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IMPROVE-PD Finder: A Web-Based Platform to Search and Share Peritoneal Dialysis Biobank, Registry, and Clinical Trial Metadata

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Received 23 September 2022; revised 12 December 2022; accepted 2 January 2023

Kidney Int Rep (2023) ■, ■–■; https://doi.org/10.1016/j.ekir.2023.01.003
KEYWORDS: cardiovascular disease; hemodialysis; inflammation; peritoneal dialysis; peritoneal membrane

INTRODUCTION

Peritoneal dialysis (PD) is a life-sustaining kidney replacement therapy for the increasing number of people with permanent kidney failure across all age groups worldwide. Although PD potentially offers socioeconomic and performance benefits over hemodialysis, both treatments severely accelerate complications of chronic kidney disease, in particular atherosclerotic disease progression that worsens outcomes when compared with non-dialysis patients.[1] Improved understanding of the underlying molecular pathogenic mechanisms should help in the design of interventions that improve outcomes.[2] Current state of the art in PD research, however, faces major limitations. Although there are numerous *in vitro* and *ex vivo* studies on complex cellular and molecular networks active in PD[3–5] and *in vivo* animal models of PD[6–8] that provide in-depth pathomechanistic insights and allow identification of promising therapeutic targets,[9,S1,S2] translation into clinical studies is a major challenge.[S3] Patient studies that aim to substantiate experimental findings with definitive clinical outcome data are mostly small. As a result, they have not provided sufficient power to derive meaningful or clinically implementable conclusions.[2] Basic PD technique has hardly changed over decades, despite high PD-related complication rates. Randomized prospective trials with hard clinical end points studied with adequate power are difficult to realize in a multifactorial setting with low patient numbers (360,000 worldwide) and are associated with high costs. To overcome these barriers intermediate end points such as PD effluent biomarkers associated (but not necessarily causally related) with hard clinical end points and composite end points are often studied.[S4,S5] Equally, combining analyses of existing cohort studies and trial data through collaborative sharing might be of considerable benefit.

IMPROVE-PD FINDER: A UNIFIED PLATFORM FOR PD BIOBANK, REGISTRY, AND CLINICAL TRIAL METADATA

The IMPROVE-PD (Identification and Management of Patients at Risk – Outcome and Vascular Events in Peritoneal Dialysis) Consortium (http://improvepd.eu/) is a pan-European PhD-level training program fostering collaboration between leading academic and industrial sectors and also working in partnership with patients and public. To optimize the use of accumulated scientific evidence and to study the specific factors determining PD patient outcomes, the consortium has established an online platform of PD registries, clinical studies/trials, and biorepositories, named the IMPROVE-PD Finder (https://www.improvepdfinder.eu/ [Access to the platform is open

to the public with the following login credentials: User: viewer and Password: viewer127894]). This tool empowers PD researchers to find and share aggregated data and metadata from participating databases. Thanks to its simple interface and intuitive search engine, the platform allows users to quickly find and share information on the availability and description of content in each biobank, registry, and clinical study/trial.

A key feature is the systematic and standardized collection of information from various sources (websites, system specifications, study protocols, etc.) into 4 sections. The Catalogue section contains all included studies with metadata on common collected data descriptors and aggregated data. The remaining 3 sections (Biobanks, Registries, and Clinical trials and studies) group information according to study type to allow for detailed presentation and searchability.

The Biobanks section is the first attempt to create a centralized directory for PD biorepositories worldwide. Currently, descriptions of individual biobanks are sparse, thus limiting the opportunity to understand if such biobanks hold viable biological samples for further research. To fill this gap, the Biobanks section contains detailed metadata on material type of each biorepository, including human and animal body fluids, tissues, cells, and nucleic acids. Information on the percentage of samples available is also collected, in addition to the type of analysis performed (e.g., omics, markers of inflammation and fibrosis, reactive metabolites). This approach will help overcome the underuse of biorepositories, a commonly observed and criticized phenomenon.[S5,S6]

The IMPROVE-PD Finder further aims to remove the barriers in finding and sharing registry data in PD. Limited attempts have been made to integrate national registry data from countries worldwide with large collaborative international registries.[S7] The Registry section of this platform seamlessly combines national and international registries, providing metadata on demography, dialysis adequacy, membrane function and outcomes, PD-related complications, mineral metabolism, and nutrition. Key aggregated data on number of patients, participating countries, and centers is made available.

