



Improving Awareness & Patient Outcomes

Mental Health in Autosomal Dominant Polycystic Kidney Disease (ADPKD)



Improving Awareness & Patient Outcomes

**This program is paid for by
Otsuka Pharmaceutical Development &
Commercialization, Inc.**

**Speakers are employees of
Otsuka Pharmaceutical Development &
Commercialization, Inc.**

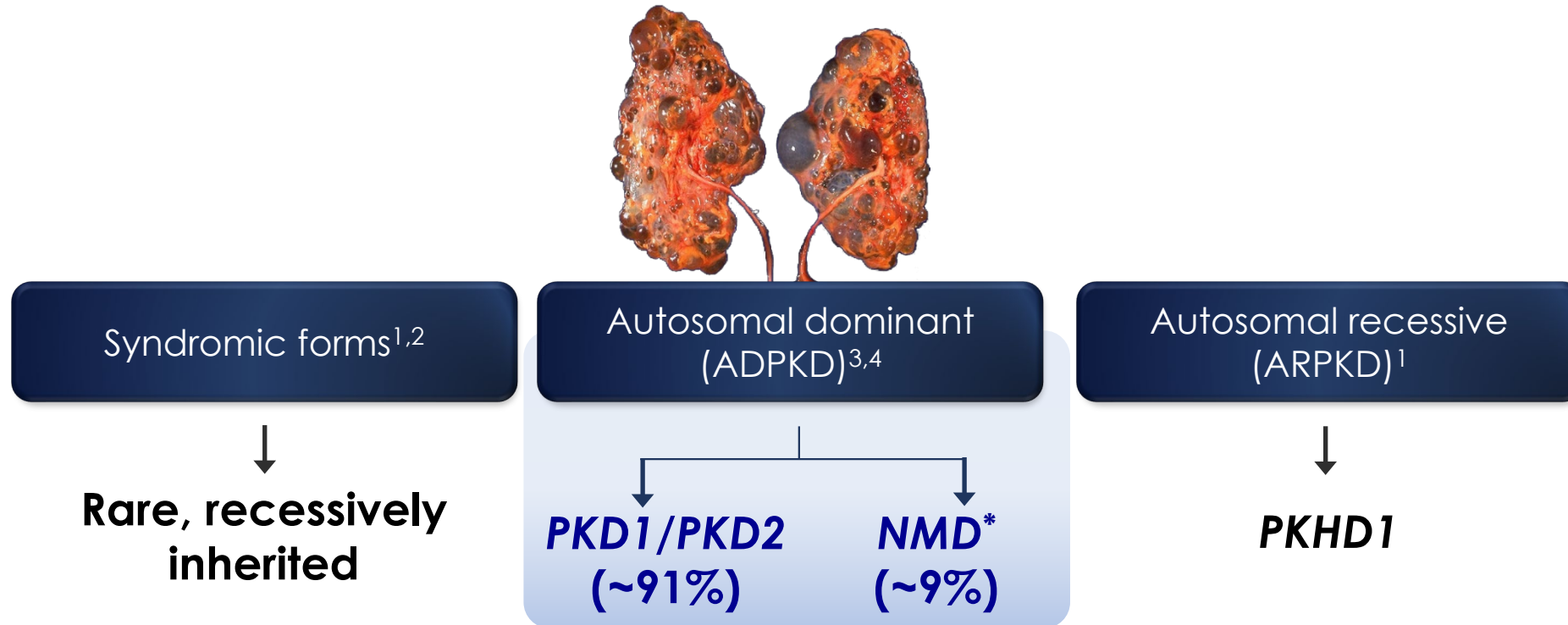


Improving Awareness & Patient Outcomes

Introduction to ADPKD

What Is PKD?

Polycystic kidney disease (PKD) is a group of monogenic disorders characterized by the propensity to develop numerous renal cysts¹



*The “no mutation detected” (NMD) group may contain those patients with mutations in other genes impacting cystic development, such as GANAB.⁵

ADPKD=autosomal dominant PKD; ARPKD=autosomal recessive PKD; GANAB=gene encoding glucosidase II subunit- α ; NMD=no mutation detected; PKD=polycystic kidney disease; PKHD1=polycystic kidney and hepatic disease 1.

1. Harris PC and Torres VE. (2009). *Annu Rev Med.* 60:321-337.
2. Jauregui AR et al. (2005). *Exp Cell Res.* 305(2):333-342.
3. Heyer CM et al. (2016). *J Am Soc Nephrol.* 27(9):2872-2884.
4. Irazabal MV et al. (2017). *Nephrol Dial Transplant.* 32(11):1857-1865.
5. Lanktree MB, Chapman AB. (2017). *Nat Rev Nephrol.* 13(12):750-768.

ADPKD Is the Most Common Life-threatening Inherited Renal Disease

ADPKD is a chronic progressive disease that does **not** discriminate on gender, race, ethnicity, or geography^{1,2}

- Affects both sexes equally, and occurs in all ethnicities³
- The most common life-threatening inherited renal disease
 - Accounts for up to ~5% of all patients with ESRD²
- The fourth leading cause of ESRD in the United States after diabetes, hypertension, and glomerulonephritis²
- As many as 1:2000 people worldwide are currently diagnosed with ADPKD,⁴ and between 1:400 and 1:1000* people living today will be diagnosed with ADPKD in their lifetime¹

*The higher prevalence value of 1:1000 is believed to be inaccurate because the data are based on a postmortem study and therefore report lifetime morbid risk rather than point prevalence.

ADPKD=autosomal dominant polycystic kidney disease; ESRD=end-stage renal disease.

1. Torres VE, Harris PC. (2009). *Kidney Int.* 76(2):149-168.

2. United States Renal Data System. 2016 USRDS Annual Data Report Volume 2: ESRD in the United States. National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, MD, 2016 (accessed 14 February 2019).

3. Chebib FT, Torres VE. (2016). *Am J Kidney Dis.* 67(5):792-810.

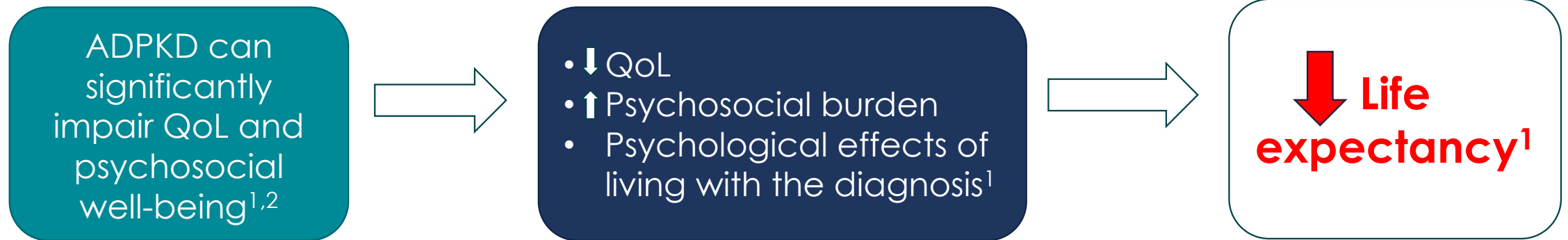
4. Willey C. DRAFT: The Descriptive Epidemiology of ADPKD in the U.S. 2017.



Improving Awareness & Patient Outcomes

Psychological Impact of ADPKD

Anxiety, Depression & Quality of Life (QoL) in ADPKD



- As renal insufficiency progresses → ↓ QoL and ↑ level of anxiety and depressive complaints¹
- Even early in the course of the disease, ADPKD patients report a lower satisfaction with life compared to healthy individuals²
- Early presentation of anxiety and depression is a predictor for higher mortality rates in later disease stages¹

Early detection and management of psychosocial difficulties can improve QoL and is as important as medical management¹

1. Yarlioglu AM et al. (2022). *Int Urol Nephrol*. 55:983-992.

2. Jankowska M et al. (2022). *Nephron*. Published online October 12, 2022:1-6.doi:<https://doi.org/10.1159/000526840>

Emotional Burden of ADPKD

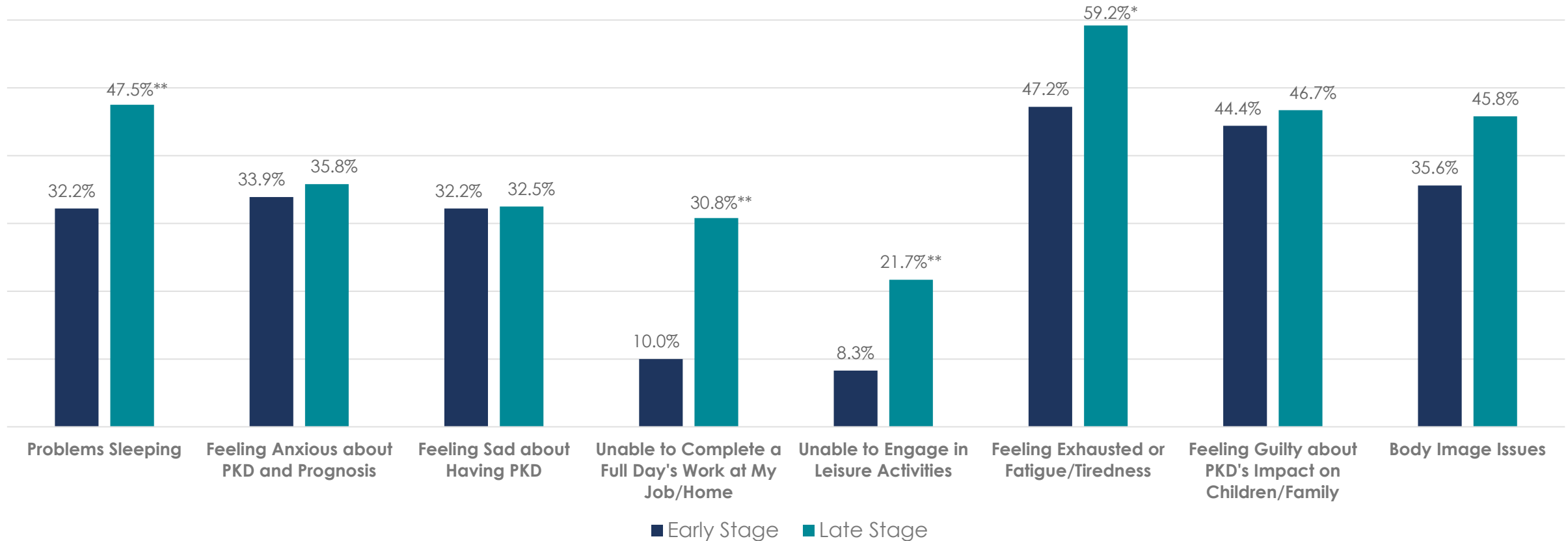


ADPKD=autosomal dominant polycystic kidney disease.

