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Patient-Reported Outcomes Measures, Polycystic Kidney Disease Burden, and Outcomes in Autosomal Dominant Polycystic Kidney Disease

February 2024 US.CORP.D.24.00003

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Speakers

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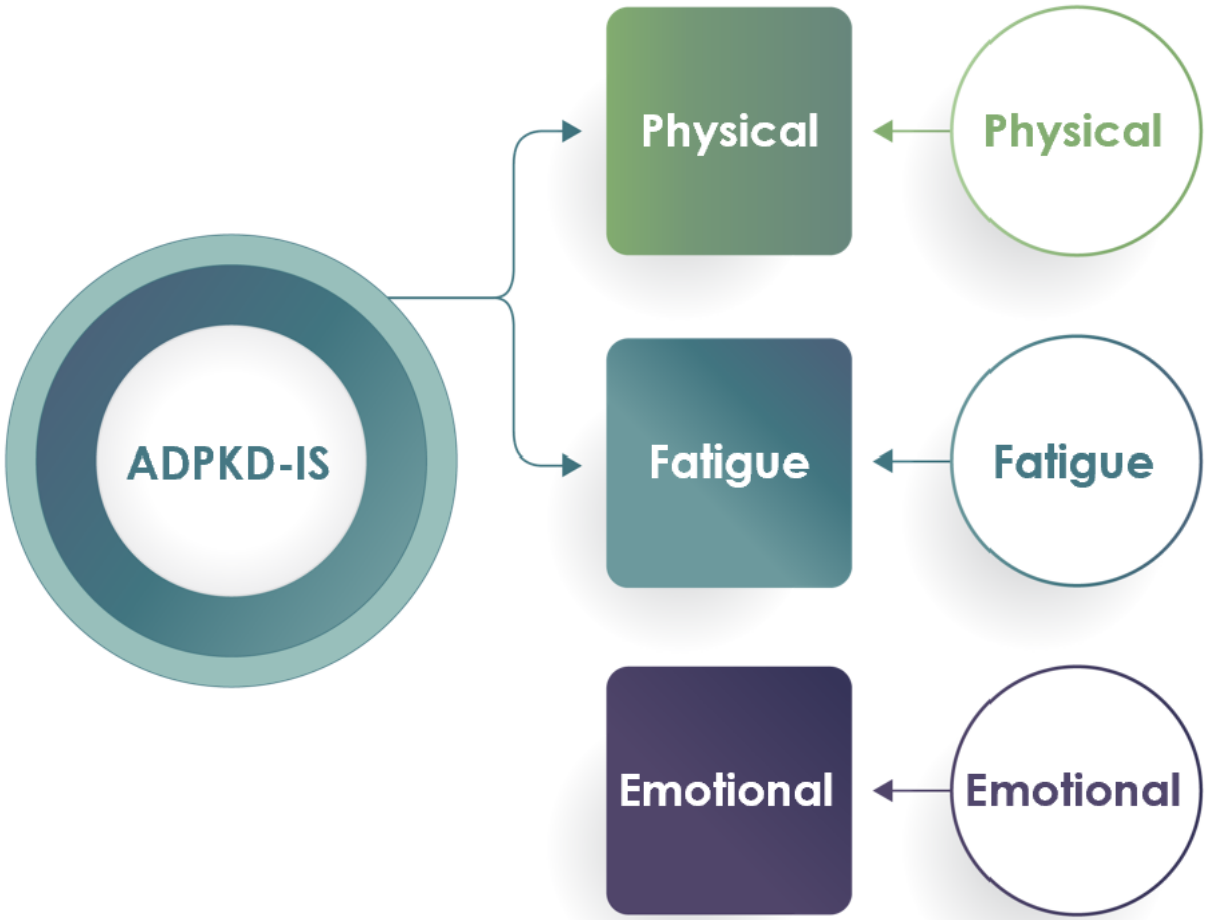
Background

Autosomal dominant polycystic kidney disease (ADPKD) imposes a substantial and progressively worsening burden on patients that may encompass multiple dimensions, including:

- **Physical Symptoms (e.g., pain)[1]**
- **Functional Impairment[3]**
- **Systemic Complications (e.g., hypertension)[1]**
- **Work Limitations[3]**
- **Psychological Burden[2]**
- **Medical Costs[4]**

1. Delaney VB et al. *Am J Kidney Dis*. 1985;5:104-111.
2. Chapman AB et al. *Kidney Int*. 2015;88:17-27.
3. Oberdhan D et al. *Am J Kidney Dis*. 2018;71:225-235.
4. Perrone RD et al. *Kidney Int Rep*. 2023;8:989-1001.

