GRIGORE T. POPA UNIVERSITY OF MEDICINE AND PHARMACY IASI

HABILITATION THESIS

MULTIDISCIPLINARY ASSESSMENT OF LIVING ENVIRONMENT- BETWEEN THREATS AND HEALTH PROMOTION

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2022

CONTENTS

ABBREVIATION LIST

ACE: Adverse Childhood Experiences
ACPA: Anti-Citrullinated Protein Antibodies
ANA: Total Antinuclear Antibodies
ASSIS: Acculturative Stress Scale for International Students
BD: Body Dissatisfaction
BDI: Beck Depression Inventory
BFI: Big Five Inventory
BMI: Body Mass Index
CBCT: Cone Beam Computed Tomography
CERQ: Cognitive Emotion Regulation Questionnaire
CF: Cystic fibrosis
CLP: Cleft Lip and Palate
COPD: Chronic Obstructive Pulmonary Disease
CRP: C Reactive Protein
DAS: Disease Activity Score
DASS: Depression, Anxiety and Stress
DMSO: Dimethyl Sulfoxide
DRG: Diagnosis Related Groups
DSM: Diagnostic and Statistical Manual of Mental Disorders
EA: Emotional Exhaustion
EDI: Eating Disorder Inventory
EPQ: Eysenck Personality Questionnaire
ESR: Erythrocyte Sedimentation Rate
EURO-URHIS: European Urban Health Indicator System
FACES: Family Adaptability and Cohesion Scale
FFQ: Food-Frequency Questionnaire
GPX: Glutathione Peroxidase
HAQ: Health Assessment Questionnaire Disability Index
IBS: Irritable bowel syndrome
IPQ-R: Illness Perception Questionnaire Revised
JSS: Job Satisfaction Scale
LSE: Low Self-Esteem
MBI: Maslach Burnout Inventory
MCP: Monocyte Chemoattractant Protein
MDA: Malondialdehyde
MSS: Medical Student Syndrome
NSJ: Number of Swollen Joints
PA: Personal Accomplishment
PKU: Phenylketonuria
RF: Rheumatoid Factor
SACS: Strategic Approach to Coping Scale
SOD: Superoxide Dismutase
SRM: Self-Regulatory Model
STZ: Streptozotocin
TAS: Toronto Alexithymia Scale
TNF: Tumor Necrosis Factor
TS: Turner Syndrome
UPP: University Preparatory Program
VAS: Visual Analogue Scale
WHO: World Health Organization

ABSTRACT

This Habilitation Thesis presents my professional/medical, scientific and academic achievements activity during the postdoctoral period, since 2007 up to 2022.

The aim of the thesis is to present an integrative view of my work in this period, with a special emphasis on the achievements in the field of scientific research.

The Habilitation Thesis entitled *"Multidisciplinary assessment of living environment-between threats and health promotion"* is developed according to the recommendations of CNATDCU and presents my research directions along with the academic career plan of development, being structured into three main sections.

Section I contains a synthesis on my professional/medical, scientific and academic activity, followed by four chapters which presents the results of the most important collaborations with different complex research teams from the last 15 years. The training during the Ph.D. period, completed with the experience of academic management in the last 10 years, allowed me to deepen the relationship of the living environment of children and young people with their health status.

In Chapter I, entitled *"Psychosocial environment - a risk factor for children and young people health"* is presented another type of relationship between the living environment and human's health, with a special emphasize on the most vulnerable group, children and young people, which are still growing and developing but being impacted by risk factors of psychosocial origin. Stressful environment (educational, medical) is the cause for anxiety, depression, burnout syndrome and, because we are in the most cosmopolite university from Romania, adapting difficulties to a new culture, experienced especially by foreign students.

Chapter II describes our results in *Assessment of harmful health behaviors related to the living environment* from distorted dietary habits to consumption of legal (alcohol, tobacco) or illegal drugs (stimulant, narcotic or hallucinogenic substances). All these habits are acquired in common living environment and represents major threats for human health, no matter they are generating addiction or not.

Chapter III presents *assessment of certain chronic diseases* (cancer and certain rare diseases) directly generated or just connected with living environment, from tertiary medical prevention perspective, which is focusing on improving life quality of affected persons.

Chapter IV may be a breakpoint for future approaches in health promotion, starting from the most important artificial environmental factor, which is our nutrition. *Health promoting nutrition and nutritional habits* are well-known but still an underrated modalities for granting an optimal health status.

All the scientific achievements were materialized in books, book chapters, publications in journals with impact factor (SCIE) and in international data basis (ESCI, PubMed).

These are the results of a complex teamwork and would not have been possible without the support of the University and the guidance of our medical school mentors, from whom I learned the importance of prevention and specifically of the living environment impact on human's health status.

Section II includes my projects on short, average and long term, regarding the scientific, academic, and professional areas in which I will focus. I have identified and I wish to develop innovative interest areas for the relation between human health - living environment quality.

Section III represent a list with over 600 of the most important references I have used along of my scientific, academic and professional evolution. There are also new references, from the last years, which proves the subject and the issues presented in my thesis are actual and still searching for their answers.

REZUMAT

Această Teză de abilitare prezintă activitatea mea profesională/medicală, științifică și academică realizată în perioada postdoctorală, din anul 2007 până în anul 2022.

Scopul tezei este de a prezenta o viziune integrativă asupra activității mele în această perioadă, cu un accent deosebit pe realizările din domeniul cercetării științifice.

Teza de abilitare intitulată *„Evaluarea multidisciplinară a mediului de viață - între amenințări și promovarea sănătății"* este elaborată în conformitate cu recomandările CNATDCU și prezintă direcțiile mele de cercetare împreună cu planul de dezvoltare a carierei academice, fiind structurată pe trei secțiuni principale.

Secțiunea I-a cuprinde o sinteză privind activitatea mea profesională / medicală, științifică și academică, urmată de patru capitole în care sunt prezentate rezultatele celor mai importante colaborări cu diferite echipe complexe de cercetare, din ultimii 15 ani. Formarea din perioada de doctorat, completată cu experiența de management academic din ultimii 10 ani, mi-au permis aprofundarea relației mediului de viață al copiilor și tinerilor cu starea lor de sănătate.

În capitolul I, intitulat *Mediul psihosocial - un factor de risc pentru sănătatea copiilor și tinerilor* este prezentat un alt tip de relație între mediul de viață și sănătatea umană, cu un accent special pe grupul cel mai vulnerabil, copiii și tinerii, care sunt încă în creștere și în curs de dezvoltare, dar care sunt afectați de factori de risc de origine psihosocială. Mediul stresant (educațional, medical) este cauza anxietății, depresiei, sindromului de epuizare și, pentru că suntem în cea mai cosmopolită universitate din România, a dificultăților de adaptare a studenților străini la un nou context cultural.

Capitolul II descrie rezultatele noastre referitoare la *Evaluarea comportamentelor nesanogene legate de mediul de viață,* de la obiceiurile alimentare incorecte la consumul de droguri legale (alcool, tutun) sau ilegale (substanțe stimulante, narcotice sau halucinogene). Toate aceste obiceiuri sunt dobândite în mediul de viață obișnuit și reprezintă amenințări majore pentru sănătatea umană, indiferent dacă generează dependență sau nu.

Capitolul III prezintă *evaluarea anumitor boli cronice (cancer și unele boli rare)* generate sau doar favorizate de mediul de viață, din perspectiva prevenției medicale terțiare, care se concentrează pe îmbunătățirea calității vieții persoanelor afectate.

Capitolul IV poate fi un punct de reper pentru abordările viitoare în promovarea sănătății, pornind de la cel mai important factor artificial de mediu care este nutriția noastră. Nutriția care promovează sănătatea și obiceiurile alimentare sanogene sunt modalități bine cunoscute, dar încă subapreciate pentru asigurarea unei stări de sănătate optimă.

Toate realizările științifice s-au materializat în cărți, capitole de carte, publicații în reviste cu factor de impact (SCIE) și reviste din baze de date internaționale (ESCI, PubMed).

Acestea sunt rezultatele unei munci complexe, în echipă și care nu ar fi fost posibilă fără sprijinul Universității noastre și îndrumarea mentorilor școlii noastre medicale, de la care am învățat importanța prevenției și în special a impactului mediului de viață asupra stării de sănătate a omului.

Secțiunea a II-a include proiectele mele pe termen scurt, mediu și lung, în ceea ce privește domeniile științific, academic și profesional pe care mă voi concentra. Am identificat și doresc să dezvolt domenii de interes, inovatoare, pentru relația sănătatea umană - calitatea mediului de viață.

Secțiunea a III-a reprezintă o listă cu peste 600 dintre cele mai importante referințe pe care le-am folosit de-a lungul evoluției mele științifice, profesionale și academice. Există, de asemenea, și referințe noi, din ultimii ani, dovadă că subiectul și problemele prezentate în această teză sunt actuale și încă își așteaptă rezolvarea.

SECTION I

OVERVIEW OF PROFESSIONAL, SCIENTIFIC AND ACADEMIC ACHIEVEMENTS

Professional achievements

My professional experience covers 27 years of medical profession and over 22 years of academic activity. After graduating the Faculty of Medicine from "Grigore T. Popa" University of Medicine and Pharmacy of Iaşi in 1995, I worked for one year in the Public Health Authority from Suceava County as a Junior Physician (1996-1997).

Following the promotion of the Residency Contest (February 1997) I was resident physician in Hygiene in the Clinical Hospital No. 1 Timișoara. Due to family reasons, I requested the transfer in Iasi County, where I was hired as a resident physician in the County Public Health Inspectorate and at the "Sf. Spiridon" County Clinical Emergency Hospital Iași.

In January 2000, when as resident physician in Hygiene, I applied and obtained through competition my first academic position, as a teaching assistant at the Discipline of Hygiene and Environmental Health, Faculty of Medicine, which is the most preeminent faculty of "Grigore T. Popa" University of Medicine and Pharmacy of Iaşi.

From that moment my academic career developed in the same rhythm with the professional one and, in constantly manner, every progress I have made in the professional field endorsed my academic evolution.

In February 2001, I completed my training in Hygiene, obtaining the title of Specialist Physician, and in January 2002 I won through competition the position of Assistant Professor at the Department of Preventive Medicine, from the Faculty of Medicine.

Between years 2003 and 2004 I was enrolled and graduated the program for achieving the Competence in Health Services Management.

Since 2005 I am a Senior Physician in Hygiene, medical degree which allowed me to become a Senior Lecturer in Hygiene in the summer of 2007.

Between 2010 and 2012, as a personal decision to enlarge my professional perspective, I applied for the second medical specialty, which was Epidemiology. After a very challenging period, at the end of year 2012, I became a Specialist Physician in Epidemiology. In the same year, realizing how important is the issue of research projects, I graduated the course for Project Manager, organized by DAL Consulting Iasi.

From January 2008 until now I have a half-time integration at the Emergency Clinical Hospital "Prof. Dr. N. Oblu" from Iasi, first as a senior physician in hygiene, with competence in health services management and, from 2012, also as a specialist physician in epidemiology. Using my entire expertise in preventive medicine, epidemiology and codifying system for Diagnosis Related Groups (DRG) in the work carried out during the last 15 years, I managed to increase the Case Mix Index (CMI) of the Emergency Clinical Hospital "Prof. Dr. N. Oblu" Iasi, from a value of 1.20 in 2008 to a value 2.04 in 2021 (increased with 70%), being now the 9th best rated as complexity and, subsequently, financed hospital in Romania (out of a total of other alike over 400 hospitals).

I have the honor and the responsibility to be the representative of the "Grigore T. Popa" University of Medicine and Pharmacy of Iaşi in the Board of Trustees of the Emergency Clinical Hospital "Prof. Dr. N. Oblu" Iasi from October 2016 till now.

I was nominated from November 2020, as medical expert on Hygiene specialty for Iasi County by the Ministry of Health from Romania. From March 2022 I was included in the professional Comission of Hygiene of College of Physicians from Romania.

Scientific achievements

My research activity was carried out in collaboration with other disciplines (Primary Health Care and Epidemiology, Behavioral Sciences/Psychology, Public Health and Management, Occupational Medicine and Occupational Diseases, Nutritional and Diabetes Diseases, Gastro-Enterology, Psychiatry, Microbiology and Biochemistry) or with other institutions such as: "Iuliu Haţieganu" University of Medicine and Pharmacy of Cluj-Napoca (2009-2011); Center for Environmental Health from Cluj-Napoca (2005-2006); Center for Anthropological Research within the Romanian Academy from Bucharest (2006-2007, 2018-2020); "Mihai Ciucă" Institute of Public Health from Iasi (2000).

I have published 4 books as principal author in national recognized publishing houses, and I have been part of the coordinating groups for other 5 books published between 2012-2016 in "Gr. T. Popa" Publishing House from Iasi, as a result of the *E-Mediqual* project.

The results of my research activity have been reflected in 19 articles rated in Web of Science Core Collection and 45 articles indexed by other international databases (PubMed, Google Academic, Scopus).

I have coordinated three National Conferences of Hygiene (2003, 2005 and 2007) and one national workshop for medical students (2008).

Scientific projects

I was the coordinator for the Iasi urban area within the Project EURO-URHIS 2 / *"European System of Urban Health Indicators Part Two: Urban Health Monitoring and Analysis System to Inform Policy"* No. 223711, funded by the European Commission through the Framework Program 7, coordinated by the University of Manchester and having as partner for Romania "Iuliu Haţieganu" U.M.Ph. of Cluj-Napoca (Director Professor Ioan Stelian Bocşan, M.D., Ph.D.). The EURO-URHIS 2 was conceived as a European research project aimed to develop several methods of comparative analysis of the health status of European citizens living in 26 urban areas, one of these methods being the monitoring of the health status. I have coordinated for 17 months all the logistic activity, as well as the activities of the entire team of investigators involved in the development of the EURO-URHIS 2 project in the Iasi urban area, all data reports and their final validation (2009-2011).

I was member of the research teams in the five grants or projects:

- "Sexual education and family planning for strengthening the health of the population" - Grant 116/108 was conducted within the Anthropological Research Centre of the Romanian Academy in Bucharest (2006-2007);
- "The National Research Assessment Exercise" (ENEC) (April-September 2011), as responsible at the level of the Faculty of Medicine for the collecting, analysis and reporting of data necessary for the evaluation process in the Information Support System for Research Evaluation (SISEC).
- SaIN - *"Création d'un réseau universitaire régional dans le domaine de la santé, la nutrition et la sécurité alimentaire"* Project financed by AUF (2017-2019);
- INCrEAsE - "Intercultural Competences for Adult Educators working with Multicultural and Multilingual Learners" Project 2019-1-RO01-KA204-063872 (2020);
- RANCARE COST ACTION - "Rationing - Missed Nursing Care: An international and multi-dimensional problem." Project CA15208 (2016-2020).

In other two research projects I was assigned a member of the target group:

- CHRONEX-RD - "The East European Network of Excellence for Research and Development in Chronic Disease" ID: MIS ETC 1840 implemented by "Grigore T. Popa" U.M.Ph. of Iaşi in partnership with the "Nicolae Testimiţanu" University of Medicine of Chisinau and the Medical University of Odessa (2014 - 2015);

- MEDICALIS - "Educational Management and Quality Education in the Information Society" POSDRU/86/1.2/S/62594 implemented by "Iuliu Haţieganu" U.M.Ph. of Cluj-Napoca in partnership with "Grigore T. Popa" U.M.Ph. of Iaşi (2010 - 2013).

Editorial activities

Since 2004 I have been member of the editorial team of *The Medical-Surgical Journal* of the Society of Physicians and Naturalists (SMN) from in Iasi, journal indexed till 2017 in PubMed, rated by UEFISC CDI B plus and currently is included in Emerging Sources Citation Index (ESCI) being evaluated by Clarivate Analytics for impact criteria and being included in Science Citation Index Expanded (SCIE).

In the editorial board I had the following tasks: Subject Editor of the Preventive Medicine Section (2004-2009), Editorial Secretary (2010-2012) and General Editorial Secretary (from 2013-2022).

Academic achievements

Starting from March 2000, my energy was dedicated to the teaching and scientific activity in this discipline, under the guidance of my Mentors, Academician Professor Gheorghe Zamfir, M.D., Ph.D., Professor of Hygiene and Professor Viorica Gavăt, M.D., Ph.D., Professor of Hygiene, which were also my Scientific Advisers during the doctoral period (2000-2007).

I was appointed after promoting the contests as Assistant Professor in 2002, Senior Lecturer in 2007 and Associate Professor from 2015.

During my teaching activity I interacted with students and resident physicians during practical classes, on lectures and in the research activity.

Starting with the 2008 academic year, I was the coordinator of the courses of Hygiene and Environmental Health for the fourth-year medical students - English section and from 2012 also for French section, both for lectures and practical classes.

As the tutor of the fourth-year French section (from 2015 to present time) I have been confronted with all the academic issues faced by my students and I counseled them regarding their professional evolution. In 2014 and 2020 I was appointed as The Dean of the Promotion for Romanian section C and for French Section, which I consider to be the highest appreciation granted by my students.

An important part of my teaching activity is the involvement in residency programs which means specialty training in Hygiene and Environmental Health, and teaching Hygiene modules for other specialties like Epidemiology, Public health and management, Diabetes and metabolic disorders. I am still connected with my former residents, debating practical problems and sharing our experience, which gives me a huge and constant challenge to be up to date with the latest news in my specialty.

More than that, I encouraged and contributed to the developing of multidisciplinary teams, composed by colleagues of different specialties from Preventive Medicine area and from our department (Psychology, Social Sciences), in order to provide and develop a wide and fresh approach to present and future problems, centered and generated by the interaction between man and his life environment.

From 2016 to present time, I was appointed coordinator of the Food Safety and Quality Management course part of the Master Program Curricula entitled *Prophylactic and Curative Nutrition and Dietetics.*

Due to our University mission to supply continuous and long-life learning programs I was first lecturer and after that coordinator of 15 Post-graduate courses for former residents and actual specialists in preventive medicine area part of *The Continuing Medical Training* (2003-2019).

Academic management

Between 2000-2008 I took part constantly in all the admission competitions and the bachelor's exams conducted in our University.

From 2009 to 2021 I was:

- Deputy Secretary of the Central Admission Commissions (2009-2010);
- Secretary of the Central Admission Commissions (2011-2021);
- Head of the Commissions for the organizing of Residency Admission Exams (2011, 2012) and member of the Commissions between 2013 and 2020);
- Head of the Admissions Commission (2013 September session);
- Coordinator of the University Bachelor's Exam (2014 September session).

Regarding my involvement in the educational management, I was assigned to be:

- President of the Faculty of Medicine Electoral Commission (2007-2008) and President of the Central Electoral Commission of "Grigore T. Popa" U.M.Ph. of Iasi (2011-2015);
- President of the Electoral Commissions that organized the elections for the Councils of Doctoral School (2016, 2020 and 2021);
- President of the Electoral Bureau of "Grigore T. Popa" U.M.Ph. of Iasi, which organized the *Referendum* for voting the actual University Charter (December 2016).

Concerning Academic achievements in May 2012, following the honoring proposal of the Faculty Dean, Professor Doina Azoicai M.D., Ph.D., I have been confirmed by Senate Decision as a Vice-Dean of the Faculty of Medicine.

As a member of the Dean's team, I have taken care of activities specific to university management such as: accreditation/re-accreditation of curricula, national and international evaluations (EUA / CIDMEF) of the Faculty and University, development of ECTS guides for all bachelor's programmes, conduct under best conditions examination sessions, competitions for the job opening positions of university structure, annual evaluation of teaching staff (2012-2016).

As Vice-Dean I took part in the organization of the National Conference of Deans, held in Iaşi (November 2013), I took part in the workshop of training about the governance of the Faculties of Medicine, organized by CIDMEF (*Conference Internationale des Doyens des Faculte de Medecine d'Expression Francaise*) in Iaşi, within the framework of the *"Ecolé des Doyens"* (April 2014).

After completing the mandate of Vice-Dean (2012-2016), I was elected by my colleagues for two mandates (in 2016 and 2020) as the Director of the Department of Preventive Medicine and Interdisciplinarity from the Faculty of Medicine, position which I held in this moment.

I was elected as a member of The Senate of the University (2016, 2020) and in both mandates I was assigned to be the President of the Senate Rules Committee.

As the Director of the Department of Preventive Medicine and Interdisciplinarity I take part as a guest member at the Faculty Council meetings, supporting all eleven study directions from the department.

SECTION I

CHAPTER I

PSYCHOSOCIAL ENVIRONMENT- A RISK FACTOR FOR YOUNG PEOPLE HEALTH

A. ACCULTURATION DUE TO STRESSFUL PSYCHOSOCIAL ENVIRONMENT

Psychosocial environment represents itself a potential health risk factor from childhood to maturity, passing through teenager period, and from acculturation, depression, distress, anxiety, to burnout, anyone can experience all these problems related to educational process.

The challenge for health system is lack of proper early diagnose and underreporting and those who are suffering are growing and developing persons, which will carry for the rest of their life this huge burden.

Any form of education is stressful and an early identifying of all these problems may be useful for implementing the concept of prevention for a better growing and developing process.

Acculturation can be stressful, and acculturative stress can be triggered by many factors.

Universities all over the world accommodate a large number of international students. In recent years, Romania, attracted many international students who enrolled especially in medical studies. The main reasons for studying in Romania are cheaper academic taxes, affordable accommodation and transport, peaceful university city, religious tolerance, and a European country (Socolov, Iorga *et al.* 2017; Socolov, Munteanu *et al.*, 2017). The choice to study abroad has a substantial impact on the student and the acculturation process can lead to acculturative stress and difficulties adjusting to the environment of the host country.

Acculturation is the process of both cultural and psychological change that occurs when two or more cultural groups come into contact (Berry, 2015). It involves changes on the group level (it entails changes in social structures and institutions and in cultural practices) and at individual level (it comprises the change of an individual's behaviors). All these changes are the result of a long-term process that should not be conceptualized as unidirectional, in that immigrants assimilate into their adopted country, but the host culture does not change (Berry, 2005). In the specific context of academic relationship, teachers working with international students must adapt themselves to multicultural and multilingual groups and must adjust their teaching styles to diminish the barriers related to language, cultural, ethnicity. Acculturation can be perceived as a stressful experience and the term acculturative stress is generally used to describe the unique stressors of immigration (Berry, 2006). The experience of acculturation is a series of major life events that can be challenging for an individual and can trigger a stress reaction called acculturative stress (Sam, 2010). Ward and Geeraert (Ward *et al.,* 2016) believe that acculturation demands facing acculturative stressors coupled with the acquisition, maintenance, and change of cultural attitudes, behaviors, values, and identities. There are several factors that may contribute to acculturative stress, including the way newcomers are regarded by members of the receiving society (Simon *et al.,* 2018), the motivation for immigrating (Organista *et al.,* 2003), and the separation of families (Suarez-Orozco *et al.,* 2001). For college students, they already are a population prone to experience higher levels of stress and depression (Kulsoom *et al.,* 2015, Iqbal *et al.,* 2015, Mayer *et al.,* 2016) and the reasons for this include demanding tasks, very busy university schedule, close deadlines, living away from families, financial problems, difficulties that have regular meals and eating unhealthy foods (Deshpande *et al.,* 2009; Zurita-Ortega *et al.,* 2018; Li KK *et al.,* 2012).

Medical students stand out and because their academic education is the longest, they are often facing numerous uncomfortable situations (communicating with ill individuals, facing palliative care patients, exploring doctor-patient-family relationship, or experiencing life-ending situations). The specificity of medical studies adds pressure and stress, and preexisting patterns established during the students' years of training can continue into adult life. International students represent an important contribution to the intellectual capital of their host country and to the workforce by bringing with them a variety of knowledge and skills in many areas (Smith *et al.,* 2011). They bring forth cultural exchange and understanding and create a more diverse learning environment (Wang, 2006).

There are numerous factors impacting upon international students' acculturation process and they may experience acculturative stress and t mental health problems: depression (Constantine *et al.*, 2004), bulimic symptoms (Perez, 2002), and body image disturbance (Menon, 2012). Understanding the factors associated with acculturative stress in this specific population is important for universities and mental health care professionals alike. One of the most well-documented such stressors is the language barrier and if English fluency is a good predictor of acculturative stress (Yeh, 2003), English competency is a predictor of adjustment in international students (Poyrazli *et al.*, 2002). Even academic stress is not unique to international students, it is likely to be more intense in their case and that's why it is added to stressors like second language anxiety, adapting to a new educational environment and to socio-cultural stressors (Smith and Khawaja 2011). Zhang and Brunton, found that 55% of the international students were unhappy with their opportunities to make friendships with locals and 71% expressed the desire to have more local friends (Zhang and Brunton, 2016). Also, Sawir found that 65% of the participants in their study reported that they had experienced periods of loneliness and/or isolation (Sawir *et al.*, 2007). When studying in another country, students might also experience practical or lifestyle acculturative stressors such as financial difficulties, accommodation, and transportation (Poyrazli *et al.*, 2007). International students' change their dietary habits (Edwards, 2010; Almohanna, 2015), but they experience emotional and physical support when they are consuming home country food (Brown, 2010).

The research on students' acculturative stress is not completely conclusive, especially from the point of view of medical studies. Accuracy is essential to ensure that appropriate interventions are introduced which will positively impact international medical students and research on this area needs to extensively identify factors that can influence acculturative stress.

My interest regarding this area is reflected by the following article:

Magdalena Iorga, Camelia Soponaru, Iulia Diana Muraru, Sofia Socolov, **Florin-Dumitru Petrariu** FACTORS ASSOCIATED WITH ACCULTURATIVE STRESS AMONG INTERNATIONAL MEDICAL STUDENTS. *BioMed Research International,* Volume 2020, Article ID 2564725, 9 pages doi.org/10.1155/2020/2564725 / **IF=3.411**

I.1. Factors associated with acculturative stress among international medical students

I.1.1. Aim

This study aimed to evaluate the presence of acculturative stress among international students from a medical university in Romania and to identify associated factors. We addressed three main categories of factors: sociodemographic (age; sex; having relatives, friends or siblings enrolled in the same university; if parents are doctors), comfortability with various aspects of living in the study city (speaking English and Romanian, neighbors, climate, transportation, and food), and satisfaction with administrative staff, colleagues, and professors. The present research is part of a larger study and previous results revealed that climate and food appeared to be the most uncomfortable aspects that students must deal with (Socolov, Munteanu *et al.*, 2017).

I.1.2. Material and methods

A number of 300 questionnaires were distributed among international medical students enrolled in General Medicine and Medical Dentistry faculties from Iasi, Romania. They were invited to participate voluntarily in the research. They had to provide information concerning sociodemographic, academic, and family data. Several items were constructed especially for the research, in order to identify the level of student's comfortability with living in the university city and the level of satisfaction with administrative staff, colleagues, and professors.

The third part of the data sheet measured the acculturative stress by using a psychological instrument. Students were informed about the purpose of the study and confidentiality of collected data; withdrawal was accepted at any time.

A total of 289 questionnaires were returned to the researchers. For statistical analysis, 265 were finally considered; 24 questionnaires were eliminated for failing to complete at least 90% of the items.

Instruments / Sociodemographic Data. Various sociodemographic, academic, and family data were registered: age, sex, year of study, nationality, if parents are doctors, if the student speaks Romanian, if parents speak Romanian, if at least one parent is a doctor, if parents visit every year, if the student is satisfied with living conditions, and having relatives, friends, or siblings enrolled in the university.

Comfortability of Living in the Study City. The degree of comfort with living in the study city was measured using a self-rated scale. Participants responded using a Likert-type scale from 1 to 5 (1-not at all comfortable, 2-somewhat comfortable, 3-comfortable, 4-very comfortable, and 5-extremely comfortable).

The items referred to their comfort with communicating in English, Romanian, and with neighbors. We also inquired about comfortability with climate, transportation, and food.

Satisfaction related to Colleagues / Staff / Teachers. To assess the satisfaction with administrative staff, colleagues, and teachers, several items were formulated, and responses were rated on a scale from 1 (very dissatisfied) to 10 (very satisfied).

The Acculturative Stress Scale for International Students (ASSIS) is a tool developed in 1994 by Sandhu and Asrabadi (Sandhu, 2016). The instrument is composed of 36 items in the form of statements about the stress caused by the adaptation to a new culture, which participants evaluate using a Likert scale from 1 (strong disagreement) to 5 (strong agreement), depending on how much it characterizes them. The measured dimensions are as follows: (I) perceived discrimination (8 items; "I am treated differently in social situations") (II) homesickness (4 items; "Homesickness for my country bothers me") (III) perceived hate/rejection (5 items; "I feel rejected when people are sarcastic toward my cultural values") (IV) fear (4 items; "I fear for my personal safety because of my different cultural background") (V) stress due to change/culture shock (3 items; "I feel uncomfortable to adjust to new cultural values") (VI) guilt (2 items; "I feel guilty to leave my family and friends behind") (VII) nonspecific concerns (10 items; "I feel nervous to communicate in English") The total scores range from 36 to 180, higher scores suggesting higher levels of stress. For the present study, the alpha Cronbach coefficient for the entire instrument is α=0:96.

Studies focusing on international students reported adequate psychometric properties for this measure of acculturative stress obtaining an internal consistency coefficient of 0.92 or above (Nguyen, 2019; Hunt *et al.* 2017).

Ethical Approval. The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by Centre de Reussite Universitaire, under the coordination of University of Medicine and Pharmacy and Agence Universitaire pour la Francophonie (AUF).

Statistical Analysis. Collected data were analyzed using IBM *SPSS Statistics version 23.0*. Percentages, means, and standard deviations were used for the descriptive analysis. *Pearson* (for quantitative variables) and Spearman (for analyses involving ordinal variables) correlations were used to investigate the associations between variables. The independent samples *t*-test was used in the case of variables where there are two independent groups to determine if there are any statistically significant differences between the means of these groups. Given the high number of independent samples *t*-tests employed, the Benjamini-Hochberg procedure was used to decrease the false discovery rate. Using a false discovery rate of 25%, the procedure indicated that all our *p* values were significant (available here).

I.1.3. Results

Descriptive Analysis. 265 students from 34 countries took part in the research (four students have dual nationality). The distribution according to gender is homogenous: 151 male (57%) and 114 females (43%). The participants were aged from 17 to 40 (M=21:38, SD=3:32). Participants were from all years of study (1st to 6th). Students were asked if they had friends, relatives, or colleagues among international students registered in the same university. Collected data showed that, of the students who reported having relatives/friends attending the same university, 33.9% of them have brothers/sisters, 32.1% have cousins, 29.4% have other friends, and 4.6% other relatives. Data regarding Romanian origins (at least one parent is Romanian but migrated to another country), if at least one parent is a physician if the student/mother/father speaks Romanian, if the parents visit them every year, and if students are satisfied with their living conditions are presented in Table I.

Table I. Sociodemographic characteristics and family related data

Variables		%
Sex	Male	57
	Female	43
Year of study	1st	44.9
	2nd	13.2
	3rd	17.4
	4th	6.4
	5th	6.8
	6th	11.3
Age ($M \pm SD$)		21.38 (3.32)
Romanian origins		9.1
Parent physician		22.6
Friends or other relatives enrolled in the same university		42.3
Student speaks Romanian		7.9
Mother speaks Romanian		9.8
Father speaks Romanian		13.6
Parents visit every year		35.1
Satisfied with living conditions		69.1

*Percentages (%), means (M), and standard deviations (SD).

The level of comfortability of international students is presented in Table II. In the extremely comfortable category, the highest score was for speaking English (31.3%) and the lowest was for city transportation (3.0%). In the not comfortable category, the highest score was for speaking Romanian (35.8%) and the lowest was for speaking English (2.6%).

Table II. The distribution of answers to items regarding students comfortability with aspects of the university life

How comfortable are you with…	Not comfortable	Somewhat comfortable	Comfortable	Very comfortable	Extremely comfortable	*M* (SD)
Speaking Romanian	35.8	34.0	18.1	7.5	4.5	2.10 (1.11)
Speaking English	2.6	4.9	25.3	35.8	31.3	3.88 (0.99)
Country's climate	12.1	24.2	40.8	18.5	4.5	2.79 (1.02)
City transportation	17.0	26.0	38.1	15.8	3.0	2.61 (1.03)
Neighbors	12.1	15.5	41.9	20.8	9.8	3.00 (1.11)
Local food	15.5	26.8	37.0	10.2	10.6	2.73 (1.16)
Communicating with the homeowner	6.4	15.1	39.2	21.9	17.4	3.28 (1.16)

*Percentages (%), means (M) and standard deviations (SD).

Mean levels of satisfaction with colleagues, teachers, and administrative staff were as follows: 7:18 ± 2:13,6:22 ± 2:32, and 5:52 ± 2:42, respectively. The results for *Acculturative Scale for International Students* (total score for ASSIS and values for each subscale) are presented in Table III; the highest scores were identified for nonspecific concerns and perceived discrimination, and the lowest scores for guilt, fear, and stress due to change/culture shock.

Table III. Total score for ASSIS and scores for each subscale of ASSIS

Total score and subscales	Results
ASSIS (total score)	85.82 (23.03)
Perceived discrimination	18.95 (5.91)
Homesickness	11.35 (3.40)
Perceived hate/rejection	11.64 (3.97)
Fear	8.74 (3.09)
Stress due to change/culture shock	7.52 (2.44)
Guilt	4.77 (1.77)
Nonspecific concerns	22.83 (6.96)

*Means (*M*) and standard deviations (SD).

Comparative Analysis. When comparing male and female students on the total score of ASSIS and each of its dimensions, two statistically significant differences emerged concerning homesickness (t ð263Þ=−5:532, p < 0:001) and stress due to change (t ð263Þ=−2:105, p=0:036). Female students were more prone to experience homesickness (M=12:61) and stress due to change (M=7:88) compared to male students (M=10:39 and M=7:25, respectively). The fact that students had Romanian origins revealed two statistically significant differences on two subscales of the ASSIS: perceived hate (t ð261Þ=−2:110, p=0:036) and stress due to change/culture shock (t ð261Þ=−2:984, p=:003). More specifically, students who had Romanian origins had lower scores on perceived hate (M=10:91) and stress due to change/culture shock (M=6:12) compared to those with no Romanian origins (M=11:80 and M=7:66, respectively). The fact that one parent was a doctor revealed two differences between participants concerning homesickness (t ð263Þ=−2:172, p=:031) and guilt (t ð263Þ=−3:063, p=:003).

Students whose parents were doctors experienced lower levels of homesickness (M=10:91) and guilt (M=4:45) compared to those whose parents had other jobs (M=11:39 and M=4:80, respectively).When considering the existence of other relatives enrolled in the same university, the results showed several statistically significant differences between international students in terms of acculturative stress (t ð263Þ=−2:062, p=0:040), perceived discrimination

(t ð263Þ=−2:299, p=0:022), perceived hate / rejection (t ð263Þ=−2:345, p=0:020), and non-specific concerns (t ð263Þ=− 2:031, p=0:043). Students with relatives enrolled in the same university had significantly lower levels of acculturative stress (M=82:43), perceived discrimination (M=17:98), perceived hate/rejection (M=10:98), and nonspecific concerns (M=21:82) compared to those who did not have relatives enrolled in the same university (M=88:30, M=19:66, M=12:13, and M=23:56, respectively). Analyses also revealed significant differences in stress due to change/culture shock between students who spoke Romanian (t ð263Þ=−4:578, p < 0:001) or having their mother (t ð263Þ=−3:595, p < 0:000) or father speaking Romanian (t ð263Þ=−2:358, p=:019). Specifically, they had lower scores on this subscale (M=5:80, M=5:92, and M=6:63, respectively) compared to those who did not speak Romanian (M=7:67) and neither did their mother (M=7:69) or father (M=7:66). Also, students whose mothers spoke Romanian experienced lower levels of acculturative stress (M=76:61) and perceived hate (M=10:07) than those whose mothers who did not speak Romanian (M=86:82, M=11:81, respectively) t ð263Þ=−2:162, p=0:032; t ð263Þ=−2:134, p=0:034, respectively. Also, there was a difference between participants whose parents visited them every year compared to those who did not visit them as often on the homesickness subscale: t ð263Þ=2:377, p=0:018. The former scored higher on this subscale (M=12:02) compared to the latter (M=10:98).

Correlation Analysis. The results of the correlation analysis revealed several significant and negative associations between the study variables and are presented in Table IV. However, the effect sizes ranged from small (*r*=−0:123) to moderate (*r*=−0:381).

Table IV. Correlations between ASSIS (total score and sub scores) and variables

	ASSIS	Perceived discrimination	Homesickness	Perceived hate/rejection	Fear	Stress due to change/culture shock	Guilt	Non-specific concerns
Age	$r=-0.170$ $p=0.005$	$r=0.078$ $p=0.207$	$r=-0.307$ $p=0.000$	$r=-0.077$ $p=0.213$	$r=-0.119$ $p=0.052$	$r=-0.221$ $p=0.000$	$r=-0.174$ $p=0.005$	$r=-0.128$ $p=0.037$
Year of study	$r=-0.118$ $p=0.055$	$r=-0.035$ $p=0.566$	$r=-0.364$ $p=0.000$	$r=0.002$ $p=0.971$	$r=-0.030$ $p=0.630$	$r=-0.165$ $p=0.007$	$r=-0.130$ $p=0.034$	$r=-0.075$ $p=0.225$
Comfortable speaking Romanian	$r=-0.092$ $p=0.137$	$r=-0.075$ $p=0.222$	$r=-0.095$ $p=0.124$	$r=-0.086$ $p=0.165$	$r=-0.106$ $p=0.085$	$r=-0.150$ $p=0.014$	$r=-0.014$ $p=0.819$	$r=-0.047$ $p=0.448$
Comfortable speaking English	$r=-0.293$ $p=0.000$	$r=-0.215$ $p=0.000$	$r=-0.172$ $p=0.005$	$r=-0.250$ $p=0.000$	$r=-0.237$ $p=0.000$	$r=-0.238$ $p=0.000$	$r=-0.288$ $p=0.000$	$r=-0.316$ $p=0.000$
Comfortable with country's climate	$r=-0.233$ $p=0.000$	$r=-0.205$ $p=0.001$	$r=-0.166$ $p=0.007$	$r=-0.190$ $p=0.002$	$r=-0.186$ $p=0.002$	$r=-0.199$ $p=0.001$	$r=-0.152$ $p=0.013$	$r=-0.184$ $p=0.003$
Comfortable with local transport	$r=-0.099$ $p=0.108$	$r=-0.130$ $p=0.035$	$r=0.067$ $p=0.277$	$r=-0.120$ $p=0.051$	$r=-0.073$ $p=0.239$	$r=-0.071$ $p=0.252$	$r=-0.017$ $p=0.780$	$r=-0.099$ $p=0.107$
Comfortable with neighbors	$r=-0.246$ $p=0.000$	$r=-0.287$ $p=0.000$	$r=-0.068$ $p=0.267$	$r=-0.186$ $p=0.002$	$r=-0.233$ $p=0.000$	$r=-0.242$ $p=0.000$	$r=-0.111$ $p=0.070$	$r=-0.277$ $p=0.000$
Comfortable with local food	r=−0.240 p=0.000	r=−0.185 p=0.003	r=−0.114 p=0.064	r=−0.210 p=0.001	r=−0.243 p=0.000	r=−0.328 p=0.000	r=−0.188 p=0.002	r=−0.205 p=0.001
Comfortable communicating with homeowner	r=−0.126 p=0.040	r=−0.131 p=0.033	r=0.053 p=0.390	r=−0.105 p=0.089	r=−0.166 p=0.007	r=−0.108 p=0.078	r=−0.015 p=0.804	r=−0.163 p=0.008
Satisfaction with colleagues	r=−0.266 p=0.000	r=−0.222 p=0.000	r=−0.155 p=0.012	r=−0.244 p=0.000	r=−0.221 p=0.000	r=−0.242 p=0.000	r=−0.135 p=0.028	r=−0.232 p=0.000
Satisfaction with teachers	r=−0.258 p=0.000	r=−0.265 p=0.000	r=−0.007 p=0.916	r=−0.220 p=0.000	r=−0.300 p=0.000	r=−0.257 p=0.000	r=−0.141 p=0.022	r=−0.234 p=0.000
Satisfaction with administrative staff	r=−0.275 p=0.000	r=−0.294 p=0.000	r=−0.047 p=0.445	r=−0.218 p=0.000	r=−0.271 p=0.000	r=−0.152 p=0.013	r=−0.169 p=0.006	r=−0.275 p=0.000

The results of our study indicated that acculturative stress and perceived discrimination correlated negatively with the degree of comfort regarding communication in English, climate, neighbors, communication with the homeowner and food in the host country; perceived discrimination correlated with local transport and acculturative stress was found to correlate with age. The statistical analysis revealed that homesickness was significantly correlated with age, year of study, the degree of comfort communicating in English, and climate of the host country. Perceived hate/rejection and fear were found to be correlated significantly and negatively with the degree of comfort with English communication, climate, neighbors, and food. Correlational analyses also showed stress due to change/-culture shock correlated negatively with age, year of study, and with the degree of comfort with communication in English, communication in Romanian, climate, neighbors, and food from Romania.

The results suggested that guilt correlated significantly with age, year of study, and with the degree of comfort with communication in English, climate, and food in Romania. According to the results, general/nonspecific concern correlated significantly with age and with the degree of comfort studied by the research (communication in English, climate, neighbors, communication with the homeowner, and food). Finally, the degree of satisfaction with colleagues was negatively correlated with the ASSIS and all its subscales. The degrees of both satisfaction with administrative staff and with teachers were correlated negatively with the total score of ASSIS and with its subscales, except homesickness.

I.1.4. Discussion

Previous studies have shown that there are a considerable number of factors associated with acculturative stress. Some of these factors include personality, social inclusiveness, language barriers, and cultural differences. Gender, age, and language competence are the most well-documented (Mesidor *et al.*, 2016, Akhtar *et al.*, 2015, Quinn *et al.*, 2016). In study women are more prone to higher levels of homesickness and stress due to change/culture shock; a fact that is congruent with another research. International female students had higher levels of acculturative stress compared to men and are more prone to experience depressive symptoms (Zahn *et al.*, 2012). The year of study was negatively related to homesickness and stress due to change/culture shock. Also, age was negatively correlated with some subscales of these students: homesickness, stress due to change/culture shock, guilt, and nonspecific concerns. Some studies found no association between age and acculturative stress (Yeh, 2003; Poyrazli *et al.*, 2004). However, Ye (Ye, 2006) found higher levels of acculturative stress among older Chinese international students compared to younger ones. The results of that study showed that older students scored higher on fear, perceived discrimination, and hatred than younger students. Akhtar and Kroners-Herwig (Akhtar *et al.*, 2015) found that younger age predicted a low level of acculturative stress. However, those studies were not conducted on medical students. Given the fact that medical studies span over a period of six years, it might be plausible for some aspects of the acculturation process to differ from other studies. It has been previously documented that international student tend to experience language difficulties (Mori *et al.*, 2000) and the challenges posed by them might make it difficult to interact with their peers (Hayes *et al.*, 1994). In the present study, the degree of comfortability of speaking in English correlated negatively with the ASSIS and all its subscales. Also, the more comfortable the students feel communicating in Romanian, the less they score on the stress due to change/culture shock subscale of the ASSIS. Accordingly, before taking into consideration the option of studying abroad, students should focus on attaining language proficiency. This allows increased chances of social interaction with the members of the host society and could be a principal factor in decreasing stressful experiences (Akhtar *et al.*, 2015). Studying the acculturative stress among international students from different specialties, Sullivan and Cashback-West (Sullivan *et al.*, 2015) assert that home country support and an emphasis on maintaining ties to the home culture are not beneficially associated with adapting to studies in the United States. In our study, having origins from the host country seemed to be a key factor that decreased the level of stress among international students. Students who had Romanian origins had lower scores on perceived hate and stress due to change/culture shock compared to international students with no Romanian origins. Our study also indicated that friends and family presence decreased the rate of acculturative stress, perceived discrimination, perceived hate/rejection, and nonspecific concerns and might indicate their influence on the choice to study in a certain country. Students speaking Romanian or having one parent speaking Romanian had lower levels of stress due to change/culture shock. Students who were not visited by their parents every year were more prone to experience homesickness. International students with Romanian origins conserved a host-country contact by parents or grandparents (language, food, relatives, family membered); therefore, the host-culture is not likely entirely new to them,

and their level of stress is low. Previous studies (Brown *et al.,* 2009, Hendrickson *et al.,* 2011) underlined the fact that acculturative stress might be decreased by the development of host country rather than home country social support. The results of our study showed that, although students still have ties with their home country (through the presence of family and friends at the same University and visits from their parents), they also have stable connections with the host country(through their origins and the fact that either them or at least one of their parents spoke Romanian), and these aspects contribute to a low level of acculturative stress. However, this result is specific to our sample (given the fact that close to half of our participants had friends or family enrolled in the same university) and might be due to the ways students choose their university (Socolov, Iorga *et al.,* 2017, Socolov, Munteanu *et al.,* 2017). Students who decide to study in another country might experience practical or lifestyle acculturative stressors. When transitioning from their home country to their host country, international college students face various perceived threats and challenges. Among them are the lack of knowledge of the host culture, difficulty in adapting to the host country customs and lifestyle, and maladjustment to the physical environment (Kuo *et al.,* 2004). The present study took into consideration some of these aspects: food, climate, transportation, neighbors, and communication with the homeowner. The results showed negative correlations between these variables and acculturative stress and some of its subscales. The students 'transition from their country to the country where they will study brings the need to adopt and assimilate the customs and culture of their host country. Adjusting to food, weather, accommodation, and local language represents an important challenge for international students (Poyrazli *et al.,* 2007, Tseng *et al.,* 2002). Ideally, international students should gather information regarding geographical and social aspects, food, and transportation in their targeted country. However, documentation does not provide the same experience as personal experience and the students must be aware of this aspect. International student satisfaction is an in-principal factor in strengthening support services for this community (Ammigan *et al.,* 2018). Previous studies have found that students struggled to develop friendships with local and international students and often felt disconnected with the wider campus community outside the classroom (Yu *et al.,* 2016). Our study showed that higher levels of satisfaction regarding the relationship with colleagues, teachers, and administrative staff were related to lower levels of acculturative stress (and most of the subscales of the ASSIS). Baranova (Baranova *et al.,* 2011) found that two of the main factors contributing to improved student experience are increased customer service training for service staff and a revitalized program that should focus on students' transition and acculturation to their new campus environment. The authors also mention that, in the case of countries with tradition in international recruitment, in order to draw and keep international students, universities must offer them suitable support services and resources; in order to be competitive in this area, there is a need to improve the international student experience (Martini *et al.,* 2019).

The drop-out rates in this medical university are about 10%, according to the rates identified by the university career counselling center. The most important reason declared by the students being the financial one even if the level of annual taxes for medical studies in Romania are among the lowest in Europe. The results of the present research must encourage teaching and counselling staff to adopt more diversified and efficient strategies for helping international students to cope with acculturative stress: establishing a more developed mentoring program for freshmen students matching them with seniors, for advice and support; increasing the number of intercultural events in order to help students socialize; providing more flexible support services in order to help them adjust to the new academic demands and cultural/local habits); organizing meetings with national and international students for networking and facilitating information change regarding lifestyle, local transportation, facilities for sports, leisure, or hobbies; and enhancing counsellors and therapist awareness in

working with international students and providing them with information and knowledge on how to work with multicultural and multilingual groups.

I.1.5. Conclusions

The existence of risk factors for acculturative stress demands institutional, social, and psychological support for international students. Multicultural environments must be provided with resources to maintain a sustainable development of international students during their education. Apart from their psychological characteristics and inner motivation, the support from family members, peers, academic community, social media, or professional staff working in the university field can provide support for students during their academic trajectory and career.

B. PSYCHOSOCIAL / ACADEMIC ENVIRONMENT IMPACT ON DEVELOPING DEPRESSION AND ANXIETY TO YOUNG STUDENTS

The academic years are usually very stressful for all medical students. The distress level is determined first by the large and diverse number of disciplines and by the continuous assessment and secondly, due to the interaction with the patients during their practice stages. Thirdly, the transition from adolescence to maturity and the changes in their personal lives also have consequences on their psychological well-being.

Apart from burnout, depression is one of the most important psychological problems experienced by students during their academic years. The scientific literature provides data for the general population of students, about 33%. Regarding the presence of depressive symptoms among nursing students, the data presented are different, depending on the country: 52.4% in Greece (Papazisis *et al.*, 2008), 22.9% in China (Xu Y *et al.*, 2014), 30.2% in Brazil (Moreira and Furegato, 2013), 30.5% in Denmark and 43% in Saudi Arabia (Zoccolillo *et al.*, 1986, Kulsoom and Afsar, 2015).

Studies have also pointed out that reports for depressive symptoms among medical students are higher compared to the general population, even before students begin their medical education (Zoccolillo *et al.*, 1986).

Showing and supplying knowledge about depression and burnout among healthcare professionals is an important aspect of medical education. Professionals in the medical field are exposed to higher risks of depression and professional exhaustion, and their negative impact on work and successful results has been proved by the research in the field: higher rates of errors and of difficulties in keeping good relationships with patients or colleagues and low rates of job-related satisfaction (Kulsoom and Afsar 2015; Iorga *et al.*, 2015).

Medical students are at risk for stress as medicine is a never-ending path and a career with high demands (Fares *et al.*, 2016). Medical studies entail a great amount of stress due to tremendous workload and great intellectual / emotional demands (Wege *et al.*, 2016).

There are two categories of factors that can generate distinct levels of stress (Fawzy and Hamed, 2017): endogenous (sex, personality traits, believes) and exogenous. Exogenous factors are divided into three categories: *academic stressors* (difficulties with understanding and learning new syllabus, difficulty with reading textbooks particularly if there is lack of a premedical university preparatory program (UPP), high workload, extensive medical curricula, long teaching hours, lack of leisure or recreation times; the poor quality of the educational process at the college; irregular schedules, frequency of tests, competition with peers and worries related to academic performance or achievement/ fear of failure), *psychosocial stressors* (the high paternal expectations; home sickness; the new living accommodation; financial strain; fear of future failure in medical career), and *socio-demographic stressors* (gender; smoking; substance abuse, marital status; working during the study; the levels of parents' education; cultural background and the socioeconomic status of the family). These

stressors can trigger various mental health problems (Fawzy and Hamed, 2017; Moutinho *et al.*, 2017; Kumar and Narayan 2018; Chen *et al.*, 2018;) and students cope by listening to music, talking to relatives or people close to them, resting or engaging in sports (Rosiek *et al.*, 2016).

Of great concern is the fact that, of the students who screened positive for depression, only a low percentage sought psychiatric treatment: 15.7% (Rotenstein *et al.*, 2016) and 12.9% (Puthran *et al.*, 2016). Elliot and Tan found that medical practitioners are also hesitant about seeking help when having mental health problems and the authors reported several barriers to help-seeking: concern about letting colleagues down; concern about stigma; concerns about losing medical staff privileges; concerns about losing medical license; negative impact on practice; confidentiality; letting patients down; letting colleagues down; lack of locum cover and career progression (Elliot and Tan, 2010).

Wege found, in a sample of German medical students, a prevalence rate of 4.7% for major depression and 5.8% for other depressive symptoms (Wege *et al.*, 2016). In their study, expected financial difficulties were associated with poor mental health (major depression, other depressive symptoms, anxiety, panic disorders and psychosomatic symptoms). Also, in Burger and Scholz's (11) study, female medical students presented higher scores of depressiveness than male students.

In Egypt were reported high frequencies of depression (65%), anxiety (73%) and stress (59.9%) among 700 Egyptian medical students (Fawzy and Hamed, 2017). This high prevalence was found to be in relation to sex (being a female), living condition (away from families), the year of study (preclinical years) and academic achievement (poor academic achievement degrees) Wahed and Hassan mentioned that 60.8% of the students in their sample had depression and higher depression scores were associated with increasing age, low socioeconomic standard and other governorates (Wahed and Hassan, 2018).

In USA, in a study conducted by Wimsatt (Wimsatt *et al.*, 2015), 14.7% of students reported a previous depression diagnosis. Moreover, most students declared that they would feel embarrassed if they were depressed and their colleagues knew. Moreover, Hardeman *et al.* found that African American students had a 59 % greater risk of being classified as having depressive symptoms than White students and female medical students had a 39% greater risk of being classified as having depressive symptoms than male students (Hardeman *et al.*, 2015).

