



The European Sleep Apnoea Database (ESADA) ERS Clinical Research Collaboration: past, present and future

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The European Sleep Apnoea Database (ESADA) ERS Clinical Research Collaboration records data in over 25 000 patients with OSA from 33 European countries, to conduct clinical research and improve OSA patient care and outcomes <http://ow.ly/DuDf30lZRP6>

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The start of the European Sleep Apnoea Database

The European Sleep Apnoea Database (ESADA) study began in 2007 as a joint project within the European Union (EU) Cooperation in Science and Technology (COST) Action B26 on obstructive sleep apnoea (OSA) and cardiovascular risk, as a network of nationally appointed sleep apnoea experts. At that time, there were few cohorts of OSA patients, mainly in the context of epidemiological studies in the general population [1–6]. The COST Action only provided funding for networking, and each participating centre entered data into the web-based database on a voluntary basis. Collected data included anthropometrics, results of blood tests, current medications, and sleep data derived from full polysomnography or cardiorespiratory nocturnal monitoring, according to the diagnostic procedure chosen by the physician. Importantly, quality controls of the dataset were performed at regular intervals since the start of the project.

During the first 2 years of the ESADA project, 5000 patients had been enrolled by 22 European sleep laboratories and stored at the coordinating centre in Gothenburg, Sweden [7]. The study continued after the end of the COST Action in 2010, thanks to financial support by the industry, and both the number of participating centres and the number of patients grew to reach the current figures of 33 and 25 000, respectively.

Before the approval of the ESADA project as a European Respiratory Society (ERS) Clinical Research Collaboration (CRC) in 2015, some important changes occurred. First, members of the ESADA group gathered each year in late winter or early spring in different European sleep centres for a 2–3-day meeting to discuss current and new projects and to work on manuscripts. Such meetings, as well as short-term exchanges of young researchers between ESADA laboratories, have strengthened the relationship between members and provided a creative, generous and friendly environment, while increasing the research productivity of the network. In 2014, four studies were published, reporting cross-sectional analyses on blood pressure [8], metabolic disorders [9, 10] and car accidents [11]. Secondly, a new generation of clinicians and scientists became involved in the ESADA study group and contributed enthusiastically to

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patient recruitment and new research projects, setting the premises for continuity of the project beyond the “founders”. Thirdly, it was recognised that it was important to set up a longitudinal cohort rather than continuing with recruitment of new patients at a high rate. Indeed, the aim of the first CRC in 2015 was to implement follow-up visits and longitudinal studies, and data on renal function [12] and body weight change [13] according to OSA treatment during follow-up have been recently published. Meanwhile, digging into the dataset in cross-sectional studies continued, with published research papers on methodological issues related to the diagnostic method [14], the association of OSA with chronic kidney disease [15], asthma [16] or dyslipidaemia [17], and the search for clinical phenotypes [18].

Where does ESADA currently stand?

The approval of the CRC by the ERS, and its recent renewal, greatly increased the visibility and prestige of ESADA worldwide, together with the cohesion and motivation of its members, in particular the commitment for further improvements, especially regarding OSA patient care and patient outcomes, which represent the ultimate goal of the ESADA project.

Current research projects include the association of OSA with cancer, definition of risk associated with mild OSA, and differences in OSA phenotypes between European countries. At the time of writing (in August 2018), there are more than 37 000 visits in the database, including first and follow-up visits. The monthly inclusion rate is ~150–200 patients and the scientific activity is high (13 abstracts accepted in international conferences in 2018 and several manuscripts in preparation/submission). The ESADA serves as a reference database on European sleep apnoea patients and continues to provide a bridge for education and knowledge transfer between the various participating centres. Following early enabling grants, the ESADA has remained a low-budget study based on strong voluntary input from participating centres.

The future of the ESADA CRC

We would like to extend the network to include new sleep centres from countries not yet represented in the current CRC. Involvement of OSA patient organisations will be promoted with the help of the European Lung Foundation, in order to jointly address the problem of treatment acceptance and non-adherence, a highly hot topic nowadays. While collection of longitudinal data will continue, contacts were established with other clinical cohorts of OSA patients in Europe during a workshop held in Palermo, Italy, in early July 2018, when the possibility of joint projects on “big data” was discussed and awaits approval by the members of ESADA and other cohorts to proceed to formal agreements.

The current debate [19, 20] on randomised controlled trials (RCTs) to evaluate the effects of continuous positive airway pressure (CPAP) on cardiovascular risk suggests that new study designs, adopted to obtain clinically relevant results applicable to different subgroups of patients, should be introduced. Inclusion of OSA patients in long-term RCTs on the effects of OSA treatment has, for ethical reasons, been limited to non-sleepy patients who are poorly compliant to CPAP treatment. Negative results of RCTs could therefore be secondary to poor treatment adherence, rather than to inefficacy of treatment [19]. In this regard, the ESADA CRC could be a powerful instrument to collect a large amount of longitudinal data in OSA patients in the European context. Adoption of the specific methodology required in pragmatic trials will be the next challenge for ESADA and other investigators in the years to come.

There are some critical issues that determine the sustainability of the ESADA project in the long term. We need to develop strategies to maintain high data quality and enable new research activities related to the database. Funding may be provided by public and academic institutions or by collaborations with industry. We plan to submit EU research or public health projects, and cooperation with other cohorts will help to reach the critical mass necessary to cover the entire European area. Again, the CRC is a very good opportunity to pursue this goal, not only for the visibility provided by the endorsement of a leading society like the ERS, but also for the practical support in submission of big projects. With these prospects, we anticipate a bright future for the highly successful collaborative ESADA project.

