

Request for Copy of Published Material

The materials provided in response to your request, unless otherwise stated, are the property of the copyright holder. Copyright and other intellectual property laws protect these materials. Reproduction or retransmission of the materials, in whole or in part, in any manner, without the prior written consent of the copyright holder, is a violation of copyright law. A single copy of the materials is provided to you pursuant to a license to do so that has been granted by the copyright holder to us. You may not redistribute or reproduce the materials in any forms without prior written consent of the copyright holder of the materials.

Enclosure:

- POSTER: McFarlane P, Bichet DG, Alam A, et al. Presented at: ISN World Congress of Nephrology 2026 (WCN'26); March 28-31, 2026; Yokohama, Japan.

Eight years of Canadian Real-World Assessment of Tolvaptan in ADPKD: Patient Reported Outcomes from the C-MAJOR study

McFarlane P,¹ Bichet DG,² Alam A,³ Oberdhan D,⁴ Bubolic S,⁵ Laplante A⁵

1. University of Toronto, St. Michael's Hospital, Toronto, ON, Canada; 2. University of Montreal & Hôpital du Sacré-Coeur, Montréal, QC, Canada; 3. McGill University Health Center, Montréal, QC, Canada; 4. Otsuka Pharmaceutical Development & Commercialization, Inc., Rockville, MD, USA; 5. Otsuka Canada Pharmaceutical Inc., Saint-Laurent, QC, Canada.

INTRODUCTION

- Tolvaptan (Jinarc®) is the first approved treatment in Canada to slow the progression of kidney enlargement and kidney function decline in patients with autosomal dominant polycystic kidney disease (ADPKD).
- C-MAJOR is an ongoing, observational, multi-center registry of people with ADPKD treated with tolvaptan, initiated in 2015, as per Health Canada requirements.

AIM

- This analysis describes the impact of tolvaptan on ADPKD health-related quality of life (HRQoL) in people with ADPKD in Canada.

METHODS

- This interim analysis includes patients enrolled in C-MAJOR between June 2015 and December 2023.
- C-MAJOR includes patients initiating tolvaptan post-enrolment (*"pure prospective", prospective only*) and those on-treatment at enrolment (*retrospective and prospective*).
- Treatment and clinical management of patients followed routine clinical practice; all treatment decisions were at the sole discretion of the treating physician, independent of participation.
- Only pure prospective patients completed patient-reported outcome (PRO) questionnaires including the Short-Form 12 Health Survey version 2 (SF-12v2), ADPKD-Impact Scale (ADPKD-IS), and ADPKD-Pain and Discomfort Scale (ADPKD-PDS).
- Repeated measures general linear models with mixed effects evaluated PRO changes from baseline over time, assessed at 6-month intervals.

RESULTS

C-MAJOR Baseline Patient and Disease Characteristics

- Among 470 patients treated with tolvaptan, 39% comprised the pure prospective population.
- Among pure prospective patients, mean age at ADPKD diagnosis and tolvaptan initiation was 29 and 43 years, respectively; 53% were female and 83% were Caucasian.
- 77% had early chronic kidney disease (CKD; category G1-3a), similar to the total population.

Table 1. Baseline demographics and disease characteristics of patients in C-MAJOR

