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HABILITATION THESIS

Titlu:

MULTIDISCIPLINARITATE ÎN MEDICINA FIZICĂ ȘI DE REABILITARE – DE LA MEDICINA CLINICĂ LA CERCETARE ȘI EDUCAȚIE

Title:

MULTIDISCIPLINARITY IN PHYSICAL MEDICINE AND REHABILITATION – FROM CLINICAL MEDICINE TO RESEARCH AND EDUCATION

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CONTENT

(A) Rezumat

Teza de abilitare „**Multidisciplinaritate în Medicina Fizică și de Reabilitare – de la medicina clinică la cercetare și educație**" reunește și combină principalele aspecte ale pregătirii academice, profesionale și de cercetare care au marcat pregătirea mea ca medic specialist și cadru didactic pe parcursul a 20 de ani.

După o scurtă sinteză a dezvoltării profesionale în Medicină fizică și de reabilitare și a parcursului științific și academic, teza detaliază principalele subiecte de cercetare din cei aproape 20 de ani de carieră universitară, în paralel cu dezvoltarea profesională ca medic primar în Medicina Fizică și de de Reabilitare:

Capitolul I, Realizări științifice (cercetare și publicații), pornește de la multidisciplinaritatea și complexitatea în Medicină Fizică și de Reabilitare și apoi marchează etapele carierei de cercetare pe parcursul a 20 de ani de predare și cercetare. Au fost structurate trei domenii principale de interes în cercetare și publicații științifice:

I. ***Inovație și tehnologie în Medicina fizică și de Reabilitare*** (include activitatea de cercetare și lucrările publicate pe tema realității virtuale aplicate în reabilitarea post-accident vascular cerebral, un domeniu foarte deschis cercetării și inovării, și cercetări dezvoltate în echipă multidisciplinară privind caracteristicile produselor polimerice bio-compozite pentru uz ortopedic, materiale utilizate în protezare și biomateriale utilizate în imprimarea 3D pentru orteze și proteze, respectiv în imprimarea materialelor sanitare utilizate în pandemia COVID 19, pretabile la sterilizare sau dezinfecție multiplă).

II. ***Cercetare interdisciplinară în Reabilitarea medicală*** (incluzând cercetări publicate în domeniul evaluarii și reabilitării pacienților cu accident vascular cerebral, cercetări în sfera reabilitării pediatrice a scoliozelor și a pectus excavatus, axate pe evaluare și programe de reabilitare respiratorie și locomotorie la copii, și studii interdisciplinare privind osteoporoza la femeile aflate în postmenopauză, un nou medicament utilizat in psihiatrie, un studiu privind sănătatea publică și managementul riscului).

III. ***Educație și Etică în Fizioterapie și Reabilitare medicală*** (detaliază etapele de cercetare în etică medicală și educație medicală sau non-medicală, abordare interdisciplinară în fizioterapie și reabilitare medicală, culminând cu perioada pandemică Covid 19, când noi provocări și asimetrii apărute în abordarea medicală, în educația medicală sau non-medicală, managementul și etica în balneologie și climatologie, respective problemele etice în posttraumă).

Capitolul II, Realizări academice, evidențiază parcursul academic și didactic de la preparator universitar până la conferențiar în 20 de ani de activitate academică și cercetare, culminând cu coordonarea programului de studii pentru licența de *Balneofiziokinetoterapie și recuperare* în centrul universitar Brașov (din 2011).

Capitolul III, Activitatea profesională, descrie pe scurt evoluția profesională de la medic rezident la medic primar cu specializări și particularități profesionale. Experiența managerială acumulată de-a lungul anilor conduce la funcția actuală de șef al Secției Clinice de Recuperare Neuropsihomotorie din Spitalul Clinic de Psihiatrie și Neurologie, Brașov, la calitatea de cadru didactic coordonator în centrul de formare universitar din Brașov pentru medicii rezidenți în specialitatea Medicină Fizică și de Reabilitare.

Capitolul IV marchează evoluția viitoare și **planurile de dezvoltare a carierei academice și de cercetare**, pornind de la domeniile de cercetare abordate până acum, în care am publicat lucrări științifice, și de la tendințele internaționale și perspectivele cercetării în domeniul Medicinei Fizice și deReabilitare. Două direcții majore de dezvoltare și cercetare sunt prezentate schematic, apoi sunt explicate temele și scopurile fiecărei direcții:

1. ***Planuri și perspective de neuroreabilitare*** (1.1. evaluare standardizată a reabilitării neurologice, 1.2. tehnologii de realitate virtuală post-accident vascular cerebral, reabilitare robotică).

2. ***Reabilitare și cercetare multidisciplinară/interdisciplinară*** (2.1. Reabilitare respiratorie după accident vascular cerebral; Reabilitare după infecție cu SARSCOV-2 a pacienților cu boli neurologice și/sau alte patologii asociate; 2.2. Gestionarea interdisciplinară a durerii și gestionarea durerii croice în programele de reabilitare; 2.3. Reabilitarea geriatrică; 2.4. Reabilitarea vezicii neurogene (post accident vascular cerebral, scleroză multiplă, scleroză laterală amiotrofică); 2.5. Gestionarea spasticității în reabilitare;)

De asemenea, unele proiecte viitoare sunt planificate pentru a combina educația cu cercetarea:
1. Continuitatea îngrijirii sănătății prin intervenție interdisciplinară centrată pe pacient. Cel mai bun model de gestionare cuprinzătoare a serviciilor de îngrijire a sănătății și de asigurare a asistenței medicale;
2. Instruire în fizioterapie la domiciliu pentru pacienții care au suferit un accident vascular cerebral;
3. Educația aparținătorilor, îngrijitorilor și a pacientului în reabilitarea post-AVC - cadru pentru îmbunătățirea funcțională și creșterea calității vieții;
4. Durerea lombară ca afecțiune frecventă și boală profesională - Evaluare, profilaxie și reabilitare terapeutică la studenți, asistenți medicali și personal de îngrijire în instituțiile medicale (obiceiuri de a ridica și a purta sarcini);
5. Evaluarea posturală și statică și profilaxia afecțiunilor coloanei vertebrale (pentru toate categoriile medicale expuse herniei de disc și posturii disfuncționale: medici, asistenți medicali, personal de îngrijire, studenți.

Fiecare dintre aceste direcții de cercetare și propuneri de proiecte poate constitui subiecte de cercetare extinse, precum și oferta de subiecte de doctorat pentru viitorii doctoranzi.

Abstract

The habilitation thesis "**Multidisciplinarity in Physical Medicine and Rehabilitation - from clinical medicine to research and education"** brings together and combines the main aspects of academic, professional and research training that marked my training as a specialist physician and teacher during 20 years. After a brief synthesis of the professional development in Physical Medicine and Rehabilitation and of the scientific and academic path, the thesis details the main research topics from the almost 20 years of university career, in parallel with the professional development as primary doctor of rehabilitation medicine.

Chapter I, Scientific achievements (research and publications) start from the multidisciplinarity and complexity in Physical Medicine and Rehabilitation and then marks the early years and stages of the research career during 20 years of teaching and research. The focus goes on three main areas of interest in research and scientific publications:

1. ***Innovation and Technology in Physical Medicine and Rehabilitation*** ((includes research and published work on virtual reality applied in post-stroke rehabilitation, a field very open to research and innovation, and research developed in a multidisciplinary team on the characteristics of bio-polymeric products, composites for orthopaedic use, materials used in prosthetics and biomaterials used in 3D printing for orthoses and prostheses, respectively in the printing of sanitary materials used in the COVID 19 pandemic, suitable for sterilization or multiple disinfection).

1. ***Cross-disciplinary rehabilitation research*** ((includes published research in the field of assessment and rehabilitation of stroke patients; research in pediatric rehabilitation of scoliosis and pectus excavatus, focusing on evaluation and respiratory and locomotor rehabilitation programs in children, interdisciplinary studies on osteoporosis in postmenopausal women and one psychiatric drug and a study on public health and risk management implementation).

1. ***Education and Ethics in Physiotherapy and Medical Rehabilitation*** (detailes the research stages in medical ethics and medical or non-medical education, culminating with the Covid 19 pandemic period, when new challenges and asymmetries in education and medical approach occur, an approach of physiotherapy and medical rehabilitation, medical or non-medical education, management and ethics in rehabilitation and balneoclimatology, respectively ethical issues in post-traumatic rehabilitation).

Chapter II, Academic achievements, points out the academic and didactic path from junior assistant to associate professor in 20 years of academic activity and research culminating with

the coordination of the residency training programme in Physical Medicine and Rehabilitation and the coordination of the Physiotherapy licence study program in the Brasov university centre.

Chapter III, Professional activity, shortly describes the professional development from resident physician to primary care physician with professional specializations and particularities. Managerial experience accumulated over the years leads to the present position as *head of department of "Clinical Department of Neuropsychomotric Rehabilitation"* in "Clinical Hospital of Psychiatry and Neurology", Brasov, as a coordinator teacher in the Brasov university training centre for resident doctors in the Physical medicine and rehabilitation specialty, as a *coordinator of Physiotherapy Study Programme* in Faculty of Medicine Brasov (since 2011).

Chapter IV scores the ***future evolution and development plans for academic and research career development, future perspectives in clinical rehabilitation research*** starting from the research fields approached so far and in which I have published scientific papers and from the international trends and perspectives of research in the field of physical medicine and rehabilitation. Two major directions of development and research are outlined schematically then the themes and purposes of each direction are explained:

1. **Neurorehabilitation plans and perspectives** (1.1. Standardized Neurorehabilitation Assessment, 1.2. Post Stroke Virtual Reality Technologies, Robotic Rehabilitation,
2. **Multidisciplinary/ interdisciplinary Rehabilitation and Research** (2.1. Respiratory rehabilitation post stroke; Post SARSCOV-2 infection rehabilitation of patients with neurological diseases or other associated pathologies; 2.2. Interdisciplinary pain management and Chronic pain management in rehabilitation programs; 2.3. Geriatric rehabilitation; 2.4. Rehabilitation of neurogenic bladder (post Stroke, Multiple sclerosis, Amyotrophic Lateral Sclerosis); 2.5. Spasticity management in Rehabilitation).

Also, some future projects are planned to combine education with research: 1. Health care continuity through interdisciplinary intervention focused on the person. Looking for the best model of comprehensive management of health care services and Health Care Assurance; 2. Home physiotherapy training for post-stroke patients; 3. Caregivers' and patient's education in post-stroke rehabilitation - framework for functional improvement and quality of life; 4. Low back pain as common condition and professional disease - Assessment, prophylaxis and therapeutic rehabilitation in students, nurses and caring staff in medical facilities (lifting habits and load burden); 5. Posture and static assessment and prophylaxis (for all medical categories exposed to disc herniation and bad posture: doctors, nurses, care staff, students.

Each of these research directions and project proposals can constitute extensive research topics as well as the offer of doctoral topics for future doctoral students.

(B) Scientific and professional achievements, evolution and plans for career development

I. Scientific achievements (research and publications)

I.1. Introduction

Multidisciplinarity and complexity in Physical Medicine and Rehabilitation

Faced with other medical specialties, which focus on patient illness and healing, sometimes even saving life, medical rehabilitation addresses the patient with a functional, often chronic and irreversible deficiency. It aims the functional rehabilitation, but also the family, social and professional reintegration of the patient, realizing a functional, applicable and long-term rehabilitation process, a three-dimensional bio-psychosocial process.

As a rehabilitation physician, medical field located at the intersection of medical specialties with surgical specialties, I have accumulated a thorough training in all these branches, to be able to understand the diagnoses and sufferings of patients addressing rehabilitation medicine, to make a relevant functional diagnosis and a short, medium and long term rehabilitation strategy for each patient, and also to formulate the recovery plan and the objectives that correspond to each stage. In this sense, through experience I managed to perfect the fineness of the recovery treatment necessary for each patient, to combine innovative and constructive rehabilitation methodology to achieve the objectives and maximum benefit for the patient, but also to practice correct planning and prioritization of patients, as well as responsibility for allocating financial and human resources.

The interdisciplinarity and complexity of medical rehabilitation derives from the treatment, care, supervision and long-term education of patients with multiple pathologies and intricate complications (which often require serial recovery programs and continuous follow-up for several years or until the end of life), but also from the daily collaboration in the multidisciplinary team of Medical Rehabilitation (physiotherapists, nurses, masseurs, specialists in orthosis-prosthesis, speech therapists, psychologists). For 11 years I have been working as a rehabilitation doctor in a neuropsychomotor rehabilitation department, with addressability for patients with neurological and vascular pathology and functional sequelae that require long-term rehabilitation and follow-up. A medium- and long-term recovery program involves more aspects of ethics, rather than recovering them on short term, such as establishing realistic goals adapted to pathology, patient motivation to collaborate and participate, complex and long-term relationship, debts and rights of

family members, making decisions, making choices with the patient and family, and advising and informing them to make their own choices.

This is how over time I have collaborated in multidisciplinary teams to treat complex patients who have been addressed to me for rehabilitation (in direct contact with fellow neurologists, psychiatrists, cardiologists, infectionists, internal medicine doctors, haematologists, doctors of functional explorations and work capacity expertise), but also with my colleagues and with distinguished academic teachers in Rehabilitation Medicine. These collaborations have been fruitful through multidisciplinary projects and team articles, presented in the subchapter **Cross-disciplinarity in Rehabilitation Research**. I have studied numerous aspects related to Rehabilitation Medicine, both in my training in the specialty, but also in teaching the activities of Rehabilitation Medicine and Physiotherapy, such as biomechanics, bioethics, medical bioengineering, materials used in prosthetic orthosis, public health, management, exercise physiology, assessment in kinesiology, etc. All these actions were constructively completed through projects and multidisciplinary articles written in the team, trying new approaches, analyses and perspectives in Rehabilitation and research, presented in the subchapter **Inovation and technology in rehabilitation** (Romanian translation of Fugl-Meyer scale, alternative therapies to classic methods of kinetic therapy as Virtual Reality therapy is as an alternative to classical physiotherapy, developing neuroplasticity, the use of e-applications in assessment of cohorts and adapting to Covid-19 pandemic, etc).

Rehabilitation medicine represent nowadays a challenging field addressing disability (including movement, mobility, and language, as well as mental health problems) as the main consequence of several categories of pathologies, following the standard steps of clinical approach and therapy: assessment, medical diagnosis and treatment, rehabilitation programs including physical therapy, social and professional readapting to disability. Beside disability, Rehabilitation medicine focuses on secondary conditions, such as pain, depression and mental disorders, respiratory and cardiovascular dysfunction, deconditioning, reaching to deal with complex and intricate pathology, located at the intersection of medical and surgical specialties, which are in phases of evolution that require rehabilitation treatment at some point or that must be continued throughout life.

The major aims of rehabilitation medicine are to increase the independence level on individuals, the daily functioning to carry out daily activities (ADL), the integration into family, society and work, to increase the quality of life (QL) of people living with disability or handicap.

Today we use in Rehabilitation medicine all the methods recognized and classically applied that have proven their therapeutic value throughout many research studies and many years of application in medical practice (physiotherapy, electrotherapy, hydrotherapy and balneal therapy, climatic therapy, massage, manual therapies and complementary, occupational therapy and ergo therapy, orthosis

and prosthesis, speech re-education therapy), but we are beginning to exceed the standard in rehabilitation and apply new tools and methods especially in electrotherapy (high frequency electrotherapy, transcranial magnetic stimulation, super inductive system) and kinesiotherapy (proprioceptive training, biofeedback, virtual reality therapy, training of balance, constraint therapy).

Research in rehabilitation medicine addresses specific issues that fall under the rehabilitation medicine umbrella, as well as research on conditions that cause disabilities, summarised below:

1. Development of best practices supported by evidence base knowledge; other activities aim to improve health outcomes related to specific diseases and conditions that cause disability (the main impact have nowadays stroke, traumatic brain injury, general trauma, degenerative diseases as osteoarthritis and spondilarthrosis)
2. Development of scientific knowledge in order to increase the level of health and education for health, work productivity, functional independence, and quality of life of disable people. In this aim research should start from basic and proceed to advanced clinical research.
3. Development and application of bioengineering principles to develop assistive technology to help people with disabilities perform daily tasks and activities. Applied sciencesresearch open the orizont to the modern rehabilitation technology including in the last decade the novel approach of biomechanical modelling and manufacturing of prosthetics (major breakthroughs in walking technologies for lower-limb amputees, wireless control of prosthetics), wheelchairs (motorized control of wheelchairs or other assistive technologies) and other devices that facilitate the locomotion and communication, and adaptation to environmental condition (for example develop ultra-lightweight, multi-geared wheels for manual wheelchairs to give users increased mobility and independence; development and testing of an instrumented glove for rehabilitation of individuals who have lost hand function from stroke, by practice gripping movements by playing a computer game.
4. Development or redevelopment of emotional, cognitive, and physical processes and characteristics, interventions to encourage behavioural development especially in children and adults with disabilities, as well as research on behavioural plasticity. [1]

The newest approach of research in rehabilitation addresses prophylaxis, treatment, lesion management both somatically and physically. It refers to the surgical, medical, psychosocial interventions necessary for the rehabilitation of critically ill and injured children, adolescents, adults and the elderly, following them throughout their developmental trajectory throughout life. [2]

I. Most evaluations and assessments of medical rehabilitation results are made in clinical or hospital practice, they do not reflect patients' perceptions of the rehabilitation process. Today, medicine wants to develop new quantifiable strategies and technologies to evaluate and monitor patient-centered outcomes, using mobile technologies and applications, behavioral

and social sciences to understand progress, the environment, involvement, and independence. Today all over the world we use large-scale data sets to quantify the responses to therapy and the use of devicesand technologies among people with disabilities.

II. Nowadays, research teams are focused on complex approaches that promote neural plasticity and sensory and motor function. The therapeutic association of physical therapy with regenerative, stimulating, but also pharmacological treatments is preferred. These approach underlines the multidisciplinary concept of Rehabilitation medicine, and emphasizes the need for modern research and application of Rehabilitation in specialized interdisciplinary teams around the world.

III. It is absolutely necessary to ensure a smooth transition without breaks or deficiencies from pediatric rehabilitation care to that of young adults and then mature ones, to improve general care and rehabilitation of adolescents and young people with physical disabilities, individually and systemically.

IV. Rehabilitation results are difficult to predict and objectively quantify. That is why it is necessary to perfect the objective evaluation of the response to the rehabilitation treatment and of the progress of the strength and functionality through rehabilitation. Today we study parameters that predict the response to rehabilitation treatment and thus can adapt the methodology of rehabilitation treatment to objectives proposed according to the individual needs of the person with disabilities.

V. Nowadays, there is still an insufficient understanding of the incidence and prevalence of secondary diseases in rehabilitation, such as pain, musculoskeletal impairment, deconditioning syndrome, skin lesions, cognitive, affective and behavioral disorders, social pathology derived from emotional and sleep dysfunctions, experienced more and more frequently by people with disabilities. Emphasis is placed on finding new methods and strategies to prevent and treat these conditions, by addressing the individual and family or social issues raised by the long and difficult process of rehabilitation.[3

VI. Disease and disability have no national borders, thus our current actions may better influence the future health status of humas all over the world. We need to better understand the long-term outcomes of individual rehabilitation and health and address more complex and multidisciplinary chronic diseases of people at risk as a global health problem. We also need to globally address to nutrition and metabolic disease prevention (obesity, sedentarism, heart diseases, atherosclerosis, alcohol and drugs consumption and dependency). In addition, but last but not least, there are always new technologies created in order to improve the assessment and motor and functional rehabilitation of people around the world with physical and cognitive disabilities. [2]

I.2. Early years and stages of the research career

I completed the licence study in General Medicine in 1997 at "Iuliu Haţieganu"University of Medicine and Pharmacy in Cluj, Romania and since 2007 I have followed the PhD studies in parallel with the residency training in Rehabilitation, Physical Medicine and Balneoclimatology. I finished and presented my PhD Thesis in 2012 at "Carol Davila" University of Medicine and Pharmacy in Bucharest, Romania, under the supervision of Professor Nicolae Marcu, with the theme " *Moments and reference contributions to the evolution of balneo-climatology in Romania in the first half of the twentieth century - scientific papers, schools, personalities, spa network*" (*"Momente şi contribuţii de referinţă la evoluţia balneo-climatologiei pe teritoriul României în prima jumătate a secolului al XX-lea - lucrări ştiinţifice, şcoli, personalităţi, reţea balneară"*).

The thesis intended to be a synthesis of the complementary and complex integrated aspects of literature, scientific personalities, education and research, legislation and *balneal (spa) and climatological* organization in Romania. I used the bibliographic research method, directly at the written source-document (for which I studied the documentary sources from the Romanian Academy Libraries, Brasov County Library, Documentary Library of History of Medicine from the Institute of Hygiene in Bucharest, Central Library of the Medico-Pharmaceutical Institute Bucharest , Library of the Society of Medical Students Bucharest, personal libraries of my distinguished reference professors) and archive documents that I analysed, ordered, synthesized and interpreted with a personal, critical imprint. I had the opportunity to discover with fascination unique images, engravings or reproductions, a true illustrated history of Romanian balneology from the nineteenth century and the first half of the twentieth century.

Being at that moment on the tortuous path of medical recovery, I was constantly encouraged to lean on the study of balneology, which I discovered with fascination.

During the study, documentation and elaboration of this paper I had the opportunity to present various aspects researched in national and Balkan symposia and congresses (having the opportunity to discuss, argue, deepen, clarify and correct aspects of the issues discussed) and to publish two chapters of books and 26 papers (in magazines and conferences proceedings), as the final fruit of the work of study and historical research, and out of the desire to accomplish something useful and that can be capitalized on further.

Another research concern was opened with the studies carried out within the Master's degree in ***Health Management*** (2004-2005) and the Master's degree in ***Medical-Surgical Emergencies*** (2005-2007), the period in which we concretized the bibliographic study and the processing of

databases for dissertation papers and 9 publications in journals in international databases and over 15 presentations at scientific events.

Articles and presentations discussed multidisciplinary topics both medical and educational, such as professional exposure to HIV and hepatitis B virus infection-statistic study, clinical diagnosis and bacterial sensibility surveillance, pandemic H1N1 influenza, new paraclinical diagnosis of lung carcinoma, triggers of acute myocardial Infarction onset and others, laparoscopy in gynaecology and oncologic surgery, endometrial cancer-statistic study.

In other 6 papers I contributed to a new perspective in medical education and practice underlying the need of a new approach followed both the aspects of medical informational novelties, but especially the *technological, structured approach of medical information* and the urgent need of *modern and continuous medical education* focused on the *correct and ethical management of medical information* (databases, online access, networks computer science, data protection, ethical regulations, electronic communication, telemedicine and tele education, medical and biomedical research).

With the deepening of medical rehabilitation methodology, then with the completion of residency and obtaining the title of specialist doctor in Physical Medicine and Rehabilitation (2009), my concerns focused on the vast field of medical practice in medical rehabilitation, in parallel with medical teaching education.

My research activity has focused on topics of neurological disease rehabilitation, paediatric evaluation and rehabilitation, materials used in orthosis and prosthesis, public health and sanitary management of pathologies that require medical rehabilitation, ethical aspects and informed consent in rehabilitation and physiotherapy, interdisciplinary concerns for research in multidisciplinary teams (neurology, psychiatry, gynaecology and endocrinology, anatomopathology, bioengineering).

Benefiting from my quality as a teacher, my training was completed by the concerns of development and correct definition of the physiotherapy field in Romania, on which occasion I documented works in the area of collaboration in the multidisciplinary rehabilitation team (Rehabilitation medicine, physiotherapy, psychology, psychiatry, occupational therapy, orthosis-prosthesis, ethics, health management) and in higher education of modern physiotherapy and aligned with European training standards in theory and practice.

This period materialized in 6 specialized books, 1 book chapter in a foreign publishing house and articles in international databases, culminating with the last 10 years of intense period of fruitful research work in 21 ISI indexed articles in Web of Science, among which 12 as principal author.

1.3. Main research area

This section includes 3 main areas of interest in research and scientific publications

I. Inovation and technology in Rehabilitation

I.a Virtual Reality Rehabilitation in post-stroke patients

This section integrates new technologies on neurorehabilitation with a significant impact on patient post-stroke rehabilitation. The research addressed post-stroke patient's neurorehabilitation focused on the use of non-immersive virtual reality exergames in the upper and lower extremities rehabilitation for post-stroke patients. The research was disseminated by two papers published in " Brain Sciences and International Journal of Environmental Research and Public Health *("Roxana Miclaus, Nadinne Roman, Silviu Caloian, Brindusa Mitoiu, Oana Suciu, Roxana Ramona Onofrei, Ecaterina Pavel and Andrea Neculau, Non-Immersive Virtual Reality for Post-Stroke Upper Extremity Rehabilitation: A Small Cohort Randomized Trial, BRAIN SCIENCE, Sept 2020, Brain Sci. 2020, 10, 655; doi:10.3390/brainsci10090655"* [4]*; "Roxana Steliana Miclaus, Nadinne Roman, Ramona Henter, Silviu Caloian, Lower Extremity Rehabilitation in Patients with Post-Stroke Sequelae through Virtual Reality Associated with Mirror Therapy, International Journal of Environmental Research and Public Health, March2021, Vol 18, Issue 5")* [5]"

The number of stroke cases in Romania is forecast to increase from 61,552 in 2015 by 24% until 2035 [6, 7]. The European Union (EU) reports state that Romania spend the lowest amount on health services per capita (in 2015, of Euro 1,029 whereas the EU average reached Euro 2,884), the highest risk factors being smoking and alcohol consumption and with male population "accounting for more than 50% of those impacted. Additionally, the level of education influences both lifestyle and life expectancy. As a result, the Romanian life expectancy is among the lowest figures registered in the EU (75.3 years in Romania and 80.9 years in the EU, in 2015)".

Stroke sequelae can be permanent. At 15-years post-stroke, 70% of survivors live with incapacity, approximately 40% have depression, and more than 25% have cognitive deterioration [8]. Post-stroke incapacity has a notable contribution to the increased use of both human and financial resources. Thus we emphasize that adequate rehabilitation can cut the expenditure in the healthcare system [9], and telerehabilitation can be a valuable tool for home community rehabilitation. "Neurorehabilitation after a stroke engages the recovery of the motor deficit and the recovery of language function, cognitive recovery, sensory and sphincter functions, and the functional reintegration as much as possible, as active as possible, into family socio-professional life components. [10].

Rehabilitation in the chronic phase begins after the patient has passed the subacute stage entering the chronic phase, followed by a constant rehabilitation program necessary to continue throughout his life. The maximum level of complexity of the physiotherapy program is reached in the chronic phase when the highest acquisition and velocity of motor improvement are also expected. Regardless of the pathology stage, the basic principle is to stimulate and activate somatic structures through different activities and tasks". [11].

VR as a supplement or replacement for conventional physiotherapy previous research has shown to be decisive in promoting the patient's rehabilitation. Nevertheless, regarding stroke, previous literature reviews suggest that VR has not returned more advantages to patients compared to conventional. On the other hand, other studies support specific VR exercise resulting from therapy that can improve motor function restore [12 - 16].

Concerning neuroplasticity and learning or re-educating capacity, previous research shows that in the new neural network pathway, "several principles of motor training, including multisensory stimulation, explicit feedback, and motor images", can influence brain activity for functional rehabilitation. Specific feedback and multisensory inducement are incorporated in the VR devices used for post-stroke rehabilitation. Hence, VR therapy can be a useful tool and an option to standard physiotherapy since it contributes to neuroplasticity. Thus,VR has emerged as a new treatment approach in stroke rehabilitation, which involves using exercise programs designed to simulate real-life objects and events using a computer [17].

This technic extends the capability to build an environment in which the power of reaction and exercise can be manipulated in particular ways and advanced to produce the most relevant paradigm of tailored motor reeducation or learning. "Most literature reviews have shown that VR has good results in the therapy of post-stroke patients, especially as an adjunct to classical physiotherapy" [18-20].

To date, previous studies have shown that VR positively influences the functional reeducation of the upper limb in post-stroke patients, as adjuvant therapy, through the use of dedicated and non-dedicated technologies [21, 22]. However, the VR therapy influences the upper limbs functional reeducation, in post-stroke rehabilitation, using non-immersive VR dedicated software and devices, and as distinct therapy has not yet been ascertained regarding staging level accordingly to the post-stroke phases.

VR has emerged as a new treatment approach in stroke rehabilitation, which involves using "exercise programs designed to simulate real-life objects and events using a computer" [17].

The research aims to use virtual reality and mirror therapy in neurorehabilitation were determined by the patient's increased needs on ADL's restore functioning and socio-economic reintegration. In addition, the research aims to investigate the efficiency of a dedicated NIVR system, with or without Mirror Therapy, for both upper and lower extremity.

Primary outcomes are: 1. Assessment of the efficiency of the proposed protocol for upper extremity rehabilitation using staged, specific therapy, and tailored non-immersive VR on 3 degrees of complexity, applying particular exercises according to patient's potential, and setting accordingly to the degree of difficulty, opposed to conventional physiotherapy; 2. How mirror therapy and VR therapy can influence the motor function of the lower extremities in post-stroke patients.

Additionally, we continued looking for 3. The variations in clinical status and functional status post stroke when using NVIR and identifying if the clinical status improves or negatively influences the functional results of the upper limb when using VR-based therapy compared to conventional physiotherapy; 4. The identification of standardized protocols in the neurorehabilitation of lower and upper extremities enhances patients' motor functions, and ADLs restore.

The study for the upper extremity developed in the "Clinical Hospital of Psychiatry and Neurology in Brasov (Romania)" included fifty-five "inpatients in the Neuro-rehabilitation Department". Although initially, sixty-four patients were selected following the inclusion criteria, nine were excluded (Table 1).

The study "was conducted over nine months, from July 2019 to March 2020, and the patients were introduced to the therapy one by one (asynchronously)". The study has the approval of "The Research and Ethics Committee of the Clinical Hospital of Psychiatry and Neurology in Brasov (no. 12534/18 July 2019) and Informed consent was obtained" from each patient. "The study was registered in clinicaltrials.gov, with no. NCT04436770".

As regards the assessment, for the upper extremity, the evaluation was performed with "Fugl Meyer Upper Extremity Assessment (FMUE), Manual Muscle Testing (MMT) and Active Range of Motion (AROM) were used to assessing muscle strength and range of motion".

For the "LE- motor function and functionality was assessed through FMLE [23-26]. Also, MMT reliability and validity proved to be a useful instrument to assess muscle motor force [27]. The Functional Reach Test (FRT) measures reaching distance and is a simple tool that provides information regarding balance capacity [28]. Time Up to Go (TUG) test was used to assess the fall risk and the progress of balance, sitting, standing and walking, and proved to have good intratester reliability and good construct validity in correlation with gait assessment" [29].

As regards post-stroke disability, "Functional Independence Measure (FIM), Modified Rankin Scale (MRS), and Modified Ashworth Scale (MAS) were used to assess patient independence. The assessments were carried out by two experienced physiotherapists trained explicitly for this research and aimed to register data in scales on stroke severity, activities of daily living, degree of spasticity, motor function and functionality, and the dynamic range of motion".

Table 1 Patient's characteristics in post-stroke rehabilitation using VR

Item	Upper extremity N=55	Lower extremity N=59
Inclusion criteria	(1) Stroke survivors after the acute phase, at least six weeks post-stroke; mild impairment (FIM ≥ 73, FMUE ≥ 13), minor cognitive impairment (Cognitive FIM ≥25); (2) Stroke survivors within no more than four years after a stroke, at least 30-degree flexion and scapulohumeral abduction against gravity, and at least 30-degree elbow flexion against gravity.	1) stroke survivors after the subacute phase, at least six months post-stroke, and less than four years; (2) stroke survivors within no more than four years after stroke, at least 20-degree hip flexion and 10 degrees hip abduction against gravity, and at least 30-degree knee flexion against gravity.
Exclusion criteria	severe cognitive impairments, global or transcortical sensory aphasia, anaemia, atrial fibrillation, NYHA class IV heart failure, other dysfunctions in the upper extremity such as surgery, fractures, scapulohumeral periarthritis, or moderate-severe pain	cognitive impairments, global or transcortical sensory aphasia, anaemia, atrial fibrillation, imbalance of anticoagulant treatment, epilepsy, NYHA class IV heart failure, other dysfunctions in the lower extremity such as surgery, fractures, periarthritis or moderate-severe pain.
Male/female patients (n/%)	Male 24/43.63% Female 35/63.63%	Male 44/74.58% Female 15/25.42%
Age (mean±SD)	62.09/6.44	59.81/9.36
Affected side (right/left)	Left 26/47.27.59% Right 29/52.72%	Left 18/43.90% Right 23/36.59%
Post-stroke duration (mean±SD)	1.61/1	2.72/1.06

"All assessment scales were found excellently related to other types of assessment, regarding the psychometric properties. Therefore, MRS was used to assess stroke severity, FIM was used for the assessment of ADLs, MAS was used to assess the degree of spasticity".

Upper extremity VR rehabilitation

Regarding the upper extremity research on the efficiency of VR and dexterity exercises, the patients were divided into four groups, based on the time since stroke.

- ✓ "Subacute Experimental (SE) enrolled patients less than six months since stroke (n = 6), and
- ✓ Chronic Experimental (CE) enrolled patients more than six months since stroke (n = 20), both groups received VR therapy;

- ✓ Subacute Control (SC) enrolled patients less than six months post-stroke (n = 5), and
- ✓ Chronic Control (CC) enrolled patients more than six months since stroke (n = 21), both groups received conventional physiotherapy".

The duration of participation: "10 working days for two consecutive weeks, all four groups received a 60-min daily therapy session for upper extremities:

The control groups (SC, CC) benefited daily from for a total time of 60 min, a standard physiotherapy protocol of exercises such as self-passive mobilization, bilateral active mobilization, and active mobilization with resistance, task-specific functional exercises to increase the ability to perform ADLs, and dexterity exercises for the hand (occupational therapy exercises)

The program of the experimental groups (SE. CE) included 20 to 40 min of VR therapy (this duration was set according to the patient's capacity) associated with dexterity exercises (occupational therapy exercises), so overall, every patient performed one 60 minutes daily of upper extremity training. The protocol for occupational therapy exercises for the hand included the use of the Canadian plate, thick and thin grip training, lateral and palmar pinch, and wrist extensor strengthening tasks, for both groups".

I. *Virtual Reality Software, Devices, and Exergames*

"The technology used consisted of a 55-inch TV screen, a computer running MIRA Rehab Limited, London, UK (a software for virtual reality therapy), and a Microsoft Kinect sensor that allows the detection of the human body, joints, and movements on all three axes".

"MIRA is a software (eHealth) telerehabilitation tool that improves physiotherapy effectiveness and convenience for patients in recovery. The software uses the Kinect sensor as an evaluation tool for the AROM assessment. It calibrates the patient's position at the beginning of each VR session or during exergames, if necessary". [30]."Through the MIRA program and the sensor, the patient receives feedback regarding the correctness of motion and posture during VR therapy sessions. During the research, the MIRA software was updated from version 2.2.3.0 (released on 16 July 2019) to version 2.2.5.8 (released on 19 December 2019)".

"MIRA Rehab software has two categories of exergames based on types of motion, respectively, a set of upper-limb analytical movements and a functional and complex set of exergames that involve muscle control, movement coordination, and isometric contraction, and multiple directions of motion".

"The games used were customized according to the functional capacity of patients, divided into three groups according to their AROM and MMT capacity: limited, low, and high".

Twenty per cent of the exergames were chosen "(mostly the same used for rehabilitation of movement coordination and kinaesthetic proprioception) to maintain the upper extremity in isometric contraction during the exercise (1–3 min)".

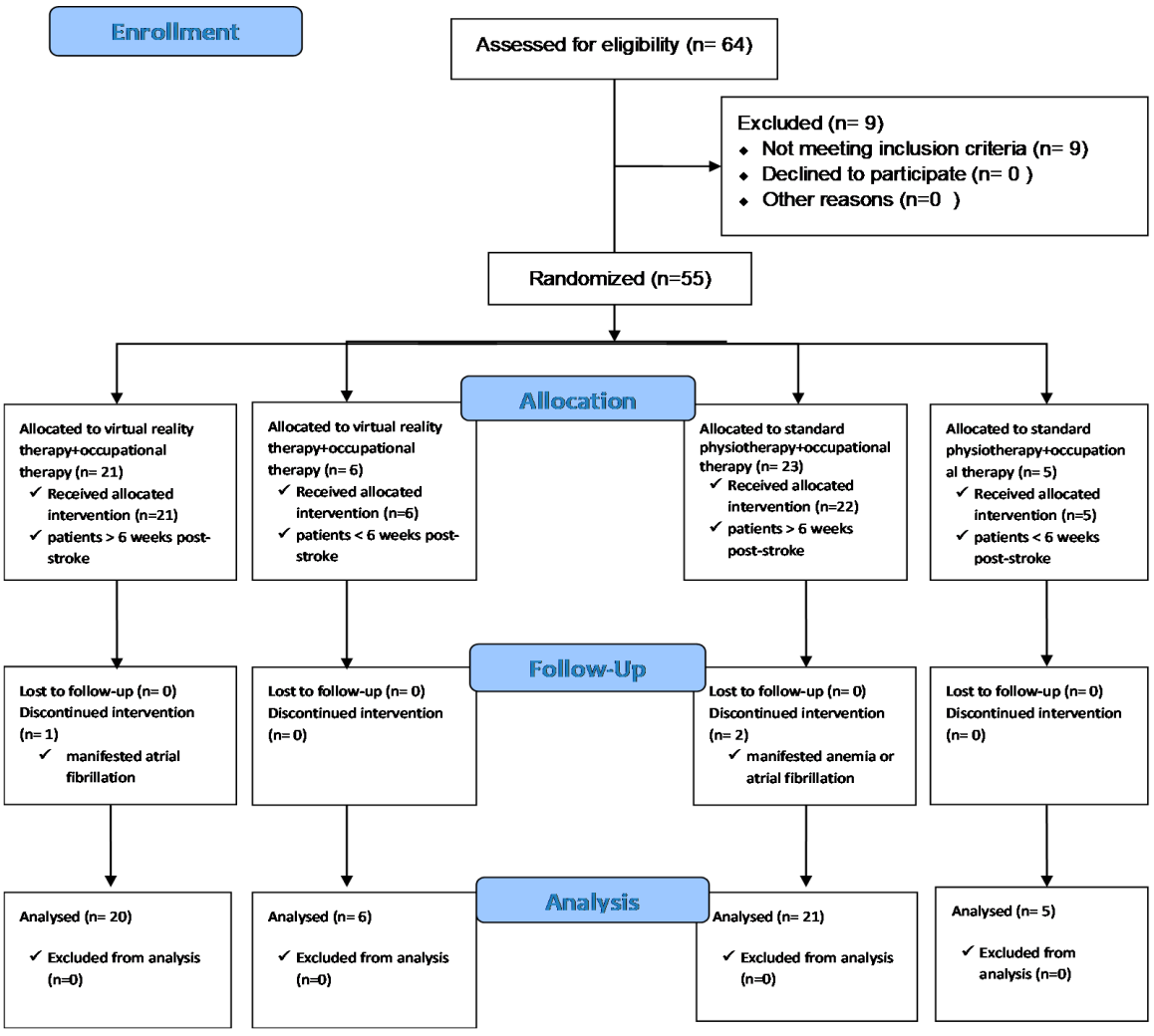


Figure 1. The CONSORT flow diagram for the upper extremity rehabilitation through VR. [4].

