# KDIGO Controversies Conference on ADPKD

## Conference Overview and Objectives

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# Disclosure of Interests

Olivier Devuyst

- Steering Committee, TEMPO Trials, Otsuka Pharmaceuticals

Vicente Torres

- Research funding from Otsuka Pharmaceuticals

# Burden of Illness Associated with ADPKD

12.5 million ADPKD patients world-wide were born with:

50% risk for ESRD by age 55 years of age (*PKD1 trunc. mut.)*

80% risk for hypertension

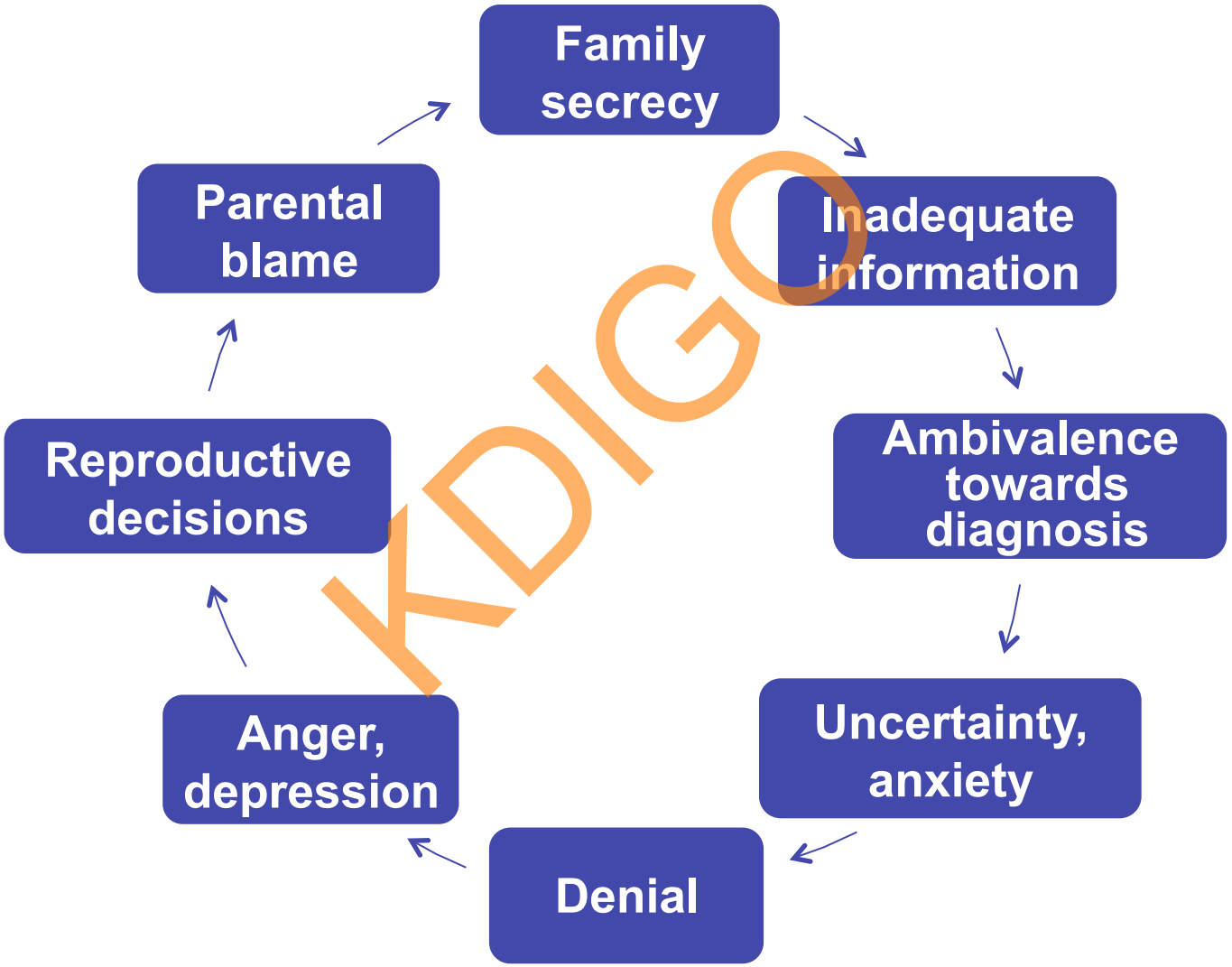
60% risk for painful kidney complications

