

A GLOBAL REGISTRY OF TREATMENTS AND OUTCOMES FOR MEN WITH SYMPTOMATIC BPH

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Protocol Revision History

Version Number: 0.4

Version Date: 2022-09-15

Summary of Revisions Made:

- Added newly elected Research Council members;
- Added information on participating centres;
- Expanded objectives;
- Expanded Background and Rationale;
- Expanded abbreviations
- Inserted links to supporting documents (Data Access Guidelines, Authorship Guidelines);
- Added Summary;
- Added recruitment chart;
- Added Study Discontinuation section
- Added References.

Version Number: 0.5

Version Date: 2022-09-16

Summary of Revisions Made: Added ClinicalTrials.gov registration number.

Summary

Rationale: There has been a significant expansion in the number of approved medical and surgical interventions with symptomatic BPH. There is a significant research interest in monitoring clinical outcomes including improvements in urinary function, impact on sexual function, postoperative morbidity as well as retreatment. A registry such as what is proposed provides real time data accounting for relevant baseline demographic characteristics in this population of men. The SIU (Société Internationale d'Urologie) is an academic organisation that is uniquely positioned to initiate such a registry because of its global outreach including countries where data are lacking.

Primary Objective: To assess peri-operative and functional outcomes of various medical and surgical interventions for symptomatic BPH in a global population.

Secondary Objective: To assess demographic characteristics of patients undergoing medical or surgical therapy for BPH at a global level.

Study design: A multicentre observational cohort study.

Study population: Male patients, less than or equal to 18 years of age, presenting at their physician's office with LUTS/BPH, who undergo medical/surgical treatment.

Intervention: All patients receive standard care for their symptoms according to their physician's practice.

Main study parameters/endpoints: There is no endpoint for follow-up. After 1 year of data collection, the registry will undergo an independent audit to verify data quality and consistency. After 3 years, a publication based on the results thus far will be submitted to appropriate journals.

Nature and extent of the burden and risks associated with participation, benefit, and group relatedness: The registry is an addition to the standard treatment and does not affect the treatment. Therefore, no negative outcomes or risks are expected.

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1. Governance

1.1. uCARE Governance

Laurence Klotz, MD, FRCS
Chair, Office of Research

Mihir Desai, MD, MPH
Office of Research-Elect

Ranan Dasgupta, MA MD FRCS(Urol)
Research Committee

1.2. Research Council

Sociedad Chilena de Urología (SCHU)
Dr. José Antonio Inzunza Navarro

Jamaica Urological Society (JUS)
Dr. Belinda Morrison

Colegio Mexicano de Urología (CMU)
Dr. Jorge Moreno-Palacios

Sociedad Mexicana de Urología (SMU)
Dr. Jose Gadu Campos Salcedo

Kenya Association of Urological Surgeons (KAUS)
Dr. Pius Musau

Hong Kong Urological Association (HKUA)
Dr. Peter Ka Fung Chiu

Indonesian Urological Association (IUA)
Dr. Lukman Hakim

Korean Urological Association (KUA)
Dr. Sang Don Lee

Malaysian Urological Association (MUA)
Prof. Shanggar Kuppusamy

Taiwanese Urological Association (TUA)
Dr. Chung-Hsin Chen

Pakistan Association of Urological Surgeons (PAUS)
Dr. Muhammad Shahzad

Georgia Urological Association (GUA)
Dr. Archil Boris Chkhotua

Associação Portuguesa de Urologia (APU)
Prof. Belmiro Parada

Iranian Urological Association (IUA)
Dr. Erfan Amini

Saudi Urological Association (SUA)

Dr. Basim Alsaywid

Urological Association of Australia and New Zealand (USANZ)

Dr. Ian Vela

Chinese Urological Association (CUA)

TBD

Turkish Urological Association (TUA)

TBD

South Africa Urological Association (SAUA)