"The Wilcoxon Signed-Rank test was used to determine the groups' differences pre-and post-therapy; consecutively, independent Kruskal–Wallis with post hoc pairwise comparison was applied. Multiple linear regressions with stepwise selection were applied to determine the best

predictors and the relationships between the physiotherapy treatments and group characteristics and also to determine if any factor influenced or predicted the physiotherapy outcomes after a stroke".

"Fifty-two participants completed the study, distributed by computer-generated randomization, out of whom six subjects were in the Subacute Experimental (SE) group, and 20 in the Chronic Experimental (CE) group, 5 in the Subacute Control (SC) group, and 21 subjects in the Chronic Control (CC) group. The characteristics of the patients from the investigated groups are presented in Table 1"

Table 2. Wilcoxon Signed-Rank test, pre- and post-therapy [4].

	SE Group (n = 6)			CE Group (n = 20)			SC Group (n = 6)			CC Group (n = 20)		
	Mean/SD	Mean Rank	p	Mean/SD	Mean Rank	p	Mean/SD	Mean Rank	p	Mean/SD	Mean Rank	p
AROM	9.41/2.86	3.50	0.028	9.00/4.48	10.50	<0.001	4.98/3.99	3.50	0.077	1.91/4.96	11.64	0.099
MMT	0.82/0.28	3.50	0.028	0.58/0.22	10.50	<0.001	0.36/0.29	3.00	0.041	0.44/0.14	11.00	<0.001
FMUE	12.66/2.42	3.50	0.027	8.45/3.61	10.50	<0.001	6.00/2.35	3.00	0.042	7.43/3.52	11.00	<0.001
FIM	10.00/2.44	3.50	0.026	3.65/4.33	9.50	<0.001	4.40/3.29	3.00	0.041	2.52/2.93	9	<0.001
FRT	5.16/2.78	3.50	0.027	4.88/4.54	9.00	<0.001	3.20/2.68	2.50	0.063	4.62/2.39	11.00	<0.001
MAS	0/0	0	1	0/0	0	1	0.40/0.55	0	1	0.05/0.22	1.50	0.157
MRS	−0.83/0.75	2	0.102	−0.10/0.31	2.5	0.056	−0.20/0.45	1	0.317	0/0	0	1

FMUE: Fugl–Meyer Assessment for Upper Extremity; MRS: Modified Rankin Scale, FIM: Functional Independence Measure; AROM: Active Range of Motion; MMT: Manual Muscle Testing; MAS: Modified Ashworth Scale; FRT: Functional Reach Test.

"No significant differences were found regarding the baseline groups comparison for the outcome measures. In Table 3, the results of the independent Kruskal–Wallis test are displayed, along with the values for group differences in the outcomes assessed".

Table 3. Independent Kruskal–Wallis. [4].

	Paired Differences						
	Mean	Std. Deviation	Minimum	Maximum	X^2	df	p
AROM	5.79	5.57	−5.58	15.39	21.21	3	<0.001
MMT	0.52	0.24	0.18	1.13	13.19	3	<0.001
FMUE	8.28	3.71	2.00	17.00	11.49	3	0.009
FIM	4.00	4.12	0	15.00	13.14	3	0.004
FRT	4.64	3.39	0	19.00	1.40	3	0.704
MAS	0.05	0.23	0	1.00	12.16	3	0.007
MRS	−0.15	0.41	−2.00	0	18.36	3	<0.001

"FMUE: Fugl–Meyer Assessment for Upper Extremity; MRS: Modified Rankin Scale, FIM: Functional Independence Measure; AROM: Active Range of Motion; MMT: Manual Muscle Testing; MAS: Modified Ashworth Scale; FRT: Functional Reach Test".

Table 4. Post hoc pairwise comparison for independent Kruskal–Wallis. [4].

Outcome Measure	Pairwise Comparison	Mean Ranks	X^2	Std. Error	*p*
AROM	SE > SC	36.50/22.00	20.08	4.73	<0.001
	SE > CC	36.50/15.79	20.71	7.01	0.019
MMT	SE > SC	41.50/12.40	29.10	9.17	0.009
	SE > CC	41.50/22.12	19.38	7.01	0.034
FMUE	SE > SC	44.58/17.00	27.58	9.13	0.015
	SE > CC	44.58/23.40	21.17	6.98	0.015
FIM	SE > SC	45.33/32.60	21.30	6.86	0.011
	SE > CC	45.33/22.02	23.31	6.82	0.004
MAS	SE < SC	25.00/35.40	−10.40	3.70	0.030
	CE < SC	25.00/35.40	−10.40	3.06	0.004
	CC < SC	26.24/35.40	9.16	3.04	0.016
MRS	SE < CE	12.42/27.45	−15.03	4.17	0.002
	SE < CC	12.42/30.00	−17.58	4.15	<0.001

SE: Subacute Experimental Group; CE: Chronic Experimental Group; SC: Subacute Control Group; CC: Chronic Control Group, FMUE: Fugl–Meyer Assessment for Upper Extremity; MRS: Modified Rankin Scale, FIM: Functional Independence Measure; AROM: Active Range of Motion; MMT: Manual Muscle Testing; MAS: Modified Ashworth Scale; FRT: Functional Reach Test.

"By merging the data from Tables 3 and 4, the results suggest that the subacute experimental group (SE) registered the most significant differences compared to control groups (subacute or chronic)".

TABLE 5 Values of the predictors which influence post-stroke physical rehabilitation[4].

Dependent Variable	Model	R^2	*p* Change	Unstandardized Coefficients		Standard Coeff.	*p*	95.0% Confidence Interval for B	
				B	Std. Error	Beta		Lower Bound	Upper Bound
AROM	(Constant)	0.47	<0.001	4.08	0.90		<0.001	2.25	5.91
	VR Time			0.38	0.06	0.64	<0.001	0.25	0.51
	Dyslipidemia			−3.72	1.15	−0.33	0.002	−6.05	−1.39
MMT	(Constant)	0.16	<0.001	0.40	0.03		<0.001	0.32	0.48
	VR Time			0.01	0.00	0.55	<0.001	0.01	0.02
FMUE	(Constant)	0.31	0.001	8,17	0.68		<0.001	6.79	9.55
	VR Time			0.17	0.04	0.42	0.001	0.07	0.26
	ICD			−3.13	0.88	−0.42	0.001	−4.90	−1.35
FIM	(Constant)	0.29	0.011	4.51	1.07		<0.001	2.36	6.67
	VR Time			0.16	0.05	0.37	0.004	0.05	0.27
	P-S.D			−1.23	0.46	−0.32	0.011	−2.17	−0.30
MRS	(Constant)	0.23	0.029	−0.19	0.10		0.069	−0.41	0.01
	VR Time			−0.02	0.01	−0.44	0.001	−0.03	−0.01
	P-S.D			0.10	0.04	0.28	0.023	0.01	0.20
	Diabetes			0.33	0.14	0.27	0.029	0.03	0.62

"Multiple linear regression analysis: in Table 5 the values of the predictors which influence post-stroke physical rehabilitation are listed, according to the outcome measures. While "VR time" has a positive influence on upper extremity rehabilitation, "dyslipidaemia, diabetes, and ICD", and "long post-stroke duration" negatively influence upper extremity functional recovery. In rehabilitation,

"long time" means more than one year since a stroke (in this research, from 1.1 to 4 years, as mentioned in Table 1"

TABLE 6 Descriptive statistics [4].

Descriptive Statistics					
Linear Regression Models	***n***	**Minimum**	**Maximum**	**Mean**	**Std. Deviation**
Model 1 AROM	52	0.35	13.71	5.79	3.83
AROM-VR	52	4.08	13.70	7.44	3.56
AROM-Dyslipidemia	52	0.35	4.08	2.43	1.86
Model 1 MMT	52	0.40	0.76	0.52	0.13
Model 1 FMUE	52	5.03	12.47	8.28	2.07
FMUE-VR	52	8.17	12.47	9.67	1.59
FMUE-ICD	52	5.04	8.17	6.78	1.57
MODEL 1 FIM	52	−0.43	8.43	4.00	2.22
FIM-VR	52	4.52	8.69	5.97	1.54
FIM-P-S.D	52	−0.44	4.39	2.54	1.34
MODEL 1 MRS	52	−0.66	0.32	−0.15	0.23
MRS-VR	52	−5.20	−0.20	−1.94	1.85
MRS-P-S.D	52	−0.19	0.23	−0.02	0.11
MRS-Diabetes	52	−0.20	0.13	−0.15	0.11

We did not find correlations between specific factors as age, gender, blood pressure, hemiparesis side, carotid artery atherosclerosis.

Lower Extremity

"Sixty-four participants were assigned to the *experimental and control groups*, using simple randomization. The participants were divided into two groups: Experimental group (n=31) and Control group (n=28)".

Table 7 Types of physiotherapy interventions [5].

Types of interventions	Experimental Group	Control Group	Minutes of therapy
Passive analytical exercises for each LE joint	No	Yes	10
Prone or supine active analytical exercises for LE joint	No	Yes	20
Active LE exercises from standing position, and proprioception	No	Yes	20
Active ergometer bicycle	Yes	Yes	10
Treadmill	Yes	Yes	10
VR exercises	Yes	No	32 ±5
MT exercises for ankle	Yes	No	18±4
Total time of physiotherapy exercises (minutes)	70	70	70

LE-Lower Extremity, VR- Virtual Therapy, MT-Mirror Therapy

"All data regarding groups allocation is presented in Figure 2, the CONSORT flow diagram. The duration of participation in the study for every patient was of 10 working days for two consecutive

weeks. Thus, each group received a 70-minute therapy session for the LE for ten days". "The control group benefited daily from a standard physiotherapy protocol of exercises. The program of the experimental group included 20 to 40 minutes of VR therapy (this duration was set according to the patient's capacity) associated with MT exercises, so overall every patient performed seventy minutes of daily LE training". "The protocol for MT therapy was set to analytical motion" with the healthy ankle and exercises of proprioception and motion control and coordination. The types of interventions for each group are found in Table 1, and as it can be seen, "the experimental group received 20 minutes of ergometer bicycle and treadmill training" like the control group.

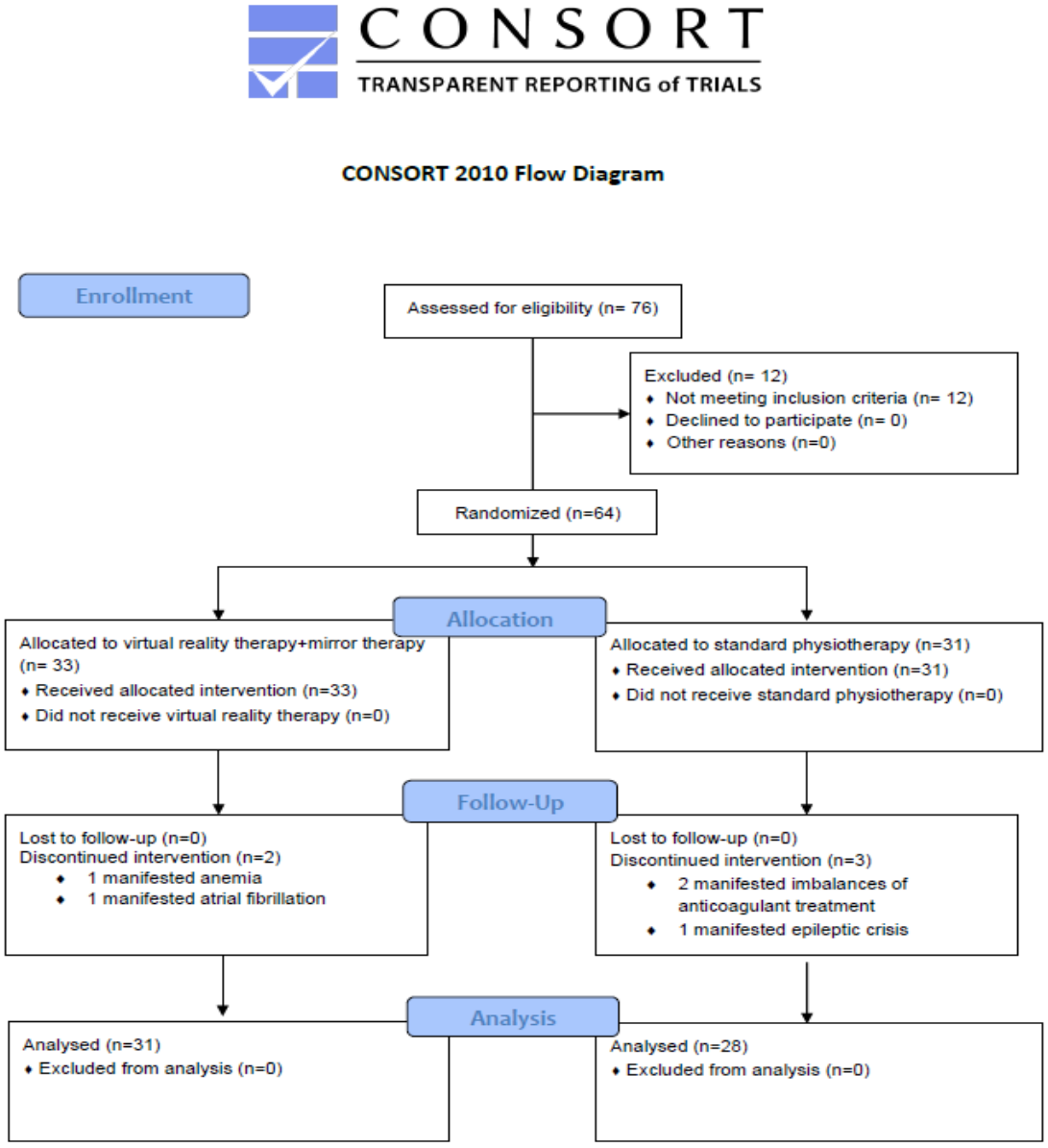


Figure 2, CONSORT flow diagram for the lower extremity rehabilitation using VR and MT [5].

The steps required by VR therapy use were "the following:

a. Assess AROM with a goniometer, assess MAS, MRS, FIM, FMLE and FRT

b. Assess AROM through Kinect sensor and MIRA software
c. Establish the limits of ROM performed during exergames based on the AROM assessment
d. Establish the level of technology tolerance to motion pattern and correctness (the adjustment of the tolerance levels for motion from 0 to 100%.
e. Assigning the patient's protocol of exergames by the results obtained from the assessments

The types of exergames used in the research were set based on three levels of difficulty:

i. For patients with only 20 degrees of hip flexion, the most comfortable types of exergames are MMT 2-3, 10 degrees of hip abduction, and 30 degrees of knee flexion.
ii. The medium types of exercises, for patients with 25-60 degrees of hip flexion, 10-20 degrees of hip abduction, MMT 3, and 30-60 degrees of knee flexion.
iii. For patients with 60-90 degrees of hip flexion, the intense level of exergames, and 20-30 degrees of hip abduction, MMT-4, and 60-90 degrees of knee flexion.

The games used were customized according to the functional capacity of patients, divided into three groups according to their AROM and MMT capacity: limited, low and high. We adjusted the virtual reality exergames for patients assigned to the easy set of exergames" by working all the ten sessions.

Mirror therapy exercises

Analytical exercises and coordination motions were performed for the ankle joint (plantar flexion, dorsiflexion, eversion, inversion) and muscle strength exercises by performing the same motions against gravity or with a weight added on the forefoot. "The exercises for coordination and muscle control included a different pattern of motions performed at physiotherapists' indication".

Table 8 Patient's characteristic [5].

Characteristic	Experimental ($n = 31$)	Control ($n = 28$)	p
Affected side (left/right)	16/15	8/20	0.074
Haemorrhagic/Ischemic stroke	18/13	13/15	0.821
Gender (male/female)	7/24	8/20	0.601
Age (mean/SD)	59.03/10.12	60.67/8.17	0.767
Post-stroke Time (mean/SD)	2.74/1.10	2.71/0.99	0.456
Mean (minutes)/SD VR Duration	22.16/4.01	0	0.317
Total Physiotherapy Duration (minutes)	70	70	1.00

"Wilcoxon Signed-Rank test was used to determine the groups' differences from pre-and post-therapy. We consecutively used Mann-Whitney to determine differences between groups; the analysis was performed by using differential score between the post-test and the pre-test in both groups. The statistical analysis was performed with a 95% confidence level, and significant values were considered $p < 0.05$. Fifty-nine participants completed the study, distributed by

computer-generated randomization, thirty-one subjects in the experimental group, and twenty-eight in the control group. The characteristics of the patients from the investigated groups are presented in Table 8".

Table 9 Related Samples Wilcoxon Signed-Rank test pre-and post-therapy for ROM and MMT, for experimental group. [5].

	ROM				MMT			
	Pre-therapy	Post-therapy			Pre-therapy	Post-therapy		
	Median (IR)	Median (IR)	p	Cohen's d	Median (IR)	Median (IR)	p	Cohen's d
Hip Flexion	85.00 (5.00)	90.00 (10.00)	.000	0.601	3.50 (0.75)	3.75 (0.75)	.000	0.538
Hip Extension	10.00 (5.00)	10.00 (5.00)	.000	0.833	3.25 (0.50)	3.50 (0.75)	.000	0.834
Hip Abduction	30.00 (15.00)	35.00 (10.00)	.000	0.853	3.25 (0.75)	3.50 (0.75)	.000	0.718
Hip Adduction	0/0	0	.083	0.090	3.25 (0.50)	3.50 (0.75)	.000	0.574
Hip Internal Rotation	10.00 (10.00)	10.00 (15.00)	.002	0.317	2.00 (1.75)	2.50 (2.00)	.001	0.204
Hip External Rotation	25.00 (15.00)	25.00 (20.00)	.000	0.349	2.75 (0.75)	3.00 (0.75)	.011	0.256
Knee Flexion	80.00 (15.00)	90.00 (15.00)	.000	0.443	3.25 (1.00)	3.25 (0.50)	.000	0.573
Knee extension	0	0	1.000	NA	3.50 (0.75)	3.75 (0.50)	.000	0.536
Dorsiflexion	15.00 (10.00)	20.00 (12.00)	.000	0.468	2.75 (1.25)	3.00 (1.25)	.000	0.302
Plantarflexion	10.00 (15.00)	15.00 (17.00)	.000	0.436	3.00 (2.00)	3.00 (1.25)	.000	0.295
Inversion	10.00 (24.00)	10.00 (25.00)	.002	0.182	2.00 (1.75)	2.00 (2.00)	.007	0.134
Eversion	6.00 (20.00)	10.00 (25.00)	.001	0.209	1.75 (2.00)	2.00 (1.75)	.002	0.238

ROM- Range of Motion, MMT-Manual Muscle Testing, IR-Interquartile Range, NA-Not Available

Table 10. Related Samples Wilcoxon Signed-Rank test pre-and post-therapy for ROM and MMT, for control group. [5].

	ROM				MMT			
	Pre-therapy	Post-therapy			Pre-therapy	Post-therapy		
	Median (IR)	Median (IR)	P	Cohen's d	Median (IR)	Median (IR)	P	Cohen's d
Hip Flexion	83.00 (27.50)	90.00 (13.75)	.011	0.324	3.25 (0.50)	3.50 (0.50)	.000	0.521
Hip Extension	5.00 (5.00)	10.00 (5.00)	.010	0.419	3.25 (0.44)	3.50 (0.75)	.001	0.456
Hip Abduction	22.50 (10.00)	27.50 (9.25)	.045	0.382	3.12 (0.50)	3.25 (0.75)	.001	0.458
Hip Adduction	0.00 (0.00)	0.00 (0.00)	1.000	NA	3.00 (0.44)	3.25 (0.75)	.006	0.436
Hip Internal Rotation	10.00 (13.75)	12.50 (12.25)	.052	0.250	2.75 (1.19)	2.87 (0.75)	.001	0.354
Hip External Rotation	15.00 (16.25)	20.00 (13.75)	.006	0.144	2.50 (0.94)	2.50 (0.94)	.025	0.064
Knee Flexion	75.00 (35.00)	80.00 (25.00)	.000	0.337	3.00 (0.25)	3.50 (0.44)	.000	0.814
Knee extension	0	0	1.000	NA	3.25 (0.50)	3.50 (0.69)	.000	0.681
Dorsiflexion	15.00 (9.50)	15.00 (25.00)	.005	0.449	3.00 (1.13)	3.00 (1.19)	.133	0.111
Plantarflexion	20.00 (15.00)	20.00 (13.75)	.630	0.057	3.00 (1.31)	3.00 (1.63)	.283	0.131
Inversion	15.00 (10.00)	20.00 (25.00)	.002	0.325	2.12 (1.44)	2.12 (1.48)	.059	0.050
Eversion	6.00 (10.00)	10.00 (18.25)	.000	0.451	2.12 (1.75)	2.12 (1.80)	.265	0.018

ROM- Range of Motion, MMT-Manual Muscle Testing, IR-Interquartile Range, NA-Not Available

"No significant differences were found regarding the baseline groups comparison for the outcome measures".

Table 11 Related Samples Wilcoxon Signed-Rank test pre-and post-therapy [5].

	Experimental group				Control Group			
	Pre-therapy	Post-therapy			Pre-therapy	Post-therapy		
	Median (IR)	Median (IR)	*p*	Cohen's d	Median (IR)	Median (IR)	*p*	Cohen's d
ROM (mean)	39.17 (5.42)	42.92 (7.42)	<0.001	0.645	37.71 (7.40)	38.83 (8.56)	<0.001	0.504
MMT (mean)	2.89 (1.02)	3.05 (0.81)	<0.001	0.533	2.86 (0.73)	3.07 (0.81)	<0.001	0.324
MAS	2.00 (2.00)	2.00 (2.00)	.157	-0.049	1.00 (1.00)	1.00 (1.00)	1.000	0.00
MRS	2.00 (1.00)	2.00 (1.00)	1.000	0.00	2.00 (0.75)	2.00 (0.75)	1.000	0
Motor FMLE	24.00 (6.00)	27.00 (7.00)	.000	0.685	24.50(6.75)	25.5 (6.50)	.000	0.254
Passive FMLE	17.00 (5.00)	20.00 (2.00)	.136	0.466	17.50 (3.75)	18.00 (3.75)	.034	0.121
Pain FMLE	20.00 (0.00)	20.00 (0.00)	.020	0.212	20.00 (4.50)	20.00 (3.00)	.063	0.157
FIM	114.00 (13.00)	114.00 (13.00)	1.000	0	121.00 (15.75)	121.00 (15.75)	.157	0.010
TUG	2.00 (0.00)	2.00 (1.00)	.083	0.011	2.00 (0.00)	2.00 (0.00)	.317	0.075
FRT	25.00 (8.00)	27.00 (5.30)	.000	0.573	23.00 (11.00)	23.00 (12.75)	.470	0.004

IR-Interquartile, Range ROM- Range of Motion, MMT-Manual Muscle Testing, FMLE: Fugl-Meyer Assessment for Lower Extremity; MRS: Modified Rankin Scale, FIM: Functional Independence Measure; MAS: Modified Ashworth Scale; TUG-Timed Up and Go test FRT: Functional Reach Test.

Table 12 Mann-Whitney test for independent samples for ROM and MMT [5].

	ROM				MMT			
	Experimental Group	Control Group			Experimental Group	Control Group		
	Median (IR)	Median (IR)	*p*	Cohen's d	Median (IR)	Median (IR)	*p*	Cohen's d
Hip Flexion	5.00 (9.00)	0.00 (5.00)	.001	0.611	0.25 (0.25)	0.25 (0.19)	.199	0.117
Hip Extension	5.00 (5.00)	0.00 (2.00)	.000	0.929	0.25 (0.25)	0.25 (0.50)	.140	0.261
Hip Abduction	5.00 (10.00)	0.00 (4.50)	.006	0.518	0.25 (0.50)	0.00 (0.25)	.030	0.568
Hip Adduction	0.00 (0.00)	0.00 (0.00)	.094	NA	0.25 (0.50)	0.00 (0.75)	.012	0.610
Hip Internal Rotation	0.00 (5.00)	0.00 (2.00)	.593	0.159	0.00 (0.25)	0.00 (0.25)	.276	0.031
Hip External Rotation	3.00 (10.00)	0.00 (5.00)	.028	0.761	0.00 (0.50)	0.00 (0.00)	.011	0.792
Knee Flexion	5.00 (13.00)	5.00 (10.00)	.249	0.287	0.25 (0.50)	0.25 (0.25)	.146	0.290
Knee extension	0.00 (0.00)	0.00 (0.00)	1.000	NA	0.25 (0.50)	0.25 (0.75)	.828	0.134
Dorsiflexion	3.00 (8.00)	0.00 (8.75)	.386	0.244	0.25 (0.75)	0.00 (0.25)	.001	0.870
Plantarflexion	5.00 (5.00)	0.00 (2.00)	.003	0.752	0.25 (0.50)	0.00 (0.00)	.002	0.520
Inversion	0.00 (5.00)	0.00 (5.00)	.354	0.299	0.00 (0.25)	0.00 (0.00)	.151	0.439
Eversion	0.00 (5.00)	2.00 (5.00)	.383	0.346	0.00 (0.25)	0.00 (0.25)	.223	0.545

"In Table 10 are presented the results of the Wilcoxon Signed-Rank test related to the other types of assessment and the means for ROM and MMT. The results suggest that VR and MT have influences on the pain scale from FMLE assessment and an improvement in the balance of the experimental group compared to the control group".

"Concerning the comparison between the two groups, the Mann-Whitney test for independent samples results suggests that the experimental group had significantly better outcomes compared to the control group regarding ROM, MMT, the motor scale of FMLE and FRT".

The results "suggest significant differences were found in both groups pre and post-therapy for ROM and MMT". While for the experimental group "ROM for hip internal rotation and plantar flexion were statistically significant pre-and post-therapy, compared to control group, the effect size was small. As it concerns muscle strength, the patients from the experimental group gained muscle force within all planes of motion regarding ankle movements, compared to the control group, also with a small effect size".

Upper extremity functionality and clinical significance in post-stroke rehabilitation using VR and dexterity exercises

This study suggests that using "NVIR-based therapy, as a standalone therapy, by a suitably established protocol, gradually staged and adapted to patients' functional and neuromotor capacity, is efficient in rehabilitating the upper extremity in post-stroke patients. VR as an adjunct to classical physiotherapy is considered efficient in patients with post-stroke sequelae, both for lower extremities, for the upper extremities, and balance [28]. Previous results suggest a significant difference between groups on the FMUE scale, while muscle strength reports have not shown significant differences pre- and post-therapy. In our study, the increase in the upper extremity muscle strength may be explained by the addition of wrist weights during VR training and the study design" [31].

"The results of the Wilcoxon Signed-Rank test prove that VR therapy positively influenced upper extremity recovery for both groups receiving this type of therapy, for most of the assessments used, except MRS and MAS. The results of the independent Kruskal–Wallis test shows statistically significant differences between the experimental and the control groups. VR therapy can explain the results as a new enriched and interactive environment that influences neuroplasticity, especially regarding the subacute experimental group, whose participants are identified in the early post-stroke period, when the cerebral reorganization is manifesting at a maximum level" [32].

"Since no significant differences were found at the baseline for the four groups, we can emphasize that the results obtained can be based on the specific VR technology used for rehabilitation and the study design". [33]

Thus, our research "brings more knowledge regarding the personalized use of VR, using specific technology, compared to standard physiotherapy, as a standalone method and not as an adjunct therapy" [21, 34].

"The use of FIM to measure the results obtained in VR training confirms that VR therapy improves the patients' functional independence and upper limb function". Furthermore, the "FIM outcomes in VR training arise even when compared to upper limb robotic therapy, as long as these new types of therapy are adapted and individualized to the patient's ability" [35].

"The post hoc pairwise comparison results for an independent Kruskal–Wallis test suggest that the group of patients who received VR therapy and dexterity exercises within less than six months post-stroke (SE) had relevant results and visible differences from the other three groups, especially the control ones".

"Most of the differences between the assessments result from the initial, and the final evaluations are found in the linear regression results, which confirm that both the length of post-stroke time and the presence of diabetes negatively influence post-stroke recovery. Therefore, despite the patients' heterogeneous profiles, ranging from subacute to chronic stroke phases, post-stroke recovery may be influenced by neuroplasticity and physiotherapy or rehabilitation". [36].

In our study, dyslipidaemia, coronary ischemic disease, and diabetes were the associated factors that negatively influenced the post-stroke physical recovery of the upper extremity. It is known that all these disorders belong to the associated risk factors of a stroke, still negatively influencing stroke.

Lower extremity clinical impact in the use of MT and VR in post-stroke patients

Our study results suggest that the combination of complex exercises (resulting from performing various tasks) "alongside visual feedback improves cognitive function in controlling the motion". Merging mirror therapy with VR therapy, kinaesthetic and proprioception training optimize brain reorganization and LE rehabilitation [37, 38]. "Our sample of patients regarding the ankle movements, both on ROM and muscle strength, suggests that the use of MT, combined with bilateral exercises and foot strengthening exercises, improves muscle strength and ankle stability".

"As the outcomes from our research show that both types of interventions have positive and significant results on LE functionality and motor function, it seems that the use of VR therapy

associated with MT has better outcomes on ROM, muscle strength and balance. As it was found in previous research, conventional physiotherapy and commercial video-gaming VR exercise improve gait and balance. A rehabilitation VR system and an adequate protocol can also achieve promising results on LE rehabilitation after stroke" [39]. The particular results of ankle strength and balance from the two groups may be approached by the biomechanics of the foot and ankle and the involvement in postural balance. Besides, the study outcomes emphasize the importance of the functionality and stability of the ankle in post-stroke patients [40].

The results obtained on hip ROM, for flexion, extension, abduction, and muscle strength suggest that VR therapy can replace classical physiotherapy in LE rehabilitation. VR adds "more value to the therapeutical exercises program by stimulating the sensorimotor components to enhance brain processes by combining visual and physical motion stimuli and visually inducing self-motion perception" [41]. The results suggest "integrating VR and MT in the rehabilitation program by stimulating LE motor and functional rehabilitation and postural balance".

"Although in the last decade, the emphasis has been on the rehabilitation therapy within the first 3-6 months post-stroke, lately, it has been shown that neuroplasticity may occur in chronic post-stroke stages. If the patient is included in rehabilitation programs", motor functions and paretic limb functionality may occur [42, 43]. "Through the use of VR, MT and other new methods of training and rehabilitation of patients in the chronic post-stroke stages, it is possible to interfere in the state of health, improving the individual's functional capacity, with chain repercussions on the family and society".

These studies suggest the efficiency of specific NVIR use both for the upper extremity and lower extremity "rehabilitation in post-stroke patients if special attention is paid to outcome measures, the length of VR therapy, and other particularities of the post-stroke population as mild impairment, aphasia, or cognitive impairment".

"Combining VR rehabilitation technology with MT exercises creates a more favourable environment for lower extremity rehabilitation in chronic patients after stroke, by combining several types of feedback, with an impact on neuroplasticity".

"A protocol of VR training exercises for lower limb after stroke, combined with MT exercises, has better outcomes than standard physiotherapy".

I.b Rehabilitation enhanced by innovative materials use in prosthesis and assistive devices

This chapter brings forward the necessity of a multidisciplinary team to research assistive devices and technologies development for patient's rehabilitation. The research focused on the innovative use of different materials and technologies to manufacture assistive devices was acknowledged by four publications.

I.b.1 Identification of secondary resources in the manufacture of hip prostheses

Orthopaedic materials properties represent a significant factor for the success of surgery in addition to self-evident factors such as "medical staff skills and medical equipment technology progress nowadays".

The research in orthopaedics materials properties is focused on different "types of loadings, especially compression and fatigue" [44], influencing the "interface between cement and bone" [45]. The success of joint cemented replacements is associated in the long-term with the danger of "mechanical failure [46] of the bone cement mantle as one of the most common causes of the reconstruction loosening". Unfortunate outcomes may also occur due to particular situations, mainly inadequate rehabilitation therapy after replacement as stretching and relaxation techniques. In addition, kinesiotherapy procedures induce "traction loads upon the insertion surface of the prosthesis and might produce damage to the prosthetic cement" over maximum stresses around 35 MPa.

Nowadays, medical studies are looking for new materials highly human-compatible and with "increased compliance between cement and patient skin" [47] *("Corneliu Druga, Radu Necula, Diana Cotoros,* ***Roxana Miclaus****, Angela Repanovici, Sarah Adriana Nica, Experimental Research Regarding the Thermomechanical Behaviour of PMMA during Recovery of Patients with Joint Replacements,* *Revista de Materiale Plastice, Vol 54, No 4/2017, pag.645-647")* [48]

This research aimed to conduct experimental research focused on observing and assessing the thermomechanical behaviour of polymethylmethacrylate (PMMA), representing the most used acrylic cement in joint replacements.

The investigation was conducted by an "interdisciplinary team of doctors and engineers" focusing their efforts on polymethylmethacrylate (PMMA), a "traditionally used material for joint replacements". The specialists are willing to investigate the optimal viscosity connected to exothermic reaction and the safe duration of cement preparation and polymerization (similar to the optimal time for a joint replacement insertion in vivo, permitting the surgeon to fix, shape, and stabilize the replacement with minimal risk).

The practical experiment took place in the Clinical County Emergency Hospital in Brasov. It aimed

to highlight the physical compliance parameters between cement and patient tissue, starting from the fact that the success rate of around 90% is influenced by various factors [47]. "Risk of tissue necrosis, fibrosis and other impairments [49] following the exothermic polymerization reaction during the material preparation [50], embolization of always a residual amount of monomer (MMA)" (the risk decreases within 2 or 3 weeks of healing and only exceptionally cause the death of the patient are the main complications[51].

Experiment description

1. *PMMA specimen manufacturing* using Plexiglas and Aluminium molds "were designed in CAD software and manufactured according to the F-2118 standard" in force. Fig 1 a, b.

a

b

Figure 3 Molds for specimens manufacturing [48]

The *PMMA cement was prepared* strictly following the instructions and closely monitoring the "exothermic radical polymerization reaction which may cause".

- ✓ "BCIS (bone cement implantation syndrome) leading to intra-operative mortality ranging from 0.02% to 6.6% of the cases [52], necrosis or impairment in blood circulation".
- ✓ As polymerization advances, an increase of viscosity occurs ("in parallel with temperature increases as 57 kJ of polymerization heat are generated per mole MMA") [53].

2. After the cement preparation, "the specimen temperature was monitored by a FLIR thermo-vision camera for 15 minutes": started at 8:20 with 26.50C (fig.4), and in 4 minutes reach 290C in the "active area of the specimens. The temperature reaches high values (like 77.20C) after 6 min from the cement preparation (fig.6), and then it starts diminishing slowly, reaching 28.40C after 15 min" (fig.7). [48]

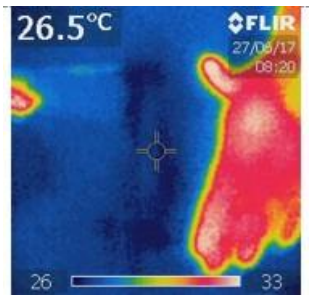


Fig. 4
Initial temperatures distribution

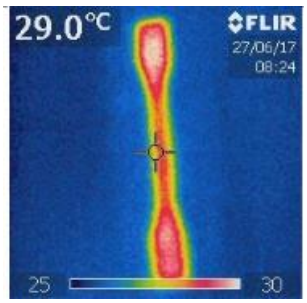


Fig.5
Temperatures distribution after 4 min

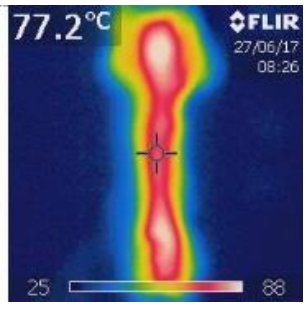


Fig.6
Temperatures distribution after 6 min

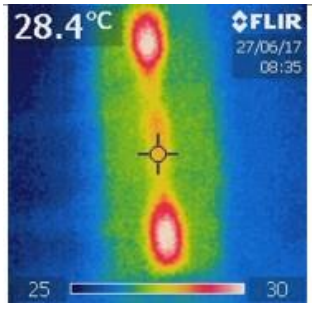


Fig.7
Temperatures distribution after 15 min

Importance in Medical application:

I. In vivo temperatures reach no such high values, around $44^{O}C$-$47^{O}C$.

II. The safe time interval "between the cement preparation and the insertion in the prosthetic joint" can be estimated by monitoring the specimen's temperature, keeping into attention that the increasing viscosity of the material"becomes more difficult to shape".

3. *The tensile test on PMMA* was performed with Lloyd Instruments equipment "capable of supporting application forces up to 50 kN". PMMA Tensile test information was collected (fig.6) for reliable data processing. All specimens were tested until destruction occurred when reaching the breaking point of the cement. The values of the parameters (forces and breaking points) during tensile test were recorded for all the specimens. Some previous tests and studies "claim that specimens have similar characteristics during tensile and compression tests [52], while others show that cement is weak in tension and strong in compression. Thus, the tensile load should be carefully monitored in order to avoid joint loosening." [53].

The tests "can only give a rough idea of the quality of the cement especially as their properties change under physiologic conditions (body temperature and fluids) and in so far the clinical relevance of test standards must be challenged" [54].

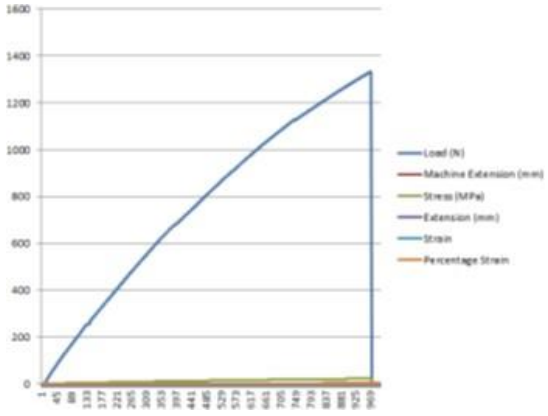


Figure 8 Specimen during tensile testing **Fig.9** Tensile testing in graphic (mechanical characteristics)

Strain value is proportional to the load along the entire elastic zone. "The average breaking load was 1334.3N for an extension of 0.02mm and maximum stress of 22.23MPa. Although, as expected, the material is not elastic, the breakage occurs suddenly for relatively high values of the load." Therefore, the breakage values are improbable to be reached during routine rehabilitation therapy. However, physiotherapists should be aware of the limits of pressure and stretching of the bone cement and consequently to "avoid applying loads comparable to the bodyweight". Furthermore, the dynamic exercise exerts a higher pressure on the cement bridges than the static (as in vitro experiments

showed). Therefore the duration of the physical therapy should be carefully monitored (long duration multiplies partial pressures with the number of loads).

