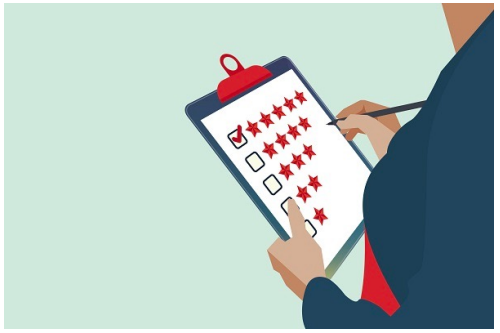
BC Renal KCC ADPKD education day

Thursday June 13, 2019

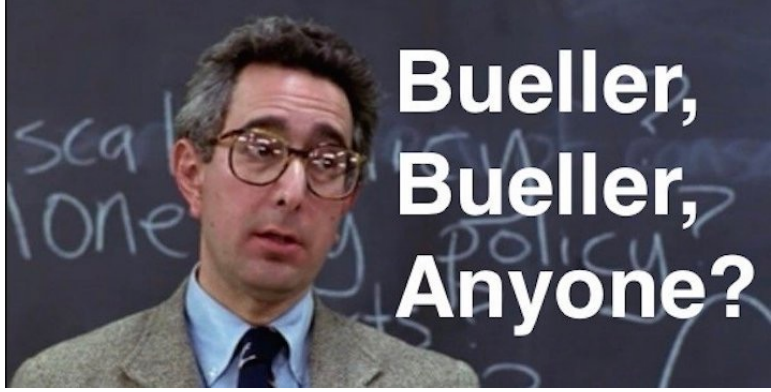
Welcome!

- The first of many KCC education days
- Thanks to all of you for attending!



Housekeeping

Agenda and format



TIME	SESSION	PRESENTOR(S)
1300	Welcome and introductions	Dr. Mike Bevilacqua
1310	Medical Management of ADPKD	Dr. Mike Bevilacqua
1340	Pharmacologic Management of ADPKD	Judith Marin
1400	Introduction to "ORUIN" - Support Program for Patients on Tolvaptan	Jonathan Leone, Otsuka Pharmaceuticals
1410	ADPKD-specific Tools Developed for BC's KCCs	Dr. Mike Bevilacqua/ Janet Williams
1430	Small Group Discussion	Small Groups
1500	Coffee Break	
1515	Dietary Management of ADPKD	Kirsten Flood & Lynn Tomita
1535	Large Group Discussion	Whole group
1545	Patient and Family Experience with ADPKD	Jeff Robertson (PKD Foundation of Canada) and Phaydy Phanouvong (Patient Rep)
1615	Small Group Discussion	Small groups, then large group discussion
1645	Regroup and Final Discussions	Dr. Mike Bevilacqua

- Lots of time built in for discussion
- Ask questions throughout
- Please participate! Your feedback is greatly valued!!

Modern Management of Polycystic Kidney Disease

Current state of the art, tools and management of ADPKD in the KCC

Outline

New insights in ADPKD management

- Better understanding of PKD
- New tools and treatments for PKD

Goals and process of ADPKD management within the KCC

- Current state of PKD in BC
- Alignment of PKD care with KCC framework
- Best practices for management of ADPKD in KCC

Disclosures

Relevant to this topic, I disclose the following from Otsuka Canada Pharmaceuticals Inc:

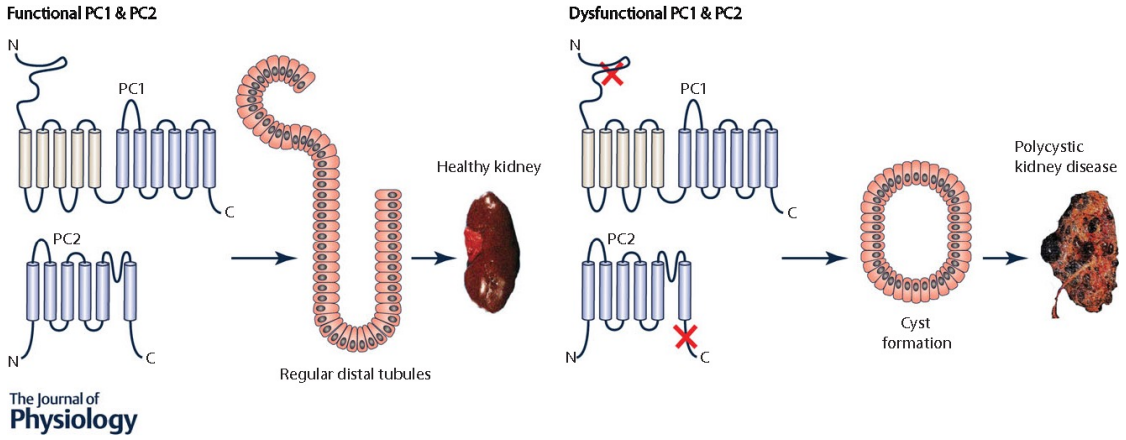
- An unrestricted grant to the BCPRA to assist in creation of the PKD registry
- Honoraria for participation in advisory boards, consultancy groups and development of educational material related to PKD

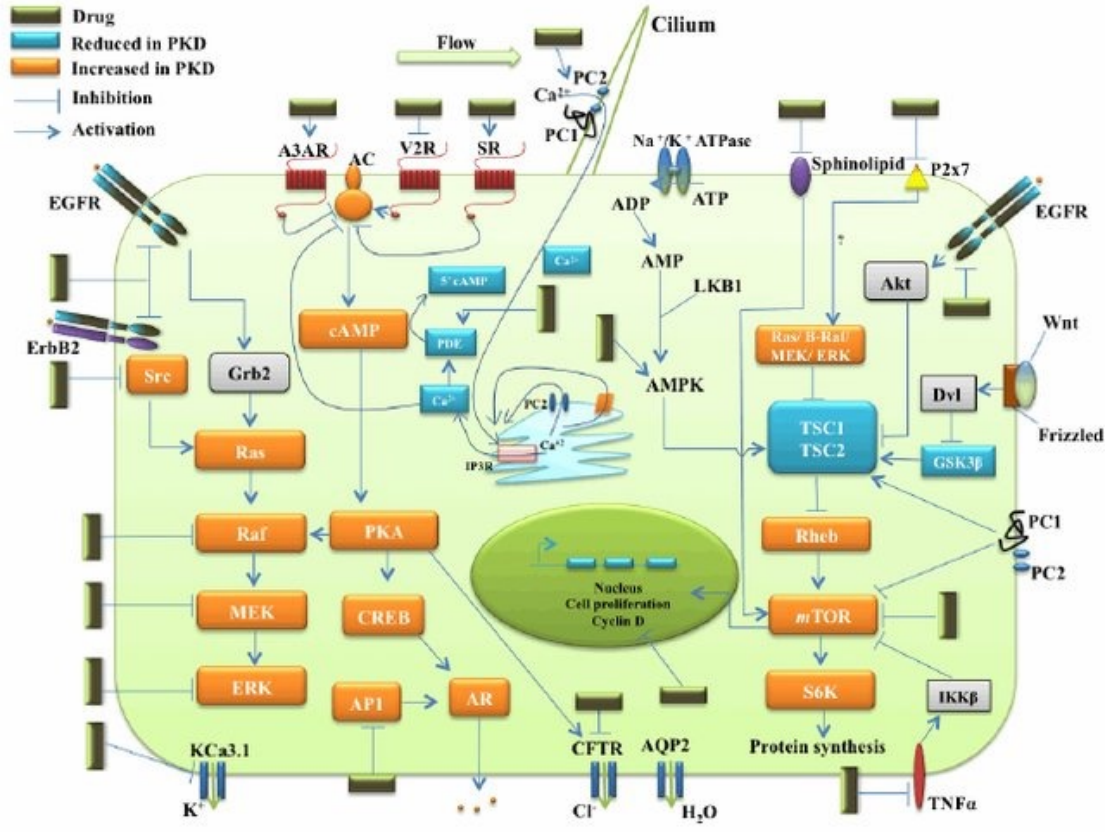
Epidemiology

- Autosomal dominant polycystic kidney disease (ADPKD) is **the most common inherited renal disorder**, affecting between 1-2.5/1000 live births
  - Although exact provincial numbers are lacking, this estimate would mean there are somewhere from **4600 to over 10000** British Columbians living with the disease.

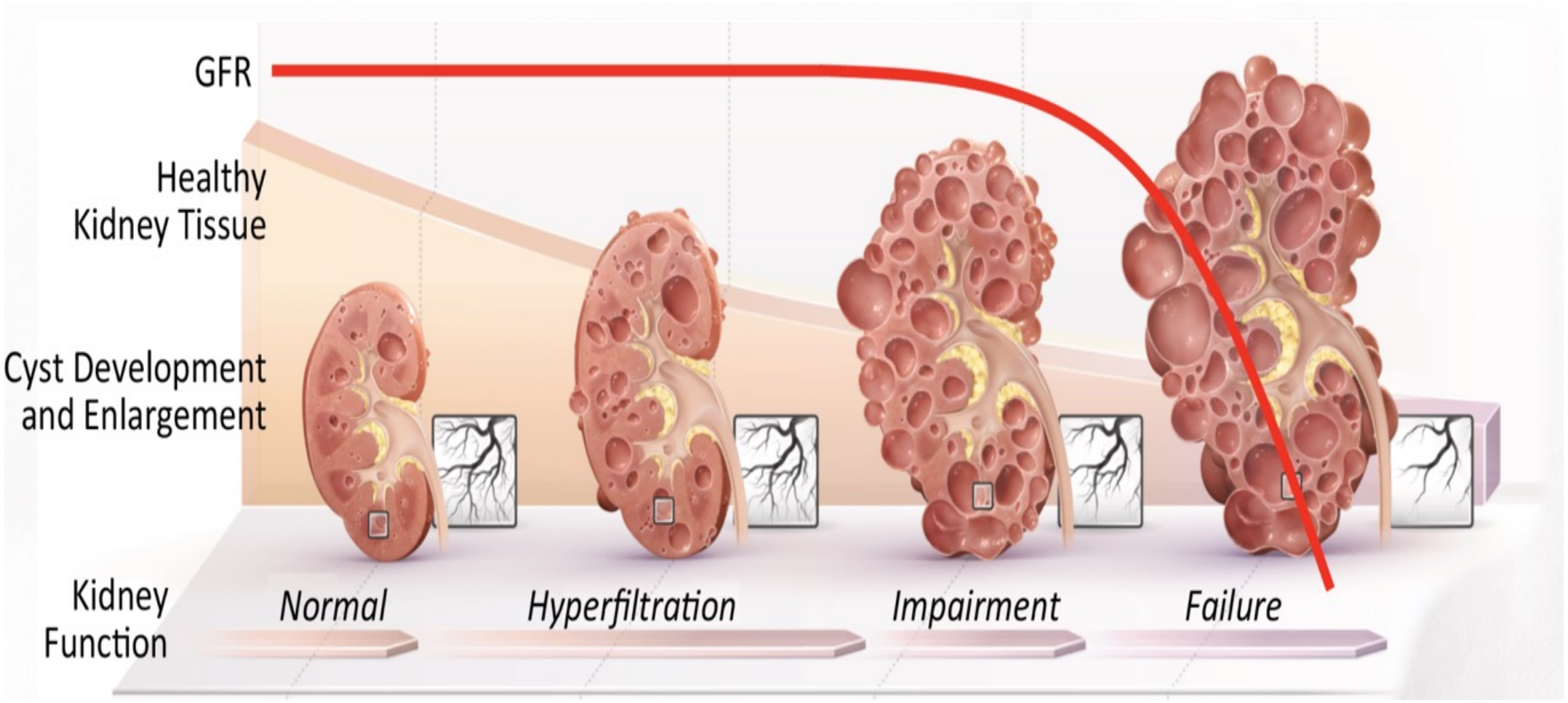
- Of patients with an identifiable etiology of ESRD, ADPKD is the 4th leading cause of ESRD in Canada

ADPKD is a more complex disease than previously appreciated


Functional PC1 & PC2
N
PC1
C
PC2
N
C
Regular distal tubules
Healthy kidney
Dysfunctional PC1 & PC2
N
PC1
C
PC2
N
C
Cyst formation
Polycystic kidney disease
The Journal of Physiology


Drug
Reduced in PKD
Increased in PKD
Inhibition
Activation
Flow
Cilium
PC2
PC1
A3AR
AC
V2R
SR
Na+/K+ ATPase
Sphinolipid
P2x7
EGFR
ADP
ATP
AMP
LKB1
Akt
EGFR
ErbB2
cAMP
PDE
Src
Grb2
AMPK
Ras/ B-Raf/ MEK/ ERK
Wnt
Dvl
Frizzled
TSC1 TSC2
GSK3β
IP3R
Ras
Raf
PKA
Rheb
PC1
PC2
Nucleus
Cell proliferation
Cyclin D
MEK
CREB
mTOR
ERK
AP1
AR
S6K
IKKβ
KCa3.1
CFTR
AQP2
Protein synthesis
TNFα
K+
Cl-
H2O

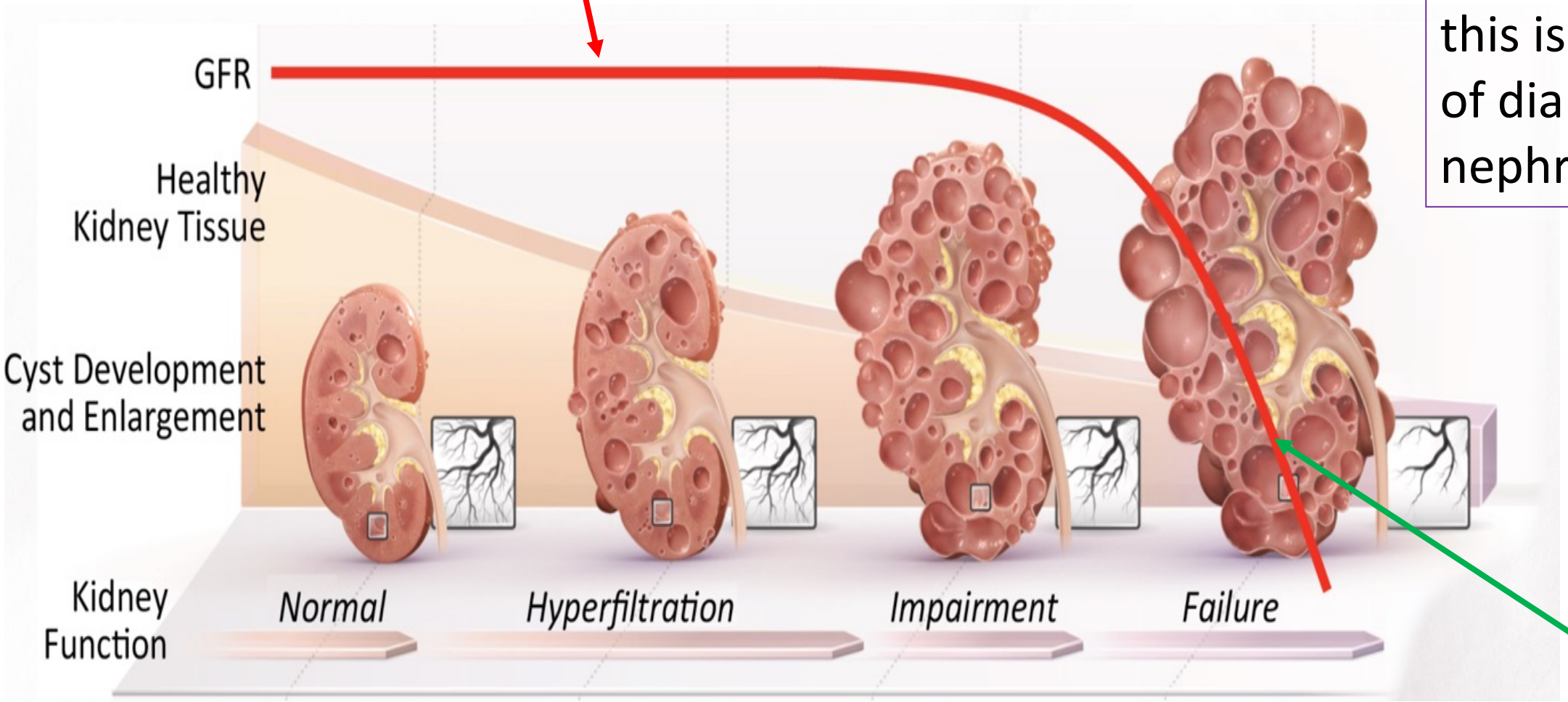
Modern understanding of ADPKD disease course



