

**UNIVERSITATEA DE MEDICINĂ ȘI FARMACIE „CAROL DAVILA”  
BUCUREȘTI**

**ȘCOALA DOCTORALĂ  
DOMENIUL MEDICINĂ**

**PSIHIATRIA ÎNTRE EPIDEMIOLOGIA CLASICĂ ȘI  
INTELIGENȚA ARTIFICIALĂ**

**Rezumatul tezei de abilitare**

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## REZUMAT

Lucrarea prezentă este o descriere de ansamblu a activității mele profesionale, didactice și de cercetare precum și o trecere în revistă a principalelor direcții de dezvoltare viitoare în fiecare dintre aceste domenii. Temele mele de interes au fost și sunt epidemiologia psihiatrică și psihofarmacologia, direcții pe care le-am urmat de-a lungul întregii mele cariere științifice, atât în cadrul studiilor doctorale, cât și ulterior acestora, și care continuă să formeze fundamentul intereselor și activității mele științifice.

Începând cu teza mea de doctorat, ce a avut ca element central studierea unei baze de date de 16153 de persoane (British Cohort Study 1970) și până în prezent cercetările mele în domeniul epidemiologiei au acoperit o gamă variată de patologii și au fost publicate în jurnale academice internaționale de prestigiu:

- Validation of the Collaborative Outcomes study on Health and Functioning during Infection Times (COH-FIT) questionnaire for adults (*Journal of Affective Disorders*)
- Quality of life in people with subjective cognitive decline (*Alpha Psychiatry*)
- Physical and mental health impact of COVID-19 on children, adolescents, and their families: The Collaborative Outcomes study on Health and Functioning during Infection Times-Children and Adolescents (COH-FIT-C&A) (*Journal of Affective Disorders*)
- How “Subjective” is Subjective Cognitive Decline? (*Psychiatry and Clinical Psychopharmacology*)
- APOE4 status and cognitive function in middle-aged and elderly people (*Journal of Medical Genetics*)
- Risk factors and consequences of traumatic brain injury in a Swiss male population cohort (*BMJ Open*)
- The collaborative outcomes study on health and functioning during infection times in adults (COH-FIT-Adults): Design and methods of an international online survey targeting physical and mental health effects of the COVID-19 pandemic (*Journal of Affective Disorders*)

- Training and retaining mental health professionals: The Romanian experience in the European Union (*Asia-Pacific Psychiatry*)
- The Use of Cannabidiol in Treating Psychiatric Disorders: A Systematic Review (*Psychiatry and Clinical Psychopharmacology*)
- Clinical Validity of Subjective Clinical Prognosis in First Episode Psychosis Schizophrenia Patients: An Analysis of Data from the European First Episode Schizophrenia Trial (EUFEST) Study (*Neuropsychiatric Disease and Treatment*)
- When Do Psychiatric Patients Get Better? Timeline and Implications of Clinical Response to Treatment in Serious Mental Illness (*Psychiatry and Clinical Psychopharmacology*)
- Knowledge of Prevention Measures and Information About Coronavirus in Romanian Male Patients with Severe Mental Illness and Severe Alcohol Use Disorder (*Neuropsychiatry Disease Treatment*)
- The Use of Cannabidiol in Treating Psychiatric Disorders: A Systematic Review (*Psychiatry and Clinical Psychopharmacology*)
- High-sensitivity C-reactive protein, possible biomarker for depression in elderly population (*Acta Endocrinologica*)
- European Union Mobility, Income and Brain Drain. The Attitudes towards Migration of Romanian Psychiatric Trainees (*Revista de Cercetare și Intervenție Socială*)
- Quality of life in Romanian patients with schizophrenia based on gender, type of schizophrenia, therapeutic approach, and family history (*Journal of Mind and Medical Sciences*)
- Prolactin level in patients with first episode schizophrenia treated for one year with atypical antipsychotics (*Acta Endocrinologica*)
- Risk factors for suicide attempts that needed medical admission in bipolar I patients. Romanian Journal of Legal Medicine (*Romanian Journal of Legal Medicine*)
- The SWITCH study: rationale and design of the trial (*European Archives of Psychiatry and Clinical Neuroscience*)
- Weight Gain and Antipsychotics. Data from EUFEST Study (*Acta Endocrinologica*)
- Is non-pharmacological treatment an option for certain schizophrenia patients? (*Psychiatria Danubina*)

Consider studierea epidemiologiei psihiatrice ca fiind un domeniu de maxim interes întrucât acest aspect este fundamental pentru înțelegerea prevalenței, incidenței și impactului acestor afecțiuni asupra populației și permite identificarea factorilor de risc, a factorilor psihopatologici precum și dezvoltarea de strategii adecvate de prevenție și intervenție.

