Kidney360

Depressive Symptoms in Adults with Autosomal Dominant Polycystic Kidney Disease

--Manuscript Draft--

Manuscript Number:	K360-2024-000708R2
Full Title:	Depressive Symptoms in Adults with Autosomal Dominant Polycystic Kidney Disease
Short Title:	Depression in ADPKD
Article Type:	Original Research
Section/Category:	Cystic Kidney Disease
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Manuscript Classifications:	15: ADPKD; 113: Depression; 147: Epidemiology and Outcomes
Abstract:	Background: Individuals with autosomal dominant polycystic kidney disease (ADPKD) face mental health challenges linked to disease progression and its heritable nature. Prior studies reported mixed associations between depressive symptoms and ADPKD severity and progression. Here, we assessed depressive symptoms and disease severity over three years in ADPKD patients without end-stage kidney disease. Methods: 283 adults with ADPKD were enrolled from April 2013 to June 2023 in a single-center prospective observational study. ADPKD severity was assessed with estimated GFR and htTKV. Depressive symptoms were assessed with the Beck Depression Inventory-II (BDI-II). Depressive symptom burden was compared to previously reported cohorts of patients with other chronic, progressive diseases. The relationship of ADPKD severity and ADPKD-related pain with depressive symptoms was estimated using multiple linear regression, adjusting for potential confounders. Results: Among 283 adult ADPKD patients(mean age 45; 81% White; 61% female), 15.5% reported moderate depressive symptoms (BDI-II ≥ 11). Depressive symptom prevalence (all ages) was lower than in primary care samples. For the older individuals in our cohort, depressive symptom prevalence was similar to those in healthy older adults. ADPKD severity [eGFR: 73±33 ml/min/1.73m2, htTKV: 1104±80 cc/meter] was unrelated to depressive symptoms, although frequent pain (abdominal, back, and/or flank pain experienced at least daily) strongly associated with higher depressive symptom levels. Baseline depressive symptoms did not predict kidney function (eGFR, htTKV) at 36 months, adjusting for baseline measures and confounders. Conclusions: Our results reveal a relatively low prevalence of clinically significant depressive symptoms in a large sample of adult patients with ADPKD who were not undergoing renal replacement therapy. However, frequent pain was associated with a greater degree of depressive symptoms, underscoring the importance of adequate pain control. While these findings highlight the resilience of patients with ADPKD, routine mental health screening is recommended, and validated pain assessment tools may provide useful resources to quantify and manage pain in ADPKD.
Funding Information:	National Institute of Diabetes and Digestive and Kidney Diseases (U54DK126114) — Dr. Terry Watnick

	National Institute of Diabetes and Digestive and Kidney Diseases (P30DK090868)	Dr. Terry Watnick
Additional Information:		
Question	**Response**	
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Kidney360 Publish Ahead of Print
DOI: 10.34067/KID.0000000683

Depressive Symptoms in Adults with Autosomal Dominant Polycystic Kidney Disease

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Abstract

Background: Individuals with autosomal dominant polycystic kidney disease (ADPKD) face mental health challenges linked to disease progression and its heritable nature. Prior studies reported mixed associations between depressive symptoms and ADPKD severity and progression. Here, we assessed depressive symptoms and disease severity over three years in ADPKD patients without end-stage kidney disease.

Methods: 283 adults with ADPKD were enrolled from April 2013 to June 2023 in a single-center prospective observational study. ADPKD severity was assessed with estimated GFR and htTKV. Depressive symptoms were assessed with the Beck Depression Inventory-II (BDI-II). Depressive symptom burden was compared to previously reported cohorts of patients with other chronic, progressive diseases. The relationship of ADPKD severity and ADPKD-related pain with depressive symptoms was estimated using multiple linear regression, adjusting for potential confounders.

Results: Among 283 adult ADPKD patients(mean age 45; 81% White; 61% female), 15.5% reported moderate depressive symptoms (BDI-II ≥ 11). Depressive symptom prevalence (all ages) was lower than in primary care samples. For the older individuals in our cohort, depressive symptom prevalence was similar to those in healthy older adults. ADPKD severity [eGFR: 73±33 ml/min/1.73m^2, htTKV: 1104±80 cc/meter] was unrelated to depressive symptoms, although frequent pain (abdominal, back, and/or flank pain experienced at least daily) strongly associated with higher depressive symptom levels. Baseline depressive symptoms did not predict kidney function (eGFR, htTKV) at 36 months, adjusting for baseline measures and confounders.

Conclusions: Our results reveal a relatively low prevalence of clinically significant depressive symptoms in a large sample of adult patients with ADPKD who were not undergoing renal replacement therapy. However, frequent pain was associated with a greater degree of depressive symptoms, underscoring the importance of adequate pain control. While these findings highlight the resilience of patients with ADPKD, routine mental health screening is recommended, and validated pain assessment tools may provide useful resources to quantify and manage pain in ADPKD.

Supplemental Digital Content: http://links.lww.com/KN9/A827

Introduction

Individuals with autosomal dominant polycystic kidney disease (ADPKD) face unique challenges to their mental health and health-related quality of life (HRQoL). Given the inherited nature of the disease, affected children and young adults may observe their older family members develop disease complications and progress to end-stage kidney disease (ESKD). The psychological burden of watching a family member die of complications from ADPKD is also striking and should not be understated. Furthermore, interpersonal relationships within families can be influenced by resentment and "genetic guilt" from passing the disease to their children.[1]

There has been limited investigation of depressive symptoms and psychological health-related quality of life in patients with ADPKD. Prior studies have found no differences in general HRQoL between pre-dialysis ADPKD patients and the general U.S. population.[2] However, among individuals with ADPKD not requiring renal replacement therapy, some investigations have found an association between declining eGFR and poorer quality of life associated with physical function.[3] In that prior study, depression was not related to ADPKD severity. Other studies have found a relationship between symptoms relating to abdominal fullness and lower eGFR only in female patients with ADPKD.[4] The relationship of depressive symptoms with PKD disease progression is also uncertain. Therefore, further investigation is required to gain a clearer understanding of the nature of depressive symptoms and polycystic kidney disease (PKD) progression in individuals with ADPKD.

