The Peritoneal Dialysis Outcomes and Practice Patterns Study (PDOPPS)

Country Participation: An Overview for Interested Investigators

1 Introduction

The Peritoneal Dialysis Outcomes and Practice Patterns Study (PDOPPS) is designed to advance the understanding of optimal practices for PD patients worldwide and to reduce barriers to PD use. Our hope is that the study will increase the appropriate use of PD, extend technique survival, and improve quality of life for PD patients. With PDOPPS, we intend to provide a much-needed infrastructure and forum to promote effective collaborative international clinical research in peritoneal dialysis as a vital means to strengthen the evidence base supporting PD treatment decisions and the use of this therapy.

The overarching study aim is to understand the impact of modifiable practices in the management of PD patients on the risk of all-cause peritoneal dialysis technique failure. Secondary aims are to assess the impact of these practices on all-cause mortality, cause-specific PD technique failure, PD-related complications, and patient-reported outcomes. Detailed hypotheses and research questions focusing on key PD-related practices have been elaborated. For each aim, we will describe the extent of variation in each PD practice and study this variation to identify practices associated with best clinical outcomes; we will publish and disseminate findings as a meaningful means to improve overall PD care and outcomes.

Arbor Research Collaborative for Health in Ann Arbor, Michigan, USA serves as the PDOPPS Data Coordinating Center (DCC). We emphasize the fully collaborative nature of this study, with development of scientific goals and study oversight provided in a partnership between Arbor Research and the International Society of Peritoneal Dialysis (ISPD), and relying on the diversity of clinical experience and investigator expertise gained from an integrated international study. Funding for PDOPPS is provided by a consortium of sponsors without restrictions on publications.

Arbor Research is responsible for securing core DCC funding, but cannot raise funds to cover costs related to data collection for most interested countries. The clearest pathway to having the opportunity to participate in PDOPPS is to raise funds locally for these within-country costs. To this end, this document provides interested investigators a summary of study design and procedures (i.e., what the study would look like in your country), study oversight at the country and international level, and opportunities for research collaboration. To secure local funding, we recognize the need for interested investigators to identify how PDOPPS will fill unmet needs, and we provide some examples. Lastly, the document provides the estimated level of effort required for within-country study operations so that interested investigators can calculate a budget.
2 Study Design and Procedures

PDOPPS is a prospective cohort study. Study design and procedures draw extensively from DOPPS, our longstanding international study of hemodialysis patients and practices.

Timeline: 3 years of study data collection are proposed. Initial countries will begin data collection in 2013. For other countries, entry in 2013 is preferred; start dates that are somewhat later will be considered.

Facility Selection: In each country, facilities will be offered participation based on stratified random sampling from the country’s census of dialysis facilities with at least 15 PD patients. This approach ensures that the study includes a nationally representative sample of dialysis facilities in each country. The recruitment goal is 20 facilities per country in most countries (goal may be lower in small countries, or higher depending on a specific country’s objectives). PDOPPS investigators will work with country leaders to identify the most relevant sampling strata, such as private versus university, central versus satellite, and large versus smaller centers.

Patient Selection: A census of all PD patients in each facility will be established. From this census, a random sample of 15-40 patients aged ≥ 18 years and able to provide informed consent will be offered study participation. The patient sample will be replenished three times per year. Over-sampling of incident dialysis patients will occur, providing capacity to study care for representative samples of incident and prevalent PD patients.

Study Data: PDOPPS will apply a common protocol and standardized questionnaires to capture detailed longitudinal data in all participating countries. Data collection instruments will include limited census data for all PD patients at the facility, detailed clinical data and patient questionnaires for enrolled patients, and facility-level questionnaires. Follow-up clinical and outcomes data will be collected thrice yearly. Numerous data will be specific to PD.

Mechanisms of Data Collection: Data collection can be implemented using three methods: the DOPPSLink web-based data collection system, electronic extraction (for facilities with standardized information management systems), or paper forms. The specific method of data collection is tailored for each study facility, thereby maximizing accuracy, efficiency, and ease of use. Paper forms are now discouraged in favor of the DOPPSLink web-based system, which as of late 2012, has been implemented in nearly 20 countries.

Coordination of Study Activities: Most often, a study coordinator at each participating dialysis facility collects study data. Other models, such as study coordinators who travel between participating facilities, can be considered. A lead study coordinator, or “CRA,” in each country oversees study activities and site performance, and liaises with the Arbor Research DCC.