The disease course is variable one, with the early disease marked by cyst proliferation and expansion with little renal dysfunction followed by a precipitous decline. The corollary here is that by the time there is a change in GFR, significant cyst expansion and proliferation has already occurred

Maintained GFR in the setting of renal parenchymal loss = hyperfiltration

A good way to conceptualize this is to think of diabetic nephropathy

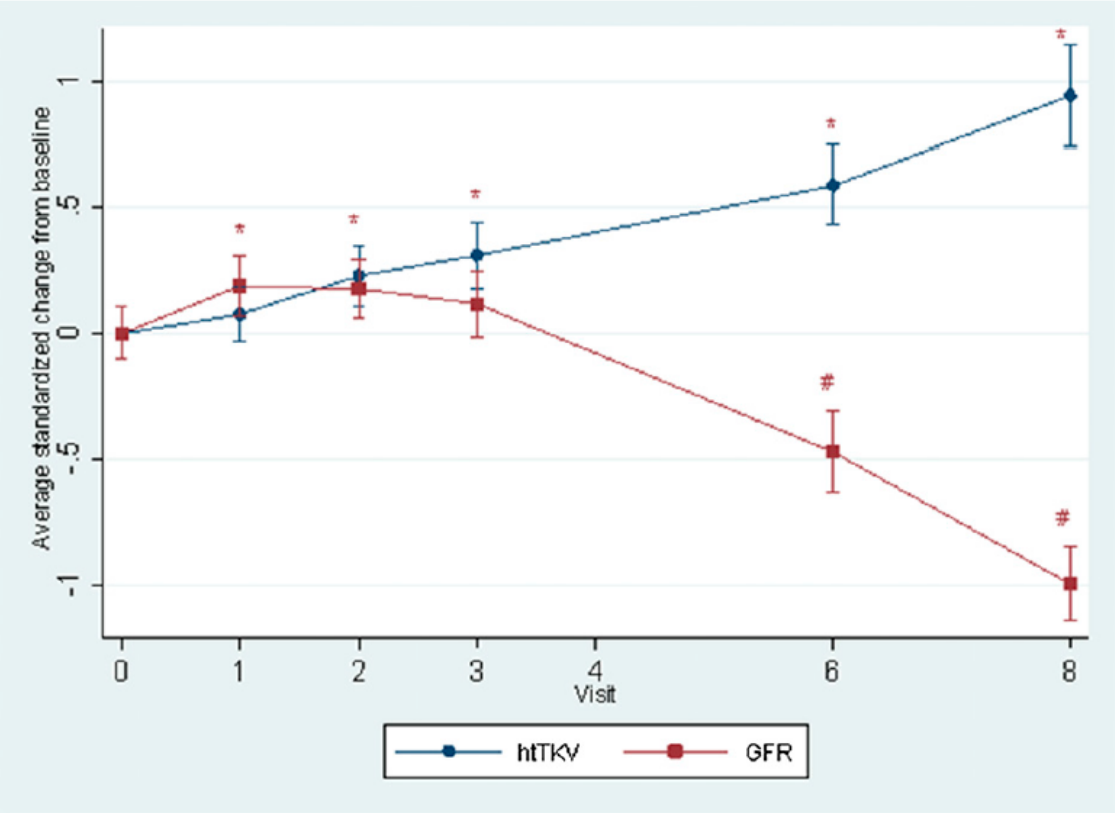


Upwards of 5ml/year decline

The disease course is variable one, with the early disease marked by cyst proliferation and expansion with little renal dysfunction followed by a precipitous decline. The corollary here is that by the time there is a change in GFR, significant cyst expansion and proliferation has already occurred

Tools to evaluate ADPKD are becoming more specialized

Changes in kidney size precede change in renal function



Significant changes in kidney volume can be detected years before changes in GFR

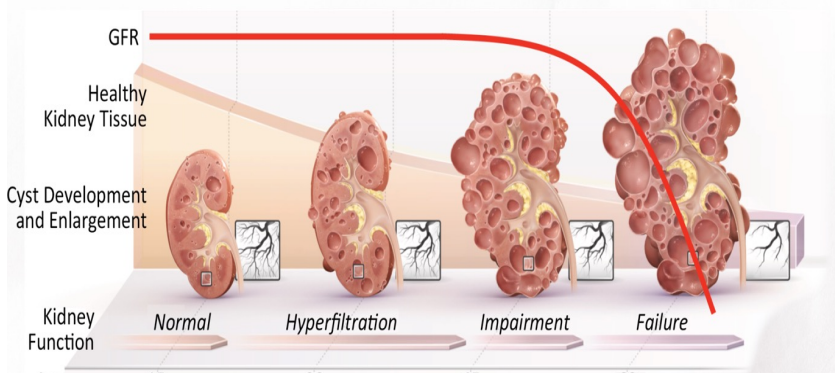
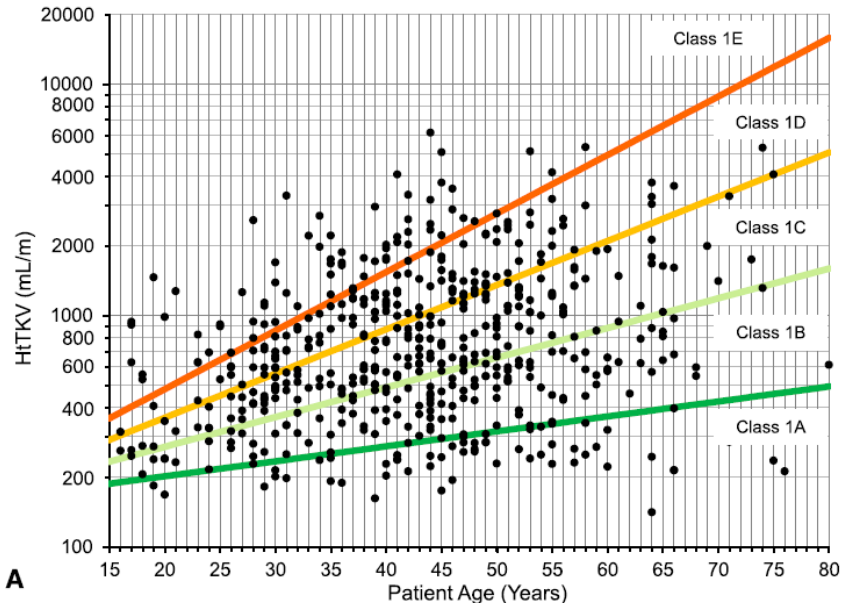


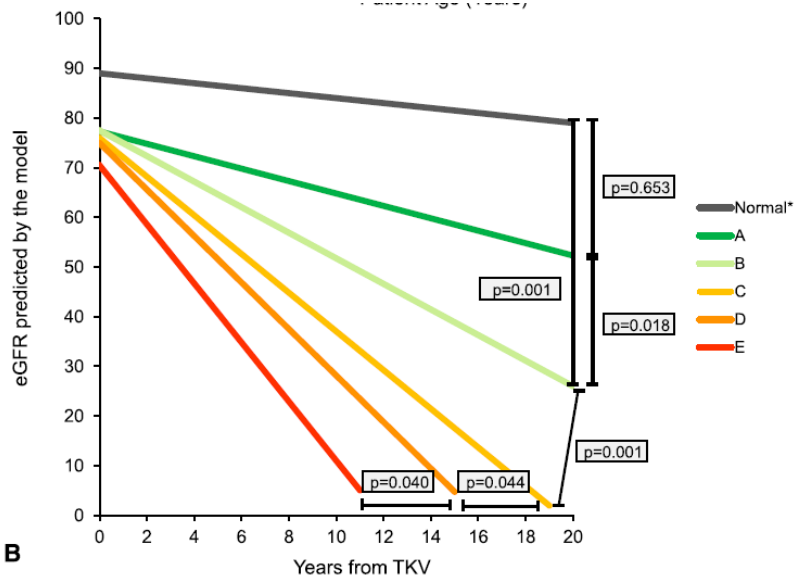
Figure 2. | Average standardized change in htTKV and iothalamate GFR. htTKV determined at baseline and iothalamate GFR at baseline and five subsequent visits until year 8 (n=93 with complete data). P<0.01 based on paired t test comparing each year to baseline for htTKV (*) and GFR (#). htTKV, height-adjusted total kidney volume.

Clin J Am Soc Nephrol 7: 479–486, 2012.

Total Kidney Volume (TKV)-based prognostication: the Mayo classification

At present this appears to be the most robust individualized predictor of **early stage** progression in PKD patients (i.e., before GFR declines)

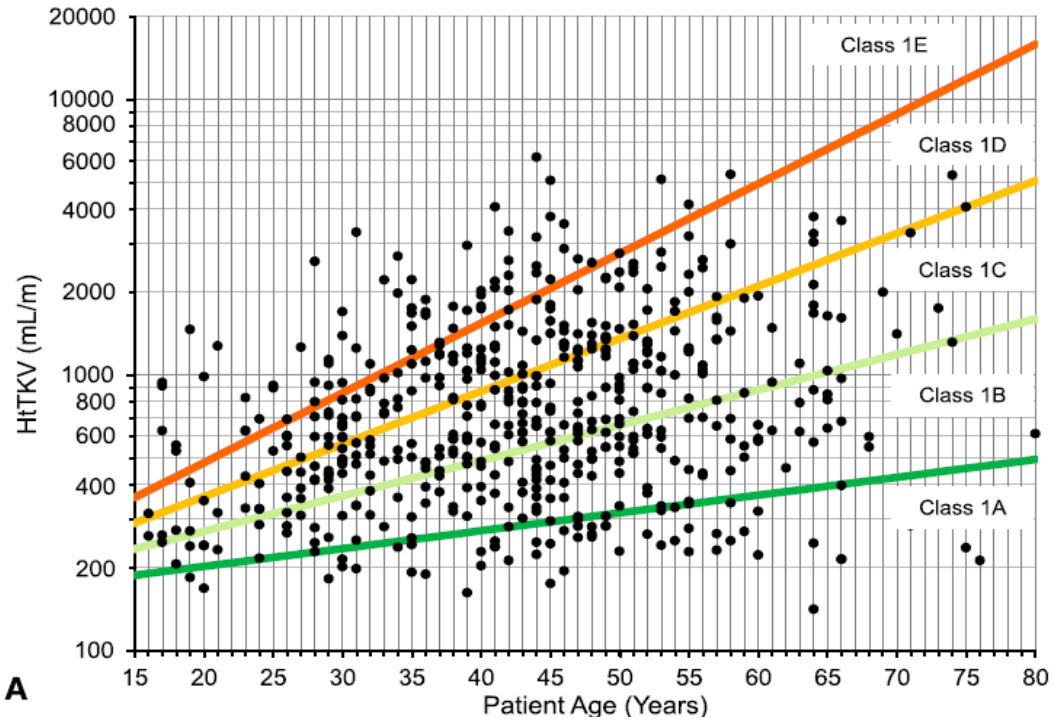




J Am Soc Nephrol 26: 160–172, 2015.

Mayo classification categorizes rate of kidney growth

Class	Average annual change in TKV
1A	<1.5%
1B	1.5-3
1C	3-4.5
1D	4.5-6
1E	>6%



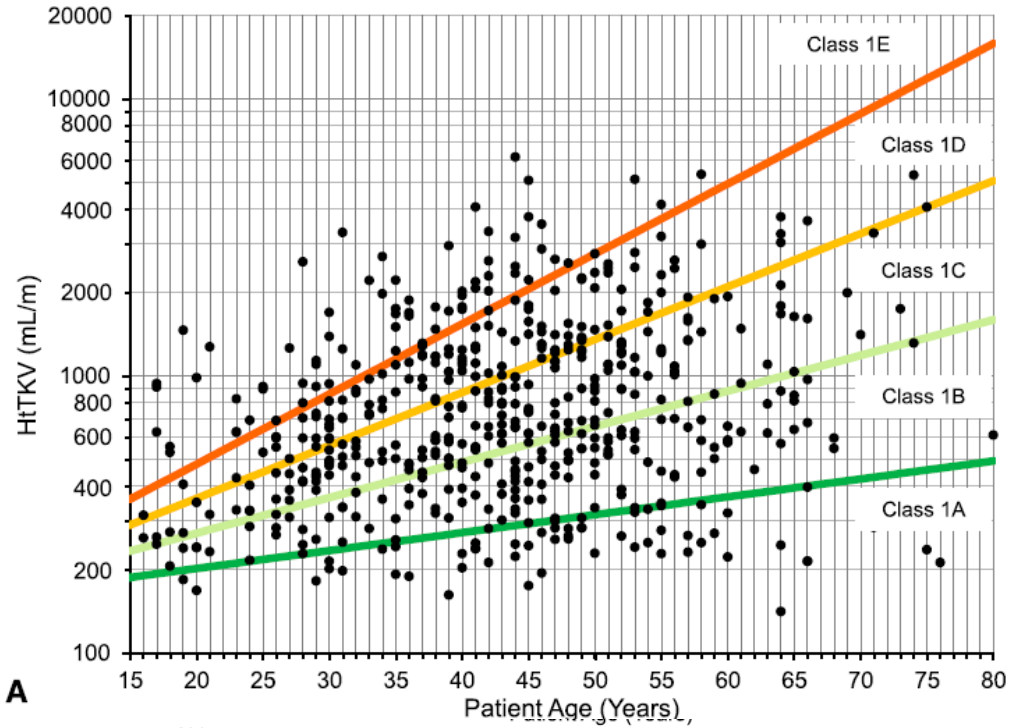
The 1A-1E classification is best thought of as a ***velocity of growth classification*** – the classes refer to the average annual growth in htTKV

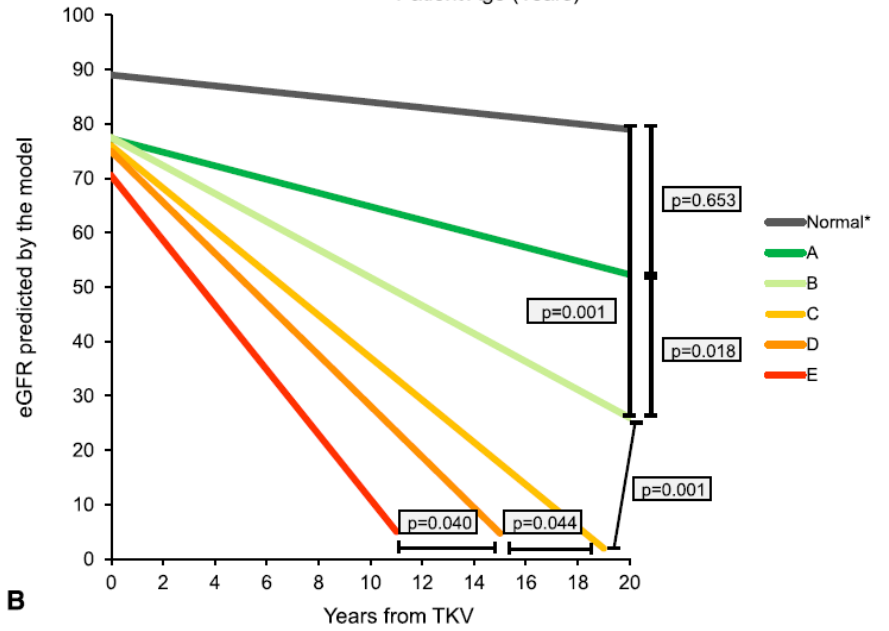
J Am Soc Nephrol 26: 160–172, 2015.