1. Baker A et al. (2015). *Clin Kidney J.* 8(5):531-537. 2. Pérez-Dominguez T et al. (2012). *Nefrologia.* 32(3):397-399.

ADPKD Patients Have Significant Emotional Burden

Symptoms Reported by Patients¹



*indicates significant difference ($p \leq 0.05$ vs. early stage)

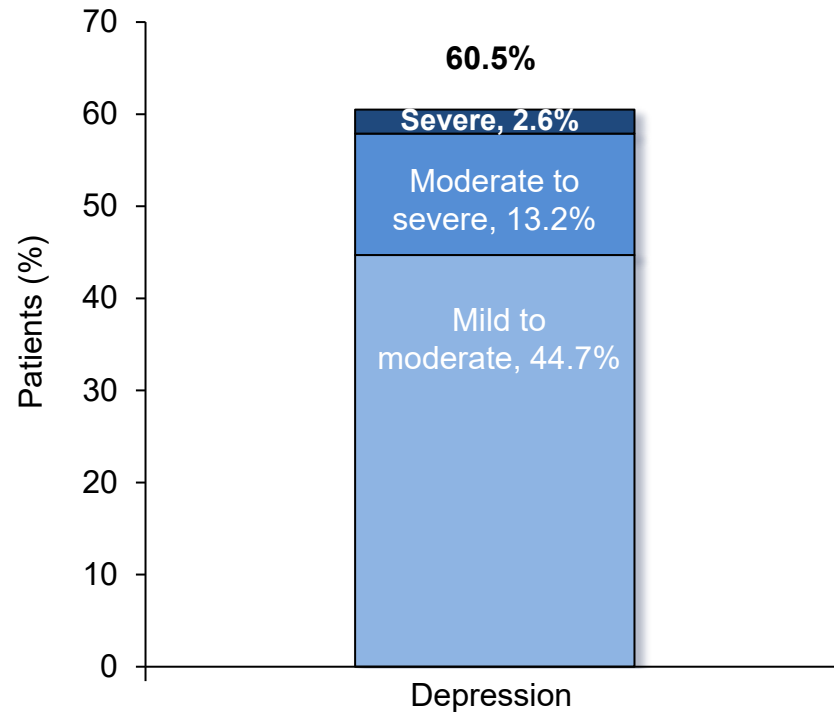
**indicates significant difference ($p \leq 0.01$ vs. early stage)

ADPKD=autosomal dominant polycystic kidney disease.

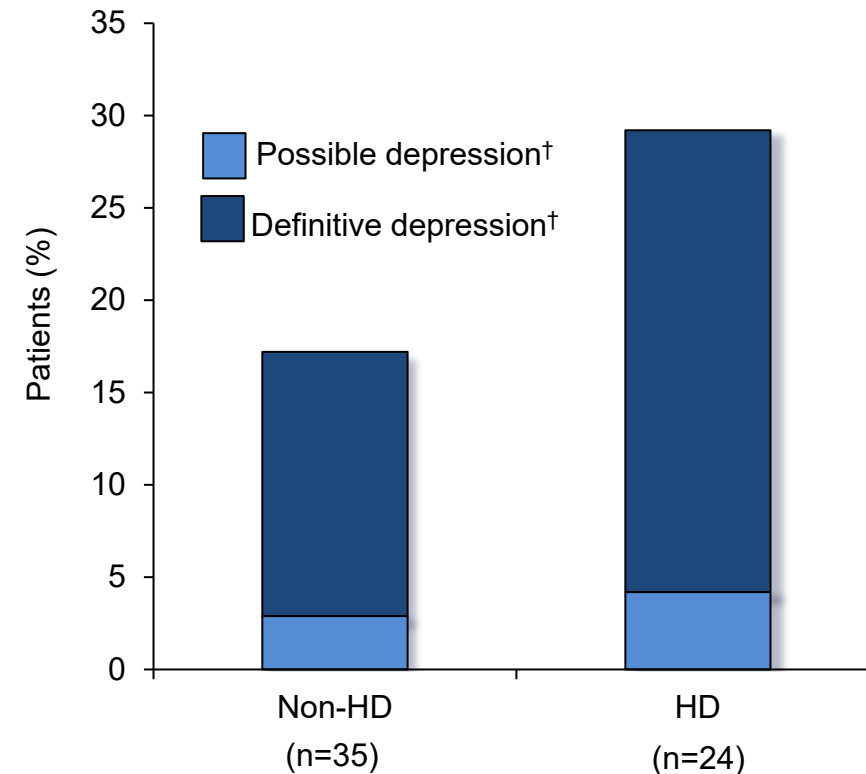
1. Sanon et al. Presented at: National Kidney Foundation 2019 Spring Clinical Meetings; May 8-12, 2019; Boston, MA.

Patients With ADPKD Have High Rates of Depression

Patients With ADPKD (n=38)^{1,*}



Patients With ADPKD According to Use of Hemodialysis (HD vs Non-HD) (N=59)²



*Diagnosed using Beck Depression Inventory; †Based on scoring of Hospital Anxiety and Depression Scale (HADS).

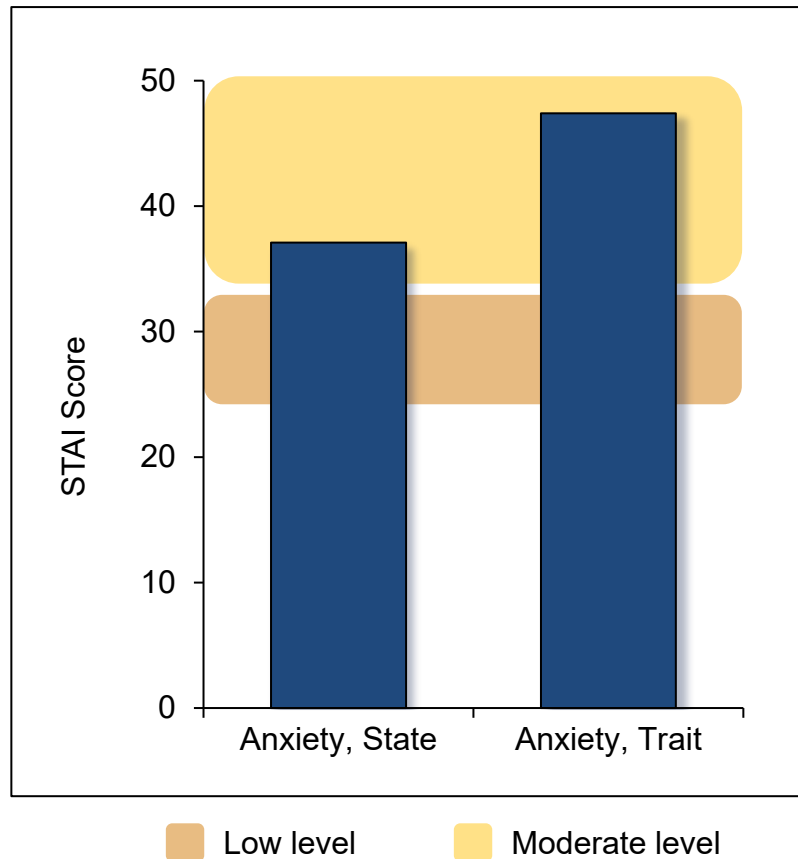
ADPKD=autosomal dominant polycystic kidney disease; HD=hemodialysis.

1. de Barros BP et al. (2011). *J Bras Nefrol.* 3(2): 120–8.

