their transformative potential for personalized cancer treatment strategies.

### 8.2. *Elucidating the Intricacies of Cytokine Release Syndrome (CRS) in Hematological Malignancies and the Associated Risk Factors: A National Study*

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Hematologic malignancies carry a heightened risk of Cytokine Release Syndrome (CRS) due to cytotoxic chemotherapies and Chimeric Antigen Receptor T (CAR-T) cellular therapies. This study explores the relationship between various risk factors and CRS in patients with hematological malignancies.

Utilizing National Inpatient Sample (NIS) data from 2019 and 2020, we identified patients with hematological malignancies and a secondary diagnosis of CRS. We examined

mortality, length of stay, and total treatment costs, conducting a multivariate regression analysis to assess the association of different risk factors with CRS.

A total of 200,590 patients were hospitalized with hematological malignancies, of whom 340 developed CRS. No statistically significant differences were observed in baseline demographic characteristics such as age, sex, insurance and income status, race, hospital teaching, rural, and size status. However, the odds of mortality were increased in CRS patients (OR 3.32, 95% CI 2.93–3.76,  $p = 0.001$ ). Total charges were significantly increased in CRS patients (+USD 654,286, 95% CI 375,835–932,636,  $p = 0.001$ ), but no difference was noted in length of stay between the two groups (+3.13, 95% CI 0.38–5.88,  $p = 0.025$ ). Fluid and electrolyte disorders (OR 2.71, 95% CI 2.47–2.97,  $p = 0.001$ ), obesity (OR 1.15, 95% CI 1.01–1.32,  $p = 0.027$ ), and heart failure (OR 1.39, 95% CI 1.2–1.6,  $p = 0.001$ ) demonstrated a higher risk of association with CRS. CRS patients were also more likely to have palliative care involvement (OR 1.71, 95% CI 1.52–1.92,  $p = 0.001$ ). Conversely, hypertension (OR 0.84, 95% CI 0.76–0.93,  $p = 0.001$ ) and major depressive disorder (OR 0.74, 95% CI 0.64–0.86,  $p = 0.001$ ) were associated with a decreased risk of CRS in hematological cancer patients.

CRS in hematological cancer patients is linked to increased mortality and hospitalization costs. Key risk factors include obesity, heart failure, and fluid and electrolyte disorders. Emphasizing holistic management of these conditions and adhering to evidence-based practices is crucial for improving patient outcomes and reducing adverse events.

### *8.3. Inflammaging: Increase in Polymorphonuclear Myeloid-Derived Suppressor Cells in Aged Healthy Individuals*

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**Introduction:** Myeloid-derived suppressor cells (MDSCs) are immature HLA-DR<sup>low</sup>/CD11b<sup>+</sup>CD33<sup>+</sup> myeloid cells, which are elevated in various human disease states that involve abnormal hemopoiesis and act mainly through suppressing T-cell responses. They are divided into two subpopulations, the CD15<sup>+</sup> (granulocytic) and the CD14<sup>+</sup> (monocytic) cells. We have previously shown that the number and functionality of MDSCs in chronic idiopathic neutropenia (CIN) are altered, contributing to a possible primary bone marrow (BM) defect and to the pathogenesis of the condition. Moreover, MDSCs are proposed in a few studies to take part in aging, in concordance with the novel theory of inflammaging. Thus, we further suggest that, in healthy individuals, their numbers increase with age through impaired myelopoiesis.

**Methods:** MDSC subsets were quantitated by flow cytometry in the peripheral blood mononuclear cells (PBMCs) of 70 healthy individuals (21–73 years old), using the combination of CD33PC7/CD15PC5/HLA-DRECD/CD14PE/CD11bFITC monoclonal antibodies and the Kaluza<sup>®</sup> analysis software. Statistical analysis was performed using the Spearman's rank correlation coefficient and the GraphPad<sup>®</sup> software. The suppression of T-cell proliferation by MDSCs was estimated in five selected cases by comparing carboxy-fluorescein succinimidyl ester (CFSE) staining of the anti-CD3/anti-CD28-activated T cells between PBMCs and CD33-depleted PBMCs after 3 days of culture.

