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Original Article

Building a network of ADPKD reference centres across Europe: the EuroCYST initiative

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ABSTRACT

Background. Autosomal dominant polycystic kidney disease (ADPKD) is the most common monogenic inherited kidney disease, affecting an estimated 600 000 individuals in Europe. The disease is characterized by age-dependent development of a multiple cysts in the kidneys, ultimately leading to end-stage renal failure and the need of renal replacement therapy in the majority of patients, typically by the fifth or sixth decade of life. The variable disease course, even within the same family, remains largely unexplained. Similarly, assessing disease severity and prognosis in an individual with ADPKD remains difficult. Epidemiological studies are limited due to the fragmentation of ADPKD research in Europe.

Methods. The EuroCYST initiative aims: (i) to harmonize and develop common standards for ADPKD research by starting a collaborative effort to build a network of ADPKD reference centres across Europe and (ii) to establish a multicentric observational cohort of ADPKD patients. This cohort will be used to study factors influencing the rate of disease progression, disease modifiers, disease stage-specific morbidity and mortality, health economic issues and to identify predictive disease progression markers. Overall, 1100 patients will be enrolled in 14 study sites across Europe. Patients will be prospectively

followed for at least 3 years. Eligible patients will not have participated in a pharmaceutical clinical trial 1 year before enrolment, have clinically proven ADPKD, an estimated glomerular filtration rate (eGFR) of 30 mL/min/1.73 m^2 and above, and be able to provide written informed consent. The baseline visit will include a physical examination and collection of blood, urine and DNA for biomarker and genetic studies. In addition, all participants will be asked to complete questionnaires detailing self-reported health status, quality of life, socioeconomic status, health-care use and reproductive planning. All subjects will undergo annual follow-up. A magnetic resonance imaging (MRI) scan will be carried out at baseline, and patients are encouraged to undergo a second MRI at 3-year follow-up for qualitative and quantitative kidney and liver assessments.

Conclusions. The ADPKD reference centre network across Europe and the observational cohort study will enable European ADPKD researchers to gain insights into the natural history, heterogeneity and associated complications of the disease as well as how it affects the lives of patients across Europe.

Keywords: ADPKD, biomarker, cohort, EuroCYST, risk factors

INTRODUCTION

Autosomal dominant polycystic kidney disease (ADPKD) is one of the most common monogenic genetic diseases, affecting ∼1 in 1000 live births, that is ∼600 000 individuals in Europe [1]. The disease is characterized by the development of multiple cysts in both kidneys and by potentially serious complications [2]. Disease manifestations impairing quality of life include hypertension, chronic pain, intracranial aneurysms, abdominal hernias, haematuria, urinary tract infection and kidney stones. Kidney function is often preserved up to the age of 40, but subsequently glomerular filtration rate (GFR) decreases and often leads to end-stage renal disease (ESRD) [3]. However, there is wide variability between subjects in disease course, even within families that share the same mutation, with some patients never reaching ESRD.

ADPKD represents a major burden for public health in the EU, estimated at €1.6 billion annually for direct medical costs related to renal replacement therapy [4]. This figure is an underestimate of the true economic burden, because it does not take into account costs related to co-morbidities that frequently occur in patients with impaired kidney function and the loss of income generation that is often observed in subjects with later stage kidney disease. Research on prevention of ADPKD-related complications could therefore offer a tremendous return on investment.