Mayo class predicts rate of GFR loss

Class	Average annual change in TKV	Average annual decrease in eGFR
1A	<1.5%	0.23
1B	1.5-3	1.33
1C	3-4.5	2.63
1D	4.5-6	3.48
1E	>6%	4.78

The average GFR comes from >8 years of CRISP and Mayo clinic follow-up data





J Am Soc Nephrol 26: 160–172, 2015.

How to get total kidney volume

- This can be done via CT or MRI
- There are standardized measurement techniques coming soon across the province – in the meantime, you can still do this – just need to discuss with your local radiation
- If you are getting a scan for TKV alone, we have recently studied an 'ultra low dose' CT protocol for this purpose
  - Similar radiation to a 3 view abdo X-ray

Effective radiation dose in this study
- LD = 1.73 mSv
- ULD = 0.88 mSv

Some comparisons based on published values
- CT abdo pelvis 10 mSv
- Cardiac CT 3 mSv
- Abdominal X-ray series (3 view) 0.7-0.8 mSv
- L-spine X-ray 1.5 mSv

FIGURE 15.—Man being bombarded by "invisible" rays.

ADPKD carries a higher disease burden than is recognized

Extra-renal manifestations of PKD

KIDNEY-RELATED

Pain and discomfort

Kidney stones

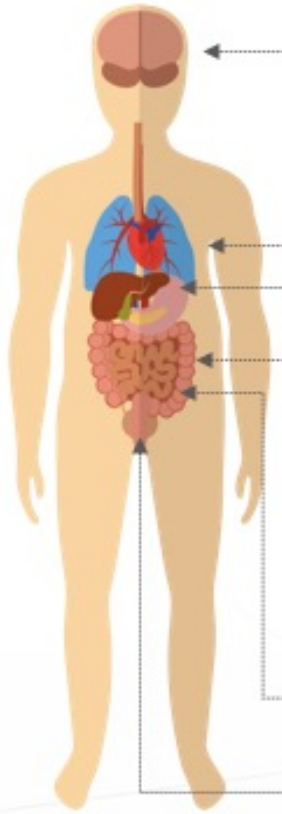
Cyst bleeds

Infected cysts

High blood pressure

Blood in urine

Worsening kidney function / kidney failure



NON-KIDNEY-RELATED

Brain aneurysm*

Cardiovascular*
(e.g., heart valve problems)

Liver cysts

Hernias of the abdomen

Diverticulosis*
(outpouchings of the large intestine)

Seminal vesicle cysts

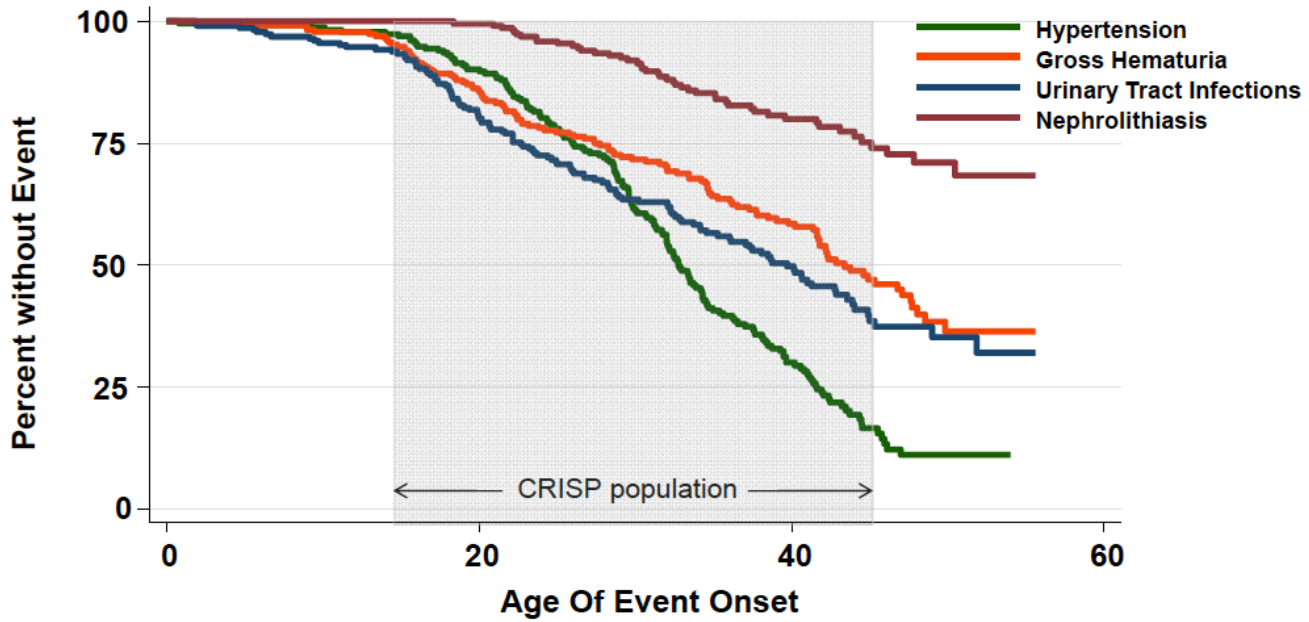
Not everybody with ADPKD will experience all of these complications

*Less frequent

ADPKD: Autosomal Dominant Polycystic Kidney Disease

Adapted from www.endpkd.ca; and Harris PC, et al. Gene Reviews, last updated June 11, 2015.

Other complications of PKD



By age 30, over 50% have at least one complications

NIH CRISP Studies; Chapman *J. Amer. Soc. Neph*, 21:384A, 2010.

CK-35

Pain, hematuria, infection and stones can occur early in the disease course

- Up to 25% of PKD patients present with these symptoms in the setting of preserved renal function
- The occurrence of these symptoms does not completely coincide with their renal disease course

Gabow PA, Duley I, Johnson AM. Clinical profiles of gross hematuria in autosomal dominant polycystic kidney disease. Am J Kidney Dis. 1992 Aug;20(2):140–3.

Bajwa ZH, Sial KA, Malik AB, Steinman TI. Pain patterns in patients with polycystic kidney disease. Kidney international. 2004;66(4):1561–9.

Abdominal symptoms

Over ¼ of people with GFR >60 have abdominal symptoms related to their PKD

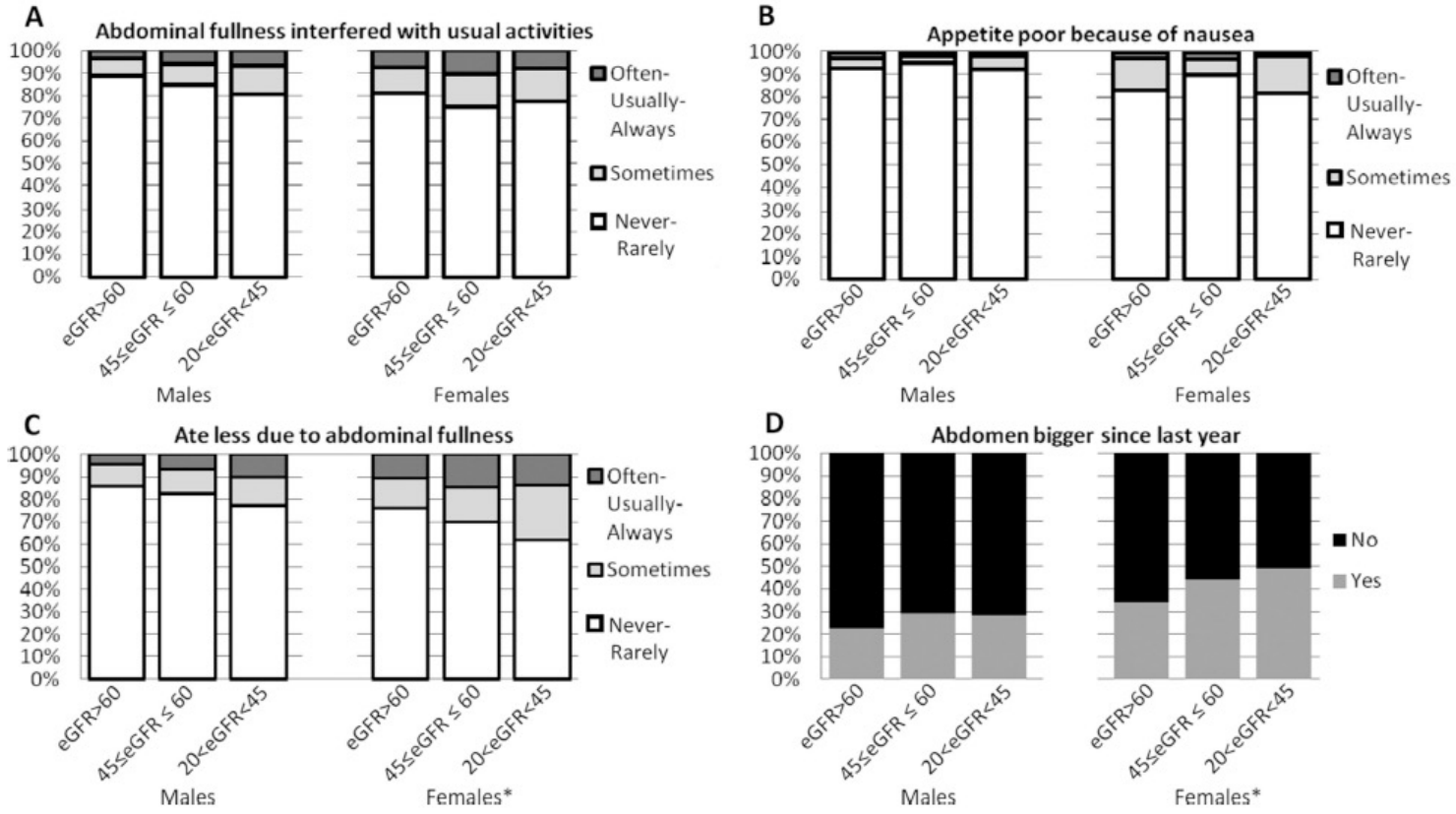
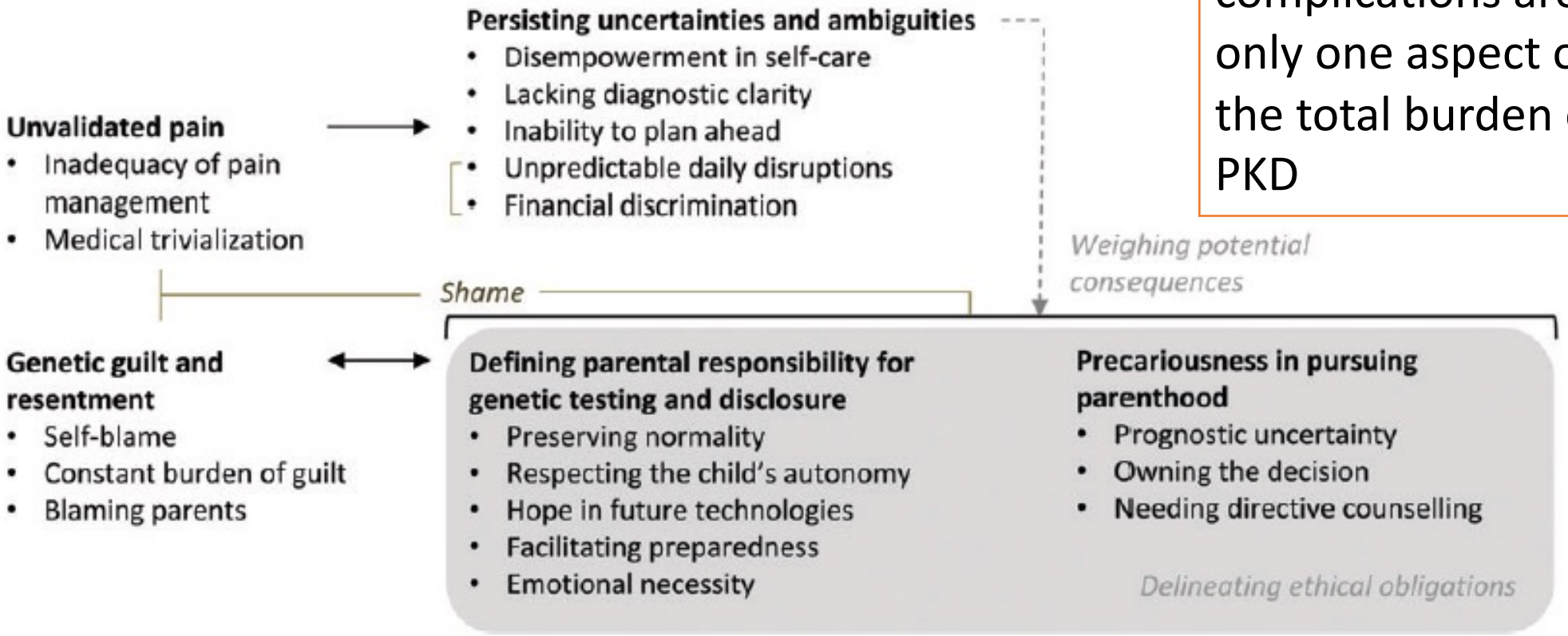


Figure 1. ADPKD patients' reports of frequency of abdominal symptoms

Miskulin DC, Abebe KZ, Chapman AB, Perrone RD, Steinman TI, Torres VE, et al. Health-Related Quality of Life in Patients With Autosomal Dominant Polycystic Kidney Disease and CKD Stages 1-4: A Cross-sectional Study. American Journal of Kidney Diseases. 2014 Feb;63(2):214–26.

Patient perspectives of PKD

The physical symptoms and complications are only one aspect of the total burden of PKD



Tong A, Rangan GK, Ruospo M, Saglimbene V, Strippoli GFM, Palmer SC, et al. A painful inheritance--patient perspectives on living with polycystic kidney disease: thematic synthesis of qualitative research. Nephrology Dialysis Transplantation. 2015 May 1;30(5):790–800.