ADPKD Impact Scale Model (ADPKD-IS)



ADPKD-IS Questions

Physical

- Engage in leisure activities
- Complete full day's work at job or home
- Conduct daily activities
- Complete everything in a day
- Perform intense physical activities
- Modify lifestyle due to pain
- Pain

Fatigue

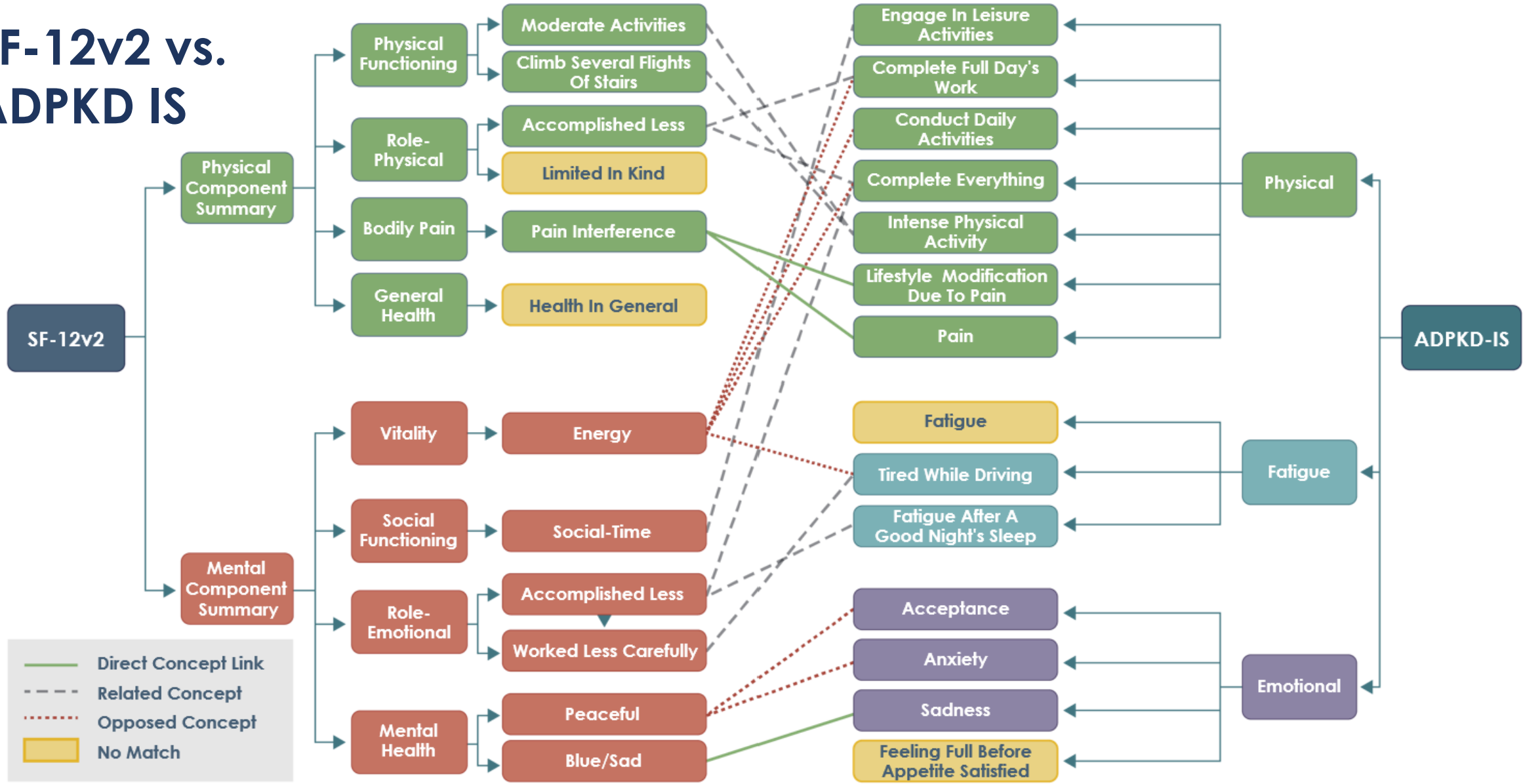
- Fatigue
- Feeling tired while driving
- Feeling fatigue after a good night's sleep