The experimental research focused on thermomechanical behaviour of polymethylmethacrylate (PMMA) representing the most used acrylic cement in joint replacements confirmed that "the material is not elastic, the breakage occurs sudden for relatively high values of the load". As per the primary concern in several types of joint replacement represents "the exothermic polymerization reaction, the monitoring by a thermo-vision camera" may provide information for an extensive database in the aim of optimal control of the procedure and reducing the patient's risk to zero: the safest time "between the cement preparation and the application on the prosthetic area, reducing the risk of BCIS (bone cement implantation syndrome)".Physical therapy before and after the surgery is mandatory, carefully following to perform exercises at low load, "by avoiding the suspension of the entire body on the arms, tractions or lifting heavy weights (in case of shoulder surgery) and also the suspension using ankles (in case of hip or knee surgery)".Further researches are welcome to study in vivo relation of the stress-load curve of PMMA or in vivo/in vitro study for other types of cement used in joints replacements. Further studies might strengthen the interdisciplinary teams of technical and medical specialists to approach other subjects in applied sciences.

I.b.2 Innovative materials and technologies used in the manufacture of assistive devices used in rehabilitation

"3D printing offers many possibilities for developing new medical devices" particularly orthosis and prosthesis manufacturing to compensate people with disabilities.

The most used techniques for medical devices manufacturing are Fused Deposition Modelling and Stereolithography. The most used biomaterials are polymers and de organic componence properties, polylactic acid or acrylonitrile butadiene styrene. *("**Roxana Miclaus**, Angela Repanovici, Nadinne Roman, Biomaterials: Polylactic Acid and 3D Printing Processes for Orthosis and Prosthesis, Revista Materiale Plastice, vol 54, nr1/2017, pag 98-102, (2017)"*) [55].

Prosthesis and orthosis devices manufacturing success depends on considering the design and the cost of these, nevertheless the specific and individual factors related to disability and social status and the necessity of increasing the patients' life quality.

3D printing aspects of these devices are associated to the adequate quality of material, especially to be suitable especially for prolonged contact with the patient's skin.

"Polymeric bio-composite materials are nowadays widely used in manufacturing processes, for daily objects or in the automotive industry, in the high-tech sector, but also in the medical fields, related to medical devices bio-engineering. Composite materials, including natural sources (like

wood), have significantly developed in recent years in bio-engineering and the medical area. They offer weight reduction, add functionality and occupational health benefits also preserve the environment. Wood fibre has a low-density structure, is a low-cost material and is a biodegradable element attracting the scientist's attention during the last decades but it seems that the principal disadvantage of the wooden fibre reinforcement is represented by the structure's hydrophilic nature when compared with carbon or glass fibres".

When incorporated in composites, wood becomes more suitable for biomedical use, increasing its mechanical strength and decreasing the risk of changing its structure once introduced into the body or in contact with the body through its hydrophilic property.

The prosthesis or orthosis prescription and training is the objective, method, and job of Physical medicine and rehabilitation. Collaborating with orthopaedists and biomechanics specialists, bioengineers, the complex rehabilitation team has the most ethical mission in medicine: to treat and assist "body impairment to orthopaedic trauma sequelae, congenital disorders of the musculoskeletal system and other movement dysfunctions". Additionally, rehabilitation aims to increase life quality and reintegrate the people into society and labour. [56]. "In the medical rehabilitation field, the recovery of motor function is the major objective. With the active orthosis, simple orthosis or external prosthesis, rehabilitation or physical therapy treatment objectives are much more achievable, but the proper rehabilitation device is crucial for recovery". [57-59].

Nowadays, "prosthesis and orthosis manufacturing is overgrowing due to 3 D printing processes and devices, computed aided design software", and biomaterials development. However, "they are also constantly subjected to dynamic shock stress due to daily activities or even accidental".

Therefore, these researches aimed to identify the leading "3D printing methods and the biomaterial properties proper to be used in orthosis and prosthesis manufacturing" and highlight medical application in prosthesis and orthosis devices manufacturing and the benefits and concerns related to biomaterials use.

3D Printing of Biomaterials

Basically, "three-dimensional printing (3D) is layered manufacturing, rapid prototyping or solid freeform fabrication represents the direct fabrication of parts, layer-by-layer, guided by digital information from a computer-aided design file, without any part-specific tooling" [60].

The table summarizes the principal 3D printing process used globally, considering the most critical factors influencing the finishing of the prototypes, the materials used and the costs: the size of printed pieces, the materials properties, and the manufacturing equipment. Also, the advantages and disadvantages of each technology were pointed out.

Biomaterials are organic polymer composite used in orthosis and prosthesis 3D printing

Properties of biomaterials recommend them for medical applications and biomedical devices, as per advantages advocated by researchers: "more compliant with biological tissue than metal and ceramics; strengths of the same magnitude with hard tissue and the mechanical and biological properties are closer to the hard biological tissue; design variability[61]; low risk of toxicity, autoimmune response and the infection, being suitable for degradation process is proportional with the length of polymer chains and the molecular weight (the higher molecular weight leads to slower degradation due to lengthy polymer chains)" [62].

Polylactic acid (PLA) characteristics:

a. PLA "is biodegradable and has similar characteristics to polypropylene (PP), polyethylene (PE) or polystyrene (PS)".
b. "The mechanical properties of PLA may vary from stiff, high-strength materials to soft, elastic materials, determined by different parameters such as polymer structure, molecular weight, material formulation (blends, plasticizers, composites) and orientation".
c. Originally known as a "brittle material, lower impact strength and elongation break, similar to polymer- polystyrene" [63].
d. "PLA is a versatile polymer made from renewable agricultural raw materials fermented to lactic acid" [64].
e. PLA has a "chiral character and are several different forms of polylactide. Poly-L-lactide (PLLA), L-lactide (also known as L-lactide). PLLA has a melting temperature of 173–178°C" [61]. In the case of the chiral lactide monomer, polymer molecular weight and stereochemistry have dramatically affected the physical properties of the polymer. Crystallinity and "thermal properties may also be controlled by polymer blending" [65].
f. "The melting temperature of PLLA may be raised by 40–50°C, and its heat deflection temperature can be raised from approximately 60°C to up to 190°C by physically blending the polymer with PDLA (poly-D-lactide)".

Table 13 3D printing processes and materials [55]

Technology	Process	Material type	Advantages and disadvantages
FDM – Fused Deposition Modeling	The device has a movabile head which deposit a thread of molten materials onto a substrate. The builted material is heated with 0,5 degrees after its melting point, so that it solidifies after 0,1 after extrusion and cold welds to the previous layers.	Structural and biopolymers, ceramic-polymer, or metalpolymer composites: ABS (acrylonitrile butadiene styrene), PLA (polylactic acid), PVA (soluble), PC (polycarbonate), polyethylene HDPE, polypropylene, elastomer, polyamide, tricalcium phosphate	Advantage – Easy to use, large variety of cheap, non-toxic materials, affordable price for printing machines and materials
			Disadvantage – Material restriction related to thermoplastic polymers - Low construction speed -Areas may appear uneven

SLA – Stereolithography –	**The use of a laser beam with UV light for solidifying a liquid photopolymer resins located inside the construction printer`s tank.**	**Photo-curable polymers, or a composite mixture of epoxide resins and cationic photoinitiators, including PLA**	Advantages: oversize pieces manufacturing, high temperature resistance
			Disadvantages: -Polymers used in 3D printing must have a low volume shrinkage at polymerization, for avoiding the solid object distortion. -The surface not well finished -High price of device - It must be studied and developed further biocompatibility in medical use
DLP – Digital Light Processing –	**Liquid resins solidified by UV light, based on a Digital Micromirror Device(DMD)-mirror modulation matrices for shaping light in space**	**Resins, photopolymers, transparent resins, polymer-based wax**	Advantages: Accuracy and finishing printed parts is high - wide range of biomedical materials including resins (certified for use in the medical field)-including PLA
			Disadvantages: High cost devices
SLS – Selective Laser Sintering	**It uses a high power laser beam for sintering powder in layers thereby achieving the desired 3D model.**	**powders (thermo) plastic (nylon, polyamide, polystyrene, elastomers, composites), powdered metal (steel, titanium alloys), ceramic powders, glass powders**	Advantages: Accuracy and finishing printed parts is very high - wide range of materials - construction`s geometries very complex without material support, - It requires no post processing operations
			Disadvantages: -High cost devices -expensive material printing -average finish area (compared to SLA)
SLM – Selective Laser Melting / Direct Metal Laser Sintering –	SLS technology sub-branch SLM metal powders used as building material are melted and welded together using a high-power laser.	metal powders	Selective Laser Melting rather be framed in the field of rapid prototyping devices than in that of 3D printing.
3DP – Three dimensional inkjet printing	It uses inkjet printing technology for powder solidification. The powder is inserted in the printer construction room and the particles are bonded with a binder material.	powder composed of a synthetic polymer polylactide–coglycolide or poly-PLA with organic solvent as binder natural, polymer powder, polyethylene glycol (PEG),	Advantage - Easy to incorporate and direct control both drug and biomolecules (proteins and living cells) -No limitations on macroarchitecture -Great range of materials
			Disadvantages: - Post-processing may be needed for some materials. - Layer thickness must be greater then porogen particle size -Use of organic solvents as binders Costs: depending on production, for industrial manufacuring is high price
LOM – Laminated Object Manufacturing	**The 3D object is manufactured using laminated paper or plastic materials, bonded and cut with a laser or knife.**	**Plastics, composites, ceramics, metals and various organic and inorganic materials with different chemical and mechanical properties**	Advantages: low cost materials -used primarily for creating scaled models and conceptual prototypes that can be tested for form or design.
			Disadvantages: usually used only on prototypes, because is doesn't create accurate models

PJP – PolyJet Printing	**Another additive manufacturing od napkin pads, somewhat similar to stereolithography (SLA) because it uses all photo-solidify a liquid photopolymer. PolyJet technology is similar with regular inkjet printing technology.**	**Photo polymers of various types (rigid, malleable, transparent, opaque, biocompatible elastomers)**	Advantages: Wide range of materials with different mechanical properties Accuracy and finishing printed parts is very high Disadvantages: Tracks do not withstand high temperature; rather large cost of building material economically inefficient for larger pieces. Cost: dependent on production, for industrial manufacturing is high price
Robotic assisted deposition/robocasting	**Direct writing of high solids loaded slurry. Good for a variety of ceramics and ceramic-polymer composites.**	**Hydroxyapatite(HA)/PLA, HA/PCL, and bioactive glass (6P53B)/PCL**	Advantage – Good for ceramics Disadvantage – May not be useful for different materials
Laser-assisted bioprinting	**Coating the desired material on transparent quartz disk (ribbon) → Deposition control by laser pulse energy → Resolution control by distance between ribbon/substrate, spot size and stage movement**	**HA Zirconia HA/MG63 osteoblast-like cell Nano HA Human osteoprogenitor cell Human umbilical vein endothelial cell**	Advantage - Ambient and mild condition is suitable for organic and inorganic materials and cells. Disadvantage - Homogeneous ribbons are needed.

PLA in biomedical applications concerning orthosis and prosthesis

1. PLA is "the most commonly used, so it was massively modified by incorporating different organic and inorganic components".
2. PLA "has a slow degradation rate providing the opportunity of long-term orthopaedics implants" production.
3. PLA has crystallinity (different configuration polymers from alfa, beta and gamma forms), with a wide melting interval (from 185,175 and 235°C).
4. PLA has a hydrophobic nature and decreases the PH of surrounding tissue when it degrades in the body, therefore in practice, "it change into polymers with a more hydrophilic nature, which degrades into fewer acid products".
5. "PLA combined with Bioactive Glasses (BG-40%), Carbonated apatite (30%), HA (50%), Calcium phosphate (50%). Halloysite nanotube (10%) offers bioactivity and neutralize the acidic degradation.
6. PLA combined with Polyurethane (PU-50%), Poly-caprolactone (PCL) (50%), PEG (20%), and offers mechanical performance" [62].

Orthosis manufacturing

A. The roles of orthosis, compensating an impairment are: "to use a low power setting; to allow patient to use his muscle power with rehabilitation device; to improve gait performance for persons with impaired lower limb function [65]; to optimize the support of a limb [65]; to prevent the excessive movement of at least one body part and still, to enable the natural movement for the healthy body parts".
B. An orthosis is used in rheumatology, traumatology or neurology, to compensate for a deficiency (stroke, multiple sclerosis, spine traumas, etc.) They are "braces for peripheral nerves dysfunctions with muscle altered function" or assist inflammatory processes, dysfunctional upper and lower limb.

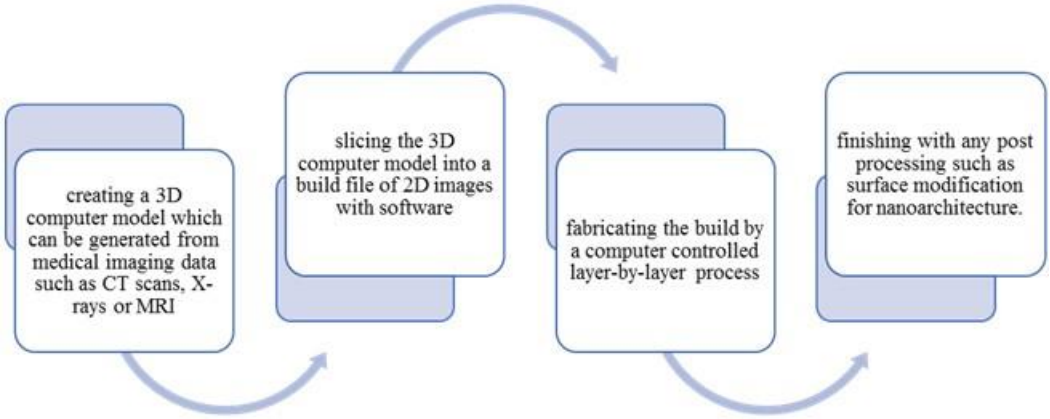


Figure 10 3D printing process

The manufacturing process follows the next steps:

1) the impaired body part is "dynamically scanning in different positions, usually using computer tomography, magnetic resonance imaging and laser scanning" [66, 67];
2) the analysis "of the plurality of scans to identify the unnatural position or motion impairment" of the body part [66];
3) obtain the digital negative model than create the orthosis shape using a design software;
4) design and create the personalized orthosis "with different types of 3D printing devices and processes" [68].

Many authors tried different materials and tested the quality of orthosis manufactured in different conditions:

a. Researchers showed that "the best mechanical damping characteristics are registered by Rilsan™ D80 (best)(polyamides), followed by DuraForm™ PA and DuraForm™ GF (worst) [67], but the thermoset materials used in orthosis manufacturing (resin, matrix and promoter) are lightweight and stronger" [68].
b. Creating a hand orthosis need a good design and production "using the 3D printing process, by offering a high degree of comfort and tolerability". In addition, clinicians have

the opportunity "to indicate pressure zones and create fully personalized orthosis, enabling the therapeutic indications in medical rehabilitation".

c. "An ankle-foot orthosis used to correct the prone foot reveals that foot type orthosis has a significant role in the muscle activity of biceps femurs, vastus lateralis and vastus medialis".
d. Personalized orthosis still might "affect pressure distribution in several patients, although even if the changes in pressure were small and it is not known if it has clinical relevance".

"CAD software is not yet sufficiently developed for use in clinical therapy" being necessary to be improved for a proper assessment and 3D printing of orthosis [68].

Secondary research regarding the use of polymers in the manufacture of the assistive devices was focused on a serial of instrumented impact tests using a "testing machine Instron Dynatup impact system" (including "an impact force transducer and falling mass velocity detector to capture load vs time information") with data acquisition and control, model 8200.

"The working principle is based on the fact that this absorbs the energy until it yields when the striker impacts the specimen. When the specimen cannot absorb more energy, fracture occurs". (*"Constantin Opran, Diana Cotoros, Nadinne Roman, Angela Repanovici, Roxana Miclaus, Research Regarding the Impact Behaviour of Some Polymeric Bio-composite Products for Orthopaedic Use MATERIALE PLASTICE, (2017))"* [69].

"Experiments were performed on materials made from polymeric bio-composites fibre reinforced wooden beech and polymeric bio-composites fibre reinforced wooden fir", and the measure was 150x100x15 mm. The used system is a "fully integrated electronics and software package that increases impact testing productivity through automated data acquisition, analysis and reporting".

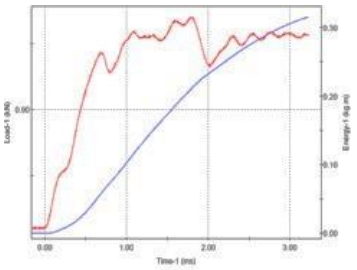
"Data collected by the impulse system was organized, analyzed and displayed both graphically and numerically based on PC software. Analysis options include automatic yield and failure point calculations and digital filtering to screen out load cell resonances and noise. Test data were exported to spreadsheets and charts for the bio-composites fibre reinforced wooden beech (figure 11) and the polymeric bio-composites fibre reinforced wooden fir material" (figure 12). "The charts show the following graphs: blue line - for variation of energy E in [kgm] and the red line – for variation of load F in [kN]. The impulse console is designed to provide intelligent test setup and control with a very flexible interface. Real-time data are displayed while providing access to test setup controls, the digital display indicates user precisely what the current settings are, including test drop height, velocity, and impact energy. The used impact mass was m = 3.94 kg. The significance of the notations are as follows: H in [mm] - the sample drop height; v - the impact velocity in [m/s]; E - the total energy in [Kgm]; and W is the total energy in [J]".

"Impulse utilizes an impact force transducer and falling mass velocity detector to capture load vs

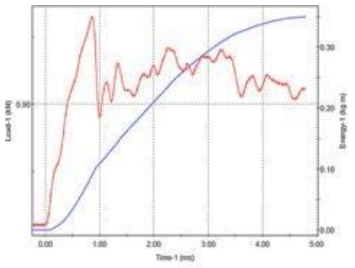
time information from instrumented impact tests".

"Table 14 presents the experimental results collected for five samples from polymeric bio-composites fibre reinforced wooden beech. Table 15 shows the results for samples made of polymeric bio-composites fibre reinforced wooden fir material".

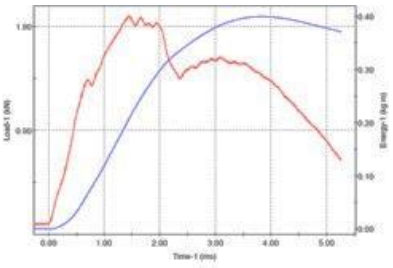
Photographs of "polymeric bio-composites fibre reinforced wooden beech and polymeric bio-composites fibre reinforced wooden fir" were taken at the moment zero of tests and after performing the impact tests for better visualization and evaluation of resistance to impact. The materials behave very differently at high rates of loading.



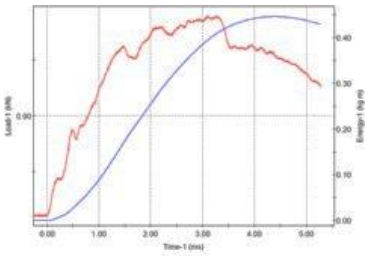
a) Sample 1, H=50 mm



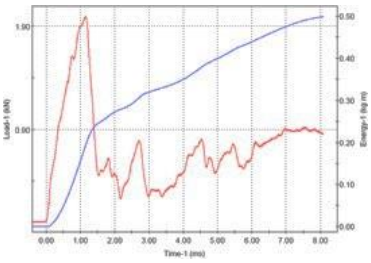
b) Sample 2, H= 60mm



c) Sample 3, H=70mm

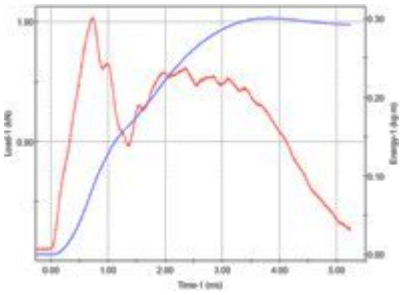


d) Sample 4, H=80mm

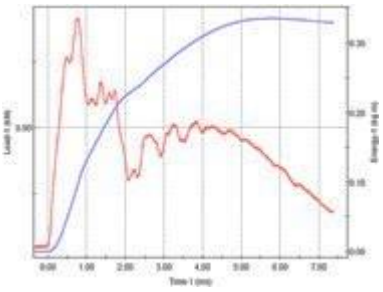


e) Sample 5, H=90mm

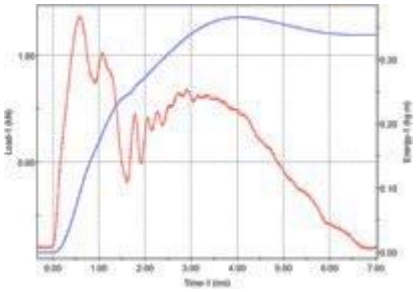
Fig. 11."Polymeric bio-composites fibre reinforced wooden beech samples' charts" [69].



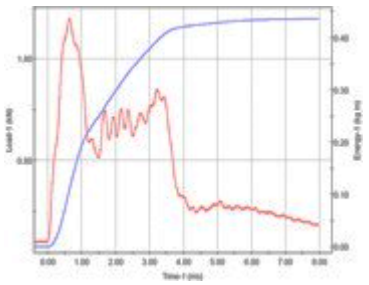
Sample 1, H=50 mm



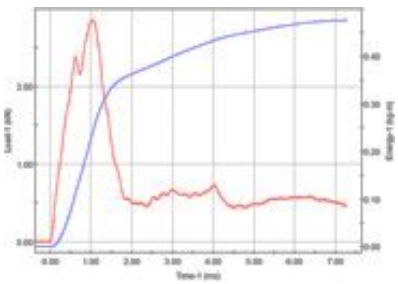
Sample 2, H=60 mm



Sample 3, H=70 mm



Sample 4, H=80 mm



Sample 5, H=90 mm

Fig. 12."Polymeric bio-composites fibre reinforced wooden fir samples charts" [69].

Sample	Characteristics					Results Type of the impact
	m [kg]	H [mm]	v [m/s]	E [Kg m]	W [J]	
1	3.94	50	1.0452	0.3156	3.0941	Without break
2		60	1.0962	0.3493	3.4245	Without break
3		70	1.1963	0.3712	3.6392	Without break
4		80	1.2720	0.4287	4.2029	Without break
5		90	1.3731	0.4985	4.8872	Without break

Table 14 "Polymeric bio- composites fibre reinforced wooden beech-experimental results" [69].

Sample	Characteristics					Results Type of the impact
	m [kg]	H [mm]	v [m/s]	E [Kg m]	W [J]	
1	3.94	50	1.0096	0.2920	2.8627	Total break
2		60	1.0952	0.3298	3.2333	Total break
3		70	1.1900	0.3371	3.3049	Total break
4		80	1.2812	0.4360	4.2745	Total break
5		90	1.3388	0.4758	4.6647	Total break

Table 15 "Polymeric bio- composites fibre reinforced wooden fir – experimental results" [69].

In figure 13 and in figure 14 "the diagrams of height variation on impact speed and energy for polymeric bio-composites fibre reinforced wooden beech are presented, while figure 15 and figure 16 show diagrams of height variation on impact speed and energy for polymeric bio-composites fibre reinforced wooden fir".

The standard impact test method "represents an essential tool for raw material research and quality control. When the total energy, W [J] accumulates in time and then increases, it achieves a level of constancy", which proves that the bio-composite polymeric material absorbs it. This property opens the possibility of various applications for "bio-composite polymers and especially in the medical field, as developing new models of equipment and instruments used in medical rehabilitation, as the biomaterials meet both conditions: nontoxic properties and biodegradable materials".

Orthosis manufacturing is applying several 3D printing technics and technology, also using many biomaterial types. Applications in the medical field are encouraging, still young in reaching high quality and reliability, and need further investigations.

The research unlighted as well the essential benefits of biomaterials as the disadvantages. 3D printing applied in medicine is an innovative and prospective area with extensive research and innovation potential. 3D printing of prosthesis and orthosis can be the future affordable solution for each patient in order to receive the best and personalized medical rehabilitation treatment, at the newest well-being standards, assessed and progressed into a solid and functional multidisciplinary team, united for the best interests of the patients: improving the patients and conditions quality of life. Using "3D printing devices in orthosis manufacturing procedures,

physical medicine and rehabilitation can improve medical services and actions and develop new technologies and functional devices collaborating with design engineers, materials or biomaterials engineers, and computing software technology specialists".

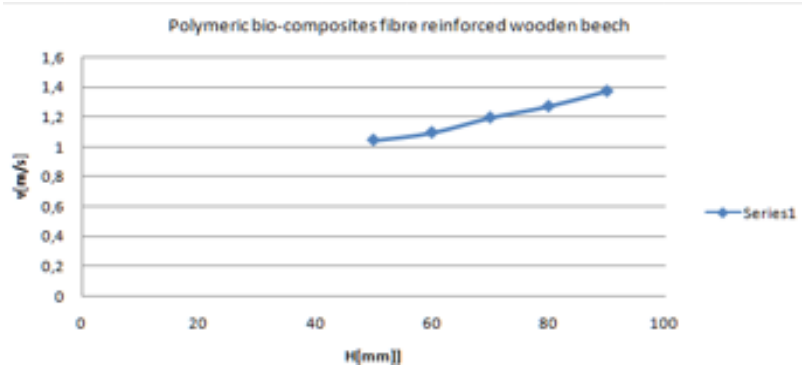


Fig. 13. "Chart speed depending on the height of impact for polymeric bio-composites fibre reinforced wooden beech" [69].

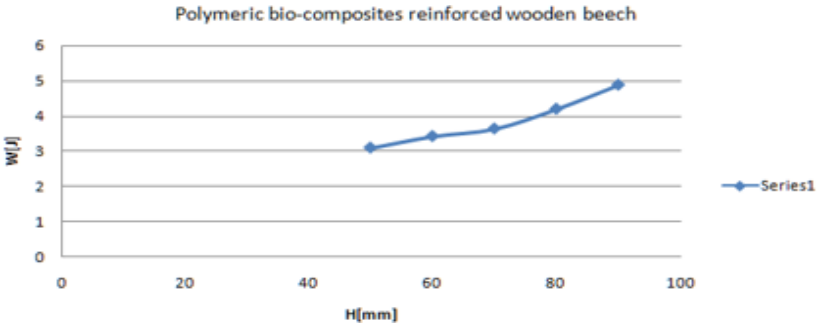


Fig. 14. "Chart total energy depending on the height of impact for polymeric bio-composites fibre reinforced wooden beech" [69].

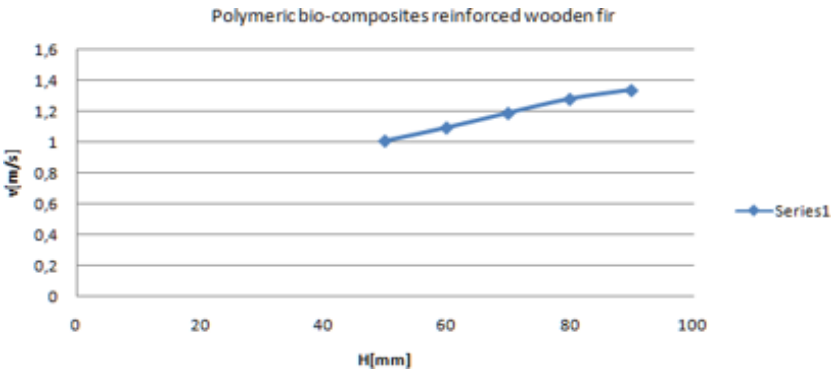


Fig. 15. "Chart of speed depending on the height of impact for polymeric bio-composites fibre reinforced wooden fir" [69].

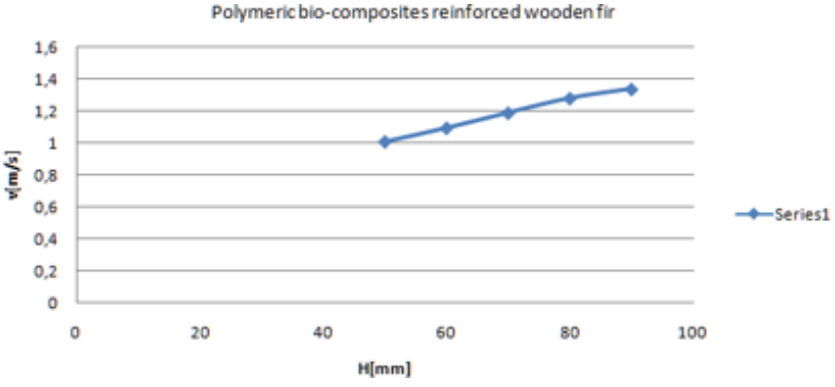


Fig. 16. "Chart of total energy depending on the height of impact for polymeric bio-composites fibre reinforced wooden fir" [69].

For polymeric bio-composites fibre reinforced wooden beech specimen, break type shreds of evidence "low dependence on the drop height, as for h: 50-90 mm there is no breakage. For polymeric bio-composites fibre reinforced wooden fir specimen, we observed that h = 50-90 mm relevant failure occurs" for the same drop height. "Polymeric bio-composites fibre reinforced wooden beech material proves good elasticity compared to polymeric bio-composites fibre reinforced wooden fir" material. The polymeric bio-composite fibre "reinforced wooden beech and polymeric bio-composites fibre reinforced wooden fir materials behave differently at different loading rates". That is why static strength tests cannot be the basis for impact behaviour prediction for orthopaedic prostheses manufactured to be used and resist in dynamic conditions.

I.b.3 3D printing materials reusable in pandemic context

This paper addresses an essential issue regarding the use of medical supplies in a pandemic. It attempts to identify the usability of 3d printing possibilities for the use of respiratory masks, which can be further sterilized using specific hygiene legislation and methodology. *("Nadinne Roman, Dan Cojocaru, Claudiu Coman, Angela Repanovici, Santiago Ferrandiz Bou, Roxana Steliana Miclaus, Materials for Respiratory Masks in the Context of COVID 19 Pandemic, Materiale Plastice, 57 (4), 2020, 236-247; (2019)")* [70].

Since January 21, 2020 World Health Organization [WHO] started to make reports on the Novel Coronavirus [2019-nCoV]. WHO China Country Office reported the first cases of unknown aetiology pneumonia beginning with December 2019 [71]. Declaration of COVID-19 infection pandemic on March 11, described as "spreading from China worldwide and being confirmed 118,319 [80 955 in China] infections at that date" [72], the number of cases and deaths rapidly increased worldwide. On March 23, 2020, the confirmed cases with "COVID infection reached 362,051 cases, with 15,496 deaths and 100,657 recovered patients" [73].

The spread of the pandemic has been rapid in Europe, especially in Italy, France, Spain, and worldwide. As a result, medical systems are facing a significant health crisis in terms of disposable protective materials [71]: gloves, surgical or respiratory masks, goggles, face shields, gowns, and disposable protective materials for covering the head, neck, and lower limbs, including the feet [74].

The health systems and the population needs regarding respiratory protection masks in the summer of 2020 were outnumbered [72]. Thus, the shortage of protective materials is accentuated and generates a global health crisis.

Starting from the experience of producing prostheses, orthoses, implants, and artificial organs that have revolutionized medicine and come to the aid of thousands of people, many manufacturers have started to manufacture face shields and protective [respiratory] masks to support the medical

systems, using 3D printing. The materials used in 3D printing play an essential role because their properties make them suitable or not for various applications such as industry, mechanics, and, last but not least, medicine. Unfortunately, one of the companies that manufacture respiratory masks uses nanomaterials that are expensive and inaccessible.

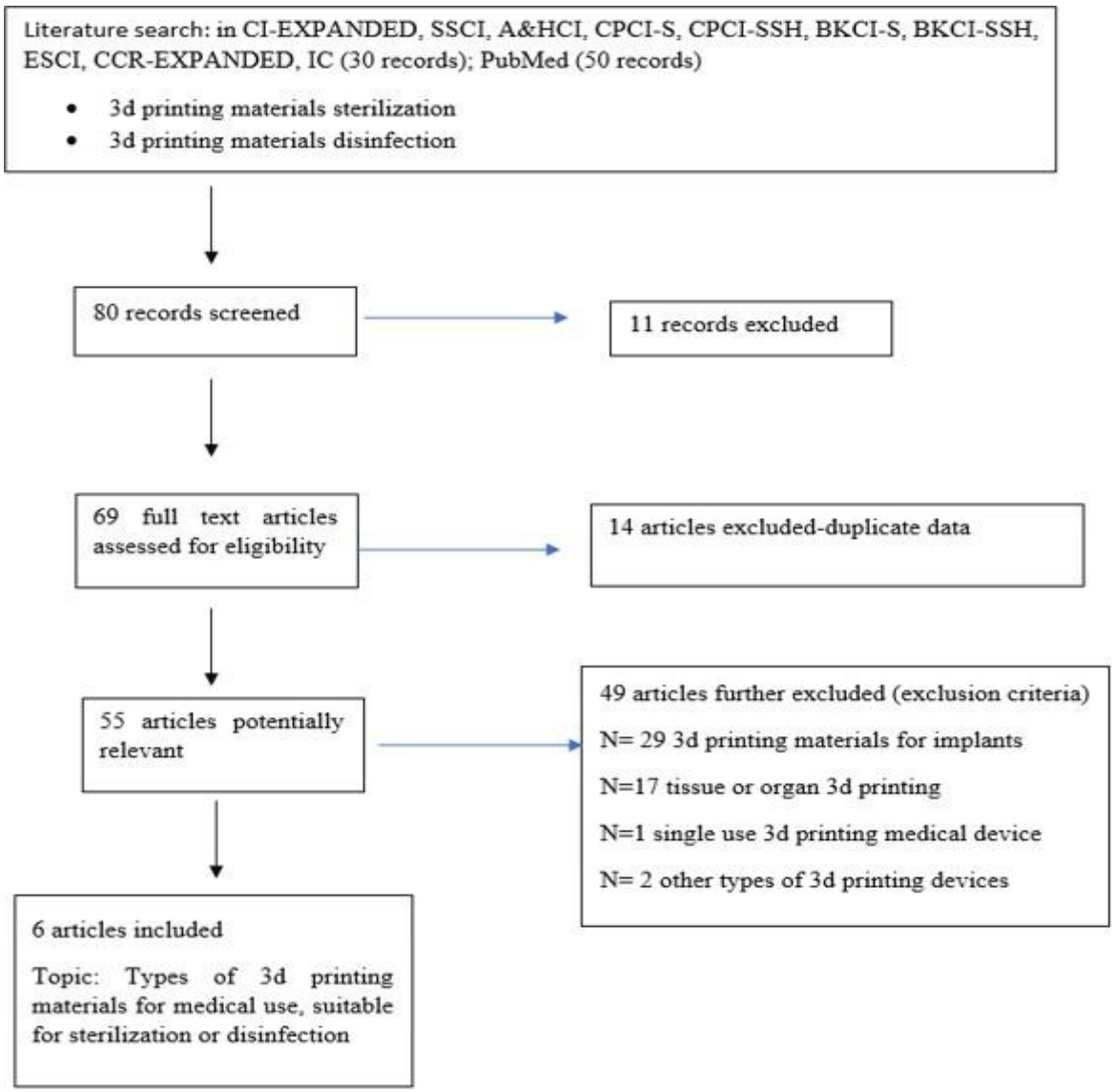
This study aimed to identify the primary materials nowadays used in 3D printing, their properties, and the possibility of sterilization or disinfection, especially multiple sterilizations, while preserving the properties of medical protection. In the context of the COVID-19 pandemic, two authors were actively involved in the epidemiological chain of planning and treating patients with COVID. I worked actively in COVID19 ward in my hospital, being preoccupied to help patients in treatment and caring and nevertheless improving the working condition in COVID pandemic: lack of materials, the stress of contamination, respecting the rules and regulation of prevention and high quality of medical treatment. We have also searched for manufacturers' information regarding 3D printing materials sterilization or disinfection. As a result, we have found seven materials that are suitable for 3D printing and sterilization with regards to multiple utilizations.

CI-EXPANDED, SSCI, A & HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, ESCI, CCR-EXPANDED, IC, and PubMed databases, were searched, using keywords such as: "3D printing materials sterilization" and "disinfection of 3D printing materials". From 80 results in databases, after refining, we selected six papers. Finally, the results obtained and the refining methods articles were selected.

Analyzing the properties and recommendations for sterilization of elements obtained by 3D printing, a thorough filaments structures/behaviour research for most of the 3D models for printing is needed regarding synthetic polymers suitable for 3D printing; also, to establish the physical and chemical properties resulted after the reactions with sterilizing substances.

The article debates all the particularities of the seven most essential materials suitable for 3D printing of masks (physical, chemical, biological properties, especially biocompatibility and biodegradability), revealing the advantages and disadvantages of medical and biomedical use on ***sterilization and multiple sterilizations***. We analyse the characteristics of Polylactic acid [PLA] and polyethylene terephthalate glycol-modified [PETG] [75], Polypropylene [PP], Nylon, Elastic material (Flex), Polycarbonate / Resins [ASA (Acrylonitrile styrene acrylate)/ABS], Chlorinated polyethene [CPE], High Impact Polystyrene [HIPS]. We conclude that dry heat sterilization is presently banned in the European Union hospitals since sterilization by radiation is used in the food and medical device industry, even considered not fitting for use in hospitals. It is recommended to avoid ethylene oxide, as it causes alterations in the polymeric structures. In opposition, sterilization at a low temperature with hydrogen peroxide produces no toxic residues on the sterilized pieces, so it is prompt, reliable. It does not demand aeration time requested by ethylene oxide [76].

Figure 17 Scientific literature survey [70].



The main advantages of polypropylene are firm, resistant, and relatively inflexible. With a small weight, mechanical properties even at high temperatures proved to have an outstanding performance related to cost. It has remarkable mechanical and breaking strength; it can be used at the autoclave or steam- sterilized and has excellent dielectric features.[77]

Steam sterilization can also be used to sterilize polypropylene and ethylene oxide since no significant modifications in properties were observed after one or three cycles.