Although the relationship between depressive symptoms and PKD progression remains poorly defined, studies in broader chronic kidney disease (CKD) populations provide relevant insights. In large pre-dialysis such as CRIC and AASK, no significant associations between depressive symptoms and eGFR have been found (CRIC[5], AASK[6] studies). In contrast, a cohort of male veterans with CKD demonstrated a strong link between depression and progression to ESRD.[7] Similarly, the Cardiovascular Health Study reported a higher baseline prevalence of CKD among depressed individuals, though no association was found between depression and incident CKD.[8] Notably, these studies excluded PKD patients or did not report on results among patients with PKD specifically, leaving gaps in our understanding of how these findings may apply to this population.

In this prospective observational study, we build on these findings by first comparing the severity of depressive symptoms between adults with ADPKD to the general population and to previously reported cohorts of patients with other chronic, progressive diseases. We used the Beck Depression Inventory (BDI-II), a well-validated self-report that assess depressive symptoms. We further investigated the association of depressive symptoms with ADPKD severity and ADPKD disease progression over 3 years, accounting for other disease progression risk factors.

Methods

Study Participants

Adults with ADPKD, as defined by the Pei-Ravine criteria, were enrolled in an observational cohort study at the Baltimore Polycystic Kidney Disease Center at the University of Maryland School of Medicine from April 2013 to June 2023.[9, 10] Individuals who were eighteen years or older were included. Individuals with a history of kidney transplant, nephrectomy, diabetes requiring insulin or with suspected diabetic nephropathy, or ESKD (eGFR < 15 mL / min / 1.73m^2 or renal replacement therapy) were excluded. The study was approved by the University of Maryland, Baltimore Institutional Review Board (protocol HP-00054815) and written informed consent was obtained from participants. This study was conducted in accordance with the declaration of Helsinki.

Study Procedures

Anthropometric and demographic information (age, sex, gender, ethnicity, education) were self-reported, while height and weight were directly measured. A detailed personal medical and family medical history was obtained by interview. Serum creatinine was measured in fasting serum specimens using an IDMS-traceable assay, and Glomerular Filtration Rate (GFR) was estimated using the "race-neutral" CKD-Epi equation.[11] Among participants without a contraindication for MRI, abdominal imaging was performed on a 3.0 Tesla Tim Trio system scanner. Total kidney volume (TKV) was estimated by an experienced radiologist blinded to clinical patient characteristics, as described previously, and indexed to height (height adjusted total kidney volume [htTKV]).[10] ADPKD severity was assessed using two measures: eGFR and

htTKV. Repeat assessments, including BDI-II, eGFR, and htTKV, were conducted at 36 months in participants without interim ESKD.

Assessment of Pain

At each visit, patients were asked about the presence and frequency of pain they experienced in the flank, abdomen, and back (**Supplemental Material 1**).

Classification of Concomitant Medications

Medication and supplement use were assessed at baseline and 36 months. Antidepressant medications were identified as those prescribed with an indication for depression. The classification of these medications was subsequently reviewed to ensure consistency with the recorded indication. Pain medications were similarly assessed. Full lists are provided in **Supplemental Materials 2 and 3.**

Classification of Comorbid medical diagnoses

Comorbid conditions potentially influencing depression were categorized based on self-reports. Cardiovascular disease included coronary artery disease, congestive heart failure, valvular heart disease, and arrythmia. Several comorbidities were grouped into broader categories for descriptive analysis. Arthritis encompassed osteoarthritis and rheumatoid arthritis, while asthma included allergic and exercise-induced subtypes. The cancer category covered malignancies such as breast, bladder, colon, and endometrial cancer, melanoma, nasopharyngeal carcinoma, dysplastic nevus, and Barrett's esophagus. Diabetes was classified as type 1 (T1DM), type 2 (T2DM), or gestational. Migraine included regular, basilar, hemiplegic, and ocular subtypes. For sleep apnea, only obstructive sleep apnea was considered, without further subcategories.

Comorbidities were self-reported and not exhaustive for each category. Asthma, arthritis, and diabetes were included based on prior World Health Surveys exploring the link between depression and chronic diseases.[12]

Ascertainment of Depressive Symptoms

Depressive symptom burden was assessed using the Beck Depression Inventory-II (BDI-II) at baseline and 36-months.[13] The BDI-II is a 21-item questionnaire scoring symptoms on a 0–3 scale, with a total score range of 0–63. In our study, clinically significant depressive symptoms were defined as a BDI-II score ≥11, based on prior CKD studies.[14] While the BDI-II correlates with clinical interviews for diagnosing depression, it serves as a screening tool and not a definitive diagnostic method.[15]

Comparison with Other Patient Samples

To interpret the severity of depressive symptoms of ADPKD patients in the context of adult patients with other chronic progressive diseases (including genetically determined diseases), we compared their BDI-II scores to those from cohorts with T1DM, chronic Hepatitis C, chronic pain, pre-manifest carriers of Huntington's Disease (HD), and amyotrophic lateral sclerosis (ALS).[16-20] We also compared a subset of older ADPKD patients (age ≥ 55) to healthy older adults, older patients with chronic kidney disease (CKD), and African American patients with CKD.[21-23]

Statistical Analyses

Baseline characteristics of the study sample were described with frequencies and medians (interquartile range). Chi-squared tests were used for categorical variables, with Fisher's exact test for small samples. Multiple linear regression models assessed the relationship between ADPKD severity and depressive symptoms, using eGFR and ln-transformed htTKV as independent variables and the BDI-II score as the dependent variable. A cube root transformation was applied to the total BDI score to adjust for strong positive skew and to ensure homoscedasticity. Adjustment covariates were selected a priori based on factors plausibly causally related to both ADPKD severity and depressive symptoms: age, gender, race, educational achievement, and the presence of daily pain in at least one location (abdomen, back, flank). Standardized regression coefficients are shown, to assist with interpretation of the magnitude of estimated associations.

The relationship between depressive symptoms and ADPKD progression within individuals over 36 months was assessed with multiple linear regression. Baseline BDI-II, baseline eGFR or htTKV and the aforementioned adjustment covariates were included as predictor variables, with eGFR or htTKV at 36 months as the dependent variable. Wilcoxon rank-sum tests compared depressive symptoms between ADPKD and chronic disease patients, due to BDI skew. Paired t-tests evaluated changes in BDI-II, eGFR, and htTKV within individuals over 36 months.

Results

Study Population

A total of 283 ADPKD participants completed baseline visits by April 2024. Participant characteristics by BDI-II category are in **Table 1**. The mean age was 45 years, 61% were female, <0.1% identified as American Indian/Alaskan Native, 7% as Asian, 12% as Black/African American, and 81% as White. Eighty-five percent had post-secondary education, and 222 reported a family history of ADPKD. Of the N=283 with baseline visits, 261 had baseline htTKV measured by MRI.