Mousa (Mousa *et al.*, 2016) found that 15.1% and 15.9% of postgraduates as well as 16.4% and 20.3% of medical students screened positive for major depressive disorder and generalized anxiety disorder. Also, both categories believe depression affects their academic performance (33.3% and 32% respectively). According to Ludwig students in their 3rd year of study are significantly at risk for depression compared to their 1st year (Ludwig *et al.*, 2015).

Wolf and Rosenstock reported that 8% of students screened positive for depression at the beginning of the year and 9.3 % in the middle of the year, with a positive association between burnout and depression. Also, the authors found positive depression screening, pathological sleepiness, and sleeping less than 7 hours / night to be independent predictors of burnout (Wolf and Rosenstock, 2017)

In India Kumar *et al.* reported an overall prevalence of depression of 21.50% in medical dentistry students. In their study, 3rd and 4th year students showed a significantly higher prevalence of depression than other years (Kumar *et al.*, 2018). The study of Iqbal (Iqbal *et al.*, 2015) revealed that 17.5% of medical undergraduate students had severe or extremely severe depression. Kumar and Narayan (Kumar and Narayan, 2018) found that 56% of the students in their sample presented depressive symptoms (there was no difference between male and female students), and they seemed to decrease as students progressed through their years of study. Jose found a high prevalence of depression (78.2% of all the students had a depression score higher than 49), with women scoring higher than men (Jose *et al.*, 2016). The authors also found a positive association between depression and insomnia. A rate of 85.3% of the students in their

study were suffering from depression and they found it to be related to internet addiction. More specifically, 95% of the participants who were addicted to the internet were found to be suffering from depression and students with internet addiction had four times the risk of being depressed when compared with those without internet addiction (Elavarasan *et al.*, 2018).

In a meta-analysis including 25 studies on depression among medical students in Brazil (Pacheco *et al.*, 2017), found the prevalence to be 30.6% and positive associations with several variables: female gender; desire to switch courses; later stages of the course; internship cycle; clinical cycle; dissatisfaction with the course; tobacco smoking; average (compared to good) academic performance; difficulties in relationships; emotional tension; evening-type preference; feeling pressured by parents; having concerns about the future; not having a parent who was a physician; not participating in social activities; parents were physicians; poor or reasonable physical health; thoughts of dropping out; religion other than Catholic; sedentary lifestyle; sporadic involvement in leisure activities; uncertainty about professional future.

In Bangladesh, Hossain and Wahab reported that 40.8% of the students at Armed Forces Medical College, Dhaka Cantonment, had depressive symptoms (with no gender differences) and they were very significantly higher in their 1st year than 2nd, 3rd and 4th year. Also, depression was significantly higher in Non-English Medium background than English Medium background participants (Hossain and Wahab, 2016). Another Bangladeshi study (Al Mamun and Griffiths, 2019) reported an even higher level of depression (46.3%). Also, depression symptoms represented a strong predictor for Facebook addiction. Said *et al.* reported that 8% of the Australian medical students reported having depression and they identified the following groups as vulnerable: women, 25-34-year-olds, students on low income, and homosexual or bisexual students (Said *et al.*, 2013).

In Romania symptoms of depression, were also found among first-year students in a medical University (Iorga *et al.*, 2017). The prevalence of depression symptoms was 20% and the authors also found significant statistical correlations between depression and a series of variables: age, experience as a nurse, emotional exhaustion, introversion, emotional instability and job satisfaction. In another Romanian study, this time centered on dental and psychotherapy students, there was a moderate association between professional stress and symptoms of depression (Dudău *et al.*, 2015).

My interest regarding this area is reflected by the following articles:

Iorga Magdalena, Muraru Iulia-Diana, Soponaru Camelia, **Petrariu FD.** FACTORS INFLUENCING THE LEVEL OF DEPRESSION AMONG FRESHMAN NURSING STUDENTS. *Medical-Surgical Journal-Revista Medico-Chirurgicala* Volume: 121 Issue: 4 Pages: 779-786 Published: 2017.Web of Science Core Collection - Emerging Sources Citation Index / **WOS:000424521200026**

Iorga Magdalena, Muraru Iulia-Diana, Munteanu Catalina, **Petrariu FD.** DEPRESSION, ANXIETY AND STRESS AMONG MEDICAL STUDENTS. *Medical-Surgical Journal-Revista Medico-Chirurgicală* Volume: 123 Issue: 3 Pages: 496-505 Published: 2019. Web of Science Core Collection - Emerging Sources Citation Index / **WOS:000489620800028**

I.2. Factors influencing the level of depression among freshman nursing students

I.2.1. Aim

The aim of the present study is to evaluate the level of depression among first-year nursing students and to find its relationship with personality traits, burnout, job satisfaction and socio-demographic variables. The article is part of an extended research focusing on psychological problems related to socio-demographic aspects and personality traits among freshman students from nursing studies.

I.2.2. Material and methods

A group of eighty-nine freshman students from the nursing specialty took part in the research. A fill-in paper recording socio-demographic data and 4 instruments were provided, after the students were informed about the goal of the research and the confidentiality of personal data. Socio-demographic data like age, sex (male, female), environment (urban/rural), marital status (single, in a partnership), the number of children in the family of origin (singleton/siblings), having children (yes/no) and length of experience as a nurse were recorded.

Four instruments were used for the research to evaluate depression and the relationship with burnout syndrome, personality traits and job-related satisfaction:

1. The level of depression was evaluated by *The Beck Depression Inventory* (BDI). The instrument has twenty-one items using a four-point scale ranging from 0 (symptom is not present) to 3 (symptom is very intense). Ratings from 0 to 13 are considered in the minimal range, 14 to 19 mild, 20 to 28 moderate, and 29 to 63 severe depressions (Beck *et al.,* 1996) The Cronbach alpha (.85) shows good internal consistency.
2. *Eysenck Personality Questionnaire* (EPQ) was used to assess participants' personality traits (Eysenck *et al.,* 1965). This instrument with fifty-seven items evaluates psychoticism, extraversion, neuroticism and social desirability. Combining scores for the two subscales, the four types of temperaments are identified (sanguine, melancholic, choleric and phlegmatic). Extroverts are usually outgoing, talkative, and in need of external stimulation, while introverts are over-stimulated and excitable; they need peace and quiet to achieve a proficient level of performance. People high on neuroticism experience important levels of negative affect, such as depression and anxiety, while emotionally stable people are calm and don't experience negative affect unless they are faced with major stressors. Psychoticism is associated with aggression and with chances of having a psychotic episode and Lie/Social Desirability measures the extent to which respondents try to be socially desirable in their answers. The instrument has good internal consistency, with a Cronbach's alpha coefficient of 0.81.
3. The burnout syndrome was evaluated using *The Maslach Burnout Inventory* (MBI). The instrument contains three scales which have nine, five and respectively eight items. MBI evaluates e*motional exhaustion* (referring to the feeling of being emotionally spent and fatigued by work), d*epersonalization* (describing coldness in responses towards the beneficiaries of one's work) and *personal achievement* (related to feelings of competence and achievement in collaborating with other people). The higher scores on *emotional exhaustion* and depersonalization subscales are related to higher degrees of burnout and lower scores on the *personal achievement* subscale correspond to higher rates of burnout (Maslach and Jackson, 1986). For the three subscales we obtained the following Cronbach's alpha scores: .828, .591 and .829.
4. Because more than half of the students are working in the medical field, we wanted to evaluate the level of job-related satisfaction with *The Job Satisfaction Scale* (JSS). The instrument contains 4 subscales with 32 items: *payment and promotions* (assessing someone's satisfaction with rewards like payment, promotion), *management and inter-personal relationships* (the employee's satisfaction with the social setting, the relationships he/she has with colleagues / manager), *organization and communication* (the employee's satisfaction with work organization and the way work is performed) and the total score for the scale - *overall job satisfaction* - providing a total score for satisfaction with all aspects of the work (Stoica-Constantin and Constantin, 2009). The Cronbach alpha scores for the subscales are: .77, .61 respectively .62 and for overall job satisfaction the score is .86.

The data were processed using *SPSS Statistics version 17.0*. We used descriptive statistics to point out the results obtained for each instrument used (mean and standard deviation). For the comparative analysis we used one-way *ANOVA* and Independent Samples

t-Test. For the correlational analysis we used *Pearson* correlations and for the regression analysis we used multiple linear regression.

I.2.3. Results

Descriptive analysis. Socio-demographic data papers and scales to be filled in were distributed among first-year nursing students in a university in north-eastern Romania. A number of 89 fully filled-in questionnaires were returned in time. The students come from 6 counties from this region (Bacau, Botoșani, Iași, Neamt, Suceava, Vaslui). Socio-demographic data are presented in Table V.

Table V. Socio-demographic data

VARIABLES		N (%)
GENDER	Male Female	8 (9) 81 (91)
ENVIRONMENT	Urban Rural	55 (62.50) 33 (37.50)
AGE (25.52 ± 9.42)	Minimum age Maximum age	19 48
RELATIONSHIP STATUS	Single (single or divorced) In partnership (couple or married)	58 (65.2) 31 (34.8)
CHILDREN	Have children No children	19 (21.3) 70 (78.7%)
EXPERIENCE AS NURSE	Yes No	24 (24.7) 65 (75.3)
LENGTH OF EMPLOYMENT AS A NURSE (3.31 ± 6.52)	Minimum length Maximum length	1 year 26 years
FAMILY OF ORIGIN	Singleton Siblings	14 (15.7%) 75 (84.3)

The research focused on depression, temperamental traits, burnout and job satisfaction scores (Table VI). Depression was evaluated for all participants. The analysis of scores proves that 9.5% of the participants have mild depression, 6.7% have moderate depression, and 2.2% have severe depression.

According to burnout subscales, we found that 15.7% of students have high levels of emotional exhaustion, for the other two subscales the scores are low.

Eysenck scores focused on revealing introvert/extrovert traits and the emotional in/stability. The analysis of data proved that 42% of participants are introverts and 58% are extroverts, while 53.4% are emotionally stable and 46.6%, emotionally unstable. The temperamental categories are: 28.1% of students are sanguine, 25.8% are phlegmatic, 14.6% melancholic, and 31.5% choleric.

I.2.4. Discussion

Correlational analyses. Pearson correlations were used for the investigated variables in the present study. A positive relation was showed between age and depression (meaning that the higher the age is, the higher the scores on depression are) and between the length of employment as a nurse and depression (the more nursing experience participants have, the higher they score on depression) (Table VII).

Table VI. Scores for BDI, EYSENCK, JSS, MBI

INSTRUMENTS	SCALE / SUBSCALE	MEAN ± STANDARD DEVIATION
BDI	level of depression	10.08 ± 8.70
EYSENCK	introversion - extraversion	11.43 ± 3.41
	stability - instability	12.34 ± 4.40
	social desirability	3.60 ± 1.82
MBI	emotional exhaustion	19.54 ± 10.08
	personal achievement	12.79 ± 8.56
	depersonalization	6.57 ± 5.41
JSS	payment and promotion	3.23 ± .70
	management-interpersonal relationships	4.05 ± .72
	organization-communication	4.28 ± .60
	overall satisfaction	3.80 ± .58

Table VII. Results regarding correlations between depression and other variables

VARIABLES		DEPRESSION
SOCIO-DEMOGRAPHIC DATA	Age	R=.256*, p=.019
	Number of children	R=.036, p=.745
	Nurse experience	R=.347*, p=.001
EYSENCK	Introversion - extraversion	R=-.271*, p=.013
	Stability - instability	R=.309**, p=.005
MBI	Emotional exhaustion	R=.362**, p=.002
	Personal accomplishment	R= -.098, p=.417
	Depersonalization	R= -.145, p =.230
JSS	Payment - promotion	R=-.257*, p=.032
	Management - interpersonal relationships	R= -.317**, p=007
	Organization - communication	R=-.333**,p=.004
	Overall job satisfaction	R=-.354**,p=.003

A negative correlation between introversion - extraversion and depression were identified, meaning that higher scores on this subscale of the *Eysenck Personality Questionnaire* correspond to lower levels of depression and a positive correlation appears to exist between the stability - instability subscale and depression. More exactly, the higher the scores on stability - instability, the higher the scores on depression; the lower the scores on stability - instability, the lower the scores on depression.

The relationship between depression and subscales of MBI was analyzed. Positive correlations were pointed between the *emotional exhaustion* subscale and depression, meaning that higher scores on *emotional exhaustion* are associated with higher scores on depression, while lower scores on *emotional exhaustion* are associated with lower scores on depression.

Negative correlations were identified between depressions and factors of job satisfaction (including the overall scores). The more satisfied participants were on *payment - promotion*, the lower they scored on depression. When considering the *management - interpersonal* relationships subdomain, the higher subjects scored on this variable, the lower their scores on depression. The more individuals were satisfied with the *organization - communication* aspect of job satisfaction, the less depressed they felt.

Finally, the higher the score is for *overall job satisfaction*, the lower the depression value is. It is important to point that the results prove that depression affect all job-related aspects. For the variables where we have three or more independent (unrelated) groups (temperament, burnout), we used the one-way analysis of variance (*ANOVA*) in order to establish if there are any statistically significant differences between the means of these groups. For the variables where we have two independent groups (nursing experience, presence of children, relationship status), we used the Independent Samples *t*-Test. This is a parametric test comparing the means of two independent groups and determining if the means are significantly different.

The number of male students is too low to proceed with a comparative analysis, to analyze if there are some differences between men and women, considering this variable. Studies from the literature point out some higher scores for depression for female students, compared to males (Bostanci *et al.,* 2005). To determine whether the type of temperament has an influence on depression, we took into consideration the four known types: sanguine, phlegmatic, melancholic, and choleric. One-way *ANOVA* results (F (3.80), p=.005) show that there is a difference in depression among participants, according to their temperament.

Multiple/post-hoc comparisons showed that sanguine individuals have lower scores on depression compared to melancholic individuals. Another difference that has emerged is that phlegmatic people have lower scores on depression compared to melancholic people. Finally, melancholic individuals have higher scores on depression compared to choleric individuals.

While the comparison between introverts and extroverts reveals no statistically significant differences (t (81)=1.733, p=.087), the Independent Samples *t*-Test shows that there is a difference between stable and unstable individuals on depression: t (81)=-2.134, p=.037. More specifically, stable individuals have lower scores on depression compared to unstable individuals.

For analyses concerning burnout subscales, we divided the variable into three groups on each of the three subscales: emotional exhaustion, personal achievement, and depersonalization. The results of one-way *ANOVA* showed that only emotional exhaustion influences depression (F (2.68)=4.126, p=.020). Multiple/post-hoc comparisons showed that individuals with low scores on emotional exhaustion have lower scores on depression compared to those with high scores on emotional exhaustion. For analyses concerning nursing experience, we divided the participants into two groups: no nursing experience and with nursing experience. The statistical analysis showed no differences in depression between participants with or without nursing experience (t (82)=-1.579, p=.129).

The results of the comparison between participants with and without children showed no differences concerning depression (t (82) =.013, p=.990).

When comparing single individuals with the ones involved in a relationship, the results of the Independent Samples *t*-test (t (82)=-.698, p=.487) showed no differences regarding the depression level between single students and those involved in a partnership. The analysis of results from the scientific literature provides different results about the scores for depression when it is about the marital status. The study of Sharokani (Sharokani *et al.,* 2013) mentioned that single students are more susceptible to higher rates of depression compared to married students. Contrary to these results, Bayram and Bilgel (Bayram and Bilgel, 2008) reported lower rates for single students.

Regression analysis. The table of correlations revealed the influence of some variables (age, nursing experience, introversion / extraversion, stability / instability, emotional exhaustion, payment - promotion, management - interpersonal relationships, organization - communication, and overall job satisfaction) on depression. We used multiple linear regression by the hierarchical method.

Of the 9 models in which the depression criterion was assessed, the fifth model explains 30% of its variance. Among the 5 predictors of the model, only stability/instability and emotional exhaustions are significant predictors of depression (p=.016, respectively p=.027), their effect on the criterion being positive (b=.613, beta=.277, respectively b=.253, beta=.266) (Table VIII).

Table VIII. Regression analysis

	MODEL	ADJUSTED R^2	F	R^2 change
Step 1	Age	.063	5.041 (p =.029)	.079
Step 2	Age, nurse experience	.120	5.106 (p =.009)	.071
Step 3	Age, nurse experience, introversion/extraversion	.167	4.997 (p =004)	.059
Step 4	Age, nurse experience, introversion/extraversion, stability/instability	.247	5.928 (p =.000)	.089
Step 5	Age, nurse experience, introversion/extraversion, stability/instability, emotional exhaustion	.300	6.132 (p =.000)	.060
Step 6	Age, nurse experience, introversion/extraversion, stability/instability, emotional exhaustion, payment-promotion	.287	5.025 (p =.000)	.000
Step 7	Age, nurse experience, introversion/extraversion, stability/instability, emotional exhaustion, payment-promotion, management-interpersonal relationships	.303	4.731 (p =.000)	.026
Step 8	Age, nurse experience, introversion/extraversion, stability/instability, emotional exhaustion, payment-promotion, management-interpersonal relationships, organization-communication	.291	4.085 (p =.001)	.001
Step 9	Age, nurse experience, introversion/extraversion, stability/instability, emotional exhaustion, payment-promotion, management-interpersonal relationships, organization-communication, overall job satisfaction	.295	3.793 (p =.001)	.015

I.2.5. Conclusions

The research proves that almost 20% of first-year nursing students have symptoms of depression, ranging from mild to severe. The factors influencing the level of depression are temperament, emotional exhaustion and emotional stability. Melancholic individuals are more prone to depression than sanguine, choleric and phlegmatic individuals. The more emotionally exhausted individuals are, the higher their chances are of developing depression. Regarding emotional stability, we identified that unstable individuals present higher risks of developing depression. The results are important for both students and teachers, to be aware that personality traits and coping strategies are important for the personal and professional life.

I.3. Depression, anxiety and stress among medical students

I.3.1. Aim

Taking into consideration the fact that poor mental health begins in medical school, it is important to gain insight into health-relevant factors early on in order to further career development of medical students. Given the fact that data on health status of medical students in Romania is scarce, we aimed at gathering some data regarding depression, anxiety and stress among them. More specifically, we examined the prevalence of the variables and their relationship with sex, sleeping hours per night, BMI, tobacco, alcohol, coffee, carbonated drinks, energy drinks, ethno-botanicals and drug use.

I.3.2. Material and methods

A number of 190 medical students from all years of study provided answers to an online questionnaire. The participants were informed about the purpose of the study, about the confidentiality of data and the use of results. The questionnaire consisted of two parts: the first

one gathered socio-demographic information, while the second one is a psychological instrument measuring the levels of depression, anxiety and stress.

Socio-demographic data and psychological tool. Students had to provide socio-demographic (sex, age, year of study, environment, faculty, living arrangements), anthropometrical (height, weight) and medical data (chronic diseases). They also had to provide information concerning dietary (tobacco, alcohol, coffee, carbonated drinks, energy drinks and drugs consumption) and sleeping habits. Academic results and family situation (siblings, level of education for both parents and having at least one parent working abroad) were also recorded.

The *Depression, Anxiety and Stress Scale* (DASS 21) (Lovibond, 1995) is a self-report instrument designed to measure the emotional states of depression, anxiety and stress. Each of its three scales consists of 7 items. The depression scale assesses dysphoria, hopelessness, devaluation of life, self-deprecation, lack of interest / involvement, anhedonia and inertia. The anxiety scale assesses autonomic arousal, skeletal musculature effects, situational anxiety, and subjective experience of anxious affect. The stress scale assesses difficulty relaxing, nervous arousal, and being easily upset/ agitated, irritable / over-reactive and impatient. The present study employed the short version of the DASS, with 21 items, due to several advantages: fewer items, a cleaner factor structure, and smaller interfactor correlations (Antony, 1998).

Statistical analysis was performed using IBM *SPSS Statistics version 21.0*. Means, standard deviations and percentages were used for descriptive analysis. Comparative analysis was performed using Independent Samples *t-test* and *One-way ANOVA*. For correlational analyses we used *Pearson* and *Spearman* correlations.

I.3.3. Results

Socio-demographic and health related data. The mean age for the sample is 21.38 (±2.18), with a majority of female participants (79.5%). Most of the students were enrolled in their third year of study (32.2%), followed by first (27%), second (23.8%), sixth year (7.4%), fourth (6.9%), and fifth year students (2.1%). The majority of the participants were from urban areas (66.3%) and the vast majority was not married (95.8%). Most of the students (90.5%) declared no chronic disease.

Academic results and family situation. The baccalaureate mean for the sample is 9.04 (±.78) and the admission mean is 8.30 (±1.20). 42.1% of the students declared that one parent or both worked abroad. Almost half of them lived in dorm rooms or rental accommodation (48.4%). The rest of them lived with family (25.3%), life partner (13.7%) or alone (12.6%).

Anthropometric data, dietary and sleep habits. Mean weight for female students in our sample is 59.01 kg (±8.92), with a mean height of 165.02 cm (±14.89). Mean weight for male participants is 78.59 kg (±11.32), with a mean height of 181.15 cm (±6.76). The body-mass index (BMI) for both genders was measured using self-declared data regarding weight and height. The values taken into consideration were WHO's standards for European population: a BMI < 18.5 kg/m^2 was categorized as underweight, 18.5-24.9 kg/m^2 as the normal range, 25.0-29.9 kg/m^2 as pre-obese, 30- 34.9 kg/m^2 as obese class I, 35.0-39.9 kg/m^2 as obese class II and ≥ 40 kg/m^2 as obese Class III (WHO, 2003). Most of the students have a normal BMI (73.4%), although we also identified underweight (11.2%), pre-obese (12.2%), and obese class I (3.2%) participants (Table IX).

Smoking and drinking habits. More specifically, 16.3% of the subjects smoke on a daily basis, 11.6% of the students drink alcohol monthly or weekly, a high percentage (42.1%) declared they drank coffee every day, 51.1% occasionally drink carbonated drinks and 33.2% occasionally drink energy drinks. The majority of students claimed they never used ethnobotanicals (95.3%) or drugs (91.6%). A small percentage of participants used ethnobotanicals (4.7%) or drugs (7.9%), while the majority declared they never used them ((95.3%, 91.6% respectively) (Table X).

Table IX. BMI for men and women

VARIABLES	Total results	Women	Men
Weight (kg)	63.03 ± 12.32	59.01 ± 8.92	78.59 ± 11.31
BMI	21.90 ± 3.21	21 ± 2.98	23.94 ± 3.31
Underweight	11.2%	13.4%	2.60%
Normal weight	73.4%	76.5%	61.5%
Pre-obese	12.2%	7.40%	30.8%
Obese class I	3.20%	2.70%	5.10%

Medical students reported a mean of 7.07 (±1.18) *sleeping hours* per night. Concerning the inquiry of whether they wake up during the night, the participants reported the following: *never* - 17.9%, *occasionally* - 68.4%, *monthly* - 1.1%, *weekly* - 4.2%, *every night* - 8.4%.

Depression, anxiety and stress. The results from the DASS-21 show elevated levels of depression, anxiety, and stress among the students from our sample (Table XI). More specifically, more than a quarter of the participants reported moderate depression (28.9%), while 17.3% appear to have severe depression and 16.3% extremely severe depression. Concerning anxiety, 30.5% of the students present moderate symptoms, 9.5% severe symptoms, and almost a quarter (23.2%) of students suffer from extremely severe anxiety. In the case of stress, 26.3% of the participants in the sample reported levels ranging from moderate to extremely severe.

Table X. The frequency of consumption

HABIT	Never (%)	Occasionally (%)	Monthly(%)	Weekly(%)	Daily(%)
Tobacco	60.0	18.9	0.50	4.20	16.3
Alcohol	21.1	67.4	3.20	8.40	0.00
Coffee	14.7	30.0	3.70	9.50	42.1
Carbonated drinks	11.6	51.1	11.1	17.9	8.40
Energy drinks	58.4	33.2	2.60	2.10	3.70
Ethnobotanicals	95.3	4.70	0.00	0.00	0.00
Drugs	91.6	7.90	0.50	0.00	0.00

Table XI. Depression, Anxiety and Stress Scale 21 results

LEVEL	Depression (%)	Anxiety (%)	Stress (%)
Normal	25.3	27.4	60.5
Mild	12.1	9.50	13.2
Moderate	28.9	30.5	11.6
Severe	17.4	9.50	10.0
Extremely severe	16.3	23.2	4.70

Correlation analysis. In order to identify the existing relationship between the DASS-21 scales and the number of sleeping hours per night and BMI, *Pearson* correlation were performed. The results showed significant negative correlations between the three scales of the DASS-21 and the hours students sleep per night: depression ($r=-.253$, $p < .001$), anxiety (r=-

.210, p=.004), and stress (r=-.249, p=.001). More specifically, the more students sleep, the lower they score on depression, anxiety, and stress; conversely, the less they sleep, the higher they score on all scales of the DASS-21. In the case of BMI, there is no association between this variable and the scales of the DASS-21.

Spearman correlations were performed in order to establish the relationship between the three scales of the DASS-21 and tobacco, alcohol, coffee, carbonated drinks, energy drinks, ethno-botanicals and drug use. The results showed positive and significant associations between depression and alcohol (r=.155, p=.03) and carbonated drinks consumption (r=.146, p=.04), meaning that students who rate themselves as consuming alcohol and carbonated drinks more frequently also score higher on depression.

Comparative analysis. Independent samples *t tests* showed statistically significant differences between male (N=39) and female (N=151) participants concerning depression (t(88)=4.40, p < .001), anxiety (t(88)=4.25, p < .001) and stress (t(88)=4.70, p < .001). More specifically, women scored higher than men on all subscales of the DASS-21: depression (Mwomen=18.58, Mmen=10.92), anxiety (Mwomen=14.95, Mmen=7.94) and stress (Mwomen=15.37, Mmen=7.48).

One-Way ANOVA showed statistically significant differences in stress according to participants' BMI (F(184)=3.81, p=.01). More specifically, participants with normal weight have lower scores (M=13.11) than pre-obese (M=13.13) and obese class I participants (M=26.33). Concerning anxiety and depression, *One-Way ANOVA* analyses showed no statistically significant differences between participants according to their BMI.

I.3.4. Discussion

Medical studies are characterized by the longest period invested in academic study, a continuously preparation for theoretical and practical achievement and require commitment, determination and responsibility. Students enrolled in medical faculties are under high stress due to high academic load, long working hours, new living accommodation, financial strain. The mental health of medical students worsens after they begin their studies and remains unsatisfactory all throughout training. More specifically, studies show high prevalence of depression among medical students from their first years of study to their last and even after completion (Sharma *et al.,* 2015). Also, studies report those medical students suffer from depression, anxiety, and stress. Other studies reported that healthy students develop depression and stress after commencing their medical education (Roberts *et al.,* 2001; Dyrbye *et al.,* 2007; Yusoff *et al.,* 2013).

Our results reveled high rates of depression, anxiety and stress among female medical students, and they tend to score higher than on these dimensions. Brenneisen found a 41% prevalence of depression among medical students, with more depressive symptoms among female students and students from schools located in capital cities (Brenneisen *et al.,* 2016). Higher scores of depressions, anxiety and stress were reported in students with the following characteristics: females, in lower semesters, younger and nonsmokers. Furthermore, students who were satisfied with their education had lower depression, anxiety and stress scores (Iqbal *et al.,* 2015). Bore *et al.* found that female students in their sample were significantly more depressed compared to the female norms, while male depression did not differ from male norms (Bore *et al.,* 2016). Moutinho *et al.* revealed a prevalence of 34.6% in medical students from all semesters of a Brazilian medical school (Moutinho *et al.,* 2017). Assessing associated factors for depression, they found the following: female gender, intrinsic religiosity, anxiety, and stress. found a high prevalence of depression (57.9%), with a higher prevalence among female students. Medical students presented higher rates of depression compared to pharmaceutical students (Ibrahim and Abdelreheem, 2015)

However, some other studies revealed no difference in depression considering gender as variable. Sharma *et al.* reported that 31% of the students in their sample (private university)

had depression (there were no gender differences) and it was higher in the first year compared to 3rd and 4th but increased after the completion of studies and the beginning of internship. They also found a significant association of depression with regularity of attendance the courses (Sharma *et al.,* 2015).

Also, some studies indicated the existence of a relationship between the DASS dimensions and the consumption of alcohol, tobacco and drugs (Iqbal *et al.,* 2015). The present research showed that there are positive and significant associations between depression and alcohol (r=.155, p=.03) and carbonated drinks consumption (r=.146, p=.04), meaning that students who rate themselves as consuming alcohol and carbonated drinks more frequently also score higher on depression.

Sleeping disorders are a real problem among medical students due to the university schedule. Compared to general population scores, medical students sleep less and have more sleep-related problems. This is due to several reasons: the long duration of the academic achievement, demanding clinical study, a lot of practical duties that include overnight on-call activities, a hard work that can be emotionally challenging (increasing the level of burnout), a high level of consummation of energy drinks, coffee or dietary supplements, and, not to be neglected, their lifestyle choices (Wong *et al.,* 2005). Also, sleep is closely related to good physical and psychological health and academic performance (Azad *et al.,* 2015; Almojali *et al.,* 2017; Alsaggaf *et al.,* 2016). Specifically, the more students sleep, the lower they score on depression, anxiety, and stress; conversely, the less they sleep, the higher they score on all scales of the psychological instrument used for this research.

There is a great need for the promotion of mental health, given the fact that medical students present high rates of depression, with a focus on vulnerable groups: female students, students with financial difficulties, students with various addictions etc. Also, mental health professionals should focus on depression stigma (Wimsatt *et al.,* 2015) and should also address the fact that neither students nor healthcare professionals are inclined to seek help when they have mental health problems (Rotenstein *et al.,* 2016; Puthran *et al.,* 2016; Elliot *et al.,* 2010).

We found that there is a statistically significant differences in stress according to participants' BMI (normal weight students having lower scores on stress comparing to over-weight students), but not when considering depression or anxiety.

I.3.5. Conclusions

High rates of depression, anxiety and stress are recorded among medical students. Increased rates of alcohol consumption, sleep-related problems, high body mass-index are found to be factors influencing students' levels of stress, anxiety and depression. Among them, females are more prone to experience these health problems. University teachers should include in their curricula topics aimed at preventing these psychological problems or to arrange schedules in order to offer students more free time and a proper sleep.

C. BURNOUT SYNDROME GENERATED BY PSYCHOSOCIAL ENVIRONMENT

In order to improve the quality of the medical act, it is important to consider medical doctors' risk of professional exhaustion, which can hinder their work performance and quality of care towards their patients. The professional activity of doctors has been analyzed from different perspectives: professional, moral, social, ethical but also economic. In recent years, studies have shown that the level of professional exhaustion has effects on personal and professional life (increasing the rate of errors, dropping out of work, substance abuse, increasing suicide attempts). Generally, burnout is also correlated with less free time, risk of experiencing work-home conflicts or high level of depression (Haik *et al.,* 2017).

Burnout in medical doctors has become a severe problem, many researchers highlighting the relationship between burnout and lower quality of care, reduced level of patient satisfaction, and problems with patient safety. Professional exhaustion in healthcare professionals become an economic problem analyzed through investments, costs and profits in health services. A satisfied physician will provide better medical services, more compassion for patients, and will reduce the cost of care (Sinsky *et al.*, 2017; Shanafelt *et al.*, 2017).

Previous studies on Romanian physicians or other healthcare professionals showed a moderate level of burnout among different specializations but also identified relationships between burnout or job satisfaction and different variables such as socio-demographic variables, alexithymia or personality traits like neuroticism (Iorga *et al.,* 2015; Iorga *et al.,* 2016a, Iorga *et al.,* 2016b, Iorga *et al.,* 2017a, Iorga *et al.,* 2018a).

Developing the ability to cope with demanding situations request a good theoretical knowledge, but also to apply it in practice, both in the framework of the university training stages and during one's professional activity as a doctor. In Romania freshman medical students are the most depressed and graduating students are the most stressed students, comparing to medical students from other years of study. Also, perceived stress and the level of alexithymia were found to influence the level of depression among medical students, with significant impact on academic results (Zugun-Eloae *et al.* 2016; Iorga *et al.,* 2017b).

My interest regarding this area is reflected by the following article:

Holman A, Gavrilescu IM, Muraru ID, **Petrariu FD.** ALEXITHYMIA AND THE BIG FIVE PERSONALITY TRAITS AS PREDICTORS OF BURNOUT AMONG MEDICAL STUDENTS. *Medical-Surgical Journal-Revista Medico-Chirurgicala* Volume: 122 Issue: 3 Pages: 592-602 Published: 2018. Web of Science Core Collection - Emerging Sources Citation Index
WOS: 000446368200037

I.4. Predictors of burnout generated by medical academic environment

I.4.1. Aim. The present study aims to assess the influence of several psychological, demo-graphic and academic characteristics on Romanian medical students' levels of burnout.

I.4.2. Material and methods

The study developed between June and October 2017. A number of 400 questionnaires were distributed among medical students from General medicine. Students had to complete a document with socio-demographic data and to answer the items of three psychological instruments. A number of 368 questionnaires were returned to the researchers. The exclusion criteria were incomplete questionnaires and documents returned after the 1st of October 2017. After analyzing the returned questionnaires, 315 were finally included in the study.

Several demographic and academic data were registered: age, sex, year of study (from one to six year of study), environment (urban/rural), department, admission mark, and information related to the accommodation in the University City (staying with parents or living by themselves in a rented apartment). One item questioned whether at least one of their parents is working abroad.

Three psychological instruments were administered: *Maslach Burnout Inventory* (MBI), *Big Five Inventory* (BFI) and *Toronto Alexithymia Scale* (TAS-20).

MBI (Maslach *et al.,* 1986) has 22 items, and it was applied to measure the level of burnout referring to its three general scales: emotional exhaustion (EA), depersonalization (D) and personal accomplishment (PA). Emotional exhaustion evaluates feelings of being emotionally overextended and exhausted by work. Depersonalization refers to the cynic responses, negative attitudes and behaviors at work, in relationship with colleagues or beneficiaries. The personal accomplishment scale evaluates one's feelings of competence and

successful achievement at work. A person is professionally exhausted if she/he has an elevated level of emotional exhaustion and depersonalization and a low level of professional accomplishment.

The second instrument, BFI (John *et al.*, 1991), was used to evaluate the Big Five Factors (dimensions) of personality: Extraversion (E), Agreeableness (A), Conscientiousness (C), Neuroticism (N), and Openness (O). The questionnaire with 44 items is divided in 5 broad domains, each of them rated on a 7-point Likert scale.

The third instrument, TAS-20 (Bagby *et al.*, 1994), has three subscales measured using 20 items and a general score. The instrument assesses the difficulties with emotional processing and emotional awareness, respectively, on three domains: difficulty of describing feelings, difficulty of identifying feelings, and externally oriented thinking. Students rated their answers on a Likert - scale, from 1 (strongly disagree) to 5 (strongly disagree).

Ethical approval. The study was approved by ethical committee of University of Medicine and Pharmacy "Grigore T. Popa" of Iasi. Informed consent was delivered together with the documents. Students were informed about the purpose of the study, the confidentiality of collected data and the fact that they could withdraw from the research with no consequences.

Statistical analysis of data. Collected data were analyzed using IBM *SPSS Statistics, version 23.0*. Means and standard deviations revealed the levels of burnout dimensions among medical students. *Pearson* and partial correlations were used to investigate the relationships between variables, and hierarchical regression analyses were used to identify the significant predictors of burnout.

I.4.3. Results

Demographic and educational data. All participants to the research (246 females and 69 males) were enrolled in general medicine studies in "Grigore T. Popa" University of Medicine and Pharmacy of Iasi. Most of the participants are coming from urban areas in the north-eastern part of the country. Almost 40% declared that they are living in the University City or in suburbia. The average age is M=22 ±3 (ranging from 18 to 27 years). 156 students were registered in preclinical (1st and 2nd) and 159 in clinical years of study (3rd to 6th). The admission process in the university is based on a final mark (minimum five from 10), resulted from a written exam with multiple answers, covering items from different disciplines (biology, chemistry and physics). The mean admission mark for the researched sample is 9.01 (±.9). 59 (18%) of them reported having at least one parent working abroad and more than half (66%) reported living in a rented apartment or in campus (Table XII).

Table XII. Demographic and educational characteristics of the sample

CHARACTERISTIC	MEAN (±SD) N (%)
Age	22 (±3)
Gender - female	246 (74)
Pre-clinical Year of study	156 (47)
Clinical Year of study	159 (53)
Department - Iasi	125 (39)
Environment - urban	232 (71)
Admission mark	9.01 (±.9)
Having at least one parent working abroad	59 (18)
Living in a rented apartment or in campus	217 (66)

The relations between the psychological factors were examined through *Pearson* and partial correlations while controlling participants' demographic and educational characteristics

(Table XIII). Specifically, the pattern of associations suggests that students' emotional exhaustion is positively associated to their neuroticism, difficulty describing feelings and difficulty identifying feelings, and negatively related to their extraversion, agreeableness, conscientious-ness and openness. In other words, the higher the score on neuroticism, the higher students' emotional exhaustion. Also, the more students have difficulties identifying and describing feelings, the higher they score on emotional exhaustion. On the other hand, students low on extraversion, agreeableness, conscientiousness and openness have high scores on emotional exhaustion.

Table XIII. Descriptive statistics, reliability, *Pearson* and correlations between the MBI, BFI, TAS-20 factors

		M and SD	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)
MBI	(1) EA	2.23 / 1.23	.85	-.12*	.52**	-.27**	-.27**	-.17**	.42**	-.20*	.23**	.42**	.03
	(2) PA	3.91 / 1.12	-.16**	.84	-.05	.24**	.21**	.28**	-.21**	.29**	-.11*	-.20**	.06
	(3) D	1.45 / 1.14	.50**	-.05	.73	-.25**	-.30**	-.19**	-.17*	-.12*	.18**	.27**	.03
BFI	(4) E	3.63 /.69	-.23**	.23**	-.21**	.81	.27**	.26**	-.22**	.28**	-.32**	-.24**	-.03
	(5) A	3.62 /.60	-.26**	.24**	-.28**	.23**	.70	.28**	-.46**	.25**	-.18**	-.37**	.01
	(6) C	3.48 / .65	-.15*	.27**	-.14*	.21**	.26**	.78	-.17**	.23**	-.10	-.23**	.07
	(7) N	2.93 / .72	.44**	-.27**	.20**	-.20**	-.50**	-.18**	.76	-.14**	.22**	.44**	.05
	(8) O	3.68 / .58	-.20**	.28**	-.11	.24**	.25**	.22**	-.17**	.77	-.07	-.17**	.10
TAS-20	(9) Difficulty Describing Feelings	2.86 / .73	.25**	-.08	.23**	-.34**	-.17**	-.07	.21**	-.06	.70	.49**	.22**
	(10) Difficulty Identifying Feelings	2.44 / .91	.39**	-.19**	.33**	-.24**	-.43**	-.26**	.46**	-.17**	.46**	.83	.15**
	(11) Externally-Oriented Thinking	3.30 / .52	-.01	.05	.05	-.04	.04	.03	.06	.08	.23**	.12*	.71

The upper triangle of the matrix shows *Pearson* correlation coefficients.
The lower triangle of the matrix shows partial correlation coefficients controlling for age, gender, year of study, department, environment, admission mark, parents' migration and accommodation.
The matrix's diagonal presents reliability coefficients (Cronbach's α). * p<.05; **p<.001.

Personal Accomplishment emerged as having an opposite pattern of correlations, being positively related to these personality factors and negatively to neuroticism and participants' difficulty in identifying feelings. Thus, students who score high on extraversion, agreeableness, conscientiousness and openness also score high on Personal Accomplishment also. Likewise, students who have higher scores on neuroticism and difficulties in identifying feelings also score low on Personal Accomplishment.

Second, hierarchical regression analyses were used in order to examine for the personality and the alexithymia factors as predictors of burnout, while controlling for the effect of participants' demographic and educational characteristics. Each of the three dimensions of burnout was included as criterion in a separate set of regression analyses. In each the demographic and educational characteristics were entered as predictors in Step 1, to assess and to control their effects on the criterion. The 5 personality factors and the 3 dimensions of alexithymia were entered in Step 2.

The first regression analysis evaluated the effect of these factors on Emotional Exhaustion (Table XIV). The first model, including only the demographic and educational characteristics, significantly predicted this trait of burnout ($p<0.01$). Two of these

characteristics emerged as significant predictors (both ps<.05), specifically year of study, with students in their clinical years reporting less emotional exhaustion, and admission mark, with students who had higher admission marks reporting more intense emotional exhaustion.

The second model also significantly predicted this facet of burnout. Neuroticism and Difficulty Identifying Feelings Two emerged as significant and positive predictors, namely (both ps < 0.01). Students reporting prominent levels of neuroticism and experiencing difficulties identifying feelings tend to also report important levels of emotional exhaustion.

Table XIV. Results of hierarchical regression analysis showing amount of variance in Emotional Exhaustion accounted for by the five personality factors and the 3 dimensions of alexithymia (S.2) while controlling for participants' demographic/educational characteristics

		Step 1 *B*	Step 2 *β*	ΔR^2
SOCIO-DEMOGRAPHIC DATA	Gender	.16	.001	
	Age	-.01	-.01	
	Study year	-.58**	-.16*	
	Department	-.24	-.03	
	Environment	-.04	-.01	
	Admission mark	.23*	.12*	
	Migration	-.21	-.03	
	Accommodation	.15	.06	
				.07**
BFI	Extraversion		-.09	
	Agreeableness		.04	
	Conscientiousness		-.01	
	Neuroticism		.31**	
	Openness		-.09	
TAS-20	Difficulty Describing Feelings		.07	
	Difficulty Identifying Feelings		.20**	
	Externally Oriented Thinking		-.06	
				.25**

Note: *p <.05; ** p<.01

Table XV. Results of hierarchical regression analysis showing amount of variance in Personal Accomplishment accounted for by the 5 personality factors and the 3 dimensions of alexithymia (S.2) while controlling for participants' demographic/educational characteristics

		Step 1 B	Step 2β	ΔR^2
SOCIO-DEMOGRAPHIC DATA	Gender	.32*	.11*	
	Age	.06*	.12*	
	Study year	.11	.04	
	Department	.12	-.02	
	Environment	.13	.04	
	Admission mark	-.05	.003	
	Migration	-.12	-.07	
	Accommodation	.01	.007	
				.06*
BFI	Extraversion		.12*	
	Agreeableness		.04	
	Conscientiousness		.18**	
	Neuroticism		-.17*	
	Openness		.16**	
TAS-20	Difficulty Describing Feelings		.01	
	Difficulty Identifying Feelings		.04	
	Externally Oriented Thinking		.06	
				.17**

The second regression analysis included Personal Accomplishment (Table XV). The first model, including only the demographic and educational characteristics, significantly predicted this facet of burnout ($p<0.01$). Gender (with females having higher self-assessments on this facet of burnout) and age yielded the significance level as predictors. Three personality factors in this model emerged as significant and positive predictors, namely Extraversion, Conscientiousness and Openness, while Neuroticism emerged as a negative predictor of Personal Accomplishment (all $ps<0.05$). Increases in Extraversion, Conscientiousness and Openness and decreases in Neuroticism are related to increases in Personal Accomplishment. Students who are more extroverted, conscientious, and open, while also scoring low on neuroticism, report feeling accomplished on personal issues.

The third regression analysis included Depersonalization as criterion (Table XVI).

Table XVI. Results of hierarchical regression analysis showing amount of variance in Depersonalization accounted for by the 5 personality factors and the 3 dimensions of alexithymia (S.2) while controlling for participants' demographic/educational characteristics

		Step 1 B	Step 2β	ΔR^2
SOCIO-DEMOGRAPHIC DATA	Gender	-.47**	-.19**	
	Age	-.005	.02	
	Study year	-.07	-.01	
	Department	-.05	-.02	
	Environment	-.35*	-.14*	
	Admission mark	.17	.11	
	Migration	-.39*	-.09	
	Accommodation	.14	.05	
				.09**
BFI	Extraversion		-.09	
	Agreeableness		-.15*	
	Conscientiousness		-.02	
	Neuroticism		-.001	
	Openness		-.008	
TAS-20	Difficulty Describing Feelings		.08	
	Difficulty Identifying Feelings		.20**	
	Externally-Oriented Thinking		-.005	
				.13**

Note: *p <.05; ** p<.01

The first model, including only the demographic and educational characteristics, significantly predicted this facet of burnout ($p<0.01$). Gender, environment and migration of parents. emerged as significant predictors (all $ps<0.05$).

Results show that females, students from urban environments and those who have at least one parent abroad have lower self-assessments on this facet of burnout, although this last variable did not yield the significance level in the second step of the analysis, in which the psychological traits were also introduced.

The second model also significantly predicted Depersonalization

Two factors in this model emerged as significant predictors, specifically Agreeableness, which is negatively related to Depersonalization, and Difficulty Identifying Feelings, which emerged as positive predictor of Depersonalization (both $ps<0.01$).

Increases in Difficulty Identifying Feelings and decreases in Agreeableness are related with increases in Depersonalization. Students who have problems with identifying feelings and are less agreeable and tend to report elevated levels of depersonalization.

I.4.4. Discussion

Burnout affects medical students from the first years (Chang *et al.,* 2012) to the final years of study (Dyrbye *et al.,* 2006) and beyond (Dyrbye *et al.,* 2014), with prevalence rates ranging from 7.0% to 75.2% (Erschens *et al.,* 2018). Furthermore, emotional exhaustion has been shown to be strongly associated with risk of psychiatric morbidity Rates of emotional exhaustion and depersonalization also appear to rise significantly during the graduate's intern year in the public hospital system (Willcock *et al.,* 2004).

Besides involving health professionals to provide psychological support to burnout sufferers, institutional involvement has also become a way to prevent or cure burnout in physicians, which emphases the need to have a deep understanding of the mechanisms and factors that predispose medical personnel to burnout. The aim of our study was to examine the factors of burnout in medical students in a Romanian University. Specifically, we assessed whether personality (5 factors: Extraversion, Conscientiousness, Openness, Agreeableness, Neuroticism) and alexithymia (Difficulty Describing Feelings, Difficulty Identifying Feelings, Externally Oriented Thinking) predict burnout (EE, PA, D). We found significant predictors for each of the three burnout dimensions.

Concerning personality factors, the results show that students with higher levels of Neuroticism also report higher levels of EE. Also, more extravert, conscientious, open, and less neurotic students experience a greater sense of Personal Accomplishment. Students low on Agreeableness score high on Depersonalization.

A study on Japanese nursing students (Takemura *et al.,* 2015) found some correlations supporting the idea of an association between personality factors and burnout. In their research, Neuroticism was positively, and Agreeableness, Conscientiousness, and Extraversion was negatively correlated with Emotional Exhaustion. Extraversion, Conscientiousness, and Agreeableness was negatively, and Neuroticism was positively correlated with Depersonalization. Extraversion, Openness, and Agreeableness was positively, and Neuroticism negatively correlated with PA.

The findings of the present study are consistent with a study of McManus (McManus *et al.*, 2004) who also showed, among others, that Emotional Exhaustion is related to Neuroticism, Personal Accomplishment is related to Extraversion, and Depersonalization is related to Agreeableness, although their study focused on doctors aged 29 and 30 years old. Also, the research of Magnano showed that emotional stability negatively predicted exhaustion in health professionals (Magnano *et al.,* 2015).

Our results are also partially supporting those of Cañadas-De la Fuente who focused on nurses. Specifically, these authors found Neuroticism, Agreeableness, and Extraversion to predict Emotional Exhaustion, while we found only Neuroticism to be linked to Emotional Exhaustion. Also, our results showed Agreeableness to be predictive of Depersonalization, while their study also added Neuroticism and Conscientiousness as predictors of this dimension of burnout. Additionally, the authors found all five dimensions to be predictors of PA, while we found support for four of them (Extraversion, Conscientiousness, Openness, and Neuroticism) (Cañadas-De la Fuente *et al.,* 2015).

In a study conducted by Bakker on volunteer counselors, emotional stability predicted EE (Bakker *et al.,* 2006,), a relationship that also emerged in our study; emotional stability, Extraversion, and intellect/autonomy predicted Depersonalization (in our study, only agreeableness negatively predicted Depersonalization); Extraversion and emotional stability predicted PA (as in our study). However, not all studies found a link between the five personality factors and burnout. For example, Extraversion, Agreeableness, and Consciousness did not significantly predict any burnout factor (Willcock *et al.,* 2004).

Nevertheless, personality seems to relate consistently to all dimensions of burnout. Neuroticism and Extraversion appear to be consistent predictors of burnout (Cañadas-De la Fuente *et al.,* 2015; Bakker *et al.,* 2006; Zellars *et al.,* 2000; Ang *et al.,* 2016). Some traits of people high in Neuroticism (the predisposition to underestimate self-performance and to respond with strong emotions in stressful situations) seem to lead to symptoms of burnout. Conscientiousness is associated with a person's perseverance and self-discipline to finish a task and, as a result, that person could also experience higher levels of PA (Bakker *et al.,* 2006). Individuals with high scores on Openness tend to view challenges as opportunities and are inclined to learn and, thus, feel more personally accomplished. Agreeable individuals have lower levels of EE and Depersonalization probably because they are more likely to be caring, nurturing, responsible, and sympathetic (Cañadas-De la Fuente *et al.,* 2015).

Concerning alexithymia, our results show an association with burnout, and students reported higher levels of Difficulties Identifying Feelings and important levels of Emotional Exhaustion and Depersonalization. Other studies point to an association between alexithymia and burnout in the medical field. Bratis found a positive correlation with Emotional Exhaustion and Depersonalization and a negative one with personal achievement (Bratis *et al.,* 2009). Katsifaraki found a significant association between Externally Oriented Thinking (a facet of alexithymia) and PA and Depersonalization (Katsifaraki *et al.,* 2013). Popa-Velea found alexithymia to have a significant role in the development of burnout syndrome, with a prevalence of 6.02% in a sample of Romanian medical students (Popa-Velea *et al.,* 2017). Researchers should focus on the impact of alexithymia and its possible connections with various psychological problems and it relationship with stress and depression during medical studies (Iorga *et al.,* 2018b).

I.4.5. Conclusions

Certain personality factors and alexithymia are associated with burnout among medical students in Romania and confirms the role they play in the experience of burnout. Our findings highlight the need for academic guidance programs to prevent burnout at younger stages of medical training. Personality profiling with the aim of identifying resources may prevent burnout among vulnerable personality medical students.