The exposure of polypropylene to gamma radiation for sterilization is preceded by stabilization with free radical scavengers to prevent discolouration and alteration. Because polypropylene maintained its stability after radiation exposure and accelerated ageing at 80°C, the stabilized polypropylene supports after nine weeks of almost 80% of its quality, compared to a standard not stabilized polypropylene loses 80% of its properties after nine weeks.

Nylon 680 material maintains a slippery nylon surface, as required by medical and industrial use. It is compatible with ethylene oxide sterilization at low temperatures and with sterilization using steam or boiling, meaning the sterilization methods that are used globally in scientific research laboratories. The material's compatibility with sterilization processes is a unique property of Nylon 680 material, and it is a rare material feature in the 3D printing industry. Thus, at the time of printing, Nylon 680 is processed at a temperature of 250- 255oC, with a melting point of 210oC. As far as the nozzle is concerned, nozzles of any size can be used. Thus, it is an excellent material for printing high-strength and functional 3D devices, more robust than **PLA and ABS**.

Elastic material (Flex) ensures ecological safety but also ensures complete biodegradability. Therefore, unlike various other plastics, the use of Flex is more rational and safer.

Chemical sterilization with formaldehyde and ethylene oxide of **ASA** (Acrylonitrile styrene acrylate) is not recommended. Also, exposure to high temperatures for a long time can reduce the life of instruments. Therefore, the use of purified or deionized water is strongly recommended. After sterilization, the instruments must be stored in sterile containers or rigid container.

Products made of ABS material can be industrially sterilized with gamma radiation. They can also be used for sterilization - plasma, oxidizing agents [hydrogen peroxide, chlorine dioxide or liquid sterilizers - glutaraldehyde]. Heat sterilization is also possible (steam, dry heat).

The following different procedures were selected for the disinfection and sterilization of CPE and **PET / PETG**: Plasma sterilization; Vacuum UV radiation and plasma-produced UV radiation Formaldehyde sterilizers; Gamma is electromagnetic, penetrating, nuclear radiation. [78].

Table 16 Selected articles (sterilization of 3D printed products) [70].

No	Title, Authors/Year	Material				Sterilization by	Observation
		PLA*	ABS *	PETG ***	PCL ****		
1	*On the intrinsic sterility of 3D printing.* Neches RY, Flynn KJ, Zaman L, Tung E, Pudlo N/ 2016. [5]	X				UV 15 watts germicidal fluorescent bulb [Philips, model G15T8]	There is no mention of the UV exposure time
2	*Reproducibility, Accuracy, and Effect of Autoclave Sterilization on a Thermoplastic Three- Dimensional Model Printed by a Desktop Fused Deposition Modelling Three-Dimensional Printer.* Boursier JF, Fournet A, Bassanino J, Manassero M, Bedu S, Leperlier D./2018 [6]	X				Autoclave sterilization	It is one-time sterilization, but it shows that PLA is compatible with autoclave sterilization
3	*3D printing surgical instruments: Are we there yet?*Rankin TM, Giovinco NA, Cucher DJ, Watts G, Hurwitz B, Armstrong DG. 2014 [7]	X				submersion in a glutaraldehyde solution concentration 2.4%, *p*H= 7.5 parameters: 20 min, 25° C	Supplementary fast protocols like "5 minutes submersion at 35C."are necessary
4	*Additive Manufacturing of Medical Instruments: A State- of-the-Art Review.* Culmone, C. Smit, G. 2019 [8]	X	X			Autoclave at 121 or 134 °C at 60 °C - PLA becomes soft at 88 °C - ABS deteriorates Low-temperature sterilization methods [below 60 °C] use Ethylene oxide gas (cycle of 12–24 h) and hydrogen peroxide gas plasma (cycle of 28–75 min)	PA 2200 *****polymer printed instruments will be sterilized by autoclave but only one time (not sufficient for solving blood contamination)
5	*How to Sterilize 3D Printed Objects for Surgical Use? An Evaluation of the Volumetric Deformation of 3D-Printed Genioplasty Guide in PLA and PETG after Sterilization by Low-Temperature Hydrogen Peroxide Gas Plasma.* Olivier Oth, César Dauchot, Maria Orellana, Régine Glineur. 2019 [9]	X		X		hydrogen peroxide sterilizer, low temperature (55 °C), one short cycle of 50 min	The best alternative in order to avoid the deformation of PLA and PETG 3D-printed objects (during autoclave)
6	*Effects of different sterilization processes on the properties of a novel 3D-printed polycaprolactone stent.* Antonio J. Guerra Paula Cano Marc Rabionet Teresa Puig Joaquim Ciurana. 2018 [10]				X	Step 1- submersion in a solution of 70% ethanol overnight Step 2 -washed two times with phosphate-buffered saline Step 3- exposed to UV light for 30 min There was no alteration of the properties	Ethanol is very effective for sterilization treatment (barely affected the material's properties)

Studies show that HIPS [High Impact Polystyrene] materials are compatible with ethylene oxide sterilization. However, five consecutive cycles of ethylene oxide sterilization will weaken the material. This is observed by decreasing the index of elongation at break. After repeated cycles of sterilization with ethylene oxides, the fragility significantly decreases so that the index of elongation at break after six months, respectively one year, is much lower than it was two weeks after sterilization.

Hydrogen peroxide is used to sterilize objects and materials that are sensitive to high temperature and heat. Compared to the sterilization cycle time for ethylene oxide [discussed above], which can be up to 18 h, some modern hydrogen peroxide sterilizers have a cycle of up to 28 min. Its vapours are also dangerous, targeting the eyes and respiratory system [76]. No information was found on how hydrogen peroxide affects HIPS materials.

The best method of sterilization is Gamma rays, as per a perfect penetrating capacity, being used as the ideal method to sterilize disposable medical equipment (syringes, cannulas, needles and other devices, especially those that cannot be sterilized with other methods). The duration of product exposure to radiation is 10 to 20 h, depending on the power of the source. There was also a slight increase in tensile strength with increasing doses of gamma radiation.

The new COVID-19 virus continues to represent a current global problem. It continuously causes disastrous effects on humanity in the economic, social and political fields. It puts more pressure on the medical system and public health policies, amplifying the risks to which the medical staff in healthcare is exposed [72]. Doctors trained in combating this virus are also facing, besides not knowing its behaviour, the lack of protective elements and elements necessary for the equipment to support and maintain human life in critical situations.

As a result, 3D printers have become an effective solution to solve existing problems partially, namely printing these missing elements by 3D modelling. However, even if the design and production of these objects were easily achievable, later, the problem of reusing printed elements that came in contact with a high-risk or contaminated infection environment was identified.

At the same time, as there is a need to reuse some printed parts, classical sterilization methods already known can be applied. Processing with saturated steam, hydrogen peroxide, ethylene oxide, electron beam radiation, gamma radiation, and others is suitable for sterilization. From the previous experience of the manufacturers of these parts for medical staff use, it has been proven that these methods are very effective for some types of material used in printing and others having harmful effects for others. Since the development of 3D printing, the domain of application has evolved significantly [101]. From the experience of making parts required during this period, both advantages and disadvantages of using 3D printers were identified.

Advantages are: (1) rapid mobility of production of the minimum required parts for protection models

at the expense of a large number of local volunteers, (2) flexibility to design new 3D models and print them, minimizing environmental pollution, involving large production systems, (3) the existence of databases on the Internet with different possible models to be printed without design intervention.

Disadvantages identified are the lack of minimum printing standards corresponding to certain quality levels and the lack of quality control of printed products from a company accredited in the field. Secondly, the multitude of 3D printers with their SOFTWARE components that impose specific model-specific processes when printing 3D parts is also a disadvantage. The use of different raw materials [PLA, ABS, PETG] and its manufacturer on the quality of printed parts, and the lack of structures dealing with the collection and the reuse of these products and which influence the short-term environmental pollution with printed parts for this purpose

Also, the risk of the inefficiency of the disinfection methods of the 3D models used is a possible disadvantage. There are some developing research directions to take into consideration to solve the limits of this research:

Q1: The mask must be able to filer the coronavirus, and the printed parts generally have tiny holes which will let the virus go through. How to sterilize these products?

Q2: Some kind of materials can be used for sterilization. The PETG or ABS can have sterilization effects?

Following the analysis of the advantages mentioned above and the disadvantages, we find a need for thorough research into the possibility of repeated sterilization of 3D printed objects and the most efficient methods to carry it out.

II. Cross-Disciplinary Rehabilitation Research

II.a. Stroke cross-disciplinary rehabilitation and assessment

II.a.1 Assessment in stroke rehabilitation

Before starting the rehabilitation program in post-stroke patients, it is imperative to perform a series of tests and assessments, to obtain a framework of the severity of the neuromotor impairments. The evaluation collects information about the patient by interpreting the assessments according to specific pre-established criteria to appreciate the degree of neurological degradation and disability of neurovascular patients is assessed using different scales used in neurorehabilitation. This study is linked to the translation, adaptation and validation of an internationally motor function assessment scale used in the upper extremity evaluation in post-stroke patients. ("*Nadinne Roman , Roxana Miclaus, Angela Repanovici, Cristina Nicolau, Equal Opportunities for Stroke Survivors' Rehabilitation: A Study on the Validity of the Upper Extremity Fugl-Meyer Assessment Scale Translated and Adapted into Romanian, MEDICINA, Medicina 2020, 56, 409; doi:10.3390/medicina56080409www.mdpi.com/journal/medicina;*" [79].

"Stroke is the third leading cause of disability worldwide". Lately, stroke mortality and disability incidence "has increased in low- and middle-income countries but has declined in high-income countries". [80].

Regarding the physical rehabilitation of patients with stroke sequelae, an adequate clinical and functional evaluation is essential for monitoring the sequelae, establishing an adequate plan of drug treatment and physiotherapy to decrease the degree of disability and regaining physical independence. Many evaluation scales have been developed at the international level to determine the level of disability, "the motor function of the upper extremity and the lower extremity, balance, cognitive function and speech, the severity of the stroke, somatosensory function, spasticity or depression".

The importance of using appropriate tools for assessing stroke patients for physical rehabilitation is primary for the development of selection criteria for rehabilitation and the selection and use of physiotherapy protocols on levels of disability and difficulty.

The majority of international guidelines and other research suggest that the Fugl Meyer Upper Limit Assessment Scale (UEFMA) represents a useful and valid tool with good psychometric properties to assess upper limb functionality after stroke. Previous studis validated UEFMA using

virtual reality technology through connection with Kinect sensor. [81, 82, 83].

Fugl-Meyer developed the initial UEFMA tool to assess motor function, balance, sensitivity and joint mobility. The complete form of the instrument has 113 items, and the subscale for assessing the upper extremity has 45 items, of which 33 related to motor function, and 12 to "joint pain and joint mobility. Each item of the evaluation scale can be marked at an ordinal level, from 0 to 2. Value 0 corresponds to the impossibility of performing a movement, and 2 represents the ability to perform" the movement entirely. However, the validity and reliability of the somatosensory balance and evaluation subscales have proven to be questionable, as they are not so reliable.

Originally in English and Swedish, UEFMA has now been translated and used in the USA, Italy, Netherlands, and Japan and validated in Danish and Colombian. [84, 85, 86, 87].

"Our research aimed to translate and validate UEFMA in Romanian" and test the reliability (reliability) test-retest and concurrent validity, taking into account the fact that the instrument is reliable. Its use internationally can analyze data related to "post-stroke rehabilitation in different countries and regions, with subsequent implications on post-stroke physical rehabilitation" worldwide. [88].

According to standard back and forth translation systems, the Romanian translation of the tool used and its cultural adjustment was conducted to manage the concept and scientific equivalents [89]. The first version of the evaluation scale has initially been examined and utilized by five physiotherapists, followed by a group study and analysis on understanding the details and agreement. The Fugl Meyer translation adaptations focused on the AII element, in synergy with the flexor; we thought clarification was needed, so "we added the words "palm upward" after the phrase "hand from the contralateral knee to the ipsilateral ear."

AIV3 element evaluates the pronation and the supination motions. "We accepted "to use the value of 30-40 degrees for shoulder flexion where "shoulder at 30◦ - 90◦ flexion" appears in the original text." Articles B3 and B4 describe the EU's initial position "with the elbow at 0" and slight shoulder flexion/abduction ". We have replaced" slight shoulder flexion/abduction "with" 20-30 shoulder flexion/abduction"."

We performed the pre-and post-therapy on patients with subacute or chronic post-stroke hemiparesis at least 6 weeks after stroke. To validate the tool used, we performed structural equation modelling (SEM); initially, "we performed an exploratory factor analysis (EFA), using Main Axis Factorization as the extraction method and Quartimax rotation with Kaiser Normalization". The Quartimax rotation was useful "because it maximizes the sum of the squares of the coefficients between the resulting vectors for each of the primary variables" [90]. Next, we explored the correlation matrix to identify assumptions because "all variables should correlate with at least one other variable, with $r \geq 0.3$. Finally, we checked the Kaiser - Meyer - Olkin (KMO) values and the Bartlett sphericity test, where KMO> 0.5 and Bartlett $p < 0.05$ considered as

appropriate values for EFA" [91].

Afterwards, a confirmation factor analysis (CFA) was performed using "structural equation modelling (SEM) and the least weighted square method for calculating estimates". [92] "Root Mean Square Residual (RMR) and Goodness-of-fit index (GFI), Normed-Fit Index (NFI) and Relative Fit Index (RFI)" were used as adhesion indices for the baseline comparison. We used Parsimonious Normed Fit Index (PNFI) to measure the parsimony. Index values are fitted "if RFI ≥ 0.9, GFI and NFI ≥ 0.95, RMR <0.08, while PNFI ≥ 0.80" [93]

Table 17. EFA (exploratory factor analysis) communalities and rotated factor matrix loading values for UEFMA (Upper Extremity Fugl-Meyer Assessment) items. [79].

Communalities			Rotated factor Matrix	
	Initial	Extraction	Factor	1
AII1	0.947	0.849	C2	0.907
AII2	0.917	0.756	B2	0.901
AII3	0.860	0.732	C1	0.890
AII4	0.823	0.675	B1	0.887
AII5	0.903	0.826	AII.8	0.879
AII6	0.922	0.785	B2	0.878
AII7	0.966	0.955	AII.9	0.869
90 AII8	0.937	0.842	B3	0.861
AII9	0.970	0.941	AII. 7	0.852
AIII 1	0.869	0.649	AII.6	0.847
AIII 2	0.918	0.754	AII. 5	0.832
AIII 3	0.895	0.744	AIV. 3	0.828
AIV1	0.898	0.763	AIII. 3	0.824
AIV2	0.929	0.777	AIII. 2	0.817
AIV3	0.858	0.740	AIV. 2	0.814
B1	0.926	0.820	AIV. 1	0.808
B2	0.945	0.888	D3	0.769
B3	0.905	0.801	C3e	0.768
B4	0.927	0.832	C3d	0.751
B5	0.750	0.576	AII.1	0.749
C1	0.957	0.895	C3b	0.746
C2	0.956	0.891	C3a	0.745
C3a	0.877	0.813	B5	0.744
C3b	0.937	0.808	D2	0.719
C3c	0.850	0.708	AII.2	0.710
C3d	0.936	0.862	AIII. 1	0.698
C3e	0.944	0.805	D1	0.696
D1	0.866	0.652	AII.3	0.695
D2	0.902	0.680	C3c	0.683
D3	0.815	0.692	AII.4	0.680

.

"Note: Each item corresponds to the numbering on the initial UEFMA scale in English".

The Cronbach Alpha index was used to determine "the internal consistency and the intraclass correlation coefficient (ICC) for test-retest reliability". "We used the Pearson correlation with the Functional Independence Measure (FIM) and the modified Rankin scale (MRS) to examine concurrent validity. We used a standardized response mean (SRM) to test responsiveness.

Regarding the exploratory factor analysis, the KMO value of 0.913 indicates that the data used were suitable for EFA, with $\chi 2$ from Bartlett's sphericity test of 2648.235 and p <0.001." Thus, a single factor was retained, so we considered the scale unidimensionality. Table 7 present the factor loadings values that emerged from the EFA.

"Alpha Cronbach's value suggests an important internal consistency. The ICC value suggests an excellent correlation regarding the first and the last evaluation. In contrast, the Pearson correlation index shows a significant correlation with the Functional Independence Measure (FIM) and the modified Rankin scale (MRS)". Moreover, "the responsiveness of the instrument used is powerful". Table 8 displayed the results.

Table 18. UEFMA reliability and responsiveness test results [79].

Intraclass Correlation Coefficient					Cronbach Alpha		Concurrent Correlation		Standardized Response Mean	
		95% CI		F Test	0.981		FIM	MRS	1.1171	
	ICC [b]	Lower Bound	Upper Bound	Sig	Mean	SD	Pearson/ Sig	Pearson/ Sig	95% CI Upper Bound	Lower Bound
Single Measures	0.984 [a]	0.974	0.990	<0.001	32.750	17.9718	0.789/ <0.001	−0.787/ <0.001	0.9394	1.2695
Average Measures	0.992 [c]	0.987	0.995	<0.001						

ICC: Intraclass Correlation Coefficient, CI: Confidence Interval, FIM: Functional Independence Measure, MRS: Modified Rankin Scale, Sig.: p, a- the estimator is the same, whether the interaction effect is present or not, b- type C intraclass correlation coefficients using a consistency definition-the between- measure variance is excluded from the denominator variance, c- the estimate is computed assuming the interaction effect is absent because it is not le otherwise

Table 19 present the coefficients of the model fit for CFA, conducted secondary to EFA".

Table 19. CFA (confirmatory factor analysis) model fit indices. [79].

Root Mean Square Residual	Godness of Fit	Baseline Comparisons		Parsimony–Adjusted Measures
RMR	GFI	NFI	RFI	PNFI
0.051	0.980	0.978	0.977	0.911

RMR: Root Mean Square Residual, GFI: Goodness-of-fit Index, NFI: Normed-Fit Index, RFI: Relative Fit Index and PNFI: Parsimonious Normed Fit Index. Note: Every item corresponds to the numbering on the initial UEFMA scale in English.

Table 20 display "the values obtained from the Bayesian modelling, with the regression weight values". "The values of the intercepts and the variation are attached to additional files. The convergence value was set to 1.002, and the results were obtained in (500 + 61,501) × 16 iterations."

"The results of our study correlate with previous research and strengthen the unidimensionality of the instrument used in the assessment of UE motor function and functionality". [94].

"Regarding the value of the coefficients obtained with EFA, the weakest factor loadings were the external rotation of the shoulder (AII4), thumb's opposition (pincer grasp, opposition) (C3c), shoulder abduction to 90 degrees (AII3), tremor (D1) and hand to the lumbar spine (AIII1). In CFA with Bayesian modelling, the lowest median regression weights were the factors related to 90-degree shoulder abduction (AII3), shoulder elevation (AII2) and shoulder external rotation (AII4), which confirm that the Bayesian ordinal CFA modelling is more robust than the EFA." [95].

Table 20. **Bayesian modelling of UEFMA regression weights values** [79].

	Mean	S.E.	S.D.	C.S.	Median	95% Lower Bound	95% Upper Bound	SkewNess	Kurtosis	Min	Max
Regression Weights											
AIV. 2 ← UE	0.906	0.005	0.122	1.001	0.904	0.678	1.154	0.201	0.100	0.514	1.420
D 3 ← UE	0.747	0.005	0.105	1.001	0.742	0.552	0.961	0.218	0.118	0.407	1.175
AII.8 ← UE	1.067	0.005	0.119	1.001	1.061	0.847	1.324	0.288	0.199	0.604	1.617
AII.4 ← UE	0.601	0.004	0.104	1.001	0.597	0.404	0.814	0.150	0.159	0.165	1.104
C3d ← UE	0.960	0.006	0.134	1.001	0.955	0.711	1.242	0.239	0.308	0.474	1.552
B2 ← UE	1.185	0.007	0.136	1.001	1.179	0.924	1.474	0.217	0.250	0.720	1.728
AIII.2 ← UE	0.972	0.006	0.124	1.001	0.969	0.736	1.230	0.281	0.619	0.552	1.595
C3.e ← UE	0.989	0.006	0.138	1.001	0.985	0.730	1.271	0.124	0.376	0.412	1.578
D2 ← UE	0.923	0.007	0.144	1.001	0.919	0.650	1.222	0.110	0.233	0.308	1.447
C3c← UE	0.739	0.004	0.119	1.001	0.735	0.516	0.981	0.175	0.107	0.323	1.258
C3a← UE	0.954	0.008	0.142	1.002	0.948	0.692	1.248	0.223	0.047	0.430	1.512
AII.2 ← UE	0.671	0.004	0.114	1.001	0.669	0.458	0.905	0.114	-0.070	0.292	1.084
AII.3← UE	0.594	0.005	0.102	1.001	0.591	0.400	0.801	0.179	0.353	0.188	1.027
AII.6 ← UE	1.088	0.005	0.129	1.001	1.081	0.850	1.355	0.233	0.202	0.626	1.629
AII.5 ← UE	1.088	0.006	0.128	1.001	1.083	0.850	1.353	0.198	0.033	0.633	1.571
AII.7 ← UE	1.063	0.004	0.123	1.001	1.061	0.826	1.316	0.176	0.372	0.607	1.586
AII.9 ← UE	1.145	0.006	0.125	1.001	1.138	0.921	1.406	0.359	0.321	0.737	1.691
AIII.1 ← UE	0.787	0.007	0.130	1.002	0.780	0.553	1.071	0.319	0.299	0.300	1.330
AIII.3 ← UE	1.006	0.005	0.121	1.001	1.000	0.788	1.259	0.339	0.298	0.631	1.571
AIV.1 ← UE	0.746	0.004	0.101	1.001	0.741	0.565	0.964	0.472	0.816	0.408	1.244
AIV.3 ← UE	1.014	0.005	0.129	1.001	1.013	0.766	1.277	0.118	0.107	0.543	1.474
B1 ← UE	1.198	0.007	0.134	1.001	1.193	0.946	1.484	0.238	0.313	0.731	1.788
B3 ← UE	1.036	0.006	0.125	1.001	1.032	0.804	1.299	0.218	-0.013	0.628	1.498
B4 ← UE	1.040	0.005	0.120	1.001	1.035	0.817	1.293	0.273	0.219	0.619	1.598
B5 ← UE	0.747	0.007	0.118	1.002	0.741	0.538	0.998	0.354	0.259	0.359	1.225
C1 ← UE	1.164	0.005	0.123	1.001	1.159	0.942	1.421	0.274	0.132	0.752	1.655
C2 ← UE	1,178	0.005	0.121	1.001	1.172	0.957	1.439	0.401	0.617	0.729	1.749
D1 ← UE	0,858	0.005	0.142	1.001	0.851	0.595	1.148	0.220	0.044	0.351	1.492
C3B ← UE	0,878	0.006	0.126	1.001	0.877	0.644	1.130	0.174	-0.009	0.484	1.401

S.E.: Standard Error, S.D.: Standard Deviation, C.S.: Convergence Statistics, UE: Upper Extremity. Note: Each item corresponds to the numbering on the initial UEFMA scale in English.

Following the use of UEFMA at the onset and completion of physiotherapy, we achieved related results with previous studies using ICC, which suggests that our version of UEFM, translated and with cultural adaptation, was performed properly. [88, 94]. The Cronbach Alpha value "is close to previous results related to the psychometric properties of UEFMA, which strengthens the results" achieved in our research on the instruments managed [95, 96].

"The test-retest reliability, simultaneous reliability and receptivity results of the translated and adapted instrument from our study validate its accuracy" [84].

The importance of transposing and adjusting clinical evaluation scales abroad is the main determinant in the improvement of the study and the formulation of a concise structure for the understanding of illnesses, inabilities and quality of life according to demographic, geographic and sociological criteria [97]. Regarding rehabilitation, it is likewise a valuable instrument in the hands of healthcare workers.

Accordingly, we estimate that "the translation, adaptation and validation of UEFMA" is a step ahead in its goal use, clinical practice and research" [98]. Furthermore, "The Romanian version of UEFMA is a stable, responsive and tested tool that can be used for motor function evaluation and upper extremity functionality in post-stroke patients".

II.a.2. Adapted Manual Muscle Testing for Assessment in Research and Chronic Post-stroke Patients' Rehabilitation

Working together in a small rehabilitation team (physician and physiotherapists), we realized that using standard methods or scientifically validated evaluation scales can be invaluable in maximizing the details of data collection and reducing the time for diagnosis and goal setting. In addition to establishing the elements related to disability, medical rehabilitation and physiotherapy evaluation includes objective and subjective evaluation modalities that allow achieving the clinical diagnosis and the functional diagnosis.

As awareness of the importance of evidence-based practice increases, researchers, clinicians, and physiotherapists need to be up-to-date on objective assessments and the effectiveness of rehabilitation assessment and therapy techniques. Objective evaluations can be achieved by correctly assessing research results or practice therapy results. Thus, correct and adequate measurement has enhanced an indispensable frame of the rehabilitation process. In addition, assessment is a method that provides a quantitative comparison of results. Nevertheless, the advantage of assessment in clinical research, clinical practice, and decision-making is conditioned on the extent to which clinicians and researchers can count on data with an accurate and significant indicator [99, 100].

Manual muscle testing (MMT) is an assessment tool used by rehabilitation physicians or physiatrists, physiotherapists, neurologists, and other clinicians who deal with the individual's functional status. The most frequently held perspective is that MMT attempts to assess the highest strength a muscle can produce.MMT emerged as a solution to assessing muscle strength impairments manifested "during the polio outbreak in the early part of the 20th century. The development of MMT links to Wilhelmine Wright and Robert W. Lovett, MD" [101-103].

Afterwards, in 1940, Florence Kendall and her husband improved the assessment technique by specific testing positions. The MMT is also known as "Oxford Scale or Medical Research Council Manual Muscle Testing scale". [104] MMT has a six points evaluation from 0 to 5.

Since MMT is a subjective assessment method, many previous research types found different conclusions regarding the use and reliability of this evaluation tool. The MMT protocol has to be very reproducible by each examiner. The earliest papers and books published related to MMT used for the functional assessment claim that a proper methodology of the evaluation is necessary before obtaining or interpreting MMT outcomes. Thus, our ongoing research is trying to provide a simple and more objective way of MMT assessment, which can also be better quantified for research purposes and clinical impact on assessment and goal setting. One of the most critical issues of MMT assessment, either in the adapted or classic type of assessment, is represented by the examiner's hands placement, especially on forces 4 and 5 [105].

Regarding the upper limb assessment in post-stroke patients, the evaluation is more complex. It requires a broader approach since hand dexterity is involved in the daily motions, and a skilled motion is necessary for writing or professional activities. Many guidelines suggest using different functional scales assessment, like Fugl Meyer Assessment for UE, Box and Block Test, Wolf Motor Function Test, Nine Hole Peg, Action Research Arm Test, Etc. Previous research reported clinically significant difference [106, 107].

Previous research showed that corticospinal tract integrity is necessary for the fine movements of the hands while it does not have a significant role in the lower extremity motor function. [53] Also, spasticity may be a favourable factor for gait (stance phase) and weight-bearing support in the standing position. At the same time, for the upper extremity coordination and hand dexterity motions. Thus, our structural equation modelling results on the upper limb try to distinguish between the wrist extensors strength and the upper extremity motor function since they had the highest loading value.

The use of the adapted MMT scoring provided in our research is a promising tool for clinicians and physiotherapists, especially in neurorehabilitation assessment. Since the functions restore in an extended period, relatively poor variations can be acquired and established in short periods of times (a few weeks or a month). Furthermore, the adapted MMT scoring system can provide a better framework even for slight variations of motor function for post-stroke patients in a short period thus can also provide better insights on short term specific goal setting.

Our research is ongoing, and further research is needed to establish the validity and usability of the modified MMT in multiple rehabilitation areas.

II.b. Children rehabilitation

II.b.1 Scoliosis and respiratory function

Scoliosis is a "sideways curvature of the spine that occurs most often during the growth spurt just before puberty", with a significant prevalence worldwide in adolescents with idiopathic scoliosis (0.93% to 12%).

The disease "can cause decreased spinal movement, weakening of muscles near the spine, chronic pain, psychological suffering, reduced pulmonary function, and respiratory dysfunction. Abnormal ventilatory patterns and respiratory muscle involvement have been reported in patients with asymptomatic mild scoliosis who may be free of any respiratory dysfunction at rest. Impaired exercise tolerance and physical deconditioning can also be early manifestations in patients with mild scoliosis. However, the study of Diarbakerli E et al. (2016) showed that adolescents with idiopathic scoliosis have similar levels of self-reported physical activity as healthy individuals" [108] ("Elena Amaricai, Oana Suciu, Roxana Ramona Onofrei, Roxana Steliana Miclaus, Radu Emil Iacob, Liliana Catan, Calin Marius Popoiu, Simona Cerbu, Eugen Boia, *Respiratory function, functional capacity and physical activity behaviours in children and adolescents with scoliosis*, Journal Of International Medical Research, 48 (4), 1-9, 2019 ", IF=1,287) [109]

"Some authors reported that staying in the sitting position for long periods and maintaining a static posture, without movement and, sometimes inadequate movement, can determine postural alterations of the spine such as scoliosis". [110]

The primary aim of this study was "to assess the pulmonary function and functional capacity in school children and adolescents with mild and moderate idiopathic scoliosis included in a rehabilitation programme." The secondary purpose was "to observe some of the physical activity behaviours in the study patients (school children and adolescents suffering from mild or moderate scoliosis)".

"Forty children (aged 9 to 17 years) with mild and moderate idiopathic scoliosis and 40 gender and age-matched healthy controls were included in the study. Physical activity behaviours (hours spent at a desk and a computer, hours of competitive and non-competitive practice of exercise per week) were recorded. Patients were assessed at the beginning of rehabilitation and twelve weeks after the exercise-based programme by spirometry and functional capacity testing (6-minute walk test)".

The inclusion criteria were set on children and adolescents who attend school; "clinically and radiologically confirmed mild and moderate idiopathic scoliosis, while the exclusion criteria focused on: secondary scoliosis (congenital scoliosis, muscular scoliosis and neurologic scoliosis), obstructive ventilatory disorders, thoracic surgery, cardiovascular disease, psychiatric or psychological disorders, and recent infectious episodes within the last 2 months".

40 gender and "age-matched healthy controls (school children and adolescents) were recruited by posters placed at public schools nearby".

"The following data related to patients and controls were collected: demographic characteristics (age, gender, weight and height) and physical activity behaviours (hours spent at a desk and the computer per week, hours of competitive and non-competitive practice of exercise per week). First, the patients were assessed clinically, and then an X-ray examination of the spinal column in standing anterior-posterior view was performed".

The protocol included "two assessments for the study group: the first one – at the beginning of the rehabilitation (T1) and the second one – twelve weeks after exercise-based rehabilitation programme" (T2). "Each evaluation consisted of spirometry tests using SPIRODOC (MRI Medical Research International) and functional capacity testing (6-minute walk test: 6MWT)".

The following parameters were recorded (the best of 3 measurements):" forced vital capacity (FVC), forced expiratory volume in 1 second (FEV1), peak expiratory flow (PEF) and FEV1/FVC ratio".

The 6MWT was conducted according to the standardized protocol and also recorded. [110] The subject walked "up and down a measured corridor, covering as much ground as possible over 6 minutes, self-paced, allowed to rest if desired", although the clock continued to run "The 6-minute walk distance".

The patients "were also evaluated at T1 and T2 for back pain using the 10-unit colour Visual Analogue Scale (VAS)". [111]

The study patients "performed a twelve-week exercise programme consisting of three sessions per week in the outpatient Rehabilitation Department to improve awareness of body alignment, axial elongation, derotation and stabilization of the spine, increasing chest expansion enhancing exercise capacity".

The programme included "stretching exercises on the scoliosis concave side, strengthening exercises on the scoliosis convex side and breathing exercises added to some specific exercises for core stabilization (spider, pelvic-tilt, cat-camel pose, basic trunk curl (crunch), exercises using a ball -back extensions, opposite arm and leg raise), and quadriceps strengthening exercises that are very important in increasing work capacity". [112] Patients "were taught to use "rotational breathing" respiratory exercises: contraction of convex areas of the trunk, directing the inspired air in the concave areas. The core stabilization programme was established according to the individual spinal characteristics. Patients with moderate scoliosis also have the prescription to wear a corrective orthosis (Chêneau brace) for 20 hours per day".

For the statistical analysis, continuous variable distributions were "tested for normality using the Shapiro-Wilk test. Descriptive statistics were calculated as mean and standard deviation for

normally distributed data (patients and controls characteristics) and as the median and interquartile range for non-normally distribution (behavioural variables, respiratory parameters, the 6-minute walk distance and VAS)".

Levene's test was applied to test the homogeneity of variances between groups. In addition, one-way ANOVA tests and Fisher's Exact test were performed to compare demographic data (age, height, weight, and sex) between patients group and control group.

"Wilcoxon signed-rank test was performed to compare respiratory and functional capacity parameters before and after twelve-week rehabilitation". The Mann-Whitney test made comparisons between the two groups. Spearman correlation coefficient was applied to investigate the relationship between pulmonary function, functional capacity and pain. A p-value less than 0.05 was considered statistically significant.

The study and control groups "were homogenous in terms of anthropometrical characteristics (Levene's test - p>0.05) (Table 21). For the study patients, Cobb angle at initial assessment was within 15-35° (mild or moderate scoliosis)". [113]

Table 22 show Pulmonary function parameters and 6-minute walk test results.

Table 21. "Patients' and controls' baseline characteristics" [109]

Variables		Patients group	Control group	*p*
Age (years)	mean ± SD	13.10 ± 2.8	13.10 ± 2.8	NS
Height (cm)	mean ± SD	156.9 ± 15.59	157.6 ± 17.44	NS
Weight (kg)	mean ± SD	49.30 ± 16.43	53.5 ± 18.06	NS
Gender	Male- N (%)	16 (40%)	16 (40%)	
	Female- N (%)	24 (60%)	24 (60%)	NS

NS: not significant

"In patients with scoliosis, all respiratory and functional capacity parameters improved significantly after physical therapy. Before rehabilitation, FVC, PEF, FEV1, FEV1/FVC and 6MWT showed significantly lower values when compared to controls. Despite the twelve-week improvement, there were still significant differences between study patients and controls in all the assessed parameters (Table 2). In addition, significant direct correlations were found between the pulmonary function and functional capacity in T1 and T2" (Table 23).

Table 22. "Pulmonary function and functional capacity of study group and controls" [109]

	Patients T1	Patients T2	Relative difference (T2-T1) (%)	95% Confidence interval	p^a T1 vs T2	Controls	p^b T1 vs control	p^c T2 vs control
FVC (l)	3.18 [1.85]	3.45 [1.98]	5.8 [3.32]		**0.001**	4.01 [1.92]	**0.001**	**0.021**
PEF (l/min)	5.12 [2.40]	5.22 [2.38]	2.16 [1.35]		**0.001**	6.44 [3.10]	**0.003**	**0.004**
FEV1 (l/s)	3.03 [1.52]	3.19 [1.65]	3.72 [4.64]		**0.001**	3.51 [1.90]	**0.045**	**0.045**
FEV1/FVC (%)	87.90 [7]	88.50 [7]	0.14 [0.13]		**0.001**	90.65 [4]	**0.021**	**0.031**
6MWT (m)	350 [61]	359 [53]	2.43 [1.74]		**0.001**	390 [53]	**0.001**	**0.003**

The parameters are given as median and [interquartile range]; "T1: first evaluation, before rehabilitation; T2: second evaluation, after rehabilitation treatment; pa relates to the differences between T1 and T2 evaluation, r>0.8; pb relates to the differences between T1 and controls; pc relates to the differences between T2 and controls".

Table 23. "Correlations between pulmonary function and functional capacity in the study group" [109]

	T1			T2		
	FVC (l)	**PEF (l/min)**	**FEV1 (l/s)**	**FVC (l)**	**PEF (l/min)**	**FEV1 (l/s)**
6MWT (m)	0.66	0.48	0.632	0.74	0.63	0.85

Spearman rank correlation coefficient; p<0.001

"At the beginning of the study, 72.5% of patients had complaints of back pain. The pain decreased significantly after the exercise programme (T1: VAS= 2.50 [4]; T2: VAS=0.50 [2]; Z= -4.83, p <0.001). None of the healthy controls had any back pain".

Regarding the physical activity behaviours, scoliosis patients had higher time spent at the computer and reduced "regular and competitive physical exercise when compared to healthy children and adolescents" (Table 24). "The negative correlations between the hours of competitive and non-competitive practice of exercise per week and VAS indicated that when higher time spent exercising, the lower reported pain intensity, both in T1 and T2 (T1: r=0.49 for regular physical exercise time and r= 0.56 for competitive physical exercise time; T2: r=0.49 for regular physical exercise time and r=0.63 for competitive physical exercise time; p<0.001)".

Table 24. "Behavioural variables in the study group and controls" [109]

	Patients group	Control group	*p*
Time at desk (hours/week)	41.50 [4]	41.5 [3]	0.88
Time at computer (hours/week)	9.50 [3]	7 [2]	**<0.001**
Regular physical exercise (hours/week)	2 [1]	4 [1.5]	**<0.001**
Competitive physical exercise (hours/week)	0.5 [2]	2 [1]	**<0.001**

The parameters are given as median and [interquartile range]

Our study showed that in 40 patients with mild and moderate idiopathic scoliosis before rehabilitation, significantly lower FVC values significantly reduced FVC, PEF and 6MWT compared to healthy controls, in opposition with the study of Szopa A and Domagalska-Szopa M in 2017. Szopa revealed that "75% of the 68 patients with mild idiopathic scoliosis had values of the basic ventilation indicator (vital lung capacity) within the normal range" [114]. The same opinion with the study from 2017 of Abdellal AAM et al. showed that "ventilatory function and functional exercise capacity in 73 adolescents with mild idiopathic scoliosis (FVC, FEV1 and 6MWT) were significantly lower" compared to healthy controls [115].

Our study revealed that ventilatory parameter improved after a twelve-week exercise programme but showing no significant differences between patients and controls. Furthermore, after rehabilitation both PEF and 6MWT were still lower when compared to controls.

Our study's plus value consists of assessing the respiratory parameters and functional capacity before and after an exercise-based programme, besides comparing children and adolescents who have scoliosis with the healthy controls.