20% risk for symptomatic PLD (if female)

3% risk for ICA rupture

Variably increased risk for cardiovascular and cerebrovascular disease, gastrointestinal disorders, hernias, neurologic and other disorders

# Emotional Burden of an Inherited Disease



# Societal Burden of ADPKD

- Loss of productivity and contribution to society

<u>European Union</u>

- Cost of renal replacement therapy: €2 billion

<u>United States</u> (cost per patient)

- Mean annualized medical and pharmacy charges (GFR ≥90): $26,521
- Mean annualized medical and pharmacy charges (GFR 60-89): $21,360
- Mean annualized medical and pharmacy charges (GFR ≥90): $31,247
- Mean annualized medical and pharmacy charges (GFR ≥90): $41,806
- Mean annualized charges for dialysis services: $131,890
- Mean charges per transplant hospitalization: $119,931

# Current Management of ADPKD

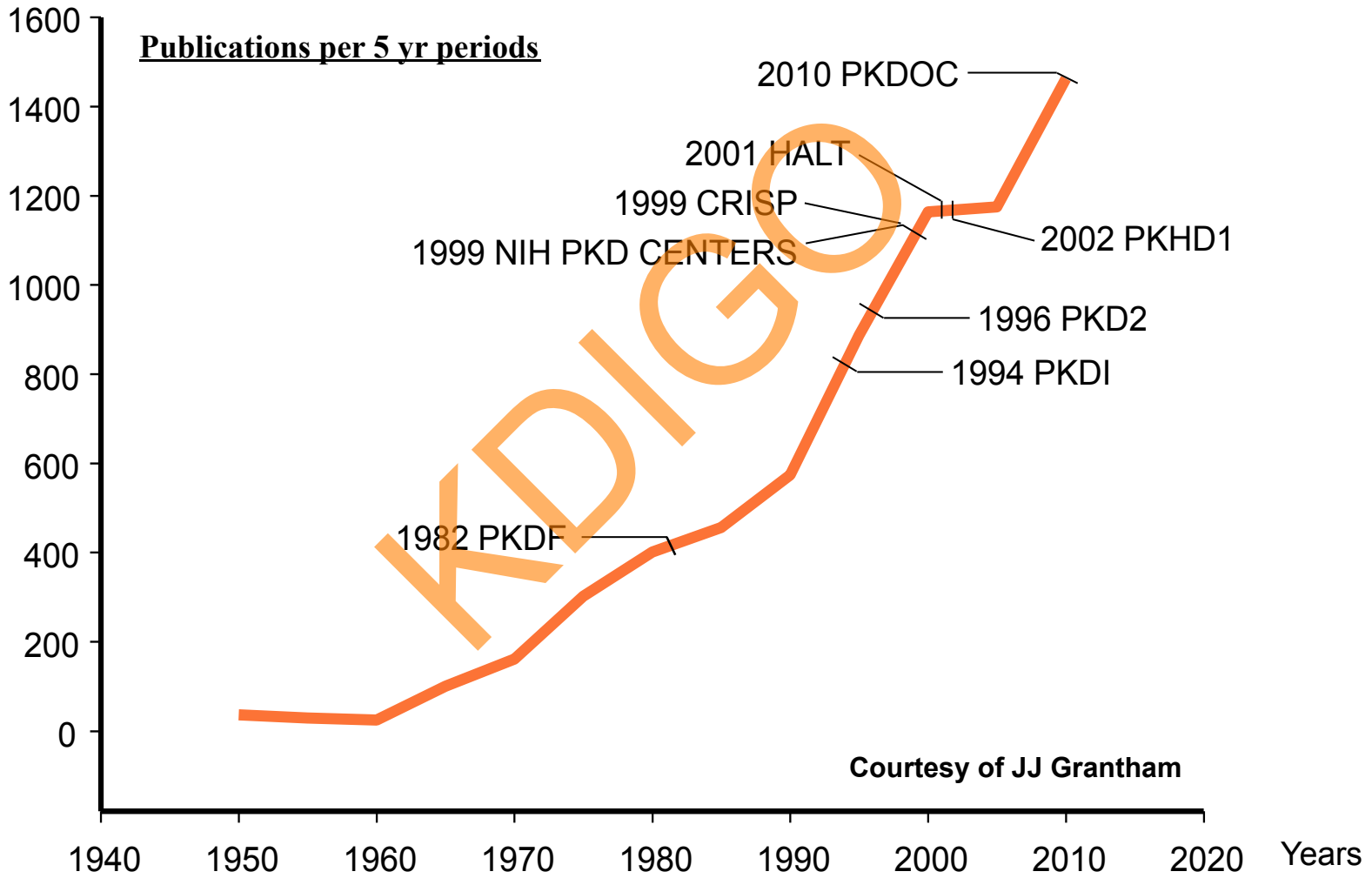
- Early detection and treatment of hypertension
- Treatment of other cardiovascular risk factors
- Treatment of renal complications
- Management of extrarenal associations
- Treatment of CKD
- Renal replacement therapy (ADPKD specific issues)