CHAPTER II

ASSESSMENT OF HARMFUL BEHAVIORS RELATED TO THE LIVING ENVIRONMENT OF CHILDREN AND YOUNG PEOPLE

A. DISTORTED DIETARY HABITS AND NEGATIVE HEALTH EFFECTS

According to the Behavioral Risk Factor Surveillance System (Deliens *et al.*, 2014), there is a constant increase in overweight and obesity between the ages of 18 and 29 years old. An unhealthy diet and a low level of physical activity during university years predispose students to future health issues (Aljadani *et al.*, 2013a). Prevention of weight excess, obesity, and related diseases has become a worldwide challenge. Given the significant association between low diet quality and weight gain, researchers have focused on evaluating the association between the nutritional quality of dietary intake and the health outcomes (Drenowatz *et al.*, 2015). Studies reported an inverse association between increased diet quality and chronic disease-specific mortality (Aljadani *et al.*, 2013b; Ezzati *et al.*, 2013; Fleming *et al.*, 2013) such that a healthy lifestyle (having a balanced diet, regular physical activity, avoiding smoking and excessive alcohol consumption) has been shown to reduce the alarming overall mortality caused especially by non-communicable diseases (Borgan *et al.*, 2015; O'Connor *et al.*, 2017). In the context of a healthy lifestyle, nutrition plays a vital role in the development of young people (Barzegari *et al.*, 2011). Eating behavioral patterns developed as adolescents and young adults influence long-term behavior and have a significant impact on adult life (Hamulka *et al.*, 2018). During their academic years, students experiment greater freedom of choice concerning their food choices, health-related behaviors, practicing sports, and shaping their own lifestyle. Consequently, the transition to a new living environment, with busy schedules, unhealthy food offers, and the risk of skipping meals, is likely to change eating behaviors over time (Tanton *et al.*, 2015; El Ansari *et al.*, 2012). Weight is strongly related to eating behaviors. The years spent in the university are a critical period for weight gain (Deliens *et al.*, 2014). It was found that, in general, students did not eat the recommended ratios of fruit and vegetables, with a significant decrease in the quantity of bread and vegetables consumed during the first year of university and significant increases in fat intake and alcohol consumption. An unhealthy diet and excessive alcohol consumption contribute significantly to the energy intake and, consequently, can facilitate the student's weight gain (Butler, 2004). In a study by Racette (Racette *et al.*, 2005), it was shown that 50% of the 764 freshmen students reported having eaten high-fat or fast food three or more times during the previous week. Moreover, the study revealed that, by the end of their sophomore year, 70% of the 290 students who were reassessed had gained weight with no apparent association with exercise or dietary patterns. Students have a significantly higher total fat and saturated fat intake and a much lower intake of polyunsaturated fats, monounsaturated fats, folic acid, vitamin E, and grains (Deliens *et al.*, 2013) compared to the instructions of the American Heart Association (Chourdakis *et al.*, 2011). Knowledge about the importance of physical activity, healthy eating habits, and nutrition was found to be the keys to a healthy lifestyle of young adults (Yahia *et al.*, 2016). Medical students are supposed to practice healthier eating habits compared to nonmedical students, but some studies have found contradictory results. A study by Ganasegeran revealed that medical students presented risk factors for early chronic disease due to their poor eating habits (Ganasegeran *et al.*, 2012). Although medical students had sufficient knowledge of healthy eating habits, it was found that they failed to apply this knowledge into practice. Similar findings were presented by Haq (Haq *et al.*, 2019) and Williams (Williams *et al.*, 2019), who

showed that medical students are more prone to have a *western dietary pattern* (processed food with low levels of fat, sugar, and salt) and to practice less physical activity. Both research teams concluded that medical students adopted less healthy dietary patterns as compared to healthy dietary patterns. Sleep-related problems and stress were also considered a problem among medical students. Studies showed that medical students have more sleep-related problems compared to non-medical students. For example, 70% of Hong Kong medical students self-reported sleep deprivation (Huen *et al.,* 2007), 40.60% of Iranian students reported poor sleep quality (2008), 28.2% of medical students in Brazil have insomnia (Jalali *et al.,* 2020), 69% of Lithuanian medical students reported good to excellent nocturnal sleep (Preišegolavičiūtė *et al.,* 2010), 47.1% of medical students in India reported refreshing sleep (Giri *et al.,* 2013), 31.5% of medical students suffered from sleep deprivation according to a study conducted in Nepal (Khadka *et al.,* 2019). Palatty (Palatty *et al.,* 2011) and Tafoya (Tafoya *et al.,* 2013) showed that the main factors which discriminate the medical students from their peers were academic loads, attitude towards study, and lifestyle. Programs to prevent unhealthy eating habits among students are necessary to counteract a growing prevalence of overweight and obesity later in life (Deliens *et al.,* 2014). Obesity is one of the most serious non-communicable diseases, classified as a chronic disease of a multifactorial origin and related to all ages. The development of dietary patterns, physical activity, and a healthy lifestyle, in general, in children and young people reduce the risk of developing obesity later in life. Dietary patterns seem to persist over the years, and thus academic years represent a crucial period for modelling a healthy lifestyle (Tanton *et al.,* 2015). The period of university studies represents, from the educator's perspective, the last opportunity to implement nutritional education among many students (Sakamaki *et al.,* 2005). The diet of students from different countries is often classified as unhealthy, poor in fruit and vegetables, with irregular eating patterns and a high frequency of fast-food choices, which is of particular concern because the eating habits established in this period of life can have a considerable effect on people's long-term health (Krešić *et al.,* 2009). Moreover, behaviors adopted by students during their university education have the potential to make an additional impact on the community because young adults can play important roles in society (physicians, lawyers, health ministers, police officers), as well as being decision-makers and having significant behavior patterns and attitudes, and therefore the health and lifestyle behaviors of university students are of interest to public health (Tanton *et al.,* 2015). Thus, strategies specifically designed to improve nutrition competence are needed, especially regarding information relating to sources of nutrition and healthy weight management (Sakamaki *et al.,* 2005). Although it has been observed that students' food habits change over the years of study, the research has focused on physical education students or has been conducted on students in general. Very few studies have looked into eating habits and a healthy lifestyle among medical students, especially due to the fact that they are much more informed about the importance of a healthy diet, physical exercise, and the negative effects of consumption of various substances on physical and mental health. Of all the specialties, medical students should be the best-informed individuals and adopt a healthy lifestyle, which they can then promote in their professional careers. Given the fact that studies conducted on medical students are extremely limited, and most of them evaluate the impact of nutrition education in the university *curriculum* on changing eating behavior (Ganasegeran *et al.,* 2012; Haq *et al.,* 2019; Williams *et al.*, 2019), this study covers an important gap.

Adverse childhood experiences (ACE) are traumatic or stressful events exposed to a child that can continue to have long-term negative health effects throughout the course of that child's life (Felitti *et al.,* 1998). There are six categorizes of ACE: physical abuse by an adult in the household, sexual abuse by a family member, sexual abuse by a non-family member, a dysfunctional household caused by the use of drugs or alcohol in the family and witnessing physical abuse by a family member on another family member (Duke *et al.,* 2010). Others

include emotional abuse, failing to provide the necessities (food, medical care, good hygiene) and being the care of a member of the family having a physical or mental illness (Murphy *et al.*, 2014). Numerous studies have found risk factors contributing to a child that has ACE such as gender, socio-economic status, family type (single parent, adopted child) and the environment they grow up. The consequences of such traumatic events are linked with self-induced harm to health, antisocial behaviors, a faster development of chronic diseases and premature death (Anda *et al.*, 2006). ACE during childhood was related to chronic disease later in life and a strong relationship was identified between ACEs and risky behaviors like drinking alcohol, consuming drugs or eating disorders.

Eating disorders represent a complex, multifactorial pathology, determined by biological, family, psychosocial and psychological factors (Kong and Bernstein, 2009). The lifetime prevalence of eating disorders in adults is about 0.6% for *anorexia nervosa*, 1% for bulimia nervosa and 3% for other eating disorders, disorders that are often chronic, relapsing and devastating. Numerous studies indicate that patients with eating disorders report a history of childhood trauma more frequently than the general population (Guillaume *et al.*, 2016).

Freud said that events that occur in the first 6 years of life are particularly important for the rest of one's life, and from this point of view, adverse childhood experiences are associated with an increased risk for acute or chronic psychosocial disorders in adult life (Maughan and McCarthy, 1997). Adverse childhood experiences are surprisingly common, generally unrecognized and may begin to show damage through somatization and illness even during childhood (Felitti, 2009).

Moreover, several studies have documented an association between traumatic events in children and the development of obesity in life, finding that, out of a sample of adult patients seeking surgical treatment for obesity, about 1/5 were exposed to sexual and physical abuse and more than a third witnessed violence. Separation from mother or father or marital problems have been associated with an increase in obesity in adulthood (Isohookana *et al.*, 2016).

Recognizing these facts provides a clear opportunity for early intervention, as it is demonstrated that what happens in childhood usually lasts a lifetime, and in this case, time will not heal the wounds, but it will hide them (Felitti, 2009). One-third of adults experienced at least two adverse childhood experiences in childhood. This finding suggests that an ACE should warn the clinician to evaluate the patient for a history of exposure to other forms of domestic abuse or dysfunction (Chapman *et al.*, 2004). Numerous studies have shown the role of trauma in the development of psychopathology in adulthood. Psychiatric comorbidity rates are higher in patients with eating disorders with a history of childhood trauma (Guillaume *et al.*, 2016). The lifetime prevalence of affective disorders in eating disorders is between 25% and 80%, most patients with eating disorders often feel lonely and desperate (Speranza *et al.*, 2003).

Psychiatric comorbidities and basic symptoms of eating disorders in patients are related to childhood traumas. Maltreatment was not associated with most lifetime psychiatric diagnoses in patients with binge eating disorders, although specific associations were observed for post-traumatic stress disorders and alcohol use disorders. The links between eating disorders severity and physical abuse as well as sexual abuse may be mediated by the presence of psychiatric comorbidities (Guillaume *et al.*, 2016).

Patients with eating disorders often report experiences of being bullied by their childhood and adolescent peers (Duarte *et al.*, 2015).

It may be clinically useful to consider all abusive experiences in the evaluation of patients with eating disorders. Treatment options will be better understood and applied when the role of different forms of childhood trauma in eating disorders is more firmly established. Certain forms of childhood trauma are predictors of eating disorders, and an early intervention for childhood trauma and the resulting depressive symptoms may help to prevent the development of eating disorders in traumatized people (Kong and Bernstein, 2009).

My interest regarding this area is reflected by the following articles and books:

Pop ML, Iorga M, Muraru ID, **Petrariu FD.** ASSESSMENT OF DIETARY HABITS, PHYSICAL ACTIVITY AND LIFESTYLE IN MEDICAL UNIVERSITY STUDENTS. *Sustainability* 2021, 13, Article Number: 3572 https://doi.org/10.3390/su13063572 / **IF=3.251**

Iorga M, Isabela Manole, Lavinia Pop, Muraru ID, **Florin-Dumitru Petrariu.** EATING DISORDERS IN RELATIONSHIP WITH DIETARY HABITS AMONG PHARMACY STUDENTS IN ROMANIA. *Pharmacy* 2018; 6: 97 / doi:10.3390/pharmacy6030097

Lavinia-Maria Pop, Iorga M, Anamika Jain, **FD Petrariu.** ADVERSE CHILDHOOD EXPERIENCES IN RELATIONSHIP WITH EATING DISORDERS. *Medical-Surgical Journal - Revista Medico-Chirurgicala* Volume: 124 Issue: 1 Pages: 133-143 Published: 2020. Web of Science Core Collection - Emerging Sources Citation Index / **WOS: 000524081400023**

Viorica Gavăt, Adriana Albu, **Florin D. Petrariu.** ALIMENTAŢIA ŞI MEDIUL DE VIAŢĂ ÎN RELAŢIE CU DEZVOLTAREA COPIILOR ŞI A TINERILOR. Publishing House "Gr. T. Popa" Iaşi, 2006, 306 pages, ISBN 973-7906-95-0

Albu A, Prejbeanu IM, **Petrariu FD.** ASSESSMENT OF NUTRITIONAL HABITS ON A GROUP OF PUPILS FROM A COUNTRYSIDE ELEMENTARY SCHOOL IN ROMANIA. *Rev Med Chir Soc Med Nat Iasi* 2013; 117(3): 764-770 / **PMID: 24502047**

Ioan Chirila, **Florin D. Petrariu**, Irina Ciortescu, Catalina Mihai, Vasile L. Drug. DIET AND IRRITABLE BOWEL SYNDROME. *J Gastrointestin Liver Dis*, December 2012 Vol. 21, No. 4, 357-362 **IF=1.855**

Chirila I, **Petrariu FD**, Bărboi OB, Drug VL (Chapter authors). Date epidemiologice despre dieta in boala de reflux gastro-esofagian şi sindromul dispeptic, 28-37. In Dan-Lucian Dumitraşcu, Vasile-Liviu Drug, Teodora Surdea-Blaga (editors) ACTUALITĂŢI ÎN GASTROENTEROLOGIE: PATOLOGIE FUNCŢIONALĂ, DE MOTILITATE ŞI INFLAMATORIE. Cluj-Napoca: Publishing House "Iuliu Haţieganu", 2014 / ISBN 978-973-693-562-6.

Chirila I, Drug VL, **Petrariu FD.** DYSPEPSIA AND DIET.
Neurogastroenterology and Motility 2012; 24(Supplement: 2): 136.

Chirila I, **Petrariu FD,** Drug VL. EPIDEMIOLOGY OF GASTRO-ESOPHAGEAL REFLUX AND RELATIONSHIP WITH DIET IN ADULT URBAN POPULATION.
Journal of Gastroenterology and Hepatology 2013; 28(Supplement: 3): 503.

Hritcu LD, Borcea D, Anton E, Morosan S, Pasca S, Trinca C, Spataru MC, **Petrariu FD**, Burtan LC, Ciobica A, Curpan A, Timofte D. EXPERIMENTAL INDUCTION OF TYPE 2 DIABETES MELLITUS AND THE EFFICIENCY OF BARIATRIC SURGERY IN ITS REVERSAL IN RATS. *Acta Endocrinologica (Buc)* 2021; 17(2): 149-156 / doi.org/10.4183/aeb.2021.149 / **IF= 0.877**

II.1. Assessment of dietary habits, physical activity and lifestyle in medical university students

II.1.1. Aim

This study aimed to investigate the eating habits, nutrition patterns, and lifestyle of students enrolled in a medical university in the North-Eastern of Romania and to assess health-related behaviors (physical activity, smoking, and alcohol consumption) considering gender and age.

II.1.2. Material and methods

The study was conducted in April-May 2019 in a public medical university in Iasi, Romania. A total of five hundred questionnaires were distributed online to medical students, all years of study. Students were informed about the purpose of the study and the confidentiality of data. No incentive was given to the participants. They were informed that they could withdraw from the study whenever they wanted, without consequences. Questionnaires fully filled in and returned before the deadline were included for the analysis of data. The criteria for excluding questionnaires from the research were incomplete questionnaires or questionnaires submitted after the deadline. Finally, 403 questionnaires were included in research (Figure 1).

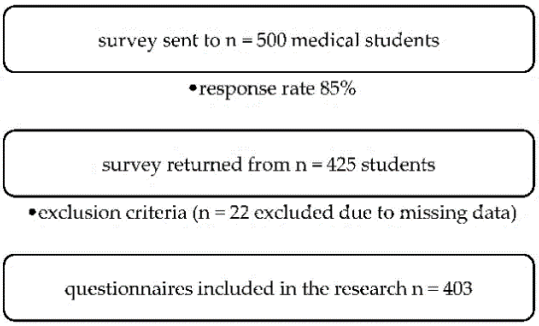

Figure 1. *Details on the response rate*

Data Collection. The questionnaire was specially created for this research, the items being formulated following extensive research of the data and tools used in scientific articles and the congruence of results obtained from their use in different countries and applied to different populations. The questionnaire was created using Google Docs and was distributed online. The first part of the questionnaire gathered socio-demographic, anthropometric, and medical self-reported information (such as age, gender, body weight, original environment, year of study, and the presence of a chronic disease). The second part of the survey inquired about dietary habits (breakfast, lunch dinner, diets, the number of snacks, eating before night sleep or the time from wake up to the first meal); sleep (number of hours and naps); engagement in physical activity (quantity and frequency); coffee, tea, carbonated drinks, and water intake (quantity and frequency); and the consumption of alcohol and cigarettes. The 3rd part collected information about the consumption of fruit, vegetables, meat, eggs, fish, sweets, and fast food.

Statistical Analysis. All analyses were performed using IBM *SPSS Statistics version 23.0*. Results for descriptive statistics were expressed as means and standard deviations (SD). Body Mass Index (BMI) was computed from self-reported weight and height (kg/m^2). The BMI calculation was conducted according to World Health Organisation (WHO) guidelines, using standards for the European population: a BMI < 18.5 kg/m^2 was categorized as underweight, 18.5-24.9 kg/m^2 as normal weight, 25.0-29.9 kg/m^2 as pre-obese, 30-34.9 kg/m^2 as obese class I, 35.0-39.9 kg/m^2 as obese class II, and ≥40 kg/m^2 as obese class III (WHO, 2020).

The normality of data distribution was assessed using the *Kolmogorov-Smirnoff* test. Given the fact that all data are not normally distributed, a bivariate analysis was performed, and non-parametric tests were applied. The *Spearman* correlation was used to assess the relationship between variables (such as age; weight; BMI; number of cigarettes smoked per day; consumption of fruit, fast food, eggs, and meat; number of hours of sleep per night; serving breakfast, lunch, dinner, and snacks). The *Mann-Whitney* test was used to identify differences depending on clinical/preclinical years of study and smoking/non-smoking status.

The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by *Centre de Reussite Universitaire*, under the coordination of University of Medicine and Pharmacy and *Agence Universitaire pour la Francophonie* (AUF)

(A5/AUF-ECO-233, approved 04.03.2014) being part of a larger research grant entitled *"Étude sur la vie des étudiants-comportement alimentaire, hygiène et style de vie"* supported by *Centre de Réussite Universitaire* - "Grigore T. Popa" University of Medicine and Pharmacy of Iași and *Agence Universitaire de la Francophonie*, Romania.

II.1.3. Results

Socio-Demographic, Anthropometric, and Medical Data. Most students were female (80.40%, N=324). More than half of the students come from urban areas (64.02%, N=258). The mean age of the students participating in the study was M=21.21 ± 4.56. A total of 349 (86.6%) of them were Christian Orthodox.

Most of the students were happy with their weight at the time (58.31%, N=235). Respondents had to declare if they suffered from chronic diseases, most of them stating they were in good health (88.20%, N=365). A small number of them (N=38, 9.20%) mentioned being previously diagnosed with gastritis (N=6, 1.40%), hypothyroidism (N=5, 1.20%), anemia (N=4, 10%), high blood pressure (N=3, 0.70%), seborrheic dermatitis (N=2, 0.50%), scoliosis (N=2, 0.50%), bronchial asthma (N=2, 0.50%), and autoimmune thyroiditis (N=20, 5%). Additionally, we registered one respondent (0.2%) for each of the following disease: gluten allergy, discopathy, renal dysfunction, endocrinological diseases, type 1 diabetes, arthropathy, and hernia. Detailed data are presented in Table XVII.

Table XVII. Anthropometric data. Comparative data by gender

	Men	Women	Total
Weight (kg)	M = 76.67 ± 12.79	M = 57.48 ± 8.94	M = 61.25 ± 12.41
BMI *	M = 23.35 ± 3.44	M = 20.90 ± 2.77	M = 21.38 ± 3.07
Underweight *	6.30% (*N* = 5)	16.70% (*N* = 54)	14.54% (*N* = 59)
Normal weight	64.60% (*N* = 51)	74.70% (*N* = 242)	72.70% (*N* = 293)
Overweight	24.10% (*N* = 19)	8.30% (*N* = 27)	11.41% (*N* = 46)
Obesity class I	5.10% (*N* = 4)	0.30% (*N* = 1)	1.24% (*N* = 5)

Data were presented as mean ± SD or n (%). *According to Diagnostic and Statistical Manual of Mental Disorders (DSM)-V (APA, 2013), a body mass index less than or equal to 17.5 kg/m^2 is considered as a diagnostic criterion for *anorexia nervosa*

Consumption of Alcohol and Cigarettes. Most students (69.40%, N=279) were non-smokers. Daily smokers, who represent 16.67% (N=67) have an M=7.77 ± 6.38 consumption of cigarettes per day. Almost half of the students drank alcohol occasionally (49.63%, N=200), and more than one-third of respondents declared they were abstinent (34.74%, N=140).

Physical Activity. Students had an average of 3.21 ± 2.71 h per week of practicing physical activity, and 18.36% of them (N=74) were practicing daily. Students declared that they practiced jogging (22.65%, N=82), going for walks (19.61%, N=71), going to the gym (11.60%, N=42), cycling (11.60%, N=42), brisk walking (6.50%, N=27), dancing (6.35%, N=23), swimming (3.60%, N=15), tennis (3.59%, N=13), and soccer (3.59%, N=13). A total of 12.16% of women (N=49) and 2.48% of men (N=10) declared they did not like to be engaged in physical activities. We also found that one-third of respondents (N=130, 31.40%) walked daily to school or downtown and the rest of them usually preferred to use local transport.

Sleep-Related Data. A series of successive items tackled sleeping habits, quality, and sleep duration. The mean hours of sleep declared by the whole group of subjects was M=6.71 ± 1.52, with no significant gender differences. One-quarter of the students (28.78%, N=116) mentioned that they usually slept during the afternoon if they had the chance.

Dietary Habits and Lifestyle

Diets. Of all participants who answered the questionnaire, 141 (34.98%) mentioned that they followed diets to lose weight. The results showed that female students resorted to diets (30.52%, N=123) more often than male students (4.47%, N=18). The most frequent numbers of kilograms lost by students following diets were 5 kg (6%, N=25), 10 kg (5.30%, N=22), 4 kg (3.10%, N=13), 3 kg (2.70%, N=11), 8 kg (2.40%, N=10), and 6 kg (2.20%, N=9). More than a quarter of the participants (33.33%, N=134) complied with religious fasts, with women (28.36%, N=114) complying more strictly than men (4.98%, N=20). The students were asked if they were deliberate in their choices of food products and ways to consume them, and more than half of the participants (53.10%, N=214) disclosed that they carefully selected food products. A higher percentage of women were more careful about food products (44.91%, N=181) than men (8.19%, N=33).

Regular Meals and Snacks

Respecting meals is especially important for physical health. Statistical analysis showed that more than half of the subjects had only two main meals a day (52.90%, N=219) and a smaller number of them had only one main meal a day (10.60%, N=44). A total of 81.89% (N=330) of the students did not eat at regular time intervals. Breakfast is considered the most important meal of the day, and one-third of students ate breakfast each morning (29.28%, N=118), while 8.68% (N=35) of students did not have breakfast at all. Half of the students (56.82%, N=229) succeeded in having lunch daily. As for supper, the results were as above, but we noted that a larger number of students had this meal every day of the week (61.79%, N=249), and equal percentages of students had supper twice or three times a week (3.97%, N=16). It appeared that the most important meal of the day for both male and female students was lunch (14.14%, N=57 for male students and 47.15%, N=190 for female students). Breakfast came in second for male students (3.47%, N=14), while supper came in second for female students (20.60%, N=83).

We found that most students (91.07%, N=367) had snacks between the main meals, and almost one-third (29.03%, N=117) declared that they ate late at night. The mean numbers of hours before bedtime when the last meal is eaten was $M=2.94 \pm 2.19$ for the whole group.

Food Consumption

The subjects were asked to estimate the consumption of foods in each food group presented in the Food Pyramid: cereals, fruits, vegetables, dairy products, meat, eggs, sweets, and fast food (Schneeman *et al.*, 2002).

Cereals. More than half of students eat cereals daily (52.61%, N=212). A small number of students (4.71%, N=19) declared that they did not eat cereals.

In Table XVIII are presented the consumption frequency of certain food categories, such as fruits, meat, and dairy, during a week. Regarding the frequency of vegetable consumption, less than half of the students (45.7%, N=189) stated that they consume vegetables daily.

Fruits. Most students seemed to prefer eating apples (63.68%, N=256); one-quarter of them did not eat any seed fruit (25.12%, N=101). More than one-third of respondents (39.80%, N=160) did not consume any subtropical fruit, while those who were consuming fruit declared they preferred to eat oranges (35.82%). In terms of tropical fruit, one-third of the students (31.09%, N=125) did not eat any fruit in this category, and 61.19% (N=248) preferred bananas from subtropical fruit.

The fruit was consumed in several ways: raw, fresh, peeled, or unpeeled, and as various beverages, such as juices or shakes. Nonetheless, most students preferred raw, unpeeled fruit (72.21%, N=291) or peeled fruit (62.28%, N=251).

Table XVIII. Fruits, meat, and dairy products

Food Item	Frequency (M ± SD) *	Total (*N* = 403)
Fruits	2.13 ± 0.90	Daily—31.2% (*n* = 129) 3–4 times/week—37.9% (*n* = 157) twice a week—25.1% (*n* = 104) no consumption—3.1% (*n* = 13)
Meat	4.72 ± 2.32	daily—30.1% (*n* = 125) 3–4 times/week—35.8% (*n* = 148) twice a week—25.4% (*n* = 105) no consumption—6% (*n* = 25)
Dairy	2.16 ± 0.89	daily—28.5% (*n* = 118) 3–4 times/week—36.2% (*n* = 150) twice a week—28.5% (*n* = 118) no consumption—4.1% (*n* = 17)

Vegetables. The most consumed vegetables were cucumbers (38.71%, N=156), tomatoes (48.14%, N=194), peppers (21.84%, N=88), green beans (10.42%, N=42), carrots (35.73%, N=144), potatoes (36.23%, N=146), cabbage (8.44%, N=34), and broccoli (7.69%, N=31).

Dairy products. Students consumed various dairy products: many types of yogurts (16.15%, N=63), distinct types of fresh cheese or cheese as part of various dishes (18.72%, N=73), as well as milk (26.92%, N=105). Most subjects (38.21%, N=149) declared that they consumed all these types of dairy products. A small number (4.22%, N=17) mentioned that they did not eat dairy products.

Meat. The types of meat students consumed most often were poultry (chicken, turkey) - 90.30%, fish - 87.20%, and pork - 36%. In addition, most students consumed the meat roasted (67.10%), fried (55.60%), or boiled (45.40%).

Eggs. Medical students consumed 3.21 ± 2.78 eggs per week. Most frequently they boiled the eggs (67.10%) or fried them (56%); a small percentage (7.50%, N=31) did not consume eggs.

Fish. Many of subjects stated that they consumed fish once (20.50%, N=85), twice (23.40%, N=97), or three times (16.20%, N=67) per month. Some of them mentioned they did not eat fish at all (9.70%, N=40). Most students preferred tuna (57.70%), most likely canned, and diverse types of oily fish such as carp (27.80%), salmon (34.10%), or mackerel (32.40%). Most of them preferred to eat the fish fried (53.10%), grilled (44.70%), or canned (45.40%).

Sweets. More than half of the students (66%, N=226) declared that they ate sweet products, like chocolate (81.40%), candies (40.60%), and cakes (44.90%).

Fast food. A large majority of medical students consumed fast food (82.38%, N=332). Approximately half of the students ate fast food only once a week (47.56%, N=185), while others ate it twice (18.25%, N=71), three times (12.08%, N=47), four times a week (7.46%, N=29), and not at all or rarely (11.31%, N=44). Students mentioned pizza (50.56%, N=180), shawarma (14.61%, N=52), hamburgers (11.80%, N=42), fries (3.37%, N=12), sandwiches (1.37%, N=12), and crispy strips (1.97%, N=7). Positive correlations were identified between participants' age and the number of sleeping hours (r=0.135 and r=0.007, respectively) and the number of eggs they ate in a week (r=0.214; $p < 0.001$), meaning that, as students aged, they slept more and tended to eat larger quantities of eggs. Furthermore, students who had more main meals also tended to consume more eggs (r=0.132; p=0.008).

Liquid intake: Water, Tea, Coffee, Carbonated Drinks

On average, students consumed 1.64 ± 0.88 liters of water per day. During classes, more than half of them hydrated themselves properly (58.85%, N=236), while a quarter of them (29.68%, N=119) rarely drank water during the hours they spent at the faculty. Almost half of the students drank coffee daily (44.42%, N=179), and a quarter of them did not drink coffee at all (25.31%, N=102); also, we found that 18.45% (N=74) preferred tea for daily consumption.

Carbonated drinks were consumed occasionally by over one-third of the students (40.69%, N=164), and a quarter of them did not consume them at all (21.84%, N=88). A low percentage of students (8.93%, N=36) declared that they consumed carbonated drinks daily.

Comparative results are presented in Table XIX. Men had lunch more often than women and women exercised less than men. Moreover, men ate more meat, eggs, and fast food compared to women. Regarding students' water intake throughout the day, women were more prone to drink a smaller quantity of water and less frequently compared to men.

Table XIX. Comparative analysis between variables considering gender

Variable	Males *	Females *	Total *	t	df	*p*-Value	95% CI
Age (years)	21.16 (±4.14)	21.22 (±4.66)	21.21 (±4.56)	−0.10	401	0.916	−1.18–1.06
Main meals/day	2.37 (±0.83)	2.23 (±0.63)	2.26 (±0.68)	1.47	101.22	0.144	−0.05–0.34
Breakfast/week	4.13 (±2.47)	4.15 (±2.27)	4.14 (±2.31)	−0.04	401	0.967	−0.58–0.55
Lunch/week	6.00 (±1.70)	5.44 (±2.00)	5.55 (±1.95)	2.52	135.82	0.013	0.12–0.99
Dinner/week	5.96 (±1.78)	5.81 (±1.80)	5.84 (±1.79)	0.63	401	0.524	−0.30–0.58
Snacks/day	1.10 (±0.03)	1.08 (±0.28)	2.49 (±1.43)	0.41	401	0.679	−0.05–0.08
Eating before sleep (h)	2.94 (±2.81)	2.93 (±2.02)	2.94 (±2.19)	0.03	98.43	0.976	−0.65–0.67
Eating after getting up (h)	3.15 (±2.20)	2.46 (±1.73)	2.58 (±1.83)	2.14	221	0.033	0.55–1.31
Fruit/day	2.25 (±1.83)	1.98 (±1.11)	2.03 (±1.28)	1.24	92.38	0.216	−0.15–0.69
Meat/week	6.02 (±2.79)	4.41 (±2.08)	4.72 (±2.32)	5.73	401	0.000	1.05–2.16
Eggs/week	4.79 (±4.56)	2.83 (±1.95)	3.21 (±2.78)	3.74	85.11	0.000	0.92–3.01
Fish/month	3.08 (±3.27)	2.85 (±2.38)	2.90 (±2.57)	0.72	401	0.471	−0.40–0.86
Fast food/week	2.14 (±1.63)	1.56 (±1.20)	1.68 (±1.31)	2.89	97.17	0.005	0,18–0.96
Water/day (litres)	2.05 (±0.97)	1.53 (±0.82)	1.63 (±0.88)	4.83	400	0.000	0.28–0.75
Exercise (hours/day)	4.07 (±3.22)	2.99 (±2.52)	3.21 (±2.71)	2.06	91.97	0.011	0.25–1.90

*Means (M) and standard deviation (SD)

We found that smokers students were more prone to consume less healthy food and to have unhealthy eating habits. The results of the *Mann-Whitney* test showed that there were significant differences depending on the status of smoker/non-smoker in terms of fast-food consumption ($z=-3.800$, $p < 0.001$) and frequency of eating breakfast per week ($z=-4.640$, $p < 0.001$), which meant that smokers ate more fast food (Mdn1=2) and had a lower frequency of eating breakfast per week (Mdn1=3) than non-smoker students (Mdn2=1 and Mdn2=5, respectively). Significant differences were also recorded in terms of fruit consumption per week ($z=-2.318$, $p=0.020$), meaning that non-smoker students (Mdn2= 2) tended to eat less fruit per week than smokers (Mdn1=3). The number of nights sleeping hours was different ($z=-2.306$, $p=0.021$) - non-smokers (Mdn2=7) had more hours of sleep than smokers (Mdn1=6).

Comparative analysis between preclinical (I-III) and clinical (IV-VI) years of study showed that there was a significant difference in terms of sleeping hours ($z=-2.382$, $p=0.017$), which showed that students in preclinical years (Mdn1=5) slept less than students in clinical years (Mdn2=7). There were also significant differences regarding the frequency of eating vegetables daily ($z=-2.748$, $p=0.006$), which means that students in the first three years of

college tended to have a higher frequency of eating vegetables daily (Mdn1=2) than students from last three years of college (Mdn2=1).

A positive correlation was identified between age and weight, age and BMI, meaning that, as students aged, their weight and BMI increased. The more students slept per night, the less fast food they consumed (Table XX).

Table XX. Correlation results

Variable	Age	BMI	Hours of Sleeping	No. of Meals	Fast Food Consumption
Age	1	0.244 **, 0.000	0.072, 0.150	−0.048, 0.334	−0.151 **, 0.003
BMI	0.244 **, 0.000	1	−0.006, 0.905	−0.043, 0.390	−0.061, 0.232
Hours of sleeping	0.072, 0.150	−0.006, 0.905	1	0.125 *, 0.012	−0.140 **, 0.006
No. of meals	−0.048, 0.334	−0.043, 0.390	0.125 *, 0.012	1	−0.194 **, 0.000
Fast food consumption	−0.151 **, 0.003	−0.061, 0.232	−0.140 **, 0.006	−0.194 **, 0.000	1

**Correlation is significant at the 0.01 level (two-tailed). *Correlation is significant at the 0.05 level (two-tailed).

II.1.4. Discussion

A total of 324 women and 79 men participated in this study. This distribution is normal for medical universities, where the percentage of female students is overwhelmingly higher. According to the Medical School Council, women outnumber men in most medical schools in the USA and Eastern and Western Europe by about 3:2 (Roter *et al.*, 2002; Dacre, 2008). During the academic years, the transition to another environment is likely to change subjects' eating patterns (Tanton *et al.*, 2015). There are many factors that were found to affect these behaviors: stress, economic status, dietary habits related to their family of origin, the cost of food, the knowledge about healthy food, the time of food preparation, culture. In the case of medical students, these factors can even be multiplied: busy schedule, skipping lunches, early wakeups with no breakfasts, long practical sessions, considering the lives of many students. Our results showed that, compared to the general population and the nonmedical students, the medical student population is more prone to eat healthier, to have more knowledge about nutrition, and to carefully select their food products; moreover, they are more prone to give up unhealthy behaviors such as drinking alcohol or smoking cigarettes and are more engaged in physical activity (Kokic *et al.*, 2019; Deshpande *et al.*, 2009; Iorga *et al.*, 2018d; Pop *et al.*, 2019; Muraru *et al.*, 2019).

Therefore, it is useful to know about food choices and preferences, as well as factors that influence students' eating habits to provide effective education and nutritional care by promoting healthy eating, a high-fiber diet, whole grains, dairy products, and low-calorie foods (Gazibara *et al.*, 2013; Alakaam *et al.*, 2015). There is a growing demand for global health strategies that would encourage body image and healthy figure among youth, initiatives that should mobilize society at national and international levels (Gazibara *et al.*, 2013). The results of our study prove that medical students have knowledge about how to maintain a healthy life and they practice it, which is important for their subsequent professional life.

In this study, we examined the eating habits of medical students and assessed their health-related behaviors; the university population is considered a suitable sample for the study of health in young adults (Nojomi and Najamabadi, 2006).

The results of this research showed that about 3/4 of the students (72.70%) had a normal BMI without significant differences according to gender; 14.54% were under-weight and 11.41% were overweight. This fact is in congruency with the results of a study conducted on 734 students in Italy, which indicated that a large part of the sample had normal weight (80.9%

in women and 71.70% in men), while 13.5% of women and 28.30% of men were overweight or obese (Zaccagni *et al.*, 2014).

These results are different to the findings of a study conducted by Mahfouz (Mahfouz *et al.*, 2016), who showed that only 45% of students had normal weight, 21% were underweight, and 34% overweight. Moreover, this study found a significant difference in the weight status of males and females; men were more likely to be obese and women were more likely to be underweight.

More than half of the students included in our study were satisfied with their body weight (58.31%), and most of them stated they were in good health (88.20%). These results are in line with the results of Piko (Piko, 2000), who showed that more than half of the students (61% of men and 66.30% of women) considered that they were in good health. In general, most students (78.6%, N= 1,667) rated their health as "good" or "very good", as indicated by the results of a study conducted by Bickerdike (Bickerdike *et al.*, 2019). Zaccagni identified that students (both men and women) had a significant preference for thinner bodies; women were especially more dissatisfied with body weight than men (Zaccagni *et al.*, 2014).

Sleep is part of a daily biological rhythm and is indispensable for health promotion (Azad *et al.*, 2015). Our results showed that the average number of hours of sleep among students was M=6.71 ± 0.88, which is consistent with the results of Band and Lee (Band and Lee, 2001). The authors found that the average sleep duration of the respondents was 6.7 ± 1.3 hrs. A recent study also indicated that the majority of students 79.3% (N=1,215) did not reach the minimum number of 8 hrs. of sleep per night during the week (Bickerdike *et al.*, 2019). Students fail to meet the current recommendations of *The American Academy of Sleep Medicine* (AASM) and *Sleep Research Society* (SRS). The two societies agreed that adults should sleep 7 hrs. a night or even longer, with sleeping less than 7 hrs. a night being associated with adverse health outcomes (Watson *et al.*, 2015). Given the medical profession of the future students, it is important for them to know that pathological drowsiness has been significantly associated with a higher prevalence of burning syndrome, and quantitatively inadequate sleep has been correlated with a significantly lower professional effectiveness and higher exhaustion scores (Wolf and Rosenstock, 2017). The results showed no statistical gender differences regarding the number of hours for night sleep.

In our study 28.78% of the students reported that they usually slept during the afternoon if they had the chance. A study by Vela-Bueno (Vela-Bueno *et al.*, 2008) showed that having a nap is a common habit among Spanish university students, a habit that can be explained by the fact that a substantial proportion of first-year students follow irregular sleep patterns, which can lead to insufficient sleep; thus, to compensate, they often have long naps, which are less effective than short naps in improving subjective alertness and cognitive performance (Dutheil *et al.*, 2020). Having naps is a healthy behavior during academic years. Naps may enhance certain cognitive and performance tasks, whereas intervening naps of 60 or 90 min halted the deterioration in the performance of a visual perception task that occurred during the day, but further studies are needed (Hershner and Chervin, 2014).

Regarding the frequency of meals, the results from the present study indicated that more than half of the students had two main meals per day. These results are in congruency with another study which showed that most students (52.70%) ate two meals per day (Yahia *et al.*, 2008). Many students in our study (81.89%) reported that they did not have meals at regular time intervals. These results are opposite to the results from a study conducted in China, which stated that most students (83.60%) ate regularly (Sakamaki *et al.*, 2005). Of great concern is the fact that only 29.28% of the students in our study ate breakfast daily, twice (13.90%) or three times (19.60%) over a week, while 8.68% did not eat breakfast at all. These results are in opposition to those obtained by Gan and Yeoh (Gan and Yeoh, 2017) who reported that about 62.20% of the female students consumed breakfast daily or 4-6 days weekly in the past 7 days.

Our results stated that most students (91.07%) ate an average of 2.49 ± 1.43 snacks per day. Al-Rethaiaa (Al-Rethaiaa *et al.,* 2010) showed that only 31.7% of students self-reported eating snacks, and Papier identified that individuals tended to increase their intake of high-calorie or high-fat snacks when they felt stressed, while other studies reported that individuals ate less of all food in stressful conditions, like academic years (Papier *et al.,* 2015).

Approximately 1/3 of students were found to have a healthy diet. More than half of the students (52.61%) ate cereals daily, 32.01% ate fruits daily, and 29.28% ate dairy every day. These results are somehow similar to another study conducted by Otemuyiwa and Adewusi which indicated that 60% of the students consumed the recommended minimum number of cereal servings (Otemuyiwa and Adewusi, 2012). Conversely, this study found that more female students (40%) consumed adequate quantities of fruits and vegetables than their male counterparts (20%), while the consumption of milk and milk substitutes was very low (10% male and 25% female).

Frequent consumption of unhealthy items is common among students from our study, given that 66% of them ate sweets daily. These results are similar with the results of a study conducted in Lebanon, which stated that 42.60% of participants consumed sweets every day (Otemuyiwa and Adewusi, 2012).

Most students from our study (82.38%) claimed they consume fast food Half of these students (47.56%) consumed fast food once a week. The results obtained by Salameh (Salameh *et al.*, 2014) had higher rates, showing that more than half of the participants (58.70%) ate fast-food less than two times a week, and 12.40% of students ate fast-food every day.

Water is essential for surviving. WHO recommends a minimum intake of water equal to 2.2 L/day for females and 2.5 L/day for males, depending on body size, in average conditions. Physical activity and elevated temperature increase this need to 4.5 liters per day for both men and women (Howard and Bartram, 2003) From this point of view, students in our study did not meet the recommendation criteria; our results showed that they drank, on average, one and a half liter of water a day, and most than half of them (58.85%) hydrated properly during classes. It was found that college students tended to choose their drinking beverages on the basis of their cost, as well as taste factors, rather than the nutritional information associated with a particular drink, which suggests that college students may be particularly at risk due to their lack of sufficient water intake, as well as a lack of understanding regarding the need to adhere to guidelines related to daily water intake (Block *et al.,* 2013; Alanazi, 2018). A high rate was identified by Teng, who showed that still water was the most consumed beverage (92.30% of the participants) (Teng *et al.,* 2019).

The findings of this study must be analyzed related to the stressful activity, demanding tasks, working in medical clinics, short breaks, or early classes all influence students' access to healthy food and regular meals, and decrease the practice of healthy habits.

Excessive alcohol consumption among students is a widespread problem on several university campuses, being associated with other unhealthy behaviors such as smoking, risky sexual behaviors, contact with multiple sexual partners, and non-use of the car seat belt (Al-Naggar *et al.,* 2013). Half of the students (49.63%) drink alcohol occasionally and 34.74% of the participants do not drink alcohol. We can conclude that medical students drink less alcohol compared to a similar age population (WHO, 2020).

Regarding coffee consumption, the results of our study showed that close to half of the students (44.42%) drink coffee every day. Results from other studies showed that consumers aged 18 to 24 yrs. old are the lightest coffee imbibers, with 2.5 cups per day, while the heaviest coffee consumers in the USA are those aged 40-59, with an average of about four cups per day (Arnot *et al.,* 2006). Thus, we can conclude that medical students drink less coffee than the normal population.

Smith and Leggat highlighted that the international prevalence of tobacco smoking among medical students varied from 2 to 58% (Smith and Leggat, 2007). Stress during college may be a contributing factor to smoking initiation. Our study revealed that most of the students did not smoke at all (69.40%), and only 16.67% of them were current smokers who consumed, on average, 7.77 ± 6.38 cigarettes in a day. These results are like those identified by other studies on medical students such as El Ansari (El Ansari *et al.,* 2011), Zarobkiewicz (Zarobkiewicz *et al.,* 2016), or Niu (Niu *et al.,* 2018). Some other studies showed that about a quarter of all U.S. students smoked (Flay, 1993), and 75% of them continued to smoke in adulthood (Tavolacci *et al.,* 2019), placing future adults at greater risk of developing lung cancer and cardiovascular disease. Similar trends were observed among students in Europe (O'Connor *et al.,* 2017; Brożek *et al.,* 2019). Considering these results, we can conclude that medical students tend to smoke less than students from nonmedical studies or adult from the general population.

Current recommendations state that adults should be engaged in aerobic physical activity for at least 150 min/week of moderate intensity or 75 min/week of vigorous intensity, or an equivalent combination (Singh *et al.,* 2020; US Department of Health and Human Services, 2018). We found that medical students were engaged in activities such as jogging, going for walks, going to the gym, or cycling and had an average of 221 minutes per week, meaning that students from medical studies reported higher levels of physical activity and met these recommendations. A relatively important percentage of students in our study did not exercise at all (14.64%), and in general, female medical students were engaged in physical activity less than male students. These findings are not similar to other results found in the literature. Studies proved that, in general, the level of physical activity of students is worrying since approximately 30% to 50% of respondents did not participate in adequate amounts of physical activity. When considering gender, studies found that male college students who participated in more vigorous activities than females tended to prefer team sports or weightlifting, while women were interested in yoga, dance, or aerobics (Kokic *et al.,* 2019; Iorga *et al.,* 2018d; Keating *et al.,* 2005; Kwan *et al.,* 2013)

It has been noticed that studying medicine and its related branches, as well as the accumulation of new knowledge, have a profound impact on students' eating practices. Thus, they internalize the information they gather, and our results showed that some self-destructive behaviors, such as smoking, decrease during university studies (Iorga *et al.,* 2018d; Zarobkiewicz *et al.,* 2016; Niu *et al.,* 2018).

Smoking decreased from the first to the sixth year of medical studies, and regarding physical activity, scores were significantly higher for first-year students compared to sixth year's students, suggesting that older students had a more sedentary lifestyle (Iorga *et al.,* 2018d; Pop *et al.,* 2019; Nola *et al.,* 2010).

The relationship between physical activity, sleep quality, and health-related quality-of-life were pointed out also by Izawa (Izawa *et al.,* 2011; Izawa *et al.,* 2004). A literature review of Blandon (Blandon *et al.,* 2017) showed that nursing students are more prone to improve their healthy habits than other non-medical students (practicing healthier behaviors, avoiding toxic intakes and risky sexual relationships).

The formation of students throughout the nursing degree improves their health-related habits. Similar findings were identified by Rizo-Baeza in health sciences students who showed also that the levels of overweight and obesity among students is less than that of the general population (Rizo-Baeza *et al.,* 2014) and Can (Can *et al.,* 2008) in nursing students-both studies proved more positive health-promoting lifestyles than those of non-medical students.

Reflections and Planning. The results of the present research proved that medical students drink alcohol and smoke cigarettes less than the normal population. Some unhealthy behaviors such as less physical activity, skipping meals, or consumption of unhealthy food must

encourage teaching and counselling staff to adopt more diversified and efficient strategies for helping medical students to develop a healthy lifestyle: developing programs about health nutrition and food to freshmen students (the most vulnerable population of students), providing access to healthy food on campus, rescheduling the sessions during semesters to facilitate breakfasts and lunches, encouraging physical activity through sports competitions, providing free snacks (fruit and vegetables), and organizing cultural events to promote specific foods and to encourage students to connect to healthy dietary patterns from different cultures.

The present study did not focus on the differences regarding the impact of nutrition knowledge on students, comparing participants from different medical specialties or different years of study. Depending on their specialty, the university curricula offer courses related to nutrition or dietetics in different years of study. Further studies should focus on measuring the effect of nutrition knowledge on the dietary habits of medical students.

II.1.5. Conclusions

Medical students have knowledge about how to maintain a healthy life and they put it into practice, which is important for their subsequent professional life as promotors of healthy physical and psychological health.

Some changes in dietary habits, physical activity, and lifestyle are related to the busy schedule and long practical stages. That is why the university campus should increase the number of facilities in order to maintain a healthy life among medical students and to fulfil the need for a healthcare environment at higher educational institutions.

II.2. Eating disorders in relationship with dietary habits among pharmacy students

Along their university studies, students change their dietary habits due to changing location, skipping home-prepared food, school schedule (which leads to snacks and skipping meals or fast food), self-administrating palatable meals (students eat preferred meals), cost and availability of food products (El Ansari *et al.*, 2007; El Ansari *et al.*, 2012; García-Meseguer *et al.*, 2014; Small *et al.*, 2013; Ganasegeran *et al.*, 2012).

Medical students are considered to be vulnerable because they fail to meet dietary requirements for a long period of time and they are practicing less healthy behaviors or eat more unhealthy food compared to non-medical students (Yahia *et al.*, 2016; Lupi *et al.*, 2015).

Students start to gain weight since freshmen years and this process slows but still increases during the adult life (WHO 2003a; Vella-Zarb 2009; Gores, 2008).

Obesity and overweight rates registered among medical students were related to skipping breakfast, frequent consumption of fast food or unhealthy food from food machines low consumption of fruits and vegetables (Boeing *et al.*, 2012; WHO 2003b; WHO 2014; Chourdakis *et al.*, 2010; Shah *et al.*, 2014).

Western cultures are more prone to accept and promote thinness compared to eastern countries and register high rates of eating disorders like anorexia and bulimia. Dietary acculturation is an extra distressful factor that may affect a student's life (Socolov *et al.*, 2017; Perez-Cueto *et al.*, 2009; Edwards *et al.*, 2010).

II.2.1. Aim

The aim of the study was to evaluate the presence of eating disorders among Romanian pharmacy students and their relationship with the patterns of dietary habits.

II.2.2. Material and methods

Study Design and Participants. A total of ninety-one students were included in the present research. All participants were enrolled, at the time of the investigation, in "Grigore T. Popa" University of Medicine and Pharmacy of Iasi, Romania, Faculty of Pharmacy, from all five years of study. In total, the number of pharmacy students registered was seven hundred, so the subjects investigated represented almost 10% of the targeted population.

All the students voluntarily participated to the research, and they were informed about the purpose of the study, and about the option to withdraw from the study anytime they wanted to, with no penalties. The survey took approximately 25 minutes to complete.

A total of 120 questionnaires (including socio-demographic, medical, anthropometric, and psychological data) were distributed directly by the investigators. From the 115 returned documents (with a rate of response of 96%), ninety-one were taken into consideration for the research. Willingness to participate was considered as an inclusion criterion.

Socio-Demographic Data. Because the present study is the first one focusing on eating habits and disease among pharmacy students in Romania, information like age, gender (male/female), environment (rural/urban), and year of study (one to five) were registered for this cross-sectional study.

Anthropometric and Medical Data. Information like weight, weight, body mass indices (BMI) and the existence of a chronic disease were also registered. Height and weight data were converted into Quetelet's BDI and the value was considered using World Health Organization (WHO) standards for European population: a BMI<18.5 kg/m^2 was categorized as underweight, 18.5–24.9 kg/m^2 as the normal range, 25.0–29.9 kg/m^2 as pre-obese, 30–34.9 kg/m^2 as obese class I, 35.0–39.9 kg/m^2 as obese class II, and ≥ 40 kg/m^2 as obese Class III (Gores, 2008). An item was added to identify if students were satisfied with their weight, to declare if they used diets in order to reduce their weight.

Dietary Data. The study focused also on gathering information regarding the consumption of vegetables, fruits, snacks, or fast-food. The selection of dietary data was collected in order to also respect the religion and the restriction imposed by the practice of it.

Health-Related Behaviors. Special items were constructed in order to identify sleep-related problems (hours of sleep), the number of weekly breakfasts, lunches, or dinners, preferred meal, serving snacks, skipping meals, eating during the night, and fasting.

Eating Disorders. Psychological problems referring to eating disorders were evaluated using Eating Disorder Inventory (EDI). The original tool was designed by Garner for identifying eating disorders, and it is widely used to screen symptoms and psychological features related to eating disorder (Garner *et al.*, 1983).

In the present study, EDI-3, Romanian Form (Miclea *et al.*, 2010) was used. The 91 items investigate the following aspects: 3 scales are related specific to eating disorders (drive for thinness - DT, bulimia - B, and body dissatisfaction - BD) and 9 are general psychological scales in strong relationship with eating disorders (low self-esteem - LSE, personal alienation - PA, interpersonal insecurity - II, interpersonal alienation - IA, interoceptive deficits - ID, emotional dysregulation - ED, perfectionism - P, ascetism - AS, and maturity fears - MF).

A 6-point scale represents the response options for the items of EDI-3, ranging from *always* to *never*. The instrument has a number of 25 reversed items. In this case, we also reverse the coding. It is mandatory to choose a response for each item and individuals have to decide which one suits those best. The score for each subscale is obtained by summing up all scores for that scale. EDI-3 is a tool to assess symptoms relevant to the development and maintaining of eating disorders. High scores on the first three scales are related to high risks of developing eating disorders. The other nine scales take into consideration important psychological aspects relevant to the evolution and persistence of eating disorders. The adaptation and validation of EDI-3 on the Romanian population used individuals from the general population from six of

the forty-one counties in Romania and individuals with a diagnosis of eating disorders. For most of the subscale, there were no significant differences between male and female participants (in accordance with other studies), with two exceptions: drive for thinness and body dissatisfaction, with women scoring higher than men on these scales.

Test-retest reliability indicates a high stability in time for EDI-3, correlation coefficients varying between 0.613 and 0.844, with $p < 0.001$. The instrument also shows a good internal consistency on all scales as measured by alpha Cronbach coefficients ranged from 0.600 to 0.899. Correlations between the scores on the scales of EDI-3 and other eating disorders relevant instruments (Eating Attitudes Test-26, Rosenberg self-esteem scale, Eysenck Personality Questionnaire, Beck Depression Inventory, Endler Multidimensional Anxiety Scales) indicate a good criterion validity. Intercorrelations between the scales of EDI-3 and factor analysis point to a good construct validity.

Statistical Analysis. The statistical analysis was done using IBM *SPSS Statistics version 23.0*. Descriptive analysis used mean and standard deviations; Independent Samples t Tests were used in the case of one independent, categorical variable that has two levels/groups and one continuous dependent variable. The one-way analysis of variance (*ANOVA*) was also used to establish whether there are any statistically significant differences between the means of three or more independent (unrelated) groups. For *Pearson* correlations, interval measured variables were used. Differences were considered statistically significant at p value <0.05.

II.2.3. Results

Socio-Demographic, Anthropometric, and Medical Data. Most of participants were females (N=83, 91.21%), age range of 18–39 (M=22.30 ± 2.71). The majority of female students is a common feature, the rate being specific to all rates registered by medical universities. Socio-demographic (gender, age, environment), anthropometric (weight and BMI), and medical (having a chronic disease or being under medical treatment) data are described in Table XXI.

Psychological Data - EDI-3. Results for EDI-3 subscales are presented in Table XXII. The results obtained for both genders are presenting together with scores for men and women from general population in Romania. Comparing with women from general population, scores for female pharmacy students are higher for all subscales. For men, only 5 scores were registered to be higher than that of Romanian males: drive for thinness, body dissatisfaction, personal alienation, interoceptive deficits, and emotional dysregulation.

There is no association between age and BMI ($r=0.059$, $p=0.582$). *Pearson* correlations revealed negative significant associations between age and number of main meals per week ($r=-0.265$, $p=0.012$) and the number of snacks per day ($r=-0.244$, $p=0.021$). Also, there is a positive correlation between age and eating after getting up in the morning ($r=0.337$, $p=0.001$). More specifically, younger students tend to eat more main meals per week, snack more, and eat later after getting up in the morning.