In our opinion, a follow-up of the study patients is necessary, and we have in view "the correction of scoliosis quantified by radiological assessment (performed at least after 6 months from the initial diagnosis), as well as the improvement of pulmonary function (PEF) and functional capacity (6MWT)". We recommend that the rehabilitation (exercise-based programme) be continued for at least twelve weeks. The study of Sperandio EF et al. from 2014 also suggested that "walking-based aerobic exercises should be encouraged in adolescents with idiopathic scoliosis". [116]

"In our study, all 40 patients with scoliosis spent at least 1 hour per day at the computer, 10 of them (25%) do not perform at all any type of physical exercise and 21 children and adolescents with scoliosis" (52.5%) do not and did not practice any type of competitive sport. These results confirmed the study of Sedrez JA et al. in 2015, evaluating "the risks factors associated with structural postural changes in the spinal column". They noticed that half of the children and

adolescents having scoliosis spent "0-3 hours per day watching TV and 0-3 hours per day at the computer, while 71% spent time reading and studying in bed)". [117]

We also assessed the back pain in scoliosis patients: at the beginning, 72.5% of patients had back pain at final evaluation, only 50% still had back pain, a significant pain decrease after the twelve-week exercise programme. Recent research by Zapata KA et al. also showed that "8 weeks of weekly spinal stabilization exercises led to significantly reduced Numeric Pain Rating Scale in adolescents with idiopathic scoliosis and low back pain". [118]

Gennary et all. in 2015 [119] on 116 adolescent with spinal pain showed that thoracolumbar scoliosis is the second most frequent aetiology (26%) and the pain has initially muscular origin. In our study, the pain was benign. None of the patients had any "red flags" signs ("pain more than 4 weeks duration, fever, chills, night sweats, awakening at night with bone pain, point tenderness, neurological symptoms, history of cancer or radiation of the anterior abdomen").

"The findings of our study have important implications for schools and school-based health professionals involved in the prevention and early diagnosis of postural changes of the spine. Our results sustain the importance of treating scoliosis as soon as possible after diagnosis in a rehabilitation centre under qualified medical supervision".

"Correction of scoliosis is still possible in children and adolescents and should be achieved if a supervised physical therapy programme is performed for a long time. The SOSORT (Scientific Society on Scoliosis Orthopaedic and Rehabilitation Treatment) recommends physiotherapeutic scoliosis-specific exercises as the first step to treat idiopathic scoliosis to prevent or limit the deformity and bracing progression". It is also recommended that specifically trained therapists should design scoliosis specific exercise programmes. The programmes "must be individualized and performed regularly throughout the treatment" [120]

As we noticed a high disproportion between the time spent in sitting positions (at the desk and the computer) and the duration of physical exercise, we recommend the increase of leisure and competitive sports activities in children and adolescents of all age groups.

In children and adolescents with mild and moderate idiopathic scoliosis, pulmonary parameters and functional capacity significantly improved after a twelve-week supervised physical therapy programme. When compared to healthy controls, "all ventilatory parameters and functional capacity had still lower values after rehabilitation". Children and adolescents diagnosed with scoliosis had higher time spent at the computer and reduced regular and competitive physical exercise when compared to healthy ones. Follow-up of the physical exercise is mandatory, both for correcting scoliosis and improving respiratory function and overall functional capacity.

II.b.2. Assessment in children with pectus excavatum

Pectus excavatum is characterized by various degrees of ribs and sternum depression on the anterior surface of the chest wall, which is the most frequent form of congenital chest wall malformation. Children with severe pectus excavatum may encounter disarrangements in cardiac and respiratory functions and may have a decreased capacity to perform dynamic cardiovascular exercises. In some cases, children with mild or moderate malformation are left without therapy if surgery is not indicated.

Our rationale to perform the current study was to consider a specific "category of children diagnosed with PE who do not have the necessary criteria for surgical treatment. These patients can benefit from a conservative treatment that aims to improve their functional status especially considering that they are in their growth and development period". "*Elena Amăricăi, Oana Suciu, Roxana Ramona Onofrei, Roxana Steliana Miclaus Liliana Cațan, Simona Cerbu & Călin Marius Popoiu, Assessment of children with pectus excavatum without surgical correction , Wiener klinische Wochenschrift The Central European Journal of Medicine ISSN 0043-5325, Vol 131, Issue 5-6, pages 126-131, Wien Klin Wochenschr DOI 10.1007/s00508-018-1406-0, MAR 2019"*[121]

Pectus excavatum (PE) is "the most common abnormality of the anterior chest wall in children. Idiopathic PE may be associated with various lung function abnormalities even in the absence of apparent clinical symptoms". Nevertheless, PE patients "often report reduced exercise tolerance, fatigue upon minimal effort and exertional dyspnea. PE is frequently associated with an asthenic build and a typical posture characterized by thoracic kyphosis, forward-sloping shoulders and a protuberant abdomen".[113]

Operative correction is usually accomplished in teenagers close to the age of skeletal maturity and if they have the specific criteria for surgical referral. Patients who require surgery "have a decreased lung function. Postoperatively, they experience an improvement in pulmonary parameters at rest and at maximal oxygen consumption and a slight increase in exercise tolerance".[122]

Although physical exercise is not seen as a method to resolve the condition independently, it has an essential role in PE treatment programs. "Exercise-based programs are used in order to halt or slow the progression of mild or moderate forms of the disease and as a method to improve the poor posture and to prevent secondary complications". [123] "A major limitation of any therapeutic or exercise program can be patient motivation, level of engagement, and adherence. Higher levels of adherence are associated with better health outcomes among children with chronic diseases".[124]

The research objectives focused on assessing respiratory function and functional capacity in children with pectus excavatum without surgical indication who followed physical therapy program and

comparing these parameters to healthy controls and to evaluate adherence of this category of patients to healthy controls a supervised exercise program.

Nineteen children diagnosed with PE were selected from the patients addressed to the Pediatric Surgery, and the parents were asked for consent to participate in the study. "Inclusion criteria were PE, Haller index (the ratio of the chest transverse diameter and the anteroposterior diameter measured on computed tomography (CT) scan sections) less than 3.25".

Exclusion criteria were: "cardiac compression or displacement on chest computed tomography, shortness of breath, chest pain, mitral valve prolapse, arrhythmias, or murmurs, exercise intolerance, previous failed open or closed repair, pre-existing chronic diseases and cognitive deficits". Three children met exclusion criteria: chest pain (1), severe learning difficulties (1), Marfan syndrome (1). We have enrolled 16 patients, from which 2 discontinued the rehabilitation program (1 was unwilling to exercise; 1 had difficulty commuting to the hospital). 14 patients completed the final assessment, and their data were analyzed. No data are missing from the training sessions.

"14 gender and age-matched healthy controls were recruited by posters placed at public schools nearby. Participation in the study was voluntary".

Assessment

Patients and controls characteristics were collected. Our study's protocol consisted of "two assessments for the study group: the first one – at the beginning of the rehabilitation (T1) and the second one – twelve weeks after exercise-based rehabilitation program (T2). The control group was assessed once. Each evaluation consisted of spirometry tests and functional capacity testing (6-minute walk test: 6MWT) for both the study and the controls. At the final assessment, the parents of PE children completed an adherence questionnaire".

"Pulmonary function was tested using SPIRODOC (MRI Medical Research International). The following parameters were recorded: forced vital capacity (FVC), forced expiratory volume in 1 second (FEV1), peak expiratory flow (PEF) and FEV1/FVC ratio. All pulmonary function parameters were measured until three reproducible recordings were obtained, with the best of three being used for analysis. All pulmonary function values were expressed as a percentage of the predicted value for sex, age, and height (mean percent of average values ± standard deviation) to exclude the effect of growth on lung volumes".

The 6MWT was conducted according to a standardized protocol and recorded. Pulse and oxygen saturation were recorded during the test.[110]

Physical therapy protocol

The study patients performed a twelve-week exercise program in the outpatient Rehabilitation Department, following the goals: "posture improvement, strengthening of the back and chest muscles, enhancing exercise capacity and increasing chest expansion. The children carried out a 30-minute exercise program. Each session began with stretching, and respiratory exercises included deep breathing and breath holding exercises. Patients learnt how to increase the vital capacity, strengthen their respiratory muscles, and increase the chest's mobility". In the first three weeks, each exercise was performed in 3 sets of ten repetitions. After that period, each exercise was performed in 4 sets of ten repetitions.

"Improving posture included adjusting the position of the head, reducing thoracic kyphosis and expanding chest. Exercises were done lying down, kneeling, sitting and standing with visual control on the mirror and then using proprioception".

After the first three weeks, "aerobic exercises (cycling and running on the treadmill) were added to improve cardiopulmonary function".[125]

The parents of PE children completed a self-report questionnaire representing the authors' contribution and "created taking into account the factors that could influence the adherence to physical therapy. Five questions addressed factors related to the training sessions, and two questions address the importance of physical activity for the child health and self-esteem. One question regarding the follow-up of a home exercise program and the last two questions assess the level of improvement in child physical capacity after rehabilitation and the parents' overall satisfaction with the physical activity program. These are measured using a scale ranging from 0 (minimum) to 10 (maximum). Great improvement and high satisfaction responses are considered for responses equal to or higher than the median".[126]

The statistical analysis was performed using the MedCalc version 17.8. Descriptive statistics were calculated for patients and controls characteristics, respiratory parameters and the 6-minute walk distance (mean and standard deviation). All patients' and controls' data and measurements "were tested for normality with the Shapiro-Wilk's test. Levene's test was applied to test the homogeneity of variances between groups. One-way ANOVA tests and Fisher's Exact test were performed to compare demographic data (age, height, weight, and sex) between patients group and controls".

Paired t-tests were performed to compare respiratory and functional capacity parameters before and after twelve-week rehabilitation. Independent t-tests did comparisons between the two groups for parameters "with equal variances and the Welch test for parameters with unequal variances. A p-value less than 0.05 was considered statistically significant. In order to compare

the magnitude of the differences between groups, Cohen's d effect size was also calculated. The effect size was considered small for d=0.2, moderate for d=0.5, and large for d≥0.8".

Fourteen PE patients "were included in the study, of whom 10 (71.4%) were boys. The PE children were between 5 and 14 years (mean age 10.14 ± 3.25 years). The study and control groups were homogenous regarding anthropometrical characteristics and measurements (Levene's test - p>0.05), except FEV1/FVC ratio".

Table 25 and Table 26 show Pulmonary function parameters and 6-minute walking test results.

Table 25. "Pulmonary function and functional capacity of study patients before and after rehabilitation" [121]

Parameters	Patients T1	Patients T2	T1 vs T2		
			t-statistic (df)	p^a	*d*
FVC (l)	1.74 ± 0.66	1.85 ± 0.69	8.65 (13)	**< 0.0001**	0.15
PEF (l/min)	236.35± 73.07	237.45 ± 74.26	1.96 (13)	0.07	0.02
FEV1 (l/s)	1.63 ± 0.6	1.73 ± 0.63	4.57 (13)	**0.0005**	0.15
FEV1/FVC (%)	93.71 ± 3.66	93.57 ± 1.65	0.17 (13)	0.86	-0.05
6-MWT (m)	463.86 ± 112.37	480.57 ± 111.35	7.94 (13)	**< 0.0001**	0.15

The parameters are given as mean ± SD; T1 - first evaluation, before rehabilitation; T2 - second evaluation, after rehabilitation treatment; p^a relates to the differences between T1 and T2 evaluation; *d* - Cohen`s d effect size
FVC forced vital capacity, *PEF* peak expiratory flow, *FEV1* forced expiratory volume in 1 second, *6-MWT* 6-minute walk test

Table 26. "Results of t-tests and descriptive statistics for patients and control group" [121]

	Patients T1	Patients T2	Controls	T1 *vs* control			T2 *vs* control		
				t-statistic (df)	p^b	*d*	*t* - statistic (df)	p^c	*d*
FVC (l)	1.74 ± 0.66	1.85 ± 0.69	2.25 ± 0.63	2.07 (26)	**0.04**	0.78	1.6 (26)	0.12	0.6
PEF (l/min)	236.35 ± 73.07	237.45 ± 74.26	240.24 ± 70.52	0.14 (26)	0.88	0.05	0.1 (26)	0.91	0.03
FEV1 (l/s)	1.63 ± 0.6	1.73 ± 0.63	2.09 ± 0.57	2.06 (26)	**0.04**	0.77	1.57 (26)	0.12	0.59
FEV1/FVC (%)	93.71 ± 3.66	93.57 ± 1.65	92.7 ± 1.9	0.89 (20)	0.37	-0.33	1.24 (25.2)	0.22	-0.47
6-MWT (m)	463.86 ± 112.37	480.57 ± 111.35	614.42 ± 105.54	3.65 (26)	**0.001**	1.38	3.26 (26)	**0.003**	1.23

The parameters are given as mean ± SD; T1 - first evaluation, before rehabilitation; T2 - second evaluation, after rehabilitation treatment; p^b relates to the differences between T1 and controls; p^c relates to the differences between T2 and controls; *d* - Cohen`s *d* effect size
FVC forced vital capacity, *PEF* peak expiratory flow, *FEV1* forced expiratory volume in 1 second, *6-MWT* 6-minute walk test

In PE children, FVC, FEV1 and 6-MWT improved significantly after the twelve-week program. Before rehabilitation, FVC, FEV1 and 6-MWT showed significant differences when compared to controls. "After rehabilitation, there were no differences between study patients and controls, except for functional capacity that has still lower values in PE children. All significant differences had minor to moderate effect size (d=0.05-0.78), except for the differences found for 6-MWT between patients and controls (large effect size)".

All PE children's parents completed the questionnaire (see Table 3). "They all agreed about fitting the training program with their child's daily routine, the low difficulty of the exercises", the child following the physiotherapist's instructions, and confidence in rehabilitation results.

"All parents considered the physical activity program important for their children health and self-esteem, necessary to continue the rehabilitation with home exercises. Twelve parents noticed a significant improvement in their children physical capacity, while all stated a high satisfaction with the twelve-week rehabilitation program".

Our study investigates the respiratory function, "functional capacity and adherence to physical therapy in children diagnosed with PE who are not candidates for surgery. They have followed a supervised physical-based exercise program for twelve weeks. To our knowledge, there is no other study that assessed the data as mentioned above in PE children who did not attend surgical correction".

At the beginning of rehabilitation, none of our study patients presented respiratory dysfunction. After performing a twelve-week exercise program, they had significantly better respiratory parameters (FVC and FEV1). The study of Fabian KM (2010), "including 30 female adolescents with idiopathic scoliosis, showed that a 5-week specialized physical rehabilitation (asymmetric respiratory exercise therapy) improved all the respiratory parameters" considerably. [127]

In our study although the functional capacity, assessed by the 6-MWT, improved after rehabilitation, there are still significant differences between PE children and healthy controls. At the end of the study PE children had still a decreased functional capacity.

Abdelaal AAM et al. showed that adolescents with mild idiopathic scoliosis had lower values of 6-MWT when compared to healthy ones. [128] Nevertheless, besides "comparing PE children with the healthy controls, we also assessed the functional capacity before and after an exercise-based program".

"Although the two subgroups were small (6 patients in the group 5-9 years and 8 patients in the group 10-14 years). We noticed a higher improvement for the respiratory parameters in 10-14 years old children after the twelve-week exercise program (Δ FVC of 0.13 l vs 0.08 l; Δ PEF of 1.92 l/min vs 0.57 l/min; Δ FEV1 of 0.13 l/s vs 0.07 l/s). In contrast, 5-9 years old patients had an increased benefit on functional capacity (Δ 6-MWT of 18.67 m vs 15.25 m)".

Taking into study 16 patients with PE who followed surgical correction, Schoenmakers MA et al. stated that in patients without postural impairments, physiotherapy is not necessary except for postoperative pulmonary care. "In our study, all 14 PE patients also had a postural thoracic kyphosis. That is why the exercise program aimed to strengthen the back extensors and stretch the pectoral muscles". We examined the posture of children with pectus excavatum after a twelve-week exercise program. We remarked that the patients "had an improved straight posture of the thoracic spine".

"Adherence to long-term therapy is a factor in achieving the best results both in adult and pediatric patients. The parents answered the questions at the end of the outpatient twelve-week rehabilitation program".

Some studies assessed adherence in children with cystic fibrosis "(examined associations between quality of family relationships and problem-solving skills and reported adherence to medical treatments for older children and adolescents with cystic fibrosis) and asthma (assessed the impact of self-directed exercise on subjective and objective indices of asthma-related health in adults, with poor adherence to a 12-week exercise program)". [129] Supervision may be required to make significant improvements in aerobic fitness and quality of life.

Exercises studies must report data on adherence to the number and length of assisted sessions and home-exercise. [130]

Having in view that "adherence refers to the extent to which a patient follows medical advice as accurate as possible, our study revealed good adherence to the physical exercise program for all children". Although the patients' age ranged from 5 to 14 years, they all had adequate participation in each supervised session without missing one. "The promoting factors for good adherence to rehabilitation were the following: involvement and availability of the families (namely their mother, father, grandparents and even older sisters or brothers), living in our city or nearby villages, the free of charge exercise sessions and not at least the quality of physical therapy and the participation of medical staff".

Assessing the long-term compliance and the long-term outcomes can be considered for future studies.

In PE children without surgical indication, forced vital capacity, forced expiratory volume in 1 second and functional capacity assessed by the 6-minute walk test improved significantly after a twelve-week supervised exercise program.

"Compared to healthy controls, functional capacity had still lower values indicating the need for follow-up of the physical exercise".

Our study showed good adherence to the exercise-based program for all patients.

IIc. Interdisciplinary research

II.c.1. Rehabilitation chalenges in pluripathology –

Policitemia Vera and stroke association, with rehabilitation inference

It resembles that patients with Polycythemia Vera have an increased risk of vaso-occlusive events and cerebral ischemia. Although previous research has shown that cerebral ischemic events are the consequence of increased blood viscosity and platelet activation in the arterial vessels of the central nervous system, there are now several case reports of microemboli presence likely from outside the brain. These founds implies different direction issues for these patients. We present another case study to highlight the particularities of the association between polycythemia vera and stroke and the implications for the neurorehabilitation of these patients. ("Adriana Sarah Nica, Roxana Nartea, Daciana Andrada Costina Stefan, Roxana Miclaus, *Link Between Biochemical, Biological and Clinical Assessment Focused on Polycythemia Vera and Stroke* , Revista de Chimie (Bucharest)", 68, No. 8 , PAG 1816-1819, 2017) [131].

"Polycythemia Vera (PV) is a myeloproliferative neoplasm characterized by an absolute erythrocytosis not driven by erythropoietin [132]. PV has a high risk of evolution to leukaemia and thrombosis. It is characterized by an increased number of leukocytes and platelets to a critical level that altercate blood flow. The onset is with non-specific signs and symptoms. Face erosion may occur, intermittent pruritus, headache, vertigo, tinnitus and peripheral and coronary manifestations. The thrombosis context may efficiently conduct to a pulmonary and cerebral embolism. In the context where coronary heart disease is essential and involves cardiomyopathy, there is a risk of sudden death". In 2008 World Health Organization established the criteria for diagnosis of PV [133]."To evaluate the complications and progression of the disease, biochemical and biological aspects are mandatory to associate the abdominal ultrasound investigation (evaluation of the liver, spleen), medullar puncture from the iliac crest". Treatment for Polycythemia Vera is symptomatic and preventive for vascular complications. Phlebotomy is performed for vascular decongestion, blood is removed and electrolyte and plasma are infused. Aspirin is often associated with anti-inflammatory and cytotoxic drugs in the treatment with hydroxyurea and/or non- interferon therapy. Patient education includes basic food hygiene rules (norm caloric, norm protein – if unchanged uric acid value), sufficient hydration (vitamin, mineral and oligo-elements)" [134].

The research focused on assessing the "biochemical and biological samples with ANALIZOR AUTOMAT - A 25 - BIOSYSTEMS analyzer and on ABACUS 3 haematology examiner during six admissions in a Rehabilitation Department. The biochemical and biological results were analyzed during 2012-2016 in connections with the biological, clinical and functional evolution in a context of severe cardiovascular, haematological, neurological and digestive plural pathology. The

biochemical and biological assessment was required to establish the appropriateness of applying the rehabilitation program (energy, caloric, hydric), mandatory adapted to the patient's physical stress and exercise training in the Rehabilitation Department".

Table 27 "**World Health Organization criteria for the diagnosis of Polycythemia Vera"** [131].

Major criteria:
A1. Hemoglobin >18.5g/dl male/16,5 g/dl female; or other evidence of increased red cell mass
A2. Presence of JAK2V617F or other functionally similar mutation
Minor criteria:
B1. Marrow morphology
B2. Low serum erythropoietin
B3. Bone marrow endogenous erythroid colony formation
Marrow morphology: hyper cellular marrow with three lines hyperplasia; clustering of pleomorphic megakaryocytes; absent stainable iron: no major inflammatory features.
Requirements for diagnosis:
A1+A2+any from B
A1+ any two from B

"This case presentation is of a 58 years old female patient who develops a stroke in 2011 with significant biochemical and biological changes. The disease was unidentified and with non-specific symptomology until the occurrence of stroke. The particularity of this case is the presence of severe cardiovascular disease (stage III hypertension, obstructive hypertrophic cardiomyopathy, chronic ischemic silent disease) associated with cerebral manifestations (stroke) and with mixt hepatitis (alcoholic and deficiency), hypercholesterolemia and hyperuricemia. This biological context represents a real challenge both etiologically and therapeutically (pharmacology and non-pharmacology). These manifestations prove to result from a haematology disorder, more precise a myeloproliferative neoplasm named Polycythemia Vera".

During five years of rehabilitation (six hospital admissions interfered with home rehabilitation), the patient was progressively degraded related to muscle force, ability, movement capacity, mentally and functionally, socially, and life quality due to comorbidities. The patient experienced especially Polycythemia Vera treatment poorly conducted, heart complications and low patient compliance.

The particularity of this case is "due to the first clinical manifestation of Polycythemia Vera identified with the debut of a stroke. Also is due to the complications of hepatic, cardiovascular and metabolic systems, which required periodical evaluation for hematologic and biochemical parametric to adjust the rehabilitation program. This evaluation represents the key in the therapeutical management of the rehabilitation program" [135, 136].

Another particularity is "the lack of patient compliance to the pharmacological and non-pharmacological treatment causing the rapid decline of cardiovascular system. The high level of uric acid must be noticed in the progression of the disease as a biochemical reaction to treatment and compliance. Interferon therapy may be considered as an alternative treatment for hepatic and

haematological pathology".

Therefore, "case management requires an interdisciplinary team to understand the particularity of the case". An individualized rehabilitation program should be applied based on repetitive assessment of the general function, cardiovascular, hematologic, and neurological level. Besides, biological and biochemical assessment often reveal undiagnosed pathology in patients referred to Rehabilitation and require rigorous assessment, fine diagnostic and competent treatment for complex and intricate pathologies addressed to Rehabilitation team.

II.c.2.Osteoporosis prevention

Osteoporosis is a disabling condition distinguished by endangered bone strength, which influences a patient to an escalation risk of fracture. It affects at least a quarter of postmenopausal "white women, and the proportion rises to 70% in women older than 80 years". This rise in the number of fractures caused by increased older people in the population enhanced survival and increased "the age-specific fracture rates of unknown aetiology. The growing number of osteoporotic fractures and their associated morbidity" marks a heavy burden on prospective healthcare resources. The main objective was to highlight the lifestyle factors that "influence bone health and/or interfere with nutrient intake and absorption" and draw the principles of a correct nutritional approach as the most adequate and less expensive way to prevent osteoporosis and lower medical costs for menopause. ("*Moga M, Preda G, Marceanu L,* ***Miclaus Roxana****, Bîgiu N., Lifestyle factors related to bone mineral density in postmenopausal women, Journal of Environmental Protection and Ecology, nr. 1 vol. 1, 2008, pag. 67-69, ISSN: 1311-5065", IF 0,168)* [137].

Postmenopausal osteoporosis causes multiple and intricate effects on the patient, complex symptoms, and a significant burden to healthcare resources. "Nutrition, lifestyle, and genetics contribute to the pathogenesis of osteoporosis". Some of the lifestyle factors "influence bone health and/or interfere with nutrient intake and absorption". For example, caffeine consumption, cigarette smoking, and alcohol abuse have been proved as being the risk factors for bone loss in postmenopausal women. From a medical and economic point of view, it would therefore be desirable to prevent loss of bone mass and not treat its' expensive consequences.

Osteoporosis, a disease characterized by the gradual loss of "low bone mass, micro-architectural deterioration of bone, and susceptibility to bone fractures, can lead to debilitating pain and deformity. The disease represents a major health problem, particularly in older women, as osteoporosis occurs most frequently in postmenopausal women following the decrease in estrogen levels". Osteoporosis is a disease we will be seeing a lot more in the decades ahead because the population's average age will continue to rise.

"Osteoporosis, like cardiovascular disease and diabetes, is associated with an increased risk of dying. Osteoporosis weakens bones to the point where relatively minor trauma can cause a fracture. There are many risk factors associated with osteoporosis", like the following:

a. Age: the loss of some "bone mass appears to be partly a natural part of the ageing process itself", and genetic factors influence its development.
b. Genetics: continuously being study.
c. Gender: women are more affected, beginning with perimenopause.
d. "Dietary and other lifestyle factors can slow down or accelerate the loss of bone strength that occurs with the increase of age". Some of the lifestyle factors that "might independently influence bone health and/or interfere with nutrient intake and absorption are alcohol, caffeine and smoking". [138]
e. "Coffee, tea, cola and cocoa are rich in caffeine, and because caffeine increases the urinary excretion of calcium", it becomes an important risk factor for bone loss in humans, depending on the intake dose. However, it appears that the risk can be offset by moderate milk consumption. "The epidemiological data addressing the association between coffee consumption and bone status are pretty contradictory". High intakes of caffeine have been shown to increase "urinary calcium excretion, which can promote bone loss when calcium or vitamin D intakes are too low to offset these losses". However, there is a shred of evidence that moderate caffeine intake may not have such an effect "it appears that the deleterious effect of caffeine becomes most pronounced when dietary Ca is inadequate and less harmful when dietary Ca is high. Those who consume substantial amounts of caffeine should be encouraged to drink milk and/or obtain calcium from other sources" [139]
f. "Chronic alcoholism leads to lower BMD and higher fracture risk due to a combination of factors:

- poor nutrition and malabsorption of critical nutrients (calcium, magnesium and zinc);
- liver disease, abnormal vitamin D metabolites and parathyroid function;
- direct toxicity to osteoblasts increased propensity to fall, thereby increasing chances for fractures".

However, "moderate alcohol consumption appears to be beneficial for bone. The possible explanation why moderate alcohol intake improves bone status may be that alcohol stimulates androstenedione conversion into estrone. Also, alcohol might inhibit osteoclasts, and by that bone resorption, significant for the elderly" [140]

"Cigarette smoking has long been recognized as a risk factor for many health problems, including bone health. According to the recent meta-analysis, smoking leads to lower BMD, and the effect is cumulative with age", and postmenopausal bone loss is more remarkable in smokers [141]

g. "Physical activity is associated with bone density", as observational studies demonstrate a significantly increased bone mineral density in women with current physical activity than sedentary postmenopausal women. Exercise should be encouraged in those at risk of osteoporosis and those with osteoporosis, along with other lifestyle measures (adequate calcium intake, stopping smoking, modest alcohol consumption, and maintaining an adequate body weight). [142]

Principles of osteoporosis prevention in young and middle-aged adults should include:

1. A healthy-eating diet with more fresh fruits and vegetables, basic food principle that provides a balanced intake of calcium (at least 800 mg/day); vitamin D3 (2000UI/day), protein, vitamin K, vitamin C and potassium decrease sodium.
2. Maintaining an adequate body weight.
3. Encouraging a physically active lifestyle;
4. Avoidance of smoking and high alcohol and caffeine intakes;
5. Minimization of glucocorticoid use.

"The overall incidence and age- and sex-related incidences of osteoporosis are increasing worldwide". Prevention of osteoporosis and osteoporosis fractures is "an urgent priority to reduce the burden placed on health care and social welfare systems". Postmenopausal bone mass can be influenced by changing individual lifestyle. Strategies for osteoporosis prevention in young and middle-aged adults should include a periodical screening of BMD, educational programs on diet, nutrition and physical activity.

II.c.3.Healthcare professionals risk management

Professional workers from healthcare are often overworking, and the workloads are frequently correlated with burnout and job dissatisfaction. Another factor that interferes and represents a risk for healthcare worker is understaffing. Consumers rank the overwork of health professionals in hospitals as higher threats to patient safety, and where is possible, the patient's caregivers are hospitalized with them. The inpatients' environments have to ensure more prominent autonomy and control, implement administrative assistance for nursing care and have sufficient staff. It should promote helpful rapport between nurses and physicians are associated with lower risk in the development of professional injuries, higher patient satisfaction, and lower personnel burnout manifestations. This research aimed to investigate the associations between satisfaction, stress and risk management practice as motivational factors of employees and "assess the most significant predictors for risk management practice in the healthcare system". ("*Daniela Drugus, Angela Repanovici, Daniela Popa, Elena Tirziman, Nadinne Roman, Liliana Rogozea,*

Roxana Miclaus, Social Impact of Public Health Care in Risk Management Implementation, Revista de cercetare și intervenție socială, 2017, vol. 56, pp. 79-87", IF =0,838[143]

Despite the certain lack of success around 2010 (Huber & Scheytt, 2013), risk management gained significant interest in the business community and practitioners in broad domains as in academics. [144]

Speculative risk and risk management practice increased in all areas of activity, underlying that risk management becomes universal practice (Hood et al., 2004; Power, 2004). Defined as a systematic methodology combining knowledge, technology, strategy, individuals and processes in has the aim to evaluate and reduce the risk that occurred in an organization (Dabari & Saidin, 2014) [145]. The Health system succeeds in designing risk management procedures to facilitate a holistic and systematic approach for the management of human resource activities (Dimitrios, 2012) and patient care activities, both targeting the patient's safety and the quality of medical services. [146]

Four functions to address when assessing Healthcare Risk Management: risk identification, evaluation loss prevention, patient safety and education (Amori, 2006). In the medical area, risk protection covers complex items regarding both patients and medical professionals: working environment, hospitalization conditions, and cares during hospitalization (asepsis conditions and manoeuvres, rigorous cleaning and disinfection, adequate knowledge and education of staff), nevertheless complex aspects of patients-caregivers interaction. [147]

The principal designation of any healthcare system is to be sustainable (to carry out quality medical services at an affordable cost -Lega, Prenestini, & Spurgeon, 2013) [148], without compromising on quality. Risk management in Health care focuses on achieving quality in human resource management, job analysis, leading, strategy and planning, stakeholder participation, knowledge management, service and outcome (Prachak, & Ngang, 2013). This approach should positively influence work performance in daily clinical practice, consisting of the sum of the motivational aspect for staff, work satisfaction, salary, work conditions and safety, stress, and task overload. Never forget about organizational factors that influence performance in clinical work as "safety climate and morale, work environment factors, managerial support", teamwork, guiding and supervision.(Sexton et al., 2006 [149].

Reaching efficiency and equity in a competitive health services market is highly conditioned by transparent policies, rich budget and competitiveness in human resource selection as principal risk adjustment issues. Wynand & Van de ven (2000), [150]

A consistent background of this study is previous research of our multidisciplinary team concluding "the necessity of implementing risk management in the Romanian health system".

We develop a prospective randomized study, on 242 persons, residence of different cities in

Romania ("Bucharest 25.1%, Iasi 23.5%, Brasov 18.3%, Cluj 16.7%, Timisoara 12.4% and Sibiu 4.0%"), with homogenous gender distribution 128 women (53%) and 114 men (47%). Professional distribution was random, 60.3% nurses and 39.7% physicians, from several hospital units (Emergency unit, Pediatrics, Orthopedics, Neurology and Oncology).

Risk management practice was investigated through 4 questionnaires (applied online through Survey Monkey, wholly anonymous and respect ethical rules of a research trial) on the following aspects:

a. Ten items Questionnaire ("5- point Likert scale, ranging from 1-never to 5 -very often"), evaluating the process of risk management implementation in the Romanian healthcare system (the support structure of risk management process, procedures, monitoring and documenting, decisions risk assessment, professional development, risk reassessment process after implementing measures)
b. Eleven items Questionnaire ("5- point Likert scale, ranging from 1-never to 5 -very often"), evaluating motivational factors for achieving performance at the workplace (work done satisfaction, working conditions and environment, competitiveness, Team relationships and subordination, wages and work reward, willingness to learn, employment continuity and fidelity, chance of promotion, prestige, gratitude expressed by superiors, and patients. The internal consistency reliability estimates (Alpha Cronbach) is 0.834. The instrument based on the researches: Judge & Ilies (2002), Dieleman et al. (2003), Mathauer & Imhoff (2006).
c. Ten items Questionnaire ("5- point Likert scale, ranging from 1-never to 5 -very often") evaluate the Level of Burnout and Congestion Degree of Professional Duties Assessment Scale. The internal consistency reliability estimates (Alpha Cronbach) is 0.82, an outstanding value for the coefficient.
d. Five items Questionnaire investigate the level of job satisfaction, assessing the work experience (correlated with demographic variables as gender, age, occupation, type of hospital unit).

The comparison between groups tested for possible bias and variance one-way ANOVA analysis compares different cities participants' response. No significant differences in the investigated variables were found.

1. Regarding the first objective of this study, the "associations between motivational factors of employees (satisfaction, stress and risk management practice), results show that **Risk Management Practice** "(RMP) highly and positively correlates with **Motivation** variable (r (242) = 0.490, p = 0.00) and with **Satisfaction** variable (r (242) = 0.485, p= 0.00), proving the more the unit concern with Risk Management Practice, the greater becomes employee

motivation. (*Table 1)* Also, Risk Management Practice negatively correlates with **Agglomeration** variable (r (242) = - 0.963, p = 0.00) and with **Burnout** variable (r (242) =- 0.778, p = 0.00). Therefore, the more disregarded risk management practices, the greater the overload with tasks and the more pronounced the exhaustion.

1.1. The *Agglomeration* and *Burnout* variables correlate highly with Risk Management Practice (RMP), despite negative correlational values.

1.2. *Motivation* highly correlates with *Satisfaction* (r (242) = 0.994, p = 0.00), and *Agglomeration* highly correlates with *Burnout* variable (r (242) = 0.801, p = 0.00).

1.3. *Motivation* is medium correlated with *Agglomeration* (242) = - 0.505, p = 0.00), and *Satisfaction* is medium correlated with *Agglomeration* (242) = - 0.505, p= 0.00).

1.4. The lowest correlational values can be observed between Motivation and Burnout variable (r (242) = -0.382, p = 0.00), and between Satisfaction and Burnout variable (r (242) = -0.397, p = 0.00).

Table 28. Correlations between research's variables [143]

Risk Management Practice		Risk Management Practice	Motivation	Satisfaction	Agglomeration	Burnout
Motivation	Pearson Correlation	,490**				
	Sig. (2-tailed)	,000				
Satisfaction	Pearson Correlation	,485**	,994**			
	Sig. (2-tailed)	,000	,000			
Agglomeration	Pearson Correlation	-,963**	-,505**	-,505**		
	Sig. (2-tailed)	,000	,000	,000		
Burnout	Pearson Correlation	-,778**	-,382**	-,397**	,801**	1
	Sig. (2-tailed)	,000	,000	,000	,000	

**. Correlation is significant at the 0.01 level (2-tailed).

2. Regarding the second aim of the research ("to assess the most significant predictors for risk management practice in the healthcare system"), we applied the hierarchical multiple linear regression method to test the efficiency of the explanatory model of Risk Management Practice. The model "based on Motivation, Burnout, Agglomeration, and Satisfaction" variables.

2.1. The data indicate the second model has a high adjusted coefficient of determination (0,928) and "explains 93% of the variance for the Risk Management Practice variable". (Table31)

2.2. Data for regression model significance (p=0,000) suggested that the prediction based on the calculated model is better than the random prediction.Regarding the second aim of

the research ("to assess the most significant predictors for risk management practice in healthcare system"), we applied the hierarchical multiple linear regression method, in order to test the "efficiency of the explanatory model of Risk Management Practice (based on Motivation, Burnout, Agglomeration, and Satisfaction" variables).

2.3. The data indicate the second model has a high adjusted coefficient of determination (0,928) and "explains 93% of the variance for Risk Management Practice variable". (*Table31*)

Table 29. Results of regression analysis regarding multiple R correlation coefficients, R square coefficients of determination for Risk Management Practice [143]

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	,964[a]	,929	,928	,33655

a. Predictors: (Constant), Motivation, Burnout, Agglomeration, Satisfaction

2.4. Data for regression model significance (p=0,000) suggested that the prediction based on the calculated model is better than the random prediction.

Table 30. ANOVA [143]

Model		Sum of Squares	df	Mean Square	F	Sig.
1	Regression	350,500	4	87,625	773,607	,000[b]
	Residual	26,845	237	,113		
	Total	377,345	241			

a. Dependent Variable: Risk Management Practice (RMP)

b. Predictors: (Constant), Motivation, Burnout, Agglomeration, Satisfaction

2.5. *Hierarchical regression analysis aimed at explaining Risk Management Practice*, shows

2.5.1. the effect size indicators for Satisfaction variable is not statistically significant: r (sp) = -,058, p=0,186

2.5.2. the effect size indicators are statistically significant for:

2.5.2.1. Agglomeration variable (r (sp) = -,973, p=0,00)

2.5.2.2. Burnout variable r (sp) = -,184, p=0,008

2.5.2.3. Motivation variable r (sp) = ,168, p=0,008.

Agglomeration, Motivation and Burnout are the coefficient predictors that contribute most.

Table 31. Results of hierarchical regression analysis aimed to explainRisk Management Practice [143]

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
1	(Constant)	10,720	,139		77,323	,000
	Satisfaction	-,058	,044	-,040	-1,325	,186
	Agglomeration	-,973	,033	-,929	-29,492	,000
	Burnout	-,184	,069	-,444	-2,678	,008
	Motivation	,168	,063	,446	2,690	,008

a. Dependent Variable: Risk Management Practice (RMP)

Regression analysis supports *hypothesis 2:* Agglomeration, Motivation and Burnout are "the most significant predictors for risk management practice in health care system".

The four questionnaires for the research were validated (1. The Risk management practice questionnaire, 2. The questionnaire investigates the motivational factors for achieving performance at the workplace, 3. The Level of Burnout and Congestion Degree of Professional Duties Assessing Scale and 4. Job satisfaction). All four questionnaires used in the research are a valid measurement for the assessment of the research variables. Construct validity and reliability proved that the questionnaires used are fit and effective instruments.

The first objective of the research has been verified obtaining "associations between motivation factors of employees, satisfaction, stress and risk management practice".

The second objective of the research revealed Agglomeration, Motivation and Burnout being the "most significant predictors for risk management practice in the healthcare system". The tested model best explains 93% of the variance for the Risk Management Practice variable.

The overload of the medical staff and the Burnout syndrome are reflected in the medical professionals, with an essential societal impact, decreasing efficiency and their ability to provide quality healthcare services, opening the gate of mistakes and malpractice, or life-threatening issues, concerning medical staff and patients.