Comorbid medical diagnoses

Overall, 35 (12%) participants reported a history of cardiovascular disease, 4 (1%) of arthritis, 43 (15%) of asthma, 10 (4%) of cancer, 6 (2%) of diabetes, 23 (8%) of migraines, and 6 (2%) of sleep apnea (**Table 1**). None of these comorbidities had showed a significant association with high degree of depressive symptoms. At baseline, 29 patients (10%) were on pain medications, increasing to 16% (18 patients of those with follow-up) at 36 months (see **Supplemental Material 3** for details).

Depressive symptoms and depression-related medications

Mean(SD) baseline BDI-II score was 5.1(6.0). Forty-four (15.5%) had a baseline score ≥ 11 and 26 (9%) had a baseline score ≥ 14. Forty-two (15%) were taking one or more medications with anti-depressant indication at baseline visits. Of these participants, sixteen (6%) had baseline BDI scores ≥ 11.

Comparison with other patient samples

Participants in this cohort (all ages) had significantly lower levels ($p < 0.05$) of depressive symptoms compared to previously published samples of primary care patients, Type 1 Diabetes Mellitus patients, chronic Hepatitis C patients, and chronic pain patients (**Figure 1**).[16-18,21] No significant differences were observed between the level of depressive symptoms in this ADPKD cohort and pre-manifest carriers of Huntington's disease.[19]

Given the association of age with depressive symptoms, and the previous examinations of depressive symptom burden in other patient populations who were older, we examined a subset of the ADPKD participants aged ≥ 55. This subset had significantly lower depressive symptoms ($p < 0.01$) (i.e., were less depressed) compared to African-American patients with hypertensive nephropathy (AASK trial) and patients with ALS (**Figure 1**).[20,23] However, older ADPKD patients exhibited comparable levels of depressive symptoms compared to a sample of healthy older adults and a cohort of older, majority-African American adults with non-PKD CKD stage G3b-4 participating in an exercise interventional trial.[21,22]

Depressive symptoms (BDI-II) and ADPKD severity

In unadjusted models, neither eGFR nor htTKV were significantly associated with depressive symptoms. After adjustment for education, gender, age, race, and ethnicity, ADPKD severity remained non-significant. Lower levels of education were significantly associated with higher depressive symptoms ($p < 0.05$). Unadjusted and adjusted models are shown in **Tables 2** (eGFR) and **3** (htTKV). Similar results were observed using serum creatinine instead of eGFR (results not shown).

Since pain has been known to affect mental health, a history of frequent pain was included as an additional covariate to the models. A history of frequent pain was defined as flank pain, back pain, and / or abdominal pain that was experienced at least daily. A history of frequent pain (*N=65, 23%*) was significantly associated with a greater severity of depressive symptoms with moderately large effects ($\hat{\beta} = 0.54, 0.56$), but htTKV and eGFR did not have significant associations with depressive symptoms in these models (Tables 2 and 3). The impact of education on depressive symptoms was attenuated in this model and did not remain statistically significant. Exploratory analyses incorporating antidepressant use, family history of ESRD, and

cardiovascular disease confirmed this association ($\hat{\beta} = 0.36, 0.38$). Baseline antidepressant use was also significantly associated with depressive symptom severity, while family history of ESRD was only significant in the eGFR model (Supplemental Materials 4 and 5). Further adjustment for family history of ADPKD did not materially change the results. A history of pain—defined as experiencing abdominal, flank, or back pain at least once—remained significantly associated with greater degree of depressive symptoms ($p < 0.05$) after adjusting for the same demographic covariates.

Family history and depressive symptoms

Participants without a family history of ESKD were more likely to have a BDI-II ≥ 11 ($p < 0.05$, **Table 1**). However, after adjustment for education, gender, age, race, and ethnicity, there was no association of family history of ESKD with depressive symptoms (BDI-II score) ($\hat{\beta} = -0.21$, $p > 0.05$).

PKD progression within individuals over time

All participants were contacted to assess their interest in completing follow-up visits. One hundred nineteen participants (42%) had 36 month follow up visits. Of the 164 participants who did not complete the follow-up, 86 (52%) had not yet reached their 36-month follow-up period at the time of data analysis. Additional reasons for non-participation are summarized in **Supplemental Material 6.** Participants who completed the 36-month follow-up MRI were modestly older and more likely to have a history of kidney stones than those who did not follow up (**Supplemental Material 7**). No significant differences were observed between the groups in terms of gender, race, ethnicity, education, BMI, eGFR, htTKV, BDI-II score, or Mayo Class (**Supplemental Material 7**, **Supplemental Material 8**). Additionally, no significant differences between the two groups were noted in terms of hypertension, gross hematuria, urinary tract infection, and coronary artery disease.

Of these with available 36 month follow-up, N=95 (81%) of participants maintained minimal levels (BDI-II < 11) of depressive symptoms at baseline and 36-month period. Thirteen (12%) of participants maintained moderate levels (BDI-II ≥ 11) of depressive symptoms, N=4 (3%) changed from minimal to moderate, and N=5 (4%) changed from moderate to minimal (**Figure 2**). Twenty-one (17%) of patients who completed follow-up visits were taking one or more

medications with an indication for depression at the 36-month follow up visit. Of these patients, N=4 (19%) had 36-month BDI scores ≥ 11. On average, eGFR declined by an average of 7.8 mL/min /1.73m^2 and htTKV increased by 116.8 mL/m within individuals over approximately 36 months (**Figure 3**).

One hundred and five participants received a follow up MRI at 36 months. Participants who received an MRI at 36 months were less likely to have a history of kidney stones compared to those who did not receive a follow-up scan ($p < 0.01$); no other differences between those with and without MRI at 36 months were noted (e.g. hypertension, gross hematuria, urinary tract infection, hernia, coronary artery disease). In adjusted models, baseline depressive symptoms were not associated with kidney function or htTKV at 36 months after accounting for baseline eGFR and htTKV and other potential confounders (**Table 4, Table 5**).

Discussion

Among 283 adult ADPKD patients without ESKD, 15.5% had moderate depressive symptoms (BDI-II ≥ 11). Notably, this prevalence of depressive symptoms was lower than that observed in a sample of primary care patients.[24] Among older ADPKD participants, depressive symptom prevalence was similar to healthy older adults.[21] ADPKD severity (eGFR and htTKV) was not associated with depressive symptoms, although frequent pain (abdominal, back, or flank) was strongly associated with a higher degree of depressive symptoms.