Emotional

- Acceptance
- Anxiety
- Sadness
- Feeling full before appetite is satisfied

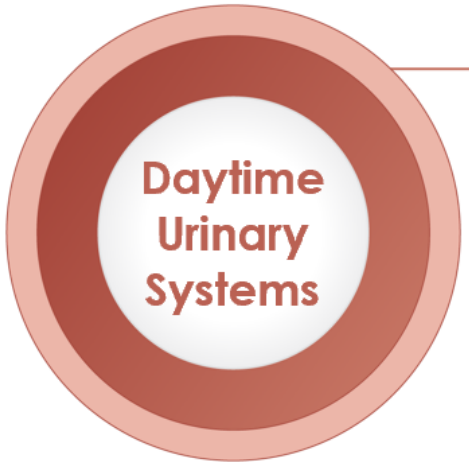
1. Oberdhan D, et al. Development of the Autosomal Dominant Polycystic Kidney Disease Impact Scale: A New Health-Related Quality of Life Instrument. Am J Kidney Disease. 2018 Feb;71(2):225-235

SF-12v2 vs. ADPKD IS



1. Oberdhan D, et al. Development of the Autosomal Dominant Polycystic Kidney Disease Impact Scale: A New Health-Related Quality of Life Instrument. Am J Kidney Disease. 2018 Feb;71(2):225-235

ADPKD Urinary Impact Scale Model (ADPKD-UIS)



Urinary Frequency

Urinary Urgency

Nocturia

Urinary Frequency

Urinary Urgency

Nocturia

ADPKD-UIS Question Topics

Urinary Frequency

- Daily activities frequency
- Social activities frequency
- Planning to use the bathroom frequency
- Need to urinate frequency

Urinary Urgency

- Daily activities urgency
- Social activities urgency
- Planning to use the bathroom urgency

Nocturia

- Ability to sleep through the night
- Waking up to urinate
- Impact on everyday life

1. Oberdhan D. et al. (2013).Value in Health, 3(16), A183
2. Oberdhan D. et al. (2013, May). Nephrology Dialysis Transplantation (Vol.28pp.143)

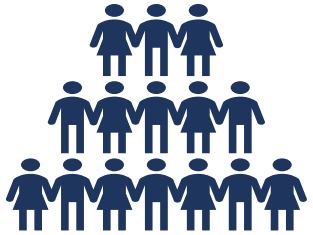
Study Objectives and Design[1]

Objectives

- **Better characterize the patient burden of ADPKD**
- **Determine whether patient-reported burden predicts risk of adverse ADPKD-related outcomes**

- *Post hoc* analysis of data from OVERTURE, a multicenter, longitudinal, observational study of patients with ADPKD (NCT01430494)
- Worldwide study conducted in 20 countries (Jun 2011 – Oct 2014)
- Patients received standard of care treatment for ADPKD in everyday clinical settings,[2] *before* disease-specific treatment was commercially available
- Study visits at 6-month intervals assessed patients for ADPKD-related clinical outcomes, PRO using disease-specific and generic instruments, and health economic and work productivity data

