European ADPKD Patient Summit

15 –16 March 2019, Brussels, Belgium

#ADPKD
@PKD_Int

PKD International

EAF
European ADPKD Forum

Summit sponsors
This event has been made possible by sponsorship from
Baxter, Otsuka Pharmaceutical Europe Ltd, Palladio Biosciences and Sanofi Genzyme.

Baxter Otsuka Palladio Biosciences Sanofi Genzyme

#ADPKD
@PKD_Int

Welcome to the European ADPKD Summit

Tess Harris
(PKD International/ EAF, UK)

EAF: the story so far …

- Collaborative platform for experts and patient advocates to raise awareness and develop policy-focused recommendations
- Communications and tools to improve patient care and empower people living ADPKD

Multidisciplinary collaboration

2016 EAF Multi-specialist Roundtable

- EAF hosted roundtable with EU societies of healthcare specialists involved in ADPKD care – basis for Multidisciplinary Position Statement and ADPKD Patient Route Map.

2017 EAF Multidisciplinary Position Statement on ADPKD Care

- Advocates for **multi-disciplinary, patient-centred care services and patient empowerment**, referencing EU policy initiatives and defining care pathway.[3]
- Published in *Nephrology Dialysis Transplantation* (ERA-EDTA journal) by EAF and specialist society representatives. Highlighted as 'Editor's choice' (special report article).
- Achieved **strong impact metrics**: 4820 views /downloads, Altmetric attention score (based on media, social media and citations): 26 (top 5% of all outputs scored).

>6000 views/downloads

Patient education and empowerment

2018 ADPKD Patient Route Map

- Interactive tool designed to **educate and empower patients and families**.[4]
- Route Map explains the care and support that patients and families should expect from their health service. Aims to help patients manage their own health with their healthcare team, to talk about ADPKD with their nephrologist, to participate in making decisions about their care, and to navigate available care and support services.
- Includes **quotes from patients** across Europe, plus **checklists** to aid patient-physician dialogue.
- Launched at ERA-EDTA 2018 Congress, with article in congress newspaper.
- Promotional video with author interviews on Youtube.
- Free online at *https://pkdinternational.org/adpkd-route-map*.
- 550 page views in first 2 weeks.
- Translations underway, to maximise reach to patients.

2019: 1st European ADPKD Patient Summit

- Collaboration between:
  - EAF
  - PKD International
  - Organisational support by Interel
- Sponsorship from:
  - Baxter
  - Otsuka
  - Palladio Biosciences
  - Sanofi Genzyme

Objective

- Bring Route Map to life as tool for patients and families to navigate the ADPKD research and care pathway
- Inform and empower patients and families to:
  - be fully involved in managing their own health
  - talk about ADPKD with healthcare team and to participate in making decisions
  - make best use of services to get right care, support and info at the right time
  - learn about ADPKD research and how to participate
  - help boost ADPKD advocacy

Attendance

54 participants in total

- 40 participants from kidney / ADPKD groups
  – patients, carers, advocates, foundations, advocacy alliances
    - 15 countries: Belgium, Finland, Denmark, France, Germany, Italy, Ireland, Lithuania, Netherlands, Spain, Sweden, Switzerland, Turkey, UK, USA
    - 2 EU level organisations (EKHA, Eurordis)
    - 4 sponsors
- EAF / Experts
- Interel

Programme

Friday 15 March 2019

19:30–22:00 **Summit Group Dinner**
Opening dinner speech – Richard Sandford *(University of Cambridge, EAF co-Chair)*

Saturday 16 March 2019

9:00–9:05 **Welcome**
Tess Harris *(PKD International/ EAF, UK)*

9:05–10:00 **Plenary I: Developments in the international ADPKD landscape**
Opportunity for patients and carers to learn about latest international developments in ADPKD research and care

SESSION CHAIR: ***Tess Harris*** *(PKD International and EAF, UK)*

PANELLISTS:

- ***Albert Ong***
  (Sheffield University, UK and EAF): Latest updates on the Polycystic Kidney Disease Outcomes Consortium (PKDOC)
- ***Djalila Mekahli***
  (KU Leuven, Belgium and EAF): Latest updates on ADPKD paediatric registries
- ***David Baron***
  (PKD Foundation, USA): Latest updates on the Standardised Outcomes in Nephrology – Polycystic Kidney Disease (SONG-PKD) study.

10:00–10:50

Breakout 1: Self-care and risk reduction
Opportunity for patients and carers to discuss latest studies and current advice on diet, lifestyle, blood pressure, issues in children etc – matters of key importance to daily living and self-care empowerment to help reduce progression and cardiovascular disease risk.

EAF/EXPERT:

- ***Tevfik Ecder***
  (Istanbul Bilim University, Turkey and EAF)
- ***Djalila Mekahli***
  (KU Leuven, Belgium and EAF)

PATIENT REPRESENTATIVE:

- ***Flavia Galletti***
  (AIRP Italy)

Breakout 2: Predicting the progress of ADPKD
Opportunity for patients and carers to learn about and discuss this increasingly important, but perhaps not widely used or understood, approach with an expert.

EAF/EXPERT:

- ***Ron Gansevoort***
  (University Medical Center Groningen, Netherlands and EAF)

PATIENT REPRESENTATIVE:

- ***Lea Münkner***
  (PKD Familiäre Zystennieren e.V., Germany)

10:50–11:10 **Coffee break**

11:10–12:00

Breakout 3: Liver cysts and pain in ADPKD
Focus on these particularly common and impactful complications for patients.

EAF/EXPERT:

- Liver: ***Lucas Bernts***
  (Radboud University Medical Center, Netherlands)
- Pain: ***Ron Gansevoort***
  (University Medical Center Groningen, Netherlands and EAF)

PATIENT REPRESENTATIVE:

- ***Natasha O'Brien***
  (PKD Charity, UK)

Breakout 4: Genetics and genetic testing
Opportunity for patients and carers to learn about and discuss genetic issues with an expert.

EAF/EXPERT:

- ***Richard Sandford***
  (University of Cambridge, UK and EAF)

PATIENT REPRESENTATIVE:

- ***Jean-Pierre Schiltz***
  (AIRG-France)

Programme

Friday 15 March 2019

19:30–22:00 **Summit Group Dinner**
Opening dinner speech – Richard Sandford *(University of Cambridge, EAF co-Chair)*

Saturday 16 March 2019

9:00–9:05 **Welcome**
Tess Harris *(PKD International/ EAF, UK)*

9:05–10:00 **Plenary I: Developments in the international ADPKD landscape**
Opportunity for patients and carers to learn about latest international developments in ADPKD research and care

SESSION CHAIR: ***Tess Harris*** *(PKD International and EAF, UK)*

PANELLISTS:

- ***Albert Ong***
  (Sheffield University, UK and EAF): Latest updates on the Polycystic Kidney Disease Outcomes Consortium (PKDOC)
- ***Djalila Mekahli***
  (KU Leuven, Belgium and EAF): Latest updates on ADPKD paediatric registries
- ***David Baron***
  (PKD Foundation, USA): Latest updates on the Standardised Outcomes in Nephrology – Polycystic Kidney Disease (SONG-PKD) study.

10:00–10:50

Breakout 1: Self-care and risk reduction
Opportunity for patients and carers to discuss latest studies and current advice on diet, lifestyle, blood pressure, issues in children etc – matters of key importance to daily living and self-care empowerment to help reduce progression and cardiovascular disease risk.

EAF/EXPERT:

- ***Tevfik Ecder***
  (Istanbul Bilim University, Turkey and EAF)
- ***Djalila Mekahli***
  (KU Leuven, Belgium and EAF)

PATIENT REPRESENTATIVE:

- ***Flavia Galletti***
  (AIRP Italy)

Breakout 2: Predicting the progress of ADPKD
Opportunity for patients and carers to learn about and discuss this increasingly important, but perhaps not widely used or understood, approach with an expert.

EAF/EXPERT:

- ***Ron Gansevoort***
  (University Medical Center Groningen, Netherlands and EAF)

PATIENT REPRESENTATIVE:

- ***Lea Münkner***
  (PKD Familiäre Zystennieren e.V. , Germany)

10:50–11:10 **Coffee break**

11:10–12:00

Breakout 3: Liver cysts and pain in ADPKD
Focus on these particularly common and impactful complications for patients.

EAF/EXPERT:

- Liver: ***Lucas Bernts***
  (Radboud University Medical Center, Netherlands)
- Pain: ***Ron Gansevoort***
  (University Medical Center Groningen, Netherlands and EAF)

PATIENT REPRESENTATIVE:

- ***Natasha O'Brien***
  (PKD Charity, UK)

Breakout 4: Genetics and genetic testing
Opportunity for patients and carers to learn about and discuss genetic issues with an expert.

EAF/EXPERT:

- ***Richard Sandford***
  (University of Cambridge, UK and EAF)

PATIENT REPRESENTATIVE:

- ***Jean-Pierre Schiltz***
  (AIRG-France)

2019: 1st European ADPKD Patient Summit

- **ADPKD Patient Summit Manifesto**
  - Advocacy outcome of the Summit: e.g. 2 aspirations per summit
  - What the future of ADPKD research and care should look like in 20 years
- **Summit material on PKDI website**
  - Slides, videos, photos (+ possibly ERA-EDTA and ERKnet / Rare Liver Network)
- **Post-summit Communication pack**
  - For national patients groups to share via web / social media

#ADPKD
@PKD_Int

PLENARY I

Developments in the international ADPKD landscape

PKD International

EAF
European ADPKD Forum

Summit sponsors
This event has been made possible by sponsorship from
Baxter, Otsuka Pharmaceutical Europe Ltd, Palladio Biosciences and Sanofi Genzyme.

Baxter Otsuka Palladio Biosciences Sanofi Genzyme

#ADPKD
@PKD_Int

Plenary I: Developments in the international ADPKD landscape

Albert Ong
(Sheffield University, UK and EAF)
Latest updates on the Polycystic Kidney Disease Outcomes Consortium (PKDOC)

Djalila Mekahli
(KU Leuven, Belgium and EAF)
Latest updates on ADPKD paediatric registries

David Baron
(PKD Foundation, USA)
Latest updates on the Standardised Outcomes in Nephrology – Polycystic Kidney Disease (SONG-PKD) study

#ADPKD
@PKD_Int

Latest updates on the Polycystic Kidney Disease Outcomes Consortium (PKDOC)

Albert Ong
(Sheffield University, UK and EAF)

C-Path Program Update

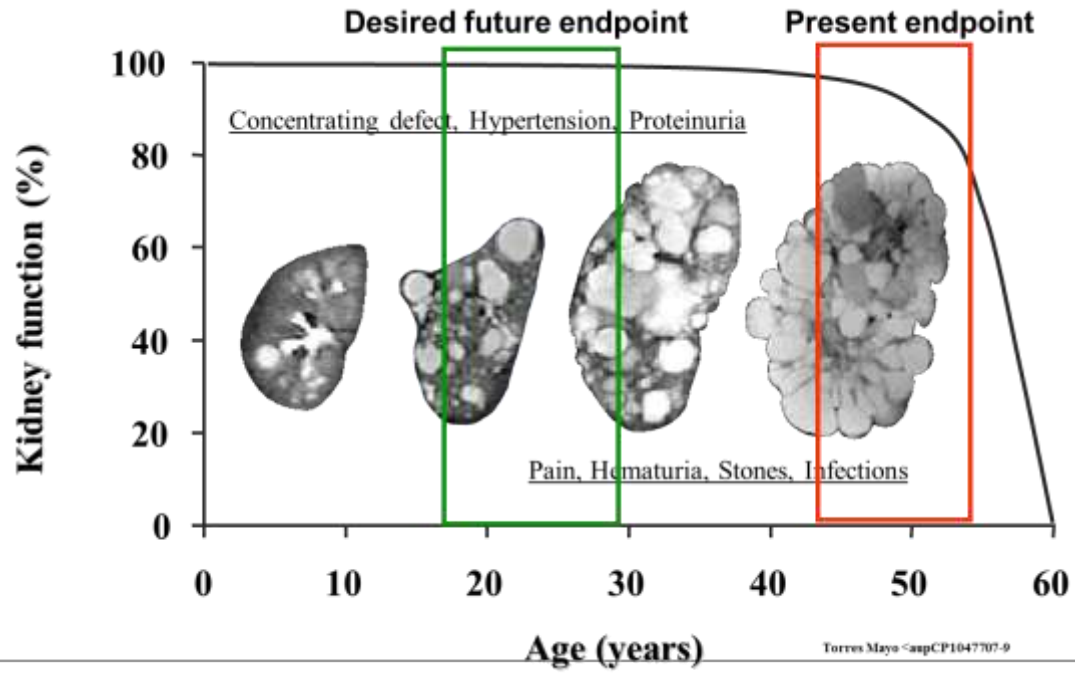
Polycystic Kidney Disease Outcomes Consortium (PKDOC)

PKD CONSORTIUM
CRITICAL PATH INSTITUTE

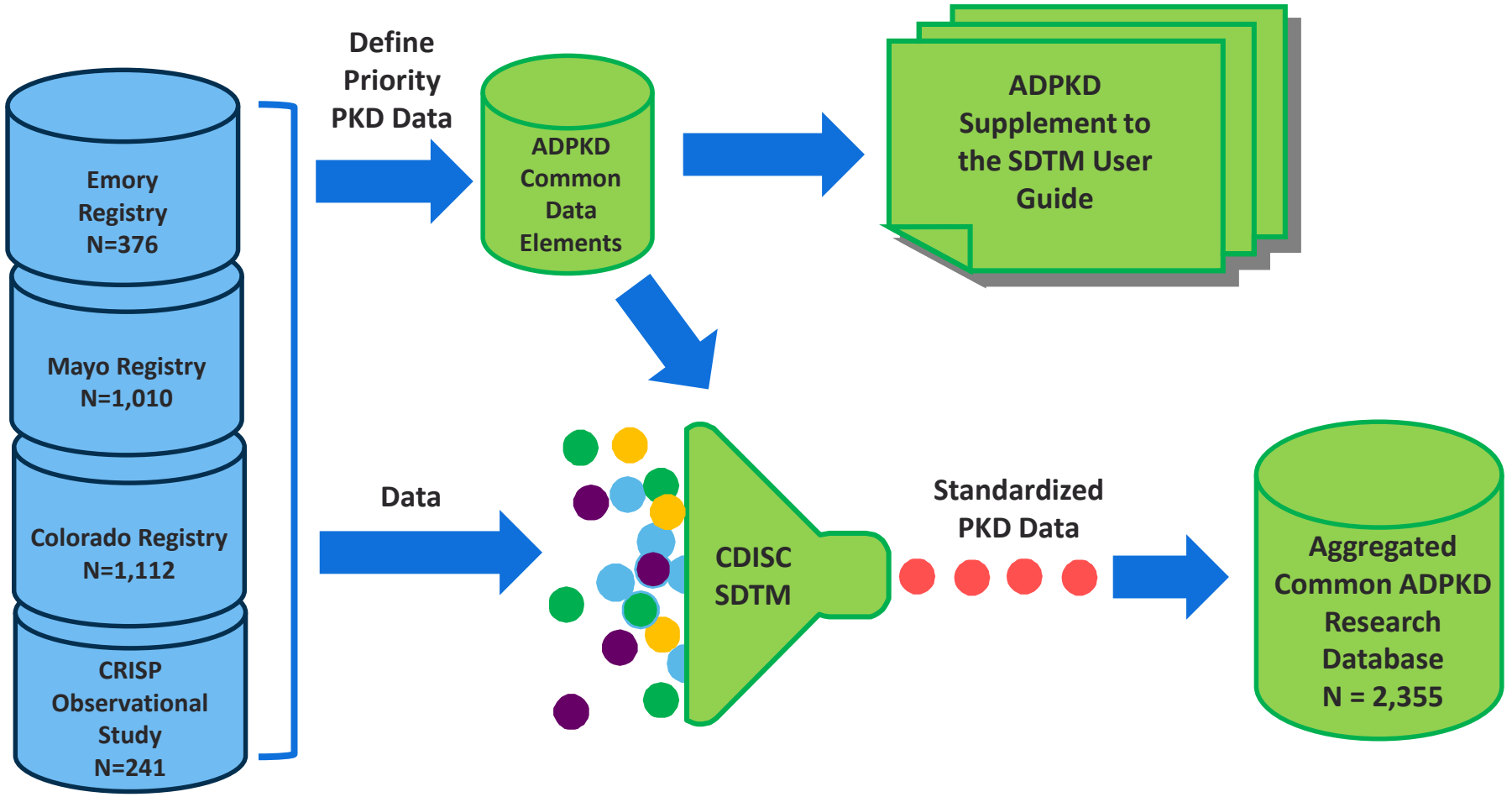
CRITICAL PATH INSTITUTE
a decade of excellence

The Challenges

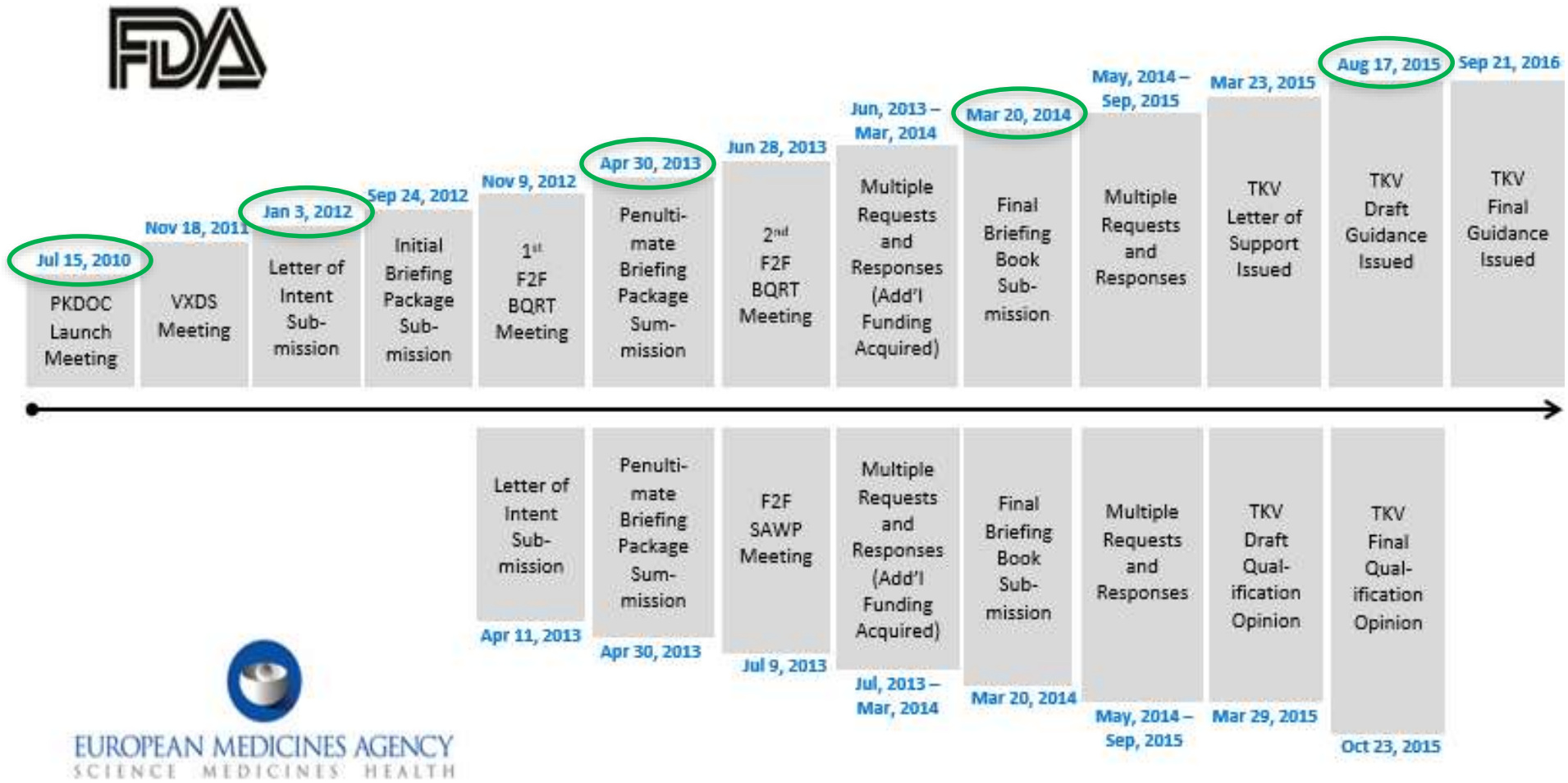
- Heterogeneous and slow progressing disease requires long trials and challenging endpoints.
- Finding clinical endpoint(s) or an accepted surrogate for measuring disease progression early in the course of the disease where kidney function is largely preserved.
- Designing a clinical trial and an acceptable post marketing study to use FDAs Accelerated Approval pathway.



Started with the Data ….

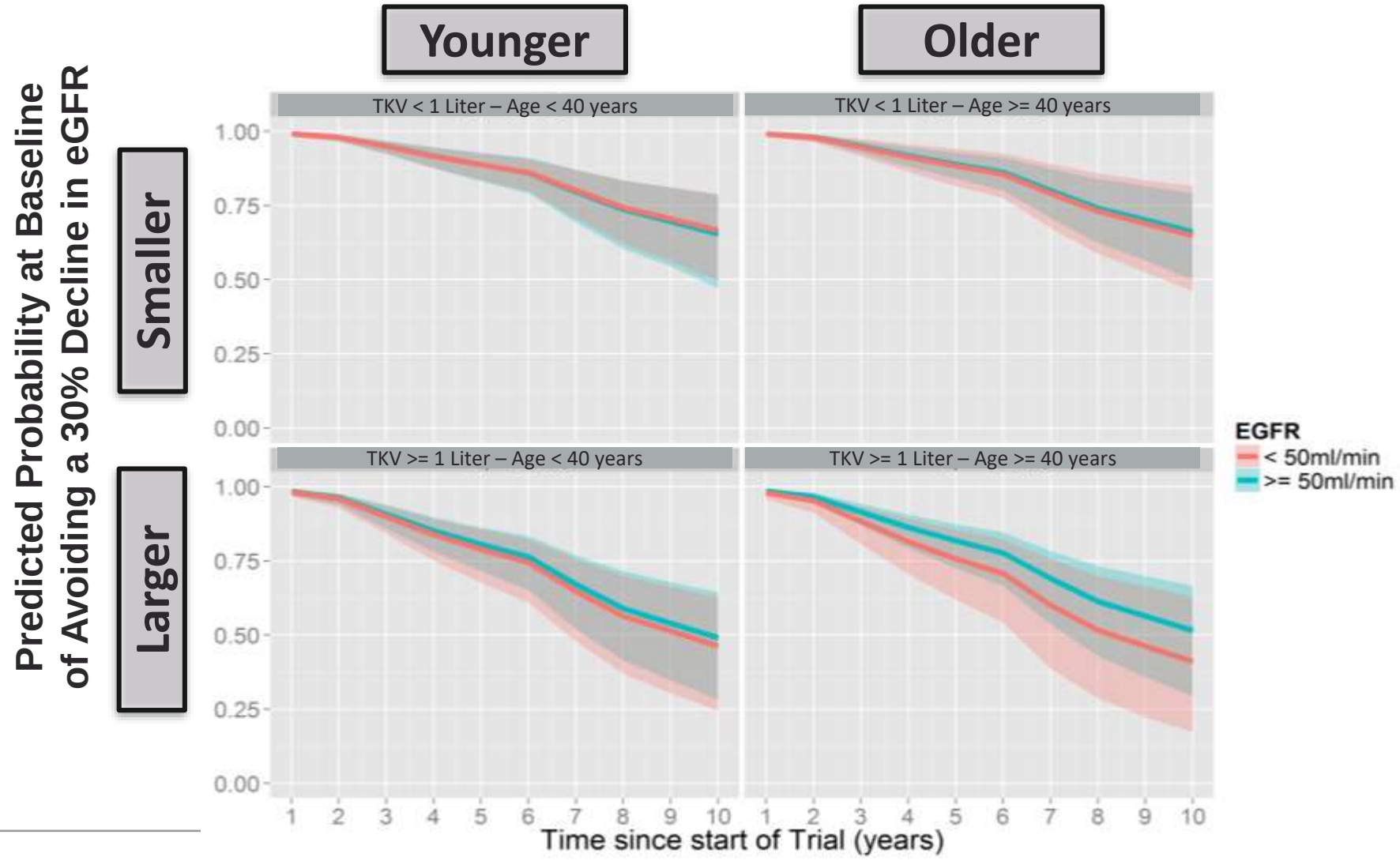


The PKD Regulatory Journey ….



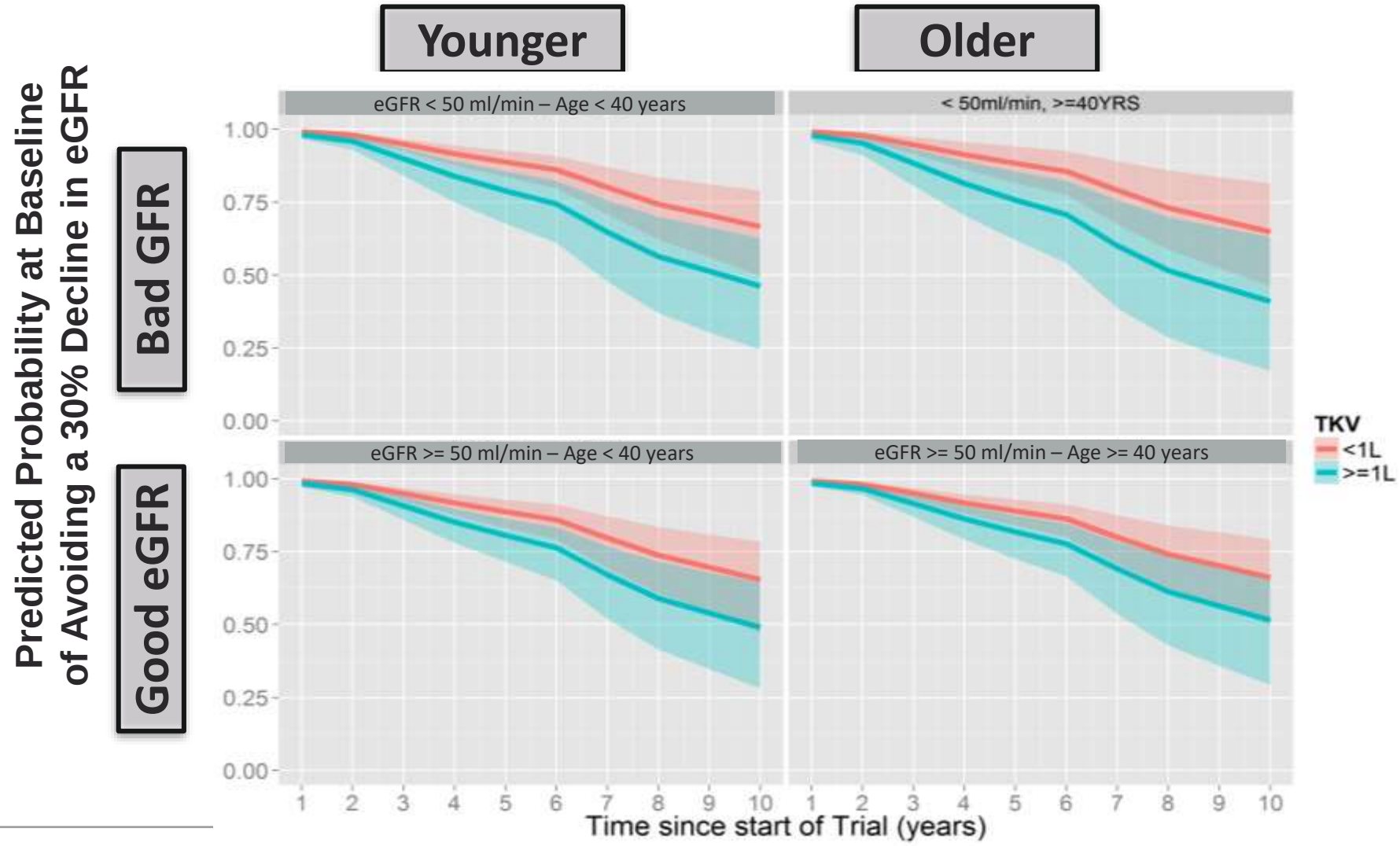
Modelling Results: Effect of Baseline eGFR

eGFR significant in older patients with large kidneys

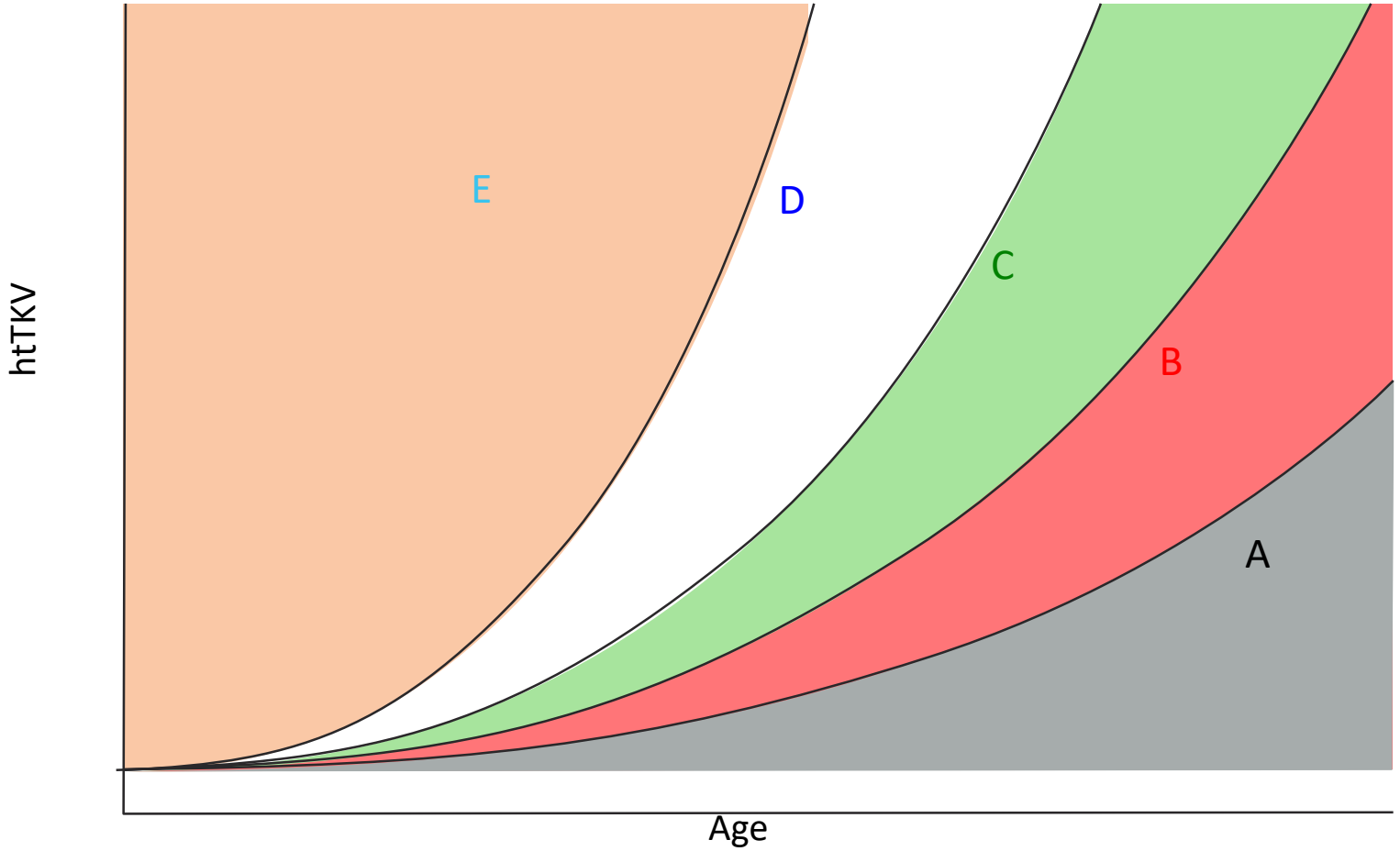


Modelling Results: Effect of Baseline TKV

TKV significant in all patients

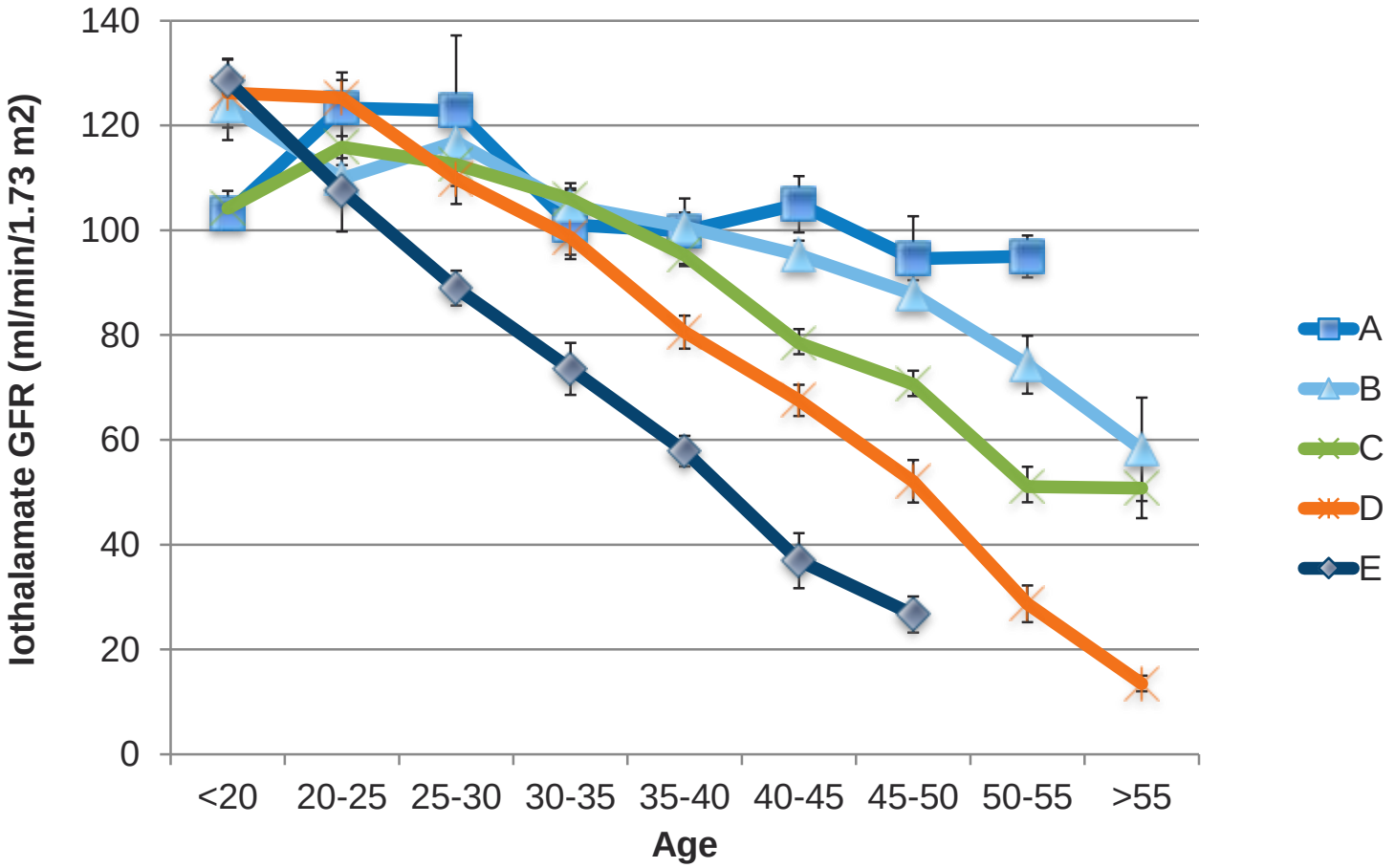


Irazabal method of stratifying by kidney growth rate



Irazabal *et al.*, JASN 2015; 26:160-72

Comparison of GFR trajectories in Irazabal subgroups



The Successes

- CDISC data standard generated
- Aggregated database created and available
- Joint model of TKV progression with PKD progression developed
- TKV qualified as a prognostic biomarker with FDA and EMA
- ADPKD Summit Meeting
- TKV considered a “Reasonably Likely Surrogate” by the FDA enabling an accelerated approval pathway
- Three companies developing drugs in this space has grown to seven
- Three papers published, one being written

Latest updates on ADPKD paediatric registries

Djalila Mekahli
(KU Leuven, Belgium and EAF)

