Tracking Outcomes and Practice in Pediatric Pulmonary Hypertension

The First Multinational Registry in Pediatric Pulmonary Hypertension

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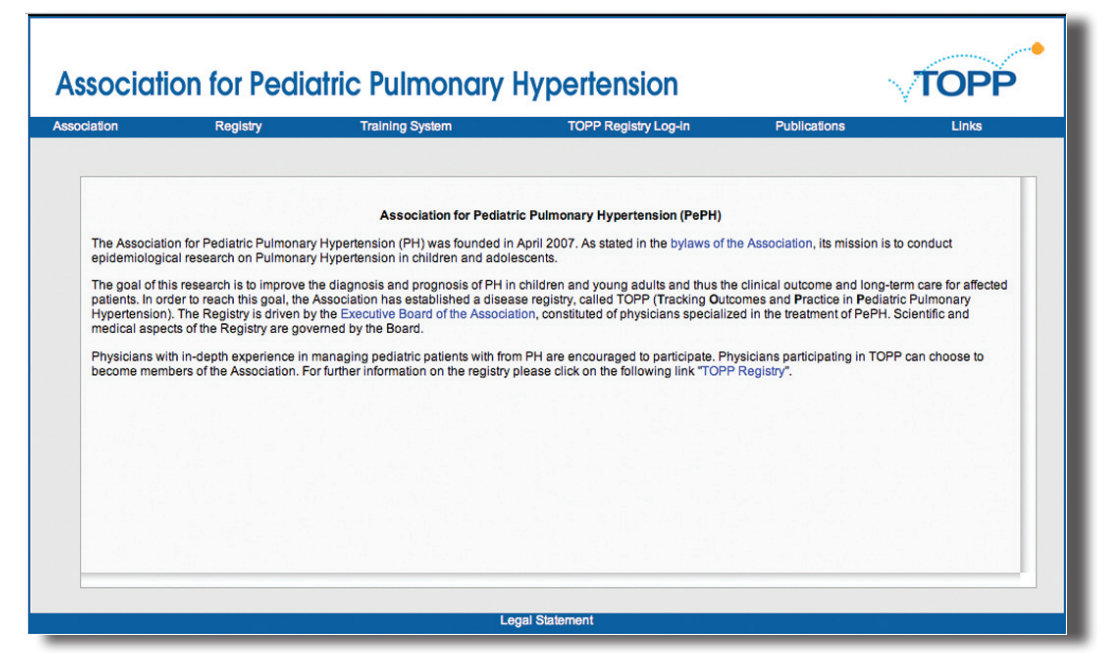
TOPP - Summary

Pulmonary hypertension (PH) reflects high blood pressure in the arteries that supply blood to the lungs, leading to shortness of breath, dizziness, fainting, and other symptoms, all of which are exacerbated by exertion. There have been recent advances in the understanding and treatment of PH in adults, but the disease and its epidemiology remain poorly understood in children and adolescents. To learn more, the Association for PePH has created the TOPP Registry—a research program aimed to gather information about the disease in children/adolescents. It is planned that 400 - 450 patients, aged between 3 months and 18 years at diagnosis, will participate over 3 years. The registry will be carried out at 38 centers in 22 countries across 4 continents. Participation will not affect or impact the standard of care that patients receive. There are no expected medical risks or immediate medical benefits. The registry should contribute to improving the management of the disease and to supporting the development and implementation of diagnosis and treatment guidelines.

Introduction

- There have been recent advances in the understanding and treatment of pulmonary hypertension (PH) in adults
- However, the natural history and epidemiology of PH in children and adolescents remain poorly understood
- TOPP (Tracking Outcomes and Practice in Pediatric PH) is the first international observational registry dedicated specifically to pediatrics to:
  - gain a better understanding of PH in children/adolescents
  - support the development of diagnosis and treatment guidelines
  - improve patient care in the long term
- TOPP was initiated and is managed by the Association for Pediatric Pulmonary Hypertension (www.peph-association.org)
- The PePH Association is a non-profit organization, founded in April 2007 with a key purpose to undertake epidemiological research on PH in children and adolescents
- The Association is headed by an Executive Board of 5 active physicians in the field of pediatric PH and 1 academic epidemiologist
- Membership to the PePH Association is open to physicians and other health care personnel interested in pediatric PH



Association for Pediatric Pulmonary Hypertension (PePH)

The Association for Pediatric Pulmonary Hypertension (PH) was founded in April 2007. As stated in the bylaws of the Association, its mission is to conduct epidemiological research on Pulmonary Hypertension in children and adolescents.