The lower prevalence of moderate depressive symptoms is unexpected, given the psychosocial effects of chronic disease and genetic guilt.[1] One possible explanation is that most of the patients in our cohort have earlier stage ADPKD (57.2% with baseline eGFR ≥ 60 ml/min/1.73m^2; 55.6% with baseline htTKV < 1000 mL/m). Depressive symptoms may increase in later stages, consistent with studies showing pre-dialysis ADPKD patients report a quality of life similar to the general population.[2] The patients in the Rizk et al. study had similar kidney size to the patients in our cohort (mean kidney volume: 936.7 ± 883.3 mL), supporting the notion that the relationship between depressive symptoms and kidney function may only become evident in later stages of disease. Of note, prior studies in the general ESKD population (comprising a range of nephropathies) have indicated high prevalence of depressive symptoms, with associations with greater mortality risk.[25] Additionally, changes in depressive symptoms may manifest over

periods longer than three years in patients with ADPKD, as our observations indicate that disease progression did not exhibit significant changes within the three-year timeframe. Lastly, as 42 participants (15%) were on antidepressants at baseline, it is possible that their depression was controlled, thus reducing the observed prevalence of depressive symptoms in this patient cohort.

While our findings suggest that depressive symptoms in our ADPKD cohort are not significantly higher than those observed in the general population, this does not imply that depressive symptoms in ADPKD patients are inherently low, nor should they be ignored by healthcare providers. Depressive symptoms are common enough in the general population that the U.S. Preventive Services Task Force recommends universal depression screening. Consensus treatment guidelines for all chronic kidney disease also support assessment of depressive symptoms.[26] Given these recommendations, routine screening in ADPKD patients remains important.

In addition, research highlights the significant impact of prescriber effects on treatment outcomes. For example, McKay et al. (2006) found that one third of psychiatrists achieved better outcomes with placebo compared to another third using antidepressants, suggesting that the clinician-patient relationship itself can influence the effectiveness of treatment. McKay's conclusion - that doctors are "not just provider[s] of treatment, but also a means of treatment" – underscores the importance of how the therapeutic alliance can shape outcomes.[27] Nephrologists, who have frequent long-term interactions with ADPKD patients, are in a unique position to leverage these relationships as a means of improving both physical and mental health outcomes.

Frequent pain was significantly associated with depressive symptoms. The effect size ($\hat{\beta} = 0.54, 0.56$) was large, although we cannot infer the directionality of this association. While specific definitions of chronic pain vary widely, it is known that pain has a complex interplay with depression, with both conditions sharing overlapping neurobiological changes.[20] Prior reports suggest interoceptive dysfunction – problems interpreting bodily signals – may affect both somatic and affective disturbances in depression.[21] In the HALT-PKD trial, pain was associated with greater kidney size only when htTKV exceeded 1,000 mL/m.[4] However, our findings show pain impacts depressive symptoms even in earlier disease. In our cohort, it was

pain, rather than kidney size or function, that was strongly associated with a greater degree of depressive symptoms. Our findings agree with Simms et al., who found that depression was significantly associated with bodily pain.[3] Ongoing discussions highlight the importance of validated patient-reported pain assessment. [30, 31]

In our exploratory analysis, baseline antidepressant use was significantly associated with a greater degree of depressive symptom severity. Individuals with more severe symptoms are more likely to receive treatment, yet antidepressants may alleviate depressive symptoms. However, given that these data were collected at a single time point, it remains challenging to disentangle the directionality of these associations.

Education appears to influence depressive symptoms in ADPKD, with patients reporting moderate symptoms (BDI-II ≥ 11) having lower education levels than those with minimal symptoms (BDI-II < 11). Lower education was also linked to a small, but significant decline in kidney function (increased htTKV, decreased eGFR). These findings align with known protective effects of higher education against depression in patients with chronic disease, ADPKD patients, and the general population.[32, 33, 2] Given that 83% of our cohort completed university, this protective effect be more pronounced in our specialized nephrology care population.

About 83% of our cohort reported a family history of ADPKD, though the true percentage may be higher due to incomplete family histories. Previous studies noted that parents with ADPKD often experience guilt about passing on the disease.[3] Although we did not use a validated separate anxiety symptoms instrument, patients have anecdotally reported significant health-related anxiety. A post hoc analysis accounting for demographics found no link between depressive symptoms and a family history of severe PKD outcomes. This suggests that the significant difference in family history of ESKD observed between the BDI-II ≥ 11 and BDI-II < 11 groups is attributable to patient-level demographic differences. One limitation of our study is the lack of psychosocial risk data, such as those measured by the Genetic Psychosocial Risk Instrument for ADPKD. Future studies using this tool could provide better explore the relationships between depressive symptoms, psychological burden, and kidney function.

Our single-center study with a three-year follow-up is limited by a predominantly White, highly educated, female cohort. Patients with more severe depressive symptoms may have been less likely to participate, limiting generalizability. Future studies should include more diverse, representative populations.

Furthermore, while our dataset includes information on concomitant medications used for pain, specific data on the efficacy of these treatments were not collected. The study's design did not target the evaluation of pain management effectiveness. As a result, we are unable to determine whether more effective pain management influences the presence or severity of depressive symptoms. Nonetheless, the observed associations between frequent or daily pain and heightened depressive symptoms underscore the need for future research to explore optimized pain management strategies in ADPKD patients.

In conclusion, our study found a low prevalence of depressive symptoms in a large sample of adult patients with ADPKD without ESKD. This relationship persisted independently of disease severity as measured by eGFR and htTKV These findings may be attributed to the relatively preserved kidney function in our population, as well as their high level of education, which is often associated with a higher quality of life and greater health literacy. Frequent pain was found to have a significant association with depressive symptoms, underscoring the need for adequate pain control in this population. These findings highlight the resilience of patients with ADPKD in coping with both the physical and psychological consequences of their disease, while also emphasizing the critical role of the clinician-patient relationship. Nephrologists, with their long-term involvement in patient care, are uniquely positioned to improve both the physical and mental health outcomes in this population.

Abbreviations

ADPKD	Autosomal Dominant Polycystic Kidney Disease
ALS	Amyotrophic Lateral Sclerosis
BDI-II	Beck Depression Inventory-II
CKD	Chronic Kidney Disease
ESKD	End Stage Kidney Disease
GFR	Glomerular Filtration Rate
HD	Huntington's Disease
HRQoL	Health Related Quality of Life
PKD	Polycystic Kidney Disease
T1DM	Type 1 Diabetes Mellitus
T2DM	Type 2 Diabetes Mellitus
TKV	Total Kidney Volume

Acknowledgements

The authors gratefully acknowledge the tireless efforts of research coordinator Charalett Diggs, RN, and the contributions and altruism of our research participants.