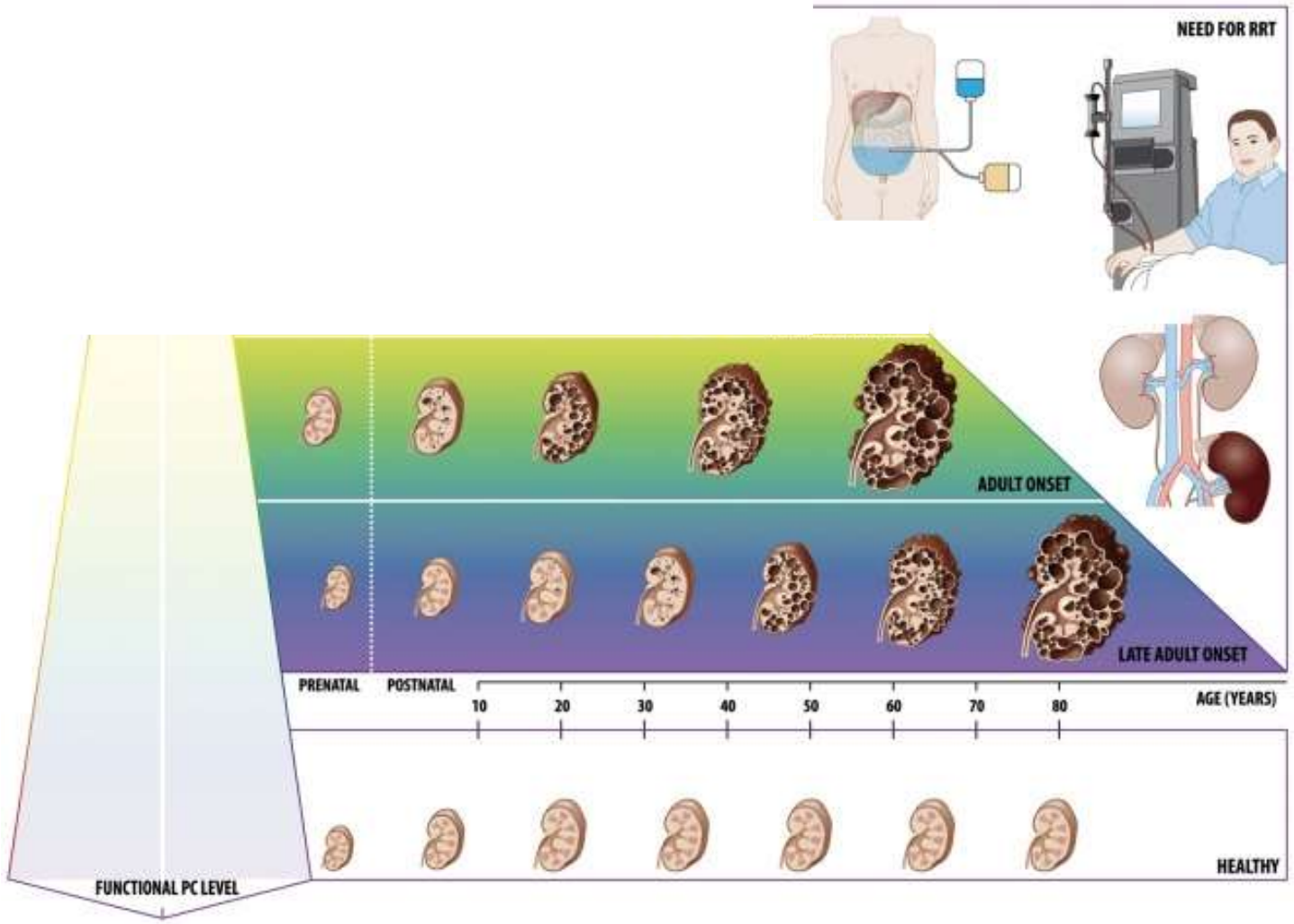
Update on ADPKD paediatric registries

Djalila Mekahli

ADPKD Patient Summit

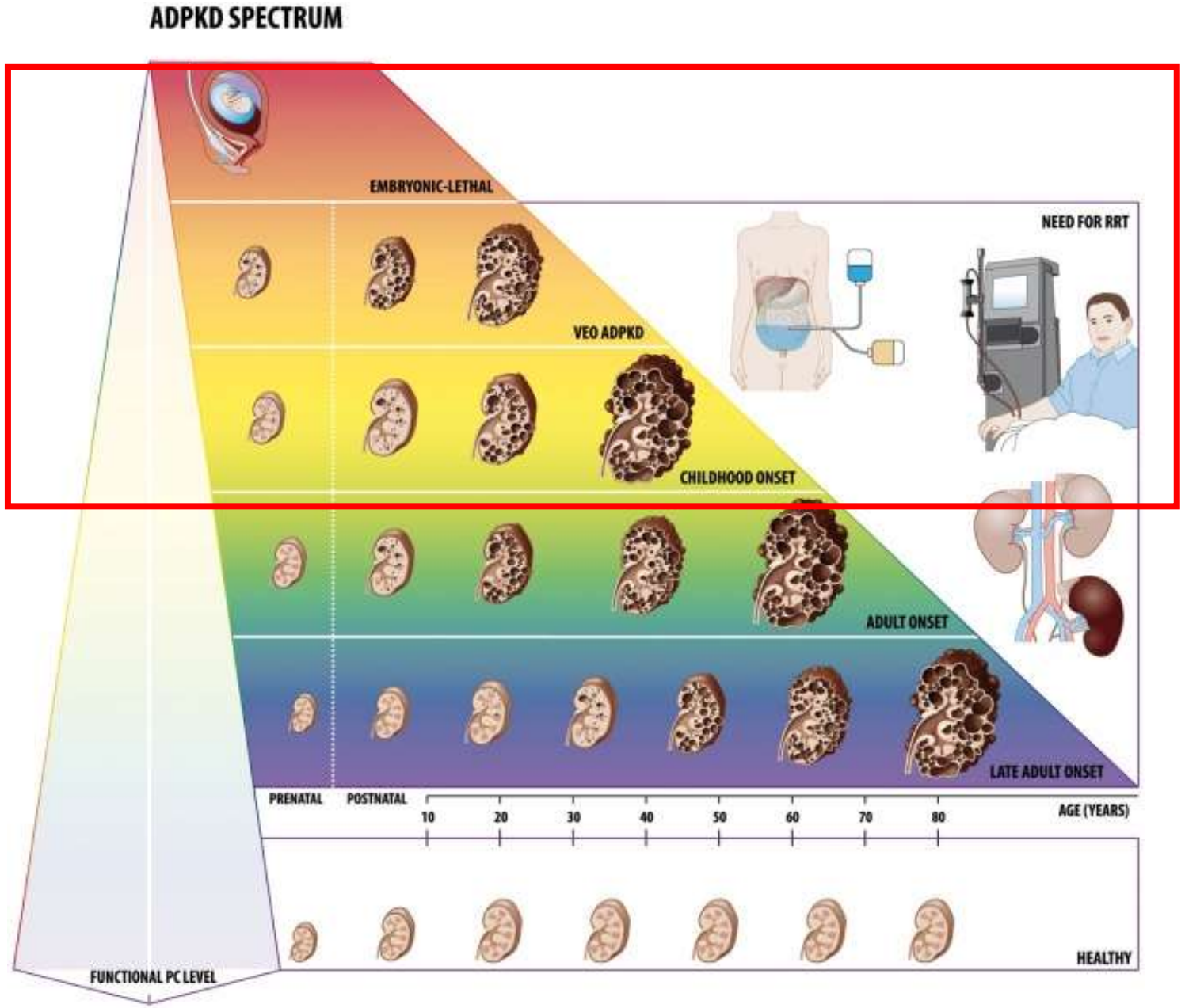
16.03.19

The clinical spectrum in ADPKD children



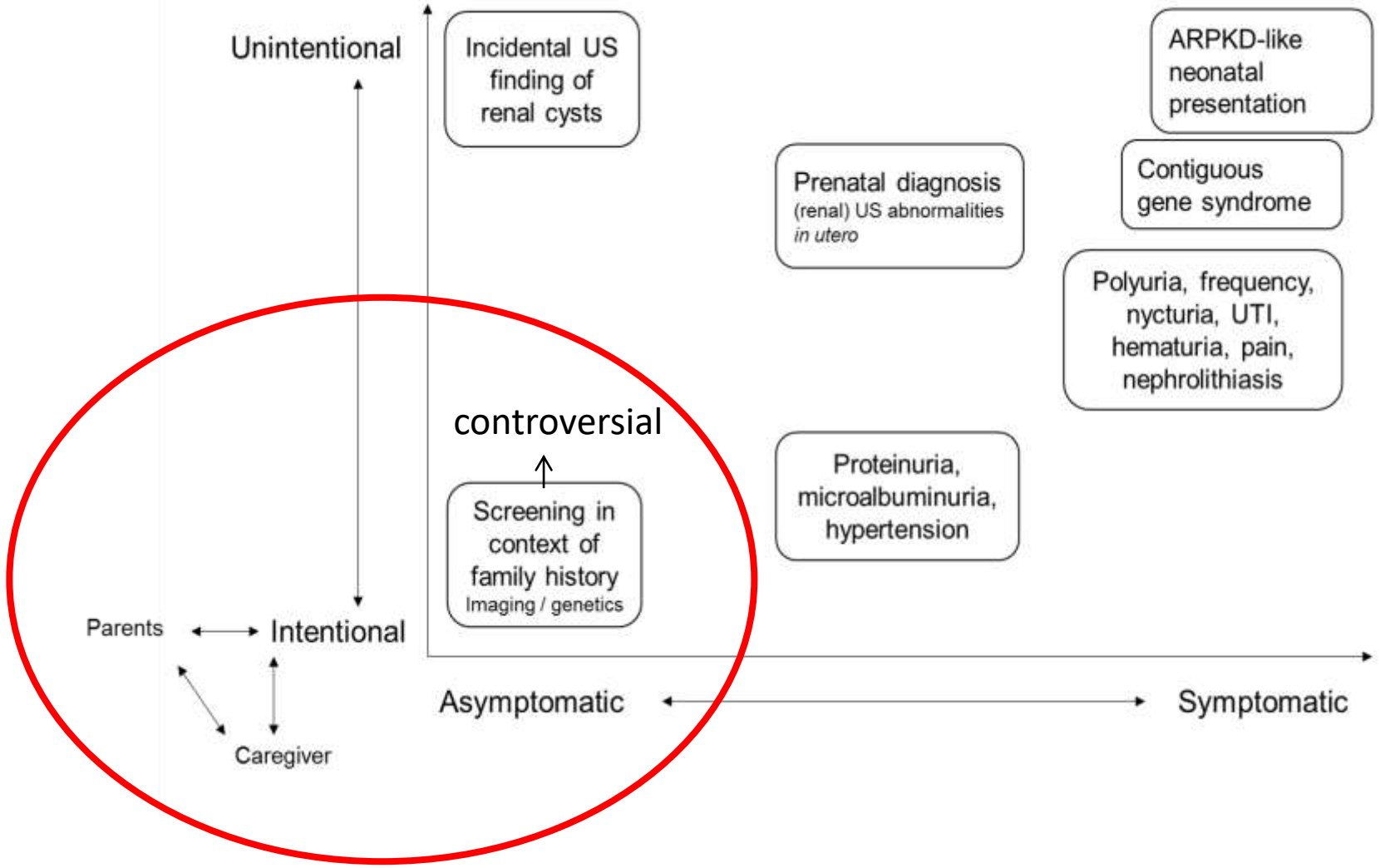
De Rechter S et al. 2018

The clinical spectrum in ADPKD children



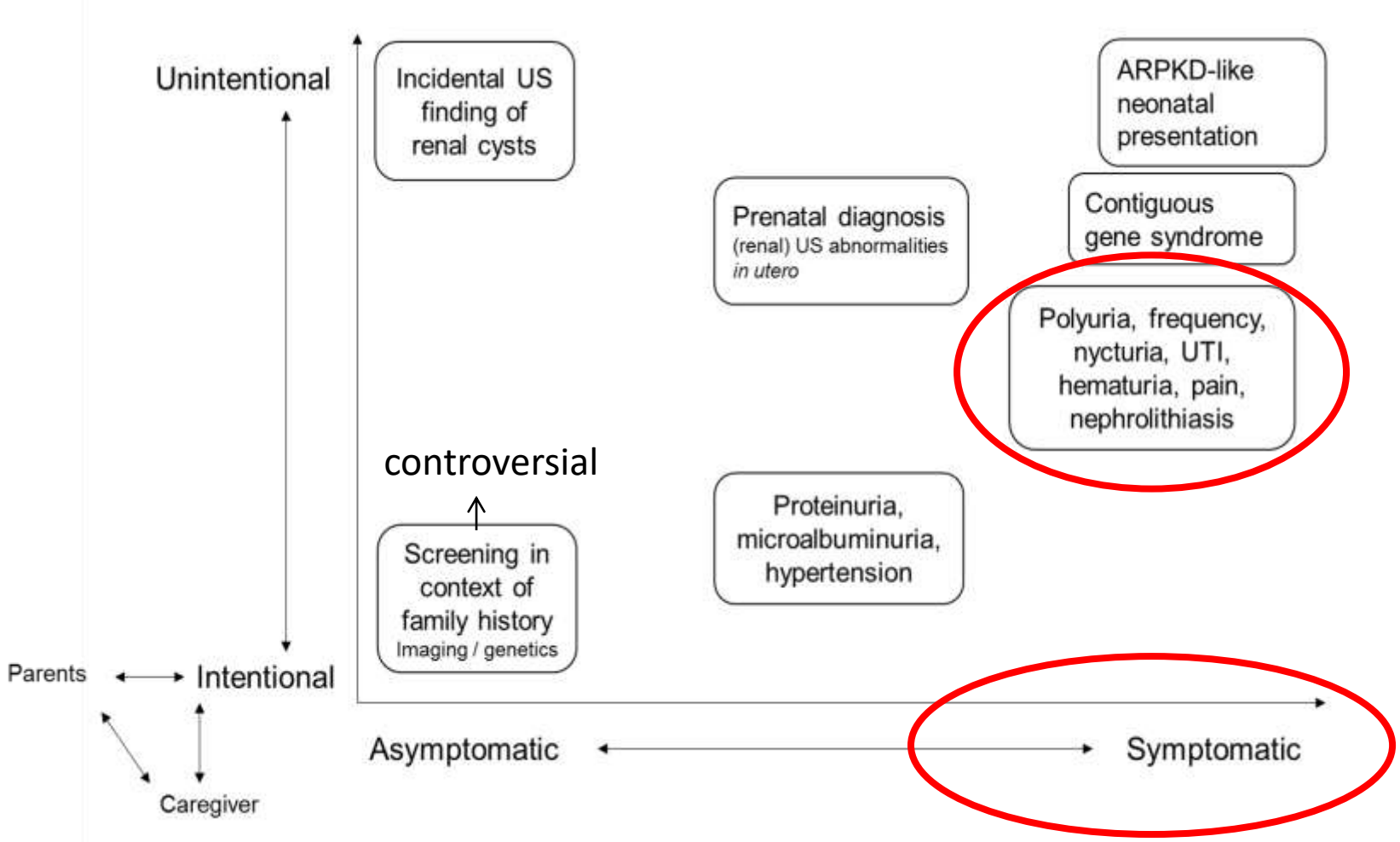
De Rechter S et al. 2018

Diagnosing ADPKD in children



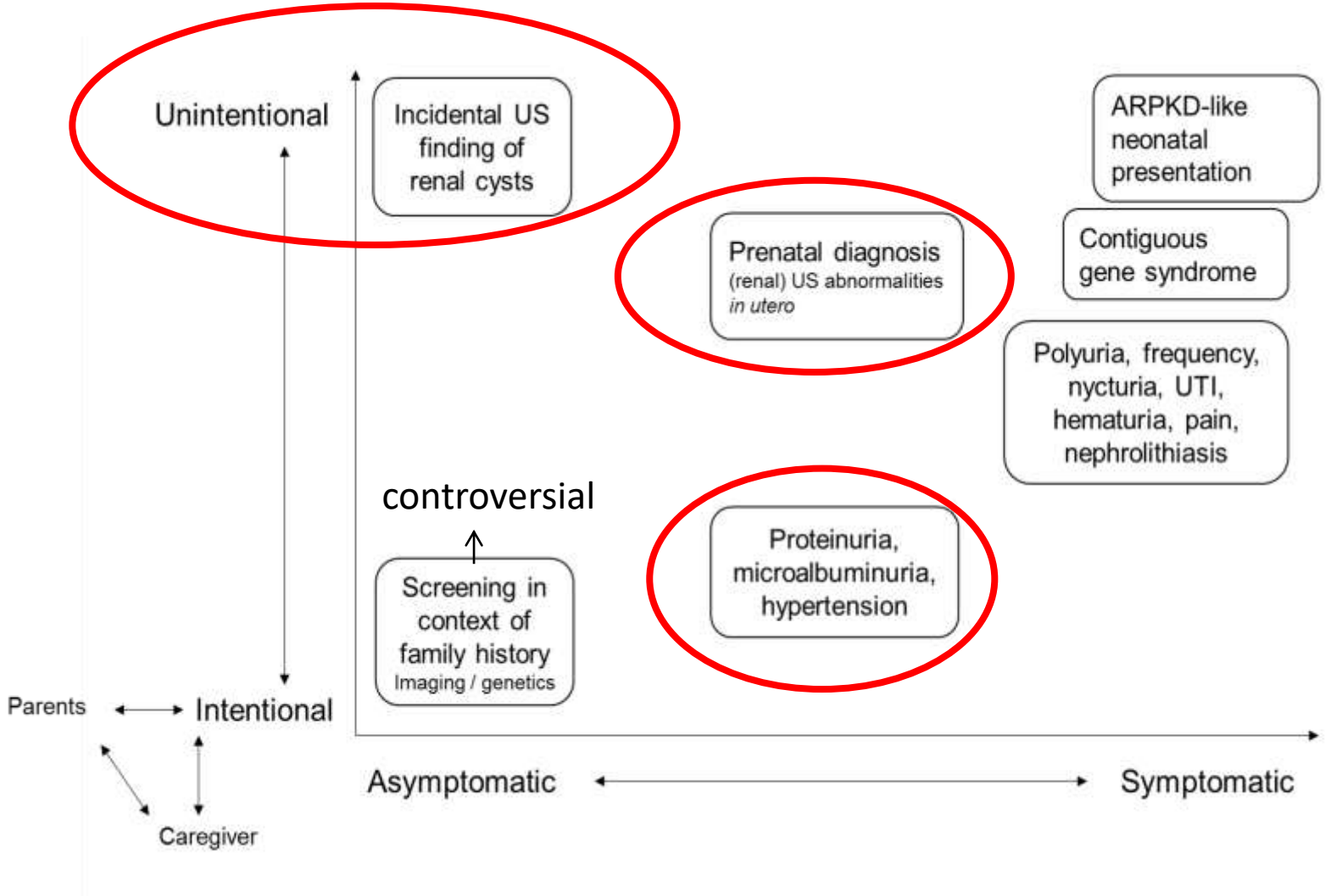
De Rechter et al. 2018

Diagnosing ADPKD in children



De Rechter et al. 2018

Diagnosing ADPKD in children



De Rechter et al. 2018

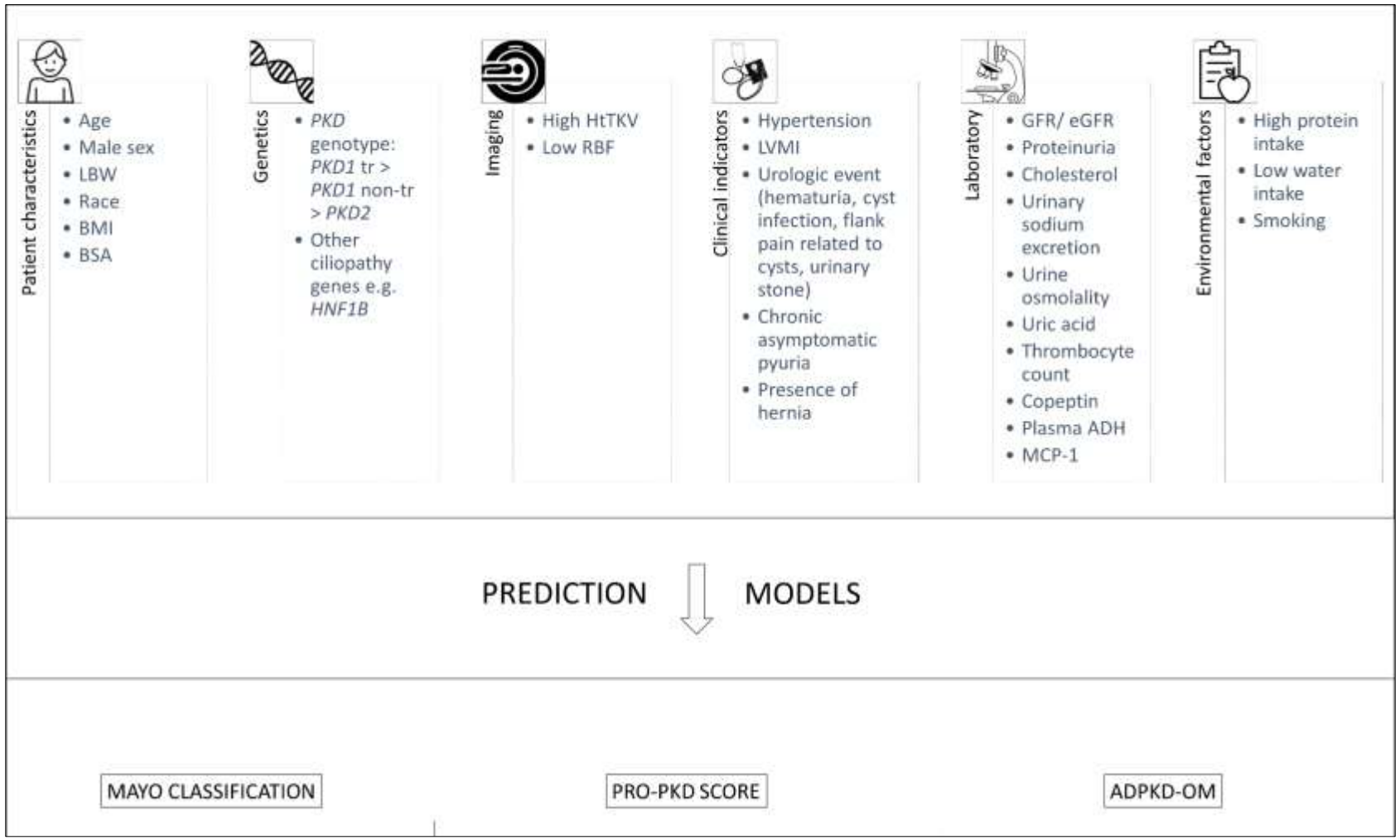
Introduction: Childhood ADPKD

- 2-5% of ADPKD patients present in childhood
- No guidelines available
- Pediatric data are scare and only derived from small cohorts

=> Controversies on the diagnosis and management in children

Chapman *et al.*, KI, 2015
Harris *et al.*, NDT, 2017
De Rechter et al., 2018

Prognosis prediction tools in ADPKD adults



De Rechter *et al.*, Clin Kidney J, 2018
Irazabal *et al.*, J Am Soc Nephrol, 2015

ADPedKD registry: Online Platform on the management of Children with ADPKD

Aims:

1. To generate data on incidence – presentation (eg. comorbidities) in childhood

2. To define a pediatric scoring system, after identification of progression factors -> stratify patients early into low and high-risk categories

3. To assess the effect of early treatment of hypertension and proteinuria on long-term renal outcome

4. To provide international guidelines for work-up, follow-up and treatment of ADPKD in childhood

ADPedKD: A Global initiative

Global Executive Committee and Regional Operational Committees

Africa (N.A. Soliman)

Asia (I. Liu)

Australia (A.J. Mallett)

Europe (D. Mekahli, S. De Rechter, F. Schaefer, M.C. Liebau)

North America (L.M. Guay-Woodford)

South America (L.C. Sylvestre)

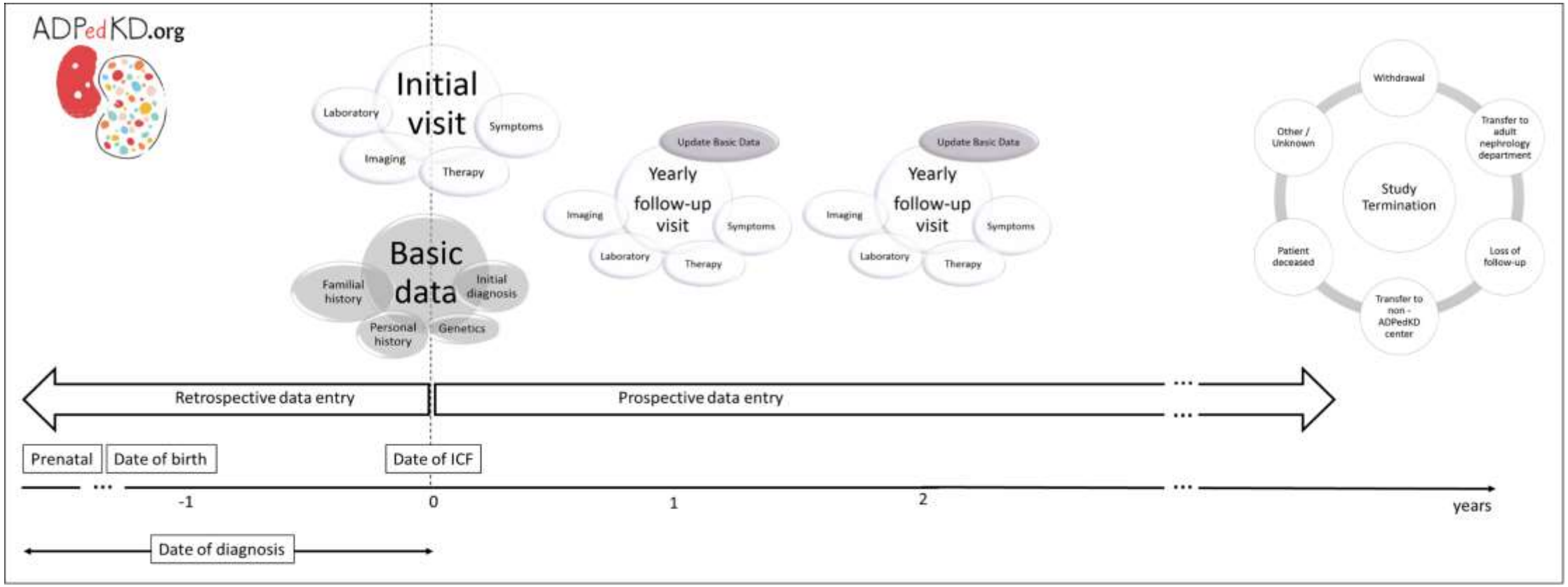
United Kingdom (D. Bockenhauer, T. Harris)

NIH-funded Hepato-Renal Fibrocystic Disease (HRFD) Database

ADPedKD global

National Registry of Rare Kidney Diseases (RaDaR)

Australasian Registry of Rare and genetic Kidney disease (ARRK)



Genotype – phenotype correlation - Incidence and presentation of comorbidities - Current medical practice information - Familial recurrence risk

Recommendations regarding modifiable risk factors

Identification of clinical / bio-markers predicting early disease progression

Current status: www.ADPedKD.org

68 centers

28 countries

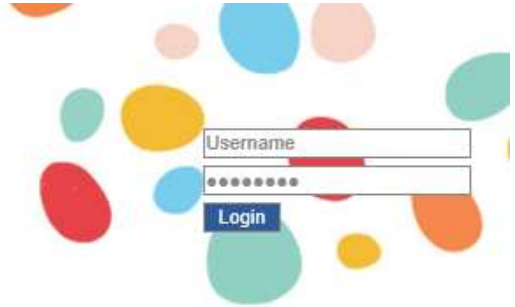
Included patients

N = 460

www.ADPedKD.org

ADPedKD

Downloads



About ADPedKD
- How to use ADPedKD
- Links & Literature
- Registration form
- **Downloads**

ADPedKD global

Participating centers

Contact

Imprint

Privacy Policy

Supported by

GPN Gesellschaft für Pädiatrische Nephrologie

A small handbook on how to use ADPedKD

How_to_use_ADPedKD.pdf

Patient Information and Informed Consent Forms

Please choose the appropriate patient information and informed consent form. The Dutch, English and French (Belgium) versions have been reviewed and approved by the Ethics Committee of the University Hospital of Leuven. The French (France) versions have been approved by the Comité d'éthique du CHU de Lyon.The German versions have been approved by Ethikkomission Uniklinik Köln. The Italian versions have been approved by Comitato Etico Milano Area 2.

Please note these may require revision by your local Ethics Committee.

Dutch

Patient_Information_and_Informed_Consent_ADPedKD_-18j_NL.pdf

Patient_Information_and_Informed_Consent_ADPedKD_adult_NL.pdf

Patient_Information_and_Informed_Consent_ADPedKD_parent_NL.pdf

English

Patient_Information_and_Informed_Consent_ADPedKD_-18j_ENG.pdf

Patient_Information_and_Informed_Consent_ADPedKD_adult_ENG.pdf

Patient_Information_and_Informed_Consent_ADPedKD_parent_ENG.pdf

French (Belgium)

Patient_Information_and_Informed_Consent_ADPedKD_-18j_FR.pdf

12 languages

Questions?

https://www.adpedkd.org/

djalila.mekahli@uzleuven.be

PKD International

european society for paediatric nephrology

ADPedKD

European Reference Network for rare or low prevalence complex diseases

Network Kidney Diseases (ERKNet)

#ADPKD
@PKD_Int

Latest updates on the Standardised Outcomes in Nephrology Polycystic Kidney Disease (SONG-PKD) study

David Baron
(PKD Foundation, USA)

EU ADPKD Patient Symposium

16 MARCH 2019

DAVID A. BARON, PHD

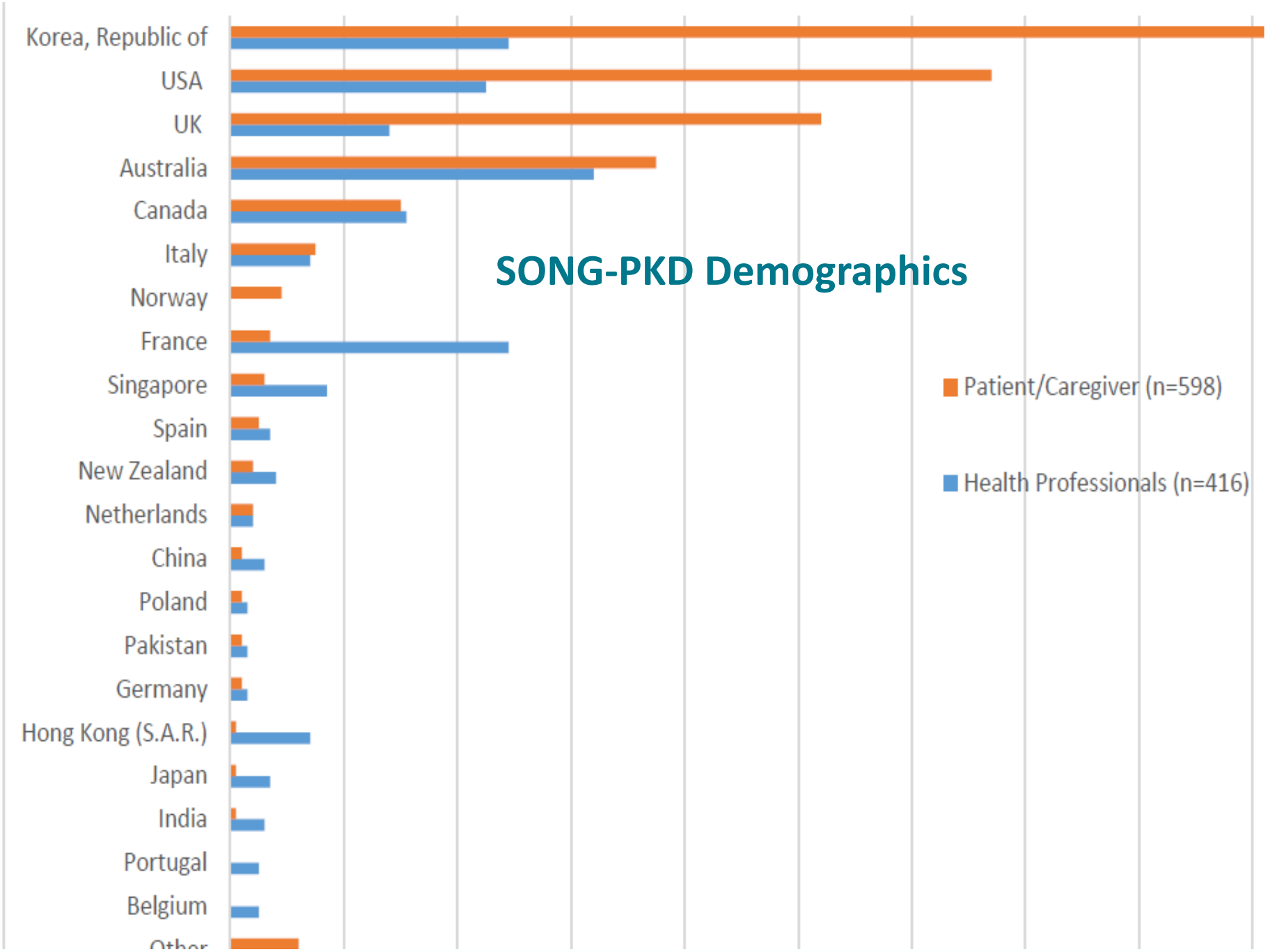
PKD FOUNDATION
Polycystic Kidney Disease

SONG-PKD

Hierarchy of Outcomes

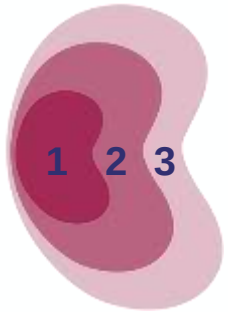
1) Core Outcomes
2) Middle Tier
3) Outer Tier

SONG-PKD Demographics



No	Outcome How important is this outcome for research in polycystic kidney disease?	Limited importance			Important, but not critical			Critical importance			
		1	2	3	4	5	6	7	8	9	Unsure
1	Kidney function Ability of the kidney to remove waste from the body and balance fluids (could be measured by creatinine in the blood)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
2	Cardiovascular disease Disease of the heart and blood vessels e.g. heart attack, stroke	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
3	Lipids Levels of cholesterol or fat in the blood	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
4	Blood pressure The number to indicate the pressure in the arteries, high (hypertension) or low (hypotension) blood pressure	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
5	Death Number of people who die, risk of death, how long the patient will live	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
6	Weight change Loss or gain in body weight (not because of fluid)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
7	Cyst size/growth Increase in the size of cysts in kidneys	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
8	Impact on family/friends On-going impact that living with a patient with polycystic kidney disease has on family, caregivers, and friends	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
9	Depression Strong feelings of sadness, hopelessness, despair for most of the time, over a long time	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
10	Ability to do usual activities Such as work, study, hobbies, etc.	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

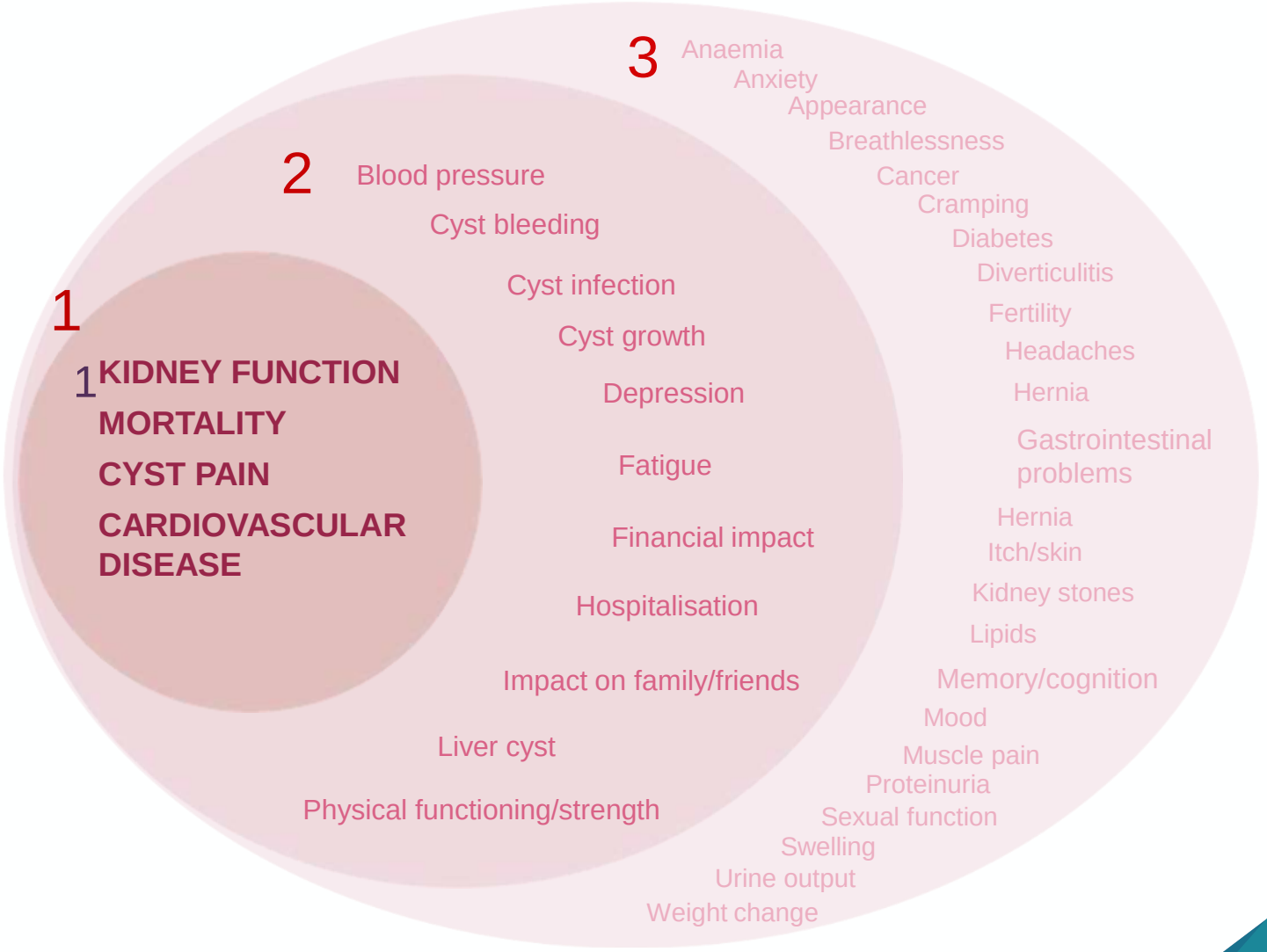
SONG-PKD (Preliminary)



1 CORE OUTCOMES
Critically important
to all stakeholder groups
Report in all trials

2 MIDDLE TIER
Critically important to
some stakeholder groups
Report in some trials

3 OUTER TIER
Important to some or
all stakeholder groups
Consider for trials



CORE OUTCOMES (TIER 1)

KIDNEY FUNCTION

MORTALITY

CYST PAIN

CARDIOVASCULAR DISEASE

MIDDLE TIER

Blood pressure

Cyst bleeding

Cyst infection

Cyst Growth

Depression

Fatigue

Financial impact

Hospitalization

Impact of family/friends

Liver cysts

Physical functioning/strength

Outer Tier

Anemia
Anxiety
Appearance
Breathlessness
Cancer
Cramping
Diabetes
Diverticulitis
Fertility
Headaches
Hernia
GI problems
Itch/skin
Kidney stones
Lipids
Memory/cognition
Mood
Muscle pain
Proteinuria
Sexual function
Swelling
Urine output
Weight change

Individual Patient Perspective

- **Apparent that only some outcomes pertain to an individual patient**
- **Middle tier and outer tier outcomes may be CORE outcomes to an individual patient**
- **CORE outcomes may not pertain to individual patients**
  - Kidney function may remain normal for years after diagnosis
  - Declines in kidney function may be asymptomatic
  - Cyst pain is not universal
  - Cardiovascular disease, i.e., bicuspid aortic valve, ascending aortic aneurysm may remain undiagnosed for years after diagnosis

PKD Foundation

- Patient-reported registry in planning phase
- Overlap with SONG-PKD Core Outcomes
- Incentive for longitudinal patient reporting
- Tool for clinical trial recruitment
- Initially US and Canada

#ADPKD
@PKD_Int

Breakout 1

Self-care and risk reduction

PKD International

EAF European ADPKD Forum

Summit sponsors
This event has been made possible by sponsorship from
Baxter, Otsuka Pharmaceutical Europe Ltd, Palladio Biosciences and Sanofi Genzyme.

Baxter Otsuka Palladio Biosciences Sanofi Genzyme

#ADPKD
@PKD_Int

BREAKOUT 1: Self-care and risk reduction

Tevfik Ecder

(Istanbul Bilim University, Turkey and EAF)

Djalila Mekahli

(KU Leuven, Belgium and EAF)

Moderator: ***Flavia Galletti*** *(AIRP Italy)*

European ADPKD Patient Summit

Saturday 16 March 2019

Novotel Brussels Airport Hotel, Brussels, Belgium

Self-care and Risk Reduction in Patients with ADPKD

Tevfik Ecder, MD

PKD International

EAF European ADPKD Forum

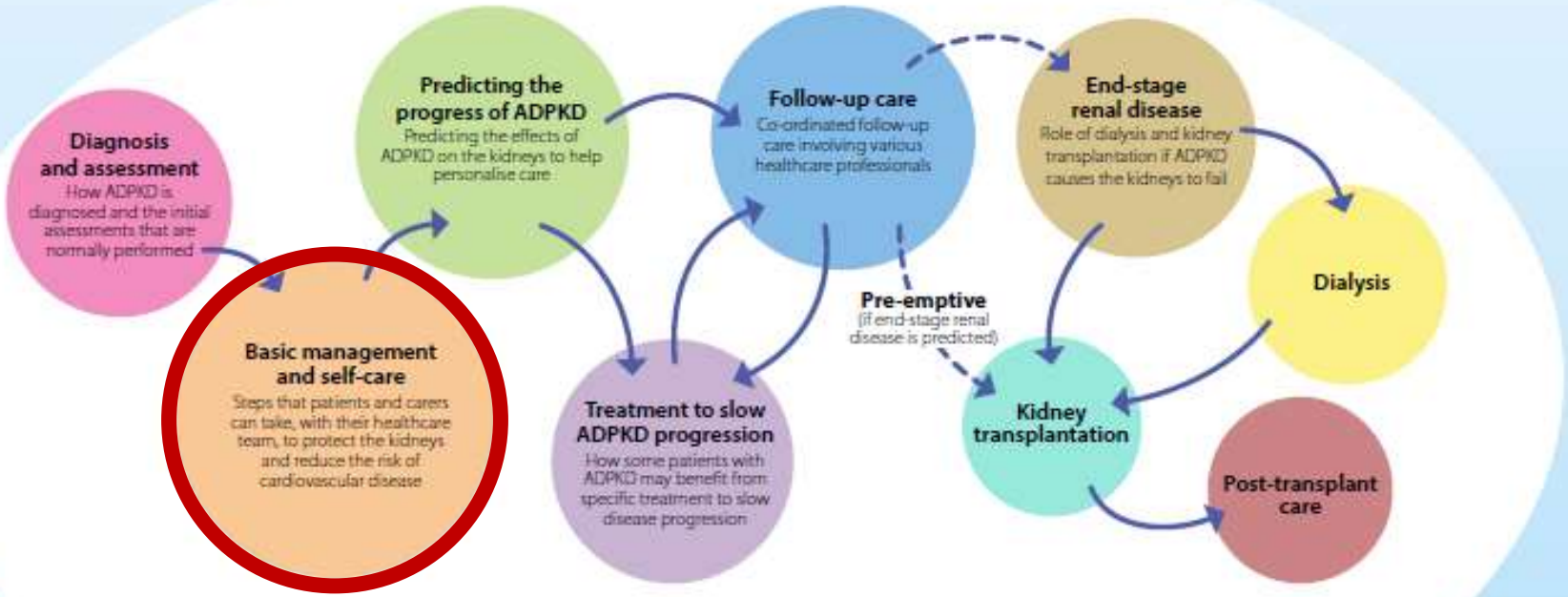
The ADPKD Patient Route Map

PKD International

EAF

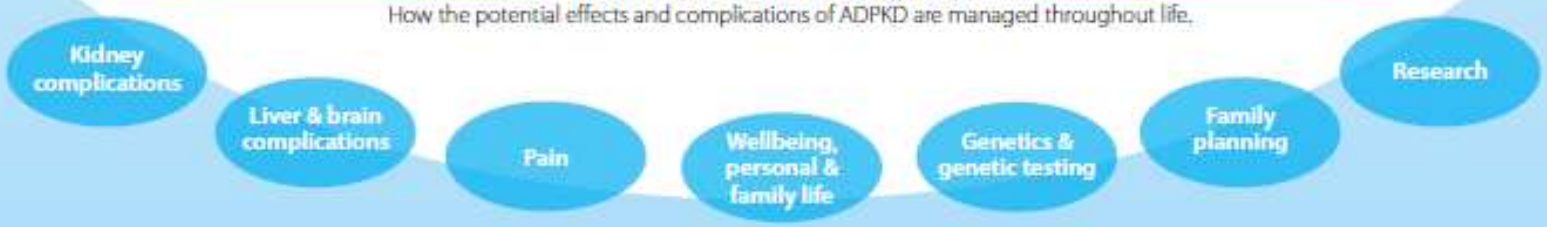
Please click on any bubble to move to that section.

Lifetime ADPKD care pathway



Ongoing care and support

How the potential effects and complications of ADPKD are managed throughout life.



General information

Basic management and self care

This section explains the steps patients can take, together with their healthcare team, to help protect their kidney function and reduce the risk of cardiovascular disease.

Lifestyle and diet

Few specific diet or lifestyle measures have yet been proven to prevent or slow the development of cysts in people with ADPKD. However, if you have ADPKD you can do many things that may help protect your kidney function and lower the risk of high blood pressure and cardiovascular disease.

Many of these are general healthy lifestyle measures also recommended for everyone else. They include:

- Drink more water to stay fully hydrated, which may protect kidney function in ADPKD.
- **Stop smoking. >**
- Maintain a healthy **body weight and do some form of regular exercise. >**
- Eat a healthy **diet. >**
- Drink less **caffeine. >** (e.g. in coffee or cola drinks) and less alcohol.

You might be advised to make other lifestyle and diet changes if you reach end-stage renal disease.

Focus on high blood pressure

Controlling long-term high blood pressure (hypertension) is very important because high blood pressure increases the risk of cardiovascular disease, such as heart attack and stroke. Controlling high blood pressure may also help to slow the growth of kidney cysts in some people with ADPKD. In people with brain aneurysms, controlling high blood pressure (and stopping smoking) can reduce the risk that the aneurysm will burst.

How can blood pressure be controlled?

If you have high blood pressure, the lifestyle and diet measures above are particularly important to reduce the risk of cardiovascular disease.

Doctors can also prescribe various **medicines >** to help control high blood pressure.

Regular **blood pressure checks >** are important to make sure treatment is working.

What do blood pressure readings and targets mean? >

Other risk factors

Your doctor may recommend you take other medicines to control **other risk factors >** for cardiovascular disease.

What about complementary or alternative therapies? >

Keeping it up!

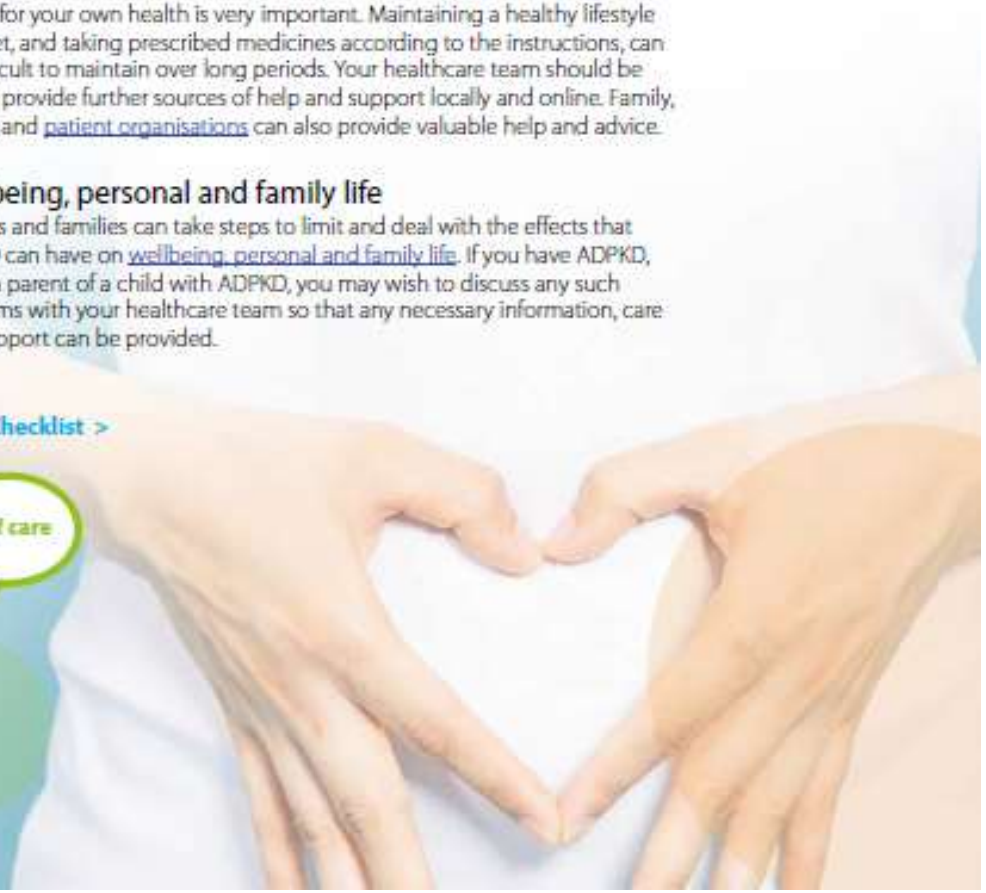
Caring for your own health is very important. Maintaining a healthy lifestyle and diet, and taking prescribed medicines according to the instructions, can be difficult to maintain over long periods. Your healthcare team should be able to provide further sources of help and support locally and online. Family, friends and patient organisations can also provide valuable help and advice.

Wellbeing, personal and family life

Patients and families can take steps to limit and deal with the effects that ADPKD can have on wellbeing, personal and family life. If you have ADPKD, or are a parent of a child with ADPKD, you may wish to discuss any such problems with your healthcare team so that any necessary information, care and support can be provided.

Checklist >

Self care



Clinical characteristics and predictors of progression of chronic kidney disease in autosomal dominant polycystic kidney disease: a single center experience

Abdullah Ozkok · Timur Selcuk Akpinar · Fatih Tufan · Nilufer Alpay Kanitez · Mukremin Uysal · Metban Guzel · Yasar Caliskan · Sabahat Alisir · Halil Yazici · Tevfik Ecder

Rapid Progressors (RP):
Median rates of decline in GFR
ΔGFR > 1ml/min/year.

Slow Progressors (SP):
Median rates of decline in GFR
ΔGFR < 1ml/min/year.

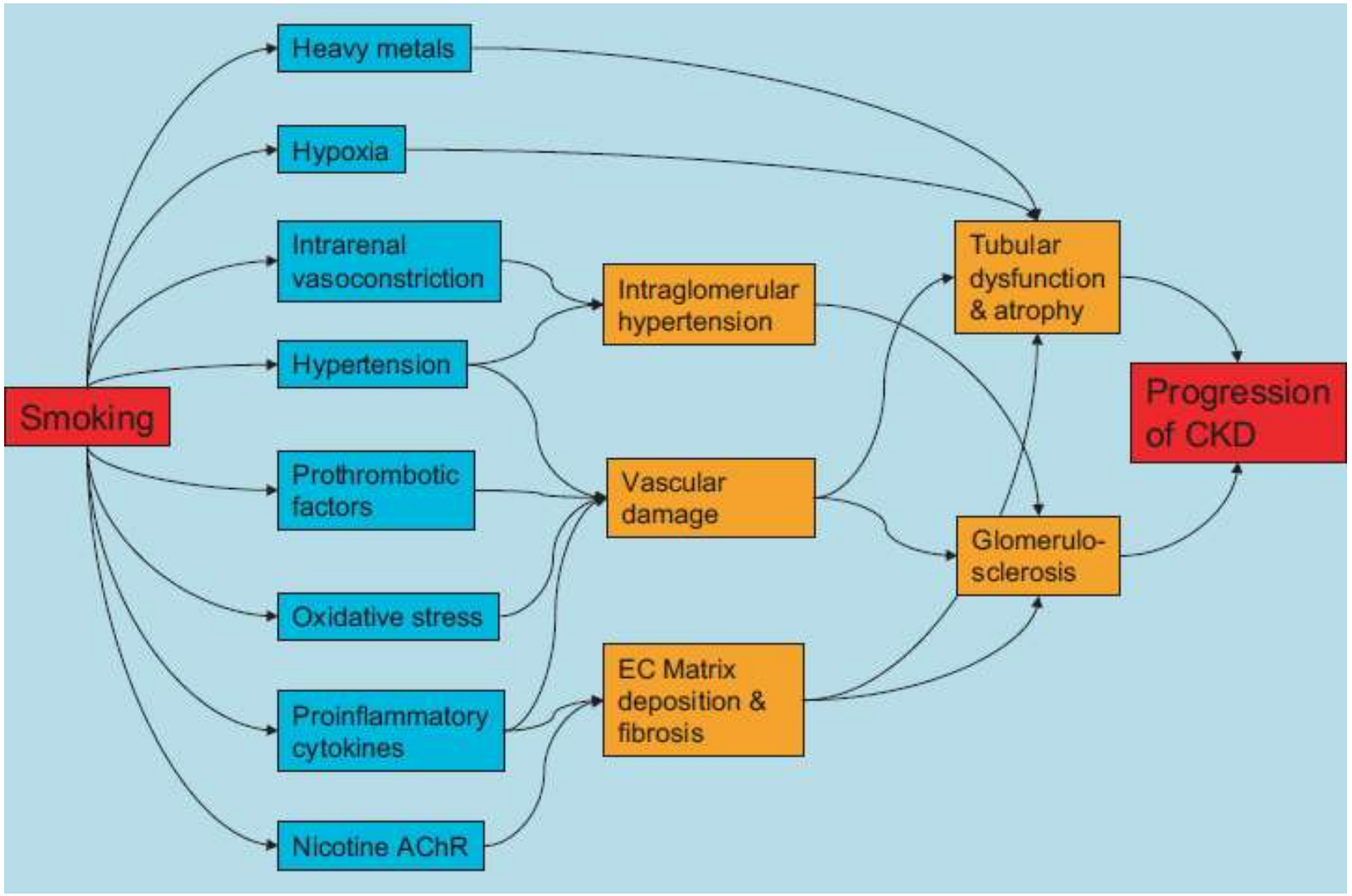
History of smoking and pack-year of cigarettes smoked were significantly higher in the RP compared to the SP group.