A doua latură majoră a activității mele o reprezintă cercetarea psihofarmacologică, fapt concretizat prin participarea în calitate de investigator principal la numeroase trialuri de medicație organizate de companii farmaceutice majore. La multe dintre studiile clinice am participat doar prin recrutarea pacienților și colectarea datelor, la altele însă, care au fost publicate în reviste prestigiu am participat și în procesul de redactare a lucrărilor (cu sugestii referitoare la analiza datelor și la identificarea unor ținte terapeutice, revederea datelor din literatură, corectură etc.) și am fost printre co-autorii acestor articole:

- A randomized controlled trial of add-on naproxen, simvastatin and their combination for the treatment of schizophrenia or schizoaffective disorder (*European Neuropsychopharmacology*)
- Changing the Antipsychotic in Early Nonimprovers to Amisulpride or Olanzapine: Randomized, Double-Blind Trial in Patients With Schizophrenia (*Schizophrenia Bulletin*)
- Add-On Pramipexole for the Treatment of Schizophrenia and Schizoaffective Disorder: A Randomized Controlled Trial (*Journal of Clinical Psychiatry*)
- Adjunctive Aspirin vs Placebo in Patients With Schizophrenia: Results of Two Randomized Controlled Trials (*Schizophrenia Bulletin*)
- Sodium Nitroprusside Infusion for the Treatment of Schizophrenia (*Schizophrenia Bulletin Open*)
- Raloxifene Plus Antipsychotics Versus Placebo Plus Antipsychotics in Severely Ill Decompensated Postmenopausal Women With Schizophrenia or Schizoaffective Disorder (*Journal of Clinical Psychiatry*)
- A randomized, double-blind, placebo-and risperidone-controlled study on valnoctamide for acute mania (*Bipolar Disorders*)

După o perioadă de ”secetă” în ceea ce privește apariția de noi medicamente atât de necesare în domeniul tratamentului afecțiunilor psihiatrice, în ultimii ani asistăm la apariția unui număr impresionant de noi molecule, unele deja introduse pe piață, altele aflate în faze avansate de cercetare, cu mecanisme de acțiune fundamental diferite de cele existente în prezent.

Primul capitol acoperă realizările mele în cadrul diferitelor domenii de cercetare, incluzând cărți sau capitole de cărți și articole în reviste indexate ISI, CNCIS sau B+ (64 de articole). De asemenea, conține descrieri succinte ale proiectelor de cercetare și ale trialurilor clinice în cadrul cărora am participat. Adițional, este conturat un scurt istoric al activității mele profesionale pe linie clinică, de la absolvirea Universității de Medicină „Grigore T. Popa” până la funcția prezentă de medic șef de secție în cadrul spitalului „Profesor Doctor Alexandru Obregia”. Este trecută în revistă activitatea mea didactică desfășurată în cadrul catedrei de psihiatrie a Universității de Medicină și Farmacie „Carol Davila”. Nu în ultimul rând, sunt enumerate rezultatele activității mele editoriale, dintre care cel mai important îl consider a fi preluarea funcției de redactor șef al Revistei Române de Psihiatrie (calitate în care am coordonat apariția a 7 numere ale Revistei Române de Psihiatrie), pe care intenționez să o aduc la standardele necesare indexării ISI.