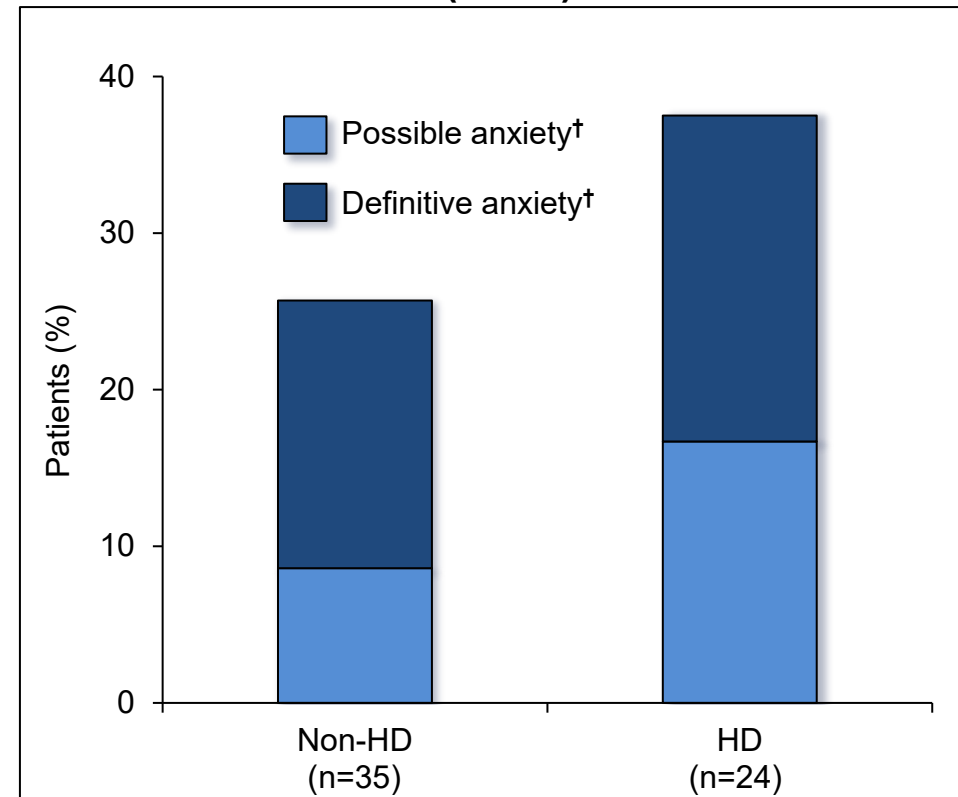
2. Pérez-Dominguez T et al. (2012). *Nefrologia.* 32(3): 397–9.

Patients With ADPKD Have High Rates of Anxiety

Anxiety in Patients with ADPKD^{1,*}



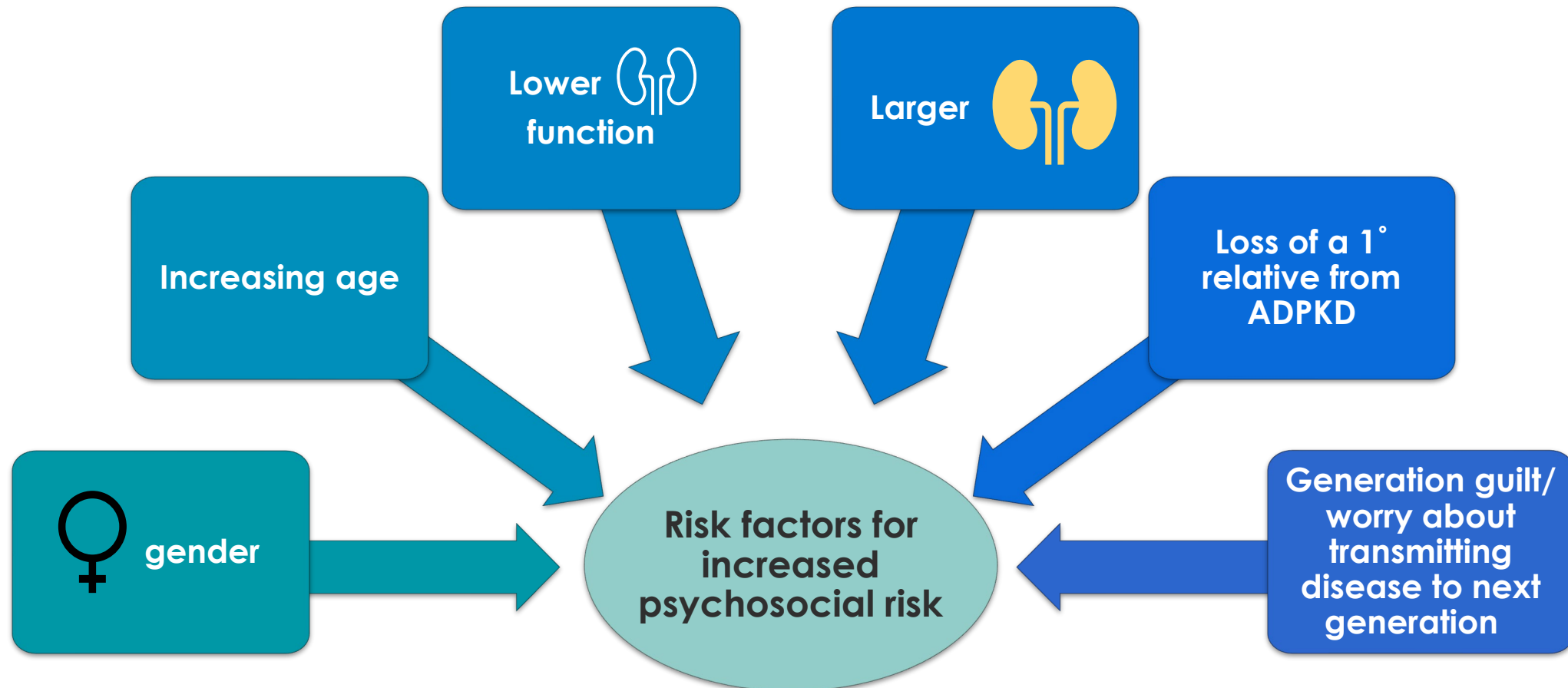
Anxiety in Patients Undergoing Dialysis (N=59)²



*Temporary or emotional-state anxiety vs longstanding personality trait; State Trait Anxiety Inventory (STAI) score: 20–30=low anxiety; 31–49=moderate; ≥50=high; †Based on scoring of Hospital Anxiety and Depression Scale (HADS).
 ADPKD=autosomal dominant polycystic kidney disease; HD=hemodialysis; STAI=State Trait Anxiety Inventory.
 1. de Barros BP et al. (2011). *J Bras Nefrol.* 3(2): 120-8. 2. Pérez-Dominguez T et al. (2012). *Nefrologia.* 32(3):397-9.

Psychosocial Risk of ADPKD

- Clinically significant depression reported in 22% of study participants
- 62% reported feeling guilty about passing ADPKD to their children