**Results:** PMN-MDSCs (1.75% of PBMCs  $\pm$  2.55, mean  $\pm$  standard deviation) showed a statistically significant positive correlation with age ( $r = 0.24$ ,  $p = 0.04$ ), while neither M-MDSCs (3.97% of PBMCs  $\pm$  2.96) nor the total population of MDSCs (PMN-MDSCs plus M-MDSCs) (6.40% of PBMCs  $\pm$  2.17) showed a statistically significant correlation with age. MDSCs displayed the capacity to suppress T-cell proliferation, as was indicated by the T-cell generations in culture experiments in the presence or absence of MDSCs, irrespective of the age of the individual.

Conclusions: In conclusion, in our study population, PMN-MDSCs increase in older individuals, contributing to the process of aging, while they retain their immunosuppressive capacity.

#### 8.4. The Combination Therapy of Transarterial Chemoembolization and Microwave Ablation Leads to Better Survival for Liver Metastases from Colorectal Cancer: A Comparative Study

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##### Introduction:

The liver remains the most frequent site of metastases from colorectal cancer (CRC). The purpose of this retrospective study was to compare the combination therapy of transarterial chemoembolization (TACE) and microwave ablation (MWA) with MWA as monotherapy in treating liver metastases from CRC (LMCRC).

##### Methods:

A total of 251 patients with unresectable LMCRC not responding to chemotherapy were enrolled. Group A consisted of 184 patients (104 M and 80 W; mean age:  $64 \pm 11.4$  years) with 442 metastases who received the combination therapy of TACE+MWA. Sixty-seven patients (49 M and 18 W; mean age:  $63.2 \pm 11.8$  years) with 173 metastases were included in group B, who were treated by MWA as monotherapy. The parameters evaluated were metastasis diameter, complications, diameter of ablation zone 24 h post-MWA, local tumor progression (LTP), hepatic distant tumor progression (hDTP), hepatic progression-free survival (hPFS), and overall survival (OS).

##### Results:

The mean metastasis diameter was 2.3 cm in group A and 2.2 cm in group B ( $p$ -value: 0.24). There were no major complications reported. The mean diameter of the ablation zone was significantly larger in group A at 5.1 cm compared to 4.9 cm in group B ( $p$ -value: 0.039). The LTP rate was 4.9% in group A and 4.5% in group B ( $p$ -value: 0.062). The hDTP rate was 71.7% and 83.6% for groups A and B, respectively ( $p$ -value: 0.81). The mean hPFS was significantly longer in group A at 13.8 months compared to 8.1 months in group B ( $p$ -value: 0.03). The median OS time for group A was 30 months and 26 months for group B ( $p$ -value: 0.67). The 1- and 2-year OS rates were 84.2% and 61.1% for group A and 82.3% and 53.2% for group B, respectively.

##### Conclusions:

The combination therapy of TACE and MWA is superior to the MWA monotherapy for LMCRC, mainly according to the size of the ablation zone, hDTP, hPFS, and OS.

#### 8.5. Aspergillosis in the Course of Childhood Acute Lymphoblastic Leukaemia: An Unexpected Enemy

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Acute lymphoblastic leukemia (ALL) is a malignant lymphoid tumor, most common in children aged 1–4. Well-diagnosed and treated ALL allows for a 5-year survival rate of up to 90% in pediatric patients.

A girl aged 3 years and 6 months was referred to the Department of Paediatric Haematology, Oncology and Transplantology of the University Children's Hospital in Lublin with suspected proliferative hematopoietic disease.

Laboratory tests revealed leucopenia, neutropenia, and significant anemia. Bone marrow aspiration biopsy showed a hypocellular marrow with 23.6% young blastic cells. Flow cytometry showed 42% B lymphocyte precursor cells. The patient's morphology results steadily improved, and a subsequent biopsy showed the absence of atypical cells. Despite the improvement in morphology results, a month later, 90% of atypical cells were found and a biopsy confirmed pre-B acute lymphoblastic leukemia. Chemotherapy according to the IA Protocol of the ALLIC-BFM Programme 2009 was started.