TBD

1.3. Steering Committee

Pending Research Council finalization

1.4. Pilot Team Roster

Dr. Mauro Gacci

AOU Careggi

Prof. Bülent Erkurt

Istanbul Medipol University

Dr. Dean Elterman

University of Toronto Health Network

Dr. Reynaldo Gomez

Hospital del Trabajador

Prof. Stavros Gravas

University of Cyprus

Dr. Mélanie Aubé-Peterkin

McGill University Health Centre

Dr. Ranan Dasgupta

Imperial College NHS Trust

1.5. Participating Study Centres

Canada

University of Toronto Health Network

McGill University Health Centre

Chile

Hospital del Trabajador

Cyprus

University of Cyprus

Italy

University of Florence

Turkey

Istanbul Medipol University

United Kingdom

Imperial College Healthcare NHS Trust

United States

University of Southern California

2. Background and Rationale

Due to a growing and ageing population, cases of benign prostatic hyperplasia (BPH) have been on a steady rise. Studies show that by age 80, 90% of men experience BPH.[1] Thus, treatment of BPH is one of the most performed surgical procedures in urology. Over the past few decades there has been an increasing development of newer surgical treatment options. Additionally, the outcome parameters for BPH treatments have been standardized. The purpose of this study is to create an ongoing prospective registry to record demographic data and clinical outcomes after medical therapy or different surgical interventions for BPH. The specific aims of the registry are to analyse demographic patterns and baseline characteristics of men undergoing surgical and medical treatments for BPH, to assess global practice patterns for various surgical and medical treatments of BPH, and to assess key outcomes for uni- and multi-modal treatments of BPH.

The ongoing global registry will provide important baseline data, functional outcomes, and complications following medical and/or surgical intervention for men with symptomatic BPH. The intention of the registry is to provide real world usage data that may be used for future investigations. It will allow providers to identify areas of interest, areas of unusually low usage or areas of unusual preference on a global scale. It will also shed light on global preferences for unimodal or multimodal approaches to treatments.

3. Study Objectives

The purpose of this study is to develop a global, multi-centre BPH registry tracking baseline data with follow-up data for at least 3 years, and thereby analyse demographic patterns, comorbidities, exacerbation, severity, and intervention selection for patients undergoing surgical treatments for BPH, to assess practice patterns (region-specific) for various surgical treatments for BPH, and to assess key outcomes (efficacy and safety) for surgical treatments of BPH. The ongoing global registry will provide important baseline data, functional outcomes and complications following medical and/or surgical intervention for men with symptomatic BPH. It aims to facilitate the identification of areas of interest for underrepresented regions and guide the implementation of regionally specific and relevant RCTs.

3.1. Primary Outcome Measures

Comparing mean score of the following measures at baseline through follow-up:

Efficacy measures

- IPSS
- QoL

Safety measures

- PVR
- Complications

3.2. Secondary Outcome Measures

Efficacy measures

- Prostate volume (cc)
- Qmax

Sexual function measures

- SHIM
- MSHQ-EjD

4. Study Design

This is a prospective longitudinal ongoing registry. The study will include medical records of all men ≥ 18 years old who have a primary diagnosis of BPH with Lower Urinary Tract Symptoms (LUTS) that are prescribed BPH medications, or a surgical intervention. Data extraction includes baseline, peri-operative, and follow-up data. Baseline data includes validated patient reported outcome tools, including International Prostate Symptom Score (IPSS), Sexual Health Inventory for Men (SHIM), Male Sexual Health Questionnaire - Ejaculatory Dysfunction (MSHQ-EjD), as well as Quality of Life (QoL), maximum flow rate (Qmax), Post-void residual (PVR), Prostate Specific Antigen (PSA), and Testosterone. Complications such as Bleeding, Urinary Tract Infection (UTI), Incontinence, Stricture, Retrograde ejaculation, and Erectile Dysfunction (ED) are also tracked from Baseline through Follow-up.

The registry has been developed using novel database technology, providing an easy-to-use user interface that enables future creation of patient portals and EMR integration.

The registry will run for 3 years with no end point for follow-up. For three years, various research studies will be formulated, and the results will be published. The possibility of extending the study for continued follow-up will be evaluated.