1. Simms RJ, et al. *Nephrol Dial Transplant*. 2016;31(7):1130-1140. doi:10.1093/ndt/gfv299

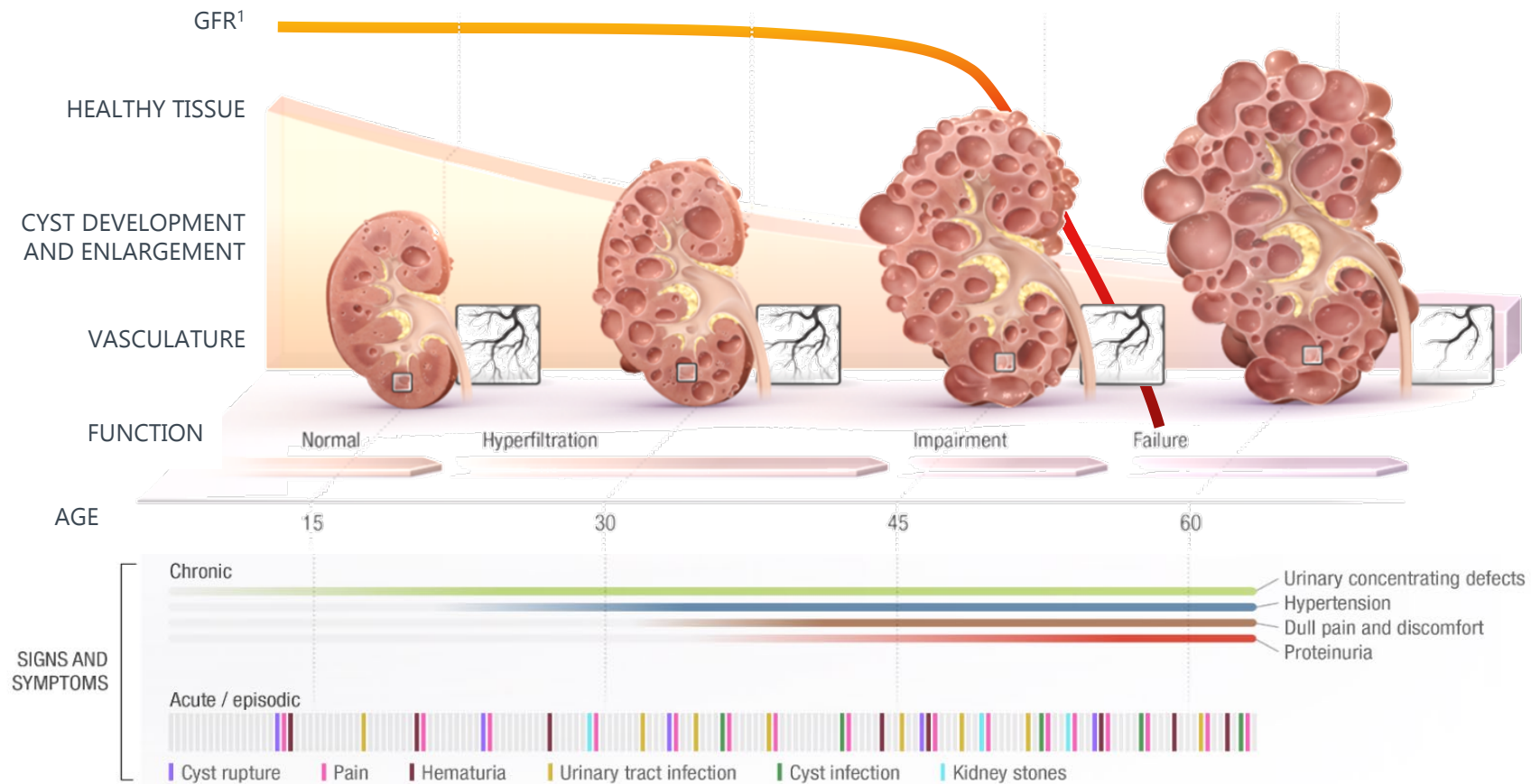


Improving Awareness & Patient Outcomes

Physical & Symptomatic Impact on ADPKD



Cyst Burden and Patient Complications in ADPKD

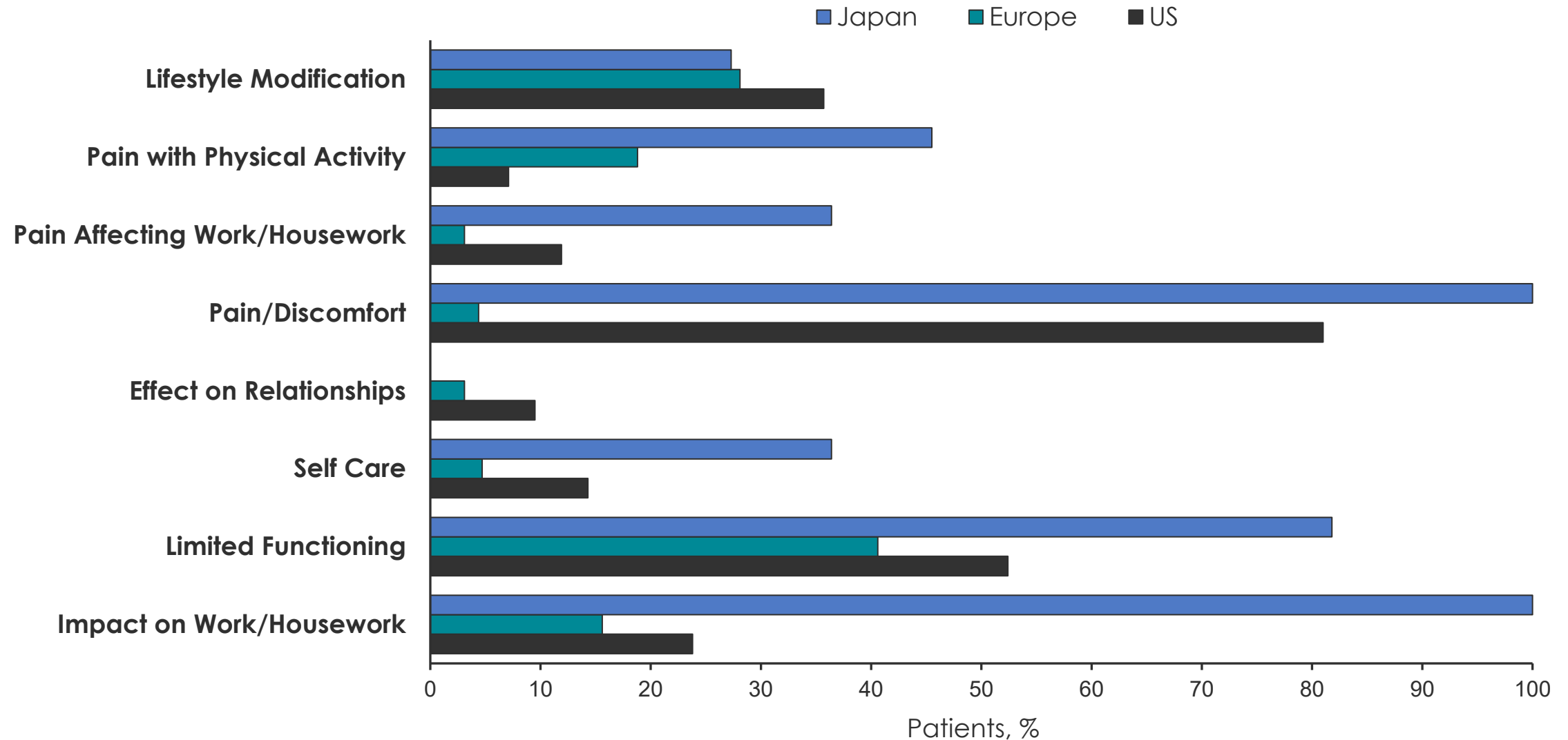


© 2013 Otsuka Pharmaceutical Development & Commercialization, Inc.

ADPKD=autosomal dominant polycystic kidney disease; GFR, glomerular filtration rate.

1. Grantham JJ et al. (2011). *Nat Rev Nephrol.* 7(10):556-566.

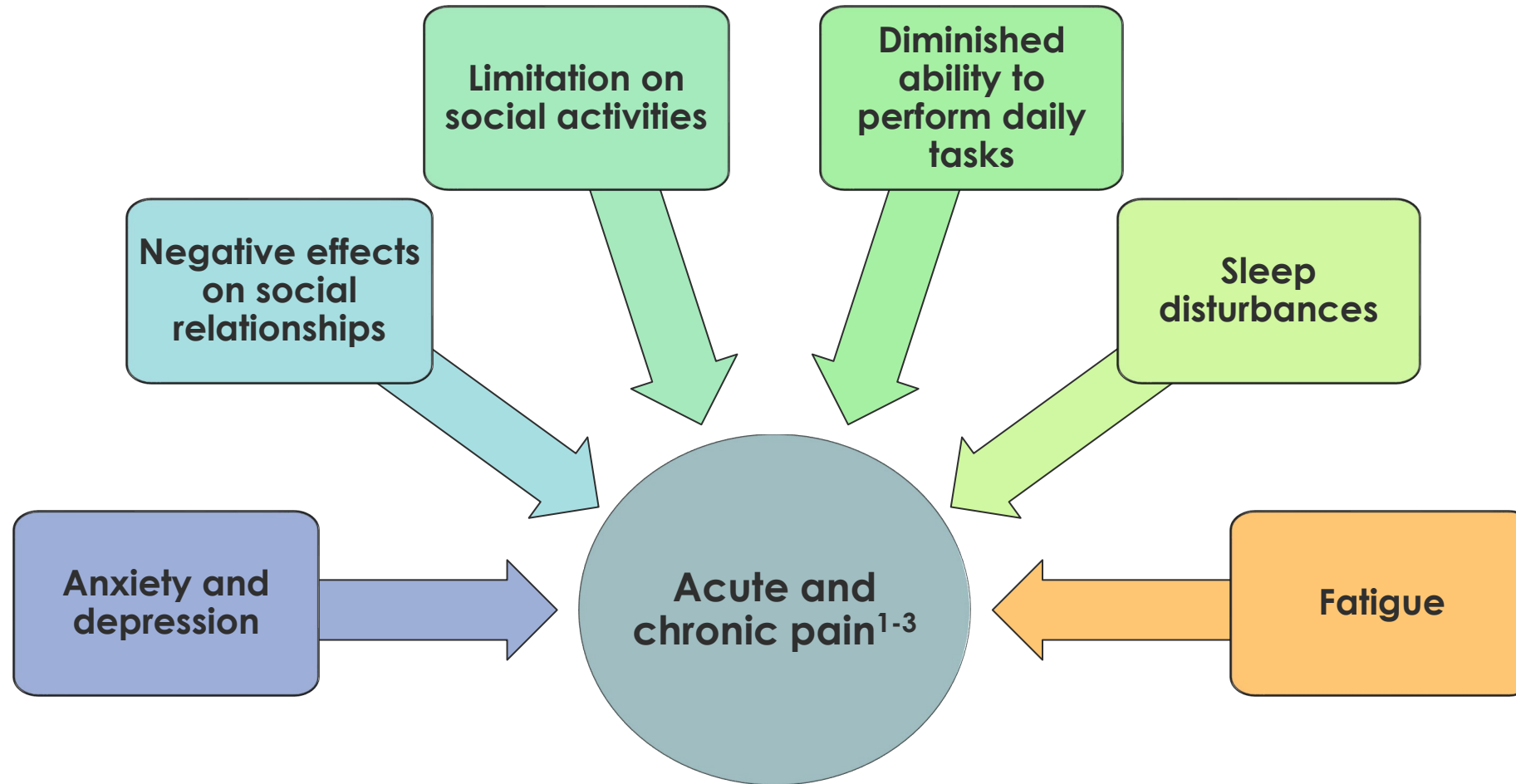
ADPKD Has Substantial Physical Impact on Patients



ADPKD=autosomal dominant polycystic kidney disease.

1. Cole JC et al. Presented at: 16th International Society for Pharmacoeconomics and Outcomes Research (ISPOR); May 21–May 25, 2011; Baltimore, MD.

Overview of the Effect of Pain in Patients with ADPKD



1. Hogan MC, et al (2010). *Adv Chronic Kidney Dis*. 17(3): e1–e16.
2. Heiwe S, et al. (2009). *Pain Manag Nurs*. 10(3): 134–41.
3. Grantham JJ et al. (2006). *Clin J Am Soc Nephrol*. 1: 148–57.