OVERTURE Study Population



Represented a Broad Spectrum of Disease Progression and Patient Characteristics

N=3,409

Age Range

12–78 Years

Female/Male

56%/44%

Baseline Chronic Kidney Disease (CKD) Stage

G1: 29%	G4: 10%
G2: 28%	G5: 3%
G3: 26%	Missing: ~3%

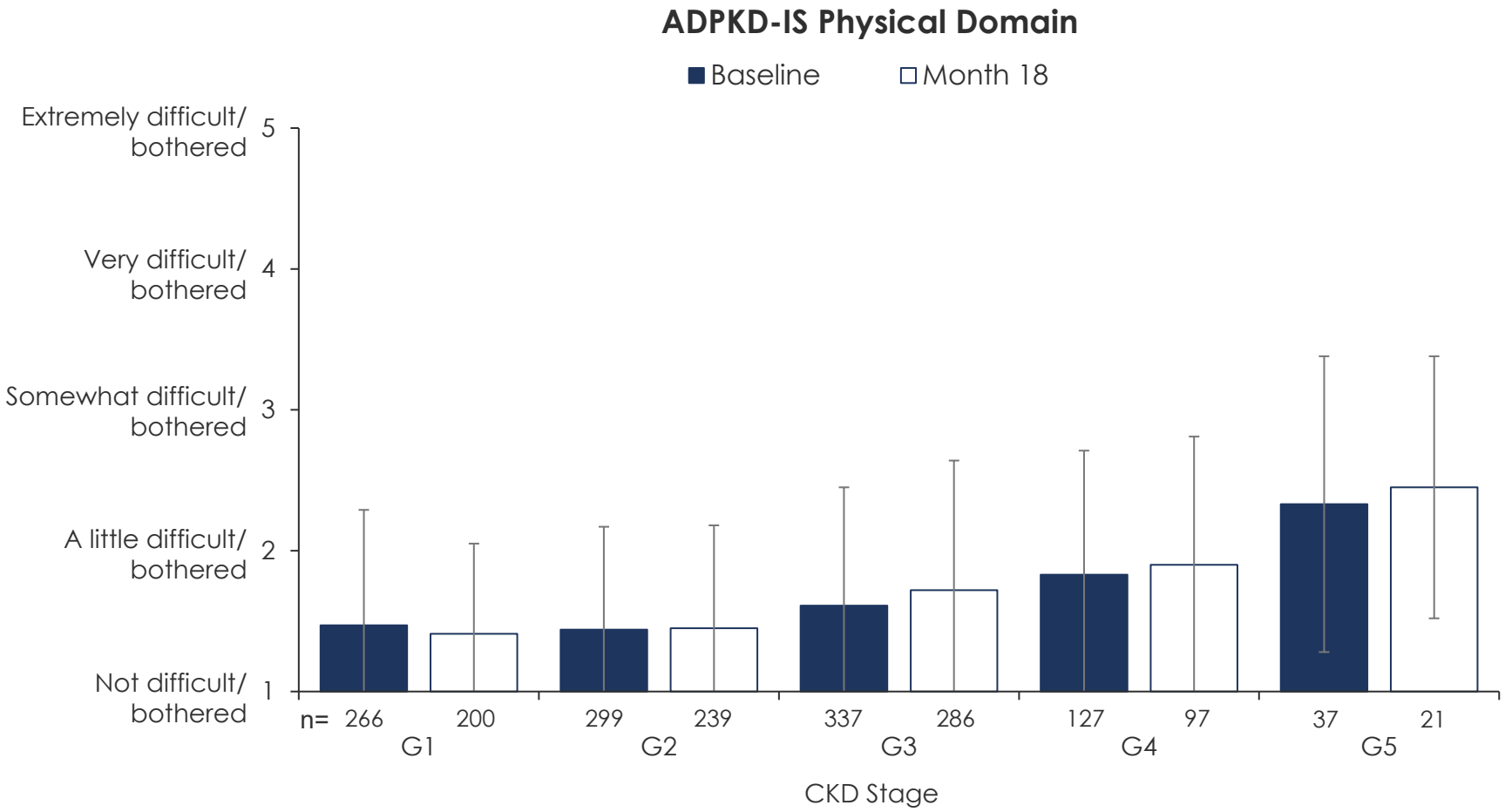
1. Oberdhan D et al. *Kidney Med*. 2024;6:100755.
2. Perrone RD et al. *Kidney Int Rep*. 2023;8:989-1001.

Study Analyses

- Scores on PRO instruments were summarized descriptively for patients in different CKD stages
- Associations between PRO scores and binary healthcare utilization and employment outcomes were analyzed using logistic regression models with PRO measure, age, gender, and race included as predictors
  - Odds ratios (ORs) were calculated for each PRO measure
- To determine if PRO scores in early disease might predict clinical outcomes, subgroup analyses were conducted that compared patients in CKD stages G1/G2 with either good or poor health-related quality of life (HRQoL) at baseline
  - Good HRQoL was defined as a score ≤3 on all 3 subscales of the ADPKD-IS, and poor HRQoL defined as a score >3 on at least 2 of the 3 subscales of the ADPKD-IS
  - The presence of ADPKD-related symptoms and conditions between these subgroups was compared using ORs
- Duration of follow-up in the analyses was limited to 18 months due to gradual drop-off in participation during OVERTURE and decreasing sample sizes