At present, there are no approved disease-modifying treatments available for ADPKD. Intensive basic research during the last three decades has contributed to a clearer understanding of the basic pathophysiological processes that lead to renal cyst formation in subjects affected by ADPKD with definition of novel therapeutic targets [5, 6]. In animal studies, some of the treatments directed at these targets, such as mammalian target of rapamycin (mTOR) inhibitors, somatostatin analogues and vasopressin V_2-receptor antagonists (V2RA), have shown promising results [7–9]. The clinical trials testing mTOR inhibitors showed no clear impact on disease progression [10–12]. However, recent results from the TEMPO 3:4 and ALADIN trials with the V2RA tolvaptan and the somatostatin analogue octreotide have shown an effect on the rates of kidney growth and kidney function decline, although long-term treatment safety needs to be addressed [13, 14]. If these therapies become available for clinical use, the pivotal question will be which patients to select for treatment. One can hypothesize that ADPKD patients with rapid disease progression would benefit most and that treatment should be started at an early stage of disease, when the kidneys are more likely to respond to an intervention. Since ADPKD is characterized by a long period of stable kidney function, due to compensatory filtration of unaffected nephrons, kidney function does not accurately reflect disease severity nor prognosis [15]. Genotype (*PKD1* as opposed to *PKD2* mutation), male gender and young age at onset of hypertension among others associate with faster disease progression in ADPKD [16, 17]. However, the predictive value of these variables is limited and untested in large prospective cohorts. The identification of surrogate markers to assess disease severity and risk of progression and to monitor the effect of interventions on the course of disease remains an important goal and is an unmet medical need. Results of smaller observational studies in ADPKD cohorts, such as CRISP and SUISSE ADPKD, suggest that changes in total kidney volume (TKV) are a predictor of subsequent loss of kidney function [18]. Magnetic resonance imaging (MRI) has a greater sensitivity for the detection of small cysts and allows to measure kidney and liver volume more precisely compared with ultrasound. It has been shown that MRI can already reliably detect changes in TKV that occur during 6 months of follow-up [19]. However, the two interventional trials with mTOR inhibitors (refs [10] and [11]) did not observe a correlation between total renal volume and disease progression (as measured by renal function) questioning whether TKV is a suitable surrogate marker for disease progression. In addition, this imaging technique is not routine clinical practice for ADPKD subjects in all European countries. Thus, there is a need to discover clinical factors or new biomarkers that predict the rate of disease progression.

Building a large, well-characterized cohort of ADPKD subjects who are followed in a longitudinal observational cohort study has the potential to identify progression factors and biomarkers, and to assess disease stage-specific mortality, morbidity and health-care costs. This knowledge should translate into new diagnostic and therapeutic modalities. This approach requires a coordinated multinational action within a network of ADPKD reference centres. The EuroCYST initiative aims to build such a network and to establish a large-scale pan-European ADPKD cohort serving as a versatile and powerful clinical research platform. Since EuroCYST is an academic initiative and not industry driven, free access to information and pseudo-anonymized biomaterial is ensured, as approved by a research oversight committee.

METHODS

Objectives

The primary objectives of the EuroCYST initiative are to:

(i) Build a network of ADPKD reference centres across Europe to provide a translational research platform that will enable EU researchers to study the pathogenesis, progression factors, morbidity, co-morbidity and health economic issues in ADPKD patients over a wide range of kidney function and kidney volume.

(ii) Harmonize and develop common standards for ADPKD-related research by a collaborative effort to establish a pan-European ADPKD cohort.

(iii) Harmonize and develop a common ADPKD biobank that includes standardized, quality-controlled biomaterials for translational research.

(iv) Create a scaffold to facilitate the integration of current and upcoming technologies to ADPKD practice.

(v) Develop evidence-based best practice and need assessments for ADPKD by utilizing the outcomes of the EuroCYST initiative and by engaging with relevant stakeholders, including patient organizations, clinical and research networks, legislators, policymakers and the pharmaceutical industry.

(vi) Serve as an impetus to expand ADPKD training programmes at all levels by establishing collaborative and educational liaisons as well as provide standard criteria for effective management protocols in ADPKD.

(vii) Improve awareness of the relevance of ADPKD including disease-specific complications and socioeconomic consequences of the disease among health-care professionals and payers.

EuroCYST strategy and organization

To build a cohort for a longitudinal observational study, 14 centres in 10 countries across Europe (Figure 1) will enrol 1100 adult ADPKD patients until the end of 2015. The study is funded by a grant of the ERA–EDTA with 1 million Euros. For optimal utilization of the funding, centres with expertise in ADPKD and already existing local clinical cohorts have been co-opted, so that efforts do not need to focus on recruitment, but can be invested into the establishment of the cohort infrastructure, uniform data recording and in-depth analysis of several time and thus resource-consuming aspects, such as assisted patient interviews using standardized questionnaires.