Table 3 Comparison results of the clinical characteristics and laboratory values of patients with rapid progressors and slow progressors

	Rapid progressors ($n = 93$)	Slow progressors ($n = 78$)	p values
Age	49 ± 13	49 ± 16	0.86
Sex (male/female)	33/60	29/49	0.81
FHX of ADPKD	62/88 (70 %)	51/73 (69 %)	0.93
Hypertension	81/93 (87 %)	61/78 (78 %)	0.12
History of MH	22/91 (24 %)	12/77(15 %)	0.16
History of UTI	22/91 (24 %)	16/76 (21 %)	0.63
History of urinary stones	29/91 (31 %)	26/77 (33 %)	0.79
New need of dialysis	18/93 (19 %)	3/78 (3 %)	<0.001
Hepatic cysts	36/92 (39 %)	27/77 (35 %)	0.58
Abdominal wall hernia	5/88 (5 %)	8/77(10 %)	0.26
History of smoking	31/84 (36 %)	14/74(18 %)	0.01
Smoking (pack-year)[a]	5.24 ± 1.20	3 ± 1.32	0.02

Ozkok et al: Clin Exp Nephrol 17: 345-351, 2013

Overview of Some Potential Mechanisms for Smoking-induced Renal Damage



Orth, Hasson: Clin J Am Soc Nephrol 3:226-236, 2009

Dietary salt restriction is beneficial to the management of autosomal dominant polycystic kidney disease

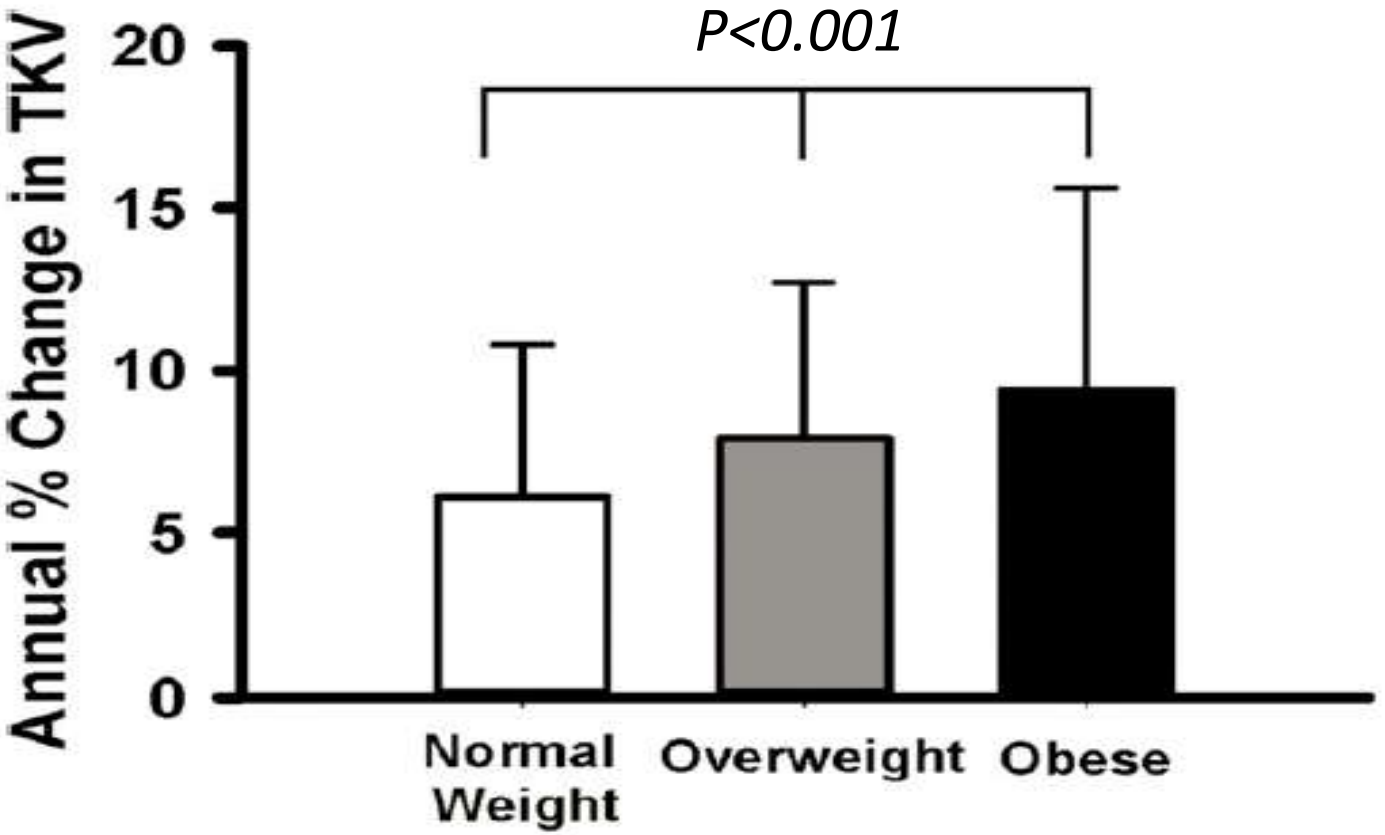
Vicente E. Torres[1], Kaleab Z. Abebe[2], Robert W. Schrier[3], Ronald D. Perrone[4], Arlene B. Chapman[5], Alan S. Yu[6], William E. Braun[7], Theodore I. Steinman[8], Godela Brosnahan[3], Marie C. Hogan[1], Frederic F. Rahbari[9], Jared J. Grantham[6], Kyongtae T. Bae[2], Charity G. Moore[10] and Michael F. Flessner[11]

respectively. In Study A, averaged and time varying urinary sodium excretions were significantly associated with kidney growth (0.43%/year and 0.09%/year, respectively, for each 18 mEq urinary sodium excretion). Averaged urinary sodium excretion was not significantly associated with faster eGFR decline (–0.07 ml/min/1.73m^2/year for each 18 mEq urinary sodium excretion). In Study B, the averaged but not time-varying urinary sodium excretion significantly associated with increased risk for the composite endpoint (hazard ratio 1.08 for each 18 mEq urinary sodium excretion) and a significantly faster eGFR decline (–0.09 ml/min/1.73m^2/year for each mEq 18 mEq urinary sodium excretion). Thus, sodium restriction is beneficial in the management of ADPKD.

Torres et al: Kidney Int 91: 453-500, 2017

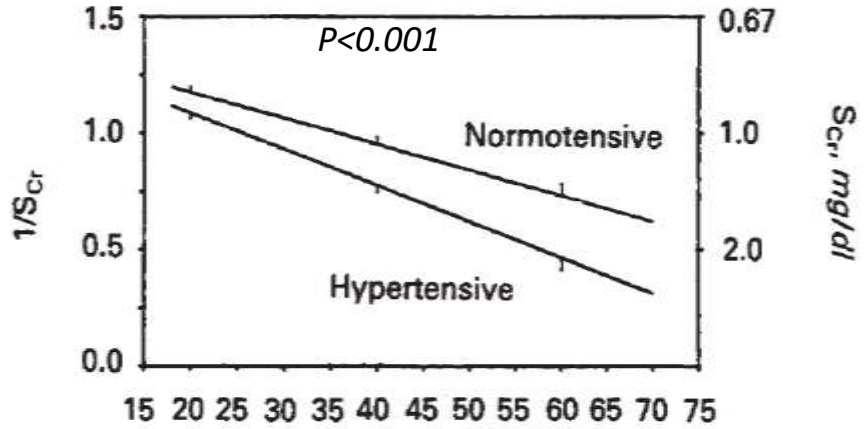
Overweight and Obesity Are Predictors of Progression in Early Autosomal Dominant Polycystic Kidney Disease

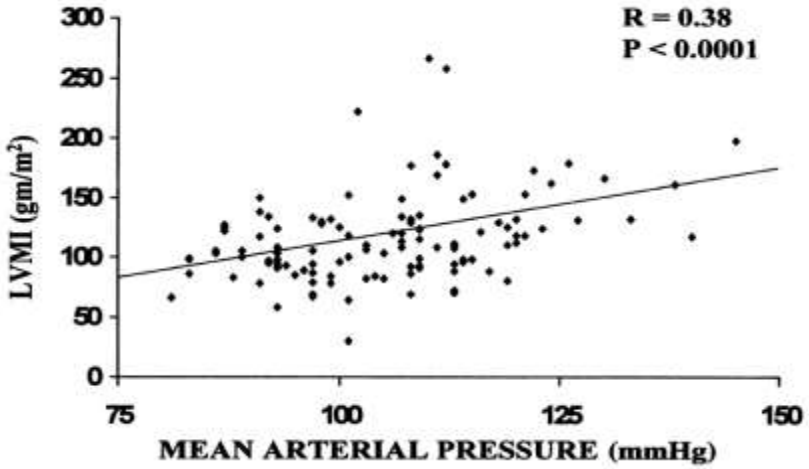
Kristen L. Nowak,[1] Zhiying You,[1] Berenice Gitomer,[1] Godela Brosnahan,[1] Vicente E. Torres,[2] Arlene B. Chapman,[3] Ronald D. Perrone,[4] Theodore I. Steinman,[5] Kaleab Z. Abebe,[6] Frederic F. Rahbari-Oskoui,[7] Alan S.L. Yu,[8] Peter C. Harris,[2] Kyongtae T. Bae,[9] Marie Hogan,[2] Dana Miskulin,[4] and Michel Chonchol[1]

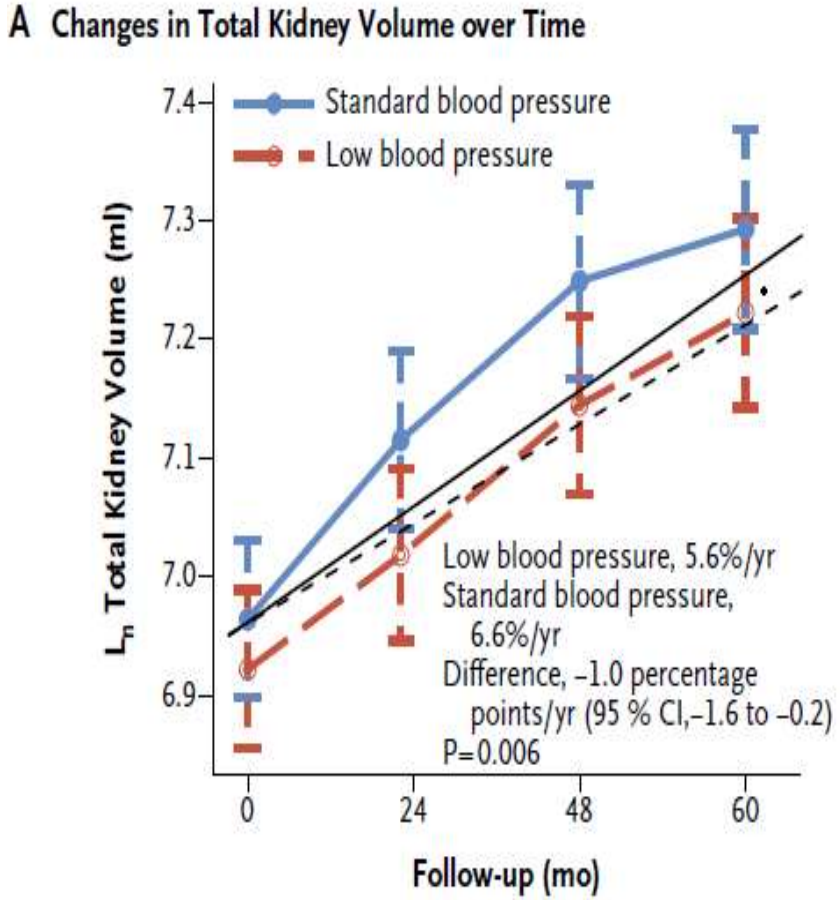


J Am Soc Nephrol 29: 571–578, 2018. doi: https://doi.org/10.1681/ASN.2017070819

Hypertension is Associated with Rapid Progression of ADPKD







Standard BP Target: 120/70 – 130/80 mm Hg

Low BP Target: 95/60 – 110/75 mm Hg

1.Gabow et al: Kidney Int 1992; 2. Chapman et al: J Am Soc Nephrol 1997; 3. Schrier et al: N Engl J Med 371: 2255-2266, 2014

Self-care and risk reduction for ADPKD children

Djalila Mekahli

ADPKD Patient Summit

16.03.19

ADPedKD

EAF
European ADPKD Forum

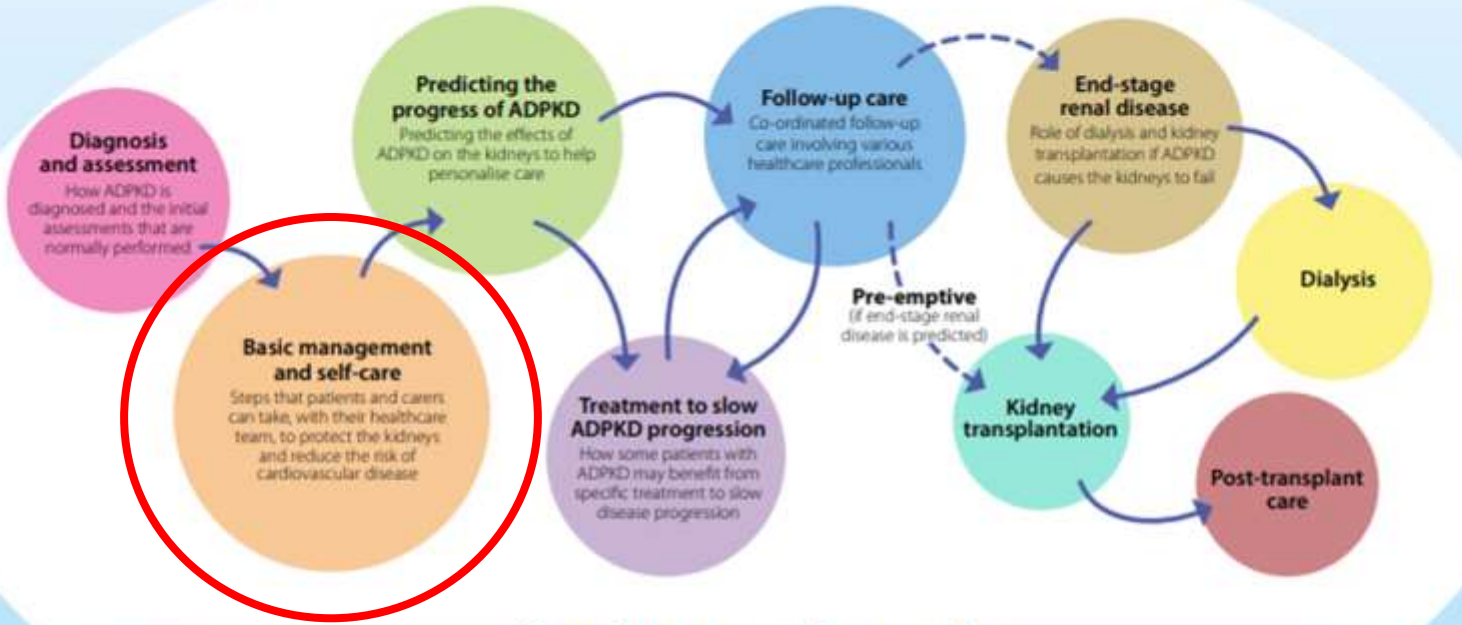
UZ LEUVEN
KU LEUVEN

The ADPKD Patient Route Map

PKD International EAF

Please click on any bubble to move to that section.

Lifetime ADPKD care pathway



Ongoing care and support

How the potential effects and complications of ADPKD are managed throughout life.

Kidney complications | Liver & brain complications | Pain | Wellbeing, personal & family life | Genetics & genetic testing | Family planning | Research

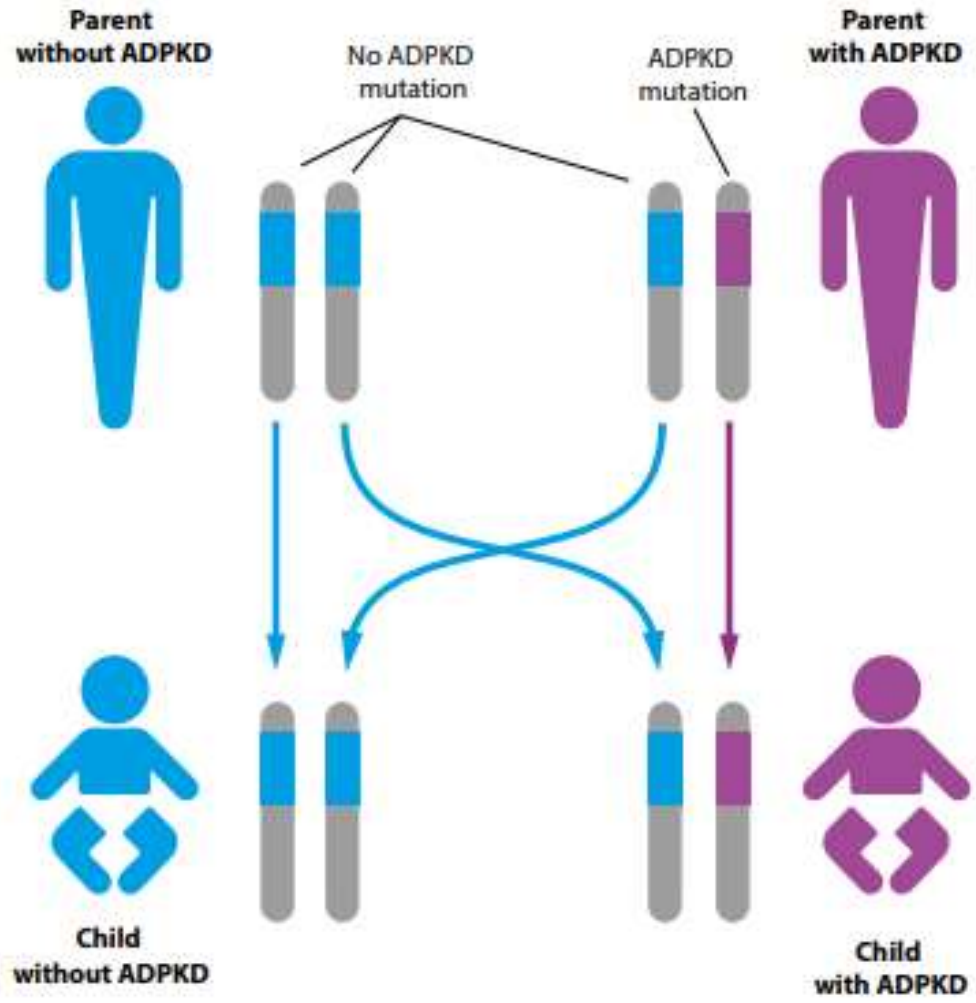
General information

Understanding ADPKD | Principles of ADPKD care | Information for health policymakers and providers | Patient organisations | Further reading | Authors and acknowledgements

Are there special issues for ADPKD children?

Are there special issues for children?

ADPKD is typically identified in adults, but it may also be diagnosed in children. Infants and children with kidney cysts should be referred to a paediatric nephrologist. ADPKD can be difficult to diagnose in children using imaging alone. A genetic test is sometimes used to confirm the diagnosis if imaging results are unclear.



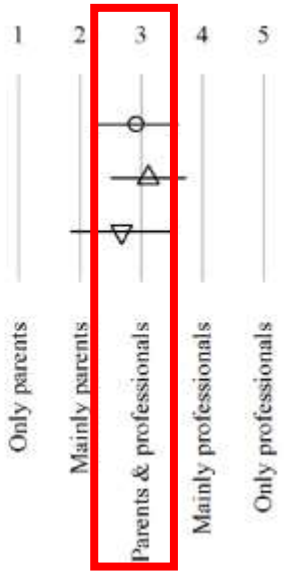
We all have two copies of most genes – one copy inherited from each parent

Each child with one parent with an ADPKD mutation has a 50% (1 in 2) chance of inheriting it

Responsibility of informing at-risk individuals about their genetic risk: Breakout 4

Who is responsible for ensuring that the minor is informed about his genetic risk for ADPKD at adulthood?

- ○ Adult Nephrologists
- △ Pediatric Nephrologists
- ▽ Geneticists



De Rechter S. *et al*, 2017

What about children and young people?

'Announcing the disease to my daughter was difficult, as one is bound to feel guilty for being responsible for transmitting a genetic disease to your child. Luckily, she seems to be coping with limited anxiety. Also, the fact that she is working in the health field will certainly provide her with further tools to confront her disease constructively.'

Corinne, France

'I found out I had a polycystic kidney when I was 40. I had three children, only one of whom is affected by the disease… At the beginning we chose not to say anything about the disease until they were 18 years old.'

Roberto, Italy

'Avoid overprotection in teenagers, they are normal and healthy people even with ADPKD. They need information and education for the future, but it takes time to accept things and go to the doctor, it's a personal decision the right time to cope with it.'

Ricardo, Spain

Deciding about me

'No decision about me, without me!'

Daniel, Spain

Basic management and self care ……for children

Blood pressure checks

The standard blood pressure target for people with ADPKD is a reading no higher than 140/90 mmHg. However, the target should be personalised, taking into account age and other diseases. It may help if you know your own blood pressure target and to monitor it at home. You should discuss with your doctor what action you should take if your readings are higher than your target.

You can measure your own blood pressure at home using simple electronic devices. In certain situations, you might be given a special device to continuously monitor your blood pressure for a period at home.

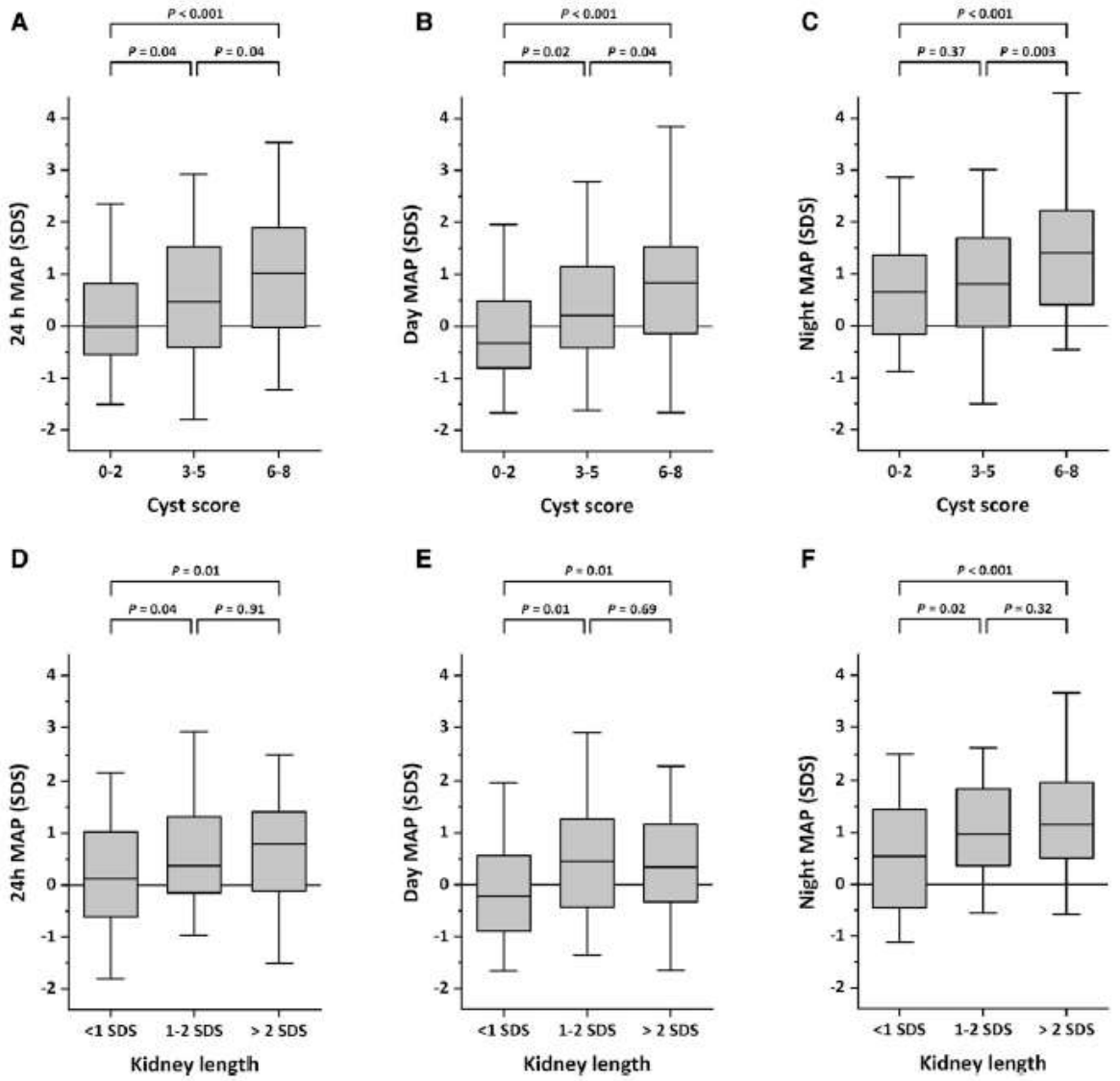
This can help to provide further information about your blood pressure at different times of the day. It is important to learn how to take these measurements properly and to provide your doctor with the measurements at your clinic visit.

Medicines to control high blood pressure

Many different types of medicines (sometimes called 'antihypertensive' drugs) can be used to treat high blood pressure. Doctors consider various factors when choosing a blood pressure medicine for an individual, including the presence of other diseases.

Usually, medicines called angiotensin converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs) are the recommended first choices for people with ADPKD. ACE inhibitors have names ending in 'pril', such as enalapril, lisinopril, perindopril and ramipril. ARBs have names ending in 'sartan', such as candesartan, irbesartan, losartan and telmistartan.

If these are not appropriate, or if additional medicines are necessary, then other medicines called beta-blockers, diuretics or calcium channel blockers may be considered depending on the individual circumstances. Your doctor might prescribe a combination of medications to control your blood pressure.



310 ADPKD (mean age of 11.5±4.1 years)

Massella L. 2018

Basic management and self care ……for children

Aspects of ADPKD management[2,13,21,22]

- *Blood pressure control – protects against cardiovascular disease and slows kidney growth*
- *Increased water intake – **may** protect kidney function*
- *Dietary salt restriction – to help control blood pressure and possibly may help protect the kidneys*
- *Dietary protein restriction (at Stage 4 chronic kidney disease with severe decline in kidney function) – to avoid waste products of metabolism accumulating in the blood*
- *Avoid high caffeine intake (which **may** promote cyst growth)*
- *Weight control, including exercise*
- *Symptom management: e.g. pain*
- *Management of kidney complications: infection, kidney stones, bleeding into cysts*
- *Avoidance of activities that risk injuring the kidneys, such as contact sports*
- *Management of other manifestations: e.g. liver cysts*
- *Management of other cardiovascular risk factors, e.g. cholesterol*
- *Renal replacement therapy: transplantation or dialysis*

Body weight and exercise

Maintaining a healthy body weight and regularly exercising are recommended to help prevent and control high blood pressure.

Exercise: this can include walking, gardening, dancing and all kinds of sports – although it may be sensible to avoid high contact sports to avoid trauma to the kidneys.

Smoking

Smoking cessation helps to reduce the risk of cardiovascular disease (i.e. coronary heart disease and stroke) and cancer. Practical help and support to stop smoking may be available.

Caffeine

Keeping caffeine intake to a moderate level (2 cups of coffee or 4 cups of tea, per day) may be advisable for general cardiovascular health, although there is no evidence that it affects kidney cyst growth in ADPKD.

Diet

Salt reduction

Recent research showed that higher dietary salt intake caused greater kidney growth in patients with ADPKD. The researchers studied data from 'HALT-PKD', a clinical trial of the effect of certain blood pressure medicines on the progression of ADPKD. They concluded that moderate salt restriction (to no more than 6 g a day) is beneficial in ADPKD, but you should not remove salt from your diet entirely. You may be referred to a dietician to provide a diet plan.

The recommended salt levels are lower for children.

Age	Salt per day (sodium equivalent)
1–3 years	2 g (0.8 g)
4–6 years	3 g (1.2 g)
7–10 years	5 g (2 g)
11 years and over	5–6 g (2–2.4 g)

Moderate protein

There is no good evidence that low-protein diets slow the progression of ADPKD. Adults with ADPKD are advised to eat the same, moderate amount of protein (0.75–1.0 g per kg of body weight per day) recommended for the general population. Guidelines for general chronic kidney disease care recommend that adults eat no more than 0.8 g of protein per kg of body weight daily when their estimated glomerular filtration rate (eGFR; see kidney function tests) falls below 30 ml/min/1.73 m^2. People at risk of CKD progression are recommended to avoid a high protein intake (>1.3 g/kg/day). Any restriction on dietary protein should preferably involve education by a renal dietician and monitoring to avoid malnutrition.

Fibre

Eating plenty of fibre in the diet may help to prevent diverticular disease.

Sources

See Further reading. Some patient organisation websites provide further information about diet and ADPKD.

ADPKD patients day


ZOUT


ZOUT
BUDGET PACK

Thanks to the children

#ADPKD
@PKD_Int

Breakout 2

Predicting the progress of ADPKD

PKD International

EAF European ADPKD Forum

Summit sponsors
This event has been made possible by sponsorship from
Baxter, Otsuka Pharmaceutical Europe Ltd, Palladio Biosciences and Sanofi Genzyme.

Baxter Otsuka Palladio Biosciences Sanofi Genzyme

#ADPKD
@PKD_Int

BREAKOUT 2: Predicting the progress of ADPKD

Ron Gansevoort

(University Medical Center Groningen, Netherlands and EAF)

Lea Münkner

(PKD Familiäre Zystennieren e.V. , Germany)

Groningen PKD Expertise Center

Predicting the progress of ADPKD

Ron Gansevoort
Chair PKD Expertise Center
University Medical Center Groningen
The Netherlands

Conflict of Interest
Consultant for Otsuka, Ipsen and Sanofi-Genzyme

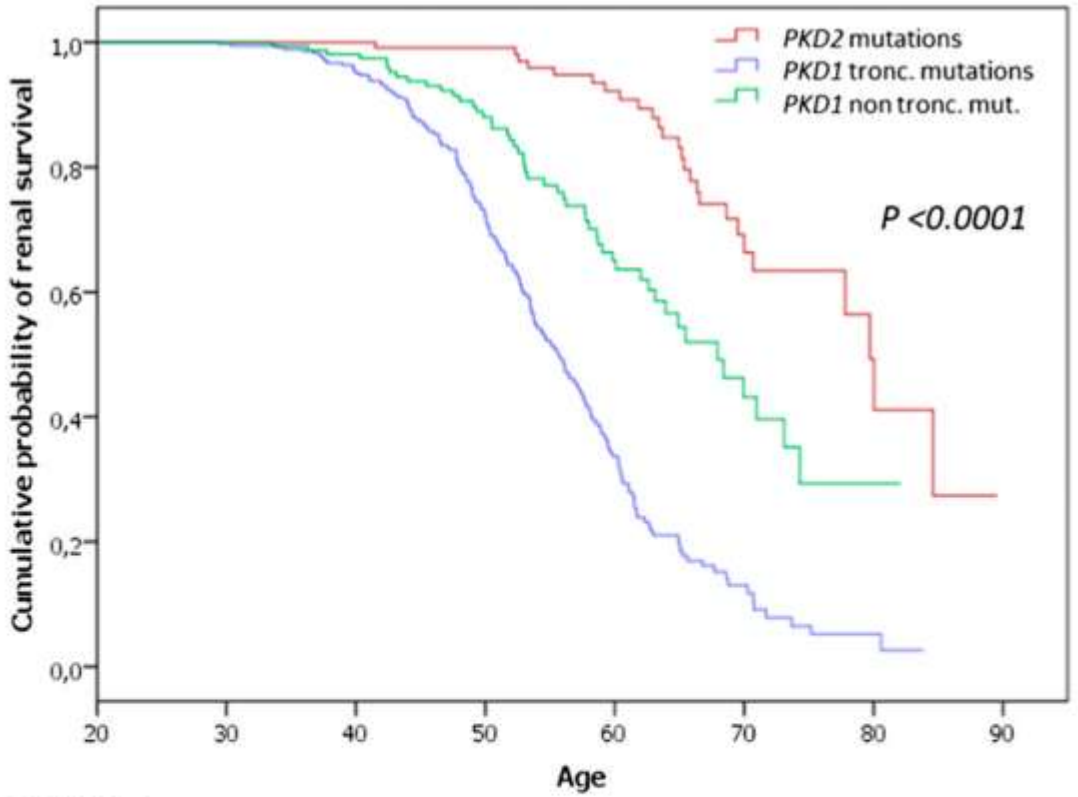
Why would we like to know prognosis?

- **Patients want to know:**
  - Social planning
    E.g.: Buy that new house?
  - Career planning
    E.g.: Do those extra courses? Go for that new job?
  - Family planning
    E.g.: Refrain from having children? IVF with Pre-implantation Genetic Diagnosis?

- **Doctors want to know:**
  - To select patients for trials or for treatment with disease modifying drugs (like V2RAs and SSAs)
    Patients with rapidly progressive disease are likely to have a better efficacy to safety ratio of these drugs

Groningen PKD Expertise Center

PKD mutation analysis to assess prognosis

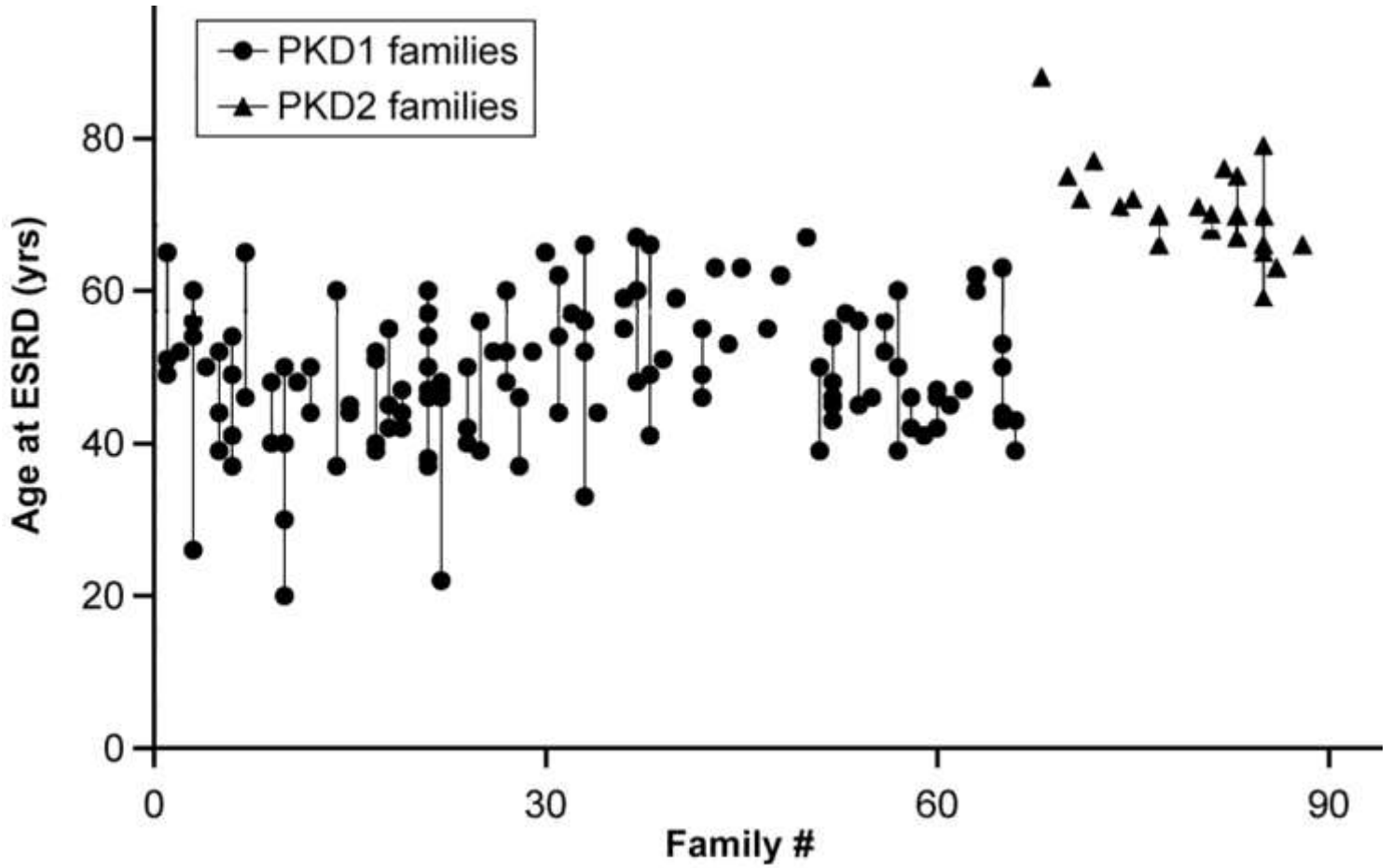


Patients at risk :						
PKD1 truncating mutations (n=387)	356	296	175	53	11	2
PKD1 non truncating mutations (n=184)	172	144	134	48	15	1
PKD2 Mutations (n=133)	127	116	99	63	23	5

Cornec-Le Gall *et al. J Am Soc Nephrol* 2013;24:1006–1013.

Groningen PKD Expertise Center

Assessing prognosis
Even within families large variability



Barua *et al*,
J Am Soc Nephrol 2009;20:1833-8

The PRO-PKD Score

Clinical or Genetic Factors	Score
Male	1 point
Hypertension <35 years of age	2 points
First urologic event <35 years of age	2 points
PKD2 mutation	0 points
Non-truncating PKD1 mutation	2 points
Truncating PKD1 mutation	4 points

Three risk categories:

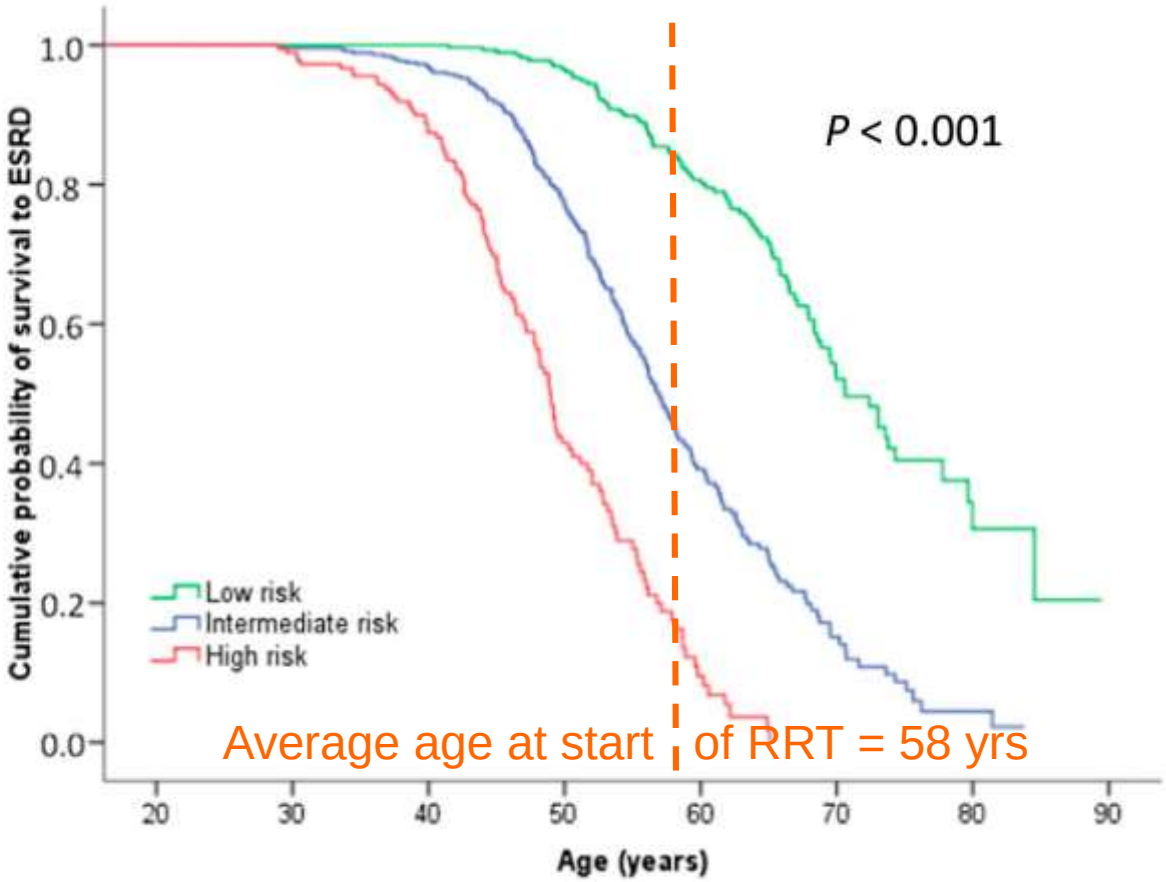
Low risk	0–3 points
Intermediate risk	4–6 points
High risk	7–9 points

The PRO-PKD score is of limited value in subjects <35 years and in subjects with a late diagnosis

Cornec-Le Gall *et al. J Am Soc Nephrol* 2015

Groningen PKD Expertise Center

The PRO-PKD Score

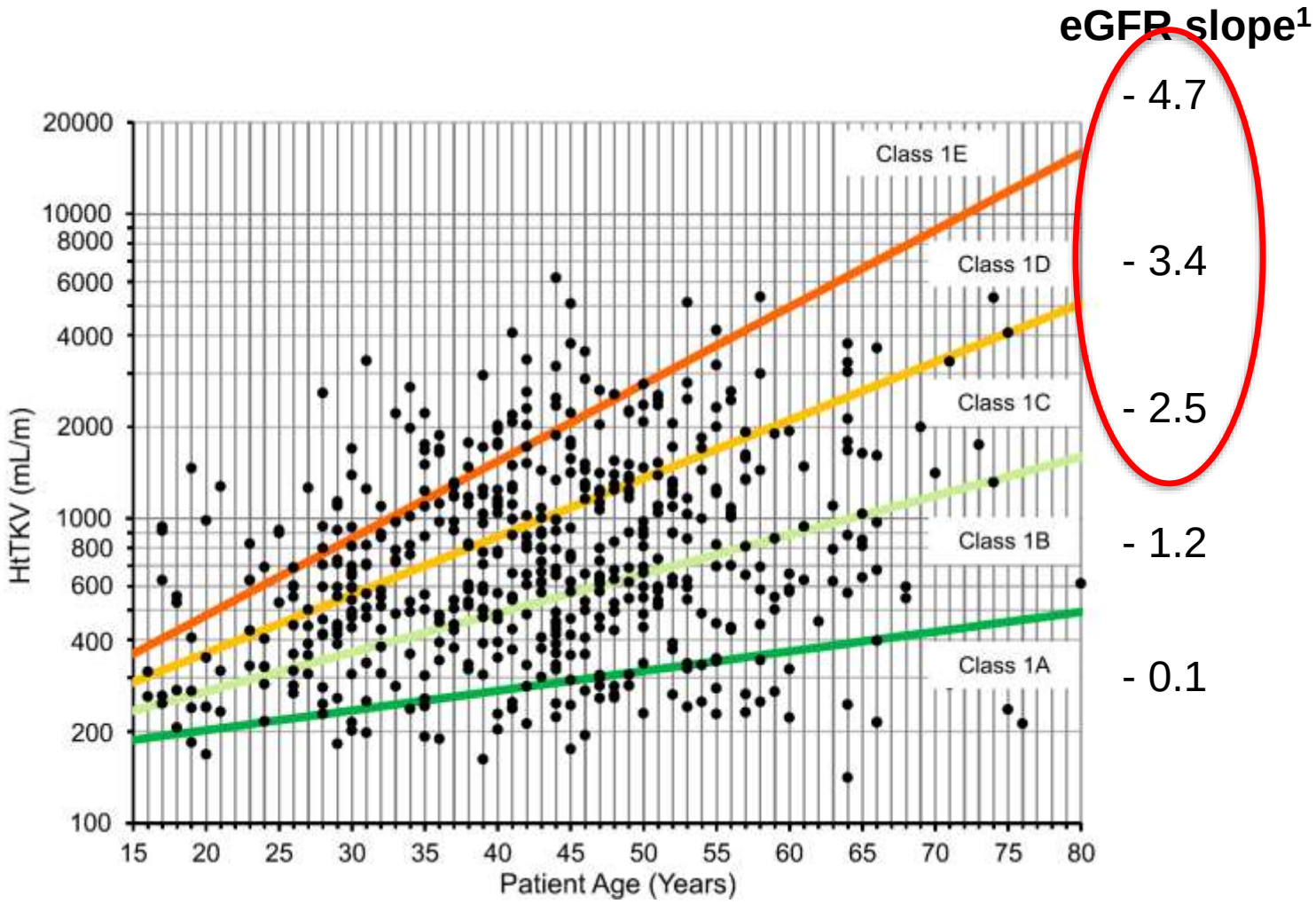


Low risk (green curve n=326)	303	234	143	45	8
Intermediate risk (blue curve n=455)	401	256	81	81	2
High risk (red curve n=192)	136	46	7	0	0

Cornec-Le Gall E *et al. J Am Soc Nephrol*

Groningen PKD Expertise Center

TKV indexed for height and age to predict rate of disease progression

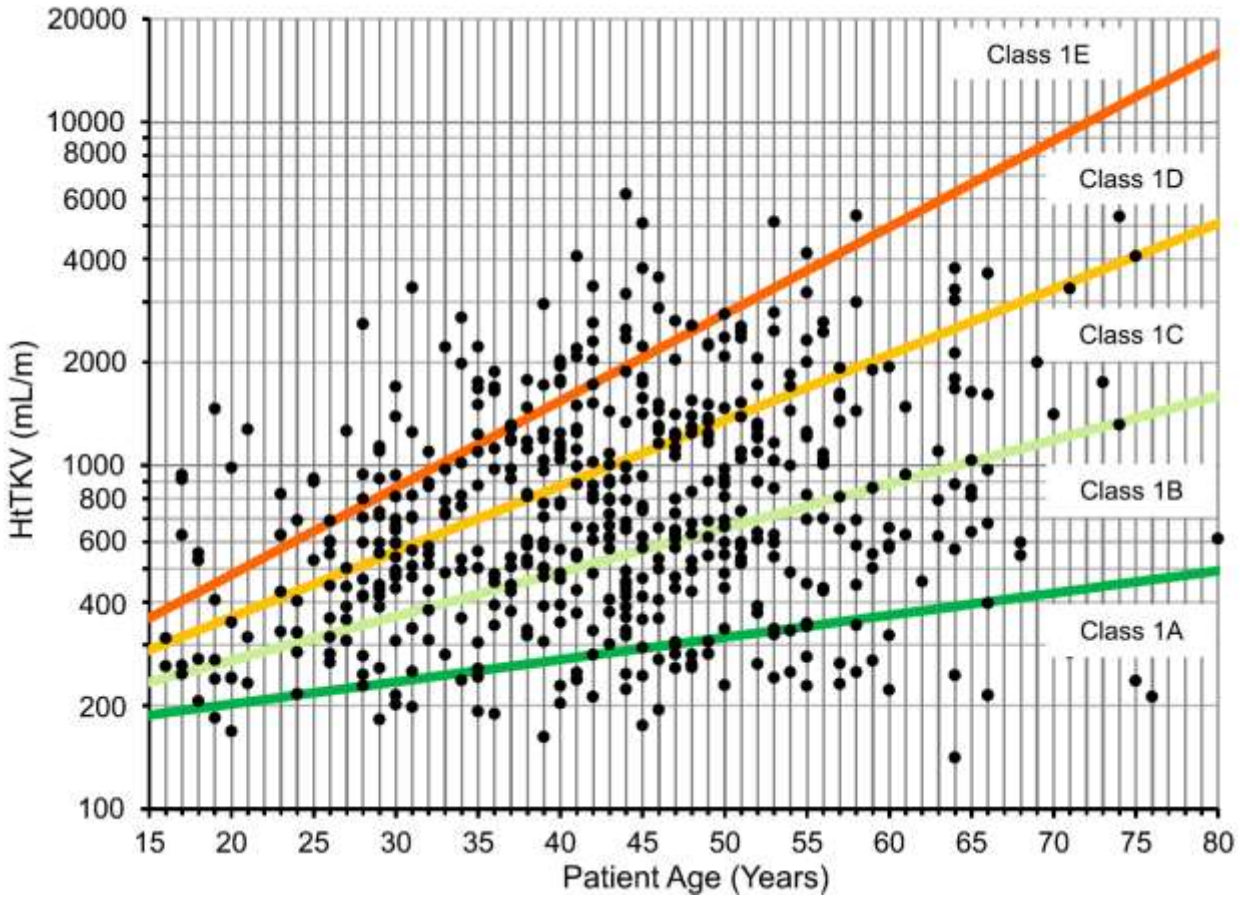


1. Future eGFR decline (ml/min/1.73 m^2 per yr) by subclass
Note: no difference between males and females in average slope !