Treatments for ADPKD are becoming more specialized

ORIGINAL ARTICLE

Tolvaptan in Patients with Autosomal Dominant Polycystic Kidney Disease

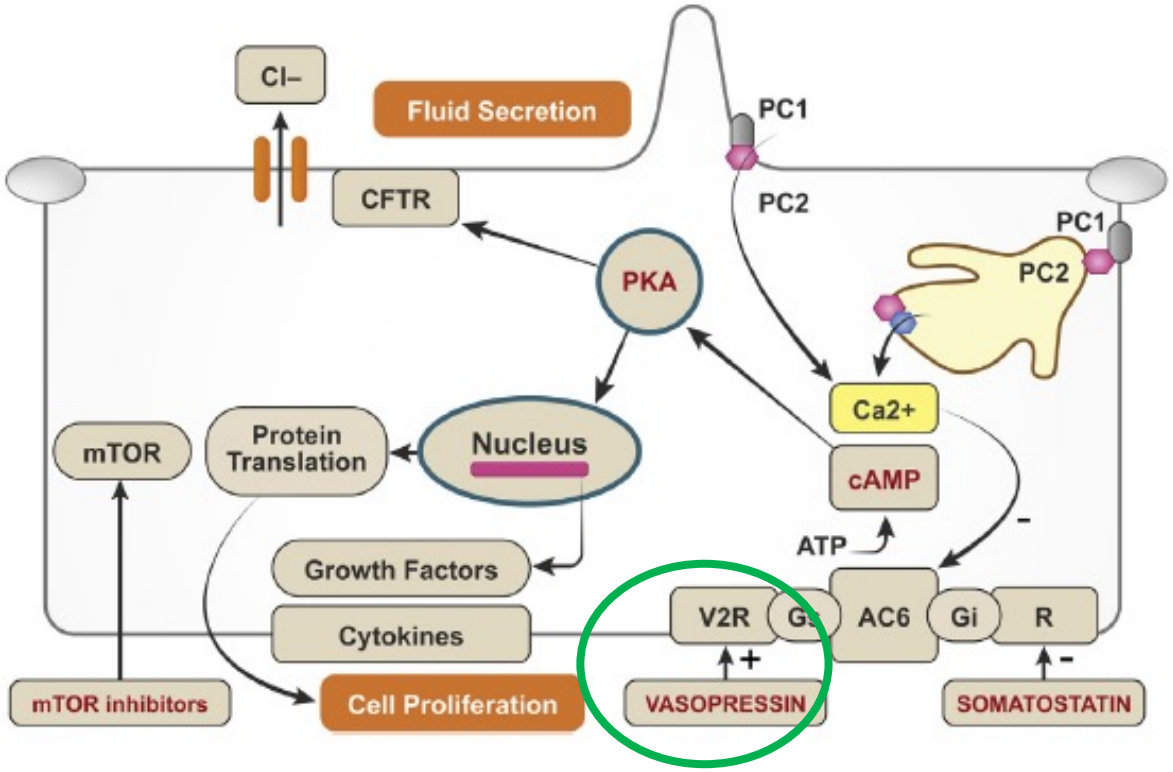
Vicente E. Torres, M.D., Ph.D., Arlene B. Chapman, M.D., Olivier Devuyst, M.D., Ph.D., Ron T. Gansevoort, M.D., Ph.D., Jared J. Grantham, M.D., Eiji Higashihara, M.D., Ph.D., Ronald D. Perrone, M.D., Holly B. Krasa, M.S., John Ouyang, Ph.D., and Frank S. Czerwiec, M.D., Ph.D., for the TEMPO 3:4 Trial Investigators*

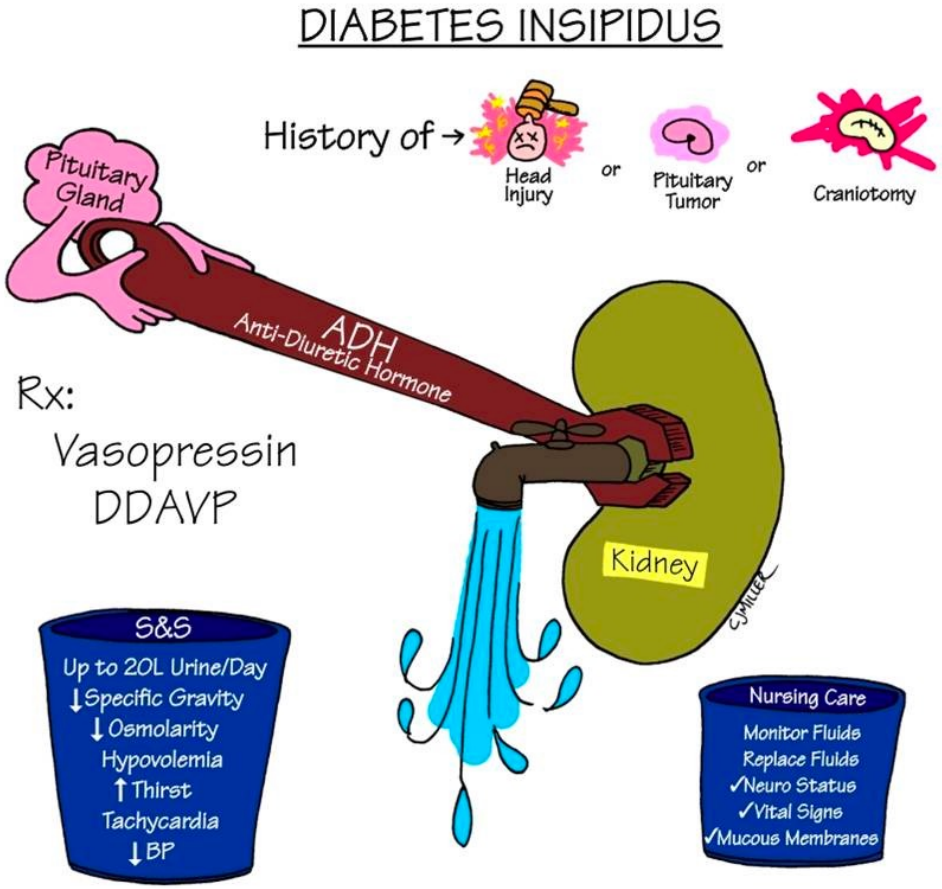
ORIGINAL ARTICLE

Tolvaptan in Later-Stage Autosomal Dominant Polycystic Kidney Disease

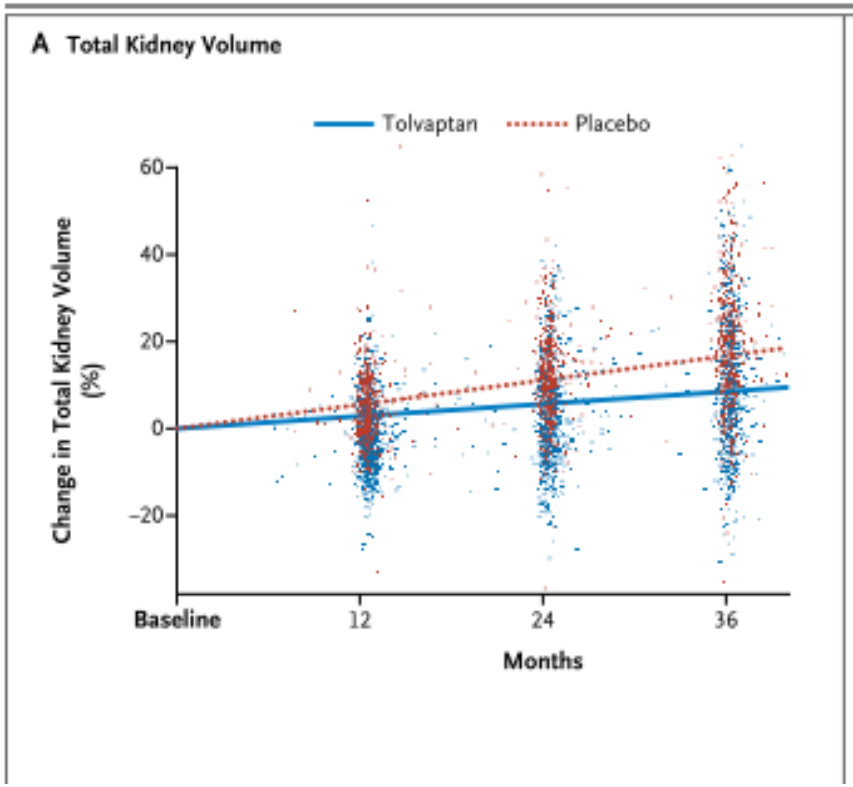
Vicente E. Torres, M.D., Ph.D., Arlene B. Chapman, M.D., Olivier Devuyst, M.D., Ph.D., Ron T. Gansevoort, M.D., Ph.D., Ronald D. Perrone, M.D., Gary Koch, Ph.D., John Ouyang, Ph.D., Robert D. McQuade, Ph.D., Jaime D. Blais, Ph.D., Frank S. Czerwiec, M.D., Ph.D., and Olga Sergeyeva, M.D., M.P.H., for the REPRISE Trial Investigators*

How tolvaptan (vasopressin 2 receptor antagonist) works





Results in early(earlier) stage patients

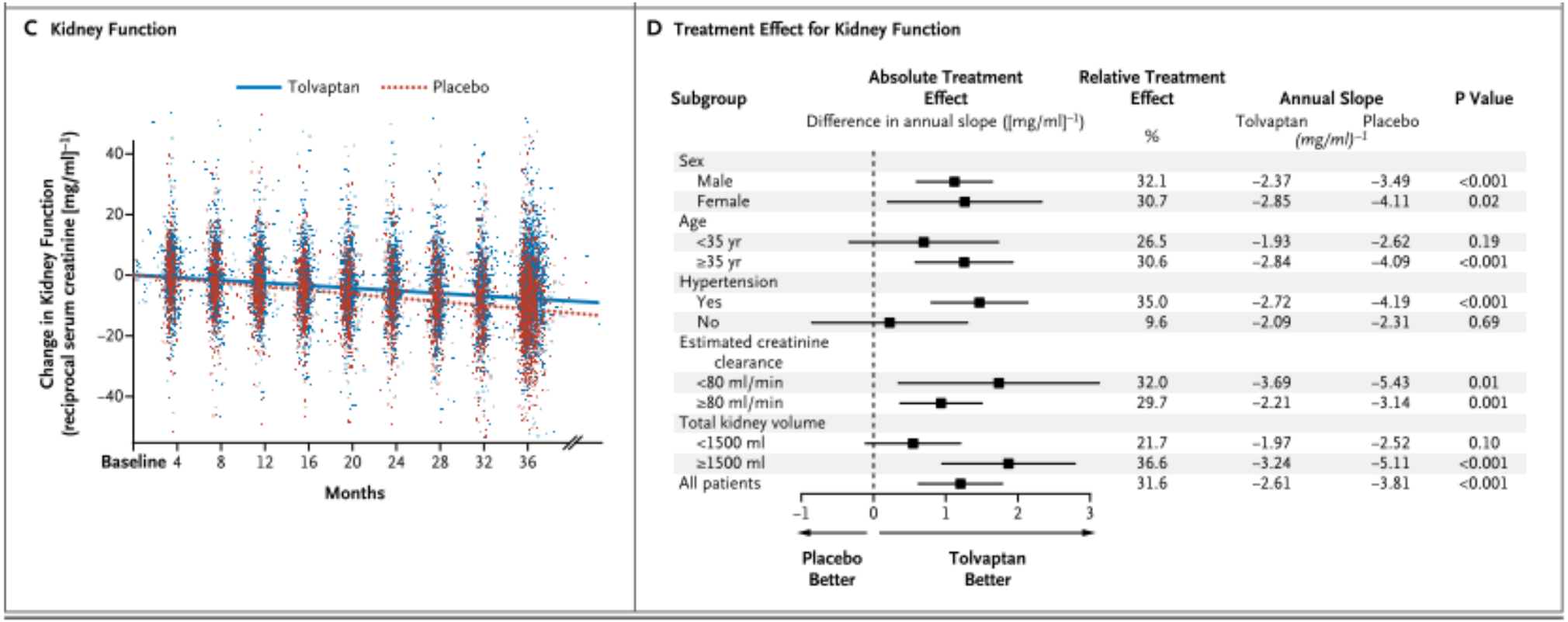


B Treatment Effect for Total Kidney Volume

Subgroup	Absolute Treatment Effect: Difference in annual slope (%/yr)	Relative Treatment Effect: %	Annual Slope: Tolvaptan %/yr	Annual Slope: Placebo %/yr	P Value
Sex					
Male		37.3	4.15	6.62	<0.001
Female		71.1	1.24	4.29	<0.001
Age					
<35 yr		28.0	4.37	6.06	0.02
≥35 yr		58.2	2.23	5.34	<0.001
Hypertension					
Yes		50.5	3.01	6.09	<0.001
No		51.2	1.62	3.32	0.008
Estimated creatinine clearance					
<80 ml/min		57.2	2.27	5.32	<0.001
≥80 ml/min		47.5	2.92	5.56	<0.001
Total kidney volume					
<1500 ml		48.8	2.24	4.37	<0.001
≥1500 ml		51.1	3.29	6.74	<0.001
All patients		49.2	2.80	5.51	<0.001

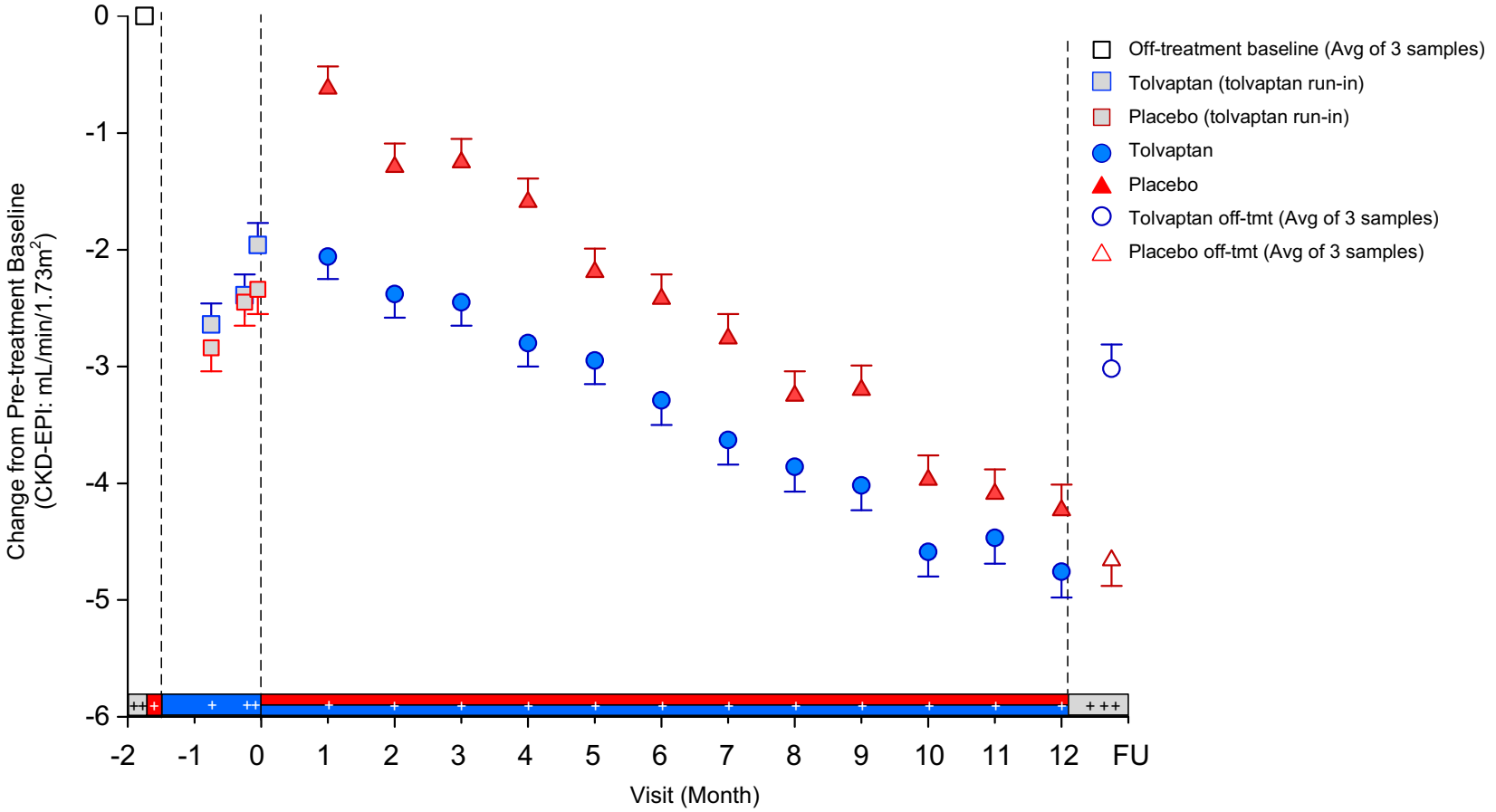
Increase in TKV was 2.8%/year(2.3-3.1%) in the tolvaptan group vs. 5.5%/year (5.1-6.0%) in the placebo group