The medical staff and patients are reluctant to include standards to solve problems addressing emerging risks in the health system, implementing risk management, and quality development cores. Also, the change of the defining and risk assessment can generate substantial changes in health systems in increasing the quality of health care.

II.c.4. Interdisciplinary research in psychiatry

During the clinical activity of Physical Medicine and Rehabilitation, we frequently face psychiatric pathology that we need to understand and manage. Rehabilitation results are conditioned by the patient's collaboration and compliance with treatment. Therefore, collaboration with fellow psychologists and psychiatrists is very important for the proper management of each patient who has temporary or chronic suffering in the psychiatric field. In particular, the neurological patients I care for daily frequently face psychological or psychiatric suffering, especially patients who have suffered a stroke and are experiencing evolving agitation, anxiety, depression, or patients with chronic pain, which is very difficult to control. In this context, I have participated in the multidisciplinary team in an observational study focused on patients with psychiatric pathology. ("*Petru ifteni, Andreea Teodorescu, Marius Alexandru Moga, Alina Mihaela Pascu, Roxana Steliana Miclaus, Switching bipolar disorder patients treated with clozapine to another antipsychotic medication: a mirror image study*, *Neuropsychiatric Disease and Treatment* 2017:13 201–204, Dovepress")[151]

Bipolar disorder (BD) "is associated with recurrent exacerbation of manic, depressed or mixed episodes, leading to functional impairment, substance abuse, risk of suicide, accidents", and increased care costs. Antipsychotics are "a proven option in the treatment of BD. Although clozapine has never been approved for treating bipolar disorder, it has shown efficacy in acute mania with psychosis and the treatment of refractory symptoms associated with BD. [152, 153] The efficacy of clozapine in severe manic patients was reported both as monotherapy and an add-on strategy. [154] Despite this evidence, clozapine remains under-utilized in general [155] and in BD treatment in particular, primarily due to tolerability and safety concerns".

"According to Good Clinical Practice rules and local regulations, this naturalistic study was conducted in the 3rd Clinical Department of Clinical Hospital of Psychiatry and Neurology, Brasov, Romania (an academic unit). The study aimed to evaluate the risks and benefits of switching from clozapine to another antipsychotic medication in BD patients with remitted manic, depression, or mixed episodes. The study took advantage of a change in local reimbursement rules, which started in 2014. The cost of clozapine was no longer reimbursed for patients with a diagnosis of BD disorder". The local Ethics Committee approved the study (Comisia de Etica). "Written informed consent has been obtained from all patients for participation in this study".

The study design tailored an "observational, naturalistic, mirror-image study of a cohort of 62 consecutive BD outpatients in remission after a severe manic episode. Clozapine was administered between 2012 and 2014, and adverse effects were monitored according to local and international guidelines. In 2014 the health insurance authorities in Romania discontinued

reimbursement of clozapine costs for BD patients, attempting to control pharmacy costs". The treating psychiatrist explained to patients and their families that "in order to continue treatment with clozapine, they would have to pay between 30 €/month (200 mg/day) and 90 €/month (600 mg/day) or they will be switched to another antipsychotic". Also, "the risks and the potential benefits of the switch to another antipsychotic" were carefully explained.

"Twenty-five patients (40%) opted to switch to another antipsychotic, and the rest remained on clozapine. All switched patients were tapered during 4 weeks. In the switched group, the first choice for replacing clozapine was quetiapine (n=10, 40%) with a mean dose of 640 mg/day (average between 400–800 mg/day)". Table 27 presents the rest of the antipsychotics used for switching. In both groups (switched and non-switched), "the augmentation of antipsychotic treatment included: mood stabilizers (sodium valproate), benzodiazepines (diazepam and lorazepam), hypnotics (zopiclone, zolpidem, clonazepam, and nitrazepam), and/or addition of a second antipsychotic (haloperidol and levomepromazine)". The patients were evaluated with "Young Mania Rating Scale (YMRS), Montgomery– Åsberg Depression Rating Scale, and Clinical Global Impression for Bipolar Disorder (CGI-BP) by two board- certificated psychiatrists". The socioeconomic status was also evaluated, and data included the total income per family, the number of rooms per person, and the number of persons who supported the patient's treatment.

Table 32 The antipsychotics used for switching [151]

Antipsychotics	n (%)
haloperidol	4 (19.04)
Olanzapine	3 (14.28)
Quetiapine	10 (47.61)
risperidone	2 (9.52)
amisulpride	1 (4.76)
aripiprazole	1 (4.76)

"Statistical analysis: Demographics and severity scores before and after clozapine switching were compared using the variance ratio test (F-test). Statistical significance was set at a two-sided P,0.05".

"Of the 62 patients included in this study, 37 (59.7%) continued clozapine (non-switched group). The rest, 25 (40.3 %), were switched to another antipsychotic (switched group). Demographics and results of the switch are shown in Table 2. The mean score of CGI-BP at admission in the study was similar in both groups (2.3 vs 2.4, respectively). After switching, a significant proportion of patients relapsed (n=21.0, 84.0%), 13 men and 8 women. In all cases, the relapse episode was manic, and patients required hospitalization. The mean YMRS score at relapse was significantly higher compared with the evaluation at the time prior to switching (31.78 standard deviations [SD] =9.72

vs 11.99 SD =7.29, P,0.01). As shown in the Table 28, more switched patients were hospitalized and exacerbated than patients who continued on clozapine".

According to the local protocol, BD patients "were switched to olanzapine, quetiapine, risperidone, aripiprazole or haloperidol. One patient continued treatment with amisulpride. The antipsychotics used after clozapine switching are presented in Table 28. There was no statistical difference between second-generation antipsychotics (SGAs) and haloperidol regarding the time until relapse or in the SGAs group. The decision to switch to a specific antipsychotic was made by the psychiatrist based on his individual preference".

The study showed that replacing clozapine with another antipsychotic might increase the risk of "relapse and hospitalization in remitted BP patients".

The use of clozapine on- and off-label and it's apparent underutilization of clozapine remains a controversial issue in clinical psychiatry. [155] "Besides treatment-resistant schizophrenia, the only other indication approved by regulatory authorities (US Food and Drug Administration) for clozapine is for suicide prevention in schizophrenia. Nevertheless, and despite the lack of randomized controlled studies, clozapine is used off-label to treat aggression in patients with BD, intermittent explosive disorder, post-traumatic stress disorder, mental retardation, manifestations of personality disorder and agitation in dementia". [153]

Table 33 Patient demographics [151]

Characteristics	Non-switched group n 37, 59.7%	Switched group n 25, 40.3%	*P*-value
gender, male, n 36, 58.1%	23	13	,0.05
age (years)	38.94 (10.59)	38.76 (10.17)	0.846
age of onset (years)	26.67 (8.17)	27.60 (7.71)	0.782
Duration of illness (years)	12.00 (7.68)	11.16 (5.51)	0.091
Number of hospitalizations (lifetime)	8.67 (5.38)	7.60 (3.65)	0.049
Days of hospitalizations (lifetime)	212.56 (123.90)	190.20 (90.76)	0.113
clozapine before replacing, months, mean (sD)	13.91 (6.20)	14.32 (5.27)	0.408
remission before clozapine discontinuation (months)	10.18 (5.55)	10.64 (4.58)	0.326
remission after clozapine discontinuation (months)	12.93 (6.24)	9.24 (3.90)	0.018
relapse after clozapine replacing	8 (21.62)	21 (77.77)	,0.0001
hospitalization after clozapine replacing	8 (24.24)	25 (75.76)	,0.0001
Total amount of money/family	€780	€821	0.884
Number of persons who support patient's treatment	2,3	2.1	0.921

Note: Data presented as n (%) unless stated otherwise.

Abbreviation: sD, standard deviation.

Furthermore, "clozapine use reduced psychiatric hospitalization and emergency room visits, numbers and length of psychiatric admissions, and psychotropic co-medications in patients with BD". [152, 156] As we know, "besides psychotropic medication, many other factors influence illness course and relapse, and many of these are related to socioeconomic circumstances". Switching antipsychotic could be influenced by one of these factors: "type of switch, low doses, too fast or too slow tapering, less sedative effect for aripiprazole or risperidone)". In our study, "there was no difference in the total amount of income per family and the number of relatives who supported the cost of the patient's treatment".

"The current study has limitations that are inherent to the naturalistic, non-randomized design, such as the possibility that the patients' and their families' decision not to discontinue clozapine was determined by a perceived likelihood of impending exacerbation, which might have affected the outcome. In addition to antipsychotics, both groups were treated with additional but different psychotropic, which might have also affected the outcome. Moreover, despite the gradual discontinuation of clozapine, a cholinergic rebound can occur in some patients". [151]

The results suggest that "switching from clozapine to another antipsychotic may increase the risk of relapses in remitted patients with BD". The study design has limitations, but shows that discontinuation of clozapine in remitted BD patients should be carefully decided considering the potential risk of symptoms' exacerbation.

III. Education and Medical Ethics in Physiotherapy and Rehabilitation

III.a Medical training and education

III.a.1. Medical training and education challanges

The new challenge of the Covid 19 pandemic has revealed several particular aspects of online education in general and medical education in particular.

The novelty, rapidity and inability to adapt to the sudden change of procedures, legislation and the effective way of carrying out activities in medicine and education have revealed positive and negative aspects. The Health and Education systems experience asymmetries and disadvantages to find efficient solutions and applications quickly.

Coronavirus SARS-CoV2 pandemic generated worldwide specific "social, economic, medical and educational issues, forcing professionals in all fields to adapt their activities to the new governmental measures and health policies". Asymmetries in education, in addition to the increase in unemployment, come to light in the pandemic. [157] "Inflation rates, generating an educational crisis with outcomes that cannot be neglected as education is the driver of any economic system in terms of knowledge transfer and competence development, including the digital teaching competencies" [158].

Nowadays, there are **issues in implementing Digital technologies in educational institutions**, initially considered to have had a positive impact

Issues	Arguments
Slow implementation process	digitalization was not perceived as a need to be rapidly addressed incorporating multimedia was not enough for teaching and training
Resistance from teachers and trainers	Face-to-face education seemed to be comfortable (not requiring changes) from the management's perspective Face-to-face education is considered successful (meeting settled standards and indicators) pedagogical methods and techniques seemed to be sufficient and efficient although less creative and lacking attractiveness in today's students' eyes.

Online learning needs interactive learning environments ("computer-aided instruction and intelligent tutoring systems") and continuously growing the World Wide Web and Internet

connections extension. Online learning will lead to a "re-shaping of the educational profession, influencing teachers and students", based on mandatory long-distance communication and efficient use of multimedia into the educational process (networks, television and computers [159].

Under the circumstances generated by the COVID-19 crisis, the main aim of this paper was to determine the educational system's capacity in a developing country like Romania "to replace face-to-face education with any form of tele-education because of the lockdown caused by this pandemic. Its general objective (GO) was identifying the level of digitalization that supports Romanian tele-education under the COVID-19 crisis, whereas the specific objectives" (SO) were as follow:

SO1—"Evaluating the asymmetries of Romanian education".

SO2—"Examining the resources used for supporting tele-education".

SO3—"Identifying key-areas for future development of tele-education in Romania". ("*Cristina Nicolau, Ramona Henter, Nadinne Roman, Andrea Neculau and Roxana Miclaus Tele-Education under the COVID-19 Crisis: Asymmetries in Romanian Education, Symmetry, Symmetry 2020, 12, 1502; doi:10.3390/sym12091502, September 2020*"[160]

Our qualitative research proposed "an innovative research methodology focused on deep analyzing the asymmetries in the digitalization" of Romanian public education as representative for developing countries. The shift from "face-to-face learning to tele-education forced by the COVID-19 pandemic" has brought significant challenges identified through a detailed qualitative study on a sample of 14 Information and Communication Technology (ICT) specialists working for/with Romanian 1–4 International Standard Classification of Education (ISCED) schools.

We investigated the development of this concept as a whole. We identified that, except medicine, where it received a lot of attention and face to face interaction with the patient. The concept of telemedicine is largely used, and two significant fields allow this concept "special attention: computer science and engineering and social sciences and language acquisition. Hence, there are two forms of tele-education" [161]: asynchronized and synchronized. Synchronized tele-education uses the Internet to publish hyperlinked multimedia content while offering "a large audience with digitalized material. Self-learning is highly encouraged as assessment may be delivered as well, not needing the assistance of a professor". Synchronized tele-education is "real-time interactive virtual classrooms supported by many applications developed to meet all students' needs".

We analyzed "three types of descriptive data related to the COVID-19 pandemic, expenditure in education and national digital performance".

The study was conducted during the most unstable period of pandemic (from the first case of COVID-19 reported on 26 February 2020 to 22 August 2020 when finished the paper), since Romania has passed through a state of emergency from 16 March to 15 May 2020, (lockdown for all the residents) and a state of alert from 16 May 2020 to August 2020, continuing while

measures of economic and social relaxation were progressively installed; 2 waves of COVID-19 infections passed over, with a peak of infections on 13 August 2020, with 1454 new cases, as presented in Figure 18

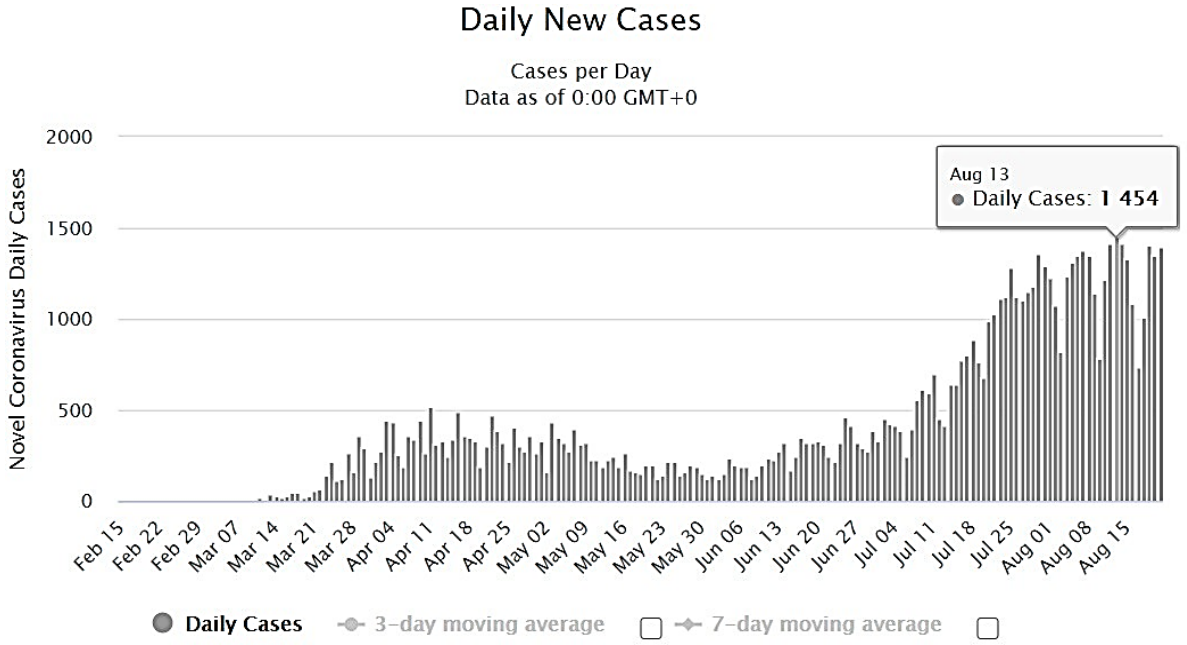


Figure 18. "Daily new cases of novel coronavirus infections" [160]:

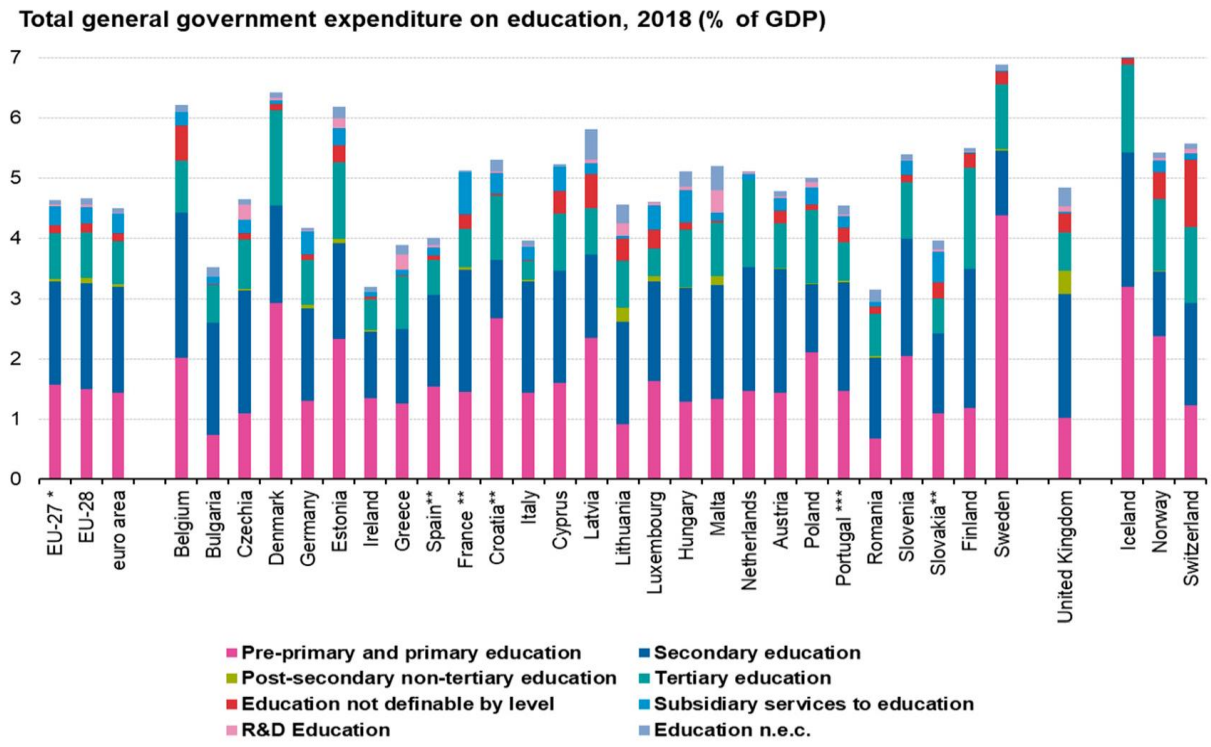


Figure 19. "Romania's expenditure on education in 2018" [160]:

"Face-to-face learning was banned in schools" starting from 11 March 2020. Three school scenarios were alternate, although no official rules ever regulated the development of the courses: Online, face-to-face (suspended due to a vast number of cases and increased epidemiological risk) mixed.

Expenditure on education became a critical indicator at the governmental, social and familial level. "In 2018, Romania spent on education 3.2% of its gross domestic product (GDP); it totalled LEI 30,100 million (approximately Euro 6468 million given the annual average exchange rate of Lei 4.6535 for 1 Euro). This expenditure (see Figure 19) ranked Romania the last within the EU in 2018".

Table 34 **"Romania's asymmetries with effects on education"** [160]:

Indicator	2017 *	2018 **	Observation
Total monthly income per household.	LEI 1,290.9 = Euro 283 per person (LEI 1,005 = Euro 220 in rural areas)	LEI 1,613 = Euro 346 per person (LEI 1,226.84 = Euro 264 in rural areas)	+Euro 63 per person (+Euro 44 in rural areas)
Total monthly expenditure on education per household.	LEI 3.72 = Euro 0.81 (LEI 2.04 = Euro 0.45 in rural areas)	LEI 5.15 = Euro 1.11 (LEI 2.01 = Euro 0.43 in rural areas)	+Euro 0.3 (-Euro 0.02 in rural areas)
Monthly average expenditure on phoning, audio, video, photo, information processing equipment and its accessories.	LEI 12.08 = Euro 2.65	LEI 14.13 = Euro 3.04	+Euro 0.39
Monthly average expenditure on information processing equipment and accessories.	LEI 2.3 = Euro 0.50	LEI 1.87 = Euro 0.40	-Euro 0.10
Share of households having access to computer at home.	65.60% (51.9% in rural areas)	n/a	-/-
Share of households having access to Internet at home.	68.60% (56.9% in rural areas)	72.40% (61.5% in rural areas)	+3.8% (+4.6% in rural areas)
Total number of the population aged 0–17.	3,704,601 persons (1,857,626 in rural areas)	3,680,850 persons (1,825,322 in rural areas)	–23,751 persons (–32,304 persons)
At-risk-of-poverty or social exclusion rate in the population aged 0–17 years.	41.70%	38.10%	-3.60%
Total number of matriculated students.	3,578,561 persons (1,022,507 persons in rural units, of which 77.84% in ISCED 1-3 units)	3,547,301 persons (994,183 persons in rural units, of which 77.50% in ISCED 1-3 units)	–31,260 persons (–28,324 persons in rural units, of which -0.34% in ISCED 1-3 units)
Total number of PC's managed by schools.	387,786 pieces (99,750 pieces in rural areas, of which 93.25% in ISCED 1–3 units)	396,614 pieces (99,275 in rural areas, of which 92.91% in ISCED 1–3 units)	+8828 pieces (–475 pieces in rural areas, of which -0.34% in ISCED 1–3 units)

* Annual average exchange rate was Lei 4.5681 for 1 Euro (source: www.bnr.ro) [34]; ** Annual average exchange rate was Lei 4.6535 for 1 Euro (source: www.bncr.ro) [34].

The lack of symmetry identified comparing "Romania's index of Digital Economy and Society (DESI), measuring digital performance" in 2019 with an average of 52.5 in EU 2019. As per Romania, the second last country in the EU range, the data "show an urgent need for capital investment in digitalizing all Romanian public services, including education". (see Table 36),

Table 35. **"The Digital Economy and Society Index (DESI)"** 2019 [160]:

Index	DESI 2019	Connectivity	Human Capital	Use of Internet	Integration of Digital Technology	Digital Public Service
The EU's score	52.5	53.5	48.0	53.4	41.1	62.9
Romania's score	36.5	59.3	31.1	31.9	20.5	43.2
Romania's rank in the UE	27th	22nd	27th	28th	27th	28th

We designed "a semi-structured in-depth research instrument (Table 3): a list of topics and sub-topics" to be discussed with participants enrolled to the study.

Sub-topic 2.3. was designed as a stimulator of creativity, encouraging the respondents' to name and describe any digital item used as learning support in Romanian school that was impressive/surprising enough to say "Wow!" "(instrument, device, tool, application, solution or platform").

Table 36. "**The qualitative research instrument"** [160]:

Analysis of Digitalization Supporting Romanian Tele-Education Under the COVID-19 Crisis	
Topic	**Sub-Topic**
1. The asymmetries within Romanian education in terms of digitalization.	1.1. The present asymmetries of the Romanian education system. 1.2. Main educational activities using ICT.
2. Digital resources needed for tele-education.	2.1. Existing infrastructure and teaching staff's hardware and software competences. 2.2. IT support for students and teachers. 2.3. Digital "Wow" in education.
3. Future digitalization of schools.	3.1. Fully digital schools and online teachers. 3.2. Costs needed to digitalize a school.

The primary data collected through interview notes was imported into this qualitative software and processed with Atlas.ti 8, into two processes:

I. "one inductive (describing seven themes and organizing the participants' words and sentences according to these themes)"
II. "one iterative (we assigned a label or code to the meanings, keeping high objectivity in the qualitative data coding)".

We grouped the respondents' answers on two paradigms:

(1) "the perception of *management's and teaching staff's intentions, planning and implementation of digitalization* in education received the following codes, (+/– management support) and (+/– teacher digitalization), used for the following pieces of information: knowledge, skills, intentions, motivations, competitions and funding";

(2) *infrastructure* received the following codes, (+/– infrastructure), used to mark the existence, use or lack of Internet, PC's, phones, labs, YouTube, smart phones, digital textbooks.

"Moreover, our respondents underlined the need to address similarities and differences between urban and rural educational environments, which received the following codes (+ urban digital development) and (+ rural digital environment)". It refers to urban digitalization, rural digitalization, funding and major houses' support.

Digitalization of Romanian Education at the Beginning of the COVID-19 Crisis

- ✓ It was shallow, no infrastructure, no Internet (some "because of the management, no acquisitions for the ICT infrastructure in the last ten years"), teachers' digital competencies are obsolete.
- ✓ Although the "implementation of modern technology in learning had been the main objective of education" and stakeholders, ICT had not reached all students. "There were schools with no Internet connectivity, and school management was mainly responsible" for the presence or lack of digitalization.
- ✓ "We identified two gaps between schools: rural versus urban (Asymmetry 1) and poor versus rich (Asymmetry 2)", as per the source of funding (local council, no money for rural schools, poor people in rural areas, children do not have any electronic devices, poor and wealthy schools even in urban).
- ✓ School management (Figure 21) represents as well the main factor of progress as an obstacle of technological advancement in schools (Asymmetry 3). Each school decision in selecting products, teachers' interest and influence in ICT help with new equipment, each school management support the influence of the local management (decisional factor in accessing funding, human resources development and development projects implementing).
- ✓ "The lack of ICT infrastructure (G = 3) is associated with the poor development of the ICT competencies of teachers (G = 14)".
- ✓ Teachers have "high digital skills (Asymmetry 4) as a result of their interest in this field (Asymmetry 5)".
- ✓ Adequate infrastructure requires public funding for the school and access and attract funding (management plan and vision, local policymakers) (Asymmetry 6). "However well-

endowed the school is, it comes down to the teachers' desire to use ICT in teaching and, more specifically, to their ability to do so".

- ✓ School management's openness and focus on digitalization shall be orientated in two directions: acquisition and donation by large companies. Usually, the companies renew their infrastructure and donate outdated or out of service equipment, not valid for students. (Asymmetry 7).
- ✓ To conclude, public policy in terms of funding infrastructure should follow a rigorous inventory of ICT-assisted activities, and acquisition should respond to students' and teachers' needs to increase educational quality and digital intelligence at the national level.

"Resources Needed to Enhance Digitalization in Romanian Public Schools"

- ✓ Our research confirmed the three types of resources a Romanian school needed "to become digital: logistics (infrastructure in terms of tangible and intangible assets), human resources, and financial resources to support tele-education (this shows how oversimplified online education is)".
- ✓ Romanian schools received infrastructure for ICT activities, especially the primary education levels (video-projectors, PCs, laptops, smartboards, scanners and printers), but they seemed not to be "enough" (Asymmetry 8).
- ✓ Romanian schools' IT infrastructure is quantitatively centred on hardware (Figure 22): no all computers are functioning, outdated donated equipment and old computers kept;
- ✓ Students' and teachers' security receive low attention: no knowledge of anti-virus software, hacking danger, no cyber-security software updates and virus scanning. (Asymmetry 9).
- ✓ Most schools had the old infrastructure, located in Computer Science labs, with limited access only during specialized computer literacy classes. (Asymmetry 10) Hence, "insufficient and/or inappropriate infrastructure, lack of access to infrastructure (kept only for the ICT Lab), and lack of cybersecurity determined teachers "use their own infrastructure" in teaching (G = 6), which underlines the need to implement a national program to digitalize Romanian schools" massively.
- ✓ "Romanian education lacks the equipment specialized for learning specific subjects (Asymmetry 11), such as science, technology, engineering and math (STEM). However, large ICT providers sell many physical devices and online synchronized and asynchronized applications and activities for education use at very affordable costs", eligible to be purchased within a national program.
- ✓ The digital competencies of teaching personnel and ICT specialists cannot correctly support tele-education. There are no updates (digital competencies or interest to develop, teachers lack basic skills, in opposition with few teachers willing to change whole schools

in digitalization) change lives with an innovative education. (Asymmetry 12)

Figure 20. "Asymmetries in the Romanian public education's digitalization". [160]:

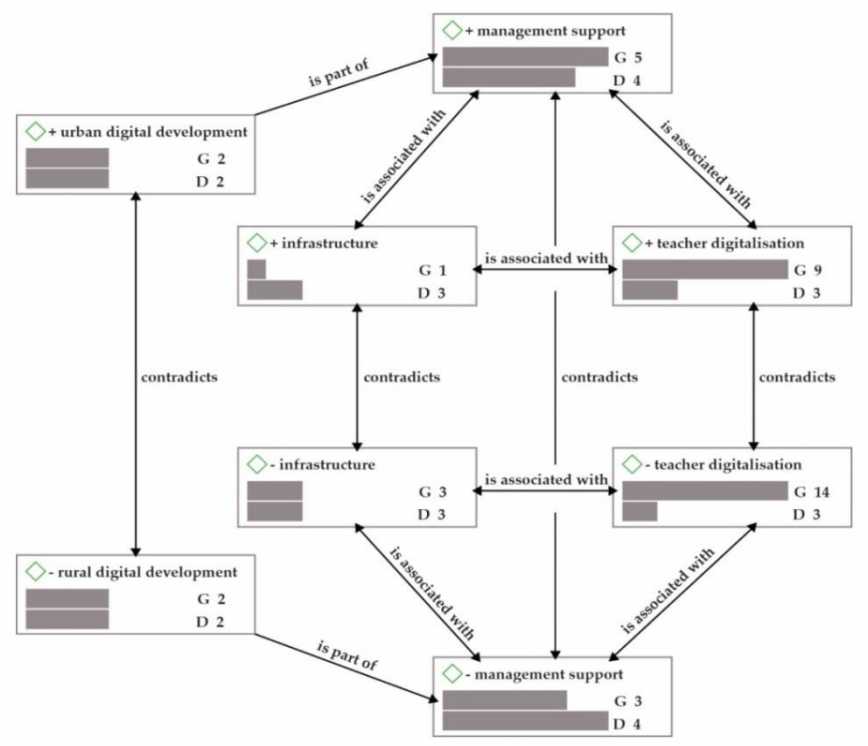


Figure 21. "Asymmetries of the logistic resources in Romanian public schools". [160]:

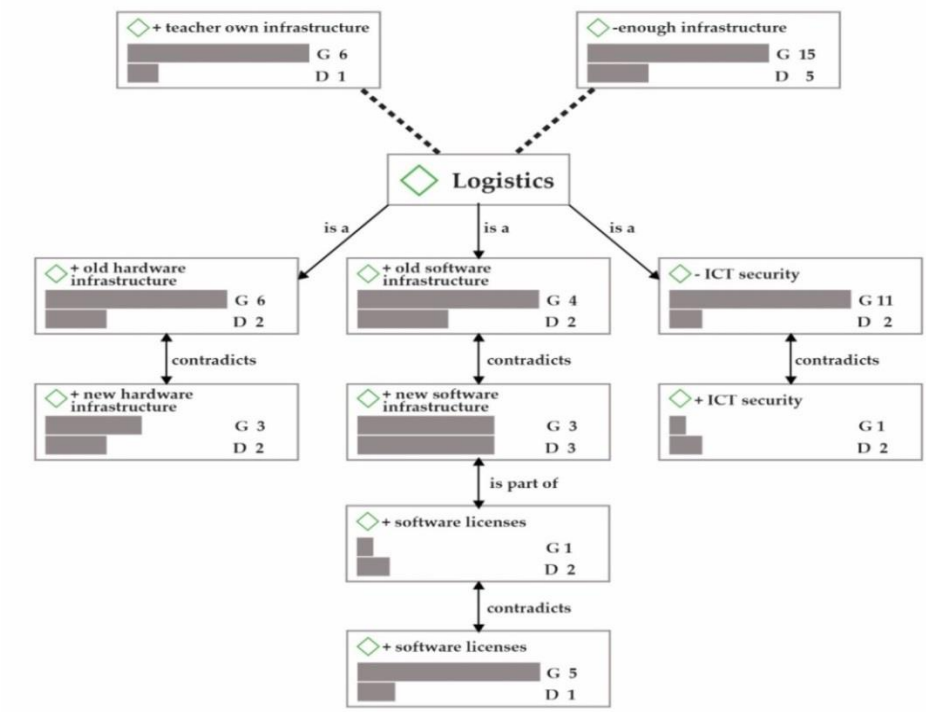


Figure 22. "Asymmetries of human resources in Romanian public schools". [160]:

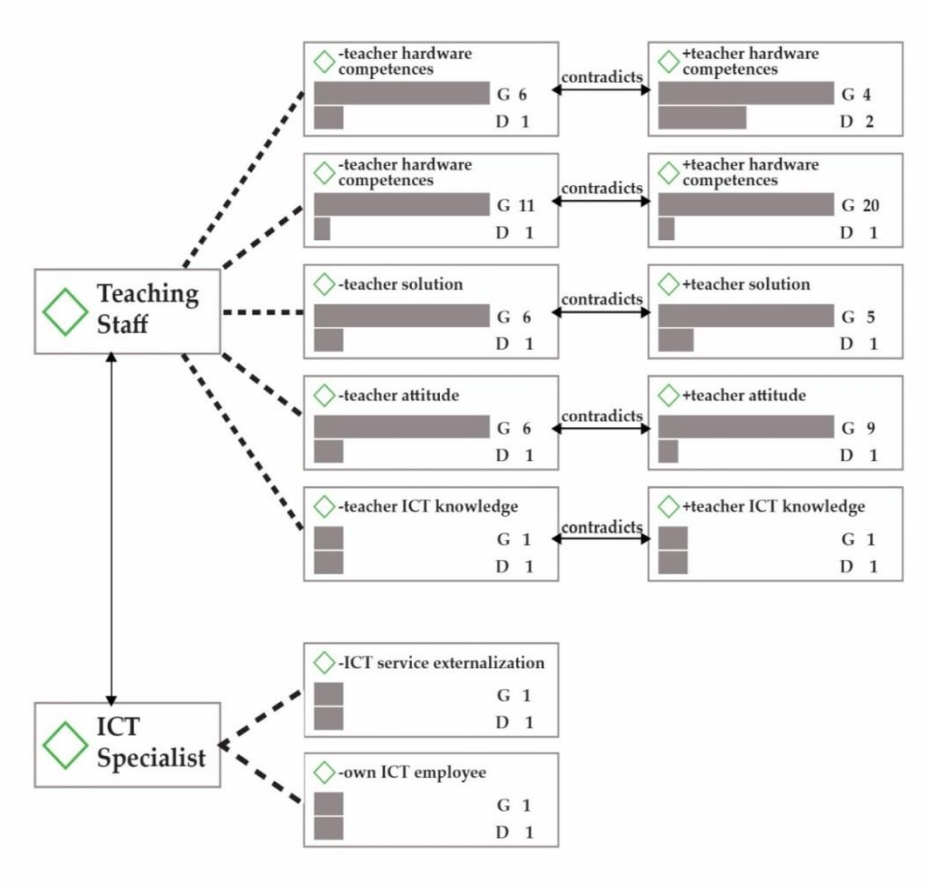
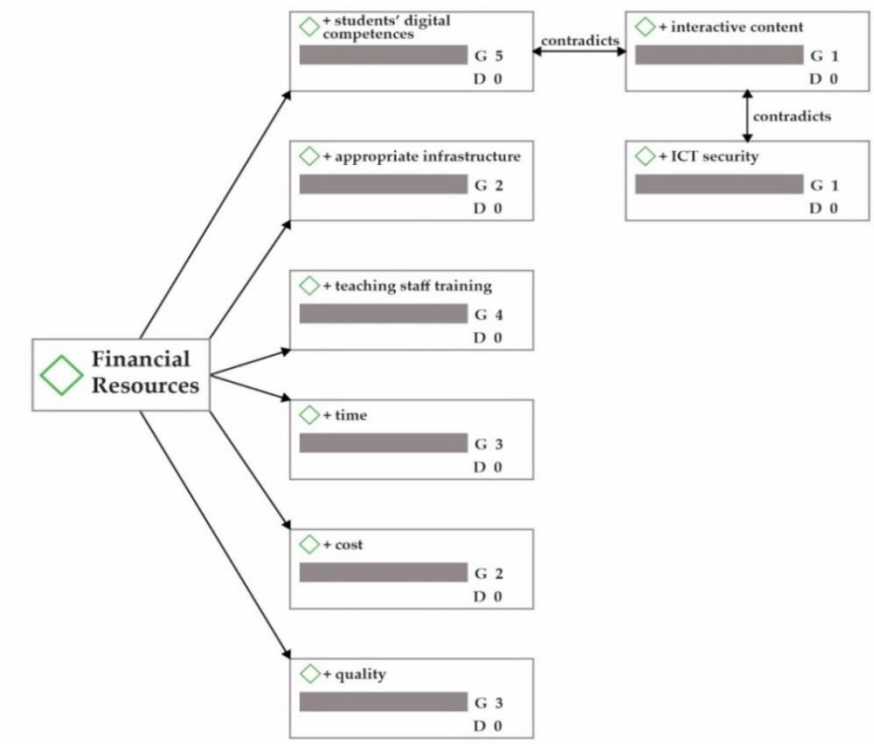


Figure 23. "Qualitative analysis of financial resources in Romanian public schools". [160]:



- ✓ "Regardless of their age, 50% of teachers are totally disinterested in using digital education".
- ✓ There is no IT support in many schools and provided by only one employee in charge of all the digital aspects of a school or through externalizing serviced to an IT company.
- ✓ "More ICT specialized jobs in public education shall build a strong education-centred, developing cooperation between ICT specialists, teachers, and students, resulting in increased students' learning outcomes (Asymmetry 13)".
- ✓ "Two participants even made a forecast of costs to provide immediate access to digital education to a student". For a school with 25 classes of 25 students, the primary digital needs can be covered with Euro.17,100 (Euro 27.36 per student). Basic infrastructure cost about 1500 euro/classroom, "affordable costs for face-to-face education".

1. *"Key Areas for Future Development of Tele-Education in Romania"*

"The three major key areas of development highlighted in this research are":

3.1. Improvement of teachers' digital skills(use a specific device, to interconnect devices "applications, software and devices to bust learning; to operate Windows, Microsoft Office, etc., to work with archives, folders, files and in the cloud, to synchronously teach by using online platforms and applications (Skype, Zoom, Google Meet, Microsoft Teams, Discord, WebEx, YouNow), to use the Internet, online platforms and online resources available, to scan the computer for viruses and work with cybersecurity";

3.2. Support for education (

3.3. Provision of fully online education.

The paper explores the asymmetries of Romanian education concerning digitalization due to the COVID-19 crisis; "this challenges education in terms of learning acquisition and educational needs, teachers' digital competencies, the ICT infrastructure available and cybersecurity".

The results showed that digitalization depends on:

1.1. the necessary infrastructure

1.2. the teachers' and students' levels of digital competences

1.3. "the capabilities of accessing and attracting funding to support digitalization (school management's and ministerial authorities capabilities"

1.4. "the stakeholders' motivations and needs to keep up with state-of-the-art technology and to use and develop the latest digital skills".