3 Study Oversight and Guidance

Within Participating Countries:

Country Investigators: Country-level activities are led by a team of two or more ‘country investigators.’ These are nephrologists who typically also have leadership roles in the local academic community, dialysis registry,
nephrology societies, and/or policy bodies. Some benefits of joining PDOPPS as a country investigator are provided herein.

**Site Investigators:** These are the medical directors at the randomly selected dialysis units that agree to participate in the study. Site investigators oversee site performance but do not have broader study responsibilities. Because a random selection of dialysis facilities participate in the study, country investigators are usually not site investigators (i.e., a country investigator’s own dialysis unit only participates in the study if randomly selected).

**For the International Study:**

This section provides an overview of the core study’s decision-making and advisory bodies, as well as leadership and scholarly opportunities for interested country investigators.

**PDOPPS Steering Committee (PDSC):** The PDSC provides guidance and authority related to the strategic direction of the PDOPPS program to ensure that the program is aligned with the mission and goals of the study and serves the needs of the PD community at-large. Policies related to ancillary studies, data release, and publications are also under Steering Committee purview. Members include DCC (Arbor Research) investigators, ISPD representatives, major study sponsors, and others as they may arise.

The PDSC reviews and approves country-level participation in the study by evaluating adequacy of funding support, operational feasibility, and alignment with overall study goals. The PDSC also ensures that a fair approach is taken toward country investigators’ access to study resources (input into research directions, data access, authorship, etc.), namely that access and resources are suitable and commensurate with funding level and overall study contributions.

**ISPD-PDOPPS Workgroups:** In collaboration with the ISPD, the PDSC has established six research workgroups:

1. Clinical application of PD therapy (includes patient selection for and access to PD therapy)
2. PD catheter access and function
3. Patient training and education
4. Dialysis prescription and fluid management
5. Infection prevention and management
6. Patient support

These workgroup domains reflect key areas of PD clinical practice guidelines and variation in PD practice. In the study planning phase, the workgroup goals are to identify the most important research questions and hypotheses, as well as to assist in instrument development to ensure that key research questions are addressed. Once data collection is underway, workgroups will help guide analytic priorities and will be offered leadership roles in scholarly activities, manuscript development, and outreach.

Though workgroups and initial membership were established in 2012, we expect to be able to offer membership to an equitable number of investigators (one or more) from countries that join the study in the future.
4 Benefits of Country Participation
In addition to the broader value of contributing to the international study, participation in PDOPPS is expected to yield direct benefits to participating countries. Because the most salient benefits may vary, we ask interested investigators to determine the value proposition most suited to your country. Based on experience with the DOPPS, examples of benefits to individual countries include:

- A national sample of PD facilities, typically 20 per country, enables regional and national comparisons to understand variation in PD practice and outcomes, trends over time, and international comparisons for benchmarking purposes.
- Because modifiable PD practices that extend time on therapy and survival will be highlighted, unwarranted practice variation identified in PDOPPS can directly inform local practice guidelines or quality improvement initiatives.
- Research hypotheses from country investigators are encouraged, so that questions directly relevant to each country can be evaluated. As a large international study, PDOPPS provides an avenue to study questions that could not otherwise be realistically addressed.
- PDOPPS data can inform policy decisions or evaluate the effect of policy on patient care and outcomes. Numerous examples from DOPPS can be provided.
- Due to the scope and depth of data collection, PDOPPS provides a data source that complements national registry data. The registry provides limited information on all PD patients, while PDOPPS provides much more detailed information on a national sample.
- PDOPPS data can be used to evaluate the reliability of national registry data.
- PDOPPS provides an infrastructure for additional investigator-initiated studies, such as PDOPPS ancillary research projects or future clinical or pragmatic trials.
- Patient-reported outcomes, including but extending well beyond quality-of-life, are an important study focus that some investigators may find particularly salient to country-level needs.

5 Access to Data
All data collected for PDOPPS will be de-identified and housed centrally at the Arbor Research DCC. When country-level support for PDOPPS is secured locally, country investigators will be granted ongoing and unrestricted access to the data collected from their own country. In these cases, analyses can be carried out within the country if desired. Depending on the level of funding, agreements can also be developed for country-specific analyses to be carried out at the Arbor Research DCC.

Use of expanded data involving multiple countries is encouraged but requires PDSC approval as per the study’s data release policy. Arbor Research has a longstanding record of releasing our international study data to qualified external collaborators and working closely with them to develop high-impact publications, as well as supporting proposals for ancillary funding for these research activities.