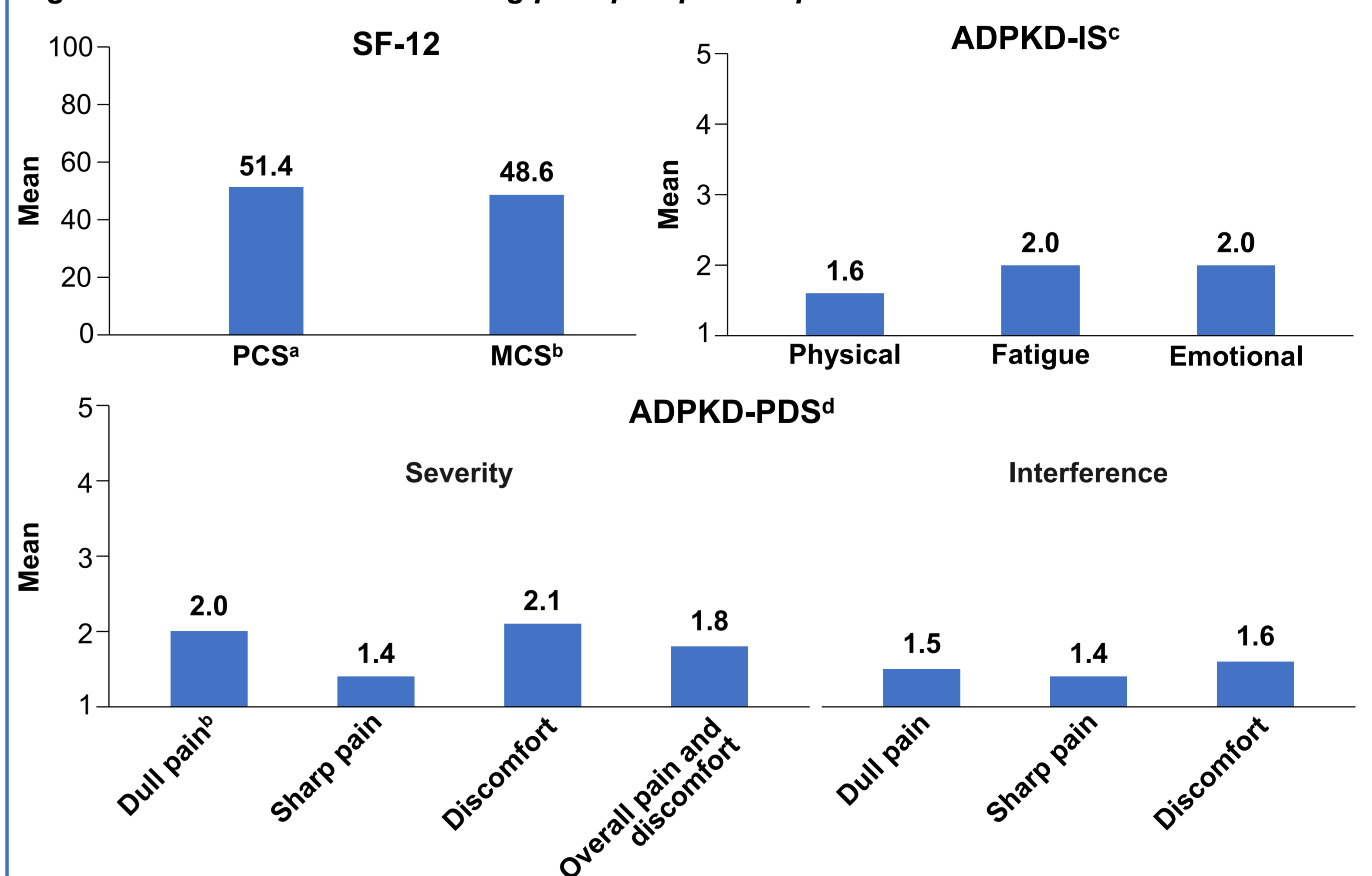
	Pure Prospective Population (N=185)	Total Population (N=470)
Demographics		
Age at diagnosis, years	28.5 (13.3)	29.8 (13.6)
Female	98 (53.0%)	239 (50.9%)
Race		
Caucasian	153 (82.7%)	394 (83.8%)
Black	4 (2.2%)	13 (2.8%)
Asian	12 (6.5%)	26 (5.5%)
Hispanic	8 (4.3%)	17 (3.6%)
Other	8 (4.3%)	20 (4.3%)
Disease characteristics		
Duration of ADPKD disease, years	14.1 (10.7)	15.0 (10.7)
Age at tolvaptan initiation, years	42.7 (11.0)	44.4 (11.4)
TKV, mL	1866.5 (1710.1) ^a	2010.8 (1559.1) ^b
ht-TKV, mL/m	1125.0 (1057.2) ^c	1158.0 (890.6) ^d
Kidney length, cm	18.1 (3.7) ^e	18.8 (4.0) ^f
eGFR, mL/min/1.73 m ²	68.3 (27.8) ^g	63.5 (27.4) ^h
CKD category		
G1	48 (26.2%) ^g	91 (19.8%) ⁱ
G2	56 (30.6%) ^g	136 (29.6%) ⁱ
G3a	36 (19.7%) ^g	90 (19.6%) ⁱ
G3b	30 (16.4%) ^g	104 (22.7%) ⁱ
G4	13 (7.1%) ^g	38 (8.3%) ⁱ
G5	0 (0.0%) ^g	0 (0.0%) ⁱ

Data are mean (SD) or n (%). ^aN=135. ^bN=278. ^cN=112. ^dN=215. ^eN=156. ^fN=417. ^gN=183. ^hN=464. ⁱN=459. CKD=chronic kidney disease; eGFR=estimated glomerular filtration rate; ht-TKV=height-adjusted total kidney volume; SD=standard deviation; TKV=total kidney volume.