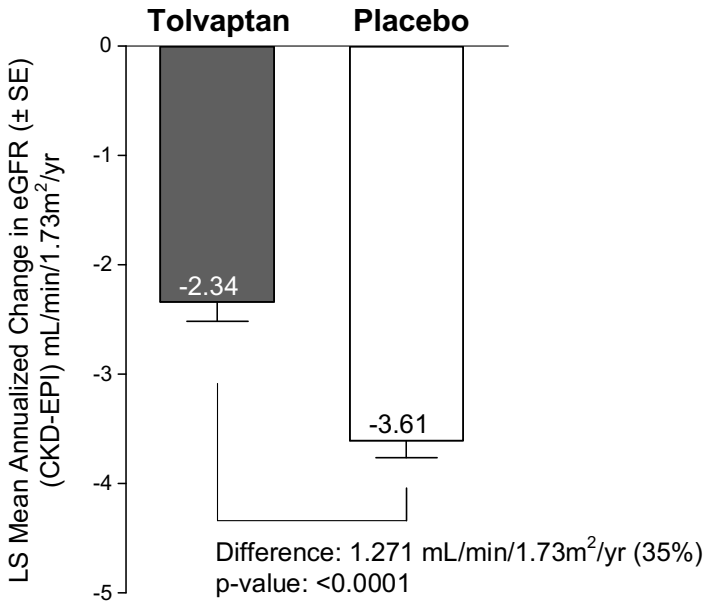
Results in early(earlier) stage patients



Slope of reciprocal of creatinine (which varies directly with GFR) was-2.61/year compared to -3.81/year in the placebo group. This corresponds to a GFR slope of -2.72ml/min/year vs. -3.70ml/min/year

Results in later stage patients



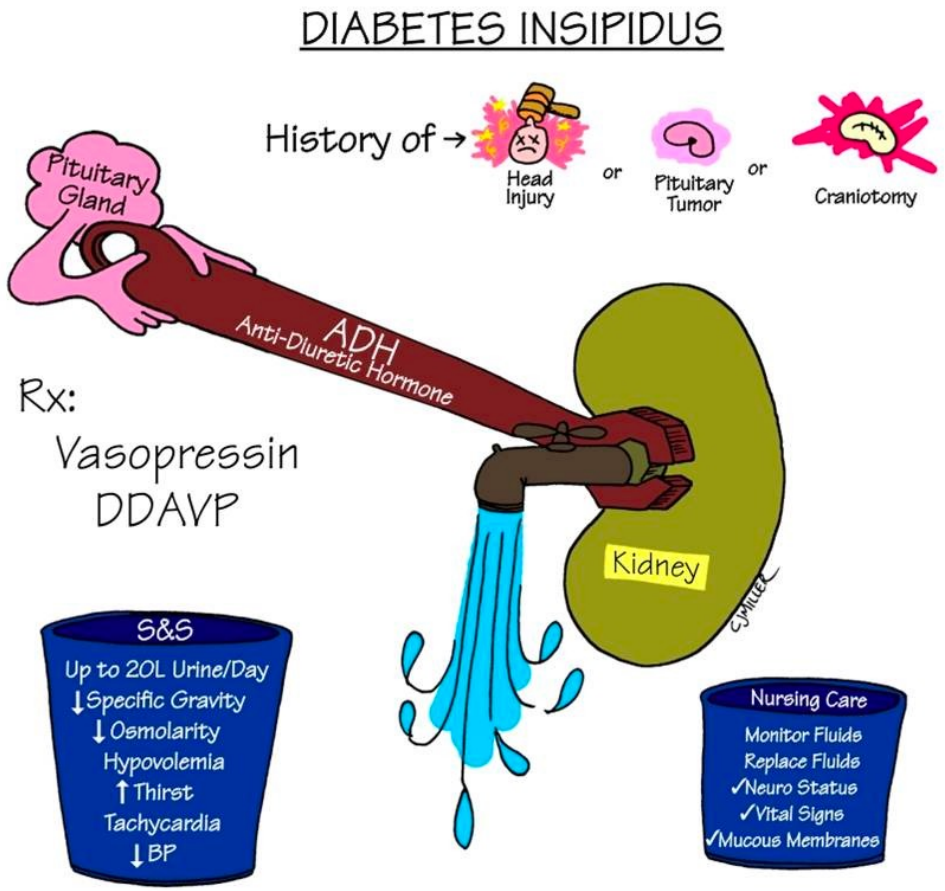


Adverse effects - aquaretic symptoms

This is a difficult drug for patients to work into their lives

It induces a different disease to slow the existing one

- There is a high rate of side effects and discontinuation



Dealing with aquaretic symptoms

- Judicious approach to dose titration
- Minimizing and distributing dietary solute intake (primarily salt and protein)
- Treat this like a ‘sick day’ medication - or more accurately, a ‘convenience day’ or ‘cheat day’ medication

Increased transaminases and need for monitoring

- Overall, there is a 4-5% rate of increased liver enzymes with tolvaptan

  To compare to other drugs associated with AST/ALT increases:
  - INH: up to 20%
  - MTX: 15%
  - Amiodarone: 3-6%
  - Lipitor: <2%

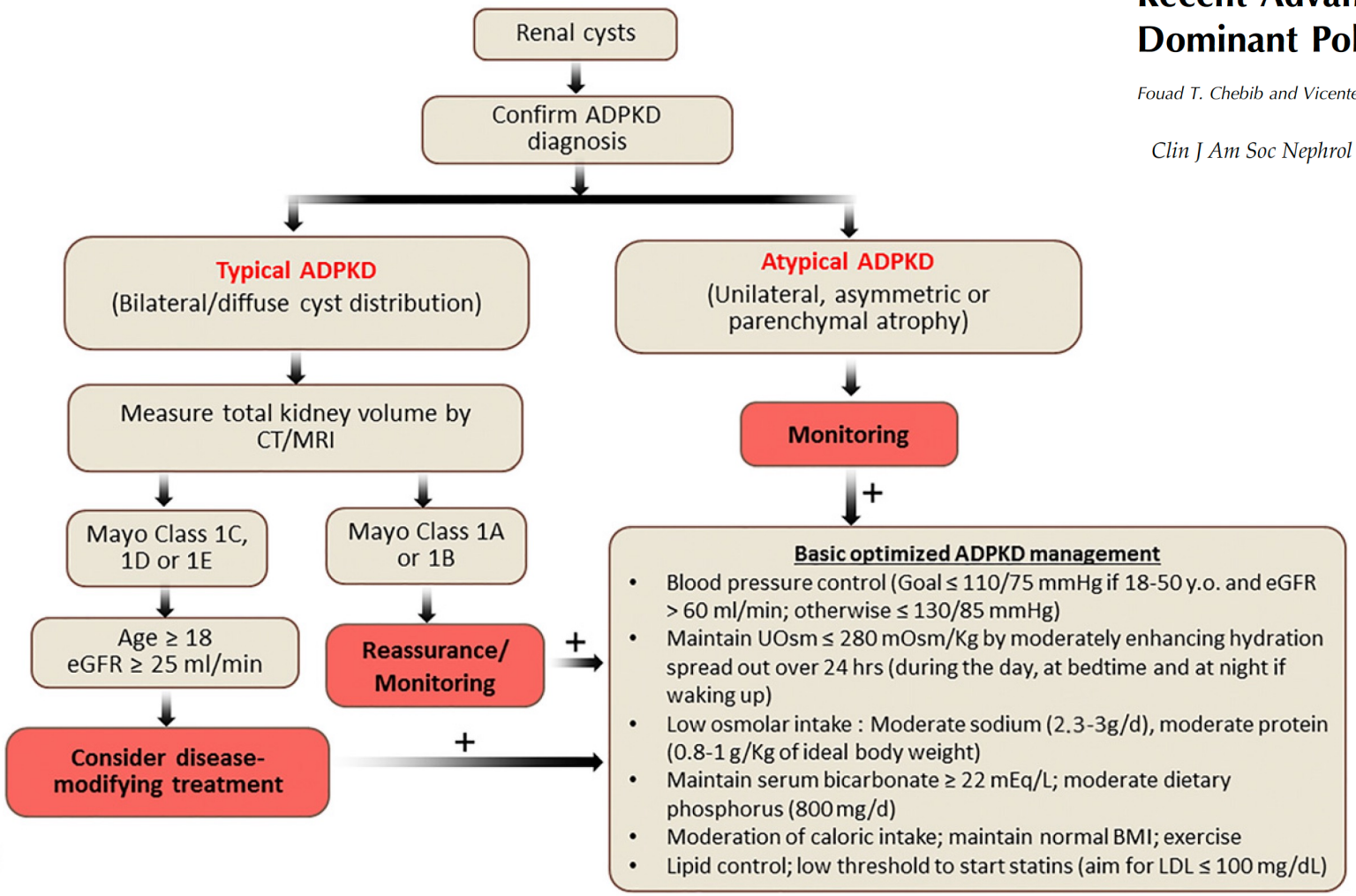
- But in the trials, 3 patients had AST/ALT >3xULN *and* bilirubin >2xULN.
  - Signal of much worse liver injury called **Hy's Law**

- The injury is reversible with drug discontinuation

- There is **mandatory** hepatic monitoring while on tolvaptan (monthly at first then q3 months)
- With this monitoring pathway, although there are incidents of transaminitis, there have been no Hy's Law patients in Canada

A new management paradigm for ADPKD

Targeted and non-target treatments



Recent Advances in the Management of Autosomal Dominant Polycystic Kidney Disease

Fouad T. Chebib and Vicente E. Torres

Clin J Am Soc Nephrol 13: ●●●–●●●, 2018. doi: https://doi.org/10.2215/CJN.03960318

MAYO CLINIC

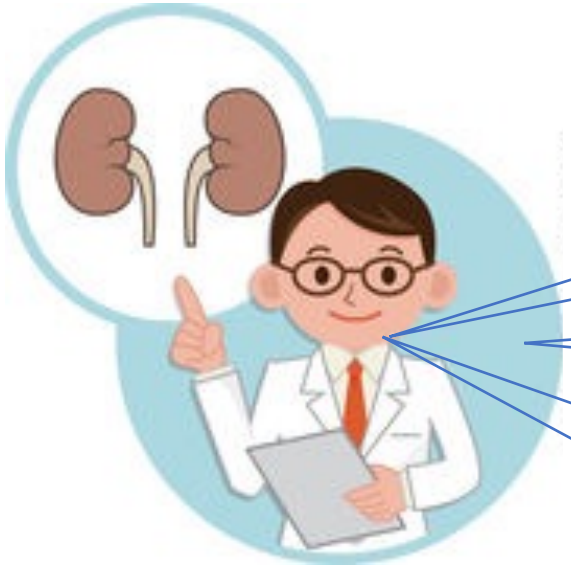
Table 2. Basic optimized management of adult patients with ADPKD

Intervention	Goal	Methods to Achieve Goal	Evidence[a]
Intensive BP control	≤110/75 mm Hg in: 1. 18–50-year-olds 2. eGFR>60 ml/min per 1.73 m^2 3. Particularly: Mayo Clinic class 1 C–E Intracranial aneurysm Valvular heart disease	Early detection is essential[b] By order of preference: 1. ACEI/ARB 2. α/β or cardioselective β-blocker 3. Dihydropyridine CCB 4. Diuretic Dietary Approaches to Stop Hypertension (DASH)-like diet at early stages	Grade 1B
	≤130/85 mm Hg in: 1. Other adult hypertensives		
Sodium	Moderate restriction (2.3–3 g/d) Adjust for extrarenal losses (hot climate, runners, sauna, bowel disease) if appropriate	Counseling Dietitian follow-up Monitor 24-h urine sodium	Grade 1C
Hydration	Moderately enhanced hydration spread out over 24 h (during the day, at bedtime, and at night if waking up) Maintain urine osmality ≤280 mOsm/kg	Counseling Monitor first morning urine osmality, plasma copeptin if available Water prescription(L)=$\frac{\text{24-hour urine solute load(mOsm)}}{280}$ + Insensible loss($\int$ 0.5 L)	Grade 1C
Protein	0.8–1.0 g/kg of ideal body wt	Dietitian Monitor protein intake: 6.25×(urine urea nitrogen in g/d+[0.03×weight in kilogram])	Grade 1C
Phosphorus	Moderate diet phosphate restriction (800 mg/d)	Dietician Read food labels and watch for food additives containing phosphates Use of phosphate binders not different from other advanced CKD when needed	Grade 2C
Acid base	Maintain plasma bicarbonate within the normal range (≥22 mEq/L)	Increase fruits/vegetables (2–4 cups/d) Oral sodium bicarbonate if needed	Grade 2B
Caloric intake	Maintain normal BMI Moderation in caloric intake	Dietitian follow-up Regular exercise	Grade 1C
Lipid control	Aim for serum LDL ≤100 mg/dl	Dietician Regular exercise Statin if needed (ezetimibe if intolerant to statin)	Grade 2B

ADPKD, autosomal dominant polycystic kidney disease; ACEI, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blockers; CCB, calcium channel blocker; BMI, body mass index.
[a]Grading of levels of evidence is provided in Supplemental Table 1.
[b]Screen children at risk every 3 years starting at age 5 years. Children with hypertension should be referred and managed by experts in pediatric hypertension.

A comprehensive approach to optimizing care for patients with ADPKD

What we have done with PKD in the past

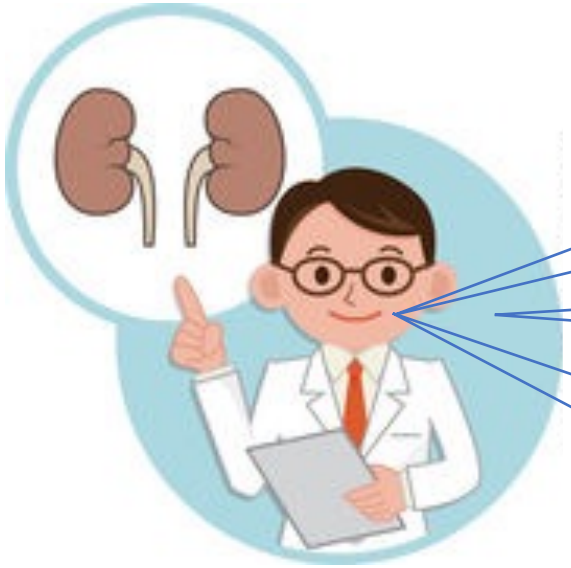


Let’s confirm the diagnosis and then we will tell you about screening your family members

Drink lots of water, keep your blood pressure in the normal range and do your bloodwork. See you back in 6-12 months.