The enrolment phase started in summer 2013; within 1 year, 250 participants should be included. To reach the goal of recruiting 1100 ADPKD patients, each participating ADPKD centre will enrol at least 50 and up to a maximum of 100 patients within 2 years to ensure a representative distribution of patients across Europe. In a second step, which is beyond the current funding period, the cohort could be extended in

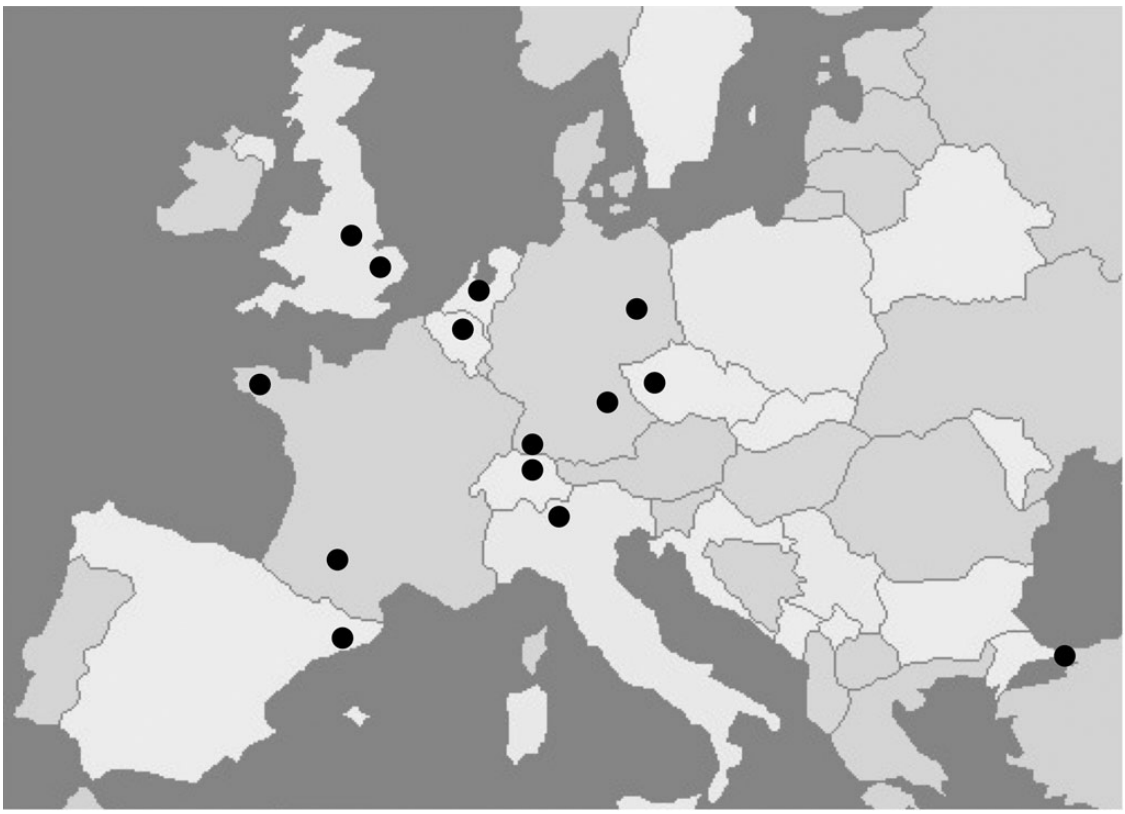

FIGURE 1: Location of participating study sites in the EuroCYST initiative.

four ways to: (i) prolong the intended duration of follow-up to longer than 3 years, (ii) increase the number of patients up to 5000 or more through the participation of additional European study centres with a minimum essential dataset, (iii) increase the information density per patient for specific aspects (e.g. cardiovascular pathology, imaging and genetics) or (iv) enrol partners, children and parents of index patients (three-generation cohort). The participation of additional centres will be possible if appropriate funding is obtained. Collaborations at various levels with other research groups to share data and biomaterials in order to achieve maximum scientific output will be encouraged. To this end, an open and transparent ancillary study policy has been established as part of the study protocol (Supplementary data S1).