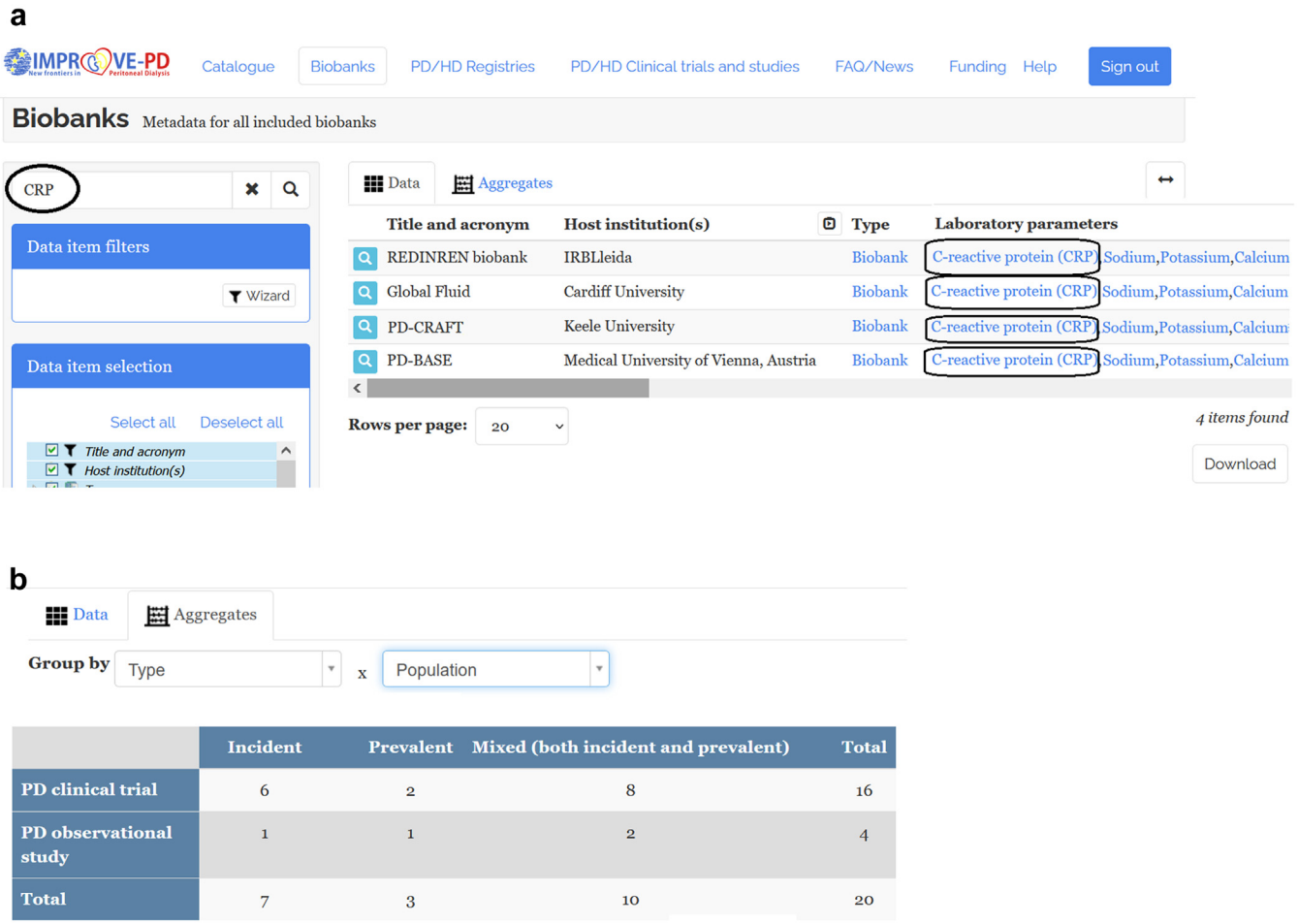
A critical view of clinical trials in PD, often characterized by small patient populations, relatively complex outcomes or end points, and a shortage of novel interventions,[S8] outlined the necessity for including the Clinical trials and studies section. In it, the user has immediate access to key descriptors of the study design and type of intervention, phase of clinical trial, randomization, sample size calculation, and duration of follow-up. Number of patients, centers and countries involved, and dropout rate of completed studies are provided. Detailed presentation of primary or secondary outcomes is accomplished with a focus on therapy-related outcomes pertaining to technique, infections, and membrane function assessment and a subsection dedicated to cardiovascular outcomes.

RESULTS

Currently, the IMPROVE-PD Finder contains information from 8 biobanks, 8 renal registries, and 20 clinical studies or trials covering 158,895 patients across 41 countries and 900 centers. This initial stage has been reached following 2 rounds of design and testing, whereby study data has been contributed by beneficiaries and partners of the IMPROVE-PD Consortium. The current snapshot of the platform indicates its successful integration of databases in PD across national borders and age groups, from infants to geriatrics. The Registries section contains a mix of national renal registries and large international multicenter pediatric registries in both PD and hemodialysis.[S9] Similarly, the Biobanks section combines single-center and international biorepositories, which have played a crucial role in recent research, for example on the role of glucose degradation products in vasculopathy.[4] True to the shared goal of the IMPROVE-PD Consortium toward innovative therapies, the Clinical trials and studies section is shaped by studies on biocompatible and inflammatory or immune modulatory PD fluids and additives,[S10–S12] delineating association between local or systemic inflammation[S13] and helping to inform practice and improve global outcomes in dialysis.[S14,S15] An overarching result of the platform is its impetus for making global PD data more findable, accessible, interoperable, and reusable (FAIR principle). Using the MOLGENIS open-source web application,[S16] accessibility is guaranteed by a secure access along with relevant web links to participating databases. Interoperability is achieved by standardizing the structure of collected information, which is synthesized from various sources, with a mix of standardized terms as well as free-text fields, and reusability is ensured by a download functionality in popular data formats. A special focus is the findability of information, realized by an intuitive search engine, filter wizard, report generation, and data summary functionality (Figure 1).