Cel de-al doilea capitol constă într-o analiză amănunțită a ceea ce consider a fi principale rezultate științifice originale obținute de-a lungul activității mele profesionale. Prima parte este o privire de ansamblu asupra concluziilor trase din studierea lotului de 16153 de persoane din cadrul British Cohort Study 1970, constând în parametri acționând în perioada copilăriei ce pot constitui factori de risc pentru depresie în perioada adultă. A doua parte se referă la colaborarea mea cu Universitatea din Lausanne pentru identificarea factorilor de risc și consecințelor traumatismelor cranio-cerebrale într-o cohortă de 5516 de bărbați elvețieni. Ulterior, sunt detaliate rezultatele obținute pe baza analizei datelor din studiul The European First Episode Schizophrenia Trial (EUFEST) referitoare la predictorii evoluției pacienților cu prim episod psihotic, precum și utilitatea procesului clinic subiectiv de prognostic în ceea ce privește primul episod psihotic, în cadrul aceluiași studiu EUFEST. Tot din cohorta românească de pacienți participanți la studiul EUFEST voi prezenta datele referitoare la “Nivelul de prolactină la pacienții cu primul episod de schizofrenie tratați timp de un an cu antipsihotice atipice” precum și “Creșterea în greutate și antipsihoticele. Date din studiul EUFEST”. În final, este descris studiul privind cunoștințele

pacienților psihiatrics în legătură cu măsurile de prevenție CoVID-19, pe care l-am derulat pe perioada pandemiei.

Al treilea capitol detaliază direcțiile viitoare de dezvoltare în planurile profesional, didactic și de cercetare. În plan profesional, ca medic șef al secției II clinic a Spitalului Clinic de Psihiatrie „Profesor Doctor Alexandru Obregia”, dezideratul principal îl reprezintă continuarea oferirii de îngrijiri psihiatrice la cele mai înalte standarde de calitate, în conformitate cu cele mai noi ghiduri de practică naționale și internaționale, adaptând datele teoretice la fiecare caz individual în parte. Din punct de vedere al activității didactice, unul dintre obiectivele mele majore este reprezentat de promovarea conceptului de mentorat în procesul de formare al rezidenților, în care am o experiență considerabilă. De asemenea, în calitate de conferențiar în cadrul Catedrei de Psihiatrie a Facultății de Medicină, doresc să asigur în continuare buna desfășurare a cursurilor și lucrărilor practice pentru studenți, precum și integrarea celor mai noi informații din domeniu în curricula acestora. Activitatea mea viitoare de cercetare se va centra în viitorul apropiat asupra unei serii de colaborări cu universitatea din Lausanne, ce va avea ca finalitate elaborarea a cinci articole științifice, având ca scop final înțelegerea a multipli factori de risc asociați cu suicidul, depresia, utilizarea nocivă a substanțelor, finalizate prin publicarea în reviste internaționale cu factor de impact ridicat. Pe termen mediu și lung doresc consolidarea unui grup redacțional concentrat asupra realizării de meta-analize și review-uri sistematice, ce consider că au potențialul de a mări semnificativ prestigiul instituției catedrei și universității din care fac parte. În plus, sunt enumerate o altă serie de proiecte de cercetare viitoare.

## SUMMARY

The present work is an overview of my professional, educational, and research activities, as well as a review of the main directions for future development in each of these areas. My main areas of interest have been and continue to be epidemiology and psychopharmacology, which I have pursued throughout my scientific career, both as part of my doctoral studies and subsequently, and which continue to form the foundation of my scientific interests and activities.

Starting with my doctoral thesis, which focused on studying a database of 16,153 individuals (British Cohort Study 1970), my epidemiological research has covered a wide range of disorders and has been published in prestigious international academic journals:

- Validation of the Collaborative Outcomes study on Health and Functioning during Infection Times (COH-FIT) questionnaire for adults (*Journal of Affective Disorders*)
- Quality of life in people with subjective cognitive decline (*Alpha Psychiatry*)
- Physical and mental health impact of COVID-19 on children, adolescents, and their families: The Collaborative Outcomes study on Health and Functioning during Infection Times-Children and Adolescents (COH-FIT-C&A) (*Journal of Affective Disorders*)
- How “Subjective” is Subjective Cognitive Decline? (*Psychiatry and Clinical Psychopharmacology*)
- APOE4 status and cognitive function in middle-aged and elderly people (*Journal of Medical Genetics*)
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- Training and retaining mental health professionals: The Romanian experience in the European Union (*Asia-Pacific Psychiatry*)
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- Is non-pharmacological treatment an option for certain schizophrenia patients? (*Psychiatria Danubina*)



I consider this field to be of utmost interest as studying the epidemiology of psychiatric disorders is crucial for understanding the impact of these conditions on the population and allows for the identification of risk factors and the development of appropriate prevention and intervention strategies.