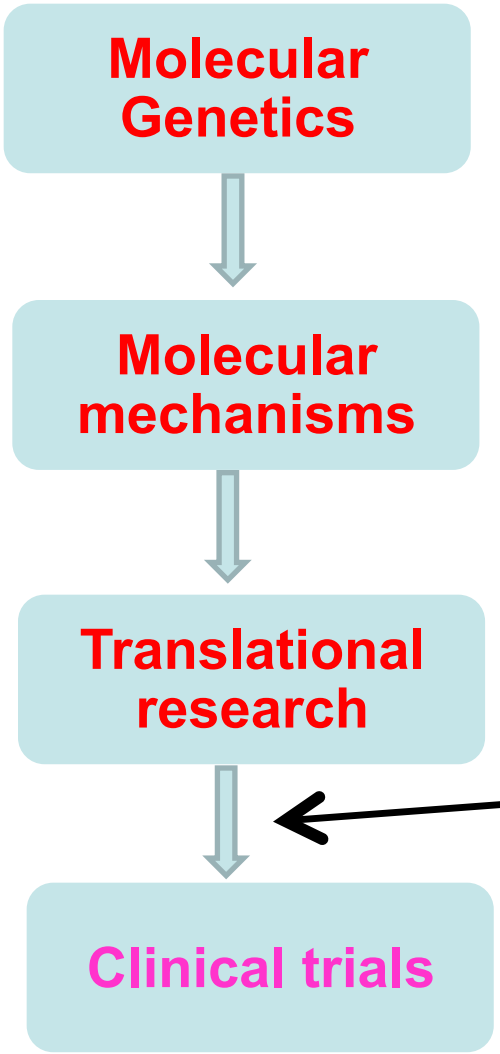
## Challenges

- No consensus for specific recommendations
- Marked phenotypic variability requires individualized therapies
- Level of evidence for specific recommendations at best C or D
- No widely accepted practice guidelines
- Challenges shared with inherited disorders in general

# Increasing Awareness & Research (1980-)



# “Hottest, most prominent area of research”

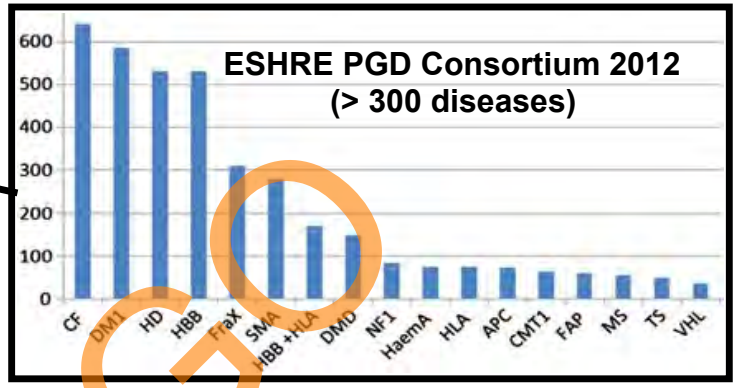



## Barriers to Clinical Trials

- Late decline of GFR: Necessitates requires very long periods of follow-up as a clinical trial endpoint (unappealing to pharmaceutical companies)
- TKV predicts renal functional decline in ADPKD, but it has not been accepted as a valid end-point by regulatory agencies
- Lack of funding for clinical trials of repurposed drugs without patent protection
- Limited resources of NIH and other government agencies to fund large clinical trials