Enlarged Kidneys Have an Emotional and Physical Impact on Patients with ADPKD

Patient Experiences: ADPKD Timeline

Diagnosis

- Loss
 - Uncertainty
 - Fear
- *'The word "'fatal' was used a lot'*
 - *'Honestly, I am scared now. As much as I did not care before, now I am scared'*
 - *'Afraid of the future. There are people who think that something bad could or couldn't happen. I already know that something bad will happen for sure.'*



Latent period

- Hopelessness and helplessness
 - Distress and frustration
 - Coping strategies
- *'It took about 12–13 years. The kidneys functioned quite well. I went for frequent follow-ups so as long as they function well you do not do anything. At least not at that point.'*
 - *'I wish I hadn't known about it because it was like living with a ticking time bomb.'*
 - *'I am just waiting for when it will get worse. It is just waiting.'*

ADPKD=autosomal dominant polycystic kidney disease.

1. Baker A et al. (2015). *Clin Kidney J.* 8(5): 531–7.

Enlarged Kidneys Are a Chronic Reminder to Patients That ADPKD Is Incurable

- The burden of ADPKD (physical and emotional) for most patients is directly linked to the size of the kidneys^{1,2}
- Enlarged kidneys cause
 - Pain³
 - High blood pressure⁴
 - Blood in urine³
 - Anxiety (body image, lifestyle, sexual dysfunction)⁵
- Patients suffer pain, discomfort, and psychosocial effects that are important, but are not always recognized by clinicians⁶

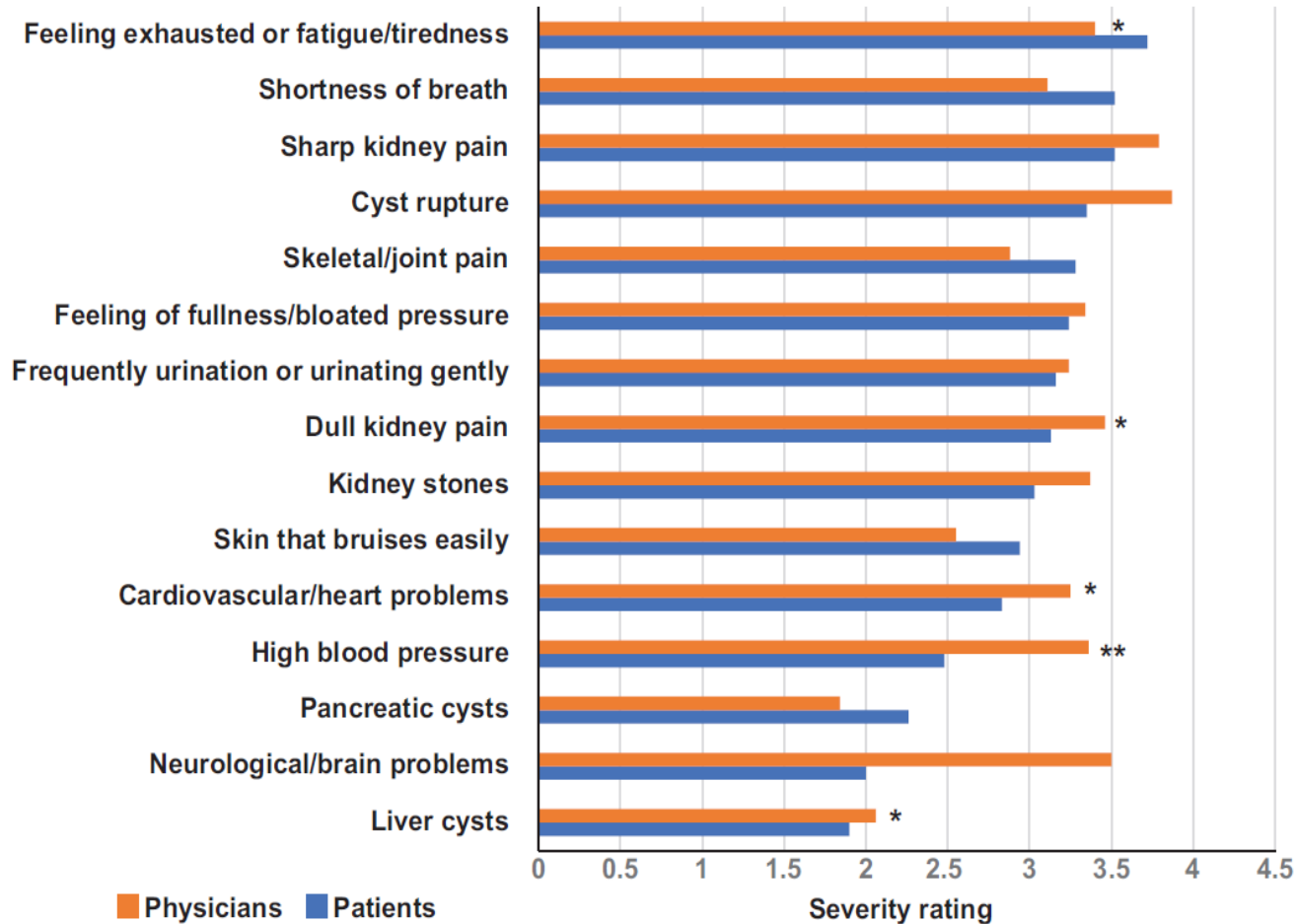


Photos courtesy of Jared Grantham, MD

ADPKD=autosomal dominant polycystic kidney disease.

1. Cole JC et al. Presented at: 16th International Society for Pharmacoeconomics and Outcomes Research (ISPOR); May 21–May 25, 2011; Baltimore, MD.

Perception of ADPKD Symptom Burden in Early-Stage Patients



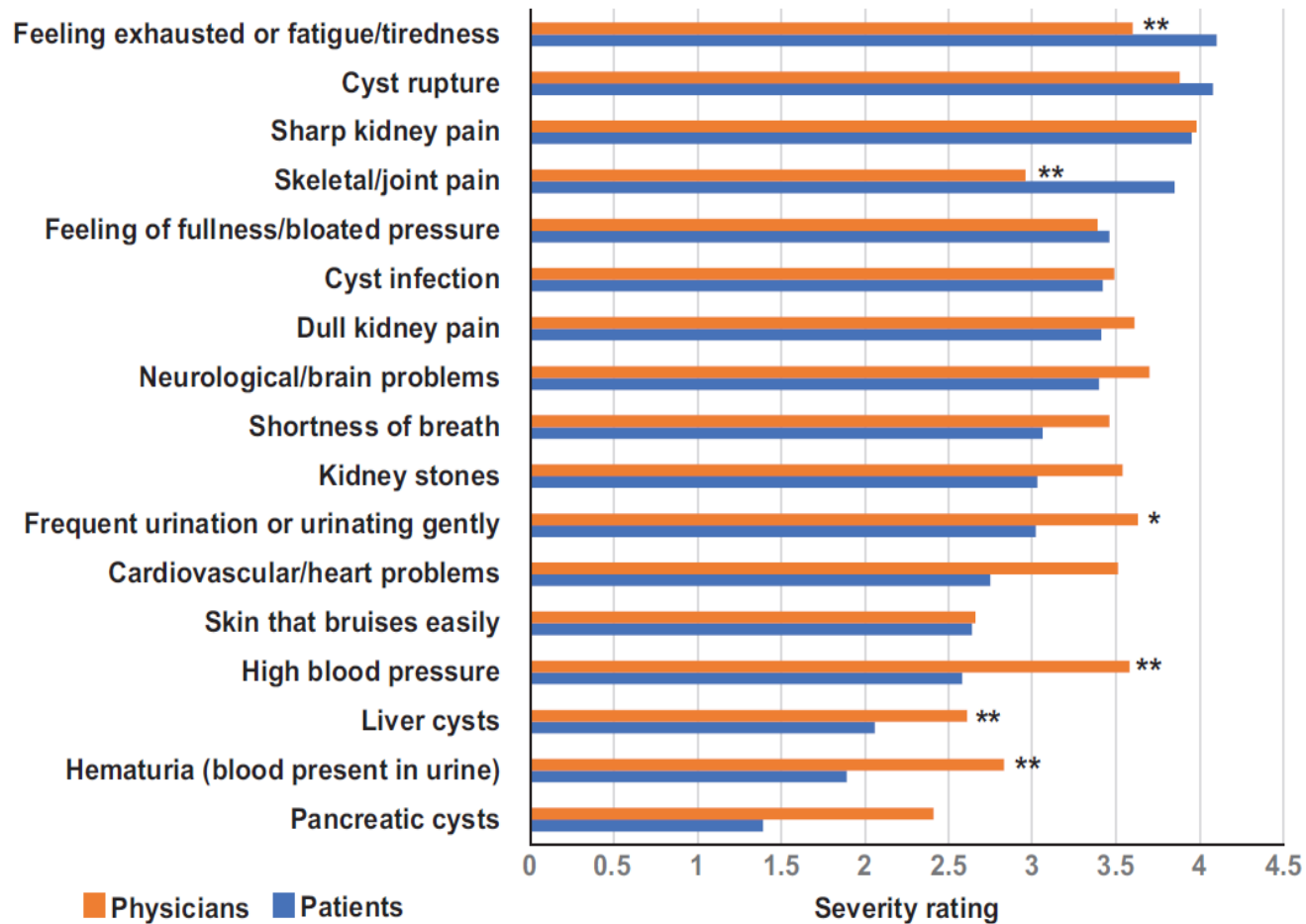
*Significant difference (p ≤ 0.05 vs patients). **Significant difference (p ≤ 0.01 vs patients). Severity rating scale: 1 (least burdensome) to 5 (most burdensome).