6 Funding Needs
Study costs are divided into within-country costs and DCC costs, as described here.
Within-Country Costs: Over half the study expenses derive from local costs related to data collection activities and logistical assistance, monitoring protocol adherence, and facilitating efficient operations. Our ability to offer market-value financial compensation for study participation is integral to ensuring high-quality data collection among a representative selection of dialysis facilities. Country-level expenses include costs for:

- Data collection at the participating dialysis facilities totaling approximately 200 hours, or 10% full-time equivalents (FTE) per year at each study site, or 4,000 total hours (2 FTE, i.e., two full-time staff) per year for a country with 20 participating sites.
- Logistical support of a research coordinator, or “CRA,” to facilitate local study activities and liaise with the Arbor Research DCC: 400-500 hours, or 20-25% FTE, per year, overseeing 20 study sites.

In the United States, we estimate the average annual data collection cost to be $10,000-$11,000 USD per study site (approximately $210,000 USD for a country having 20 study sites) and approximately $40,000-$45,000 USD in CRA costs. These costs total ~$250,000 annually and are spent wholly within the country.

Based on many years of experience with the DOPPS programs, the level of required effort is very consistent across participating countries. We recognize that market-value financial compensation for this level of effort will vary by country, and we ask interested investigators to determine the funding amount required to meet these resource needs.

Models for study participation that include more limited data collection have been considered for some countries, but are not yet operational. Thus far, we have determined this to be a suboptimal approach.

DCC Costs: In addition to within-country costs, PDOPPS requires funding support for an anticipated 6-8 FTEs of DCC staff at Arbor Research during each study year, totaling (over the study’s duration) about 30 FTE investigators, biostatisticians, health information technology specialists, and program management staff. Additional resources are required for other infrastructure costs, study visibility, and dissemination of results in leading journals and at major nephrology meetings internationally.

Suggested Approach for Interested Country Investigators: Arbor Research cannot raise funds for ‘within-country costs’ for most interested countries. Therefore, raising funds locally is the clearest pathway to have the opportunity to participate in PDOPPS. We present a two-tiered approach to local fund-raising for joining the study:

- Partial Funding – Funds raised by a country cover the local, within-country costs of the study. The country’s proportional share of the global DCC cost is paid from worldwide PDOPPS funding. Participation in PDOPPS is considered likely but not assured; the decision to include the country in PDOPPS requires adequate core (DCC) funding and PDSC approval.
- Full Funding – Funding is raised to cover local costs plus the country’s proportional share of the global DCC cost. Countries with this funding level will have guaranteed study participation. At a certain funding level, PDSC membership will be offered to a country investigator, and the DCC can prepare analyses and manuscripts of particular interest to the country. This option is typically exercised with an increased study size (number of facilities) and/or research scope.
7 Summary

PDOPPS is becoming a highly visible resource to the PD community, providing a much-needed infrastructure and forum to promote effective international collaborative clinical research. The extensive detail and breadth of data will serve as an extremely valuable source of PD practice and outcomes data in participating countries, and country investigators will have many opportunities for research and collaboration. Based on the recent successful launch of DOPPS programs in a range of countries worldwide, the introduction of PDOPPS will generate great enthusiasm and focus efforts to understand and improve dialysis care in each country joining the study.

The clearest path to PDOPPS participation is to raise funds locally to cover within-country costs. Interested investigators are asked to determine the most important benefits of study participation, the funding amount required to meet the resource needs specified above, and the best sources to approach for funding support. We strongly encourage interested investigators to consider seeking funding from a diversity of public (e.g., health authorities, research funding agencies) and/or private (e.g., commercial industry) entities. **We ask that investigators not rely solely on approaching current sponsors of the international study, as this is not a means to generate new study funding.** Expanding the diversity of funding sources to include local public or private entities not only adds to total study support, but is also preferred because it helps to enrich the study’s scope, scientific goals, and ultimate impact on PD care.

Arbor Research and the PDOPPS leadership at ISPD hope to be as helpful and transparent as possible as you consider ways to secure funding, implement PDOPPS, and realize the benefits of your country’s participation. We encourage you to contact us and are happy to provide additional support such as central study materials (core protocol, questionnaires, etc.) that may markedly facilitate your funding submissions.

For additional information, please contact dopps@arborresearch.org.