The goal of this research is to improve the diagnosis and prognosis of PH in children and young adults and thus the clinical outcome and long-term care for affected patients. In order to reach this goal, the Association has established a disease registry, called TOPP (Tracking **O**utcomes and **P**ractice in **P**ediatric Pulmonary Hypertension). The Registry is driven by the Executive Board of the Association, constituted of physicians specialized in the treatment of PePH. Scientific and medical aspects of the Registry are governed by the Board.

Physicians with in-depth experience in managing pediatric patients with from PH are encouraged to participate. Physicians participating in TOPP can choose to become members of the Association. For further information on the registry please click on the following link "TOPP Registry".

TOPP Goals

Key objectives of this prospective registry are to describe the:

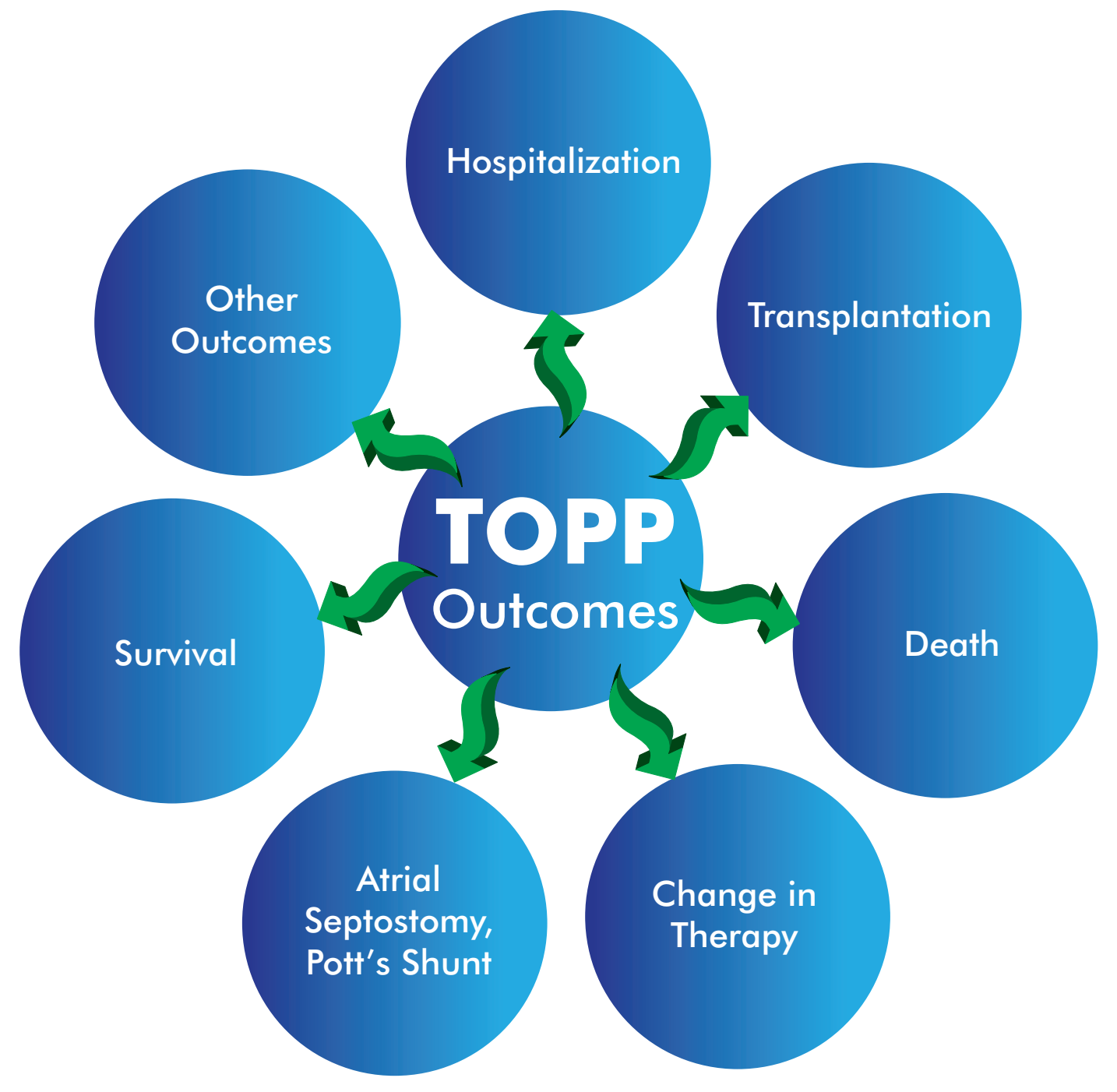
- Demographic and clinical characteristics of PH in children and adolescents
- Current treatment regimens
- Disease management patterns in real-world clinical practice settings