- **Early-stage patients** reported a significantly **greater** symptom burden, or feeling exhausted or fatigue/tiredness compared with the burden perceived by physicians¹

- **Physicians** perceived several symptoms to be more burdensome than they actually were to early-stage patients:
 - Dull kidney pain
 - Cardiovascular problems
 - High blood pressure
 - Liver cysts¹

1. Sanon et al. Presented at: National Kidney Foundation 2019 Spring Clinical Meetings; May 8-12, 2019; Boston, MA.

Perception of ADPKD Symptom Burden in Late-Stage Patients



*Significant difference (p ≤ 0.05 vs. patients). **Significant difference (p ≤ 0.01 vs patients). Severity rating scale: 1 (least burdensome) to 5 (most burdensome).

- **Late-stage patients** reported a significantly **greater** symptom burden for feeling exhausted or fatigue/tiredness and skeletal/joint pain compared with the burden perceived by physicians¹

- **Physicians** perceived several symptoms to be more burdensome than they actually were to late-stage patients:
 - Frequent urination or urinating urgently
 - High blood pressure
 - Liver cysts
 - Hematuria¹

1. Sanon et al. Presented at: National Kidney Foundation 2019 Spring Clinical Meetings; May 8-12, 2019; Boston, MA.



Improving Awareness & Patient Outcomes

Quality of Life in ADPKD Patients & Impact on Family/Caregivers

Pain and QoL in ADPKD patients: CYSTic QoL Study

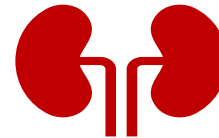
Observational study assessing QoL in European ADPKD patients with eGFR ≥ 30 ml/min/1.73 m² ¹

Health-related Quality of Life (HR-QoL)¹

- 465 patients administered KDQoL-SF V1.3 questionnaire
- Combination of the kidney disease QoL (disease specific) and SF-36 (generic)

ADPKD patients uniformly reported:¹

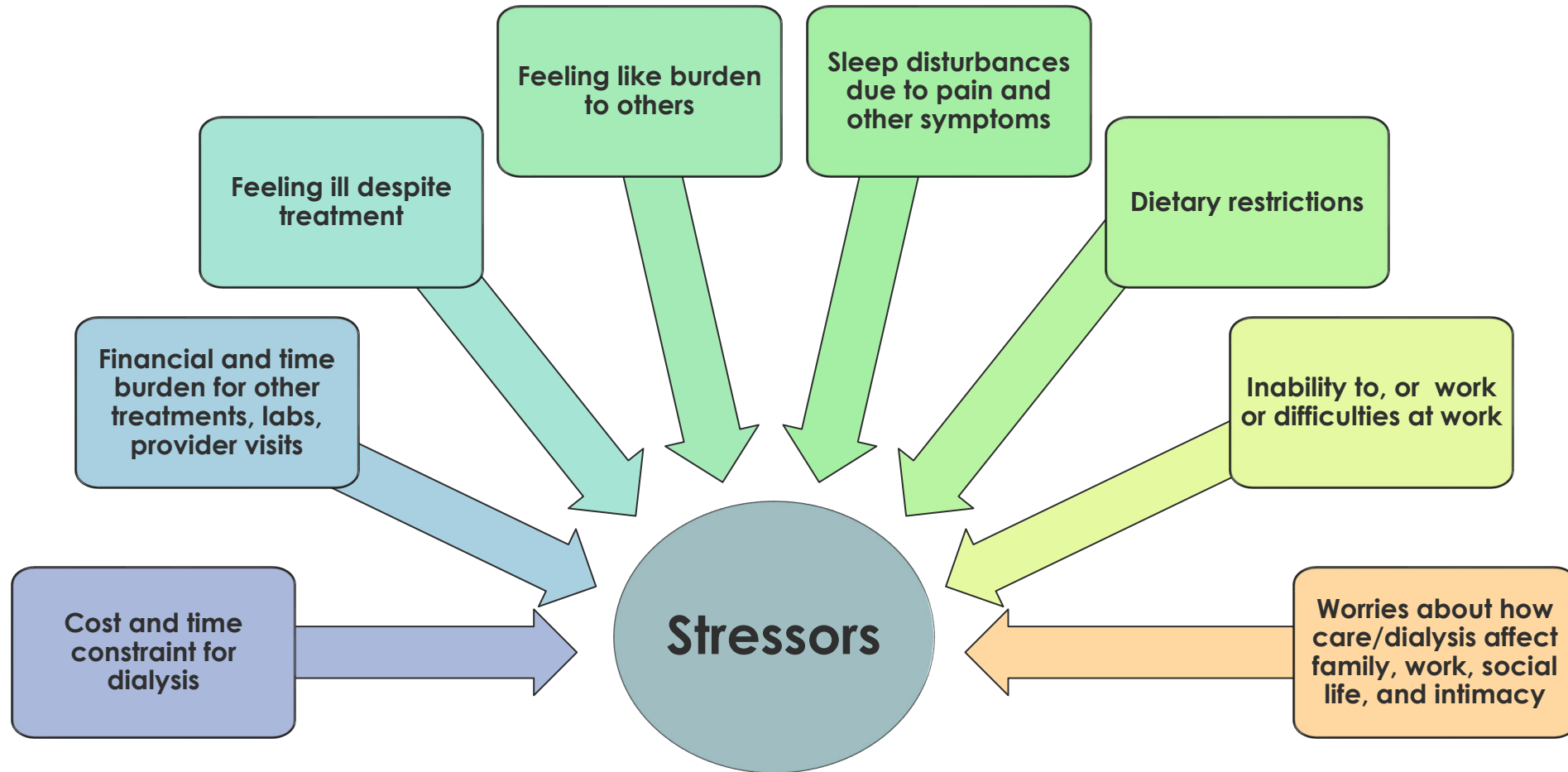
- ↓ general health and energy
- Poorer physical, mental and emotional health
- Limitations in social functioning and work



- **32.5% of patients experienced flank pain**
- Significantly and negatively correlated with 10/20 KDQoL-SF subscales
- Larger kidney size and lower kidney function was negatively associated with reduced energy and poorer physical health respectively¹

1. Winterbottom J, et al. Clinical Kidney Journal. 2022

Burden of ADPKD on QoL



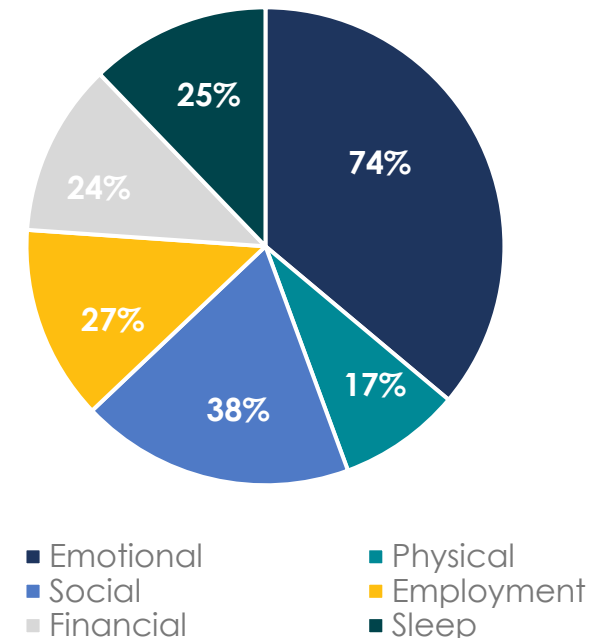
1. Barhum L. Living With Autosomal Dominant Polycystic Kidney Disease Coping, Support, and Living Well. December 07, 2021. Accessed April 18, 2023. <https://www.verywellhealth.com/autosomal-dominant-polycystic-kidney-disease-coping-5211944#toc-emotional>

Burden on Caregivers Results in Substantial Emotional, Social and Financial Impact

Caregivers reported difficulties in their QoL, with emotional well-being as most negatively impacted

- Constant stress & anxiety of health status or risk of worsening health for ADPKD-individual
- Difficult to leave home for work, social/leisure activities or travel
- Anger/frustration because there is no cure
- Feeling hopeless & surrendered to the disease
- Financial burden due to reduction of work hours and cost of care

Caregiver Burden On Domain of Life (N = 139)