From the 18th day of treatment, the patient's condition worsened; she started to have a fever, and her inflammatory parameters were increasing. Broad-spectrum antibiotic therapy was ineffective. Chest CT scan revealed massive inflammatory densities in the left lung. Antifungal drugs (v-fend) were included. The girl's condition continued to deteriorate; a seizure occurred, and head CT showed hypodense foci in the parietal lobes. After 5 days, in the area of the skull, a protrusion of the skin occurred, and diagnostic tests confirmed the presence of mycelial strands of *Aspergillus* (*Aspergillosis*) in the liquefied brain tissue, necessitating neurosurgical evacuation of the necrotic lesions. Intensive antifungal treatment was continued.

Five months later, a resection of the lower lobe of the left lung was performed. After 1.5 years, there was a recurrence of the proliferative process, without reactivation of invasive mycosis.

Regular monitoring and treatment of complications are crucial for the long-term survival of patients.

#### *8.6. In Vitro Studies on the Use of Extremely Low Frequency (ELF) Electromagnetic Fields as a Means of Increasing the Effectiveness of Anticancer Drugs*

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#### Introduction

Extremely low frequency (ELF) electromagnetic fields (EFs) represent an innovative means of treating cancer. They affect various biological processes in cells, such as proliferation, metabolism, and the cell cycle, which play a key role in the development of cancer cells. Intercellular interactions based on the EFs regulate cell migration and morphogenesis. These processes are closely related to the function of the centrosome and intercellular communication. EFs can increase apoptosis and inhibit the angiogenesis and proliferation of tumor cells.

#### Methods

In order to investigate the effect of ELF on the action of anticancer drugs, a device was developed that allows for the assessment of the effect on cell cultures of various cancer cell lines (including those taken from the patient) and the use of anticancer drugs in the appropriate concentration. It is possible to investigate the effect of the selected EF intensity in the ELF range to determine the optimal time of field exposure.

#### Results

The initial evaluation of device performance and the determination of EF parameters were performed on three human cancer cell lines (LoVo, MC7, and A431) treated with doxorubicin. In relation to the EF parameters, the operating range of the field with a frequency of 50 Hz and an induction of 1.25 mT was established. The EF distribution inside the solenoid was examined. Only cells within an area no greater than 5 cm from the central

point of the solenoid may be considered as having been subjected to uniform exposure with non-uniformities not exceeding +10%.

#### Conclusion

The described method allows for an effective and fast way of checking the influence of EF on the pharmacological effect of the drug for a given type of cancer. This model can thus help in selecting the appropriate EF parameters, allowing for a reduction in the cytostatic dose while maintaining the effectiveness of the therapy.

#### 8.7. L-Arabinose Suppresses the Epithelial–Mesenchymal Transition Through the Autophagy-Dependent Wnt/ $\beta$ -Catenin Signaling Pathway in Breast Cancer

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Breast cancer (BC) is one of the major causes of cancer death among women around the world, and the available therapeutic strategies still need to be improved. Monosaccharides, as a natural product, possess the capability to impair the growth of cancer cells, which has been confirmed, but the efficacy of L-arabinose on the epithelial–mesenchymal transition (EMT) of tumor cells remains unclear. In the present study, we found that L-arabinose treatment significantly influences EMT marker protein (N-cadherin, E-cadherin, and Vimentin) expression and decreases migration and invasion potential *in vivo* and *in vitro*. Mechanistically, L-arabinose induced autophagy and abrogated the nuclear and cytoplasmic expression of  $\beta$ -catenin in BC cells. After adding the Wnt/ $\beta$ -catenin activator LiCl, the efficacy of L-arabinose on the EMT of BC cells was reversed. Intriguingly, the expression of  $\beta$ -catenin was elevated by the suppression of autophagy using the sh-Atg5 lentivirus under L-arabinose treatment. Here, we found L-arabinose contributed to the inhibition of the epithelial–mesenchymal transition (EMT) in breast cancer cells. Moreover, the suppressive effects of L-arabinose on the EMT were regulated by autophagy in BC cells. In addition, we demonstrated that L-arabinose affected the EMT via downregulating the Wnt/ $\beta$ -catenin signaling pathway, which is dependent on autophagy. Thus, this study provides a novel potential drug for breast cancer therapy.