A Steering Committee has been established and is meeting at least twice a year. All decisions by the Steering Committee will be approved on a 75% majority. The establishment of a Central Study Coordination Team, which meets on a bi-weekly basis, will ensure rapid and successful project implementation and progress.

Eligibility of cohort participants

Following a consecutive enrolment approach, all patients with ADPKD are considered as potentially eligible for the study at pre-screening and will undergo screening for the study. Patients aged 18 years and older with an estimated GFR (eGFR) of 30 mL/min/1.73 m^2 and higher [chronic kidney disease-epidemiology collaboration (CKD-EPI) formula], having a diagnosis of ADPKD established based on kidney ultrasound and family history (modified Ravine criteria) who have not taken part in a disease-modifying trial at least 1 year or shorter before enrolment and are able to provide written informed consent, will be eligible for enrolment into the EuroCYST cohort [20, 21]. Table 1 displays the inclusion and exclusion criteria. Exclusion criteria include the likelihood of reaching ESRD within 1 year after enrolment or significant heart disease according to New York Heart Association Stage IV (NYHA Stage IV) [22]. A stratification strategy based on subjects' eGFR will avoid a selection bias. Thus, 40 to 60% of included patients in each study center need to have an eGFR of 60 mL/min/1.73 m^2 and more.

Table 1. Inclusion and exclusion criteria for the EuroCYST observational cohort study

Inclusion criteria
Age ≥18
eGFR ≥30 mL/min/1.73 m^2 (CKD-EPI formula)
Clinical diagnosis of ADPKD based on kidney imaging and family history (modified Ravine criteria)
Patient provided written informed consent
Exclusion criteria
Receiving chronic renal replacement therapy before enrolment (dialysis and allograft) or anticipated to receive such therapy within 12 months after enrolment
Participation in a clinical trial aiming to modify disease outcome 1 year or less before enrolment in the EuroCYST study
NYHA stage IV

ADPKD, autosomal dominant polycystic kidney disease; eGFR, estimated glomerular filtration rate; NYHA, New York Heart Association.

Study design

Patients who meet the inclusion criteria will be invited to participate. All potential participants will receive detailed information about the study both verbally and in writing. Local ethical committees will approve the study, and the protocol has to fulfil the local regulatory requirements and complies with Good Clinical Practice (GCP) Guidelines.

The study design is shown in Figure 2. At baseline, a detailed medical and ADPKD-specific assessment will be performed. Family history/pedigree information will be collected, as well as information on medical resource use (health-care visits, hospital admission, procedures and medication), productivity (employment and absenteeism), information culture within families and reproductive planning. The economic and social position, based on income, education and occupation, will be assessed. Quality of life will be measured by asking patients to complete the KDQOL-SF 1.2™ questionnaire, which includes questions relating to patients' general health, kidney disease and about the effect of the disease on activities of daily living. The protocol will also require a physical examination.

Follow-up visits will be conducted on an annual basis until the end of study, withdrawal, ESRD or death. Follow-up visits will include physical examination, laboratory analyses and completing the aforementioned ADPKD-related questionnaires. Participating patients will be treated according to current standards of care in routine clinical practice within each country.

Magnetic resonance imaging

MRI will be used to measure the different magnitudes and volume parameters of kidney and liver. MRI will be performed at the baseline visit and is recommended at 3-year follow-up. To obtain high-quality renal and hepatic imaging and maintain consistency between the centres participating in the trial, a standardized protocol has been developed. The MRI acquisition protocol includes T_2 single-shot fast/turbo spin-echo images with fat-saturation, FISP or FIESTA 3D spoiled gradient echo and T_1-3D spoiled gradient echo. Images will be sent using the Picture Archiving and Communication System