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Table 1: Demographics

	Overall (N=283)	BDI-II < 11 (N=239)	BDI-II ≥ 11 (N=44)	P-value
Gender				
Female	173 (61.1%)	145 (60.7%)	28 (63.6%)	0.84
Male	110 (38.9%)	94 (39.3%)	16 (36.4%)	
Age *(years)*				
Mean (SD)	45 (14)	45 (13)	47 (14)	0.40
Race				
American Indian or Alaskan Native	1 (< 0.1%)	1 (0.4%)	0 (0%)	0.92
Asian	19 (6.7%)	17 (7.1%)	2 (4.5%)	
Black or African American	35 (12.4%)	30 (12.6%)	5 (11.4%)	
White	228 (80.6%)	191 (79.9%)	37 (84.1%)	
Ethnicity				
Hispanic or Latinx	17 (6.0%)	14 (5.9%)	3 (6.8%)	0.73
Not Hispanic or Latinx	266 (94.0%)	225 (94.1%)	41 (93.2%)	
Highest Education				
University	236 (83.4%)	207 (86.6%)	29 (65.9%)	**<0.001***
Up to High School	42 (14.8%)	27 (11.3%)	15 (34.1%)	
Missing	5 (1.8%)	5 (2.1%)	0 (0%)	
BMI *(per kg/m^2)*				
Mean (SD)	27.1 (5.1)	27.0 (5.0)	27.8 (5.6)	0.39
Avg SBP				
Mean (SD)	126 (15)	126 (15)	126 (14)	0.86
Avg DBP				
Mean (SD)	78 (11)	77 (11)	80 (11)	0.10
eGFR *(ml/min/1.73m^2)*				
Mean (SD)	73 (33)	73 (33)	69 (34)	0.47
htTKV *(mL/m)*				
Mean (SD)	1104 (805)	1100 (831)	1140 (650)	0.69
Missing	22 (7.8%)	18 (7.5%)	4 (9.1%)	
Mayo Class				
1A	14 (5.0%)	13 (5.4%)	1 (2.3%)	0.32
1B	47 (16.6%)	43 (18.0%)	4 (9.1%)	

	Overall (N=283)	BDI-II < 11 (N=239)	BDI-II ≥ 11 (N=44)	P-value
1C	89 (31.4%)	71 (29.7%)	18 (40.9%)	
1D	59 (20.8%)	48 (20.1%)	11 (25.0%)	
1E	52 (18.3%)	46 (19.2%)	6 (13.6%)	
Missing	22 (7.8%)	18 (7.5%)	4 (9.1%)	
Pain Med Usage				
Yes	29 (10%)	23 (10%)	6 (14%)	0.59
Antidepressant Usage				
Yes	41 (14%)	25 (11%)	16 (34%)	**<0.001***
Frequent Pain				
Yes	75 (27%)	43 (18%)	22 (50%)	**<0.001***
Family Hx of ESRD				
Yes	134 (47%)	120 (50%)	14 (32%)	**<0.05***
Hx of cardiovascular disease				
Yes	35 (12%)	27 (11%)	8 (18%)	0.31
Hx of arthritis				
Yes	4 (1%)	3 (1%)	1 (2%)	0.49
Hx of asthma				
Yes	43 (15%)	38 (16%)	5 (11%)	0.59
Hx of cancer				
Yes	10 (4%)	9 (4%)	1 (2%)	1
Hx of diabetes				
Yes	6 (2%)	4 (2%)	2(5%)	0.24
Hx of migraines				
Yes	23 (8%)	20 (8%)	3 (7%)	1
Hx of sleep apnea				
Yes	6 (2%)	4 (2%)	2 (5%)	0.24

Table 2: Association between eGFR and Depressive Symptoms (N = 278)

	Unadjusted					*Adjusted*					*Adjusted + Frequent Pain*				
Predictors	***Beta***	***CI***	***Std. Beta***	***Std. CI***	***p***	***Beta***	***CI***	***Std. Beta***	***Std. CI***	***p***	***Beta***	***CI***	***Std. Beta***	***Std. CI***	***p***
Intercept	1.49	1.26 – 1.72	0.00	0.12 – 0.12	<0.001	1.12	0.29 – 1.95	0.00	0.17 – 0.17	0.01	1.04	0.23 – 1.84	0.12	0.29 – 0.06	0.01
eGFR *(ml/min/1.73m^2)*	0.00	0.00 – 0.00	-0.06	0.18 – 0.05	0.30	0.00	0.00 – 0.00	0.02	0.17 – 0.14	0.84	0.00	0.00 – 0.00	0.00	0.15 – 0.15	0.97
Education: Up to High School						0.34	0.07 – 0.61	0.42	0.09 – 0.76	**0.01***	0.24	0.02 – 0.51	0.30	0.03 – 0.64	0.07
Gender: Male						0.05	0.25 – 0.14	0.06	0.31 – 0.18	0.61	0.06	0.25 – 0.13	0.08	0.31 – 0.16	0.53
Age *(years)*						0.00	0.01 – 0.01	0.05	0.10 – 0.21	0.51	0.00	0.01 – 0.01	0.04	0.11 – 0.19	0.57
Race															
American Indian or Alaskan Native						0.01	1.60 – 1.58	0.02	2.00 – 1.97	0.99	0.05	1.50 – 1.60	0.06	1.87 – 2.00	0.95
Asian						0.04	0.41 – 0.34	0.05	0.52 – 0.43	0.85	0.03	0.40 – 0.33	0.04	0.50 – 0.42	0.86
Black or African American						0.22	0.51 – 0.08	0.27	0.63 – 0.09	0.15	0.16	0.45 – 0.12	0.21	0.56 – 0.15	0.26
Hispanic or Latinx						0.03	0.43 – 0.37	0.03	0.53 – 0.46	0.89	0.00	0.39 – 0.39	0.00	0.48 – 0.48	1.00
BMI *(per kg/m^2)*						0.01	0.01 – 0.02	0.04	0.09 – 0.16	0.55	0.01	0.01 – 0.02	0.04	0.08 – 0.15	0.57
Frequent Pain: Yes											0.45	0.23 – 0.67	0.56	0.28 – 0.84	**<0.001***

Standardized estimates are shown in the Std. Beta and Std. CI columns. Reference groups were those that had the largest number of participants (Education: University; Gender: Female; Race: White).