#### 8.8. Small Molecules of Great Importance

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**Introduction:** Acute lymphoblastic leukemia (ALL) is the most common childhood malignancy. The cure rates for ALL are remarkably high (90%). This has been achieved due to chemotherapy protocols based on high doses of drugs. Unfortunately, this is associated with adverse effects of therapy in almost 75% of patients. Therefore, biomarkers that could indicate a higher risk of adverse effects are being searched for so that they can be prevented. miRNAs have recently been explored as such potential markers.

**Material and Methods:** A systematic review of scientific articles available in the PubMed, WOS, Medline, and Google Scholar databases was conducted using the following keywords: “miRNA”, “chemotherapy toxicity”, “acute lymphoblastic leukemia”. Only full-text articles from 2014–2024 about children were included. We analyzed 21 studies.

**Results:** miRNAs are a good potential diagnostic, prognostic, and predictive marker in ALL. Moreover, overexpression of miR-29b (AUC = 0.75) and miR-499 (AUC = 0.82) is useful in identifying patients at high risk of cardiomyopathy after anthracycline treatment and as an early marker of myocardial damage. Furthermore, some miRNAs have been associated with hepatotoxicity (miR-1208; OR = 1.15), oral mucositis (miR-4268, OR = 1.31; miR-1206; OR = 3.6), hematotoxicity (miR-1206, OR = 2.3; miR-323b, OR = 0.36), and

gastrotoxicity (miR-323b, OR = 0.23; miR-4751, OR = 12.38; miR-3117, OR = 0.24) caused by methotrexate administration. Reduced expression of miR-24 (OR = 0.43) also correlates with the toxicity of this drug at higher doses. In addition, changes in the expression and/or specific single-nucleotide polymorphisms of the target genes of miR-202 (OR = 2.88), miR-4481 (OR = 2.56), miR-3117, (OR = 0.18), and miR-6067 (OR = 0.58) correlate with vincristine neurotoxicity. Moreover, overexpression of miR-155 ( $\rho = 0.7$ ) and reduced expression of miR-146a ( $\rho = -0.67$ ) are associated with gastrotoxicity after myeloablative conditioning before allogeneic hematopoietic stem cell transplantation.

Conclusions: The determination of changes in expression levels and/or single-nucleotide polymorphisms of target genes for specific miRNAs is a good potential tool for identifying patients at risk of developing complications during chemotherapy.

## 9. Dermatology

### 9.1. *Bergenia Crassifolia Extract-Loaded Nanogel to Untangle the Web of Psoriasis: Characterization and in Vivo Evaluation in an IMQ-Induced Rat Model*

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Background: The high surface-to-volume ratio, tiny size, general non-toxicity, and ease of functionalization of nanostructured lipid carriers make them an excellent option for topical drug delivery systems.

Methods: The NLC of *Bergenia crassifolia* extract composed of soy wax as a solid lipid and sea buckthorn seed oil were prepared using the hot melt method and embedded in a topical gel. The Box–Behnken experimental design was run, and the gels were prepared using 1% carbopol-934. The characterization of NLC and nanogels was carried out using bergenin as a biomarker. A mouse model of imiquimod-induced psoriasis was used to carry out our in vivo study.

Results: The characterization of NLC showed the encapsulation of the extract. Studies on histopathology showed that the produced nanogel had a potentially effective anti-psoriatic effect. The findings indicated that, in comparison to plain extract gel, nanogel demonstrated anti-psoriatic action in a shorter amount of time. Additionally, the nanogel showed prolonged drug release for 12 h and decreased the inflammatory markers IL-23 and IL-17 associated with psoriasis.

