

**"VICTOR BABEȘ" UNIVERSITY OF
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DOCTORAL SCHOOL
MEDICINE DOMAIN**



**RESPIRATORY AND SLEEP MEDICINE
MEET NETWORK SCIENCE: FROM PHENOTYPING
TO SEVERITY PREDICTION, COMORBIDITIES
AND PERSONALIZED MANAGEMENT**

ABSTRACT

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The habilitation thesis entitled **"RESPIRATORY AND SLEEP MEDICINE MEET NETWORK SCIENCE: FROM PHENOTYPING TO SEVERITY PREDICTION, COMORBIDITIES AND PERSONALIZED MANAGEMENT "** summarizes the personal scientific, academic, and professional achievements in the postdoctoral period 2008-2021, together with the main directions of development in research and academic areas.

The first chapter presents the **scientific achievements**. The first subchapter states the research motivation, research path, multiple team research areas, research grants and the most important published papers (ISI articles, book chapters, in extenso and abstract papers published at conferences) and participation in scientific research projects. According to the Web of Science Citation Report (Clarivate Analytics), the author's H-index is 8, based on 269 citations; the Scopus citation database lists an H-index of 9 based on 394 citations, and Google Scholar citations' report indicates an H-index of 10 based on 435 citations. In the PubMed there are 51 papers.

As the principal author, 14 ISI scientific papers have been published, with an impact factor between 1.8 and 11.6, with a cumulative impact factor of 52.882. As a co-author, I published 15 ISI papers with an impact factor between 0.83 and 12.83. As an-author/co-author we have 78 conference papers published in ISI journals (Web of Science) with impact factor from 3.1 to 16.5.

The author was also involved in 7 research projects: three international grants, and four national projects. Of these, one grant is in progress, as a director at national level "Revolution of sleep diagnostics and personalized health care based on digital diagnostics and therapeutics with health data integration" - SLEEP REVOLUTION, ID 965417, in the European competition HORIZON 2020 (March 2021 – February 2025).

The following subchapter presents results from three areas of research: sleep medicine, asthma, tobacco control.

Network science analysis can contribute to a better prediction, screening and treatment response in OSA. There were four major topics with significant contributions and novelties that were published in high impact factor journals: a new score and new application of Network Science in sleep medicine with software for AHI and apnea severity prediction; a new network-based clustering algorithms to uncover gender-

specific phenotypes; complex network approach in combination with symptoms, age, gender, and BMI as the best qualitative indicator of treatment response.

As a member of experts from European Respiratory Society and European Sleep Research Society we published an updated standard for procedures and scoring in Europe, and the about the challenges and perspectives in OSA. Novelties: first assessment of practice for the standard procedure for diagnosis of sleep-disordered breathing throughout Europe; a new expert analysis of challenges and perspectives in obstructive sleep apnoea;

ESADA is the largest European data base. As a member from 2019, we published paper from the largest database related to impact of OSA on cardiometabolic risk in atrial fibrillation and the residual daytime sleepiness in CPAP treated patients.

Together with colleagues from Budapest and Manchester University we published new data related comorbidities in OSA, metabolic markers in plasma of apneic patients. Novelties: the first retrospective study describing the profile of comorbidities in patients with OSA in Hungary and Romania; the first study that evaluates atherosclerotic index of plasma as a predictive biomarker for cardiovascular disease in Central Europe; an up-to-date review in an high impact factor journal about asthma and OSA in adults and children; long-term CPAP use associated with significant weight loss; patients with OSAS and heart failure with mid-range ejection fraction may represent a new group with increased risk of developing life-long chronic kidney disease, diabetes mellitus, tricuspid and aortic insufficiency.

Asthma research focused on an international cooperation with Inter Asthma network and we published 7 papers. Novelties: four predictors may identify elderly patients with uncontrolled asthma and facilitate early medical interventions; the definition of asthma phenotypes and underlying mechanisms (endotypes) is a key point in the development of new asthma treatments; successful strategies for adherence to treatment in allergic respiratory diseases should combine different interventions (i.e., education, counselling, more convenient care, self-monitoring, reinforcement, and reminders); a multidisciplinary group is needed with focus on the patient and the multimorbid concept and united airway disease; obesity-associated asthma is more severe, difficult to control, and less responsive to standard controller

therapy; recognizing asthma occupational triggers in the workplace, early diagnosis and removal of the workers from the exposure, education and development of institutional medical-surveillance programs; a first analysis that shows uncertainties and inconsistencies regarding the use of biological medications in asthma world-wide; a manifesto describes the evidence upper airway diseases (rhinitis, rhinosinusitis and nasal polyposis), and concomitant/comorbid lower airways disorders (asthma, chronic obstructive pulmonary disease, bronchiectasis, cystic fibrosis, obstructive sleep apnoea) with the aim of challenging assumptions, fostering commitment, and bringing about change.