TOPP Detailed Objectives

- Describe the clinical and socio-demographic characteristics of pediatric PH patients at time of diagnosis for incident and prevalent cases
- Describe co-morbidities before and at PH diagnosis
- Describe PH therapies ongoing at time of PH diagnosis and during subsequent follow-up for a minimum of three years
- Describe referral patterns before and at PH diagnosis
- Describe treatment patterns by age, gender, etiology, and other covariates
- Describe the time course of disease progression and differences in outcomes according to risk factors such as associated conditions, disease severity, age at time of diagnosis and available treatment options

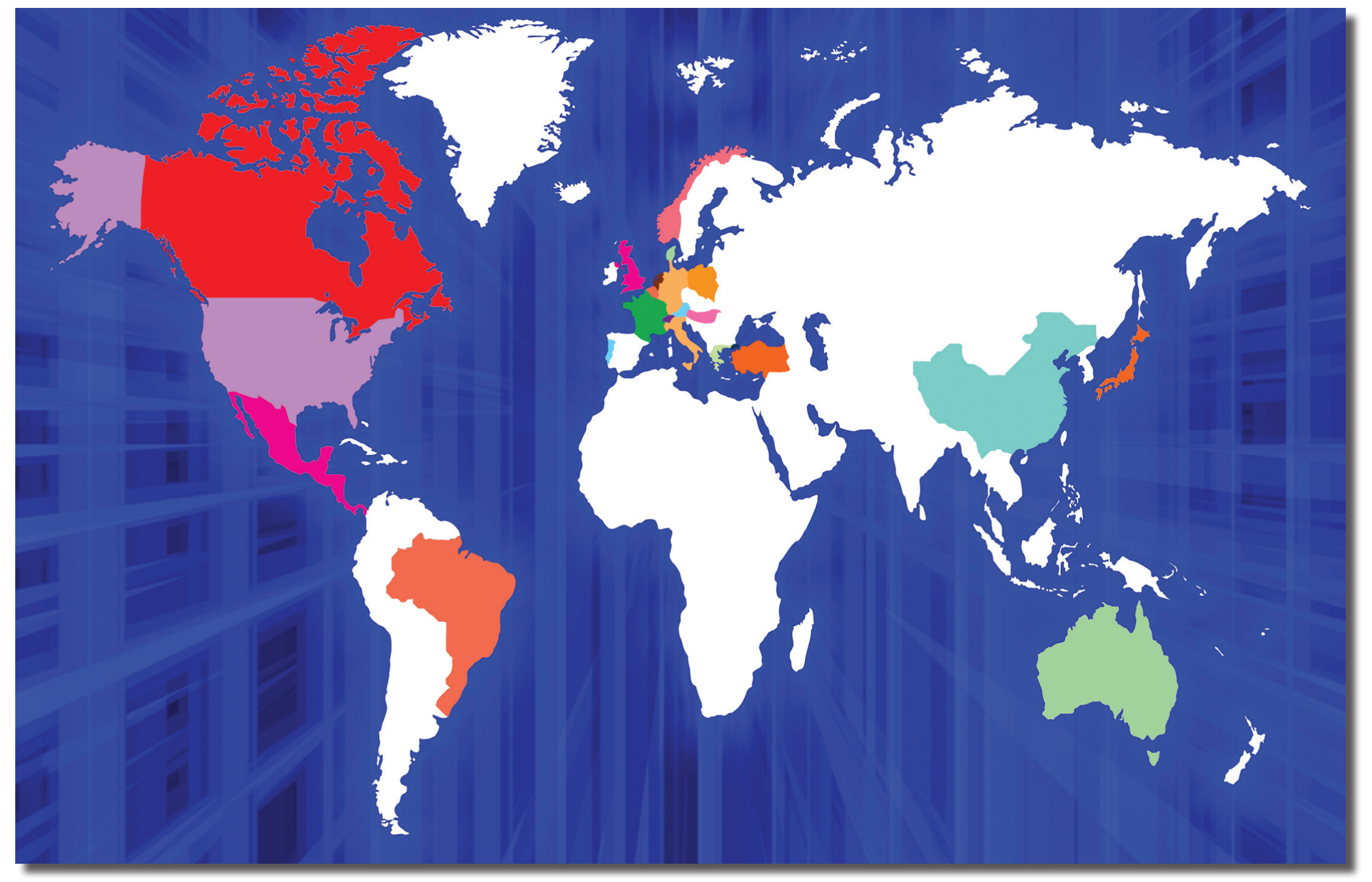
Outcomes

Outcomes, including survival, hospitalization, transplantation, change in therapy and interventions such as atrial septostomy and Pott's Shunt, will be described prospectively and in an observational as opposed to controlled study manner



TOPP Registry Features

- Prospective, clinician-driven, international, multi-center, observational program
- TOPP encompasses 38 specialist PH centers from 22 countries across 4 continents: *Australia, Austria, Belgium, Brazil, Canada, China, Denmark, France, Germany, Greece, Hungary, Italy, Japan, Mexico, Netherlands, Norway, Poland, Portugal, Switzerland, Turkey, UK and USA*



- Inclusion of patient data started in Jan 2008
- TOPP is planned to run for at least three years
- Patients will be treated according to standard local clinical practices
- Frequency of follow-up visits will be determined by the physician and the health care needs of the patient

Inclusion Criteria

- Patients aged between 3 months and 18 years at time of diagnosis
- Diagnosed with PH on or after 01 January 2001
- Presenting with PH categorized into WHO Groups I, III, IV or V
- PH diagnosis must be confirmed by heart catheterization
  - PAP mean ≥ 25 mmHg at rest; or ≥ 30 mmHg upon exercise
  - PVRi ≥ 3 Wood Units*m²
  - PCWP mean ≤ 12 mmHg
- Patients (or their legal guardians) must provide written informed consent