Table 3: Association between htTKV and Depressive Symptoms (N=256)

	Unadjusted					*Adjusted*					*Adjusted + Frequent Pain*				
Predictors	***Beta***	***CI***	***Std. Beta***	***Std. CI***	***p***	***Beta***	***CI***	***Std. Beta***	***Std. CI***	***p***	***Beta***	***CI***	***Std. Beta***	***Std. CI***	***p***
Intercept	1.31	1.14 – 1.47	0.00	0.12 – 0.12	<0.001	1.28	0.63 – 1.93	0.02	0.20 – 0.16	<0.001	1.21	0.57 – 1.84	0.12	0.31 – 0.06	<0.001
htTKV *(mL/m)*	0.00	0.00 – 0.00	0.04	0.08 – 0.17	0.47	0.00	0.00 – 0.00	0.02	0.12 – 0.16	0.77	0.00	0.00 – 0.00	0.04	0.09 – 0.18	0.53
Education: Up to High School						0.39	0.10 – 0.68	0.49	0.12 – 0.85	**0.009***	0.29	0.00 – 0.58	0.36	0.00 – 0.72	**0.05***
Gender: Male						0.03	0.24 – 0.18	0.04	0.30 – 0.22	0.77	0.05	0.25 – 0.16	0.06	0.31 – 0.20	0.65
Age *(years)*						0.00	0.01 – 0.01	0.05	0.08 – 0.18	0.47	0.00	0.01 – 0.01	0.03	0.10 – 0.16	0.67
Race															
American Indian or Alaskan Native						0.03	1.63 – 1.56	0.04	2.03 – 1.95	0.97	0.05	1.51 – 1.60	0.06	1.89 – 2.00	0.95
Asian						0.03	0.41 – 0.35	0.03	0.51 – 0.44	0.89	0.03	0.40 – 0.34	0.03	0.50 – 0.43	0.89
Black or African American						0.21	0.54 – 0.11	0.27	0.67 – 0.13	0.19	0.15	0.47 – 0.16	0.19	0.59 – 0.20	0.34
Hispanic or Latinx						0.02	0.38 – 0.42	0.02	0.48 – 0.53	0.92	0.04	0.35 – 0.43	0.05	0.44 – 0.54	0.85
BMI *(per kg/m^2)*						0.00	0.02 – 0.02	0.02	0.15 – 0.11	0.76	0.00	0.02 – 0.02	0.01	0.14 – 0.11	0.82
Frequent Pain: Yes											0.43	0.19 – 0.67	0.54	0.24 – 0.83	**0.001***

Standardized estimates are shown in the Std. Beta and Std. CI columns. Reference groups were those that had the largest number of participants (Education: University; Gender: Female; Race: White).

Table 4: Association between baseline BDI-II and 36 Month eGFR (N = 130)

Predictors	***Beta***	***Std. Beta***	***Std. CI***	***p***
Intercept	1.07	0.03	-0.06 – 0.12	0.91
Baseline BDI	-0.24	-0.04	-0.11 – 0.03	0.28
Baseline eGFR *(ml/min/1.73m^2)*	1.00	0.96	0.88 – 1.04	**<0.001**
Gender: Male	-0.21	-0.01	-0.15 – 0.14	0.93
Age *(years)*	0.18	0.07	-0.01 – 0.15	0.08
Race				
American Indian or Alaskan Native	-22.59	-0.72	-1.48 – 0.05	0.07
Asian	-10.62	-0.34	-0.65 – -0.02	**0.04**
Black or African American	-1.24	-0.04	-0.28 – 0.20	0.75
Hispanic or Latinx	-3.31	-0.10	-0.46 – 0.25	0.56
BMI *(per kg/m^2)*	-0.57	-0.09	-0.16 – -0.02	**0.01**
Education: Up to High School	0.05	0.00	-0.21 – 0.22	0.99

Standardized estimates are shown in the Std. Beta and Std. CI columns. Reference groups were those that had the largest number of participants (Education: University, Gender: Female, Race: White).

Table 5: Association between baseline BDI-II and 36 month htTKV (N = 104)

Predictors	*Beta*	*Std. Beta*	*Std. CI*	*p*
Intercept	5.33	-0.02	-0.15 – 0.10	**<0.001**
Baseline BDI	0.01	0.06	-0.04 – 0.16	0.22
Baseline htTKV *(mL/m)*	0.00	0.83	0.73 – 0.93	**<0.001**
Gender: Male	0.14	0.20	-0.01 – 0.41	0.06
Age *(years)*	0.00	0.05	-0.05 – 0.15	0.31
Race				
American Indian or Alaskan Native	-0.29	-0.41	-1.37 – 0.55	0.40
Asian	-0.14	-0.21	-0.64 – 0.23	0.34
Black or African American	0.02	0.02	-0.32 – 0.37	0.90
Hispanic or Latinx	-0.11	-0.15	-0.73 – 0.43	0.61
BMI *(per kg/m^2)*	0.02	0.12	0.02 – 0.22	**0.02**
Education: Up to High School	-0.13	-0.19	-0.50 – 0.12	0.22

Standardized estimates are shown in the Std. Beta and Std. CI columns. Reference groups were those that had the largest number of participants (Education: University, Gender: Female, Race: White).

Figure 1
Healthy older adults (Stewart 2009), CKD (Weiner 2023), African American CKD (Fischer 2010), ALS (Taylor 2010), Primary care (Arnau 2001), Pre-manifest carriers of Huntington's Disease (Aziz 2010), Type 1 Diabetes Mellitus (Gendelman 2009), Chronic Hepatitis C (Dbouk 2009), Chronic pain (Harris 2008).

The y-axis ("Depressive Symptoms") depicts the test statistic for the Wilcoxon Rank Sum test, which represents a 'difference in location.' This describes the median of the differences between a sample from group X and a sample from group Y. For example, the test statistic for the ALS group can be interpreted as follows: the median difference in total BDI-II scores between a patient with ALS and a patient from our ADPKD cohort (age ≥ 55) was 11. The confidence interval indicates that if we repeated the study 100 times, 95% of the 'differences in location' would fall between 8.3 and 12.9.