When your GFR drops, we’ll start talking about transplant and dialysis

What we need to do with ADPKD now



Tell us what your family screening, reproductive, financial, symptom and renal failure concerns are and we will discuss those

We will use imaging and other tools to more accurately predict your renal progression

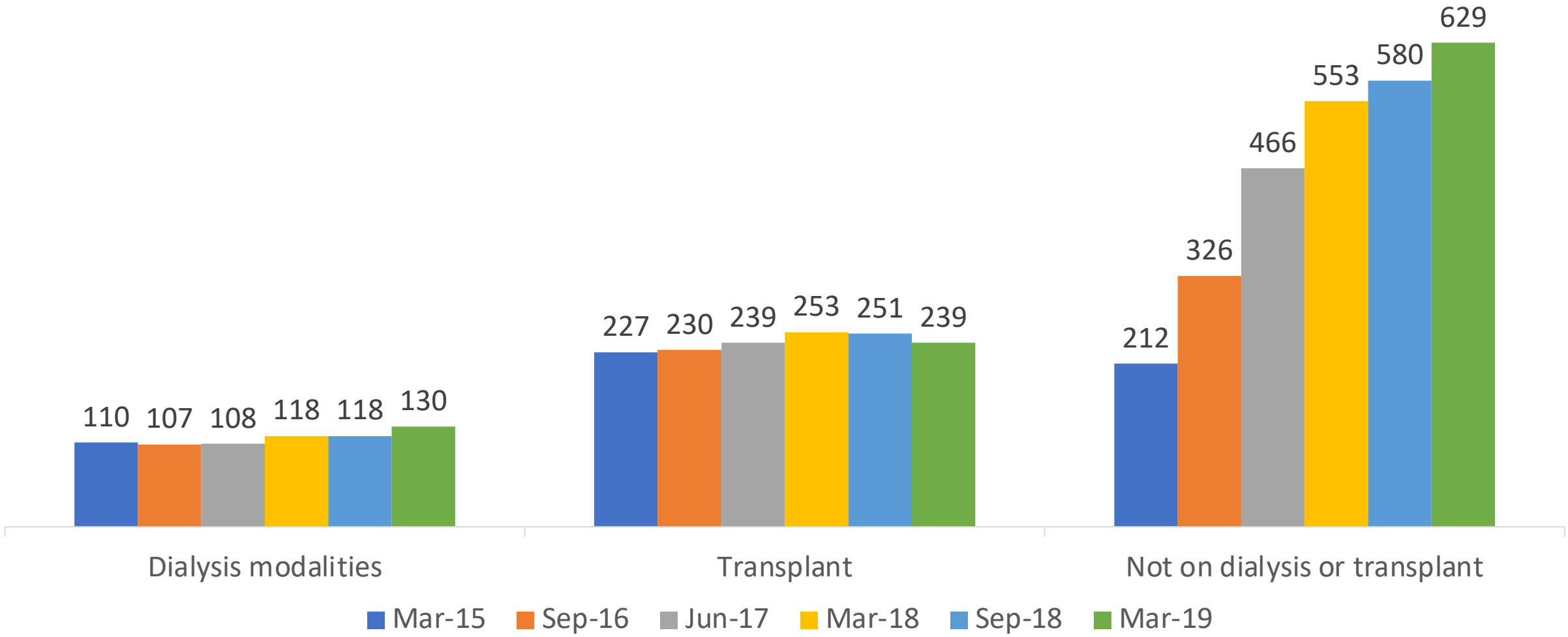
We will discuss conventional treatments like BP reduction that apply to everyone with PKD and will also assess whether you are a candidate for new disease specific treatments

Summary

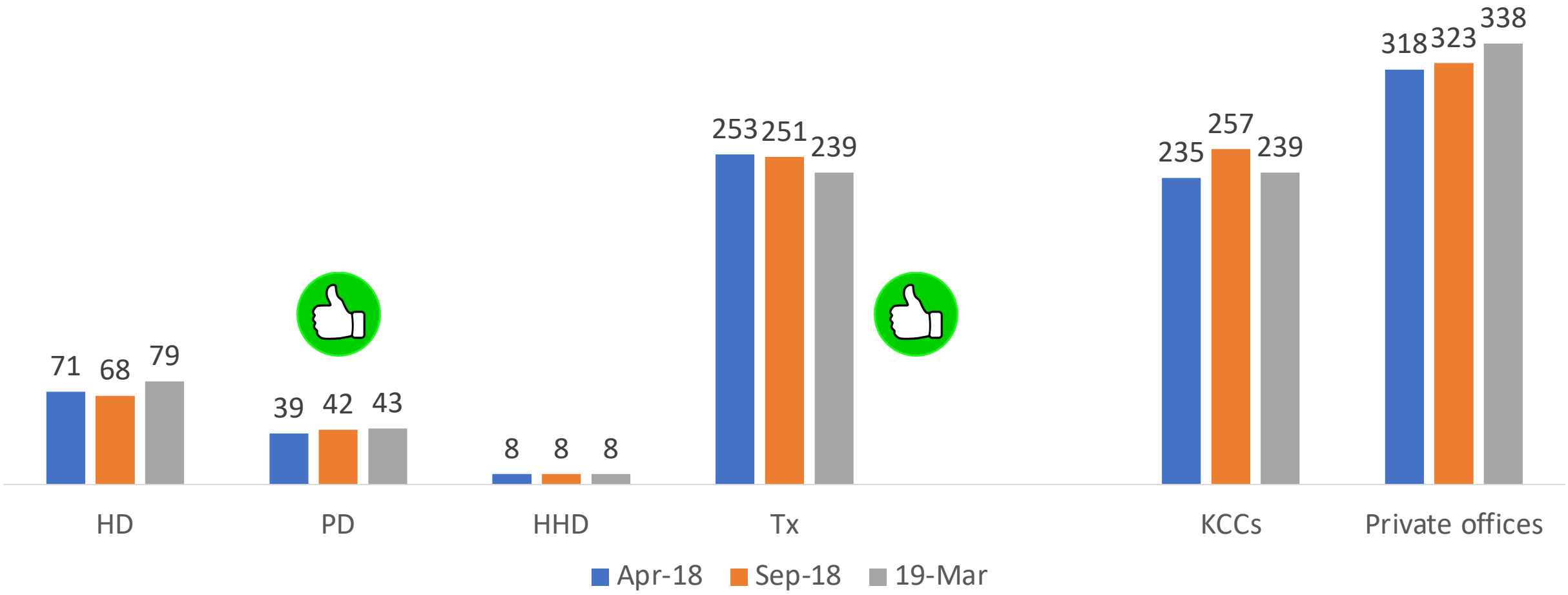
- Our understanding of ADPKD is evolving, new treatment strategies exist
- Modern management includes predicting risk of progression, tailoring treatments
- There are a host of management strategies encompassing many dimensions of care to consider in ADPKD

Current state of ADPKD in BC and moving to provincial best practices

PKD patients in BC that we know of (ADPKD registry)



Many are in KCC, more are not



Modern management of ADPKD aligns with goals of KCC

- Early identification and care
  - All documents (KCC best practices, ADPKD guidelines) suggest early referral
- Evaluation of risk of progression, implementation of tailored treatment strategies
- Interprofessional programs focusing on different aspects of the disease process and experience

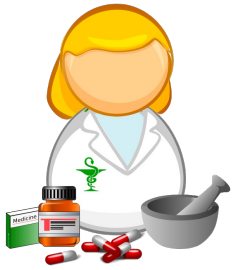


Table 2. Basic optimized management of adult patients with ADPKD

Intervention	Goal	Methods to Achieve Goal	Evidence[a]
Intensive BP control	≤110/75 mm Hg in: 1. 18–50-year-olds 2. eGFR>60 ml/min per 1.73 m^2 3. Particularly: Mayo Clinic class 1 C–E Intracranial aneurysm Valvular heart disease	Early detection is essential[b] By order of preference: 1. ACEI/ARB 2. α/β or cardioselective β-blocker 3. Dihydropyridine CCB 4. Diuretic Dietary Approaches to Stop Hypertension (DASH)-like diet at early stages	Grade 1B
	≤130/85 mm Hg in: 1. Other adult hypertensives		
Sodium	Moderate restriction (2.3–3 g/d)	Counseling	Grade 1C
	Adjust for extrarenal losses (hot climate, runners, sauna, bowel disease) if appropriate	Dietitian follow-up Monitor 24-h urine sodium	
Hydration	Moderately enhanced hydration spread out over 24 h (during the day, at bedtime, and at night if waking up)	Counseling	Grade 1C
	Maintain urine osmality ≤280 mOsm/kg	Monitor first morning urine osmality, plasma copeptin if available Water prescription(L) $= \frac{\text{24-hour urine solute load(mOsm)}}{280}$ + Insensible loss($\int$ 0.5 L)	
Protein	0.8–1.0 g/kg of ideal body wt	Dietitian Monitor protein intake: 6.25×(urine urea nitrogen in g/d+[0.03×weight in kilogram])	Grade 1C
Phosphorus	Moderate diet phosphate restriction (800 mg/d)	Dietician Read food labels and watch for food additives containing phosphates Use of phosphate binders not different from other advanced CKD when needed	Grade 2C
Acid base	Maintain plasma bicarbonate within the normal range (≥22 mEq/L)	Increase fruits/vegetables (2–4 cups/d) Oral sodium bicarbonate if needed	Grade 2B
Caloric intake	Maintain normal BMI Moderation in caloric intake	Dietitian follow-up Regular exercise	Grade 1C
Lipid control	Aim for serum LDL ≤100 mg/dl	Dietician Regular exercise Statin if needed (ezetimibe if intolerant to statin)	Grade 2B

ADPKD, autosomal dominant polycystic kidney disease; ACEI, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blockers; CCB, calcium channel blocker; BMI, body mass index.
[a]Grading of levels of evidence is provided in Supplemental Table 1.
[b]Screen children at risk every 3 years starting at age 5 years. Children with hypertension should be referred and managed by experts in pediatric hypertension.

Best Practices: Care of Patients with Autosomal Dominant Polycystic Kidney Disease in BC's Kidney Care Clinics

- Draft available for review and feedback here
- Huge amount of work done right here in BC
  - Working groups, subgroups and lots of work!!

Best Practices: Care of Patients with Autosomal Dominant Polycystic Kidney Disease in BC's Kidney Care Clinics

- Goal is a complement to existing best practices
- How to implement modern treatment strategies within the existing KCC
  - Best care, where patients receive their care
- Not a standalone document, not meant to be a standalone clinic

Best Practices: Care of Patients with Autosomal Dominant Polycystic Kidney Disease in BC's Kidney Care Clinics

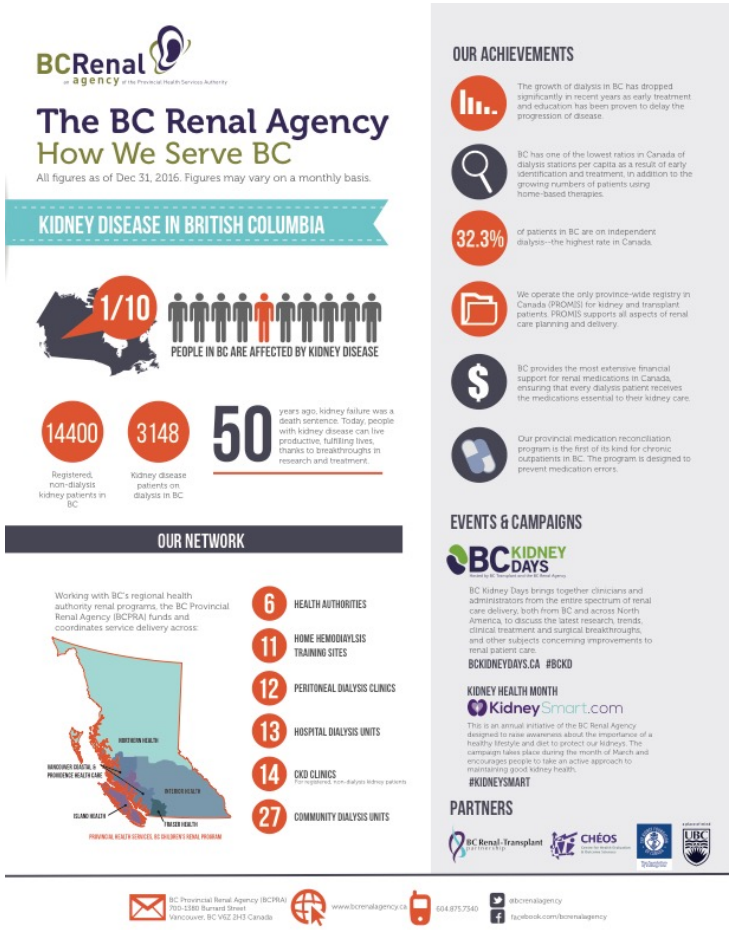
BEST PRACTICES:
KIDNEY CARE CLINICS

Guiding principle # 1

Not a substitute for existing best practices

- Goal is a complement to existing best practices
- Not a standalone document, not meant to be a standalone clinic
- Think of this as a 'add-on' to core services to allow a treatment stream for specific patients

Best Practices: Care of Patients with Autosomal Dominant Polycystic Kidney Disease in BC's Kidney Care Clinics



Guiding principle # 2

Best practices, close to home

- How to implement modern treatment strategies within the existing KCC
  - Best care, where patients receive their care
- Aim is to foster a Network of PKD clinicians and services
- Focus on utilizing resources that are already locally available

Goals

Goals for KCC patients with ADPKD

KCCs work collaboratively with patients with ***rapidly progressing ADPKD and/or a high burden of symptoms or complications*** and their families to provide evidence-based, interprofessional care which aims includes:

1. Early identification and accurate diagnosis and prognostication of kidney outcomes and disease trajectory.
2. Selection of appropriate ADPKD management and treatment strategies throughout a patient's disease course.
3. Screening for complications, monitoring and managing symptoms and treatment of comorbidities.
4. Attention to the unique implications of inherited kidney disease that has impacts on multiple generations as well as a patient's current or future family planning.
5. Support for planning and preparation for management of later stage CKD as outlined for all other CKD patients.
6. Focusing on empowering patients and families throughout these steps to maximize active participation in care plans and disease self-management.

Contents

Best Practices: Care of Patients with Autosomal Dominant Polycystic Kidney Disease in BC's Kidney Care Clinics

Contents

This paper is a supplement to the ***Best Practices: Kidney Care Clinics*** document developed by BC's Kidney Care Clinic Committee and available at: http://www.bcrenalagency.ca/resource-gallery/Documents/Best%20Practices-%20Kidney%20Care%20Clinic_0.pdf

- Intentionally mirrors KCC Best Practices
- Key areas of difference are highlighted
- We will go through an overview of content a little later on

Summary

- The KCC framework is well suited to meet the specific needs of ADPKD
  - Some core services are the same, others are tailored to ADPKD
- The goal is empowering local KCCs to deliver best ADPKD care as part of a provincial network of clinicians
- There are many new tools to help support this, created in BC
  - Please provide feedback!

Questions/comments

ADPKD tools developed for BC KCCs

Best practices document and associated tools

Best practices content: Patient population

3.0 Referral of patients with ADPKD to KCC and repatriation to primary care

Because the majority of concepts described in the *Best Practices: Kidney Care Clinics* document also apply to ADPKD patients, the next sections focus on **variations in practice specific to the care of ADKD patients.**

3.1 Referral criteria

While the management strategies contained in this document are applicable to all patients with ADPKD, the patients mostly likely to benefit from the interdisciplinary expertise available within Kidney Care Clinics include:

- Patients with rapidly progressing ADPKD
- Patients with a high burden of symptoms or complications
- Patients with treatments that require more intensive monitoring and support (e.g., vasopressin antagonism)
- Any other ADPKD patients whose clinicians expect would benefit from the interdisciplinary environment and approach of the KCC

Best practices content : Assessment, education, planning

5.2.3 KCC team assessment, education, goal-setting & treatment planning

Refer to *Best Practices: Kidney Care Clinics* document for a general overview of assessment, education, goal-setting and treatment planning. Most of these concepts also apply to ADPKD patients. The focus of this section is on **additional considerations specific to ADPKD and its management.**

KCC team assessment and education

In addition to the general topics covered in *Best Practices: Kidney Care Clinics,* the following ADPKD specific topics are suggested:

- Disease specific education about the ADPKD disease process and its management. This is facilitated by the provision of ADPKD-specific materials at the orientation visit (section 5.2.2).
- An ADPKD specific educational needs assessment (as part of the initial assessment - LINK). In addition to general knowledge and self-management, this needs assessment covers the additional domains of understanding of the ADPKD disease process, specific management options and genetic/family planning implications.