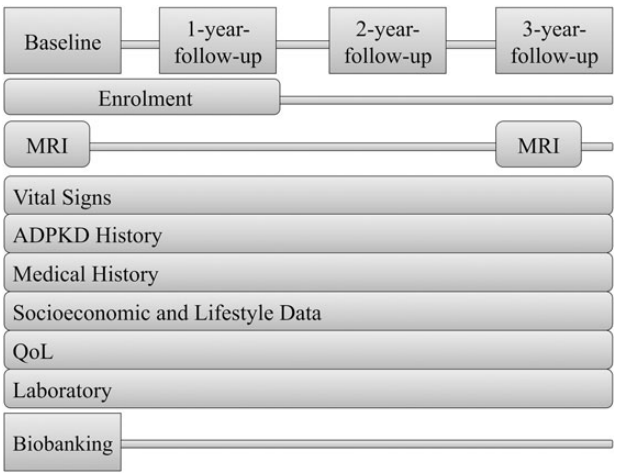

FIGURE 2: Study design.

(PACS) to the centres in Zurich and Bergamo, where a read out by trained personnel will be performed. Read out of the scans includes whole kidney and cyst volume, length, depth, width of the kidney, numbers of cysts and also liver and liver cyst volume, using the workstation GE Advantage and the programme volume viewer.

Collection and storage of biomaterials

The collection of material for biobanking will be conducted at the baseline visit. A standard operating procedure (SOP) harmonizes the procedure for sampling, pre-processing and storage of biobanking material within the EuroCYST initiative. Serum, plasma and whole blood collected on EDTA and spotted, and a 24-h urine sample will be collected, processed and aliquoted. They will be shipped in batches to a central biobank storage facility where an automated −80°C sample library management system is in place to handle the de-identified 2D bar-coded sample vials. The whole blood tubes will be shipped to a central, certified genetic laboratory for DNA extraction and storage. The database will be kept separately with a secure method to link clinical information to biological samples.

Data management and protection

Data collection and data management will be conducted using the web-based data management system SecuTrial®, with a data capture, which has been approved by the US Food and Drug Administration (FDA) and that fulfils the requirements of the International Conference on Harmonization Good Clinical Practice (ICH GCP) and Good Clinical Data Management Practices (GCDMP). All electronic case report forms (eCRF) have been implemented into this system. Figure 3 shows the different subject areas of the data bank that are reflected in the eCRF. Data will be stored for at least 10 years after study termination and a daily back up will be performed. The study data are saved on a separate server at the University Hospital Zurich, where the clinical trial centre, provider of the data management system, is located. Server access is controlled physically and electronically. Each patient will be pseudo-anonymized in a reversible manner, and all data introduced into the data management system are coded. Subject identification will only be possible at the local study site. Access to the system will be role specific and will only be possible with a unique user-ID and password. High data quality will be ensured by performing regular monitoring and reporting of entered data by the coordination centre in Zurich. All study site data entered in the eCRF will be checked for completeness and plausibility according to predefined rules to draw attention to missing data or errors. Certified personnel will monitor the participating centre annually. All patients' written informed consent forms and all study files will be checked for completeness, and remain at the individual sites. In 10% of locally enrolled patients, the source files and eCRFs will be checked for accuracy. In addition, frequent communications and annual meetings of reference centre principal investigators will ensure study compliance. The centre's individual results of the study shall be owned by the centre. Each centre will provide copies of all results, including but not limited to case report forms, to the study coordination centre in Zurich. Owner of the overall data of the initiative is the EuroCYST Steering Committee.