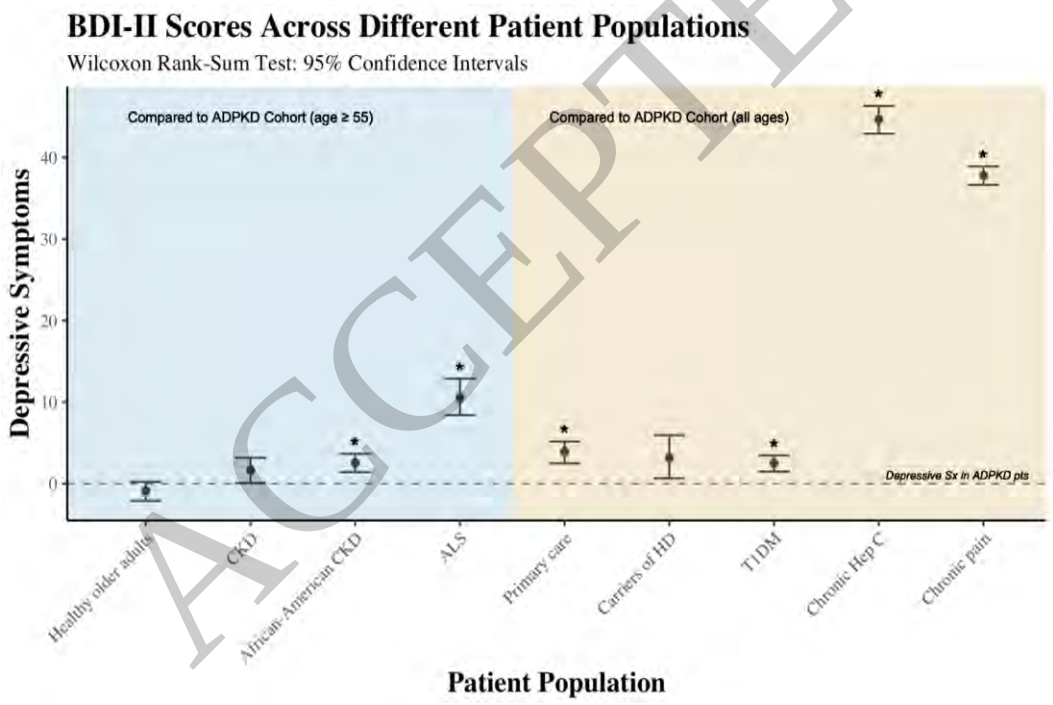


Figure 2
Individual Change in BDI-II

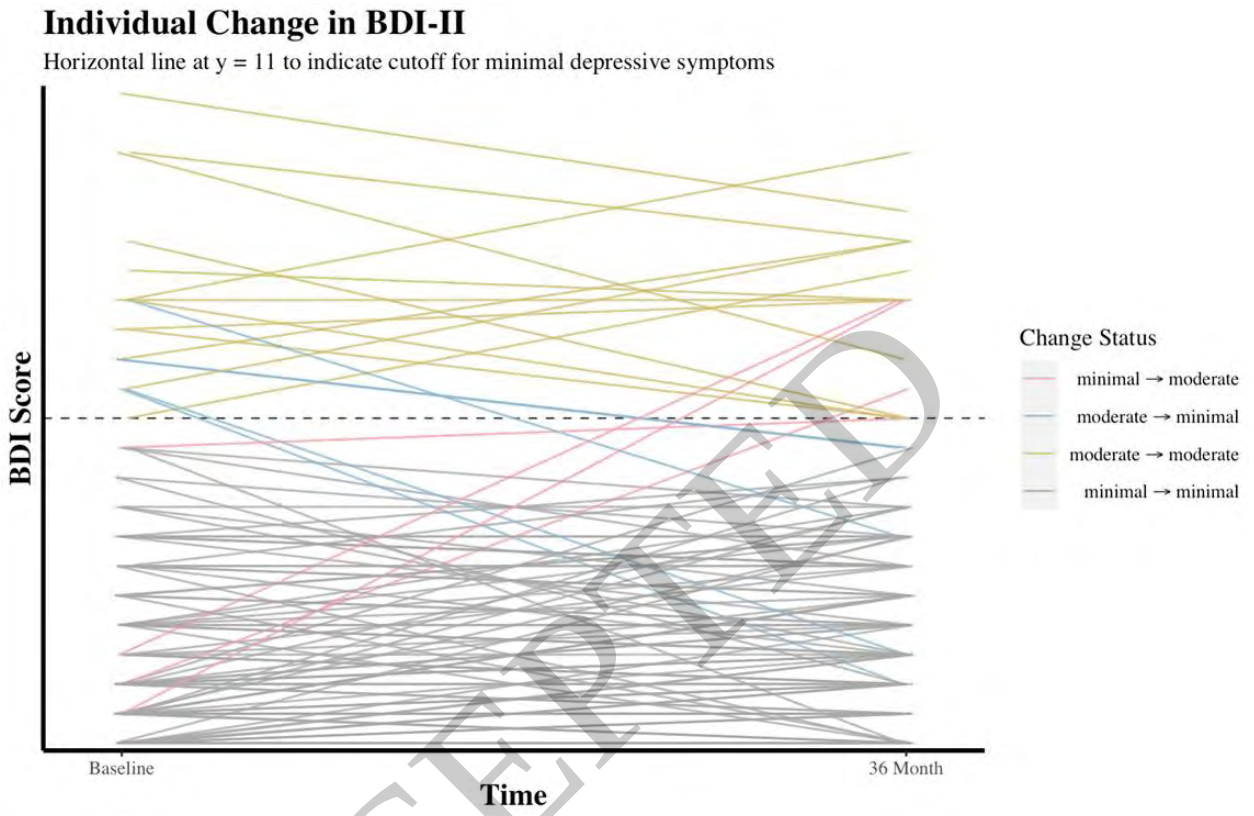
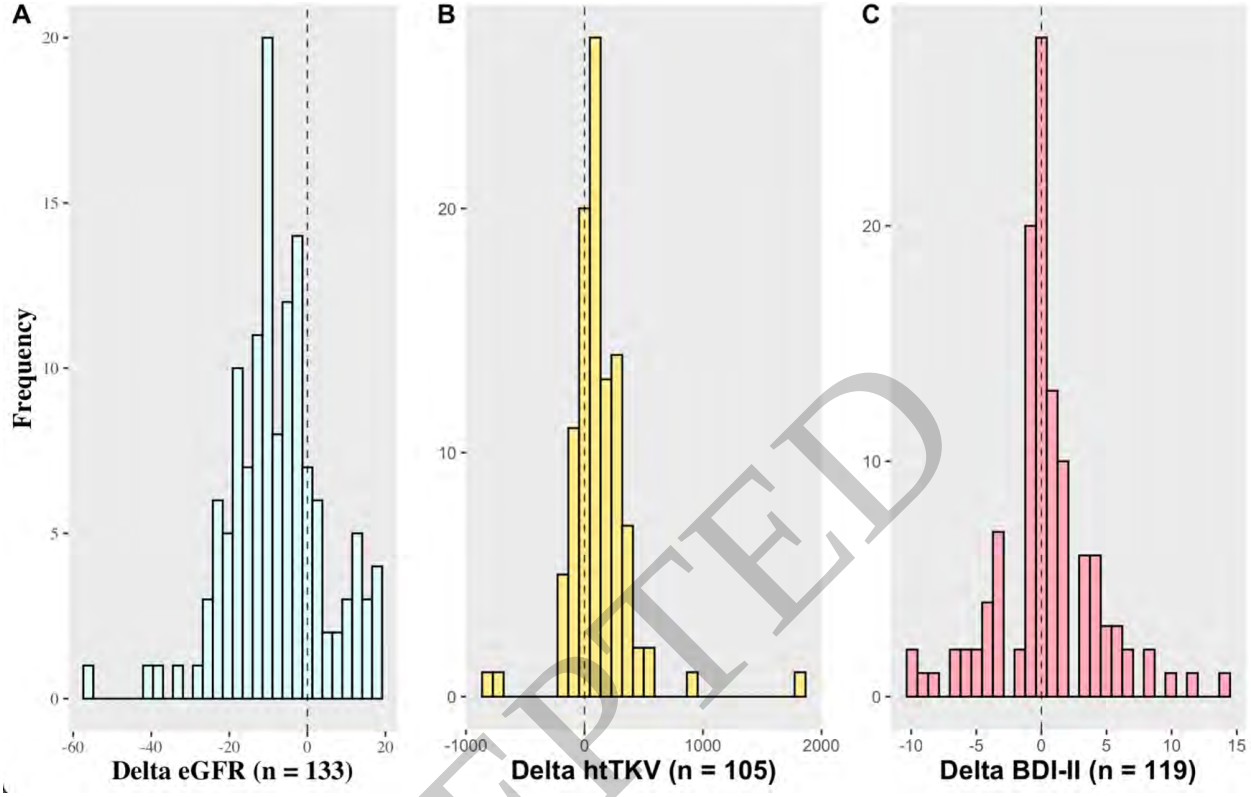