Add HA/Hospital Logo	Add Label/Addressograph
Kidney Care Clinic: Learning Needs Questionnaire for New Patients with ADPKD	
Form #: xxxxxx | Rev: Jun 2019 | Page 1/2	

To help us know what you would like to learn more about, please tell us what you know now by putting a check mark (✓) in the box that best describes you.

	I do not know much about this	I know something about this but would like to know more	I understand this very well	This does not apply to me
Polycystic Kidney Disease (PKD) and how it affects me				
Blood tests and what they mean for me				
Blood pressure and kidney care				
Diabetes and kidney care				
Resources to self-manage my care				
Diet measures to protect my kidneys				
Stress and coping with kidney disease				
Lifestyle changes necessary for kidney health				
How will PKD affect my work				
How will PKD affect my family				
Concerns about having children related to PKD and kidney disease				

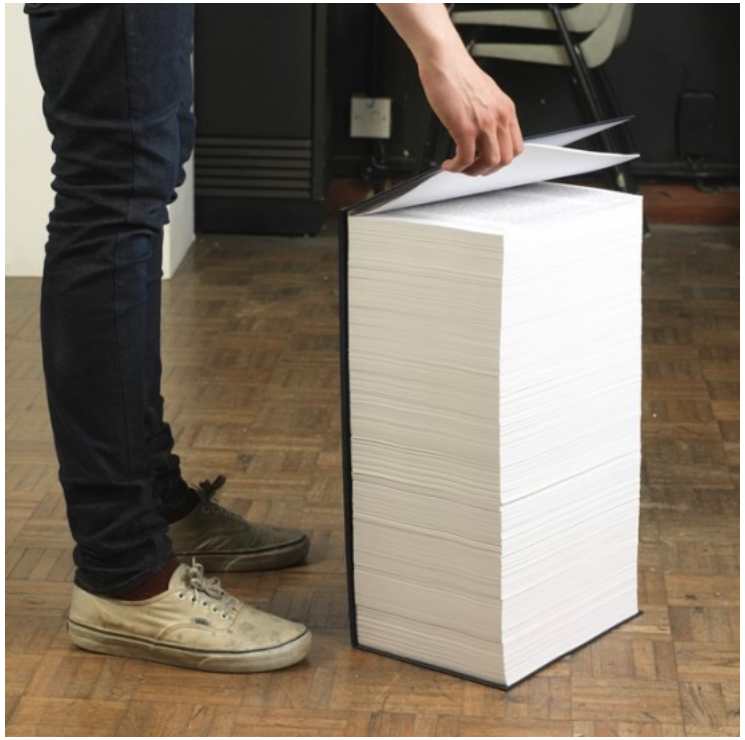
Please turn over the page ➔

Best practices content : Imaging, genetics, screening for complications, family screening

Guidance on:

- Renal imaging
  - Choice, frequency of tests
- Genetic testing
- Screening of family members
- Screening for complications
  - ICAs
  - Other extra-renal complications

5.2.4.2 Renal Imaging, Genetic Testing and Screening for Patients with ADPKD



Not meant to replace clinical judgement/individual decision making, but guidance for those unfamiliar with these items

Best practices content : pharmacologic management

Lipid management in ADPKD

For a more detailed review, refer to *Supporting evidence: lipid-lowering therapy in patients with ADPKD* (LINK).

Blood pressure management in ADPKD

For a more detailed review, refer to *Supporting evidence: blood pressure targets in patients with ADPKD* (LINK) and *Supporting evidence: antihypertensive agents in patients with ADPKD* (LINK).

5.2.4.3 Treatment protocols/guidelines for patients with ADPKD

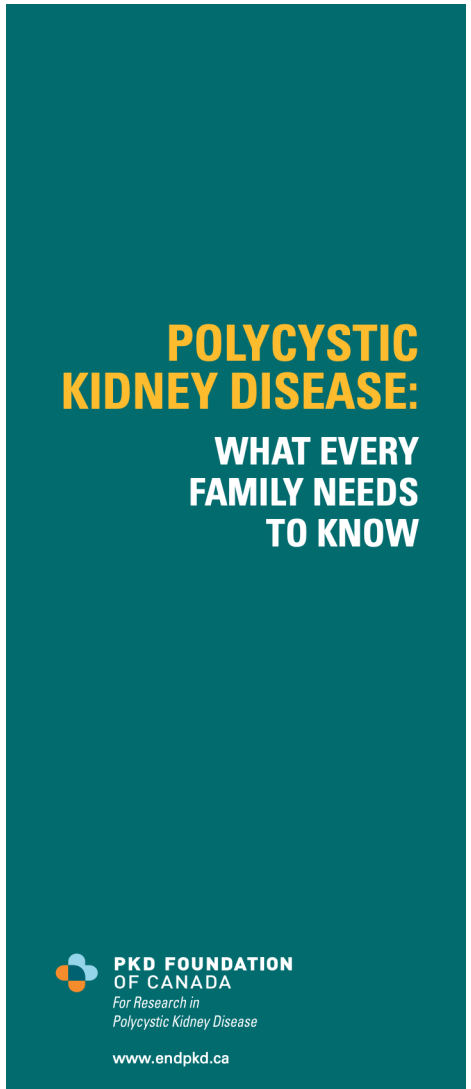
Treatment with tolvaptan

Application for tolvaptan treatment in ADPKD

TOLVAPTAN
FREQUENTLY ASKED QUESTIONS (FOR PATIENTS) BCRenal an agency of the Provincial Health Services Authority

TOLVAPTAN
FREQUENTLY ASKED QUESTIONS (FOR PRESCRIBERS) BCRenal an agency of the Provincial Health Services Authority

Patient/family information



Diet: staff and patient resources

Staff Guide: Dietary Recommendations for Patients with Autosomal Dominant Polycystic Kidney Disease (ADPKD)

BCRenal
Provincial Health Services Authority

This teaching sheet is intended as a reference sheet for staff working in a BC Kidney Care Clinic.

Fluid

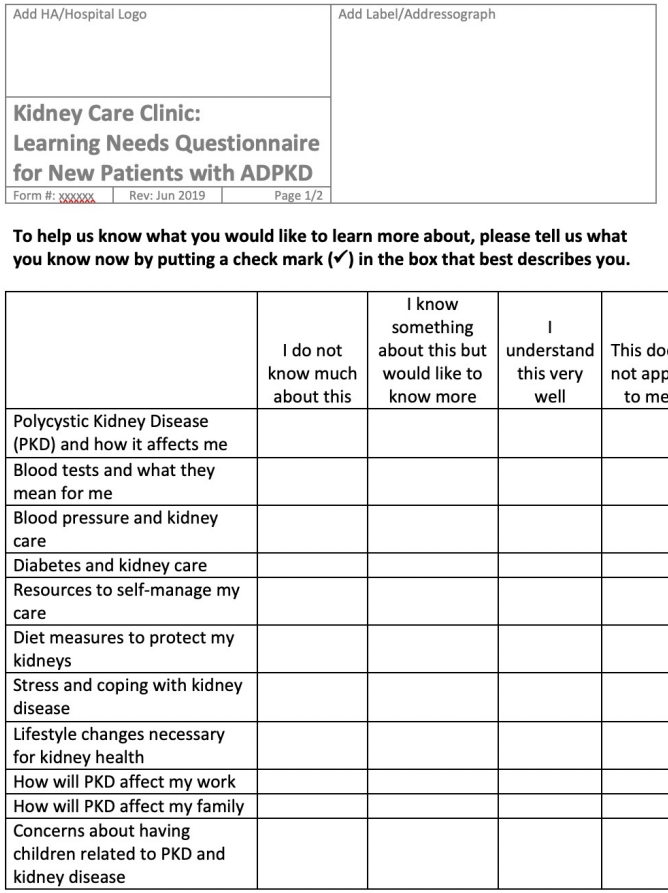
- Increased water intake has the potential to slow cyst formation by limiting cellular proliferation and transepithelial fluid secretion
- Goal is to lower urine osmolarity to reduce antidiuretic system
- Water prescription needed to lower urine osmolarity will be in relation to solute intake of meals (sodium, protein). As patients reduce solute intake (especially sodium), they should not need as high water intake and therefore, have reduced urination
- Water prescription is individual, however, in general it is suggested that 3-4L of water per day efficiently and safely lowers serum vasopressin
- Need to drink water evenly over the period of waking hours to have desired effect to suppress ADH. Patients need to drink through the night and drink a glass of water when waking to urinate to keep vasopressin levels low .
- Important to drink water with meals to limit release of vasopressin in response to sodium intake
- Water should be first choice, but other sugar-free, caffeine-free, low-sodium drinks can be acceptable
- Alcohol has an unknown effect on cyst growth. However, alcohol is known to increase blood pressure and should be limited to moderate amounts (1-2 drinks/day)
- Goal is to maintain urine osmolarity of < 280 mOsm/L

Sodium

- ADPKD = sodium-sensitive hypertension
- High sodium intake is associated with the release of vasopressin and therefore impacts the growth of cysts
- Recommendation 2300mg/day
- For patients on Tolvaptan therapy, a 24 hour urine collection can help to evaluate sodium intake

Protein

ADPKD patient learning needs



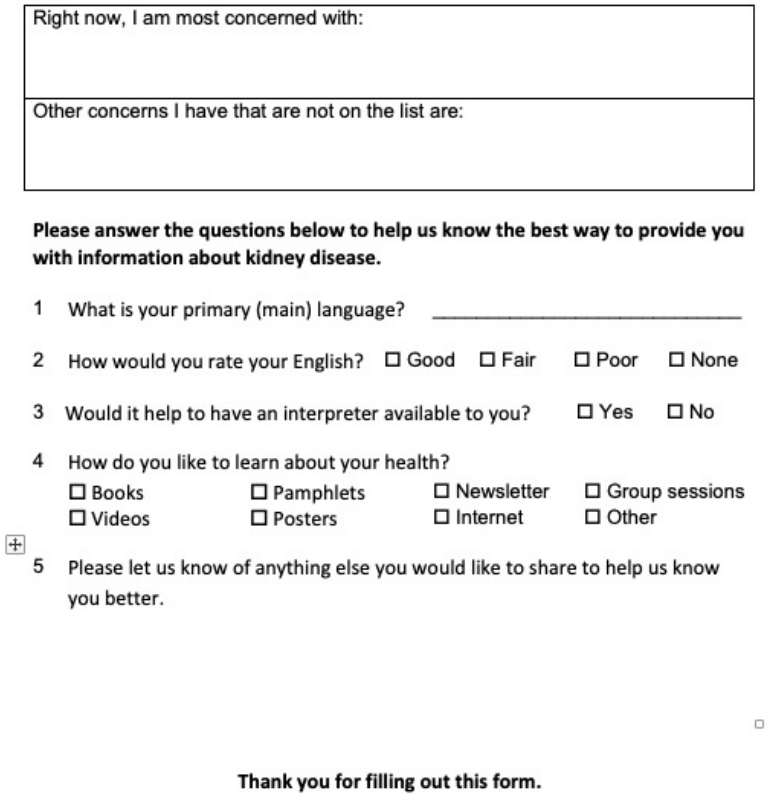
Add HA/Hospital Logo	Add Label/Addressograph
Kidney Care Clinic: Learning Needs Questionnaire for New Patients with ADPKD	
Form #: xxxxxx | Rev: Jun 2019 | Page 1/2	

To help us know what you would like to learn more about, please tell us what you know now by putting a check mark (✓) in the box that best describes you.

	I do not know much about this	I know something about this but would like to know more	I understand this very well	This does not apply to me
Polycystic Kidney Disease (PKD) and how it affects me				
Blood tests and what they mean for me				
Blood pressure and kidney care				
Diabetes and kidney care				
Resources to self-manage my care				
Diet measures to protect my kidneys				
Stress and coping with kidney disease				
Lifestyle changes necessary for kidney health				
How will PKD affect my work				
How will PKD affect my family				
Concerns about having children related to PKD and kidney disease				

Please turn over the page ➔

DRAFT June 4, 2019 1



Right now, I am most concerned with:

Other concerns I have that are not on the list are:

Please answer the questions below to help us know the best way to provide you with information about kidney disease.

1 What is your primary (main) language? _____

2 How would you rate your English? ☐ Good ☐ Fair ☐ Poor ☐ None

3 Would it help to have an interpreter available to you? ☐ Yes ☐ No

4 How do you like to learn about your health?

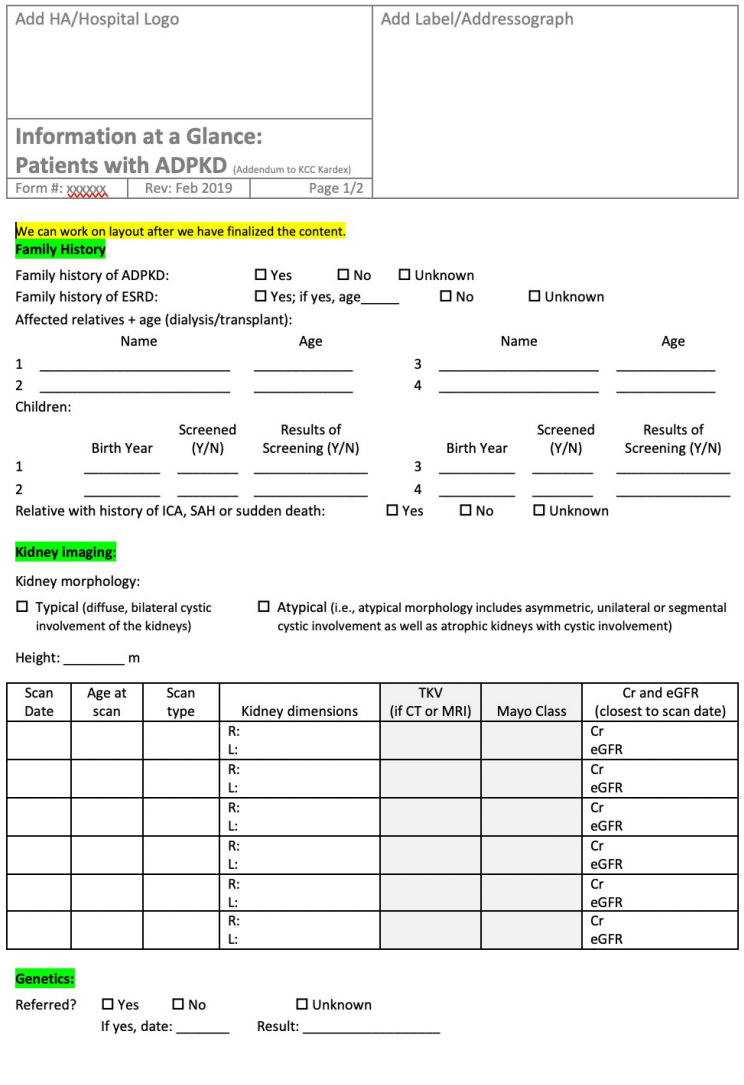
☐ Books ☐ Pamphlets ☐ Newsletter ☐ Group sessions
☐ Videos ☐ Posters ☐ Internet ☐ Other

5 Please let us know of anything else you would like to share to help us know you better.

Thank you for filling out this form.

- An initial needs assessment
- Will likely serve an ongoing evaluation role as well

ADPKD information at a glance



Add HA/Hospital Logo | Add Label/Addressograph

Information at a Glance: Patients with ADPKD (Addendum to KCC Kardex)

Form #: xxxxxx | Rev: Feb 2019 | Page 1/2

We can work on layout after we have finalized the content.