Pearson correlations revealed that students with a high drive for thinness have higher body weights ($r=0.282$, $p < 0.001$) and tend to skip dinners ($r=-0.344$, $p < 0.001$). As expected, a positive correlation was identified between weight and the subscales body dissatisfaction ($r=0.342$, $p < 0.001$) and drive for thinness ($r=-0.285$, $p < 0.001$). Also, participants with high body dissatisfaction tend to have fewer main meals ($r=-0.265$, $p=0.011$) and to skip breakfasts ($r=-0.235$, $p=0.025$) and dinners ($r=-0.303$, $p < 0.001$).

Table XXI. Socio-demographic, anthropometric and medical data

	VARIABLES	RESULTS
Gender	female	83 (91.21%)
	male	8 (8.79%)
Environment	urban	54 (53.94%)
	rural	37 (40.66%)
Religion	Orthodox	70 (77.78%)
	Catholic	10 (11%)
	Others (Pentecostal, Adventist)	11 (11.21%)
	Respecting religious fasts	29 (31.87%)
Body Mass Index (BMI)	Weight (kg)	60.2 ± 10.56 (42 to 105)
	underweight	13 (14.3%)
	normal weight	63 (69.2%)
	pre-obese	12 (13.2%)
	obese	0
Medical data	Having a chronic disease	13 (14.29%)
	Under a medical treatment	15 (16.49%)

Table XXII. Comparative results for EDI-3 subscales for men and women

EDI-3 SUBSCALES	Pharmacy Students		General Population	
	Male	Female	Male	Female
Drive for thinness	3.37 ± 4.30	9.26 ± 7.65	2.66 ± 3.66	8.03 ± 7.54
Bulimia	1.12 ± 1.80	4.87 ± 5.97	2.04 ± 2.38	2.00 ± 3.18
Body dissatisfaction	7.25 ± 6.62	17.03 ± 10.62	5.18 ± 6.13	10.29 ± 9.28
Low self-esteem	2.75 ± 2.37	8.08 ± 5.98	3.28 ± 4.85	2.97 ± 3.19
Personal alienation	6.62 ± 1.40	10.40 ± 4.48	3.55 ± 4.12	4.48 ± 3.45
Interpersonal insecurity	6.35 ± 5.75	13.81 ± 7.75	7.07 ± 5.87	6.73 ± 4.95
Interpersonal alienation	5.03 ± 6.34	11.98 ± 9.62	7.04 ± 4.48	7.13 ± 4.06
Interoceptive deficits	7.82 ± 2.72	12.20 ± 3.50	4.79 ± 5.16	6.10 ± 4.34
Emotional dysregulation	6.24 ± 1.88	7.74 ± 2.12	5.36 ± 5.83	6.03 ± 4.60
Perfectionism	4.68 ± 7.84	10.96 ± 10.87	11.79 ± 5.34	10.42 ± 5.42
Ascetism	5.19 ± 3.29	7.77 ± 4.00	6.41 ± 3.66	6.81 ± 3.82
Maturity fears	6.65 ± 5.28	17.97 ± 10.37	10.62 ± 4.07	13.23 ± 5.81

Means (M) and standard deviations (SD).

Interpersonal alienation (reluctance to form close relationship) and maturity fears (the fear to face the demands specific to an adult life) had a negative correlation with number of lunches per week ($r=-0.295$, $p < 0.001$ and $r=-0.214$, $p=0.042$, respectively), meaning that participants with high scores on this subscale tend to skip lunch.

For the subscale interoceptive deficits, it was identified a positive correlation with the number of eaten fruits ($r=0.252$, $p=0.021$). Interoceptive deficits scale measures the ability of an individual to discriminate between sensations (of hunger and satiety) and feelings.

A negative correlation was identified between emotional dysregulation and the number of hours of night sleep and number of breakfasts ($r=-0.222$, $p=0.035$), that means the subjects presented higher rate of emotional problems, tend to sleep less and they skip breakfast.

A negative correlation was identified between ascetism and the number of main meals per week ($r=-0.265$, $p=0.012$), meaning that students with high scores on ascetism tend to skip more main meals.

Dietary Habits and Health-Related Behaviors

Sleep-Related Data. Students were asked to estimate the number of night sleep hours. The results revealed an $M=7 \pm 1.02$ h of sleep every night and almost a quarter of them (24.12%) were having a nap after lunch almost every day. The t-test revealed significant differences between subjects who eat during nights ($M=11.85$) and those who do not ($M=9.54$) on personal alienation ($t(89)=2.31$, $p=0.035$). Personal alienation refers to low self-esteem. Results proved that students who used to eat during nights had higher scores on personal alienation.

Meals, Snacks, and Diets. Students were asked to mention which was their preferred meal: 64.84% of them usually prefer have lunch, 23.08% dinner, and 12.09% enjoy having breakfasts. A number of 21 subjects (23.08%) declared that they eat during nights. They had also to mentions how many times they succeed in serving breakfasts, lunches, and dinners and the results are presented in Table XXIII.

Table XXIII. Meals (breakfasts, lunches, dinners) per week

How many times per week do you eat…	Never	1	2	3	4	5	6	Daily	M ±SD
Breakfast	7.69%	5.49%	8.79%	16.48%	4.40%	14.29%	9.89%	32.97%	4.51 ± 2.34
Lunch	1.10%	0%	2.20%	4.40%	12.09%	14.29%	6.59%	59.34%	5.92 ± 1.54
Dinner	1.10%	0%	4.40%	9.89%	4.40%	13.19%	2.20%	64.84%	5.89 ± 1.72

Number of meals (%).

Students were also asked to report whether they eat snacks or not. The majority of them (95.6%), sustained that they eat snacks daily, with an $M=2.33 \pm 1.25$. More than one-third of students declared that they used to keep diets to reduce their weight ($N=37$, 40.7%). When comparing students who dieted for reducing weight to those who did not, the first group obtained statistically significant higher scores on each of the following six subscales: drive for thinness ($t(89)=6.14$, $p<0.001$), bulimia ($t(89)=3.03$, $p=0.004$), body dissatisfaction ($t(89)=3.71$, <0.001), personal alienation ($t(89)=2.01$, $p=0.047$), emotional dysregulation ($t(89)=2.02$, $p=0.046$), and ascetism ($t(89)=3.25$, $p=0.002$).

Religious Fasts and Vegetable / Fruit Diet. The results of the Independent Samples t-Test revealed that students who fast (M=9.24) had lower scores than those who do not (M=12.96) on interpersonal alienation (t(89)=−3.21, p=0.002). The answers to the items regarding the daily consumption of fruits and vegetables proved that 35.2% of students eat fruits daily and 57.1% of them declared they eat daily vegetables, with an M= 2.02 ± 1.41 fruits and M=5.92 ± 1.54 vegetables per day.

One-Way *ANOVA* analyses showed significant differences between fruit consumption (1 - daily, 2 - two times a week, 3 - three, four times a week, 4 - not at all) and three of the subscales: drive for thinness (F(3.87)=4.57, p=0.005), emotional dysregulation (F(3.87)=3.24, p=0.026), and perfectionism (F(3.87)=3.86, p=0.012). The multiple comparisons analysis showed that students who ate fruits daily (M=11.53) had a higher drive for thinness than those who eat fruits twice a week (M=5.23); those who do not eat fruits (M=14.80) had higher scores on emotional dysregulation than those who eat fruits three/four times a week (M=6.00); and participants who do not eat fruits (M=16.60) had higher scores on perfectionism than those who used to eat fruits two times (M=9.52) or three/four times a week (M=9.97).

Satisfaction with Personal Weight

A number of 53 (58.2%) students declared that they are content with their weight. The results of the Independent Samples *t*-Tests showed significant differences between subjects who are content with their weight and those who are not on 9 of the 12 subscales of the EDI-3: drive for thinness (t(89)=−5.40, p < 0.001), bulimia (t(89)=−4.42, p < 0.001), body dissatisfaction (t(89)=−8.31, p < 0.001), low self-esteem (t(89)=−3.08, p=0.003), personal alienation (t(89)=−4.36, p < 0.001), interpersonal alienation (t(89)=−3.21, p=0.002), interoceptive deficits (t(89)=−3.78, p < 0.001), emotional dysregulation (t(89)=−3.47, p=0.001), and ascetism (t(89)=−4.85, p < 0.001). More specifically, students who are content with their weight have a lower drive for thinness, lower scores on bulimia, higher self-esteem, lower scores on personal and interpersonal alienation, lower interoceptive deficits and emotional dysregulation, lower scores on ascetism, and are more satisfied with their bodies comparative with students dissatisfied with their weight.

Environment

Environment is closely link to several aspects of nutrition (more healthy food, private gardeners with fruits and vegetables) and more religious people. The analysis of data focused on the relationship between environment and the consumption of food (vegetables, fruits) or respecting religious fasts.

The chi square test revealed no statistical difference between students from rural areas and those from urban areas according to whether they respect religious fasts or not ($\chi^2(2)=3.716$, p=0.054) or whether they eat fruits ($\chi^2(3)=1.173$, p=0.759) or vegetables ($\chi^2(1)=0.004$, p=0.951) on a daily basis.

Regarding EDI-3 analysis of data, the Independent Samples *t*-Test, reveled a significant difference between students from rural areas (M=15.59) and those from urban areas (M=11.70) concerning the interpersonal insecurity (II) subscale of the EDI-3 (t(89)=−2.91, p=0.004). More specifically, students from rural area score higher on interpersonal insecurity (II) than those from urban areas.

BMI

One-way *ANOVA* was used in order to identify the statistically significant differences between BMI categories. Significant differences were identified between underweight (M=3.92), normal weight (M=8.74), and pre-obese (M=13.71) participants regarding the subscale DT (F(2.85)=5.43, p=0.006). Multiple comparisons using the Bonferroni method showed a significant difference between underweight and pre-obese students, the first group having a lower drive for thinness than the last group.

Significant statistical differences were also identified between underweight (M=11.38), normal weight (M=15.11), and pre-obese (M=25.08) participants concerning the body dissatisfaction (BD) subscale ($F(2.85)=6.98$, $p=0.002$). Underweight students had lower scores on body dissatisfaction than pre-obese participants, the latter obtained higher scores than the former. Positive correlations were identified between BMI and drive for thinness ($r=0.291$, $p < 0.001$), bulimia, ($r=0.391$, $p < 0.001$), body dissatisfaction ($r=0.447$, $p < 0.001$), and ascetism ($r=0.246$, $p=0.019$).

II.2.4. Discussion

The present study identified a weight of M=60.2 ± 10.56 (ranged from 42 to 105 kg) and 69% of students are normal weight. No obese persons were identified among the questioned students. Because no other study was lead on pharmacy students' weight-related aspects, no comparative analysis could be done considering other results on Romanian pharmacy students. A previous study lead on Romanian students from many specialties, developed in 2012, registered a lower M=54.3 ± 4.7 for investigated Romanian student population. At that time, the score was lower in comparison with German students, with an M=60.3 ± 9.3 (Joja and Von Wietersheim, 2012).

For female participants, our sample had higher mean score on all subscales than those found among Romanian women. For men, the majority of mean scores were higher than those reported among men from Romania, with the exception of low self-esteem, interpersonal insecurity, interpersonal alienation, ascetism, and maturity fears, where the means were lower (Miclea *et al.*, 2011).

A study lead on Hungarian medical and pharmacy students showed a low administration of milk, fruits, and vegetables (Biró *et al.*, 2005). Similar results were found by Allen *et al.* focusing on Canadian pharmacy students, identifying that students' dietary habits were far below *Canadians' Food Guide recommendations* (Allen *et al.*, 2011). Interesting results targeting students in Egypt showed that there is an important effect of nutrition awareness and knowledge on health habits and performance among Egyptian pharmacy students, meaning that knowledge is not sufficient to stimulate students from Pharmacy to practice healthy habits, this must be doubled by nutrition awareness (El-Ahmady and El-Wakeel, 2017). Tiralongo and Wallis results showed that Australian pharmacy students must internalize first information prior respecting nutritional alternatives (Tiralongo and Wallis, 2008).

Sleep has consequences on both physical and psychological health. The results regarding the duration of night sleep showed that questioned students had an M=7 ± 1.02 hours of sleep every night. *American Academy of Sleep Medicine* recommended for this category of age 7-9 hours for an optimal health (Paruthi *et al.*, 2016).

Several studies lead on pharmacist students in USA (Rabinowitz *et al.*, 1993), Malaysia (Al-Naggar and Chen, 2011), and Poland (Jaworowska and Bazylak, 2007) or focusing on working pharmacists (Gardiner *et al.*, 2006) revealed that there is a high rate of consumption of vitamins, minerals, or other supplements and rates are even higher compared to other medical specialties or other science studies. It is natural to think that students or health professionals who are well-trained in drugs and their effect on health to consume with precociousness these medications (Rabinowitz *et al.*,1993). One raison for high rate for the consumption of supplements could be related to the fact that these medical specialists are trained to be more aware about the importance of nutritional status and they are able to evaluate the fact that skipping meals or consuming unhealthy food led to an unbalanced nutritional status with negative consequences on health. This self-evaluation of their dietary behaviors doubled by the knowledge in drug's component could be a reason for a self-administration of medicines. This habit was identified among medical students by a lot of researches focusing on this population (Iorga *et al.*, 2016a; Gavrilescu *et al.*, 2017) and among working pharmacists, with or without presenting a chronic disease (Iorga *et al.*, 2017 Iorga *et al.*, 2018). The rates of self-

administration of dietary supplements among pharmacy students balanced in different studies between 20% in Japan (Shimizu *et al.,* 2007) and 47% in USA ((Rabinowitz *et al.,* 1993).

Our study identified that over 40% of the students admitted to dieting to lose weight, a higher rate than those observed in other studies (Tavolacci *et al.,* 2015). Our results concerning the positive correlation between three scales of the EDI-3 (specifically the drive for thinness, bulimia, and body dissatisfaction) and weight and BMI are in accordance with those found in the Romanian population, with the exception of the relationship between bulimia and weight, where we found no associations (Miclea *et al.,* 2011).

Results pointed out that higher BMIs are associated with higher score on body dissatisfaction. Jaworowska and Bazylak (Jaworowska and Bazylak, 2009) which identified a relatively low percentage of pharmacy students satisfied with their body weights (34.4% for female and 37.1% for male participants), despite the fact that they were not overweight or obese. As-Sa'edi *et al.* (As-Sa'edi *et al.,* 2013) also found, a low percentage of female medical students satisfied with their bodies (26.40%), while the rest perceived themselves as either too thin or too heavy and expressed a desire to lose weight. In our study, only students with high BMIs tend to have a higher drive for thinness.

Female students desire a significantly thinner figure than men (Zaccagni *et al.,* 2014) and that their ideal figure is underweight (Yahia *et al.,* 2016). In our study, a high desire to be thin is associated with high BMI. Albertson showed that a self-compassion meditation training spanning a period of 3 weeks improved body satisfaction for women (Albertson *et al.,* 2015).

In our sample is students with high BMIs tend to score high on the bulimia scale of EDI-3, suggesting that this group of students are at a higher risk of developing symptoms for bulimia. Findings from other studies (Bodell *et al.,* 2017) point to the fact that weight suppression has an important effect on bulimic symptoms and this association could be maintained by the preoccupation with thinness.

When comparing college students and eating disorder patients, findings showed that the latter have lower mean levels of self-esteem (Kelly *et al.,* 2014) and that students with greater positive body image have higher levels of self-esteem (Gillen, 2015). Research suggests that, when comparing individuals with eating disorders with individuals without eating disorders, the first group has a tendency towards perfectionism in maladaptive ways (Ashby *et al.,* 1998). Our results that students who do not eat fruits have higher scores on perfectionism than those who eat fruits two times or three, four times a week, suggesting that perfectionism could have significant implications for health and well-being.

Also, the results showed that that students with high scores on ascetism tend to skip more main meals. The results are in concordance with Garner's results (Garner *et al.,* 1983). The ascetic motive for weight loss was common in early writings on anorexia nervosa and is still an important theme in some cases.

The present findings showed that students who fast had lower scores than those who do not fast on interpersonal alienation. The majority of subjects were Christians, also representing the major religion in Romania. Fasting is respected in general by the religious persons. Meaning that subjects are closed to religious rules, are used to going to church and fulfilling dietary restrictions during festal times. The result that students who fast are presenting less personal alienation is in congruency with the majority of studies, showing that the practice of religion has positive effects on personal, familial, social life, and on health (Alcorta *et al.,* 2017; Lucchetti and Lucchetti, 2014; Scott *et al.,* 2014). Some recent study showed that a high prevalence of religious practice was associated with overweight/obesity, especially among Christian women (Peltzer *et al.,* 2014).

Results proved that students who used to eat during nights obtained higher scores on personal alienation, so they had a low level of self-esteem. These findings are similar with previous research on night-eaters. Individuals who used to eat during nights had higher scores

on depression and lower self-esteem and usually eat later in the morning and present sleeping disturbance (Gluck *et al.,* 2001). Further research would be interesting to focus on night-eating syndrome, in order to identify this psycho-pathological problem among students.

II.2.5. Conclusions

The results of the present study showed that eating disorders were identified having higher rates among pharmacy students than in general population in Romania. Considering some key factors like age, environment, fasting, sleeping, respecting main meals, or encouraging the consumption of fruits and vegetables could help students and university policy makers to promote healthier eating behaviors among pharmacy students.

II.3. Modern diet associated with irritable bowel syndrome

Functional bowel disorders are highly prevalent among people worldwide and are considered to represent up to 50% of medical consultations in gastroenterology (Phillips 1994). *Irritable Bowel Syndrome* (IBS) is a common cause for medical referral and has a clear impact on the patient quality of life and also on the medical system costs. Over the years, the definition criteria for IBS have evolved from Manning and Kruise's criteria to Rome I and Rome III criteria. However, clear conclusions are difficult when comparing studies with different definitions for IBS. The worldwide prevalence of IBS varies according to the location and design of the study from 1.1% (Sorouri *et al.,* 2010; Khoshkrood-Mansoori *et al.,* 2009) - to 22% (Rey and Talley, 2009). Most western studies have revealed prevalence between 15-20% (Grundmann and Yoon, 2010). IBS is more prevalent in women, independently of age (Chang *et al.,* 2006), and ethnic groups. IBS is somehow more frequently present in western European than in Asia Pacific countries (Gwee *et al.,* 2009) and in the white population compared with Afro-Americans (Dapoigny, 2009).

Although many patients recognize the impact of specific food in symptom occurrence, very few population-base studies have evaluated the importance of diet in IBS and its role remains uncertain (Eswaran *et al.,* 2011; Morcos *et al.,* 2009). Even though many patients have reported that food may precipitate or aggravate their symptoms, only one population-based study has evaluated its role in IBS and the results suggested that food sensitivity rather than different diet composition may be related to IBS (Rey and Talley, 2009).

The single study conducted on the general population in Romania, using Rome I criteria, revealed IBS prevalence of 14.49% (8.4% man and 17.7% women) with no significant difference between the age groups (Drug *et al.,* 2000). The study was conducted in 1998 in the same area as the present study, on 338 subjects (220 women, 118 men), mean age 44 (standard deviation 14.8, range 17 to 80 years old) and had a home visiting design.

II.3.1. Aim

The aim of the study was to determine the prevalence of IBS in the general urban population and to evaluate the type of diet associated with IBS symptoms.

II.3.2. Material and methods

The study included a sample of 300 subjects (more than 18 years old) from a population of 18,000 subjects living in the Pacurari urban area, from Iasi, Romania. The sample size and demographic characteristics were estimated to be representative for the general population of the geographic area using *EpiInfo™ 3.5.2* (Centers for Diseases Control) software. According to an expected frequency of 14%, and a worst acceptable value of 8%, the minimum sample size would be 128 for a confidence interval (CI) of 95% and 219 for a CI of 99%. The inclusion criteria were age over 18 years and residency in this urban area, with no exclusion criteria. The selection of subjects was randomized, using a function in *Microsoft Excel™* software, from

family doctors' patient lists. The family doctors invited the selected subjects by phone for interview and measurement in their offices.

Measurements. Two interview-based questionnaires were delivered to all subjects: a Rome III questionnaire (Drossman, 2006; Drossman and Dumitrascu 2006; Drossman *et al.*, 2006) for diagnosis of IBS and a *food-frequency questionnaire (*FFQ) for evaluation of eating habits and frequency of food intake for the last six months. A general medical history (overweight, obesity, diabetes mellitus, hypertension, cancer, cardiovascular, liver, digestive, endocrine, locomotor system, skin, respiratory, neuro-psychiatric diseases and sleep disorders) was also included in the interview together with an objective evaluation of obesity (weight and height were measured by doctors, in their offices).

Age, gender and educational level were studied as demographic factors. Educational level was categorized into three classes: low (no school or elementary school only), medium (high school) and high (college or university). Health-related conditions were investigated: smoking (dichotomized as "current smokers" and "non-smokers"), physical activity (dichotomized as "physically active" if exercise moderate to vigorous at least weekly and "physically inactive" for less) and general well-being (using a 5-point scale "very good - good - acceptable - poor - very poor condition"). Body mass index (BMI) was also calculated, and subjects were grouped into four categories: underweight (<18.5 kg/m^2), normal weight (18.5-24.9 kg/m^2), overweight (25.0-29.9 kg/m^2), and obese (≥30.0 kg/m^2)(WHO, 2000).

A FFQ was designed to reveal habitual intake over a six-month period. This questionnaire was based on a FFQ developed for use among adults in Romania but was modified to include more dietary questions. We asked about the main categories of foods consumed in our region, detailing the foods considered of interest to our study. Consumption frequencies were noted: "never or rarely", "monthly", "once a week", "several times a week", "once a day" and "several times a day". We also investigated individual eating habits (including daily breakfast, number of meals and snacks a day, use of home prepared food, meal with family, eating in a hurry as subjective perception).

Descriptive statistics were performed with IBM *SPSS Statistics version 17.0*. Mean was used for parametric characteristics and median for non-parametric or ordinal variables. The median was used to characterize the frequency of food consumption in the studied population and subjects were divided into two categories of consumers (less than median frequency and equal or more than median frequency). *Spearman's* correlation and cross-tabulation analysis (chi square test) was used initially to reveal any association between medical personal history, eating habits, food consumption frequency and other associated conditions. Finally, we used logistic regression (binary, univariate) and calculated odd ratios (ORs) and 95 % confidence interval for significant predictors of IBS derived from initial analysis. A value of $p<0.05$ in both analyses was considered to be statistically relevant.

The study was approved by the Ethics Committee of the "Grigore T. Popa" University of Medicine and Pharmacy of Iasi, and a patient informed consent was obtained from all subjects.

II.3.3. Results

During a period of four months (January - April 2011) three hundred persons were invited to enroll in the study. A group of 193 subjects (80 males and 113 women) agreed to participate. Participation rate was 64.3%, with no socio-demographic differences between participants and non-participant subjects (for gender, age and educational level, $p>0.05$). The mean age of the sample was 50.8±16.2 years (range: 20-85).

The prevalence of IBS was 19.17% (19.47% for females and 18.75% for males) (Figure 2). Evaluation of the age distribution indicated increased prevalence of IBS in subjects above the mean age of sample, with a maximum in the decade 60-69 years (37.5%, $p <0.01$) (Figure

3). Educational level of subjects influenced the prevalence of IBS in the studied population, but not significantly (p=0.066).

The trend showed higher prevalence of IBS symptoms toward low educated people (12.5% among high-educated people, 23.0% in medium and 30.3 % in low-educated people). Profession did not reveal any difference between subject; with and without IBS. A history of digestive diseases was more common in subjects with IBS *vs.* non-IBS subjects (29.7% *vs.* 7.7%, p<0.01).

Also, patients with IBS had more commonly cardio-vascular diseases (64.9% *vs.* 18.6%, p<0.01), including arterial hypertension (75.7 % *vs.* 31.4%, p<0.01). Obesity (59.5% *vs.* 24.4%, p<0.01) and diseases of the loco-motor system (27% *vs.* 12.2%, p<0.05) were more common in IBS subjects. History of other diseases, including psychiatric disorders, did not feature often in IBS subjects (p>0.05).

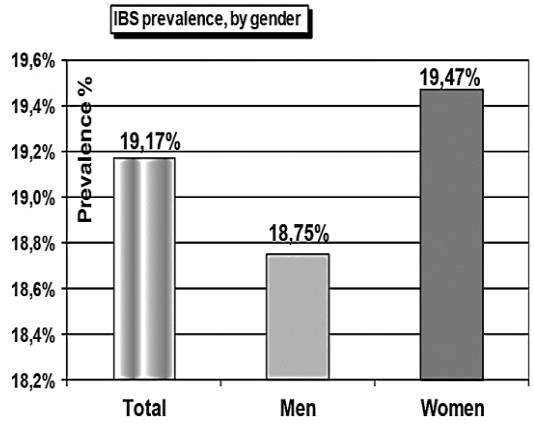

Figure 2. *IBS prevalence, by gender.*

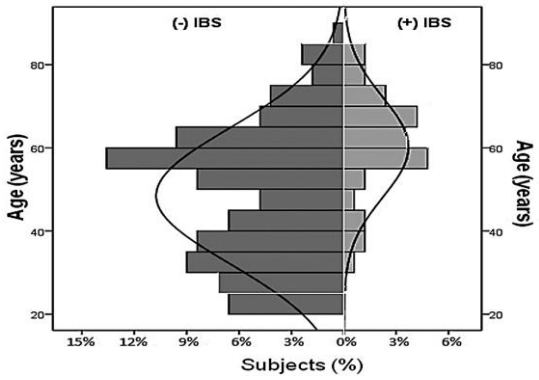

Figure 3. *Age distribution of IBS and non-IBS subjects*

IBS and health-related behaviors. Smoking was not associated with IBS: 13.5 % of IBS subjects were smokers, *vs.* 29.5% non-IBS subjects (p>0.05). Alcohol (beer, wine or spirits) was also not associated with IBS symptoms (p>0.05). 10.9 % participants had an alcoholic beverage daily. However, 86.5% of IBS subjects and 60.2% of non-IBS subjects were physically inactive (p<0.01). IBS *vs.* non-IBS subjects perceived their well-being status to be poor: 13.3% *vs.* 7.6% (p>0.05), acceptable (50% *vs.* 34.7%, p>0.05), good (36.7% *vs.* 40.7%, p>0.05). No IBS subjects and 16.9% of non-IBS subjects perceived themselves as in very good condition while no subject perceived themselves to be in a very poor condition of well-being. In the sample studied, 49.5% were overweight and 20.8% obese. Presence of obesity was not significantly different in IBS (21.6%) and non-IBS subjects (20.6%) (p>0.05).

IBS and diet. Median frequency of food consumption in the studied population is presented in Figure 4. Using median as the cutoff point, the IBS subjects ate significantly more frequently the following foods (chi square test and OR derived from logistic regression, Table XXIV): canned food (p<0.001), processed meat (p<0.01), beef (p<0.001), milk (p<0.05), pulses (legumes) (p<0.05), cereals or grain bread /pasta (p<0.01), cafeteria products (p<0.01), fruit compotes (canned or not) (p<0.001), herb teas (p<0.001). The difference between IBS and non-IBS subjects was not significantly different (p>0.05) for the consumption of the following type of foods: fish, eggs, fats, vegetables with 5% carbohydrate (lettuce, spinach, tomatoes, peppers), white bread, sugar and sweets, alcoholic beverages and coffee. *Spearman* correlation found an association between IBS and several types of food consumption frequency (Table XXV).

Eating habits and IBS .Subjective perception of eating in a hurry was more frequent among the IBS patients (41.6 %) than non-IBS subjects (22%) (p<0.05). Other eating habits

(daily breakfast, number of meals per day, meals with the family or frequent use of home-prepared food) were not significantly different (Table XXVI).

II.3.4. Discussion

The recent literature using Rome III criteria reports a mean prevalence for IBS of 12-15 % (range 1 to 33 %) (Sorouri *et al.*, 2010; Khoshkrood-Mansoori *et al.*, 2009; Hillilä and Färkkilä 2004; Hori *et al.*, 2009; Wang A, *et al.* 2008; Dumitrascu *et al.*, 2006). The only IBS prevalence study in the Romanian general population revealed an IBS prevalence of 14.49% (8.4% men and 17.7% women) (Drug *et al.*, 2000). Comparing the two studies a modest, not significant increase of the prevalence (19.47 %: 95% CI) in the present study can be seen ($p>0.05$). Although the geographic area was the same, the design was somehow different, and this could have influenced the results.

Table XXIV. Associations of IBS with frequency of food consumption

Food categories Frequency of food consumption	Chi square test	OR (95% CI) derived from logistic regression
Canned food		
No, rarely	18.662***	1
At least monthly		23.74 (3.17-177.7)**
Processed meat		
Less than once a week	9.158**	1
At least once a week		4.75 (1.60-14.09)**
Milk		
Once a week or less	7.343**	1
At least several times a week		10.03 (1.55-418.93)*
Vegetables (10% CH)		
Once a week or less	5.143*	1
At least several times a week		7.53 (1.15-316.93)*
Pulses (legumes)		
Less than once a week	7.027**	1
At least once a week		4.01 (1.31-16.31)**
Grain bread /pasta / cereals		
Once a week or less	11.576***	1
At least several times a week		8.75 (2.03-37.8)**
Confectionary (Cakes, cream, ice-cream)		
Rarely	11.965***	1
At least monthly		5.74 (1.89-23.22)**
Fruits compotes		
Less than once a week	19.578***	1
At least once a week		7.47 (2.59-23.11)***
Herb teas		
Less than once a day	12.465***	1
At least once a day		4.78 (1.77-13.59)***

OR: odds ratio; CI: confidence interval; CH: carbohydrates;
*p<0.05; **p<0.01; ***p<0.001

In the present study, the subjects were invited to the doctor's office, and the population sample had a higher mean age. It is recognized that inviting the subjects to the doctor's office may influence the selection. Recruitment by invitation may select primarily subjects with a higher availability, more free time or possible co-morbidities. This may explain the high prevalence of IBS subjects in our sample.

The prevalence of IBS was higher in women (as most studies have found), but it did not reach statistical significance (Chang *et al.,* 2006; Spiller, 2005). The prevalence was also increased in older people. Even if the IBS incidence was shown to decrease with age (Hillilä and Färkkilä, 2004), the prevalence was high in elderly (Grundmann and Yoon, 2010) making it an overlooked problem (Agrawal *et al.,* 2009). Female gender and increasing age are associated with higher consultation rates in most studies in both western and developing countries, although not all agree (Rey and Talley, 2009).

Education level and profession did not influence the prevalence of IBS. In different populations those with higher educational levels or professional people were more likely to be physically active (Dowler *et al.,* 2001) and have a healthy diet (Johansson *et al.,* 1999). However, no association with socioeconomic class or education has been reported (Hillilä and Färkkilä 2004, Ford *et al.,* 2008). Also, low socioeconomic status in childhood may carry an increased risk of suffering with IBS in adulthood (Rey and Talley, 2009). Similar with other data, IBS subjects in our study had more commonly gastrointestinal co-morbidities in their past history, but not psychiatric disorders (Talley *et al.,* 2001). Higher mean age in IBS subjects may explain the increased prevalence of cardiovascular and loco-motor diseases in the IBS subjects. Comparable with other studies, smoking and alcohol was not more common in IBS subjects. The general self-perceived well-being of IBS subjects was worse than in non-IBS. In a 10-year longitudinal study, inferior quality of life at baseline was a strong predictor for the new onset of IBS (Ford *et al.,* 2008). We used a food frequency questionnaire (FFQ) to capture habitual intake over an extended period (McNeill *et al.,* 2009). The FFQ is appropriate for exploring dietary patterns based on frequencies but has not been validated for estimating total intakes of energy or nutrients (Oellingrath *et al.,* 2011). The FFQ did not include portion sizes and calculating energy and nutrient intakes was not feasible. However, the reproducibility and validity of major dietary patterns assessed using FFQs have previously been found to be satisfactory for studying diet- disease relationships (Hu *et al.,* 1999). In our study, certain categories of food (canned food, processed meat, milk, high carbohydrates vegetables, pulses, whole cereals, confectionary, compotes or herb teas) were significantly related to IBS. Food may contribute to symptom onset through several mechanisms including food allergy and intolerance. Also, certain food may alter the composition of the luminal milieu, either directly or indirectly through effects on bacterial metabolism. Finally, IBS symptoms may develop following exposure to food-borne pathogens (Morcos *et al.,* 2009).

A specific food intolerance (for example, lactase deficiency) may explain the symptoms for a part of the patients (Spiller, 2005; Matthews 2005; Newcomer and McGill 1983; Arvanitakis *et al.,* 1977; Nanda *et al.,* 1989). Our study did not explore this kind of association: observational or interventional longitudinal studies are necessary for this (Mann, 2003; Ligthelm *et al.,* 2007).

Table XXV. Associations of IBS with frequency of food consumption - *Spearman test*

FOOD CATEGORIES	CORRELATION COEFFICIENT (R)
Canned food	0.279***
Processed meat	0.218 **
Potatoes	0.216 **
Cereals	0.208 **
Grain bread /pasta	0.162 *
Fruits compotes	0.337***
Herb teas	0.220 **

*p<0.05; **p<0.01; ***p<0.001

A cross-sectional study such as the present one may only reveal association and not causality between the studied elements. A correlation between the studied elements may have several explanations in our case.

Frequent consumption of a particular food may positively or negatively influence the presence of disease. For example, canned food, processed meat, milk, or fiber-rich products - 10% carbohydrate vegetables (carrots, onions, beets), pulses (beans, peas, soybeans, lentils), grain cereals / bread / pasta or sweet foods, like confectionary (cakes, cream, ice-cream), compotes, may affect digestive transit, gas production, gut biota and also may cause abdominal discomfort or pain.

The presence of IBS may lead, on the other hand to a specific lifestyle or diet, which may explain the increased use of herb teas in IBS subjects. The relationship between dietary factors and IBS independent of other potential confounding factors (for example, socioeconomic status) could not be evaluated without a multivariate modelling. A further study using a larger sample may permit a multivariate analysis and consequently may reduce the confounding factors.

Table XXVI. Eating habits among IBS and non-IBS subjects

EATING HABITS	Answers	Non- IBS		IBS		Significance
		No.	%	No.	%	
Breakfast	Not daily	55	35.3	14	37.8	
	Daily	101	64.7	23	62.2	p>0.05
Number of meals and snacks / day	1-2/day	57	42.2	18	51.4	
	3/day	48	35.6	14	40.0	p>0.05
	More than 3/day	30	22.2	3	8.6	
Home cooked food	1 /day or less	65	42.2	16	43.2	
	2 /day or more	89	57.8	21	56.8	p>0.05
Meal with family / day	1 /day or less	101	66.0	22	59.5	
	2 /day or more	52	34.0	15	40.5	p>0.05
Eating in a hurry (subjective perception)	No	117	78.0	21	58.3	
	Yes	33	22.0	15	41.7	p<0.05

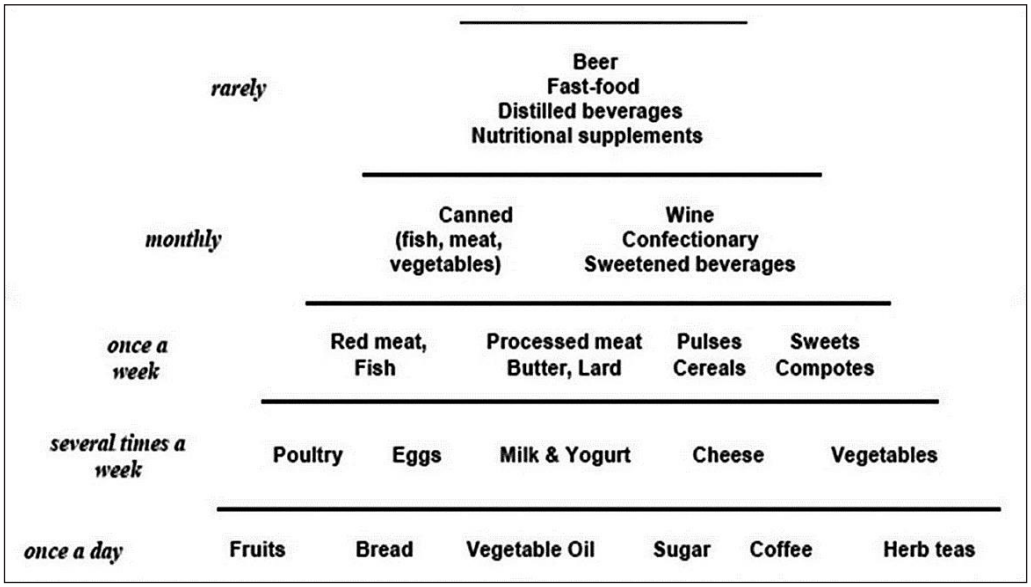

Figure 4. *Median frequency of food consumption*

II.3.5. Conclusions

This survey, conducted in a general urban population and using Rome III criteria revealed that IBS may be associated with a higher consumption of canned food, processed meat, legumes, whole cereals, confectionary, fruit compotes and herb tea. Further studies are needed to explore the mechanisms that may explain the association.

II.4. Nutritional and chemical induction of Type 2 Diabetes Mellitus (T2DM) and the efficiency of bariatric surgery in its reversal in animal models

For a long time, there has been an increasing interest in studying diabetes mellitus (DM), both in inducing and treating it, therefore experiments have been conducted on animal models and human subjects. From animal models, rats are often used because they are small, easy-to-maintain animals, have an acceptable life expectancy for experiments, respond well to the experimental factors to which they are subject, have a good recovery capacity and a high similarity to human anatomy and physiology thus they are representing viable models for a plethora of disorders (Dufrane *et al.*, 2006; Kleinert *et al.*, 2018).

DM is described as a chronic metabolic disease characterized by an impairment of the body's ability to produce or respond to insulin, which results in abnormal metabolism of ingested carbohydrates and, therefore, in increased levels of blood glucose. Besides its widespread in humans, DM is also one of the most common metabolic disorders that have been diagnosed in canines and felines (Catchpole *et al.*, 2013).

The molecular mechanisms of DM in humans and animals are described in the literature as almost similar. Hence, small laboratory animals, such as rats, are often used in research studies (Akash 2013). The most important clinical feature of DM is considered to be the incapacity of β-cells to generate enough insulin for the organism's metabolic pathway (Ganguly *et al.*, 2014). Also, lately there has been an increased interest in the connections that might exist between DM and the bariatric surgery (Kashyap *et al.*, 2010; Koliaki *et al.*, 2017). The treatment and reversing of diabetes have become a topic of high interest at the worldwide level with an increasing number of institutions dedicating resources and time into elucidating the best approach for this disease.

Advantages and disadvantages between bariatric surgery and low-calorie intake as a means of treatment are now debated (Hallberg *et al.*, 2019). Bariatric surgery stands by advantages such as glycemia improvement shortly post-op compared to low calorie intake (Steven *et al.*, 2015), high rates of T2DM remission compared to non-surgical groups (Salminen *et al.*, 2018) and 3-year remission rates over 60% (Purnell *et al.*, 2017). Bariatric surgery involves risks of complications, mortality, morbidity as well as the cost of the surgery itself, whereas the low calory intake imposes a substantial caloric restriction with severe energy restriction eventually leading to maintenance difficulties and possible negative long-term effects (8). A study conducted by Patkar on mice fed with a high-fat diet and then subject to either bariatric surgery or caloric restriction, has illustrated that Roux-en-Y gastric bypass surgery prevents the biologically adaptive hunger response (through hypothalamic AgRP responsible for feeding behavior and Neuropeptide Y - stimulates food intake with a preference for sources of carbohydrates) triggered by undernutrition and weight loss and suppresses weight-loss induced hypothalamic inflammation markers highlighting some of the molecular effects of bariatric surgery (Patkar *et al.* 2019).

Several studies have reported that postsurgical patients with T2DM showed more immediate improvements of insulin secretion, raising the possibility that bariatric procedures might induce specific responses to rectify abnormalities in β-cell function (Douros *et al.*, 2019a; Malin *et al.*, 2016).

It has been observed that prior to the actual weight loss, bariatric surgery lowers the glucose blood level in diabetic patients and studies on mice subject to vertical sleeve gastrectomy surgery displayed improved glucose tolerance and insulin secretion *in vivo* within 2 weeks of surgery (Douros *et al.*, 2019b; Batterham *et al.*, 2016). The most often used mechanism to induce DM in rats, is the chemical one because it is considered the fastest and the most cost-effective option. The most common chemical substance used for inducing DM is streptozotocin (Carneiro *et al.*, 2010; Rakieten *et al.*, 1963).

II.4.1. Aim

The main goal of the present animal model of induced T2DM was to assess the pathological consequences of diabetes and to screen potential therapies for the treatment of this condition as an alternative to current therapies used in house pets. Specifically, in our experiment we wanted to assess the potential benefits of a bariatric procedure using T2DM in rats as, despite its numerous advantages and rapid and definite improvements, it is not always the treatment of choice especially in house animals. Despite the increasing prevalence of this disease, it still has a broad area of unknown mechanisms regarding how the treatments work. For pharmaceutical and molecular findings, the easier and significantly less risky way is by using animal models, in our case Wistar rats, as they are a potential model for diet-induced obesity.

II.4.2. Material and methods

Our experimental study group consisted of 40 young Wistar rats (3 months old). For our experiment involving the bariatric surgery, we decided to use a low dose of STZ after a prolonged high fat diet (56 days), to induce T2DM in healthy, young, Wistar rats in order to avoid surgical complications and postoperative complications (Mossman *et al.*, 1986).

The protocol we used for inducing T2DM was previously validated in the literature (Damasceno *et al.*, 2011; Volpato *et al.*, 2008; Magalhães *et al.*, 2019).The experimental design of our study was structured in three well-built stages leading to the final results. The designed stages were the following: the pre-experimental phase, the experimental phase and the post-experimental phase. The study was approved by the Ethical Committee with the registration number 882/12.09.2018 and the animals were housed, cared for and managed according to Council Directive 86/609/EEC (Figure 5).

In the first phase of our study, we created the experimental groups, the diets and weighted each individual weekly.

The second phase involved the induction of T2DM and the bariatric surgery.

The last stage was conducted after the surgery and included observation and monitoring of the operated rats and the possible underlying mechanisms of the visible changes. Regarding the physical and biological materials, for the accommodation of subjects, we had specific cages with a grille for food and water.

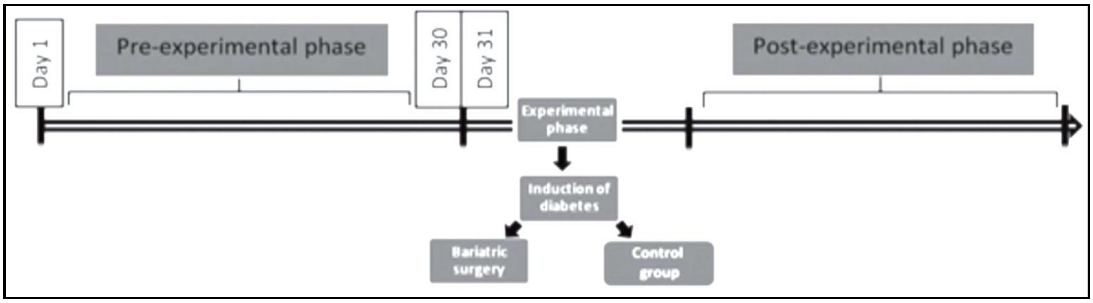

Figure 5. *The experimental protocol of the study*

For the weighting of the animals, we used an electronic weighing scale. Blood tests were performed at the Physiology Laboratory whereas the bariatric surgery was performed in collaboration with the surgical department. The measurement of glycaemia was performed using the *Glucometer OneTouch Select Plus*.

The pre-experimental protocol. The first stage of this protocol consisted of the allocation of the study groups: 40 Wistar male rats were randomly distributed in: the high fat diet group and the control group.

The next step was the establishment of the rats' diets. Food was chosen to cover all three macronutrients (proteins/lipids/carbohydrates). The difference between the two groups was the addition of excess saturated and unsaturated fat, with a ratio of 17.4% protein, 42.9% carbohydrates and 39.7% fat in the high fat diet group. The composition of the hypercaloric diet as well as the macronutrients can be observed in Table XXVII. The control group received smaller weights of mixed seeds and sunflower seeds.

Food was given at two different intervals during the day, in the morning and in the evening whereas the water was changed once every two days. The light cycle was the natural one (12 hrs. day/ 12 hrs. night) without artificial lighting.

Table XXVII. The foods utilized for the normal diet and the hypercaloric diet with their corresponding macronutrients and weights used

FOOD		Fats				Carbohydrates			Protein	Cal. Breakdown (100g)		
		Total	Sat	Poly unsaturated	Mono unsaturated	Total	Diet Fibers	Sugar	Total	Fat	Carb	Prot.
Mixed Seeds	ND (50)	23.8g	3.46g	13.41g	5.93g	9.140g	3.60g	0.905g	11.83g	72%	12%	16%
	HD (100)	47.7g	6.93g	26.82g	11.86g	18.28	7.20g	1.81g	23.66g			
Puffed wheat with sugar	ND (40)	0.64g	0.10g	0.29gg	0.22g	35.98g	0.64g	21.98g	2.380g	4%	90%	6%
	HD (20)	0.32g	0.05g	0.145g	0.11g	17.99g	0.36g	10.99g	1.190g			
Sunflower seeds	ND (50)	25.0g	2.50g	16.665g	5.00g	10.00g	5.00g	1.665g	6.830g	77%	13%	8%
	HD (100)	50.0g	5.00g	33.33g	10.00g	20.00g	10.00g	3.33g	13.66g			
Fruit yoghurt (Activia)	ND (50)	1.00g	0.50g	0.00g	0.00g	11.00g	0.00g	9.50g	2.05g	15%	72%	13%
	HD (50)	1.00g	0.50g	0.00g	0.00g	11.00g	0.00g	9.50g	2.05g			
Plain biscuits	ND (20)	1.00g	0.00g	0.00g	0.00g	13.50g	0.00g	1.50g	1.50g	13%	78%	9%
	HD (20)	1.00g	0.00g	0.00g	0.00g	13.50g	0.00g	1.50g	1.50g			
Cornflakes	ND (40)	0.18g	0.054g	0.096g	0.034g	35.98g	1.24g	3.74g	2.652g	1%	90%	9%
	HD (20)	0.09g	0.027g	0.048g	0.017g	17.99g	0.62g	1.87g	1.326g			
Green lettuce	ND (100)	0.15g	0.020g	0.082g	0.006g	2.79g	1.30g	0.78g	1.36g	8%	62%	30%
	HD 100)	0.15g	0.020g	0.082g	0.006g	2.79g	1.30g	0.78g	1.36g			
Carrots	ND (25g)	0.06g	0.008g	0.028g	0.002g	2.395g	0.70g	1135.0g	0.232g	5%	87%	8%
	HD (25g)	0.06g	0.008g	0.028g	0.002g	2.395g	0.70g	1135.0g	0.232g			
Apples	ND (40)	0.06g	0.01g	0.020g	0.002g	5.524g	0.96g	0.104g	4.156g	3%	95%	2%
	HD (20)	0.03g	0.005g	0.010g	0.001g	2.762g	0.48g	0.052g	2.078g			
Total daily food intake	ND HD	787.680 kcal 1471.96 kcal										

After we created the groups and established the hypercaloric diet, the animals were weighted weekly in order to monitor their progress regarding the weight gain. The purpose of these procedures was to induce obesity and to create a proper environment for the development of T2DM.

The glycemic control was conducted in the mornings before food was given. At baseline, the fasting glucose of all animals was in the normal range.

It is important to be mentioned that side veins, dorsal vein and ventral artery were used for the peripheral blood sampling. After the blood sampling was finished, the experiment continued with either hypercaloric diet or normal diet, depending on the experimental group, for another period of 30 days. The purpose of this part of our study was to try to induce a pronounced increase in insulin resistance in the high fat diet group.

Induction of diabetes. The animals from the high fat diet group received their respective diets for a period of 30 days, and on the day 31, a single dose of STZ was administered intraperitoneally (35 mg/ kg body weight) to animals fasted for 12 hrs.

We used this dose of STZ because it is low enough to guarantee the development of type 2 diabetes in rats which received a high fat diet without causing absolute insulin absence for evaluating the bariatric procedure.

We have induced diabetes to our animals following specified protocol. Blood glucose, temperature and vital functions were monitored the day before the substance was used. The dose of streptozotocin used was calculated for the current weight of each individual. After the injection of the substance at the intraperitoneal level, an individual daily observation file was kept with all the data observed during the development and manifestation of diabetes.

For the next stage of our experiment, we randomly assigned the rats from the high fat diet group in two groups: 10 rats received the bariatric surgery intervention, the other 10 were used as controls.

Bariatric surgery. A sleeve gastrectomy was conducted, resecting about 70% of the stomach, including most of the fundic portion (which in the rat is the bottom of the stomach). A vascular forceps was used to outline the area to be removed.

The gastrorrhaphy was conducted with an invaginating continuous polypropylene hand-sewn suture (Schimieden pattern). Hemostasis and suture-line integrity was checked, and an additional stitch was applied when necessary. Subcutaneous fluids were administered, and body warming was performed.

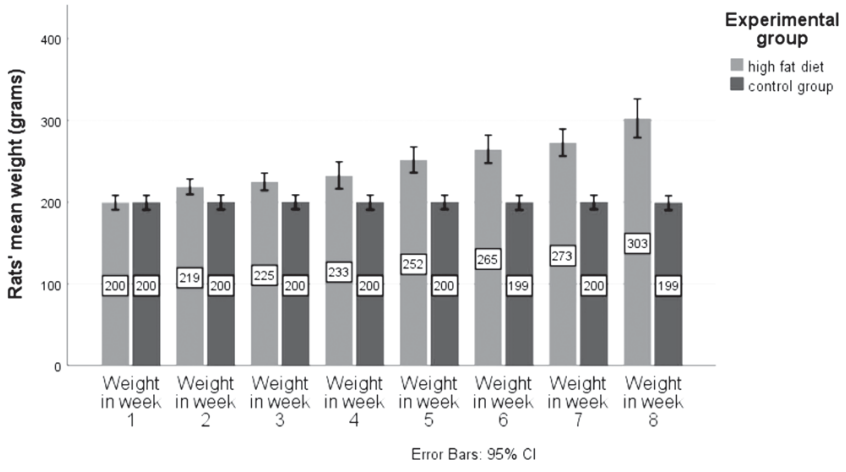

Figure 6. *The evolution of the rats' mean weight from week 1 to week 8 of normal diet, as well as hypercaloric diet.*

Both groups started at a weight of 200 g and significant differences were observed from week 2 as follows week 2- $p=0.004$, week 3- $p<0.001$, week 4- $p=0.001$, week 5- $p<0.001$, week 6- $p<0.001$, week 7- $p<0.001$, week 8- $p<0.001$. The high fat diet group exhibited a significant

and constant increase in weight over the 8 weeks period going from a mean weight of 200g to a mean weight of 303g, while the control group maintained a constant 200g mean weight.

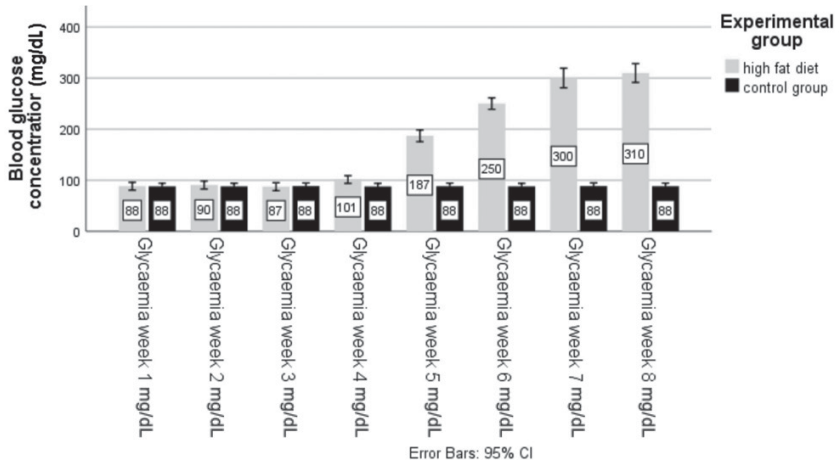

Figure 7. *The evolution of the rats' glycemia from week 1 to week 8 pre-surgeries on normal diet (control group) and hypercaloric diet (high fat diet).*

Both groups started at the same glycaemia level (88 mg/dL) and no significant differences were observed for the first 3 weeks between the 2 groups (week 1- p=0.623, week 2- p=0.111, week 3- p=0.238) with this aspect changing from week 4 (week 4- p<0.001, week 5- p<0.001, week 6- p<0.001, week 7- p<0.001, week 8- p<0.001.Throught the 8 week period, the control group maintained a constant glycaemia level (88 mg/dL) while for the fat-diet group it kept increasing and reached 310 mg/dL.