Exclusion Criteria

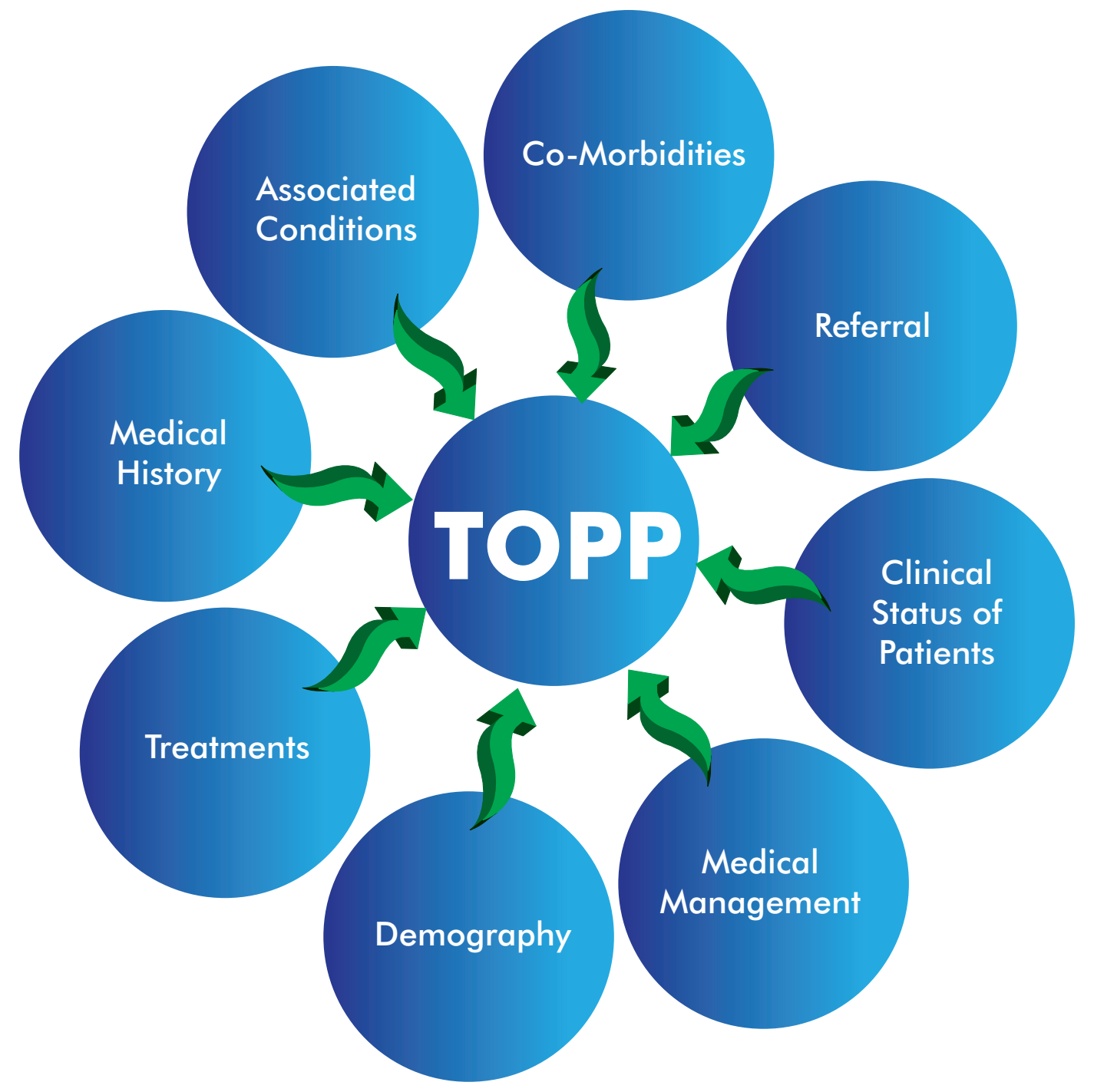
- Patients diagnosed with PH belonging to WHO Group II
- Patients who underwent interventional surgery/procedure for closure or partial closure of systemic-to-pulmonary shunt(s) and/or palliative pulmonary artery banding — unless PH persists beyond a year after the intervention
- Centers will not enrol patients approaching 18 years of age unless they provide care for adult PH

Patient Population

- Target inclusion is 400-450 children and adolescents with PH
- To eliminate selection bias all consecutive eligible patients will be screened and given the opportunity to participate
- Both incident (diagnosed within 3 months of enrollment) and prevalent (diagnosed more than 3 months prior to enrollment) patients will be included
- The Executive Board may request centers to stop inclusion if
  - The proportion of incident to prevalent exceeds two-thirds prevalent
  - More than half the total population have congenital heart disease