Family History

Family history of ADPKD: ☐ Yes ☐ No ☐ Unknown

Family history of ESRD: ☐ Yes; if yes, age____ ☐ No ☐ Unknown

Affected relatives + age (dialysis/transplant):

	Name	Age		Name	Age
1			3		
2			4		

Children:

	Birth Year	Screened (Y/N)	Results of Screening (Y/N)		Birth Year	Screened (Y/N)	Results of Screening (Y/N)
1				3			
2				4			

Relative with history of ICA, SAH or sudden death: ☐ Yes ☐ No ☐ Unknown

Kidney imaging:

Kidney morphology:

☐ Typical (diffuse, bilateral cystic involvement of the kidneys)

☐ Atypical (i.e., atypical morphology includes asymmetric, unilateral or segmental cystic involvement as well as atrophic kidneys with cystic involvement)

Height: _____ m

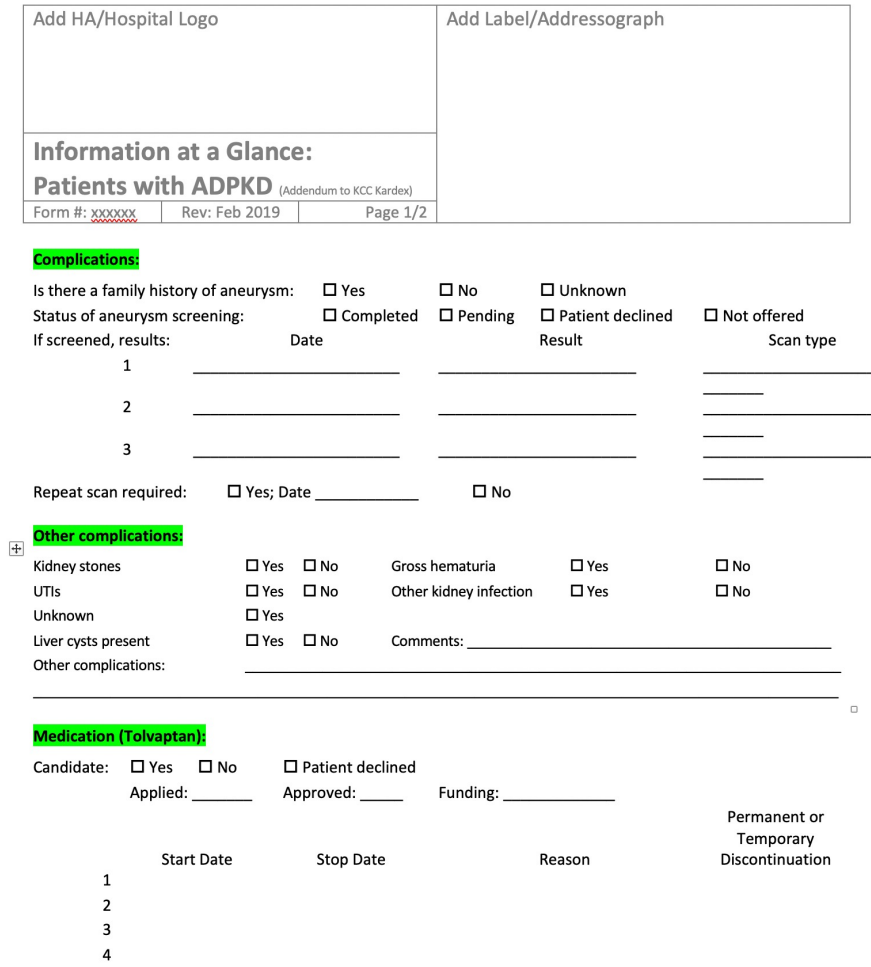
Scan Date	Age at scan	Scan type	Kidney dimensions	TKV (if CT or MRI)	Mayo Class	Cr and eGFR (closest to scan date)
			R: L:			Cr eGFR
			R: L:			Cr eGFR
			R: L:			Cr eGFR
			R: L:			Cr eGFR
			R: L:			Cr eGFR
			R: L:			Cr eGFR

Genetics:

Referred? ☐ Yes ☐ No ☐ Unknown

If yes, date: _____ Result: _____

DRAFT Mar 7, 2019 Page 1



Add HA/Hospital Logo | Add Label/Addressograph

Information at a Glance: Patients with ADPKD (Addendum to KCC Kardex)

Form #: xxxxxx | Rev: Feb 2019 | Page 1/2

Complications:

Is there a family history of aneurysm: ☐ Yes ☐ No ☐ Unknown

Status of aneurysm screening: ☐ Completed ☐ Pending ☐ Patient declined ☐ Not offered

If screened, results:	Date	Result	Scan type
1			
2			
3			

Repeat scan required: ☐ Yes; Date _____ ☐ No

Other complications:

Kidney stones	☐ Yes	☐ No	Gross hematuria	☐ Yes	☐ No
UTIs	☐ Yes	☐ No	Other kidney infection	☐ Yes	☐ No
Unknown	☐ Yes				
Liver cysts present	☐ Yes	☐ No	Comments: _____		

Other complications: _____

Medication (Tolvaptan):

Candidate: ☐ Yes ☐ No ☐ Patient declined

Applied: _____ Approved: _____ Funding: _____

	Start Date	Stop Date	Reason	Permanent or Temporary Discontinuation
1				
2				
3				
4				

Will not replace existing Kardex

A place to collect ‘bigger picture’ PKD related care planning

ADPKD Clinic worksheet

Add HA/Hospital Logo	Add Label/Addressograph
Clinic Visit Form for Patients with ADPKD (Kidney Care Clinic)	
Form #: xxxxxx | Rev: Feb 2019 | Page 1/2	

Will work on layout after we have finalized the content. Will set up as front and back of page so only need label on front page.

Visit date: _____

BP sitting: _____ BP standing: _____ BP at home: _____ BP target: _____
Current weight: _____ Weight at previous clinic visit: _____

Tolvaptan: ☐ Yes ☐ No
If yes, date started: _____ Dose: _____

Current Symptoms and Recent Events

- ☐ Thirst
- ☐ Nocturia
- ☐ Decreased appetite
- ☐ Fullness/early satiety
- ☐ Bloating
- ☐ Constipation
- ☐ Diarrhea
- ☐ Kidney/flank pain
- ☐ Hematuria
- ☐ UTI/Other kidney infection
- ☐ Kidney stones
- ☐ Nausea
- ☐ Vomiting
- ☐ Headache
- ☐ Fatigue or weakness
- ☐ Dizziness
- ☐ Shortness of breath
- ☐ Sleep disturbance
- ☐ Other: _____
- ☐ None

Nurse:

Dietitian: Results of most recent 24 hour urine collection: Na: _____ mmol/day Protein: _____ gm/day

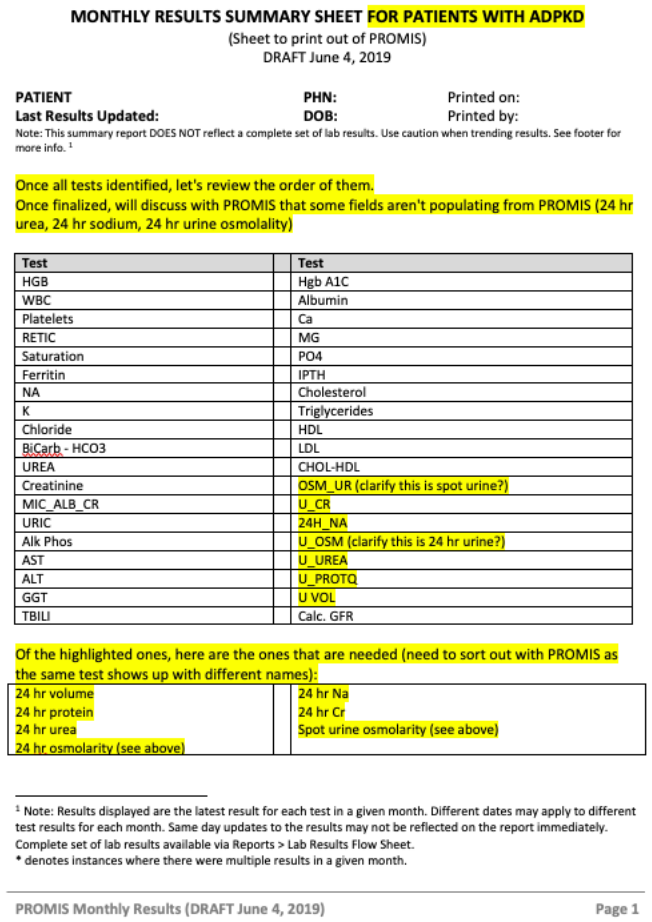
Social Worker:

Pharmacist:

Physician:

Comments/plans:

ADPKD Promis flowsheet and lab forms



MONTHLY RESULTS SUMMARY SHEET FOR PATIENTS WITH ADPKD

(Sheet to print out of PROMIS)
DRAFT June 4, 2019

PATIENT **PHN:** Printed on:
Last Results Updated: **DOB:** Printed by:

Note: This summary report DOES NOT reflect a complete set of lab results. Use caution when trending results. See footer for more info. [1]

Once all tests identified, let's review the order of them.
Once finalized, will discuss with PROMIS that some fields aren't populating from PROMIS (24 hr urea, 24 hr sodium, 24 hr urine osmolality)

Test		Test
HGB		Hgb A1C
WBC		Albumin
Platelets		Ca
RETIC		MG
Saturation		PO4
Ferritin		IPTH
NA		Cholesterol
K		Triglycerides
Chloride		HDL
BiCarb - HCO3		LDL
UREA		CHOL-HDL
Creatinine		OSM_UR (clarify this is spot urine?)
MIC_ALB_CR		U_CR
URIC		24H_NA
Alk Phos		U_OSM (clarify this is 24 hr urine?)
AST		U_UREA
ALT		U_PROTQ
GGT		U VOL
TBILI		Calc. GFR

Of the highlighted ones, here are the ones that are needed (need to sort out with PROMIS as the same test shows up with different names):

24 hr volume 24 hr protein 24 hr urea 24 hr osmolarity (see above)		24 hr Na 24 hr Cr Spot urine osmolarity (see above)

[1] Note: Results displayed are the latest result for each test in a given month. Different dates may apply to different test results for each month. Same day updates to the results may not be reflected on the report immediately. Complete set of lab results available via Reports > Lab Results Flow Sheet.
* denotes instances where there were multiple results in a given month.

PROMIS Monthly Results (DRAFT June 4, 2019) Page 1

- Still under development
- PROMIS updates
- Provincial lab req update

Staff resources: pharmacologic management

Application for tolvaptan treatment in ADPKD

- Ensure the patient is registered in PROMIS, with a diagnosis of ADPKD
- Complete the information below, fax this form along with the PPAF/Tolvaptan consent for monitoring and any supporting documentation (e.g., imaging reports) to XXXXX

The following information is required for approval:

*Confirmed diagnosis of ADPKD: Yes____ No____
Tolvaptan is only indicated for use in ADPKD and not in any other renal cystic disease

Current patient characteristics

*Current Age_____ years DOB___/____/_____

*Most recent BP___/_____ mmHg

Imaging

To interpret these results please provide confirmation of typical morphology of ADPKD ***and*** renal sizes. 'Typical morphology' is defined as diffuse, bilateral cystic involvement of the kidneys (i.e., not atypical morphology which includes asymmetric, unilateral or segmental cystic involvement)

*Typical morphology? Yes ____No ____ Unknown_____

Current renal size - At least one of these measurements must be included. If both are available, include TKV. *Please attach a copy of the imaging report along with this application.*

Ultrasound kidney length: R_____cm L_____cm Date_____

TKV _____mL_____ Date _____

If TKV is included, record patient height_____ cm Mayo Class (if known) _____

Evidence of disease progression

Demonstration of disease progression may assist with determining candidacy; this would include evidence of GFR decline or rapidly increasing kidney volume over the course of the last ≥2 years

Historical renal size – provide values at least 1 year apart to determine rate of growth

Previous TKV _____ Date _____
Previous TKV _____ Date _____
Previous TKV _____ Date _____

GFR – Please provide values approximately 1 year apart rather than just the 3 most recent values to determine annual decline

*Current GFR_____ mL/min/1.73m^2 *Date _____
Previous GFR_____ mL/min/1.73m^2 Date _____
Previous GFR_____ mL/min/1.73m^2 Date _____

Please list any other clinical criteria not listed above that may impact patient's candidacy:

Please attach all supporting documents along with this application
*Indicates Mandatory fields

Application for tolvaptan treatment in ADPKD

Criteria for tolvaptan use in ADPKD

Potential candidates for treatment with tolvaptan are those with ADPKD and more rapidly progressing disease. These criteria are based on evidence from clinical trials[1,2], and the *Updated Canadian Expert Consensus on Assessing Risk of Disease Progression and Pharmacological Management of Autosomal Dominant Polycystic Kidney Disease*[3].

Please indicate which group (**A, B or C**) best reflects your patient's characteristics, as well as which criteria within that group are met

☐ **Group A:** Patients 18-55 years old who are similar to those in clinical trials[1,2]:

eGFR >25 mL/min/1.73 m2 AND Evidence of renal enlargement
Renal enlargement can be documented as any of:
- ☐ TKV >750 mL in those with eGFR >45 mL/min/1.73m2
- ☐ Ultrasound kidney length >16.5 cm bilaterally in those with eGFR > 45 mL/min/1.73 m2, if TKV is not available
- ☐ Class 1C, 1D or 1E on the Mayo Clinic Classification

Although not a criterion in the REPRISE trials, documentation of renal enlargement has been included here as a criterion. In those patients with advanced or rapidly progressive CKD without enlarged kidneys, an alternate diagnosis for CKD should be investigated.

☐ **Group B:** Patients 55-65 years old who would have met criteria for the REPRISE trial[2], and who also have evidence of rapid disease progression. **All three** of these criteria must be met:
- ☐ eGFR of 25 to 44 mL/min/1.73 m2
  AND
- ☐ Historical evidence of a decline in eGFR >2.0 mL/min/1.73 m2/year
  AND
- ☐ Class 1D or 1E on the Mayo Clinic Classification

Although not a criterion in the REPRISE trial, documentation of renal enlargement has been included here as a criterion to ensure that only the more rapidly progressing patients are chosen for tolvaptan treatment. In those patients with advanced or rapidly progressive CKD without enlarged kidneys, an alternate diagnosis for CKD should be investigated.

☐ **Group C:** Patients 18-65 years of age with eGFR ≥25 mL/min/1.73 m2 who do not otherwise fit into the trial criteria may also be considered if they display other markers of rapid disease progression, such as:
- ☐ Annual decrease in eGFR of >2.5 mL/min/1.73 m2 and alternate CKD diagnoses have been excluded
- ☐ Increase in TKV of >5% per year.
- ☐ Mayo Clinic Classification groups 1D or 1E
- ☐ PKD 1 protein truncating mutation
- ☐ Classified as high risk via the PROPKD risk score (7-9 points)
- ☐ Consideration can be given to patients with high symptom burden related to renal expansion but this alone is not generally an indication for treatment. Symptom burden should be considered in addition to other clinical criteria

1 Torres VE, Chapman AB, Devuyst O, Gansevoort RT, Grantham JJ, Higashihara E, et al. Tolvaptan in Patients with Autosomal Dominant Polycystic Kidney Disease. New England Journal of Medicine. 2012 Dec 20;367(25):2407–18.
2 Torres VE, Chapman AB, Devuyst O, Gansevoort RT, Perrone RD, Koch G, et al. Tolvaptan in Later-Stage Autosomal Dominant Polycystic Kidney Disease. New England Journal of Medicine. 2017 Nov 16;377(20):1930–42.
3 Soroka S, Alam A, Bevilacqua M, Girard L-P, Komenda P, Loertscher R, et al. Updated Canadian Expert Consensus on Assessing Risk of Disease Progression and Pharmacological Management of Autosomal Dominant Polycystic Kidney Disease. Canadian Journal of Kidney Health and Disease. 2018 Jan;5:2054358118801588.

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Staff resources: pharmacologic management

- Great, comprehensive work!
- Summary statements are included in the best practices document
- The comprehensive information will be posted in these standalone documents

Questions/comments/discussion