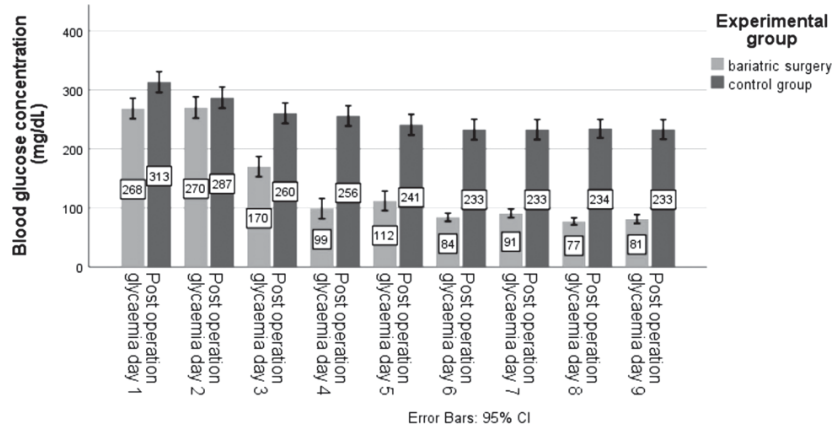

Figure 8. *The evolution of the fasted glycaemia after the bariatric procedure over a 9 days' period in control and bariatric surgery group, both fed with a hypocaloric diet.*

The control group started with a glycaemia of 313 mg/dL, while the bariatric group started at 268 mg/dL. All post-operation glycaemia values were significantly different between groups for all supervised days (p<0.001) (day 1- p<0.001, day 2- p<0.001, day 3- p<0.001, day 4- p<0.001, day 5- p<0.001, day 6- p<0.001, day 7- p<0.001, day 8- p<0.001, day 9- p<0.001). After a 9 days observation period, the glycaemia of the bariatric group reached normal values (81 mg/dL) while for the control group it still remained high (233 mg/dL).

No food was given for 48 hrs. and starting with day three post-operated rats were given low- caloric foods (Table XXVIII).

Data were statistically analyzed, and all results are expressed as mean± standard error of the mean (SEM) and *ANOVA* for repeated measurements was applied using IBM *SPSS Statistics version 17.0.*

Table XXVIII. The foods utilized for the hypocaloric diet fed to both groups (control and bariatric surgery) post-op with their corresponding macronutrients and weights used

FOOD		Fats				Carbohydrates			Proteins	Cal. Breakdown (100g)		
		Total	Sat	Poly unsaturated	Mono unsaturated	Total	Diet Fibers	Sugar	Total	Fat	Carb	Prot.
Green lettuce	(100g)	0.150g	0,02	0.082g	0.006g	2.79g	1.30g	0.780g	1.360g	8%	62%	30%
Arugula	(50 g)	0.330g	0.043g	0.159g	0.024g	1.825g	0.80g	1.025g	1.290g	19.4%	47.2%	33.4%
Carrots	(25 g)	0.060g	0.008g	0.028g	0.020g	2.395g	0.70g	1.135g	0.232g	5%	87%	8%
Apples	(20 g)	0,034g	0.005g	0.010g	0.001g	2.762g	0.48g	0.052g	2.078g	3%	95%	2%
Organic Pap Multicereal	(100g)	3.900g	0.600g	0.000g	0.000g	69.70g	7.90g	1.000g	12.10g	3%	83%	14%

Table XXIX. The glycemia of the rats (mean) after the bariatric surgery compared to controls with warm blankets.

Day	Control group	Bariatric group
Day 1	313 mg/dL	268 mg/dL
Day 2	286 mg/dL	270 mg/dL
Day 3	260 mg/dL	170 mg/dL
Day 4	256 mg/dL	99 mg/dL
Day 5	241 mg/dL	112 mg/dL
Day 6	232 mg/dL	84 mg/dL
Day 7	232 mg/dL	91 mg/dL
Day 8	234 mg/dL	77 mg/dL
Day 9	233 mg/dL	81 mg/dL

II.4.3. Results

The pre-experimental results. The animals from the high fat diet group gained constant weight during the 8-week period, while the weight of the control group remained constant.

When we analyzed the weight gain only in the high fat diet group, the results showed statistically significant increases from week to week (week 1 to week 2 $p= 0.001$, week 2 to week 3 $p= 0.022$, week 3 to week 4 $p= 0.028$, week 4 to week 5 $p=0.023$, week 5 to week 6 $p=0.003$, week 6 to week 7 $p=0.003$, week 7 to week 8 $p=0.022$) (Figure 6).

In addition, as expected, the differences regarding the weight between the high fat diet group and the control group were statistically significant from week 2 to week 8 ($p<0.05$).

Regarding the glycaemia (measured in mg/ dL) our statistical analysis revealed that it took some time until the differences between groups became significant. For the first three weeks p was non- significant ($p>0.05$), but the differences became significant starting from week 4 ($p<0.05$) (Figure 7).

After this statistical analysis, it was possible to conclude this first stage. In the next part of our experiment, we divided the twenty rats from the high fat diet group which already met the obesity criteria, in two distinct groups: one group received the bariatric procedure, the other group of rats was used as a control.

Post-operative evolution and results. After the bariatric surgery, the ten subjects were observed. The operation was shown to be well performed without the occurrence of post-operative complications. Due to the lack of food administration for the first two days post-operation but only the use of infusion food (saline, glucose 33%), the rats lost about 20g of body weight. Blood glucose was checked only in the mornings before food was given.

The post operation glycaemia values were significantly different between the bariatric surgery group and the control group starting from day one($p<0.005$) (Figure 8).

Based on the presented figures and data, we can see that from the second post-operative period, the fasted blood glucose level begins to return to normal physiological values. Starting from days 4 and 5, normal values were observed in the bariatric surgery group. In Table XXIX, it can also be observed a decrease in the glycemia of diabetic control groups that is most likely due to the low-calorie diet they have been fed with, that started at the same time as the bariatric group. As expected, the surgical procedure showed the benefit of stimulating a rapid decrease of blood glucose concentration. Therefore, when the pancreas and liver lose some of the lipid tissue, they can perform their functions under normal conditions.

II.4.4. Discussion

The symptoms of diabetes are relatively similar between humans and animals. The similarities continue as it is known that sedentary and inadequate nutrition rich in simple carbohydrates and lipids leads to obesity in both humans and animals.

Knowing the evolution and symptoms of diabetes mellitus, we decided to study through an animal experimental model a therapeutic process applicable by a bariatric surgery technique in obese rats. We induced diabetes mellitus through a prolonged high fat diet followed by the administration of a beta- cytotoxic drug, streptozotocin (STZ).

Regarding the molecular mechanism, "streptozotocin diabetes" is caused by the necrosis of the pancreatic beta-cells, and this agent is the first choice for diabetes induction in animal models (Magalhães *et al.,* 2019; Damasceno *et al.*,2014)

The results of our study suggest that the bariatric procedure in obese, type-2 diabetes suffering animals may lead to rapid and visible improvement by counteracting on the metabolic effects due to diet-induced body weight gain and streptozotocin injection. The rats from the bariatric procedure group presented a lower glycaemia just after a few days post operation. These results are not surprising, and they are in concordance with those found in the literature (Kleinert *et al.,* 2018; Rodrigues *et al.,*1997). The improvements brought by the various bariatric procedures are well documented (Chouinard *et al.,* 1992).

Regarding the underlying mechanism of action of vertical sleeve gastrectomy (VSG), currently there are several possible hypotheses on how and why it affects the impaired glucose homeostasis specific to T2DM by normalizing it, but subsequent studies on the matter are required. An impaired glucose homeostasis is determined by a combination between insulin resistance and pancreatic β-cell's incapacity to release sufficient insulin with elevated blood glucose levels as a consequence. One possible explanation of how VSG can repair the imbalance is through the weight loss, rapidly observed post-op, determined by a reduced energy intake as a consequence of little to no malabsorption of nutrients; VSG determines the rate increase at which nutrients enter the small intestine. Through procedures like bypass and VSG, the delivery of ingested glucose into the systemic circulation is improved causing a spike in plasma glucose concentrations (Bradley *et al.,* 2012). VSG determines an accelerated gastric emptying of liquid and solid nutrients therefore it affects the nutrients absorption leading to faster and higher peaks of blood glucose levels following the rapid delivery of carbohydrates to the absorptive surface of the intestine, but also a rapid clearance from the circulation. These changes have been linked to increased glucagon-like peptide 1 levels and insulin responses. Gut peptides like gastrin or peptide YY and cholecystokinin have been observed to be increased after VSG (Douros *et al.,* 2019). Another interesting hypothesis involves the gut microbiome

changes as it was observed that post surgery the bacterial profile becomes leaner, and several studies have illustrated that by the use of fecal transplants from surgery treated mice to recipient/germ-free mice has led to weight-loss and reduced adiposity. Altogether, changes in weight, nutrient absorption, gut microbiota, circulation bile acids, GLP-1 are likely to contribute to the antidiabetics effects (Batterham *et al.,* 2016).

Although it is established as a well proven method to combat obesity in humans, bariatric procedures are rarely used as a therapeutic method to combat obesity and/or diabetes in house animals (Suzuki *et al.,* 1986; Al Wadani *et al.,* 2017). In the present study, this therapeutic approach was based on the desire to treat the cause of diabetes and not the symptoms by influencing the level of glucose present in the blood. All pharmaceutical drugs with biological or hormonal synthesis are strictly aimed at regulating glycemic levels.

The objectives of this study were to observe the efficiency of such a therapeutic protocol on the recovery from T2DM through bariatric surgery as a potential therapy for house pets by using animal models - Wistar rats. In addition, this experimental design was intended as a scientific model for obesity research and type 2 diabetes using animal protocols.

Based on this study, it was possible to demonstrate that the non-specific diet based on a hypercaloric consume of lipids (saturated and unsaturated) and carbohydrates (simple and complex) causes a debilitating state of health which is mainly characterized by obesity. It is also important to note that, according to the diet composition, the amount of saturated fatty acids is very limited, but considering our results, the obesity induction was successful and allowed us to continue with STZ injection and bariatric surgery as it also determined elevated glycaemia levels.

Maintaining such a chaotic eating pattern that causes obesity in subjects may lead to complications characterized by increased insulin resistance and secondary to type-2 diabetes, but such parameters were not measured in our present study in the absence of streptozotocin injection.

Therefore, treating obesity problems in pet animals may include a variety of therapeutic protocols consisting of a combination of medications, specific diets and surgical bariatric techniques. In order to perform the bariatric surgery, the patient must be monitored and examined in such way not to affect its health more by this intervention. By applying the bariatric method of reducing the stomach by surgical removal along the greater curvature, visible improvements were seen on both weight loss and plasma glucose adjustment without the use of insulin in less than 4 days after the operation.

II.4.5. Conclusions

The positive effect of bariatric surgery on glycemic control of type-2 diabetes is already well known as the bariatric procedure provides a therapeutic response faster than conventional diets that pet-owners often do not administer or do not follow in a well-established program although our study is limited by not measuring a set of parameters (glycemia before streptozotocin administration, circulation insulin, peptide C) important to such an experimental design. Thus, alternative diets to the ones provided by literature have been illustrated and we strongly encourage further studies to add on our results and go even further, by trying to better characterize the mechanism by which VSG actions.

However, it is important that after the bariatric procedure, the animals maintain a hypocaloric diet, specific for their species and their physiological needs in order to avoid a possible relapse.

B. CONSUMPTION OF ALCOHOL, TOBACCO AND DRUGS IMPACT ON HEALTH STATUS

Alcoholism is a chronic disease which affects multiple organs and tissues and an adjusted management of it may have an overall positive impact on individual health. A possible mechanism of inducing toxicity in alcoholism could be the mechanism of oxidative stress. Even it is accepted that there is an increased oxidative stress status at the patients with alcohol dependence, mainly expressed through a reduction in the general antioxidant activity and a significant increase of the lipid peroxidation processes (Seiva, 2009a), the precise impact of the oxidative stress markers after the complex processes of alcohol withdrawal is questioned (Zima *et al.,* 2001). The relevance of the oxidative stress markers after the complex processes of alcohol withdrawal is still controversial, so for all the markers of the oxidative stress, as in the case of the main antioxidant enzymes (superoxide dismutase-SOD and glutathione peroxidase-GPX), there are previous reports stating both increased and decreased activities ((Guemouri *et al.,* 1993) - increased; (Huang *et al.,* 2009) - decreased, for superoxide dismutase) ((Lecomte *et al.,* 1994) - decreased; (Girre *et al.,* 1990) - no modification at all, for glutathione peroxidase). The other side of the oxidative stress balance, which is represented by the reactive oxygen species, is reported to suffer controversial modifications during the process of abstinence. Thus, when talking about malondialdehyde-MDA as the main marker of the lipid peroxidation processes, previous reports described increased level in patients with alcohol withdrawal (Soardo *et al.,* 2005; Peng *et al.,* 2005) as well as clear reductions in MDA levels following alcohol withdrawal (Lecomte *et al.,* 1994, Situnayake *et al.,* 1990). In the case of all three markers of oxidative stress status which we determined (SOD, GPX and MDA), the levels after one week or one month of abstinence were significantly altered when compared to controls (Alexinschi *et al.,* 2014).

Tobacco consumption or smoking cigarettes it is a voluntarily habit which causes addiction. In the cigarette smoke were identified 4,800 toxic substances existing, and nicotine is the one that causes addiction, which is classified by The Diagnostic and Statistical Manual of Mental Disorders, 4th Edition, Text Revision (DSM-IV-TR) (American Psychiatric Association, 2000) and 5th Edition (DSM-5) (American Psychiatric Association, 2013) as a disease. Criteria for this diagnosis include for a smoker at least three of the following situations, in the last year: -Smoking more intense than normal; -Strong desire to smoke, despite all efforts to reduce the number of cigarettes smoked per day; -Tolerance to nicotine, manifested by the reduction of its effect and the need of increasing the number of cigarettes to achieve the same effect; -Withdrawal symptoms after discontinuing smoking; -Increase time spent smoking / acquiring cigarette, giving up to different social / educational activities; -Continue smoking despite the danger of ill health awareness.

The nicotinic withdrawal was also classified apart as a disease induced by nicotine consumption, according to DSM-IV-TR and DSM-5. It occurs in some people with major symptoms in the early days: a strong desire to smoke, difficulty concentrating, headache, nervousness, insomnia, irritability and even depression, increased appetite, reduced heart rate.

These symptoms may disappear within a month. Smoking is responsible worldwide for more than 85% of all deaths due to lung cancer, being the major cause of emphysema, bronchitis, Chronic Obstructive Pulmonary Disease (COPD) and cardiovascular diseases.

Tobacco may also determine neoplasms in the oral cavity, esophagus, pancreas, stomach, larynx, it can complicate recovery after surgery, delay healing of wounds and fractures, decreases bone density, causing osteoporosis and it can affect the excretory and genital systems, skin and mucous membranes (Eriksen *et al.,* 2012; Bosînceanu *et al.,* 2014; Postolache *et al.,* 2013; Postolache *et al.,* 2014).

Drugs consumption represents one of the most dramatic issues for Romanian youth health status and one of the most challenging problems for medical prevention, since Romania is no more a transit country, and it became a place where consumption of illegal substances is a real fact. Licit or socially accepted drugs (tobacco or alcohol) or illicit drugs (stimulant, narcotic or hallucinogenic substances) consumed by high school students affect their nervous system, which is in the process of development, and anticipate extensive drug use later or as university students (Atkinson *et al.*, 2003; Zani and Palmonari 2003; Bellido *et al.*, 2008).

Lifestyles involving regular drug use include nonconformism over traditional values, a trait found among most adolescents today. Difficult family relationships, lack of educational interests or states of alienation and revolt, as well as negative emotional experiences are factors that determine drug use among adolescents (Zani and Palmonari 2003; Bellido *et al.*, 2008).).

Studies do not indicate a specific type of personality associated with drug use. Teenagers are tempted to try drugs for a multitude of reasons, such as curiosity, the desire to live another state of consciousness, to integrate into a new group, to avoid physical pain or any other severe problem, or simply to "spice" a lifestyle become boring (Ieniştea, 1982; Nădăşan, 2003).

Health related problems first among high school students and later to university students is the consequence of the developing of these noxious habits.

Alcohol and tobacco advertising is frequently associated with earlier initiation and higher rates of consumption among youth (Jernigan *et al.*, 2017)

Recent research proved that alcohol overconsumption plays a mediating role in the relationship between tobacco smoking and illegal drugs use (Delgado-Lobete L *et al.* 2020).

During their academic years, medical students are taught about diseases, how to identify symptoms and to give a correct diagnostic. It is proved that students can suffer from diseases they learn about, and it is speeded among students who are trained in Psychology or Medical Sciences. When studying a psychological disturbance, students may experience more psychological distress regarding the members of their families or their own psychological health. Also, while learning about a physical disease, students can interpret a physical disturbance as a sign of a serious illness.

Medical students by misinterpreting could experience the fear that they suffer from a disease. Some studies showed that this kind of beliefs (about having a severe disease) is persistent in time, despite medical examination or laboratory analysis and it is a temporary kind of hypochondria (Harding *et al.*, 2008a; Sinthubua *et al.*, 2016).

This situation is like hypochondria and could be related to *Medical Student Syndrome* (MSS). Other used terms were nosophobia, hypochondria of medical students it is, a mild form of anxiety or transient hypochondriasis.

In the case of hypochondria, the patient always seeks a medical diagnosis, but in case of MSS no increase in the number of medical consultations is revealed. Students identified with MSS will not look more frequently to have a medical check but the belief or the fear that they were having a disease is present. This is a unique type of hypochondriasis which can lead to health anxiety in strong relationship with the diseases medical students focus their attention on during medical training.

The rates of MSS among medical students vary from 5-70% (Harding *et al.*, 2008b; Howes and Salkovskis 1998; Weck *et al.*, 2014). Consequently, scientific reports regarding the effects of progressing through medical education on health anxiety are scarce and contradictory. Studies show that the fear of having a disease may persist over the years during medical studies (Collier, 2008; Woods *et al.*, 1966; Zahid *et al.*, 2016) and that some factors influence the level of fear: personality traits, fantasy proneness, clinical year, thought suppression (Candel and Merckelbach, 2003). Nevertheless, results focusing on medical students' stress, fear of illness or burnout show contradictory data when are compared to other students (Hardy *et al.*, 1997).

My interest regarding this area is reflected by the following articles:

Florin Petrariu, Ovidiu Alexinschi, Roxana Chirita, Vasile Chirita, Alin Ciobica, Manuela Padurariu, Radu Lefter, Romeo Dobrin, Radu Popescu, Emil Anton, Oana Arcan, Daniel Timofte .THE DYNAMICS OF SOME OXIDATIVE STRESS MARKERS IN 3, 6 AND 12-MONTHS ALCOHOL ABSTINENT PATIENTS: POSSIBLE RELEVANCE FOR THE USAGE OF ANTIOXIDANTS IN ALCOHOL WITHDRAWAL *Revista Română de Medicină de Laborator* 2014; 22(4): 451-457 / doi:10.2478/rrlm-2014 / **IF=0.239**

Ovidiu Alexinschi, Roxana Chirita, Padurariu Manuela, Alin Ciobica, Romeo Dobrin, **Florin Dumitru Petrariu,** Daniel Timofte, Vasile Chirita. ADDITIONAL DEMOGRAPHIC AND CLINICAL EVIDENCE ON THE RELEVANCE OF THE SYSTEMIC THERAPY IN ALCOHOL DEPENDENCE. *Revista Medico-Chirurgicala* 2015; 119(4): 1120-1127 / **PMID: 26793858**

Roxana-Maria Nemeş, Paraschiva Postolache, Adeline Ţintilă, FD Mihălţan, **FD Petrariu.** ASPECTS OF PHYSICIAN-PATIENT COMMUNICATION IN THE PROGRAM OF SMOKING CESSATION. *Revista Medico-Chirurgicala* 2015; 119(1): 23-30 **/ PMID: 25970938**

Petrariu FD, Mezei A, Huţuleac A, Dobrin PR, Knieling A. STUDY ABOUT THE ASSOCIATED USE OF DIFFERENT TYPES OF DRUGS BY HIGH SCHOOL STUDENTS
Revista Medico-Chirurgicala 2011; 115(3): 919-926 / **PMID: 22046809**

Muraru ID, Catalina Munteanu, Iorga M, **Petrariu FD**. INVESTIGATING MEDICAL STUDENTS' HEALTH CONCERNS DURING THEIR ACADEMIC STUDIES
Medical-Surgical Journal - Revista Medico-Chirurgicala 2019; 123(4): 728-734
Web of Science Core Collection - Emerging Sources Citation Index **/ WOS: 000504019200022**

PROJECT EURO-URHIS 2 / "EUROPEAN SYSTEM OF URBAN HEALTH INDICATORS PART TWO: URBAN HEALTH MONITORING AND ANALYSIS SYSTEM TO INFORM POLICY" No. 223711. Project funded by the European Commission through the Framework Program 7 (2009-2011).

PROJECT e-Mediqual POSDRU 86/1.2/S/63815. MODUL INTEGRATIV PENTRU STUDIUL PLĂMÂNULUI. Editors: Doina Azoicăi, Daniela Boișteanu, Irina Draga Căruntu, Manuela Ciocoiu, Daniela Cristina Dimitriu, Daniela Druguș, Laura Gheucă-Solovăstru, Cristina Grigorescu, Beatrice Gabriela Ioan, Traian Mihăescu, Cristina Elena Moldoveanu, **Florin Dumitru Petrariu**, Ovidiu Rusalim Petriș, Cristinel Ionel Stan, Dragomir Nicolae Șerban, Ionela Lăcrămioara Șerban, Antigona Trofor, Traian Țăranu. Editura „Gr. T. Popa" U.M.F. Iași, 2016, 237 pages, ISBN 978-606-544-410-2
CAPITOLUL XVI. Florin-Dumitru Petrariu. Managementul organizațional modern al patologiei pulmonare obstructive cronice, 229-237.

II.5. The dynamics of some oxidative stress markers in 3, 6 and 12-months alcohol abstinent patients: possible relevance for the usage of antioxidants in alcohol withdrawal

II.5.1. Aim

In the present report we were interested in studying the importance of oxidative stress status in the alcohol withdrawal processes, by determining some oxidative stress markers after an even longer term at 3, 6 and 12 months of abstinence and comparing them to the baseline and the control group.

II.5.2. Material and methods

62 patients were selected between January 2013- July 2014, aged between 26 to 79 years old (average 44.8 ± 3.7 years), all of them males. They met the *Diagnostic and Statistical Manual of Mental Disorders IV* Text Revision diagnostic criteria for alcohol dependence. Of

course, alcohol consumption was stopped abruptly at admission. Exclusion criteria were the following: illicit drug use, chronic systemic disease or severe mental disorders. All the patients were treated with diazepam or lorazepam. In this way, 33 (at baseline), 14 (at 3 months), 14 (at 6 months) and 15 (at 12 months) patients from the initial 62 had their blood collected, since some of them decided to drop out of the study or refused blood collection at some point. The control group (n=32) included healthy, sex and aged-matched subjects without any psychiatric or physical illnesses. Also, the controls did not meet the criteria for alcohol abuse/dependence or any abusive alcohol consumption in the last 2 months. Blood samples were obtained in the morning, before breakfast; after being centrifuged, the serum was then put into plastic tubes and stored at −40°C until measurement. Determination of SOD, GPX and MDA were performed by using "19160 SOD" or "GPX CGP1" Cellular Activity Assay Commercial Kits or by using classical and well-known methods (for MDA-10). The current study was performed under the approval of the Socola Hospital Ethics Committee. Also, signed consent was obtained from all patients, according to the World Medical Association Declaration of Helsinki, revised in 2000, Edinburgh.

Data Analysis The levels of oxidative stress markers were statistically analyzed using one-way analysis of variance (*ANOVA*). All results are expressed as mean ± SEM. Post hoc analysis were then performed using Tukey's honestly significant difference test in order to compare all groups (except control) between them. F values for which $p<0.05$ were regarded as statistically significant.

II.5.3. Results

Regarding the superoxide dismutase results, we observed a significant group difference ($p<0.0001$) (Figure 9), suggesting significant effects of alcohol abstinence on SOD specific activity. Also, post hoc comparisons showed a significant increase in the specific activity in all 3 time-related abstinence cases, when compared to baseline results: ($p < 0.0001$ at 3 months), ($p < 0.0001$ at 6 months) and ($p < 0.0001$ at 12 months) (Figure 9).

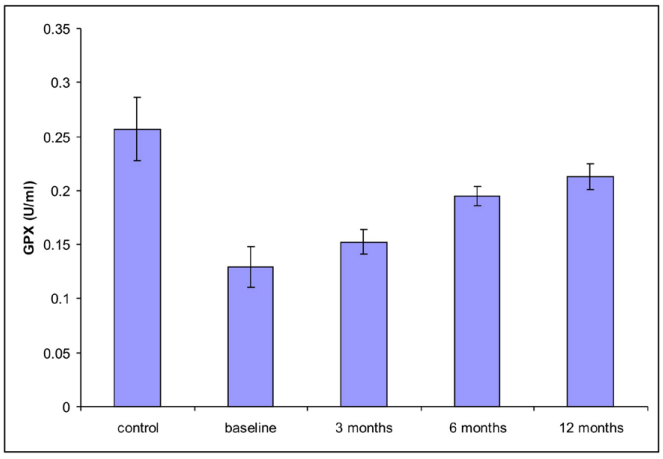

Figure 9. *Superoxide dismutase (SOD) specific activity in the serum of control subjects, baseline and alcohol abstinent patients after 3, 6 and 12 months. The values are mean ± SEM (n=32 in control group, n=33 in baseline, n=14 in 3 months group, n=14 in 6 months group, n=15 in 12 months group)*

Still, there was a significant decrease in the SOD specific activity at 3 ($p < 0.0001$) and 6 ($p < 0.0001$) months, when compared to the control group. On the other hand, there were no significant modifications when we compared the control group with the 12 months group ($p =0.99$). In addition, we also observed a progressive increase in SOD's specific activity, as the

time from withdrawal increased, especially from 3 to 12 months (p =0.0003) and also from 6 to 12 months (p =0.009) (Figure 9).

When it comes to the results of the other antioxidant enzyme, which was GPX, we could also observe a significant overall effect of the abstinence on enzymatic specific activity in our groups (p=0.0003) (Figure 10). Moreover, when we performed the post hoc analysis, we observed a significant increase in the specific activity of the enzyme, especially at 6 months (p =0.03) and 12 months (p =0.006), compared to the baseline group (Figure 10). However, the specific activity at 3 months was still significantly decreased (p =0.026), when compared to the control group (Figure 10). Additionally, there was a progressive increase in the GPX specific activity from the time of withdrawal, as showed for example by the significant increase in the 6 months group, when compared to the 3 months group (p =0.007). A significant difference was observed in the GPX specific activity between the 3 *vs.* 12 months group (p =0.001) (Figure 10).

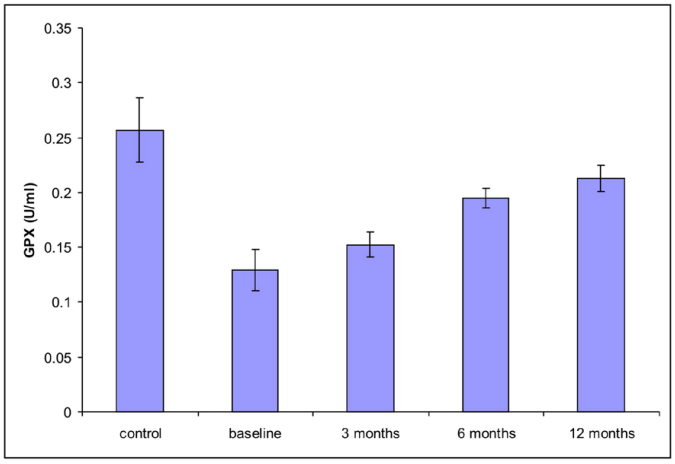

Figure 10. *Glutathione peroxidase (GPX) specific activity in the serum of control subjects, baseline and alcohol abstinent patients after 3, 6 and 12 months. The values are mean ± SEM (n=32 in control group, n=33 in baseline, n=14 in 3 months group, n=14 in 6 months group, n=15 in 12 months group)*

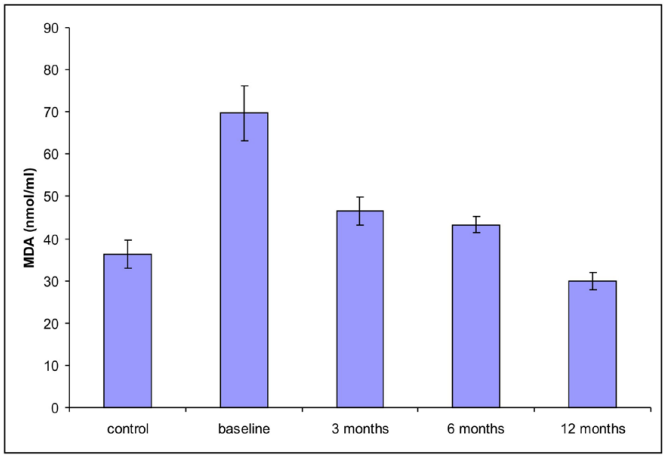

Figure 11. *The levels of malondialdehyde (MDA) in the serum of control subjects, baseline and alcohol abstinent patients after 3, 6 and 12 months. The values are mean ± SEM (n=32 in control group, n= 33 in baseline, n=14 in 3 months group, n=14 in 6 months group, n=15 in 12 months group).*

Regarding the levels of malondialdehyde, as a main marker for the lipid peroxidation processes, we also found significant differences between our study groups (p<0.0001). In

addition to that, when we performed the post hoc analysis, we observed a significant decrease for all the 3 cases we studied, when compared to the baseline group ($p = 0.003$ at 3 months), ($p = 0.01$ at 6 months) and ($p = 0.0002$ at 12 months) (Figure 11). Still, no significant modifications were noticed when we compared our 3 study groups ($p = 0.07$ at 3 months), ($p = 0.19$ at 6 months) and ($p = 0.23$ at 12 months) with the controls (Figure 11). Also, we observed a tendency for a progressive decrease of MDA in time, as showed for example by the significant decrease of the MDA levels in the 12 months group, as compared to the 6 months patients ($p < 0.0001$). Furthermore, a significant difference was observed in the GPX specific activity between the 3 vs. 12 months group ($p = 0.0001$) (Figure 11).

II.5.4. Discussion

In this way, the data we presented in this study confirmed again the increased oxidative stress status in alcoholic patients and even more importantly, we showed that there is a significant and progressive decrease in the oxidative stress status at 3, 6 and 12 months after the withdrawal process, as demonstrated by the increased levels of antioxidant enzymes and decreased rate of lipid peroxidation, when compared to baseline values. This data is an important continuation of our previous studies, in which we demonstrated a decrease in the oxidative stress status, one week and one month following the withdrawal, as showed by a significant increase in the specific activity of SOD, as well as by a decrease in MDA levels, when compared to baseline. In the case of all three markers of the oxidative stress status which we determined back then, the levels from one week or one month of abstinence were significantly altered when compared to controls, suggesting that severe and prolonged deficiency in their levels needs more than one month of abstinence to normalize (Alexinschi *et al.*, 2014).

All these aspects could lead to the idea of using antioxidant compounds in order to reduce or improve the damages produced by alcohol consumption/withdrawal. In this way, it was showed for example that procysteine, which is a glutathione precursor (Sinha-Hikim *et al.,* 2010), could increase the alcohol-depleted glutathione stores in various muscles of a rat model, following a period of abstinence, especially since it is known that alcohol consumption may result in numerous negative muscular effects (Otis *et al.,* 2010). Otis suggested that glutathione restoration therapy could provide therapeutic benefits to the overall antioxidant state of skeletal muscles, especially when it is used in conjunction with an established detoxification program for the recovering alcoholics (Otis *et al.,* 2010).

Another important antioxidant drug in this area of research is represented by N-acetylcysteine, which was experimentally used, for example, for the myocardial oxidative stress in alcoholic heart disease (Seiva *et al.,* 2009a). Also, it seems that alcohol related oxidative stress could be in fact inhibited by N-acetylcysteine (Ozaras *et al.,* 2003). Moreover, there seems to be an interaction between N-acetylcysteine's metabolism and the withdrawal processes, which could result in decreased oxidative stress levels (Seiva *et al.,* 2009b). Importantly, as in the case of the procysteine, the protective effects of N-acetylcysteine could also be explained by the fact that it is required for glutathione biosynthesis (Diniz *et al.,* 2006), which is of course an important antioxidant, with fundamental roles in preventing damages induced to important cellular components by the free radicals and various peroxides (Sies, 1997). Thus, drugs like glutathione, procysteine and NAC are right now in our attention for their possible therapeutic actions in the withdrawal processes, both in animal models, as well as for human patient studies. In this way, we generally demonstrated the fact that a decrease of the oxidative stress level is sustained by all measured parameters both on short term (Alexinschi *et al.,* 2014) and long term, as demonstrated through the results of the present report.

Thus, the metabolism of the oxidative stress could be a fundamental aspect in the mechanistic of withdrawal and perhaps it may represent a crucial point where other negative factors are meeting, resulting in this complicated set of events. However, there is a long way

until we can establish a clear relationship between antioxidant-related deficiencies and alcohol consumption/withdrawal time, especially considering the importance of free radicals in many metabolic reactions, but also due to the fact that in the present paper we actually showed a natural evolution for the oxidative stress status.

Regarding the limitations of the present study, we could add the fact that all the groups received B vitamins supplements that could have influenced our results (however all the subjects received the same combination of vitamins B_1 and B_6), also the lack of calculation power for this study, in order to see the number of subjects included (we used the patients which met the inclusion and exclusion criteria through the mentioned duration of the study, while trying to have a large enough group of subjects and controls), but also a more strict diet, BMI and alcohol quantity determinations before withdrawal.

II.5.5. Conclusions

Our results are suggesting that there is a significant and progressive decrease in the oxidative stress status at 3, 6 and 12 months after the withdrawal process, as demonstrated by the increased levels of antioxidant enzymes and decreased rate of lipid peroxidation, when compared to baseline values. This could be relevant for the beneficial and therapeutical actions of the antioxidants usage in the withdrawal processes.

II.6. Tobacco consumption - from daily habit to cessation

In Romania ISRA Center Marketing Research conducted a study in 2007 for Pfizer Romania Pharmaceutical Company which aimed to evaluate the incidence of tobacco consumption and the assessment of smoking behavior in Romania. Being asked: *"Is it possible to have health problems due to smoking?"* the majority of the respondents answered: "Yes!" (ISRA-Center-Marketing-Research, 2007). Due to the incidence and prevalence of smoking which increases every year, in 2007, the Ministry of Health started The National Program "Stop Smoking", which supplies medical and psychological counselling and therapy for smoking cessation. During the "Stop Smoking" program were established counseling and therapy centers for smoking cessation across the country, which were coordinated by pulmonologists with special training regarding the counseling of smokers (PN "STOP-FUMAT", 2007).

During the medical counseling meetings, usually the physician explains to the patient the harmful effects of smoking on health and its negative economic consequences. In the "Stop Smoking" program, after the initial counseling session, conducted by the specialist physician, patients voluntarily returned and attended a medical and psychological counseling provided. Pharmacological therapy included Bupropion and Varenicline for 2-3 months and helped the smoker to over-come the withdrawal syndrome by inhibiting the wish to smoke.

After the first consultation, patients followed 2 weeks of treatment, with a preliminary assessment of the efficacy. The second period of treatment was scheduled, for 2 to 3 months, depending on the drug used. Subsequently this treatment, the patient was checked for another 6 months.

The medical specialist-patient communication is a complex process of transmission of information, data and knowledge, connecting individuals, communities, groups, companies, ensuring collaboration and collaboration between them. The doctor-patient communication represents a social interaction which implies the existence of the two partners, one being the message emitter, and the other one the message receiver. Interpersonal communication is examined and analyzed according to several possible classifications. The communication channel can be auditory, olfactory, visual or tactile. Another classification is verbal and non-verbal. Communication can be written or oral. After the means used in the transmission of information, communication can be realized through auditory media, print media, audiovisual,

and electronic media (e-mail, audio and video files). Considering communication conditions, it can be face-to-face or remote communication (Knapp *et al.*, 2011).

The chronic respiratory pathology has brought us face-to-face with the effects of smoking, due to the patients suffering from COPD, chronic bronchitis and pulmonary emphysema. The communication with these smoking patients is present in the day-by-day activity, but even more within the anti-smoking program at the Rehabilitation Clinical Hospital from Iasi requires abilities in the interpersonal relationships like listening, asking, speaking, analysis and evaluation. All these native skills need to be tailored by a specific education and also on the basis of the subjective experiences, as the ability of advising is acquired in time.

Informing the people from Iasi about the existence of the program "Stop Smoking" used all the available means of communication, ranging from inpatients, hospital staff and students, to written press, radio and television. We encouraged smokers and their entourage to contact the counseling center a by using a mix between the positive and negative messages. We tried to change the vision of smokers and non-smokers, convincing smokers to be more responsible towards their own health and of the people around them and the nonsmokers to convince the smokers to give up this habit. All the details were previously debated with the media representatives, all the aspects concerning the communication being paid attention, even to the apparently minor ones. When the message was delivered audio-visually, the aspects of the posture, voice, audio-visual amplification were carefully analyzed. During the radio and television broadcasts, the persons showing interest could interact with us live and that were recommended to address to our center. Each time possible, the interaction with the audience was ensured, avoiding as much as possible the speeches. The message was insistently repeated using as much as possible present tense and imperative verbs.

The written press was used to underline the consequences on morbidity and mortality of the diseases caused by the active and passive smoking. The message *"These consequences equally affect both the men and women and depend on the number of cigarettes smoked per day, age and moment of start"* was spread presenting advantages of giving up smoking on short and extended periods, urging immediate action in giving up. Messages that underlined the negative aspects of smoking and the positive ones of giving up, confessions of the former smokers were used for the inpatients and the smokers in the hospital's staff, emphasizing the possibility of direct addressing to the center. The inpatients with chronic addiction had two different attitudes after discussing with the physician. Some of them requested help in giving up smoking, some others had no reaction.

For the smoking in patients who did not request out help, we started the minimal advice three minutes intervention, which is the most efficacious prevention action. The chances to succeed are bigger if the patient attends the counseling center compared to trying to give up by them. We avoided mentioning percent and we used assertions such as: *"A smoker dies each 5 minutes!"* or *"Give up smoking gives years to the life and life to the years".* If the medical staff would give the three minutes intervention minimal advice to each smoker, 2,200 years of life every one million people would be saved each year by preventing the occurrence of diseases caused by smoking (Trofor *et al.*, 2010).

Psychologically, the nonsmoking staff is more credible than the smoking one. Mass-media gave us the chance to implement educational programs which recommended that the nonsmokers not accept smoking and the smokers to give up by applying to the anti-smoking counseling center within the Rehabilitation Clinical Hospital from Iasi. It is important to mention that the smokers usually are tempted to ignore the danger in which they put the entourage. The process of counseling is possible, useful and needs to take place gradually.

The therapy starts at the moment the patient comes to the counseling center for giving up smoking, admitting that he/she wants to give up. This acceptance represents the first step in the therapeutic success.

In the first phase when communicator explains to the patient the path that needs to be followed, the moment of nicotine withdrawal syndrome is crucial. This syndrome is defined by the sum of all symptoms which occur when the intake of nicotine is cut-off after a long period of use. A special attention is granted to realize that giving up is difficult, to recognize this fact and to avoid panic.

The communication in this phase with the smokers and their relatives takes place in all the four situations: - one emitter and one receptor (face to face communication with the patient during the session); - one emitter and more receptors (the communication with the smoker and his relatives or a group of smokers, during the first session); - more emitters and one receptor: (medical counseling followed by the psychologically one, both given by a specialized person); - more emitters and more receptors (the public presentations with supportive and educational role) (Postolache *et al.*, 2013; Knapp *et al.*, 2011; Trofor *et al.*, 2010).

The style of communication is influenced by the personal sensitivity and the persuasion skills of the person who promotes the message, each physician having a particular style of interaction with patients, shaped up by his instruction, exercise and experience. The persuasion ability of the physician is revealed by his ability to formulate questions and make affirmations in the moment of interaction with the patient, while the personal sensitivity is the degree of the control over expressing his emotions.

In practice there are four personal communication styles are known to influence the quality of physician-patient relationship: analytical, respectful, expressive, and directive. The verbal and nonverbal communication between the physician and the smoker has different percentages, depending on the emitter and the receptor, the verbal part (7-10%), the vocal one (35-38%) and the visual one being the most representative (55%) (Knapp *et al.*, 2011; Trofor *et al.*, 2010).

Communication between transmitter and receiver can be disrupted by psychological, social, structural or environmental barriers that are technically called *"noise"*. The process of communication with the smokers must be persuasive, so that the smoker listens to the message, accepts it and implements it. Once the smoker knows how dangerous smoking is and tries to abandon tobacco consumption, usually problems occur due to psychological dependence because smoking cessation causes demotivating issues like weight gain, withdrawal symptoms, sudden desire to smoke, depression and insomnia.

Tobacco addiction requires medical treatment that consists of two essential components: *the behavior intervention* (education, information, advice) and the *pharmacological support* (treatment of the withdrawal syndrome).

Stages of *smoking cessation* were formalized by British researchers in the **5A**:

- **A**SK (asking the subject if he is a smoker or to admit their status)
- **A**DVISE (advising to quit smoking)
- **A**SSESS (assessing the desire to give up smoking)
- **A**SSIST (helping him to try to quit smoking)
- **A**RRANGE (maintaining constant contact for support)

For the smokers with *compliance issues*, we can apply to the **5R** in persuasive form:

- **R**ELEVANCE (personalized information)
- **R**ISKS (both for the smokers and their entourage)
- **R**EWARDS (smoking cessation benefits)
- **R**OADBLOCKS (obstacles that may arise)
- **R**EPETITION (repeating the information)

Non-pharmacological therapy is based on social support during and after the treatment. Learning practice involves models, strategies, methods and materials (Knapp *et al.*, 2011; Trofor *et al.*, 2010).

In the post-treatment period, physicians should stay connected to ensure free addressability when the patient feels the need to discuss. Physician-patient relationship is a key part of a good clinical practice in the anti-tobacco treatment throughout its duration, but also in post-treatment period in order to combine the success and avoid relapse.

The pre-and post-therapy counseling depends entirely on the physician -patient relationship, the patient's level of participation and the patient's satisfaction. Practical experience has put us in front of all situations about possible types of patient-physician relationship. There are three well-known views of the physician-patient relationship: as a consensual event - Parson model (Parson, 1951), Szasz and Hollender model (Szasz and Hollender, 1956), Stewart and Roter model (Stewart and Roter, 1989), as a conflict event - model Freidson, or as a negotiation.

Stewart and Roter identified three types of relationships based on the degree of control: *paternalistic* (physician -centered relationship; use of closed questions; model focused on defining illness and diagnosis), *consumerist* (patient-centered relationship; he knows exactly what he wants) and *absent* (focusing on patient fails; the physician abandons the control of the patient; he is not willing to accept the physician; the final result is a stalemate) (Stewart and Roter 1989).

Mutuality (using open questions, encouraging the patient to talk about his suffering) (Gillespie and Moon, 2005) concerns the physician-patient relationship in terms of consensus, being a static model, but in practice the relationship has a dynamic character due to issues occurring during the treatment and the post-treatment. The situation is kept even after leaving the program as any event can cause a relapse and long-term failure if abandoning tobacco was not blended as a habit.

Practical activity in the anti-smoking counseling center has made us confront with different issues about the medical staff of the hospital, various medical units and students from "Grigore T. Popa" University of Medicine and Pharmacy of Iasi (Stratulat *et al.,* 2013).

The habit of smoking on healthcare professionals has an influence on their professional credibility and effectiveness in tobacco control activities. Studies shown that non-smoking male doctors recommend that patients more often quit smoking, than the male doctors that smoke. The negative attitude of the latter affects the success of their therapeutic practices. For women doctors, differences are less significant between smokers and nonsmokers. Smoker healthcare professionals, as well as medical students, are a special target group because they can supply an assessment of the effectiveness of anti-smoking counseling program (Szász *et al.,* 2014).

II.7. Study about the associated use of different types of drugs by high school students

II.7.1. Aim

In this paper we set out to evaluate comparatively, at different ages (high school grades) how adolescent students perceive drugs, both socially accepted drugs (tobacco and alcohol) and illicit psychotropic substances, if they consume them, which they consume and how often they associate them, and whether they are aware of the risks associated with their health.

II.7.2. Material and methods

We developed and applied a questionnaire with twenty-three items to 200 students from a high school in urban area II (teenagers between the ages of 15 and 19, enrolled in grades 9^{th}, 10^{th}, 11^{th} and 12^{th}). From each year of study were randomly selected at the beginning of the second semester of the 2009-2010 school year two grades, totaling fifty students, who answered the questionnaire questions in the direction grades, in the presence of qualified persons.

The data obtained (which is strictly confidential in order to increase the accuracy of the analysis) was statistically processed using *EpiInfo™ 3.5.1* (Centers for Diseases Control) through uni-variate analysis, using descriptive statistical indicators.

For the determination of statistical significance between different frequencies, were applied the variants of the test χ^2 Mantel-Haenszel and Yates (corrected formula).

II.7.3. Results

The subjects included in the study are predominantly boys compared to girls (in the whole group the M:F ratio being 1.70:1). Most of the students included in the study (59%) come from rural areas and only 41% come from urban areas, with a stature-weight development within the normal limits for their age (norm weight, harmonically developed).

Tobacco consumption, or smoking, appears to be the lowest at the ninth graders, being significantly better represented in the 10^{th} grade (χ^2=4.54 and p=0.0329), the 11^{th} (χ^2=6.3529 and p=0.00117) and the 12^{th} (χ^2=14.77 and p=0.0001).

Regardless of the grade in which 55% of the students smoked the first cigarette before the age of 15 years old (the moment of entering high school), respectively there are significant differences between the proportion of boys and girls who smoke.

Of all the students surveyed, 16% of those in the ninth-grade smoke daily, respectively there are significantly more those who have the same habit, but they are registered in the 11^{th} grade (χ^2=7.071 and p=0.007) respectively in the $12t^h$ grade (χ^2=20.33 and p=0.000006).

As far as smoking motivation is concerned, 32% of all students are, regardless of grade, they maintain curiosity or lack of a specific reason.

Regarding the risks of smoking, over 80% of those surveyed, regardless of grade, know that it leads to a change in the appearance / color of the teeth and to different forms of cancer (laryngeal, esophageal, lung).

The motivation that would cause smoking cessation, acquires other valences over time, as the adolescent grows. Thus, if in the ninth grader the threat of parents is significantly stronger (χ^2=7.04 and p=0.0079) than in those of 11^{th} and 12^{th} grades, the possible alteration of their own health is significantly more important for those in the higher grades (11^{th} and 12^{th}) (χ^2=6.35 and p =0.001 and χ^2= 5.26 and p=0.0217). It should be noted that the cost price of cigarettes is not a reason enough to give up this habit at any age.

Most of the students surveyed on smoking (between 88 and 96%, with an average of 91.5%) admit that smoking has no real benefit for the teenager consumer.

Alcohol consumption. Among the alcoholic beverages preferred by teenagers, beer stands out. Thus, 71.5% of all students included in the study consumed a maximum of twice beer in the last month, with no differences between one grade or another. The abuse of beer is the prerogative of the boys, without dis-tinctions related to the age of the consumer.

A comparable situation is found in the case of wine where 72.5% of the students have consumed up to twice the wine in the last month. An interesting aspect is that all the girls surveyed have not consumed wine more than 5 times in the last 30 days.

As for the spirits drinks, there is a common aspect of those surveyed, namely that 64.5% did not consume such drinks at all in the last month and only 20% consumed them 1-2 times.

An immediate consequence, but also with possible medium and long-term effects, is drunkenness. The larger the search area, the less accurate the answers are, the most accurate (sincere) being the answers of the students from the ninth grade.

Another detail related to the consumption of alcoholic beverages is the “age of the first drink/glass.” Analyzing this moment, but in connection with the alcoholic strength of the drink (degrees of pure alcohol), we can notice for beer the temptation of early consumption before 11 years in about a quarter of all those surveyed. If in those in the middle grades there are no differences between boys and girls, in extreme grades boys who consumed beer before 11 years are 2 and 12 times, respectively, more numerous compared to girls.

Drinking a glass of wine for the first time shifts the focus to the age of 14 years old in boys and 15 years old in girls. Spirits were not (at least declaratively) consumed by 48%, 44%, respectively 30% of the youngest students and only by 14% of the older students (χ^2=13.37 and p= 0.0002).

Sweet alcoholic beverages were not consumed by 40% of the youngest students and only by 14% of the older students (χ^2=8.48 and p=0.003).

The last aspect analyzed by our questionnaire on alcohol consumption was the *"age of first drunkenness."* The proportion of those who deny that they have reached drunkenness decreases, from 20% to 12% for boys and from 26% to 16% for girls. The event is placed after the age of 15 years old for those in the 9th grade and over 16 for the others. Half of the students in the final year admit to being intoxicated, boys being 2.5 times more numerous than girls.

Drugs use was analyzed in the last section of the questionnaire applied to the two hundred adolescents was dedicated to the use of "illicit" drugs or psychotropic substances. Drugs use is lowest in 9th graders and significantly better represented in the 10th grade ($\chi^{2=}$5.019 and p=0.02), the 11th (χ^2=7.087 and p=0.007) and the 12th grade (χ^2=4.069 and p=0.043). There are also significant differences between the proportion of children who use drugs in the 10th grade (3 times more) and 12th grade (4.5 times more).

Regarding the type of drug that is preferred by each grade, it is noticed that marijuana is the drug exclusively for those in 11th grade who say they are consumers, but also holds the supremacy in consumers in the other grades: 71.43% in 10th grade, 76.92% in 11th grade and 58.34% in 12th grade.

The declared frequency of consumption indicates for 11th grade only one test as predominant, while in the higher grades occasional consumption predominates: 58.33% in 10th grade, 64.28% in 11th grade and 81.81% in 12th grade.

The motivation of the first contact with psychotropic substances and then the repetition of the experience in those surveyed consists mainly in generating a state of well-being regardless of age: in 75% of the students who are consumers of the 11th grade; in 63,64% of the pupils who are consumers of the 10th grade; in 92.30% of the pupils who are consumers of the 12th grade and in all the pupils who are consumers of the 12th grade.

II.7.4. Discussion

The level of information of the students in the high school grades about the possible effects of the consumption of psychotropic substances on their health status:

- physical and mental dependence is known by 58% of respondents, without significant differences between grades;
- mental disorders are known by 24.5% of respondents, without significant differences between grades;
- memory impairment is known by 17.5% of respondents, without significant differences between grades;
- heart damage is known by 13.5% of respondents, with significant differences between 9th and 10th grades (χ^2=5.65 and p=0.017).

The associative type of grid, which aimed to highlight whether the students and what action they have immediately the different psychotropic substances, was filled-in most correctly by the students from:

- 09th grade for amphetamines (70%) and barbiturates (68%);
- 10th grade for barbiturates (62%), amphetamines and marijuana (56% each);
- 11th grade for barbiturates (64%) and amphetamines (60%);
- 12th grade for barbiturates (76%) and cocaine (70%).

This fact reveals the existence of an above-average level of information and/or interest for barbiturates (regardless of grade), amphetamines (all grades) and cocaine only in students in 12th grade.

High school students look differently at the possibility of quitting drug use. Ninth graders are significantly less convinced that they could give up without specialized help, compared to students in the 10th grade (χ^2=6.55 and p=0.0104), 11th grade (χ^2=9.79 and p=0.00175) and the 12th grade (χ^2=3.849 and p=0.0484).

The association of risks posed by alcohol, tobacco and drug use is represented differently in this group of adolescents and evolves in diverse ways as students grow-up and mature in a positive sense or not for their future existence.