Smoking cessation and research with an international team brought some novelties: web-based, multimedia smoking prevention programs may be effective tools to prevent smoking initiation among multi-ethnic adolescents; the first study to report the prevalence, correlates and patterns of e-cigarette use of among multi-ethnic high school students in central Romania.

The following **two chapters** present the most important **academic and professional achievements** since graduating from the Faculty of Medicine, the specialization General Medicine of the "Timisoara Medicine Institute" in 1990 until now, as well as elements of professional activity recognition, reflected by citations in high-impact scientific journals, reviewer activity for scientific journals from prestigious editorial groups and the position of guest academic editor at medical journals.

Author of a chapter in 3 international textbooks, 18 monography CNCSIS, guidelines, and courses, 16 book chapters. The author coordinated 38 license dissertations for students from Romanian and English sections and 16 Master Degree - Bachelor in Science, Department of Master Studies, Prevention and Rehabilitation in cardio- pulmonary disease.

Principal investigator in over 40 international clinical trials related to asthma, COPD, pneumonia, bronchiectasis. Some results can be found in PubMed in papers published in New England Journal of Medicine as a member Flame Investigators, Galathea Study Investigators, Terranova Study Investigators.

Executive position at the European Sleep Research Society for 3 mandates. President of the Sleep Section of the Romanian Society of Pulmonology.

Competences (Attestate): 4 at a national level, one at European level (Sleep Medicine Expert Somnologist from 2013). Reviewer for journals from well-known and acknowledged publishing houses: 52 verified reviews in Web of Science.

The last chapter presents the **academic and scientific development project** to be undertaken after obtaining the habilitation qualification. There are teaching development proposals by diversifying the undergraduate topics, the recommendation of optional and postgraduate courses. A second plan is that of the research development proposal, focused mainly on OSA and COPD.

OSA is under research within Sleep Revolution grant that started in 2021 and will be completed in 2024 in a multi-disciplinary and multi-national team of experts in sleep medicine, data technology, state-of-the-art machine learning, and skilled small-to-medium enterprises. It proposes a revolution of sleep diagnostics and personalized health care based on digital diagnostics and therapeutics with health data integration with creating an integrated network that extends across Europe, including major stakeholders to transform sleep medicine in Europe with key opinion leaders in sleep medicine, data engineers, patient representatives, and the two leading European expert organisations (European Research Society and European Sleep Research Societies).

For the next years, I will work in an international team (Romania is represented by our university and Polytechnic University of Timisoara) for standardizing self-applied state-of-the-art polysomnography utilizing automatic sleep scoring which allows multiple night home sleep studies, constructing a European Sleep Questionnaire that integrates standardized patient-reported outcome measures, and creating a cloud-based data storage for multi-centre analysis and a digital platform which enables integration of the data source needed for complete clinical disease management from sleep medicine centres across Europe.

Pilot studies will validate a new self-applied PSG, using a simple three-night set-up at home instead of the traditional one night in the laboratory or at home. We will implement the state-of-the-art deep learning methodologies which have already achieved remarkable results in automatic sleep staging. We will be one of 25 clinical centres representing 15 European countries that will perform a large prospective

standardized clinical trial in 1000 OSA patients treated with CPAP or mandibular advancement devices.

For the COPD research we want to build a complex network model for clustering patients in order to predict the disease evolution trajectory for individuals that were already diagnosed with COPD. The goal consists of predicting exacerbations and issuing alerts when physiological signals degrade. The network approach will hopefully provide a precise patient phenotype identification. A first paper (Fractional dynamics foster deep learning of COPD stage prediction) together with a team from the University of Southern California led by Professor Paul Bogdan is under review at Science Advances.

This project will help us to develop the research infrastructure of our university and will continue partnerships both to perform the experiments entailed by the research topics proposed in this habilitation thesis.