1. Oberdhan D et al. *Kidney Med*. 2024;6:100755.

The ADPKD-IS Captured Differences by Baseline CKD Stage



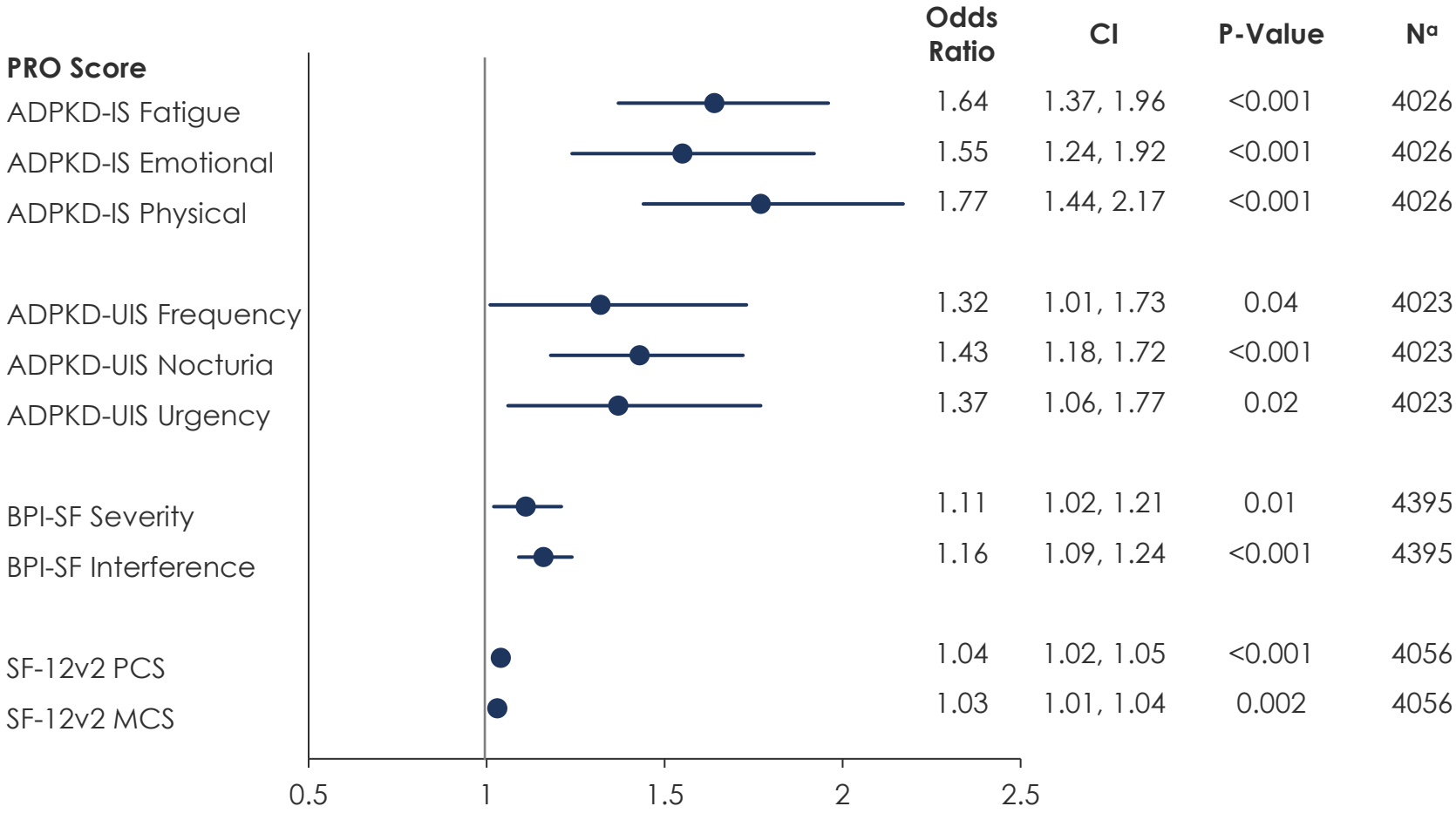
1. Oberdhan D et al. *Kidney Med*. 2024;6:100755.

Worse PRO Scores Predict Risk of Hospitalization

Worse PRO scores predicted hospitalization (0 vs. ≥1 hospitalizations) over 6–18 months of follow-up

Associations were strongest for the disease-specific ADPKD-IS

Pain (BPI-SF) and urinary symptoms (ADPKD-UIS) were also associated with hospitalization



The direction of all associations is increased odds of hospitalization with worse PRO assessment scores (i.e., higher scores on ADPKD-IS, ADPKD-UIS, and BPI-SF scales, lower scores on SF-12v2 scales).