1. Oberdhan D et al. (2023). *Kidney Med.* Published online 2022 Dec 14. doi: 10.1016/j.xkme.2022.100587



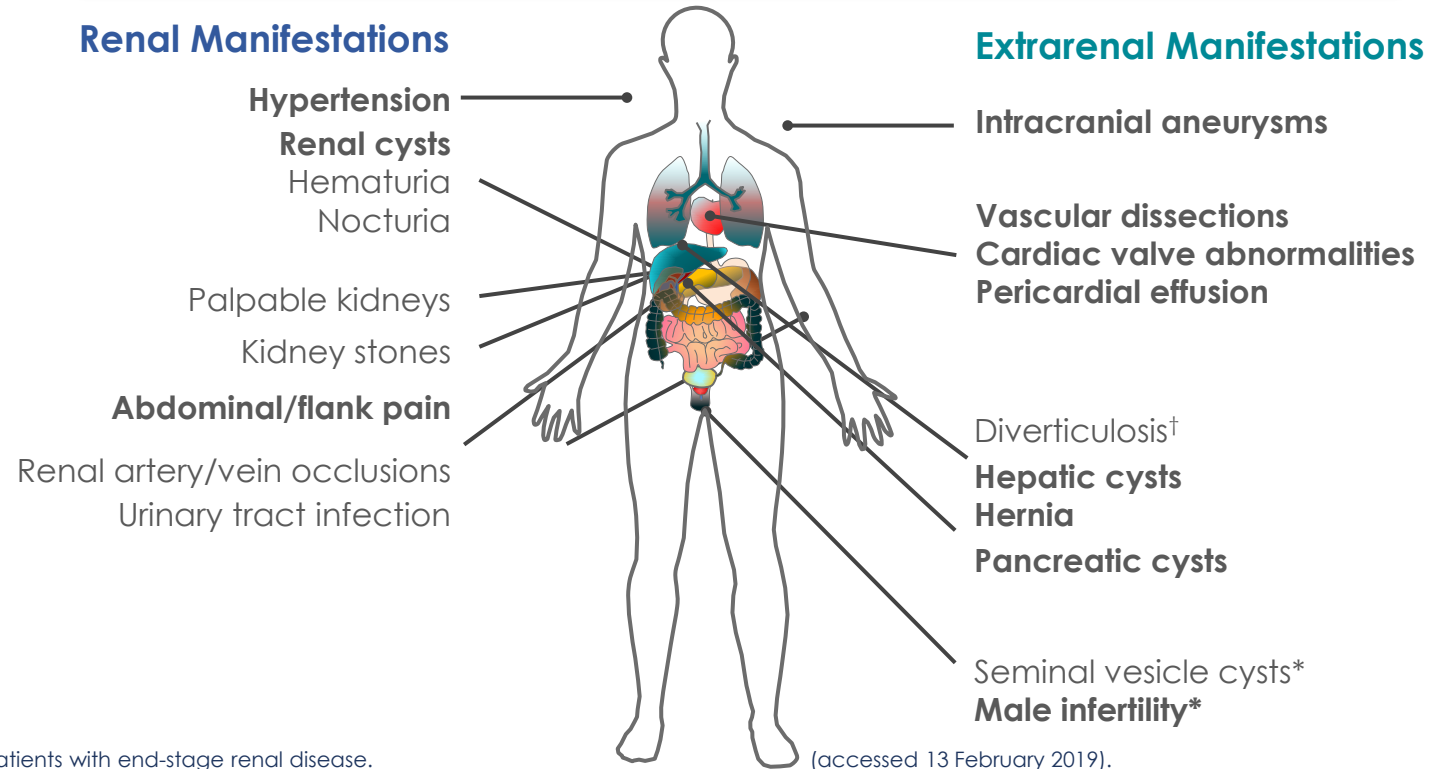
NephU[™]

Improving Awareness & Patient Outcomes

Morbidity & Mortality in ADPKD Patients

ADPKD Is a Systemic Disease

Renal cysts are the first manifestation of ADPKD and precede changes in kidney function by many years¹⁻⁸



*In male patients. [†]Most common in patients with end-stage renal disease.

ADPKD=autosomal dominant polycystic kidney disease.

1. Halvorson CR et al. (2010). *Int J Nephrol Renovasc Dis.* 3:69-83.
2. Torres VE, and Harris PC. (2009). *Kidney Int.* 76(2):149-168.
3. Chebib FT and Torres VE. (2016). *Am J Kidney Dis.* 67(5):792-810.
4. Patient Platform. <http://www.patient.co.uk/doctor/autosomal-dominant-polycystic-kidney-disease>
5. Luciano RL and Dahl NK. (2014). *Nephrol Dial Transplant.* 29(2):247-254.
6. Mikolajczyk AE, et al. (2017). *Clin Gastroenterol Hepatol.* 15(1):17-24.
7. Chapman AB and Rahbari-Oskui FF. Renal Cystic Disorders. In: Wilcox CS et al. eds. *Therapy in Nephrology & Hypertension.* 3rd ed. Philadelphia, PA: Saunders; 2008.
8. Chauveau D et al. (1994) *Kidney Int.* 45:1140-1146.

Extra-Renal Manifestations May Result in Increased Morbidity and Mortality

Manifestation	Prevalence	Recommendation
Hepatic Cysts	>90%	None
HTN	70%	Routine BP in all patients
LVH	50%	HTN Control in all patients
Valvular Abnormalities	30%	Echocardiography in patients with murmur
ICA	6-20%	MRA in patients with family hx/prior ICA rupture
Hernias	45%	Physical Exam in all patients with high cyst burden
Diverticula	40%	None
Depression	60%	Depression screen in all patients yearly
Pain	60%	QOL Screen in all patients yearly

- Cardiovascular abnormalities (i.e. HTN, LVH and valvular abnormalities) pose significant morbidity and mortality

- Aneurysmal rupture results in a mortality rate of 60% and if the patient survives, significant morbidity

- Higher prevalence of hernias increases risk of intestinal incarceration leading to significant morbidity

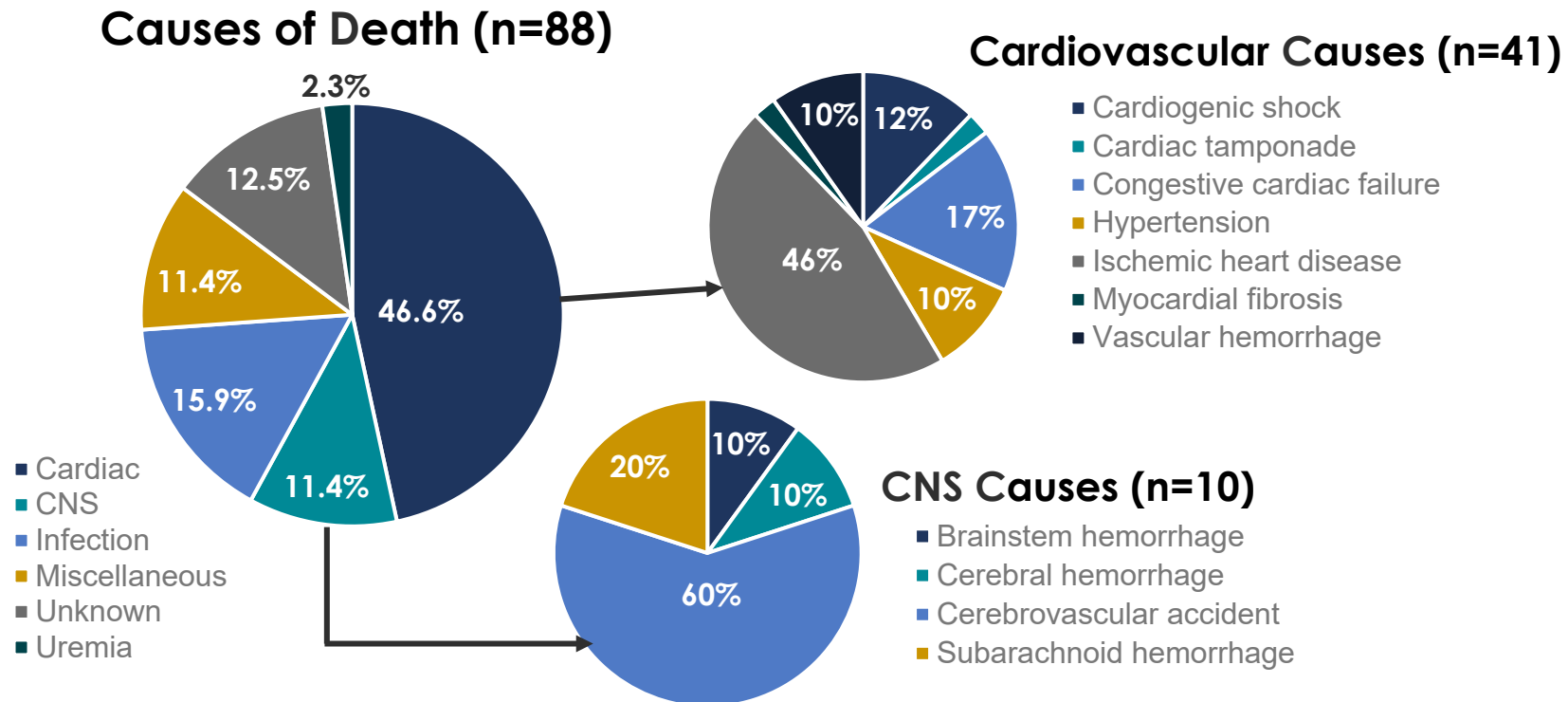
- Pregnant females with ADPKD have higher morbidity than non-ADPKD females

LVH = left ventricular hypertrophy

1. Luciano RL et al. (2014). *Nephrology Dialysis Transplantation*. 2(29):247-254

Cardiovascular Disease Is the Most Common Cause of Death in ADPKD

Mortality is estimated to be 1.6- to 3.2-fold higher in ADPKD patients than the general population, with cardiac-related death being the most common cause of mortality⁴



ADPKD=autosomal dominant polycystic kidney disease; CNS=central nervous system.