C-MAJOR Baseline PROs

- Among pure prospective patients, 113 completed PROs at baseline, and scores indicated minimal impact on HRQoL.
- Scores were generally comparable between early (G1-3a) and late (G3b-4) CKD (data not shown).

Figure 2. PROs at baseline among pure prospective patients

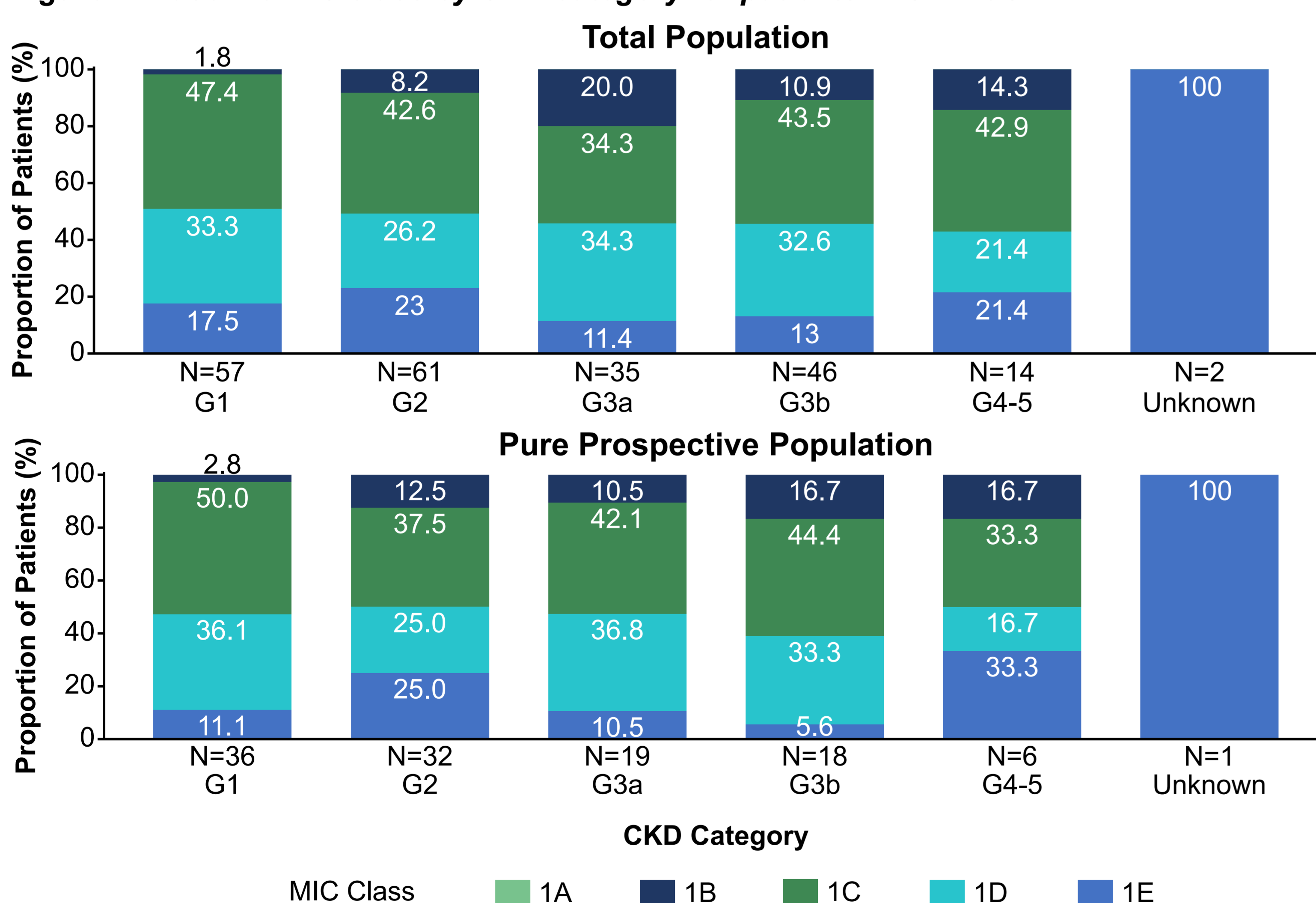


Data are mean (SD). ^aN=111. ^bN=112. ^cADPKD-IS scale ranges from 1 (not bothered/not difficult at all) to 5 (bothered/extremely difficult). ^dADPKD-PDS ranges from 1 (not bothered and not difficult) to 5 (extremely bothered and extremely difficult). IS=Impact Score; MCS=Mental Component Summary; PCS=Physical Component Summary; PDS=Pain and Discomfort Scale.

Baseline MIC Class by CKD Category

- Among both the total population and pure prospective patients, ~90% were identified as fast progressors using the Mayo Imaging Classification (MIC class 1C-E).

Figure 1. Baseline MIC class by CKD category for patients in C-MAJOR



Baseline MIC class by CKD category at tolvaptan initiation in the registry study patient population with available ht-TKV. Percentages were calculated using the respective number of patients in each CKD category as the denominator.

PROs Over Time

- Despite disease progression, PRO scores remained generally stable over time.
- Statistically significant changes were seen in SF-12 PCS, ADPKD-IS physical and emotional scales, and ADPKD-PDS Dull Pain and Discomfort Interference scores, although small effect sizes were likely not clinically meaningful.
- Patients with early CKD had greater improvements in ADPKD-related physical, fatigue, and emotional domains, and pain/discomfort measures.
- A notable decline in PRO completion rates over time limited interpretation (baseline n: 111-113; 36 months n: 41-42).