5. Selection and Enrollment of Participants

5.1. Clinical Recruitment

The registry will run for a period of 3 months starting from May 2022 as a pilot study. After 3 months, we will evaluate outcomes, adapt the protocol if needed. Registry enrollment will be

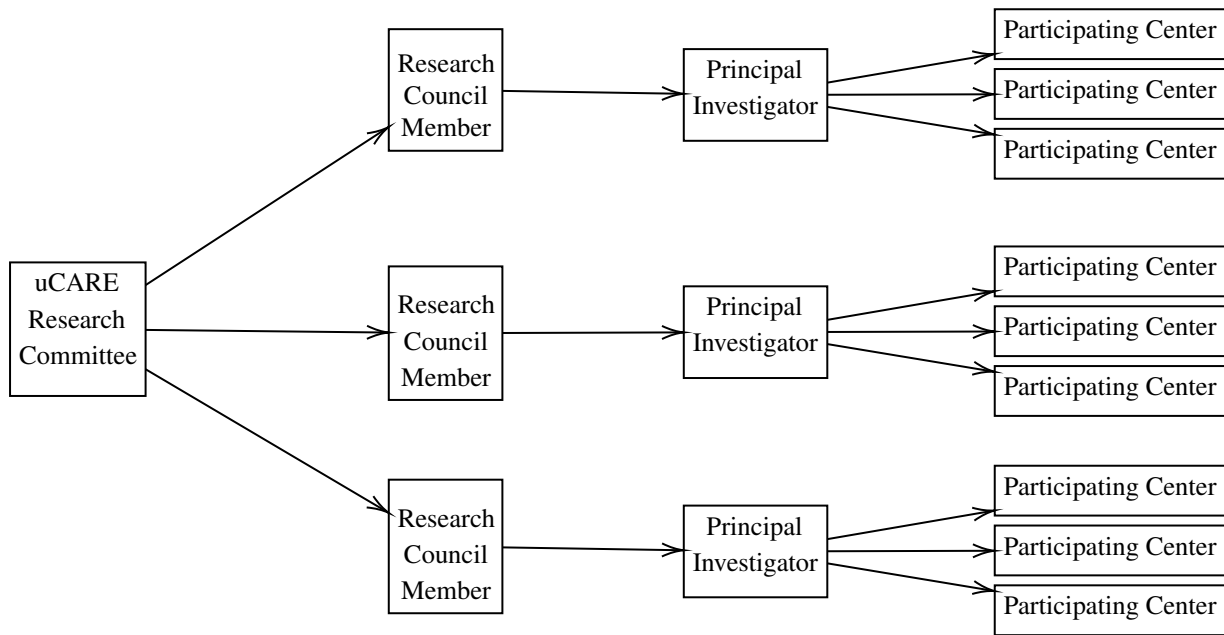


Figure 1: Research Council recruitment structure.

offered to all members of the Société Internationale d’Urologie (SIU), including the robust network of international uCARE member countries. The registry will also be opened to non-SIU members.

Sites for this pilot study are primarily recruited by the uCARE Research Council Members and must be approved for participation by the Research Council. Each Council Member will approach three high-volume national centres and will appoint one Principal Investigator (PI) who will be part of the Steering Committee of this study (Figure 1).

The PI is responsible for contacting the clinicians at the individual sites recruited for the registry and is responsible for the national data collection. It is the responsibility of each participating centre to obtain ethical approval, as needed, according to local regulations.

Each participating centre will include all consecutive eligible patients during the study period beginning from August 2022. Treatment procedures are performed according to local protocols.

The Steering Committee of this study will coordinate data analysis.

5.2. Study Population

Records and cases of all men ≥ 18 with a primary diagnosis of BPH with LUTS that are prescribed BPH medications, or a surgical intervention will be identified and included in the registry.

5.3. Inclusion Criteria

- A clinical history consistent with Benign Prostatic Hyperplasia
- Prescribed medication or surgical intervention for BPH

5.4. Exclusion Criteria

- Patients <18 years old
- Patients with no planned intervention

6. DATA COLLECTION, HANDLING AND STORAGE

In this study, we have multiple timepoints for data collection.

1. The first moment of data collection (**T1**) starts on the day of surgery/intervention. Baseline characteristics, peri-, intra-, and post-operative data are entered then.
2. The next collection moment (**T2**) is at the first follow-up appointment with the patient, within 3 months of the initial intervention.
3. Data collection will occur at each follow-up (**T3+**). There is no end point for follow-up.

Data will be collected in a central electronic data management system, which is selected and developed by Hefficient Analytics, under the supervision of uCARE. A data manager from SIU will coordinate the electronic data collection and will regularly provide feedback to the individual study sites and to the Research Council.