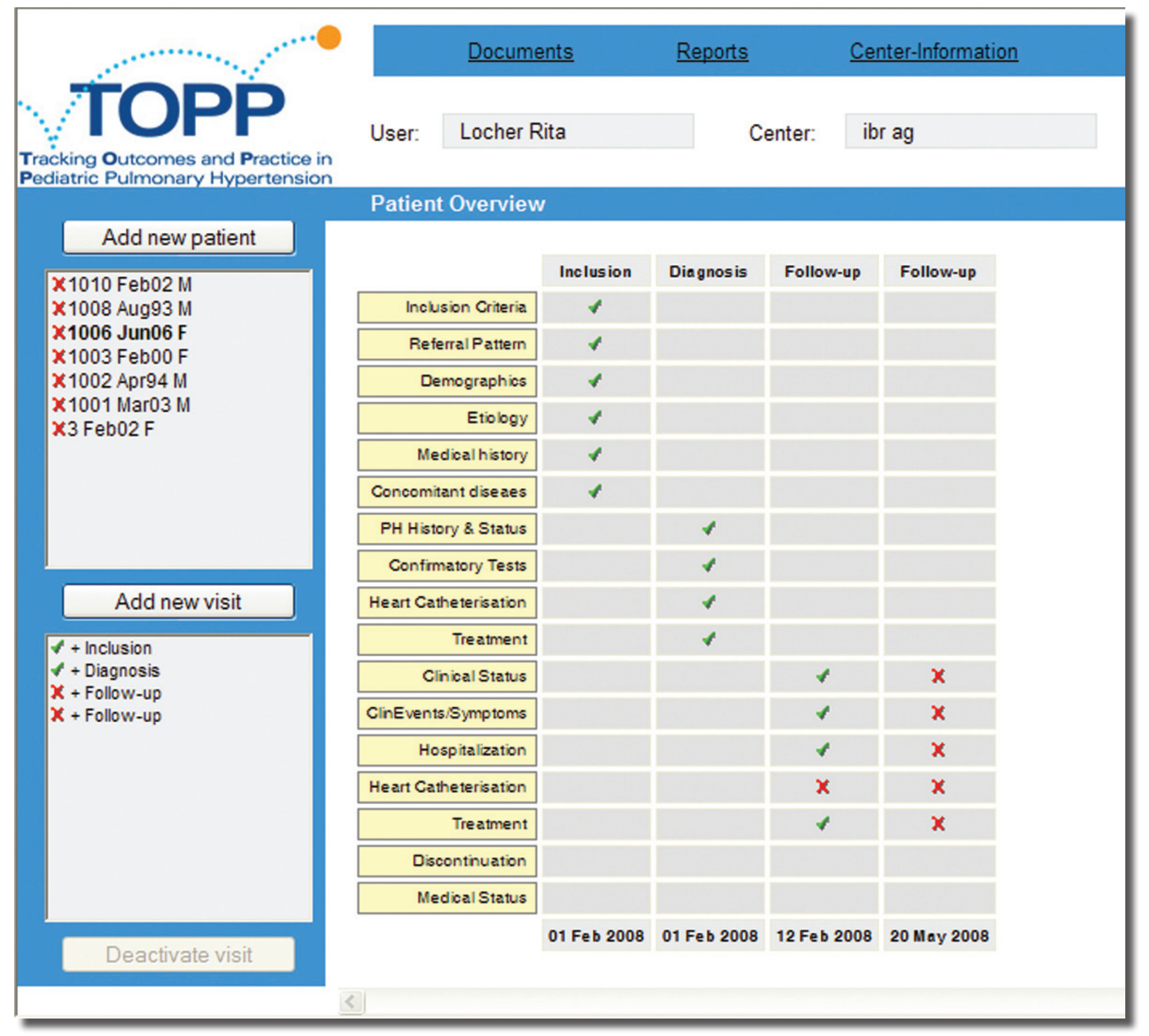
Data Collection

An auditable and secure web-based Electronic Data Capture (EDC) system is used for data collection in the following categories:



- The database is available via the Internet for direct data entry by the participating centers
- Only data collected from assessments that are routinely performed in the real-world clinical setting are reported

Collected Information



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✗1010 Feb02 M
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✗1003 Feb00 F
✗1002 Apr94 M
✗1001 Mar03 M
✗3 Feb02 F

✓ + Inclusion
✓ + Diagnosis
✗ + Follow-up
✗ + Follow-up

	Inclusion	Diagnosis	Follow-up	Follow-up
Inclusion Criteria	✓			
Referral Pattern	✓			
Demographics	✓			
Etiology	✓			
Medical history	✓			
Concomitant diseaes	✓			
PH History & Status		✓		
Confirmatory Tests		✓		
Heart Catheterisation		✓		
Treatment		✓		
Clinical Status			✓	✗
ClinEvents/Symptoms			✓	✗
Hospitalization			✓	✗
Heart Catheterisation			✗	✗
Treatment			✓	✗
Discontinuation				
Medical Status				
	01 Feb 2008	01 Feb 2008	12 Feb 2008	20 May 2008

Statistical Analysis

- Statistical analysis will be exploratory and descriptive
- Periodic reports will be available to participating physicians
- Modelling techniques will explore relationships between potential risk factors and outcomes
- Exploratory analyses will be made between subgroups (e.g., etiologic types)
- Age, gender, time since diagnosis and additional prognostic parameters, as appropriate, will be analyzed as covariates
- Confounding factors associated with bias will be accounted for

Conclusion

The TOPP registry should provide well-defined data on PH in children and adolescents according to real-world experience thereby allowing the opportunity to:

- Address lack of epidemiologic data in pediatric PH
- Better characterize natural history
- Support the elaboration of diagnosis and treatment guidelines
- Improve patient care in the long-term

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