Update on Provincial initiatives in ADPKD
Bringing new insights into clinical practice
Objectives

Update on the status of current provincial initiatives in PKD care

Understand the role of new tools in PKD and how they are being incorporated into care of patients with PKD
Disclosures

Relevant to this topic, I disclose the following interactions with Otsuka Canada Pharmaceuticals Inc.:

– An unrestricted grant to the BCPRA to assist in creation of the PKD registry

– Honoraria for participation in advisory boards related to PKD; these have been directed to the BCPRA educational fund
Understanding the burden and characteristics of PKD in BC
Live polling question

How many people would you estimate are currently living with PKD in BC?

A) 0 – 1,000
B) 1,000 – 5,000
C) 5,000 – 10,000
D) >10,000
Early identification of people with PKD is crucial if we want to impact their disease course.

We are very good at identifying people with advanced disease, but not those early in their disease.
The PKD registry

Through the use of PROMIS, BC has developed a first of its kind provincial registry that aims to include all British Columbians with ADPKD, regardless of disease or treatment status.

Based on successes of the GN registry

The PKD registry started enrollment about 4 months ago

Much of this work is being done in individual offices and clinics
Known PKD patients in BC: Mar 2015

- Dialysis modalities: 110
- Transplant: 357
- Not on dialysis or transplant: 212
Known PKD patients in BC: Sept 2016

- Dialysis modalities:
  - Mar-15: 110
  - Sep-16: 107

- Transplant:
  - Mar-15: 357
  - Sep-16: 370

- Not on dialysis or transplant:
  - Mar-15: 212
  - Sep-16: 485
Registered PKD patients not at ESRD

<table>
<thead>
<tr>
<th>eGFR</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-30</td>
<td>101</td>
</tr>
<tr>
<td>30-60</td>
<td>97</td>
</tr>
<tr>
<td>&gt;60</td>
<td>241</td>
</tr>
</tbody>
</table>
Patients registered across BC

| Health Authorities | 165 | 140 | 28 | 437 | 183 |
Use of the PKD registry so far

Thank you for your participation in the registry!

There is still more work to do:
   Ongoing registration
   More detailed data will follow as the registry grows

Ultimately, this process will be a model for other diseases
Bringing new imaging-based tools into clinical practice
Live polling question

What would be considered a ‘big’ kidney for an average sized 30 year old person living with PKD? (Answer refers to the size of each kidney)

A) Size of a pear
B) Size of a grapefruit
C) Size of a mango
D) Size of a head of cauliflower
Live polling question

What would be considered a ‘big’ kidney for an average sized 60 year old person living with PKD? (Answer refers to the size of each kidney)

A) Size of a pear
B) Size of a grapefruit
C) Size of a mango
D) Size of a head of cauliflower
Modern understanding of PKD natural history
Individualizing prognosis in PKD

A hallmark of PKD is its variability – between families and within families

Usual endpoints (loss of GFR, hypertension, proteinuria, urologic complications) are variable and sometimes late findings

Need an early, reliable and readily available marker to provide individualized prognostication
Rate of kidney growth is an early and robust prognosticator.

Methods of determining renal size

Exciting new tests

What’s old is new again
Getting the most out of ultrasound via standardization

>90% of PKD patients have a renal ultrasound as their first imaging test

There is some strong and reliable information that can be obtained from US such as kidney length

The key is standardization to reduce variability
In collaboration with the BC Radiological Society we are standardizing ultrasound reporting to enhance the utility of ultrasound in PKD

<table>
<thead>
<tr>
<th>Old report</th>
<th>New report</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kidneys are enlarged and display multiple bilateral cysts consistent with polycystic kidney disease</td>
<td>Study confirms phenotypic diagnostic criteria for polycystic kidney disease</td>
</tr>
<tr>
<td>The largest cyst on the right is 3.6cm by 2.4cm and is unchanged in size. There is no dominant cyst on the left.</td>
<td>Typical morphology of cyst involvement with diffuse bilateral cystic expansion.</td>
</tr>
<tr>
<td></td>
<td>Right kidney 17.8cm, left kidney 18cm in long axis.</td>
</tr>
<tr>
<td></td>
<td>Measurement of renal length is less precise at lengths exceeding 17cm. If more accurate determination of renal size is required, suggest cross-sectional imaging.</td>
</tr>
</tbody>
</table>
TKV and the challenge of implementation into everyday practice

Total Kidney Volume (TKV) is the most accurate and best studied method of measuring kidney size but it is difficult to obtain in the clinical setting:

- This is a new and unfamiliar measurement for most radiologists
- Most studies use multiphase MRI (limited access)
- The gold standard evaluation is time consuming and requires substantial expertise
Pilot of TKV measurement at St Paul’s

In collaboration with radiology we are performing a pilot of TKV measurement that includes:

- An abbreviated MRI protocol (7min per scan vs 45min)
- Use of validated equations to approximate TKV (shorter interpretation time)
- Includes an ‘ultra-low dose’ CT protocol for places with limited MRI access

Goal: To identify a real world clinical solution that is comparable to gold standard research measurements
Coming soon: standardized TKV reporting

Based on the results of the pilot we will standardize a method of TKV measurement across the province

All British Columbians with PKD will have local access to these diagnostics

Standardized approach to interpretation and reporting, and a ‘core lab’ system will be implemented
Improving treatment of PKD
By age 30, approximately what percentage of PKD patients will have experienced a complication such as pain, hypertension or urologic complications?

A)~25%  
B)~50%  
C)~75%  
D)~100%
Recent evidence points to three areas that we can improve care for people living with PKD

- Maximizing use of existing treatments
- Using novel disease-modifying treatments when appropriate
- Addressing symptom burden in PKD
Maximizing the use of existing treatments
Maximizing the use of existing treatments

An area where the PKD registry can use the powerful informatics available in PROMIS to improve quality of care

As the registry and PROMIS-related tools develop this will be a great tool for practice audit to help implement findings like HALT-PKD
Using novel disease modifying treatments

Tolvaptan is approved for use as the first disease-modifying treatment in ADPKD

Present evidence suggests it is not for all patients with PKD but a select subset with more aggressive disease

In BC, clinicians wanted to address uncertainty, collect real world information and contribute to the evidence around this drug
Using novel disease modifying treatments

Based on feedback from across BC we independently created tools to assist clinicians (available on BCPRA website)

Based on PROMIS and the PKD registry there is enhanced monitoring and data collection for all patients on tolvaptan

Moving forward, this will allow for real time analysis of safety and outcomes
Addressing symptom burden in PKD

There is a high and often unrecognized burden of complications in early stages of PKD.

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

The physical symptoms and complications are only one aspect of the total burden of PKD.
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 should aim for 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.
How we will get there: upcoming initiatives

BC has a strong track record of incorporating existing evidence and navigating uncertainty to create standardized best practices in kidney care

We will build on this experience, our existing infrastructure of multidisciplinary care and strong relationships with patient groups (PKD Canada and Kidney Foundation of Canada) to help clinicians bring care of PKD patients to the next level

Stay tuned for updates!
Summary

Early identification will enable better management
Keep going with the PKD registry!

Translating evidence into accessible clinical practice
Standardization and access to new imaging tools
Supporting use and monitoring new treatments
Understand and address the total burden of PKD

Stay tuned for more updates and if you would like to be involved in these initiatives, let me know!