6.1. Data Collection Schedule

	Time	Data collection
T1	Before intervention	Baseline characteristics
T2	Immediately after intervention	Intraoperative information
T3+	Outpatient Clinic/Self-report	Postoperative information
END		

6.2. Handling and Storage of Data

All data is hashed (i.e., protected from decryption) except for a medical record number (MRN), which will be used to add follow-up data to the patient's record. This number is encrypted and linked to the hashed and randomly generated institution code. For security purposes, biographical information is not saved on the registry.

The registry provides secure access to registered users using a web browser. Registrations are site-specific, which means that users can only access the data that is specific to their own site. The registry application and databases are hosted on secure, encrypted servers behind a firewall. They can only be accessed by registered users via a specific port.

No encryption keys or any other mechanism for identifying the data will be retained at the end of the study. uCARE and the SIU will retain ownership of the registry data. The uCARE Research Council will be responsible for monitoring registry accrual. The principal investigators along with the uCARE council will entertain study proposals related to the registry.

Private, non-publishable data will be provided to industry registry sponsors for internal quality control. This will include overall practice patterns and demographics as well as outcome

data related to their specific technology only. The research sponsor will have an input on the procedure specific PI nomination.

6.2.1 Database Management System

uCARE has chosen Hefficient Analytics to develop the data management software. The registry software provides secure access to registered users using a web browser. Users are registered for use and set up with username and password authentication. User registrations are site-specific, meaning that users can only access data from their site. Any biographical data is stored using HIPAA-approved mechanisms for encryption.

6.2.2 Data transfer and storage

Biographical data is stored in a physically separate database from the registry database. That database holds site and patient biographical information only. The registry database holds an internal site code and the encrypted MRN of the patient.

The registry application and databases are hosted in AWS on servers running Ubuntu Linux LTS. The application sits behind an AWS WAF and a Reverse Proxy using NGINX. Registry database servers are protected by a firewall and made accessible only to the Registry application servers on a specific port. All other routes and ports are blocked by the firewall. All databases are held on encrypted disks.

6.2.3 Data audit

A built-in quality control using data validation during the input process decreases the chance that invalid data will be entered or that datapoints will be omitted. Periodic audits will be performed to verify accuracy of source data by our audit committee based on our audit committee guidelines.

uCARE is in the process of putting together an Audit committee, which will be independent from the study to ensure the accuracy and quality of the data collected.

6.2.4 Data access

See Data Storage, Access, Ownership and Transfer Guidelines

7. INVESTIGATOR RESPONSIBILITY

Except where the Principal Investigator's signature is specifically required, it is understood that the term 'Investigator,' as used in this Protocol and on the CRFs, refers to the Principal Investigator or an appropriately qualified member of the staff that the Principal Investigator designates to perform specified duties of the Protocol. The Principal Investigator is responsible for the conduct of all aspects of the study.

Each Investigator will comply with the local regulations regarding clinical trials, the clinical research standards of uCARE, and the Investigator responsibilities outlined in the ICH GCP guidelines.

It is the responsibility of the Investigator to report study progress to the Reviewing Ethics Committee or Governance Office as required or at intervals not greater than one year.

The Principal Investigator, or his/her nominee, will be responsible for reporting any serious adverse events to the Reviewing Ethics Committee and Site Governance Office as soon as possible, and in accordance with uCARE guidelines.

8. ETHICS

8.1. Institutional Review Board (IRB) Review

It is the responsibility of each participating centre to obtain ethical approval, as needed, according to local regulations.

8.2. Informed Consent

We will be retrospectively reviewing and collecting data that exist in patient's medical records. We will not be contacting participants or including any sensitive data included in the HIPAA section (i.e., HIV/AIDS status, mental health, and alcohol/drug abuse records). A full waiver of informed consent is requested in the IRB submission form.

8.3. Participant Confidentiality

The study will access limited PHI (Protected Health Information) (MRN without identifier for the clinical site), which will undergo HIPAA-approved methods for maintaining data security. Full waiver of HIPAA authorisation is being requested in the IRB submission form.

8.4. Study Discontinuation

When deemed necessary, the study may be discontinued at any time to ensure the research participants are protected. In case the study was ended prematurely, the coordinating investigator will notify the individual centres, including the reason(s) for the premature termination.

9. PUBLICATION OF RESEARCH FINDINGS

See Authorship Guidelines

References

- [1] WM Garraway, RJ Lee, and GN Collins. High prevalence of benign prostatic hypertrophy in the community. *The Lancet*, 338(8765):469–471, 1991.