2. For the identified challenges, there appears to led to an educational crisis:

2.1. "a need for national infrastructure development for Challenges 1 to 4: 1-students' lack of Internet connectivity and/or electric power; 2-students' lack of proper ICT infrastructure; 3-students' lack of digital competencies or ICT support; 4-teaching staff's lack of Internet

connectivity, proper ICT infrastructure and digital competences";

2.2. "a need of changes in the education curricula (for Challenges 3, 4 and 6)"

2.3. "a need of new legal support (for Challenges 5 and 6: 5-legal issues with remote and online job tasks; and 6-cyber risks".

3. "In Romania, the present educational crisis has three major players:
   3.1. tele-learners who are or should be/become skilled users of ICT devices;
   3.2. educational institutions that are improperly digitalized in terms of infrastructure;
   3.3. tele-teaching staff is low skilled (according to the E-Didactics framework)".

4. "The differences between these two generations seem too deep to overcome, and the asymmetry is even more profound, considering that today's students are digital natives. In contrast, most teachers are digital immigrants as in both generations; there are people with high and low digital skills. This approach better highlights our findings that there are skilled and unskilled users of digital instruments in both younger and older generations, and the difference lies in the individual's digital literacy". [163].

5. "We also identified asymmetries in the use of digital skills and infrastructure in learning (Table 4) that need to be addressed at the national policy level. The socio-economic and technical disparities lead to educational disparities and a lack of equality of chances for all students in Romania".

6. The necessary infrastructure is still insufficient as tele-teaching requires an entirely different set of pedagogical competencies than traditional teaching (Comenius's) and specific personality traits.

The teaching and learning process, including the assessments and final evaluation of knowledge, were deeply challenged during the latest pandemic of COVID-19, and a huge mandatory change for the core of the education system, accustomed to face-to-face education as a unique option.

All teachers and education stakeholders faced students' readiness to adjust to learning in virtual environments instead of many teachers' reluctance to teach in virtual environments".

The pandemic has accelerated the application of online education, which needs rapid recovery and adjustments to improve the quality and involvement of both students and science providers.

The whole architecture of the teaching and training system should be redrawn and rethought to include e-didactics as a new mandatory topic for educating future generations.

III.a.2. Medical education and ethical knowledge – development and implementation

"Education, Ethics and E-Communication in Medicine"

Among the first studies and researches concerns were the modern concept of Ethics, Education and Communication, with the complex aspects of approach and application in education and health. These concepts were relatively unknown at the beginning of the 21st century, and while there were scientific approaches in research and literature projects, there were few practical applications in education. This was the reason why ethics papers, intertwined with education and medical activity, had a significant impact in the 2000's, as evidenced by the quantification of their impact and frequent citation in papers and presentations at medical and educational conferences. *("Rogozea Liliana, Miclăuş R., Nemet C., Bălescu A., Moleavin I. "Education, Ethics and E-Communication in Medicine" WSEAS-International Conferences – Santander, Cantabria, Spain")* [164].

This first article was an endorsement statement for introducing Ethics in medical and non-medical education curricula, underlying a complex list of characteristics and implications of using Internet and technics in learning and communication. Starting from the reality that e-Health became very important in medical students' education, the article presents a summary statistic data about the internet influence on medical students in University Transylvania of Brasov. Although ethics is an ancient concern of humanity and ethics gained the attention of specialists worldwide in 2000th, there are not so many approaches of medical ethics in students (as future specialists). The main characteristics of internet actions and how to use multiple forms of internet and e-communication (e-mail, chat rooms, online discussion group, forums, blogs or instant messaging) could influence the students.

Synthetizing the ethical implication in educating human behaviour, the paper states the adequate interventions connected with a fine understanding of the following issues, becoming educational goals:

I. To educate the proper Internet-individual relation, especially to whom we are communicating with?
II. To stimulate the appropriate individual attitude in internet communication and learning: cultivating active involvement and action, combating the passive taking part and the refuge reaction, encouraging a superior valorization of information sources and preventing an overdue reaction of its importance.
III. To identify the negative behavioural changes induced by the Internet (egocentrism, dependence, anxiety, depression, narrowed of concerns area) and find the best tools to prevent or fight against them.
IV. To search the signs and ways of potential alteration of an individual's social status while using e-communication and e-tools and to prevent the individual or collective attitude of disregarding the obligations or escaping responsibilities.

The ethical approach of cyber tools and Internet using is not to equalize the individual way of use or live but to increase the awareness of golden rules of bilateral respect, trust, flexibility, tolerance, no prejudice or discrimination.

"Health promotion - strategies and topics. Educating the medical students"

Other papers in the area of Education and Health sciences debate in 2010 the subject of Health promotion as definition, topic, content and factors to consider in awareness and education, ethical issues facing young people rights, training and responsibilities for Health sciences future specialist and future Health educators. ("*Rogozea, Liliana; Miclaus, Roxana; Repanovici, Angela; Burtea, Victoria, "Health promotion - strategies and topics. Educating the students from nursing and optometry department", Published in "Selected topics in education and educational technology", 2010, Editors Fujita, H; Sasaki, J, pag 263-267")* [165].

In 2010, in most universities worldwide, "nursing and optometrist students never got appropriate training in health promotion. Health professionals did not have updated knowledge in health promotion, especially in human well-being standards".

The paper explained the idea of developing a "standard curriculum in adolescent health promotion topics for students studying in two completely different faculties: Medicine (Nursing Program) and Mechanical engineering" (Optometry Program), and started from a study on the adolescent problems developed in the department. Paying attention to adolescents' needs and rights and considering the ethical issues related to people rights in Medical care, the paper developed a structured health promotion curriculum for both Educational programs.

We start from the concept of a healthy lifestyle that should include a lot of factors, as 3-5 times per week moderate physical activity and 2-3 times a week strenuous physical exercise as recommended in addition with healthy food, a good sleep in quality and quantity and a healthy "sleeping-working balance, mandatory preventive activities and behaviours -regular medical examinations, vaccinations, sexually transmitted disease prevention, safety compliance measures- use of protective equipment, safety belt". In order to determine adolescent's needs and behaviour, we developed a study on 300 adolescents age 14 to 18 between 2008 and 2010. The authors developed and applied a questionnaire with 24 questions regarding adolescents' evaluation of their health status.

The results of the study showed:

1. 75% of young people evaluate their health as pretty good in opposition with 25% believing their health is bad. 82.5% of teens recognized "difficulty concentrating" (26.5% - rarely, 51% - sometimes, 4% - often, 2% -all the time had difficulty concentrating). Regarding feeling stressed, half of the studied adolescents admitted "they are sometimes stressed, 25% are

rarely stressed, 12.5% often feel stressed", and 12.5% always feel stressed. Considering the body mass index, 18.07% of adolescents are underweight, the majority of them were girls (23.07% of all girls), a mark of social behaviour adapted to fashion, related to body image and beauty pressure.

2. The study confirmed smoking as one of the main unhealthy behaviours, even though "most teens responded that they have never smoked". In opposition, 12% of adolescents smoke every day (14.45% of boys use tobacco daily, more than in girls -10.25%).
3. The data confirm bad behaviour in adolescence (42% of adolescents recognized alcohol abuse and only 37% of teenagers never use alcohol), knowing that alcohol abuse is a principal health determinant directly related to disability and early death.
4. Daily consumption of fizzy drinks is highly connected with "a high consumption of fast-food (50% of the subjects eat at least 2-3 times per week hamburgers, cheeseburgers"), so fast food as diet associated with sweet drinks is a normal behavior, promoted by advertising (indicator of low quality of diet at apparently low budget).

Conclusions revealed two main ideas: "Evaluate the adolescent needs is the first step in developing a curriculum", with beneficial and attractive topics and Young people have to learn, more precisely need to be taught to understand and then how to develop a healthy lifestyle, especially how to balance good healthy things with things they like.

To successfully implement these ideas, we need to develop links between school professionals and community professionals, health professionals or others, meaning to redesign public health policies and often impose health policies to the detriment of advertising and consumption.

Also, Health promotion curriculum design has to respect human ethics, equality, and respect for human life to improve humans' health and extend life. In addition, a critical pedagogical approach within health promotion curricula, a perspective of qualitative research and skills for self-expressing each personality should be considered when teaching Health Promotion. We have to consider the mandatory characteristics for a good student and professional like initiative, implication, dynamism, personal attitude and point of view, the capacity of communication and listening to others, and lead a team).

So, it is crucial to redirect financial resources for preventive medicine, enabling to help more people by preventing grave health problems (healthy life, early diagnosis, and early treatment). Using money for health promotion campaigns remains the most important ethical challenge. Nowadays, people with economic background and education are still asking "why using the financial and human resources for preventive and not for curing medicine". [166]

Nowadays, challenges are to educate the students but also "to develop modern e-Health sites, health promotion forums for young people", coordinated by adequate professionals, in order to maintain the

quality of the information and education provided by these sites ("human good sense, good practice and professionalism in health sciences practice").

Ethical issues should represent a fine instrument to measure health promotion adequacy, not an obstacle in developing health promotion activities.

"Ethics and human behaviour – two topics for medical engineering students"

Also presented in the "WSEAS/IASME International Conference on Educational Technologies", in 2008, resulted from multidisciplinary team work. ("*Rogozea Liliana, Repanovici Angela, Cristea Luciana, Baritz Mihaela, Miclăuş Roxana, Pascu Alina,. "Ethics and human behaviour – two topics for medical engineering students", "WSEAS-International Conferences – Santander, Cantabria, Spain Sept. 23-25 2008 ISSN: 1790-5109 ISBN: 978-960-474-005-5, pg.87-90").* [166]

We start from the research and conclusion of the first paper underlying the importance of evaluating the ethical role of e-Health, awareness of computer sciences importance in the health system, the study of e-technologies in the medical and non-medical curriculum). The present study endorses the arguments for studying Ethics and Behavioural sciences in the medical engineering students' curriculum, based on the expertise of Medicine and Mechanical engineering teachers.

Medical licensed Engineering must understand malpractice as the most critical ethical issues linked with medical gestures and manoeuvres. They have to be prepared to meet the necessity of reducing the risk of medical error by developing special projects which decrease the potential life risk and increase the odds of life-saving and by efficiently using financial resources as much as possible.

Additionally, in 2008 the paper supports the implementation of Behavioral Sciences in the Medical Engineering curriculum giving a modern perspective of understanding new technologies and development linked with human interaction, relationship, unmediated relations, and empathy. The study endorsed the new technologies implementation as tools for human beings to increase their quality of life and allow multidisciplinary teams to collaborate.

In parallel, in the last ten years, Behavioral Sciences was introduced as a subject into the Medical Sciences curriculum in General Medicine, Nursing and Physiotherapy to prepare good specialists in Health sciences, trained to approach, interact, care, treat and educate people. In this way, university education gives the chance of meeting at the half road, physicians and Health specialists with medical engineers, working together to focus on people and their benefit. Both categories of specialists use modern communication and investigation tools to increase the quality of medical actions and ensure a proper human relation between physician and patient. Another aim is to minimize the risk of professional addiction to machines (value the role of clinical approach more than Para clinical-technological simply interpretation).

III.b. Ethical issues in Physical Medicine and Rehabilitation

III.b.1. Informed consent in physiotherapy in Romania

Physiotherapy becomes an important field nowadays inside the medical system. Physiotherapists are competent to apply the rehabilitation program designed by a physician and have become responsible for the rehabilitation of patients worldwide. [167]

Bioethical questions in Physiotherapy have grown in parallel with the field development but asymmetric assimilated to academic studies. We observed the lack of scientific literature to define and debate ethical specificity framework for physiotherapy. The subjects as informed consent (IC), medical practice, applied technology in rehabilitation and physiotherapy are rarely studied. We identified the imperiousness of coherent moral and ethical policies, mandatory to protect the patient and human life. [168] ("*Nadinne Roman, Roxana Miclaus, Liliana Rogozea Ethical considerations about informed consent in physiotherapy in Romania, Medicine and Pharmacy Reports. 1222- 2119,2066-8872 13., DOI: 10.15386/mpr-1223, July 2019").* [169]

The physiotherapist has to work mainly and progressively with the patient, to change techniques and treatment methods according to daily evaluation or health status of the patient. There is no framework or guidelines about how informed consent should be obtained in physiotherapy, and most of the time is related only to giving information to patients. [170] There is a surge need for comprehending the physiotherapy process of care with ethical implications, given the responsibilities of physiotherapists raised with new medical equipment utilization, including robotic therapy [171, 172]

Our research aimed to explore IC in physiotherapy services from an interdisciplinary perspective related to the patient's and physiotherapist's views. Social aspects of the patient's perception of IC were discussed and hypothesized within better perception and understanding amongst graduate patients. ("Nadinne Roman, Elena Tirziman, Daniela Sorea, Roxana Miclaus, Angela Repanovici, Elena Amaricai, Liliana Rogozea, *Ethical Dilemmas in the Interdisciplinary Approach to Informed Consent to Patients in Physiotherapy Services in Romania*, Revista de Cercetare si Interventie Sociala, 2018, vol. 63, pp. 290-303, ISSN: 1583-3410 (print), ISSN: 1584-5397 (electronic)")[173]

Two questionnaires regarding IC obtaining process were applied to physiotherapists and patients to investigate the frequency and level of understanding of the IC process. In both s, there were similar items. Each questionnaire contains similar items related to demographics, age, occupation, educational level, designed in compliance with European Data Protection Registry (European Parliament, 2016). In order to carry out the research, approvals have been obtained from the

Ethics Committee of Transylvania University in Brasov, but also Management Teams and the Ethics Committees of the County Emergency Clinical Hospital in Brasov and the "Clinical Hospital of Psychiatry and Neurology in Brasov".

The questionnaire for physiotherapists was made up of 39 items, with 2 open questions. It was applied from May to August 2018, distributed through a social network, within a group of physiotherapists' community in Romania, due to the lack of other access methods according to the lack of a professional association.

The questionnaire addressed to patients contained 22 items. One open question was distributed in written form within the County Emergency Clinical Hospital in Brasov and at the "Clinical Hospital of Psychiatry and Neurology in Brasov" and also applied from May to August 2018. From 535 respondents 148 were physiotherapists and 397 patients, with a rate of effective completion of 91.4% among physiotherapists (148 out of 162) and 98% among the patients (397 out of 405).

The data were processed using the SPSS 20 statistical analysis software, realizing a descriptive statistical analysis to generate a complex framework for the interpretation of data.

Mann-Whitney test was applied with the aim to determine significant differences between physiotherapists and patients. Kruskal-Wallis test was used to identify the differences in IC perception related to education level. Validation of the questionnaires was done through confirmatory factor analysis and Cronbach Alpha's appreciation

The value of the Cronbach Alpha index for:

- ✓ the physiotherapist questionnaire was 0.836,
- ✓ the patient questionnaire was 0.743.

Of the total number of participants, 27.7% carry out professional activities in public health, 67.6% in the private environment and 6.7% in the units of older people's homes, social associations or other units not in the public or private system.

We observed the frequency of CI when admission to medical word for rehabilitation treatment versus during the ongoing physiotherapy plan. Both aspects were debited from the patient's perspective versus the physiotherapist's perspective.

I1. IC provided at admission in physiotherapy: confirms the delayed patient- physiotherapist contact. IC is requested by the Rehabilitation physician when admission in rehabilitation department and assessment of each patient, but also, must be achieved by the physiotherapist as approval when beginning physical therapy and during the therapy, if necessary. 69.8% of the patients reported that IC at admission and of physiotherapy versus 40.5% of frequency reported by professionals (physiotherapists).

Tabel 37 Demografic characteristics of study' groups [173]

	Gender		Age group distribution							Education				
			Age (years)							secon dary	High school	higher Univer sity)	master's graduates	doctoral studies
Patients 397	Mal e	Fem ale	15-25	25-35	35-45	45-55	55-65	65-75	over 75					
	45.7 %	54.3 %	4.7%	3.6%	11.9 %	22%	31.5 %	21.4 %	4.9%	19.6%	62.5% bachelor	17.8%	-	-
Physioth erapists 148				49.3 %	38.5 %	9.5%	1.4%				60.1% Students	5.4%	33.1%	1.4 %

National legislation requires patient informing and IC provided by each patient. However, there are no specific requirements related to physiotherapy, taking advantage of the lack of a professional association, ethical, deontological norms, and the lack of a standard good practice in Physiotherapy. All these factors add up and lead to poor perception and misleading of IC process and management. [174, 175]

I2. IC provided at the contact with the physiotherapist and the onset of physical therapy, confirm a decrease in frequency reporting, both physiotherapists and patients and a mismatch in the frequencies reported, as the patients reported a higher frequency of IC acquired at the onset of kinetic therapy compared to physiotherapists.

The modality of obtaining IC (Verbally, Written, Verbally and Written, I3, I4, I5) showed differences in perception.

Written form IC is asymmetric understood and practice as physiotherapists do not perceive obtaining IC in written form as their professional duty. Additionally, obtaining CI in both verbal and written form was similarly reported and considered valid. [176]

Verbal is the most commonly used method of obtaining CI, for both physiotherapists and patients, both in the majority. Although National legislation does not impose obtaining CI in written form as mandatory, except for clinical trials. According to the purpose of IC obtaining, for treatment or research on human subjects, obtaining IC for physical therapy has legal, ethical and moral implications correlated to risk management [177]

The time spent by physiotherapists to give complete information about detailed physical therapy plan and progress (type of exercise applied, methods, techniques and outcomes) was investigated in patients and physiotherapists perspectives.

The extreme values, less the 3 minutes and more than 15 minutes, are at low frequency or never happened in practice, confessed by patients and physiotherapists. Because the results showed differences in physiotherapists' perception versus patients, we have developed a comparative statistical analysis, applying Mann- Whitney test to identify if there are statistically significant difference s between groups.

Mann-Whitney test was applied for comparative statistical analysis to identify significant

statistically differences between physiotherapists (PT group) and patients (P group) regarding IC obtaining in physiotherapy. Only three items from 10 analyzed, shown no significant statistically difference between the two groups, items related to frequency of reobtain IC during physiotherapy changing program (I6), time spent less than 3 minutes to inform the patient (I7) and time spent over 15 to inform the patient regarding physical therapy plan (I10).

The other 7 items showed "statistically significant difference between the two groups", leading to the discussions about:

A. Patients are more aware of the process of getting IC as well at admission as at the onset of physical therapy, revealing a discrepancy between answers and a mislead of obtaining IC by physiotherapists at the onset or during treatment. Going further and analyzing the distribution of physiotherapists' public or private practice, only 27.7% carry out professional activities in the public health facilities, which might be one reason behind the results.
B. There are significant statistically difference between Pt and P groups, in the disadvantage of Pt group, regarding the type of IC provided when admission. Patients have chosen high-end options with a higher frequency for IC types, compared to physiotherapists, underlying the importance of the first contact of the patient with other medical staff upon admission to the physiotherapy department (quality of time spend, quality of information, empathy)
C. There are significant statistically difference between Pt and P groups, in the disadvantage of P group, regarding the time spent by physiotherapists to explain physical therapy plan and inform patient about technical procedures and outcomes of physiotherapy exercises. (I8 and I9). Pt group have chosen high-end options with a higher frequency for these two quantities of time (3-5 minutes versus 5-10 minutes).

Social aspects regarding patient's IC understandings regarding physiotherapy have been analyzed linked with the ***educational level*** (graduates of secondary education, high school graduates and university graduates) and Kruskal-Wallis Nonparametric Test was applied to investigate the differences between the participants, as per a not normal distribution.

1. I1 analyzed showed "a statistically significant difference" between the University (U) and Secondary education (SE) group, but also a difference between U group and High School group (HS). Also, the mean rank and p values proved "a statistically significant difference between" the U group and SE groups, with a lower mean rank for U group (224.90, versus 287.48).
2. I2 analyzed showed statistically significant differences (by X2 and p <0.001) and a strong statistical significance in differences between U group and SE (mean rank and p). The second notable group difference is represented by the U and HS groups with a higher mean rank for the HS group and a statistical significance threshold p <0.001.

In both items analyzed, there were no differences between the SE and HS groups; the

university graduates rated a lower frequency as well in IC obtaining at physiotherapy admission, as in IC obtaining at physiotherapy onset. Another questionable issue is the level of perception and understanding of the analyzed groups regarding IC. SE and HS groups may overestimate their assessment of services generally assimilated to medical services or have a poor perception of IC process and its reasons.

3. I4 (CI in written form) determined the group differences (the threshold p <0.001 and X2). Thus, statistically significant differences were found for U and HS groups \
4. I6 (reobtain IC during physiotherapy intervention in the treatment plan), according to the level of studies, showed statistically significant differences, by p and X2. Thus, higher education has again reported a lower frequency of IC reoccurrence in treatment reassessment.
5. I 9 and I10 (the amount of time provided by physiotherapists for patients to give information and details about the therapeutic program) show statistically significant differences after Kruskal-Wallis test in (by X2 and p). The U group has in both variants a lower mean rank compared to SE and HS groups. The results confirm a poorly process of IC obtaining in physiotherapy usually associated with both patients and physiotherapists perspectives.

One ethical aspect of IC raised from patient autonomy and his right to decide on his treatment. Due to the health system in Romania, where the physiotherapy component is public, the patient can often feel disillusioned about the issues of consent, information and perception of decision-making processes. However, IC also requires background information and mandatory education to enable patient's understanding and decision.

In Romanian physiotherapy services, higher educated patients are better informed and more aware of the IC process, even if lower educated patients overestimate their IC knowledge.

Further research should focus on identifying the gaps of patient's knowledge, information process and consent in physiotherapy services with a specific objective to build adequate instruments for patient education. Since most public health institutions have a CI form, an interdisciplinary approach is the best tool to individualize the IC process, based on appropriate information techniques, the use the most appropriate language and multidisciplinary perspective tailed on patients' individual level of understanding.

The perception and understandings of the IC process and the treatment aspects related to patient information regarding physical therapy tend to be disregarded and overrated as frequency by patients with average or lower education levels. Higher education is linked with greater attention to the circumstances of the medical services, including physical therapy, with better information, especially IC. It has a higher level of expectations regarding the amount of time and information from professionals performing physiotherapy.

Further research is needed to identify elements and tools related to the knowledge required to improve patients' understanding of IC in physiotherapy from an interdisciplinary perspective.

III.b.2. Ethical issues in the practice of Physical Medicine and Rehabilitation

III.b.2.1. Ethical issues in rehabilitation of the post-traumatic patient

Physical Medicine and Rehabilitation "developed after 1947 based on the needs of patients with functional locomotor sequelae of infectious pathologies (poliomyelitis epidemics) or of various posttraumatic pathologies - interpreted as public health issues related to impairments and disabilities". Restoring maximum locomotor functioning is the main therapeutic objective, thus increasing the degree of physical and psycho-behavioural independence of the posttraumatic patient referred to rehabilitation. Patients are extremely physically and mentally vulnerable. They are not "psychologically prepared for the long-term therapeutic program and must be informed and motivated to follow a medical routine involving many healthcare professionals. The trauma patient needs empathy and communication for reaching coping, adapting and complying with the rehabilitation program". Patients with dysfunctional locomotor pathologies and disabilities in posttraumatic context are usually referred from orthopedics, neurology, neurosurgery or rheumatology. The goals of the rehabilitation program have to be understood reasonably. Also, "they must carry out its different sequences by following the given recommendations based on the experience and professional competence of the rehabilitation team. In many situations developing conflicts and ethical dilemmas related to the communication and information process, patient monitoring, quality of the relationships and communication in the rehabilitation team", of specific equipment, assistive devices and infrastructure The particular elements of ethics in Rehabilitation "were progressively structured starting from other models such as the US bioethical model and the general principles of medical ethics. To address the specific issues of Ethics in Rehabilitation, various challenging situations related to compliance of physician-patient and patient-family relationship might be analyzed". [178, 179].

The main objective of the research was to identify the main ethical issues in posttraumatic rehabilitation, focusing on the main steps of the rehabilitation process after trauma. ("*Adriana Sarah Nica, Mariana Constantinovici, Roxana Miclaus, Ethical issues in rehabilitation of the post-traumatic patient, Romanian Journal of Legal Medicine , Volume: 25 , Issue: 3 ,Pages: 309-313 , DOI: 10.4323/rjlm.2017.309")* [180].

We analyze in detail the situation of a posttraumatic patient referred for rehabilitation services, discussing each step of rehabilitation considering various parameters involved: patient, the patient

family, the rehabilitation team and the medical system, financial aspects, social and professional aspects, goals and tools of rehabilitation.

The terms "ethical" and "moral" are closely linked to behavioural values and they may be correctly interpreted or not. Thus, a biomedical ethical system has been developed with general principles and rules and particularities for rehabilitation. "This system may solve dilemmas and conflicts from clinical rehabilitation practice, including posttraumatic or polytrauma patient's particularities in various scenarios".

All road accident at fault, "negligence, trauma secondary to other health problems, trauma in elderly and in patients with important physical deconditioning syndrome require to make correct decisions based on the understanding of the case scenario". [181].

The debated topics and the problems to be solved are the following: 1. "the reforms in the healthcare system and the complex issues related to posttraumatic patient's journey" 2. "the main responsibilities in rehabilitation for all the players involved: rehabilitation specialists, physiotherapists, psychologist, speech therapist, nurses and caregivers and other healthcare professionals"; 3. "direction of resources and healthcare costs"; 4. "particular events in the rehabilitation platform and related to the patient's journey and that of his family as well as that of the rehabilitation specialist and his team".

Considering the more extended period necessary to carry out gradually the rehabilitation program in a posttraumatic patient and the journey of the patient with posttraumatic disabilities between several rehabilitation settings, the effects of the rehabilitation program do not occur "in few days after application". "According to the international guidelines, in most situations, rehabilitation requires several weeks or even months. In chronic patients care, the development of a partnership with many players from the rehabilitation platform brings interest to the characteristics of bioethics in rehabilitation. Also, setting the rehabilitation goals and professional obligations, the professional relationship with the patient and the role and involvement of the family of the posttraumatic disabled patients are real challenges. This experience might negatively affect the patient's self-esteem for reasons related to psycho-behavioural issues and physical dependence".

The main ethical principles related are (1) "Beneficence (with connotation for moral obligation to help "the others")" and (2) "Prevention of illness and injury, pain management, maximal autonomy and justice advocacy";

There are several unique topics of interest in the rehabilitation of posttraumatic patients, related to "the age of the patient, the traumatic context, and the perception of the disease by the patient and his family, their expectations, the development and implementation of the rehabilitation

program and patient's journey". From the clinical and functional perspective, "pain is an essential element with an important ethical position for posttraumatic patients that requires compliance with specific ethical norms and dynamic evaluation".

A special posttraumatic situation is "Traumatic Brain Injury (TBI), a severe problematic health care field in connection with disability. Medical evidence suggests that the primary goal of rehabilitation for TBI is community integration" and the evolution is connected with variation in the individual characteristics (family background and support, education programs, quality and availability of community services, financial conditions), rehabilitation infrastructure, the experience and professional competencies of the rehab team members". "The patients may experience long term physical, cognitive and psycho behavioural impairment due to extremely variant lesions resulting in many potential disabilities. Thus, the rehabilitation process needs to be carefully planned. The goals need to be holistic, considering long-term outcomes and must be individualized to each survivor and his or her family. The TBI may cause long-term physical disability and neurological impairments, such as motor dysfunction (impairing coordination, balance, walking, hand function, speech) and sensory loss. These critical functional consequences affect the patient's quality of life. Physical therapy and rehabilitation identify these impairments and may help the person achieve the maximum degree of return to their previous level of functioning"

Bioethics of the posttraumatic patient and the related costs are essential; "the decision to select the therapeutic offer depends on the healthcare cost"s, the application methodology, the quality, and the case-solving speed additional risks in evolution. Particularly in the posttraumatic elderly patient, "there are ethical dilemmas related to the economic and financial aspects. In advanced countries, the public opinion indicates moderate support (about 30%) for the criterion of healthcare in the elderly, a situation in which, on the long-term, there is a risk of elderly exclusion. In these conditions, the dependence of posttraumatic elderly patient regarding healthcare and rehabilitation program is a real challenge. Rehabilitation in the elderly posttraumatic patient with disabilities gives a new chance of improving the patient's quality of life".

The physiotherapy (PT) team and Occupational therapy (OT) team are involved in "ethical procedures: PT goals and physical procedures should be very explicit, every patient should be directly involved in the rehab program", in decisions, exchange of information, initiation and review of practice's mechanism, cooperation with patients and their relatives "when establishing goals and making decisions during their rehabilitation program, respect the right of the patient to refuse a specific service, scientific or research activity" [182].

In the context of the rehabilitation program for chronic posttraumatic patients, "following multiple evaluation and therapy sessions, the relationship between the patient (and his family) and the rehabilitation specialist (and his team) requires a long-term climate of trust, understanding and respecting all rules".

The rehabilitation team must try "to communicate better and find institutional solutions for identifying and reporting moral dilemmas and sustaining the ethical consultation in rehabilitation of the posttraumatic patient". The identified situations must be registered and periodically analyzed and not be minimized, but presented and solved for every case to avoid repetition and the waste of time and energy, trust, material and economic and financial loss.

III.b.2.2. Management and ethics issues in rehabilitation and balneoclimatology

The medical and paramedical recovery team often faces ethical dilemmas during practice. Team members must adhere to ethical principles and give importance to conflicting moral obligations [183]. Examples of balneology difficult decisions are: directing patients in the resort based on medical history, lack of screening in patients sent to different resorts, involvement of other domains (labour medicine) in sending tickets to the resorts. Decisions of a moral nature differ from those governed by law, religion or politics. They emphasize what is right rather than what is possibly or legally permissible. Etiquette, cost, and convenience considerations play an insignificant role in making moral decisions. The moral and ethical principles are closely correlated; both emphasize manners, habits and character. Ethics concerns the theoretical representation of values. Morality describes and analyses behaviours, identifying what is right or wrong. There are also described inherent moral conflicts and problems commonly encountered in clinical recovery practice and the approaches recommended to resolve these dilemmas. However, new situations are emerging in the medical practice of rehabilitation.

The codes of medical practices have evolved in response to medical challenges.

Therefore, this research's main objectives focused on identifying, summarising, and structuring the particular ethical problems in the field of rehabilitation medicine and specific situations when specific ethical issues arise and to determine physicians' duties and responsibilities in medical ethics and their contribution to the development of sound public policy.("*Adriana Sarah Nica, Ioana Ghiorghiu, Mariana Constantinovici, Roxana Steliana Miclaus, Brindusa Ilinca Mitoiu, Management and ethics issues in rehabilitation and balneoclimatology, Romanian Journal of Legal Medicine, Jun 2019, vol XXVII, No 2, pag 195-199 DOI: 10.4323/rjlm.2019.195")* [184]

The analysis starts from ethical principles explained exhaustively (the principle of beneficence: "moral obligation to help others not to harm them, implies the obligation to promote health, the well-being of patients and prevent illness, injury, pain and suffering)", the principle of autonomy: obtaining informed consent, respect for the values and beliefs of others (obligation to inform the patient of the diagnosis and therapeutic options and obtain their consent prior treatment beginning [185] and the principle of justice as the distribution of burdens and benefits in society, to provide health services to all members equally. However, limited resources or competition for them can create conflicts [186].

Faced with other medical specialities, which focus on patient illness and healing, sometimes even saving a life, medical rehabilitation addresses the patient with a functional, often chronic and irreversible deficiency. It aims both at the functional rehabilitation and in the family, social and professional reintegration of the patient, realizing the practical definition of the complex and long-term rehabilitation process, a three-dimensional bio-psychosocial process. This approach requires both the presence and active participation of the patient and the existence of an environmental platform (infrastructure and human resources) to support rehabilitation policy. Also, the constant and stimulating presence of the family and the activity of a complete rehabilitation team (rehabilitation physician, physiotherapist, psychologist, speech therapist and sociologist, orthosis specialist, social assistant, nurse) is mandatory. The team focus on somatic and visceral functional objectives in the context of psycho-behavioural particularities.

A. Practical clinical problems in Rehabilitation

1. *Patient identification* is based on *general clinical assessment* (the presence of pathologies with impact on rehabilitation), somatic and functional assessment (locomotor and neurological), and psycho-behavioural adherence to treatment. It will consider the type of functional deficit, patient communication and learning capacity, patient age, family support, financial capacity, and the specificity of the rehabilitation department to assess his / her rehabilitation capacity. All these categories can emerge many ethical issues, an excellent reason to use a standardized selection guideline containing the inclusion and exclusion criteria.
2. Rehabilitation Goals setting is done by the complex medical team, based on good communication and information with the patient and the family related to possibilities and outcomes, risks and benefits, pain, costs, health and illness, treatment benefits and alternative therapeutic options. Individual perception of patient and famiily is influenced by their level of education, experience and values). [186] Patient's autonomy can be compromised by lack of medical knowledge and might waste time, money and effort without need. Also, a physician's experience in recovering dysfunctions can overstep the choice of

family or patient [187], but should never impose personal values on patients and should never involve moral authority.

3. Patient-doctor relationship is a long-lasting one [188]. Caplan describes two patterns:

   3.1. *The contractual model* requires the patient to be informed about medical condition and all treatment options and respect for the patient's autonomy. The problems related to habits and levels of education, understanding and involvement of patients and family into the treatment are commonly encountered.

   3.2. Patients with extensive disabilities need time to accept the new physical and psycho-behavioural status and to adapt to the new reality and feel unprepared to make crucial decisions; the family does not know to care for a disabled person and cannot make appropriate decisions [188].

   3.3. *The educational model* bases on the patient's ability to accept, learn, understand and cooperate during the long rehabilitation program while the doctor is attempting to understand the patient's options and values. Caplan suggests that doctors are entitled to try to predict, simulate scenarios, to have arguments to persuade the patient to follow the rehabilitation program in the first phase of recovery. The doctors can orientate the medical decision when the patient has not yet adapted to the new condition and is not prepared to decide the treatment. In rehabilitation, it is necessary to evaluate the patient's autonomy periodically and becomes essential to quantify the dynamics of the functional acquisitions. .

4. *Professional and team issues*. The patient of the rehabilitation program crosses a long medical experience and begins with a family doctor or other specialties (neurology, neurosurgery, orthopedics, rheumatology, geriatrics, etc.), crossing a medical and relational experience which he will prepare for confrontations and acceptances in rehabilitation. Therefore, it is considered that the rehabilitation program is provided by a multidisciplinary group of professionals working together as a team, improving the patient's functional deficit, psychosocial challenges and professional needs. Experienced teams can provide efficient and well-organized services, well-coordinated and appropriate program that cannot be provided by a self-employed professional.
5. *Debts and rights of family members*.

Most patients are home-grown affects freedom, independence and responsibility of "falls".

   5.1. Family members taking care of patients with disabilities are subject to emotionally, physically, and social chronic variable stress. They can also progressively develop an increased rate of depression, overwork, social isolation, family misconduct, and poor

health towards people who are not responsible.

5.2. The financial effort for the family is substantial and is an ethical obligation to allow the family to participate in making financial management decisions. Conflicts arise when the family's opinion differs from that of the patient, increasing pressure on the parts and compromising the patient's autonomy.

5.3. Ideally, family members benefit from tools, devices and facilities to support them, such as daycare centres, counselling, support groups, and providing medical devices. Nowadays, there is no social infrastructure mandatory to continue the rehabilitation program after discharge (social assistance, the ability to adapt the home to the patient's needs). Society should develop mechanisms to reward financial and psychological services that can lessen people who care for a person with disabilities.

6. *Quality of life and cessation of treatment*. Many factors occur in the decision to stop the rehabilitation treatment (high expectation, disappointment after long rehabilitation with low benefit, non-compliant, non-cooperative or insufficiently motivated patients cause the team to cease treatment relatively early, short. Duration of treatment, insufficient imposed by health insurance policy, patient and relatives do not appreciate the importance of the evaluated factors. Physicians have to present the objective data that led to the decision to stop the rehabilitation program. Patient and family participation in team discussions about the cessation of treatment is critical to accept the decision.

B. **Professional and legal decision**

B.1. Resource allocation raises the central questions: the challenge for the healthcare system is and will continue to be the imminent increase in the need for medical services. Increasing the elderly population, the number of chronic diseases and increasing life expectancy) with the financial limitation of the system, increased demand for medical services while resources are insufficient will be the challenges for the next 20 years in Public healthcare. The human resource is deficient, and the responsibilities and the low number of the medical staff negatively influence the quality of the medical act by overworking the medical professionals [143, 191].

Calling for specialized services should be discouraged. Access to primary care improves health outcomes; the use of more specialized care should depend on evidence of effectiveness and understanding of the effectiveness with which it can be assured. Costly care of marginal benefits should be replaced by treatments that improve quality of life.

B.2. Medical insurance and implications for rehabilitation: allows in Romania not enough wage per person as expense on rehabilitation treatment (21 days a year of rehabilitation or balneary treatment are insufficient for patients with posttraumatic or post-stroke pathologies, and the continuation of the treatment implies costs which majority of patients and families cannot bear.

As conclusions, rehabilitation doctors will continue to face significant moral challenges in the coming years (criteria of inclusion and exclusion in Rehabilitation, prioritizing, patient-doctor-team relationship, human and financial resources management and allocation). Thus they must ensure that patients are treated with compassion and respect in an era dominated by financial pressure and rapid technological innovation.

Physicians' duties and responsibilities in medical ethics are priority focused on recognizing and addressing the inequalities of our current medical system, on discussing the role of medical rehabilitation in a time of limited resources. Being aware that some medical needs remain unsatisfied in a society with other vital needs, they must recognize and limit the care of marginal benefits or high costs.

As the Romanian society strives to balance the needs of vulnerable people with those of the larger society, Rehabilitation doctors must contribute to the development of sound public policy to harmonize the reality of differences between people and how patients and families are participating in health care. The critical implication of today's complex health care environment is to think complexly and find the best solution for the suffering of each patient and the development and progress of Physical Medicine and Rehabilitation in Romania as a safe and competent medical field.

(B-II) Academic Achievements

In 2001 I started my academic activity as a junior assistant in the Faculty of Medicine, Transylvania University of Brasov, Romania, in the Nursing discipline. Then, I was promoted assistant through a competition in 2004. The experience gained during this period allowed me to accumulate instrumental knowledge related to the Rehabilitation speciality. I trained as a resident physician in parallel and combined the didactic and mentoring activity with the national and international projects to coordinate the international exchange of teachers and students within the Erasmus program.

Since September 2007, I was a lecturer (by competition) in the Faculty of Medicine, Transylvania University of Brasov, Romania, teaching courses and laboratory for Medical students in the 5th year in Medicine Faculty and teaching General and Clinical Nursing in Nursing licence programme.