1. Fick GM et al. (1995). *JASN*. 5:2048-2056.

2. Rahman E et al. (2009). *Saudi J Kidney Dis Transpl*. 20(5):806-810.

3. Orskov B et al. (2012). *Nephrol Dial Transplant*. 27:1607-1613.

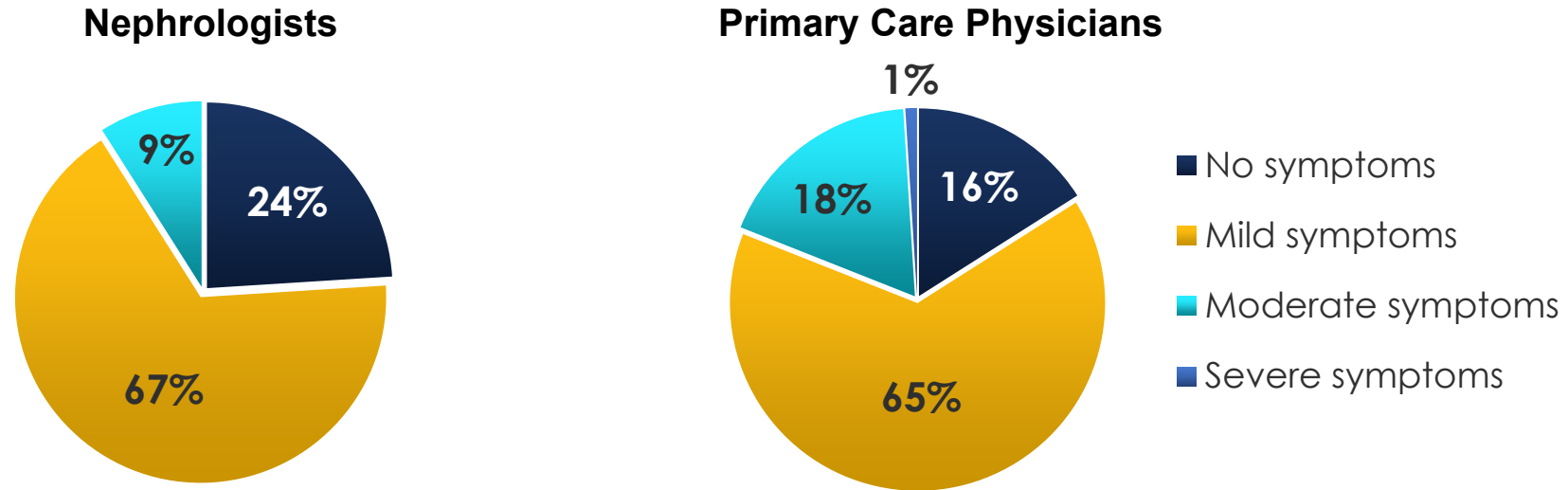
4. Luciano RL et al. (2013). *Nephrology Dialysis Transplantation*. 29(2):247-254.



Improving Awareness & Patient Outcomes

Empowering Healthcare Providers and Patients to Prioritize Mental Health

Impact of ADPKD on Patients May Be Underestimated by Healthcare Professionals

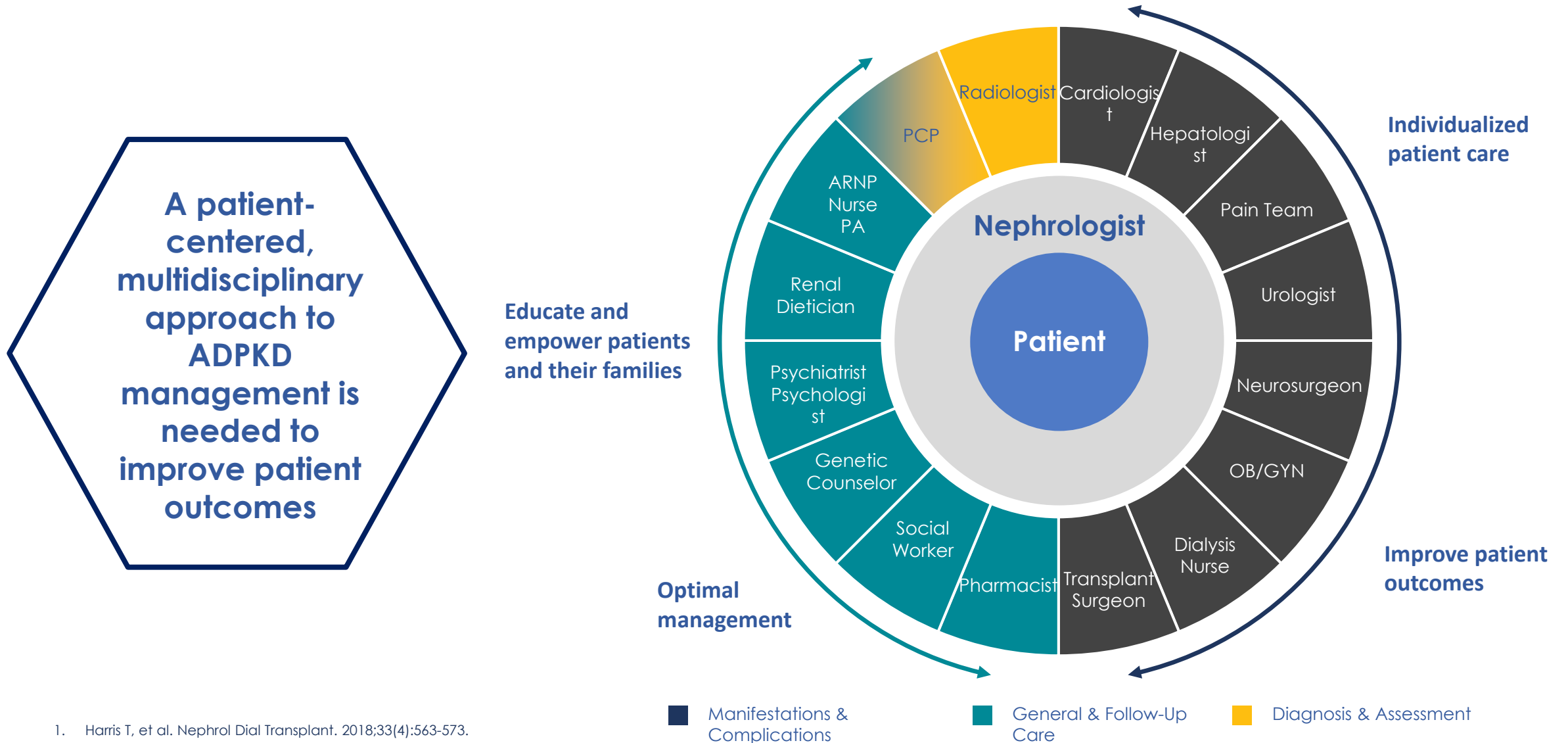


- European Survey¹:
 - Approximately two-thirds of nephrologists and primary care physicians believed that patients with early-stage ADPKD had only mild symptoms
 - A quarter believed that these patients had no symptoms at all
 - Approximately half of both groups (52%) believed that early-stage ADPKD was not associated with any emotional symptoms, or was associated with only mild symptoms

ADPKD=autosomal dominant polycystic kidney disease.

1. Carr A et al. Abstract SP020 Presented at: 51st ERA-EDTA Congress; May 31–June 3, 2014; Amsterdam, Netherlands.

Multidisciplinary Team Approach to Managing ADPKD



1. Harris T, et al. Nephrol Dial Transplant. 2018;33(4):563-573.

Patient Centered Approach to Improving Care in ADPKD

Health Care Providers should recognize the potential psychological, social and functional effects of ADPKD at all disease stages

- **Early** identification and screening
 - Self-Assessments
 - PHQ9, BAI, BDI
 - ADPKD Genetic Psychosocial Risk Instrument (GPRI-ADPKD)
 - ADPKD Impact Scale (ADPKD-IS)
 - Clinical interview
- Comprehensive assessment of manifestations
- Holistic assessment of physical, psychological & social impact of the disease on the patient and family
- Access to treatment to relieve symptoms, manage complications, preserve kidney function, lower risk of CVD & maintain QoL
- Information to help patients and families act as active partners in care

1. Harris T, et al. Nephrol Dial Transplant. 2018;33(4):563-573.

Resources for Patients, Families and Caregivers to Enable Informed & Active Participation in Care*

- **Access to psychological and social support services¹**
- **Foundations & Informative Sites:**
 - **PKD Foundation** | pkdcure.org
 - **PKD International** | pkdinternational.org
- **Peer mentor programs**
 - **PKD Connect Peer to Peer Mentor Program** | connect.pkdcure.org
- **Support Call Lines**
 - **PKD HOPE LINE** | 844-PKD-HOPE
- **Patient/Caregiver education**
 - **OPEN** | otsukapatiented.com
 - **PKD Foundation** | resources.pkdcure.org
 - **NKF** | kidney.org
- **Referral to Centers of Excellence & Partner Clinics**
 - **PKD Foundation** | pkdcure.org
- **Participate in research¹**
 - Registry entry, clinical trials, patient reported outcome data collection
- **Family planning¹**
 - Genetic counseling
 - Pre-implantation genetic diagnosis
 - Contraception
 - Pregnancy issues
- **Renal Replacement Therapy & Transplant¹**
 - Explore options for living kidney donors early on for preemptive kidney transplant

* Not an exhaustive list

1. Harris T, et al. Nephrol Dial Transplant. 2018;33(4):563-573.

What Can We do to Empower Patients & Caregivers?

Patient centered approach to ADPKD is one in which patients, family members and caregivers are empowered to act as fully informed and active partners in decision-making regarding their care

- Partnering with patients to enable them to take control of their own health and well-being requires:
 - Effective communication, adequate information, access to support services and specialist advice
 - Reframing traditional models of communication and learning to truly listen to patients
 - Refraining from minimizing emotions and understanding that it is a disease that affects quality of life

1. Harris T, et al. Nephrol Dial Transplant. 2018;33(4):563-573.

Like What You Learned Today? See What's Up Next!



NephU.org/events

The NephU Community
Grows Stronger When
You're Engaged.

Follow Us
@NephUCommunity





Improving Awareness & Patient Outcomes

Mental Health in Autosomal Dominant Polycystic Kidney Disease (ADPKD)