Irazabal MV *et al.*
J Am Soc Nephrol 2015;26:160–72.

Groningen PKD Expertise Center

TKV indexed for height and age to predict rate of disease progression



eGFR slope[1]

-4.7
(-3.2 to -6.4)

-3.4
(-2.2 to -4.7)

-2.5
(-1.5 to -3.7)

-1.2
(-0.2 to -2.4)

- 0.1

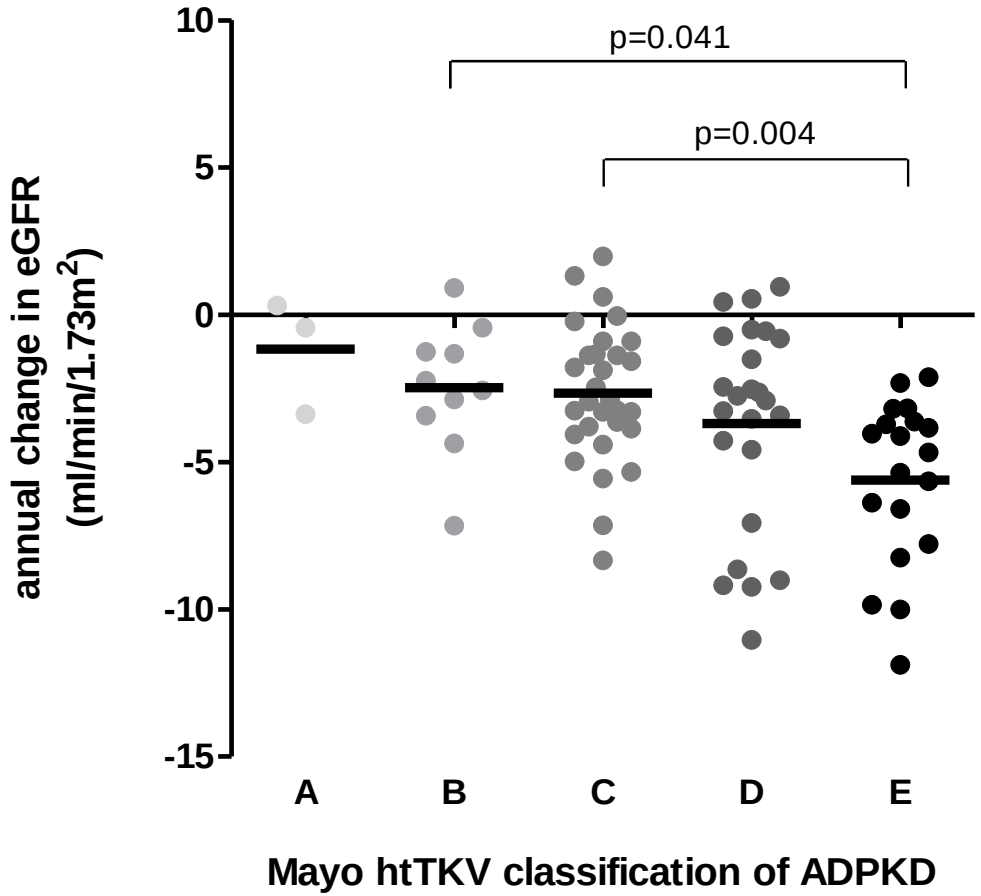
1. Future eGFR decline (ml/min/1.73 m^2 per yr) by subclass
Note: no difference between males and females in average slope !

Irazabal MV *et al.*
J Am Soc Nephrol 2015;26:160–72.

Groningen PKD Expertise Center

Associations with disease progression

Longitudinal analysis, n=108 ADPDK



Longitudinal, observational analysis
n=104 ADPDK, wide eGFR range, >5 yr FU

Messchendorp *et al*
Submitted

Groningen PKD Expertise Center

Factors to assess prognosis

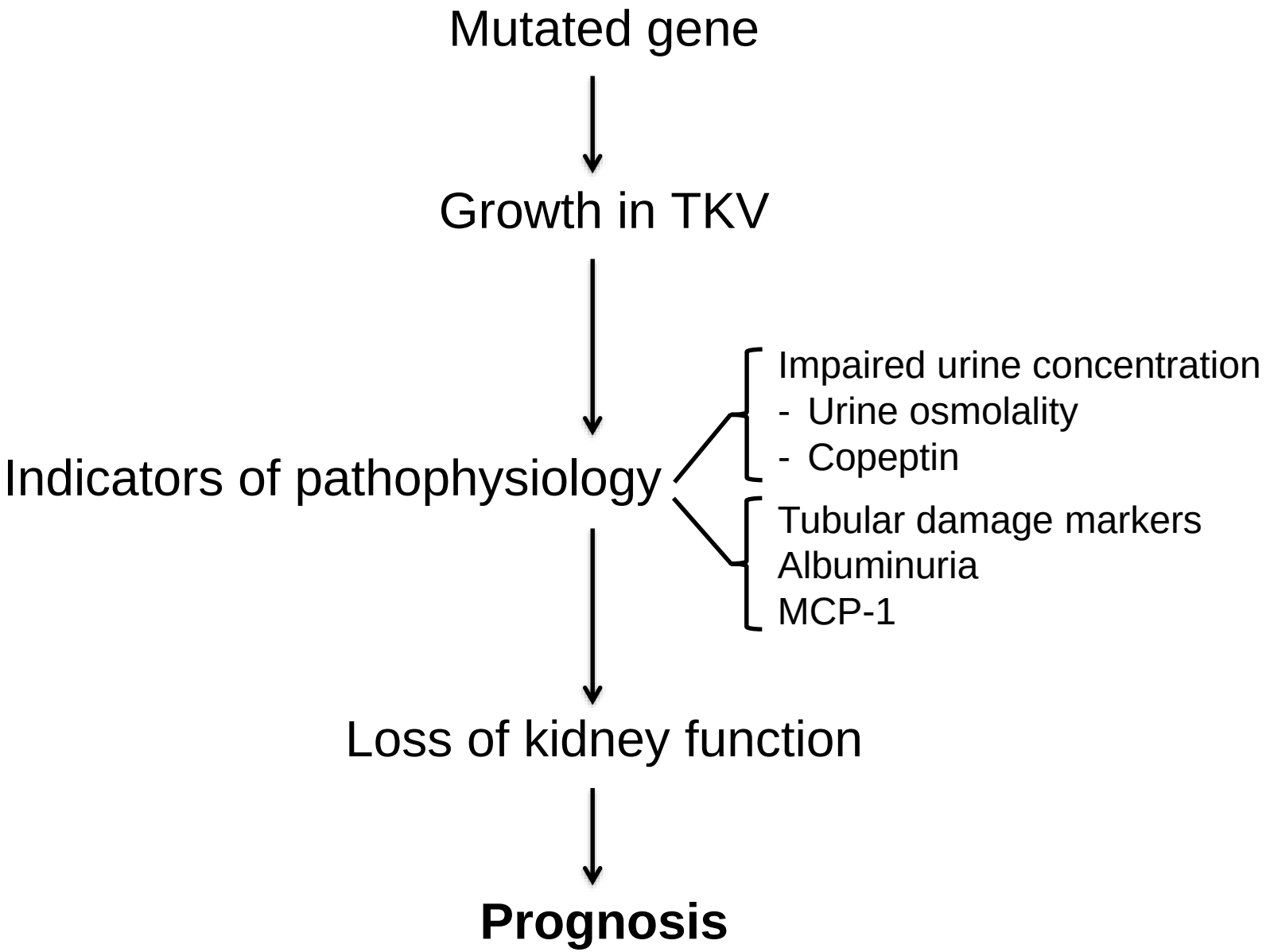
- Function — eGFR given a certain age
- Genetics: — *PKD1* / *PKD2* (non)truncating mutations
- Size: — TKV indexed for age and length (MRI or US)
- Symptoms: — Early haematuria, hypertension or pain
- Demographics: — Family history of young age at ESRD

- Biomarkers: — [1]Plasma copeptin concentration?
  [2]Albuminuria
  [3]Urinary excretion tubular damage markers?
  [4]MCP1
  Etc etc

1. Gansevoort R *et al. ASN abstract 2016*
2. Gansevoort R *et al. Nephrol Dial Transpl* 2016;31:1887-94. Boertien WE *et al. Am J Kidney Dis* 2013;61:420–9.
3. Meijer E *et al. Am J Kidney Dis* 2010;56:883–95. Boertien WE *et al. Kidney Int* 2013;84:1278–86
4. Grantham J *et al. Nephrol Dial Transplant*. 2016 [Epub ahead of print]

Groningen PKD Expertise Center

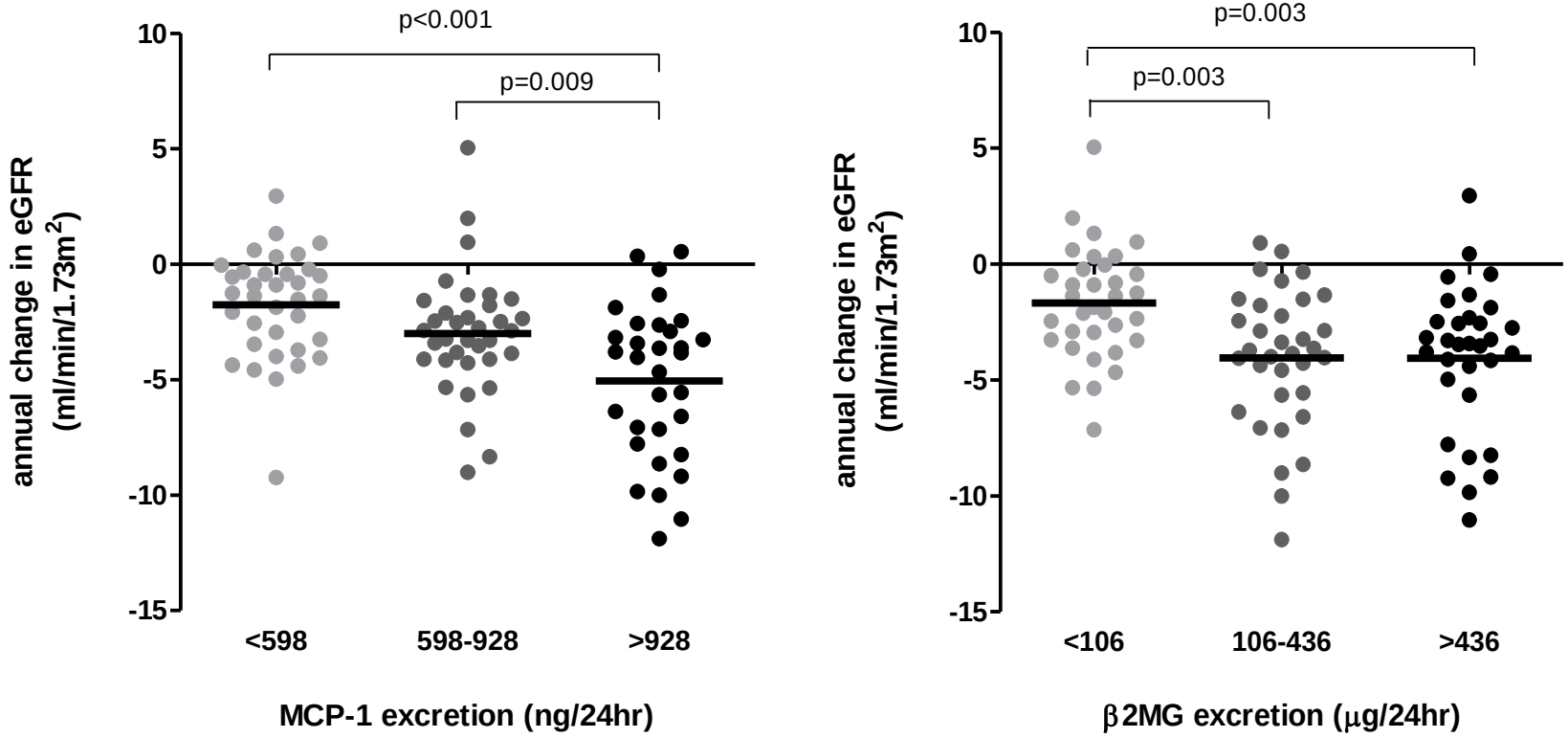
Which prognostic factors to aim for?



Groningen PKD Expertise Center

Associations with disease progression

Longitudinal analysis, n=108 ADPDK

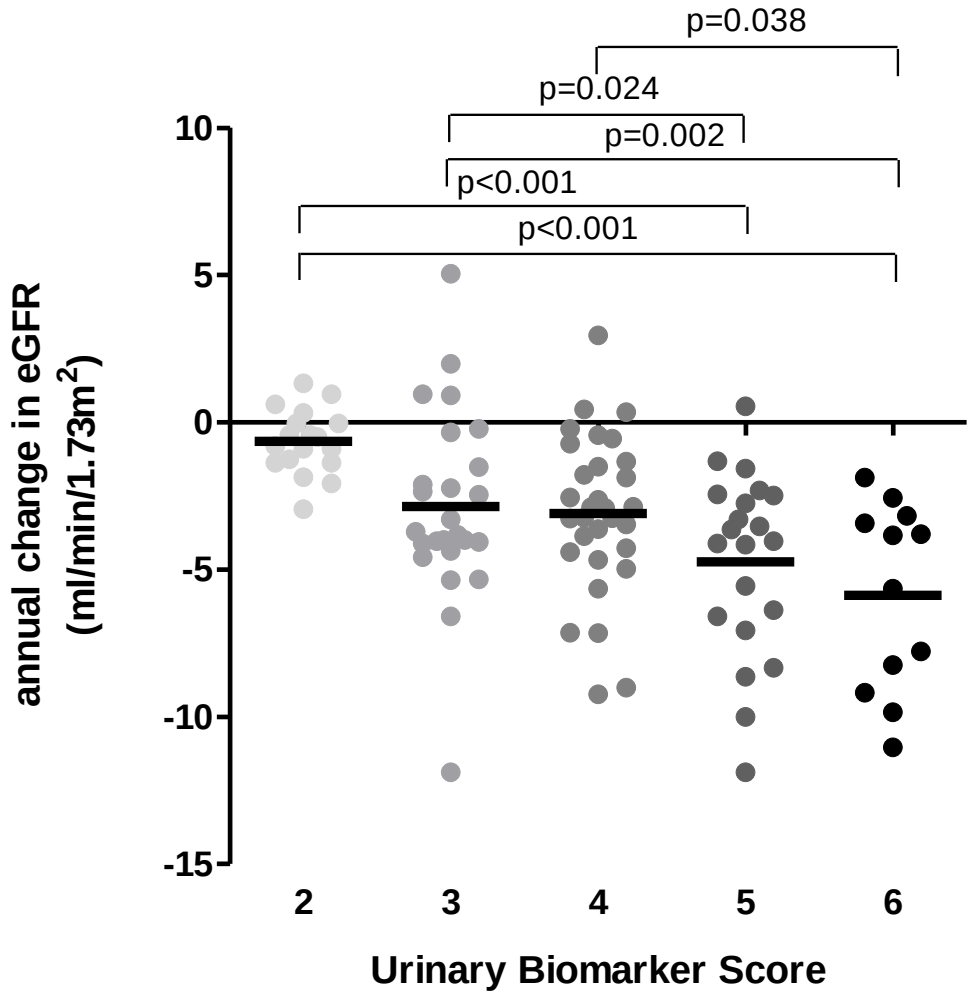


Messchendorp et al. (submitted)

Groningen PKD Expertise Center

Associations with disease progression (δeGFR)

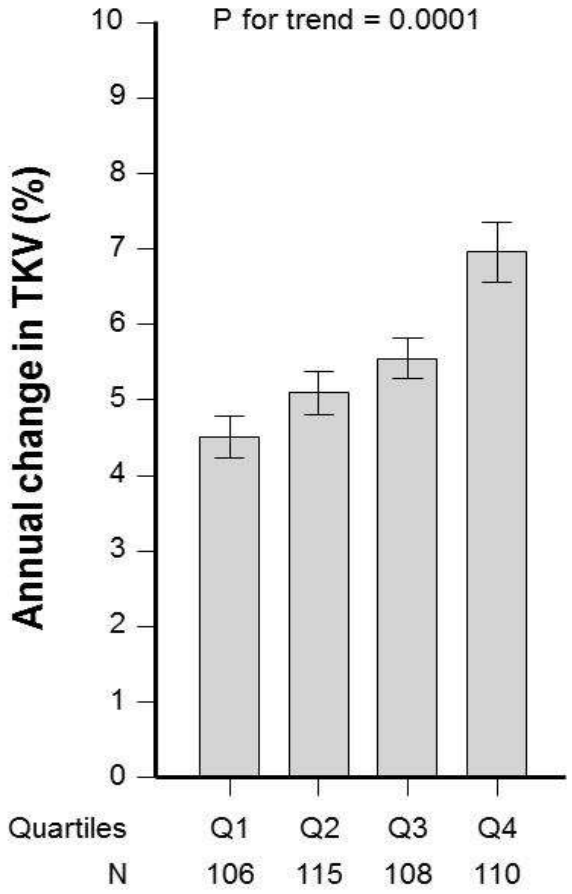
Longitudinal analysis, n=108 ADPDK, wide eGFR range

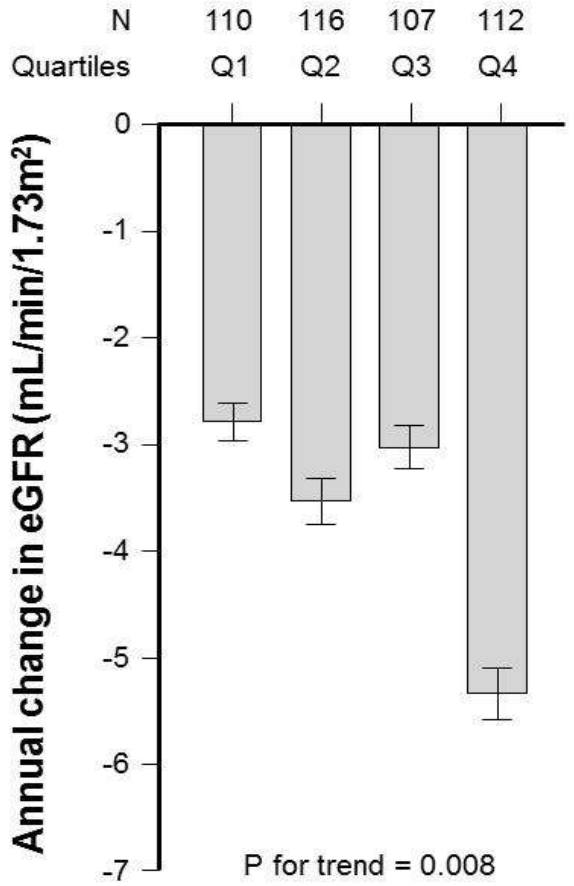


Messchendorp et al. (submitted)

Groningen PKD Expertise Center

The need for additional prognostic markers
- Copeptin as an example -



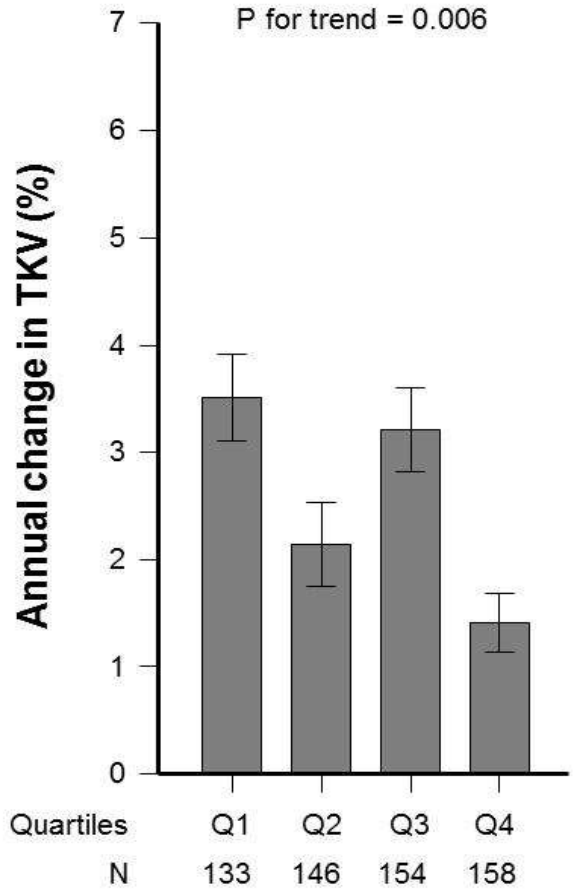


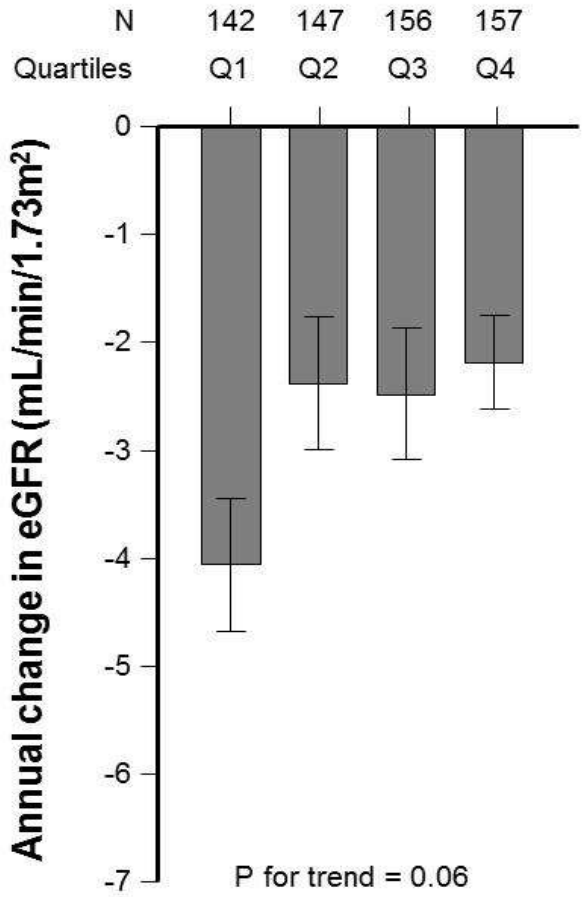
TEMPO 3:4, N=484 ADPKD, placebo treated patients only
Age 18–50 yr, eCrCl≥60 ml/min, TKV≥750 ml

Gansevoort RT *et al*
Kidney Int. In press

Groningen PKD Expertise Center

The need for additional prognostic markers
- Predicting efficacy of treatment -



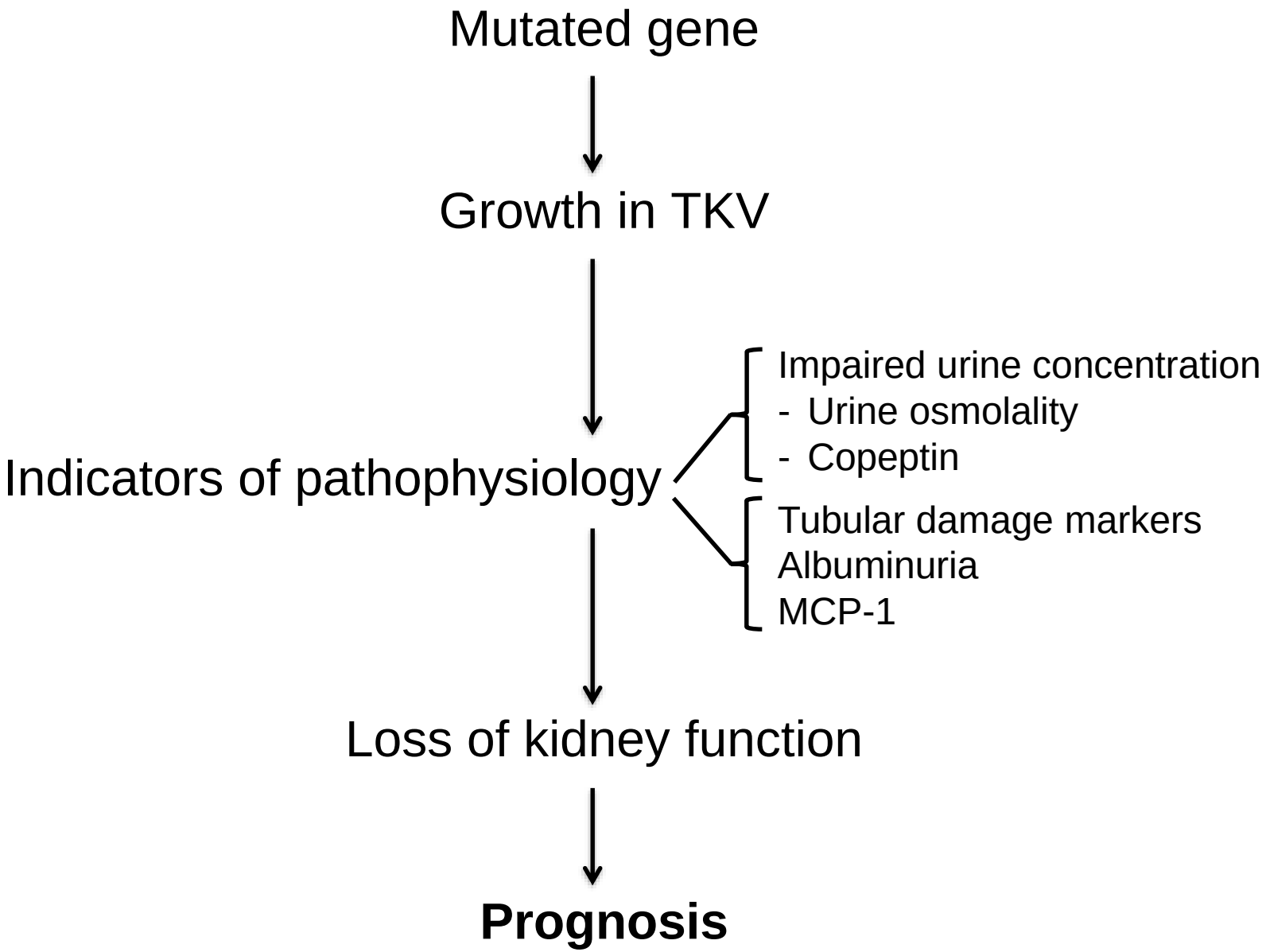


N=961 ADPKD, tolvaptan treated patients only
Age 18–50 yr, eCrCl≥60 ml/min, TKV≥750 ml

Gansevoort RT *et al*
Kidney Int. In press

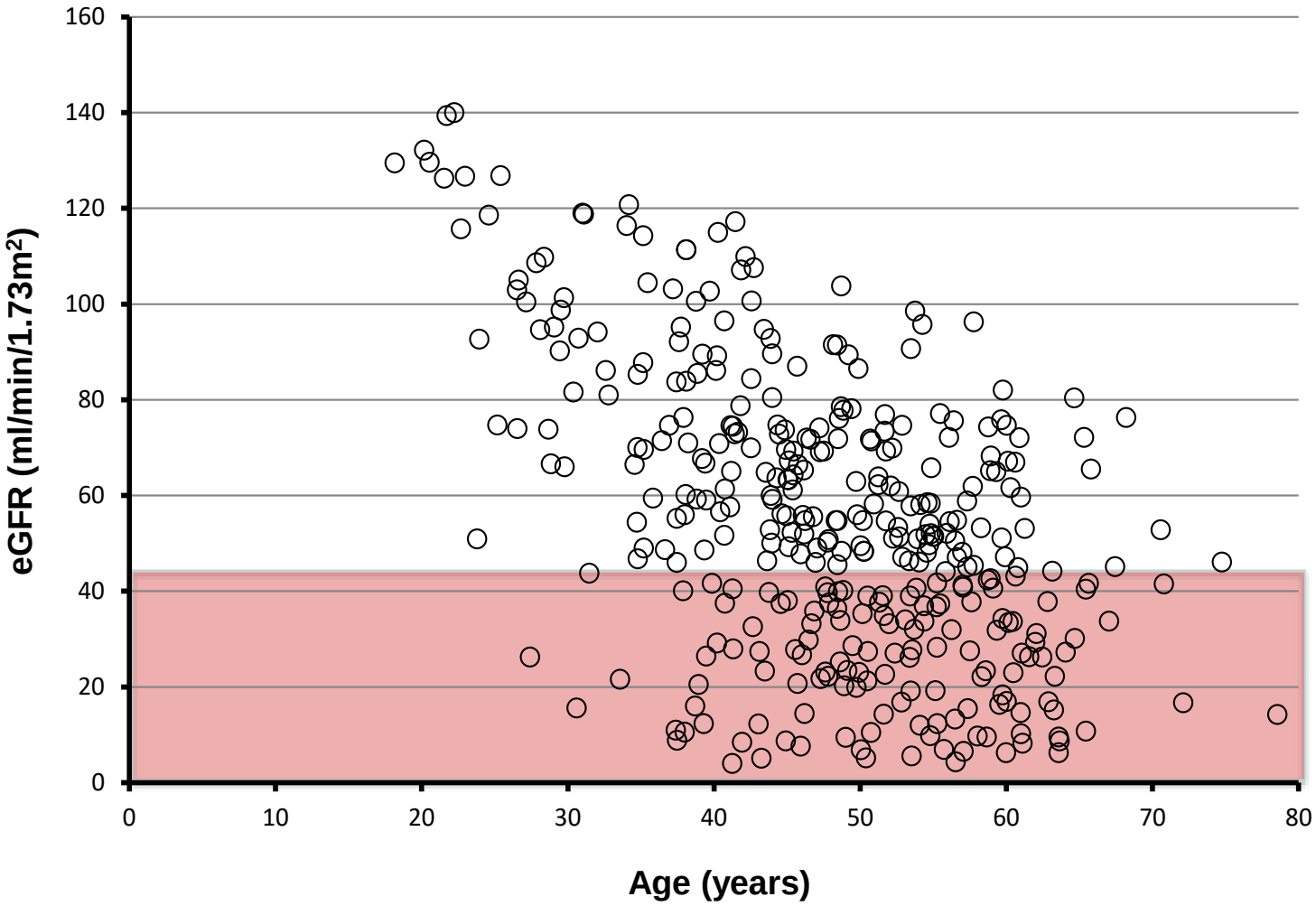
Groningen PKD Expertise Center

Which prognostic factors to aim for?



Groningen PKD Expertise Center

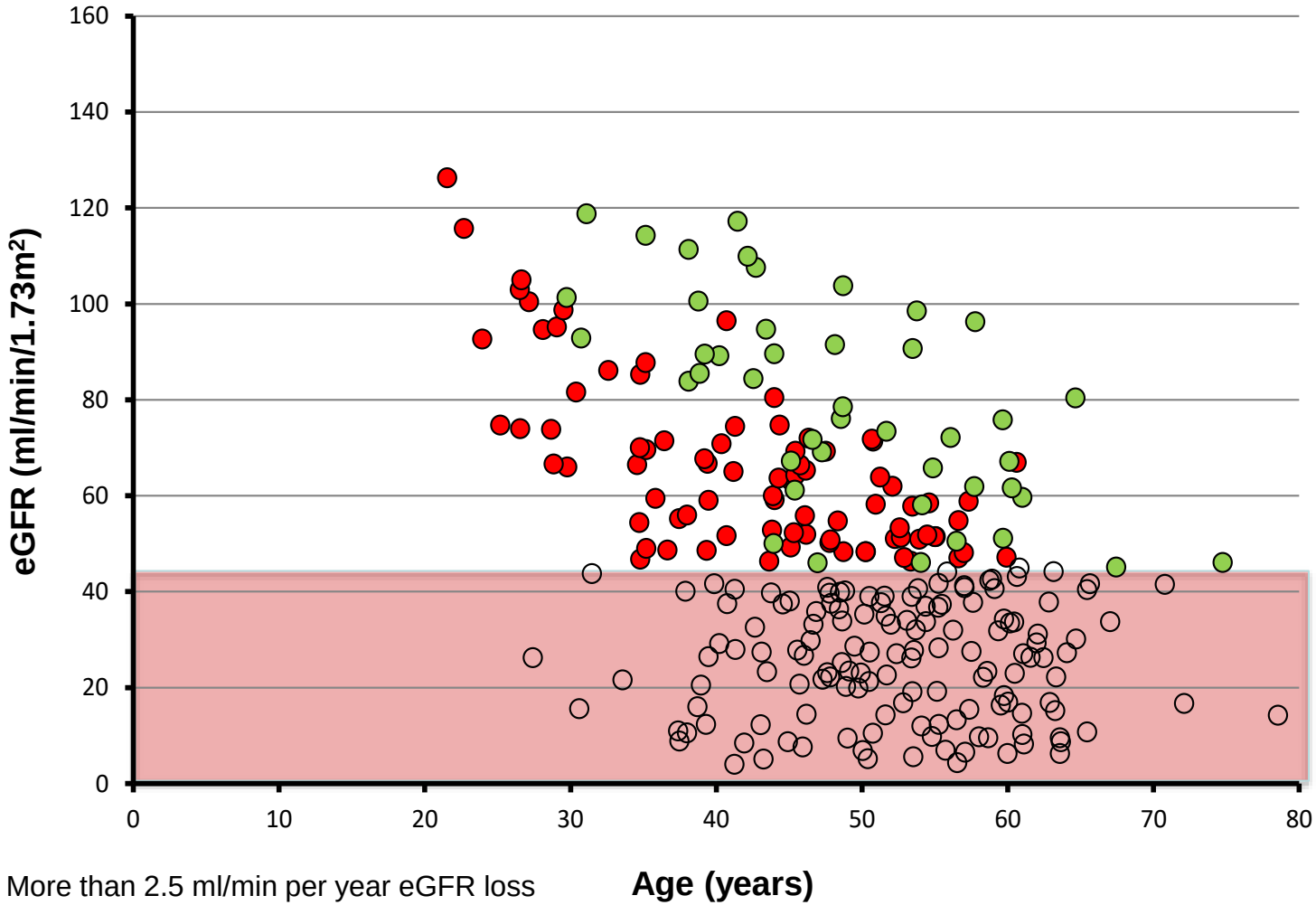
eGFR indexed for age for risk prediction



May 2017
N=371, Groningen PKD Expertise Center, Netherlands

Groningen PKD Expertise Center

eGFR indexed for age for risk prediction



- More than 2.5 ml/min per year eGFR loss
- Less than 2.5 ml/min per year eGFR loss
- eGFR<45, no risk prediction needed anymore

May 2017
N=371, Groningen PKD Expertise Center, Netherlands

Groningen PKD Expertise Center

Will the future lie in multitude?
Biomarker panels to predict disease progression

	Model 1			Model 2			Model 3			Model 4		
	St. β	**p-val.**	**R^2**	**St. β**	**p-val.**	**R^2**	**St. β**	**p-val.**	**R^2**	**St. β**	**p-val.**	**R^2**
Annual change in eGFR			0.15			0.25*			0.22*			0.29**
Age	0.20	0.17		0.11	0.44		0.13	0.19		0.05	0.69	
Male sex	-0.07	0.51		-0.05	0.63		-0.08	0.41		-0.06	0.51	
eGFR	0.13	0.34		-0.04	0.79		0.05	0.73		-0.09	0.51	
htTKV	-0.44	<0.001		-0.43	<0.001		-0.30	0.009		-0.31	0.004	
PKD1 truncating$	-0.44	0.008		-0.51	0.001		-0.32	0.045		-0.41	0.009	
PKD1 non-trunc.$	-0.45	0.004		-0.49	0.001		-0.35	0.022		-0.40	0.005	
β2MG				-0.35	0.001					-0.31	0.002	
MCP-1							-0.33	0.003		-0.28	0.008	

$ Reference group is *PKD2.*
* Significant compared to model 1 (p=0.003 for model 2 and p=0.02 for model 3);
** Significant compared to model 1, 2 and 3 (p=0.001, p=0.03 and p=0.006 respectively);

Longitudinal, observational analysis
n=104 ADPDK, wide eGFR range, >5 yr FU

Messchendorp *et al*
Submitted

Groningen PKD Expertise Center

Mr. X, 36 years

Medical specialist. Diagnosed himself with PKD during US training. Negative family history. Because of fear hid this knowledge for years. Changed life (job, holidays, no 3rd child). Now asks for consultation. Normal seize, 1.95m, 88 kg

- eGFR over time: ?
- eGFR for age: 92 ml/min/1.73m^2 at age 36 yr
  - Low risk
- htTKV: low class 1C.
  - Intermediate (to low) risk
- Mutation analysis: truncating *Pkd2* mutation
  - Low risk

Conclusion: low risk for rapid progression, i.e. it is likely that you will remain without need for RRT during working life

Conclusions

- There are many prognostic markers in ADPKD, but individually they all have limited predictive value.
- There is a need for “risk scores” that integrate the predictive value of various markers. Such risk scores:
  - should contain preferably “downstream”, easy to measure variables, and at least eGFR and age
  - should be validated in appropiately sized independent cohorts
- There is a need for markers that can change due to treatment, as these may help to titrate such treatment

Theses related to “Predicting Progress”

In 2025:

- ADPKD patients are entitled to know (*or not know*) their prognosis.
- Caregivers are able to provide an evidence based estimate of prognosis. To do so, there is consensus
  - how to assess prognosis
  - how to translate an evidence based estimate of prognosis in understandable lay language

Question: should all care givers be able to estimate prognosis, or just a subset (e.g. expertise centers).

#ADPKD
@PKD_Int

Breakout 3

Liver Cysts and Pain in ADPKD

PKD International

EAF European ADPKD Forum

Summit sponsors
This event has been made possible by sponsorship from
Baxter, Otsuka Pharmaceutical Europe Ltd, Palladio Biosciences and Sanofi Genzyme.

Baxter Otsuka Palladio Biosciences Sanofi Genzyme

BREAKOUT 3: Liver Cysts and Pain in ADPKD

Lucas Bernts

(Radboud University Medical Center, Netherlands)

Ron Gansevoort

(University Medical Center Groningen, Netherlands and EAF)

Natasha O'Brien

(PKD Charity, UK)

European ADPKD Patient Summit
Breakout 3: Liver cysts and pain

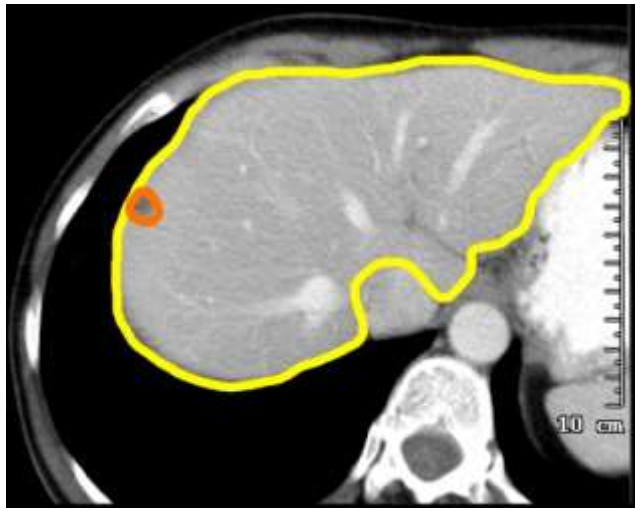
Lucas Bernts, MD, PhD-candidate

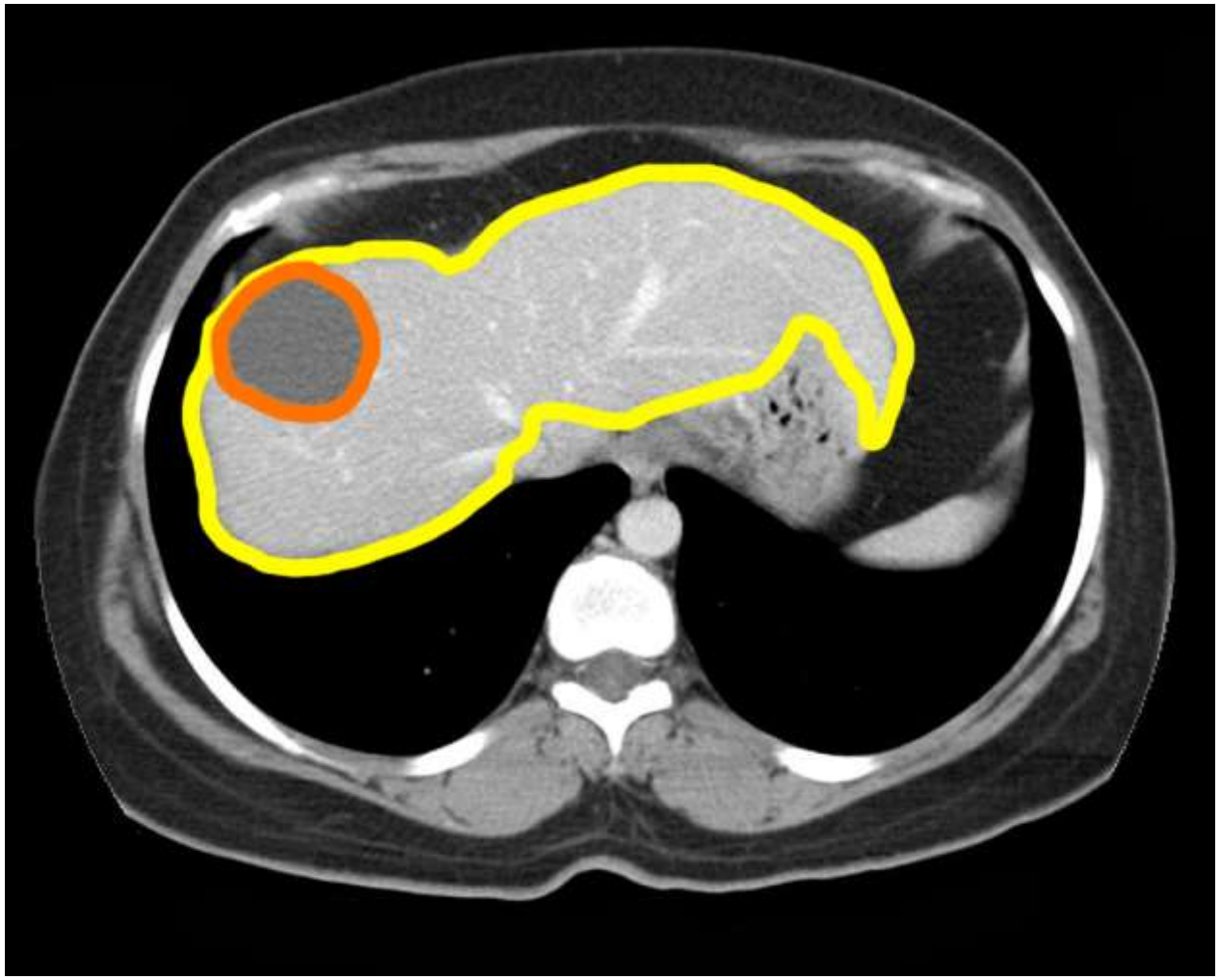
16-03-2019

Radboudumc

Liver Cysts

- Very common
- Usually no symptoms

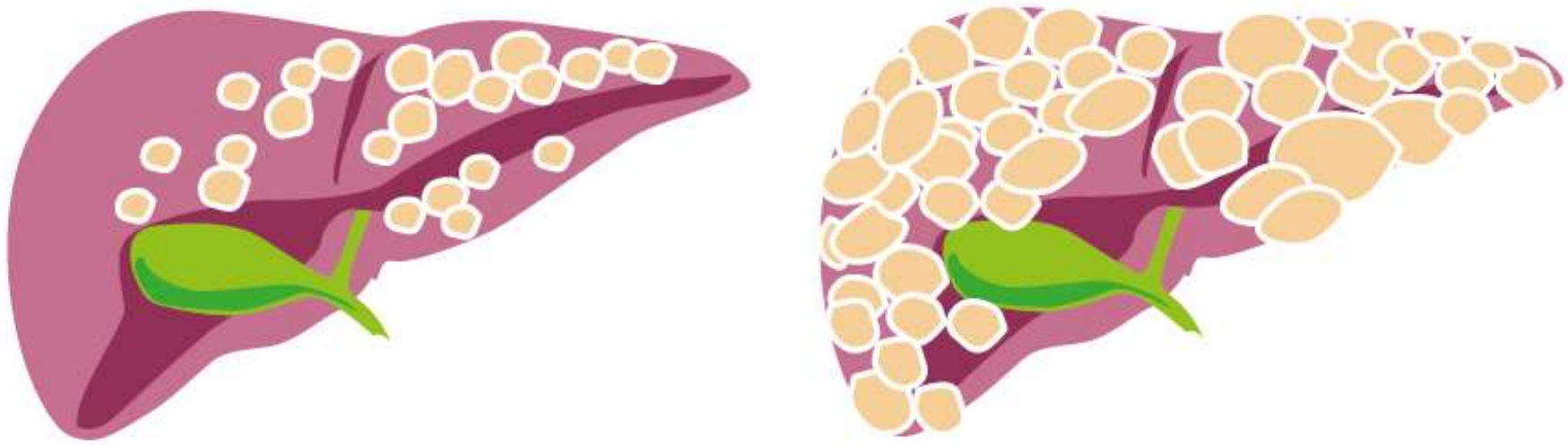




Case courtesy of Dr Hani Salam, Radiopaedia.org, rID: 9942

Polycystic Liver Disease (PLD)

- >10 liver cysts
- Genetic disease (ADPKD/ADPLD)