Statistical considerations

Formal sample size estimation has not been performed for this study. While chronic kidney disease cohorts currently aim to enrol at least 3000 and up to 5000 patients (CRIC, CKD JAC and GCKD) to identify valid associations in subgroups, the common genetic origin in APDKD allows important

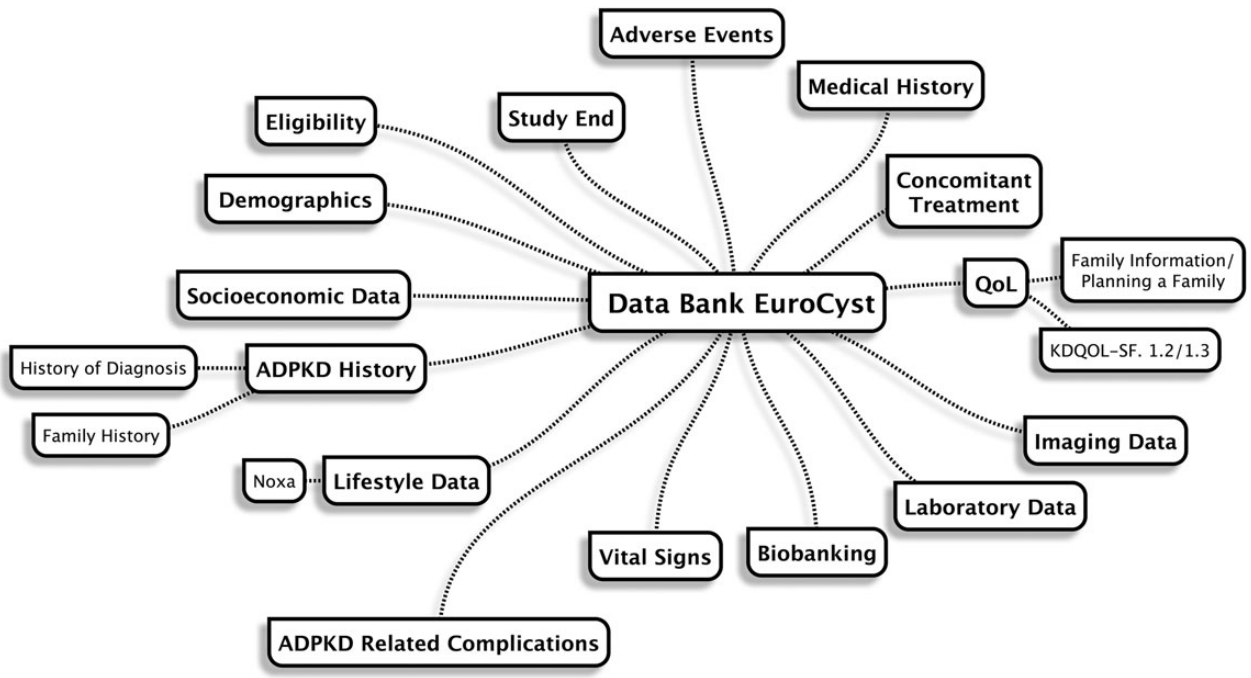

FIGURE 3: Content of the databank.

conclusions to be drawn using a smaller sample size [23–25]. On the other hand, groups of several hundred patients enrolled in recent randomized controlled trials as well as already existing ADPKD cohorts have displayed large variability in the disease progression rate as assessed by the change in eGFR rate and TKV despite restrictive inclusion and exclusion criteria. Therefore, a larger sample size is required to account for the broader range in age and renal function in our cohort. A mixed-effects regression model will be used as the modelling framework, with a random effect for each patient (this allows correlation between repeated eGFR or TKV measurements in the same patient) and with fixed effects for time with a spline structure to model change in eGFR and TKV.

Study outcomes

The primary outcome measure of the study will be disease progression, assessed as change in eGFR (CKD-EPI) and change in TKV. Secondary outcome measure will be: first, onset and severity of ADPKD-related clinical outcomes, such as hypertension, albuminuria, renal urine concentrating ability, haematuria, renal pain, cyst infection and nephrolithiasis; secondly, self-reported health status, quality of life and pain; and thirdly, health-related resource use and ADPKD-related health burden.

Enrolment start

The study started enrolling patients in July 2013 and will run for 36 months.