Figure 3

Change in Kidney Function and Depressive Symptoms over 36 Months



Supplemental Table of Contents

ASN American Society of Nephrology
JASN Journal of the American Society of Nephrology
KIDNEY360 Accessing Our World From Every Angle
CJASN Clinical Journal of the American Society of Nephrology

ASN Journal Disclosure Form

As per ASN journal policy, I have disclosed any financial relationships or commitments I have held in the past 36 months as included below. I have listed my Current Employer below to indicate there is a relationship requiring disclosure. If no relationship exists, my Current Employer is not listed.

S. Seliger reports the following:
Employer: University of Maryland School of Medicine; Baltimore VA Medical Center; University of Maryland Medical Center; Ownership Interest: Apple, Inc; Costco; Research Funding: Regulus Therapeutics; Sanofi; Patents or Royalties: University of Maryland, Baltimore and University of Texas, Southwestern: Methods for Assessing Differential Risk for Developing Heart Failure; and Advisory or Leadership Role: Member, Medical Review Board, ESRD Network 5 - unpaid. ; Member, Editorial Board - Circulation - unpaid ; Member- Polycystic Kidney Disease Foundation Patient Registry Advisory Committee (PRAC) - unpaid.

I understand that the information above will be published within the journal article, if accepted, and that failure to comply and/or to accurately and completely report the potential financial conflicts of interest could lead to the following: 1) Prior to publication, article rejection, or 2) Post-publication, sanctions ranging from, but not limited to, issuing a correction, reporting the inaccurate information to the authors' institution, banning authors from submitting work to ASN journals for varying lengths of time, and/or retraction of the published work.

Name: Stephen L. Seliger
Manuscript ID: K360-2024-000708R2
Manuscript Title: Depressive Symptoms in Adults with Autosomal Dominant Polycystic Kidney Disease
Date of Completion: November 27, 2024
Disclosure Updated Date: November 27, 2024

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T. Watnick reports the following:
Employer: The University of Maryland School of Medicine; Research Funding: Co site PI for the Falcon Study (reata pharmaceutical)-this study has been terminated; Co site PI for a clinical trial funded by Regulus. The terms are governed by a research contract.; Honoraria: I recorded a video on the genetics of PKD for medscape and there was an honorarium. I don't know if this is a continuing education activity so will disclose.; Patents or Royalties: PKD DNA testing AThena Diagnostics; royalties, but both my spouse and I have declined these; I receive royalties from Uptodate for a chapter on polycystic kidney disease.; Advisory or Leadership Role: Scientific Advisory Committee for the Polycystic Kidney Disease Foundation registry and centers of excellence program; and Other Interests or Relationships: I serve on advisory committees for the PKD Foundation.

I understand that the information above will be published within the journal article, if accepted, and that failure to comply and/or to accurately and completely report the potential financial conflicts of interest could lead to the following: 1) Prior to publication, article rejection, or 2) Post-publication, sanctions ranging from, but not limited to, issuing a correction, reporting the inaccurate information to the authors' institution, banning authors from submitting work to ASN journals for varying lengths of time, and/or retraction of the published work.

Name: Terry J. Watnick
Manuscript ID: K360-2024-000708R2
Manuscript Title: Depressive Symptoms in Adults with Autosomal Dominant Polycystic Kidney Disease
Date of Completion: December 1, 2024
Disclosure Updated Date: December 1, 2024

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C. Yi has nothing to disclose.

I understand that the information above will be published within the journal article, if accepted, and that failure to comply and/or to accurately and completely report the potential financial conflicts of interest could lead to the following: 1) Prior to publication, article rejection, or 2) Post-publication, sanctions ranging from, but not limited to, issuing a correction, reporting the inaccurate information to the authors' institution, banning authors from submitting work to ASN journals for varying lengths of time, and/or retraction of the published work.

Name: Caroline Yi
Manuscript ID: K360-2024-000708R1
Manuscript Title: Depressive Symptoms in Adults with Autosomal Dominant Polycystic Kidney Disease
Date of Completion: September 30, 2024
Disclosure Updated Date: September 30, 2024