Database of Pulmonary Hypertension in the Polish Population (BNP-PL): design of the registry

Grzegorz Kopeć, MD, PhD, email: grzegorzkrakow1@gmail.com
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Anna Doboszyńska17, Agnieszka Pawlak18,19, Zbigniew Gąsior20, Wiesława Zabłocka21
24 Department of Paediatric Cardiology and Congenital Heart Defects, Medical University of Gdańsk, Gdańsk, Poland
22 Department of Cardiology and Internal Medicine, Military Institute of Medicine in Warsaw, Warsaw, Poland
23 Department of Cardiology, Copper Health Center, Lubin, Poland
21 Department of Cardiology, General Hospital in Szczecin, Szczecin, Poland
20 Department of Cardiology, School of Health Sciences, Medical University of Silesia, Katowice, Poland
19 Central Clinical Hospital of the Ministry of Interior, Department of Invasive Cardiology, Warsaw, Poland
18 Department of Cardiology, Pomeranian Medical University, Szczecin, Poland
17 Pulmonology Department, University of Warmia and Mazury, Olsztyn, Poland
16 Department of Cardiology, Pomeranian Medical University, Szczecin, Poland
15 Department of Cardiology, Medical University of Białystok, Białystok, Poland
14 2nd Department of Cardiology, School of Medicine with Dentistry Division in Zabrze, Medical University of Silesia, Zabrze, Poland
13 Department of Cardiology, Medical University of Lublin, Lublin, Poland
12 1st Department of Cardiology, School of Medicine in Katowice, Medical University of Silesia, Katowice, Poland
11 2nd Department of Cardiology, Faculty of Medical Sciences in Zabrze, Medical University of Silesia, Zabrze, Poland
10 Department of Cardiology and Electrotherapy, Medical University of Gdańsk, Gdańsk, Poland
9 Department of Cardiology, Cardinal Wyszynski Hospital, Lublin, Poland
8 Department of Internal Medicine and Cardiology, Medical University of Warsaw, Warsaw, Poland
7 Department of Congenital Heart Disease Institute of Cardiology, Warsaw, Poland
6 3rd Department of Cardiology, Faculty of Medical Sciences in Lublin, Medical University of Lublin, Lublin, Poland
5 Department of Cardiology, Poznan University of Medical Sciences, Poznań, Poland.
4 Cardiology Department, Medical University of Łódź, Łódź, Poland
3 Department of Cardiology Provincial Specialist Hospital Research and Development Center, Wrocław, Poland
2 Department of Pulmonary Hypertension, Thromboembolic Diseases and Cardiology, Centre of Postgraduate Medical Education, Otwock, Poland
1 Department of Cardiac and Vascular Diseases, Institute of Cardiology, Jagiellonian University Medical College, John Paul II Hospital, Kraków, Poland

Introduction Pulmonary arterial hypertension (PAH) and chronic thromboembolic pulmonary hypertension (CTEPH) are rare types of pulmonary hypertension (PH). Consequently, patient registries are key instruments that provide data for clinical research and improve patient care and healthcare planning.1

Currently, most of our knowledge on PAH and CTEPH epidemiology, management, and treatment outcomes come from registries originating in the Western populations.2-5 However, a global view on the epidemiology of PH reveals important geographical differences.1

The Database of Pulmonary Hypertension in the Polish population (Baza Nadciśnienia Płucnego [BNP-PL]) (ClinicalTrials.gov identifier, NCT03959748) is the first multicenter and prospective registry of adult and pediatric patients with PAH and CTEPH created in any of the Central-Eastern European countries. In the present report, we describe the design of the registry.

Objectives of the BNP-PL registry The BNP-PL registry is an initiative of the Working Group on Pulmonary Circulation of the Polish Cardiac Society in cooperation with Polish PH reference centers2-5 to assess prospectively the epidemiology, clinical course, and disease management of patients with PAH and CTEPH. The specific objectives of the study are shown in Supplementary material, Table S1.
Methods  Organization of the BNP-PL registry  An invitation to participate in the study was sent to Polish centers (22 adult and 8 pediatric centers) that were accredited to treat PAH or CTEPH by the Polish National Health Fund (Narodowy Fundusz Zdrowia, NFZ), the only healthcare payer in Poland. Of the invited centers, all of the adult and pediatric centers accepted the invitation and were formally involved in the project. Design of the registry is shown in Figure 1 and is further described in Supplementary material, Methods S1.

The protocol of the study was reviewed and accepted by the Bioethical Committee of Physicians and Dentists Chamber in Kraków.

