Two New Instruments to Measure Autosomal Dominant Polycystic Kidney Disease (ADPKD) Related Burden: ADPKD-Impact Scale (ADPKD-IS) and ADPKD-Urinary Impact Scale (ADPKD-UIS)

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BACKGROUND

- Autosomal dominant polycystic kidney disease (ADPKD) is a hereditary disease that affects approximately 1:1,000-1:4,000 diagnosed patients.[1,2]
- ADPKD is characterized by cyst development and growth, associated with increasing kidney size, potentially resulting in a progressive loss of renal function.[1] Signs and symptoms include kidney, abdominal, or flank pain; hypertension; hematuria; kidney stones and infections.[3]
- Patient-reported disease burden in ADPKD has not been sufficiently quantified. There are no sound psychometric instruments designed specifically to measure ADPKD-related burden, nor are there any general measures of health-related quality of life (HRQoL) validated for use in ADPKD patients.
- Extensive international qualitative research into disease-impact of ADPKD has led to the development of 2 instruments that capture patient-reported outcomes (PRO):
  - ADPKD-IS: the ADPKD-Impact Scale measures the impact of ADPKD on a patient's HRQoL on a 5-point response scale and has 18 items capturing 3 domains (i.e., physical, fatigue, emotional) using a 14-day recall period.
  - ADPKD-UIS: the ADPKD-Urinary Impact Scale measures the burden of urinary concerns on a 5-point response scale and has 11 items assessing 3 domains (i.e., daytime urinary urgency, daytime urinary frequency, and nocturia) using a 7-day recall period.

OBJECTIVES

Cross-sectional data from a sample of patients in the United States were analyzed to establish reliability and validity of both instruments.

METHODS

- For these analyses, preliminary baseline data from an ongoing observational study (ClinicalTrials.gov identifier NCT01430494) were used.
- US English versions of ADPKD-IS and ADPKD-UIS were administered to adults in the United States with ADPKD (CKD stages 1-5).
- Descriptive information about the items and scales were summarized using the range and distribution of responses.
- Reliability and validity of both instruments were investigated using confirmatory factor analysis (CFA) to ensure data fit with concepts patient noted as most important in qualitative research, as well as item-response theory (IRT) and classical test theory psychometric statistics at the item- and scale-level for each instrument/domain.
- Convergent validity correlations with SF-12v2 and Brief Pain Inventory – Short Form (BPI-SF) were examined.

RESULTS

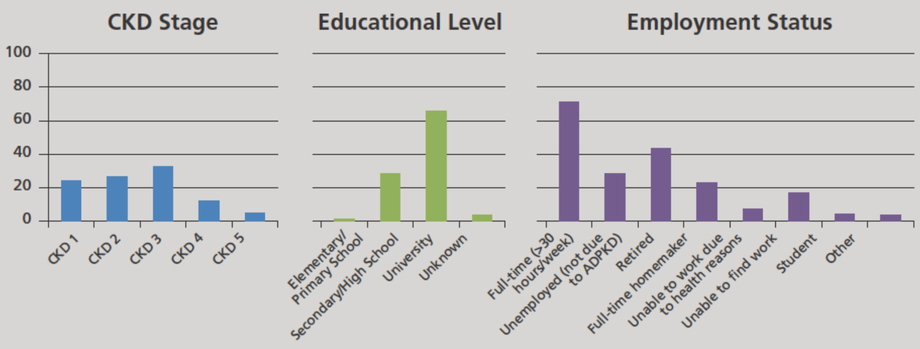
Table 1 describes the demographic characteristics of the sample of patients used to analyze the reliability and validity of the two ADPKD specific PRO instruments.

Table 1. Demographic Characteristics

Disease Group	Subjects (N = 665)
Age, years	
Mean (SD)	**49 (11.9)**
Gender, n (%)	
Male	263 (39.5)
Ethnicity, n (%)	
Caucasian	596 (89.6)
Black/African American	45 (6.8)
Other	24 (3.6)

Figure 1 describes the socio-demographic and clinical characteristics of the population.