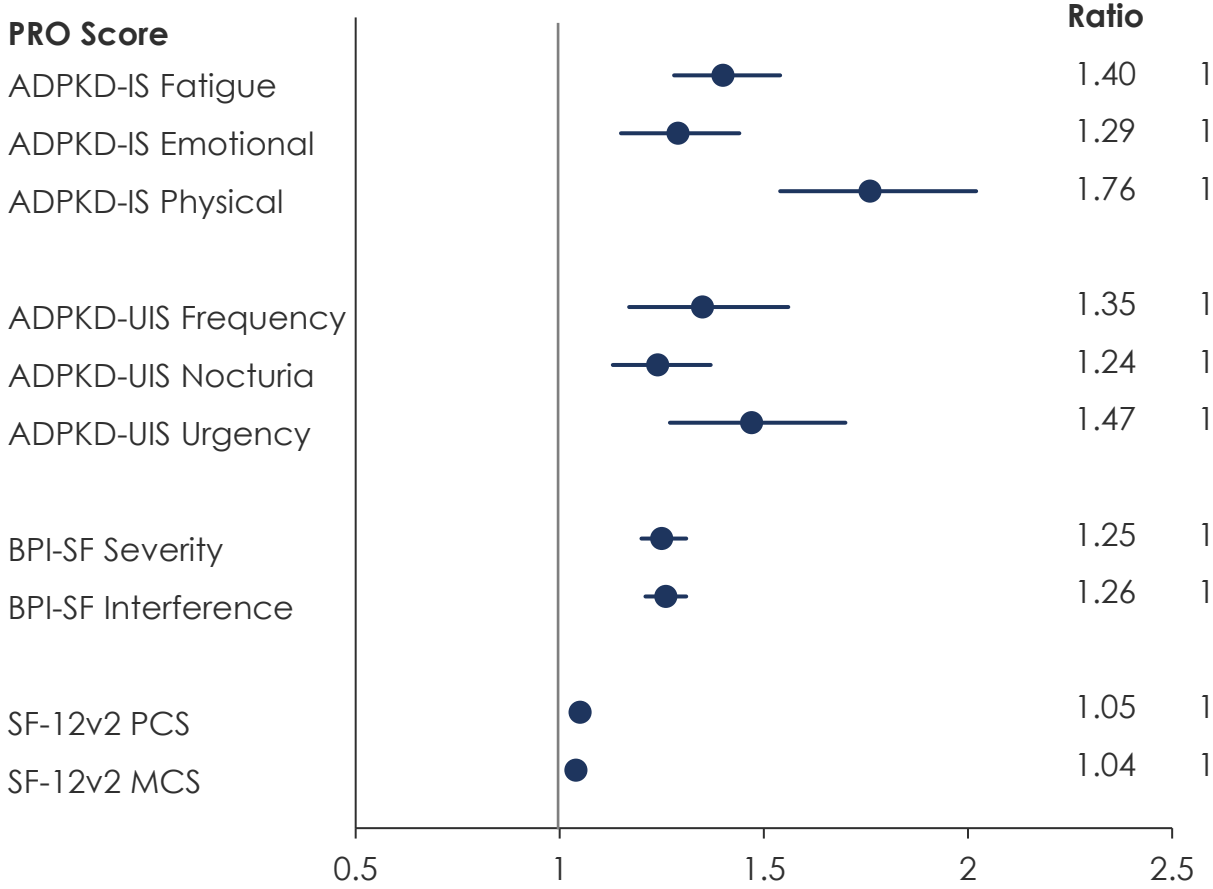
[a] The number of assessments available for the PRO score during the follow-up period in subjects with hospitalization data.

1. Oberdhan D et al. *Kidney Med*. 2024;6:100755.

Worse PRO Scores Predict Sick Days

Worse PRO scores predicted sick days (0 vs. ≥1 sick days) over 6–18 months of follow-up

The strongest associations were for the ADPKD-IS Physical subscale and the ADPKD-UIS Urgency subscale



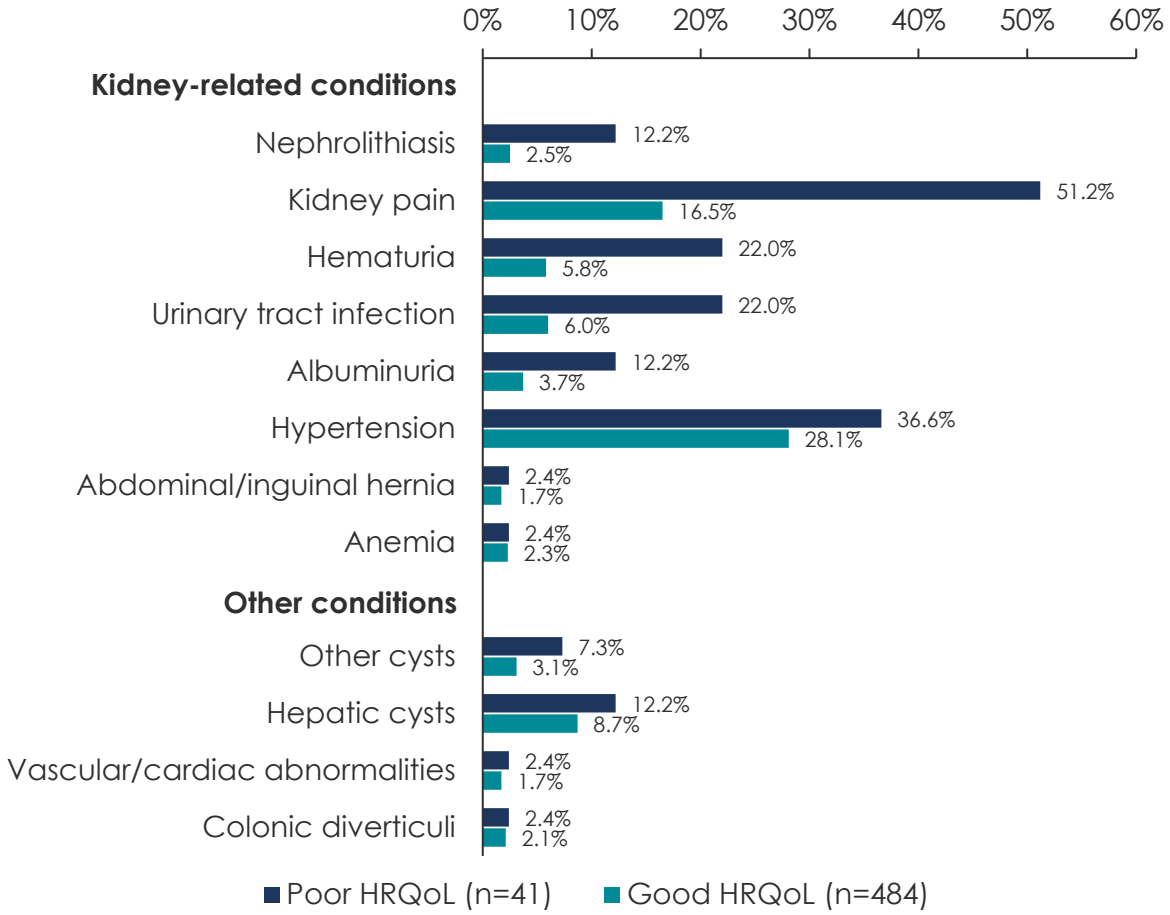
PRO Score	Odds Ratio	CI	P-Value	N[a]
ADPKD-IS Fatigue	1.40	1.28, 1.54	<0.001	2142
ADPKD-IS Emotional	1.29	1.15, 1.44	<0.001	2142
ADPKD-IS Physical	1.76	1.54, 2.02	<0.001	2142
ADPKD-UIS Frequency	1.35	1.17, 1.56	<0.001	2140
ADPKD-UIS Nocturia	1.24	1.13, 1.37	<0.001	2140
ADPKD-UIS Urgency	1.47	1.27, 1.70	<0.001	2140
BPI-SF Severity	1.25	1.20, 1.31	<0.001	4950
BPI-SF Interference	1.26	1.21, 1.31	<0.001	4950
SF-12v2 PCS	1.05	1.04, 1.06	<0.001	3643
SF-12v2 MCS	1.04	1.03, 1.04	<0.001	3643