In 2007 I participated in creating the curriculum and the structure of the bachelor's degree in Physiotherapy (Balneofiziokinetoterapie și recuperare), which ARACIS authorized started operating starting in the University of Transylvania in October 2009. I taught the specialized subjects within this bachelor program, respectively: Kinesiology, Nursing, Electrotherapy, Kinesiotherapy, Somatic and Functional Assessment, Balneoclimatology, Hydrotherapy, and Hospital Practice three years of study, Research activity and licence dissertation. Since 2011 (by appointing the Teachers' Council, starting with 1.11.2011), I am intensely involved in the coordination activity, management of the study and training program. I am the mentor and coordinator of the bachelor theses of Physiotherapy graduates of the Physiotherapy study programme.

In parallel, I coordinated the Erasmus activity of international partnership in Nursing and Physiotherapy until 2012. On this occasion, I continued to participate in international exchanges of teaching courses at partner foreign universities:

1. "Partnership in the Area of Health Promotion and Well-being, summer school", "Jyväskylä University of Applied Sciences, School of Health and Social Studies", 25-29.08.2003
2. "Promoting Well-Being and Sexual Health", Jyvaskyla, 4-5.X.2004
3. "2nd International Conference on Trends in Environmental Education EnvEdu 2005", 8-10.09.2005, Brasov, Romania
4. "3st International Conference on Trends in Environmental Education EnvEdu 2005", 8-10.09.2005, Brasov, Romania
5. "Summer School, Family and Health Promotion, 10-14 septembrie 2007", "Jyväskylä University of Applied Sciences, School of Health and Social Studies", Finland

6. "Summer School, Family Health Promotion: Men's Health 15-19 September 2008", Poznań, Poland
7. "Symposium and Summer school: The Promotion of Family Health - The Mental Health, a Theoretical and Practical Approach", Brasov, 10-12.06.2009
8. Erasmus Teaching Program 06.2010- University Antalya, Turkey
9. Erasmus Teaching Program 11.2010- Escola Superior d' Enfermagem do Porto, Portugal
10. Erasmus Teaching Program 11.2010- University Almeria, Spain
11. Erasmus Teaching Program 2011- University Larisa, Grecia

I have actively participated to the **international projects**, the most important beingincluded in the table below:

Table 38 **International Research projects participation and the role into the projects**

International Research project/ Programme		Role	Period
1.	Research project no. 5/ 2005 in the partnership of Medicine Faculty and SC Hiperdia SA: „Elaborarea unui plan strategic privind armonizarea curicullei şi a pregătirii asistenților medicali din România în concordanță cu standardele Uniunii Europene şi ale pregătirii din Statele Unite ale Americii"	member	February 1st– December 1st 2005
2.	„Bioanalytical methods – linking environmental protection and public health", SOCRATES/ERASMUS project- director Mihaela Badea	member	2004-2005
3.	"Leonardo da Vinci - Community Vocational Training Action Programme - PMH – PROMENTALHEALTH, Exchange of Competencies for Trainers on Mental Health Promotion RO/2006/97125/EX", inside the project TEMPUS Contract No.S-JEP 12156-97, coordinator Ann Alty, University Lancashire, UK	beneficiary	2006-2007
4.	Leonardo da Vinci – E health in European Community Training 2007-2009	member	2007-2009
5.	"Masters in Health Rehabilitation through Physical Exercise – HARPE, Lifelong Learning Programme, ERASMUS Curriculum Development Projects", coordinator: Buckinghamshire New University, 2009-2011	management team member	2009-2011
6.	„Equal opportunities for health: action for development", Contract DCI-NSAED/2010/239-187, EuropeAid/129493/C/ACT/Multi, coordinator CUAMM Italy	Project Director	2011-2014
7.	"HELP Healthy Europe through learning practice"- 2011-1-GB2-LEO05-05499	Member	2010-2012
8.	"Ring transferring supports for caregivers – Leonardo da Vinci"	member	2010-2014
9.	Guidelines for training of Information Literacy teachers/practiconers, Methodology for teaching information literacy. Mobility Project in Higher	member	20th-25th

	Education EEA-FINANCIAL MECHANISM – Teaching/Training Mobility Programme de burse şi cooperare inter-instituțională in domeniul învățământului superior finanțat prin Mecanismul Financiar al Spațiului Economic European 2009-2014, Măsura 2 - Proiecte de mobilitate în învățământul superior, Universitatea Bergen Norvegia (F-SEE-017_List_select_MOB_SEE TU BRASOV)		Jan 2014

My participation in all these projects and international exchanges has contributed to the formation of partnership teams in education and research and have materialized in the didactic and scientific works and publications that I sign as an author, including extensive interdisciplinary research topics.

In 2017, I was promoted through competition in associate professor position in the Faculty of Medicine, continuing the teaching activity, mentoring of students in Medicine and Physiotherapy.

Since 2018, I continue to coordinate the residency training activity of 17 resident doctors in the speciality of Physical Medicine and Rehabilitation (Rehabilitation, Physical Medicine, Balneoclimatology). Each resident doctor si integrated into the clinical activity, the treatment and care of patients, and the study and research of the nucleus developed in the Clinical Department I lead. Young doctors can find the condition for study and research and find their way both in training as doctors and future teachers.

In 2018 I won as a **project director** an internal competition of Transilvania University iin the partnership with Brasov County Counsil ("***Recuperarea pacienților cu AVC prin Realitate Virtuală***"). Inside this project, I managed to purchase modern rehabilitation equipment within a value of 10.000 euro, and I started an intense research activity in the "Clinical Department of Neurological Rehabilitation" of "Clinical Hospital of Psychiatry and Neurology", in parallel with the training of rehabilitation doctors and physiotherapists. Since then, the research activity of the team I lead has focused on neurological rehabilitation, materialized through works and studies published internationally.

I intend to consolidate a strong research nucleus in the Rehabilitation Clinical Department in neurological rehabilitation and cardiovascular, posttraumatic and respiratory rehabilitation. The complexity of the cases we treat in rehabilitation requires a multidisciplinary approach and the construction of complex rehabilitation programs, which gradually combine the rehabilitation of complex pathology associated with secondary and tertiary prophylaxis, preparing the patient for reintegration into family, society, and possible work reintegration.

I have contributed as a principal author or a co-author at writing book and teaching materials for Physiotherapy students and Medical students: Esențialul în recuperarea medicală, Ed. Lux libris, 2015 (single author);"Kinesiologie curs și kinesiologie aplicată", Editura Lux Libris, 2016 (co-author); Electroterapie. Note de curs, Ed. Lux Libris, Brasov, 2015 (single author); Recuperare în chirurgie, note de curs, Ed. Lux Libris, Brasov, 2014 (co-author), Managementul mobilizării pacientului, Editura Universității Transilvania, 2007 (prime autor).

In twenty years of academic activity, I have coordinated more than 100 bachelor theses for Physiotherapy program graduates, more than fifty for Nursing graduates and nine theses for students in Medicine. I have also coordinated students work and papers for scientific communications and congresses, and annually Students' Scientific Communication Session (Organized annually after Easter students' holiday).

Since 2001 I took part as a member in the commission of the admission exam for the Medicine Faculty. Between 2016 and 2020 I served as secretary or vice-chairman of the admission committee in the Faculty of Medicine.

Between 2011 and 2017, I was a member of the bachelor exam commision for the Physiotherapy programme and since 2018, I served as President of the same commission.

Starting from 2007 I took part a member in several commissions of teaching positions vacancies at Faculty of Medicine, University Transilvania of Brasov: four commissions for assistant and five for lecturer. I was a member in three commissions of Associated professor, one at the University of Oradea (2020) and two at "Victor Babeș" University of Medicine and Pharmacy (2020). Also, in the last five years, I had the honour to be a member of two PhD dissertations at the University of Medicine and Pharmacy "Carol Davila" Bucharest.

Due to experience as a lecturer and associate professor, I was invited to be a speaker at conferences and presentations inside projects, organized by prestigious entities, as follow:

1. "***AVC - de la educatia pacientului la managementul multidisciplinar***" as the fourth event inside National Program " AVC 360° - Calatoria pacientului, 2018,11th of July, project sustaind by Academia de Stiinte Medicale, in partnership with Faculty of Medicine, Transilvania University of Brasov, Romanian Society of Medical Rehabilitation, Neuroaxis, Romanian Society of Geriatry and Gerontology, Romanian National Society of Family Doctors, Proffesional Society of Family doctors, and Hiperdia Brasov., organised in Romanian Physicians' College, Brasov branch.
2. Speaker for Zentiva Symposium "***Date noi privind siguranța și eficiența tratamentului cu Celecoxib si Etoricoxib***", 2018, June 7th, Brasov
3. ***"Recuperarea pacientului cu pluripatologie: complexitate si multidisciplinaritate"***, Conferinta Med Academy Brasov, 2017, November, 24 – 25th, Brasov

(B-III) Professional Activity

I have started my training as a resident doctor in Rehabilitation, Physical Medicine and Balneoclimatology (Physical Medicine and Rehabilitation) in 2004. I have completed my full training in Brasov university centre and Bucharest university centre.

I finished my residency training with the specialist doctor exam held in the university centre of Bucharest (commission chaired by Professor Gelu Onose) in October 2009, with a grade of 9.51. I was then temporarily employed, then with clinical integration (being lecturer of Faculty of Medicine) at the "Clinical Hospital of Psychiatry and Neurology" in Brasov, where I work since April 2011 until now on the "Clinical Department of Neuropsychomotric Rehabilitation". I must mention that my activity in the rehabilitation department of this hospital benefited from treating many neurological patients, being the only neuropsychomotor rehabilitation profile department and serving several counties around Brasov city. Also, the patients who address the rehabilitation department are pluripathological patients with vascular and neurological sequelae and diabetes and metabolic diseases, cardiovascular and respiratory diseases, polyarthritis and traumatic and degenerative diseases of the spine dysfunctions and disabilities.

Having the chance to assess, interact, and treat these complex patients, one of the characteristics of the Rehabilitation speciality, I gained the professional experience that I was able to apply and enrich in research and in the educational activity in which I ascended.

I took the primary physician exam in Physical Medicine and Rehabilitation in 2014 at the University of Oradea, a commission led by Professor Lazar Liviu, graduated with an average of 9.87.

Since April 2019, I lead the Neuropsychomotor Rehabilitation Clinical Department as head of the department. I am also the coordinating teacher in the Brasov University training centre for resident doctors in the Physical Medicine and Rehabilitation speciality.

Our department address the rehabilitation programmes and periodical assessment requested by the disability commissions and the work capacity evaluation commission for the following disorders: stroke in the subacute and chronic stage, craniocerebral trauma, vertebro-medullary trauma, disc herniation, spondylolisthesis, multiple sclerosis, amyotrophic lateral sclerosis, tetraparesis and paraparesis of various causes, polyradiculoneuritis, polyneuropathy, polymyositis, muscular dystrophy, infantile spastic tetraparesis (in adult), and others.
My concern regarding healthcare and emergencies management was deepened in studies within the ***Master's degree in Medical-Surgical Emergencies*** (2005-2007). The organization and leadership skills were started through the course "Quality management in higher education" (2004) and then continued through the ***master studies in Health Management*** (2004-2005).

I also graduated the following **courses**:

1. 4th MONTESCANO EFIC (European Pain Federation) SCHOOL 2012 - Montescano (Italy), 8-11 October 2012 (Pain School- Neuropathic Pain)
2. Spasticity management and Injection of botulinum toxine (Cluj, 2017).
3. TECAR application in rehabilitation (Brasov, 2018)
4. 9th European Teaching course on Neurorehabilitation, Poiana Brasov, Romania (2019, 6th-7th July)
5. 14th International summer school of Neurology, Poiana Brasov, Romania (2019, 8th-10th July)

During the Coronavirus pandemic, I participated in scientific events held online, among which I mention:

1. "Multifactorial control of diabetes always a challenge!", June 16, 2021, online
2. "Palliative care at the interface with curative medicine", 2nd edition, May 14-16, 2021, online
3. "Pulmonary rehabilitation in the context of the Covid-19 pandemic", June 10, 2021, online
4. "Tratamentul anticoagulant cu Xarelto - mai mult decât Eficiență și Siguranță", June 29, 2020.

I participated as chairman of the commission or member of competition commissions for Physical Medicine and Rehabilitation doctors and physiotherapists in Rehabilitation departments and compartments from Brasov County (Clinical Emergency Hospital Brasov, Zarnesti City Hospital).

I am an active member of the Romanian Society of Rehabilitation Medicine, attending the annual congresses. I have also been member in the Romanian Society of History of Medicine, the Balcanic Medical Union, and the Romanian Society of Chinese Traditional Medicine.

Managerial experience has taken shape and accumulated over the years as a head of the department of "Clinical Department of Neuropsychomotric Rehabilitation" in "Clinical Hospital of Psychiatry and Neurology", Brasov, as coordinating teacher in the Brasov University training centre for resident doctors in the Physical Medicine and Rehabilitation speciality, as a coordinator of Physiotherapy Study Programme in Faculty of Medicine Brasov (since 2011), as coordinator of Erasmus programme of international cooperation and exchange for universities (Nursing 2005-2012 and Physiotherapy 2009-2012).

Managerial experience has taken shape and accumulated over the years as a head of the department of "Clinical Department of Neuropsychomotric Rehabilitation" in "Clinical Hospital of Psychiatry and Neurology", Brasov, as coordinating teacher in the Brasov University training centre for resident doctors in the Physical Medicine and Rehabilitation speciality, as a coordinator of Physiotherapy Study Programme in Faculty of Medicine Brasov (since 2011), as coordinator of Erasmus programme of international cooperation and exchange for universities (Nursing 2005-2012 and Physiotherapy 2009-2012).

(B-IV) The evolution and plans for career development

Future perspectives in clinical rehabilitation research

Starting from the research fields approached so far, and I have published scientific papers, I intend to continue and consolidate the documentation activity, applied research in the same directions, and focused on studies performed on patients admitted for treatment and medical and medical educational applicability. Thus, I will stay focused on disability as a large umbrella of disorders covering movement, mobility and language, mental health problems, and secondary conditions connected with disability (pain, depression and mental disorders, respiratory and cardiovascular dysfunction, deconditioning, etc.

I will also try to lobby for the allocation of more financial and human resources to enhance rehabilitative activities dedicated to the reintegration of disabled patients.

I will carry out these actions on two levels within the clinical medical activity in parallel with the education of the new generations of rehabilitation doctors and physiotherapists dedicated to increasing the functionality and quality of the patient's life.

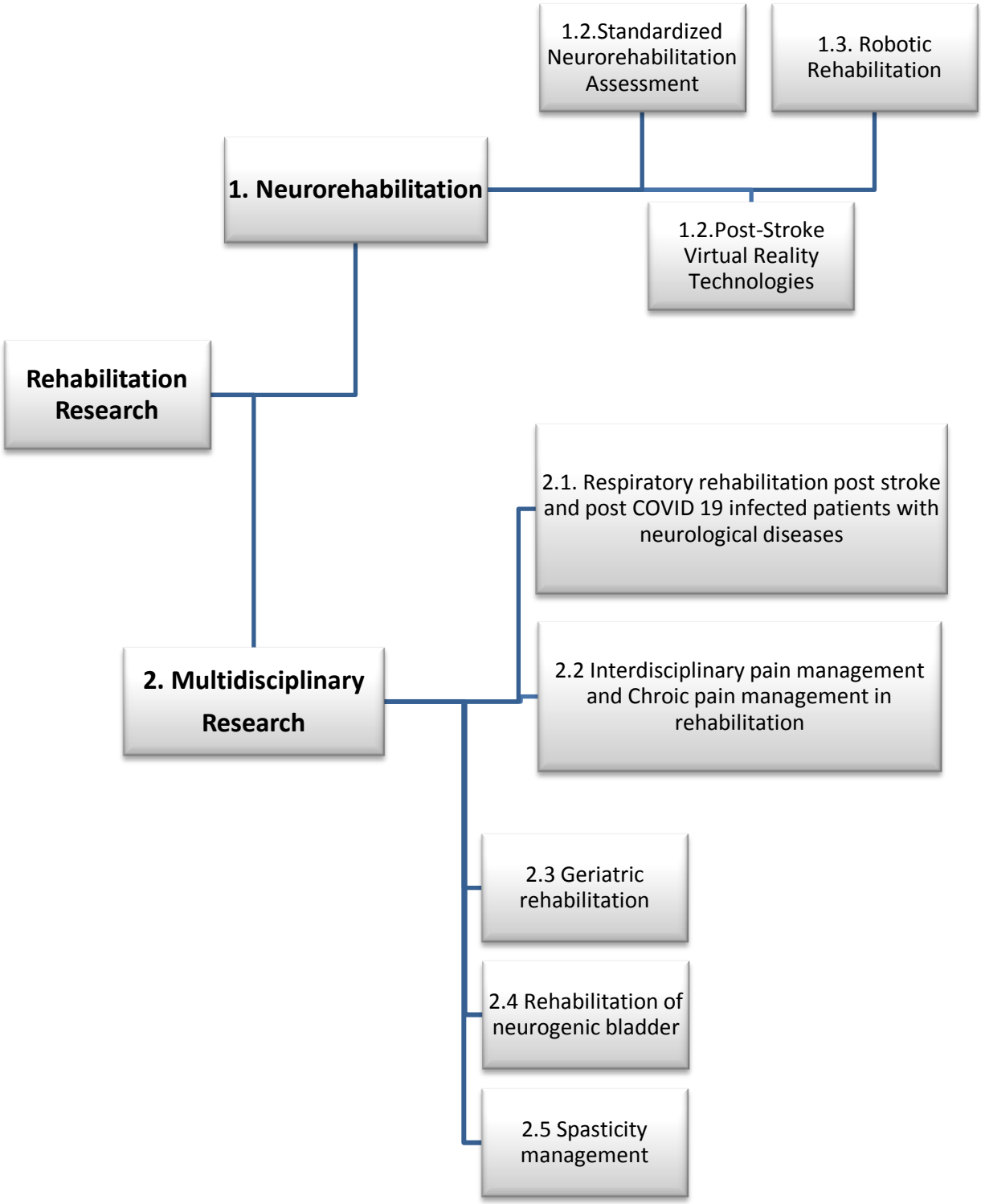


Figure 24 Reabilitation research plans and perpectives

1. Neuroreabilitation plans and perpectives

1.1 Standardized Neurorehabilitation Assessment

The rehabilitation results are difficult to evaluate objectively and predict, so it is necessary to improve the methods of objective evaluation of the effects of rehabilitation treatment and especially of objective assessment of functional progress. Evaluating the response to the treatment that can give the rehabilitation prognosis allows the modification of the rehabilitation methodology and the interventions to the needs, abilities, and resources of the person with disabilities. [3]

One of the main goals is represented by the translation of new international scales, cultural adaptation and validation in Romanian. As per the lack of many translated scales into Romanian language, very useful scales in the fine, complex and accurate assessment of the patient's clinical status and the prediction of the possibility of rehabilitating it are necessary for the international alignment of the patient evaluation. The main direction of this goal is to perform a standardized assessment in neurorehabilitation, improve the rehabilitation goal setting, and increase assessment in rehabilitation at the European or international level.

Another goal of this objective is to increase the complexity of assessment ideas by associating several scales of somatic with functional assessment and correlate them with cognitive and sensory assessment scales.

Another perspective is the comparison of complex, multiparametric, manual and clinical assessment performed by the rehabilitation physician and physiotherapist with the evaluation performed by motion sensors integrated into rehabilitation devices. Sensors created to collect posture, movement and position data are used today in podometry and posturology, walking platforms, proprioceptive and equilibrium, re-education devices, robotics and motor re-education platforms through virtual reality. The challenges come from the fact that many rehabilitation new technologies based on sensors, robotic therapy or virtual reality have their own assessment programs. Often, these programs are not validated and do not provide sufficient information for a complex assessment framework.

Besides motor impairments, stroke cause cognitive and behavioural impairments like depression, speech and communication difficulties like dysarthria and/or apraxia of speech, and aphasia. Thus, focusing on evaluating and evolving the post-stroke patient's cognitive, mental and behavioural status and developing new working methods for the psycho-behavioural improvement of the sequelae stroke patient is another goal of my research in assessment inclusion in the rehabilitation program.

1.2 Post Stroke Virtual Reality Technologies

Virtual Reality technology has flourished in the last decade, becoming a valuable tool for rehabilitation and great potential for the development and transformation of rehabilitation, especially in neurological pathology, in particular stroke. Virtual reality technology uses digital images that allow interaction with a virtual environment that transposes the patient into a world equivalent to the real world.

Many virtual reality technologies, either augmented or immersive besides motor and functional training, provide cognitive training and allow the user to perform a complete rehabilitation. Some of the technologies also ensure home rehabilitation programs.

The differences between augmented (non-immersive) and immersive virtual reality technologies useful in rehabilitation are vast. Even if non-immersive virtual reality technologies allow the user to fill in a simulated environment, the patient is not fully inserted in the virtual environment. Thus, one of my further research goals in this perspective is to identify the best potential of these two different virtual reality technologies for rehabilitation after stroke.

New technologies offering different modules for different types of rehabilitation emerged. Besides motor and functional recovery, modules for proprioception, hand dexterity, balance, sensitivity, cognitive or speech therapy are available with different virtual reality technologies. Stroke or neurological rehabilitation is one of the most complex types of rehabilitation requiring the fusion of these types of activities into the rehabilitation program. Virtual reality techniques become advantageous through specific features such as the execution of "goal-oriented tasks and the repetition of tasks, proven to be important in neurological rehabilitation". Thus, my further research aims to use these modules in the neurorehabilitation program and identify the parameters used to enhance an increased quality of post-stroke or neurologic rehabilitation.

Another significant advantage provided by the most virtual reality technologies used in rehabilitation is the possibility of patient home training. Some new technologies enable interaction with the physiotherapist or speech-language therapist during home program training. The majority of the Virtual technologies provide feedback of motion or activity accuracy based on exergames setting made by the physiotherapist or speech therapist. My further research aims to identify the parameters of virtual reality training exergames needed in neurorehabilitation to further use of home virtual reality training. The significance of this issue is crucial in virtual reality technologies that do not provide interaction with the physiotherapist or speech-language therapist during home program training. Thus further research can create a better framework for the home working program in neurorehabilitation.

Also, home neurorehabilitation using virtual reality technologies may be a valuable tool to maintain and progress functional, motor and cognitive obtained during patient hospitalization and rehabilitation. Unfortunately, the time spent by the patient in the rehabilitation unit after stroke or other central nervous disease is only two weeks in one admission, not enough to acquire sufficient motor, functional or speech skills. Also, short term rehabilitation is not enough to improve daily activities performance, walking, running or cardiorespiratory activities or socio-professional reinsertion. Therefore, the use of a virtual reality home working program for neurorehabilitation besides many advantages provided by this type of rehabilitation training can also substitute the presence of a physiotherapist for further goal setting achievements or maintain the gained motor, functional or speech functions during rehabilitation hospitalization. Thus, I hope that my future research can provide a sufficient framework for the benefit of virtual reality devices in home working programs and identify the usability of these therapies in neurorehabilitation and ***telerehabilitation***.

I plan to start using immersive VR systems and those that combine modules of motor rehabilitation, proprioceptive, sensitivity, cognitive, development of thinking and intelligence and speech therapy.

1.3 Robotic Rehabilitation

Robotic therapy has emerged as a modern alternative to classical physical therapy, increasing the intensity of therapy and standardization of methods. The most recent meta-analysis (2020) suggests that robotic therapy may improve the muscle strength of the upper and lower limbs and overall functionality and ability after stroke. Some studies claim no quantitative differences exist between functional motor progression through conventional therapy and robot therapy.

Other recent studies demonstrate the efficacy of robotics in enhancing motor function. No study ever explored the restoration of the cognitive deficits until 2020.

Robotic devices stimulate patients' physically and mentally active participation in therapy, activating patient's attention and motivation. The assistance by the physiotherapist is adaptive, maximizing the patient's involvement, adapting to the ever-increasing difficulty of the task to be performed, training motor performance through visual and auditory feedback. At the same time, the motivation is increased, and the plasticity of the motor cortex and cortical remodelling is facilitated. [192]

The use of robots in rehabilitation allows the use of high doses and high intensity, necessary in the advanced stages of post-stroke rehabilitation.

However, in the context in which patients with post-stroke sequelae require continuous medical care and intensive rehabilitation that often requires individual manual interaction with the physiotherapist, it involves high costs for health systems. Unfortunately, current demands and budgetary constraints do not allow for this intensive rehabilitation. Therefore, the need for new technologies to improve the effectiveness and efficiency of post-stroke rehabilitation is growing.

Therefore, future research in the usability and tailored physiotherapy using robotic therapy is needed to enhance motor function rehabilitation in post-stroke patients. Furthermore, since robotic rehabilitation is novel for patient recovery, a solid framework and research for developing standards of practice can improve post-stroke patients rehabilitation. Hence, my aims for future research using robotic therapy involve end-effector devices for the lower and upper extremity and exoskeletons, especially for gait rehabilitation, through tailored interventions.

II. Multidisciplinarity Research in Reabilitation

2.1. Respiratory rehabilitation post stroke and post COVID 19 infected patients with neurological diseases

In the difficult, long and complex process of patients' rehabilitation after stroke, the aspect of respiratory rehabilitation is often neglected, especially if the patient has not previously had a respiratory pathology that requires prioritization of this goal. Post-stroke patients experience a reduction in the respiratory capacity, FEV1 and exertion due to restrictive respiratory phenomena and stroke and immobilization in bed. Hypotonia of the respiratory and accessory respiratory muscles, the decreased deep inspiratory force and deep expiration, diminishing of the cough force are the physiopathological changes induced by the bed immobilization. All these will add to the changes induced by lateral decubitus on the disabled hemibody, limitation of motor activity and ADLs, limitation of chest mobility and costal horizontalization, adoption of vicious positions with kyphoscoliosis on the healthy side, and all will lead to the reduction of the thoracic respiratory and cardio-pulmonary functional volume. Also, obstructive phenomena are installed through stasis, secondary to immobilization and dorsal decubitus, decreased clearance capacity, and bronchial defence.

The Covid 19 pandemic period revealed aspects of the formidable complications of inflammation following viral infection and then healing of the lung's fibrosis and connective tissue in general, added to the harmful effects of bed rest. These pathophysiological aspects make the Covid infected patient a particular patient, who requires a complex approach in the multidisciplinary team of neurology, infectious diseases, internal medicine, intensive care, but also rehabilitation, in

order to treat each phase of evolution properly and prevent short term and long-term complications, respectively for the aim of fully functional and professional recovery of the patient.

For this purpose, I will focus on the research of the most appropriate way to associate the goal of increasing respiratory function with other objectives of physiotherapy specific to the neurological patient to respect its limited capacity for effort and to minimize the risks of complications in an attempt to optimize the respiratory and effort performance in parallel with mobility, coordination, balance, ability and gait, essential to be restored in neurological rehabilitation.

2.2. Interdisciplinary pain management and Chroic pain management in rehabilitation

Chronic pain is an important, common and financially consuming problem in all countries and health insurance systems. The effectiveness and efficiency of traditional medical interventions have led to perfect performance of the medical act, leaving room for alternative therapies to treat chronic pain. The biopsychosocial model of pain described around the 2000s has led to the emergence of modern interdisciplinary management models of chronic pain, increasing therapeutic efficacy, lowering patients' costs and quality of life. [193]

The holistic approach to chronic pain, including physical, behavioural, and psychological, has provided clear evidence of efficacy, increased functionality, reduced suffering, and increased quality of life for the patient with chronic pain.

This approach reduces the already escalating costs of chronic pain care, being a model accepted by society, taxpayers and health insurance systems worldwide.

Rehabilitation addresses methods of pain control specific to the speciality, such as relaxation, sedative massage, and analgesic electrotherapy associated with ongoing medication.

I will advocate in medical practice and research the use of the rehabilitation methodology as specific tools for pain control and an alternative to analgesic medication to study quantitatively and qualitatively the potential for complete replacement of analgesic and anti-inflammatory medication with rehabilitation treatment methods.

2.3.Geriatric rehabilitation

The ageing of our population is an inevitable reality. It is increasing in the last decades, at the same time as chronic diseases and pluripatology or multimorbidity, defined by the presence of two or more chronic diseases. Sometimes our vascular patients have more than twenty diagnoses at the age of 60.

For this reason, the WHO (World Health Organization) promoted and prioritized their knowledge in order to improve their management to give "life to years". We are not treated the patients for a single disease, but comprehensively, considering all interdependent complex factors of health and social aspects, without forgetting their individual values and preferences. The main goal of rehabilitation is to improve health status, global function (motor, psychic, social, professional) and the quality of life increasing performance. Associated, we add the objectives of reducing possible complications, improve care and, ultimately, the balance health quality versus health costs.

2.4 Rehabilitation of neurogenic bladder (Stroke, Multiple sclerosis, Amyotrophic Lateral Sclerosis) through standard kinesiotherapy of pelvic muscles girdle and electrostimulation of external bladder sphincter

The neurogenic bladder is one of the significant dysfunctions of neurological patients that affect the quality of life. It can be manifested in Parkinson disease, Multiple Sclerosis, Spinal Cord Injuries or Stroke. Besides urinary incontinence, the neurogenic bladder can also manifest urinary tract infections, renal calculi, nephrolithiasis, urolithiasis, urinary frequency and urgency and small urine volume during voiding. All these symptoms and manifestations alter the quality of life, kidneys and urinary tract functions. Electrical stimulation was developed as a second- or third-line treatment for neurogenic bladder and is now well-validated and accepted. However, many forms of electrical currents can act on the neurological bladder and the position of the electrodes. Also, the electrical stimulation parameters are heterogeneous. The transcutaneous electrical nerve stimulation (with the variation of pulse width, pulse form and frequency), interferential currents (with the variation of modulation, carrier and base frequency), Russian currents, Diadinamic's Rhythm Syncopal form can be used for bladder electrical stimulation.

Different areas of application of electro bladder stimulation were also tested, with different rates of effectiveness. If in the past, electrodes for stimulating bladder function were placed on the bladder, skin, sacral roots or spinal cord, today the training of the pelvic muscles is preferred. Blader stimulation has also shown effectiveness in spinal cord injuries with lower urinary tract symptoms (stress incontinence and bladder overactivity).

Thus, by further research, I plan to study the different parameters and application sites of currents associated with pelvic girdle muscle training. The main aim is to identify an efficient form of neurogenic bladder electrical stimulation, with the secondary outcomes to improve kidney function and quality of life for neurologic patients.

2.5 **Spasticity management** with electrotherapy, massage therapy and botulinic toxin injection associated with intensive and constant physiotherapy (inpatient and at-home physiotherapy)

Spasticity management challenges a multidisciplinary strategy fusing nurses, physicians like physiatrists, neurologists, physiotherapists, and occupational therapists, working simultaneously to implement different treatments specifically designed to meet the patient's needs and solve his individualized problems.

Patients with overactive muscle activity have multiple needs where spasticity is caused by and is producing multiple difficulties. Unfortunately, it can be challenging or too late to manage spasticity in many cases, given the range of secondary complications, including biomechanical changes/contractures involving muscles and tendons, pain, skin integrity issues, and associated motion and handling difficulties. Secondary complications can often impact a huge cost to healthcare and decrease the quality of life, increasing the daily life difficulties for patients with spasticity.

Spasticity management involves a combination of therapies since none alone was clinically proved to be effective in spasticity treatment. Therefore, my future research in spasticity management involves the use of different electrical therapy (TENS, High voltage pulsed current, ultrasound, shortwave therapy, TECAR therapy, thermal therapy), or physiotherapy exercises and techniques, the use of prosthesis, in combination with antispasticity medication, or botulinic toxin injections.

Future professional development and projects in Rehabilitation and Education

I. **Health care services continuity** through interdisciplinary intervention focused on the person. Looking for the best model of comprehensive management of health care services and Health Care Assurance

Our team starts from the reality of the discontinuity of the complex neurological and cardiovascular treatment of vascular (stroke) or posttraumatic patients. We try to build a comprehensive rehabilitation model, combining and merging the treatment of primary and associated diseases with physiotherapy, psychotherapy and care of patients who need long-term rehabilitation, nursing and complex stimulation. A nursing model and a medical model for long-term treatment are mandatory to be organized and institutionalized to avoid the interruptions of the correct rehabilitation treatment and expose to risks of complications, recurrences, and regression in rehabilitation, increasing morbidity and mortality.

II. **Home physiotherapy training for post-stroke patients**

The project aims to train master students, physiotherapy graduates to apply for recovery programs at patients' homes in teams with resident recovery doctors and other specialties, under specialispecialitiesctising physiotherapists' direct coordination and guidance.

The project aims to train master students and physiotherapy graduates to apply for rehabilitation therapy programs at patients' homes in teams with resident rehabilitation physicians and practicing physiotherapists' direct coordination and guidance.

I propose approaching this future direction related to education and rehabilitation by realizing and accessing a future project on European funds by accessing the health program from 2021-2027. One of the health sub-programs within the European funds is intended for post-stroke patients, respectively the Operation Program of Strategic Importance - Increasing the medical care capacity of the critical patient with acute cerebral vascular pathology. Thus, future projects related to patient care with post-stroke pathology, both in the acute and subacute stages, can be designed and implemented. This direction related to education and rehabilitation is more important considering patients' limited access in the medical rehabilitation departments through the health insurance system (14 days in the subacute period once every 3 months and 14 days in the chronic period o date to six months).

III. Caregivers' and patient's education in post-stroke rehabilitation, a concise framework for functional and quality of life improvement

The project aims to train family members to help the physiotherapy team and learn to continue the application of rehabilitation programs at patients' homes and thus ensure continuity of care and accelerate rehabilitation.

This aspect is extremely important, both from the perspective of the increased burden of the health system in terms of material and human resources, but especially from the perspective of the burden of post-stroke patients. Unfortunately, in the case of hemorrhagic strokes, most patients are left with disabling sequelae that do not allow them to perform daily activities, often burdening family members for their care. The design, implementation and implementation of an educational program for patients and relatives in terms of individual and family adaptation of patients with post-stroke sequelae is essential for socio-familial and why not professional reintegration of these patients. There is no national framework to guide and educate patients and patients from this perspective. Thus, I propose, together with PhD students, physiotherapy students, nurses, physiotherapists, and other doctors (neurologist, psychiatrist) and psychologists, speech therapists to create a directional framework for the education of relatives and patients after stroke. At the same time, in this context, I propose to draw up guidelines on stroke prophylaxis.

IV. Low back pain as common condition and proffessional disease

The project aims to provide *Assesment, profilaxy and therapeutic rehabilitation in students* and *Assessment and prophylaxis in nurses and caring staff in medical facilities.* (lifting habits and load burden).

Unfortunately, most medical staff perform physically and demanding professional activities during the nursing activities of patients with neuromotor pathology in all three stages - acute subacute and chronic. Through this direction, I propose designing a project through which to carry out the objective evaluation of the lumbar disc pathology in the case of the medical staff working with the neuromotor pathology. The evaluation involves clinical testing through specific questionnaires of low back pain and inability to perform daily or professional activities and functional evaluation. Following the results obtained, an educational program can be developed for healthcare workers to prevent lumbar disc pathology, maintain the health of the lumbar spine, and educate medical staff on the correct way to handle patients also to lumbar spine protection.

V. **Posture and static assessment and prophylaxis,** focus on all medical categories exposed to disc herniation and bad posture: Doctors, Nurses, care staff, students.

Posture in the human body is based on the interaction and the coordination of the musculoskeletal system components and the upper and peripheral nervous system. It involves stability, balance and constant connections between body parts and between body and environment.

Postural stability is achieved due to the memory of the neural network, through the messages received from the receptors, stores reference models for all the fundamental and derived positions of the body in space. A correct posture is necessary to produce an efficient movement along the kinetic chain.

Researchers in the field have concluded that most people do not have a suitable posture, which often indicates muscles issues. Therefore, during effort or repetitive functional task performing, the muscles can not develop enough strength to perform the motions correctly. As a future project, posture assessment will include assessment of spinal deviations in the three planes - frontal, sagittal and transverse, axial misalignments of the limbs, especially of the lower limbs and functional assessment of the musculoskeletal system - joint and muscle balance, but also specific tests. This project can represent research and educational opportunity for future PhD students, physiotherapist students and doctors of different specialities. The educational component involves creating guiding elements for the prophylaxis of musculoskeletal dysfunctions due to vicious postures.

Each of these research directions and project proposals can constitute extensive research topics as well as the offer of doctoral topics for future doctoral students.

The first research topics I will launch to PhD students will study working hypotheses for:

1. *Proprioceptive and balance reabiliatation in patients with central motor neuron syndrome*
2. *Spasticity management in neuropsychomotor rehabilitation.*

The Clinical Rehabilitation Department I lead is a very appropriate environment for developing doctoral research and learning within a young research team. PhD students will have access to the clinical activity in the Clinical Rehabilitation Department, will be able to evaluate patients daily and follow their evolution during the physical therapy and rehabilitation program, will be able to interact with all related medical specialities, will be able to develop professionally and individually with their colleagues, by the entire research team in the doctoral school.

The Clinical Rehabilitation Department I lead and where I carry out my medical and academic activity provides multiple personal and team development conditions to the resident physicians studying Physical Medicine and Rehabilitation.

Each potential doctoral student meet the appropriate environment for clinical, academic and research training, having access to learn together with high-level specialists and professionals who are part of the multidisciplinary rehabilitation team and part of the rehabilitation research team.

The Neuropsychomotor Rehabilitation department's infrastructure is equipped with electrical stimulation devices (low and medium frequency currents, high-intensity currents, galvanic baths, laser therapy, TECAR therapy, shock wave therapy). The physiotherapy unit is also equipped with virtual reality technology, proprioception and balance training device, functional electrical stimulation, and all the tools necessary for physical therapy exercises). The unit contains eight cabinets for electrical stimulation therapy, thermal therapy and physical therapy. Within the unit can be hospitalized 36 patients with neuropsychomotor impairments which can be further enrolled in clinical trials. Our unit also collaborates with the Neurology unit, where acute post-stroke patients are hospitalized and receive massage therapy and physical therapy training in the acute stage post-stroke. Therefore, further research can be conducted regarding the patient's transition from the acute to subacute stage post-stroke regarding physiotherapy care.

Furthermore, a previous European Funds project wan by the Hospital of Psychiatry and Neurology and County Council will provide new modern equipment in the Neuropsychomotor department. Robotic therapy devices for neuromotor rehabilitation, both end-effect devices and exoskeletons for gait training, proprioception training devices, augmented virtual reality devices and gait assisted devices will fulfill the existent hard and soft equipments for complex Rehabilitation.

Accordingly, my future PhD students will have access to the latest technology in neurorehabilitation, from electrical stimulation devices to thermal therapy, robotic therapy and virtual reality therapy. Thus, all my future research directions can be accomplished in partnership with PhD students within my coordination, resulting in multiple multidisciplinary and individual research possibilities.

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