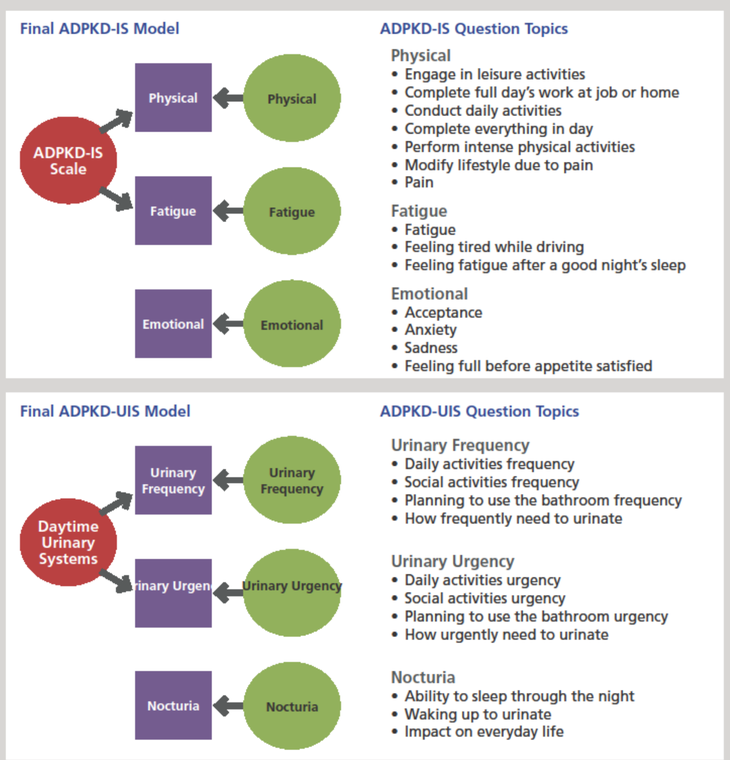
Figure 1. Clinical and Socio-demographic Characteristics



CONFIRMATORY FACTOR ANALYSES

Confirmatory factor analysis (CFA) is used to test whether measures of a construct are consistent with the model of concepts used to create the PRO instruments and to confirm the factor structure of the instruments. The final CFA models, as confirmed by these analyses, are presented in Figures 2A and 2B.

Figure 2. Final Models and Question Topics for Both Instruments



The evaluation also includes testing how well a model fits and reproduces the data. Good fit of items in both instruments with their respective domains was observed with respect to:

- Comparative fit index (CFI) = 0.970 and 0.998 for ADPKD-IS and ADPKD-UIS respectively). CFI ranges from 0 – 1 with larger values indicating better fit. CFI should be equal to or greater than 0.90 to accept the model, indicating that 90% of the co-variation in the data can be reproduced by the given model.[4]
- Non-normed fit index (NNFI) = 0.954 and 0.996 for ADPKD-IS and ADPKD-UIS respectively). NNFI ≥0.95 is suggested for a good model fit.[5]
- Root mean square error of approximation (RMSEA) = 0.051 and 0.080 for ADPKD-IS and ADPKD-UIS respectively. RMSEA ranges from 0 – 1 with smaller values indicating better fit. Target should be below 0.08, ideally even below 0.05.[6]

INTERNAL CONSISTENCY RELIABILITY

Internal consistency reliability describes the consistency of results delivered, ensuring that the various items measuring the different constructs deliver consistent scores.

It also evaluates the range of responses that is observed as well as the percentage of responses that are at the floor (lowest scoring response option = not bothered/difficult at all) versus the ceiling (highest scoring response option = extremely bothered/difficult) of the range.

- Internal consistency reliability for all domains ranged from the mid 0.80s to mid 0.90s (Table 2). Good reliability is achieved with α ≥0.8.
- Substantial floor effects were observed across all domains. This could potentially be a sign of constant impact of across disease stages.

Table 2. Internal Consistency Reliability for Both ADPKD-IS and ADPKD-UIS

Disease Group	Mean (SD)	Observed Range	% Floor	% Ceiling	Coefficient α	Average inter-item correlation r_{ii}
ADPKD-IS						
ADPKD-IS Scale Overall	24.1 (11.7)	14 – 70	17.7%	0.2%	0.95	0.61
Physical	11.2 (6.0)	7 – 35	43.8%	0.5%	0.94	0.71
Fatigue	5.8 (3.4)	3 – 15	41.2%	2.3%	0.94	0.84
Emotional	7.2 (3.5)	4 – 20	30.1%	0.3%	0.85	0.58
ADPKD-UIS						
Daytime Urinary Symptoms	11.5 (6.0)	8 – 40	54.1%	0.6%	0.97	0.78
Urgency	5.7 (3.0)	4 – 20	62.7%	0.6%	0.94	0.80
Frequency	5.9 (3.1)	4 – 20	58.4%	0.8%	0.94	0.79
Nocturia	5.6 (3.1)	3 – 15	38.5%	2.6%	0.93	0.82

ITEM RESPONSE THEORY

Item Response Theory (IRT) models the response of each patient to each item in the instrument. In this evaluation IRT provided further evidence of item and instrument efficacy for both instruments.

IRT- and item-level analyses revealed no misclassified items with their intended scales and domains or problems with skew or inappropriate heterogeneity of variance throughout the response scale (Tables 3 and 4).