The direction of all associations is increased odds of sick days with worse PRO assessment scores (i.e., higher scores on ADPKD-IS, ADPKD-UIS, and BPI-SF scales, lower scores on SF-12v2 scales).

[a] The number of assessments available for the PRO score during the follow-up period in subjects with sick days data.

1. Oberdhan D et al. *Kidney Med*. 2024;6:100755.

Poor vs Good Health-Related Quality of Life at Baseline Predicted ADPKD-Related Symptoms and Conditions



	Odds Ratio	95% CI	P-value
Kidney-related conditions			
Nephrolithiasis	5.5	1.82, 16.36	0.002
Kidney pain	5.3	2.75, 10.24	<0.001
Hematuria	4.6	1.99, 10.53	<0.001
Urinary tract infection	4.4	1.93, 10.11	<0.001
Albuminuria	3.6	1.26, 10.25	0.02
Hypertension	1.5	0.76, 2.87	0.3
Abdominal/inguinal hernia	1.5	0.18, 12.19	0.7
Anemia	1.1	0.14, 8.54	0.9
Other conditions			
Other cysts	2.5	0.68, 8.90	0.2
Hepatic cysts	1.5	0.54, 3.92	0.5
Vascular/cardiac abnormalities	1.5	0.18, 12.19	0.7
Colonic diverticuli	1.2	0.15, 9.49	0.9

In a subgroup analysis comparing CKD G1/G2 patients with good (n=484) vs. poor (n=41) ADPKD-specific HRQoL at baseline, those with poor HRQoL were significantly more likely to report ADPKD-related signs and symptoms during up to 18 months of follow-up

Differences were especially large for conditions related to kidney pain and urinary disorders (i.e., nephrolithiasis, hematuria, urinary tract infection)

Good HRQoL = a score ≤3 on all 3 ADPKD-IS subscales; poor HRQoL = a score >3 on at least 2 of the 3 ADPKD-IS subscales. The odds ratio compares the likelihood of the outcome occurring in the poor HRQoL group versus the good HRQoL group.