Conclusion: Nanogel improves penetration, deposits drugs deeper into the skin layers, and reduces systemic absorption compared to extracts, highlighting the potential of nanosizing to enhance biological activities. Dermatokinetics and preclinical findings show the downregulation of inflammatory mediators IL-23 and IL-17. The skin irritation study score indicated that the gel was not irritating. The results show that the nanogel is an effective and safe carrier for plant extracts. Clinical studies are needed to evaluate the efficacy of this treatment as an alternative or supplement to conventional treatments for psoriasis.

### 9.2. *Formulation and Evaluation of an Antilice Hair Cream Using *Annona Muricata**

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*Annona muricata*, also known as soursop, is a member of the Annonaceae family and has a long history of traditional uses. It is an evergreen plant that grows in tropical and subtropical regions of the world, primarily in Africa, South America, and Southeast Asia. The *A. muricata* plant's miraculous nature is a boon to mankind, and it has been widely used in folk medicine. *A. muricata* preparations on the market include candies, syrups,

beverages, ice creams, and shakes. Several studies have concluded that the plant contains over 212 chemical constituents, such as acetogenins, alkaloids, and phenols. The plant has antibacterial, antiviral, antifungal, antitumor, anthelmintic, analgesic, antiarthritic, hypotensive, anti-inflammatory, and immune-enhancing effects, as well as anti-diabetic activity. Although some toxicities have been reported, the extract of *A. muricata* is effective and safe. This study aims to formulate and evaluate an herbal antilice cream containing the ethanolic extract of *Annona muricata* (leaves). Soursop leaves were blended, and the extract was obtained by a maceration process. Then, a cream was obtained using the slab technique or an extemporaneous method. The antilice cream was optimized by preparing three formulations (F1, F2, F3) using different concentrations of the extract and ingredients. The formulation was evaluated for various parameters, like physical appearance, irritancy, pH, viscosity, spreadability, washability, greasiness, and antilice activity.

### 9.3. Management of a Squamous Cell Carcinoma Arising from an Unusually Large and Long-Standing Condyloma Acuminatum of Low-Risk Subtype

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Condyloma acuminata are a cutaneous manifestation of human papillomavirus (HPV), with lesions varying in clinical presentation, ranging from small, sessile, or pedunculated growths to flat papules or large cauliflower-like plaques. Condyloma acuminata are categorized into high-risk and low-risk genotypes based on their association with carcinomas. High-risk HPV genotypes, HPV 16, 18, 31, 33, and 35, are more commonly associated with malignant transformation into squamous cell carcinoma (SCC). In contrast, low-risk subtypes, including HPV 6 and 11, are typically not associated with SCC. The development of SCC in this context is exceptionally rare, with malignant transformation likely being secondary to chronic infection and persistent inflammation. A thorough clinical evaluation of all HPV-associated cutaneous lesions is sometimes necessary in order to assess malignant potential, including physical examination, biopsy, and gene testing. Treatment methods including topical agents and surgical debridement are utilized on a case-by-case basis, guided by clinical features and histopathology. Similarly, SCC arising from pre-existing HPV lesions is systematically evaluated, with consideration of tumor stage, depth, and patient comorbidities guiding treatment decisions. Here, we present a unique SCC case arising out of a large and long-standing condylomatous plaque on the thigh, expressing a low-risk HPV subtype in a 71-year-old male. The diagnosis and management are discussed.

### 9.4. Nanoparticles for Enhanced Drug Delivery to Hair Follicles: A Comprehensive Review

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Nanoparticles (NPs) have emerged as attractive vehicles for targeted medication delivery to hair follicles (HFs), providing increased therapeutic efficacy while minimizing systemic side effects. This comprehensive review investigates the various applications of NPs in HF-targeted drug delivery, emphasizing polymeric, lipid, metallic, and other specialized NPs. Key physicochemical features such as size and content influence NP penetration depth and follicular targeting efficacy. NPs ranging in size from 400 nm to 700 nm penetrate