# Opportunities for intervention at multiple stages

**PGD**




**Nephroprevention**

**PKD specific therapies**

- Early diagnosis feasible in most cases
- Cause of the disease is known
- Pathophysiology partially understood
- Large window for intervention

**CKD therapies**

Late progression by mechanisms similar to other chronic nephropathies: Nephron loss, hyperfiltration, proteinuria, oxidative stress, and interstitial inflammation and fibrosis

# KDIGO Controversies Conference on ADPKD

## Goals

- Assess the current state of knowledge related to the evaluation, management and treatment of ADPKD
- Identify controversial topics and outstanding knowledge gaps
- Propose a research agenda to resolve these issues
- Determine whether there is sufficient evidence base for the development of a practice guideline
- Help pave the way to harmonize and standardize the care of ADPKD patients

# KDIGO Controversies Conference on ADPKD

"A goal without a plan is just a wish"

(Attributed to Antoine Saint-Exupéry)

# KDIGO Controversies Conference on ADPKD

→ Participants divided into 6 Breakout Groups:

- Diagnosis *(Drs. Pei & Torra)*
- Mgmt. of renal manifestations *(Drs. Chapman & Horie)*
- Mgmt. of hypertension & renal function decline *(Drs. Schrier & Gansevoort)*
- Mgmt. of ESRD in ADPKD *(Drs. Eckardt & Perrone)*
- Mgmt. of extra-renal complications *(Drs. Pirson & Watnick)*
- Practical integrated patient support *(Tess Harris & Dwight Odland)*



Specific questions

Essential literature

# Plenary Session 1: Friday January 17, 8:15 to 14:20 hrs

- Two plenary lectures for each Breakout Group (15+5min)

  → *Balanced review of the literature*

  → *Highlighting controversial issues*

  → *Introduction to the prioritized breakout questions*

# Breakout Session 1: Friday, January 17, 14:20 to 18:30 hrs

- Manage time to address all prioritized questions
- One group Co-Chair moderates and the other takes notes
- Objective: Reach conclusions regarding
  - *Areas of consensus*
  - *Areas of controversy*
  - *Gaps in knowledge*
- Prepare report to for Plenary Session 2 (PPT presentation)

- If time allows, some optional questions can be addressed

# Plenary Session 2: Saturday, January 18, 8:00 to 11:30 hrs

- Preliminary report from 6 Breakout Groups (20 min each)
- Questions/comments to Breakout Groups (10 min each)
- Feedback to be addressed during next breakout session

# Breakout Session 2: Saturday, January 18 11:30 to 15:00 hrs

- Manage time to address all prioritized questions
- Objective:
  - Discuss feedback from Plenary Session
  - Finalize areas of consensus, controversy and gaps in knowledge
  - Propose research agenda (controversies and knowledge gaps)
  - Determine whether there is sufficient evidence base for the development of practice guidelines
- Prepare report for Plenary Session 3

- If time allows, some optional questions can be addressed

# Plenary Session 3:

Saturday, January 18 15:30 to 18:30 hrs
& Sunday, January 19 8:00 to 13:00 hrs

- Final reports from Breakout Groups (30 min each)
- Discussion (30 min each)

- Need for Guidelines: Discussion (30 min)
- Research Agenda & Priorities: Discussion (30 min)

- Final Conference Summation: Wrap up and next steps

# Can we provide acceptable guidance in rare/ inherited disorders ?

- ADPKD is not *stricto sensu* a rare disease – but close
- In rare diseases, the basis of evidence for clinical practice guidelines is generally weak: need for pragmatic attitude
- Transparency: literature search, interpretation of evidence, considerations taken when formulating recommendations
- Position document by European Medicines Agency (EMA):
  - *Rules for the production of guidelines on common diseases are also applicable to rare diseases*
  - ***All forms of evidence, even anecdotal case-reports, may provide relevant information and should then be taken into consideration***

EMA Guideline on clinical trials in small populations, 2007
Bolignano D et al. Nephrol Dial Transplant 2013

# Post-Conference Report and Publication

- Report from co-chairs of each Breakout Group due to the conference co-chairs by February 15, 2014
- Compiled and revised manuscript by conference co-chairs due to conference participants by March 15, 2014
- Feedback from conference participants to conference co-chairs due by April 1, 2014
- MS. submitted to *Kidney International* by April 15, 2014