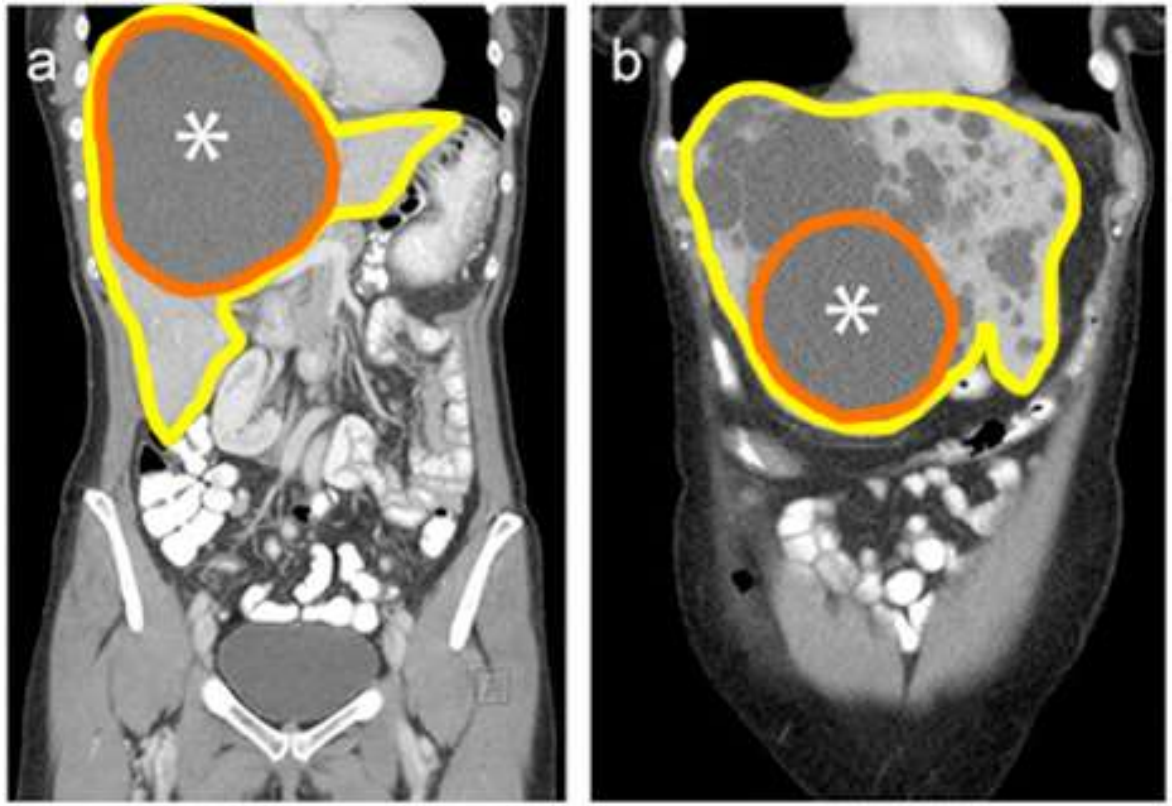


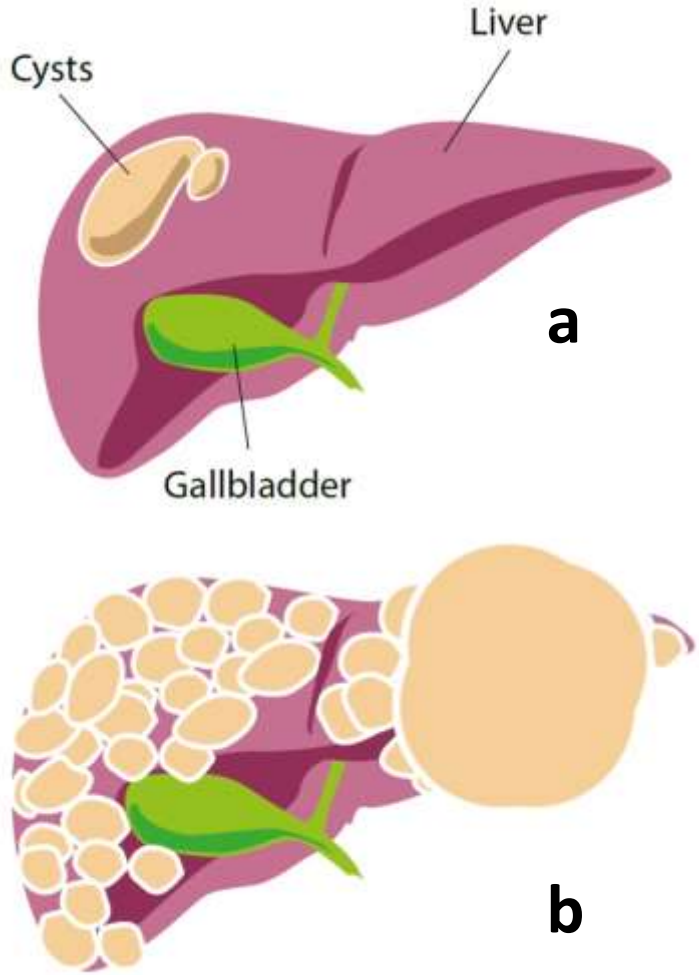
Complications of Liver Cysts

Three problems:

1. Large cysts
2. Large livers
3. Cyst infections

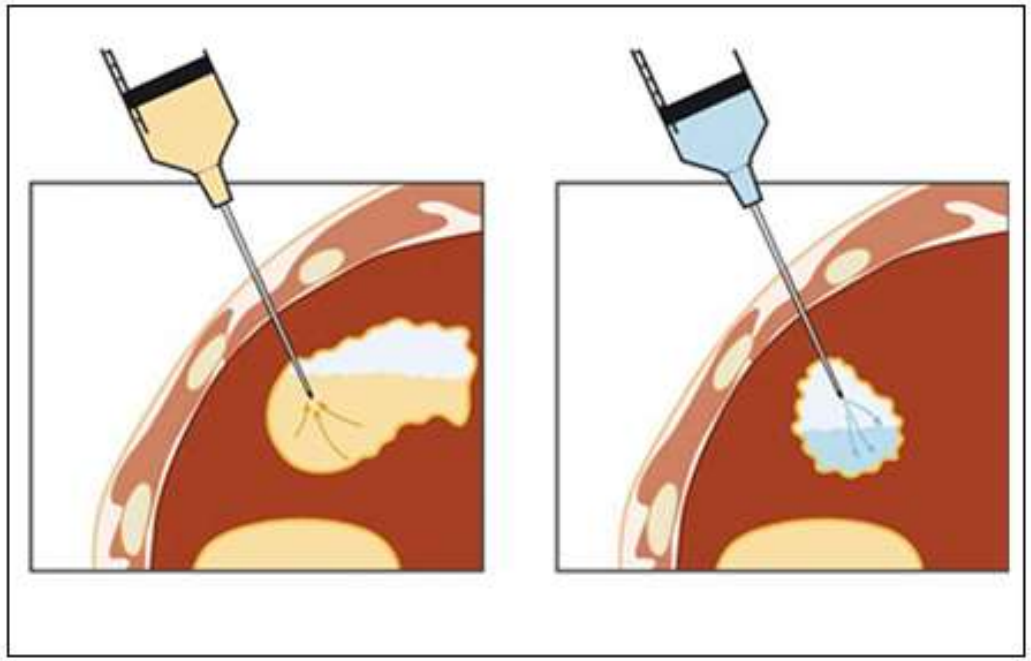
Problem 1: Large Cysts



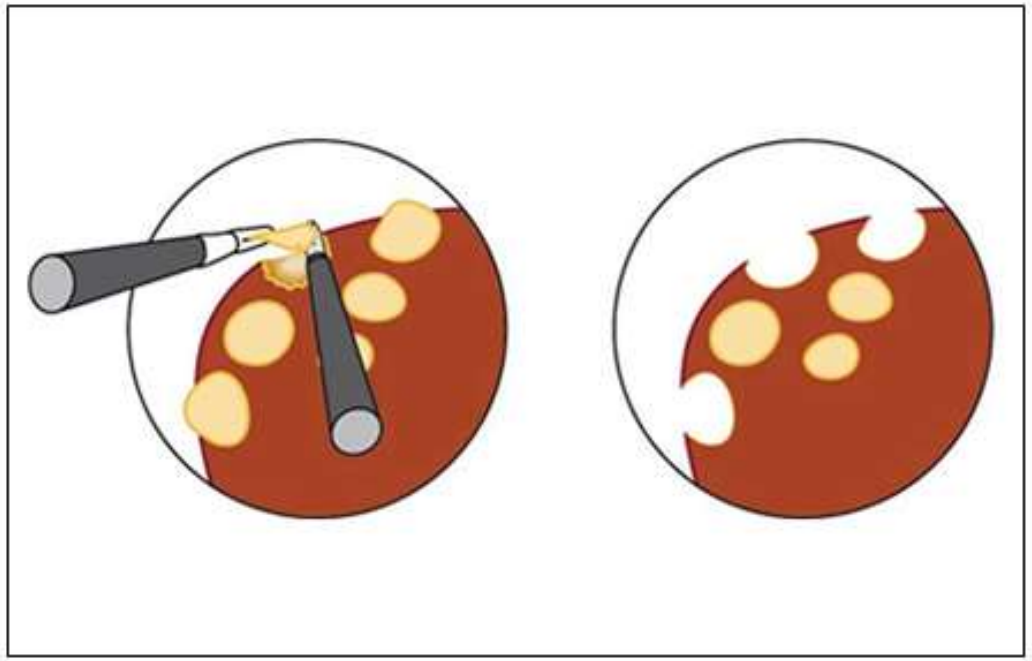


Problem 1: Large Cysts

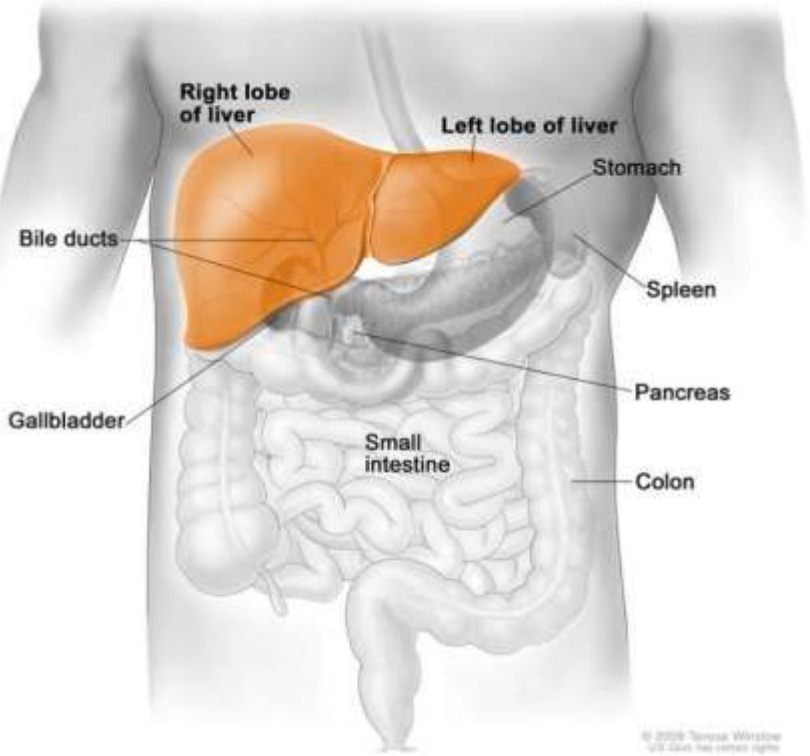
1. Aspiration Sclerotherapy



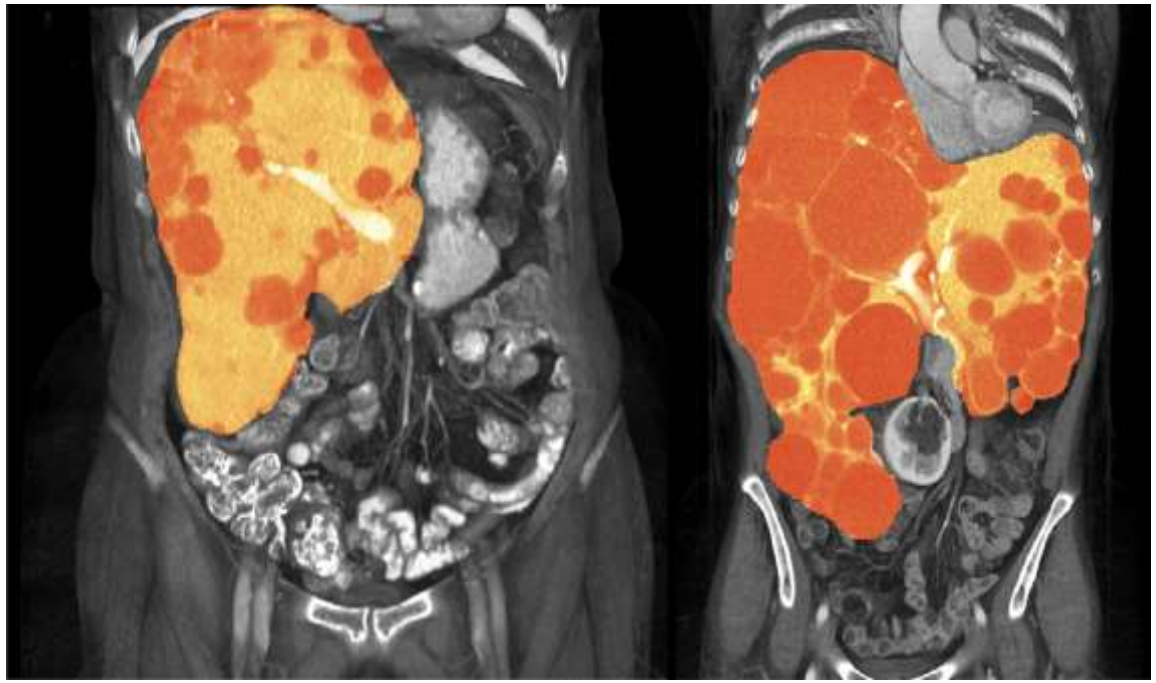
2. Laparoscopic Fenestration



Problem 2: Large Livers



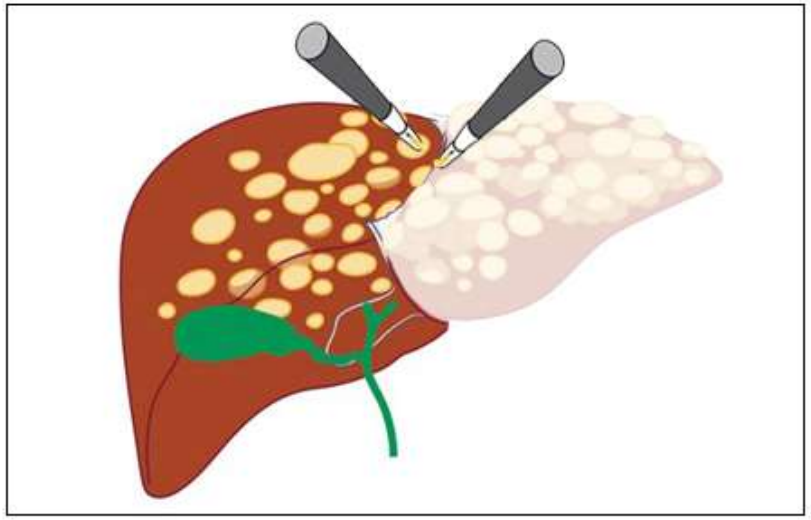
Normal



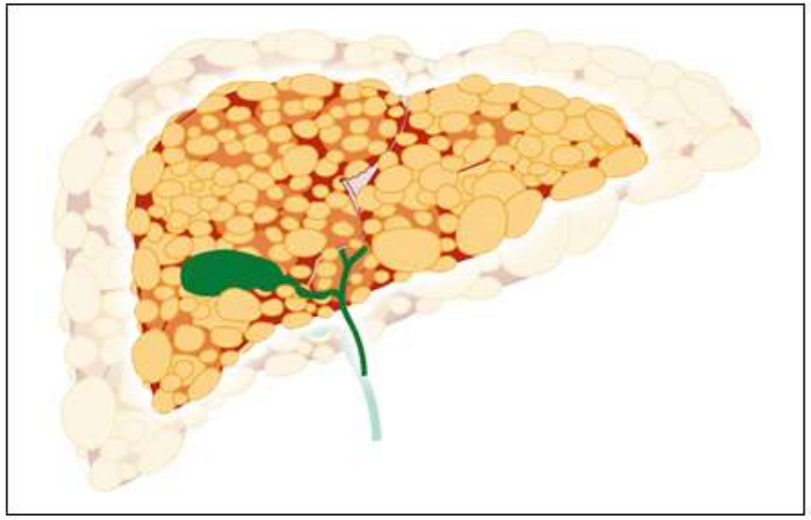
Polycystic Liver Disease

Problem 2: Large Livers

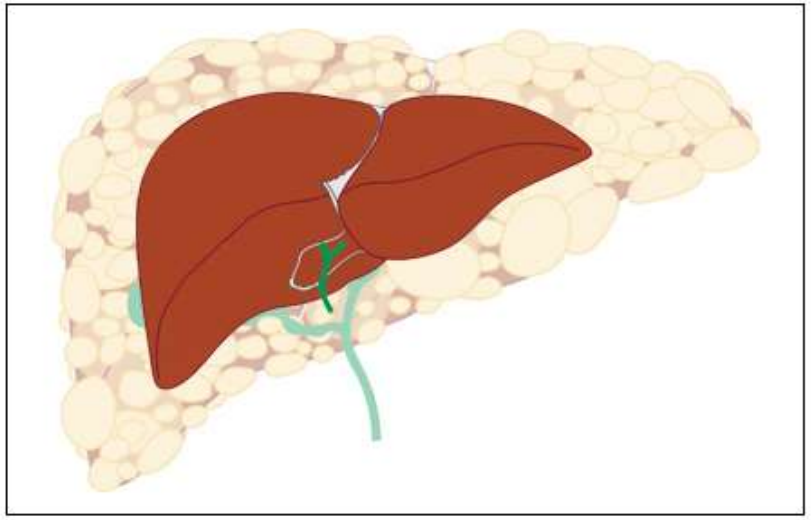
3. Segmentresection



4. Somatostatin Analogues



5. Transplantation



Problem 2: Large Livers

- **Estrogen birth control pills** increase liver volume
- **Hormonal replacement therapy** increases liver volume
- Female patients (and daughters) should use **estrogen-free** options

Problem 3: Cyst infections

- Fever

- Pain

Problem 3: Cyst infections

- Seek medical advice
- 6 weeks of antibiotics

Summary

- Liver cysts are the most common sign of ADPKD outside the kidneys.
- Problems are:
  - Large cysts
  - Large livers
  - Cyst infections

- Treatment has to be **tailored** to the patient
- Treatment preferably by a **hepatologist** (liver specialist)
- European Reference Network RARE-LIVER: https://www.rare-liver.eu/

Pain in ADPKD

Ron Gansevoort

Chair PKD Expertise Center
University Medical Center Groningen
The Netherlands

GRONINGEN
KIDNEY
CENTER

Conflict of Interest

Consultant for Otsuka, Ipsen and Sanofi-Genzyme

Pain in ADPKD

- Common symptom in ADPKD patients (about 60%)

- Acute
  ~ infection, renal stones and cyst bleeding

- Chronic
  > 6 weeks, multifactorial
  - non-ADPKD
  - ADPKD
    - distension capsule
    - compression adjacent tissue

- Chronic pain is sometimes difficult to treat
  - Pharmacological options
  - Invasive options

Casteleijn et al, NDT 2014

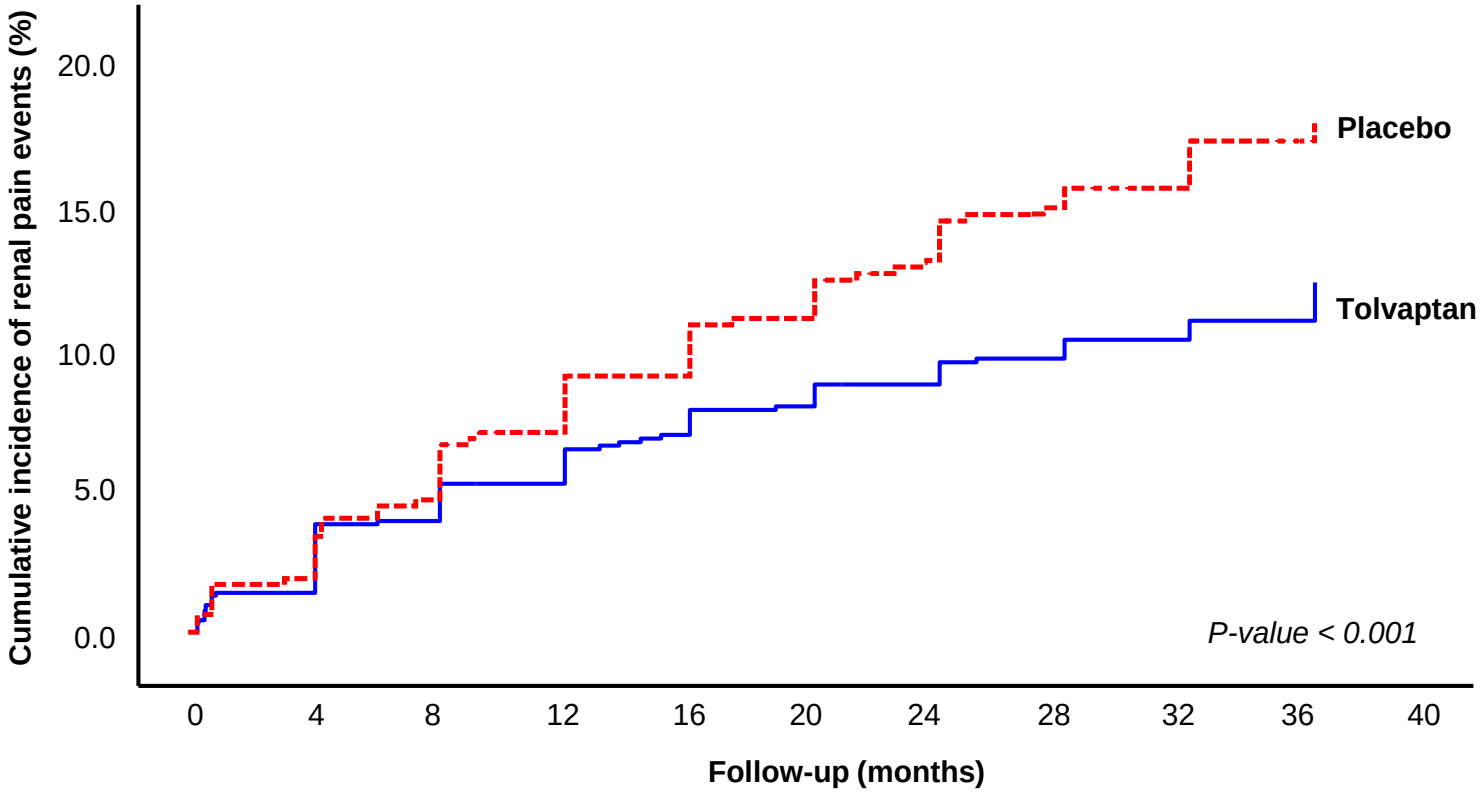
Acute pain in ADPKD

- Symptomatic treatment
  - Analgesics
  - Antimicrobial treatment by UTI or cyst infection

- Causal treatment
  - Vasopressin V2 receptor antagonists (tolvaptan)
    - only in case of renal pain
  - Somatostain analogues (lanreotide, ocreotide)
    - in case of renal and/or liver pain

Casteleijn et al, NDT 2014

Cumulative incidence of renal pain events

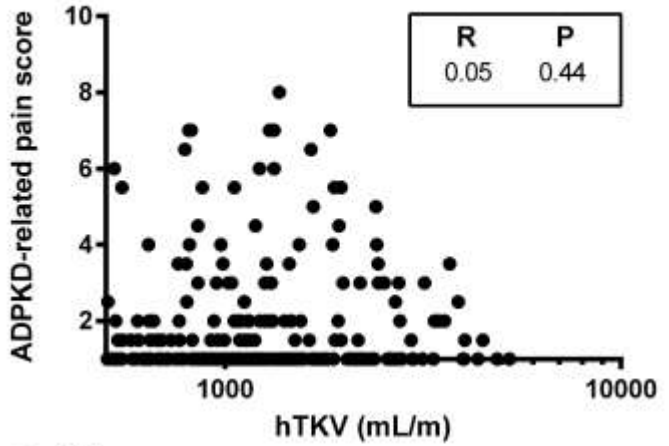


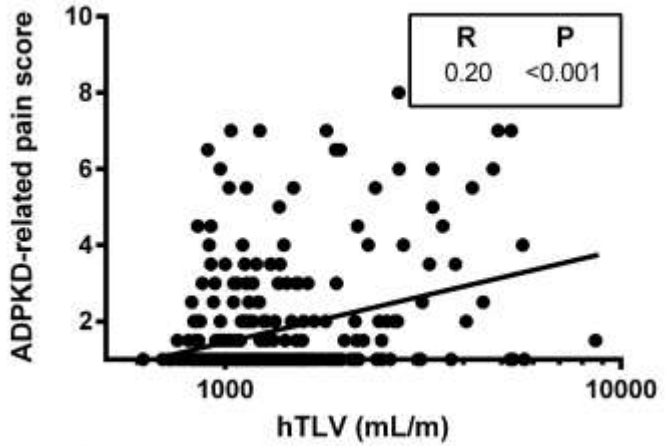
Tolvaptan resulted in a significantly lower incidence of renal pain events with a risk reduction of 36% (HR= 0.64; 95% CI 0.48-0.86)

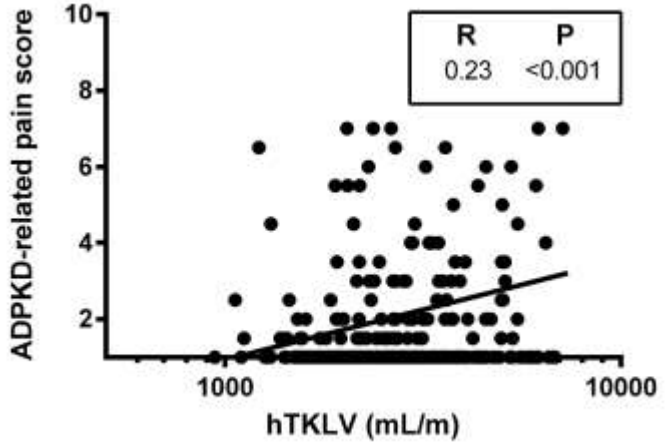
Casteleijn et al. AJKD 2016

Chronic pain

- Kidney volume does not play a major role
- Liver volume does correlate with severity of chronic pain
- Combined liver and kidney volume is even better correlated
- Women experience more pain, yet sex itself is not a determinant







Casteleijn et al, AJN 2017

Our ADPKD Pain Clinic

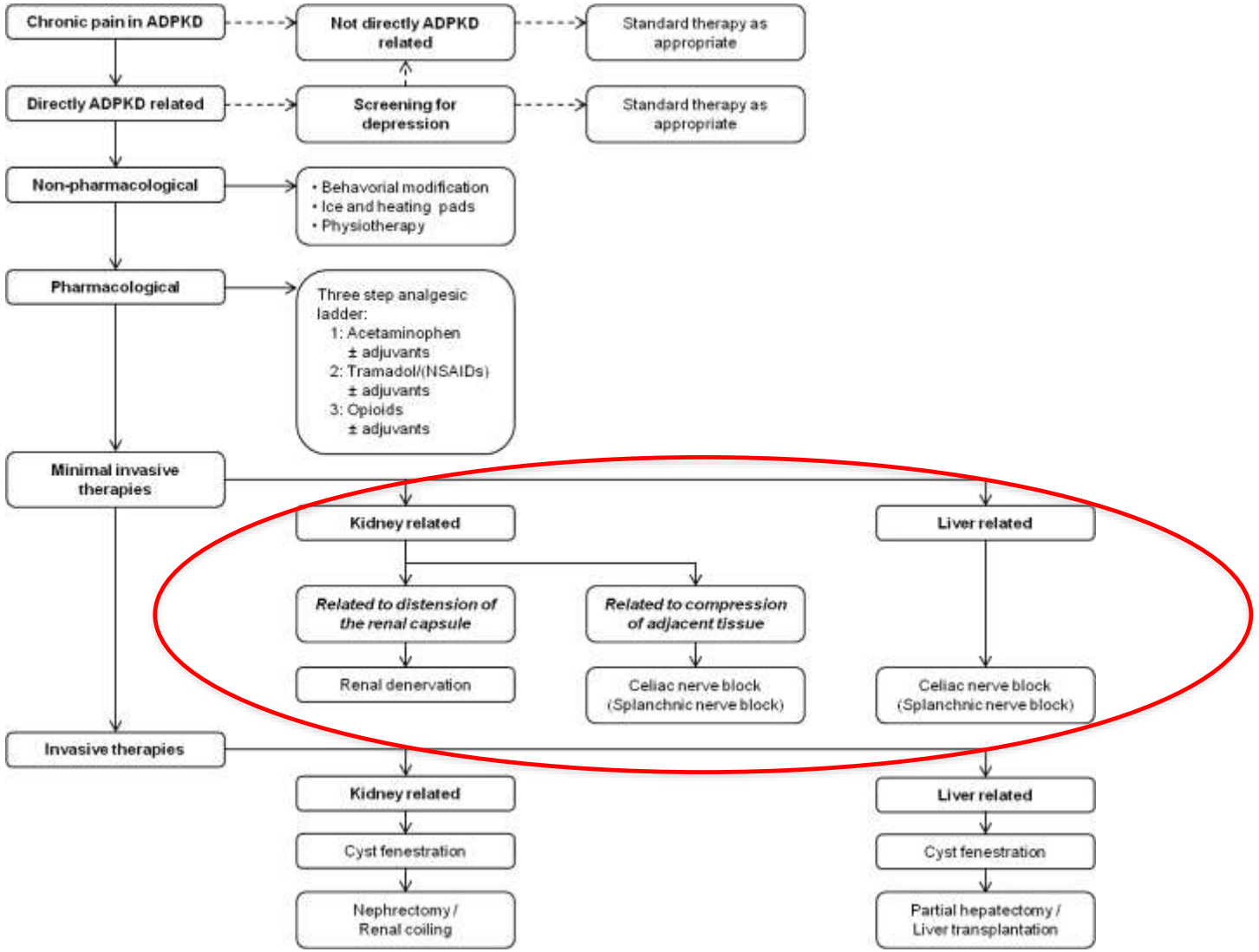
- Multidisciplinary approach:
  - Screening by Nephrologist/Urologist
  - Screening by Pain Specialist

- Investigations:
  - Standard measurements (blood, spot urine, 24hr urine)
  - CT or MR images of the kidneys and liver
  - Renography

- After screening, patients are discussed by our multidisciplinary team (nephrologist and pain specialist, but also radiologist, urologist, gastro-enterologist and when needed a transplant surgeon and gynecologist)

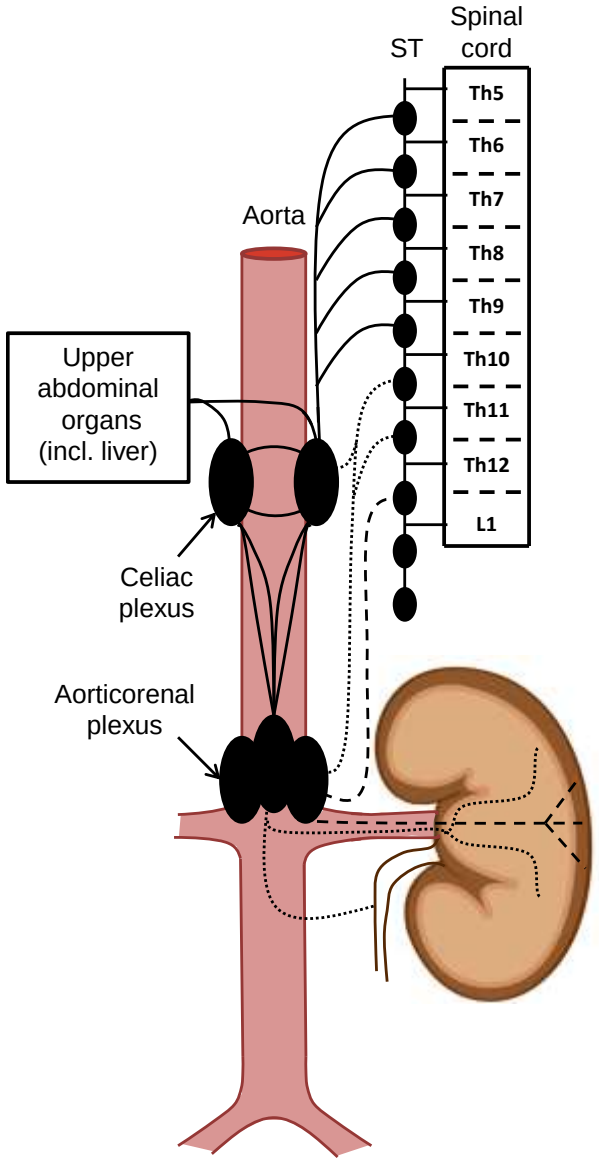
Casteleijn et al. Kidney Int 2017

A stepwise approach to manage chronic pain



Casteleijn et al, NDT 2014

Sensory nerve supply of kidneys and other upper abdominal organs

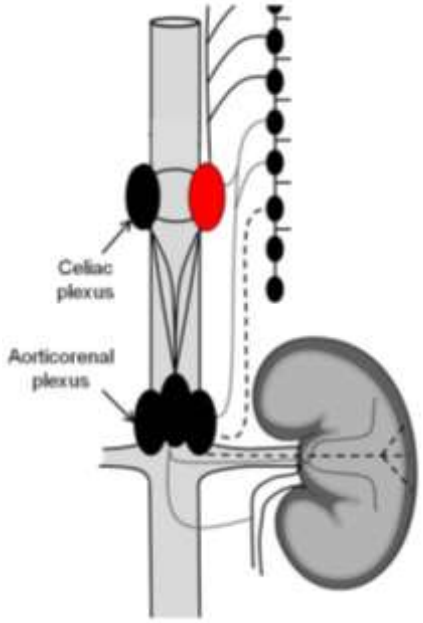


ADPKD-related pain:

- *Distension of renal capsule:* pain <u>not</u> via celiac plexus (but via least splanchnic nerve[1])
- *Compression of adjacent tissue:* pain pathway via celiac plexus[2]
- Difference in referred pain pattern T(6-9) vs. T(10-12) pattern, but overlap

1: Cousins et al, Pain 2008
2: Loukas et al., Clinc Ant 2010

How to distinguish between causes of pain?



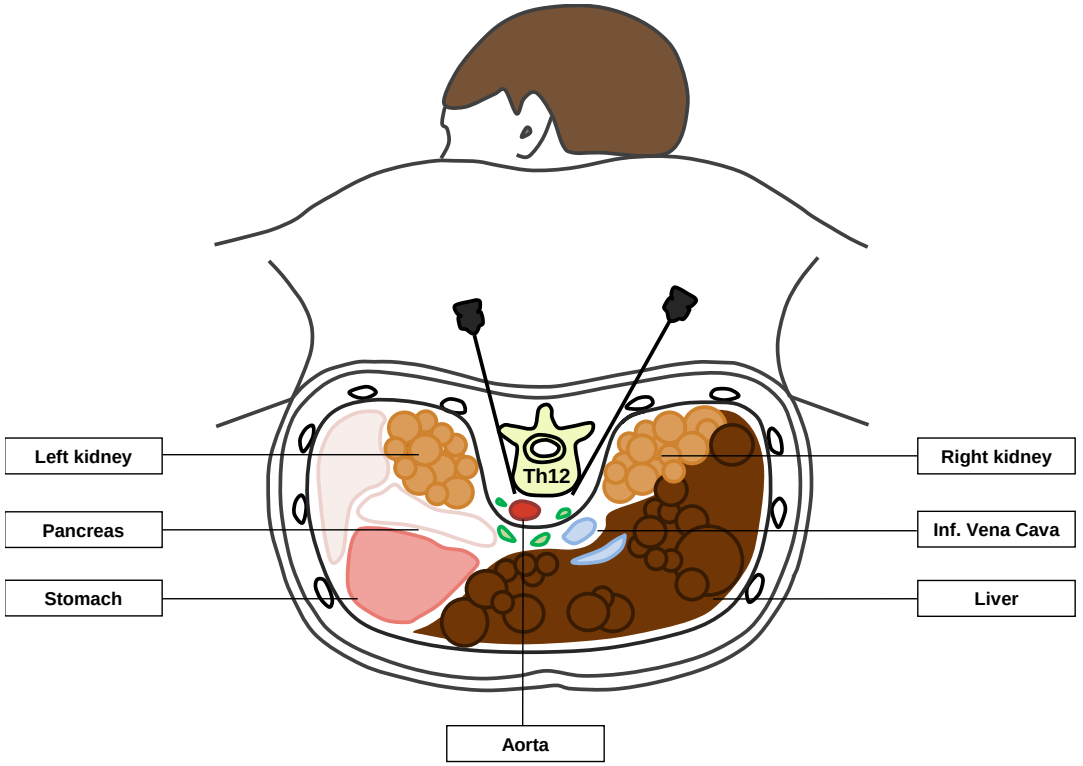
Diagnostic ipsilateral celiac block with LA (5-10 ml 0.25% bupivacaine)

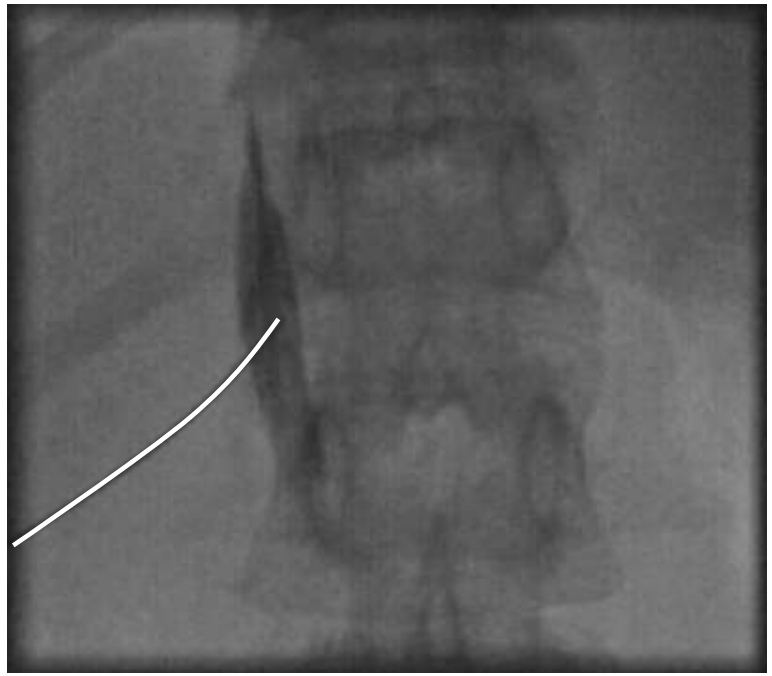
In case of pain relief, but pain recurs
→ planning for RF-MSN block

Good experience in patients with abdominal pain related to chronic pancreatitis, pancreatic and gastric cancer, hepatoblastoma and neuroblastoma[1,2]

1: Eisenberg et al, Anest Analg 1995
2: Akan et al., AJR 2004

Diagnostic celiac block with local anesthetic





Patients eligible for nerve blocks

- ADPKD-related pain ≥ 3 months
- VAS score ≥ 50 out of 100
- Chronic pain is invalidating, e.g. influencing social life and / or leading to an inability to work
- Use of opioids therapy
- Insufficient effect of previous pain therapies; non-pharmaco-logical as well as pharmacological

Casteleijn et al. Kidney Int 2017

Eligible patients

60 patients participated

- 16 patients did not receive a nerve block:
  - Option rejected by patient: 4
  - Pain not invalidating: 5
  - Pain deemed not ADPKD-related: 2
  - Cyst aspiration as preferred therapy: 2
  - Nephrectomy as preferred therapy: 3
- 44 patients received a diagnostic temporary celiac block with LA

Casteleijn et al. Kidney Int 2017

Results

- After 1 year 82% of patients experienced a sustaining improvement in pain intensity, leading to cessation of daily opioid use in 64%.
- Remarkably, in 30% this is obtained with one injection of a local anesthetic with temporary action
- These data indicate that a multidisciplinary stepwise treatment protocol, that applies sequential nerve blocks, is effective in obtaining substantial and sustained pain relief in most ADPKD patients with invalidating chronic pain.
- Patients should be carefully selected, and other treatment options should be considered (also for ineligible patients).

Casteleijn et al. Kidney Int 2017

Theses about chronic pain and abdominal volume related complaints in ADPKD

In 2025:

- No ADPKD/PLD patients will have invalidating chronic pain
  - To meet this aim there is a network of centers of expertise with a specialized multidisciplinary ADPKD Pain Clinic

    Problem: renal denervation is not reimbursed anymore

- No ADPKD/PLD patient will have major abdominal volume related complaints
  - To meet this aim there is consensus when to perform volume reducing interventions (i.e. cyst fenestration, nephrectomy, partial hepatectomy and liver transplantation)

#ADPKD
@PKD_Int

Breakout 4

Genetics and genetic testing

PKD International

EAF
European ADPKD Forum

Summit sponsors
This event has been made possible by sponsorship from
Baxter, Otsuka Pharmaceutical Europe Ltd, Palladio Biosciences and Sanofi Genzyme.

Baxter Otsuka Palladio Biosciences Sanofi Genzyme

#ADPKD
@PKD_Int

BREAKOUT 4: Genetics and genetic testing

Richard Sandford

(University of Cambridge, UK and EAF)

Jean-Pierre Schiltz

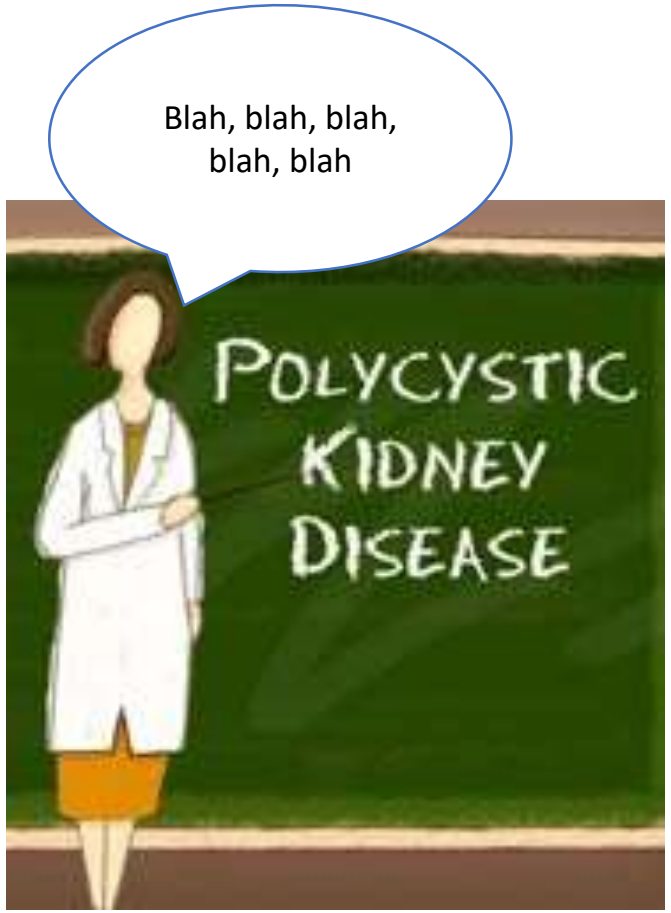
(AIRG-France)

ADPKD Genetics with Dr Richard Sandford and Jean-Pierre Schiltz

Dr Sandford is a Consultant in Clinical Genetics in the East of England.

He works in a multidisciplinary renal genetics clinic in Cambridge, UK and sees many individuals and families living with ADPKD.

He has a particular interest in understanding how ADPKD progresses over time, the factors that influence this and how genetic testing can be widely implemented in clinical practice.



http://thirtywhat.blogspot.co.uk/2007_10_01_archive.html

This session will briefly cover the following areas and provide ample time for questions:

- Genetics and ADPKD
- What do we mean by genetic testing?
- Why might I be offered genetic testing?
- What do the results mean?
- Do I have to have genetic testing?
- Should I tell my family the result?
- Can I test my children?

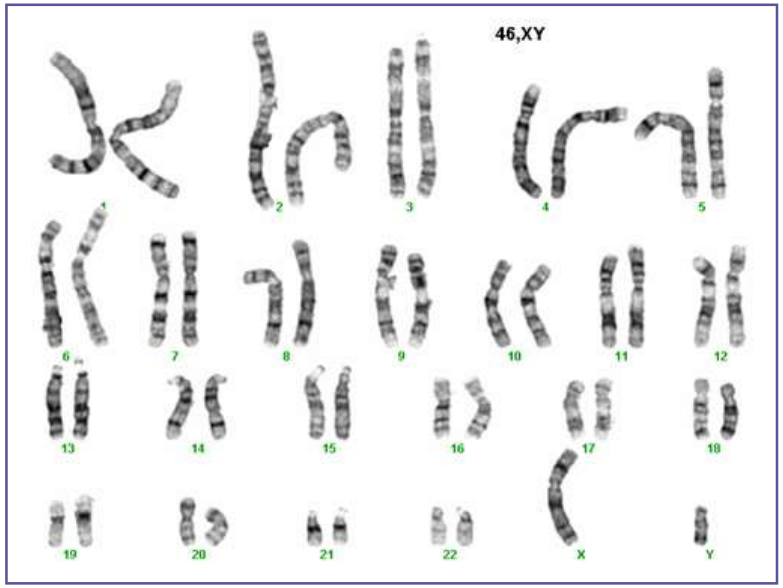
We need to think about our aspirations for the future!

- Genetics and ADPKD
- What do we mean by genetic testing?
- Why might I be offered genetic testing?
- What do the results mean?
- Do I have to have genetic testing?
- Should I tell my family the result?
- Can I test my children?

Autosomal Dominant Polycystic Kidney Disease

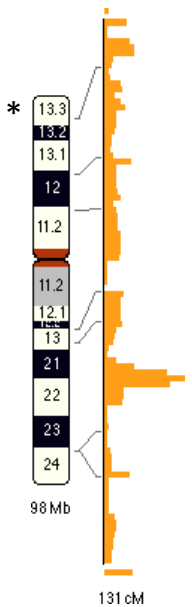
- A is autosomal not adult!
- What does autosomal mean?

- Human body cells contain 46 chromosomes in 23 pairs – one of each pair inherited from each parent
- Chromosome pairs 1 – 22 are called autosomes.
- The 23rd pair are called sex chromosomes:
  XX is female, XY is male.