DISCUSSION

A great advantage of the platform is its unlimited potential to grow. The platform is open to all researchers worldwide upon request to the authors. There are no geographical limitations to neither accessing nor



	Incident	Prevalent	Mixed (both incident and prevalent)	Total
PD clinical trial	6	2	8	16
PD observational study	1	1	2	4
Total	7	3	10	20

Figure 1. (a) To demonstrate the intuitive search engine, a query with the keyword "CRP" (search box in the top left corner) results in 4 biobanks collecting C-reactive protein. (b) A dedicated module generates summarized counts for queries on the data in the form of 2 × 2 tables. In this example, a summary of PD study type by population (i.e., incident, prevalent, mixed) is presented. CRP, C-reactive protein; PD, peritoneal dialysis.

contributing to the IMPROVE-PD Finder platform. Workload is limited because no personal patient data are collected, but study descriptors and aggregated data. Another benefit is the close relation to the influential SONG-PD initiative, which established standardized outcomes for PD trials.[S17] In fact, the core SONG-PD outcomes of PD - infection, cardiovascular disease, mortality, and technique survival underpin the structure of all sections of the IMPROVE-PD Finder platform, with life participation represented in the patient-reported outcome measures collected in Registries and Clinical trials and studies sections. Finally, to encourage comparative research, the platform also includes hemodialysis-based studies with domain-specific subsections. Most principal investigators and their teams provided comprehensive information, whereas in some instances, we collected data from different sources (i.e., system specifications, annual reports), potentially introducing inaccuracy. This stresses the collaborative and iterative nature of the platform and the need for constructive feedback on its design and contents. IMPROVE-PD Finder is an intersectoral research resource, which gives a comprehensive global overview of collected data on PD. It promotes equality of access to information among researchers worldwide, facilitating basic, translational, and clinical research. Being a step forward in characterizing the patient's clinical, social, and treatment-related risk profile, it encourages comparative research and validation of findings in independent and sufficiently powered patient cohorts. All researchers are welcome to join the platform as well as to contribute to its contents. Please see the homepage https://www.improvepdfinder.eu/ on how to contact the authors.

APPENDIX

List of Members of IMPROVE-PD Consortium

Prof. Andreas Vychytil, Dr. Anne-Catherine Raby, Dr. Chantal Colmont, Prof. Cristoph Aufricht, Prof. David W. Johnson, Prof. Donald Fraser, Prof. Ed Eringa, Prof. Johann Morelle, Prof. Jose M. Valdivielso, Prof. Klaus Kratochwill, Dr. Lily Jakulj, Prof. Marc Vervloet, Prof.

Marta Ruiz-Ortega, Prof. Olivier Devuyst, Prof. Patrick Rossignol, Dr. Peter Rutherford, Dr. Rebecca Herzog and Dr. Soma Meran.

DISCLOSURE

All the authors declared no competing interests.

ACKNOWLEDGMENTS

We sincerely thank Javier Carrero and Professor López-Cabrera for providing expert and technical support for the platform, as well as the representatives of IMPROVE-PD beneficiaries and partner organizations for their data contributions and advice as follows: Prof. Andreas Vychytil, Dr. Anne-Catherine Raby, Dr. Chantal Colmont, Prof. Cristoph Aufricht, Prof. David W. Johnson, Prof. Donald Fraser, Prof. Ed Eringa, Prof. Johann Morelle, Prof. Jose M. Valdivielso, Prof. Klaus Kratochwill, Dr. Lily Jakulj, Prof. Marc Vervloet, Prof. Marta Ruiz-Ortega, Prof. Olivier Devuyst, Prof. Patrick Rossignol, Dr. Peter Rutherford, Dr. Rebecca Herzog, and Dr. Soma Meran.

This work is part of "Identification and Management of Patients at Risk – Outcome and Vascular Events in Peritoneal Dialysis" (IMPROVE-PD), a project that receives funding from the European Union's Horizon 2020 research and innovation program under the Marie Skłodowska-Curie Actions, grant agreement No 812699. MB is funded by the Deutsche Forschungsgemeinschaft (DFG, German Research Foundation)-Projektnummer 419826430 and by Olympia Morata Fellowship from Heidelberg University.

SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Supplementary References.

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