Thus, we can identify 7 subgroups of students who consume with different frequencies:

- only alcohol (beer being the common element for all grades) (53%);
- alcohol and tobacco (27.5%);
- alcohol, tobacco and occasionally drugs (9.5%);
- alcohol, tobacco and at least once tried to use drugs (3.5%);
- alcohol and occasionally drugs (3.0%);
- alcohol, tobacco and daily drugs (2%);
- alcohol and at least once tried to consume and drugs (1.5%)

By applying the test χ^2 we have identified the following aspects:

- there are significantly more students who consume only alcohol in the 9th grade compared to 12th grade (χ^2=20.19 and p=0.0000007), the tendency being to reduce monoconsumption as the adolescent grows.
- there are significantly more students who associate alcohol with tobacco in 12th grade compared 9th grade (χ^2=7.821 and p=0.0051).

In the 12th grade, there is another distribution compared to the smaller grades, in terms of drug associations: 44% drink and smoke; 36% just drink; 12% drink, smoke and occasionally take drugs; 4% drink, smoke and have tried drugs at least once; 4% drink and occasionally take drugs.

II.7.5. Conclusions

Tobacco use is lowest in ninth graders and is significantly better represented in students in older grades. There are no significant differences between the proportion of children who smoke, regardless of grade. In over a third of all students, regardless of grade, a motivational similarity is noted for tobacco consumption, namely curiosity or absence of a motivation. The risks involved by smoking (changing the appearance/color of the teeth and the appearance of neoplasia) are known by over 80% of the surveyed students. Among the reasons that could cause the smoking cessation, the threat of parents (significantly stronger than in the eleventh and twelfth grade students, predominate in the ninth grader), unlike the older students, who value more a possible alteration of their own health.

The cost price of cigarettes is not a percussive enough reason to determine the teenager to quit smoking at any age, between 14 and 19 years old. The majority of surveyed students (91.5%) agree that smoking does not bring any real benefit to the adolescent consumer.

Alcohol, considered the most accepted social drug, is also the favorite of teenagers, especially if we are talking about beer (the most wanted) or wine and less about spirits with an alcoholic strength over 40º. The onset of alcohol consumption, correlated with the alcoholic strength of the drink (degrees of pure alcohol), showed in about a quarter of all those surveyed the temptation of early consumption (before 11 years old) of beer. In the extreme grades, boys who consumed beer before the age of 11 are 2-12 times, respectively, more numerous compared to girls. Regarding this aspect between students in the 10th and 11th grades, there are no statistically significant differences between boys and girls. The first-time consumption of a glass of wine is identified around the age of fourteen in boys and fifteen in girls.

Marijuana is the drug exclusively used by ninth-grade users, but which holds supremacy in the other grades as well. About 2/3 of the students surveyed have correct information about what barbiturates and amphetamines are and what immediate effects their consumption

produces. The medium- and long-term consequences known to most students (58%) are physical and mental dependence.

The combination of alcohol, tobacco and drug use is a dynamic process, with the reduction to mono consumption as the students grow and become mature.

Although the questionnaire was confidential, a fine shade of distrust can be observed in the interviewed subjects, when addressing issues such as drunkenness and, especially, the use of illicit drugs, the temptation being to mystify the reality.

II.8. Medical students' health concerns related legal and illegal drugs consumption

II.8.1. Aim

The aim of the study is to identify medical students' thoughts regarding their health and behaviors related to maintaining physical health.

II.8.2. Material and methods

The study was developed between January and March 2019. The research targeted medical students from all years of study and was divided in three parts: the first one collected socio-demographic, medical and academic data. The second part of the questionnaire consisted of a number of self-rated items developed with the purpose of identifying aspects related to students' health. The third part included items targeting their health-related behaviors regarding physical health or limiting exposure to diseases during practical stages and worries about catching a disease. The participants had to rate their responses on a Likert-like scale from 1 to 5 (*1 - strongly disagree; 2 - disagree; 3 - neutral; 4 - agree; 5 - strongly agree).*

A number of 220 medical students provided online answers to the questionnaire. Google Forms was used due to its familiarity with students. Socio-demographic data (sex, age, year of study, environment, living arrangements), medical (chronic disease) and anthropometrical data (weight, height) were collected. Supplementary items were gathered related to academic results or family situation (siblings, level of education for both parents and having at least one parent working abroad).

Statistical analysis of collected data. Collected data were analyzed using IBM *SPSS Statistics, version 23.0.*

II.8.3. Results

Demographic, academic and family-related data

All the participants were domestic students enrolled in the "Grigore T. Popa" University of Medicine and Pharmacy of Iasi. 46.8% of them were in their third year of study, followed by second year (15%), fourth year (12.7%), first and fifth year (both of them 8.2%) and sixth year (9.1%).

Most of the participants were female students (82.5%), with age ranging from 19 to 32 years old ($M=21.92 \pm 1.96$). This gender majority is specific to medical students.

About their living environment, 78% of the participants declared that they were living in urban areas. Most of the students lived with their families and in rental accommodation or dorm rooms (33.6%, 38.6% respectively); a smaller percentage lived either alone (12.7%) or with their life partner (15%).

The admission process in the university is based on a final mark (minimum 5, maximum 10) resulted from a written exam with multiple answers, covering items from different disciplines (biology, chemistry and physics) and the mark from the baccalaureate exam.

The mean admission mark for the researched sample is 8.76 (± 0.85). For the baccalaureate exam the mean was 9.26 ± 0.58.

In case of 5% of the students, both parents were working abroad at the time of the investigation and another 14,1% declared that one parent is working in another country (9.1% for fathers and 5% for mothers).

Anthropometric, dietary habits, and health-related data

Students had to declare if they suffer from a chronic disease and 9.5% of them claimed that they had a chronic disease. As anthropometric data, it was obtained an M=63.29 (± 12.26) for weight and M=168.19 (± 8.22) for height.

Regarding the consumption of alcohol, tabaco, coffee, carbonated/energizing drinks or psychoactive substances, 9 XXV presents the frequency of answers. Almost a fifth of the students (20.9%) smoke daily, 13.1% of the students drink alcohol monthly or weekly, almost half of them (45.9%) drink coffee every day, 51.8% occasionally drink carbonated drinks and 34.1% occasionally drink energizing drinks. Most students claimed that they never used ethnobotanicals (95.9%) or drugs (94.0%) and only a small percentage revealed that they have used them occasionally (3.6%, 5% respectively) (Table XXX).

Students were also asked about their *sleeping* and *dietary habits*. Respondents reported an average of 6.73 (±1.09) hours of sleep per night, with a minimum of 3 and a maximum of 11. Also, 13.1% of the students reported that they wake up every night, while 59.5% of them wake up occasionally. The students had a rich diet in fruits and vegetables (43.2%), sweets (25.9%) and fat (16.8%). Only 10.5% of the students self-rated as having a balanced diet.

Health-related thoughts and behaviors. Students were asked to read five statements and decide to what extent they agreed with them, in order to identify their concern about their physical health. Almost 20% of the students strongly agreed with the fact that they were always preoccupied with their health. Also, 11.1% of the students in our sample agree or strongly agree that people around them paid little attention to their health.

Table XXX. The consumption of tobacco, drinks or drugs (%)

FREQUENCY OF USE	Tobacco	Alcohol	Coffee	Carbonated drinks	Energizing drinks	Ethno-botanics	Drugs
Never	60.0	15.0	11.8	9.50	62.3	95.9	94.0
Occasionally	15.9	71.8	22.7	51.8	34.1	3.60	5.00
Monthly	0.90	7.30	1.40	12.3	1.40	0.50	0.50
Weekly	2.30	5.90	18.2	21.8	2.30	0.00	0.50
Daily	20.9	0.00	45.9	04.5	0.00	0.00	0.00

While consulting patients, 7.7% of the students are very concerned they could have the same disease. A small percentage (4.1%) strongly believe they have a disease the doctors haven't discovered yet. Finally, 21.9% of the students agree or strongly agree with the statement that there is something wrong with their bodies (Table XXXI).

We were also interested in students' feelings during their practical stages. Almost a quarter of students (22.7%) were scared for no apparent reason, or they felt it was hard for them to calm down (21.9%). Students agreed or strongly agreed that they had a challenging time swallowing (19.4%), they lacked enthusiasm (35.4%), they were afraid they did not have enough time for all the assignments (44.5%), they were tense during clinical hours (48.2%) and, more importantly, they felt life didn't have a meaning (30.9%) (Table XXXII).

Behaviors regarding physical health. A percentage of 30.9% of the students believe they lose more hair than others; 58.6% of them carry hand sanitizing with them, rarely take medication without medical prescription (69.5%), use dietary supplements seasonally to improve their health (53.2%) and never bit their nails (65.9%). 15.5% of the students in our sample think very frequently that they could have a serious affection.

Half of the students declared they were healthy, while the rest declared various affections; digestive (15.5%), genital (7.3%) and endocrinological (5.9%) problems. 53.2% of the students were afraid of developing cancer, followed by diabetes (6.8%).

Table XXXI. The frequency of answers

ITEMS	Strongly disagree	Disagree	Neutral	Agree	Strongly agree
I am very preoccupied about my health	1.80	18.6	30.5	29.5	19.5
People around me pay little attention to my health	33.2	36.4	19.4	9.70	1.40
While I consult patients, I am afraid I could have the same disease	33.2	32.3	15.5	11.4	7.70
I think I have a disease the doctors haven't discovered yet	74.1	9.50	5.90	6.40	4.10
I always have the feeling there is something wrong with my body	30.0	31.8	16.4	11.4	10.5

Table XXXII. The distribution of answers to items regarding the feeling during stages

ITEMS	Strongly disagree	Disagree	Neutral	Agree	Strongly agree
I was scared for no apparent reason	23.6	25.9	17.7	19.1	13.6
It was hard for me to calm down	34.1	24.1	20.0	11.4	10.5
I had a hard time swallowing	41.8	26.4	12.3	11.4	8.2
I lacked enthusiasm	12.3	26.4	25.9	18.6	16.8
I was afraid of lack of time for assignments	13.2	21.4	20.9	26.8	17.7
I felt tense	8.2	22.7	20.9	26.8	21.4
Life doesn't have a meaning	39.1	17.3	12.7	13.2	17.7

Comparative analysis showed a significant difference between students with and without parents working abroad regarding the admission $t(199)=2.48$, $p=0.002$ and baccalaureate means $t(207)a=4.43$, $p=0.004$. The results showed that students with parents working in another country obtained lower marks for both baccalaureate ($M_{with}=9.35$, $M_{without}=8.92$) and faculty admission exams ($M_{with}=8.46$, $M_{without}=8.83$).

II.8.4. Discussion

The results of similar studies showed contradictory rates concerning two aspects: the level of fear of having a disease or the tendency to identify themselves as having the signs of a studied physical or mental illness. With rates ranging from 5-70%, various researchers tried to identify different variables linked to this tendency (Harding *et al.,* 2008b; Weck *et al.,* 2014; Hardy *et al.*,1997).

More than half of the respondents are afraid of developing cancer (53.2%), a major fear also identified by other studies led on medical students (Candel and Merckelbach, 2003). Studies focusing on medical students revealed that 70% of them have groundless medical fears during training. On the contrary, some other studies found no difference regarding health-seeking behaviors and fear of illness between medical and non-medical students (Waterman and Weinman 2014; Salkovskis and Howes, 1998).

Students tend to diagnose themselves or to self-administrate dietary supplements with no medical prescription in order to improve their physical and mental power.

The rates for this study correspond to results obtained by other studies focusing on medical students: more than 50% in USA (Spencer *et al.,* 2006), 37.4% in Italy (Lirico *et al.,* 2018) or 76.1% in Saudi Arabia (Alfawaz *et al.,* 2017).

Even if some studies point out that there is no significant difference between students with and without medical knowledge, other findings show that there are differences in the knowledge of health sciences and non-health sciences students pertaining to health benefits and safety of the consumption of dietary supplements (Alhomoud *et al.,* 2016).

We identified that 1/5 of the students smoke and then drink coffee (33%) or energizing drinks (35%). Aljaloud identified that 71.5% of students use energizing drinks (Aljaloud, 2016).

A study conducted by Casuccio revealed that 22% of medical students were regular consumers of energizing drinks (Casuccio *et al.,* 2015). The consumption of these drinks was associated with a high rate of alcohol consumption and 45% of the students declared that they felt side-effects like insomnia, palpitations and irritability after the consumption these drinks. In Canada 73.8% of all students consume the same drinks (Hammond *et al.,* 2018).

Regarding the consumption of tobacco, studies show that the rates are decreasing. With a percentage of smokers of 40, this study reveals an increased rate, compared to studies on medical students from Europe (19%), Africa (19%) or SUA (21%) (Pérez-Pazos, 2015).

II.8.5. Conclusions

Medical education is a long and demanding academic training. Apart from psychological aspects or social characteristics, other aspects influence students' psychological, physical and social health during their academic years.

The contact with patients, the knowledge about illness, suffering and dying determines the individuals to deal with objective or imaginative fears.

CHAPTER III

LIVING ENVIRONMENT QUALITY AND CERTAIN CHRONIC DISEASES (CANCER, RARE DISEASES)

Chronic diseases directly, or by their complications, are proven to be the leading causes of death and functional incapacity worldwide.

Thus, 71% of all deaths recorded worldwide are due to chronic diseases, and 15 million people die annually from a chronic disease, aged between 30 and 69 years. Every two seconds a person between the ages of 30 and 69 suffers a premature death.

Chronic diseases tend to be long-lasting and are the result of a combination of genetic, physiological, mesological factors and type of behavior. Chronic pathology does not disappear suddenly and, above all, cannot be considered as curable definitively and totally.

Chronic diseases disproportionately affect people in low- and middle-income countries, areas where more than 78% of all deaths related to chronic pathology are recorded.

The early diagnosis of chronic diseases through the development and implementation of screening programs has a double connotation both for the patient (ensuring a better quality of life) and for the health insurance systems (reducing the pressure represented by the additional costs related to the treatment of chronic diseases).

Prevention of chronic diseases depends on the early identification of risk factors that can be influenced and that depend on the clinical context (tension values, glycemic and lipid profile) or on the general way of life (unbalanced nutrition, obesity, tobacco consumption, alcohol, lack of physical movement / sedentary lifestyle, psychosocial stress).

We develop our research in this area due to the necessity to understand better chronic disease, and how to prevent these medical conditions through an adapted lifestyle (Iorga, 2020).

Frequently rare diseases are misdiagnosed which leads to a delayed treatment and subsequently a lower life quality. Among all the chronic diseases we have investigated cancer and certain rare diseases (phenylketonuria, cystic fibrosis, hypothyroidism, Turner syndrome and orocraniodigital syndrome cleft lip/cleft palate).

A. COPING WITH CANCER AS A MULTIFACTORIAL CHRONIC DISEASE

Living under the influence of stress factors that are associated with being diagnosed with cancer demands the development of coping strategies that help the patient regain a *sense of balance* (Moos and Schaefer, 1984). Adapting to cancer is similar to adapting to a major stress event and can be analyzed from the point of view of the intensity of the strain on the adaptive resources of the individual (Lazarus and Folkman 1984) and on the coping resources or on self-efficacy (Bandura, 1989).

Adapting to the oncological disease depends on a series of factors, such as the individual's illness representations, the psychoemotional implications of the disease, the specific clinical characteristics of the disease and its evolution, the presence of a history of direct contact with the disease through family members, and the sociocultural context (Popa-Velea, 2010).

Most studies which set out to investigate the relationship between the perception of the illness and the coping strategies used by oncology patients used instruments based on the division of coping strategies into problem-focused coping (active-passive) and emotion-focused coping (positive-negative). *Leventhal's Self-Regulatory Model* (SRM) is the cognitive-affective model which emphasizes the existence of the emotional and cognitive components, which play a role in the perception of the threat of disease, and which influence each other.

Leventhal consider that the representation of health threats, at an individual level, is updated and enriched by actions aimed at health promotion, risk perception, and disease prevention, by disease management behaviors (Leventhal *et al.,* 2005). The model explains that problem-focused coping focuses on resolving the stressful situation or altering the source of stress, taking control of stress by solving the problem or eliminating the source of stress, seeking information or assistance in managing the situation, and removing oneself from the disturbing situation. Emotion-focused coping is focused on managing the emotions associated with the situation, rather than changing it (Carroll, 2013). But drawing this distinction generates a major conceptual problem, as there is a dimension that goes beyond the limits of this dichotomy: the cognitive dimension (thoughts) versus the behavioral one (behaviors) (Holahan *et al.,*1996; Hamilton *et al.,* 2009.), which is less explored in the other studies of coping strategies for oncology patients, especially for those with a family history of cancer.

In this study, performed on oncological patients and healthy individuals with a family history of cancer, we used the model combining problem-focused active-passive behavioral coping, addressed directly to the stressor, and described in the following dimensions: active-passive, prosocial-antisocial, direct-indirect (giving the person the possibility of directly or actively confronting the causes of the stressful situation or of avoiding them, to retreat from this situation), with cognitive coping strategies centered on emotions (giving the possibility of cognitive adjustment of emotional responses to events with aggravating consequences for individual emotions).

Previous literature in the USA shows that the cognitive coping strategy contributes to the management and regulation of emotions aimed at adapting to the illness, in order to avoid patients' becoming overwhelmed by the negative event they are facing, such as the oncological diagnosis in the context of a family history of cancer (Garnefski *et al.,* 2001).

On the other hand, as asserted by Edwards and Clarke in their study about levels of depression and anxiety in newly diagnosed adult patients and their adult relatives (Edwards and Clarke, 2004), cancer affects not just the patient but family functioning, family members' communication, roles and interactions, clinical levels of depression, and severe levels of anxiety and stress reactions being ascertained; therefore, research and health service providers should focus on the family not just on the individual. Another study about long-term effects of cancer treatment, performed on the wives of oncological patients, reported a similar level of distress and negative consequences of the diagnosis and intervention on intrafamilial interactions, changes in family roles and communication difficulties, just as in families without a history of cancer (Harden *et al.,* 2013), families with a history of cancer who were able to act openly, to express feelings directly, to manage problems effectively, and to communicate information directly within the family, had lower levels of depression and anxiety.

In the case of oncogenetic counseling for hereditary breast/ovarian cancer, families perceived higher anxiety and depression at genetic test result communication even if, at baseline, subjects perceived families as functional; in other words, they were pleased with their own family (Condello *et al.,* 2007). At the same time, in the case of hereditary cancer, the assessment of the family history is very important for determining risk. Thus, the family health history of cancer is considered an important instrument for prevention and health promotion. Better family cohesion and flexibility correlated with better communication between family members and better disclosure of information regarding the history of cancer (Rodríguez *et al.,* 2016). In addition to a low level of information and education, poor family communication is also considered to be a barrier related to collecting data on the family history of cancer by health service providers (Sussner *et al.,* 2011).

My interest regarding this area is reflected by the following articles and book chapter:

Roxana Postolica, Iorga M, **Florin Dumitru Petrariu**, Doina Azoicai. COGNITIVE-BEHAVIORAL COPING, ILLNESS PERCEPTION, AND FAMILY ADAPTABILITY IN ONCOLOGICAL PATIENTS WITH A FAMILY HISTORY OF CANCER. *Hindawi BioMed Research International Volume* 2017, Article ID 8104397, 11 pages / **IF=2.583**

Florin Dumitru Petrariu, Iorga M. Chapter 1. *Bolile cronice. Clasificare și factori de risc*, 25-41. BOALA CRONICĂ. O PERSPECTIVĂ INTERDISCIPLINARĂ. Editura Polirom, 2020, ISBN 978-973-46-8321-5

Miron L, Bosanceanu M, Filimon R, **Petrariu FD.** CLINICAL-EPIDEMIOLOGICAL STUDY ON ADVANCED NON-SMALL CELL LUNG CANCER. *Rev Med Chir Soc Med Nat Iasi* 2014; 118(2): 492-496 / **PMID: 25076720**

Surlin V, Bintintan V, **Petrariu FD**, Dobrin R, Lefter R, Ciobică A, Timofte D. PROGNOSTIC FACTORS IN RESECTABLE PANCREATIC CANCER. *Rev Med Chir Soc Med Nat Iasi* 2014; 118(4): 924-931 / **PMID: 25581949**

III.1. Cognitive-behavioral coping, illness perception, and family adaptability in oncological patients with a family history of cancer

III.1.1. Aim

This study aims to analyze the cognitive/emotional coping strategies of cancer patients with and without a family history of cancer and the way in which these coping mechanisms influence the perception of the illness in the context of the family system. The importance of this study comes from the fact that, to date, no study has emphasized the underlying cognitive and behavioral mechanisms used by patients with a family history of cancer in order to cope with the illness, the perception of the illness, and the characteristics of these patients' family system, in what concerns communication, family cohesion, and flexibility. Therefore, the paper outlines several aspects related to the profile of strategic coping used for adapting to illness by patients with a family history of cancer. The goal of the study is to identify the main coping strategies of patients with a genetic risk of cancer and to analyze the impact of the diagnosis on family adaptability and cohesion, by comparing the coping strategies of patients with and without a family history of cancer.

III.1.2. Material and methods

The research has the approval of the Ethics Committee at the "Grigore T. Popa" University of Medicine and Pharmacy of Iasi. Between January and May 2016, 200 questionnaires were sent to oncology patient associations in 6 Romanian counties. The patient selection criteria considered age (over 18), the unimpeded ability to understand information, the absence of cognitive, personality, or psychiatric disorders, and the completion in full of the received questionnaires. The two hundred patients voluntarily took part in the research and agreed to complete our questionnaires, they were informed about the purpose of the investigation and data privacy was ensured; before filling in the questionnaire, they all signed an informed consent. A number of 124 of these questionnaires were filled in fully and returned.

As the patients come from various regions of the country, we may consider that this study analyzes a heterogeneous group of individuals from the point of view of socio-demographic data and it is not limited to the analysis of a closely defined region of the country.

After all the participants in the research provided their informed consent, sociodemographic and medical data were filled in and tests were self-administered. All these participants went through a comprehensive medical evaluation and genetic testing that provided

information about their illness and their genetic risk for cancer. For a better understanding and a useful description of the data, it is important to note that the patients with a genetic risk of cancer are a subgroup of the patients with a family history of cancer.

The questionnaire included a set of specific questions designed to record socio-demographic characteristics such as sex, age, marital status, level of education, parenthood, and medical data like genetic risk, type of therapy, age at the time of diagnosis, and time since the diagnosis. In addition to this, they responded to 4 questionnaires assessing their coping mechanisms, illness perception, and family situation in connection with their illness.

Cognitive Emotion Regulation Questionnaire (CERQ) (Perte and Miclea, 2011), the Romanian version, comprising of 36 items, is a multidimensional questionnaire that measures the cognitive coping strategies at nine different levels: self-blame, other-blame, rumination, catastrophizing, putting things into perspective, positive refocusing, positive reappraisal, acceptance, and refocusing on planning; respondents were asked to indicate to what extent they used certain cognitive coping strategies on a 5-point Likert scale (*1=(almost) never, 2=sometimes, 3=usually, 4=often, and 5=(almost) always*). The sum of shares of the four items included in a scale may vary from 4 (the strategy is never used) to 20 (the cognitive coping strategy is often used); the total score of the scale has values from 4 to 20.

The Strategic Approach to Coping Scale (SACS), in Romanian (Budău *et al.*, 2011), is a scale that comprises 52 items, that evaluates behavioral coping strategies on a 5-point Likert scale (1=it is not at all what I would do; 5=it is what I would do, categorically); the items are organized on nine subscales: assertive action, social joining, seeking social support, cautious action, instinctive action, avoidance, indirect action, antisocial action, and aggressive action.

The Family Adaptability and Cohesion Scale - FACES IV (Olson *et al.,* 2011) is a self-report questionnaire including 62 items organized in six subscales, that evaluates the mid ranges of adaptability and cohesion of the family (two subscales) and the extremes of adaptability and cohesion-rigid, chaotic, disengaged, and enmeshed (four subscales); respondents must express appraisals on a 5-point Likert scale, from strong disagreement (1) to strong agreement (5) and a percentile score must be used for the results (%), as well as specific computation formulas: the dimension scores for cohesion and flexibility are only used for plotting the one location of the family onto the updated graphic representation of the *Circumplex Model of Couple and Family Systems*.

Illness Perception Questionnaire revised (IPQ-R) (Moss-Morris *et al.,* 2002) is a method that measures the cognitive representation of illness; it contains 38 items organized on five scales assessing *identity*, the symptoms the patient associates with the illness; the *cause*, personal ideas about etiology; *timeline,* the perceived duration of the illness; the *consequences*, the expected effects and outcome; *cure control*, how one controls or recovers from the illness; respondents were asked to choose from 1-5 answers (*1=strongly disagree, 2=disagree, 3=neither agree or disagree, 4=agree, and 5=strongly agree*); it is recommended to start analysis with separate items by grouping variables; high scores on the identity, timeline, consequences, and cyclical dimensions represent strongly held beliefs about the number of symptoms attributed to the illness, the chronicity of the condition, the negative consequences of the illness, and the cyclical nature of the condition; high scores on the personal control, treatment control, and coherence dimensions represent positive beliefs about the controllability of the illness and a personal understanding of the condition.

Statistical Analysis. A descriptive analysis was conducted to report demographic, social, and illness characteristics of the subjects enrolled. The *Pearson* product-moment coefficient was used to measure the multivariate correlation between the time elapsed between the diagnosis and 4 FACES factors: disengaged, enmeshed, rigid, and cohesion ratio (2-tailed, $p< 0.05$*)*, considering all types of patients (cured patients, patients undergoing treatment, and patients undergoing posttreatment monitoring).

Linear regression analysis was used to evaluate whether the length of treatment predicted the increase in unbalanced family relationships for the families of cancer patients.

Student's *t*-test comparison was calculated for the 124 oncological patients on the criteria of the family history of cancer and coping strategies (CERQ self-blame, CERQ acceptance, CERQ rumination, CERQ positive refocusing, CERQ catastrophizing, CERQ other-blame, SACS indirect action, SACS antisocial action, CERQ positive refocusing, CERQ refocusing on planning, CERQ positive reassessment, and CERQ putting things into perspective) as dependent variable (2-tailed, $p < 0.05$).

The *Pearson* product-moment coefficient was also used to measure the multivariate correlation between the time elapsed between diagnosis and 4 FACES factors: disengaged, enmeshed, rigid, and cohesion ratio (2-tailed, $p < 0.05$), considering all types of patients (cured patients, patients undergoing treatment, and patients undergoing posttreatment monitoring).

The *Pearson* product-moment coefficient was also used to measure the multivariate correlation between the 124 oncological patients on the criterion of coping strategies and the influence of family records of cancer, namely, between illness coherence, the influence of family records of cancer, coping strategies, and perception of the disease. *Student's t*-test comparison was calculated for the 124 oncological patients on the criterion of the influence of the genetic risk of cancer for patients with a family history of this illness.

The data were processed, and analyses were performed with the IBM *SPSS Statistics version 21.0*.

III.1.3. Results

Sociodemographic and Medical Data. At the moment of data gathering, 39.52% of the 124 patients were declared cured, while 41.13% were still undergoing treatment. Only 19.35% of the participants were undergoing posttreatment monitoring. Sociodemographic and medical data are presented in Table XXXIII.

Table XXXIII. Socio-demographic and medical data

Variables	Characteristics	Variables	Characteristics
Sex of the participants	Male: *N* = 18 (14.51%) Female: *N* = 106 (85.48%)	The age at the time of diagnosis	M = 48.91, SD = 8.72 minimum = 27 and maximum = 70
Age	M = 55.25, SD = 9.33 minimum = 27 and maximum = 70	The time since the diagnosis	1–32 years
Level of education	Primary school: 8.1% Secondary school: 39.5% High school: 14.5% Bachelor's degree: 37.9%	Types of cancer	Breast cancer (65.32%) Colorectal cancer (11.29%) Ovarian cancer (6.45%) Cervical cancer (8.06%) ORL neoplasm (5.65%) Lung cancer (2.42%) Melanoma (0.81%)
Marital status	Single (34.7%) Unmarried (7.3%) Divorced (12.9%) Widowed (14.5%) In relationship (65.3%) First marriage (58.95%) Remarried (4.8%) In relationship (1.6%)	Course of treatment	Surgery (94.45) Chemotherapy (90.3%) Radiotherapy (64.5%) Other therapy: hormonal, biological (29%)

Of all subjects, 21.8% were assessed with a genetic risk of cancer evaluated by a geneticist considering the analysis of pedigree in the context of family history of cancer. The patients were asked about their knowledge regarding genetic testing (Table XXXIV).

Table XXXIV. Stage of disease and family history of cancer

Stage of disease	%	Family history of cancer	%	Genetic risk of cancer	%
Cured	39.52	Family history of cancer	44.4	With a genetic risk of cancer	21.8
Undergoing treatment	41.13	No family history of cancer	55.6	Without a genetic risk of cancer	79.2
Posttreatment monitoring	19.35				

Almost one-third (32.45%) of them claimed that they had had no information regarding genetic testing prior to enrolling in the program, while 28.23% declared that they had had little information. Only 12.90% of participants stated they had sufficient information about genetic testing for cancer.

Of all respondents, 31.5% never considered the idea that their illness could be genetically determined. Yet 59.1% of participants in the study were worried that they might carry a cancer gene that could be transmitted to their offspring (Table XXXV).

Table XXXV. Knowledge about genetic testing and the possibility that the disease to be inherited

Knowledge about genetic testing	%	The possibility that the disease be inherited	%
No information	32.45	Worried about carrying a cancer gene	59.1
Little information	28.23	Not worried about carrying a cancer gene	41.9
Sufficient information	12.90	Never considered illness = genetically determined	31.5

The Duration of Treatment and Its Impact on Adaptability and Family Cohesion

The time between the diagnosis and the present study correlates significantly, in patients under- going treatment (N=51), with the following FACES factors: disengaged ($r=0.339$, $p < 0.02$), enmeshed ($r=.524$, $p < 0.01$), rigid ($r=0.422$, $p < 0.01$), and cohesion ratio ($r=-0.317$, $p < 0.05$). The longer the duration of the illness is, the more unbalanced the family relationships become. Also, cohesion within the family tends to decrease with time in patients undergoing treatment. These correlations seem to be more significant for the group of participants still undergoing treatment (they are not statistically significant for patients who are declared cured or undergoing posttreatment monitoring) (Table XXXVI).

Table XXXVI. Correlation between FACES factors and duration of treatment

FACES factors	Cured patients			Patients undergoing treatment			Patients undergoing posttreatment monitoring		
	r	*p*	*N*	*r*	*p*	*N*	*r*	*p*	*N*
Disengaged	.141	0.336	49	.339*	0.015	51	−.178	0.406	24
Enmeshed	.098	0.503	49	.524**	0.000	51	−.066	0.760	24
Rigid	.000	0.999	49	.422**	0.002	51	.243	0.252	24
Cohesion ratio	−.078	0.595	49	−.317*	0.024	51	.307	0.145	24

Linear regression analysis explores the valid model for the prediction of unbalanced family relationships for the families of cancer patients using as a predictor the variable *length of treatment*. The regression analyses were conducted for the group of patients undergoing treatment. Analyzing the relations between the predictor and criterion variables leading to the rise in unbalanced family relationships, for the sample of 51 respondents (patients undergoing treatment), namely, 1 predictor represented by the length of treatment, in turn for all 4 FACES factors (disengaged, enmeshed, rigid, and cohesion ratio), we find that each prediction model of "unbalanced family relationships" differs significantly from the previous one ($p < 0.01$).

The results obtained show that the variable length of treatment contributes significantly ($R2$=0.13; p= 0.015)to the explanation of the disengaged factor (F(1;49)=6.35; p=0.015), contributes significantly ($R2$=0.27; p=0.001) to the explanation of the enmeshed factor (F(1;49)=18.589; p=0.001), contributes significantly ($R2$=0.18; p=0.001) to the explanation of the rigid factor(F(1;49)=10.61; p=0.001), and contributes significantly ($R2$=0.10; p= 0.024) to the explanation of the cohesion ratio (F(1;49)=5.461; p =0.024). From each final model, one can notice that the predictor length of treatment significantly influences the variance of the 4 FACES factors: disengaged (β=0.339; p=0.015), enmeshed (β=0.524; p =0.001), rigid (β=0.422; p=0.001), and cohesion ratio(β=−0.317; p = 0.024). The results of the regression indicated that the length of time since diagnosis could be used as a predictor for the FACES IV factors (Table XXXVII).

Table XXXVII. Summary of models for FACES IV factors and length of time since diagnosis

FACES factors	R^2	df	F	p	β	t
Disengaged	0.13	1; 49	6.35	0.015	0.339	2.522
Enmeshed	0.27	1; 49	18.589	0.001	0.524	4.312
Rigid	0.18	1; 49	10.61	0.001	0.422	3.252
Cohesion ratio	0.10	1; 49	5.461	0.024	−0.317	−2.337

Coping Strategies and the Influence of Family Records of Cancer

Comparing the results obtained by the 124 oncological patients, based on the family history of cancer, our research identified that patients with cancer scored significantly higher in the following coping strategies: CERQ self-blame, CERQ acceptance, CERQ rumination, CERQ positive refocusing, CERQ catastrophizing, CERQ other-blame, SACS indirect action, SACS antisocial action, CERQ positive refocusing, CERQ refocusing on planning, CERQ positive reassessment, and CERQ putting things into perspective.

Moreover, they scored insignificantly in the following factors: SACS assertive action, SACS social relationing, SACS seeking social support, SACS cautious action, SACS instinctive action, SACS avoidance, and SACS aggressive action.

The results obtained prove that cancer patients use acceptance and positive refocusing on planning, positive reassessment, putting things into perspective as cognitive-adaptive coping strategies. In what concerns prosocial behavioral coping strategies, cancer patients are less prone to use social relationing and seeking social support, assertive action, in addition to passive behavioral coping strategies - avoidance and indirect action. At the same time, the results reveal that, when faced with a negative event such as illness, the patients also use maladaptive cognitive coping strategies: rumination, catastrophizing, and antisocial behavioral coping strategies, such as other-blame. This could be explained by the fact that the cancer diagnosis is a factor threatening not just their health but their existence. Nonetheless, cancer patients use other-blame for the onset of the illness as a cognitive coping strategy significantly less than average for the general population (Table XXXVIII).

There were significant differences between patients with a family history of cancer (M= 9.47, SD= 2.52) and patients with no such history (M=10.66, SD=3.18) regarding the following factors of strategic coping: indirect action [t(122; 121.998)=−2.27, p < 0.05], and there were significant differences between patients with a family history of cancer (M=9.69, SD=3.29) and patients with no such history (M=11.13, SD=4.16) regarding antisocial interaction [t(122; 121.998)=−2.09, p < 0.05]. These results support the idea that patients with a family history of cancer use antisocial action and indirect action as behavioral coping strategies less than patients with no family history of cancer. For both factors, the score mean of the genetic risk of cancer group was significantly lower.

Table XXXVIII. Coping strategies and the influence of family records of cancer

Coping strategy scale	Mean	SD	*T*	df	*p*
Self-blame	9.66	3.63	−.442	122	0.005
	10.01	3.55		40.903	
Acceptance	14.81	2.96	.620	122	0.036
	14.30	3.93		54.243	
Rumination	12.81	3.11	.803	122	0.024
	12.19	3.65		47.805	
Positive refocusing	13.07	4.07	−.009	122	0.003
	13.08	4.15		42.263	
Catastrophizing	9.18	4.24	−.804	122	0.023
	9.80	3.32		35.350	
Other-blame	6.55	2.65	−1.994	122	0.034
	6.42	2.65		119.620	
Indirect action	9.47	2.52	−2.270	122	0.025
	10.66	3.18		121.998	
Antisocial action	9.69	3.29	−2.092	122	0.038
	11.13	4.16		121.998	
Refocusing on planning	15.37	3.15	1.646	122	0.002
	14.06	3.77		48.828	
Positive reassessment	15.33	3.59	1.930	122	0.036
	13.60	4.23		48.045	
Putting things into perspective	15.00	3.74	2.008	122	0.047
	13.22	4.13		45.309	
Illness coherence	17.05	3.41	2.352	122	0.020
	15.33	4.48		121.774	

The patients from the group with a family record of cancer (M=6.42, SD=2.65) scored significantly lower than those with no family record of cancer (M=6.55, SD=2.65) at blaming others [t(122; 119.620)=−1.99, $p < 0.05$] as a coping strategy. The patients from the group with a family record of cancer (M=9.66, SD=3.63) scored significantly lower than those with no family record of cancer (M=10, SD=3.55) at self-blame [t(122; 40.903)=−.442, $p < 0.05$] as a coping strategy. The patients from the group with a family record of cancer (M=13.07, SD=4.07) scored significantly lower than those with no family record of cancer (M=13.08, SD=4.15) at positive refocusing [t(122; 42.263)=−.009, $p < 0.05$] as a coping strategy.

The patients from the group with a family record of cancer (M=9.18, SD=4.24) scored significantly lower than those with no family record of cancer (M=9.80, SD=3.32) at catastrophizing [t(122; 35.350)=−.804, $p < 0.05$] as a coping strategy. The patients from the group with a family record of cancer (M=14.81, SD=2.96) scored significantly higher than those with no family record of cancer (M= 14.30, SD= 3.93) at acceptance [t(122; 54.243)=.620, $p < 0.05$] as a coping strategy.

The patients from the group with a family record of cancer (M=12.81, SD=3.11) scored significantly higher than those with no family record of cancer (M=12.19, SD=3.65) at rumination [t(122; 47.805)=.803, $p < 0.05$], as a coping strategy. The patients from the group with a family record of cancer (M= 15.37, SD= 3.15) scored significantly higher than those with no family record of cancer (M=14.06, SD=3.77) at refocusing on planning [t(122; 48.828)=1.646, $p < 0.05$] as a coping strategy.

The patients from the group with a family record of cancer (M=15.33, SD=3.59) scored significantly higher than those with no family record of cancer (M=13.33, SD=4.23) at positive reassessment [t(122; 48.045)=1.930, $p < 0.05$] as a coping strategy. The patients from the group with a family record of cancer (M=15, SD=3.74) scored significantly higher than those with no family record of cancer (M=13.22, SD=4.13) at putting things into perspective [t(122; 45.309)=2.008, $p < 0.05$] as a coping strategy. There were no significant differences ($p > 0.05$) between participants with a family history of cancer and the others regarding factors of the *Family Adaptability and Cohesion Scale* (FACES IV).

When it comes to the perception of illness, patients with family records of cancer (M=17.05, SD=3.41) get significantly higher scores than patients with no such records (M=15.33, SD=4.48) for the illness coherence factor [$t(122; 121.774)=2.35$, $p < 0.05$].

The patients from the group with a family record of cancer scored significantly lower than those with no family record of cancer at blaming others, self-blame, positive refocusing, and catastrophizing as a coping strategy, and they scored significantly higher at acceptance, rumination, refocusing on planning, positive reassessment, and putting things into perspective as coping strategies. The efforts of patients with a family history of cancer to face the requirements of life as patients, assessed or perceived as exceeding or overloading their own resources, are supported by coping strategies such as acceptance, rumination, refocusing on planning, positive reassessment, and putting things into perspective and less supported by blaming others, self-blame, positive refocusing, and catastrophizing, as efficient coping strategies for the situation of being ill.

Functional cognitive coping strategies ensure the regulation of emotions in oncological patients with a family history of cancer; stable ways of facing negative life events and emotional responses to situations which might worsen individual emotions are as follows: resignation to what has occurred, the continual analysis of feelings and ideas associated with the negative event, the analysis of future steps necessary to face the event, assigning positive meanings to the event, in terms of personal development, and minimizing the gravity of the event by comparison with other events. Due to the genetic factors involved, these patients perceive the illness as being more coherent, easier to explain.

They believe, to a greater extent than the group of participants with no family history of cancer, that genetic factors are the cause of their disease ($p < 0.01$, $r=0.52$). Patients with a family history of cancer also believe more than those with no family history of cancer that an accident or a trauma caused their disease ($p < 0.04$, $r=0.18$). On the other hand, when there is a family history of cancer, patients tend to attribute their illness to luck and chance less often than the ones with no family history of cancer ($p < 0.03$, $r=0.19$). In what concerns the details of patients with a family history of cancer, the statistical data analysis reveals these results:

i. The adoption of a functional cognitive coping style, based on refocusing on planning ($p=0.0001$, $r=0.464$), positive reassessment ($p=0.006$, $r=0.363$), and putting things into perspective ($p=0.001$, $r=0.452$) correlates with an adaptive sense of illness coherence.
ii. Positive refocusing correlates with an adaptive emotional representation of the illness ($p=0.05$, $r=-0.266$), in contrast to catastrophizing as a cognitive coping strategy, which correlates with a maladaptive emotional representation of the illness ($p=0.001$, $r=0.431$).
iii. Adopting a behavioral coping strategy which involves assertiveness correlates with positive control beliefs about the illness, personal ($p=0.015$, $r=0.327$) and through treatment ($p=0.005$, $r=0.369$), as well as with a sense of illness coherence ($p=0.012$, $r=0.338$).
iv. Adopting a cautious behavior is a prosocial behavioral coping strategy which correlates with a positive emotional perception of the illness ($p=0.007$, $r=0.361$).
v. Adopting an aggressive behavior correlate weakly with control beliefs about the illness, personal ($p=0.031$, $r=0.292$) and through treatment ($p=0.006$, $r=0.366$). This result could be explained by the fact that oncological treatment, as well as the diagnosis, is perceived by patients as particularly harsh, both physically and emotionally; therefore, a direct and individualistic approach when it comes to fighting the illness could be useful.
vi. A balanced, cohesive family system correlates with an adaptive emotional representation of the illness ($p=0.012$, $r=-0.338$) (Table XXXIX).

Table XXXIX. Correlation between illness coherence, the influence of family records of cancer, coping strategies, and perception of the illness

	r	*p*
	The influence of family records of cancer	
Illness coherence		
Genetic factors, cause of the disease	0.52	<0.01
Accident or a trauma caused the disease	0.18	<0.04
Luck and chance	0.19	<0.03
	Adaptive sense of illness coherence	
Coping strategies		
Self-blame	0.52	0.001
Positive refocusing	−0.266	0.05
Catastrophizing	−0.431	0.001
Refocusing on planning	0.464	0.001
Positive reassessment	0.363	0.006
	Assertiveness	
Personal control beliefs about the illness	0.327	0.015
Control beliefs about the illness through treatment	0.369	0.005
Sense of illness coherence	0.338	0.012
	Prosocial behavioral	
Positive emotional perception of the illness	0.361	0.007
	Aggressive behavior	
Personal control beliefs about the illness	0.292	0.031
Control beliefs about the illness through treatment	0.366	0.006
	Cohesive family system	
Adaptive emotional representation of the illness	−0.338	0.012

The Influence of the Genetic Risk of Cancer for Patients with a Family History of This Illness. Patients with a genetic risk of cancer (M=15, SD=3.74) broaden their perspective as a coping strategy more often than patients with no genetic risk (M=13.22, SD=4.13), [t(122; 45.30)=2.00, $p < 0.05$]. Family satisfaction seems to be significantly higher for patients with a genetic risk of cancer (M=38.33, SD=6.97) compared to the one reported by patients who suffer from the disease (M=34.88, SD=7.15) but have no genetic risk [t(121; 42.60)=2.22, $p < 0.05$].

Illness coherence is significantly higher for patients with a genetic risk of cancer (M=18.48 SD=3.67) compared to patients with no such risk (M=15.43 SD=4.01), [t(122; 44.782)=13.56, $p < 0.01$].

These results are confirmed by other studies in the field, showing that patients evaluated before the oncogenetic counseling are satisfied with their family adaptability, in that better family cohesion and flexibility are correlated with better communication between family members and better disclosure of information regarding family history of cancer. If problem-focused or emotion-focused coping efforts are insufficient or inadequate, patients feel fear or worry regarding disease risk; family cohesion has positive influences on the patient's coping with the disease (Rodríguez *et al.*, 2016). The results are important in shaping therapeutic strategies, pointing out the importance of family involvement in the patient's recovery program (Table XL).

Table XL. The influence of the genetic risk of cancer for patients with a family history of this illness

Genetic risk of cancer	Mean	SD	*t*	df	*p*
Putting things into perspective	15.00	3.74	2.00	122	0.047
	13.22	4.13		45.30	
Family satisfaction	38.33	6.97	2.22	121	0.028
	34.88	7.15		42.60	
Illness coherence	18.48	3.67	3.55	122	0.001
	15.43	4.01		44.782	

Participants in the group with a genetic risk of cancer believe more than the other group that their illness is inherited ($p < 0.01$, $r=0.34$). They also attribute the cause of their illness more to their own behavior than the others ($p=0.37$, $r=0.19$).

III.1.4. Discussion

The present study aims at offering a more thorough understanding of the way in which oncological patients with a family history of cancer deal with the cancer diagnosis and the way in which these patients assess coping mechanisms which influence the perception of the illness in the context of the family system: the cancer diagnosis represents a negative life event carrying a major impact on the quality of life. Adapting to the oncological disease depends on several factors: the individual's illness representations, the psychoemotional implications of the disease (characteristics and evolution), especially the presence of a history of direct contact with the disease (through family members), and the coping strategies. *Self-Regulatory Model* (SRM) is the explanatory cognitive-affective model adopted in this study, which emphasizes the emotional and cognitive components involved in disease management behaviors. The practical efficiency of these cognitive-behavioral coping strategies in accordance with SRM manifests itself in a functional perception of the disease in the context of good family communication and cohesion.

The results of this research prove that cancer patients faced illness frequently using acceptance and positive refocusing on planning, positive reassessment, putting things into perspective as cognitive-adaptive coping strategies, less often prosocial behavioral coping strategies (social relationing, seeking social support, assertive action, and passive behavioral coping strategies as avoidance and indirect action) and maladaptive cognitive coping strategies (rumination, catastrophizing, and antisocial behavioral coping strategies, such as other-blame). These data could be explained by the fact that the cancer diagnosis is a factor which threatens not just their health but their existence.

The Self-Regulation Theory predicted that illness representations would be directly associated with coping and, via this association, with other outcomes such as mood and disability (Weinman *et al.*, 1996). Researchers found that a negative coping style predisposes individuals with a family history of cancer to stronger psychological distress (Liu and Cao, 2014). Some studies reported that 46% of women with a family history of cancer were concerned about the possibility of developing the disease (Gorin, 2010). An extremely important factor is the patient's satisfaction, which is determined by a positive relationship with the doctor, good compliance, and a low rate of complications; consequently, it minimizes the psychological and physical distress.

The evidence of relationships between illness cognitions and psychological distress was proved in many research in the field and pointed the way to the development of a psychological intervention for women diagnosed with breast cancer, based on the modification of their cognitions (Rozema *et al.*, 2009; McCorry *et al.*, 2013; Defrank *et al.*, 2013; Danhauer *et al.*, 2009). Variables such as personal history of cancer, female gender, family history of cancer, negative perception of the illness, and coping style are factors associated with maladaptive psychological manifestations (psychological distress and low level of quality of life) in people under oncogenetic surveillance for hereditary cancer (Lifford *et al.*, 2012; Gopie *et al.*, 2012). These variables were proved to be crucial factors influencing compliance with cancer screening programs. In this way, the results of this study on oncological patients promote the benefits of an early identification of individuals with an elevated risk of developing cancer due to family history, so that they can be included in personalized psychological intervention programs with the purpose of reducing the maladaptive coping strategies and helping them and their families deal with the diagnosis and the treatment in an adequate way. In the updated recommendations on *Genetic Cancer Risk Assessment, Counseling and Testing*, health practitioners recommend genetic counseling using: the input (medical and family histories), psychosocial assessment,

cancer risk assessment (consultation and inquiring about the patient's current understanding of cancer genetic risk assessment and testing processes), genetic testing for an inherited cancer syndrome (regulations, informed consent, and counseling). The authors add follow-up considerations for better representations of the illness and coping mechanisms in order to influence the entire family system (family cohesion and family satisfaction) (Riley *et al.*, 2012). Other studies proved that the belief that the illness was part of family history could determine or maintain certain behaviors with negative consequences on the individual's health (Lijovic *et al.*, 2009; Kaphingst *et al.*, 2009; Fantini Hauwel *et al.*, 2011). The direct connection between a high level of family cohesion and a patient's functional, adaptive representation of the disease supports the fact that, for patients with a family history of cancer, therapeutic intervention must address both patients and their families, in order to build balanced, functional systems within these families. Most people with a family history of the illness have at least some beliefs and relevant knowledge regarding their own risk of developing the illness. According to Leventhal's *Self-Regulation Model*, which supports the role of external, environmental, social, and familial factors in forming representations of the illness, these beliefs generate a cognitive-emotional-behavioral model of illness representations through which people process information and act.

The chronology, consequences, and coherence of the illness have been significantly correlated with passive adaptation (van Oostrom *et al.*, 2007). Simultaneously, passive adaptation has anticipated the emotional suffering caused by hereditary cancer but also concerns about cancer. In addition, significant associations have been found between the (personal and/or family) history of cancer and perceptions of cancer (Kowalkowski *et al.*, 2012) between beliefs about inheriting cancer and adopting protective behaviors (Kaphingst *et al.*, 2009). Cognitive coping, based on refocusing on planning, positive reassessment, and broadening one's perspective correlate with an important level of the sense of illness coherence, underpinning the adoption of healthy behaviors. These results thoroughly complement the results of the study conducted by Delgado, which claimed that, for chronic diseases, even when accompanied by severe physical symptoms, the positive perception of illness-generated stress and of quality of life is moderated by a strong feeling of coherence (Delgado, 2007).

Catastrophizing as a maladaptive cognitive coping strategy, frequently encountered in oncological patients, directly correlates with a dysfunctional emotional perception of the illness. Adopting prosocial behaviors for social relationing and assertive action are closely connected to positive control beliefs and an adaptive emotional perception of the illness in the case of oncological patients with a family history of cancer. These results complete the findings of research supporting the significant correlation between coping strategies and illness perception (Rozema *et al.*, 2009; Gould, 2010; Travado and Reis, 2013; Postolica *et al.*, 2016; Woźniacki *et al.*, 2017), considering the family adaptability in the context of a family history of cancer.

III.1.5. Conclusions

In Romania, there is no analysis, at the level of the individual and the family, on patients with a family history of cancer from the perspective of coping strategies and the perception of the illness in the context of the family system. The results of the research are important for clinical practice, especially when treatment and therapeutic interventions are determined. Illness perception, family adaptability, and coping mechanisms are principal factors for the quality of life of a patient with a chronic disease. The success of the recovery therapy is ensured by an extended team including doctors, psychologists, and family members. Every therapeutic program must take into consideration the family history of cancer and the genetic factor, due to the fact that the representation of the disease depends on the discussed variables. The results of this study could be useful in developing screening tools to facilitate an individual and familial functioning adaptability of patients with a family history of cancer.

B. RARE DISEASES ASSESSMENT - A WAY TO IMPROVE LIFE QUALITY

A rare disease is a challenge, with national programs providing equal access to medical services for all patients with healthcare problems and to support costs related to them.

Living with a rare disease is also a challenge for both pediatric patients and their families. Affected children experience loss of social, educational and economic opportunities and difficulties in receiving medical care in suitable time caused by the need for a specialized medical team or proper medical investigation, with the latter sometimes being delayed (Schieppati *et al.*,2008; Iorga *et al.*, 2018c). After a clear diagnosis, the relationship with the medical encounter is crucial, the doctor-patient relationship influences the quality of life of a patient with a rare disease. The difficulties and importance of providing information about a rare dis-ease represents a challenge also for the healthcare provider (Budych *et al.*, 2012).

Most of the families are affected by the child's health condition: more financial expenses are needed to cover the specialized medical care, medical treatment, specialized equipment, and special education services (Angelis *et al.*, 2015).

Considering the type of disease, some families must travel to obtain a clear diagnosis, or they have to settle in a new location in order to have access to the treatment or medical equipment. Greater geographical distances between patients and physicians have been identified in a study lead by *EURORDIS* (EURORDIS. The voice of 12,000 patients: experiences and expectations of rare disease patients on diagnosis and care in Europe; 2009). Professional difficulties for parents are also noted, like an elevated level of unemployment among parents of children with rare diseases (Mulroy *et al.* 2007; Dellve L, *et al.* 2006).

A rare disease does not influence only a patient's and caregiver's life, but also the other children in the family and the quality of life of the sibling of a child with a rare disease is also affected (Zurynski *et al.*, 2008).