HFs most successfully, with polymeric and lipid NPs showing particular promise because of their biocompatibility and customized release patterns. Drug delivery using polymeric nanoparticles (NPs) is a reliable method, and finasteride (FIN) and dutasteride for alopecia treatments have been effectively administered by NPs like poly(lactic acid) (PLA) and poly(lactic-co-glycolic acid) (PLGA). Lipid nanoparticles (NPs), such as solid lipid NPs (SLNs) and nanostructured lipid carriers (NLCs), provide long-term drug release and have a preference for high-sebum HF settings, which improves follicular absorption. Deeper penetration into HFs is made possible by the special qualities of metallic NPs, such as gold and iron oxide NPs, through treatments like plasmonic heating and magnetic targeting. Effective medication distribution to the hair bulb and supra bulbar region—critical areas for controlling hair growth cycles—remains a challenge. Techniques like surface modification with bioactive compounds and NP size optimization show potential for improving NP delivery to these deep HF areas. To ensure the safe and efficient treatment of hair diseases, more research is required despite breakthroughs to optimize NP formulations for therapeutic uses. The promise of NPs to transform therapeutic methods for alopecia and other HF-related illnesses is highlighted in this review, which compiles recent developments and obstacles in NP-based drug delivery to HFs.

#### 9.5. Prevalence and Impact of Skin Disorders in Palliative Care: A Systematic Review

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Skin disorders are a significant concern in palliative care settings, often complicating symptom management and reducing the quality of life for patients with life-limiting illnesses. Despite their prevalence and impact, there is a lack of comprehensive research synthesizing the scope of skin disorders in palliative care. This systematic review explores the range of skin disorders experienced by palliative care patients, providing a thorough understanding essential for effective clinical management and improved patient outcomes. A meticulous literature search was performed across databases including b-on, PubMed, Web of Science, and Scopus, focusing on studies involving human participants aged 18 and older in palliative care settings. The inclusion criteria covered randomized controlled trials, observational studies, and quantitative studies published in peer-reviewed journals, specifically addressing skin disorders as a primary focus or a significant aspect of palliative care. Out of an initial 347 articles, 17 studies met the inclusion criteria. This review identified pruritus, pressure ulcers, and dermatitis as the most common skin disorders, significantly affecting patients' physical comfort, emotional well-being, and social interactions. These findings emphasize the complexity of managing skin disorders in palliative care, highlighting the need for interdisciplinary collaboration and tailored interventions to meet the diverse needs of this population. This review underscores the critical role of recognizing, assessing, and managing skin disorders to improve the quality of life for palliative care patients. Future research should prioritize developing and implementing targeted strategies

to mitigate the burden of skin disorders in this vulnerable group, ultimately enhancing patient care and outcomes.

#### 9.6. Recent Advancements in 3D Bioprinting for Pediatric Burn Treatment

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Recent advancements in 3D bioprinting technology have shown significant promise in developing innovative treatments for pediatric burn victims. This systematic literature analysis examines the progress in isolating and expanding autologous skin cells, specifically keratinocytes and fibroblasts, from pediatric patients for use in bioprinting applications. Key studies demonstrate the ability to effectively culture these cells, which are crucial for generating viable skin grafts. The systematic review also explores the evolution of bio-inks and the optimization of 3D bioprinting protocols aimed at creating multi-layered skin constructs that closely mimic natural skin architecture. Preclinical studies have been analyzed to evaluate the integration, functionality, and cosmetic outcomes of bioprinted skin grafts in animal models, highlighting their potential to improve healing and reduce scarring. Additionally, the review addresses the challenges of translating these promising preclinical findings into clinical trials, considering factors such as biocompatibility, immune response, and the scalability of bioprinting techniques. This comprehensive review underscores the transformative potential of 3D bioprinting in pediatric burn treatment, while also identifying the critical areas where further research and development are needed to bring these advancements to clinical practice. To fully realize the clinical application of 3D bioprinting for pediatric burn victims, interdisciplinary collaboration and long-term studies are essential in addressing the complex ethical, regulatory, and technical challenges associated with this cutting-edge technology.

**Conflicts of Interest:** The authors declare no conflicts of interest.

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