SHORT COMMUNICATION

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

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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 centers[6-9] 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.

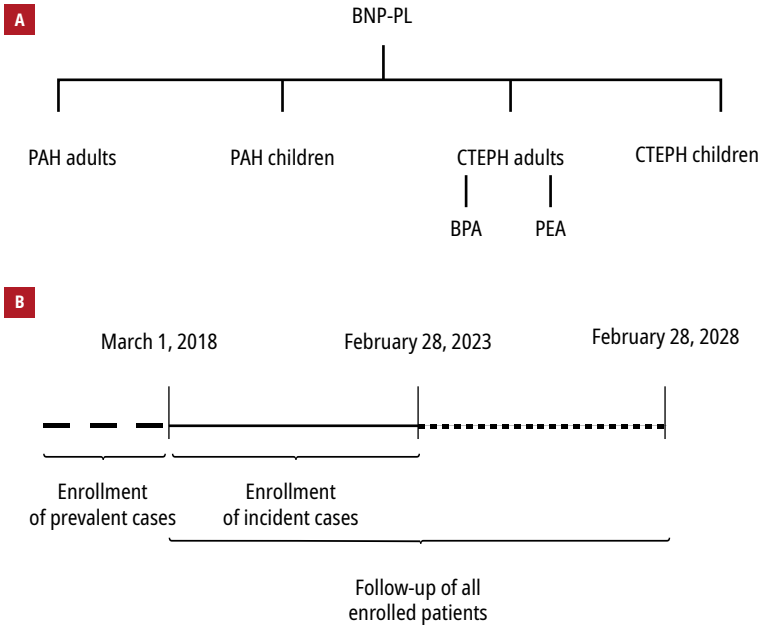

FIGURE 1 Design of the Database of Pulmonary Hypertension in the Polish Population (BNP-PL) registry: **A** – four arms of the BNP-PL registry including adults and children with pulmonary arterial hypertension (PAH) and chronic thromboembolic pulmonary hypertension (CTEPH). Two additional arms of the CTEPH group represent patients treated with balloon pulmonary angioplasty (BPA) and pulmonary endarterectomy (PEA). **B** – time points of enrollment and follow-up of prevalent and incident cases

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 catheterization[11] 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

recorded. Accordingly, we plan to perform separate analysis in prevalent and incident groups. Additional bias may be related to the enrollment of patients participating in clinical trials since they may be receiving better care than others. However, exclusion of these patients would affect the real-life profile of our population.

Due to specific organization of treatment of patients with PAH and CTEPH in Poland in centers accredited by the NFZ, we believe that we will enroll to enroll almost all affected individuals in our analysis. In that way, our results will be representative of the recently diagnosed patients with PAH or CTEPH and of patients who lived with PAH or CTEPH long enough to be represented in the registry. Still, our data will not be generalizable to patients with PAH or CTEPH who have not been yet diagnosed.

Comparison with other registries on pulmonary hypertension In their recent systematic literature search, Skride et al[12] 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).[13] 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 1 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.[8] Another registry by Jansa et al[14] 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.[1] 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,[3-5] 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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