CONCLUSION

The fragmentation of cohorts of ADPKD patients in Europe has been an obstacle to a better understanding of disease characteristics. Individual efforts in different countries often have little inter-changeability and it can be almost impossible to connect detailed clinical information held in one database with genetic information or biomaterial sample availability held in other databases. Our increasing knowledge of the basic biology of ADPKD has led to the identification of multiple novel targets in pre-clinical studies, which will need to be tested in patients. Positive results from recent clinical trials also now compel nephrologists to find new ways of risk stratification to identify patients at higher risk of disease progression and who may benefit most from early intervention. So far, limited data are available addressing patients' quality of life, disease-related health burden, health-care resource use and reproductive planning. Currently, available data regarding quality of life for ADPKD patients are limited and often only applicable to those on dialysis or transplanted patients [26–29].

These issues motivated the EuroCYST initiative, which aims to build an ADPKD reference centre network in Europe in order to establish a large pan-European observational cohort that will serve as a scaffold and platform enabling researchers to study the pathogenesis, progression factors, mortality, comorbidity as well as health economic issues relevant to ADPKD as a major cause of kidney disease. Although there is an interest of the pharmaceutical industry to establish ADPKD databases, an independent academic network with a transparent open access policy remains essential. The recent establishment of the ERA–EDTA Working Group on Inherited Kidney Disorders demonstrates the interest and need for a consolidated pan-European approach in the field of inherited kidney diseases at large [30].

The establishment of such a cohort has the potential to strengthen European ADPKD investigators by harmonizing and standardizing research efforts and will guarantee that current and upcoming technologies to study chronic kidney disease can be applied to ADPKD patients across Europe. Affected patients and their relatives will benefit from the scientific-medical innovations by improved prevention and awareness, treatment of disease-specific complications and development of new diagnostic and therapeutic modalities.

SUPPLEMENTARY DATA

Supplementary data are available online at http://ndt.oxfordjournals.org.

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CONFLICT OF INTEREST STATEMENT

None declared.

REFERENCES

1. Torres VE, Harris PC, Pirson Y. Autosomal dominant polycystic kidney disease. Lancet 2007; 369: 1287–1301
2. Liebau MC, Serra AL. Looking at the (w)hole: magnet resonance imaging in polycystic kidney disease. Pediatr Nephrol 2013; 28: 1771–1783
3. Grantham JJ, Mulamalla S, Swenson-Fields KI. Why kidneys fail in autosomal dominant polycystic kidney disease. Nat Rev Nephrol 2011; 7: 556–566
4. Lentine KL, Xiao H, Machnicki G *et al.* Renal function and healthcare costs in patients with polycystic kidney disease. Clin J Am Soc Nephrol 2010; 5: 1471–1479
5. Torres VE, Harris PC. Autosomal dominant polycystic kidney disease: the last 3 years. Kidney Int 2009; 76: 149–168
6. Chang MY, Ong AC. Autosomal dominant polycystic kidney disease: recent advances in pathogenesis and treatment. Nephron Physiol 2008; 108: p1–p7
7. Wu M, Wahl PR, Le Hir M *et al.* Everolimus retards cyst growth and preserves kidney function in a rodent model for polycystic kidney disease. Kidney Blood Press Res 2007; 30: 253–259
8. Masyuk TV, Radtke BN, Stroope AJ. Pasireotide is more effective than octreotide in reducing hepatorenal cystogenesis in rodents with polycystic kidney and liver diseases. Hepatology 2013; 58: 409–421
9. Gattone VH, II, Wang X, Harris PC *et al.* Inhibition of renal cystic disease development and progression by a vasopressin V2 receptor antagonist. Nat Med 2003; 9: 1323–1326
10. Serra AL, Poster D, Kistler AD *et al.* Sirolimus and kidney growth in autosomal dominant polycystic kidney disease. N Engl J Med 2010; 363: 820–829
11. Walz G, Budde K, Mannaa M *et al.* Everolimus in patients with autosomal dominant polycystic kidney disease. N Engl J Med 2010; 363: 830–840