The second major aspect of my work is psychopharmacological research, as evidenced by my participation as a principal investigator in numerous clinical trials organized by major pharmaceutical companies:

- A randomized controlled trial of add-on naproxen, simvastatin and their combination for the treatment of schizophrenia or schizoaffective disorder (*European Neuropsychopharmacology*)
- Changing the Antipsychotic in Early Nonimprovers to Amisulpride or Olanzapine: Randomized, Double-Blind Trial in Patients With Schizophrenia (*Schizophrenia Bulletin*)
- Add-On Pramipexole for the Treatment of Schizophrenia and Schizoaffective Disorder: A Randomized Controlled Trial (*Journal of Clinical Psychiatry*)
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- A randomized, double-blind, placebo-and risperidone-controlled study on valnoctamide for acute mania (*Bipolar Disorders*)

After a period of "drought" in terms of the emergence of new molecules that are much needed in the field of psychiatric disorder treatment, we have witnessed an impressive number of new

molecules in recent years, some being already on the market, and others in advanced stages of research, with fundamentally different mechanisms of action from those currently available.

The first chapter covers my achievements in various research areas, including books or book chapters and articles in ISI, CNCIS, or B+ indexed journals. It also includes brief descriptions of research projects and clinical trials in which I have participated. Additionally, a brief history of my professional clinical activity is outlined, from graduating from the "Grigore T. Popa" University of Medicine to my current position as Chief Medical Officer of the "Professor Doctor Alexandru Obregia" Psychiatry Hospital. My teaching activities within the Psychiatry Department of the "Carol Davila" University of Medicine and Pharmacy are reviewed. Lastly, the results of my editorial activities are listed, with the most significant being the assumption of the role of Editor-in-Chief of the Romanian Journal of Psychiatry, which I intend to bring to the standards required for ISI indexing.

The second chapter consists of a detailed analysis of what I consider to be the main original scientific results obtained throughout my professional career. The first part provides an overview of the conclusions drawn from studying the cohort of 16,153 individuals in the British Cohort Study 1970, focusing on parameters acting during childhood that can constitute risk factors for depression in adulthood. The second part relates to my collaboration with the University of Lausanne in identifying risk factors and consequences of cranio-cerebral traumas in a cohort of 5,516 Swiss men. Subsequently, the results obtained based on data analysis from "The European First Episode Schizophrenia Trial" (EUFEST) are detailed, concerning the predictors of outcome for patients suffering from a first psychotic episode, as well as the usefulness of the subjective clinical process in predicting the first psychotic episode, also within the same EUFEST study. From the Romanian cohort of patients participating in the EUFEST study, data on "Prolactin levels in patients with first episode schizophrenia treated with atypical antipsychotics for one year" and "Weight gain and antipsychotics: Data from the EUFEST study" will be presented. Finally, the study on the psychiatric patients' knowledge of COVID-19 prevention measures, which I conducted during the pandemic, is described.

The third chapter details the future directions for development in my professional, educational, and research plans. In terms of my professional role as Chief Medical Officer of the Clinical Section II of the "Professor Doctor Alexandru Obregia" Hospital, the main goal is to continue providing psychiatric care at the highest quality standards, in accordance with the latest national and international practice guidelines, adapting theoretical knowledge to each individual case. In terms of my teaching activities, one of my major objectives is to promote the concept of mentoring in the training process of residents, in which I have considerable experience. Additionally, as a lecturer in the Psychiatry Department of the Faculty of Medicine, I aim to ensure the smooth running of lectures and practical work for students, as well as the integration of the latest information in the field into their curricula. My future research activities will focus on a series of collaborations with the University of Lausanne, culminating in the development of five scientific articles aimed towards understanding multiple risk factors associated with suicide, depression, and harmful substance use, with the final goal of publishing them in high-impact international journals. In the medium and long term, I aim to consolidate an editorial group that will focus on conducting meta-analyses and systematic reviews, which I believe have the potential to significantly increase the prestige of the Psychiatry Department and the university to which I belong. Additionally, a series of other future research projects are outlined.