Participants  Patients with PAH and CTEPH older than 3 months of age and treated in the participating centers are enrolled to the BNP-PL registry to form 4 separate arms as shown in Figure 1A. Patients with both newly and previously diagnosed PAH or CTEPH are eligible. Newly diagnosed is defined as diagnosis established after March 1, 2018 (termed “incident cases”). Patients who were diagnosed earlier are classified as “prevalent cases” (Figure 1B). For the purpose of the study, we use the most recent definitions of PAH and CTEPH as recommended by the European Society of Cardiology (Supplementary material, Methods S2).10

Patient records are submitted by local coordinators to a dedicated internet platform created and managed by the Informatics Centre of the Jagiellonian University Medical College, which ensures system integrity and data protection.

Cohort size and study duration  Enrollment to our study started on March 1, 2018 and is planned to continue at least until February 28, 2023. We plan to collect the follow-up data for a minimum of 5 years from the enrollment of the last patient. As our registry is mostly descriptive, the study size is not prespecified.

Prevalence and incidence  The prevalence of PAH and CTEPH will be calculated separately for adults (≥18 years of age) and children (≥3 months and <18 years of age) as the number of cases per 1,000,000 inhabitants, and the incidence, as the number of new cases of PAH or CTEPH per 1,000,000 inhabitants each year. Data for the number of adults and children living in Poland will be acquired from the publications of Statistics Poland (https://stat.gov.pl)

Baseline assessment  In incident cases, the baseline assessment includes data acquired at the diagnosis of PAH or CTEPH, including the first prescribed treatment (Supplementary material, Table S2). We also collect information about the first symptoms and the time elapsed from the first symptoms to diagnosis. In prevalent cases, the baseline assessment includes data obtained at the most recent visit after March 1, 2018 and also from the most recent right heart catheterization. We also record the date of diagnosis and patient’s functional class at that time. The date of PAH or CTEPH diagnosis is defined as the date of the first right heart catheterization11 fulfilling the hemodynamic criteria for precapillary PH.

Follow-up assessment  Follow-up data (Supplementary material, Table S3) will be recorded in the database every year between September 1 and October 30, starting in 2019. Accordingly, follow-up data will include the most recent information on patients’ status before September 1 each year, including changes in treatment, major clinical events and outcomes, and results of additional tests performed in a patient in the last 12 months.

Treatment  Medical therapy in patients with PAH and CTEPH in Poland is reimbursed by the NFZ in a structured program with specific inclusion and exclusion criteria. This program is subject to change along with new drug approvals.

Discussion  Bias and generalizability of the results  Enrollment of both prevalent and incident patients may bias the outcome analysis as data on patients with prevalent cases who did not survive until the study enrollment will not be
Comparison with other registries on pulmonary hypertension In their recent systematic literature search, Skride et al identified 11 prospective registries performed in patients with PH from Europe. Most of them were national (4 single-center and 6 multicenter registries) and only 1 involved multiple international centers. Three registries involved all groups of patients with PH, while others were limited exclusively to patients with PAH and CTEPH (3 studies), with PAH (2 studies), with IPAH (1 study), or with CTEPH (1 study). Six studies recruited only incident cases while the other 5 registries enrolled patients both with incident and prevalent cases. With 1 exception, the registries were performed in Western European countries, which shows that patients with PH from the Central-Eastern European countries have not been well represented in the literature. In a single-center prospective study, 130 adult patients with PAH and 44 with CTEPH were followed for a median of 33 months to report the survival rates in the Latvian population. Another registry by Jansa et al was a retrospective analysis of 191 prevalent and incident adult patients diagnosed with PAH in 2 specialized centers in Czech Republic. The BNP-PL registry is the first multicenter, nationwide prospective registry compiled in a Central-Eastern European country to assess patients with PAH and CTEPH. The design of the BNP-PL registry has some similarities with the largest ever PAH registry (Registry to Evaluate Early and Long-term PAH Disease Management; REVEAL) which was initiated in the United States in 2006 to prospectively analyze characteristics of patients with PAH in the modern era of novel treatment options. Similarly to the REVEAL registry, our patients are recruited from several pulmonary hypertension reference centers and we include both adults and children as well as patients with prevalent and incident diseases. In contrast to the REVEAL study, and similarly to the large European registries, we have planned a long-term continuous enrollment of incident patients.

Conclusions The BNP-PL registry is designed to show the epidemiology and characteristics of PAH and CTEPH in a large Central-Eastern post-communist European country with a relatively short history of availability of modern PAH diagnostics and therapies.

SUPPLEMENTARY MATERIAL
Supplementary material is available at www.mp.pl/kardiologiapolska.

CORRECTIONS
This article was corrected on December 19, 2019. The list of corrections is available at www.mp.pl/kardiologiapolska.

ARTICLE INFORMATION
CONFLICT OF INTEREST None declared.

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