12. Perico N, Antiga L, Caroli A *et al.* Sirolimus therapy to halt the progression of ADPKD. J Am Soc Nephrol 2010; 21: 1031–1040
13. Torres VE, Gansevoort RT, Czerwiec FS *et al.* Tolvaptan in patients with autosomal dominant polycystic kidney disease. N Engl J Med 2012; 367: 2407–2418
14. Caroli A, Perico N, Perna A *et al.* Effect of longacting somatostatin analogue on kidney and cyst growth in autosomal dominant polycystic kidney disease (ALADIN): a randomised, placebo-controlled, multicentre trial. Lancet 2013; 382: 1485–1495
15. Grantham JJ, Chapman AB, Torres VE. Volume progression in autosomal dominant polycystic kidney disease: the major factor determining clinical outcomes. J Am Soc Nephrol 2006; 1: 148–157
16. Helal I, Reed B, Schrier RW. Emergent early markers of renal progression in autosomal-dominant polycystic kidney disease patients: implications for prevention and treatment. Am J Nephrol 2012; 36: 162–167
17. Cornec-Le Gall E, Audrézet MP, Chen JM *et al.* Type of PKD1 mutation influences renal outcome in ADPKD. J Am Soc Nephrol 2013; 24: 1006–1013
18. Chapman AB, Guay-Woodford LM, Grantham JJ *et al.* Consortium for radiologic imaging studies of polycystic kidney disease cohort: renal structure in early autosomal-dominant polycystic kidney disease (ADPKD): the consortium for radiologic imaging studies of polycystic kidney disease (CRISP) cohort. Kidney Int 2003; 64: 1035–1045
19. Kistler AD, Poster D, Krauer F *et al.* Increases in kidney volume in autosomal dominant polycystic kidney disease can be detected within 6 months. Kidney Int 2009; 75: 235–241
20. Pei Y, Obaji J, Dupuis A *et al.* Unified criteria for ultrasonographic diagnosis of ADPKD. J Am Soc Nephrol 2009; 20: 205–212
21. Levey AS, Stevens LA, Schmid CH *et al.* A new equation to estimate glomerular filtration rate. Ann Intern Med 2009; 150: 604–612
22. Hunt SA, Abraham WT, Chin MH. ACC/AHA 2005 Guideline Update for the Diagnosis and Management of Chronic Heart Failure in the Adult: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (writing committee to update the 2001 Guidelines for the Evaluation and Management of Heart Failure): developed in collaboration with the American College of Chest Physicians and the International Society for Heart and Lung Transplantation: endorsed by the Heart Rhythm Society. Circulation 2005; 112: e154–e235
23. Lash JP, Go AS, Appel LJ *et al.* Chronic Renal Insufficiency Cohort (CRIC) Study: baseline characteristics and associations with kidney function. Clin J Am Soc Nephrol 2009; 4: 1302–1311
24. Imai E, Matsuo S, Makino H *et al.* Chronic Kidney Disease Japan Cohort (CKD-JAC) study: design and methods. Hypertens Res 2008; 31: 1101–1107
25. Eckardt KU, Bärthlein B, Baid-Agrawal S *et al.* The German Chronic Kidney Disease (GCKD) study: design and methods. Nephrol Dial Transplant 2012; 27: 1454–1460
26. Peterson RA, Kimmel PL, Sacks CR *et al.* Depression, perception of illness and mortality in patients with end-stage renal disease. Int J Psychiatry Med 1991; 21: 343–354
27. Kimmel PL, Weihs K, Peterson RA. Survival in hemodialysis patients: the role of depression. J Am Soc Nephrol 1993; 4: 12–27
28. Devins GM. Psychosocial issues in end-stage renal disease: introduction. Adv Ren Replace Ther 1994; 1: 195–197
29. Miskulin DC, Abebe KZ, Chapman AB *et al.* Health-related quality of life in patients with autosomal dominant polycystic kidney disease and CKD stages 1–4: a cross-sectional study. Am J Kidney Dis 2014; 63: 214–226
30. Devuyst O, Antignac C, Bindels R *et al.* The ERA-EDTA Working Group on inherited kidney disorders. Nephrol Dial Transplant 2012; 27: 67–69

APPENDIX

EUROCYST STUDY SITES AND PRINCIPAL INVESTIGATORS

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Erratum

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