1. Oberdhan D et al. *Kidney Med*. 2024;6:100755.

Limitations

- The 18-month period of follow-up did not allow assessment of change measured by PRO instruments or significant decline in kidney function longitudinally
- Study visit intervals were 6 months apart in OVERTURE, and the recall period was only 1 month or less for the PRO assessment measures used, so events or perspectives falling outside the recall periods may have been missed
- Medical resource use and other outcomes were self-reported and therefore subject to recall bias

1. Oberdhan D et al. *Kidney Med*. 2024;6:100755.

Conclusions

- The disease-specific ADPKD-IS best captured differences in burden across baseline CKD stages
- ADPKD-specific PRO instruments predicted hospitalization and work absences, further supporting the use of disease-specific assessment instruments designed for the ADPKD population
- Patients with poor HRQoL at baseline were at significantly increased risk for experiencing pain and urinary-related disorders at follow-up

PRO assessment instruments document the burden of disease across the spectrum of ADPKD progression, and PRO scores have utility in predicting clinical and health-economic outcomes

1. Oberdhan D et al. *Kidney Med*. 2024;6:100755.

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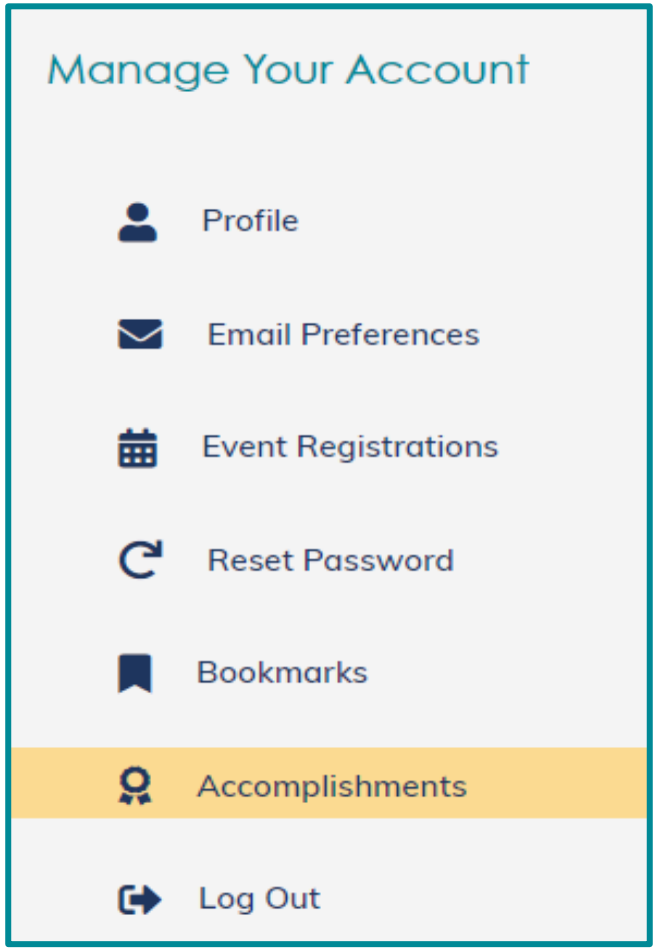

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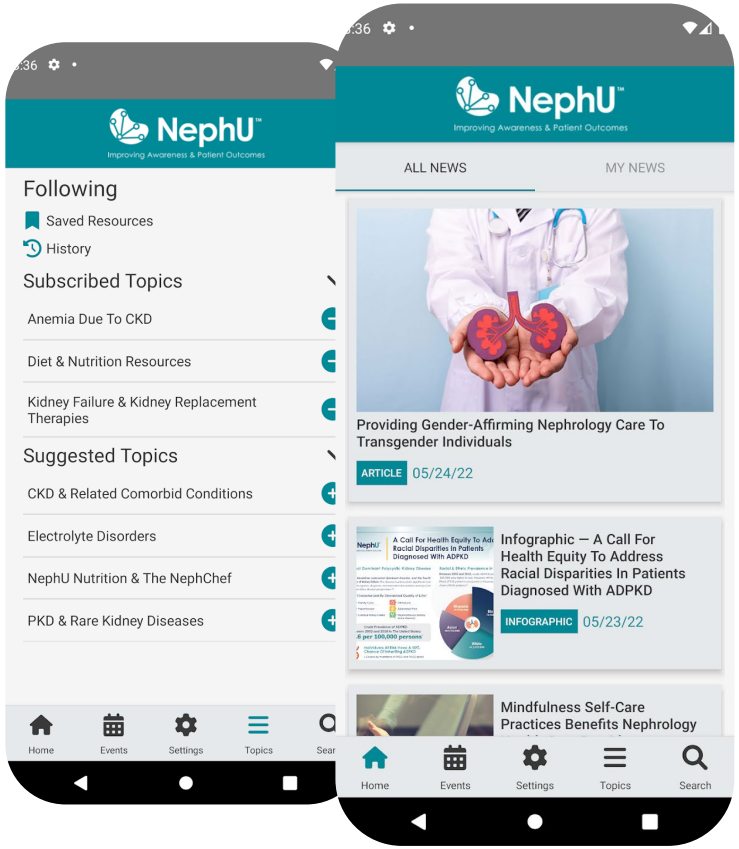

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