Table 3. ADPKD-IS: Item-Level Psychometrics

Domain		Correlations: Physical Domain	Fatigue Domain	Emotional Domain	Physical vs. Fatigue zdiff (p)	Physical vs. Emotional zdiff (p)	Fatigue vs. Emotional zdiff (p)
Leisure activities/mild exercise	Item 1	0.87	0.66	0.58	<0.0001	<0.0001	–
Full day of work	Item 2	0.89	0.68	0.59	<0.0001	<0.0001	–
Daily activities	Item 3	0.88	0.62	0.60	<0.0001	<0.0001	–
Sense of accomplishment	Item 4	0.88	0.84	0.65	0.0251	<0.0001	–
Intense physical activities	Item 5	0.88	0.76	0.60	<0.0001	<0.0001	–
Lifestyle modification	Item 15	0.85	0.66	0.69	<0.0001	<0.0001	–
Pain	Item 16	0.81	0.62	0.62	<0.0001	<0.0001	–
Exhaustion/fatigue	Item 10	0.79	0.94	0.67	<0.0001	–	<0.0001
Tiredness	Item 17	0.75	0.94	0.63	<0.0001	–	<0.0001
Next day fatigue	Item 18	0.75	0.96	0.62	<0.0001	–	<0.0001
Acceptance of PKD	Item 6	0.58	0.51	0.81	–	<0.0001	<0.0001
Anxiety	Item 11	0.60	0.58	0.91	–	<0.0001	<0.0001
Sadness	Item 12	0.55	0.55	0.89	–	<0.0001	<0.0001
Early satiety	Item 13	0.66	0.62	0.70	–	0.1326	0.0033

Table 4. ADPKD-UIS: Item-Level Psychometrics

Domain		Correlations: Urinary Frequency	Urinary Urgency	Nocturia	Urinary Frequency vs. Urinary Urgency zdiff (p)	Urinary Frequency vs. Nocturia zdiff (p)	Urinary Urgency vs. Nocturia zdiff (p)
Daily activities	Item 1	0.92	0.83	0.64	<0.0001	<0.0001	–
Social activities	Item 3	0.92	0.88	0.60	0.0118	<0.0001	–
Planning	Item 6	0.92	0.84	0.67	<0.0001	<0.0001	–
Frequency	Item 8	0.91	0.81	0.64	<0.0001	<0.0001	–
Daily activities	Item 2	0.86	0.93	0.63	<0.0001	–	<0.0001
Social activities	Item 4	0.85	0.93	0.60	<0.0001	–	<0.0001
Planning	Item 7	0.85	0.92	0.63	<0.0001	–	<0.0001
Urgency	Item 9	0.87	0.91	0.61	<0.0001	–	<0.0001
Sleeping through the night	Item 5	0.60	0.59	0.93	–	<0.0001	<0.0001
Nighttime awakening	Item 10	0.66	0.62	0.96	–	<0.0001	<0.0001
Impact	Item 11	0.71	0.67	0.92	–	<0.0001	<0.0001

CONVERGENT VALIDITY

Convergent validity refers to the degree to which items and score correlate with each other and describes the degree of how closely related or differentiated items are. Convergent validity of the ADPKD-IS and ADPKD-UIS domains was supported by correlations with the SF-12 (both physical [PCS] and mental component [MCS] scores) and BPI-SF (pain intensity/severity and impact/interference) domains which ranged from the mid 0.40s to mid 0.60s, and the magnitude of correlations supported interpretation of physical and emotional domains on the new instruments (Tables 5 and 6).

Table 5. ADPKD-IS correlations with SF-12 and BPI (Convergent Validity)

	ADPKD-IS Domains: Physical	Fatigue	Emotional
IS Physical Domain	–	0.81	0.72
IS Fatigue Domain	0.81	–	0.68
IS Emotional Domain	0.72	0.68	–
UIS Frequency Domain	0.58	0.51	0.45
UIS Urgency Domain	0.56	0.49	0.42
UIS Nocturia Domain	0.54	0.56	0.46
SF-12 PCS	-0.68	-0.58	-0.41
SF-12 MCS	-0.48	-0.51	-0.54
BPI-SF Intensity	0.62	0.53	0.43
BPI-SF Impact	0.69	0.61	0.53

Table 6. ADPKD-UIS Correlations with SF-12 and BPI (Convergent Validity)

	ADPKD-UIS Domains: Frequency	Urgency	Nocturia
UIS Frequency Domain	–	0.91	0.70
UIS Urgency Domain	0.91	–	0.67
UIS Nocturia Domain	0.70	0.67	–
SF-12 PCS	-0.39	-0.39	-0.39
SF-12 MCS	-0.38	-0.37	-0.32
BPI-SF Intensity	0.44	0.42	0.38
BPI-SF Impact	0.45	0.43	0.42

CONCLUSIONS

- For ADPKD-IS and ADPKD-UIS high reliability and validity has been confirmed in a general ADPKD population based on cross-sectional data.
- ADPKD-IS provides patient-endorsed and psychometrically strong measures of HRQoL for physical impact, fatigue, and emotional impact.
- ADPKD-UIS provides quantitatively strong measures for urinary symptom impact of daytime urinary urgency and frequency, as well as nocturia.
- Disease burden of ADPKD can be established based on patients' responses on ADPKD-IS and ADPKD-UIS
- Future research is needed to evaluate stability of the instruments over time and their ability to detect true change in symptoms within an individual.

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