Table 2. Repeated measures mixed models of change from baseline in PROs in C-MAJOR

	Time (per month)		CKD (early ^a vs late ^b)	
	β (95% CI)	p-value	β (95% CI)	p-value
SF-12v2^c				
PCS	-0.055 (-0.09;-0.02)	0.002	1.810 (0.10;3.52)	0.038
MCS	-0.027 (-0.07;-0.02)	0.233	0.330 (-1.74;2.40)	0.752
ADPKD-IS^d				
Physical	0.006 (0.00;0.01)	<0.001	-0.191 (-0.33;-0.06)	0.006
Fatigue	0.001 (-0.00;0.01)	0.518	-0.247 (-0.43;-0.06)	0.009
Emotional	0.006 (0.00;0.01)	<0.001	-0.435 (-0.59;-0.28)	<0.001
ADPKD-PDS^d				
Dull Pain Severity	0.001(-0.00;0.01)	0.466	-0.071 (-0.24;0.10)	0.417
Sharp Pain Severity	0.003 (-0.00;0.01)	0.146	-0.330 (-0.50;-0.16)	<0.001
Discomfort Severity	0.001 (-0.00;0.00)	0.631	-0.056 (-0.25;0.13)	0.555
Overall Pain and Discomfort Severity	0.002 (-0.00;0.01)	0.137	-0.147 (-0.28;-0.01)	0.033
Dull Pain Interference	0.005 (0.00;0.01)	<0.001	-0.191 (-0.32;-0.06)	0.004
Discomfort Interference	0.004 (0.00;0.01)	0.005	-0.202 (-0.34;-0.06)	0.006
Sharp pain Interference	0.002 (-0.00;0.01)	0.333	-0.155 (-0.33;0.02)	0.078

Models were also adjusted for outcome score at baseline. ^aCKD category G1-3a. ^bCKD category G3b-5. ^cHigher scores indicate better health status/HRQoL. ^dLower scores indicate less impact/better HRQoL. CI=confidence interval.

CONCLUSION

- This first report of PRO data from C-MAJOR helps inform our understanding of ADPKD impact in patients treated with tolvaptan in Canada.
- Findings showed people with early category ADPKD had minimally impacted ADPKD-related burden of illness at baseline, with PRO scores remaining constant over time with tolvaptan despite disease progression.
- Greater improvements in PROs were seen for patients with early vs late CKD.
- Rates of PRO completion declined over an extended timeframe, highlighting challenges of gathering such data in real-world settings.