Family plays a leading role in assuring the quality of life of children affected by rare diseases. Around the world, support programs for parents of children with rare diseases were developed within the last decade. They help the caregiver cope with stress and train them to develop parental skills in order adjust properly to life with a rare disease. That is why factors like eco-nomic status, professional duties or other socio-demographic data like marital status, type of chronic disease, geographic area or the possibility to access medical services are also studied. The psychological and physical well-being of the career will in-fluence the quality of life of the affected child. In a recent study in Germany (Wallenwein *et al.*, 2017) it was revealed that the marital status influences this level, with single parents of children with cystic fibrosis obtaining significantly lower scores for quality of life than partnered parents. The mother of children with rare disease are usually affected mentally and physically, having significantly lower than average physical and mental well-being scores (Mulroy *et al.*, 2007; Laurvick *et al.*, 2006; Iorga *et al.*, 2018). Fathers are more likely to need supportive programs than mothers focusing on family competence (Dellve, 2006).

Since the parent psychological and physical health is important, the present study focuses on the opinion of parents regarding the disease and on some difficulties that they must deal with personal problems or issues related to their child's life.

For both patients and families, living with a rare disease is an ongoing learning experience. Research should address the many challenges in the management of rare disease and focus on identifying factors that improve life for people with rare diseases. Patient well-being does not involve only medical care, but also psychological support, for both patient and caregivers, especially mothers, single parents or the unemployed. Financial expenses and investments in studying rare diseases is approached differently by medical teams from different countries. This vulnerable population must be cared for care-fully to reduce psychological and physical distress for those affected by this type of illness.

They are between 5,000 and 8,000 rare diseases, most of them genetic. A rare disease is, according to the definition of World Health Organization (de Vrueh *et al.*,2013), a life-threatening or chronically debilitating condition from which not more than 5% of citizens in the European Community suffer. It is estimated that 30 million Europeans and 25 million Americans are suffering from a rare disease, which coincide with 6-8% of the total population (www.orpha.net).

As WHO guidelines, there is a strong recommendation to sustain and develop research in this area in order to help knowledge about rare diseases and to improve quality of life of patients suffering from orphan diseases. Social support should not be neglected also, *EURORDIS Care Survey Program* conducted in 23 countries between 2002-2008 included 12,000 patients with rare diseases (*EURORDIS*, 2009). The survey concluded that "social security systems are usually designed around common diseases are not flexible enough to take into consideration unprecedented health need" as is an orphan disease.

Phenylketonuria (PKU) is a rare metabolic disease that has consequences on cognitive development. The cognitive impairment appears if the patient is not treated with a strict protein-restricted diet. Even with early diagnosis and treatment of PKU children, these patients present some deficiencies intellectually compared to normal children (Aghasi *et al.*, 2015). Following the medical recommendation regarding diet are extremely important for medical development of the disease and for the quality of life of patient. In many cases, diet and its restrictions are the most stressful factor for parents having a child diagnosed with this disease and perceived social support and diagnosis resolutions seems to improve coping strategies and quality of life for caregivers (Medford *et al.,* 2017; Borghi *et al.,* 2017). Some studies assessing the occurrence of psychiatric disorders identified in patients with early treatment for PKU a high rate of anxiety disorder and the tendency of withdrawal were mentioned being the most frequent self-reported symptoms. A study of Manti showed that patients with good metabolic control in the first eleven years of life proved higher frequency of psychiatric diagnosis comparing to those having more years from diagnosis, meaning that respecting diet represents a distressful situation and children, or adolescents are feeling more frustrating (Manti *et al.*, 2016). Psychological and psychiatric evaluation is recommended for all children under medical treatment.

Cystic fibrosis (CF) is a genetic disease of the exocrine glands that affects all races but primarily whites. For this reason, since 2001, the American College of Obstetricians and Gynecologists recommends that white women be tested for the gene if they are pregnant or considering pregnancy (Grody *et al.,* 2001) and three years later, in 2004, the Centers for Disease Control and Prevention (CDC) published their pivotal recommendation that regions "begin newborn screening for CF" (Grosse *et al.*, 2004; Groose *et al.,* 2010). A patient with CF and also members of the family may have tremendous physical, psychosocial, and educational needs. As the patient get older, some recent problems may arise, or existing problems may worsen requiring comprehensive, multidisciplinary lifelong care (Gardner, 2017). Sometimes patients with CF could be misdiagnosed earlier in life as having asthma or chronic bronchitis.

Hypothyroidism can manifest with different signs and symptoms. In the pediatric population, the prevalence of this thyroid disorder is estimated to be less than 10% (Wu *et al.*, 2006). This disorder has a wide range of presentation from subclinical hypothyroidism to overt form. Hearing loss is more common in hypothyroid patients than normal population so diagnosing earlier the deafness will help children to be cognitively stimulated. Dental problems and cardiac manifestations must be identified to improve the quality of life for these patients.

Living with these rare diseases demand a lot of effort of family members, multidisciplinary team and a strong determination to empower the patient (if it is possible) to care about own medical and psychological problems. Early diagnosis, adherence to treatment, family, medical and social support are important for an important level of quality of life.

The care for the patients must be doubled by the care for the family members in order to improve life standards for all persons touched by the diseases.

One of the most common behaviors identified in mothers having a child with a rare disease is the hyper-protection, attitude with a negative impact over the years, causing a lot of reactiveness in children during their pre/adolescence period. That is why mothers or caregivers must be well trained to help, supervise, interfere and treat their children.

Turner Syndrome (TS) is a rare chromosomal disease which affects girls. At puberty ovarian function can sometimes be normal, with development of mammary glands in 25% of patients and spontaneous menarche in 3% of cases with homogeneous X monosomy and 10% of cases with X monosomy mosaicism. These persons present secondary amenorrhea, with progressive degradation of functional ovarian tissue. Under these circumstances, the spontaneous pregnancy in a woman with TS is a rarely event. Until the introduction of in vitro fertilization techniques (IVF), there were cited fewer than 200 pregnancies in women with TS (Gravholt, 2004; Pasquino *et al.*, 1997; Sybert and McCauley, 2004)

Craniofacial anomalies as *Cleft lip and palate* (CLP), affects the physical wellbeing and the development of children presenting this condition, their social and emotional wellbeing (Mossey *et al.*, 2009) and their quality of life (Felce and Perry, 1995). Children with CLP represent a socially disadvantaged group, with a tendency toward social inhibition, social anxiety and low self-esteem, due to their medical condition, facial appearance and speech difficulties (Wyszysnski, 2002; Hunt *et al.*, 2006; Piombino *et al.*, 2014). CLP patients require a multidisciplinary medical approach, the main goal being to offer the optimum patient care and to achieve the best possible treatment outcome (Jones *et al.*, 2011).

All physicians involved in the management of CLP patients need to use multiple radiologic examinations. This raises an ethical consideration: the need for a careful judgment on radiation exposure of these pediatric patients, considering its significant impacton their future quality of life (Holmberg *et al.*, 2010; Slovis, 2011; Khong *et al.*, 2013). CT becomes a valuable tool and leads to a relatively high radiation doses associated with CT scans, raising concerns for the pediatric patient's health and quality of life, potential risks, and the management of patient dose (Slovis, 2011; Goske *et al.*, 2014). Cone Beam Computed Tomography (CBCT), as a three-dimensional (3D) imaging technique, provides a lower dosage of radiation exposure, compared to the classic CT (Wortche *et al.*, 2006; Silva *et al.*, 2008; Ludlow and Ivanovic, 2008).

My interest regarding this area is reflected by the following articles:

Iorga Magdalena, Muraru Diana, Drochioi Ana-Simona, **Petrariu FD.** SOCIO-DEMOGRAPHIC CHARACTERISTICS AND REPORTED PSYCHO-MEDICAL SYMPTOMS FOR CHILDREN WITH RARE DISEASES. A COMPARATIVE STUDY BETWEEN PATIENTS WITH PHENYL-KETONURIA, CYSTIC FIBROSIS AND HYPOTHYROIDISM. *Medical-Surgical Journal-Revista Medico-Chirurgicala* Volume: 121, Issue: 3, Pages: 510-518, Published: 2017.
Web of Science Core Collection - Emerging Sources Citation Index / **WOS: 00042442800009**

Florescu L, Paduraru DT, Mîndru DE, Temneanu OR, **Petrariu FD,** Matei MC. EPIDEMIOLOGICAL EVALUATION REGARDING THE ROLE OF CYSTIC FIBROSIS AS A RISK FACTOR FOR CHILD MALNUTRITION. *Rev Med Chir Soc Med Nat Iasi* 2014; 118(2): 450-456 / **PMID: 25076714**

Gorduza V, **Petrariu FD.** OUTCOME OF SPONTANEOUS PREGNANCY IN TURNER SYNDROME. *Acta Endo (Buc)* 2015; 11: 348-355 / doi.org/10.4183/aeb.2015.348 / **IF=0.235**

Yllka Decolli, Danisia Haba, **Florin D. Petrariu,** Olga-Odetta Duma, Ana Elena Petcu. IMPROVEMENT OF HEALTH CARE FOR SOCIALLY DISADVANTAGED CHILDREN WITH CLEFT LIP AND PALATE ANOMALY BY USING PROPER RADIOLOGIC EXAMINATIONS *Revista de Cercetare si Intervenție Sociala* 2015; 51: 176-186 / **IF = 0.424**

III.2. Socio-demographic characteristics and reported psycho-medical symptoms for children with rare diseases

III.2.1. Aim

The aim of this study is to identify psychological and medical symptoms of pediatric patients suffering from these three rare diseases (cystic fibrosis, hypothyroidism and phenylketonuria) as that are declared by their mothers.

III.2.2. Material and methods

A number of 37 patients aged 1-22 years old were included in the study (M=7.61 ± 6.37). In Romania, patients older than eighteen are continuing to be hospitalized in pediatric clinics till the age of 25 if they are registered in the educational system. The children were diagnosed and under medical supervision in "Sf. Maria" Emergency University Hospital for Children from Iasi, Romania with one of the following three rare disease: cystic fibrosis, hypothyroidism and phenylketonuria.

The study has been approved by the Ethical Committee of "Sf. Maria" Emergency Clinical Hospital for Children from Iasi and questioned mothers and children were informed about the confidentiality and use of data and results and mothers signed an informed consent before filling in the items. Socio-demographic and family member's information (age for patient and both parents, sex, religion, department, environment and level of education for both parents) were registered. The mothers of the patients had to indicate psychological, social and physical symptoms that they have been identified to their children. Statistical analysis was performed using IBM *SPSS Statistics version 23.0*.

III.2.3. Results

Socio-demographic and self-reported data were gathered during their hospitalizations from 2016. For 24 boys and 13 girls hospitalized in 2016, mothers reported psychological and medical symptoms for their children and appreciated their social interactions with peers.

More than half of the patients (69.4%) are aged between 2 and 6 years old, 27.8% are aged between 6 and 12 years old, and the rest (2.8%) are older than 12 years old.

The patients are coming from six districts of North-Eastern part of the country (Bacau, Botosani, Iasi, Neamt, Suceava, Vaslui), 17 of patients (45.95%) living in urban area and 20 (54.05%) living in countryside (Table XLI).

Table XLI. Data referring to the distribution of patients accordingly to disease, sex and age at diagnostics

DISEASE	Male	Female	Age at diagnostic (Mean ± SD)
Phenylketonuria	10 (41.7%)	1 (7.7%)	1.12 ± 1.24 months
Hypothyroidism	3 (12.5%)	6 (46.2%)	1.66 ± 0.70 months
Cystic fibrosis	11 (45.8%)	6 (46.2%)	20.58 ± 34.71 months

Family data. Mothers were asked about their marital situation at the time of diagnosis and 25 of them (67.57%) declared that they were married. A number of 11 of them (32.35%) are having one child, 18 (52.94%) are having 2 children, 3 (8.82%) are having 3 children and 2 (5.88%) are having 4 children (the number of births / mothers is M = 2 ± 0.76).

Data about the religion of the family members revealed that the majority patients are Orthodox-Christian (92.1%), and a small number is Pentecostal (5.3%) and Adventist (2.6%).

The minimum age of mothers is 18 and the maximum is 55 years old (M = 33.05 ± 8.52). For the fathers, age varied from 21 to 56 years old (M = 37.87 ± 7.79).

Data regarding the educational level of parents was also registered. A total of 6.1% of the mothers have primary education background, 21.2% gymnasium level, 57.6% have reached high school level, and 15.2% graduated college. In what concern the level of education of fathers, 5.7% have primary education background, 22.9% gymnasium level, 68.6% have reached high school level, and 2.9% graduated college.

III.2.4. Discussion

Patients with phenylketonuria. The minimum registered age at diagnosis for this category of pediatric patients is 0 months (3 weeks) and the maximum is 4 months, with a mean of 1.12 ± 1.24 months. In the case of *phenylketonuria* none of the patients (with M =3.36 ± 3.29, minimum age of 1 year old and maximum age of 13 years old) displayed loss of appetite, bowel movement problems, muscular dystrophy, intellectual disability, bradypsychia, language difficulties, memory difficulties, unhealthy behaviors, bruxism, night terrors, bed wetting, behavioral problems, isolation (by others or themselves), panic attacks, or a high caloric diet. 40% of the patients presented nutritional problems and 40% of the patients presented sleep-related problems. Most of them (80%) complied with their treatment. Considering anger outbursts, 25% of the patients had them, and more than half of the patients (60%) were advised on a nutrition diet, 20% of the children had depression, and more than half of the patients (66.7%) followed nutritional recommendation.

Patients with hypothyroidism. The minimum registered age at diagnosis for this category of disease is at birth (more frequent is the third week of life) and the maximum is 3 months, with a mean of 1.66 ± 0.70 months. The age at the time of the study is M =3.62 ± 1.68, with a minimum age of 1 and a maximum age of 7. In the case of *hypothyroidism*, patients did not display bowel movement problems, muscular dystrophy, bradypsychia, memory difficulties, nutrition problems, bruxism, night terrors, bed wetting, panic attacks or a high caloric diet. 16.7% we identified a loss of appetite, and 33.3% presented intellectual disability. Almost 40% of the patients had language problems and 20% of the patients displayed unhealthy behaviors. For 16.7% of the patients, were reported sleep problems.

In case of 20% of the patients, mothers were reported having depressive symptoms. More than half of the patients (60%) complied with their treatment and 83.3% were taking medication. Twenty percent of the patients experienced isolation (by others or themselves) and 20% of the patients displayed anger outbursts. Half of the patients were advised on a diet. Many of the patients (80%) followed their nutritional recommendations.

Our findings are congruent to the scientific data from the literature. Findings published by Rovet, and Ehrlich indicated cognitive problems for children with hypothyroidism that persist into adolescence (memory, attention, or visual and spatial processing areas) (Rovet and Ehrlich, 2000). For these problems, the educational support is extremely important, to supervise medical condition, intellectual achievement and behavior.

Mothers identified for 20% of those children suffering from hypothyroidism they are having depression symptoms, angriness, unhealthy behaviors and isolation. Their physical aspect, the cognitive impairment, language problems and motor skills (Fuggle *et al.,* 1991; Campos *et al.,* 2017) are factors that influence their social interaction so, family members, and teachers must diminish the child's distress. Social and educational difficulties should not be underestimated, as the scientific results are proving that physical condition is usually more supervised and cared compared to psychological and social well-being (Bongers-Schokking *et al.,* 2016; Soonawala *et al.,* 2015). Despite the negative cognitive development in case of under-treatment, few studies have been focused on the effects of overtreatment of patients with this disease. Bongers-Schokking shows that overtreatment during the first two years determines lower cognitive outcomes (the study being lead on patients aged 11 years old). A fast TSH normalization at initial treatment leads to above-normal development scores at a youthful age

but does not affect the quotient of intelligence at the age of 11 years old (Bongers-Schokking *et al.*, 2013).

Patients with cystic fibrosis (CF). The age registered at diagnosis for this category of disease varied from first month) to 132 months, with a mean of 20.58 ± 34.71 months. The age at the moment of the study is M =12.23±6.13 (from 5 years old to 22 years old).

The patients diagnosed with CF have no record of bradylalia, memory difficulties, unhealthy behaviors, night terrors, behavioral problems or panic attacks. 23.1% had a loss of appetite, 66.7% had bowel movements problems, 30.8% had muscular dystrophy and 9.1% presented intellectual disability and bradypsychia (Table XLII).

Table XLII. Comparative results for variables in PKU, hypothyroidism and CF

VARIABLES		Phenylketonuria (%)	Hypothyroidism (%)	Cystic fibrosis (%)
Loss of appetite	Yes	0	16.7	23.1
	No	100	83.3	76.9
Bowel movement problems	Yes	0	0	66.7
	No	100	100	33.3
Muscular dystrophy	Yes	0	0	30.8
	No	100	100	69.2
Intellectual disability	Yes	0	33.3	9.1
	No	100	66.7	90.9
Bradypsychia	Yes	0	0	9.1
	No	100	100	90.9
Bradylalia	Yes	0	40	0
	No	100	60	100
Memory difficulties	Yes	0	0	0
	No	100	100	100
Fertility problems	Yes	0	0	28.6
	No	100	100	71.4
Unhealthy behaviors	Yes	0	20	0
	No	100	80	100
Nutrition problems	Yes	40	0	25
	No	60	100	75
Sleep problems	Yes	40	16.7	10
	No	60	83.3	90
Bruxism	Yes	0	0	20
	No	100	100	80
Night terrors	Yes	0	0	0
	No	100	100	100
Bed wetting	Yes	0	0	18.2
	No	100	100	81.8
Behavioral problems	Yes	0	0	0
	No	100	100	100
Depression	Yes	20	20	9.1
	No	80	80	90.1
Compliance with treatment	Yes	80	60	45.5
	No	20	40	54.5
Medication	Yes	0	83.3	91.7
	No	100	16.7	8.3
Isolation	Yes	0	20	7.7
	No	100	80	92.3
Panic attacks	Yes	0	0	0
	No	100	100	100
Anger outbursts	Yes	25	20	8.3
	No	75	80	91.7
High caloric diet	Yes	0	0	41.7
	No	100	100	58.3
Diet	Yes	60	50	69.2
	No	40	50	30.8
Following nutritional recommendations	Yes	66.7	80	100
	No	33.3	20	0

Most of the patients suffering from CF present nutritional problems (25%), 10% had sleep problems, 20% present bruxism and 18.2% were diagnosed with enuresis. A small number of pediatric patients (9.1%) presented symptoms of depression. Almost half of the patients (45.5%) complied with their treatment and large majority of patients (91.7%) took medication.

For 7.7% of patients' mothers declared that children experienced isolation and 8.3% of the patients displayed anger outbursts. 41.7% from the patients were on a high caloric diet and 69.2% received a diet, and all the patients followed their nutritional recommendations.

Early medical intervention is essential for these patients so neonatal screening is demanded. Understanding the ethical issues in CF is a key factor for providing optimal care of newborn with CF (Anton-Paduraru and Iorga, 2015). Our results prove that children with CF have an older age at the moment of their diagnostic comparing to the pediatric patients suffering from the other two disease. Comparative results for the three diseases are presented in table XLI. The higher number of symptoms identified by mother are those having children diagnosed with cystic fibrosis.

Regarding the nutritional recommendations, the rate of affirmative responses is very high, for all 3 of diseases. This result proves that families understand very well importance of the nutritional diet and respect the medical recommendation to negative effects on child's development. Prevention or prompt treatment of iron deficiency may improve cognitive development and behavior of children with PKU (Anton-Păduraru *et al.,* 2017). It is important to register from the beginning of the diagnostic family rules for food and nutrition and to identify restriction imposed, for example, by the religious believes. Multidisciplinary assessment is imposed for all these medical cases.

We found that an important rate of pediatric patients questioned are presenting nutritional problems and sleep disturbance (higher rate in phenylketonuria), cognitive impairment (higher rate for hypothyroidism), and enuresis and bowel syndrome (higher rate for cystic fibrosis). Almost 20% of diagnosed children with hypothyroidism and phenylketonuria were found to have depression symptoms, as their mothers declared. The physical and psychological problems seem to be frequent and care for these patients must be done in a multidisciplinary team, as soon as possible after the diagnostic. Personalized educational support plan is required for children that have cognitive delay such those with congenital hypothyroidism and hearing tests, memory deficit, speech and visual development must be targeted from the beginning (Léger *et al.,* 2014).

III.2.5. Conclusions

Children with a rare disease present several psychological symptoms and social difficulties that can been identified by the family members, especially mothers who are the most frequent the responsible and dependable caregiver.

The educational support of pediatric patient and psychotherapy intervention for both patients and families are needed as soon as possible after the medical diagnostic. Psychological support must not be neglected or not prioritized due to the medical outcomes.

III.3. Cleft lip and palate paraclinical assessment

III.3.1. The aim of this study was to assess the level of knowledge in this area among medical residents involved in *Cleft Lip and Palate* (CLP) treatment through the means of a questionnaire and to address its impact on their patients' quality of life.

III.3.2.Material and methods

A questionnaire was designed and applied to residents training in four medical specialties involved in CLP treatment: Pediatric surgery, Plastic surgery and reconstructive

microsurgery, Oral and maxillofacial surgery, Orthodontics and Orthopedics at "Grigore T. Popa" University of Medicine and Pharmacy of Iasi, Romania. The content validity of the questionnaire was assessedby one expert in dent maxillofacial radiology (Burns *et al.*, 2008). The questionnaire consisted in 3 sections and 10 items: (1) *The first section* (I 1-3) contained personal data (age, sex, medical specialty); (2) The items of *the second section* (I 4-6) targeted the residents' concepts on the necessity and the importance of 3D imaging, and also their indications of choice in CLP management, using multiple response questions; (3) *The third section* (I 7-10) aimed to assess the residents' self-evaluation on their current knowledge regarding 3D imaging modalities. Simple Yes/No responses items were used, alternating with 5-point Likert scale items (options: *very low, low, medium, high, very high*).

The pretest survey was conducted on a sample of 20 residents training in another similar medical specialty: dentoalveolar surgery (Burns *et al.*, 2008;Krosnick and Presser, 2010; Stone, 1993). The pretesting resulted in small changes regarding enunciation, and the revised form of the questionnaire was then applied to the studied sample, consisting in 104 residents. 55 residents agreed to participate in the testing phase, filling in the questionnaire that was distributed to them (Table XLIII). Before the testing, the respondents were encouraged to answer all items honestly, being ensured of the preservation of their anonymity. The retest phase took place by distributing the same questionnaire to the respondents, two weeks after their participation to the testing phase (Burns *et al.*, 2008). From all 55 residents physians, 33 agreed to respond to the second application of the questionnaire (Table XLIII). The questionnaires in both test and retest phases had a specific ID code for every participant, allowing the evaluation of test-retest reliability assessment (Burns *et al.*, 2008).

Statistical analysis was performed by using IBM *SPSS Statistics version 16.0*, to compare test and retest applications of the questionnaire. Corresponding to the type of questions found under section 2 and 3 of the questionnaires we have used: (1) The *McNemar* test, used to compare discordance of two dichotomous responses, was used for questions with multiple possible answers; (2) The *Marginal homogeneity* test, an extension of *McNemar* test, was used just for single response questions; (3) *Spearman* correlation coefficient was used for *Likert* scale response questions.

Table XLIII. Participating residents in test and retest phases

	Values	Test (55)	Re-test (33)
Pediatric surgery	N	12	10
	%	21.8	30.3
Plastic surgery / reconstructive microsurgery	N	19	13
	%	34.5	39.4
Oral and maxillofacial surgery	N	11	1
	%	20.0	3.0
Orthodontics and dentofacial orthopedics	N	13	9
	%	23.6	27.3

III.3.3. Results

Test-retest reliability. The results of *McNemar* test and of the *Marginal homogeneity* test showed no significant difference between the two applications of the questionnaire for each participant (Table XLIV).

The *Spearman* correlation coefficient calculated for items 8 and 10 showed a good or strong correlation (Table XLV). The *t*-test values ($p<0.01$) showed a statistically significant correlation between test and retest results, with a confidence interval of 99% (CI). These data confirm the questionnaire's reliability and reproducibility.

Section I of the questionnaire. Out of 104 residents training in the selected medical specialties involved in CLP treatment, 55 agreed to participate in the present study, achieving a response rate of 52.88%. The participants' ages ranged from 25 to 41 years, with a balanced male/female distribution (about 4/5). The subjects' distribution on specialties was balanced.

Table XLIV. Results of the *McNemar* test for multiple answer items

ANSWERS	Item 4	Item 6
1	1.000	1.000
2	0.453	0.250
3	0.774	1.000
4	0.727	1.000
5	1.000	0.125
6	0.549	0.092
7	0.125	*
8	0.065	0.021
9	0.500	1.000
10	-	1.000
11	-	0.500
12	-	1.000
13	-	0.070
14	-	0.549
15	-	*

*Answer chosen by none of the respondents

Table XLV. Test-retest reliability results for single answer items and *Likert* scale answer

ITEMS	Spearman Coefficient[1]	Marginal Homogeneity Test[2]	t-test[1]
Item 05	-	0.782	0.000
Item 07	-	1	0.000
Item 08	0.942	-	0.000
Item 09	-	0.317	0.000
Item 10	0.804	-	0.000

[1] p=0.01 , [2] p=0.05

Section II of the questionnaire. When asked to choose imaging modalities they deemed necessary to prescribe during CLP management, participants chose both two-dimensional (2D) and 3D procedures. Nevertheless, CT was considered the most useful imaging modality by 58.2% of the respondents, followed by CBCT (29.1%), pointing out the perceived importance of 3D imaging among residents (Figure 12). Fewer Plastic surgery and reconstructive microsurgery residents opted for CBCT, as being a necessary imaging modality, compared to residents from the other three medical specialties.

The same tendency was observed when opting for the most useful imaging modality in CLP management. On both occasions, a statistically significant difference was found (pairwise t-test, 95% CI). In their clinical practice with CLP patients, 63.6% of the interviewed residents would opt for simultaneous indication of 2 or 3 imaging techniques – of which at least one is a 3D imaging modality (80% of cases). Again, fewer Plastic surgery and reconstructive micro-

surgery residents opted for CBCT, compared to the other three medical specialties (pairwise t-test, 95% CI).

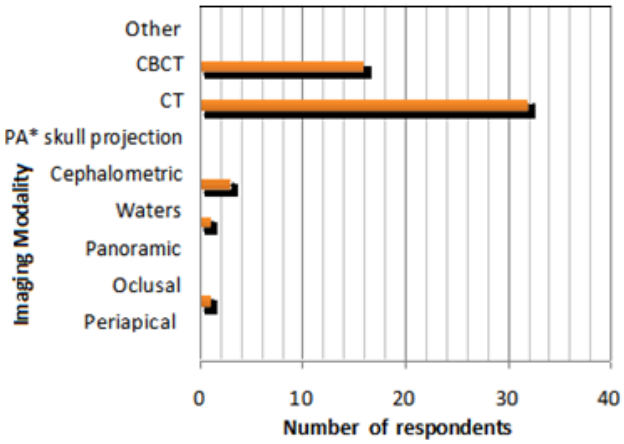

Figure 12. *Residents' perception on the most useful imaging modality in CLP management*

Comparing the prescription of digital and conventional 2D imaging modalities, no statistically significant difference was found. Nevertheless, fewer Plastic surgery and reconstructive microsurgery residents opted for digital techniques, compared to their colleagues (pairwise t-test, 95% CI).

Table XLVI. Residents' perceptions of their knowledge in 3D imaging interpretation

LEVEL OF KNOWLEDGE ON INTERPRETATION			
		CT	CBCT
Total	N	55	55
	%	100	100
1-Very low	N	15	29
	%	27.3	52.7
2-Low	N	15	12
	%	27.3	21.8
3-Medium	N	20	10
	%	36.4	18.2
4-High	N	4	3
	%	7.3	5.5
5-Very high	N	1	1
	%	1.8	1.8

Table XLVII. Mean scores on 5 points scale

LEVEL OF KNOWLEDGE ON INTERPRETATION		
	CT	CBCT
Valid Number	55	55
Mean	2.29	1.82
Minimum	1	1
Maximum	5	5
Standard Deviation	1	1

Section III of the questionnaire. Most of the residents considered that they cannot correctly interpret CT and CBCT examinations (78.2%, respectively 83.6%). More than half

of the respondents (Table XLVI) self-assessed their level of knowledge on the interpretation of 3D imaging results as being very low or low (54.6%in the case of CT, respectively 74.5% for CBCT). The calculated mean scores for the self-assessed level of knowledge on interpreting 3D imaging results are showed in Table XLVII. The score regarding CT results interpretation was significantly higher when compared to CBCT (pairwise t-test, 95% confidence interval).

III.3.4. Discussion

The recognition of the effects of radiation in children has conducted to substantial effort to train physicians to request only the indicated imaging modalities, for diminishing the radiation exposure from diagnostic medical imaging and respect the *As Low As Reasonably Achievable* principle (ALARA) (Farman, 2005; Fazel *et al.*, 2009; Slovis, 2011; Goske *et al.*, 2014). Other studies reported cumulative radiation exposure to increase the risk of producing cancer and other pathologies among children (Holmberg *et al.*, 2010; Khong *et al.*, 2013; Miglioretti *et al.*, 2013).

Previous studies have shown stress, anxiety, depression among children with CLP and their parents, related to satisfaction with facial appearances, concerns on the quality of health care provided and their involvement in treatment planning (De Sousa *et al.*, 2009).

CLP patients undergo multiple imaging procedures, indicated to examine the size, its position and the structures involved by the cleft. Considering the complexity and the fragmentation of CLP treatment, as well as the young age of the patients, radiation exposure dictates a careful judgment and balance betweenpotential risks and the clinical benefits of each radiologic examination (Fazel *et al.*, 2009; Connolly, *et al.*, 2006). Since a specialized multidisciplinary treatment center for CLP patients in yet not available in Romania, CLP management is conducted by physicians working in different clinics and hospitals.That makes it difficult to access the patient's exposure history, considering the absence of a national radiologic data base and the lack of communication among different medical specialties. Technology in 3D imaging, alongside with digital 2D imaging, is a valuable tool in the preoperative assessment, as well as in the outcome evaluation during different stages of the CLP treatment (Albuquerque *et al.*,2011; Kapila *et al.*,2011). CBCT technique for maxillofacial imaging was introduced in the late 90's (Mozzo *et al.*, 1998; Arai *et al.*, 1999) and since then, its applications have been growing rapidly, offering a lower dosage of radiation exposure compared to CT (Wortche *et al.*, 2006; Silva *et al.*, 2008). The use of CBCT scans instead of classic CT whenever is possible, applies a dose-reduction strategy, contributing to radiation protection and to a better medical care for these pediatric patients. Statistical processing of data pooled from the 2nd section of our questionnaire showed that the respondents understand the importance of 3D imaging and indicate these modalities during CLP management. While the results obtained in the 3rd section of the questionnaire indicate low scores for both 3D imaging techniques, a more pronounced lack of knowledgecan be observed when referring to CBCT, compared to CT. This may explain the more frequent indication for CT scans, as observed from the answers of the participating residents. Another explanation is the availability of CT units in hospitals, compared to CBCT equipment which are not covered by medical assurance. This may influence the physician's decision because a large number of CLP patients come from vulnerable families. Other results showed no statistically significant difference when comparing the indication of digital techniques to the conventional 2D imaging modalities. This fact highlights those digital techniques reduces in great measure the radiation dose compared to conventional 2D imaging (Shah *et al.*, 2014).

III.3.5. Conclusions

Our results indicate the necessity to improve the physicians' awareness on the necessity of high-quality health services for CLP patients - as socially disadvantaged children, and pediatric patients in general, but also on the effect of improper radiation on these patients' quality of life.

CHAPTER IV

HEALTH PROMOTING NUTRITION AND NUTRITIONAL HABITS

Health promoting nutrition may be another way to value one of the Hippocrates of Kos most debated recommendation "*Let food be your medicine, and medicine be your food."*

A well-balanced nutrition is the simplest way to preserve human health status, but also to fight against medical problems like cardiovascular diseases, diabetes, systemic pathologies.

Analyzing the intake of nutrients from this perspective can offer new possibilities to prevent tissular damages, to protect or regenerate certain tissular structures. This approach is considered to be significant less harmful than intake of chemical synthetic non-self-substances.

A. NUTRITIONAL PREVENTION IN ATHEROSCLEROTIC DISEASE

Atherosclerotic cardiovascular disease represents nowadays a leading cause of death worldwide (Laslett *et al.*, 2012; De Backer, 2018). Surveys data of coronary patients prove that the implementation of guidelines regarding cardiovascular diseases prevention in clinical practice needs improvement (De Backer, 2018; Kotseva *et al.*, 2016). Scientific studies related to atherosclerosis are being constantly published, in time with an increase in morbidity and mortality due to ischemic heart disease. The medical community is justifiably focused on cardiovascular diseases prevention, following the control of risk factors involved in the etiology of these disease (total cholesterol, low-density lipoprotein-cholesterol, glycemia, uric acid, smoking, hypertension, hyperhomocysteinemia) (Yuan *et al.*, 2014; Tuñón *et al.*, 2018; Filip *et al.*, 2010).

Recent epidemiological data support the idea that hypertriglyceridemia is a prevalent risk factor for cardiovascular diseases and plays a significant role in the pathogenesis of atherosclerosis. Consequently, current perspectives of how dyslipidemia is treated should be renewed to also target the normalization of triglyceride levels (Goldberg *et al.*, 2018). Upon correction of serum LDL, both with medication as well as via a hygienic-dietetic regimen, there is still a residual risk of atherosclerosis mainly due to the lipoproteins which are known to transport triglycerides (Peng *et al.*, 2017). The mechanism by which lowering the level of plasma triglycerides leads to a decrease of the total cardiovascular risk appears to be the apoB (apolipoprotein B) reduction (Ference *et al.*, 2019).

The fact that triglycerides stimulate the production of inflammatory cytokines, of fibrinogen, and coagulation factors, thus affecting fibrinolysis, is another confirmation of its role in the atherosclerotic process (Tenenbaum *et al.*, 2014). The involvement of triglycerides in atherosclerosis and in increasing the total cardiovascular risk is therefore evident, but additional research is necessary in order to establish if elevated levels of serum triglycerides cause ischemic heart disease per se or by association with other known cardiovascular risk factors such as diabetes mellitus or obesity (Simha, 2020; Packard *et al.*, 2020).

We have investigated the anti-atherogenic potential of valine and leucine, two non-polar amino acids, in the context of hypercholesterolemia induced by a cholesterol-rich diet, and we followed their effects on lipid metabolism (total cholesterol, HDL (high-density lipoprotein)-cholesterol, LDL-cholesterol) and oxidative stress parameters (Cojocaru *et al.*, 2010; Cojocaru *et al.*, 2012a; Cojocaru *et al.*, 2012b; Cojocaru *et al.*, 2014).

These two essential aminoacids are provided by food-rich in leucine, like salmon, eggs, different types of seeds (sesame, pumpkin seeds, hemp) and algae (spirulina), or by food-rich in valine, like eggs (egg white), soybeans, beans, oats, wheat, spinach, broccoli and avocado.

My interest regarding this area is reflected by the following article:

Cojocaru E, Leon-Constantin M, Ungureanu C, Trandafir MF, Mastaleru A, Trandafir L, **Petrariu FD**, Badulescu OV, Filip N. HYPOLIPEMIANT ACTIONS AND POSSIBLE CARDIOPROTECTIVE EFFECTS OF VALINE AND LEUCINE: AN EXPERIMENTAL STUDY *Medicina* 2021; 57, 239, https://doi.org/10.3390/Medicina57030239 / **IF= 2.430**

IV.1. Hypolipemiant actions and possible cardioprotective effects of valine and leucine: an experimental study

IV1.1. Aim

In this paper, we focus on our results regarding the study of triglycerides levels, agreeing that hypertriglyceridemia could become an important therapeutic target in the management of atherosclerosis.

IV1.2. Material and methods

The experimental study conducted over a period of 60 days. Male Wistar rats weighing 250-280 g was obtained from the animal farm of the "Grigore T. Popa" University of Medicine and Pharmacy of Iași. All animal protocols were conducted in accordance with the instructions of the Guide regarding animal care and scientific use, in strict accordance with international ethical regulations (NACLAR Guidelines 2021; AVMA Guidelines for the Euthanasia of Animals: 2013).

The rats were divided into four groups as follows:

1. Control group I (n = 8): Fed with a regular diet composed of agricultural byproducts.
2. Group II-C (n = 8): Received regular diet supplemented with 0.4 g/kg/day cholesterol.
3. Group III-C + V (n = 8): Received regular diet supplemented with 0.4 g/kg/day cholesterol and 62.5 mg/kg/day valine powder for animal nutrition.
4. Group IV-C + L (n = 8): Received regular diet supplemented with 0.4 g/kg/day cholesterol and 69.985 mg/kg/day leucine powder for animal nutrition.

Blood samples were collected from the retro-orbital plexus, under anesthesia of animals with 75 mg/kg of intraperitoneal ketamine, in three moments of the experiment as follows: R0-1st day, R1-30th day R2-60th day. The measurement of triglycerides levels was made using Diagnosticum Zrt kit bought from Budapest, Hungary, as in our previous studies (Fossati and Prencipe, 1982).

The study was conducted in accordance with the 2010/63/EU directive and followed the recommendations of the National Institutes of Health (NIH) Guide for the Care and the Use of Laboratory Animals. Prior to the beginning of the study, the protocol received ethical approval from the ethics committee of the "Grigore T. Popa" University of Medicine and Pharmacy of Iași, Ethics Committee approval number 15186/2008.

The data were centralized in *Microsoft Excel* and IBM *SPSS* databases and processed with their respective suitable statistical. Statistical confidence intervals (CI) with a 95% significance level were used. In order to evaluate the statistically significance between our groups we used *ANOVA* test (including repeated measures *ANOVA*). The threshold for statistical significance is the maximum level of probability which affords an error.

IV.1.3. Results

For each group, triglycerides were measured in R0, R1 and R2. Table XLVIII and Figure 13 shows the levels of triglycerides throughout the experiment, as well as the variance of the measured values series.

In the control group, the variance was low, ranging from 3.27 to 3.77 CV (coefficient of variation) %, with R2 results being the most homogenous (3.27 CV%).

In groups II, III and IV, the coefficients of variation ranged from 2.45 to 14.82 CV%.

In these cases, the most homogenous results were registered in R2 in group II—C (8.04 CV%) and group IV—C + L (4.36 CV%), and in R1 in group III—C + V (2.45 CV%).

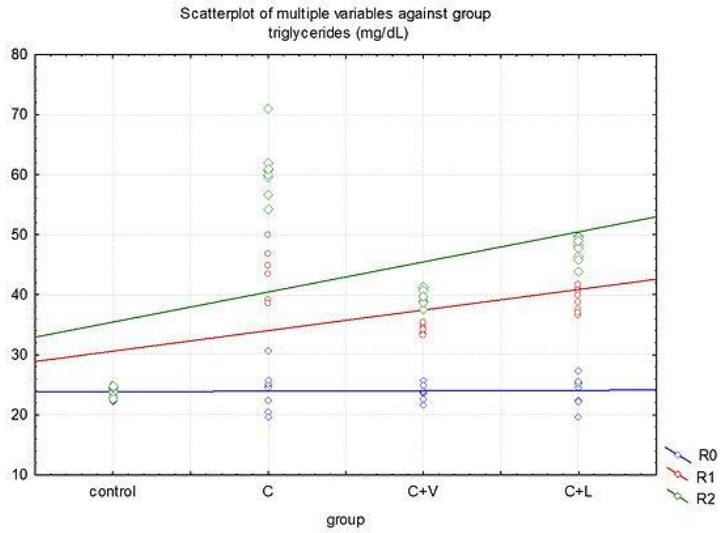

Figure 13. *Individual levels of triglycerides in all groups.*

Table XLVIII. Levels of triglycerides in all groups

Group	R0	R1	R2
Group I: control			
Average mg/dL	23.70	23.88	23.90
SD	0.89	0.90	0.78
CV%	3.76	3.77	3.27
Group II: C			
Average mg/dL	24.19	45.73	60.61
SD	3.44	6.78	4.87
CV%	14.22	14.82	8.04
Group III: C + V			
Average mg/dL	23.91	34.15	39.73
SD	1.31	0.84	1.30
CV%	5.48	2.45	3.27
Group IV: C + L			
Average mg/dL	24.04	39.15	47.56
SD	2.43	2.01	2.07
CV%	10.13	5.14	4.36

The highest individual levels of triglycerides were found in group II corresponding to the rats who received cholesterol only (Figure 13).

A one-way repeated measure analysis of variance (*ANOVA*) was conducted to evaluate the null hypothesis that there is no change in the triglycerides values in different subgroups measured in R0, R1 and R2 ($N = 32$) (Table XLIX).

The results of the *ANOVA* indicated a significant time effect, Wilks' Lambda = 0.015, $F(2, 27) = 879.33$, $p < 0.01$, $\eta^2 = 0.98$. Thus, there is significant evidence to reject the null hypothesis.

Table XLIX. Multivariate tests using one-way repeated measure analysis of variance

Multivariate Tests [d]									
Effect		Value	F	Hypothesis df	Error df	Sig.	Partial Eta Squared	Noncent. Parameter	Observed Power [b]
Time	Pillai's Trace	0.985	879.337 [a]	2.000	27.000	0.000	0.985	1758.674	1.000
	Wilks' Lambda	0.015	879.337 [a]	2.000	27.000	0.000	0.985	1758.674	1.000
	Hotelling's Trace	65.136	879.337 [a]	2.000	27.000	0.000	0.985	1758.674	1.000
	Roy's Largest Root	65.136	879.337 [a]	2.000	27.000	0.000	0.985	1758.674	1.000
Time * Type	Pillai's Trace	1.058	10.487	6.000	56.000	0.000	0.529	62.920	1.000
	Wilks' Lambda	0.028	44.831 [a]	6.000	54.000	0.000	0.833	268.989	1.000
	Hotelling's Trace	31.694	137.340	6.000	52.000	0.000	0.941	824.037	1.000
	Roy's Largest Root	31.596	294.898 [c]	3.000	28.000	0.000	0.969	884.694	1.000

[a] Exact statistic. [b] Computed using alpha = 0.05. [c] The statistic is an upper bound on F that yields a lower bound on the significance level. [d] Design: Intercept + Type. Within Subjects Design: Time. * Statistical difference between time and type (groups).

Follow-up comparisons indicate that each pairwise difference was significant, $p < 0.01$. There was a significant increase of values over time (Table L).

Table L. Pairwise comparisons between the studied groups.

Pairwise Comparisons								
(I) Time		(J) Time		Mean Difference (I-J)	Std. Error	Sig.[a]	95% Confidence Interval for Difference [a]	
							Lower Bound	Upper Bound
dimension1	R0	dimension2	R1	−11.766 *	0.459	0.000	−12.934	−10.597
			R2	−18.986 *	0.454	0.000	−20.143	−17.829
	R1	dimension2	R0	11.766 *	0.459	0.000	10.597	12.934
			R2	−7.220 *	0.321	0.000	−8.038	−6.401
	R2	dimension2	R0	18.986 *	0.454	0.000	17.829	20.143
			R1	7.220 *	0.321	0.000	6.401	8.038

Based on estimated marginal means. *. The mean difference is significant at the 0.05 level. [a] Adjustment for multiple comparisons: Bonferroni.

In R0, there were no significant differences between the average levels of triglycerides in groups II, III and IV and neither between these and the control group ($p < 0.05$). Compared to the control group, the average levels of triglycerides were significantly higher in all groups in R1 and R2 ($p < 0.001$).

Also, in R1 and R2 measurements, the average triglycerides in group II receiving cholesterol only (C) were significantly higher than those in group III receiving valine (C + V) as well as in group IV receiving leucine (C + L) ($p < 0.001$; $p < 0.05$).

At the end of the experiment (R2), the average triglycerides in group III were significantly lower than in the case of rats who received leucine ($p < 0.001$) (Table LI, Figure 14).

As described before, in previous studies, we evaluated the anti-atherogenic potential of valine and leucine in the context of hypercholesterolemia induced by a cholesterol-rich diet, following their effects on lipid metabolism (total cholesterol, HDL-cholesterol, LDL-cholesterol) and oxidative stress parameters (Cojocaru *et al.*, 2010; Cojocaru *et al.*, 2012a; Cojocaru *et al.*, 2012b; Cojocaru *et al.*, 2014) (Table LII).

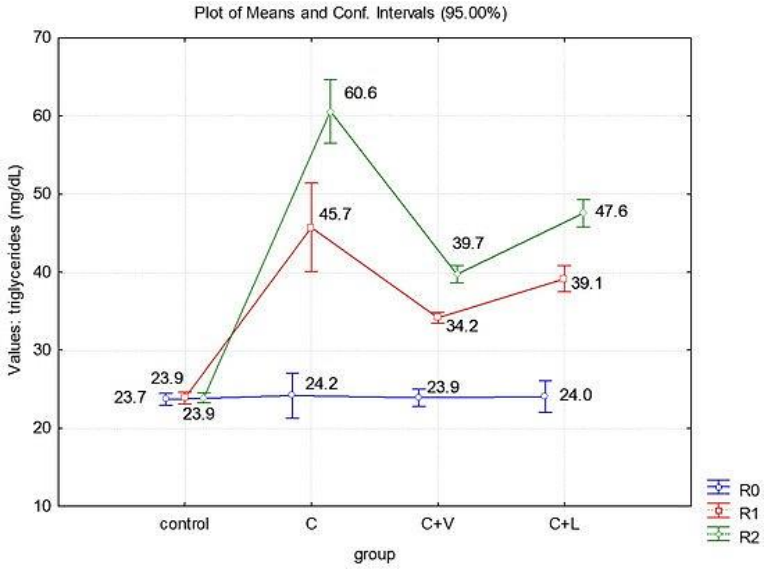

Figure 14. *Average levels of triglycerides in all groups*.

Table LI. Statistical differences between the average levels of triglycerides in all groups.

Time	Group	Control Group (n = 8)	C (n = 8)	C + V (n = 8)
R0	C (n = 8)	p = 0.737	-	
	C + V (n = 8)	p = 0.884	p = 0.849	-
	C + L (n = 8)	p = 0.814	p = 0.919	p = 0.928
R1	C (n = 8)	p < 0.001 *	-	
	C + V (n = 8)	p < 0.001 *	p < 0.001 *	-
	C + L (n = 8)	p < 0.002 *	p = 0.001 *	p = 0.0422 *
R2	C (n = 8)	p < 0.001 *	-	
	C + V (n = 8)	p < 0.001 *	p < 0.001 *	-
	C + L (n = 8)	p < 0.001 *	p < 0.001 *	p < 0.001 *

Post-hoc analysis: Newman–Keuls test; (*) Marked differences are significant at p < 0.05.

Our results showed that valine and leucine increased the serum levels of HDL-cholesterol. More specifically, after one month and at the end of the experiment, the HDL-cholesterol values in animals who received only cholesterol (C) were significantly lower compared with group III who received cholesterol and valine (C + V) or group IV that received cholesterol and leucine (C + L) (p < 0.001) (Cojocaru *et al.*, 2012a).

We also showed that valine and leucine decreased the serum levels of LDL-cholesterol proving lipid-lowering properties (Cojocaru *et al.*, 2012b). In our experiment we also evaluated the glucose value, and we found an important increase when cholesterol is added to the diet, but when the amino acids (valine and leucine) are added, the glycemic values decrease compared to group II.

According to our results, the two amino acids proved their antioxidant abilities, which could improve the endothelial damage related to atherosclerosis (Cojocaru *et al.*, 2014).The literature mentions that the appearance of atheroma plaque in the vessel's intima in rats subjected to a hypercholesterolemic diet occurs in approximately 8 months.

Table LII. Mean values of HDL, LDL and glucose at R0, R1 and R2.

	Group	R0	R1	R2	*p*-Value
Cholesterol I mean ± SD	Control group	37.14 ± 2.56	37.50 ± 2.09	37.61 ± 1.45	0.0783
	C (*n* = 8)	36.41 ± 4.15	49.89 ± 3.99	76.61 ± 3.46	<0.001 *
	C + V (*n* = 8)	36.67 ± 1.28	41.12 ± 1.27	44.87 ± 1.22	0.001 *
	C + L (*n* = 8)	36.50 ± 2.70	46.04 ± 2.71	49.53 ± 2.12	<0.001 *
	***p*-value**	**0.577**	**0.006 ***	**<0.001 ***	
HDL mean ± SD	Control group	23 ± 1.48	22.88 ± 1.22	22.89 ± 1.68	0.911
	C (*n* = 8)	22.43 ± 3.29	19.44 ± 1.45	15.93 ± 1.20	0.004
	C + V (*n* = 8)	22.98 ± 1.48	24.64 ± 2.79	26.85 ± 2.95	0.114
	C + L (*n* = 8)	22.51 ± 2.15	22.97 ± 1.90	23.17 ± 1.81	0.523
	***p*-value**	**0.637**	**0.001 ***	**<0.001 ***	
LDL mean ± SD	Control group	9.39 ± 3.39	9.83 ± 2.52	9.93 ± 2.71	0.749
	C (*n* = 8)	7.73 ± 4.54	21.3 ± 3.64	47.94 ± 5.47	<0.001 *
	C + V (*n* = 8)	8.9 ± 2.01	9.64 ± 2.79	10.07 ± 2.75	0.486
	C + L (*n* = 8)	9.17 ± 3.43	15.23 ± 2.73	16.84 ± 2.28	0.0004 *
	***p*-value**	**0.319**	**0.001 ***	**<0.001 ***	
Glucose mean ± SD	Control group	122.75 ± 5.87	122.61 ± 5.84	122.77 ± 6.08	0.962
	C (*n* = 8)	122.78 ± 8.77	149.26 ± 7.73	162.82 ± 5.83	<0.001 *
	C + V (*n* = 8)	121.98 ± 4.71	140.93 ± 4.84	142.37 ± 4.70	<0.001 *
	C + L (*n* = 8)	121.93 ± 5.13	143.79 ± 6.32	148.08 ± 4.78	<0.001 *
	***p*-value**	**0.994**	**<0.001 ***	**<0.001 ***	

Post–hoc analysis: Newman–Keuls test; (*) Marked differences are significant at $p < 0.05$. SD–standard deviation.

In our study, we did not obtain atherosclerotic plaques because the length of the experiment was 60 days, which is not long enough to produce severe lesions. Instead, at the biochemical level, we found changes in the parameters of lipid metabolism and oxidative stress that characterize atherosclerosis in the pre-lesional phases. In addition, according to our results, valine and leucine added to this diet have a direct influence on the lipid metabolism parameters by lowering the level of triglycerides, total cholesterol and LDL-cholesterol. Comparing the two essential amino acids, we noted that valine acts more promptly and rapidly than leucine. Therefore, we assume a possible hypolipemiant action and a consequently anti-atherogenic action of the two compounds.

IV.1.4. Discussion

Triglycerides are present in the lipoprotein particles known as chylomicrons, which contain the largest amount of lipids absorbed in the intestines as well as in the very-low-density lipoproteins (VLDL) containing triglycerides synthesized in the liver. An increased amount of any of these two leads to elevated levels of serum triglycerides and to hypertriglyceridemia as a clinical condition, which is a heterogeneous ensemble of features, each of them contributing to a certain degree in the increase of the total cardiovascular risk (Navar *et al.*, 2019).

In the present experimental model, we aimed to study the antiatherogenic potential of 2 amino acids (valine and leucine), based on the physiopathological mechanisms of atherosclerosis, in conditions of induced hypercholesterolemia via a cholesterol-rich diet. We analyzed many animal models discussed in the literature (Leong *et al.*, 2015) and we chose the atherosclerosis experimental model proposed by Anitschkow in 1913 (Anitschkow and Chalatow, 1913).

Amino acids are essential precursors for the synthesis of numerous molecules playing a major role in homeostasis (Harris *et al.*, 2004; Wu *et al.*, 2009). Leucine, valine and isoleucine are branched-chain essential amino acids involved in protein biosynthesis as well as in regulating the cell-division cycle. Leucine, in particular, participates in growth and development of cells in a mTOR-dependent manner (Chotechuang *et al.*, 2009).

In a study performed in 2018, we assessed the role of valine, leucine and isoleucine on the occurrence and progression of atherosclerosis in rats receiving hypercholesteremic diet. The comparative study of the three essential amino acids revealed that valine induced a faster response than leucine and isoleucine on the improvement of biochemical parameters, but no significant differences between the three amino acids in terms of their protective ability, according to the histopathological lesion assessment (Ifrim *et al.*, 2018). Still, further studies in order to assess the precise molecular mechanism by which these amino acids influence the triglyceride levels are necessary.