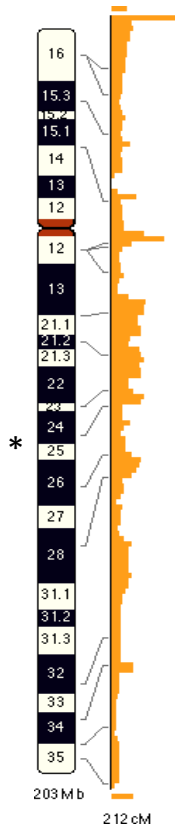
- Genetics and ADPKD
- What do we mean by genetic testing?
- Why might I be offered genetic testing?
- What do the results mean?
- Do I have to have genetic testing?
- Should I tell my family the result?
- Can I test my children?

- Genetic alterations (mutations) in two genes, *PKD1* and *PKD2*, are responsible for most cases of ADPKD
- New genes are being discovered but are responsible for very few cases



Chromosome 16

- *PKD1* is located on chromosome 16 (1995)
- *PKD2* is on chromosome 4 (1996)
- 85% of ADPKD families have a ‘mutation’ in in *PKD1*

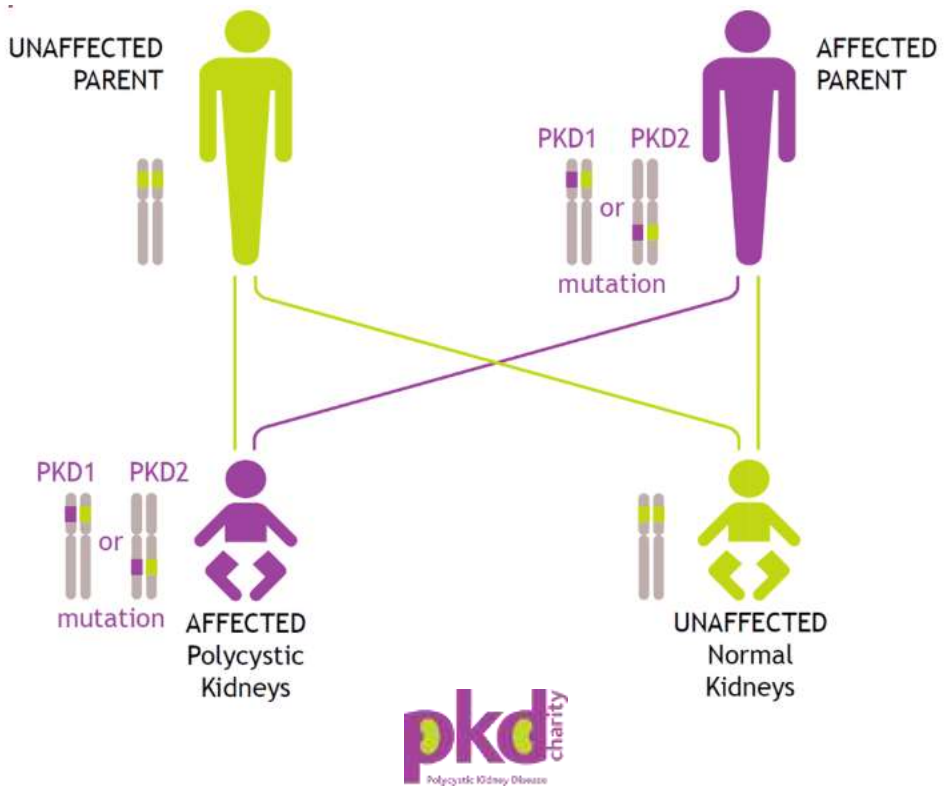


Chromosome 4

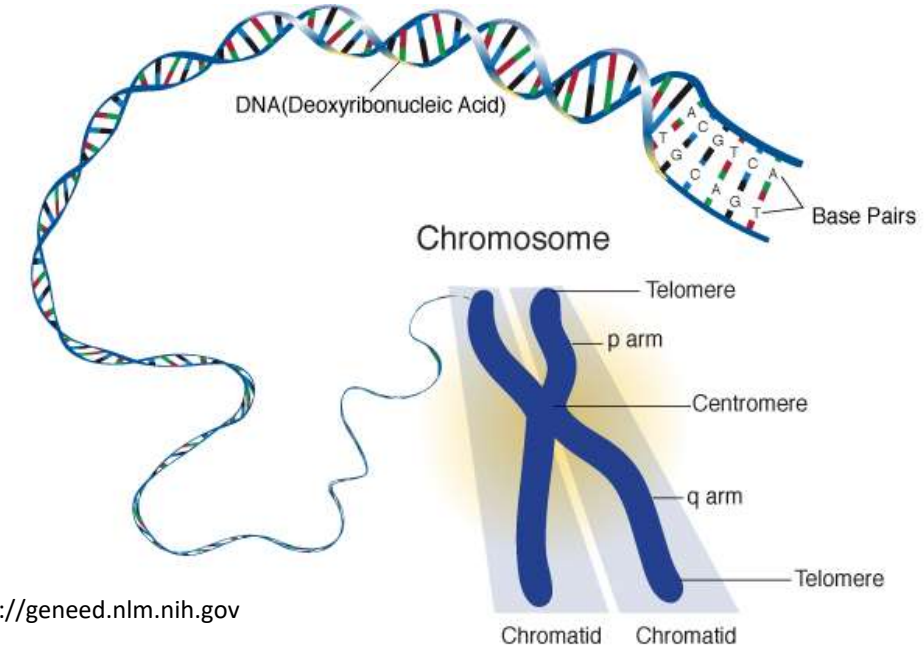
- Genetics and ADPKD
- What do we mean by genetic testing?
- Why might I be offered genetic testing?
- What do the results mean?
- Do I have to have genetic testing?
- Should I tell my family the result?
- Can I test my children?

Autosomal Dominant inheritance:

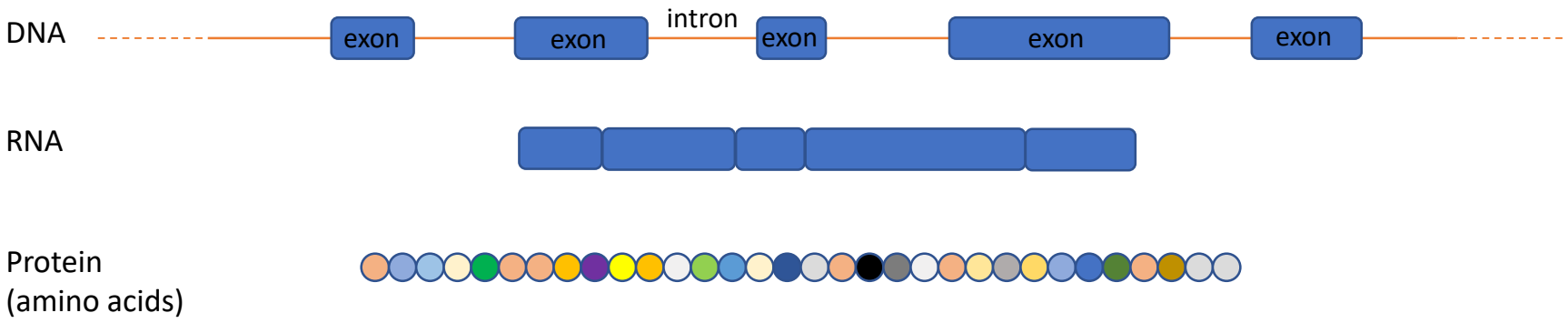
- Condition can be passed from generation to generation and affect males and females
- Only one altered copy of a gene is required to cause the condition
- An affected individual will have a 1 in 2 (50%) chance of having a child with the same condition
- An individual with ADPKD but no family history still has a 1 in 2 chance of having a child with the same condition
- The risk is the same for each child



- Genetics and ADPKD
- What do we mean by genetic testing?
- Why might I be offered genetic testing?
- What do the results mean?
- Do I have to have genetic testing?
- Should I tell my family the result?
- Can I test my children?

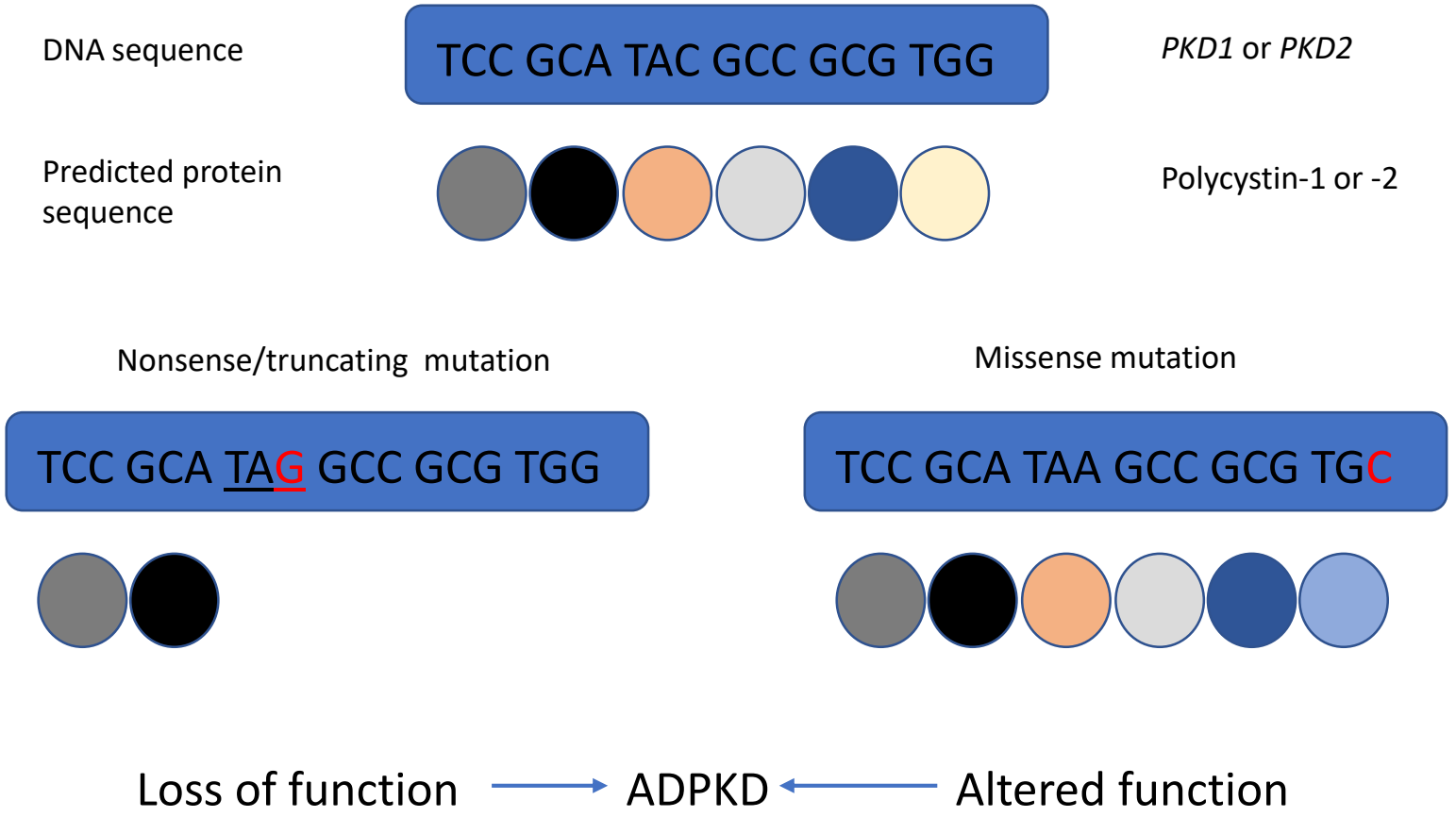


https://geneed.nlm.nih.gov



- Genetics and ADPKD
- What do we mean by genetic testing?
- Why might I be offered genetic testing?
- What do the results mean?
- Do I have to have genetic testing?
- Should I tell my family the result?
- Can I test my children?

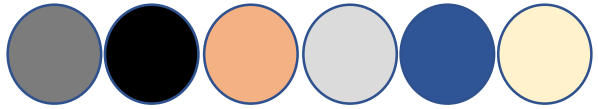
We are trying to find a genetic alteration or mutation that causes ADPKD. This is not always possible in someone with ADPKD.



- Genetics and ADPKD
- What do we mean by genetic testing?
- Why might I be offered genetic testing?
- What do the results mean?
- Do I have to have genetic testing?
- Should I tell my family the result?
- Can I test my children?

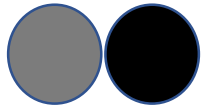
There are several different types of ‘mutation’ that are identified by genetic testing. For example:

TCC GCA TAC GCC GCG TGG



Deletion mutation

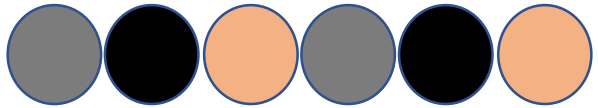
TCC GCA TAG CCG CGT GG



Loss of function

Duplication mutation

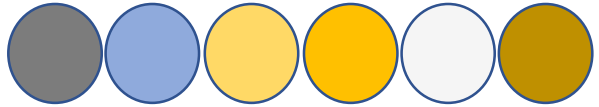
TCC GCA TAC TCC GCA TAC



Loss/altered function

Insertion mutation

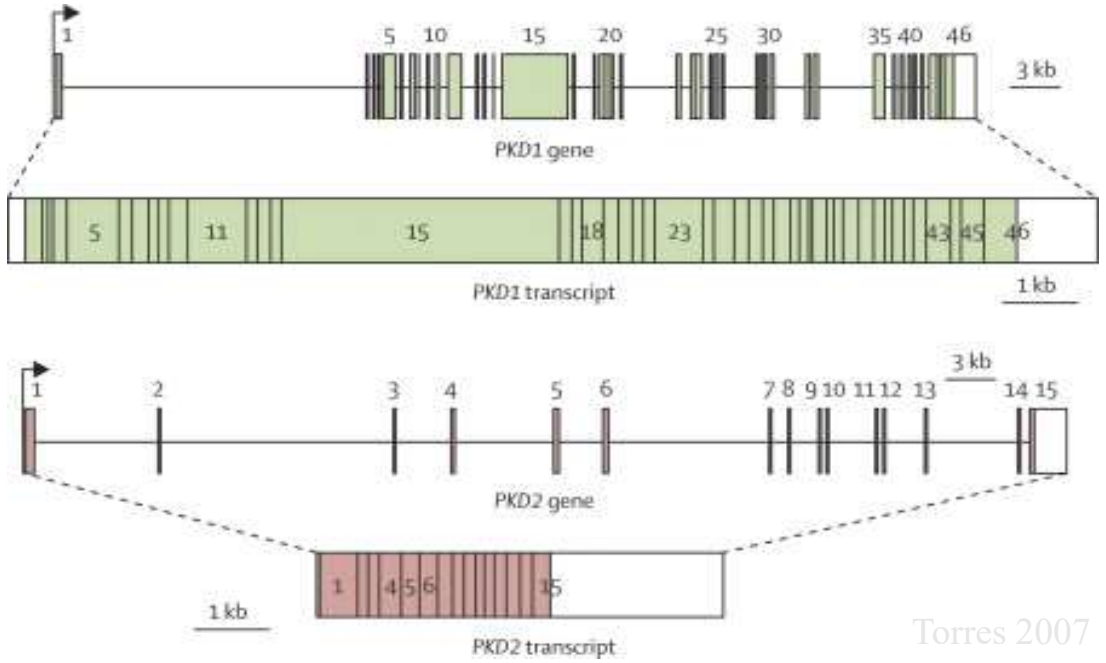
TCC GGC ATA CGC CGC GTG G



Loss/altered function

- Genetics and ADPKD
- What do we mean by genetic testing?
- Why might I be offered genetic testing?
- What do the results mean?
- Do I have to have genetic testing?
- Should I tell my family the result?
- Can I test my children?

- Currently genetic testing for ADPKD is focused on *PKD1* and *PKD2*
- *PKD1* and *PKD2* may also be tested together with a few or many additional genes or even the whole genome



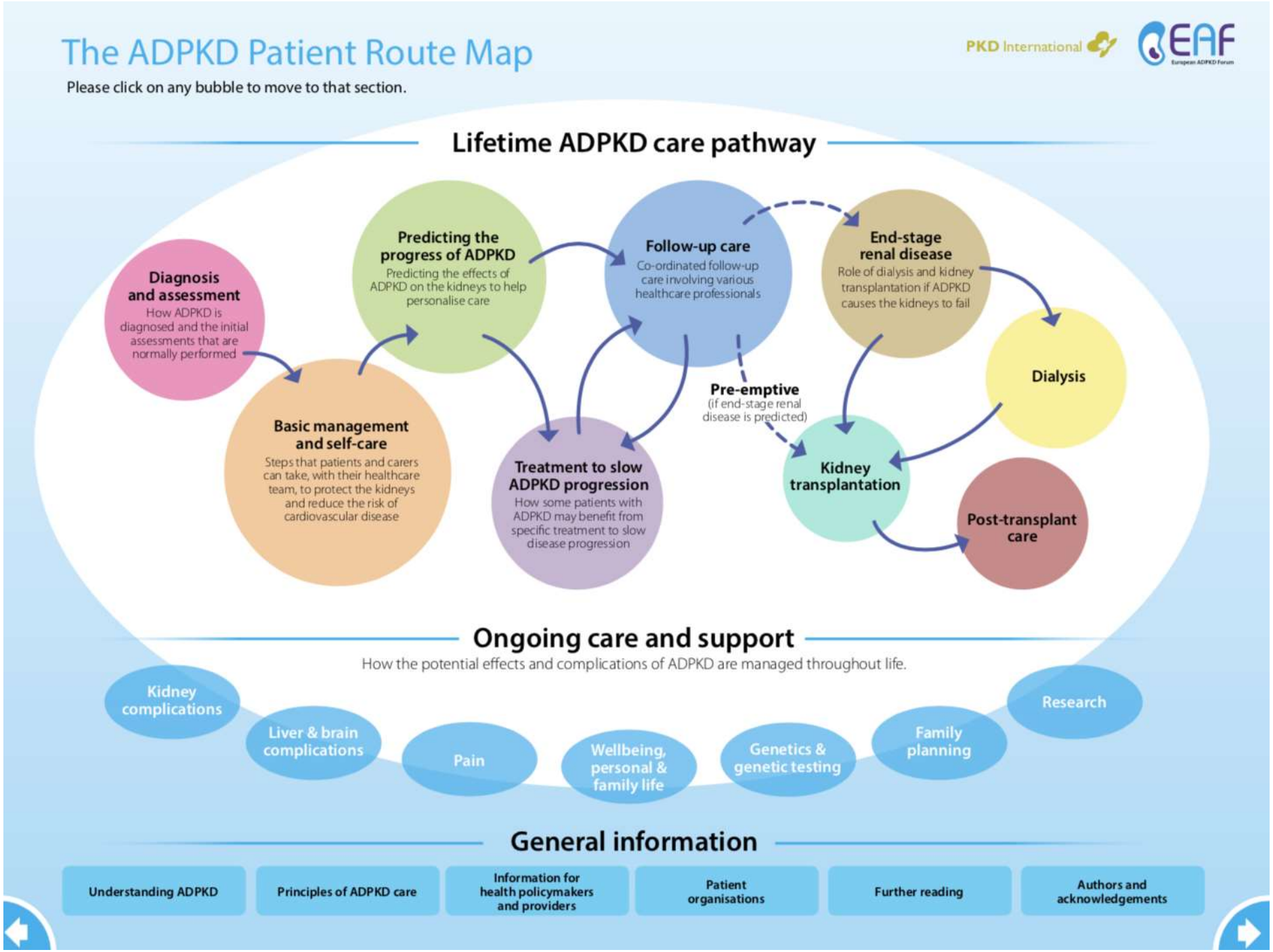
Torres 2007

The ADPKD Patient Route Map

PKD International

EAF European ADPKD Forum

Please click on any bubble to move to that section.



- Genetics and ADPKD
- What do we mean by genetic testing?
- Why might I be offered genetic testing?
- What do the results mean?
- Do I have to have genetic testing?
- Should I tell my family the result?
- Can I test my children?

The reasons for offering genetic testing are evolving, are not always clear and may differ from individual to individual.

For the majority of individuals with a family history of ADPKD imaging (ultrasound, CT or MRI) remains the commonest diagnostic and screening investigation

- Diagnostic testing e.g. in infants and children
- Likely ADPKD but equivocal/unusual scan results
- Likely ADPKD but no family history
- Is there a ‘syndromic’ cause of renal cysts?
- Predictive testing especially in younger individuals (may be with a normal ultrasound scan)
- Living-related donor evaluation
- Prenatal and preimplantation genetic diagnosis
- Prognosis/risk scores (risk assessment)

- Genetics and ADPKD
- What do we mean by genetic testing?
- Why might I be offered genetic testing?
- What do the results mean?
- Do I have to have genetic testing?
- Should I tell my family the result?
- Can I test my children?

Your genetic test report:

- PKD1 c.4968delT, p.(Arg1657Glyfs*65)
- Variant results in an abnormal protein and is highly likely to be pathogenic
- Variant has not been reported previously (ADPKD Mayo database, ClinVar and HGMD)
- Test confirms a diagnosis of ADPKD
- Testing is available for other family members

Which gene and where?
Is it predicted to cause ADPKD?

Is it unique to me?

What does the result mean to me and my family?

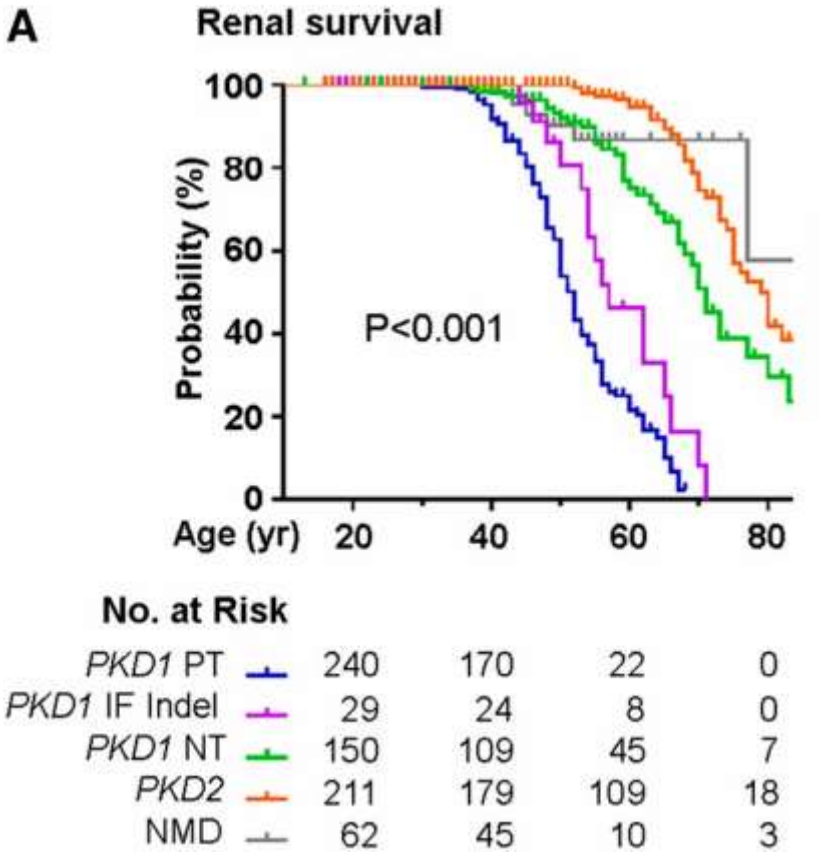
Other test result outcomes:

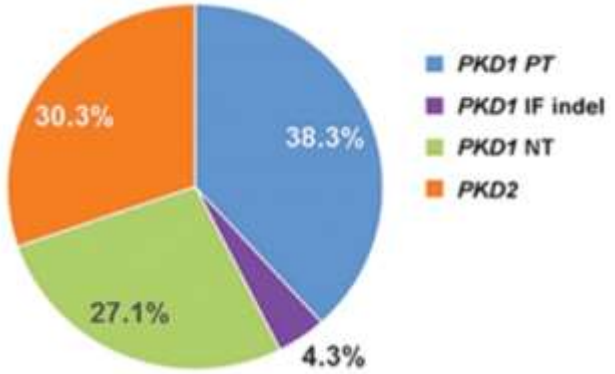
- Likely pathogenic-do other affected family members carry the same variant?
- VUS (variant of unknown significance)
- No mutation detected NMD 5-10% (often interpreted as ‘normal’)

- Genetics and ADPKD
- What do we mean by genetic testing?
- Why might I be offered genetic testing?
- What do the results mean?
- Do I have to have genetic testing?
- Should I tell my family the result?
- Can I test my children?

Renal survival in TGESP

Young-Hwan Hwang et al. JASN 2016;27:1861-1868





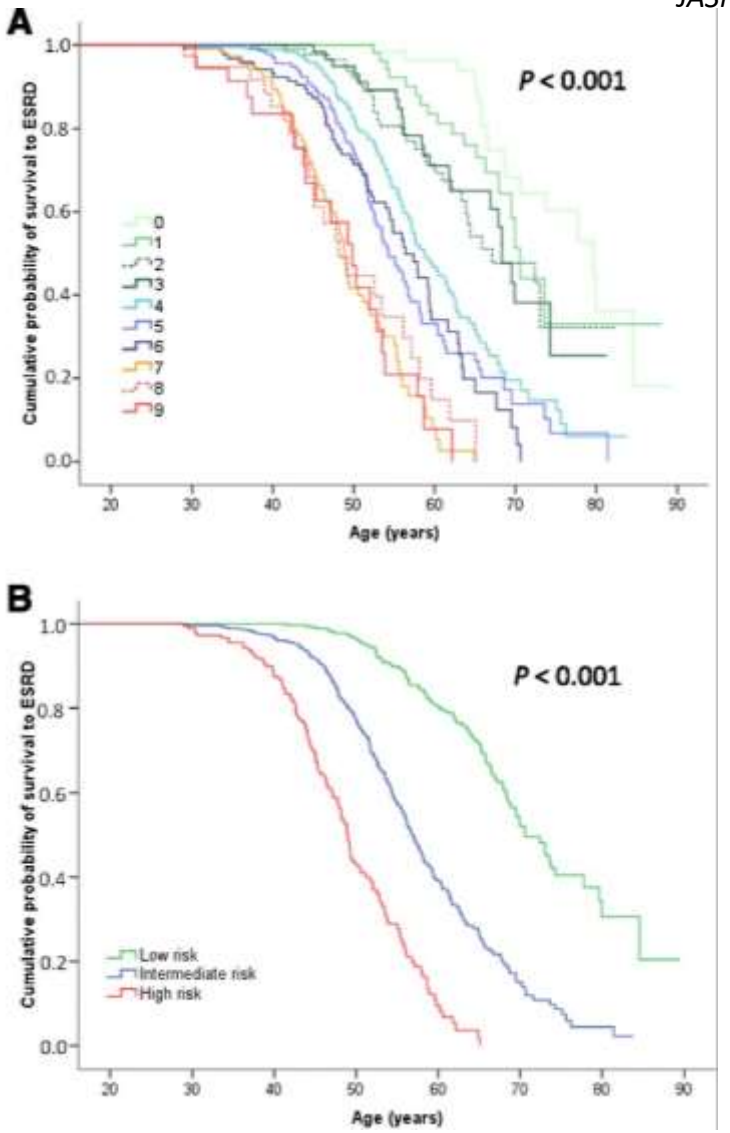
Mutation Class	*N*	Age (yr) at ESRD[a]
PKD1 truncating	249	52.5 (51.2 to 53.9)
PKD1 IF indel	32	58.6 (54.9 to 62.4)
PKD1 NT	152	70.8 (67.5 to 74.2)
PKD2	213	80.0 (77.1 to 82.8)
NMD	61	77.5 (72.1 to 82.9)

- Genetics and ADPKD
- What do we mean by genetic testing?
- Why might I be offered genetic testing?
- What do the results mean?
- Do I have to have genetic testing?
- Should I tell my family the result?
- Can I test my children?

The PROPKD Score

Cornec-Le Gall et al 2015
JASN 27 942-51

Points	
1	Male gender
2	HT before age 35
2	First urologic event before age 35
0	*PKD2* mutation
2	Non-truncating *PKD1* mutation
4	Truncating *PKD1* mutation

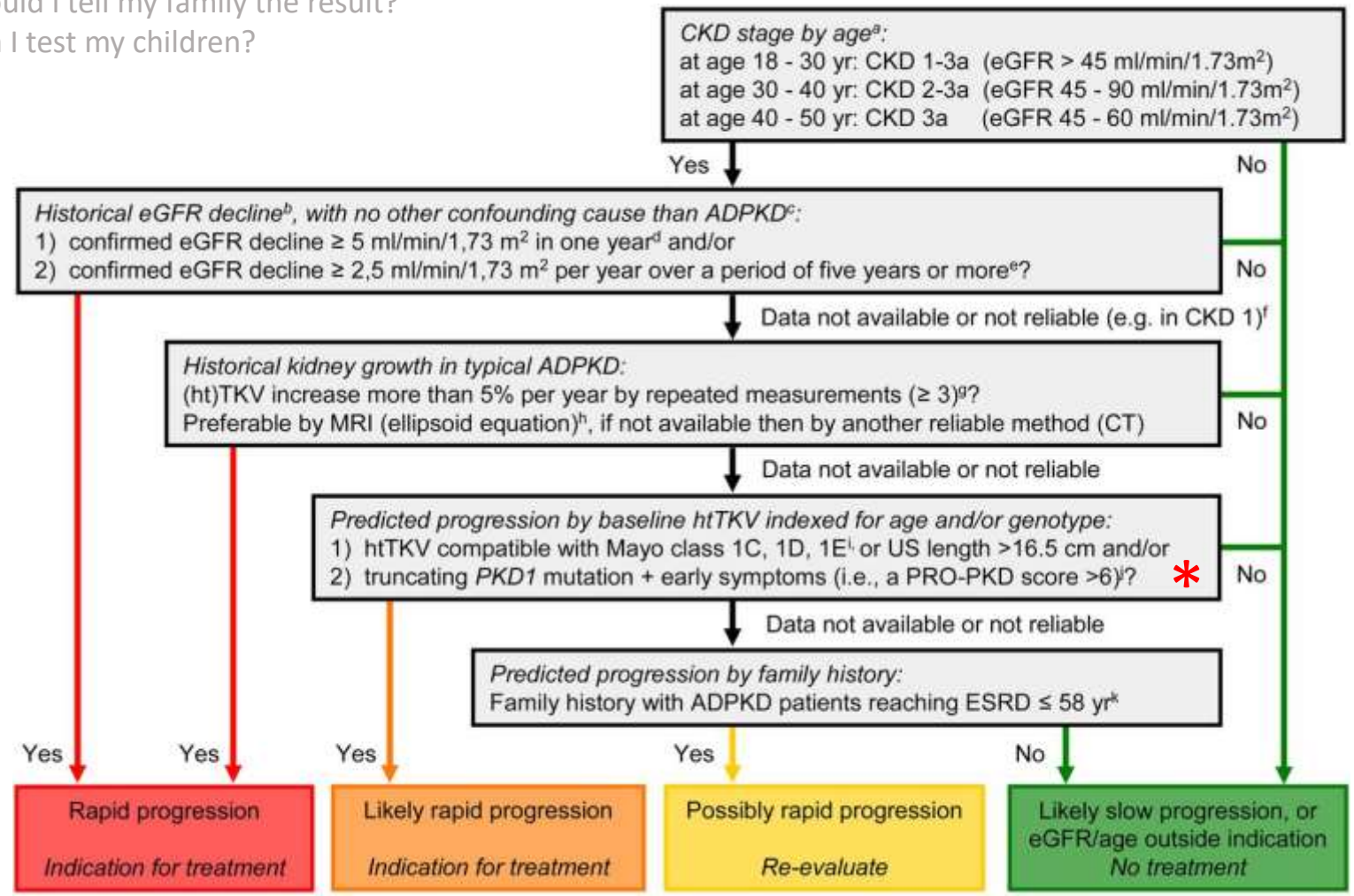


- Genetics and ADPKD
- What do we mean by genetic testing?
- Why might I be offered genetic testing?
- What do the results mean?
- Do I have to have genetic testing?
- Should I tell my family the result?
- Can I test my children?

Prognostic group	patients (n)	Kaplan-Meier analysis			
		Median age at ESRD	Age at ESRD	p value	Risk of ESRD at age 60
		(IQR yrs)	range yrs		yrs± SEM (%)
low risk	326	70.6 (63.6-84.5)	41.5-84.6		19.3±2.7
Intermediate risk	455	56.9 (50.7-65.4)	28.9-81.5	<0.001	60.8±3.0
High risk	192	49 (43.8-55.6)	29-65.5	<0.001	91.9±3.2

- Genetics and ADPKD
- What do we mean by genetic testing?
- Why might I be offered genetic testing?
- What do the results mean?
- Do I have to have genetic testing?
- Should I tell my family the result?
- Can I test my children?

Algorithm to assess indications for initiation of Tolvaptan treatment in ADPKD.



Gansevoort et al. 2016;31:337-348

- Genetics and ADPKD
- What do we mean by genetic testing?
- Why might I be offered genetic testing?
- What do the results mean?
- Do I have to have genetic testing?
- Should I tell my family the result?
- Can I test my children?

Pros:

- Confirm diagnosis
- Pre-symptomatic testing
- Confirm gene- *PKD1* or *PKD2*
- Information for family members
- Donor evaluation
- Treatment options
- Family planning

Cons:

- Worry and anxiety
- Uncertainty
- Future risks
- Uncertain result
- Insurance and careers

Genetic counselling is an important part of seeking genetic testing

- Genetics and ADPKD
- What do we mean by genetic testing?
- Why might I be offered genetic testing?
- What do the results mean?
- Do I have to have genetic testing?
- Should I tell my family the result?
- Can I test my children?

- This remains a difficult area!
- Most commonly requested for diagnostic testing
- Respect child's autonomy and ability to consent
- Requires genetic counselling
- Familial mutation typically needs to be known but there may be no family history
- Not 'just to find out'
- Consider blood pressure monitoring and 'one-off' ultrasound scanning (see UK Renal Association Clinical Practice Guideline)
- Individual family reasons

Where I can find out more?

- Your own GP or kidney specialist may be able to offer you further advice about genetic testing or screening. They may also refer you to your local genetics clinic. You should ask!

- ADPKD organisations including PKD International, PKD Charity, PKD Foundation and many others.

- New resources are required that reflect the current variation in practice across Europe but which aspire to equitable access to genetic testing if appropriate for clinical care and to support individuals and families in key decision making.

Questions?

For example……

- Who should be tested?
- When should testing be offered?
- Should testing be offered to all families with ADPKD?
- Should testing be offered to children?
- Are there any negative impacts on testing?

#ADPKD
@PKD_Int

Jean-Pierre Schiltz

AIRG FRANCE

www.airg-france.fr
airg.permanence@orange.fr

AIRG BELGIQUE AIRG ESPAGNE AIRG SUISSE AIRG MAROC

#ADPKD
@PKD_Int

Meet the Industry

PKD International

EAF
European ADPKD Forum

Summit sponsors
This event has been made possible by sponsorship from
Baxter, Otsuka Pharmaceutical Europe Ltd, Palladio Biosciences and Sanofi Genzyme.

Baxter Otsuka Palladio Biosciences Sanofi Genzyme

European ADPKD Patient Summit

15 –16 March 2019, Brussels, Belgium

PKD International

EAF European ADPKD Forum

Neil Shusterman
(Palladio Biosciences)

Manish Maski
(Sanofi Genzyme)

Carmen Walbert
(Baxter)

Moderator: ***Lee Baker*** *(Interel European Affairs)*

#ADPKD
@PKD_Int

Palladio Biosciences

PKD International

EAF
European ADPKD Forum

Summit sponsors
This event has been made possible by sponsorship from
Baxter, Otsuka Pharmaceutical Europe Ltd, Palladio Biosciences and Sanofi Genzyme.

Baxter Otsuka PALLADIO BIOSCIENCES SANOFI GENZYME

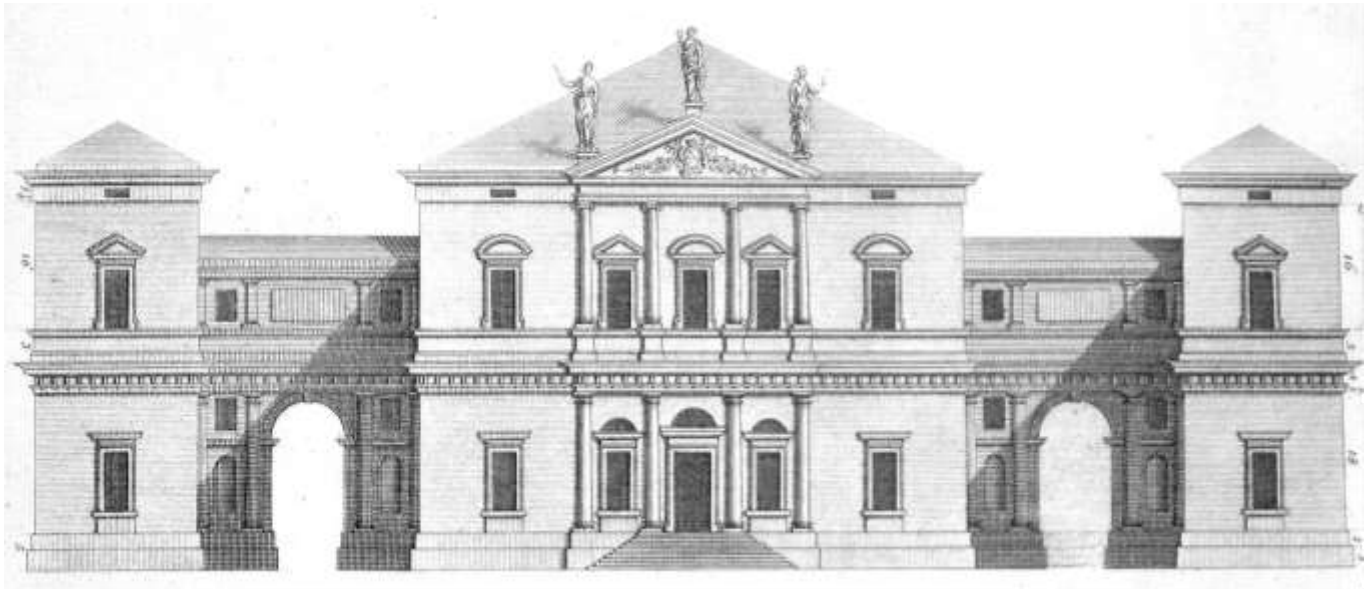
PALLADIO BIOSCIENCES

Working to Bring New Hope to Patients with Polycystic Kidney Disease

European ADPKD Patient Summit
March 2019

Introduction – Palladio Biosciences

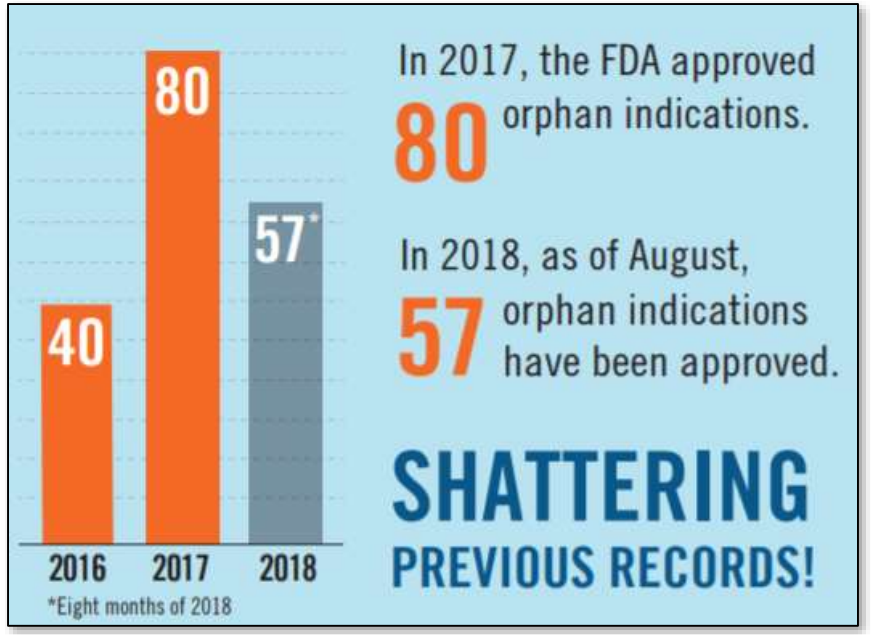
- Private drug development company based outside Philadelphia, PA USA
- Founded in 2015
- Working to bring new hope to patients with orphan diseases of the kidney
  - → Lixivaptan for Autosomal Dominant Polycystic Kidney Disease (ADPKD)
  - → Potentially other cystic kidney diseases



"Building a Biotech like a Classical Architect Would"

Orphan & Rare Diseases

- In the US, defined as conditions affecting less than 200,000 individuals
- In the EU, defined as less than 5 per 10,000 persons
- Estimated to be ~7,000 disorders
- Previously neglected by the pharmaceutical industry
- New developments in the regulation of drugs have created incentives for manufacturers to pursue research for these disorders
  - There has been an upward trend in research and approvals



Orphan & Rare Kidney Diseases

- Over 100 rare kidney diseases have been cataloged
- Partial list shown here:

Glomerular, tubular and metabolic disorders		Disorders of kidney development/morphology	
(i)	Adenine-phosphoribosyl-transferase deficiency	(i)	Alström syndrome
(ii)	Alport syndrome (XL, AR, AD)	(ii)	Bardet–Biedl syndrome types 1–12
(iii)	Alport syndrome with leiomyomatosis	(iii)	Branchio-oto-renal syndrome
(iv)	Bartter syndrome types 1–4	(iv)	Fraser syndrome
(v)	Cystinosis	(v)	Ellis–van Creveld syndrome
(vi)	Cystinuria—dent disease—lysinuric proteinintolerance	(vi)	Hypoparathyroidism, deafness, renal syndrome
(vii)	Denys–Drash syndrome	(vii)	Ivemark syndrome
(viii)	Diabetes insipidus, nephrogenic	(viii)	Jeune syndrome
(ix)	Distal renal tubular acidosis	(ix)	Joubert syndrome-related disorders
(x)	Fabry disease	(x)	Kallman syndrome
(xi)	Frasier syndrome	(xi)	Meckel–Gruber syndrome
(xii)	Gitelman syndrome	(xii)	Medullary cystic kidney disease
(xiii)	Gordon syndrome	(xiii)	Multicystic renal dysplasia
(xiv)	Hypophosphatemic rickets	(xiv)	Nephronophthisis types 1–11
(xv)	Liddle syndrome	(xv)	Oral-facial-digital syndrome 1
(xvi)	Lowe syndrome	(xvi)	Polycystic Kidney Diseases (autosomal dominant, types 1 and 2, autosomal recessive)
(xvii)	Nail–Patella syndrome	(xvii)	Renal agenesis
(xviii)	Nephrotic syndrome (Congenital-Finnish type)	(xviii)	Renal coloboma syndrome
(xix)	Nephrotic syndrome (due to mitochondrial or lysosomal disorders)	(xix)	Renal cysts and diabetes syndrome
(xx)	Nephrotic syndrome (steroid resistant) types 2, 3 and 4	(xx)	Renal hypoplasia/dysplasia syndrome
(xxi)	Pierson syndrome	(xxi)	Sensenbrenner syndrome
(xxii)	Primary hyperoxaluria type 1, 2 and 3	(xxii)	Townes–Brocks syndrome
(xxiii)	Proximal renal tubular acidosis	(xxiii)	Vesicoureteral reflux
(xxiv)	Pseudohypoaldosteronism types 1 and 2		
(xxv)	Renal amyloidosis (familiar)		
(xxvi)	Renal glicosuria		
(xxvii)	Schimke immuno-osseous dystrophy		
(xxviii)	'SeSAME' syndrome		
(xxix)	Xanthinuria—distal renal tubular acidosis		

ADPKD Drugs in Development

Stage (US)	Drug	Mechanism of Action	Sponsor
Approval	Tolvaptan	Vasopressin V2 antagonist	Otsuka
Phase 2	Lixivaptan	Vasopressin V2 antagonist	Palladio Bio
Phase 2	Tesevatinib	Multiple TK Inhibitor	Kadmon
Phase 2 / 3	Venglustat	GCS inhibitor	Sanofi-Genzyme
Phase 2	Bardoxolone	Nrf2 activator	Reata
Phase 1	RGLS4326	miR-17 inhibitor	Regulus

+ Research efforts by Vertex, Glaxo SmithKline
  List may not be complete

Vasopressin Hypothesis:

In ADPKD, vasopressin attaching to a specific receptor advances disease and blocking the receptor would be beneficial

PKD rats without vasopressin do not develop cysts

Vasopressin blockade in humans slows the decline in renal function

Patient Involvement in Clinical Research

1. Provide input and feedback to the research process
2. Learn about clinical trials
3. Participate in clinical trials

→ Why participate in clinical trials?

- → New drugs cannot be advanced without clinical trials
- → Clinical trials require the participation of patients
- → Clinical trials are highly regulated
- → Clinical trials are conducted under ethics' committee approval and require informed consent

#ADPKD
@PKD_Int

Sanofi-Genzyme

PKD International

EAF European ADPKD Forum

Summit sponsors
This event has been made possible by sponsorship from
Baxter, Otsuka Pharmaceutical Europe Ltd, Palladio Biosciences and Sanofi Genzyme.