Collaborators: M.R. Bonsignore and J. Hedner are Chairs of the ESADA Clinical Research Collaboration. Collaborators in the ESADA project (current and past) by country and sleep centre were as follows. Belgium: J. Verbraecken and E. Petiet (Multidisciplinary Sleep Disorders Centre, Antwerp University Hospital and University of Antwerp, Antwerp); D. Rodenstein (Cliniques Universitaires Saint-Luc, Brussels). Croatia: Z. Dogas and T. Galic (Sleep Medicine Center, Dept of Neuroscience, University of Split School of Medicine, Split). Czech Republic: O. Ludka (Dept of Cardiology, University Hospital Brno and International Clinical Research Center, St Ann’s University Hospital, Brno); M. Pretl (Centre for Sleep and Waking Disorders, Dept of Neurology, First Faculty of Medicine, Charles University, Prague, and InSpamed, Neurology and Sleep Laboratory, Prague). Finland: U. Anttalainen and T. Saaresranta (Division of Medicine, Dept of Pulmonary Diseases, Turku University Hospital and Sleep Research Centre, Dept of Pulmonary Diseases and Clinical Allergology, University of Turku). France: P. Levy and J-L. Pépin (Université Grenoble Alpes, INSERM HP2 (U1042) and Grenoble University Hospital, Grenoble); P. Escourrou and G. Roisman (Service d’Explorations Fonctionnelles Multidisciplinaires and Unité de Médecine du Sommeil, Hospital Antoine Beclere, Clamart). Germany:

I. Fietze and T. Penzel (Schlafmedizinisches Zentrum, Charité – Universitätsmedizin Berlin); R. Schulz (Sleep Disorders Centre, University of Giessen, Lung Centre, Giessen); H. Hein (Sleep Disorders Center, St Adolf Stift, Reinbeck). Greece: P. Steiropoulos (Sleep Unit, Dept of Pneumology, Democritus University of Thrace, Alexandroupolis); G. Trakada (Pulmonary Medicine, National and Kapodistrian University of Athens, Athens); I. Bouloukaki and S. Schiza (Sleep Disorders Unit, Dept of Respiratory Medicine, Medical School, University of Crete); A. Pataka (Respiratory Failure Unit, G. Papanikolaou Hospital, Thessalonika). Ireland: W.T. McNicholas (Dept of Respiratory Medicine, St Vincent’s University Hospital, Dublin); S. Ryan (Pulmonary and Sleep Disorders Unit, St Vincent’s University Hospital, Dublin). Israel: L. Lavie and P. Lavie (Centre for Sleep Medicine, Technion Institute of Technology, Haifa). Italy: C. Lombardi and G. Parati (Istituto Auxologico Italiano, Ospedale San Luca, Milan); M.R. Bonsignore (Biomedical Department of Internal Medicine and Medical Specialties (DiBiMIS), Section of Pneumology, University of Palermo, and CNR Institute of Biomedicine and Molecular Immunology, Palermo); O. Marrone (CNR Institute of Biomedicine and Molecular Immunology, Palermo). Latvia: A. Vitols (Institute of Cardiology, University of Latvia, Riga). Lithuania: G. Varoneckas (Institute Psychophysiology and Rehabilitation, Palanga). Norway: J.A. Kvamme (Sleep Laboratory, ENT Department, Førde Central Hospital, Førde). Poland: P. Sliwinski and R. Plywaczewski (Institute of Tuberculosis and Lung Diseases, Dept of Diagnosis and Treatment of Respiratory Failure, Warsaw); P. Bielicki and J. Zielinski (Dept of Internal Medicine, Pneumology and Allergology, Warsaw Medical University, Warsaw). Portugal: R. Staats (Dept of Respiratory Medicine, Hospital de Santa Maria, Lisbon); M. Drummond and M. van Zeller (Pulmonology Dept, Hospital São João, Medicine Faculty of Porto University, Porto). Slovakia: P. Joppa and R. Tkacova (Dept of Respiratory Medicine and Tuberculosis, Faculty of Medicine, P.J. Safarik University and L. Pasteur University Hospital, Kosice). Spain: J.M. Montserrat (Hospital Clinic i Provincial de Barcelona, Barcelona, IDIBAPS Barcelona and CIBERes, Madrid); J.F. Masa (Hospital San Pedro de Alcántara, Cáceres); F. Barbé (Servei Pneumologia Hospital Arnau de Vilanova and Hospital Santa Maria, Lleida, and CIBERes, Madrid). Sweden: J. Hedner and L. Grote (Dept of Sleep Medicine, Sahlgrenska University Hospital, Gothenburg). UK: B. Kent (Guy’s and St Thomas’ NHS Foundation Trust, Guy’s Hospital, London); R.L. Riha (Dept of Sleep Medicine, Royal Infirmary Edinburgh). Turkey: O.K. Basoglu and M.S. Tasbakan (Dept of Chest Diseases, Ege University, Izmir). In addition, the following were centres in the start-up process: ENT Dept at Mainz University, Germany; Pulmonary Dept, University Hospital, Istanbul, Turkey.

Conflict of interest: M.R. Bonsignore has nothing to disclose. J. Hedner reports grants from ResMed, Respironics and Bayer, for conduct of the ESASA database, and an issued patent related to sleep apnoea treatment.

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