Numerous theories have been issued with regard to the role of essential amino acids in the modulation of atherosclerotic pathophysiology. The exact impact and timing of these amino acids intervention are not fully elucidated, as research has so far yielded contradictory results (Rom and Aviram, 2017).

Researchers are now engaged in a debate about a possible proatherogenic effect and a potential antiatherogenic role of branched-chain amino acids (Grajeda-Iglesias *et al.*, 2018).

Unlike our results, Bhattacharya presented the idea in 2013 that branched-chain amino acids are responsible for increasing cardiovascular-related mortality, being associated with extreme forms of ischemic heart disease. They were able to demonstrate that the relationship is there even after the more traditionally accepted risk factors, such as diabetes mellitus or insulin resistance have been corrected (Bhattacharya *et al.*, 2014).

In a study from 2016, Ruiz-Canela hypothesized that elevated serum levels of branched-chain amino acids as valine, leucine and isoleucine correlate with increased global cardiovascular risk which may not be altered by dieting (Ruiz-Canela *et al.*, 2016). In addition, Sun *et al.* demonstrated via an experimental study on mice that defective catabolism of branched-chain amino acids mediated by Kruppel-like factor 15 (KLF 15) is responsible for cardiac depression manifestations (Sun *et al.*, 2016).

Based on the results of a prospective cohort study over a period of 18.6 years, Tobias *et al.*, were able to conclude that the connection between branched-chain amino acids and cardiovascular disease is similar to the causal relationship between plasma levels of LDL cholesterol and cardiac mortality (Tobias *et al.*, 2018).

On the other hand, numerous published studies support the beneficial effects of branched-chain amino acids in regulating lipid metabolism and functional cardiac parameters.

Similar to our results, Noguchi in 2006, highlighted the role that valine and leucine play in counteracting the impact of abnormal lipid concentration, directly involved in the production of atherosclerotic lesions (Noguchi *et al.*, 2006).

Terakura demonstrated that supplementing the diet with branched-chain amino acids decreases the hepatic triglycerides accumulation and the chronic inflammatory process associated with obesity, most likely by inhibiting interleukin-6 (IL-6), Tumor Necrosis Factor-alpha (TNF-alpha) and monocyte chemoattractant protein-1 (MCP-1) expression. Also, in mice fed with branched-chain amino acids, their average adiposity was lower, probably mediated by peroxisome proliferator-activated receptor gamma (PPAR-gamma) (Terakura *et al.*, 2012).

In 2012, Chen *et al.* shared their results regarding the influence of leucine on body weight and blood lipids. They witnessed a regulation of carbohydrate and lipid metabolism regardless of how the amino acid was administered (orally or intracerebroventricularly) (Chen, *et al.*, 2012).

Pedroso showed that in rats with metabolic syndrome, restricting their caloric intake concurrent with adding leucine to their diet facilitates an improved protein anabolism, as well as an increase in the levels of leptin and IL-6. The study drew attention to the fact that supplementing the diet with branched-chain amino acids modifies the hepatic metabolism by influencing the metabolism of fatty acids and cholesterol (Pedroso *et al.*, 2013).

Another study confirming the role of leucine in lowering the levels of triglycerides and LDL and in raising HDL-cholesterol in diabetic rats to which food was supplemented with this amino acid was published by Sadri in 2017 (Sadri *et al.*, 2017). However, the therapeutic effect of nor leucine is notably inferior to that of leucine. A possible increase in the level of leptin as a result of a leucine-rich diet has been discussed in the literature. The leptin levels obtained, however, have not proven to be statistically significant (Lynch, *et al.*, 2006).

Research results are still contradictory and different views are being presented. Some point to the effects of branched-chain amino acids with regard to an increasing in the global cardiovascular risk, while numerous studies highlight the benefits of supplementing the diet with leucine, valine and isoleucine in order to lower the lipid metabolism parameters. Our study evidently supports the latter by showing that leucine and valine lower the level of plasma triglycerides, thus having a positive effect on lipid balance and, consequently, on the integrity of the vascular wall.

IV.1.5. Conclusions

By comparing the measured triglyceride values across different groups according to the experimental design, the biochemical analysis revealed the fact that essential amino acids such as valine and leucine lower the level of triglyceride. Consequently, the vascular endothelium is protected, and the risk of endothelial dysfunction diminished.

The comparison of the two essential amino acids indicated that valine acts more promptly and rapidly than leucine. The results of this experiment support the idea that valine and leucine play a distinct and specific role in the evolution of induced atherosclerosis. How these two amino acids behave affords several subsequent research avenues in terms of therapeutic goals, and our study is an attempt to highlight a potential novel therapeutic strategy.

B. ACTUAL ISSUES ABOUT PREVENTION AND TREATMENT ON DIABETES

People have always resorted to natural resources, which were an important food source as well as solution for finding prophylaxis and treatment. Although there have been periods when different synthetic drugs were considered irreplaceable and eclipsed plant sources, once with the world development and the appearance of illnesses related to the modern civilization, obliged the scientific world once again to turn its attention to herbal resources, hoping to find valuable solutions for modern therapy (Rejhová *et al.*, 2018).

Therefore, our attention is focused on easily accessible species on which there is little information in the literature from a chemical and biological point of view, and we started from the information available in the traditional medicine. Currently, diabetes is a major pathology all around the world that implicates dysfunctions in glucose metabolism (Albu *et al.*, 2013). Either the glucose cannot be used by the cells in order to normalize the blood level if there is not enough insulin or the receptors for insulin not recognise it. The manifestations of insulin-resistant glucose metabolism include reduced glucose transport and phosphorylation and reduced rates of glycogen synthesis (DeFronzo, 2004), whereas abnormal fatty acid metabolism entails increased accumulation of triglycerides and other lipid structures as well as dysregulation of lipid oxidation during fasting and insulin-stimulated conditions.

Diabetes is a leading cause of death in most developed countries and there is substantial evidence that it is epidemic in many developing and newly industrialized nations. Complications from diabetes, such as coronary artery and peripheral vascular disease, stroke, diabetic neuropathy, amputations, renal failure and blindness are resulting in increasing disability, reduced life expectancy, and enormous health costs for virtually every society (Evert *et al.*, 2019).

Chronic hyperglycemia, the predominant metabolic state of diabetes, can exacerbate defective glucose disposal by interfering with insulin action in insulin-target tissues, such as

skeletal muscle (Banerjee *et al.*, 2019; Borse *et al.*, 2018; Rejhová *et al.*, 2018). The vegetal extracts are rich in polyphenolic compounds that have also an antioxidant capacity, therefore the combination between normalization of the glucose blood level and the antioxidant capacity is revolutionary for diabetic patients (Mircea *et al.*, 2018). It is well known that these patients present many complications because of the production of reactive oxygen species and of inflammatory conditions (Serban *et al.*, 2018).

Pelargonium species can be found in the history of modern medicine from the time of British Major Stevens, who, in 1897, launched the Stevens' Consumption Cure drug, which treated tuberculosis (Sharifi-Rad *et al.*, 2017). The experience he had gained in South Africa was the basis for the introduction of umckaloabo preparations (decoction of the roots of *Pelargonium sidoides*), although the first clinical trial was conducted in 1920 on eight hundred patients (Helmstädter, 1996).

Our previous studies indicated the antioxidant properties of extracts from *Pelargonium species* on *in vitro* tests (Iancu *et al.*, 2016). Side effects of current antidiabetic drugs and negative consequences of postprandial hyperglycemia stimulated the researchers to find new drugs for type 2 diabetes, able to delay or to reduce glucose absorption (Hoza *et al.*, 2018).

Due to the side effects of some antidiabetic drugs, many present studies try to identify functional foods and plant-based medicines able to influence metabolic processes and to be used in the prevention and cure of diabetes and obesity. Hence, the attractive targets like *in vitro* inhibition of alpha-glucosidase and alpha-amylase are currently studied. Previously, several *in vitro* studies have been performed yielding potential α-glucosidase inhibitors from various food components and plants like cranberry, *Cuscuta reflexa*, pepper, soybean extracts and alpha-amylase inhibitors from cheese, oregano, cranberry extract, Fenugreek and Balanite, but never on *Pelargonium species* extracts (Anis *et al.*, 2002; Apostolidis *et al.*, 2006; Pullela *et al.*, 2006). Natural alpha-glucosidase and alpha-amylase inhibitors from plant sources offer an attractive strategy for the control of postprandial hyperglycemia (Afolabi *et al.*, 2018; Apostolidis *et al.*, 2006; Georgetti *et al.*, 2006; McCue *et al.*, 2004).

Inhibition of alpha-glucosidase and alpha-amylase, enzymes involved in the digestion of carbohydrates, can significantly decrease the postprandial increasing of blood glucose after a mixed carbohydrate diet and therefore can be an important strategy in the management of postprandial blood glucose level in type 2 diabetic patients and borderline patients (Gad *et al.*, 2006; Mircea *et al.*, 2013).

Plant extracts have long been used in ethno-medicine to treat diabetes and are currently accepted as an alternative for diabetic therapy or to complete this. However, for many plant extracts, there is no clear understanding of the mechanism of action. The *in vitro* alpha-glucosidase inhibitory activity may not always correlate with the *in vivo* one (Afolabi *et al.*, 2018; Shen *et al.*, 2002). There are no previous reports of any *in vitro* alpha-glucosidase and alpha-amylase inhibitory activity of *Pelargonium species*, so in our study we tried to identify these properties and the ability of extracts to control the inflammatory process.

My interest regarding this area is reflected by the following articles:

Cristina Iancu, Cornelia Mircea, **Florin Petrariu*,** Oana Cioancă, Cătălina Stan, Andreia Corciovă, Andreea Murărașu, Nina Filip, Monica Hăncianu *Corresponding Author. THE EVALUATION OF NORMO-GLYCEMIC AND CYTO-REGENERATIVE EFFECTS OF *PELARGONIUM SPECIES* EXTRACTS *Farmacia* 2020; 68(1): 135-141. https://Doi.Org/10.31925/Farmacia.2020.1.19 **IF=1.433.**

Ana Petcu, Alexandru Nemțoi, Sorin Pașca, Eusebiu-Viorel Sindilar, Danisia Haba, **Florin Dumitru Petrariu.** SCANNING ELECTRON MICROSCOPY INVESTIGATION OF BONE AROUND TWO DIFFERENT SANDBLASTED ACIDS ETCHED TITANIUM IMPLANT SURFACES IN DIABETIC RATS**.** *Revista de Chimie* 2015; 66(9): 1331-1335 / ISSN: 0034-7752, **IF= 0.956.**

IV.2. The evaluation of normo-glycemic and cyto-regenerative effects of *Pelargonium species* extracts

IV.2.1. Aim

In order to evaluate the cyto-regenerative effect of the extracts, we did the Scratch assay that involves the assessment of the migrating capacity of the cells and the rebounding capacity of the cells in the presence of the vegetal extracts.

IV.2.2. Materials and methods

Reagents, cell line and animals. Ethanol (Chimopar SA, Romania), methanol (SC Chimreactiv, Romania), dimethyl sulfoxide - DMSO (Merck, Germany), monopotassium phosphate (Merck,Germany), dipotassium phosphate (Merck, Germany),3,5-dinitrosalicylic acid (DNS) (Sigma-Aldrich, Germany), p-nitrophenyl-D-glucopyranoside (Sigma-Aldrich, Germany), sodium chloride (Merck, Germany),alpha-glucosidase (Sigma-Aldrich, Germany), alpha-amylase (Sigma-Aldrich, Germany), acarbose CRS (European Pharmacopoeia Reference Standard, EDQM Strasbourg, France), indomethacin MK 4% (Fiterman Pharma SRL, Romania), tetradecanoyl phorbol-13-acetate-TPA (Sigma-Aldrich, Germany), Dulbecco's modified Eagle Medium with high glucose and fetal bovine serum (FBS) (Sigma-Aldrich, Germany), penicillin / streptomycin (Sigma-Aldrich, Germany), HaCaT cell line (was offered by the University of Debrecen, Hungary), SKH-1 mice (Charles River Laboratories, Hungary).

Plant material. The subjects of the current research are two *Pelargonium* species: *hispidum* (P1) and *grandiflorum* (P2). Specimens were obtained from the "Anastasie Fătu" Botanical Garden, Iași, Romania.The plants were kept in similar growth conditionsto provide a minimum environmental impact.

Preparing of the hydro-alcoholic/methanolic extracts 2 g of dried and powdered leaves were extracted with2 x 50 mL ethanol-water 1:1, respectively 2 x 50 mL methanol, on water bath, at reflux, for 45 minutes.The extracts are filtered and washed to complete theobtained volume to 100 mL using the same solvent.After cooling, the extracts were dried using a rotary evaporator. Dried extracts were solved in dimethyl sulfoxide (DMSO) in order to obtain solutions withconcentrations between 0.039 and 5 mg/mL (Burlec *et al.*, 2019).

Alpha-amylase inhibition test. The method is based on enzyme inhibition, so the transformation of starch to reducing oligosaccharidesthat react with 3,5-dinitrosalicylic acid is blocked. The extracts in different concentrations and 20 mM phosphate buffer pH 6.9, containing porcine alpha- amylase (0.5 mg/mL) were incubated at 25°C for 10min. 0.5% starch solution in 20 mM phosphate bufferpH 6.9, was added and the mixture was incubated at25°C for 10 min. The reaction was stopped with 96 mM 3,5-dinitrosalicylic acid (DNS) color reagent. After boiling and cooling the mixture, the absorbancewas measured at 540 nm.

The percent of alpha-amylaseinhibition was calculated as follows: (1–B/A) × 100,where A is the absorbance of control and B is the absorbance of samples containing extracts. The concentration of the extract required to inhibit the activity of the enzyme by 50%, IC50 was calculated by regression analysis. Experiments were performed in triplicate (Grădinariu *et al.*, 2013).

Alpha-glucosidase inhibition test. The method is based on the inhibition of alpha-glucosidase that catalyzes the hydrolysis of p-nitro-phenyl-D-glucopyranoside to p-nitro-phenol. The extracts in different concentrations, were made up withequal volumes of DMSO and distilled water. Sample solutions mixed with alpha-glucosidase (0.1 U/mL) in 100 mM phosphate buffer, pH 7.0 were incubatedfor 5 minutes. After the incubation, p-nitrophenyl-alpha-d-glucopyranoside was added and incubated again. The absorbance of the final solution was measured at405 nm. The percent of alpha-glucosidase inhibitionwas calculated as follows: (1–B/A) × 100, where A isthe absorbance of control and B is the absorbance ofsamples containing extracts. The inhibitory concentration of the extract required to inhibit the activity of the enzyme

by 50%, IC50 was calculated by regression analysis. Experiments were performed in triplicate. Acarbose was used as positive control (Apostolidis *et al.,* 2006).

The anti-edematous/anti-inflammatory effect of the investigated samples was demonstrated on a TPA- induced animal model. We used 15 mice, SKH-1 females without hair, 3 mice for each group. SKH-1 female mice were kept under standard conditions (24ºC,55% relative humidity). There were five groups: Control group - not treated, TPA group - treated with TPA, Indomethacin group - treated with TPA and indomethacin - topical administration, Group 1 - TPA+P1M (*P. hispidum* methanolic extract 5 mg/mL) and Group 2 - TPA+P2M (*P. grandiflorum* methanolic extract 5 mg/mL). The protocol was approved by the Bioethics Committee of "Victor Babeș" University of Medicine and Pharmacy, Timișoara, Romania. After 24 hours from the topical administration, we measured the inflammatory parameters (ear base size, length, and mass) (Dehelean *et al.,* 2012; Kim *et al.,* 2000).

The scratch assays. The evaluation of cell division capacity by using the scratch technique is based on *in vitro* assessment of the ability of plant extracts to stimulate the process of restoring intercellular bonds that were destroyed mechanically. We used keratinocyte cell line (HaCat) that were cultivated in 12 wells plates and then treated with DMSO (control), 0.0195 mg/mL and 1.25 mg/mL methanolic extract of P1 and P2 (Dehelean *et al.,* 2012).

IV.2.3. Results

The *Pelargonium species* were studied less from this therapeutic point of view and this research will contribute to the biological characterization of this group of plants. The methanolic extracts of *Pelargonium species* showed a great antioxidant activity by assessing the free-radical scavenging capacity (DPPH radical, ABTS cation), also ferrous ion-chelating capacity, and super-oxide anion radical scavenging capacity (Certegy *et al.,* 2013). Moreover, the antibacterial, antifungal and anti-inflammatory activity were studied on these types of extracts and showed good results (Dehelean *et al.,* 2012). This is the reason of choosing the methanolic extracts for the anti-inflammatory assay.

The results of the UHPLC analysis showed that *P. hispidum* was richer in cyanidol, flavonols and its derivatives, whereas *P. grandiflorum* contains more catechins (Tadera *et al.,* 2006). Our data were in accordance with the literature related to the types of compounds usually found in *Pelargonium species*, but unlike other authors we found only relatively small amounts of tannins in both samples (less than 0.5 mg/g), these results have been published before (Iancu *et al.,* 2016). The values obtained for the alpha-amylase and alpha-glucosidase inhibition assays are showed in Table LIII and Table LIV.

Table LIII. The results of the alpha-amylase inhibition test

SOURCE – % INHIBITION ± STANDARD DEVIATION								
Sample conc. (mg/mL)	0.039	0.078	0.156	0.3125	0.625	1.25	2.5	5
P1E	30.30 ± 0.26	42.73 ± 0.20	48.12 ± 0.16	50 ± 0.02	53.64 ± 0.23	56.67 ± 0.17	59.22 ± 0.10	73.41 ± 0.17
P1M	40.09 ± 0.21	47.45 ± 0.28	51.81 ± 0.06	56.59 ± 0.28	57.64 ± 0.17	75.48 ± 0.29	88.52 ± 0.14	91.74 ± 0.07
P2E	48.63 ± 0.31	66.60 ± 0.31	76.35 ± 0.11	82.63 ± 0.29	88.63 ± 0.27	91.36 ± 0.11	93.05 ± 0.05	94.26 ± 0.07
P2M	38.43 ± 0.21	42.62 ± 0.21	46.71 ± 021	50.57 ± 0.17	54.39 ± 0.09	62.59 ± 0.31	68.58 ± 0.32	80.54 ± 0.14
Acarbose	34.55 ± 0.04	44.87 ± 0.08	55.68 ± 0.05	60.87 ± 0.12	67.58 ± 0.04	75.44 ± 0.03	82.77 ± 0.04	95.47 ± 0.11

*P1E – hydro-alcoholic extract of *Pelargonium hispidum*, P1M – methanolic extract of *Pelargonium hispidum*,
*P2E – hydro-alcoholic extract of *Pelargonium grandiflorum*,
P2M – methanolic extract of *Pelargonium grandiflorum*.

Table LIV. The results of the alpha-glucosidase inhibition test

SOURCE – % INHIBITION ± STANDARD DEVIATION								
Sample conc. (mg/mL)	0.039	0.078	0.156	0.3125	0.625	1.25	2.5	5
P1E	17.49 ± 0.17	21.64 ± 0.23	29.55 ± 0.27	38.71 ± 0.22	45.34 ± 0.05	50.56 ± 0.08	65.83 ± 0.03	69.38 ± 0.03
P1M	20.33 ± 0.12	29.92 ± 0.05	35.68 ± 0.23	48.40 ± 0.08	51.27 ± 0.06	59.64 ± 0.17	64.36 ± 0.13	75.83 ± 0.04
P2E	35.35 ± 0.21	40.21 ± 0.11	48.32 ± 0.03	52.35 ± 0.05	61.45 ± 0.15	70.52 ± 0.02	81.81 ± 0.02	90.18 ± 0.03
P2M	19.84 ± 0.08	25.52 ± 0.04	39.51 ± 0.03	47.27 ± 0.06	55.67 ± 0.06	67.25 ± 0.07	78.21 ± 0.07	83.37 ± 0.11
Acarbose	20.47 ± 0.03	39.56 ± 0.02	48.99 ± 0.01	57.54 ± 0.05	67.78 ± 0.04	70.99 ± 0.07	82.47 ± 0.01	93.65 ± 0.04

*P1E – hydro-alcoholic extract of *Pelargonium hispidum*, P1M – methanolic extract of *Pelargonium hispidum*,
*P2E – hydro-alcoholic extract of *Pelargonium grandiflorum*,
P2M – methanolic extract of *Pelargonium grandiflorum*

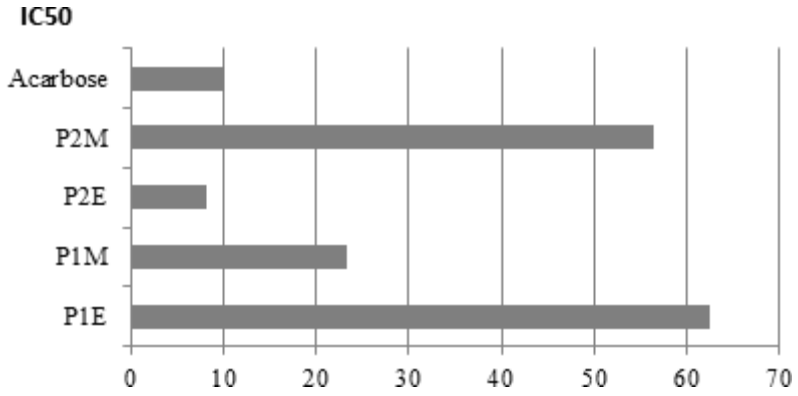

Figure 15. *The results of the IC50 (μg/mL) in the alpha-amylase inhibition test*

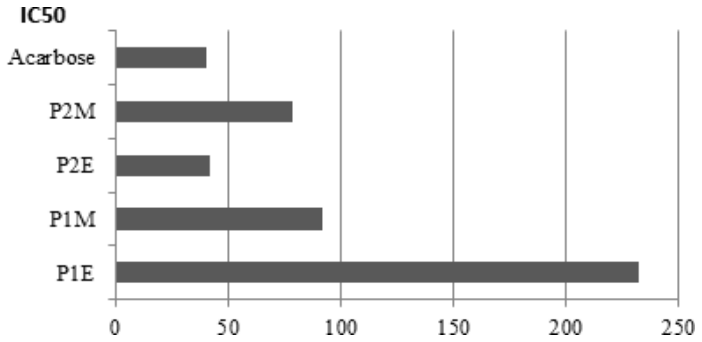

Figure 16. *The results of the IC50 (μg/mL) in the alpha-glucosidase inhibition test*

IV.2.4. Discussion

On the alpha-amylase inhibition assay the best activity was showed by the methanolic extract of *Pelargonium hispidum* (P1M) and also the hydro-alcoholic extract of *Pelargonium grandiflorum* (P2E). On the other hand, at the alpha-glucosidase inhibition assay the methanolic extract of *P. grandiflorum* (P2M) had an IC50 = 78.29 ± 0.02 μg/mL compared with acarbose that had an IC50 = 40.25 ± 0.05 μg/mL (Figures 15 and 16).

Following the results on these assays, we observe that the IC50 on the alpha-amylase inhibition is lower than the alpha-glucosidase inhibition because alpha-amylase has larger substrate specificity and could transform more compounds than the alpha-glucosidase that transform just glucose. The best activity was showed by the hydroalcoholic extract of the *P. grandiflorum* (P2E) with an IC50 = 41.68 ± 0.1 µg/mL.

Vegetal extracts with mild enzyme inhibitory effects have some advantages compared to acarbose that could induce digestive side effects such as flatulence, diarrhea, abdominal distension and bloating (Oboh *et al.,* 2012). These effects are the consequences of carbohydrates transformation by intestinal bacteria on the large intestine (Pak *et al.,* 2015).

The type of polyphenols is important for biological properties of extracts, so, catechol catechins were twice more active than the pyrogallol catechins on the inhibition of alpha-amylase and alpha-glucosidase (Hora *et al.,* 2014). Tadera *et al.,* proved that inhibitory activity of flavonols against alpha-amylase and alpha-glucosidase is correlated to the chemical structure of the compounds. It was shown that the luteolin, myricetin and quercetin were potent inhibitors. This capacity is depended by the position and the number of hydroxyl groups on the rings in the polyphenols structure (Williams *et al.,* 2000). Inhibitory activity against alpha-amylase is more important for und phenolic extract such as hydro-alcoholic extract than free phenolic extract such as methanolic extract (Afolabi *et al.,* 2018). For our samples, just *P. grandiflorum* hydro-alcoholic extract was more active than methanolic extract against alpha-amylase, and it is dependent on the complex composition of these extracts.

According to the results obtained from previous assays and using the information obtained in the UHPLC analysis (Iancu *et al.,* 2016), we decided to evaluate only the methanolic extracts in the TPA-induced oedema assay and the scratch test on the cell line.

The values obtained on the *TPA-induced oedema* were determined after a single topical application of TPA. The maximum expression of oedema was observed 24 hours after the administration of TPA with important differences for the groups treated with the investigated *Pelargonium* extracts. For the same dose (5 mg/mL) applied topically, the most intense oedema reduction effect was present in the group 2 treated with the methanolic extract of *P. grandiflorum*, in which inflammation compared to the negative control (TPA group) decreased by about 50%, and, compared to the positive control (treated with indomethacin-TPA+IND group), decreased by about 30%. *P. hispidum* methanolic extract (group 1) showed an anti-edematous effect of 45% compared to the negative control.

The parameters we obtained in this assay are presented in table LV, after measuring the base (mm) of the ear, the length (mm) and the weight (g).

Table LV. The results of the TPA-induced oedema test

GROUP	EAR PARAMETERS		
	BASE (mm)	LENGTH (mm)	WEIGHT (g)
Control	5.46 ± 0.023	14.50 ± 0.03	0.05 ± 0.016
TPA group	8.33 ± 0.023	16.80 ± 0.03	0.29 ± 0.016
TPA + indomethacin group	7.69 ± 0.023 [a]	16.05 ± 0.03 [a]	0.20 ± 0.016 [a]
Group 1	6.37 ± 0.023 [a]	16.11 ± 0.03 [a]	0.18 ± 0.016 [a]
Group 2	6.60 ± 0.023 [a]	16.80 ± 0.03	0.16 ± 0.016 [a]

[a] extremely statistically significant ($p < 0.0001$) – treated groups *vs.* TPA group

In the process of restoring intercellular bonds, it was clear that the P1M and P2M, after 24 hours of cell treatment, the antimigrating process is low, which proves the fact that it has no cytotoxic effect on cells, especially at 0.0195mg/mL (Figure 17).

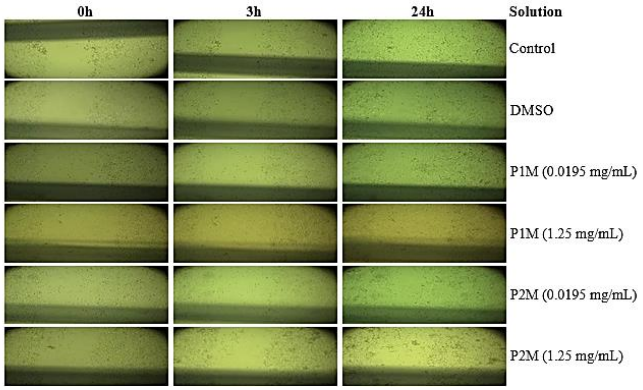

Figure 17. *The anti-migrating effect of methanol extracts on HaCaT cells*

These results are promising and lead us to the information that the extracts can be used in rebounding tissues. The antioxidant activity and the ability of polyphenolsto inhibit enzymes involved in the synthesis of pro- inflammatory eicosanoids, cytokines or chemokinesexplain the anti-inflammatory properties of these (Yahfoufi *et al.*, 2018).

Mueller showed that the anti-inflammatory activity of some plant extracts with rich content in quercetin, resveratrol, kaempferol reduced the pro-inflammatory interleukin (IL)-6 (Mueller *et al.*, 2010). TPA-oedema induced test and our previously antioxidant tests reveal the anti-inflammatory propertiesof extracts with higher polyphenols content.

Oxidative stress with overproduction of reactive oxygenspecies could induce or promote tissue injuries and finally will affect tissue regeneration. *In vivo*, vegetal extracts increase the activity of endogenous antioxidant enzymes. The vegetal extracts with high concentrations in polyphenols have the biggest effect on tissueregeneration (Zubair *et al.*, 2012; Yahfoufi *et al.*, 2018). These results can be correlated with ours and sustainsthe fact that the ethanolic extract of *P. grandiflorum*presents a higher activity on the inhibitory assays due to its composition and higher extractability in flavonols compounds, also their important effect in anti-inflammatory mechanism and tissue regeneration. Flavonols such as myricetin and quercetin possess antioxidant and anti-inflammatory properties and havethe ability to protect keratinocytes and endothelial cells. Also, polyphenols increase the biosynthesis ofcollagen and elastin, stabilize collagen, and inhibit enzymes involved in their degradation. The hydro-alcoholic extracts improve collagen cross-linking andimprove the properties of dentin depending on the time of exposure. These properties sustain the use of polyphenols rich vegetal extracts in tissue engineering for tissue regeneration, bone regeneration, and to improve the mechanical and chemical properties of biomaterials used in medicine (Shavandi *et al.*, 2018).

IV.2.5. Conclusions

Polyphenols protect cells against the damages caused by reactive oxygen species as a product of energy metabolism. It is well known that diabetes islinked with oxidative stress in the body. The polyphenol-rich extracts can be a potential source of anti-diabetic agents for the postprandial hyperglycemia control and diabetic damages arising from oxidativestress (Oboh *et al.*, 2012). As far as we got with the determination and correlating the results it is clear that the extracts of the *Pelargonium species* that we tested have promising utility in the diabetes therapy.

The targeted pathologies are inflammatory conditions, such as rheumatism, rheumatoid arthritis, as well as many others for which the allopathicsolution proposes classes of selective and/or non-selective steroidal and/or non-steroidal anti-inflammatory drugs, but which come with numerous side effects thatlead to the treatment discontinuation.

C. MODERN APPROACHES OF CHRONIC INFLAMMATORY CONDITIONS

Inflammation is closely linked to significant fracture risk (Vasile *et al.*, 2017; Salaffi *et al.*, 2018) in chronic inflammatory conditions, such as rheumatoid arthritis (Dehghan *et al.*, 2014; Vaananen *et al.*, 2000) or ankylosing spondylitis, as well as when a low degree of inflammation is detected in apparently healthy individuals.

Rheumatoid arthritis is one of the most important inflammatory conditions since in addition to its triggering local juxta-articular bone impairment, it also entails bone mass loss at considerable distances from the joints (Fautrel *et al.*, 2018). In rheumatoid arthritis the bone is a major target for chronic inflammation, this condition being caused by the numerous interactions and interconnections between the bone and the immune system (Dankers *et al.*, 2017). Inflammation occurring in the bone leads to bone resorption increase and it determines local bone formation suppression (Caraba *et al.*, 2017; Franco *et al.*, 2017).

Research in this field has shown that juxta-articular bone mass loss and bone inflammation occur during the early stages of the disease and that they precede and are also predictive of erosive bone destruction specific to rheumatoid arthritis (Adami *et al.*, 2019). A European multi-center study published in 2017 revealed that patients with rheumatoid arthritis usually exhibit vitamin D insufficiency or even deficiency, with significant differences among various countries. The serum levels of vitamin D in the patients included in this study were inversely proportional to life quality indices, to the stage of the disease and to the degree of disability (Vojinovic *et al.*,2017). Fortified food (e.g., bread, milk, cottage cheese) with vitamin D, as a food-based solution, may prevent the deficiency of this vitamin and, subsequently, the chronic inflammatory conditions (Itkonen *et al.*, 2016).

My interest regarding this area is reflected by the following articles:

Barzoi Raluca-Oana, Rezus Elena, **Petrariu FD**, Badescu Codruta, Ciocoiu Manuela. IMPLICATIONS OF VITAMIN D DEFICIENCY IN INFLAMMATION DUE TO RHEUMATOID ARTHRITIS. *Medical-Surgical Journal-Revista Medico-Chirurgicală* Volume: 122, Issue: 4, Pages: 676-681, Published: 2018. Web of Science Core Collection - Emerging Sources Citation Index / **WOS: 000457410000005**

Cardoneanu Anca, Cozma, Sebastian, Rezus Ciprian, **Petrariu Florin,** Burlui Alexandra Maria, Rezus Elena. CHARACTERISTICS OF THE INTESTINAL MICROBIOME IN ANKYLOSING SPONDYLITIS. *Experimental and Therapeutic Medicine*, 2021, Volume: 22, Issue: 1, Article Number: 676 / https://doi.org/10.3892/etm.2021.10108 / **IF= 2.447**

IV.3. Implications of vitamin D deficiency in inflammation due to rheumatoid arthritis.

IV.3.1. Aim

The research was aimed to analyze the factors involved in bone mass loss in patients with rheumatoid arthritis, as well as at determining the connection between the serum level of 25-(OH) vitamin D and the extent of the inflammation, and also the impact of vitamin D supplement delivery on the status of these patients.

IV.3.2. Material and methods

The observational prospective case-control study was conducted for about one year, from January 2017 to January 2018.

There were initially ninety-three patients with rheumatoid arthritis included in the study, who were selected based on the inclusion criteria set in the study protocol (20 to 65 years of age, confirmed rheumatoid arthritis diagnosis in various disease evolution stages: I, II or III),

but also according to the exclusion criteria (less than 20 or more than 65 years of age, related diseases - endocrine or neoplastic conditions). Only 82 patients were left in the study group after reassessment.

Patient data (personal and family medical history), anthropometric indices (weight, height, BMI), data on socio-demographic factors and lifestyle (exercise, active smoking) and data on clinical parameters (number of painful joints, number of swollen joints, morning stiffness) were collected on the initial assessment. Patients were also selected depending on the rheumatoid arthritis stage and maintenance therapy administered before.

A series of biological parameters of inflammation, such as erythrocyte sedimentation rate (ESR) and C reactive protein (CRP), as well as certain biological parameters assessing the possible complications of the basic disease or side effects of the maintenance therapy, among which certain hematological, hepatic or renal factors, were also determined in order to set the stage of the disease. Also, in this study, we dosed 25-OH vitamin D in order to determine whether mild or severe vitamin D deficiency is linked with the extent of bone mass loss, with the level of pain and possibly with the level of disease activity and degree of disability. We calculated internationally acknowledged scores (DAS-28, HAQ, SDAI, CDAI) for all the patients included in the study, in order to be able to assess the level of disease activity and degree of disability. The immunological markers of the disease were determined in all the patients: rheumatoid factor (RF), anti-citrullinated protein antibodies (ACPA), total antinuclear antibodies (ANA), using ELISA-type tests.

On the 6-month follow-up, we analyzed the inflammation parameters again (ESR, CRP), we studied the new values of the immunological markers (rheumatoid factor, ACPA), and we calculated the new internationally-used disease activity scores (DAS_{28}, CDAI, SDAI, HAQ), in order to be able to monitor disease activity dynamics and its functional impact.

Throughout the study, all the patients underwent classical or biological DMARDs therapy. After their initial assessment, 95% of the patients also received vitamin D supplements and this was decided since we found significant vitamin D deficiency in the patients included in the study.

IV.3.3. Results

The number of painful joints was 0 to 24, and the value series median was 6. The results of the Skewness test suggest that number of painful joints (NPJ) is a continuous variable (p=0.851). The mean NPJ was 7.46±6.53, i.e., significantly lower than the number of painful joints before the treatment – 8.77±7.67 joints (p=0.001).

The number of swollen joints (NSJ) was 0 to 16, and the value series median was 1, whereas the mean was 2.11, and the results of the Skewness test suggest that NSJ is a discontinuous variable (p=2.488), which restricts the application of parametric significance tests. On reassessment, the mean NSJ was 2.11±0.36, i.e., significantly lower than the number of swollen joints detected before therapy – 2.46±0.48 joints (p=0.037).

Pain visual analogue scale (VAS) ranged between 1 and 8. The value series median was 4, close to the mean value of 4.01. The results of the Skewness test suggest that the VAS value series was homogeneous (p=0.266). On reassessment, the mean VAS was 4.01±2.22, which was significantly lower than the VAS determined at the beginning of the study, which was 4.70±2.44 (p=0.001) (Figure 18).

In the patients included in the research, the disease activity score DAS_{28} had normal distribution (p= -0.026), ranging from 2 to 7 and exhibiting a value series median of 4.03. The second assessment revealed a mean DAS-28 of 3.97±1.39, which was slightly lower than the score recorded during the first assessment, which was 3.99±1.52 (p=0.813) (Figure 19).

On reassessment, the ESR ranged from 4 to 115 mm/h, with a homogeneous value series (p=1.259), the mean reading being 34.39±22.25 mm/hr., without being significantly different from the initial one of 34.18±22.25 mm/hr. (p=0.834) (p=0.834).

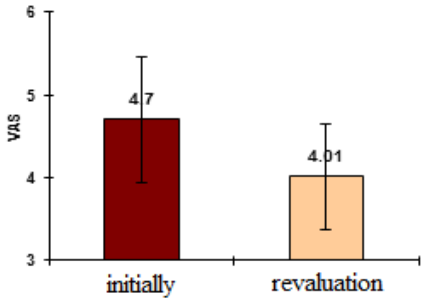

Figure 18. *Evolution of mean VAS*

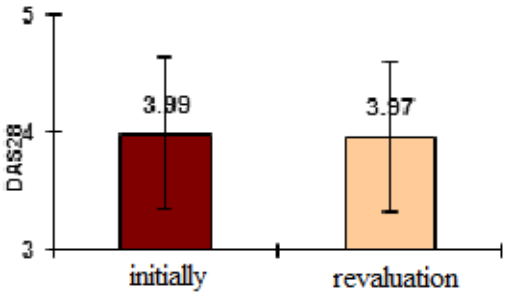

Figure 19. *Evolution of mean DAS_{28}*

On reassessment, the CRP showed wide variations within the 0.40-102 mg/dL range, the mean level being 7.28±8.63 mg/dL, i.e., slightly lower than the reading at the beginning of the research 7.55±4.06 mg/dL (p=0.710).

Of all the clinical parameters, only VAS varied significantly depending on Latex rheumatoid factor positivity (4.39 *vs.* 3.39; p=0.046).

The mean level of clinical parameters did not show significant differences depending on Waller Rose rheumatoid factor positivity, with the exception of VAS (4.39 *vs.* 3.39; p=0.046).

The rheumatoid factor assessed positive especially in the female sex (p=0.247) and in the urban environment (p=0.582), but the percentage distributions were not statistically significant. 46.9% of the high titre patients and 73.3% of the low titre patients were 60 and older, whereas 63.6% of the negative titre patients had not reached this age (p=0.039).

Serum calcium and ESR were apparently independent parameters both at the beginning of the study (r= -0.004; p=0.973) and on reassessment (r= -0.068; p=0.546) (Figure 20).

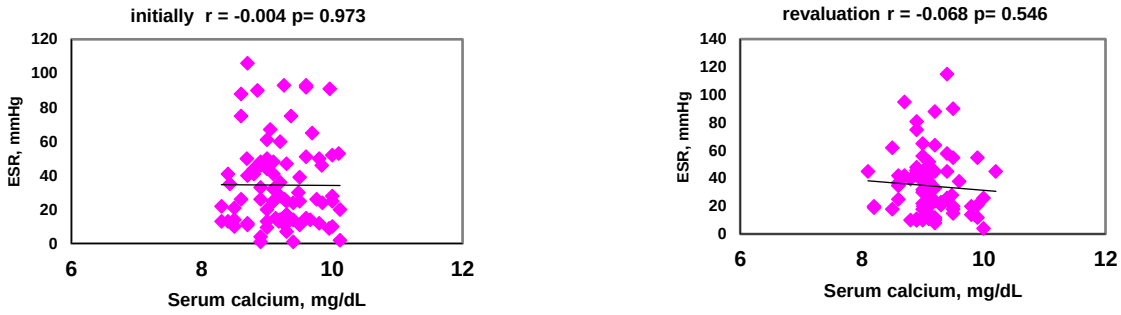

Figure 20. *Serum calcium correlation with ESR*

Vitamin D values showed negative correlation with both VAS and HAQ, both on the first assessment and on reassessment. The vitamin D and ESR correlation was indirect and weak, both at the beginning of the study (r= -0.146; p=0.169) and on reassessment (r= -0.169; p=0.130) (Figure 21).

On the first assessment, the lower vitamin D and serum calcium levels were associated with higher ESR values (Figure 22).

On the other hand, on reassessment, the higher vitamin D and serum calcium levels were associated with lower CRP values (Figure 23). Vitamin D and CRP were also apparently independent parameters both at the beginning of the study (r= -0.017; p=0.881) and on reassessment (r= +0.026; p=0.814) (Figure 24).

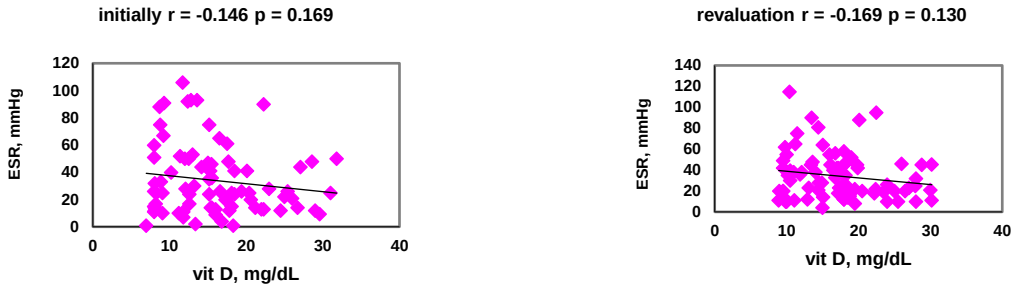

Figure 21. *Vitamin D and ESR correlation*

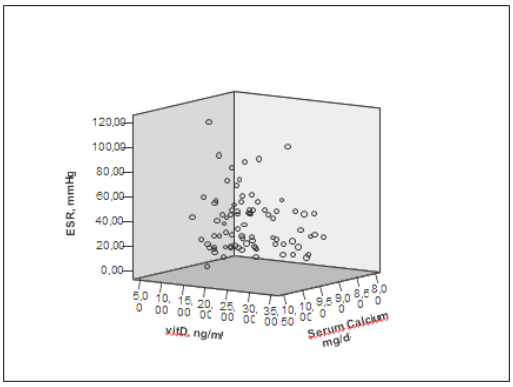

Figure 22. *Serum calcium and vitamin D correlation with ESR*

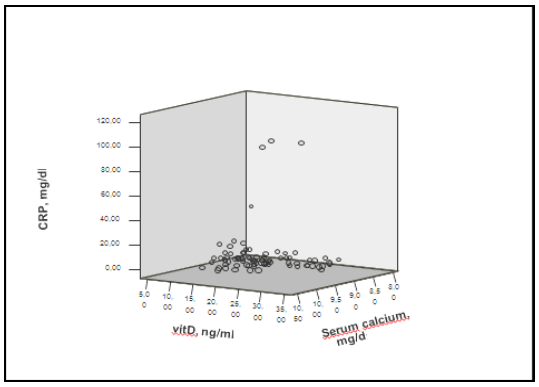

Figure 23. *Serum calcium and vitamin D correlation with CRP*

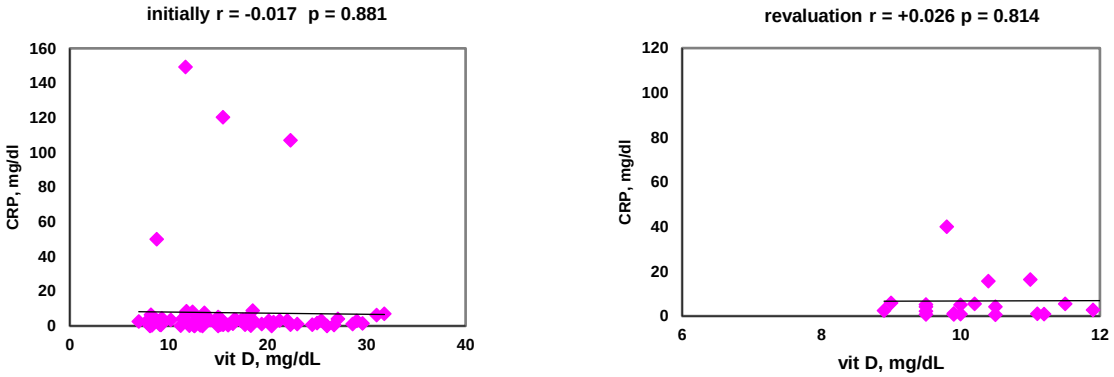

Figure 24. *Vitamin D and CRP correlation*

At the beginning of the study, 21% of the patients had higher serum calcium values and higher white cell counts (r= +0.210; p=0.05), whereas on reassessment only 15.5% of them still exhibited this characteristic (r= +0.155; p=0.165). Nevertheless, these findings cannot be extrapolated to the general population.

IV.3.4. Discussion

A study published in 2018 revealed that low vitamin D values in the serum were associated with a series of autoimmune diseases. This research revealed a negative correlation of serum 25-(OH) vitamin D concentrations with pain and disease activity score in patients with rheumatoid arthritis, yet it was unable to clearly determine the cause-effect relation. The same research found that vitamin D supplements were associated with significant effects on pain and on disease activity in patients suffering from rheumatoid arthritis. It was also found that vitamin D deficiency seems to be tightly connected to pain, whereas high serum concentrations of 25-

(OH) vitamin D seem to have immunomodulating effects (Chandrashekara and Patted, 2015; Lin J *et al.*, 2016).

On reassessment, the analysis of our group of patients showed a significantly lower mean NPJ level compared to the number of painful joints detected in the patients at the beginning of the research, which proves a positive evolution of pain, correlated with improved 25-OH vitamin D levels. This also stands for a mean NSJ level.

On reassessment, the mean VAS level was significantly lower than the VAS determined before the therapy, and it was also correlated with 25-(OH) vitamin D values. 6 months after the beginning of the study, the mean DAS_{28} of these patients was slightly lower than the one determined on the first assessment. The VAS scale on reassessment improved and it was correlated with improved NPJ and NSJ values, as well as with 25-(OH) vitamin D values.

The vitamin D and ESR correlation was indirect and weak, both at the beginning and on reassessment. On the first assessment, the lower vitamin D and serum calcium levels were associated with higher ESR values. On reassessment, the higher vitamin D and serum calcium levels were associated with lower CRP values. We also detected negative correlations of the vitamin D level with the pain and disability.

IV.3.5. Conclusions

The assessment of the patients 6 months after the beginning of the study showed a slight improvement of the inflammatory and immunological syndrome, knowing that in addition to their anti-inflammatory maintenance therapy they were also given vitamin D supplements.

Our research showed that strong inflammation was linked to lower vitamin D and serum calcium levels, especially on the first assessment.

The findings of our study are in line with the research in the field, as they reveal that the intake of vitamin D supplements since the onset or since the early stages of rheumatoid arthritis may lead to an improvement of these patients' status, both from the viewpoint of joint and muscle pain and of mobility and stability improvement, and from the viewpoint of bone mass loss slowdown.

SECTION II

FUTURE PROJECTS IN THE PROFESSIONAL, ACADEMIC AND SCIENTIFIC FIELD AND DEVELOPMENT PROJECTS

The development of my future career it is supported by the following arguments:

- Expertise gathered from the professional evolution.
- Experience accumulated so far during the academic community.
- I am motivated person by everything I intend to do;
- I have participated in various activities and projects with different responsibilities to accomplish.

Perspectives in professional activity

During all my activity, I tried continuously to develop a proper harmonious connection between the human living environment research and educational activity, to improve level of knowledge, communication and teamwork skills.

Collaborating with different specialists in the preventive medicine area from North-Eastern part of Romania, helped me to understand their constant need for training and up-dating the information. This observation determined me to organize lectures workshops for both for residents and specialists based on my professional experience

Professionally, I intend to improve my management skills and also to acquire new professional competences.

I want to create mixed research teams with members from University and Emergency Clinical Hospital "Prof. Dr. N. Oblu" from Iasi, capable to access funding in open competitions for updating and optimizing the actual medical infrastructure.

Another goal will be the development of different primary, secondary and tertiary prevention programs for nutritional disorders, hospital acquired infections and food safety, by collaborating with other medical specialties which are in the same area of expertise.

Improving and extending interdisciplinary collaborations will be also a professional objective I want to accomplish in the next years.

All the professional approaches I intend to develop in the next years are aiming to change the image and the medical school graduates perception generally for preventive medicine and particularly for the hygiene specialty.

Perspectives in academic activity

One of my goals is to change the actual paradigm of medical education that needs to be interactive, student-centered, skills-training and not just informative.

From the point of view of academic management, I propose at the local level to develop much closer working relationships between the departments within our University and at the national level, in order to stimulate scientific and educational collaborations with all colleagues from the other disciplines of Hygiene and Environmental Health/Ecology from all the academic centers in Romania.

Ensuring a medical education to the highest standards at all levels (Licence / Master / Ph.D.) at the same time as developing innovative research programs, being aware that we work in a highly prestigious University, but also in a highly competitive global academic community.

I intend continue and extent the fruitful collaboration with other chairs like Social Sciences, Epidemiology and Primary Healthcare, Public Health, Biochemistry, Medical Genetics and other clinical specialties, in order to find new ways to emphasize on the impact of living environment over the health status and life quality of human beings.

An increased number of multicentric studies which will include extended groups of persons is compulsory if we want to identify different relationships between human health and environment heath.

I will encourage an active strategy aiming for student's involvement in the teaching-learning and researching process and also, I will involve the most valuable resident physicians in scientific research programs.

Developing new methods of teaching, assimilation and assessment of information's understanding will fulfill the educational partnership we have with our students.

I am aware that I must be, first a model and second a mentor, for the Ph.D. students, who are entitled to receive the best counseling for structuring and developing their own genuine research.

On the other hand, I will plead for permanent up-dating of the hygiene and preventive medicine *curriculum* content, both for students and young residents or specialist physicians, focused on the last and most important discoveries in this medical field.

I will elaborate with my colleagues a new *Hygiene and Environmental Health Textbook* for students in Romanian, English and French sections, to fit into the challenging international tendencies in this field.

All these educational approaches are ment to provide a better knowledge, and also a different statute for *hygiene* and *preventive medicine* as important and innovative parts of modern medicine.

Perspectives in scientific activity

European Charter on Environment and Health elaborated in 1989 at Frankfurt, established for the first time that *"Good health and well-being require a clean and harmonious environment in which physical, psychological, social and aesthetic factors are all given their due importance".*

After more than one social generation, in year 2022, the concept of *good health* appears to be, more than ever, a synthesis of all relationships between human and environmental health.

Reckless of mankind activity imprints dramatically the living environment and endangering even our existence among other species.

Due to anthropic activity and dysfunctional environmental management, we generate every day new challenging pathologies.

Using the information and expertise of the partners in the previous projects I want to develop local projects to identify ways of secondary and tertiary prevention, with immediate application to children / teenagers development and chronic degenerative diseases, in people of third age. The results we intend to publish in SCIE and ESCI listed journals.

As a mainstream long-term goal, I will enroll both for research funds in competitions for CNCSIS-funded projects, and in those initiated by Faculty of Medicine and our University.

Another goal is to identify new and challenging areas of interdisciplinary research, which are at the interference between preventive medicine, clinical medicine and fundamental sciences.

Starting from my previous experience I intend to look beyond the classical approaches in environmental health and give a real and consistent chance to an *integrative assessment* of living environment from quality of water, air, food, habitat and, above all, psycho-social component.

Education for all the members of the community about their relationship with the living environment should be a major care regardless their age and educational background.

Early education concept may be used in designing and shaping correct future habits as a primary preventive mechanism to prevent the onset of the disease.

Psychonutrition is a borderline area between different areas of expertise (nutrition, psychology and ecology) where information about eating and healthy habits must be reassessed and transferred to all the people, in order to prevent nutritional disorders or to improve their health status.

In a historical moment when an increased number of scientists talk about *food security*, the solution seems to be *food safety* for preserving the health status and avoiding other health problems.

Last but not least, all the future medical doctors and specialists in medical field must discover that the most challenging aspects of the research activity are generated mainly by knowledge and surely endorsed by creativity and pragmatism.

Final remarks

This habilitation summarizes research, educational/learning and management activities, conducted within the Department of Preventive Medicine and Interdisciplinarity and at the University level and proves that such a challenging approach can be achieved only with hard working, creativity and the support of an extremely complex and complete team.

I am proud and honored to be part of the "Grigore T. Popa" University of Medicine and Pharmacy of Iasi and all my future activity will be dedicated to give back at least as much as I received from it.

SECTION III

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