Baxter Otsuka Palladio Biosciences Sanofi Genzyme

SANOFI GENZYME

STAGED-PKD:

A clinical trial for certain ADPKD patients

Company Commitment to Patients

PKD Conference (US) 2018

Rare Disease Day 2018

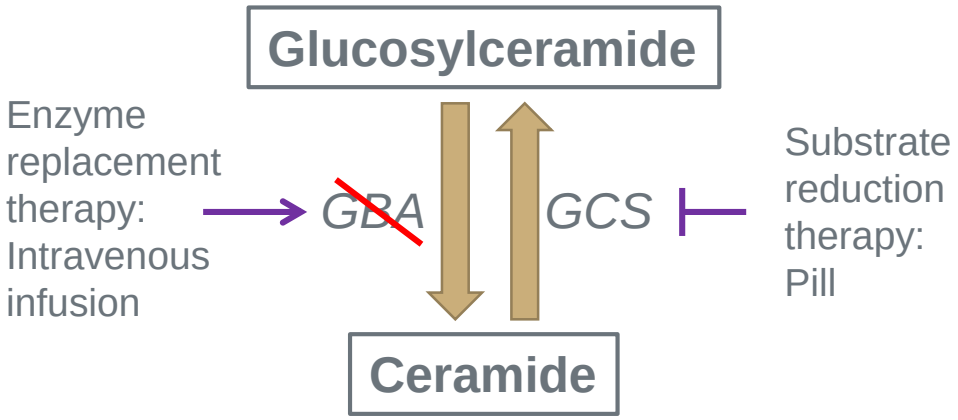
ASN 2018

PKD New England Walk 2018

Testing a hypothesis about GCS

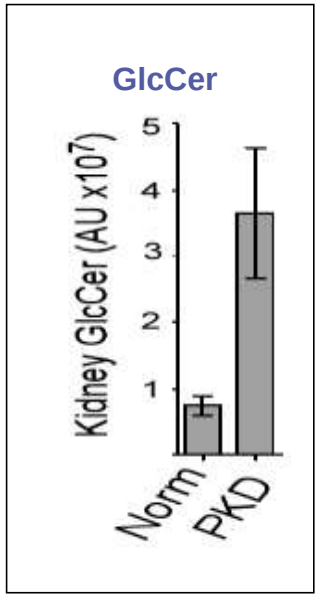
Glucosylceramide (GCS) plays a role in Gaucher disease and ADPKD

Gaucher Disease: Accumulation of glucosylceramide in liver & spleen

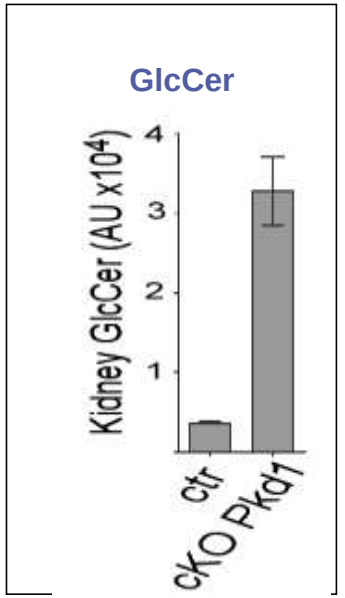


ADPKD: Accumulation of glucosylceramide in kidneys

Human ADPKD



Mouse ADPKD



Hypothesis: Glucosylceramide (GCS) accumulation promotes cyst growth in ADPKD.

Natoli et al (2010) Nature Medicine

STAGED-PKD: Trial Overview

EudraCT2017-004084-12

Study Design: 2 stages

Stage One: 240 participants

- *Timing:* Screening (15 days) + run-in (2 weeks) + 24 months treatment
- *Assignment:* Randomized, three dose groups – placebo, dose 1, dose 2 (1:2)
- *Assessments*: MRI, eGFR, plasma PK, safety/tolerability

Stage Two: 320 participants

- *Timing:* Screening (15 days) + run-in (2 weeks) + 24 months treatment
- *Assignment:* Randomized; two dose groups - placebo or stage one dose (1:1)
- *Assessments*: MRI, eGFR, urine osmolality, plasma PK, safety/tolerability

Study Objectives

Primary

Rate of Total Kidney Volume (TKV) Growth: *Baseline – 18 months*

Estimated Glomerular Filtration Rate (eGFR) decline: *Baseline – 24 months*

Secondary

Rate of renal function decline (Stage 1) and TKV growth (Stage 2)

Evaluate effect on mood using Beck Depression Inventory

Evaluate change in nocturia based on patient-reported diary

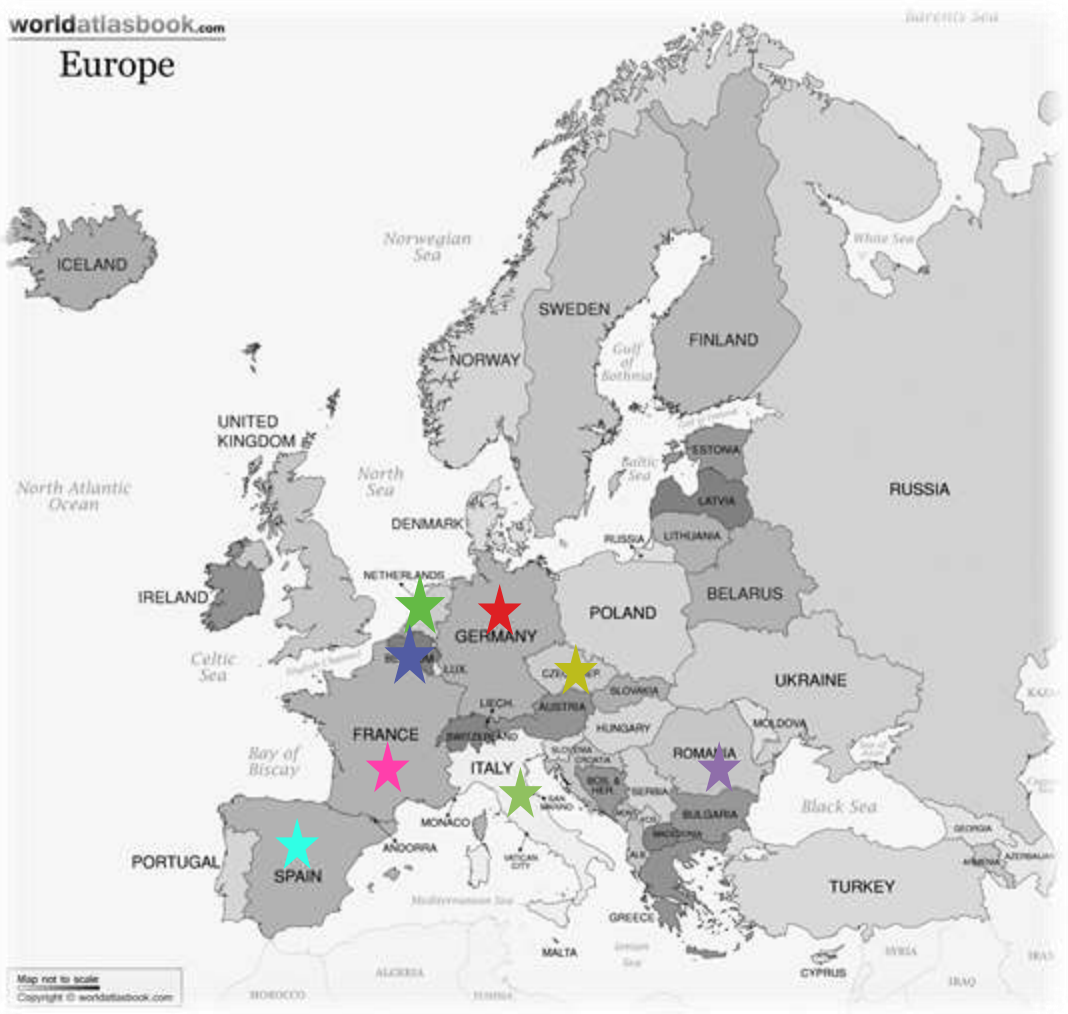
Evaluate effect of on kidney concentrating ability by assessing urine osmolality

Characterize safety profile and evaluate PK of venglustat

Evaluate change in lens clarity by ophthalmological exam

STAGED-PKD: A Global Study

European Sites (March, 2019)



Belgium:
- Cliniques universitaires Saint-Luc *(Olivier DEVUYST)*
- Universitair Ziekenhuis Leuven *(Bert BAMMENS)*

Czechia:
- Institut klinicke a experimentalni mediciny *(Ondrej VIKLICKY)*

France:
- CHU De Toulouse - Hôpital De Rangueil *(Dominique CHAUVEAU)*
- Hôpital Necker Enfants Malades *(Bertrand KNEBELMANN)*
- Hopital de la Cavale Blanche *(Yannick LE MEUR)*

Germany:
- Charité Universitätsmedizin Berlin *(Christian ROSENBERGER)*

Italy:
- Spedali di Brescia Ospedaliero Montichiari *(Francesco SCOLARI)*
- HSR – IRCCS *(Paolo MANUNTA)*

The Netherlands:
- UMC Groningen *(Esther MEIJER)*
- UMC St Radboud *(Joost DRENTH)*

Romania:
- Spitalul Clinic Judetean de Urgenta “Pius Branzeu” Timisoara *(Flaviu BOB)*

Spain:
- Fundacion Jimenez Diaz *(Alberto ORTIZ)*
- Hospital Del Mar *(Laia Sans ATXER)*

SANOFI GENZYME

“It was a shot in the dark, and it was magnificent.”

Henri Termeer, on coming to Genzyme*

Source: https://www.bostonglobe.com/metro/2017/05/13/henri-termeer-key-biotech-leader-who-built-genzyme-into-industry-giant-dies/HUbclNVfURdx1ARCH2OK1M/story.html

THANK YOU!

Manish MASKI, MD, MMSc
Global Medical Director, ADPKD

Kathleen TIGHE
AD, Global Rare Patient Advocacy, Nephrology

Contact-US@sanofi.com
Trial Team

Reference Staged-PKD and include location

#ADPKD
@PKD_Int

Baxter

PKD International

EAF
European ADPKD Forum

Summit sponsors
This event has been made possible by sponsorship from
Baxter, Otsuka Pharmaceutical Europe Ltd, Palladio Biosciences and Sanofi Genzyme.

Baxter Otsuka Palladio Biosciences Sanofi Genzyme

SUPPORTING EMPOWERMENT OF PATIENTS WITH RENAL DISEASES IN THEIR CHOICE OF OPTIMAL TREATMENT

DR CARMEN WALBERT MD

HEAD OF MEDICAL AFFAIRS BAXTER EUROPE, MIDDLE EAST AND AFRICA

MARCH 16, 2019

ADVANCING HEALTHCARE: OUR SIX GLOBAL BUSINESS UNITS

OUR MISSION: SAVE AND SUSTAIN LIVES

RENAL CARE
Pioneering therapy options for people with kidney diseases, including peritoneal dialysis and hemodialysis

ADVANCED SURGERY
Enabling surgeons to act with precision and speed to minimize complications and increase efficiency

PHARMACEUTICALS
Providing generic injectable medicines and inhaled anesthetics that are critical to effective patient care across the globe

MEDICATION DELIVERY
Advanced infusion systems and solutions to help ensure the right treatment is delivered safely and efficiently

NUTRITION
Leading clinical nutrition solutions formulated to help patients maintain or regain their health

ACUTE THERAPIES
Innovative products and therapies that treat life-threatening conditions in the ICU

BAXTER: A PIONEER IN RENAL REPLACEMENT CARE

DIALYSERS

DIALYSIS SYSTEMS

DIALYSIS FLUIDS

IN THE HOME

PERITONEAL DIALYSIS AND HEMODIALYSIS

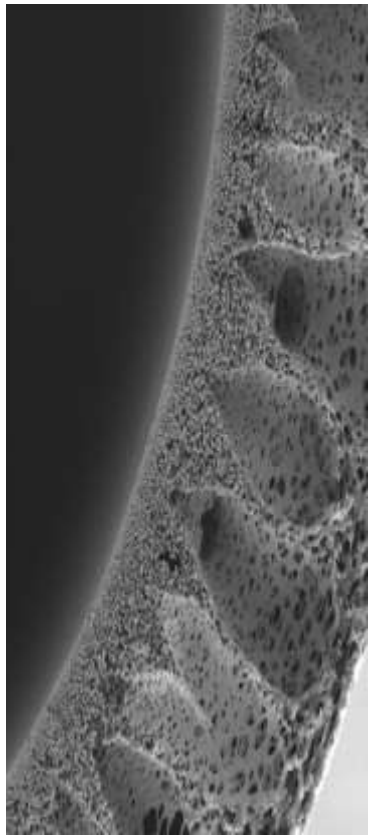
IN THE DIALYSIS CENTER

HEMODIALYSIS

IN THE ICU

ACUTE CARE

RECENT DIALYSER INNOVATION IN HEMODIALYSIS



Editorial

Blood Purification

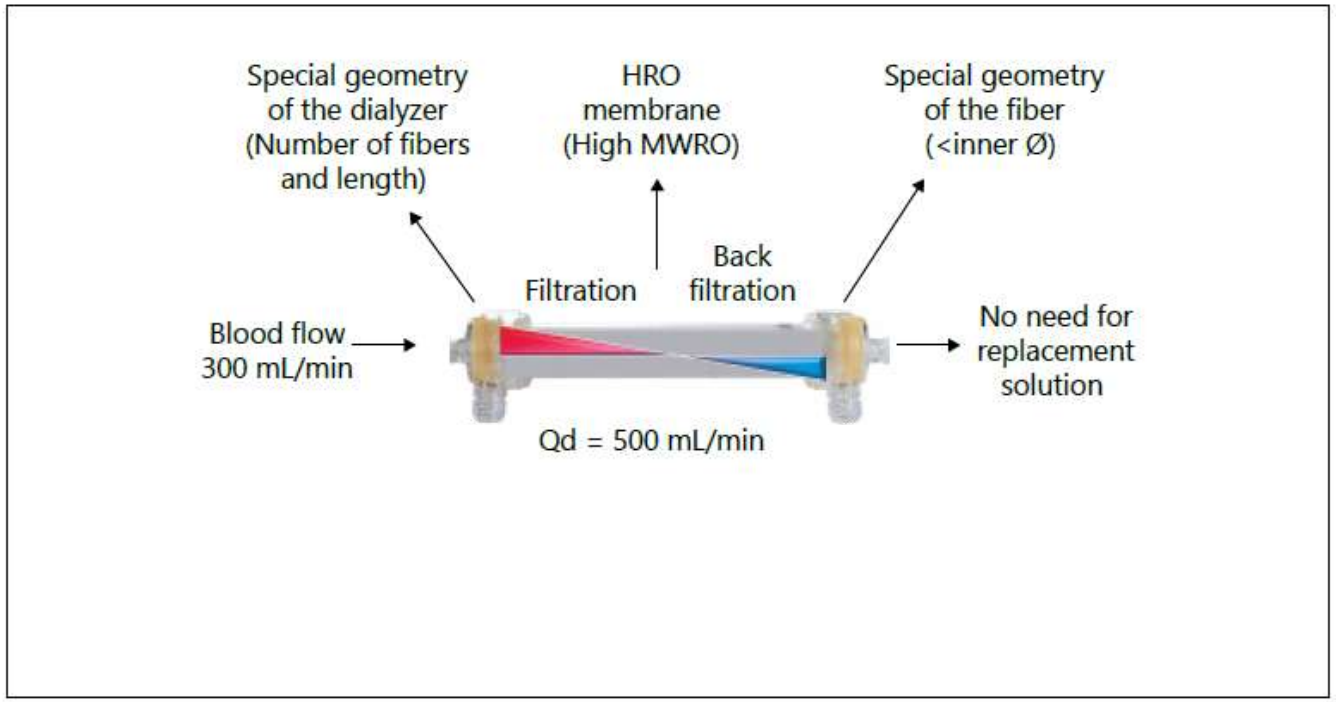
Blood Purif 2017;44:I–VIII
DOI: 10.1159/000476012

Published online: May 10, 2017

The Rise of Expanded Hemodialysis

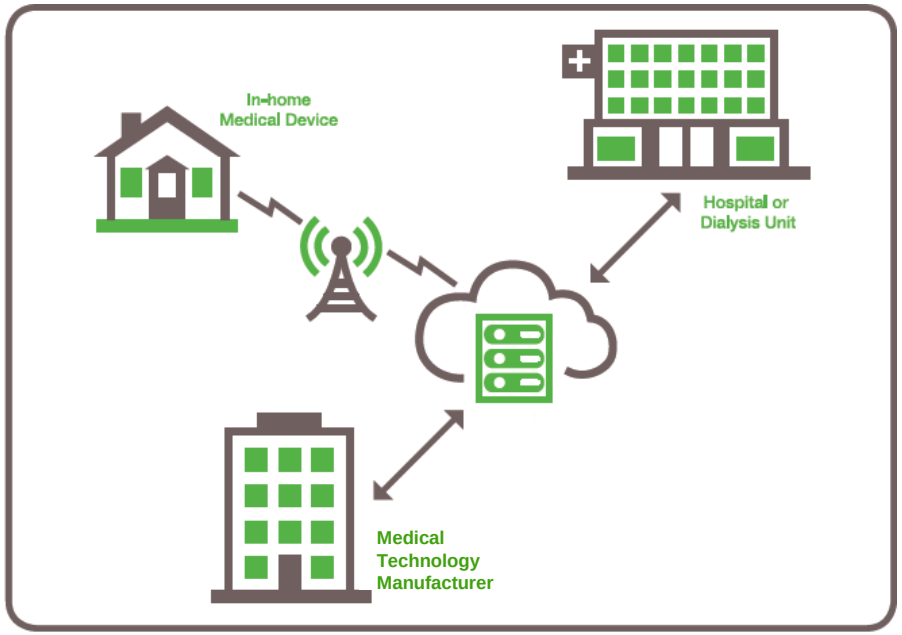
Claudio Ronco[a, b]

[a]Department of Nephrology Dialysis and Transplantation, St. Bortolo Hospital, and [b]International Renal Research Institute, Vicenza, Italy



https://www.karger.com/Book/Toc/276628#toc

RECENT INNOVATION IN PERITONEAL DIALYSIS - RPM[1] ENABLER FOR BETTER CARE AND PATIENT OUTCOMES



2015:
First patient in the UK

2017:
In the Benelux

2018:
In Europe 27 countries & 5656 patients

1. RPM: Remote Patient Monitoring

RECENT INNOVATIONS IN HOME DIALYSIS TREATMENTS

‘Next door dialysis’

GROWING NEED FOR KIDNEY DISEASE TREATMENTS

1 in 10 Europeans

has some degree **of Kidney Disease**[1]

1 in 3 Europeans

is at risk of developing **chronic kidney disease.**[1]

Globally, over **12 million patients** suffering from **ADPKD**[4]

~2.6 million ESRD patients **treated with dialysis** worldwide[1] and numbers are rising steadily

Dialysis treatment accounts for **2% of national healthcare budgets** This will double in the next 5 years[1]

[1] European Kidney Health Alliance (2015) Recommendations for Sustainable Kidney Care
[2] Liyanage Lancet 2015 22014
[3] Annual Data Report. Volume 2: End-Stage Renal Disease in the United States. Chapter 10: International Comparisons. http://www.usrds.org; 2014; Accessed 1/23/15; p1. 2011 data.
4 ttps://pkdinternational.org/what-is-pkd/adpkd

WE ARE COMMITTED TO WORKING IN PARTNERSHIP

EUROPEAN CANCER PATIENT COALITION

World Kidney Day

EKHA EUROPEAN KIDNEY HEALTH ALLIANCE

Ogólnopolskie Stowarzyszenie Osób Dializowanych

EPF European Patients Forum

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

Kidney Care UK

ALCER Federación Nacional

ERA EDTA

The European Nutrition for Health Alliance

ISN International Society of Nephrology
Advancing Nephrology Around the World

ESPEN The European Society for Clinical Nutrition and Metabolism

PATIENT EMPOWERMENT

The five “E” of Empowerment stand for[1]:

- **Education:** informed decisions about their health
- **Expertise:** self-manage their condition so they have a unique expertise
- **Equality:** need support to become equal partners with health professionals
- **Experience**: work with patient organizations to represent them
- **Engagement**: be involved in designing more effective healthcare and research

1. European Patient’ s Forum, Website, March 10, 2019

#ADPKD
@PKD_Int

Breakout 5

Renal Replacement Therapy

PKD International

EAF European ADPKD Forum

Summit sponsors
This event has been made possible by sponsorship from
Baxter, Otsuka Pharmaceutical Europe Ltd, Palladio Biosciences and Sanofi Genzyme.

Baxter Otsuka Palladio Biosciences Sanofi Genzyme

#ADPKD
@PKD_Int

BREAKOUT 5: Renal Replacement Therapy

Yves Pirson

(Université Catholique de Louvain, Belgium)

Tom Oostrom

(Dutch Kidney Foundation, Netherlands)

Brenda de Coninck

(EAF)

European ADPKD Patient Summit

Renal Replacement Therapy

Pr Yves PIRSON
Cliniques univ. St Luc – Brussels – Belgium

16 March 2019

- Up to 70% of patients with ADPKD progress to ESKD by the age of 65 yrs, needing RRT

- Among 55 patient-important outcomes in ADPKD, the 3 top ranked issues were kidney function, ESKD and survival

(Cho Y et al, Nephrology (Carlton) 2019, in press)

What is the optimal choice of RRT ?

What is the best dialysis modality ?

What is the place of nephrectomy in patients on RRT ?

What about liver disease on RRT ?

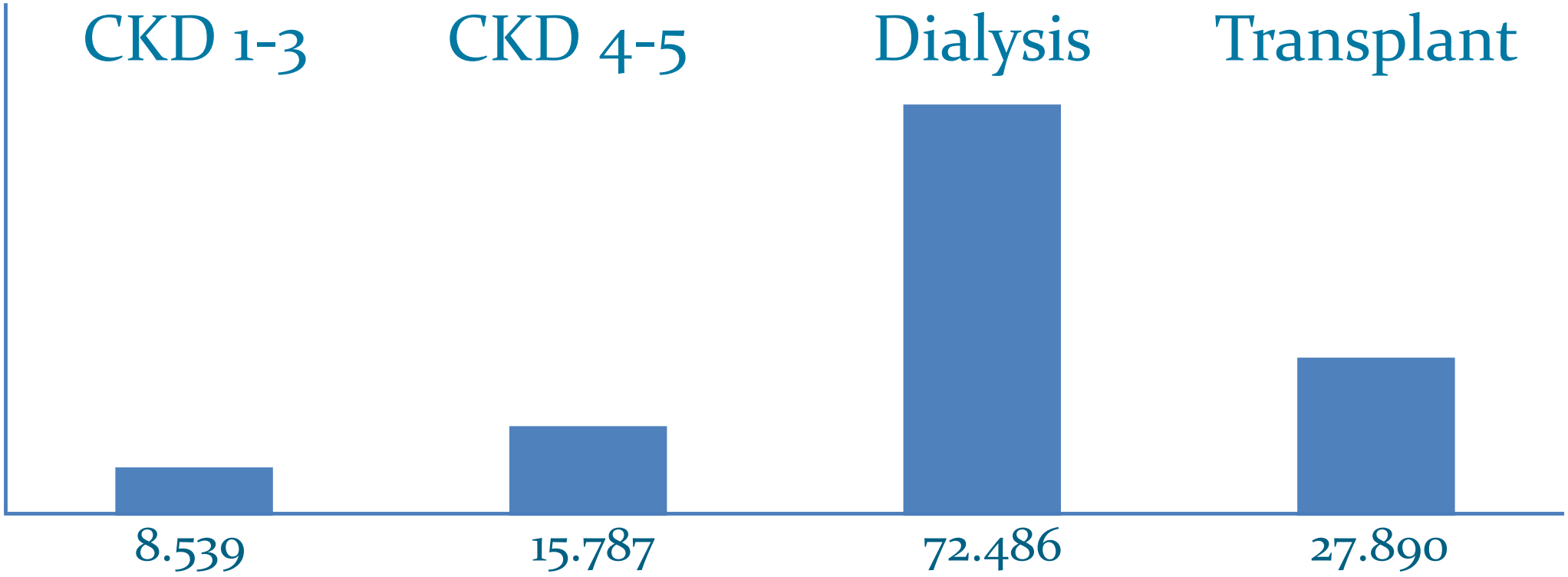
- Transplantation in the optimal choice of RRT

- … with living kidney donation, ideally preemptive, as the best option

➡ better survival
➡ better quality of life
➡ lower cost

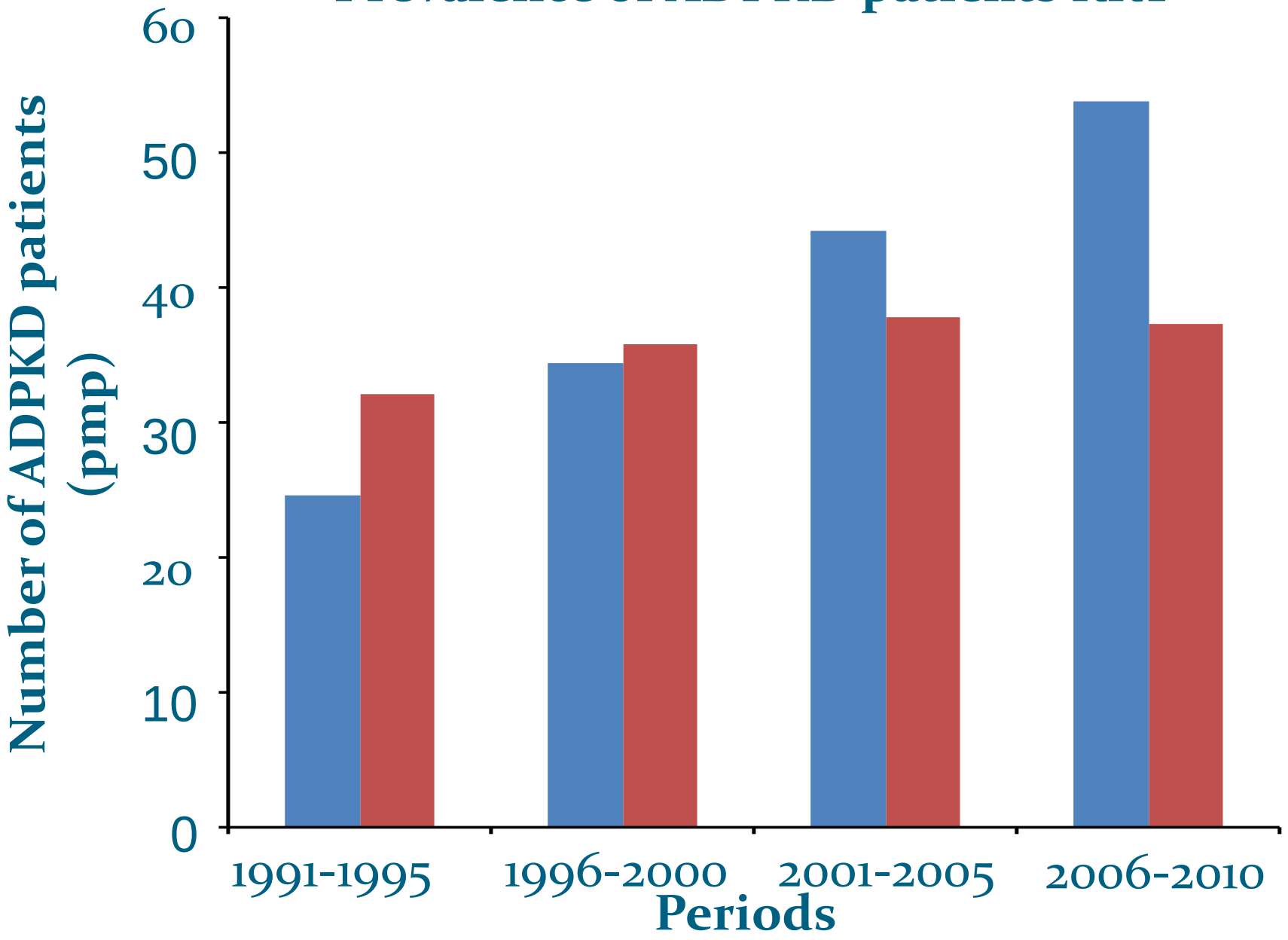
(Chapman A. ADPKD – KDIGO Kidney Int 2015)

Annual costs (€) in Finland for ADPKD patients



(Eriksson D et al – BMC Health Services Research 2017)

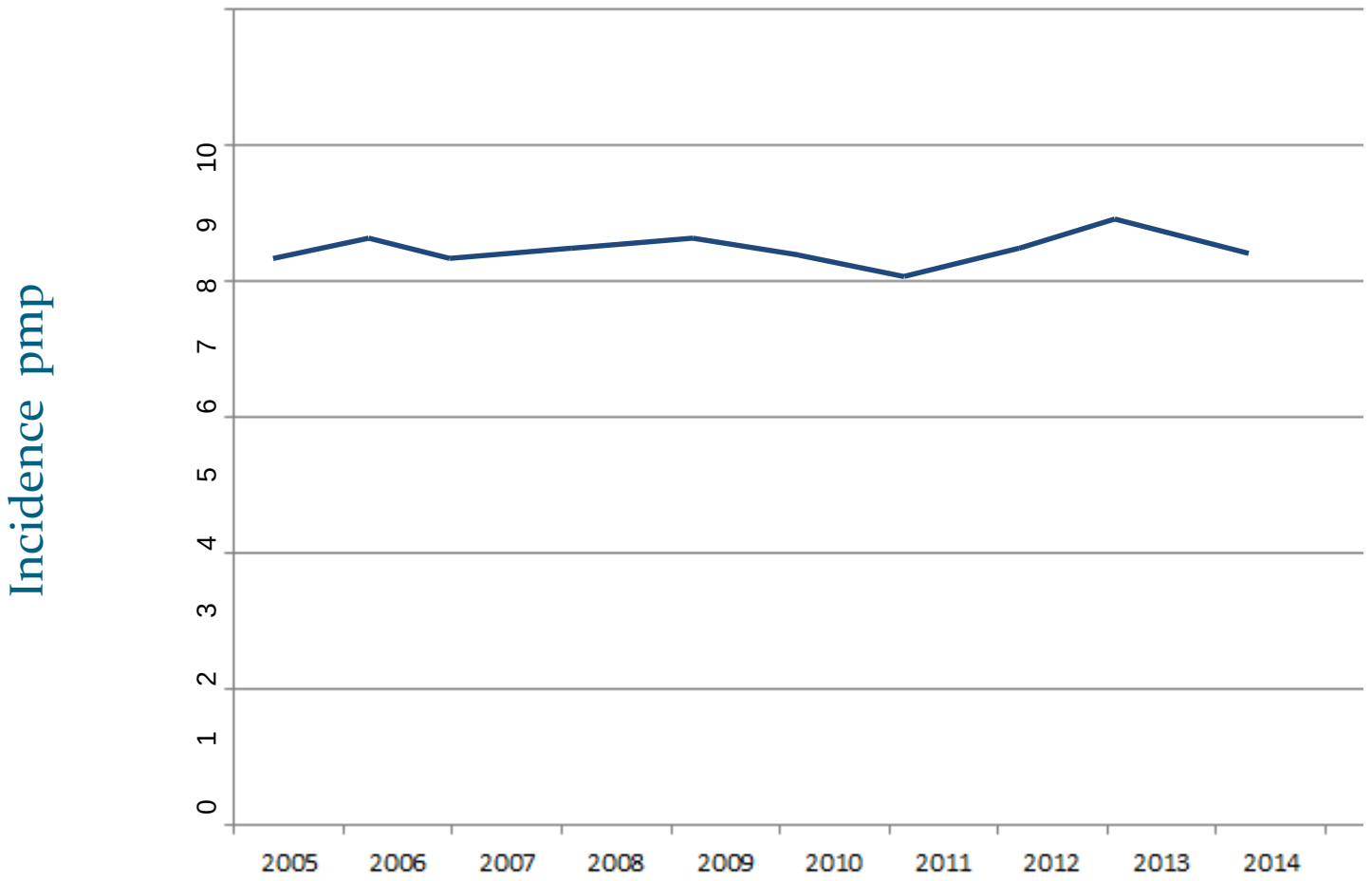
Prevalence of ADPKD patients RRT



ERA-EDTA Registry data
12 countries with individual data
206 million people

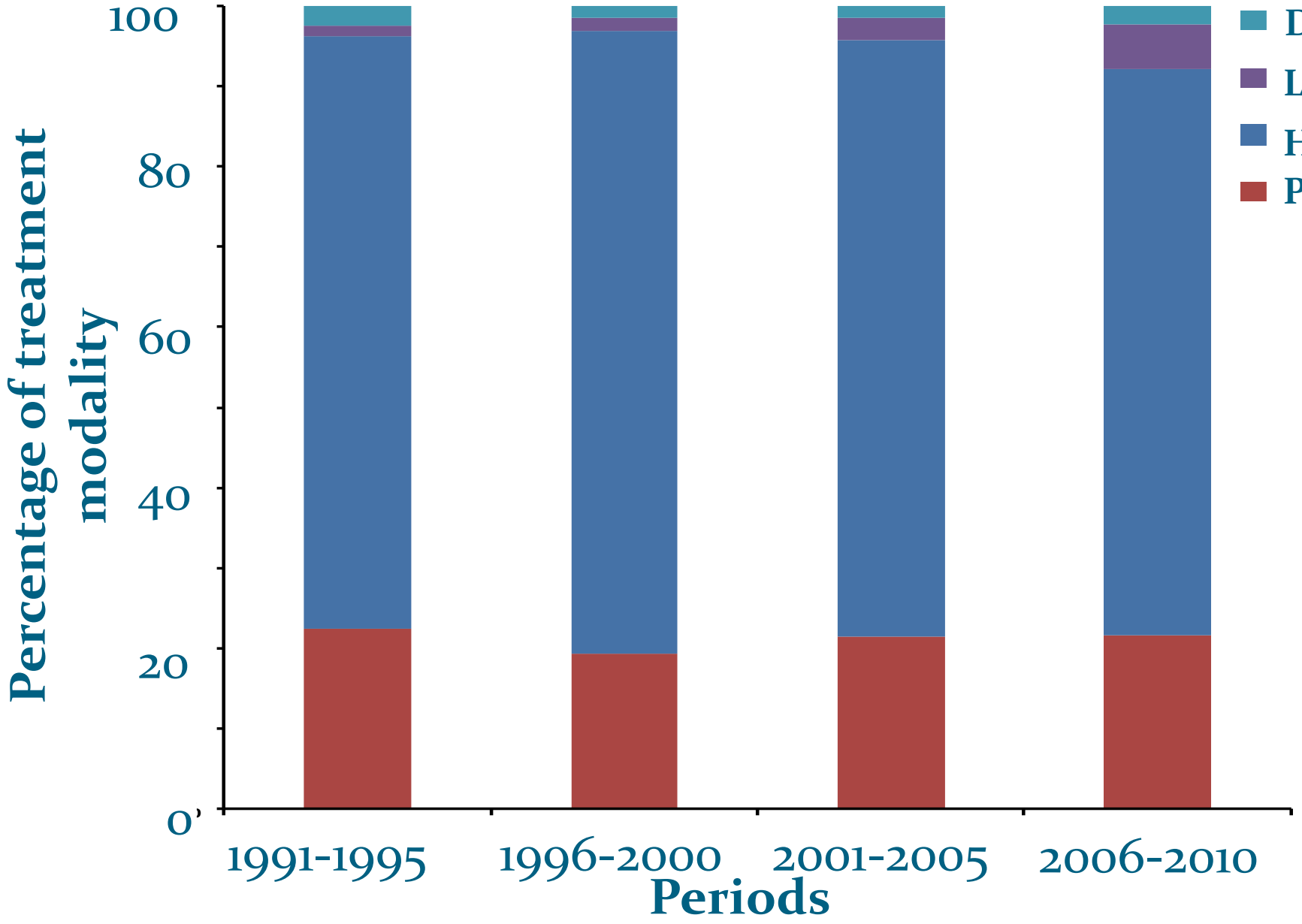
(Spithoven, Kramer, Jager, Gansevoort et al. Nephrol Dial Transplant 2014)

The incidence rate of RRT for ADPKD in Europe was stable from 2005 to 2014



(Stel VS. Nephrology (Carlton) 2019, in press)

Treatment modality at start RRT



ERA-EDTA Registry data
12 countries with individual data
206 million people

(Spithoven, Kramer, Jager, Gansevoort et al. Nephrol Dial Transplant 2014)

What is the optimal choice of RRT ?

What is the best dialysis modality ?

What is the place of nephrectomy in patients on RRT ?

What about liver disease on RRT ?

- 2-yr survival rate : HD = PD

- No difference in ADPKD and non-ADPKD patients for :
  - **Technique survival**
  - **Peritonitis**
  - **Dialysis adequacy**

But x2-risk of **hernia**
-> automated PD treatment while supine

(Khan S et al. Perit Dial Int 2017;Dupont V et al PLoS One 2018)

What is the optimal choice of RRT ?

What is the best dialysis modality ?

What is the place of nephrectomy in patients on RRT ?

What about liver disease on RRT ?

Nephrectomy is to be avoided

- noticeable morbi-mortality
- ↗ risk for blood transfusions → allosensitization
- suppression of residual renal function

Indications for nephrectomy

- severe bleeding
- recurrent and severe cyst infection
- infected stone
- intractable pain
- space for transplantation

(Kanaan N. Nat Rev Nephrol 2014)

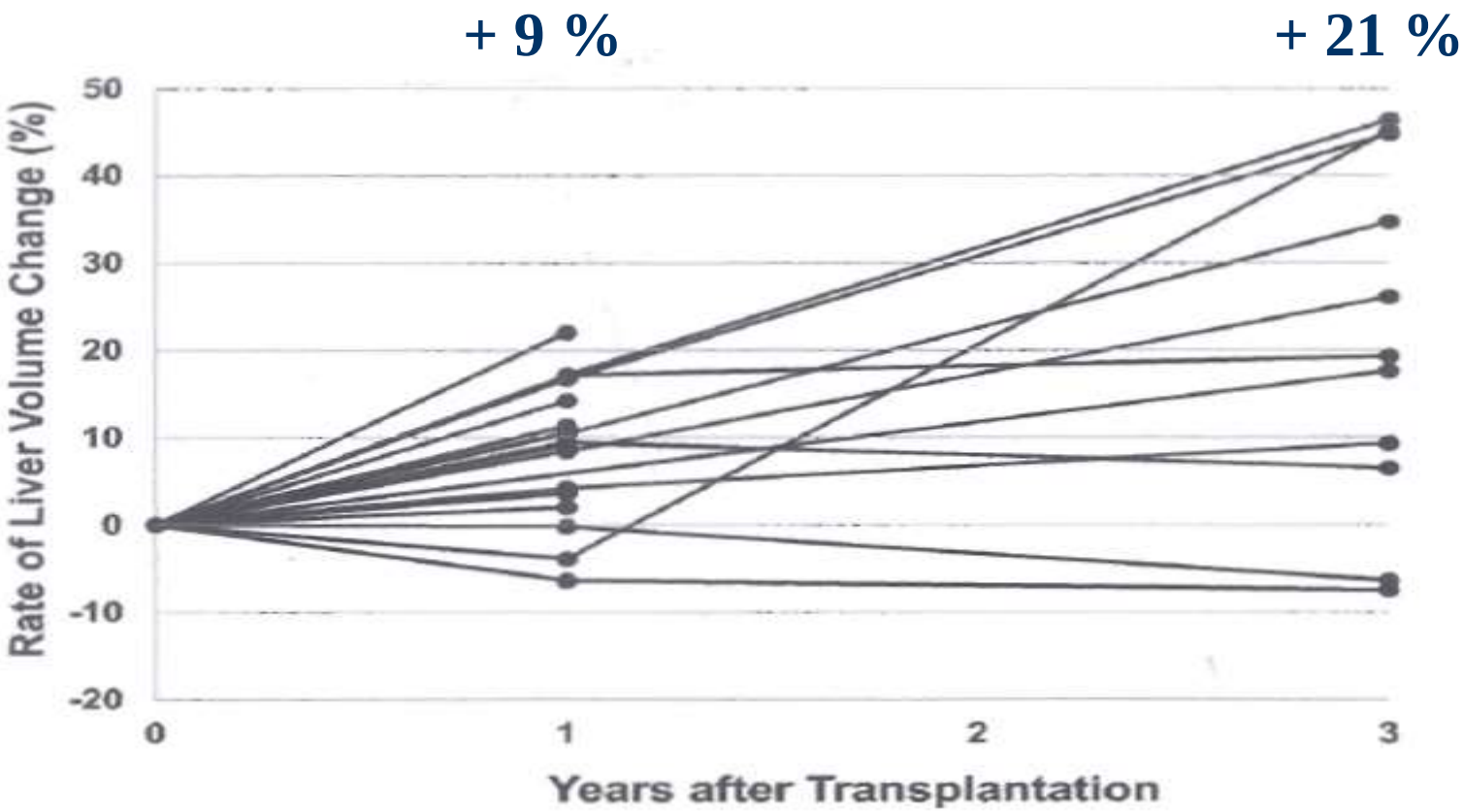
What is the optimal choice of RRT ?

What is the best dialysis modality ?

What is the place of nephrectomy in patients on RRT ?

What about liver disease on RRT ?

Liver cysts usually continue to grow after kidney TP



(Yamamoto T, Transplantion 2012)

- CT/MRI with liver volume determination at time of transplantation
- Avoid use of oestrogen in women with substantial liver involvement
- Consider combined liver-kidney TP for pts with highly symptomatic liver or recurrent cholangitis and GFR <30

ADPKD on RRT : key points

- Excellent survival rates
- PD is a valuable modality
- Nephrectomy is to be restricted to some recognized indications
- More attention is to be paid to liver involvement before and after kidney TP

More promotion on pre-emptive TP !

Tom Oostrom
(Dutch Kidney Foundation, Netherlands)

NIERSTICHTING
Leven gaat voor.

NEOKIDNEY
A Dutch Kidney Foundation initiative

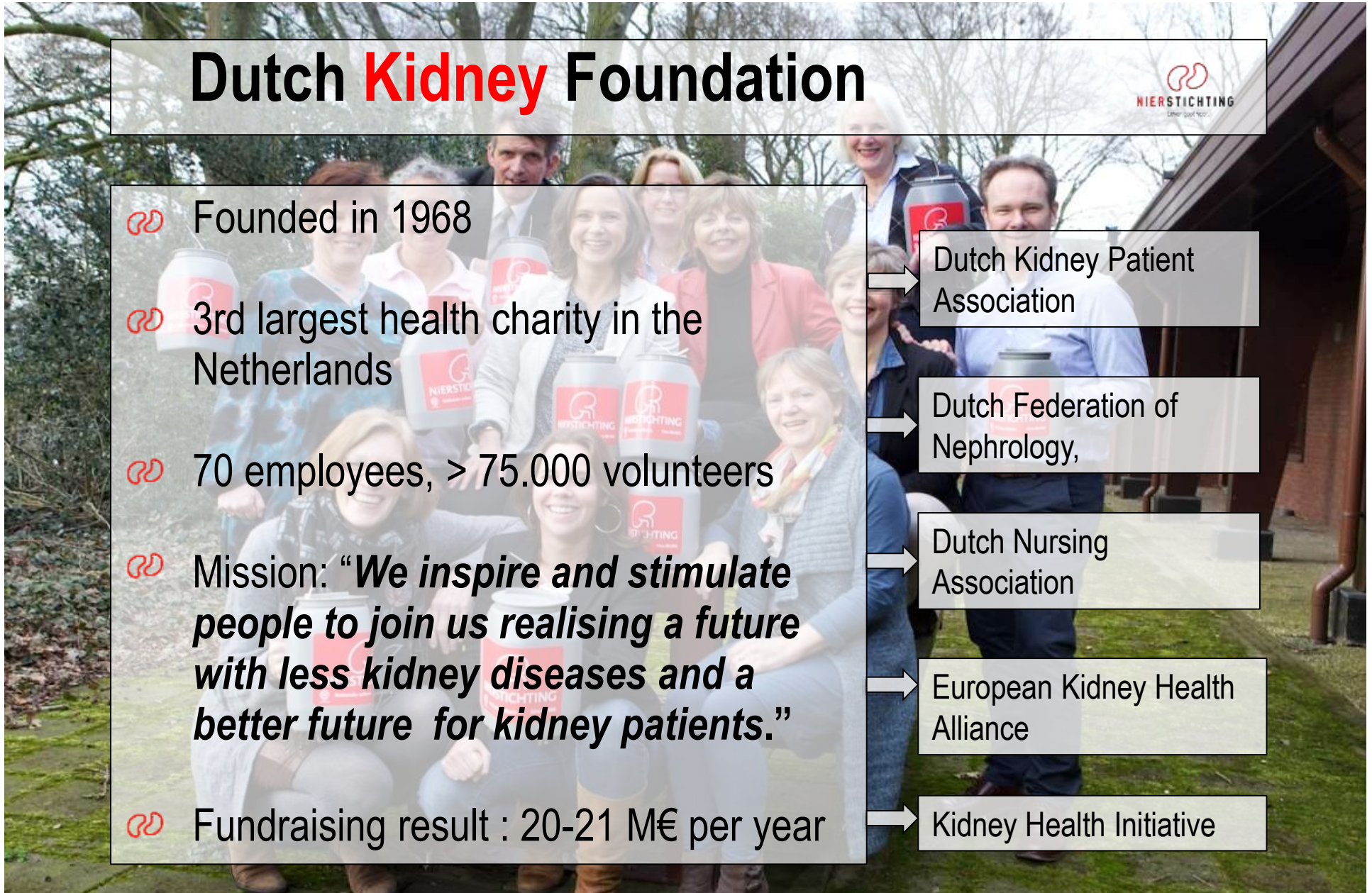
The Neokidney project

towards portable hemodialysis

European ADPKD Patient Summit
Brussels, March 16, 2019

EAF
European ADPKD Forum

PKD International



Dutch Kidney Foundation

- Founded in 1968
- 3rd largest health charity in the Netherlands
- 70 employees, > 75.000 volunteers
- Mission: "***We inspire and stimulate people to join us realising a future with less kidney diseases and a better future for kidney patients.***"
- Fundraising result : 20-21 M€ per year

- Dutch Kidney Patient Association
- Dutch Federation of Nephrology,
- Dutch Nursing Association
- European Kidney Health Alliance
- Kidney Health Initiative

A truly portable HHD device enabling the shift from “patient compliance” to ”therapy compliance”

Centre dialysis → **Neokidney home dialysis**

- 60-100 kg
- >60-120 litre dialysis fluids
- Old technique
- 3 x a week 4 hours

“Patient adapts life to the treatment“

- 5-10 kg
- 6 litre dialysis fluids
- Sorbent-based dialysate recycling
- Small and portable
- 5-7 x a week (better clearance)
- Take along anywhere

“Therapy adapts to the patients life”

>> DKF started the NeoKidney social enterprise to build the first portable artificial kidney

Current technology is a hurdle in itself for patients to leave the clinic

Home hemodialysis today

- Water purification needed
- Adaption of electric wiring
- Adaption of plumbing
- Storage of large volumes
- Training
- Paperwork

Technological innovation

Care provider

Patient

Insurer

Technological innovation

Social innovation

Care provider

Patient

Insurer

Support from doctors, nurses and patients is key

ERA EDTA – Nephrologist (EU)

EKPF – Dialysis patients

IFKF – International kidney foundations

EDTNA – Dialyse nurses

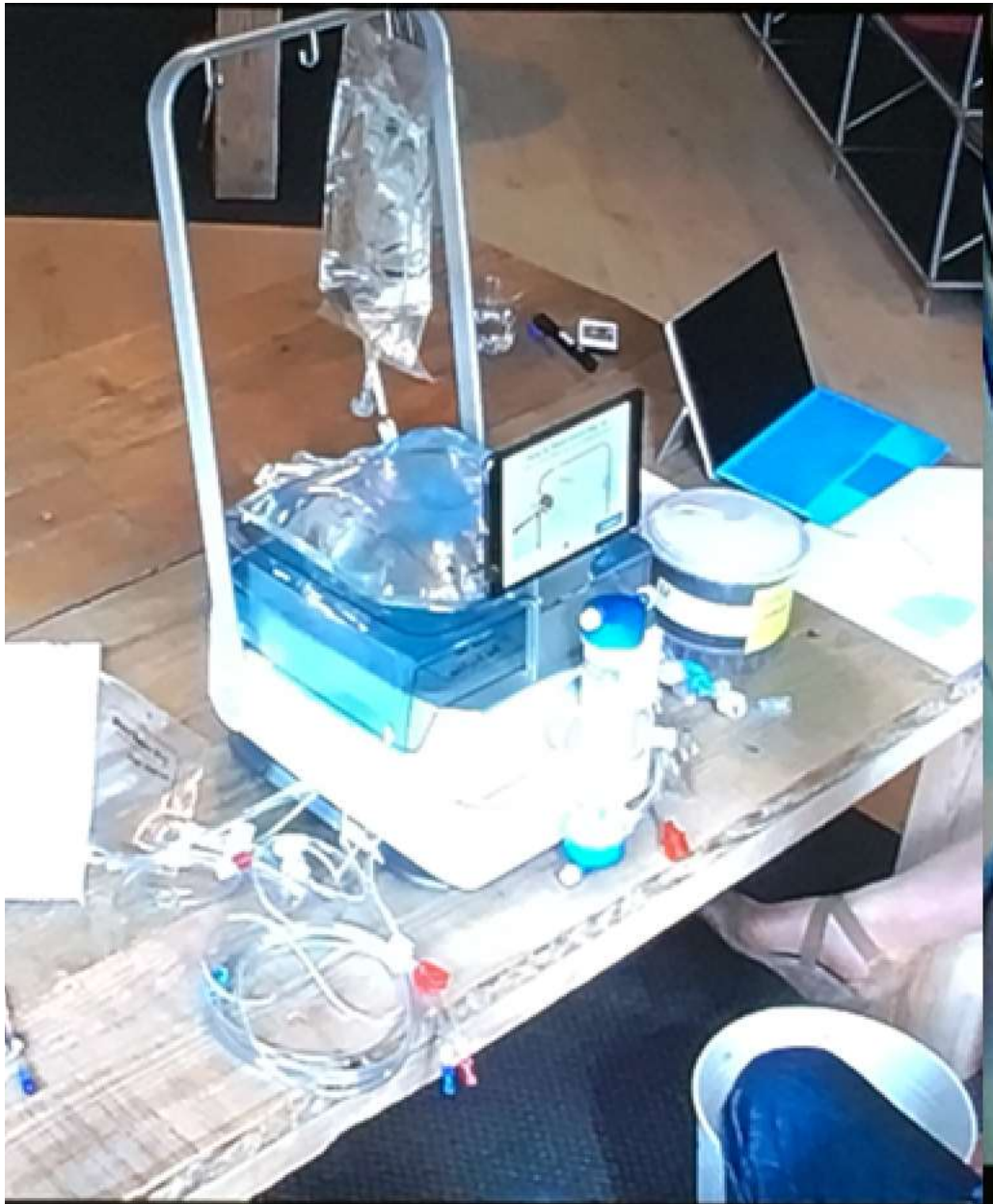
National Advisory board:

- prof. dr. Ton Rabelink (LUMC)
- prof. dr. Norbert Lameire (Universiteit Gent)
- prof. dr. ir. Clemens van Blitterswijk (UM)
- prof. dr. Jeroen Kooman (AZM)
- dr. Walther Boer (UMCU)

International Medical Advisory Board:

- prof. dr. James Tattersall (Leeds, UK)
- dr. Francesco Locatelli (Lecco, IT)
- prof. dr. Raymond Vanholder (Gent, BE)
- dr. Michel Burnier (Lausanne, CH)
- prof. dr. Norbert Lameire (Universiteit Gent)

Patient tests



Technological innovation

Care provider

Social innovation

Care innovation

Patient

Insurer

8 june 2016: 6,8 mio euro support from 3 health insurance companies

vlnr) Frank Janssen (Menzis), Joep de Groot (CZ/CbusineZ), Gerke Witteveen (Zilveren Kruis/Achmea) en Tom Oostrom (Neokidney)

ZilverenKruis | achmea

CZ

menzis

Technological innovation

Care provider

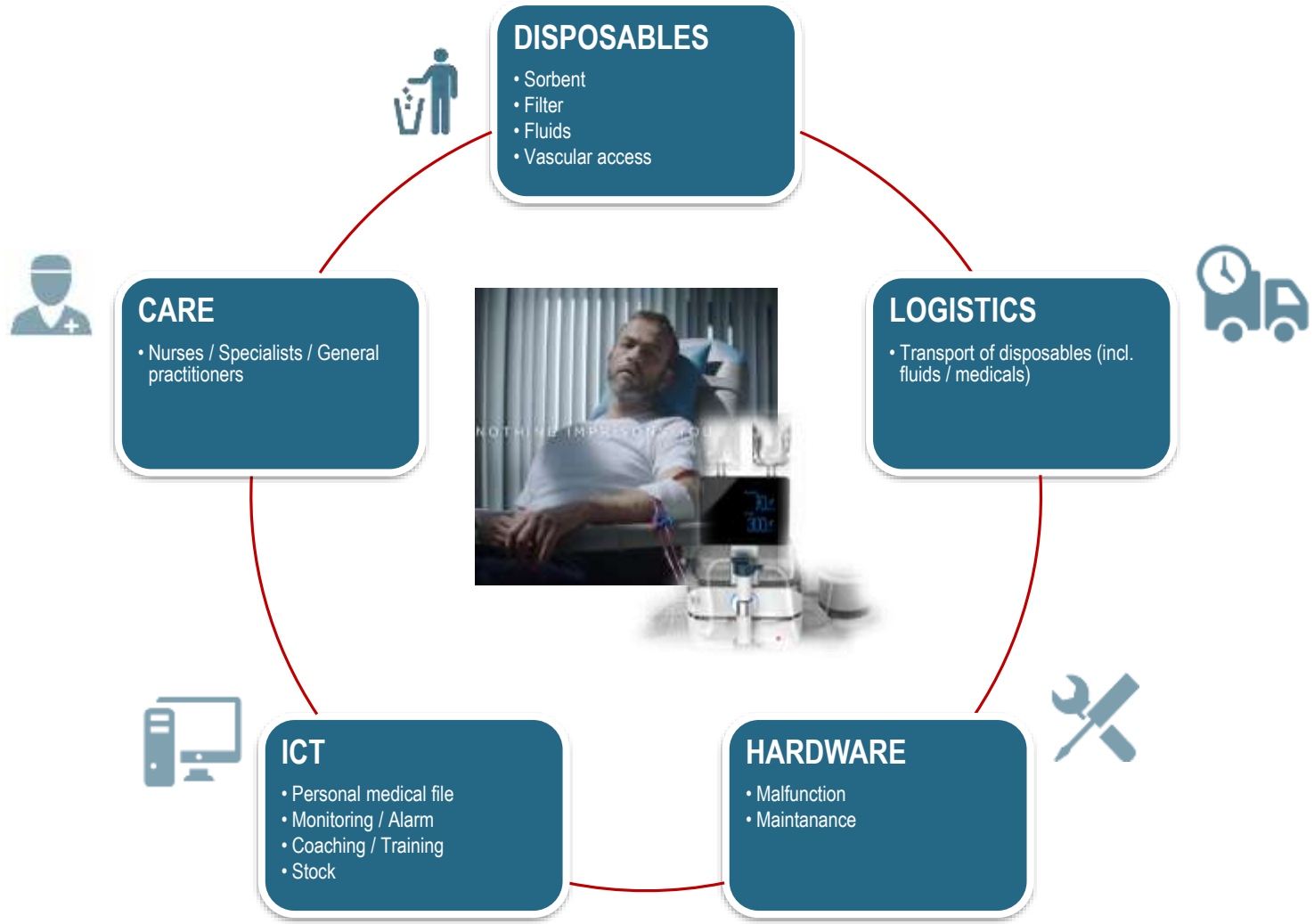
Social innovation

Care innovation

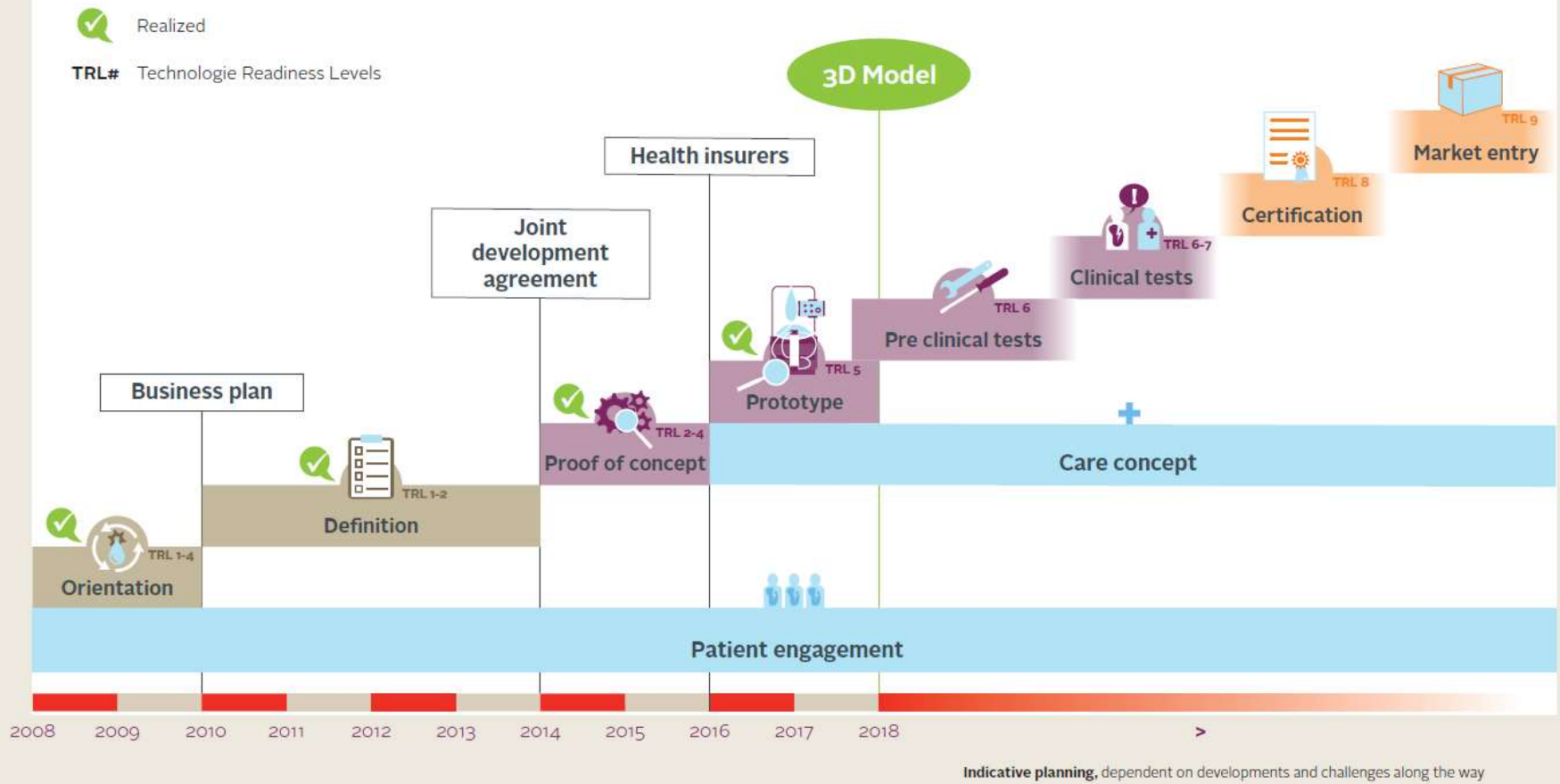
Patient

Insurer

Together with health insurers, nephrologistst and home hemodialysis organizations we develop a service concept



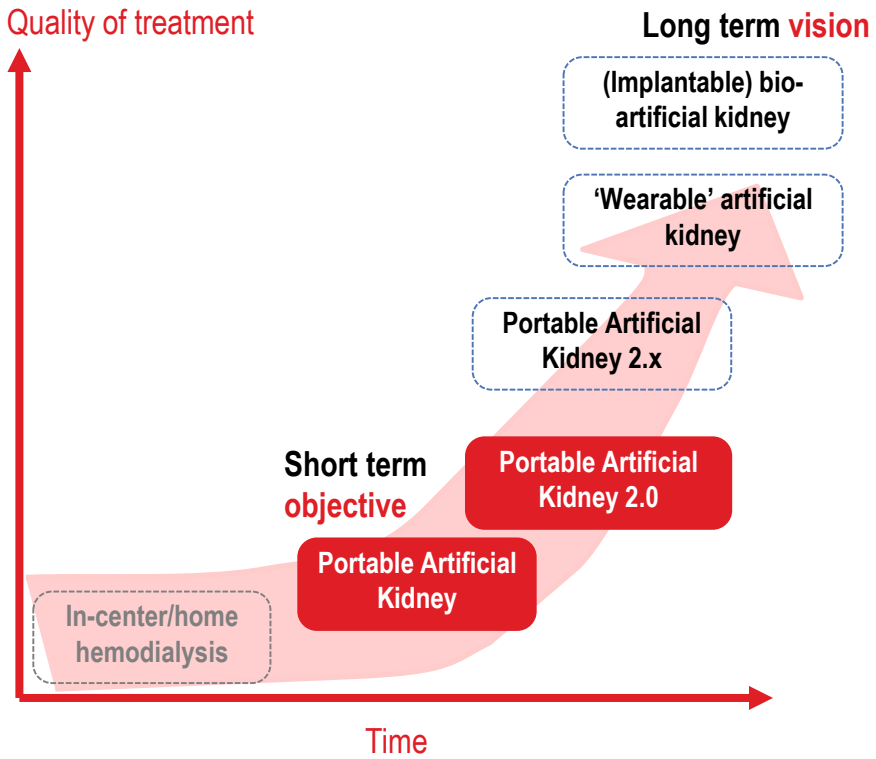
Steps development portable artificial kidney



Indicative planning, dependent on developments and challenges along the way

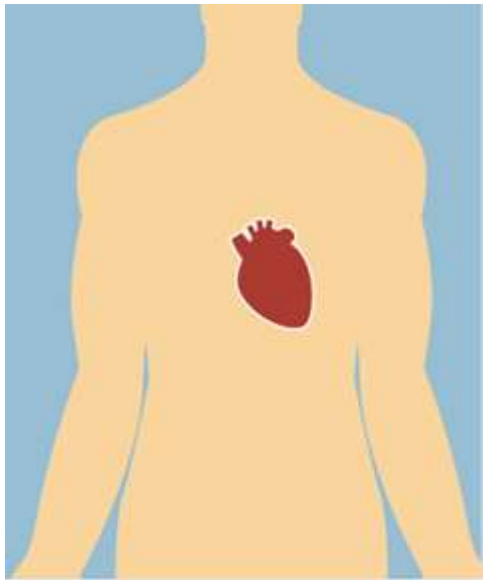
Dutch Kidney Foundation aims for continuous development of “artificial kidney” concepts that improve patients’ lives

Our vision from Portable to Wearable, to Implantable…

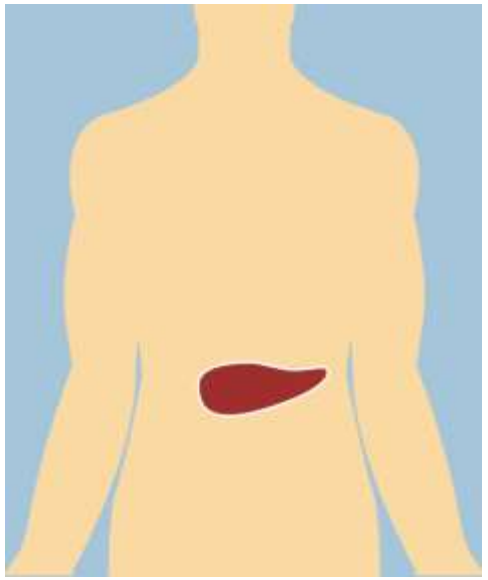


DKF is one of the founding partners in the Dutch/Flemish regenerative medicine consortium RegMed XB

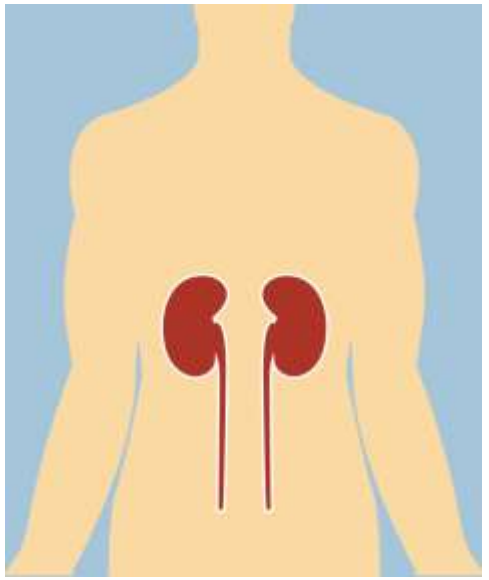
Regeneration of the human heart



A proof-of-concept therapy for type 1 diabetes



A first subunit of a bioengineered kidney



Taking steps towards a bioengineered joint

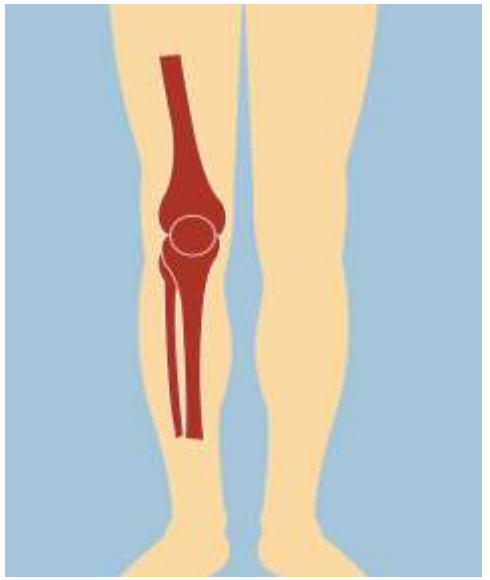


Fig. 6 W. J. Kolff met de draagbare nier, juli 1976. Het gewicht van de W.A.K. is 5 kg.

12

'The main aim of my endeavors has been, and still is, to restore people to an enjoyable existence. If it is not enjoyable, it should not be done.'

W.J. Kolff 1911-2009
Inventor of the artificial kidney

#ADPKD
@PKD_Int

Breakout 6

Understanding research and getting involved

PKD International

EAF
European ADPKD Forum

Summit sponsors
This event has been made possible by sponsorship from
Baxter, Otsuka Pharmaceutical Europe Ltd, Palladio Biosciences and Sanofi Genzyme.

Baxter Otsuka Palladio Biosciences Sanofi Genzyme

#ADPKD
@PKD_Int

BREAKOUT 6: Understanding research and getting involved

Albert Ong

(Sheffield University, UK and EAF)

Daniel Gallego

(ALCER, Spain)

Albert Ong
(Sheffield University, UK and EAF)

Patient centered approach to ADPKD Research

Patients should be placed at the centre of their care and treatment journey. Patients have crucial roles in managing their own ADPKD throughout their lives. Patients and families are given the knowledge and opportunity to act as fully informed partners in making decisions about:

- their own care
- healthcare policies
- services
- **research related to ADPKD**

Research Registries

- **Databases that collect information about patients with a specific disease**
  - Allows researchers to study diseases:
  - how it affects people
  - how it progresses over time
  - how effective treatments are in practice
- ADPKD registries exist in several **European countries**
- There is also an international registry for children with ADPKD, called ADPedKD.
- To join an ADPKD registry, discuss with your nephrologist.
- If you join, you will be asked to sign a consent form for the use of your information to be included in the registry.

Clinical Trials

- Clinical trials are research studies that test:
  - **efficacy** (i.e. the ability to produce a desired or intended result)
  - **safety** of medicines or other types of treatment.
- Some clinical trials involve healthy volunteers, while others involve patients with specific diseases such as ADPKD.
- If you are interested in participating in this type of research, ask your nephrologist
- You can also find out more about clinical trials at
  - EU Clinical Trials Register
  - ClinicalTrials.gov
  - the PKD Foundation.

European Reference Network for Rare Kidney Diseases (ERKnet)

- Links together expert paediatric and adult nephrology centres in Europe
  - uses uniform clinical guidelines and pathways
  - monitors the quality and outcomes of treatment
  - provides education for nephrologists, and
  - **supports research**
  - also offers ‘virtual consultations’ for doctors who need advice and provides links to information for patients.
- There is also a European Reference Network on Rare Liver Diseases (RARE-LIVER), including polycystic liver disease.

ERKNet
The European Rare Kidney Disease Reference Network

European Reference Networks

"Understanding Research and Getting Involved"

ALCER
Federación Nacional

Daniel Gallego
Figthing Against Kidney Diseases Federation

Brussels, March 16th 2019

Patients´Mantras

“Empowerment”

“PATIENTS AT THE HEART”

“Shared decision making”

“Patients as drivers of innovation”

“Patient in the DNA of the clinical trials”

“Humanization of healthcare”

What We See of a Chronic Disease

S.O.N.G.

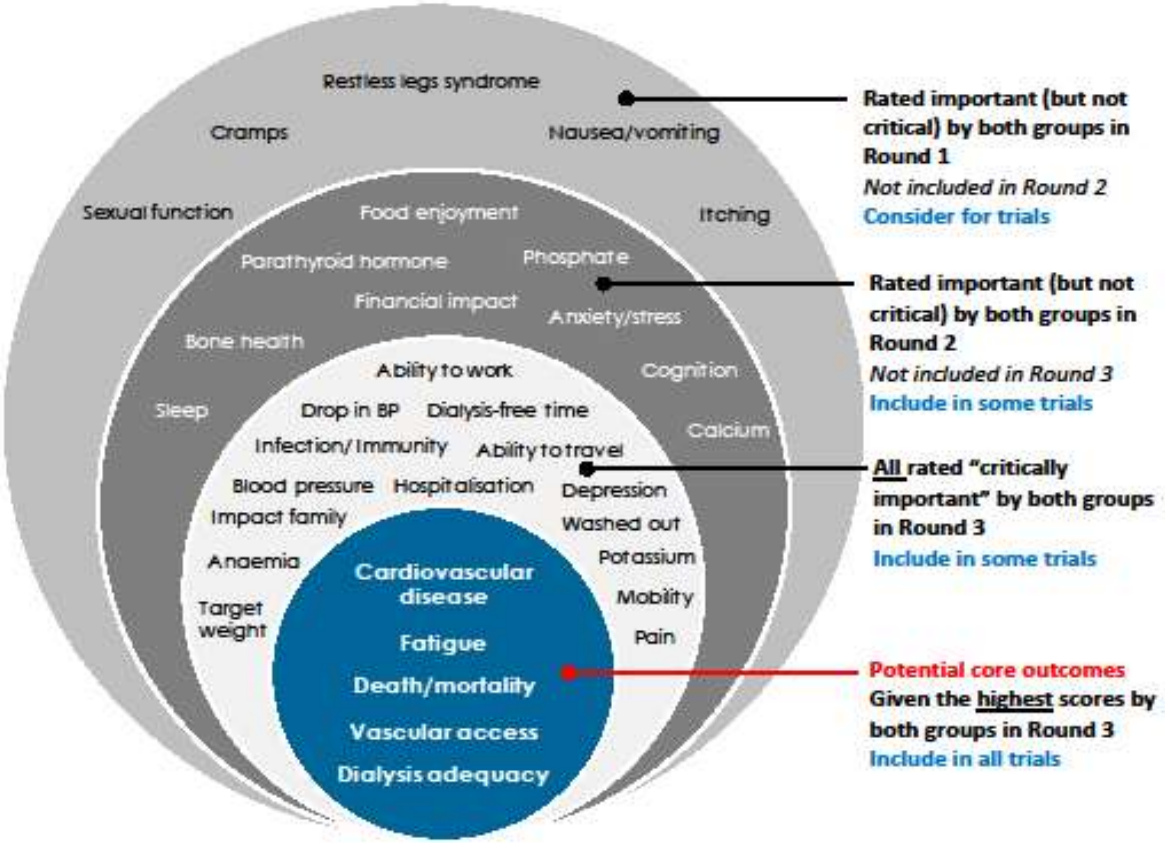
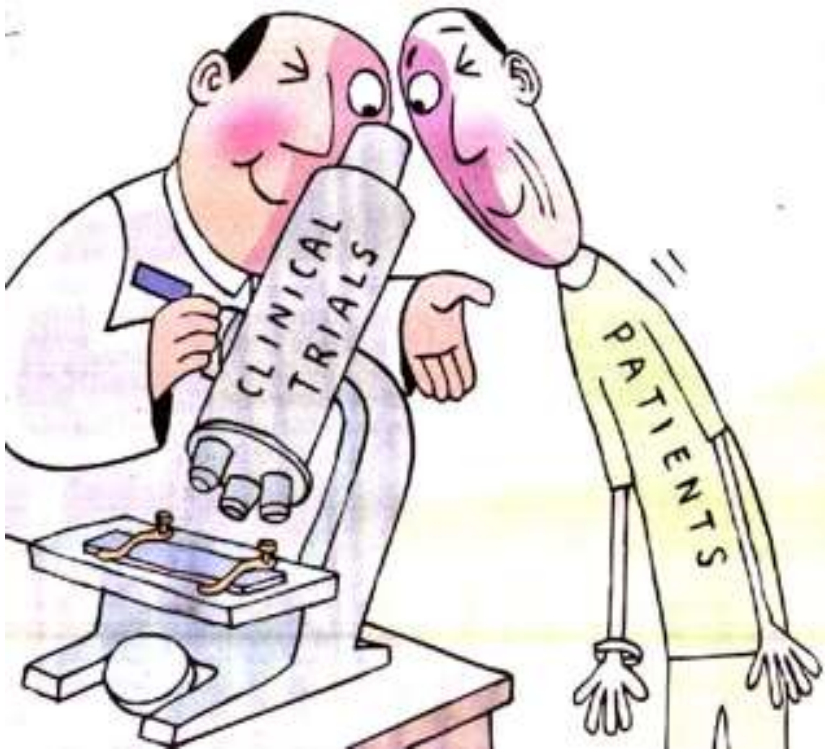


Table 1. Delphi participants

Patients/caregivers 202 165 (82) 150 (74)
Health professionals* 979 784 (80) 688 (70)
TOTAL 1181 949 (80) 838 (71)
*Includes nephrologists, surgeons, nursing and allied health professionals, researchers, policy makers, industry

Patient Engagement

- ❑ Clinical Research Ethics Committee
- ❑ Patient Representative
- ❑ WE ARE IN
- ❑ **Expertise and Experiences**
- ❑ EUPATI Academy Formation
- ❑ ¿Volunteers or Gainful?
- ❑ **P.R.O.M.s y P.R.E.M.s**



#ADPKD
@PKD_Int

PLENARY II

Patient engagement and disease advocacy

PKD International

EAF European ADPKD Forum

Summit sponsors
This event has been made possible by sponsorship from
Baxter, Otsuka Pharmaceutical Europe Ltd, Palladio Biosciences and Sanofi Genzyme.

Baxter Otsuka Palladio Biosciences Sanofi Genzyme

Plenary II: Patient engagement and disease advoacy

Clim van Daelen
(Nierpatiënten Vereniging Nederland (NVN), Netherlands)

#ADPKD
@PKD_Int

Ines Hernando
(EURORDIS, Belgium)

Juan Carlos Julian Mauro
(ALCER, Spain)

Ray Vanholder
(University of Ghent, Belgium and European Kidney Health Alliance)

Moderator: ***Tess Harris*** *(PKD International and EAF)*

European ADPKD Patient Summit

15 –16 March 2019, Brussels, Belgium

PKD International

EAF European ADPKD Forum

#ADPKD
@PKD_Int

Clim van Daelen
(Nierpatiënten Vereniging Nederland (NVN), Netherlands)

The Dutch Kidney Patients Association

- National association for kidney patients and their relatives, transplant recipients & living donors
- 7.500 members
- 20 employees and >150 volunteers
- For ADPKD: - Diagnose Group
  - Facebook Group
  - Theme Day

nvn nierpatiënten vereniging nederland

Patient empowerment by information

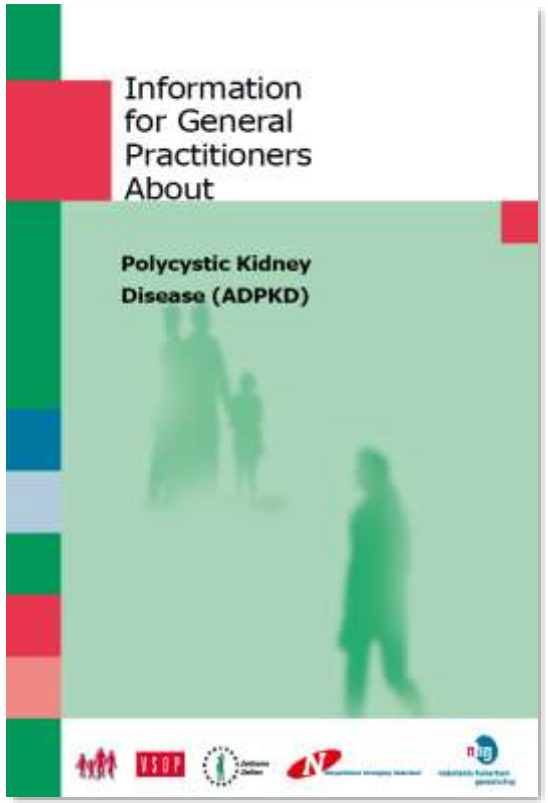
For patients…

on ADPKD

on genetics

…the general public…

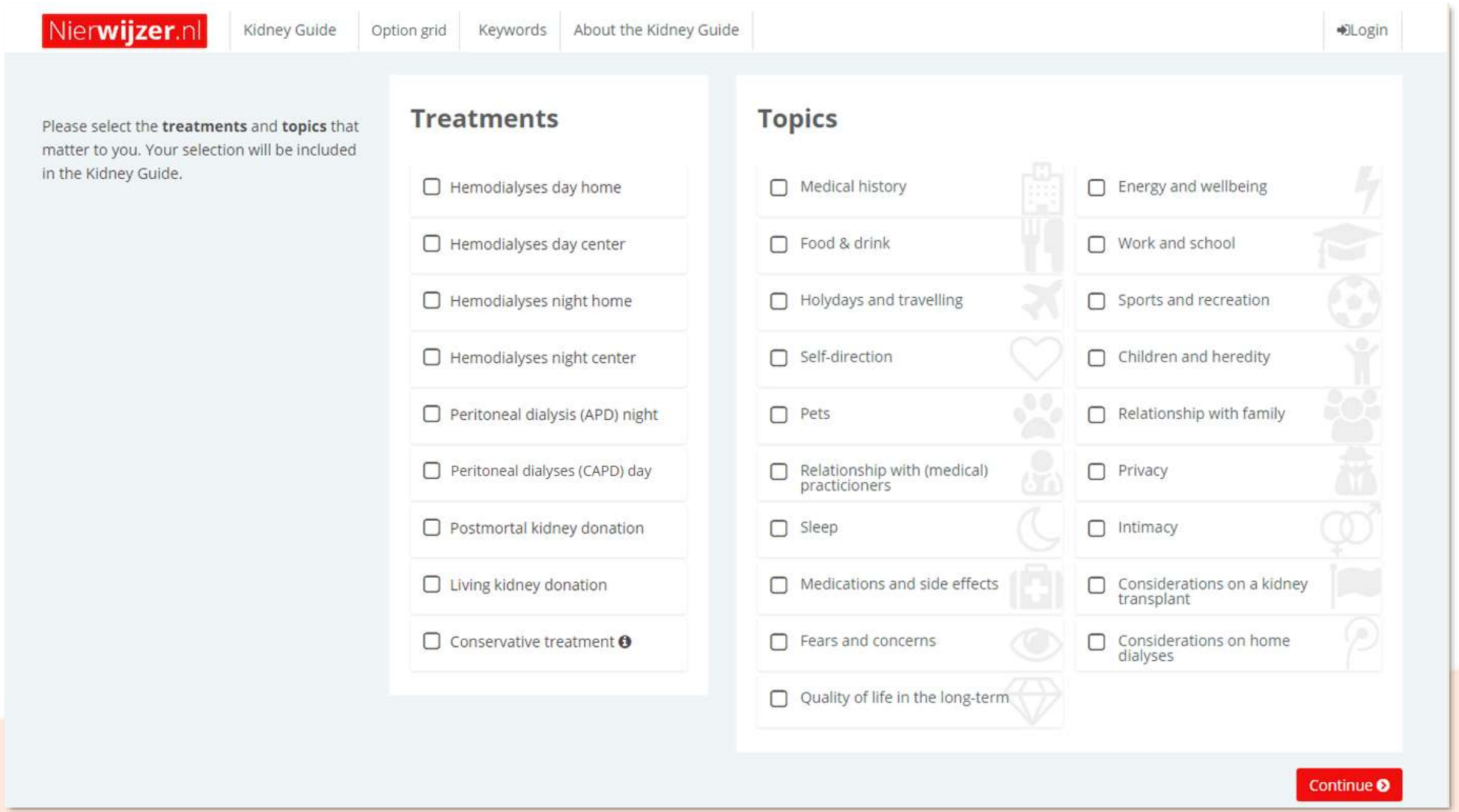
…and General Practitioners



nvn nierpatiënten vereniging nederland

Facilitating Shared Decision Making

Online Decison Aid



nvn nierpatiënten vereniging nederland

#ADPKD
@PKD_Int

Ines Hernando
(EURORDIS, Belgium)

EUROPEAN AND INTERNATIONAL ADVOCACY AND PATIENT ENGAGEMENT ON EUROPEAN REFERENCE NETWORKS

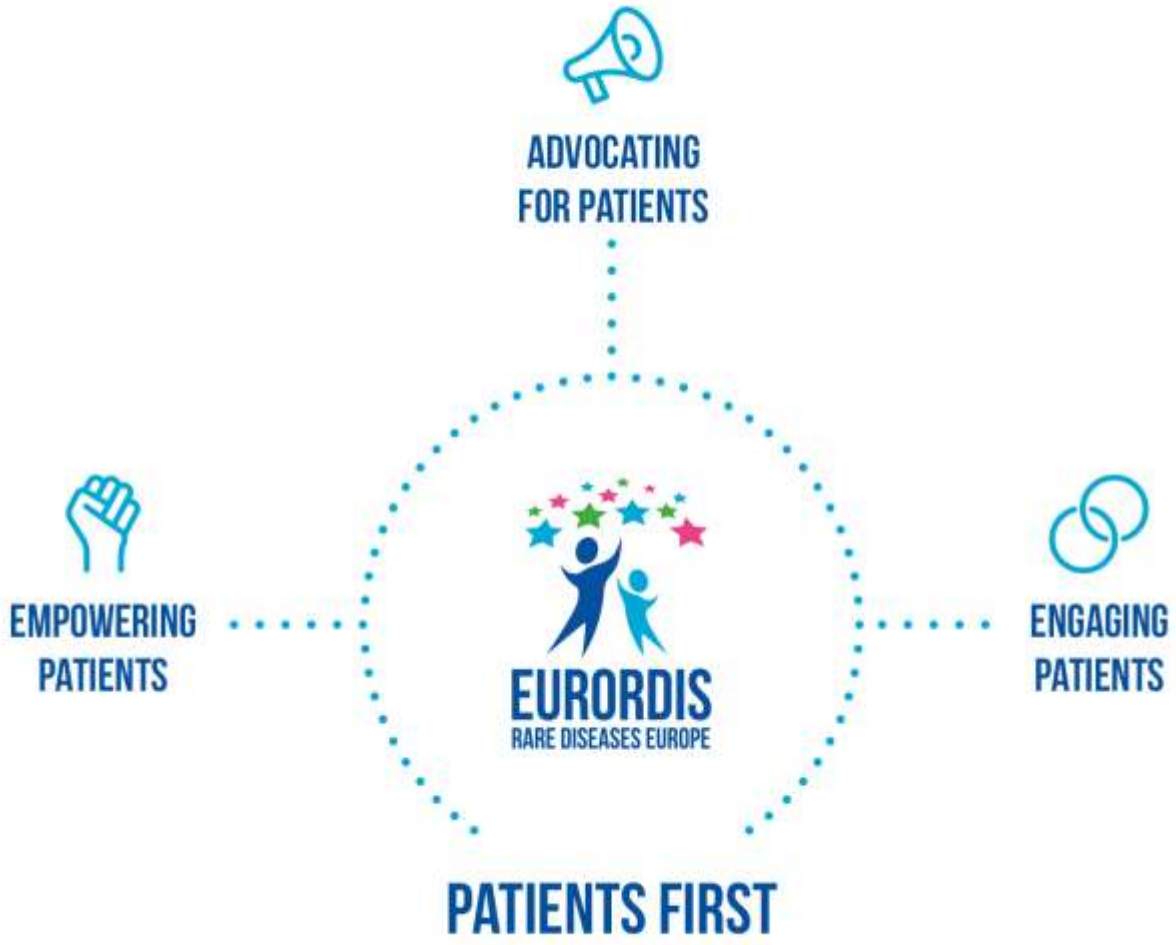
European ADPKD Summit

Ines Hernando, ERN and Healthcare Director. EURORDIS

16th March 2019

EURORDIS.ORG

1. Supporting RD patients through advocacy, facilitating their engagement and empowering patient advocates



2. Patients' involvement in the ERNs - ePAG advocates represent the wider patient community

They represent the voice of patients within ERNs to ensure that the needs of people living with a rare disease are well understood and included in the strategic and operational delivery of the Networks. Most of them have a dual role

They create a bridge between the ERN and the wider European patient community (having a strong national and international network facilitates this interaction)

3. Your ERNs… ErkNET and Rare Liver

ERKNet

Autosomal dominant structural kidney disorders' WG and Renal malformations WG (incl. ciliopathies) (Tess Harris is ePAG patient advocate in both)

1. Registry – just received funding; early days

2. They have developed an extensive webinar curriculum – open to patients
View 2019 webinars here and past webinars here

3. Endorsed guidelines and consensus statements
   - Perinatal Diagnosis, Management, and Follow-up of Cystic Renal Diseases: A Clinical Practice Recommendation with Systematic Literature Reviews
   - Imaging of Kidney Cysts and Cystic Kidney Diseases in Children: An International Working Group Consensus Statement

ErkNET website: https://www.erknet.org/index.php?id=home

4. Your ERNs… ErkNET and ERN Rare Liver

European Reference Network
for rare or low prevalence complex diseases
Network Hepatological Diseases (ERN RARE-LIVER)

PLD in ADPKD is within the 'Structural disorders' (Tess Harris is ePAG patient advocate)

1. Registry – just received funding. Aims to recruit 2 newly diagnosed PLD patients from each centre for follow – up to 1000 patients potentially

1. Patient information resources being added to new website

3. Endorsed guidelines and consensus statements: work in progress

ERN Rare Liver website: https://www.rare-liver.eu

5. Why patient involvement in ERNs is important and how can you contribute?

If you're not at the table, then you're on the menu. Patient advocates are around the table; they participate in the strategic and operational discussions of the networks – for example by giving their perspective on how to best organise transition from children to adult care or helping to identify research priorities -

YOUR involvement is necessary at national and European level:

1. Engage with other PO and with the RD national alliances on ERNs to facilitate the integration of ERNs into national health systems (common voice on all the aspects related to the integration)

2. Reach out and further develop your network with other PO to mirror ePAGs at national level (organise around the same disease groupings). This will strengthen your advocacy efforts towards the integration of ERNs and the interaction with the ePAG groups.

3. Liaise with the patient advocates in ErkNet, Liver or other ERNs to organise how you can best provide feedback. You can also be actively involved as an ePAG patient advocate, depending on your time available – ongoing recruitment process to ensure full representation -

3. Resources

European Patient Advocacy and Engagement Resources

EURORDIS Summer, Winter, Leadership and Digital Health Schools
EUPATI online, open source training
European Patient ambassador programme https://www.epaponline.org/ - online course

UK

Kidney Patients Involvement Network (new network, launching June 2019)
INVOLVE

Others:

PFMD https://patientfocusedmedicine.org/
Patients centred outcomes research Institute - PCORI https://www.pcori.org/
Find a cure https://portal.findacure.org.uk/ - online courses and other resources
7 ways to find information on your RD
https://www.eurordis.org/find-information-on-your-disease

Thank you!

EURORDIS
RARE DISEASES EUROPE

European ADPKD Patient Summit

15 –16 March 2019, Brussels, Belgium

#ADPKD
@PKD_Int

Juan Carlos Julian Mauro
(ALCER, Spain)

ALCER
Federación Nacional

Juan Carlos Julián
Managing Director

European ADPKD Patient Summit

Saturday 16 March 2019

Novotel Brussels Airport Hotel, Brussels, Belgium

Spanish Alliance Against ADPKD

- Was created in 2015
- Multi-stakeholders Alliance
- Promotion of Common actions and activities

European ADPKD Patient Summit

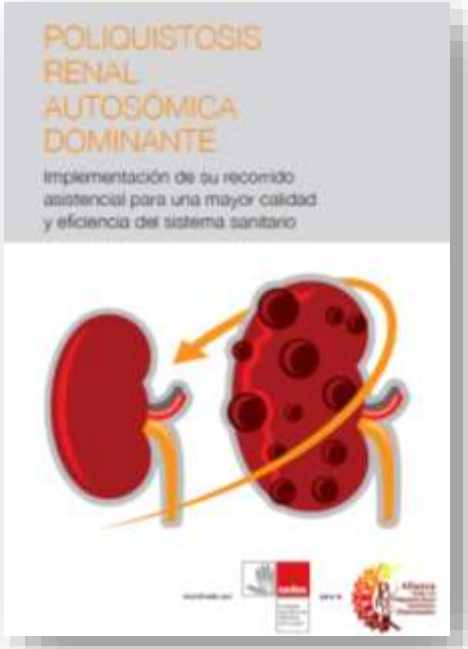
Alianza frente a la Poliquistosis Renal Autosómica Dominante

2017
Awards
Best ADPKD Multidisciplinary Project

2016 Manifiesto against ADPKD

2016 ADPKD White Paper

2018 ADPKD
Health Care Route



2019 Regional Forums
With Public Administrations

ALCER Federación Nacional

European ADPKD Patient Summit

2016
ADPKD Patient Journey

2016-17
Regional Patient Meetings

2016:
- Gran Canaria
- Bilbao
- Sevilla

2017:
- Valencia
- Pamplona
- Valladolid
- Málaga
- Madrid
- Toledo
- Santiago de Compostela
- Zaragoza
- Badajoz
- Mallorca

2018
***ADPKD* Action Plan**

Key Goals

- Encourage training on ADPKD for health professionals
- Access to genetic studies of people affected ADPKD in the Public Health System
- Implement a ADPKD Information and Screening Plan for patients and relatives
- Access to preimplantation genetic diagnosis

2019
Cooking Workshops

Barcelona	Valencia
Alicante	Álava
Vizcaya	Guipúzcoa
Málaga	Asturias
Valladolid	Murcia

ALCER Federación Nacional

Thank you!

ALCER Federación Nacional

European ADPKD Patient Summit

15 –16 March 2019, Brussels, Belgium

#ADPKD
@PKD_Int

Ray Vanholder
(University of Ghent, Belgium and European Kidney Health Alliance EKHA)

European Kidney Health Alliance

Working together to influence EU policy

Raymond Vanholder, Chairman EKHA

EKHA is an NGO representing the key stakeholders (including patients) focused on kidney health

- Physicians
- Nurses
- Patients
- Foundations

EKPF EUROPEAN KIDNEY PATIENTS' FEDERATION

EDTNA/ERCA Caring Together

era edta LEADING EUROPEAN NEPHROLOGY

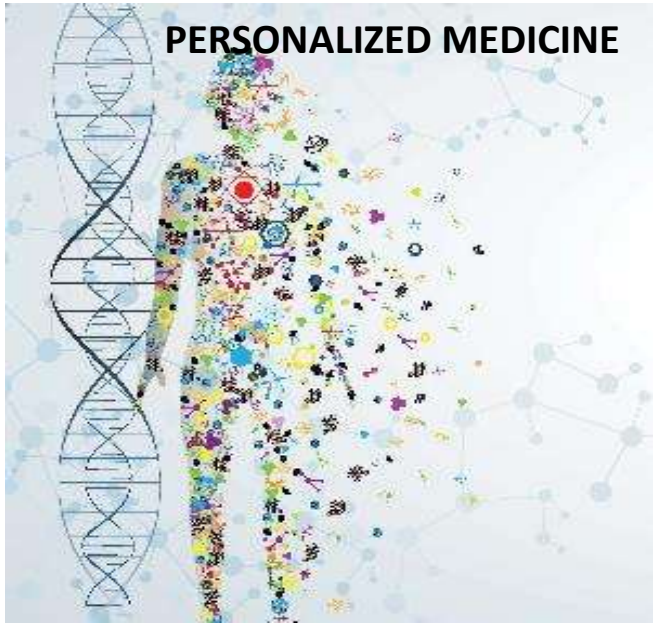
DUTCH KIDNEY FOUNDATION

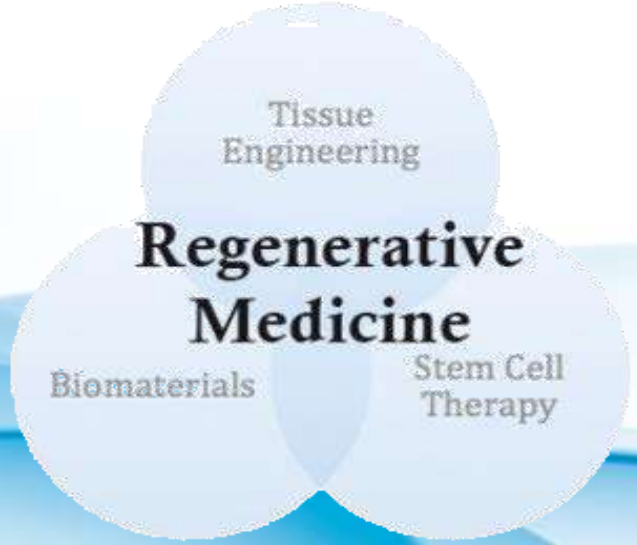
EKHA EUROPEAN KIDNEY HEALTH ALLIANCE

EKHA Recommendations for Sustainable Kidney Care

- *Prevention and early detection*
- *Patient's choice of treatment*
- *Increasing access to transplantation*
- *Treatment reimbursement strategies*

RESEARCH AVENUES





#ADPKD
@PKD_Int

Summit Closure

Richard Sandford
(University of Cambridge / EAF, UK)